# MATHEMATICAL MODELLING OF ANTHRAX AND LISTERIOSIS CO-DYNAMICS WITH OPTIMAL CONTROL

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# Mathematical Modelling of Anthrax and Listeriosis Co-dynamics with Optimal Control

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# Declaration

This thesis is my original work and has not been submitted to any other university for examination.

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# Dedication

I dedicate this thesis to my late grandmother, Amina Kande Danbaba.

.

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# Nomenclature

Variable and Description

$S_h$ : Susceptible population of humans.

$S_v$ : Susceptible population of animals.

$I_h$ : Infected group.

$I_v$ : Infectious animals

$V_v$ : Vaccinated animals.

$R_h$ : Recovered humans.

$R_v$ : Recovered animals

$N_h$ : Total humanpopulation.

$N_v$ : Total animal population.

$\rho$ : Vaccination rate.

$\beta$ : Susceptible contact rate of disease from exposed group.

$\mu_h$ : Natural death rate for all the human compartments.

$\mu_v$ : Natural death rate for all the animal compartments.

$\alpha$ : Progression rate from infected to recovered group due to treatment.

$\pi$ : Proportion of susceptible that are vaccinated at birth.

$\sigma$ : Death rate due to disease infection.

$\delta_h$ : Progression rate from exposed to infected group.

$\Lambda_h$ : Human recruitment rate.

$\Lambda_v$ : Animal recruitment rate.

$\delta_h$ : Human treatment rate

$\delta_v$ : Animal treatment rate.

$R_{0a}$ : Basic reproductive number of only Anthrax model .

$R_{0l}$ : Basic reproductive number of only Listeriosis model.

$R_{al}$ : Basic reproductive number of Anthrax-Listeriosis co-infection model.

# Abbreviations

*SIR* : Susceptible Infected Recovered

*SIRS* : Susceptible Infected Recovered Susceptible

*SEIR* : Susceptible Exposed Infected Recovered

*WHO* : World Health Organisation

*CDC* : Center for Disease Control

*HIV* : Acquired Immune Deficiency Syndrome

*NICD* : National Institute for Communicable Diseases

*NHLS* :National Health Laboratory Services

# Abstract

In this research, three mathematical models were developed to explain the transmission dynamics of zoonotic diseases that are bacteria related, specifically Listeriosis, Anthrax and their co-infection. Ordinary differential equations were used in the formulation of the Anthrax, Listeriosis and Anthrax-Listeriosis co-infection deterministic models. These deterministic models were formulated and analysed qualitatively and quantitatively. A vaccination compartment with waning immunity was incorporated into the Anthrax model. The local and global stability analysis of equilibrium points were analysed and found to be locally asymptotically stable whenever the basic reproductive number is less than one and unstable if the basic reproductive number is greater than one. The basic reproductive numbers were computed and used as the threshold parameter that governs the spread of Anthrax, Listeriosis and Anthrax-Listeriosis co-infection. Moreover, the extension of the Anthrax, Listeriosis and the co-infection models to optimal control theory seek to minimise the objective functional subject to some controls variables were determined. The resulting control problem was solved numerically in order to determine the most effective control measure in combating the Anthrax infections.

It established that Anthrax and Listeriosis models exhibited multiple endemic equilibrium. Sensitivity analysis of the basic reproduction numbers of all the three models were determined. It was established that, increasing animal (livestock) recovery rate, would lead a decrease in the basic reproduction number. The qualitative analysis of optimal control of the Anthrax, Listeriosis and Anthrax-Listeriosis co-infection were performed and the necessary conditions for the optimality of Anthrax, Listeriosis and Anthrax-Listeriosis infections were analysed. The two most effective control strategies of the Listeriosis model were the combination of treatment of infectious vectors and treatment of infectious humans, combination of prevention of susceptible humans and the treatment of infectious vectors.

Anthrax-Listeriosis co-infection model analysis reveals that the disease free equilibrium was locally asymptotically stable whenever the reproduction number is less one. The co-infection model exhibited the phenomenon of backward bifurcation. Mathematically, it implies that the idea of the model been locally asymptotically stable whenever the reproduction number is less than unity and unstable otherwise is not a sufficient condition for disease eradication. The impact of Listeriosis on Anthrax infections reveals that Anthrax infections can be attributed to increased risk of Listeriosis but the reverse is not the same. However, optimal prevention and treatment of Anthrax and not keeping Listeriosis under control is not the best strategy for eradicating either of the disease.

# Chapter 1

# Introduction

## 1.1 Background of the study

### 1.1.1 Anthrax

Anthrax is an infectious disease that can be categorized under zoonotic diseases and it is caused by a bacteria called Bacillus anthracis. The disease is found naturally in soil and mostly affects wild and domestic and animals worldwide. The disease is mostly common in developing countries. Susceptible individuals can easily get sick with anthrax if they interact with infected animals or consume contaminated dairy foods and animal products. Routine vaccination can help prevent outbreaks of anthrax in areas where domestics animals have had it in the past (Samad, 2013). The human population are usually infected with the disease when spores enter into the body. When anthrax spores enter into the body, they are usually "activated". They produce toxins and this causes serious illness. This may usually happen when the individual inhales the spores, ingest contaminated food or drink contaminated water containing spores or comes in contact with spores in a cut on the skin. Humans contract the disease from direct contact with animals or indirectly from animal products (Samad, 2013).

Figure 1.1 shows how the effects of anthrax usually occur on the human skin. A typical skin lesion from an Anthrax infections.

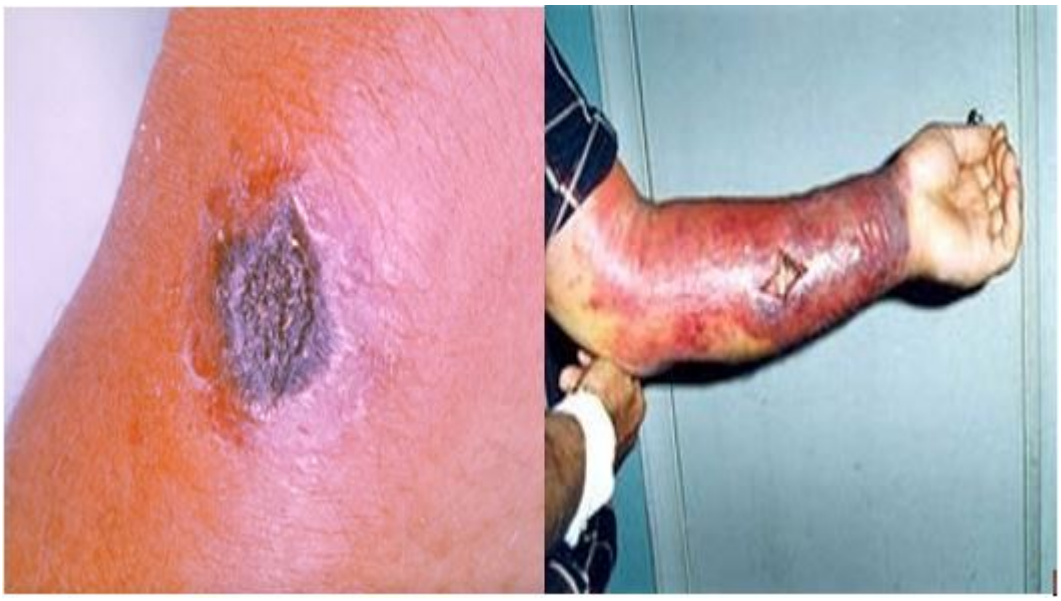

Figure 1.1: Skin Lesion from Anthrax infections.
Skin Lesion from Anthrax. Source:(https://www.cdc.gov/anthrax/basics).

Figure 1.2 shows how animals usually get infected with the Anthrax disease. They contract anthrax infections by grassing in an anthrax infected areas as a results of the contamination of the grass. This happens when an infected dies and decomposed. The area becomes infected with the anthrax bacteria.

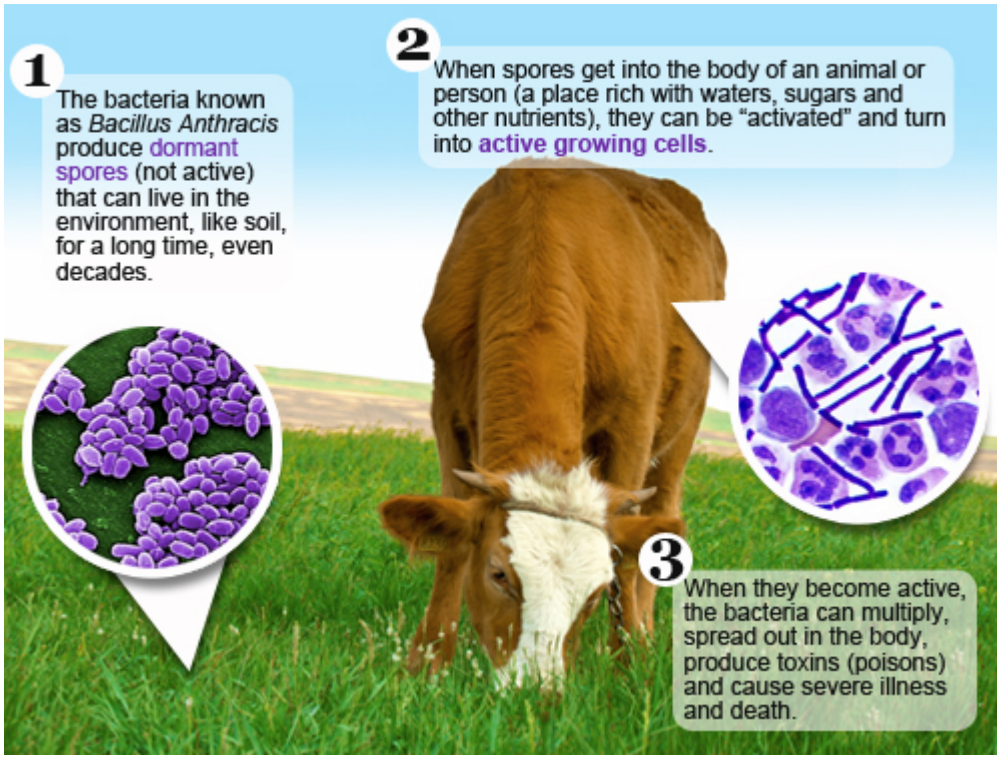


Figure 1.2: Anthrax life cycle
Cycle of Anthrax infection. Source: (https: //www.WHO/CDS/2008).

Anthrax in humans is generally grouped into two forms; Industrial and Non-industrial anthrax. Non-industrial anthrax occurs in farmers, veterinarians, butchers. Industrial anthrax, occurs in those employed in the processing of bones, hides, wool and other animal products. The occupation of the individual determines how exposed he is to the disease. Good hygiene can prevent the infection of Anthrax when practiced properly by avoiding the swallowing contaminated water from recreational parks, lakes, streams and pools. Anthrax still remains one of the most global cause of morbidity and mortality, that is capable of causing periodic epidemic disease Samad (2013). Therefore, a critical understanding of the transmission dynamics of Listeriosis-Anthrax co-infection in emergent epidemic areas can help policy makers and health professionals to improve the control of future epidemics. Animals generally contract the disease by ingestion of spores while grassing. The diagram in Figure 1.3 shows the transmission processes of Anthrax disease between humans and animal populations.

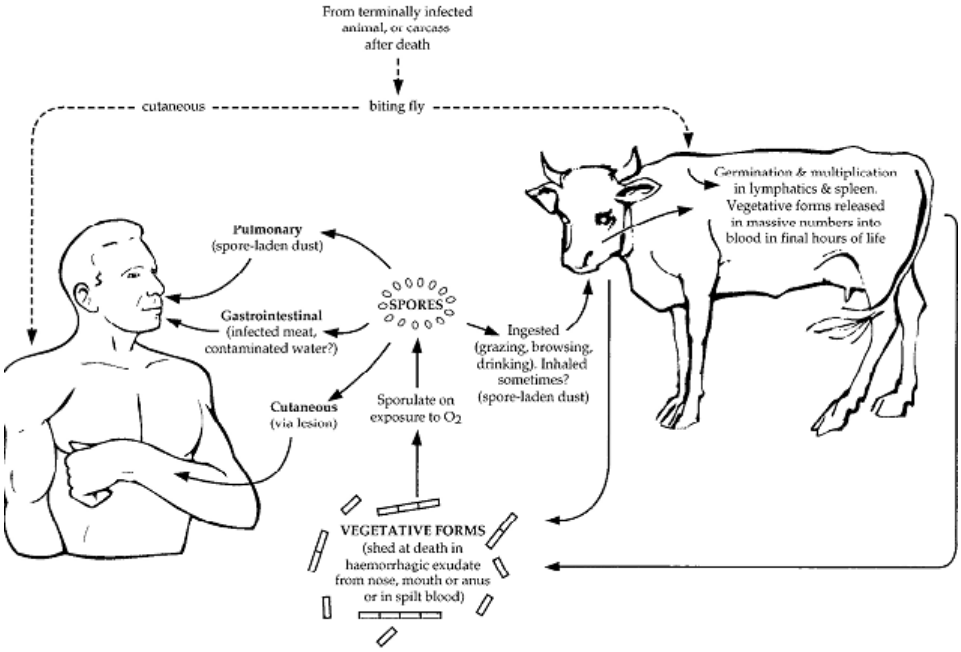


Figure 1.3: Cycle of Bacillus Anthracis.
Cycle of Bacillus Anthracis. Source:(https://www.cdc.gov/ncezid/dw-index)

### 1.1.2 Listeriosis

Listeria monocytogenes is the causative agent of Listeriosis which is in the field of bacteriology. The organism was initially described as a cause of epizootics in veld rodents from South Africa (Tiger River disease) by Pier et al., 1926. (Murray et al., 1926) established and explained a septic illness in laboratory rabbits that was described by peripheral monocytosis. The organism was used to be called Bacterium monocytogenes when the genus name was changed from Listerella to Listeria. Most clinical descriptions of both human and animal infection caused by listeria monocytogenes were published in the 1920; But, the organism remained a laboratory problem until the World War II, when it was known to be the major cause of neonatal sepsis and meningitis . With the advancement in immunosuppressive drugs and chemotherapy for malignancy in the early sixty's, the disease in adult patients with compromised immune systems was appreciated. In recent times, HIV epidemic has increased the susceptible population at risk Schlech and Acheson (2000).

Listeria monocytogenes can be found mostly in the environment and it is responsible for meningoencephalitis and stillbirths in a number of animals. The disease usually occurs in human in the setting of pregnancy, immunosuppressive and as the individual ages. The investigations of the outbreak of the disease during the early eighty's revealed that Listeriosis is a food borne disease. Greater attention has therefore been given to Listeriosis as a clinical entity of increasing importance and as a substantial problem for the food industry (Schuchat et al., 1991a).

Figure 1.4: Sources of Listeriosis.
Source:(https://www.healthmap.org/site/disease-daily/article/listeria-death-toll-rises).

The diagram in Figure 1.4 shows some of the common sources of Listeriosis infections. The commonest sources are raw meat, milk and vegetables. These products are usually contaminated with listeria monocytogenes. The Listeriosis outbreak in South Africa was as a result of food products that are contaminated in most the malls and supermarkets in the country.

Figure 1.5: Sources of Listeriosis.
Source:(https://www.healthmap.org/site/disease-daily/article/listeria-causes-yet-another-dole-recall).

The diagram in Figure 1.5 shows some of the common sources of Listeriosis food products. These products are so common in our malls and supermarkets. The consumption of these products when contaminated can easily lead to the outbreak of Listeriosis infections.

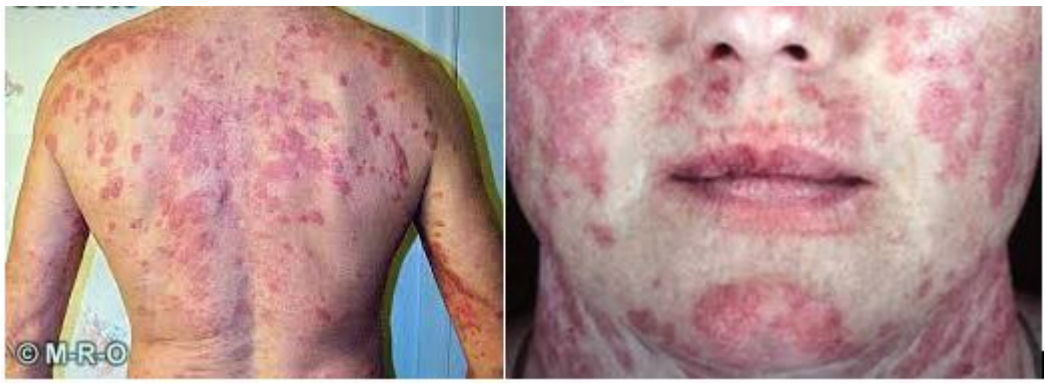


Figure 1.6: Listeriosis infections on the skin.
Source:(https://www.healthmap.org/site/disease-daily/article/listeria.

The diagram in Figure 1.6 shows the effects of Listeriosis on the skin. The symptoms of Listeriosis infections can easily be reflected on the skin indicated on Figure 1.6.

## 1.2 Statement of the problem

Zoonotic diseases are the most common infectious diseases worldwide. Anthrax disease is endemic and claims so many lives in developing countries. Veterinary Officers, farmers and people who work in the food processing industry are mostly at risk. Efforts to eradicate and control the spread of these diseases through vaccination has resulted to some extent the decline in the spread of the diseases. Incidence of these diseases has reduced significantly in many developed nations as a result of proper vaccination campaigns. Unfortunately, zoonotic diseases are still a threat to many developing nations especially Africa Samad (2013).

Saad-Roy et al. (2017) developed an epidemic models on anthrax transmission in animals. But never considered anthrax as a zoonotic disease. Anthrax disease affects both human and animal population in an environment. The model has not incorporated human populations. Since there exist vaccines for animals against anthrax, we incorporated the vaccination compartment in the animal population to improve the work on the existing anthrax models.

However, there has not been any existing model or work on Anthrax-Listeriosis co-dynamics. Since both infections are bacteria related and share common source of infection and transmission mechanism, it calls for a co-dynamics model and optimal control analysis to combat both diseases in our environment.

### 1.2.1 Anthrax outbreaks in Ghana between 2005-2016

Table 1.1 shows the cases of anthrax outbreaks in Ghana between 2005 to 2016. The highest outbreak occurred in the year 2011 with a total number of 12 outbreaks and lowest outbreak recorded in the country was in the year 2009.

| Year | Number | Percentage |
|---|---|---|
| 2005 | 7 | 10 |
| 2006 | 5 | 7.5 |
| 2007 | 5 | 7.5 |
| 2008 | 7 | 10 |
| 2009 | 2 | 3.0 |
| 2010 | 5 | 7.5 |
| 2011 | 12 | 17.9 |
| 2012 | 5 | 7.5 |
| 2013 | 6 | 9.0 |
| 2014 | 6 | 9.0 |
| 2015 | 3 | 4.5 |
| 2016 | 4 | 6.0 |

Table 1.1: Anthrax outbreaks in Ghana between 2005 to 2016.

Table 1.2 shows the cases of anthrax by livestock types in Ghana between the year 2005 to the year 2016. Cattle recorded the highest cases of anthrax in the country and goats recorded the lowest cases of anthrax in the country.

| Year | Cattle | Sheep | Goats | Pigs |
|---|---|---|---|---|
| 2005 | 27 | 1 | 0 | 0 |
| 2006 | 17 | 15 | 0 | 0 |
| 2007 | 15 | 9 | 3 | 0 |
| 2008 | 21 | 6 | 11 | 0 |
| 2009 | 0 | 2 | 0 | 0 |
| 2010 | 2 | 1 | 0 | 0 |
| 2011 | 13 | 7 | 0 | 3 |
| 2012 | 6 | 66 | 1 | 500 |
| 2013 | 50 | 14 | 0 | 0 |
| 2014 | 3 | 1 | 0 | 1 |
| 2015 | 26 | 1 | 0 | 0 |
| 2016 | 4 | 6 | 19 | 0 |
| Total | 184 | 129 | 34 | 504 |

Table 1.2: Cases of anthrax outbreaks in animals between 2005 to 2016 in Ghana.

Friedman and Yakubu (2013) analysed the compartmental model using the basic reproduction number but did not consider sensitivity analysis. We improved the model by considering sensitivity analysis to see the contribution of each parameter on the model.

The contribution of each parameter to the basic reproduction number is paramount to disease reduction. Sensitivity analysis determines which parameter contributes to the reduction of the reproduction number. This is because the reproduction number should always be less than one in order to reduce the infections in the environment.

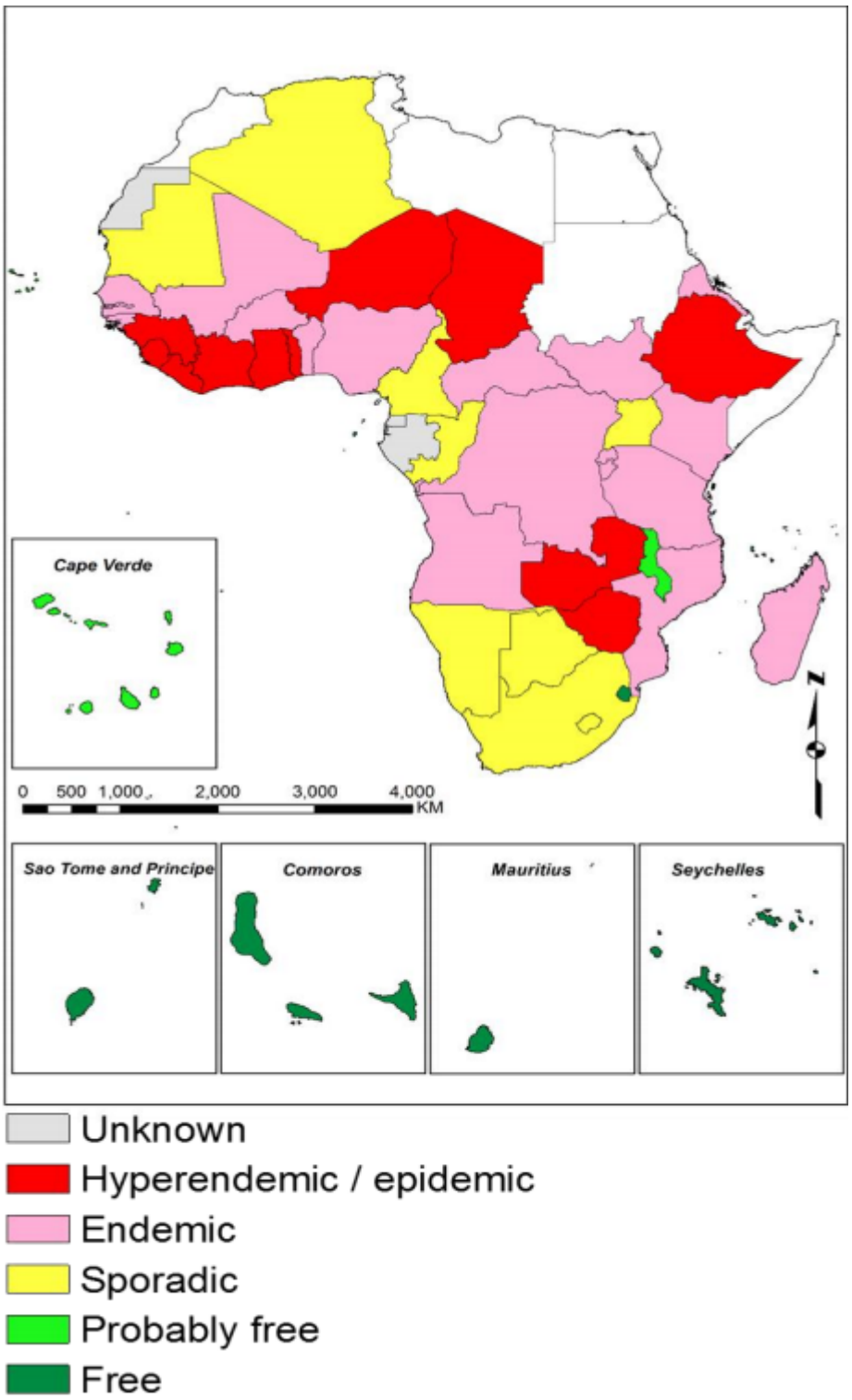


Figure 1.7: Prevalence of Anthrax in Africa
Anthrax ecological zones based on reported cases in humans and animals. Source: (https://www.WHO/AFRO library/2016).

Figure 1.7 shows the prevalence of Anthrax infections in the African continent. These

are Anthrax ecological zones based on reported cases in human and animal population in the continent. The infection is hyper-endemic in some western, central, eastern and southern African countries. There are also sporadic cases of Anthrax infections in most parts of northern and the extreme parts of southern Africa countries. Based on reported cases, there are just some probably Anthrax infection free zones in the entire Africa continent as shown in Figure 1.7.

Listeriosis is a less common zoonotic disease but it continues to pose a series of problems in veterinary medicine. Listeriosis is the major cause of encephalitis in ruminants. This encephalitis is usually refereed to as "circling disease" because it occurs in the hind brain and can lead to ataxia in infected animals before death (Schlech and Acheson, 2000).

### 1.2.2 A situational report on listeriosis outbreak in South Africa

The data bellow gives the outcome of persons with laboratory-confirmed Listeriosis by province in South Africa. The data is from the National Institute for Communicable Diseases (NICB). A division of the National Health Laboratory Services (NHLS). This data is between January, 2017 to March, 2018.

| Province | Died | Discharged | Pending | Total |
|---|---|---|---|---|
| EC | 10 | 18 | 22 | 50 |
| FS | 8 | 19 | 7 | 34 |
| GA | 98 | 261 | 213 | 572 |
| KZ | 11 | 30 | 27 | 68 |
| LP | 7 | 25 | 15 | 47 |
| MP | 10 | 34 | 2 | 46 |
| NC | 3 | 2 | 1 | 6 |
| NW | 7 | 17 | 5 | 29 |
| WC | 29 | 80 | 6 | 115 |
| Total | 183 | 486 | 298 | 967 |

Table 1.3: Outcome of 967 persons with laboratory-confirmed Listeriosis by province in South Africa between January, 2017 to March, 2018.

## 1.3 Objective of the study

### 1.3.1 General objective

The general objective of this research is to develop and examine a deterministic model for the spread and transmission mechanisms of Listeriosis and Anthrax in animal and human populations with optimal control.

### 1.3.2 Specific objectives

1. To formulate an epidemic model for Anthrax in animal and human population with optimal control.
2. To formulate an epidemic model for Listeriosis in animal and human population with optimal control.
3. To formulate an epidemic model for the Co-dynamics of Anthrax and Listeriosis in animal and human populations with optimal control.
4. To perform both qualitative and quantitative analysis of the Co-dynamics model and determine the parameters for eradication or control of the diseases.
5. To perform sensitivity analysis of the Co-dynamics model parameters to determine the effects of each parameter on the control or die out of the diseases.

## 1.4 Research questions

1. How is basic reproductive number associated with stability of the equilibrium points of Anthrax and Listeriosis diseases?
2. How is basic reproductive number associated with control of Anthrax and Listeriosis diseases?

3. Which is the best control strategy in combating Anthrax and Listeriosis diseases?

4. Which is the most sensitive parameter that influence the spread of Anthrax and Listeriosis diseases?

## 1.5 Significance of the study

Socioeconomic impacts of emerging and re-emerging infectious diseases like Anthrax and Listeriosis are significant. This study will help the health care sector to optimize controls and minimize the cost of control strategies in order to reduce the spread of Anthrax and Listeriosis diseases in the society. It will also help to improve control strategies for the occurrence of Listeriosis and Anthrax diseases outbreak in a community. Moreover, public health policy makers will be guided on optimal control strategies which can be used to control the diseases. Furthermore, the health sector would see the need for organising seminars, workshops or training programmes to educate the general public about the dangers and control strategies of Anthrax and Listeriosis diseases. The study will provide information for further research on optimal control of Anthrax and Listeriosis diseases and zoonotic diseases as a whole.

## 1.6 Scope of the study

In this section, the basic mathematical concepts that govern the methods and theories used in thesis are presented. The main diseases that were considered in this research are Anthrax and Listeriosis infections. These diseases are treated as zoonotic diseases. The transmissions of these are considered in both animal and human populations. The methodologies used to study the transmission dynamics of infectious diseases can be grouped under two categories: Stochastic and non-stochastic methodologies. The theory of differential equations falls under non-stochastic methodology. This concept

is the most widely used in infectious disease modelling. The application of differential equations in infectious disease modelling is as a result of its ability to handle nonlinear problems and can easily be implemented. Therefore, all the models developed and analysed in this thesis employ the concepts of differential equations. These proposed mathematical models are analysed quantitatively and qualitatively. Some aspects of both the qualitative and quantitative analysis aspect were carried out by the use of mathematical software. Strategies of effectively controlling the disease are been carried out by applying the concepts of optimal control. The control problems are designed by introducing controls such as treatment, prevention and vaccination that are aimed at reducing the spread of infections. The basic concepts in critical analysis of infectious disease modelling are presented in this chapter.

## 1.7 Organisation of the study

The study is organized into seven chapters. Chapter one which is the introduction consists of the following section: Background of the study, problem statement, objective of the study and significance of the study. Chapter two has to do with the review of literature. The integration of the study into a broader framework of relevant theory and research. Chapter three comprises of the methodologies used in the underlining assumptions. The mathematical description, analysis of the model and the underlying assumptions are presented in this chapter. In chapter four, the dynamics of Anthrax in animal and human population with optimal control was considered. The existence and stability of the disease free equilibrium and the endemic equilibrium points have been analysed. Chapter five basically deals with the dynamics of Listeriosis in animal and human populations with optimal control. Also, the the existence and stability of the disease free equilibrium and the endemic equilibrium points have been investigated. The Co-dynamics of Anthrax and Listeriosis in animal and human populations have been analysed to give a mathematical interpretations of the effects of each parameter

on the control or die out of the diseases in chapter six. The numerical results, analysis and discussions are as well incorporated in chapter four, chapter five and chapter six. Finally, chapter seven comprised of discussions, conclusion and recommendations of the findings of the research for policy makers, regulatory bodies and health professionals in their decision making and policy implementations.

# Chapter 2

# Review of Related Literature

## 2.1 Anthrax

(Samad, 2013) investigated zoonotic diseases in Bangladesh. Diseases and infections that are shared between human population and animals are usually referred to as zoonotic diseases. Zoonotic diseases occur worldwide especially in developing countries and Bangladesh is not exception. The findings and analysis of the results on prevalence and effects of zoonotic diseases in the country were analysed presented. The statistics revealed that, there were approximately 1415 human pathogens of which sixty one percent are zoonotic related diseases. The commonest zoonotic diseases recorded in the country are Anthrax, Tuberculosis, Brucellosis, Salmonellosis, and Leptospirosis Samad (2013).

Anthrax has been reported in both humans and cattle. Between 2009 to 2012, the disease caused death of many animals and more than 650 cases of cutaneous anthrax were reported. The findings showed that all types of zoonotic diseases are widely spread and they pose a serious threat to public health in the country. Lack of policy framework by government for Veterinary and extension officers are responsible for the disease spread. Moreover, ignorance of the dynamics of zoonotic diseases by farmers who

are in contact with infected animals and contaminated food products, and improper processing of diary products by most food processing industries have complicated the problems in Bangladesh (Samad, 2013).

(Lu et al., 2002) investigated the effectiveness of constant and pulse vaccination policies using SIR model. From the theoretical results of their study under constant vaccination, the dynamics of the disease model is similar to dynamics without vaccination. Several studies have used the methods of optimal control theory in the formulation of the models (Lashari and Zaman, 2012)(Lashari, 2016). However, a number of these studies focused on the effect of vaccination on the spread and transmission of the diseases as in the case of the authors in (Mushayabasa and Bhunu, 2012).

Also, (Gumel and Moghadas, 2003) studied a disease transmission model by considering the impact of a protective vaccine and came out with the optimal vaccine coverage threshold required for disease control and eradication. Moreover, in (Kar and Batabyal, 2011), optimal control was used to study a nonlinear SIR epidemic model with a vaccination strategy. Several mathematical modeling techniques have been employed to study the role of optimal control using SIR epidemic model (Makinde, 2007; Yusuf and Benyah, 2012; Zaman et al., 2009)).

Zaman et al. (2008), formulated an SIR epidemic model by considering vaccination as a control. Makinde and Okosun (2011), also considered and applied optimal control to investigate the impact of chemo-therapy on malaria disease with infection immigrants and applied optimal control methods associated with preventing exogenous reinfection based on a exogenous reinfection tuberculosis model. Lashari et al. (2012), considered and studied essential role of three basic types of control: personal protection, treatment, and mosquito reduction approaches in the control of malaria. But much studies have not been done on the mathematical model, formulation and analysis to Listeriosis, Anthrax or Co-dynamics of Listeriosis and Anthrax in animals and human population. Also, the authors developed a more general mathematical model in (Rogers, 1988) of

a vector-borne disease comprising of two vertebrate host species and one insect vector species. To the best of the authors' knowledge, no studies or research has been done to examine, analyse and investigate Listeriosis and Anthrax co-infection dynamics in animals and human population. Hence the study is to develop an SIRS (Susceptible, Infected, Recovered, Susceptible) model for Listeriosis-Anthrax co- infection dynamics in animal and human population Rogers (1988).

Lashari (2016) formulated an optimal control problem for an SIR epidemic model with saturated incidence and saturated treatment. Treatment and vaccination are basically the two main efforts that are considered to reduce the disease transmission. The concept of basic reproduction number was used to discuss the impacts of vaccination and treatment on the disease transmission Lashari (2016).

A control problem was formulated and the existence of the control is shown. Two control functions were used: one for vaccinating the susceptible and the other for treatment efforts for infectious individuals. Appropriate optimal control methods are used to characterize the optimal levels of the two controls. The effectiveness of the proposed control solution is shown by comparing the behavior of controlled and uncontrolled systems. Numerical results show the impacts of two controls in decreasing both susceptible and infectious members of the population Lashari (2016).

A compartmental and simulation models for evaluating Med-kits propositioning strategies for anthrax attack response was developed (Houck, 2011). After the 2001 anthrax attacks, policy makers and health officials have increasingly showed much interest in planning for a possible large scale attack. Mathematicians and Epidemiologists have developed model attack scenarios in order to determine various response policies. One of such models has proposed the distribution of antibiotics to the general population in the form of Med-kits in advance Houck (2011).

However, despite existence of all these models, no model has studied the effects of distributing Med-kits on the expected number of deaths in an attack. Houck (2011)

developed a discrete-time compartmental difference equation model that analysed the policy. Their findings showed that distributing any number of Med-kits has a significant impact on the reduction of deaths expected Houck (2011).

Bacteria are usually organisms that are responsible for the causes of most zoonotic diseases and Anthrax is no exception. Moreover, many of the bacteria are not harmful and others are beneficial to animal and human population. Most bacteria are usually useful in the food processing industries (Tamma et al., 2012).

They are useful in the production of cheese, chemicals, yogurt and medicines. Bacteria play important roles to manufacture and synthesize food particles in the digestive system to produce energy. Insulin that saves Millions of diabetic patients are mostly saved by the use of Insulin and it is produced from genetically modified bacteria Tamma et al. (2012).

But ironically, most bacteria are harmful and are a threat to public health worldwide. Gastritis, pneumonia, meningitis, gonorrhea are some examples of diseases caused by various bacteria. However, most zoonotic diseases that are bacteria related can be treated by antibiotics. Some the diseases usually caused by bacteria are meningitis, gonorrhea, pneumonia, gastritis and anthrax. Also, bacteria organisms are responsible for many zoonotic diseases (Wexler, 2007).

Domestic and agricultural use of compost can really increase the possibility of disease transmission and infections by direct contact of humans and animals with the waste matter. The question of whether the use of compost can cause any serious risks as compared to the use of human and animal wastes as agricultural fertilisers still remains unanswered Jones and Martin (2003). Food-borne infections are the major human diseases that should be taking with serious considerations and attention in the United Kingdom as well as intoxication caused by other zoonotic diseases. Further research work should concentrate on determining the conditions for heat-resistant bacteria in experimental and industrial composting systems accurately Jones and Martin (2003).

Studies on experimental anthrax by Robert Koch in the early 1870, demonstrated for the first time the bacterial origin of a specific disease and realised the spore stage that allows persistence of listeria monocytogenes in the environment (Pile et al., 1998).

Later, John Bell established Bacillus anthracis as responsible for inhalation anthrax and the bacteria plays a major role in establishing wool disinfection measures and procedures. The disinfection procedures proved effective in reducing the incidence of inhalation anthrax and they emerged as standard in the British woolen industry Pile et al. (1998).

Shortly afterwards, successful immunization of livestock against anthrax soon followed in 1880 by William Greenfield's . Even although Louis Pasteur's 1881 trial of a heat-cured anthrax vaccine in sheep would always be remembered as the initial use of a live vaccine (Pile et al., 1998).

Moreover, vultures have been linked to the persistence and spread of the disease in Africa. The incidence of anthrax has actually increased in African continent in recent years. This prompted the World Health Organization (WHO) to look for alternative measures of improving surveillance and control efforts (Pile et al., 1998).

The spread of diseases causes deaths of millions of people and cost of treatment of these diseases are of a great concern to every human endeavour. Public health is a major concern to the world at large. Adequate attention must be given to eradicate the spread of these diseases (Li et al., 2010; Lashari, 2016). Many studies in the literature have been carried out to determine the role of treatment and vaccination on the spread of diseases. A discrete-time epidemic model with vaccination for measles is formulated in (Allen, 2007).

(Lu et al., 2002) investigated the effectiveness of constant and pulse vaccination policies using SIR model. From the theoretical results of their study under constant vaccination, the dynamics of the disease model is similar to dynamics without vaccination. Several studies have used the methods of optimal control theory in the formulation of

the models (Lashari and Zaman, 2012; Lashari, 2016).

Moreover, (Gumel and Moghadas, 2003) studied a disease transmission model by considering the impact of a protective vaccine and came out with the optimal vaccine coverage threshold required for disease control and eradication. Moreover, optimal control was used to formulate a nonlinear SIR epidemic model with a vaccination strategy by authors in (Kar and Batabyal, 2011).

## 2.2 Listeriosis

A study conducted by (Rebagliati et al., 2009) showed that Listeria monocytogenes is a food borne pathogen that is responsible for the cause of serious invasive illness, mostly in certain class of individuals including elderly and immune compromised patients, new born children and pregnant women . The disease is primarily the cause of stillbirth and meningitis Rebagliati et al. (2009).

Dairy products, contaminated meats and seafood have all been proved to be the major causes of the outbreaks of Listeriosis. Much importance of the effects and its associated consequences of the disease as a threat to public health is not always observed, because Listeriosis is a relatively rare disease as compared to other zoonotic diseases such as anthrax, salmonellosis and other food borne diseases Rebagliati et al. (2009).

In a study conducted by (Jemmi and Stephan, 2006), Listeria monocytogenes has been rated among the most increasing and major food-associated pathogen and many countries of the European Union have always recorded an annual cases of human Listeriosis of between two and ten reported cases per million. Listeriosis has been placed among the highly frequent diseases responsible for death due to food-borne illness. Listeria monocytogenes infections has the highest hospitalisation rates among all the known food-borne pathogens Jemmi and Stephan (2006).

Investigations conducted by (Lianou and Sofos, 2007) on the incidence and transmis-

sion of listeria monocytogenes in ready-to-eat products in retail and food services environments proved that contamination of food products with Listeria monocytogenes can exist or show up at multiple stages before consumption. Lack of control interventions at retail and food service environments as compared with the the food processing industries and the low regulatory framework is solely responsible for the increase of this pathogen into most of these foods environment Lianou and Sofos (2007).

Moreover, they reviewed existing data available on information on the incidence and transmission of listeria monocytogenes on all ready-to-eat products at the food service environments. Potential transmission of the disease in those environments has been elaborated by survey data Lianou and Sofos (2007).

The likelihood sources of the organism in these places are incoming raw ingredients, food handlers, processed products that are contaminated and the environment. The pathogens can be present at retail and food service environments in various food products especially those that have been packaged in the food establishments Lianou and Sofos (2007). Educational campaign on food safety and training programmes for all persons in the food processing industries must be ensured (Lianou and Sofos, 2007).

A research conducted by (Rossi et al., 2008) showed that Listeria monocytogenes is among the food borne pathogens responsible for invasive illness in certain class of people. The outbreaks of the disease has been reported in Japan,North America and Europe. The commonest sources of getting infected with the disease are raw milk and meats Swaminathan and Gerner-Smidt (2007). These are high risk food products for vulnerable individuals. The food regulatory agencies, public health authorities and food processing industries have made a significant impact in the fight against Listeriosis and this has reduced the incidence of the disease significantly (Swaminathan and Gerner-Smidt, 2007).

In an article published by (Little et al., 2010), Listeriosis in human are rare but it is among the top serious food borne diseases in susceptible and vulnerable individuals in

a population such as the immune compromised and pregnant women. The high-risk sources of the disease are contaminated ready-to-eat foods. There have been outbreaks of Listeriosis in many European countries since 2001. England and Wales recording the highest incidence of the disease Little et al. (2010).

The Salmonella Bayesian model was used to quantify the contribution of different food products and sources to human Listeriosis in England and Wales between 2004 to 2007 Little et al. (2010). The major sources for the entire population were multi component foods such as salad vegetables and sandwiches accounting for twenty three percent Little et al. (2010).

Also, fish was approximately seventeen percent and beef was fifteen percent. Moreover, for pregnancy related cases: beef was twelve percent, dairy products was approximately twelve percent and fish was eleven percent Little et al. (2010).

The resurgence of food borne Listeriosis was investigated by (Allerberger and Wagner, 2010). The causative agent of human Listeriosis is listeria monocytogenes and it is noted as one of fatal food borne infection. The clinical manifestations of Listeriosis can range from febrile gastroenteritis to a severe invasive forms like meningitis, perinatal infections, abortions and sepsis. The significance of separating the pathogens as a necessary requirement for a correct epidemiological research and eradicating transmission can not be overemphasised Allerberger and Wagner (2010).

Moreover, Donnelly (2001), stated Listeriosis as one of leading causes of death from food borne pathogens. The disease continues to spread and cause sporadic outbreaks of illness. Investigation of many huge epidemics of Listeriosis revealed that transmission of listeria monocytogenes in food are responsible for human diseases in the early 1980 (Schuchat et al., 1991b).

Advancement in laboratory detection of the organism has enabled our ability to compare human and environmental isolates of listeria monocytogenes. The transmission by food borne organisms has now been accepted as responsible for both epidemic and

sporadic Listeriosis Schuchat et al. (1991b).

Continued investigation of dietary risk factors associated with the disease is required in order to develop dietary recommendations for the increasing population at the continuous risk of disease. Recent research and application of new molecular methods of studying listeria monocytogenes can improve the tendency of diagnosing pregnancy related disease and allows quick detection and control of the disease in the food supply (Schuchat et al., 1991b).

An investigation conducted by (Hof, 2001) showed that listeria monocytogenes are the causative agent of gastrointestinal. The intestinal tract can be the main point of entry for Listeria monocytogenes. These are ingested via contaminated food substances. The pathogens enter the mucous tissue either through engulfment by erythrocytes, or through active penetration of the Peyer's patches Hof (2001).

Borucki et al. (2004) researched on the identification and reservours of pathogens for effective control of sporadic disease and epidemics. Listeria monocytogenes is among the major zoonotic food borne pathogen that is responsible for approximately twenty eight percent of most food-related deaths in the United States annually and a major cause of serious product recalls worldwide. The dairy farm has been observed as a potential point and reservour for listeria monocytogenes Borucki et al. (2004).

Listeriosis infection is less common and when active examination of sepsis and meningitis has been carried out, the following were revealed: 10 cases per $100,000$ population and in the elderly, 1.4 cases per $100,000$ population Schlech and Acheson (2000).

The infection is predominant among males. Listeriosis in infants can be acquired in two forms. Mothers usually acquire it after eating foods that are contaminated with listeria monocytogenes and can develop sepsis resulting in chorioamnionitis and delivering a septic infant or fetus Schlech and Acheson (2000).

Also, mothers carrying the pathogens in the gastrointestinal tract can contaminate the skin and respiratory tract of their babies during childbirth. Listeria monocytogenes

is the third major and common pathogen responsible for bacterial meningitis among neonates in North America. Factors that are responsible and can increase the risk of Listeriosis include acquired and induced immune suppression linked with HIV infection, hematologic malignancies,cirrhosis, diabetes, hemochromatosis and renal failure with hemodialysis (Schlech and Acheson, 2000).

In an article published by (Little et al., 2010), Listeriosis in human are rare but it is among the top serious food borne diseases in susceptible and vulnerable individuals in a population such as the immune compromised and pregnant women. The resurgence of food borne Listeriosis was investigated by (Allerberger and Wagner, 2010).

The significance of separating the pathogens as a necessary requirement for a correct epidemiological research and eradicating transmission can not be overemphasised. Moreover, a study conducted on the effects of Listeriosis revealed that the diseases causes death from food borne pathogens. The disease continues to spread and cause sporadic outbreaks of illness Donnelly (2001).

## 2.3 Biological and epidemiological models

Biological and epidemiological models are usually used in the study of transmission and dynamics of infectious diseases generally. In recent times, mathematical models are employed in the study of infectious diseases. Their use have increased tremendously in real life phenomenon. Rapid diagnostic test, existence of health data and electronic surveillance has aided the use of mathematical models to critically examine the scientific hypotheses and the formulation of strategies to controlling infectious diseases (Hethcote, 1976; Grassly and Fraser, 2008).

Interest in biological modeling arose from the emerging and reemerging of complex and strange infectious diseases. Mathematical models can estimate an underlying parameter of a natural phenomenon that is sometimes tedious to be found and analysed

through experiment Hethcote (1976).

This can be obtained by estimating transmission rate, reproduction number and some variables and parameters. A model is capable of predicting relationship between an infectious diseases and as well determine whether or not the associated disease will spread in a population or die out with time. Moreover, models can equally predict the effects, impact of a certain control measure by outlining useful strategies to authority and government units in charge of health for combating the infections. Mathematical modelling emerged during the $18th$ century Hethcote (1976).

A model was formulated for predicting the effectiveness of differences in healthy population with smallpox infected population by authors in (Hethcote, 1976). Generally, models have recently gained recognition since the middle of the $20th$ century when Kermack and McKendrick published a paper on epidemic models in 1927. The findings contains threshold results that determines whether an epidemic outbreak would occur or not (Hethcote, 1976; Kermack and McKendrick, 1927).

There have been a growing interest in biological modelling and its applications has in all fields biological sciences (Anderson et al., 1982; Hethcote, 1976; Smith and Zhao, 2000)). Models have solved many problems in biological sciences such as the association between infectious diseases, levels of infection, spatial spread, chemotherapy, vaccination, quarantine, waning immunity, vertical transmission, zoonotic disease, age structure, acquired immunity (Anderson et al., 1982; Grassly and Fraser, 2008; Hethcote, 1976)).

# Chapter 3

# Mathematical Preliminaries

## 3.1 Introduction

In this this chapter, the basic concepts and theories in mathematical and epidemiological models are considered. The underlining theories of dynamical systems, differential equations, local and global stability analysis of dynamical systems, bifurcation analysis and optimal control theory applied to infectious disease modelling were considered.

## 3.2 Dynamical systems

**Definition 1.** Dynamical system is the process or way of describing the passage in time of all points of a given space $(\mathscr{L})$.

This space $\mathscr{L}$ could be thought of as the space of a state of some physical system. This phenomena of dynamical systems arises in all field of human endeavour. Particularly, in the areas of biological sciences where knowing the behaviour of a given system at a given times in space is paramount. A dynamical system can be said to be either continuous or discrete. The groupings mostly depends on whether the interest has to do with the state of the system at integer time values or not. A dynamical system is

generally of the form;

$$\Theta_t = \mathbb{R}^n \rightarrow \mathbb{R}^n \tag{3.2.1}$$

A smooth dynamical system on $\mathbb{R}^n$ is a continuous and differentiable function;

$\Theta_t = \mathbb{R}^n \rightarrow \mathbb{R}^n$ , where $\Theta(t,X) = \Theta_t(X)$

satisfies;

1. $\Theta_t = \mathbb{R}^n \rightarrow \mathbb{R}^n$ is an identity function: $\Theta_0(x_0) = (x_0)$;
2. The composition $\Theta_t \circ \Theta_s = \Theta_{t+s}$ for each $t$, $s \in \mathbb{R}$.

Mostly, dynamical systems that are employed in infectious or biological modelling are in the form of differential equations. Hence, all systems considered in this thesis would be treated in the concept of differential equations.

## 3.3 Differential equations

**Definition 2.** A differential equation is an equation involving a function together with its derivatives with respect to some independent variable(s).

There are two types of differential equations; An ordinary and partial differential equations.

A differential equation is said to be an ordinary differential equation if the derivative depends on only one variable. A differential equation is said to be a partial differential equation when the derivative of the function depends on more than one independent variable. Infectious disease modelling are mostly deterministic models and are ordinary differential equations. This thesis involves deterministic models and therefore emphasis would be on ordinary differential equations.

**Definition 3.** Consider $x$ to be the state of a dynamical system. Then a generalised deterministic model that involves $x$ would be given by;

$$\frac{dx}{dt} = f(t, x, \lambda) \tag{3.3.1}$$

Where $x \in \mathbb{R}^n$, $t$ denotes time, and $\lambda \in \mathbb{R}^m$, denotes the parameters upon which the evolution of the system depends.

An ordinary differential equation in which the time variable$t$, is explicitly defined is said to be non-autonomous. Those equations in which time variable are not usually defined explicitly are referred to as autonomous ordinary differential equations. Generally, infectious disease models (epidemic models) especially those considered in this thesis are autonomous systems and are generally written as;

$$\dot{x} = f(x) \tag{3.3.2}$$

where $x = x_1, x_2, x_3 \ldots x_n$ and $\dot{x} = \frac{dx}{dt}$ denotes a point-wise time-derivatives of the state variable $x$. In situations or instances where the information about the initial conditions of the system are provided together with equation $\dot{x} = f(x)$, then the resulting equations are said to be initial-value problems $(IVP)$, and are generally in the form:

$$\dot{x} = f(x) \quad , \quad x(t_0) = x_0 \in \mathbb{R}^n \tag{3.3.3}$$

When the initial and final conditions are declared, then the differential equation with these conditions are generally referred to as boundary value problem $(BVP)$. Basically, biological or epidemic models are mostly compartmental models that involves rate of change of populations with time of several compartments of a given system. Considering a given system of differential equations with $n$ compartments, a precise dynamical system describing the dynamics of the system are generally written as;

$$\left.\begin{aligned} \frac{dx_1}{dt} &= f_1(x_1, x_2, x_3, \ldots, x_n) \\ \frac{dx_2}{dt} &= f_2(x_1, x_2, x_3, \ldots, x_n) \\ &\vdots \\ \frac{dx_{n-1}}{dt} &= f_{n-1}(x_1, x_2, x_3, \ldots, x_n) \\ \frac{dx_n}{dt} &= f_n(x_1, x_2, x_3, \ldots, x_n) \end{aligned}\right\} \tag{3.3.4}$$

The system of equations in (3.3.4) are generally represented in a compact form as; $x = (x, x_2, x_3, \ldots, x_n)$ and $f = f_1(f_1, f_2, f_3, \ldots, f_n)$.

**Lemma 1.** *Let $\Delta$ be an open subset of $\mathbb{R}^n$ and let $f : \Delta \to \mathbb{R}^n$ then, if $f \in C^1(\Delta)$, $f$ is locally Lipschitz on $\Delta$.*

**Definition 4.** Let $f : \Delta \to \mathbb{R}^n$ where $\Delta$ is an open subset of $\mathbb{R}^n$. We say $f \in C^1(\Delta)$, if the partial derivatives $\frac{\partial f_i}{\partial x_j}$, $i, j = 1 \ldots n$ exist and are continuous on $\Delta$.

The notation $C^k$ denotes the space of all functions with continuous $k^{th}$ order derivatives.

**Definition 5.** The function $f : \Delta \to \mathbb{R}^n$ is differentiable at $x_0 \in \mathbb{R}^n$, if there is a linear transformation $Df(x_0) \in \mathscr{L}(\mathbb{R}^n)$ that satisfies;

$$\lim_{|h \to 0|} \frac{|f(x_0 + h) - f(x_0) - Df(x_0)h|}{|h|} = 0 \tag{3.3.5}$$

The linear transformation $Df(x_0)$ is called the derivative of $f$ at $x_0$.

The derivative of a function at any point can be calculated by the help of the following theorems;

**Theorem 1.** *If $f : \mathbb{R}^n \to \mathbb{R}^n$ is differentiable at $x_0$, then the partial derivatives $\frac{\partial f_i}{\partial x_j}, i, j = 1 \ldots n$ all exist at $x_0$ and for all $x \to \mathbb{R}^n$;*

$$Df(x_0)x = \sum_{j=1}^{n} \frac{\partial f}{\partial x_j}(x_0)x_j, \tag{3.3.6}$$

Hence, for a differentiable function $f$, the derivative is given by the *nxn* Jacobian matrix; $Df = \dfrac{\partial f_i}{\partial x_j}$.

**Definition 6.** Suppose $A_1$ and $A_2$ are considered to be two normed linear spaces with respective norms, $|\cdot|$ and $|\cdot|$. Then $f : A_1 \to A_2$ is continuous at $x_0 \in A_1$ if for all $\varepsilon > 0$, there exists a $\delta > 0$ such that for any $x \in A_1$, if $\|x - x_0\|_1 < \delta$ then $\|f(x) - f(x_0)\|_2 < \varepsilon$.

The function $f$ is said to be continuous on the set $\Delta \in A_1$ if it is continuous at every point in $\Delta$ and when this is the case, then the notation $f \in C(\Delta)$ is used to mean that $f$ is continuous on $\Delta$.

**Theorem 2.** *(Fundamental Existence-Uniqueness theorem (Hirsch et al., 2004)). Consider the initial value problem of equation* (3.3.3). *Suppose that $f$ is $C^1$. Then firstly, there exists a solutions of this initial value problem and secondly, this is the only such solution. Moreover, there exists an $a > 0$ and a unique solution of equation* (3.3.3) *on the interval $[-a, a]$ satisfying the initial condition $x(t_0) = x_0$.*

### 3.3.1 Equilibrium and linearisation of autonomous systems

**Definition 7.** Considering an autonomous deterministic model in equation (3.3.2) , a state $x^*$ is said to be an equilibrium point of the model if $f(x^*) = 0$ (the function-value at $x^*$ is zero). The equilibrium points are generally referred to as critical points of the model.

In general, ordinary differential equation epidemic models in the form of equation (3.3.2), their equilibrium points are always obtained or computed by equating the left-hand-sides of the equations zero and then evaluate for the state variable $x$.

**Definition 8.** Generally an equilibrium point, $(x^*)$, of equation (3.3.2) is said to be locally stable if $\forall\ \varepsilon > 0$, $\exists \delta > 0$ such that $\|x_0 - x^*\| < \delta \Longrightarrow \|x(t) - x^*\| < \varepsilon$. An equilibrium point which is not locally stable is said to be unstable.

This stability is in the context of Lyaponuv perspective.

**Definition 9.** Considering an equilibrium point, $(x^*)$, of an epidemic model in equation $(3.3.2)$ is said to be locally asymptotically stable if it is locally stable and all solutions starting near equilibrium point tend towards it as $t \to \infty$.

This implies that, $\exists \delta > 0$ such that $\|x_0 - x^*\| < \delta \Longrightarrow \lim_{t \to \infty} x(t) = x^*$.

### 3.3.2 Local stability of equilibrium points

Understanding the concepts and behaviour of a dynamical system near equilibrium point is paramount in infectious disease modelling. Knowing whether or not future evolution of the system would remain close to the equilibrium point base on the initial conditions close to equilibrium is very key. Concept of local stability analysis is used in the determination of this phenomena. Indirect Lyaponuv technique is used in the determination of local stability of critical points.

**Definition 10.** An equilibrium point (critical point), $(x^*)$, of a dynamical system is said to be locally stable if all eigenvalues of the Jacobian matrix evaluated at $x^*$ are negative.

The Jacobian matrix of the dynamical system denoted in equation$(3.3.4)$is given by:

$$J = Df(x) = \begin{bmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} & \cdots & \frac{\partial f_1}{\partial x_{n-1}} & \frac{\partial f_1}{\partial x_n} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} & \cdots & \frac{\partial f_2}{\partial x_{n-1}} & \frac{\partial f_2}{\partial x_n} \\ \vdots & \vdots & \cdots & \vdots & \vdots \\ \frac{\partial f_{n-1}}{\partial x_1} & \frac{\partial f_{n-1}}{\partial x_2} & \cdots & \frac{\partial f_{n-1}}{\partial x_{n-1}} & \frac{\partial f_{n-1}}{\partial x_n} \\ \frac{\partial f_n}{\partial x_1} & \frac{\partial f_n}{\partial x_2} & \cdots & \frac{\partial f_n}{\partial x_{n-1}} & \frac{\partial f_n}{\partial x_n} \end{bmatrix} \tag{3.3.7}$$

**Definition 11.** An equilibrium point $(x^*)$ of equation $(3.3.2)$is said to be hyperbolic if none of the eigenvalues of the Jacobian matrix evaluated at $x^*$, has a zero real part.

The equilibrium point $x^*$is said to be non-hyperbolic otherwise.

**Theorem 3.** *(Linearisation theorem Hirsch et al.,* $(2004)$*. Suppose the nonlinear system* $(3.3.2)$ *has an equilibrium point,* $(x^*)$ *that is hyperbolic. Then the nonlinear flow is conjugate to the flow of the linearised system in a neighborhood of* $x^*$*.*

The concept of linearisation are generally referred to as the Hartman-Grobman Theorem. This theorem states that, local behaviour of an equilibrium point of a nonlinear dynamical system can be evaluated or approximated by its linearisation.

## 3.4 Global stability of dynamical systems

Establishing the local stability of equilibrium point by using or employing the indirect methods of Lyapunov function, generally has its limitations. This concept can be applicable only in cases or situations where there are very small perturbations about the equilibrium. Information about the extent of the basis of attractions are usually not provided (that is the idea of all solutions starting within that domain approach the critical point). The concept of direct Lyapunov approach addresses this issue.

**Definition 12.** An equilibrium point $x^*$ is said to be globally asymptotically stable, if it is asymptotically stable for all initial conditions $x_0 \in \mathbb{R}^n$.

The concept of Lyapunov can be used to obtain the global stability of equilibrium points of dynamical systems in $(3.3.2)$without necessarily computing its trajectories. The concept of direct Lyapunov method is to obtain the properties of the equilibrium point of the dynamical system by examining and analysing the behaviour of selected scalar functions of the state as the system state evolves with time. Suppose there exist a function $V(x)$, continuous and differentiable over a given time interval. The partial derivatives exists such that:

1. $V(x)$is a positive definite; $V(0) = 0$; $V(x) > 0$ for all $x \neq 0$.

2. The derivative of $V(x)$is negative: $\frac{dV(x)}{dt} < 0$.

**Definition 13.** A continuous and differentiable function, $V : \mathbb{R}^n \to \mathbb{R}_+$ is said to be positive definite in a region $U \in \mathbb{R}^n$if and only if;

- $V(0) = 0$
- $V(x) > 0$

for all $U \in \mathbb{R}^n$, and $x \neq 0$.

$V(x)$is said to be positive semi-definite if $V(x) \geq 0$ for every $x \in U$. Conversely, $V(x)$is said to be negative definite if $V(x) < 0$ and $V(x)$is said to be negative semi-definite if $V(x) \leq 0$.

**Theorem 4.** *(Global stability in terms of Lyapunov)*

*Considering* $x^* = 0$ *as an equilibrium point of the dynamical system in* (3.3.2)*,*

*where* $f : U \to \mathbb{R}^n$ *is locally Lipschitz and* $U \subset \mathbb{R}^n$*be a domain that contains the origin.*

*Consider* $V : U \to \mathbb{R}$ *be continuously differentiable and positive definite function in* $U$*.*

1. If $\frac{\partial V}{\partial x} * f \leq 0$, then $x^* = 0$ is globally stable.
2. If $\frac{\partial V}{\partial x} * f < 0$, then $x^* = 0$ is globally asymptotically stable.

A function can be referred to as a Lyapunov function if it satisfies conditions 1 and 2 , called Lyapunov stability theorem. Moreover, the applications of this theorem is often complicated and difficult as there are no set rules for constructing the Lyapunov functions. Some functional forms and their variants are often serve as baseline for Lyapunov functions:

- Quadratic functions: $V(x) = \sum_{i=1}^{n} (x_i - x_i^*)$.

- Logarithmic functions: $V(x) = \sum_{i=1}^{n} \left( x_i - x_i^* \ln \left( \frac{x_i}{x^*} \right) \right)$.

Where $x^* = \left( x_1^*, \ x_2^*, \ ,,,,, \ x_n^* \right)$ are the equilibrium points.

## 3.5 Bifurcation analysis

The qualitative change in the behaviour of a dynamical system as the parameter varies is called Bifurcation. The points at which the changes usually occur are generally referred to as bifurcation points.

**Definition 14.** Consider $\frac{dx}{dt} = (x, \alpha)$, for every $x \in \mathbb{R}$ and $\alpha \in \mathbb{R}$ be a family of one dimensional ordinary differential equations of one parameter. The equilibrium solution given by $(x, \alpha) = (0,0)$ is said to experience bifurcation at $\alpha = 0$ if the flow for $\alpha$ near zero and $x$ near zero is not qualitatively the same as the flow near $x = 0$ at $\alpha = 0$.

Local stability of disease free equilibrium of most epidemic models are often studied by using the indirect method of Lyapunov theorem. These concepts are usually employed by linearising the dynamical system around the disease free equilibrium and applying the eigenvalues of the resultant Jacobian matrix to determine conditions for stability. However, employing this concept for endemic equilibrium points for some epidemic models can be tedious and complicated. Generally, the concept of the center manifold theory is employed as an alternative Hethcote (1976); Blayneh et al. (2010).

**Theorem 5.** *Considering the general system of ordinary differential equations with a parameter* $\theta$.

$$\frac{dx}{dt} = \quad f(x, \theta), \quad f : \mathbb{R}^n X \mathbb{R} \to \mathbb{R} \quad \textit{and} \quad f \in C^2(\mathbb{R}^n X \mathbb{R}), \tag{3.5.1}$$

*where* 0 *is an equilibrium point of the system of differential equations* $f(0, \theta) \equiv 0$, *for every* $\theta$*and assume;*

1. $A = D_x f(0,0) = \left( \frac{\partial f_i}{\partial x_j}(0,0) \right)$ is the linearisation matrix of $(3.5.1)$at equilibrium point 0 with with $\theta$evaluated at 0. Where zero is simply an eigenvalue of $A$ and other eigenvalues of $A$ have negative real parts.

2. The matrix $A$ has a right eigenvector $u$ and a left eigenvector $v$ with each corresponding to the zero eigenvalue.

Let $f_k$ be the $k^{th}$ component of $f$ and;

$$a = \sum_{k,i,j=1}^{n} v_k u_i u_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0) \tag{3.5.2}$$

$$b = \sum_{k,i=1}^{n} v_k u_i \frac{\partial^2 f_k}{\partial x_i \partial \theta}(0,0) \tag{3.5.3}$$

The local stability of the system of ordinary differential equations in $(3.5.1)$at 0 is completely determined by the signs of $a$ and $b$:

- If $a > 0$ , $b > 0$ and $\theta < 0$ with $|\theta| \leq 1$, then 0 is locally asymptotically stable and there exists a positive unstable equilibrium; when $0 < \theta \leq 1$, 0 is unstable and there exists a negative and locally asymptotically stable equilibrium.

- If $a < 0$ , $b < 0$ and $\theta < 0$ with $|\theta| \leq 1$, then 0 is unstable; when $0 < \theta \leq 1$, 0 is locally asymptotically stable and there exists a positive unstable equilibrium.

- If $a > 0$ , $b < 0$ and $\theta < 0$ with $|\theta| \leq 1$, then 0 is unstable; when $0 < \theta \leq 1$, 0 is unstable and there exists a locally asymptotically stable negative equilibrium; when $0 < \theta \leq 1$, 0 is stable and there exists a positive unstable equilibrium.

- If $a < 0$ , $b > 0$ and $\theta$changes from positive to negative , then 0 changes its stability from stable to unstable; A negative unstable equilibrium turns positive and locally asymptotically stable.

However, when $a > 0$ and $b > 0$ , then a backward bifurcation is said to occur at $\theta = 0$ Hethcote (1976); Blayneh et al. (2010).

### 3.5.1 Bifurcation coefficients, $a$ and $b$

In this section, we concentrate on the computations of the bifurcation coefficients $(a)$and $(b)$. Using the relationships defined in equations $(3.5.2)$ and $(3.5.3)$to determine the bifurcation coefficients can so cumbersome and tedious when dealing with large system of ordinary differential equations. A simplified relations for computing the bifurcation coefficients for $a$ and $b$ are presented for easy use of software in the computations.

Consider a system of $n$ ordinary differential equations of the form;

$$\frac{dx}{dt} = f(x, \theta) \tag{3.5.4}$$

where $x = (x_1, \ x_2, \ ...., \ x_n)$ and $f = (f_1, \ f_2, \ ...., \ f_n)$.

Let $u = (u_1, \ u_2, \ ...., \ u_n)^T$ and $v = (v_1, \ v_2, \ ...., \ v_n)$ be the right and left eigenvector associated with a simple eigenvalue of the Jacobian matrix evaluated at equilibrium point $(0,0)$ of the system of ordinary differential equations in $(3.5.4)$, then the bifurcation coefficients $a$ and $b$ can be obtained using the relations;

$$a = v. \begin{pmatrix} u^T H_1 u \\ u^T H_2 u \\ . \\ . \\ u^T H_n u \end{pmatrix} \tag{3.5.5}$$

$$b = v^T M u \tag{3.5.6}$$

## 3.6 Basic reproduction number

In epidemic models, the concept of the basic reproduction number plays a central role as it determines whether the disease would persist or die out with time in the system. The basic reproduction number gives or tells the state of disease with time. It is obtained by computing the Jacobian of the system at the disease free equilibrium by posing the condition that all eigenvalues of the corresponding characteristic equation must have negative real parts.

**Definition 15.** The basic reproduction number, is defined as the average number of secondary infections generated by one infectious individual introduced into a completely susceptible population. It is the number of secondary cases produced on average by one infected person when all are completely susceptible. It combines the biology of infections with the social and behavioural factors influencing contact rate.

If $\mathfrak{R}_0 < 1$, then the infectious individual infects less than one percent susceptible over the course of its infectious periods and the disease can not grow. But when $\mathfrak{R}_0 > 1$, then an infectious individual infects more than one susceptible over the course of its infectious period and the infection (disease) would persist.

**Definition 16.** However, when dealing with cases of one compartment of infection, $\mathfrak{R}_0 > 1$ is usually considered as the product of mean duration of infection and infection rate. But for complex models with two or more infectious compartments, this definition of the basic reproduction number $(\mathfrak{R}_0)$is not a sufficient condition Van den Driessche and Watmough (2002). There are instances that all the population might not be susceptible to infections. Some would be immune to the infection which are permanent or as a result of immunisation. Since there might exists immunity of permanent immunity, not all interactions would result to infections and the number of secondary incidence of infections will reduce. This phenomenon is usually measured by the effective reproductive number..

### 3.6.1 Effective reproductive number

In epidemiological models, a population can never be totally susceptible to an infection in reality. There are those who are infected $(I)$and others who have recovered$(R)$and are immune. Effective reproductive number, measures the average number of secondary cases produced by one infectious case in a population that comprises of both susceptible and non-susceptible individuals.

The effective reproductive rate is the number of secondary cases produced on average by one infected person when a fraction of the population are susceptible. Simply, when $S$ out of $N$ are susceptible.

Mathematically:

$$R_{eff} = R_0 \left( \frac{S}{N} \right). \tag{3.6.1}$$

Assuming the population mix randomly.

If $R_{eff} \geq 1$, the disease persists.

If $R_{eff} < 1$, the disease dies out.

The effective reproductive rate is more realistic because in every population, not everyone is susceptible . There are those who are infected $(I)$and others who have recovered$(R)$and are immune. The effective reproductive rate must always be less than unity to ensure that the disease dies out of the population. It is important to achieve $R_{eff} < 1$. This can only be possible if a fraction of the population are treated or vaccinated large enough. As $R_{eff} = R_0 \left( \frac{S}{N} \right)$, the number of the susceptible must be reduce so that $R_{eff} < 1$.

Researchers in disease modelling have attached great importance to effective reproduction number $(R_{eff})$, by determining basic reproductive number $(R_0)$ and its proxies. A review of methodologies employed to estimate reproductive number and effective reproductive number are critically examined. The methodology employed in Van den Driessche and Watmough (2002) was used in this research to estimate the basic repro-

ductive number ($R_0$) and the effective reproductive number ($R_{eff}$).

### 3.6.2 Method employed in Van den Driessche and Watmough (2002).

Let a system of differential equations ( compartmental disease model ) be of the form: $\dot{x} = f(x)$, where $x = x_1, x_2, x_3 \ldots x_n$. Let $\mathscr{F}_i(x)$ and $\mathscr{V}_i^+(x)$ denote the rate of appearance of new infections and the rate of transfer of new infections into the infection class $(I)$respectively.

Let $\mathscr{V}_i^-(x)$ represent the rate of transfer of infections out of class $(I)$ and

$\mathscr{V}(x) = \mathscr{V}_i^-(x) - \mathscr{V}_i^+(x)$.

Let $X_s = \{ \quad x \geq 0 | x_i \quad = 0, \quad i = 1, \quad ...., \quad m \}$ be the set of all disease free states.

Assuming all the conditions on these functions are satisfied, then:

1. If $x \geq 0$ then $\mathscr{F}_i, \quad \mathscr{V}_i^+, \quad \mathscr{V}_i^- \quad \geq 0$ for all $i = \quad 1 \quad , ....., \quad n$ .
2. If $x_i = 0$ then $\mathscr{V}_i^- = 0$ . When $x \in X_s$ then $\mathscr{V}_i^- = 0$ for $i = \quad 1 \quad , ....., \quad m$ .
3. $\mathscr{F}_i = 0$ if $i > m$
4. If $x \in X_s$ then $\mathscr{F}_i(x) = 0$ and $\mathscr{V}_i^+(x) = 0$ for $i = \quad 1 \quad , ....., \quad m$ .
5. If $\mathscr{F}_i(x)$ is set to zero, then all eigenvalues of $Df(x_0)$ have negative real parts and the Jacobian matrix of $Df(x_0)$ is usually partitioned as illustrated in the following lemma:

**Lemma 2.** *If $x_0$ is a disease free equilibrium of system of differential equations of the form:*

*$\dot{x} = f(x)$, and $f(x_i)$ satisfies conditions $(1) - (5)$, then the derivatives $D\mathscr{F}(x_0)$ and $D\mathscr{V}(x_0)$are partitioned*

*as follows:* $D\mathscr{F}(x_0) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix}$, $D\mathscr{V}(x_0) = \begin{pmatrix} V & 0 \\ J_3 & J_4 \end{pmatrix}$,

*where F and V are mxm matrices defined by;*

$F = \left[\frac{\partial \mathscr{F}_i}{\partial x_i}(x_0)\right]$ *and* $V = \left[\frac{\partial \mathscr{V}_i}{\partial x_i}(x_0)\right]$, *with* $i \leq m$ , $j \leq m$.

*Moreover, F and V are non-negative matrices and all the eigenvalues of* $J_4$ *have positive real parts Van den Driessche and Watmough (2002).*

The threshold value of the basic reproductive number $(\Re_0)$, is computed by employing the concept of the theorem;

**Lemma 3.** *Consider a system of differential equations of the form:* $\dot{x} = f(x)$, *and* $f(x_i)$ *satisfies conditions* $(1)-(5)$. *If* $x_0$ *is a disease free equilibrium of the system of differential equations, then* $x_0$ *is said to be locally asymptotically stable if* $\Re_0 < 1$ *and unstable if* $\Re_0 > 1$ , *where* $\Re_0$ *is defined by:* $\Re_0 = \rho\left(FV^{-1}\right)$ *and* $\rho(A)$ *represents the spectral radius of A Van den Driessche and Watmough (2002).*

The threshold value of the basic reproductive number, $(\Re_0)$, has a significant role when determining the qualitative behaviour of epidemic models. Both the DFE and EE exchange stability when the basic reproduction number is equal to one, $(\Re_0 = 1)$. Changes in stability which is usually referred to as forward bifurcation mostly occurs in several epidemic models Kermack and McKendrick (1927). When the basic reproductive number is less than or equal to one, $(\Re_0 \leq 1)$, then forward bifurcation occurs. This is a necessary and sufficient condition for disease eradication.

Moreover, when the stable disease free equilibrium and the stable endemic equilibrium co-exists and the basic reproductive number is less than or equal to one $(\Re_0 \leq 1)$, then a backward bifurcation is said to occur. When backward bifurcation occurs, then $\Re_0 \leq 1$ becomes a necessary but not sufficient condition for disease eradication. In this case, disease elimination can not be achieved by ensuring that the basic reproductive number is always less than one $(\Re_0 < 1)$. Many epidemic models have exhibited the phenomenon of backward bifurcation Van den Driessche and Watmough (2002).

## 3.7 The analysis of optimal control theory

An optimal control problem is simply an optimisation problem that tends to minimise or maximise the objective functional subject to a system of equations (Dynamical system) under some constraints (boundary or initial conditions). Optimal control theory has been employed in the analysis of the models to determine the significace of the various control efforts in controlling Anthrax and Listeriosis diseases.

Consider a dynamical system;

$$\dot{X}(t) = f(\ t,\ \ x(t),\ \ u(t)\ ) \tag{3.7.1}$$

where
$$\left.\begin{array}{rcl} \dot{X}(t) & = & nx1 \\ f & = & nx1 \\ x(t) & = & nx1 \\ u(t) & = & mx1 \end{array}\right\}$$

The Performing Index (Optimal Control) $J(\cdot)$ is given by;

$$J(\cdot) = S(x(t),t)|_{t=t_f} + \int_{t=0}^{t_f} V(x(t),u(t),t)dt \tag{3.7.2}$$

subject to $\dot{X}(t) = f(\ t,\ \ x(t),\ \ u(t)\ ),\ \ x(t_0)\ \ = x(0), x(t_f)$ and $u(t) \in \mathfrak{U}, \forall t \in \left[0, t_f\right]$.

where $S$ and $V$ are the Terminal Cost and Cost Function respectively. The problem is to find the control $u(t)$ such that the Performing Index $J(\cdot)$ is minimise.

### 3.7.1 Pontryagin's maximum principle

The Pontryagin's Maximum Principle provides the necessary conditions that an optimal control must satisfy. The principle changes the system of differential equations in (3.7.1) and equation (3.7.2)into minimisation problem point-wise Hamiltonian ($H$),

with respect to the controls$(u_i(t))$ . This principle is the main tool used in solving optimal control problems. It determines how the state variables $(x_i)$, controls $(u_i)$and the co-state variables $(\lambda_i)$change over time through the equation of motion for $x$ and $\lambda$.

**Theorem 6.** *Let $u(t)$ be an optimal control and the corresponding response of the dynamical system be $X(t)$, then there exists a function $\lambda(t) : [0,t_f] \longrightarrow \mathbb{R}^n$ , such that;*

$$\left.\begin{aligned} \dot{x} = & \quad \frac{\partial H}{\partial \lambda}(x,\lambda,u,x(t_0)) = x_0 \\ \dot{\lambda} = & \quad -\frac{\partial H}{\partial \lambda}(x,\lambda,u,) \\ \lambda(t_t) = & \quad 0 \\ \frac{\partial H}{\partial u} = & \quad 0 \end{aligned}\right\}$$

*where $\dot{x}$ ,$\dot{\lambda}$ and $\lambda(t_f)$ are the State Equation, Co-state or adjoint equation and the Transversality condition respectively.*

### 3.7.2 Numerical solution of optimal control problems

Optimal control problems in epidemiology and engineering can be so complex in nature that their solutions can not be obtained analytically. Generally, numerical methods are often employed in solving these problems. This concept involves finding piecewise continuous functions $u_i(t)$ that maximise the objective functional. This can be done either by linear programming techniques or total enumeration methods with the consideration that, solutions of these problems must satisfy the state equations, co-state equations and the optimal conditions. The optimal conditions are usually manipulated to obtain explicit expressions and substituted into the state equations as well as the co-state equations. The state and co-state equations then form a two boundary value problem. The problem is then solved using the method of solving an ordinary differential equation with two boundary value conditions.

The outline of the numerical scheme employed in solving the optimal control problem in this thesis are those in Grassly and Fraser (2008); Martcheva (2015);

1. An initial guess is made for the control $(u)$ over a time interval.

2. The initial condition $x(t_0) = x_0$and the control $(u)$ are used in solving for $x$ forward in time depending on the differential equation in the optimal system.

3. The transversality condition $\lambda(t_f) = 0$ and the values of $x$ and $u$ are used in solving for $\lambda$ backward in time depending on the differential equation in the optimal system.

4. The control $(u)$ is then updated by using new $x$ and $\lambda$ values into the characterisation.

5. The convergence is then checked. When values of the current iteration and the last iteration are negligibly small, output current values otherwise return to step two $(2)$.

# Chapter 4

# Dynamics of Anthrax with Optimal Control.

## 4.1 Introduction

In this chapter, the analysis and transmission dynamics of anthrax infection in both human and animal populations with optimal control is considered. A vaccination compartment is incorporated into the model.

## 4.2 Anthrax model description and formulation

The model divides the total human and vector populations at any time $(t)$into seven sub-populations (compartments) with respect to their disease status in the system.

The total vector population, represented by $N_v(t)$, is divided into sub-populations of Susceptible vector $(S_v)$, Infectious vector $(I_v)$, Vaccinated vector $(V_v)$, and Recovered vector $(R_v)$.

The total vector population becomes:

$N_v(t) = S_v(t) + V_v(t) + I_v(t) + R_v(t)$.

The total human population also represented by $N_h$, is divided into sub-populations of

Susceptible humans $(S_h)$, Infected humans $(I_h)$, and Recovered humans $(R_h)$.

The total human population is given by:

$N_h(t) = S_h(t) + I_h(t) + R_h(t)$.

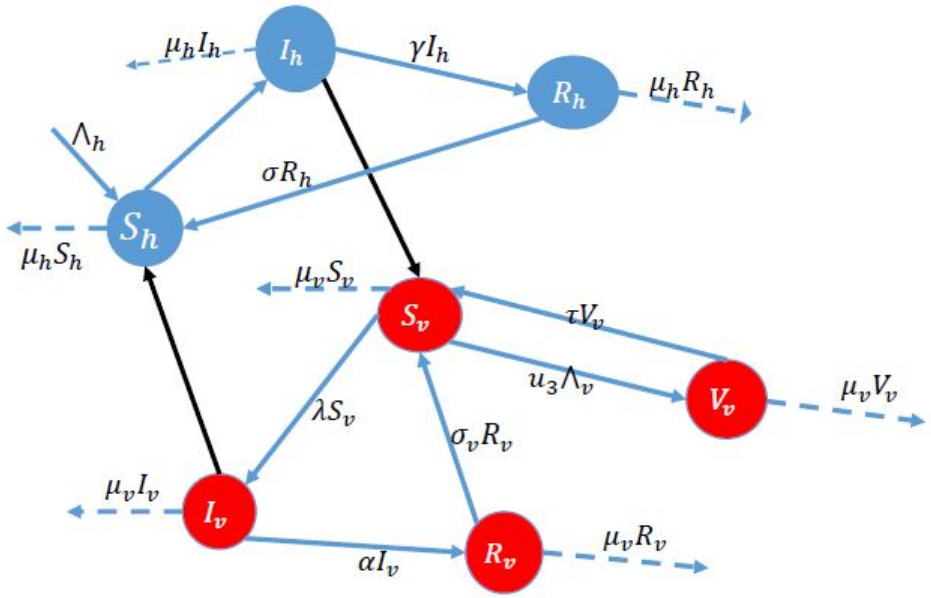


Figure 4.1: Flow diagram for the anthrax disease transmission dynamics.

$S_v(t)$; these include animals(livestock) that are at risk of developing an infection from the Anthrax disease, $V_v(t)$; these include animals that are vaccinated before the Anthrax disease out break, $I_v(t)$; this compartment consists all animals(livestock) that are showing the symptoms of the Anthrax disease, $R_v(t)$; these include animals that have recovered from the Anthrax disease and got temporal immunity, $S_h(t)$; these include individuals who are at risk of developing an infection from the Anthrax disease and $I_h(t)$; these include individuals that are showing the symptoms of at risk of the Anthrax disease, $R_h(t)$; these are individuals who have recovered from the Anthrax disease and got temporal immunity.

The Susceptible humans are recruited into the population at a rate $\Lambda_h$. Susceptible humans acquire Anthrax through inhalation of spores, ingestion of contaminated foods from infected animals, contact with infectious animals and humans at a rate $(I_v + I_h)\beta$. Individuals recover from the disease at a rate $\gamma$. Humans who are infected with An-

thrax die at a rate $\delta_h$ and the recovered humans may loose immunity and return to the susceptible compartment at a rate $\sigma_h$. The natural death rate of the entire human compartments is $\mu_h$.

The susceptible vector $S_v$ are recruited into the population at a rate $\Lambda_v$, but a fraction of the animals are successfully vaccinated at a rate $u_3$, where $u_3 \in [0,1]$. Anthrax can be acquired through contacts with infectious animals and humans at a rate $(I_v + I_h)\lambda$. The natural death rate of the animals is $\mu_v$and the death rate as a result of the disease is $\delta_v$. The animals recover at a rate $\alpha$ and a fraction of the vaccinated animals may move to the infected animal compartment at a rate $b\beta_m^*\lambda$ due to waning effect. Where $(1-b) \in [0,1]$ is the efficacy of the vaccine. This is because the animals may loose immunity and move back to the susceptible compartment at a rate $\tau$. Humans are infected through inhalation of spores and ingestion of contaminated foods at a rate, $\beta$ and animals can be infected through the inhalation of spores and ingestion of contaminated grass as a result of carcasses in the soil at a rate, $\lambda$.

Where $\beta_m^* = I_h + I_v$ .

The following system of ordinary differential equations are obtained from the the model flow diagram in Figure 4.1:

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= \Lambda_h + \sigma_h R_h - \beta_m^* \beta S_h - \mu_h S_h \\
\frac{dI_h}{dt} &= \beta_m^* \beta S_h - \gamma I_h - (\mu_h + \delta_h) I_h \\
\frac{dR_h}{dt} &= \gamma I_h - (\sigma_h + \mu_h) R_h \\
\frac{dS_v}{dt} &= (1-u_3)\Lambda_v - \beta_m^* \lambda S_v - \mu_v S_v + \sigma_v R_v + \tau V_v \\
\frac{dI_v}{dt} &= \beta_m^* \lambda S_v + b\beta_m^* \lambda V_v - \alpha I_v - (\mu_v + \delta_v) I_v \\
\frac{dR_v}{dt} &= \alpha I_v - (\sigma_v + \mu_v) R_v \\
\frac{dV_v}{dt} &= u_3 \Lambda_v - (\tau + \mu_v) V_v - b\lambda \beta_m^* V_v
\end{aligned}\right\} \qquad (4.2.1)$$

## 4.3 Mathematical analysis of the Anthrax model

### 4.3.1 Positivity and boundedness of solutions

When dealing with human population model, we are aiming at getting non-negative solutions. Therefore, the conditions under which the system of differential equations under study has non-negative solutions is of great importance. The Anthrax model would be epidemically meaningful on condition that all the solutions with non-negative initial data remain non-negative at every time. The concept of the derivative of a function would be applied. The derivative of a function at a point is one of the basic properties that determines the behaviour of that particular function even when that function is unknown. If the derivative of a function at a point is positive, then the function is said to be increasing at that point. If the derivative of the function at a point is negative, then it is said to be decreasing and if the derivative of the function at a point is equal to zero, then the function is constant.

**Theorem 7.** *Let* $\Pi = \{(S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), V_v(t), R_v(t)) \in \mathbb{R}^7_+ :$

$(S_h(0), I_h(0), R_h(0), S_v(0), I_v(0), V_v(0), R_v(0)) > 0\}$,

*then the solution of* $\{(S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), V_v(t), R_v(t))\}$*are non-negative for all time* $t \geq 0$.

*This implies that, if* $S_h(0), I_h(0), R_h(0), S_v(0), I_v(0), V_v(0), R_v(0)$*are non-negative, then*

$S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), V_v(t), R_v(t)$*are also non-negative for all time* $t > 0$.

The total human population at any time $(t)$is given by:

$$N_h(t) = S_h(t) + I_h(t) + R_h(t).$$

$$\frac{dN_h}{dt} = \frac{dS_h}{dt} + \frac{dI_h}{dt} + \frac{dR_h}{dt}$$

$$\left.\begin{aligned}\frac{dN_h}{dt} = \quad & \Lambda_h - \mu_h S_h - \beta_m^* \beta S_h - \mu_h S_h + \beta_m^* \beta S_h \\ & -\gamma I_h - (\mu_h + \delta_h) I_h + \gamma I_h - (\sigma_h + \mu_h) R_h\end{aligned}\right\}$$

$$\frac{dN_h}{dt} = \quad \Lambda_h - \mu_h S_h \quad - (\mu_h + \delta_h) I_h - (\sigma_h + \mu_h) R_h.$$

In the absence of mortality due to Anthrax infections, the above becomes;

$$\frac{dN_h}{dt} \leq \quad \Lambda_h - \quad \mu_h N_h.$$

$$\left(\frac{dN_h}{\Lambda_h - \mu_h N_h}\right) = dt$$

Taking integral of both sides;

$$\int \left(\frac{dN_h}{\Lambda_h - \mu_h N_h}\right) = \int dt$$

$$-\frac{1}{\mu_h} \ln(\Lambda_h - \mu_h N_h) \leq t + A$$

$\Lambda_h - \mu_h N_h \quad \geq \quad A e^{-\mu_h t}$ , where $A$ is constant.

Applying the initial condition, $N_h(0) \quad = \quad N_{h(0)}$ ,

$\Lambda_h - \mu_h N_{h(0)} \quad = \quad A$

Therefore, $\Lambda_h - \mu_h N_h \quad \geq \quad \left(\Lambda_h - \mu_h N_{h(0)}\right) e^{-\mu_h t}$ .

$$N_h \quad \leq \quad \frac{\Lambda_h}{\mu_h} - \left(\frac{\Lambda_h - \mu_h N_{h(0)}}{\mu_h}\right) e^{-\mu_h t}.$$

As $t \to \infty$, the population size, $N_h \to \frac{\Lambda_h}{\mu_h}$.

This implies that, $0 \leq \quad N_h \leq \quad \frac{\Lambda_h}{\mu_h}$ and $N_h(t) \leq \frac{\Lambda_h}{\mu_h}$.

Also, if $N_h(0) \leq \frac{\Lambda_h}{\mu_h}$, then $N_h(t) \leq \frac{\Lambda_h}{\mu_h}$.

$$\Pi_h = \left\{(S_h, I_h, R_h) \in \mathbb{R}_+^3 : S_h + I_h + R_h \leq \frac{\Lambda_h}{\mu_h}\right\} \tag{4.3.1}$$

The total vector(livestock) population at any time $(t)$is given by:

$$N_v(t) = S_v(t) + V_v(t) + I_v(t) + R_v(t)$$

This implies that;

$$\frac{dN_v}{dt} = \frac{dS_v}{dt} + \frac{dV_v}{dt} + \frac{dI_v}{dt} + \frac{dR_v}{dt} \ .$$

By substituting the derivatives on the right hand side and simplifying;

$\frac{dN_v}{dt} = \Lambda_v - \mu_v N_v - \delta_v I_v.$

In the absence of mortality due to Anthrax infections, the above becomes;

$\frac{dN_v}{dt} \leq \Lambda_v - \mu_v N_v.$

$\left(\frac{dN_v}{\Lambda_v - \mu_v N_v}\right) = dt$

Taking integral of both sides;

$\int \left(\frac{dN_v}{\Lambda_v - \mu_v N_v}\right) = \int dt$

$-\frac{1}{\mu_v}\ln(\Lambda_v - \mu_v N_v) \leq t + A$

$\Lambda_v - \mu_v N_v \geq Ae^{-\mu_v t}$ , where $A$ is constant.

Applying the initial condition, $N_v(0) = N_{v(0)}$ ,

We obtain the relation;

$\Lambda_v - \mu_v N_{v(0)} = A$

Therefore, $\Lambda_v - \mu_v N_v \geq \left(\Lambda_v - \mu_v N_{v(0)}\right) e^{-\mu_v t}$ .

$N_v \leq \frac{\Lambda_v}{\mu_v} - \left(\frac{\Lambda_v - \mu_v N_{v(0)}}{\mu_v}\right) e^{-\mu_v t}.$

As $t \to \infty$, the population size, $N_v \to \frac{\Lambda_v}{\mu_v}$.

This implies that, $0 \leq N_v \leq \frac{\Lambda_v}{\mu_v}$ and $N_v(t) \leq \frac{\Lambda_v}{\mu_v}$.

Also, if $N_v(0) \leq \frac{\Lambda_v}{\mu_v}$, then $N_v(t) \leq \frac{\Lambda_v}{\mu_v}$.

Therefore,

$$\Pi_v = \left\{(S_h, I_h, R_h, V_v) \in \mathbb{R}_+^4 : S_h + I_h + R_h + V_v \leq \frac{\Lambda_h}{\mu_h}\right\}. \tag{4.3.2}$$

The feasible region for the system of ordinary differential equations in $(0.2.1)$ is given by:

$$\Pi = \Pi_h \times \Pi_v \subset \mathbb{R}_+^3 \times \mathbb{R}_+^4 \ . \tag{4.3.3}$$

Where ,

$$\Pi_h = \left\{ (S_h, I_h, R_h) \in \mathbb{R}^3_+ : S_h + I_h + R_h \leq \frac{\Lambda_h}{\mu_h} \right\} \tag{4.3.4}$$

and

$$\Pi_v = \left\{ (S_h, I_h, R_h, V_v) \in \mathbb{R}^4_+ : S_h + I_h + R_h + V_v \leq \frac{\Lambda_h}{\mu_h} \right\}. \tag{4.3.5}$$

Where $\Pi$ is positively invariant.

### 4.3.2 Disease-free equilibrium for the Anthrax model.

The disease-free equilibrium of the Anthrax model is obtained by setting the system of differential equations to zero. At disease free equilibrium, there are no infections and recovery. This is given by:

$\xi_0 = (S_h^*, I_h^*, R_h^*, S_h^*, I_h^*, R_h^*, V_h^*)$.

$\frac{dS_h}{dt} = \Lambda_h + \sigma_h R_h - \beta_m^* \beta S_h - \mu_h S_h = 0$

$S_h^* = \frac{\Lambda_h}{\mu_h}$ .

At disease free equilibrium, there are no infections and recovery.

$$\left.\begin{array}{rcl} I_h^* & = & 0 \\ R_h^* & = & 0 \end{array}\right\} \text{and} \quad \left.\begin{array}{rcl} I_v^* & = & 0 \\ R_v^* & = & 0 \end{array}\right\}.$$

$\frac{dV_v}{dt} = u_3 \Lambda_v - (\tau + \mu_v) V_v - b\lambda \beta_m^* V_v = 0$

$u_3 \Lambda_v - (\tau + \mu_v) V_v = 0$

$V_v^* = \frac{u_3 \Lambda_v}{\tau + \mu_v}$.

Also, from the relation;

$\frac{dS_v}{dt} = (1 - u_3)\Lambda_v - \beta_m^* \lambda S_v - \mu_v S_v + \sigma_v R_v + \tau V_v = 0$

$(1 - u_3)\Lambda_v - \mu_v S_v + \tau V_v = 0$

$$S_v^* = \frac{(1-u_3)\Lambda_v + \tau V_v}{\mu_v} \quad .$$
$$S_v^* = \frac{\Lambda_v(\tau + \mu_v(1-u_3))}{\mu_v(\tau+\mu_v)}.$$

$$\xi_0 = \left( \frac{\Lambda_h}{\mu_h}, \quad 0, \quad 0, \frac{\Lambda_v(\tau+\mu_v(1-u_3))}{\mu_v(\tau+\mu_v)} \quad , \quad 0, \quad 0, \quad \frac{u_3\Lambda_v}{\tau+\mu_v} \right). \tag{4.3.6}$$

### 4.3.3 The basic reproductive number

Using the Next Generation Matrix, the linear stability of the disease-free equilibrium $(\xi_0)$ can be established. The basic reproductive rate gives the number of secondary cases one infectious individual will produce in a population consisting only of susceptible individuals Van den Driessche and Watmough (2002); Grassly and Fraser (2008). It is the threshold parameter that governs the spread of a disease Muia et al. (2018).

The next-generation matrix is defined as; $K = FV^{-1}$ and $R_0 = \rho(FV^{-1})$

Where $\rho(FV^{-1})$ denotes the spectral radius of $FV^{-1}$.

The basic reproductive number $R_0$, is defined as the spectral radius of the next-generation matrix.

**Definition 17.** The spectral radius of a matrix $A$ is defined as the maximum of the absolute values of the eigenvalues of the matrix $A$ : $\rho(A) = sup\{|\lambda| : \lambda \varepsilon \rho(A)\}$, where $\rho(A)$ denotes the set of eigenvalues of the matrix $A$.

Using the Next Generation Matrix, we consider only the infectious classes in the system of differential equations in $(4.2.1)$ :

$$\left.\begin{array}{rcl} \frac{dI_h}{dt} & = & (I_h+I_v)\beta S_h - \gamma I_h - (\mu_h+\delta_h) I_h \\ \frac{dI_v}{dt} & = & (I_h+I_v)\lambda S_v + (I_h+I_v) b\lambda V_v - \alpha I_v \quad -(\mu_v+\delta_v) I_v \end{array}\right\} \tag{4.3.7}$$

Let $f$ be the number of new infection coming into the system and $v$ be the number of infectious that are leaving the system either by death or birth.

$$f = \begin{bmatrix} (I_h + I_v)\beta S_h \\ (I_h + I_v)\lambda S_v \quad + \quad (I_h + I_v) b\lambda V_v \end{bmatrix},$$

and

$$v = \begin{bmatrix} \gamma I_h + (\mu_h + \delta_h) I_h \\ \alpha I_v + (\mu_v + \delta_v) I_v \end{bmatrix}.$$

The Jacobian matrix of $f$ and $v$ are obtained by $F$ and $V$ as follows:

$$F = \begin{bmatrix} \frac{\partial f_1}{\partial I_h} & \frac{\partial f_1}{\partial I_v} \\ \frac{\partial f_2}{\partial I_h} & \frac{\partial f_2}{\partial I_v} \end{bmatrix} = \begin{bmatrix} \beta S_h & \beta S_h \\ \lambda S_v + b\lambda V_v & \lambda S_v + b\lambda V_v \end{bmatrix},$$

$$V = \begin{bmatrix} \frac{\partial v_1}{\partial I_h} & \frac{\partial v_1}{\partial I_v} \\ \frac{\partial v_2}{\partial I_h} & \frac{\partial v_2}{\partial I_v} \end{bmatrix} = \begin{bmatrix} \gamma + (\mu_h + \delta_h) & 0 \\ 0 & \alpha + (\mu_v + \delta_v) \end{bmatrix}.$$

The Jacobian matrix of $f$ and $v$ at disease free equilibrium is obtained by $F$ and $V$ as follows:

$$F = \begin{bmatrix} \frac{\partial f_1}{\partial I_h} & \frac{\partial f_1}{\partial I_v} \\ \frac{\partial f_2}{\partial I_h} & \frac{\partial f_2}{\partial I_v} \end{bmatrix} = \begin{bmatrix} \beta S_h^* & \beta S_h^* \\ \lambda S_v^* + b\lambda V_v^* & \lambda S_v^* + b\lambda V_v^* \end{bmatrix},$$

$$V = \begin{bmatrix} \frac{\partial v_1}{\partial I_h} & \frac{\partial v_1}{\partial I_v} \\ \frac{\partial v_2}{\partial I_h} & \frac{\partial v_2}{\partial I_v} \end{bmatrix} = \begin{bmatrix} \gamma + (\mu_h + \delta_h) & 0 \\ 0 & \alpha + (\mu_v + \delta_v) \end{bmatrix}.$$

From the relation; $FV^{-1}$, the inverse of $V$ can be computed as ;

$$V^{-1} = \begin{bmatrix} \frac{1}{\gamma + (\mu_h + \delta_h)} & 0 \\ 0 & \frac{1}{\alpha + (\mu_v + \delta_v)} \end{bmatrix}$$

Computing the product of $FV^{-1}$.

$$FV^{-1} = \begin{bmatrix} \frac{\beta S_h^*}{\gamma + (\mu_h + \delta_h)} & \frac{\beta S_h^*}{\alpha + (\mu_v + \delta_v)} \\ \frac{\lambda S_v^* + b\lambda V_v^*}{\gamma + (\mu_h + \delta_h)} & \frac{\lambda S_v^* + b\lambda V_v^*}{\alpha + (\mu_v + \delta_v)} \end{bmatrix} \tag{4.3.8}$$

By computing the eigenvalues of $FV^{-1}$ and selecting the dominant eigenvalue. Let $A$ represent the eigenvalue of the matrix.

$$\begin{vmatrix} \frac{\beta S_h^*}{\gamma+(\mu_h+\delta_h)} - A & \frac{\beta S_h^*}{\alpha+(\mu_v+\delta_v)} \\ \frac{\lambda S_v^* + b\lambda V_v^*}{\gamma+(\mu_h+\delta_h)} & \frac{\lambda S_v^* + b\lambda V_v^*}{\alpha+(\mu_v+\delta_v)} - A \end{vmatrix} = 0$$

By computing the determinant and re-arranging;

$$A^2 - \left[\left(\frac{\lambda S_v^* + b\lambda V_v^*}{\alpha+(\mu_v+\delta_v)}\right) + \left(\frac{\beta S_h^*}{\gamma+(\mu_h+\delta_h)}\right)\right] A = 0$$

Solving the quadratic equation;

$$A_1 = 0 \text{ and } A_2 = \left[\left(\frac{\lambda S_v^* + b\lambda V_v^*}{\alpha+(\mu_v+\delta_v)}\right) + \left(\frac{\beta S_h^*}{\gamma+(\mu_h+\delta_h)}\right)\right].$$

The dominant eigenvalue is $A_2$. This implies that;

$$R_{hv} = \left[\left(\frac{\beta S_h^*}{\gamma+(\mu_h+\delta_h)}\right) + \left(\frac{\lambda S_v^* + b\lambda V_v^*}{[\alpha+(\mu_v+\delta_v)]}\right)\right]. \tag{4.3.9}$$

At disease free equilibrium,

$S_h^* = \frac{\Lambda_h}{\mu_h}$, $S_v^* = \frac{\Lambda_v(\tau+\mu_v(1-u_3))}{\mu_v(\tau+\mu_v)}$, and $V_v^* = \frac{u_3\Lambda_v}{\tau+\mu_v}$.

Substituting the above into the basic reproductive number, $R_{hv}$:

$$R_{hv} = \left(\frac{\beta\Lambda_h}{\mu_h[\gamma+(\mu_h+\delta_h)]}\right) + \frac{b\lambda\Lambda_v(\tau+\mu_v(1-2u_3))}{\mu_v(\tau+\mu_v)[\alpha+(\mu_v+\delta_v)]} \tag{4.3.10}$$

If the mode of infection is from infected animals, then the parameters in the reproduction number, $(R_{vq})$ are the contributing to the rise in the value of $R_{hv}$. Moreover, if the mode of infection is as a result of infected humans, then the parameters in the reproduction number, $(R_{hq})$ are the contributing factors in the value of $R_{hv}$.

The inhalation of spores and the ingestion of contaminated foods affects the basic reproduction number, $(R_{hv})$ by the rate of interaction between susceptible humans and infected animals as well as the interaction between susceptible animals and infected humans.

Where, $R_{hq} = \left(\frac{\beta\Lambda_h}{\mu_h[\gamma+(\mu_h+\delta_h)]}\right)$ is the basic reproduction number of Anthrax in human population.

Where, $R_{vq} = \frac{b\lambda\Lambda_v(\tau+\mu_v(1-2u_3))}{\mu_v(\tau+\mu_v)[\alpha+(\mu_v+\delta_v)]}$ is the basic reproduction number of Anthrax

in animal population.

**Proposition 1.** *The disease-free equilibrium of model* $(4.2.1)$ *is locally asymptotically stable if* $R_{hv} < 1$,*and unstable if* $R_{hv} > 1$ .

### 4.3.4 Global stability of the disease-free equilibrium.

**Theorem 8.** *If* $R_{hv} \leq 1$, *the disease-free equilibrium is globally asymptotically stable in the interior of* $\Omega$.

Proof: Considering the Lyapunov function below;

$$P(t) = (\alpha + \mu_v + \delta_v) I_h + (\gamma + \mu_h + \delta_h) I_v \tag{4.3.11}$$

By computing the time derivative of P along the solutions of the system of ordinary differential equations in$(4.2.1)$, the following is obtained,

$$
\left.
\begin{aligned}
\frac{dP(t)}{dt} = & \quad (\alpha+\mu_v+\delta_v)\frac{dI_h}{dt}+(\gamma+\mu_h+\delta_h)\frac{dI_v}{dt} \\
= & \quad (\beta S_h(I_h+I_v)-\gamma I_h-(\mu_h+\delta_h)I_h) \\
& \quad +\lambda S_v(I_h+I_v) \\
& \quad +b(I_h+I_v)\lambda V_v-\alpha I_v-(\mu_v+\delta_v)I_v] \\
\leq & \quad (\alpha+\mu_v+\delta_v)\frac{\beta\Lambda_h I_h}{\mu_h}+(\alpha+\mu_v+\delta_v)\frac{\beta\Lambda_h I_v}{\mu_h} \\
& \quad -(\alpha+\mu_v+\delta_v)(\gamma+\mu_h+\delta_h)I_h \\
& \quad +I_h(\gamma+\mu_h+\delta_h)\left(\frac{\lambda\Lambda_v(\tau+\mu_v(I-u_3))}{\mu_v(\tau+\mu_v)}\right) \\
& \quad +I_v(\gamma+\mu_h+\delta)\left(\frac{\lambda\Lambda_v(\tau+\mu_v(I-u_3))}{\mu_v(\tau+\mu_v)}\right) \\
& \quad +I_h(\gamma+\mu_h+\delta_h)\left(\frac{bu_3\lambda\Lambda_v}{\tau+\mu_v}\right)+I_v(\gamma+\mu_h+\delta)\left(\frac{bu_3\lambda\Lambda_v}{\tau+\mu_v}\right) \\
& \quad -I_v(\gamma+\mu_h+\delta)(\alpha+\mu_v+\delta_v) \\
\leq & \quad -I_h(\gamma+\mu_h+\delta_h)(\alpha+\mu_v+\delta_v)(1-R_{hv}) \\
& \quad -I_v(\gamma+\mu_h+\delta_h)(\alpha+\mu_v+\delta_v)(1-R_{hv}) \\
= & \quad -(I_h+I_v)(\gamma+\mu_h+\delta_h)(\alpha+\mu_v+\delta_v)(1-R_{hv})
\end{aligned}
\right\} \quad (4.3.12)
$$

Time derivative of P along the solutions of the system of differential equations in (4.2.1) yields:

$\left(\frac{dP(t)}{dt}\right) \leq 0$, if and only if $R_{hv} < 0$

$\left(\frac{dP(t)}{dt}\right) = 1$, if and only if $I_h + I_v = 0$ or $R_{hv} = 1$.

The highest compact invariant set in $S_h,\ I_h,\ I_v,\ \in\ \Omega\ ,\ \frac{dP(t)}{dt} = 0,$ if $R_{hv} \leq 1$, is the singleton $\xi_0$.

It shows that $\xi_0$ is globally asymptotically stable in $\Omega$. By LaSalle's invariant principle (LaSalle, 1976; Grassly and Fraser, 2008).

### 4.3.5 Endemic equilibrium

Considering the system of differential equations in 4.2.1, at equilibrium, $\beta_m^* = I_h + I_v = 0$. It corresponds to the disease free equilibrium or the relation:

$$H_0\beta_m^{*3} + H_1\beta_m^{*2} + H_2\beta_m^* + H_3 = 0 \tag{4.3.13}$$

*Remark.* The system of differential equations in equation $(4.2.1)$ is said to have an endemic equilibrium $E^*$, if $R_{hv} > 1$.This is satisfied by cases $(2,4,6)$ in 4.1. The system of differential equations can have more than one endemic equilibrium points if $R_{hv} > 1$. This is satisfied by case $(8)$ in table 4.1. The system of differential equations in equation $(4.2.1)$, have more than one equilibrium points if $R_{hv} < 1$, as satisfied by case $(3,5,7)$.

| Cases | $H_0$ | $H_1$ | $H_2$ | $H_3$ | $R_{hv}$ | No. of sign change | No. of positive real roots |
|---|---|---|---|---|---|---|---|
| 1 | + | + | + | + | $R_{hv}<1$ | 0 | 0 |
| 2 | + | + | + | - | $R_{hv}>1$ | 1 | 1 |
| 3 | + | + | - | + | $R_{hv}<1$ | 2 | 0,2 |
| 4 | + | + | - | - | $R_{hv}>1$ | 1 | 1 |
| 5 | + | - | - | + | $R_{hv}<1$ | 2 | 0,2 |
| 6 | + | - | - | - | $R_{hv}>1$ | 1 | 1 |
| 7 | + | - | + | + | $R_{hv}<1$ | 2 | 0,2 |
| 8 | + | - | + | - | $R_{hv}>1$ | 3 | 1,3 |

Table 4.1: Possible positive real roots of $P(\beta_m^*)$ for $R_{hv} > 1$ and $R_{hv} < 1$.

From the table 4.1, it can be deduced that the existence of multiple endemic equilibrium exists when the basic reproduction number $(R_{hv})$is less than unity. This indicates the tendency of backward bifurcation, a situation where the disease free equilibrium coexists with the stable endemic equilibrium, when the basic reproduction number is less than one. The existence of backward bifurcation has significant implication for epidemiological control measures because an epidemic may persist at steady state even when the basic reproduction number is less than one $(R_{hv} < 1)$.

### 4.3.6 Global stability of endemic equilibrium

In this section, global behaviour of the system of differential equations in equation (4.2.1)is analysed. This is done by considering the non-linear Lyapunov function.

**Theorem 9.** *The system of differential equations in equation* (4.2.1)*, is said to have a unique endemic equilibrium if* $R_{hv} > 1$ *and it is globally asymptotically stable.*

The endemic equilibrium can only exists if and only if $R_{hv} > 1$ So by letting $R_{hv} > 1$ it implies that the endemic equilibrium exists.

Considering the non-linear Lyapunov function below;

$$\left.\begin{array}{rcll} L & = & S_h^{**}\left(\frac{S_h}{S_h^{**}} - ln\frac{S_h}{S_h^{**}}\right) & + \quad I_h^{**}\left(\frac{I_h}{I_h**} - ln\frac{I_h}{I_h^{**}}\right) \\ & + & \frac{g_1 R_h^{**}}{\gamma}\left(\frac{R_h}{R_h^{**}} - ln\frac{R_h}{R_h**}\right) & + \quad S_v^{**}\left(\frac{S_v}{S_v^{**}} - ln\frac{S_v}{S_v^{**}}\right) \\ & + & I_v^{**}\left(\frac{I_v}{I**} - ln\frac{I_v}{I_v^{**}}\right) & + \quad R_v^{**}\left(\frac{R_v}{R_h^{**}} - ln\frac{R_v}{R**}\right) \\ & + & V_v^{**}\left(\frac{Vv}{V_v^{**}} - ln\frac{V_v}{V_v^{**}}\right). & \end{array}\right\} \tag{4.3.14}$$

Where;

$$\begin{aligned} g_1 &= \gamma + (\mu_h + \delta_h), \\ g_2 &= (\sigma_2 + \mu_h), \\ g_3 &= \alpha + (\mu_v + \delta_v), \\ g_4 &= (\sigma_v + \mu_v), \end{aligned}$$

When the above Lyapunov function is differentiated with respect to time, we obtain the equation;

$$\left.\begin{array}{rcccccccc}
\frac{dL}{dt} & = & \left(1-\frac{S_h^{**}}{S_h}\right)\frac{dS_h}{dt} & + & \left(1-\frac{I_h^{**}}{I_h}\right)\frac{dI_h}{dt} & + & \frac{g_1}{\gamma}\left(1-\frac{R**}{R_h}\right)\frac{dR_h}{dt} \\
 & + & \left(1-\frac{S_v^{**}}{S_v}\right)\frac{dS_v}{dt} & + & \left(1-\frac{I_v^{**}}{I_v}\right)\frac{dI_v}{dt} & + & \left(1-\frac{R_v^{**}}{R_v}\right)\frac{dR_v}{dt} \\
 & + & \left(1-\frac{V_v^{**}}{V_v}\right)\frac{dV_v}{dt}. & & & & \\
\end{array}\right\} \tag{4.3.15}$$

Therefore, this implies that;

$$\left.\begin{array}{l}
\frac{dL}{dt} = \left(1-\frac{S_h^{**}}{S_h}\right)\left[\Lambda_h+\sigma_h R_h^{**}+\beta\beta_m^{**}S_h^{**}+\mu_h S_h^{**}-\Lambda_h\right. \\
\left.-\sigma R_h-\beta\beta_m S_h-\mu_h S_h\right]+\left(1-\frac{I_h^{**}}{I_h}\right)\left[\beta\beta_m S_h-g_1 I_h\right. \\
\left.+\frac{g_1}{\gamma}\left(1-\frac{R_h^{**}}{R_h}\right)\left[\gamma I_h-g_2 R_h\right]+\left(1-\frac{S_v^{**}}{S_v}\right)\left[(1-u_3)\Lambda_v\right.\right. \\
\left.+\lambda\beta\beta_m^{**}S_v^{**}+\mu_v S_v^{**}+\sigma_v R_v^{**}+\tau V_v^{**}-(1-u_3)\Lambda_v\right. \\
\left.-\lambda\beta_m S_v-\mu_v S_v-\sigma_v R_v-\tau V_v\right]+\left(1-\frac{I_v^{**}}{I_v}\right) \\
\left[\lambda\beta_m S_v+b\lambda\beta_m V_v-g_3 I_v\right]+\frac{g_3}{\alpha}\left(1-\frac{R_v^{**}}{R_v}\right) \\
\left[\alpha I_v-g_4 R_v\right]+\left(1-\frac{V_v^{**}}{V_v}\right)\left[u_3\Lambda_v+b\lambda\beta_m^{**}V_v^{**}\right. \\
\left.+(\tau+\mu_v)V_v^{**}-u_3\Lambda_v-b\lambda\beta_m V_v-(\tau+\mu_v)V_v\right].
\end{array}\right\} \tag{4.3.16}$$

Basically, however, the arithmetic mean value exceeds the geometric mean value(Safi and Garba, 2012; Grassly and Fraser, 2008). This follows that;

$$
\left.
\begin{array}{lll}
2 & -\dfrac{S_h^{**}}{S_h} - \dfrac{S_h}{S_h^{**}} & \leq 0 \\
1 & -\dfrac{R_h}{R_h^{**}} & \leq 0 \\
1 & -\dfrac{R_h^{**}}{R_h} - \dfrac{g_1 g_2 S_h}{\gamma) S_h^{**}} \left(1 - \dfrac{R_h^{**}}{R_h}\right) & \leq 0 \\
1 & -\dfrac{\beta_m}{\beta_h^{**}} - \dfrac{S_h^{**}}{S_h} - \dfrac{S_h \beta_m I_h^{**}}{S_h^{**} \beta_m^{**}} & \leq 0 \\
1 & -\dfrac{I_h}{I_h^{**}} - \dfrac{\gamma) I_h}{I_h^{**}} \left(1 - \dfrac{R_h^{**}}{R_h}\right) & \leq 0 \\
2 & -\dfrac{S_v^{**}}{S_v} - \dfrac{S_v}{S_v^{**}} & \leq 0 \\
1 & -\dfrac{S_v^{**}}{S_v} - \dfrac{R_v}{R_v^{**}} + \dfrac{R_v S_v^{**}}{R_v^{**} S_v} & \leq 0 \\
1 & -\dfrac{S_v^{**}}{S_v} - \dfrac{V_v}{V_v^{**}} - \dfrac{V_v S_v^{**}}{V_v^{**} S_v} & \leq 0 \\
1 & -\dfrac{S_v^{**}}{S_v} + \dfrac{\beta_m}{\beta_h^{**}} - \dfrac{S_v \beta_m I_v^{**}}{S_v^{**} \beta_m^{**} I_v} & \leq 0 \\
1 & -\dfrac{I_v}{I_v^{**}} - g_3 \alpha \dfrac{I_v}{I_v^{**}} - g_3 \alpha \dfrac{I_v R_v^{**}}{I_v^{**} R_v} & \leq 0 \\
1 & -\dfrac{R_v}{R_v^{**}} & \leq 0 \\
2 & -\dfrac{V_v^{**}}{V_v} - \dfrac{V_v}{V_v^{**}} & \leq 0 \\
1 & -\dfrac{V_v^{**}}{V_v} + \dfrac{\beta_m}{\beta_h^{**}} - \dfrac{V_v \beta_m I_v^{**}}{V_v^{**} \beta_m^{**} I_v} & \leq 0
\end{array}
\right\} \tag{4.3.17}
$$

From the assumption that all the model parameters are non-negative, it implies that the derivative of the Lyapunov function is less than zero $\left(\dfrac{dL}{dt} \leq 0\right)$, if the basic reproduction number of the system of differential equation in equation$(4.2.1)$ is greater than one $(R_{hv} > 1)$ Kanyaa et al. (2018). Therefore by LaSalle's Invariant Principle (LaSalle, 1976), as $t$ approaches infinity, all the solution of the equations of the system of differential equations in the model approaches the endemic equilibrium point if $(R_{hv} > 1)$.

#### 4.3.6.1 Backward Bifurcation and Multiple Equilibrium

In this section, we discuss the phenomenon of Backward Bifurcation. In this case, the bifurcating endemic equilibrium exists only when the basic reproduction number is less

than one $(R_{hv} < 1)$. Our model has exhibited this property and backward bifurcation exists. When backward bifurcation occurs, the range of the reproduction number $(R_{hv})$ is between $R^*_{hv} < R_{hv} < 1$. There exits at least one endemic equilibrium. Usually, at least one is stable and the disease free equilibrium is not globally stable when the basic reproduction number is less than one. In this case, the infection would exist even when $R_{hv} < 1$. Below is the backward bifurcation diagram of the force of infection against the basic reproduction number that the model has exhibited.

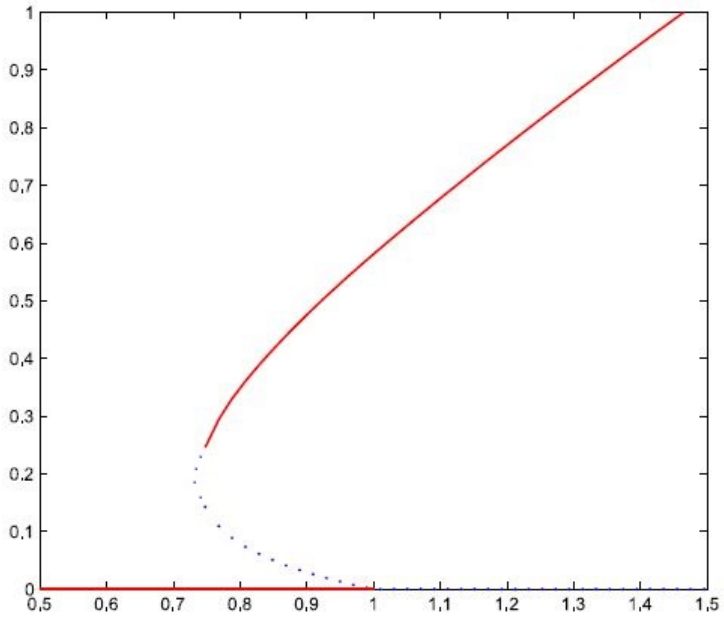


Figure 4.2: Backward bifurcation of the endemic equilibrium when $R_{hv} > 1$.

## 4.4 Sensitivity Analysis of the Anthrax model

Basically, the essence of sensitivity analysis is to determine how robust a model is to parameter values. This is usually done to help identify the parameters with high impact on the basic reproduction number $(R_{hv})$. The basic reproduction number is usually analysed to find out whether or not treatment of the infective, mortality and vaccination could help in the control or eradication of the disease in the population Eustace et al. (2018).

**Definition 18.** The normalised forward sensitivity index of a variable, $y$, which depends deferentially on a parameter, $x$, defined as:

$$\Upsilon_x^y = \frac{\partial y}{\partial x} \times \frac{x}{y}. \tag{4.4.1}$$

### 4.4.1 Sensitivity indices of the basic reproduction number $R_{hv}$.

In biological models, the reproductive number determines the ability of the disease to spread within the population. We will determine the reduction in infection due to the diseases by computing the sensitivity indices of the basic reproduction Number $R_{hv}$, with respect to the parameter values in the model. The sensitivity indices serve as determinants of the significance of each parameter in the dynamics and prevalence of the diseases. They measure the change in model variables when a parameter changes. In this study, we will compute the sensitivity indices of $R_{hv}$ to parameter values for the model which will be estimated from data available or already published papers in the literature. Considering the thirteen different parameters of the system of differential equations in model $(4.2.1)$, we therefore derive the sensitivity of $R_{hv}$ to each of the parameters in the model. Consider the parameter values in table 4.3 bellow:

The sensitivity indices of the basic reproduction number of $R_{hv}$ with respect to each of the parameters of the system of differential equations in model $(4.2.1)$, are given in the table bellow:

| Parameter | Description | Sensitivity index(+ve/-ve) |
|---|---|---|
| $\Lambda_h$ | humans recruitment rate | +ve |
| $\Lambda_v$ | animals recruitment rate | +ve |
| $\mu_h$ | death rate in humans | -ve |
| $\mu_v$ | death rate in animals | -ve |
| $\delta_h$ | human disease induced death rate | -ve |
| $\delta_v$ | animals disease induced death rate | -ve |
| $u_3$ | proportion vaccinated | -ve |
| $\alpha$ | animals recovery rate | -ve |
| $\beta$ | human transmission rate | +ve |
| $\gamma$ | human rate of recovery | -ve |
| $\tau$ | waning rate | +ve |
| $\lambda$ | animals transmission rate | +ve |
| $b$ | vaccine efficacy | +ve |

Table 4.2: Sensitivity indices of parameters to $R_{hv}$.

The detailed sensitivity analysis of the basic reproductive number $(R_{hv})$ as a result of evaluation of the other parameters of the model shows that increasing $\alpha$ would decrease the basic reproduction number $R_{hv}$. Moreover, decreasing $\alpha$ would increase the basic reproductive number $(R_{hv})$. Also, by increasing $\beta$ and $\lambda$ would cause an increase in the basic reproduction number $R_{hv}$ and by decreasing $\beta$, and $\lambda$ would cause a decrease in the basic reproduction number $R_{hv}$.

## 4.5 Optimal control of the Anthrax model

In this section, the analysis of an optimal control is carried out to determine the impact of the four intervention schemes. The optimal control problem is derived by incorporating the following controls into the Anthrax model(4.2.1)and the introduction of an objective functional that seeks to minimise: $(u_1, u_2, u_3, u_4)$.

1. $u_1$ : This is the preventive measures of the susceptible human population $(S_h)$. These are efforts to reduce the acquisition of Anthrax through education.

2. $u_2$: This is the treatment efforts given to the infected humans $(I_h)$ as a result of

complications of infections. These are efforts to minimise infections by treating the infective human population.

3. $u_3$: This is the vaccination effort of the susceptible animals $(S_v)$. This is the use of antimicrobial drugs.

4. $u_4$: This is the treatment efforts given to the infected animals $(I_v)$ as a result of complications of infections. These are efforts to minimise infections by treating the infective animal population.

The following system of differential equations are obtained as a result of incorporating all the controls into the model in 4.1;

$$\left.\begin{array}{rcl}
\frac{dS_h}{dt} &=& \Lambda_h + \sigma_h R_h - (1-u_1)\,\beta_m^* \beta S_h - \mu_h S_h \\
\frac{dI_h}{dt} &=& (1-u_1)\,\beta_m^* \beta S_h - (u_2+\gamma) I_h - (\mu_h + \delta_h) I_h \\
\frac{dR_h}{dt} &=& (u_2+\gamma) I_h - (\sigma_h + \mu_h)\, R_h \\
\frac{dS_v}{dt} &=& (1-u_3)\,\Lambda_v - (1-u_1)\,\beta_m^* \lambda S_v - \mu_v S_v + \sigma_v R_v + \tau V_v \\
\frac{dI_v}{dt} &=& (1-u_1)\,\beta_m^* \lambda S_v + (1-u_1)\, b\beta_m^* \lambda V_v - (u_4+\alpha) I_v - (\mu_v + \delta_v) I_v \\
\frac{dR_v}{dt} &=& (u_4+\alpha) I_v - (\sigma_v + \mu_v)\, R_v \\
\frac{dV_v}{dt} &=& u_3 \Lambda_v - (\tau + \mu_v)\, V_v - (1-u_1)\, b\lambda \beta_m^* V_v
\end{array}\right\}$$

In epidemiological models, the essence of optimal control analysis is to minimise the spread or number of infections and the cost of treatment, preventive measures and vaccination controls. The objective functional that can be used to achieve this is given by:

$$J = min_{(u_1,u_2,u_3,u_4)} \int_0^{t_f} \left(A_1 I_v + A_2 I_h + A_3 u_1^2 + A_4 u_2^2 + A_5 m u_3^2 + A_6 u_4^2\right) dt. \quad (4.5.1)$$

subject to the system of differential equations in $(4.2.1)$.

Where;

$A_1, A_2, A_3, A_4, A_5, A_6$; these are referred to as the weight constants to aid balance the terms in the integral to avoid the dominance of one another. They are termed as the balancing cost factors.

$A_1 I_h, A_2 I_v$; these are the costs associated with infected humans and animals respectively.

$A_3 u_1^2$ : this is the cost associated with preventive measures of the susceptible human population $(S_h)$.

$A_5 m u_3^2$ : this is the cost associated with vaccination of the susceptible animals $(S_v)$. The costs is as a result of antimicrobial drugs, where $(m)$is the number of infected animals.

$A_4 u_2^2$ : this is the costs involved in the treatment of the infected humans $(I_h)$ as a result of complications of infections. This is the cost associated with treatment of infected humans.

$A_6 u_4^2$ : this is the cost associated with the treatment of infected animals $(I_v)$. The costs involved in the treatment of the infected animals as a result of complications of infections.

$t_f$ : This is the period of the intervention. $(A_1 I_h, A_2 I_v)$, represents a linear function for the cost associated with infections and

$\left(A_3 u_1^2, A_4 u_2^2, A_5 m u_3^2, A_6 u_4^2\right)$, represents a quadratic function for the cost associated with controls(Joshi et al., 2006; Grassly and Fraser, 2008).

The model control efforts is by linear combination of $u_i^2(t)$, $(i = 1,2)$ . It is a quadratic in nature because of the assumption that costs are generally non-linear in nature. Moreover, the nature of the functional is chosen in line with existing literature on epidemic models. Thus, our aim is to minimise the number of infective and reduce cost of treatment.

The objective is finding the optimal functions $\left(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t)\right)$ such that;

$$J\left(u_1^*(t),u_2^*(t),u_3^*(t),u_4^*(t)\right) = min_{(u_1,u_2,u_3,u_4)}\varepsilon \cup J(u_1,u_2,u_3,u_4) \tag{4.5.2}$$

Where

$\cup = \left\{ u : u,\ 0 \leq u_i(t) \leq 1,\ t \varepsilon \left[0,t_f\right],\ i = 1,2,3,4 \right\}$ is referred to as the control set.

### 4.5.1 Pontryagin's maximum principle

Considering the Lagrangian function;

$$L(I_h,I_v,u_1,u_2,u_3,u_4,t) = A_1I_h + A_2I_v + A_3u_1^2 + A_4u_2^2 + A_5mu_3^2 + A_6u_4^2. \tag{4.5.3}$$

The Pontryagin's Maximum Principle provides the necessary conditions that an optimal must satisfy. The principle changes the system of differential equations in $(4.2.1)$and equation $(4.5.1)$into minimisation problem point-wise Hamiltonian $(H)$, with respect to $(u_1,u_2,u_3,u_4)$ .

$$\left.\begin{aligned} H(S_h,I_h,R_h,S_v,I_v,R_v,V_v,t) = L(I_h,I_v,u_1,u_2,u_3,u_4,t) + \lambda_1\frac{dS_h}{dt} \\ +\lambda_2\frac{dI_h}{dt} + \lambda_3\frac{dR_h}{dt} + \lambda_4\frac{dS_v}{dt} + \lambda_5\frac{dI_v}{dt} + \lambda_6\frac{dR_v}{dt} + \lambda_7\frac{dV_v}{dt} \end{aligned}\right\}$$

The Hamiltonian can be written as;

$$\left.\begin{aligned} H &= A_1 I_v + A_2 I_h + A_3 u_1^2 + A_4 u_2^2 + A_5 m u_3^2 + A_6 u_6^2 \\ &+ \lambda_1 \{\Lambda_h + \sigma_h R_h - (1-u_1)\beta (I_v + I_h) S_h - \mu_h S_h\} \\ &+ \lambda_2 \{(1-u_1)\beta_m^* \beta S_h - (u_2+\gamma) I_h - (\mu_h + \delta_h) I_h\} \\ &+ \lambda_3 \{(u_2+\gamma) I_h - (\sigma_h + \mu_h) R_h\} \\ &+ \lambda_4 \{(1-u_3)\Lambda_v - (1-u_1)\lambda (I_v + I_h) S_v - (\mu_v S_v + \sigma_v R_v + \tau V_v)\} \\ &+ \lambda_5 \{(1-u_1)\beta_m^* \lambda S_v + (1-u_1) b \beta_m^* \lambda V_v - (u_4+\alpha) I_v - (\mu_v + \delta_v) I_v\} \\ &+ \lambda_6 \{(u_4+\alpha) I_v - (\sigma_v + \mu_v) R_v\} \\ &+ \lambda_7 \{u_3 \Lambda_v - (\tau + \mu_v) V_v - (1-u_1) b\lambda (I_v + I_h) V_v\} \end{aligned}\right\} \tag{4.5.4}$$

Where;

$\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7$ are referred to as the adjoint variables.

Considering the relation;

$$\frac{d\lambda_i}{dt} = -\frac{\partial H}{\partial \dot{x}(t)} \tag{4.5.5}$$

By differentiating the Hamiltonian function with respect to $S_h$;

$$\left.\begin{aligned} \frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S_h} &= -[-(1-u_1)\beta (I_v + I_h)\beta\lambda_1 - \mu_h\lambda_1 + (1-u_1)\beta (I_v + I_h)\beta\lambda_2] \\ &= [(1-u_1)\beta (I_v + I_h)\beta\lambda_1 + \mu_h\lambda_1 - (1-u_1)\beta (I_v + I_h)\beta\lambda_2] \\ &= (1-u_1)\beta (I_v + I_h)\beta (\lambda_1 - \lambda_2) + \mu_h\lambda_1 \end{aligned}\right\}$$

By taking the partial derivatives of the Hamiltonian function with respect to $(S_h, I_h, R_h, S_v, I_v, R_v, V_v)$ and negating each of them, the following adjoint or co-state variables are solutions of adjoint systems;

$$\left.\begin{aligned}
\frac{d\lambda_1}{dt} &= (1-u_1)(I_v+I_h)\beta(\lambda_1-\lambda_2)+\mu_h\lambda_1 \\
\frac{d\lambda_2}{dt} &= -A_2+(1-u_1)\beta S_h(\lambda_1-\lambda_2)+(u_2+\gamma)(\lambda_2-\lambda_3) \\
&+ \lambda_2(\mu_h+\delta_h)+(1-u_1)\lambda S_v(\lambda_4-\lambda_5)+(1-u_1)b\lambda V_v(\lambda_7-\lambda_5) \\
\frac{d\lambda_3}{dt} &= -\sigma_h\lambda_1+(\sigma_h+\mu_h)\lambda_3 \\
\frac{d\lambda_4}{dt} &= (1-u_1)\lambda(I_v+I_h)(\lambda_4-\lambda_5)+\mu_v\lambda_4 \\
\frac{d\lambda_5}{dt} &= -A_1+(1-u_1)\beta S_h(\lambda_1-\lambda_2)+(1-u_1)\lambda S_v(\lambda_4-\lambda_5) \\
&+ b\lambda(\lambda_7-\lambda_5)V_v+(\lambda_5-\lambda_6)(u_4+\alpha)+\lambda_5(\mu_v+\delta_v) \\
\frac{d\lambda_6}{dt} &= -\sigma_v\lambda_4+(\sigma_v+\mu_v)\lambda_6 \\
\frac{d\lambda_7}{dt} &= -\tau\lambda_4+(1-u_1)b\lambda(I_v+I_h)(\lambda_7-\lambda_5)+(\tau+\mu_v)\lambda_7
\end{aligned}\right\} \tag{4.5.6}$$

The above satisfies the transversality condition;

$$\lambda_1(tf)=\lambda_2(tf)=\lambda_3(tf)=\lambda_4(tf)=\lambda_5(tf)=\lambda_6(tf)=\lambda_7(tf)=0. \tag{4.5.7}$$

Now, combining the Pontryagin's Maximum Principle and the existence result of the optimal control(Pontryagin, 1987; Fleming and Rishel, 2012).

Moreover, the characterisation of the optimal control is obtained by solving;

$$\frac{\partial H}{\partial u_i}=0 \tag{4.5.8}$$

$u_i=u_i^*$, where $i=1,2,3,\ldots,n$.

$$\left.\begin{aligned}
\frac{\partial H}{\partial u_1} &= 2A_3u_1+(I_v+I_h)\beta S_h\lambda_1-(I_v+I_h)\beta S_h\lambda_2+(I_v+I_h)\lambda S_v\lambda_4 \\
&-(I_v+I_h)\lambda S_v\lambda_5-(I_v+I_h)b\lambda V_v\lambda_5+(I_v+I_h)b\lambda V_v\lambda_7=0
\end{aligned}\right\}$$

By simplifications;

$$\left.\begin{aligned}\frac{\partial H}{\partial u_1} = 2A_3u_1 + (\lambda_1-\lambda_2)\left[(I_v+I_h)\beta S_h\right] + \\ (\lambda_4-\lambda_5)\left[(I_v+I_h)\lambda S_v\right] + (\lambda_7-\lambda_5)\left[(I_v+I_h)b\lambda V_v\right] = 0\end{aligned}\right\}$$

Therefore;

$$u_1^* = \frac{(\lambda_2-\lambda_1)\left[(I_v+I_h)\beta S_h^*\right] + (\lambda_5-\lambda_4)\left[(I_v+I_h)\lambda S_v^*\right] + (\lambda_5-\lambda_7)\left[(I_v+I_h)b\lambda V_v^*\right]}{2A_3}$$

Differentiating the Hamiltonian function evaluated at optimal control and equating the derivatives of the Hamiltonian with respect to the controls to zero, the following are obtained;

$$\left.\begin{aligned}u_1^* = \left\{\left(\frac{\beta(\lambda_2-\lambda_1)(I_v+I_h)S_h^*}{2A_3} + \right.\right. \\ \left.\left.\frac{\lambda(\lambda_5-\lambda_4)(I_v+I_h)S_v^* + b\lambda(\lambda_5-\lambda_7)(I_v+I_h)V_v^*}{2A_3}\right)\right\} \\ u_2^* = \left\{\left(\frac{(\lambda_2-\lambda_3)I_h^*}{2A_4}\right)\right\} \\ u_3^* = \left\{\left(\frac{\Lambda_v(\lambda_4-\lambda_7)}{2mA_5}\right)\right\} \\ u_4^* = \left\{\left(\frac{(\lambda_5-\lambda_6)I_v^*}{2A_6}\right)\right\}\end{aligned}\right\}$$

**Theorem 10.** *The optimal control vector* $\left(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t)\right)$ *that maximise the objective functional,* $(J)$ *over* $\cup$*, given by;*

$$\left.\begin{aligned}u_1^*(t) = max\left\{0, min\left(1, \frac{\beta(\lambda_2-\lambda_1)(I_v+I_h)S_h^*}{2A_3} + \right.\right. \\ \left.\left.\frac{\lambda(\lambda_5-\lambda_4)(I_v+I_h)S_v^* + b\lambda(\lambda_5-\lambda_7)(I_v+I_h)V_v^*}{2A_3}\right)\right\} \\ u_2^*(t) = max\left\{0, min\left(1, \frac{(\lambda_2-\lambda_3)I_h^*}{2A_4}\right)\right\} \\ u_3^*(t) = max\left\{0, min\left(1, \frac{\Lambda_v(\lambda_4-\lambda_7)}{2mA_5}\right)\right\} \\ u_4^*(t) = max\left\{0, min\left(1, \frac{\alpha(\lambda_5-\lambda_6)I_v^*}{2A_6}\right)\right\}\end{aligned}\right\} \tag{4.5.9}$$

Where;

$\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7$ are the solutions of equation $(4.5.4)$ and $(4.5.5)$.

*Proof.* The existence of an optimal control is as a result the convexity of the integral of $J$ with respect to $u_1$,$u_2$,$u_3$and $u_4$, the Lipschitz property of the state system with

respect to the state variables and a priori Boundedness of the state solutions(Fleming and Rishel, 2012).

$$\left.\begin{aligned} u_1 = \tilde{u_1} := \left\{ \left( \frac{\beta\left(\lambda_2-\lambda_1\right)\left(I_v+I_h\right)S_h^*}{2A_3} + \right.\right. \\ \left.\left. \frac{\lambda\left(\lambda_5-\lambda_4\right)\left(I_v+I_h\right)S_v^* + b\lambda\left(\lambda_5-\lambda_7\right)\left(I_v+I_h\right)V_v^*}{2A_3} \right) \right\} \\ u_2 = \tilde{u_2} := \left\{ \left( \frac{\left(\lambda_2-\lambda_3\right)I_h^*}{2A_4} \right) \right\} \\ u_3 = \tilde{u_3} := \left\{ \left( \frac{\Lambda_v\left(\lambda_4-\lambda_7\right)}{2mA_5} \right) \right\} \\ u_4 = \tilde{u_4} := \left\{ \left( \frac{\left(\lambda_5-\lambda_6\right)I_v^*}{2A_6} \right) \right\} \end{aligned}\right\}$$

Therefore, it can be concluded by standard control arguments involving the bounds on the controls that;

$$\left.\begin{aligned} u_1^* = \begin{cases} 0, & if\ \tilde{u_1} \le 0 \\ \tilde{u_1} & if\ 0 < \tilde{u_1} < 1 \\ 1 & if\ \tilde{u_1} \ge 1 \end{cases} \quad , \quad u_2^* = \begin{cases} 0, & if\ \tilde{u_2} \le 0 \\ \tilde{u_2} & if\ 0 < \tilde{u_2} < 1 \\ 1 & if\ \tilde{u_2} \ge 1 \end{cases} \\ u_3^* = \begin{cases} 0, & if\ \tilde{u_3} \le 0 \\ \tilde{u_3} & if\ 0 < \tilde{u_3} < 1 \\ 1 & if\ \tilde{u_3} \ge 1 \end{cases} \quad , \quad u_4^* = \begin{cases} 0, & if\ \tilde{u_4} \le 0 \\ \tilde{u_4} & if\ 0 < \tilde{u_4} < 1 \\ 1 & if\ \tilde{u_4} \ge 1 \end{cases} \end{aligned}\right\} \tag{4.5.10}$$

The system in equation (4.5.7) above leads to the system in equation (4.5.6). Optimal control uniqueness for small $t_f$ was obtained as a result of the Lipschitz structure of the Ordinary Differential Equations and the priori Boundedness of the state solutions and adjoint functions. The existence optimal control uniqueness quadruple is in line with the uniqueness of the optimal system, that comprises of equations (4.2.1) ,(4.5.4) ,(4.5.5)and (4.5.6).

The uniqueness of the optimal of the system is guaranteed, by imposing a condition on the time interval. This is as a result of the opposite time orientations of the optimal system. This is always the case because, the adjoint problem has the final values whereas the the state problem has the initial values. In optimal control problems, imposing a condition or applying a restriction is always common(Joshi et al., 2006).

□

## 4.6 Numerical results

In this section, the numerical simulations of the effects of the optimal control strategies on Anthrax dynamics is shown. We obtained the optimal control by solving the optimal system comprising the state equations (4.2.1) and co-state equations (adjoint equations) (4.5.4), the transversality conditions (4.5.5) and the characterisation (4.5.6). We solve the optimal system applying an iterative scheme. We apply a fourth order Range-Kutta scheme to solve the state equations by guessing the controls over time. We also use the current iterations solutions of the state systems to evaluate the co-state equations (adjoint equations) by a backward fourth order Range-Kutta scheme. We then finally update the controls by using a convex combination of the previous controls and the value from the characterizations (4.5.6). We repeat this process and iterations are stopped if the values of the unknowns at the previous iterations are very close to the ones at the present iterations Joshi et al. (2006).

The following strategies were considered and the most effective strategies were selected and presented for convenience purposes: Combination of prevention on humans and treatment of infectious humans. Combination of treatment of humans, vaccination and treatment of infectious vectors. Combination of treatment of humans and treatment of infectious vectors. Combination of treatment of humans and vaccination of vectors. Combination of prevention control on humans and vaccination of vectors. Combination of prevention of humans, treatment of infective humans and vaccination of susceptible vectors. Combination of vaccination of vectors and treatment of infectious vectors. Combination of prevention control on humans, vaccination and treatment of infectious vectors. Combination of prevention of humans and treatment of infective vectors.

| Parameter | Estimated value | Reference |
|---|---|---|
| $\mu_h$ | 0.2 | Mushayabasa et al. (2015) |
| $\delta_h$ | 0.2 | Steven Kim (Health line, Dec 2015) |
| $\Lambda_v$ | 0.005 | Mushayabasa et al. (2015) |
| $\Lambda_h$ | 0.001 | assumed |
| $\mu_v$ | 0.0004 | Mushayabasa et al. (2015) |
| $\delta_v$ | 0.45 | assumed |
| $\alpha$ | 0.0025 | assumed |
| $\beta$ | 0.0001 | Mushayabasa et al. (2015) |
| $\tau$ | 0.002 | assume |
| $\lambda$ | 0.00002 | assumed |
| $b$ | 0.003 | assumed |

Table 4.3: Variable and parameter values of Anthrax model.

## Strategy 1: Optimal treatment of infectious vectors and treatment of humans.

Using the control treatment on infectious vectors, $(u_4)$ and the control treatment on infective humans, $(u_2)$, we optimise the objective functional $(J)$ by setting the prevention control on humans $(u_1)$and the control on vaccination of susceptible vectors, $(u_3)$ to zero. Due to the control strategies employed, we observed that the number of infective vectors, $(I_v)$ and infective humans, $(I_h)$ have reduced drastically. This implies that the spread of Anthrax can be eradicated or curbed through effective treatment of infectious vectors and the treatment of infective humans. This optimal strategy can be achieved by the treatment all infective animals and humans that are infected with the disease.

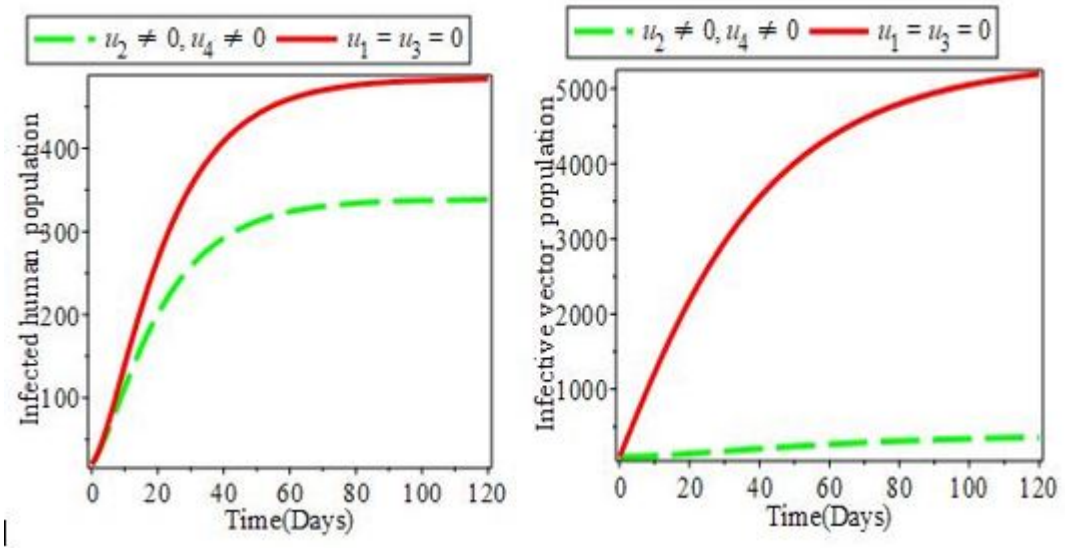


Figure 4.3: Simulation of Anthrax model indicating the effects of optimal strategies: Optimal treatment of infectious vectors and treatment of susceptible humans. Cases without control are indicated by red lines and cases with control are indicated with blue lines.

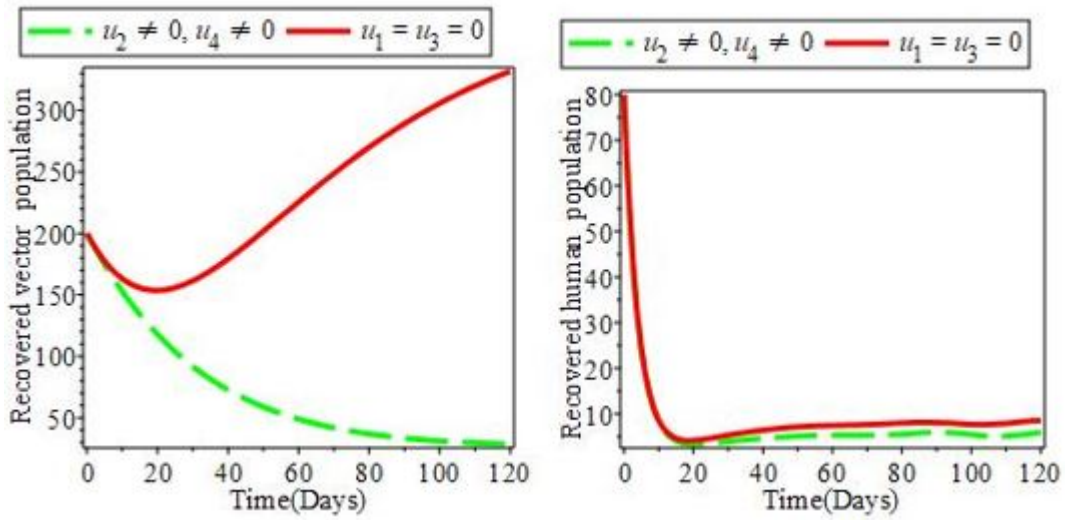


Figure 4.4: Simulation of Anthrax model indicating the effects of optimal strategies: Optimal treatment of infectious vectors and treatment of susceptible humans. Cases without control are indicated by red lines and cases with control are indicated with blue lines.

## Strategy 2: Optimal vaccination of vectors and prevention of humans.

Using the vaccination control of susceptible vectors $(u_3)$and the prevention control on susceptible humans $(u_1)$, we optimise the objective functional $(J)$by setting the treatment control on infective humans $(u_2)$and the treatment control on infective vectors $(u_4)$ to zero. Due to the control strategies employed, we observed that the number of infective vectors $(I_v)$and infective humans $(I_h)$have reduced drastically. This implies that the spread of Anthrax can be eradicated or curbed through effective vaccination of susceptible vectors and the prevention of susceptible humans. This strategy can be achieved by educating and encouraging farmers on the need to vaccinate their animals against anthrax and also educating the general public the dangers associated with the consumption of infected meat and products from animals that infected with Anthrax.

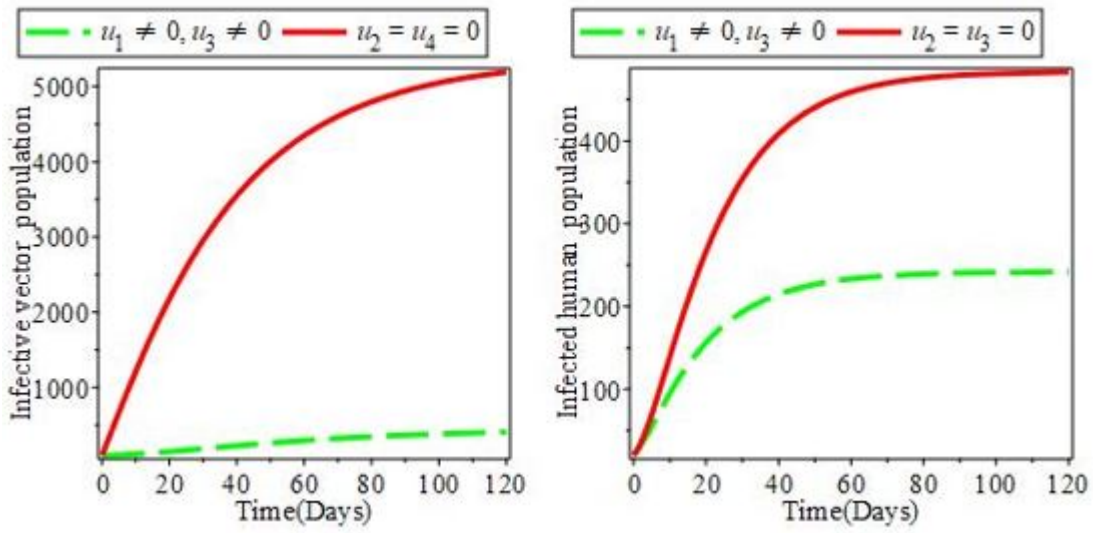


Figure 4.5: Simulation of Anthrax model indicating the effects of optimal strategies: Optimal vaccination of susceptible vectors and prevention of susceptible humans. Cases without control are indicated by red lines and cases with control are indicated with blue lines.

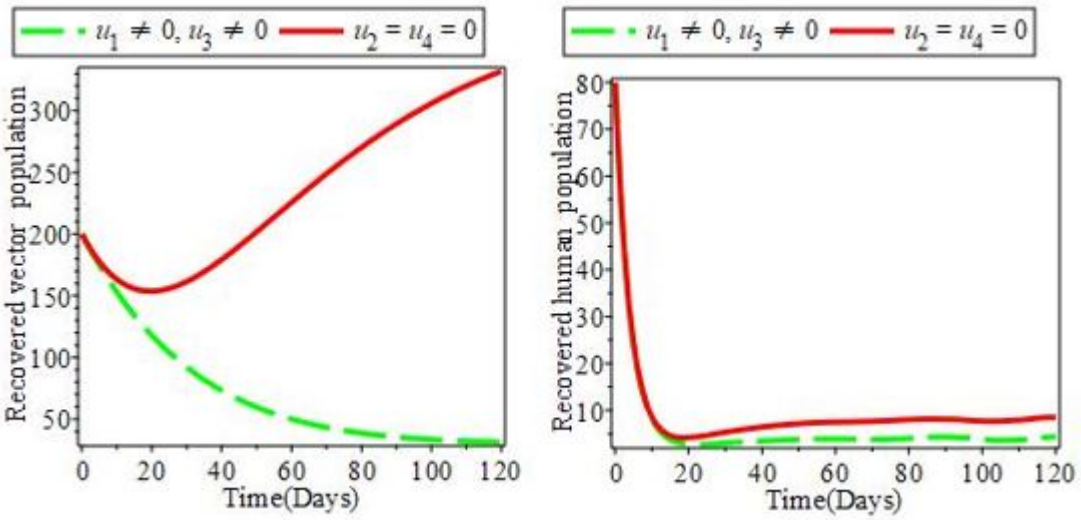


Figure 4.6: Simulation of Anthrax model indicating the effects of optimal strategies: Optimal vaccination of susceptible vectors and prevention of susceptible humans. Cases without control are indicated by red lines and cases with control are indicated with blue lines.

## Strategy 3: Optimal vaccination susceptible vectors and treatment of infectious vectors.

Using the vaccination control on vectors $(u_3)$and the control treatment on infective vectors $(u_4)$, we optimise the objective functional $(J)$by setting the prevention control on humans $(u_1)$and the control on treatment of infective humans $(u_2)$ to zero. Due to the control strategies employed, we observed that the number of infective vectors $(I_v)$and infective humans $(I_h)$have reduced drastically. This implies that the spread of Anthrax can be eradicated or curbed through effective vaccination of susceptible vectors and the treatment of infective vectors. This optimal strategy can best be achieved by the proper vaccination of susceptible animals and the treatment of all infected animals in the community.

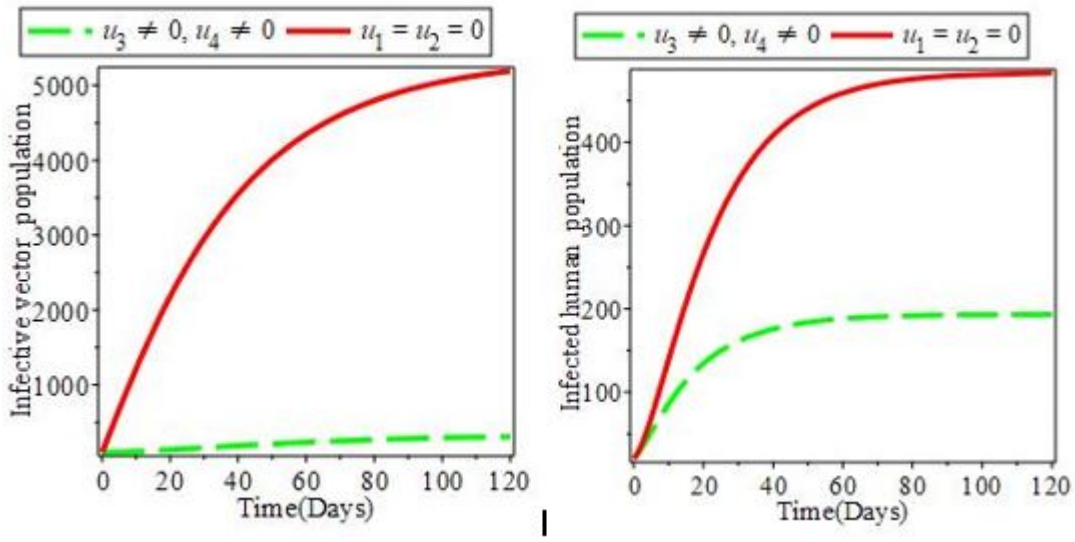


Figure 4.7: Simulation of Anthrax model indicating the effects of optimal strategies: Optimal vaccination of susceptible vectors and treatment of infectious vectors. Cases without control are indicated by red lines and cases with control are indicated with blue lines.

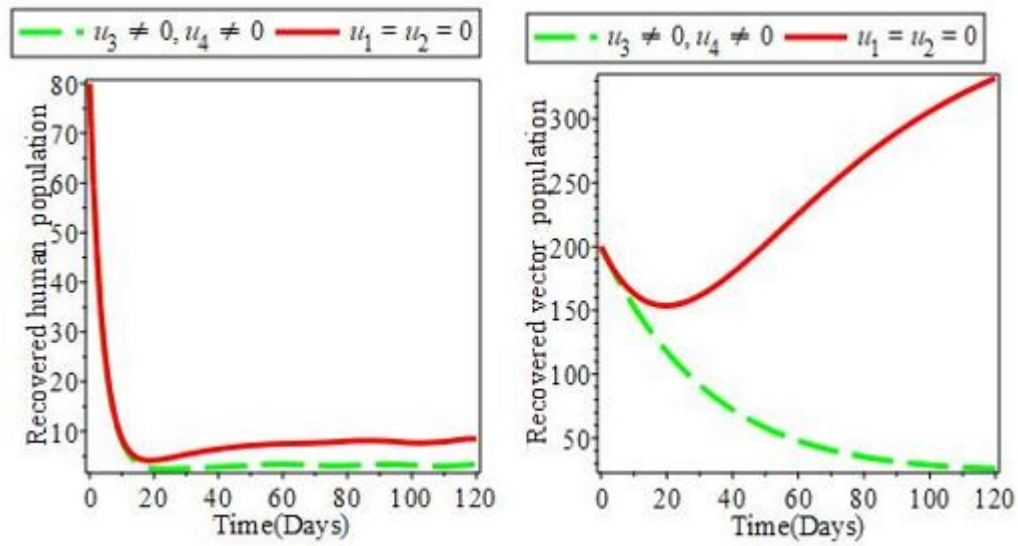


Figure 4.8: Simulation of Anthrax model indicating the effects of optimal strategies: Optimal vaccination of susceptible vectors and treatment of infectious vectors. Cases without control are indicated by red lines and cases with control are indicated with blue lines.

## 4.7 Conclusion

In this chapter, a deterministic model for the dynamic mechanism of anthrax with the addition of vaccination with waning immunity, treatment of infectious humans and treatment of infectious vectors is derived and analysed. The basic reproductive number, stability and existence of the various equilibrium points qualitatively were determined. The qualitative analysis of the model showed an existence of multiple endemic equilibrium points. In epidemiological models, this implies that, proper control of the disease can not be achieved if the basic reproductive number, is less than unity (the critical value). The idea of the reproductive number is no longer a sufficient condition for disease eradication.

The sensitivity analysis of the basic reproduction number indicated that, increasing $\alpha$would decrease the basic reproduction number. Moreover, decreasing $\alpha$would increase the basic reproductive number. Also, by increasing $\beta$ and $\lambda$would cause an increase in the basic reproduction number, and by decreasing $\beta$ and $\lambda$would cause a decrease in the basic reproduction number.

The rate of Anthrax infection can be reduced by ensuring that the rate of interaction between susceptible humans and infectious animals, $(\beta)$ is minimised. Moreover, the spread of Anthrax infection can be curbed by reducing the rate of interaction between susceptible animals and contact with infected environment and grassing fields.

We performed the qualitative analysis of optimal control of our model and derived the necessary conditions for the optimal of anthrax. The most effective strategies according to our model are as follows: The combination of treatment of infectious vectors and treatment of infectious humans, combination of vaccination of susceptible vectors and the prevention of susceptible humans and combination of vaccination of susceptible vectors and the treatment of infectious vectors.

# Chapter 5

# Dynamics of Listeriosis with Optimal Control.

## 5.1 Introduction

In this chapter, the qualitative and quantitative analysis of the dynamics of Listeriosis in human and animal populations are considered. The contribution of each parameter to the basic reproduction number of Listeriosis in human and animal population are considered using sensitivity analysis. The best optimal strategy in combating the Listeriosis infection is determined using optimal control.

## 5.2 Listeriosis model description and formulation

In this section, we divide the model into two parts, the total human and vector populations. These populations at any time $(t)$ are also divided into six sub-populations (compartments) with respect to their disease status in the system. The total human population also represented by $N_h$, is divided into sub-populations of Susceptible humans $(S_h)$, Infected humans $(I_h)$, and Recovered humans $(R_h)$.

The total human population is given by:

$N_h(t) = S_h(t) + I_h(t) + R_h(t)$.

The total vector population, represented by $N_v(t)$, is divided into sub-populations of Susceptible vector $(S_v)$, Infectious vector $(I_v)$, and Recovered vector $(R_v)$.

The total vector population becomes:

$N_v(t) = S_v(t) + I_v(t) + R_v(t)$.

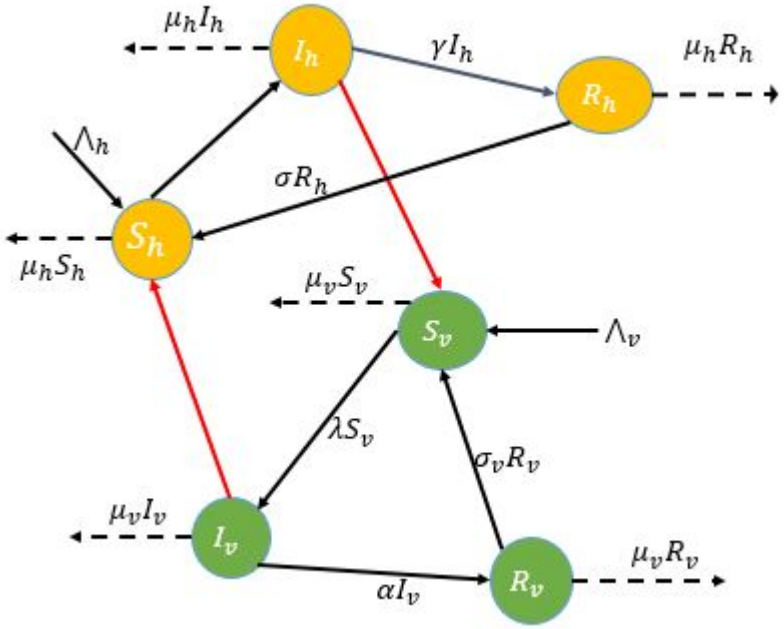


Figure 5.1: Flow diagram for the Listeriosis disease transmission. The gold balls indicates the human compartments and the green colour indicates the animal compartments.

The susceptible human compartment $(S_h(t))$, include individuals who are at risk of developing an infection from the Listeriosis disease. Infectious human compartment $(I_h(t))$ includes individuals that are showing the symptoms of the disease. The recovered human class $(R_h(t))$, are those individuals who have recovered from the disease and got temporal immunity. The susceptible vector$(S_v(t))$; these include animals(livestock) that are at risk of developing an infection from the Listeriosis. The infectious vector $(I_v(t))$ ; this compartment consists all animals(livestock) that are show-

ing the symptoms of Listeriosis. The recovered vector $(R_v(t))$ ; these compartment is made up of animals(livestock) that have recovered from Listeriosis and got temporal immunity.

The Susceptible humans are recruited into the population at a rate $\Lambda_h$. They are infected by the Listeriosis through ingestion of contaminated foods from infected animals, inhalation of spores and contact with infectious animals and humans at a rate $(I_v + I_h)\beta$. Infected individuals recover from the disease at a rate $\gamma$. Individuals who are infected with Listeriosis die at a rate $\delta_h$ and they may loose immunity after recovery and return to the susceptible compartment at a rate $\sigma_h$. Natural death rate of all the human compartments is $\mu_h$.

Susceptible vector population $S_v$ are usually recruited into the population at a rate $\Lambda_v$. Listeriosis can be acquired through contacts with infectious animals and humans at a rate $(I_v + I_h)\lambda$. The natural death rate of the animals is $\mu_v$and the death rate as a result of the disease is $\delta_v$. The animals recover at a rate $\alpha$. Where, $\beta_m^* = I_h + I_v$. The following system of ordinary differential equations are obtained from the model:

$$\left.\begin{array}{rcl} \frac{dS_h}{dt} &=& \Lambda_h + \sigma_h R_h - \beta_m^* \beta S_h - \mu_h S_h \\ \frac{dI_h}{dt} &=& \beta_m^* \beta S_h - \gamma I_h - (\mu_h + \delta_h) I_h \\ \frac{dR_h}{dt} &=& \gamma I_h - (\sigma_h + \mu_h) R_h \\ \frac{dS_v}{dt} &=& \Lambda_v - \beta_m^* \lambda S_v - \mu_v S_v + \sigma_v R_v \\ \frac{dI_v}{dt} &=& \beta_m^* \lambda S_v - \alpha I_v - (\mu_v + \delta_v) I_v \\ \frac{dR_v}{dt} &=& \alpha I_v - (\sigma_v + \mu_v) R_v \end{array}\right\} \quad (5.2.1)$$

## 5.3 Analysis of the Listeriosis model.

### 5.3.1 Positivity and Boundedness of Solutions

In this section, the objective or goal is to show that the solutions are non-negative because we are dealing with human population model. The conditions under which a system of differential equations under study has non-negative solutions is of paramount importance when dealing with human population models. Our Listeriosis model is epidemically meaningful on condition that all the solutions with non-negative initial data remain non-negative at every point in time. We apply the concept of a derivative of a function. The derivative of a function at a point determines the behaviour of that particular function. If the derivative of a function at a point is positive, we can conclude that the function is said to be increasing at that point. If the derivative of the function at a point is negative, we can conclude that the function is decreasing and if the derivative at any point is equal to zero, we say that the function is constant.

**Theorem 11.** *Let* $\Theta = \{(S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), R_v(t)) \in \mathbb{R}^6_+ :$
$(S_h(0), I_h(0), R_h(0), S_v(0), I_v(0), R_v(0)) > 0\}$*, then the solution of*
$\{(S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), R_v(t))\}$*are non-negative at all time* $t \geq 0$.

This implies that, if $S_h(0), I_h(0), R_h(0), S_v(0), I_v(0), R_v(0)$are non-negative, then $S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), R_v(t)$are also non-negative for all time $t > 0$.

The total human population at any time $(t)$is given by:

$$N_h(t) = S_h(t) + I_h(t) + R_h(t). \tag{5.3.1}$$

$$\left.\begin{aligned} \frac{dN_h}{dt} &= \frac{dS_h}{dt} + \frac{dI_h}{dt} + \frac{dR_h}{dt} \\ \frac{dN_h}{dt} &= \Lambda_h - \mu_h S_h - \beta^*_m \beta S_h - \mu_h S_h + \beta^*_m \beta S_h \\ &\quad -\gamma I_h - (\mu_h + \delta_h) I_h + \gamma I_h - (\sigma_h + \mu_h) R_h \end{aligned}\right\}$$

$$\frac{dN_h}{dt} = \Lambda_h - \mu_h S_h - \beta_m^* \beta S_h - \mu_h S_h + \beta_m^* \beta S_h - \gamma I_h - (\mu_h + \delta_h) I_h + \gamma I_h - (\sigma_h + \mu_h) R_h$$
$$\frac{dN_h}{dt} = \quad \Lambda_h - \mu_h S_h \quad - (\mu_h + \delta_h) I_h - (\sigma_h + \mu_h) R_h.$$

In the absence of mortality due to Listeriosis infections, the above becomes;

$$\frac{dN_h}{dt} \leq \quad \Lambda_h - \quad \mu_h N_h.$$
$$\int \left( \frac{dN_h}{\Lambda_h - \mu_h N_h} \right) = \int dt$$
$$-\frac{1}{\mu_h} \quad \ln(\Lambda_h - \mu_h N_h) \quad \leq t + A.$$

$\Lambda_h - \mu_h N_h \quad \geq \quad A e^{-\mu_h t}$ , where $A$ is constant. $N_h(0) \quad = \quad N_{h(0)}$ ,

$$\Lambda_h - \mu_h N_{h(0)} \quad = \quad A$$

$$\Lambda_h - \mu_h N_h \quad \geq \quad \left(\Lambda_h - \mu_h N_{h(0)}\right) e^{-\mu_h t} \quad .$$
$$N_h \quad \leq \quad \frac{\Lambda_h}{\mu_h} - \left( \frac{\Lambda_h - \mu_h N_{h(0)}}{\mu_h} \right) e^{-\mu_h t}.$$

As $t \to \infty$, the population size, $N_h \to \dfrac{\Lambda_h}{\mu_h}$.

$$0 \leq \quad N_h \leq \quad \frac{\Lambda_h}{\mu_h} \text{ and } N_h(t) \leq \frac{\Lambda_h}{\mu_h}.$$

Also, if $N_h(0) \leq \dfrac{\Lambda_h}{\mu_h}$, then $N_h(t) \leq \dfrac{\Lambda_h}{\mu_h}$.

$$\Theta_h \quad = \left\{ (S_h, I_h, R_h) \in \mathbb{R}_3^3 : S_h + I_h + R_h \leq \frac{\Lambda_h}{\mu_h} \right\} \tag{5.3.2}$$

The total vector(livestock) population at any time $(t)$is given by:

$$N_v(t) \quad = S_v(t) + I_v(t) + R_v(t) \quad . \tag{5.3.3}$$

$$\frac{dN_v}{dt} \quad = \frac{dS_v}{dt} + \frac{dI_v}{dt} + \frac{dR_v}{dt} \quad .$$
$$\frac{dN_v}{dt} = \Lambda_v - \mu_v S_v - (\mu_v + \delta_v) I_v \quad .$$

In the absence of mortality due to Listeriosis infections, the above becomes;

$$\frac{dN_v}{dt} \leq \Lambda_v - \mu_v N_v \quad .$$
$$\int \left( \frac{dN_v}{\Lambda_v - \mu_v N_v} \right) = \int dt$$

$$-\frac{1}{\mu_v} \quad \ln(\Lambda_v - \mu_v N_v) \quad \leq t + c.$$

$\Lambda_v - \mu_v N_v \quad \geq \quad A e^{-\mu_v t}$ , where $A$ is constant. $N_v(0) \quad = \quad N_{v(0)}$ ,

$\Lambda_v - \mu_v N_{v(0)} = A$

$\Lambda_v - \mu_v N_v \quad \geq \quad \left(\Lambda_v - \mu_v N_{v(0)}\right) e^{-\mu_v t}$ .

$$N_v \quad \leq \quad \frac{\Lambda_v}{\mu_v} - \left(\frac{\Lambda_v - \mu_v N_{v(0)}}{\mu_v}\right) e^{-\mu_v t}.$$

As $t \to \infty$, the population size, $N_v \to \frac{\Lambda_v}{\mu_v}$.

$0 \leq \quad N_v \leq \quad \frac{\Lambda_v}{\mu_v}$ and $N_v(t) \leq \frac{\Lambda_v}{\mu_v}$.

Also, if $N_v(0) \leq \frac{\Lambda_v}{\mu_v}$, then $N_v(t) \leq \frac{\Lambda_v}{\mu_v}$.

Therefore,

$$\Theta_v = \left\{ \quad (S_v, I_v, R_v) \in \mathbb{R}^3_+ : S_v + I_v + R_v \leq \frac{\Lambda_v}{\mu_v} \quad \right\}. \tag{5.3.4}$$

The feasible region for the system of ordinary differential equations in $(5.3.1)$ is given by:

$$\Theta = \Theta_h \times \Theta_v \quad \subset \mathbb{R}^3_+ \times \mathbb{R}^3_+ \tag{5.3.5}$$

Where, $\Theta_h \quad = \left\{ (S_h, I_h, R_h) \in \mathbb{R}^3_3 : S_h + I_h + R_h \leq \frac{\Lambda_h}{\mu_h} \right\}$

and

$\Theta_v = \left\{ \quad (S_v, I_v, R_v) \in \mathbb{R}^3_+ : S_v + I_v + R_v \leq \frac{\Lambda_v}{\mu_v} \quad \right\}$

Where $\Theta$ is positively invariant.

### 5.3.2 Disease-free equilibrium for the Listeriosis model.

By setting the system of differential equations in $(5.3.1)$ to zero:

$$\frac{dS_h}{dt} = \Lambda_h + \sigma_h R_h - \beta^*_m \beta S_h - \mu_h S_h = 0 \tag{5.3.6}$$

$$S_h^* = \frac{\Lambda_h}{\mu_h} \quad .$$

At disease free equilibrium (DFE), there are no infections and recovery.

$$\left.\begin{array}{l} I_h^* = 0 \\ R_h^* = 0 \end{array}\right\} \text{and} \left.\begin{array}{l} I_v^* = 0 \\ R_v^* = 0 \end{array}\right\}$$

$$\frac{dS_v}{dt} = \Lambda_v - \beta_m^* \lambda S_v - \mu_v S_v + \sigma_v R_v = 0 \tag{5.3.7}$$

$$S_v^* = \frac{\Lambda_v}{\mu_v}$$

$$\xi_0 = \left(\frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_v}{\mu_v}, 0, 0\right) \tag{5.3.8}$$

### 5.3.3 The Basic Reproductive Number

In this section, we use the Next Generation Matrix approach to determine the linear stability of the disease-free equilibrium $(\xi_0)$. The basic reproductive number or rate is the number of secondary cases produced on average by one infected animal or person when all are susceptible. It combines the biology of infections with the social and behaviour of the factors influencing contact rate. The basic reproduction rate gives the number of secondary cases one infectious individual will produce in a population consisting only of susceptible individualsVan den Driessche and Watmough (2002). The basic reproductive number is the threshold parameter that governs the spread of a disease. The next-generation matrix is defined as; $K = FV^{-1}$and $R_0 = \rho\left(FV^{-1}\right)$ . Where $\rho\left(FV^{-1}\right)$ denotes the spectral radius of $FV^{-1}$. The basic reproductive number $R_0$, is defined as the spectral radius of the next-generation matrix.

**Definition 19.** The spectral radius of a matrix $A$ is defined as the maximum of the absolute values of the eigenvalues of the matrix

$A : \rho(A) = sup\{|\lambda| : \lambda \varepsilon \rho(A)\}$, where $\rho(A)$ represents the set of eigenvalues of the matrix $A$.

Considering only the infective classes in the system of differential equations in (5.3.1) :

$$\left.\begin{array}{rcl} \frac{dI_h}{dt} & = & (I_h+I_v)\,\beta S_h-\gamma I_h-(\mu_h+\delta_h)\,I_h \\ \frac{dI_v}{dt} & = & (I_h+I_v)\,\lambda S_v-\alpha I_v-(\mu_v+\delta_v)\,I_v \end{array}\right\} \tag{5.3.9}$$

Let $f$ be the number of new infection coming into the system and $v$ be the number of infective that are leaving the system either by death or birth.

$$f=\begin{bmatrix} (I_h+I_v)\,\beta S_h \\ (I_h+I_v)\,\lambda S_v \end{bmatrix},\ v=\begin{bmatrix} \gamma I_h+(\mu_h+\delta_h)\,I_h \\ \alpha I_v+(\mu_v+\delta_v)\,I_v \end{bmatrix}.$$

The Jacobian matrix of $f$ and $v$ are obtained by $F$ and $V$ as follows:

$$F=\begin{bmatrix} \frac{\partial f_1}{\partial I_h} & \frac{\partial f_1}{\partial I_v} \\ \frac{\partial f_2}{\partial I_h} & \frac{\partial f_2}{\partial I_v} \end{bmatrix}=\begin{bmatrix} \beta S_h & \beta S_h \\ \lambda S_v & \lambda S_v \end{bmatrix} \tag{5.3.10}$$

$$V=\begin{bmatrix} \frac{\partial v_1}{\partial I_h} & \frac{\partial v_1}{\partial I_v} \\ \frac{\partial v_2}{\partial I_h} & \frac{\partial v_2}{\partial I_v} \end{bmatrix}=\begin{bmatrix} \gamma+(\mu_h+\delta_h) & 0 \\ 0 & \alpha+(\mu_v+\delta_v) \end{bmatrix} \tag{5.3.11}$$

The Jacobian matrix of $f$ and $v$ at disease free equilibrium is obtained by $F$ and $V$ as follows:

$$F=\begin{bmatrix} \frac{\partial f_1}{\partial I_h} & \frac{\partial f_1}{\partial I_v} \\ \frac{\partial f_2}{\partial I_h} & \frac{\partial f_2}{\partial I_v} \end{bmatrix}=\begin{bmatrix} \beta S_h^* & \beta S_h^* \\ \lambda S_v^* & \lambda S_v^* \end{bmatrix}, \tag{5.3.12}$$

$$V=\begin{bmatrix} \frac{\partial v_1}{\partial I_h} & \frac{\partial v_1}{\partial I_v} \\ \frac{\partial v_2}{\partial I_h} & \frac{\partial v_2}{\partial I_v} \end{bmatrix}=\begin{bmatrix} \gamma+(\mu_h+\delta_h) & 0 \\ 0 & \alpha+(\mu_v+\delta_v) \end{bmatrix}. \tag{5.3.13}$$

$$V^{-1}=\begin{bmatrix} \frac{1}{\gamma+(\mu_h+\delta_h)} & 0 \\ 0 & \frac{1}{\alpha+(\mu_v+\delta_v)} \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} \dfrac{\beta S_h^*}{(u_2+\gamma)+(\mu_h+\delta_h)} & \dfrac{\beta S_h^*}{(u_4+\alpha)+(\mu_v+\delta_v)} \\ \dfrac{\lambda S_v^*}{\gamma+(\mu_h+\delta_h)} & \dfrac{\lambda S_v^*}{\alpha+(\mu_v+\delta_v)} \end{bmatrix} \tag{5.3.14}$$

$$FV^{-1} = \begin{bmatrix} \dfrac{\beta S_h^*}{\gamma+(\mu_h+\delta_h)} & \dfrac{\beta S_h^*}{\alpha+(\mu_v+\delta_v)} \\ \dfrac{\lambda S_v^*}{\gamma+(\mu_h+\delta_h)} & \dfrac{\lambda S_v^*}{\alpha+(\mu_v+\delta_v)} \end{bmatrix} \tag{5.3.15}$$

Now, computing the eigenvalues of $FV^{-1}$ and selecting the dominant eigenvalue. Let $A$ represent the eigenvalue of the matrix.

$$\begin{vmatrix} \dfrac{\beta S_h^*}{\gamma+(\mu_h+\delta_h)} - A & \dfrac{\beta S_h^*}{\alpha+(\mu_v+\delta_v)} \\ \dfrac{\lambda S_v^*}{\gamma+(\mu_h+\delta_h)} & \dfrac{\lambda S_v^*}{\alpha+(\mu_v+\delta_v)} - A \end{vmatrix} = 0$$

$$A^2 - \left[\left(\frac{\lambda S_v^*}{\alpha+(\mu_v+\delta_v)}\right) + \left(\frac{\beta S_h^*}{\gamma+(\mu_h+\delta_h)}\right)\right] A = 0 \tag{5.3.16}$$

$A_1 = 0$ and $A_2 = \left[\left(\dfrac{\lambda S_v^*}{\alpha+(\mu_v+\delta_v)}\right) + \left(\dfrac{\beta S_h^*}{\gamma+(\mu_h+\delta_h)}\right)\right]$.

Dominant eigenvalue is $A_2$. This implies that;

$$R_{hv} = \left[\left(\frac{\beta S_h^*}{\gamma+(\mu_h+\delta_h)}\right) + \left(\frac{\lambda S_v^*}{[\alpha+(\mu_v+\delta_v)]}\right)\right] .. \tag{5.3.17}$$

But at disease free equilibrium,

$S_h^* = \dfrac{\Lambda_h}{\mu_h}, S_v^* = \dfrac{\Lambda_v}{\mu_v},$

$$R_{hv} = \left(\frac{\beta\Lambda_h}{\mu_h(\gamma)+(\mu_h+\delta_h)}\right) + \left(\frac{\lambda\Lambda_v}{\mu_v[(\alpha)+(\mu_v+\delta_v)]}\right) . \tag{5.3.18}$$

If the mode of infection is from infected animals, then the parameters in the reproduction number, $(R_{vq})$ are contributing to the rise in the value of $R_{hv}$. Moreover, if the mode of infection is as a result of infected humans, then the parameters in the reproduction number, $(R_{hq})$ are the contributing factors in the value of $R_{hv}$.

The ingestion of contaminated foods affects the basic reproduction number, $(R_{hv})$ by

the rate of interaction between susceptible humans and infected animals as well as the interaction between susceptible animals and infected humans.

Where;

$R_{hq} = \left( \frac{\beta \Lambda_h}{\mu_h(\gamma) + (\mu_h + \delta_h)} \right)$ is the basic reproduction number of Listeriosis in human population.

$R_{vq} = \frac{\lambda \Lambda_v}{\mu_v [\alpha + (\mu_v + \delta_v)]}$ is the basic reproduction number of Listeriosis in animal population.

**Proposition 2.** *The disease-free equilibrium (DFE) of model* (5.3.1) *is locally asymptotically stable if*

$R_{hv} < 1$, *and unstable if* $R_{hv} > 1$.

### 5.3.4 Local stability of the disease free equilibrium

**Theorem 12.** *The disease free equilibrium is locally asymptotically stable if* $R_0 < 1$ *and unstable if* $R_0 > 1$.

The disease free equilibrium was obtained as; $\left( \frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_v}{\mu_v}, 0, 0 \right)$.

The jacobian matrix of the system of differential equations is given by:

$$\begin{pmatrix} -(\beta_m^* \beta + \mu_h) & -\beta S_h^* I_v^* & \sigma_h & 0 & \beta S_h I_h & 0 \\ \beta_m^* \beta & r_1 & 0 & 0 & \beta S_h I_h & 0 \\ 0 & \gamma & -(\sigma_h + \mu_h) & 0 & 0 & 0 \\ 0 & -\lambda S_v^* I_h^* & 0 & -(\beta_m^* \lambda + \mu_v) & -\lambda S_v^* I_h^* & \sigma_v \\ 0 & \lambda S_v^* I_h^* & 0 & \beta_m^* \lambda & r_2 & 0 \\ 0 & 0 & 0 & 0 & \alpha & -(\sigma_v + \mu_v) \end{pmatrix}$$

Where;

$r_1 = \left( \beta S_h^* I_v^* - \mu_h - \delta_h - \gamma \right)$

$r_2 = \lambda S_v^* I_h^* - (\alpha + \mu_v + \delta_v)$

The jacobian matrix at disease free equilibrium; $DFE = \left( \frac{\Lambda_h}{\mu_h}, 0, 0, \frac{\Lambda_v}{\mu_v}, 0, 0 \right)$

$$\begin{pmatrix} -\mu_h & 0 & \sigma_h & 0 & 0 & 0 \\ 0 & -(\mu_h+\delta_h+\gamma) & 0 & 0 & 0 & 0 \\ 0 & \gamma & -(\sigma_h+\mu_h) & 0 & 0 & 0 \\ 0 & 0 & 0 & \mu_v & 0 & \sigma_v \\ 0 & 0 & 0 & 0 & -(\alpha+\mu_v+\delta_v) & 0 \\ 0 & 0 & 0 & 0 & \alpha & -(\sigma_v+\mu_v) \end{pmatrix}$$

Now determining the eigenvalues of the jacobian matrix at DFE;

$$\begin{pmatrix} -\mu_h & 0 & \sigma_h & 0 & 0 & 0 \\ 0 & -(\mu_h+\delta_h+\gamma) & 0 & 0 & 0 & 0 \\ 0 & \gamma & -(\sigma_h+\mu_h) & 0 & 0 & 0 \\ 0 & 0 & 0 & \mu_v & 0 & \sigma_v \\ 0 & 0 & 0 & 0 & -(\alpha+\mu_v+\delta_v) & 0 \\ 0 & 0 & 0 & 0 & \alpha & -(\sigma_v+\mu_v) \end{pmatrix}$$

By computing the eigenvalues, the following were obtained;

$$\left.\begin{array}{c} A_1 = -\mu_v \\ A_2 = -\mu_h \\ A_3 = -(\mu_v+\delta_v) \end{array}\right\}, \quad \left.\begin{array}{c} A_4 = -(\mu_h+\delta_h) \\ A_5 = -(\alpha+\mu_v+\delta_v) \\ A_6 = -(\gamma+\mu_h+\delta_h) \end{array}\right\}$$

Where $A$ is referred to as the eigenvalue.

Since all the eigenvalues are negative, it implies that the disease free equilibrium is locally asymptotically stable.

### 5.3.5 Global stability of the disease-free equilibrium.

**Theorem 13.** *If $R_{hv} \leq 1$, the disease-free equilibrium is globally asymptotically stable in the interior of $\Phi$.*

Proof: Considering the Lyapunov function below,

$$P(t) = (\alpha+\mu_v+\delta_v) I_h + (\gamma+\mu_h+\delta_h) I_v \tag{5.3.19}$$

By computing the time derivative of P along the solutions of the system of ordinary differential equations in$(0.3.1)$, the following is obtained,

$$\left.\begin{array}{rcl}
\frac{dP(t)}{dt} = & (\alpha+\mu_v+\delta_v)\frac{dI_h}{dt}+(\gamma+\mu_h+\delta_h)\frac{dI_v}{dt} \\
= & (\alpha+\mu_v+\delta_v)(\beta S_h(I_h+I_v)-(\gamma+\mu_h+\delta_h)I_v) \\
& +(\gamma+\mu_h+\delta_h)[\lambda S_v(I_h+I_v) \\
& -(\alpha+\mu_v+\delta_v)I_v] \\
\leq & (\alpha+\mu_v+\delta_v)\frac{\beta\Lambda_h I_h}{\mu_h}+(\alpha+\mu_v+\delta_v)\frac{\beta\Lambda_h I_v}{\mu_h} \\
& -(\alpha+\mu_v+\delta_v)(\gamma+\mu_h+\delta_h)I_h \\
& +I_h(\gamma+\mu_h+\delta_h)\left(\frac{\lambda\Lambda_v}{\mu_v(\tau+\mu_v)}\right) \\
& +I_v(\gamma+\mu_h+\delta)\left(\frac{\lambda\Lambda_v}{\mu_v(\tau+\mu_v)}\right) \\
& +I_h(\gamma+\mu_h+\delta_h)+I_v(\gamma+\mu_h+\delta) \\
& -I_v(\gamma+\mu_h+\delta)(\alpha+\mu_v+\delta_v) \\
\leq & -I_h(\gamma+\mu_h+\delta_h)(\alpha+\mu_v+\delta_v)(1-R_{hv}) \\
& -I_v(\gamma+\mu_h+\delta_h)(\alpha+\mu_v+\delta_v)(1-R_{hv}) \\
= & -(I_h+I_v)(\gamma+\mu_h+\delta_h)(\alpha+\mu_v+\delta_v)(1-R_{hv})
\end{array}\right\} \quad (5.3.20)$$

The time derivative of P along the solutions of the system of differential equations in $(5.3.1)$ gives the following:

$\left(\frac{dP(t)}{dt}\right) \leq 0$, if and only if $R_{hv} < 0$

$\left(\frac{dP(t)}{dt}\right) = 1$, if and only if $I_h + I_v = 0$ or $R_{hv} = 1$.

Therefore, the highest compact invariant set in $\left\{S_h, I_h, I_v, \in \Phi, \frac{dP(t)}{dt} = 0\right\}$ ,if $R_{hv} \leq 1$, is the singleton $\xi_0$.

This implies that is $\xi_0$ globally asymptotically stable in $\Phi$. By LaSalle's invariant principle(LaSalle, 1976; Joshi et al., 2006; Okosun et al., 2016).

### 5.3.6 Endemic Equilibrium

Considering the system of differential equations in (5.3.1), at equilibrium,

$\beta_m^* = I_h + I_v = 0$. This corresponds to the disease free equilibrium or the relation:

$$\Phi_0 \beta_m^{*3} + \Phi_1 \beta_m^{*2} + \Phi_2 \beta_m^* \quad + \Phi_3 = 0 \quad . \tag{5.3.21}$$

$\Phi_0 = 1$, $\Phi_1 = \dfrac{Q_*}{C}(1 - R_w)$, $\Phi_2 = \dfrac{T_1}{C}\left(1 - R_f\right)$, $\Phi_3 = \chi\,(1 - R_{hv})$.

Where;

$$\left.\begin{array}{rcl}
R_{hv}^2 & = & R_{hq} + R_{vq} = \dfrac{\beta \Lambda_h}{\mu_h\,(\gamma + \delta_h + \mu_h)} + \dfrac{\lambda \Lambda_v}{(\alpha + \delta_v + \mu_v)}, \\
C & = & \beta \lambda^2 \left[\mu_v\,(\alpha + \delta_v + \mu_v) + (\mu_v + \delta_v)\,\sigma_v\right]\left[\mu_h\,(\gamma + \delta_h + \mu_h) + (\mu_h + \delta_h)\,\sigma_h\right], \\
G_1 & = & \lambda^2\,(\gamma + \delta_h + \mu_h)\,(\mu_h + \sigma_h)\left[\mu_v\,(\alpha + \delta_v + \mu_v) + (\mu_v + \delta_v)\,\sigma_v\right], \\
G_2 & = & \beta \lambda \left[\mu_h\,(\gamma + \delta_h + \mu_h) + (\mu_h + \delta_h)\,\sigma_h\right] F_3\,(\mu_v + \delta_v)\,(\tau + \mu_v)\,(\alpha + \delta_v + \mu_v), \\
Q_* & = & G_1 + G_2, \\
R_w^2 & = & \dfrac{G_1 R_{hq} + G_2 R_{vq}}{Q_*}, \\
F_1 & = \lambda \mu_h & (\mu_h + \sigma_h)\,(\gamma + \delta_h + \mu_h)\left[\mu_v\,(\alpha + \delta_v + \mu_v) + (\mu_v + \delta_v)\,\sigma_v\right], \\
F_2 & = & \beta \mu_h\,(\alpha + \delta_v + \mu_v)\,(\mu_v + \sigma_v)\left[\mu_h\,(\gamma + \delta_h + \mu_h) + (\mu_h + \delta_h)\,\sigma_h\right], \\
F_3 & = & \left[\left[\mu_v\,(\alpha + \delta_v + \mu_v) + (\mu_v + \delta_v)\,\sigma_v\right] + \alpha \mu_v\right], \\
T_1 & = & \lambda \left[\mu_h\,(\mu_h + \sigma_h)\,(\gamma + \delta_h + \mu_h)\left[\mu_v\,(\alpha + \delta_v + \mu_v) + (\mu_v + \delta_v)\,\sigma_v\right]\right] \\
 & - & \left[\Lambda_v\,(\mu_v + \sigma_v) + \beta \Lambda_h \alpha \mu_v \sigma_v\,(\mu_h + \sigma_h) + (\alpha + \delta_v + \mu_v)\,(\mu_v + \sigma_v)\right], \\
\chi & = & \dfrac{\mu_h \mu_v\,(\mu_v + \sigma_v)\,(\mu_h + \sigma_h)\,(\alpha + \delta_v + \mu_v)\,(\gamma + \delta_h + \mu_h)}{\beta \lambda^2 \left[\mu_v\,(\alpha + \delta_v + \mu_v) + (\mu_v + \delta_v)\,\sigma_v\right]\left[\mu_h\,(\gamma + \delta_h + \mu_h) + (\mu_h + \delta_h)\,\sigma_h\right]}, \\
R_f^2 & = & \dfrac{F_1^2 R_{hq} + F_1^2 R_{vq}}{T_1},
\end{array}\right\} \tag{5.3.22}$$

| Cases | $\Phi_0$ | $\Phi_1$ | $\Phi_2$ | $\Phi_3$ | $R_{hv}$ | No. of sign change | No. of positive real roots |
|---|---|---|---|---|---|---|---|
| 1 | + | + | + | + | $R_{hv} < 1$ | 0 | 0 |
| 2 | + | + | + | - | $R_{hv} > 1$ | 1 | 1 |
| 3 | + | + | - | + | $R_{hv} < 1$ | 2 | 0,2 |
| 4 | + | + | - | - | $R_{hv} > 1$ | 1 | 1 |
| 5 | + | - | - | + | $R_{hv} < 1$ | 2 | 0,2 |
| 6 | + | - | - | - | $R_{hv} > 1$ | 1 | 1 |
| 7 | + | - | + | + | $R_{hv} < 1$ | 2 | 0,2 |
| 8 | + | - | + | - | $R_{hv} > 1$ | 3 | 1,3 |

Table 5.1: Possible positive real roots of $P(\beta_m^*)$ for $R_{hv} > 1$ and $R_{hv} < 1$.

*Remark.* The system of differential equations in equation $(5.3.1)$ is said to have an endemic equilibrium $E^*$, if $R_{hv} > 1$. This is satisfied by cases $(2,4,6)$ in 5.1. The system of differential equations can have more than one endemic equilibrium points if $R_{hv} > 1$. This is satisfied by case $(8)$ in table 5.1. The system of differential equations in equation $(5.3.1)$, have more than one equilibrium points if $R_{hv} > 1$, as satisfied by case $(3,5,7)$.

### 5.3.7 Global stability of endemic equilibrium

The Global behaviour of the system of differential equations in equation $(5.3.1)$ is analysed.

**Theorem 14.** *The system of differential equations in equation* $(5.3.1)$*, is said to have a unique endemic equilibrium if* $R_{hv} > 1$*, and it is globally asymptotically stable.*

The endemic equilibrium can only exists if and only if $R_{hv} > 1$. So by letting $R_{hv} > 1$, it implies that the endemic equilibrium exists.

Considering the Lyapunov function defined by:

$$\left.\begin{aligned} L\left(S_h^*, I_h^*, R_h^* S_v^*, I_v^* R_v^*\right) &= \left(S_h - S_h^* - S_h^* \ln \frac{S_h^*}{S_h}\right) \\ &+ \left(I_h - I_h^* - I_h^* \ln \frac{I_h^*}{I_h}\right) + \left(R_h - R_h^* - R_h^* \ln \frac{R_h^*}{R_h}\right) + \\ \left(S_v - S_v^* - S_v^* \ln \frac{S_v^*}{S_v}\right) &+ \left(I_v - I_v^* - I_v^* \ln \frac{I_v^*}{I_v}\right) + \left(R_v - R_v^* - R_v^* \ln \frac{R_v^*}{R_v}\right) \end{aligned}\right\} \quad (5.3.23)$$

Computing the derivative of L along the solution of the system directly;

$$\left.\begin{aligned} \frac{dL}{dt} &= \left(\frac{S_h - S_h^*}{S_h}\right)\frac{dS_h}{dt} + \left(\frac{I_h - I_h^*}{I_h}\right)\frac{dI_h}{dt} + \left(\frac{R_h - R_h^*}{R_h}\right)\frac{dR_h}{dt} \\ &+ \left(\frac{S_v - S_v^*}{S_v}\right)\frac{dS_v}{dt} + \left(\frac{I_v - I_v^*}{I_v}\right)\frac{dI_v}{dt} + \left(\frac{R_v - R_v^*}{R_v}\right)\frac{dR_v}{dt} \end{aligned}\right\} \quad (5.3.24)$$

This implies that;

$$\left\{\begin{aligned} \frac{dL}{dt} = &\left(\frac{S_h - S_h^*}{S_h}\right)\left[\Lambda_h + \sigma_h R_h - \beta_m^* \beta S_h - \mu_h S_h\right] \\ &+ \left(\frac{I_h - I_h^*}{I_h}\right)\left[\beta_m^* \beta S_h - \gamma I_h - (\mu_h + \delta_h) I_h\right] \\ &+ \left(\frac{R_h - R_h^*}{R_h}\right)\left[\gamma I_h - (\sigma_h + \mu_h) R_h\right] + \\ &\left(\frac{S_v - S_v^*}{S_v}\right)\left[\Lambda_v - \beta_m^* \lambda S_v - \mu_v S_v + \sigma_v R_v\right] \\ &+ \left(\frac{I_v - I_v^*}{I_v}\right)\left[\beta_m^* \lambda S_v - \alpha I_v - (\mu_v + \delta_v) I_v\right] \\ &+ \left(\frac{R_v - R_v^*}{R_v}\right)\left[\alpha I_v - (\sigma_v + \mu_v) R_v\right] \end{aligned}\right\}$$

Which can also be written as;

$$\left\{\begin{aligned} &\frac{dL}{dt} = \Lambda_h + \sigma_h R_h - \beta_m^* \beta S_h - \mu_h S_h - \frac{\Lambda_h S_h^*}{S_h} + \beta_m^* \beta S_h^* - \frac{\sigma_h R_h S_h^*}{S_h} + \mu_h S_h^* \\ &+\beta_m^* \beta S_h - \gamma I_h - (\mu_h + \delta_h) I_h - \frac{\beta_m^* S_h I_h^*}{I_h} + \gamma I_h^* + \mu I_h^* + \delta I_h^* + \gamma I_h - \\ &(\sigma_h + \mu_h) R_h - \frac{\gamma_h I_h R_h^*}{R_h} + \sigma_h R_h^* + \mu_h R_h^* + \Lambda_v - \beta_m^* \lambda S_v - \mu_v S_v + \sigma_v R_v - \\ &\frac{\Lambda_v S_v^*}{S_v} + \beta_m^* \lambda S_v^* - \frac{\sigma_v R_v S_v^*}{S_v} + \mu_v S_v^* + \beta_m^* \lambda S_v - \alpha I_v - \mu_v I_v - \delta_v I_v - \frac{\beta_m^* S_v I_v^*}{I_v} \\ &+\alpha I_v^* + \mu_v I_v^* + \delta_v I_v^* + \alpha I_v - \sigma_v R_v - \mu_v R_v - \frac{\alpha I_v R_v^*}{R_v} + \sigma_v R_v^* + \mu_v R_v^* \end{aligned}\right\}$$

Given;

$$\frac{dL}{dt} = M - N \quad (5.3.25)$$

where $M$ and $N$ are positive and negative respectively.

Therefore;

$$\left.\begin{aligned} M = \Lambda_h + \sigma_h R_h + \mu_h S_h^* + \beta_m^* \beta S_h + \gamma I_h^* + \mu I_h^* + \delta I_h^* + \gamma I_h + \sigma_h R_h^* + \mu_h R_h^* + \Lambda_v \\ + \sigma_v R_v + \beta_m^* \lambda S_v^* + \mu_v S_v^* + \beta_m^* \lambda S_v + \alpha I_v^* + \mu_v I_v^* + \delta_v I_v^* + \alpha I_v + \sigma_v R_v^* + \mu_v R_v^* \end{aligned}\right\}$$

and

$$\left.\begin{aligned} N = \mu_h S_h + \frac{\Lambda_h S_h^*}{S_h} + \frac{\sigma_h R_h S_h^*}{S_h} + \gamma I_h + (\mu_h + \delta_h) I_h + \frac{\beta_m^* S_h I_h^*}{I_h} + (\sigma_h + \mu_h) R_h + \frac{\gamma_h I_h R_h^*}{R_h} + \\ \beta_m^* \lambda S_v + \mu_v S_v + \frac{\Lambda_v S_v^*}{S_v} + \frac{\sigma_v R_v S_v^*}{S_v} + \alpha I_v + \mu_v I_v + \delta_v I_v + \frac{\beta_m^* S_v I_v^*}{I_v} + \sigma_v R_v + \mu_v R_v + \frac{\alpha I_v R_v^*}{R_v} \end{aligned}\right\}$$

By imposing the condition that if $M < N$, then the derivative of the Lyaponuv function with respect to time is less than or equal to zero.

If $M < N$, then $\frac{dL}{dt} \leqslant 0$.

But $\frac{dL}{dt} = 0$, if and only if $S_h = S_h^*, I_h = I_h^*, R_h = R_h*, S_v = S_v^*, I_v = I_v^*, R_v = R_v^*$

The largest invariant set in;

$$\left\{ (S_h^*, I_h^*, R_h^* S_v^*, I_v^* R_v^*) \in \Phi : \frac{dL}{dt} = 0 \right\} \tag{5.3.26}$$

is singleton $E^*$, where $E^*$is the endemic equilibrium.

Since all the model parameters are assumed to be non-negative, it implies that the derivative of the Lyapunov function is less than or equal to one, if the reproduction number of the system of differential equation in equation$(5.3.1)$ is greater than one $(R_{hv} > 1)$. Therefore by LaSalle's Invariant Principle(LaSalle, 1976; Joshi et al., 2006), as $t$ approaches infinity, all the solution of the equations of the system of differential equations in the model approaches the endemic equilibrium point if $R_{hv}$> 1. Hence, the endemic equilibrium is globally asymptotically stable in the invariant set if $M < N$.

## 5.4 Sensitivity analysis of the Listeriosis model

In this section, we employ sensitivity analysis approach to determine how robust a model is to parameter values. This approach helps identify the parameters with high impact on the basic reproduction number $(R_{hv})$. The essence of the basic reproduction number is to determine whether or not treatment of the infective and mortality could help in the control of the disease in the populationVan den Driessche and Watmough (2002)

**Definition 20.** The normalised forward sensitivity index of a variable, $q$, which depends differential on a parameter, $r$, defined as:

$$\Upsilon_r^q = \frac{\partial q}{\partial r} \times \frac{r}{q}. \tag{5.4.1}$$

### 5.4.1 Sensitivity indices of the basic reproduction number $R_{hv}$.

In epidemiological models, the value of the basic reproductive number determines the ability of the disease or infection to spread within the population. We will determine the reduction in infection due to the diseases by computing the sensitivity indices of the basic reproduction Number $R_{hv}$, with respect to the parameter values in the model. The sensitivity indices serve as determinants of the significance of each parameter in the dynamics and prevalence of the diseases. They measure the change in model variables when a parameter changes. In this study, the sensitivity indices of $R_{hv}$ to parameter values for the model is computed and estimated from data available or already published in literature. Considering the thirteen different parameters of the system of differential equations in model $(5.3.1)$, we therefore derive the sensitivity of $R_{hv}$ to each of the parameters in the model. The sensitivity indices of the basic reproduction number of $R_{hv}$ with respect to each of the parameters of the system of differential equations in model $(5.3.1)$, are given in the table 5.2bellow:

| Parameter | Description | Sensitivity index(+ve/-ve) |
|---|---|---|
| $\Lambda_h$ | human recruitment rate | +ve |
| $\Lambda_v$ | livestock's recruitment rate | +ve |
| $\mu_h$ | death rate in humans | -ve |
| $\mu_v$ | death rate in livestock's | -ve |
| $\delta_h$ | human disease induced death rate | -ve |
| $\delta_v$ | livestock's disease induced death rate | -ve |
| $\alpha$ | livestock's recovery rate | -ve |
| $\beta$ | human transmission rate | +ve |
| $\gamma$ | human rate of recovery | -ve |
| $\lambda$ | livestock transmission rate | +ve |

Table 5.2: Sensitivity indices of parameters to $R_{hv}$.

## 5.5 Listeriosis Model Extension to Optimal Control

In this section, the analysis of an optimal control is carried out to determine the impact of the four intervention control schemes. The optimal control problem is derived by incorporating the following controls into the Listeriosis disease model $(5.3.1)$ and the introduction of an objective functional that seeks to minimise: $(u_1, u_2, u_3)$, where $u_1$ is the preventive measures of the susceptible human population $(S_h)$. These are efforts to reduce the acquisition of Anthrax through education. $u_2$ is the treatment efforts given to the infected humans $(I_h)$ as a result of complications of infections. These are efforts to minimise infections by treating the infective human population and $u_3$ is the treatment efforts given to the infected animals $(I_v)$ as a result of complications of infections. These are efforts to minimise infections by treating the infective animal population.

By incorporating the various controls, the system of differential equations of the model becomes;

$$\left.\begin{array}{rcl}
\frac{dS_h}{dt} &=& \Lambda_h + \sigma_h - (1-u_1)\,\beta\,(I_v + I_h)\,S_h - \mu_h S_h \\
\frac{dI_h}{dt} &=& (1-u_1)\,\beta\,(I_v + I_h)\,S_h - (u_2+\gamma)\,I_h - (\delta_h + \mu_h)\,I_h \\
\frac{dR_h}{dt} &=& (u_2+\gamma)\,I_h - (\sigma_h + \mu_h)\,R_h \\
\frac{dS_v}{dt} &=& \Lambda_v - (1-u_1)\,\lambda\,(I_v + I_h)\,S_v - (\mu_v S_v + \sigma_v R_v) \\
\frac{dI_v}{dt} &=& (1-u_1)\,\lambda\,(I_v + I_h)\,S_v - (u_4+\alpha)\,I_v - (\delta_v + \mu_v)\,I_v \\
\frac{dR_v}{dt} &=& (u_4+\alpha)\,I_v - (\sigma_v + \mu_v)\,R_v
\end{array}\right\}$$

In epidemiological models, the essence of optimal control analysis is to minimise the spread or number of infections and the cost of treatment, preventive measures and vaccination controls. The objective functional that can be used to achieve this is given by:

$$J = min_{(u_1,u_2,u_3)} \int_0^{t_f} \left(B_1 I_v + B_2 I_h + B_3 u_1^2 + B_4 u_2^2 + B_5 u_3^2\right) dt. \tag{5.5.1}$$

subject to the system of differential equations in $(5.3.1)$.

Where; $B_1, B_2, B_3, B_4, B_5$ are referred to as the weight constants to aid balance the terms in the integral to avoid the dominance of one another. They are termed as the balancing cost factors.

$B_1 I_h, B_2 I_v$ , are the costs associated with infected humans $(I_h)$ and the infected animals $(I_v)$. $B_3 u_1^2$ , is the cost associated with preventive measures of the susceptible human population, $(S_h)$. $B_4 u_2^2$ , this is the costs involved in the treatment of the infected humans $(I_h)$ as a result of complications of infections. This is the cost associated with treatment of infected animals. $B_5 u_3^2$ , this is the cost associated with the treatment of infected animals $(I_v)$. the costs involved in the treatment of the infected animals as a result of complications of infections. $t_f$, is the period of the intervention. This implies that $\left( B_1 I_h, B_2 I_v \right)$, represents a linear function for the cost associated with infections and $\left(B_3 u_1^2, B_4 u_2^2, B_5 u_3^2\right)$, represents a quadratic function for the cost associated with controls (Joshi et al., 2006).

The model control efforts is by linear combination of $u_i^2(t)$, $(i=1,2)$ . It is a quadratic in nature because of the assumption that costs are generally non-linear in nature. Moreover, the nature of the functional is chosen in line with existing literature on epidemic models. Thus, our aim is to minimise the number of infective and reduce cost of treatment.

The objective is finding the optimal functions $\left(u_1^*(t), u_2^*(t), u_3^*(t)\right)$ such that;

$$J\left(u_1^*(t), u_2^*(t), u_3^*(t)\right) = min_{(u_1,u_2,u_3)}\varepsilon \cup J\left(u_1, u_2, u_3\right) \tag{5.5.2}$$

Where

$\cup = \left\{ u : u, \quad 0 \leq \quad u_i(t) \leq 1 \quad , \quad t\varepsilon \left[0, t_f\right], \quad i = 1,2,3 \right\}$ is referred to as the control set.

### 5.5.1 Pontryagin's Maximum Principle

The Pontryagin's Maximum Principle provides the necessary conditions that an optimal must satisfy. The principle changes the system of differential equations in (5.3.1) and equation (5.6.2) into minimisation problem point-wise Hamiltonian $(H)$, with respect to $\left( u_1, u_2, u_3 \right)$.

$$\left.\begin{aligned} H &= B_1 I_v + B_2 I_h + B_3 u_1^2 + B_4 u_2^2 + B_5 u_3^2 \\ &+ M_{S_h}\left\{\Lambda_h + \sigma_h - (1-u_1)\beta\left(I_v + I_h\right) S_h - \mu_h S_h\right\} \\ &+ M_{I_h}\left\{(1-u_1)\beta\left(I_v + I_h\right) S_h - (u_2+\gamma) I_h - (\delta_h + \mu_h) I_h\right\} \\ &+ M_{R_h}\left\{(u_2+\gamma) I_h - (\sigma_h + \mu_h) R_h\right\} \\ &+ M_{S_v}\left\{\Lambda_v - (1-u_1)\lambda\left(I_v + I_h\right) S_v - (\mu_v S_v + \sigma_v R_v)\right\} \\ &+ M_{I_v}\left\{(1-u_1)\lambda\left(I_v + I_h\right) S_v - (u_3+\alpha) I_v - (\delta_v + \mu_v) I_v\right\} \\ &+ M_{R_v}\left\{(u_3+\alpha) I_v - (\sigma_v + \mu_v) R_v\right\} \end{aligned}\right\} \tag{5.5.3}$$

Where;

$M_{S_h}, M_{I_h}, M_{R_h}, M_{S_v}, M_{I_v}, M_{R_v}$ are referred to as the adjoint variables.

The adjoint or co-state variables are solutions of adjoint systems below;

$$\left.\begin{array}{rcl}
\frac{dM_{S_h}}{dt} &=& \left((1-u_1)(I_v+I_h)\beta\left(M_{S_h}-M_{I_h}\right)+\mu_h M_{S_h}\right) \\
\frac{dM_{I_h}}{dt} &=& -B_2+(1-u_1)\beta S_h\left(M_{S_h}-M_{I_h}\right)+(u_2+\gamma)\left(M_{I_h}-M_{R_h}\right) \\
&+& (\mu_h+\delta_h)M_{I_h}+(1-u_1)\lambda S_v\left(M_{S_v}-M_{I_v}\right)+b\lambda V_v\left(M_{V_v}-M_{I_v}\right) \\
\frac{dM_{R_h}}{dt} &=& -\sigma_h M_{S_h}+(\sigma_h+\mu_h)M_{R_h} \\
\frac{dM_{S_v}}{dt} &=& (1-u_1)\lambda\left(I_v+I_h\right)\left(M_{S_v}-M_{I_v}\right)+\mu_v M_{S_v} \\
\frac{dM_{I_v}}{dt} &=& -B_1+(1-u_1)\beta S_h\left(M_{S_h}-M_{I_h}\right)+(1-u_1)\lambda S_v\left(M_{S_v}-M_{I_v}\right) \\
&+& (\mu_v+\delta_v)M_{I_v}+(u_4+\alpha)\left(M_{I_v}-M_{R_v}\right) \\
\frac{dM_{R_v}}{dt} &=& -\sigma_h M_{S_v}+(\sigma_v+\mu_v)M_{R_v}
\end{array}\right\} \tag{5.5.4}$$

The above satisfies the transversality condition;

$$M_{S_h}(tf)=M_{I_h}(tf)=M_{R_h}(tf)=M_{S_v}(tf)=M_{I_v}(tf)=M_{R_v}(tf)=0. \tag{5.5.5}$$

Now, combining the Pontryagin's Maximum Principle and the existence result of the optimal control (Pontryagin, 1987; Fleming and Rishel, 2012).

**Theorem 15.** *The optimal control vector* $\left(u_1^*(t),u_2^*(t),u_3^*(t)\right)$ *that maximises the objective function* $(J)$ *over* $\cup$, *given by;*

$$\left.\begin{array}{rcl}
u_1^*(t) &=& max\left\{0,min\left(1,\frac{\beta\left(M_{I_h}-M_{S_h}\right)(I_v+I_h)S_h^*}{2B_3}\right.\right. \\
&& \left.\left.+\frac{\lambda\left(M_{I_v}-M_{S_v}\right)(I_v+I_h)S_v^*}{2B_3}\right)\right\} \\
u_2^*(t) &=& max\left\{0,min\left(1,\frac{\left(M_{I_h}-M_{R_h}\right)I_h^*}{2B_4}\right)\right\} \\
u_3^*(t) &=& max\left\{0,min\left(1,\frac{\left(M_{I_v}-M_{R_v}\right)I_v^*}{2B_5}\right)\right\}
\end{array}\right\} \tag{5.5.6}$$

Where;

$M_{S_h}, M_{I_h}, M_{R_h}, M_{S_v}, M_{I_v}, M_{R_v}$ are the solutions of equation (5.6.4) and (5.6.5).

*Proof.* The existence of an optimal control is as a result the convexity of the integral of $J$ with respect to $u_1$,$u_2$,*and* $u_3$, the Lipschitz property of the state system with respect to the state variables and a priori Boundedness of the state solutions (Fleming and Rishel, 2012). The system in equation (5.6.4) was derived by differentiating the Hamiltonian function evaluated at optimal control. However, equating the derivatives of the Hamiltonian with respect to the controls to zero, the following are obtained;

$$\left.\begin{aligned} u_1 = \tilde{u_1} := \left\{ \left( \frac{\beta \left(M_{I_h} - M_{S_h}\right)(I_v + I_h) S_h^*}{2B_3} \right.\right. \\ \left.\left. + \frac{\lambda \left(M_{I_v} - M_{S_v}\right)(I_v + I_h) S_v^*}{2B_3} \right) \right\} \\ u_2 = \tilde{u_2} := \left\{ \left( \frac{(M_{I_h} - M_{R_h}) I_h^*}{2B_4} \right) \right\} \\ u_3 = \tilde{u_3} := \left\{ \left( \frac{(M_{I_v} - M_{R_v}) I_v^*}{2B_5} \right) \right\} \end{aligned} \right\}$$

Therefore, it can be concluded by standard control arguments involving the bounds on the controls that;

$$\left.\begin{aligned} u_1^* = \begin{cases} 0, & if\, \tilde{u_1} \leq 0 \\ \tilde{u_1} & if\, 0 < \tilde{u_1} < 1 \\ 1 & if\, \tilde{u_1} \geq 1 \end{cases}, \quad u_2^* = \begin{cases} 0, & if\, \tilde{u_2} \leq 0 \\ \tilde{u_2} & if\, 0 < \tilde{u_2} < 1 \\ 1 & if\, \tilde{u_2} \geq 1 \end{cases} \\ u_3^* = \begin{cases} 0, & if\, \tilde{u_3} \leq 0 \\ \tilde{u_3} & if\, 0 < \tilde{u_3} < 1 \\ 1 & if\, \tilde{u_3} \geq 1 \end{cases}, \end{aligned} \right\} \tag{5.5.7}$$

The system in equation (5.6.7) above leads to the system in equation (5.6.6) in Theorem (7). Optimal control uniqueness for small $tf$ was obtained as a result of the Lipschitz structure of the Ordinary Differential Equations and the priori boundedness of the state solutions and adjoint functions. The existence optimal control uniqueness quadruple is in line with the uniqueness of the optimal system, that comprises of equa-

tions $(5.3.1)$ ,$(5.6.4)$ ,$(5.6.5)$and $(5.6.6)$.

The uniqueness of the optimal of the system is guaranteed, by imposing a condition on the time interval. This is always the case as a result of the opposite time orientations of the optimal system. This is always the case because, the adjoint problem has the final values whereas the the state problem has the initial values. In optimal control problems, imposing a condition or applying a restriction is always common (Joshi et al., 2006). □

## 5.6 Numerical Results

In this section, we solve the optimal system by using Range-Kutta fourth order scheme. This optimal strategy was achieved as a results solving the state systems, adjoints equations and the transversality conditions. The problem is a two-point boundary-value problem which has two separate boundary conditions at times $t = 0$ and $t = t_f$. Our ultimate objective is to solve this optimal problem for the value $t_f = 120$ days. This chosen value represents the time at which treatment and vaccination is expected to be stopped. We conducted the numerical simulation by solving the state equations$(5.3.1)$ using Range-Kutta fourth order scheme by guessing the controls over a simulated time. Secondly, we then use the current iteration of the state equations $(5.3.1)$, the adjoint equations and the transversality conditions by a backward method. The controls are then updated by the use of a convex combination of the controls in the previous iterations as well as values from the characterizations of the system. We repeat the process and the iteration is stopped if the values of unknowns at the previous iteration are very close to those at the present iteration Van den Driessche and Watmough (2002).

We considered the following combinations of optimal control strategies and selected the best three most effective strategies:

Prevention of and treatment control of humans. Prevention of humans and the treat-

ment of infective vectors. Treatment of humans and treatment of infective vectors. Treatment of infective vectors, prevention of susceptible humans and the treatment of infective humans. Prevention of susceptible humans only. Treatment of infective vectors only. Treatment of infective humans only. Table 5.3 shows values of parameters and variables used in the simulation of the model in equation (5.3.1).

| Parameter | Estimated value | Reference |
|---|---|---|
| $\mu_h$ | 0.004 | assumed |
| $\delta_h$ | 0.20 | Adak et al., 2002. |
| $\Lambda_v$ | 0.0273 | assumed |
| $\Lambda_h$ | 0.1 | assumed |
| $\mu_v$ | 0.002 | assumed |
| $\delta_v$ | 0.30 | Adak et al., 2002. |
| $\alpha$ | 0.002 | assumed |
| $\beta$ | 0.200 | assumed |
| $\lambda$ | 0.27 | http://www.about-listeria.com |
| $b$ | 0.005 | assumed |

Table 5.3: Variable and parameter values of Anthrax model.

## Strategy A: Optimal prevention of susceptible humans and treatment of infected animals.

We optimise the objective functional by using the prevention control of susceptible humans $(u_1)$ and the treatment control of infected animals $(u_3)$. This was done by setting treatment control of infected humans to zero. It can be observed from the figure that there has been a significant reduction in the number of infective vectors $(I_v)$ and infective humans $(I_h)$. The epidemiological implication is that the spread of Listeriosis can be effectively tackled through the treatment of infective animals and prevention of susceptible humans. Achieving this strategy, there should be proper prevention of susceptible humans as well as treatment of infective animals in the community.

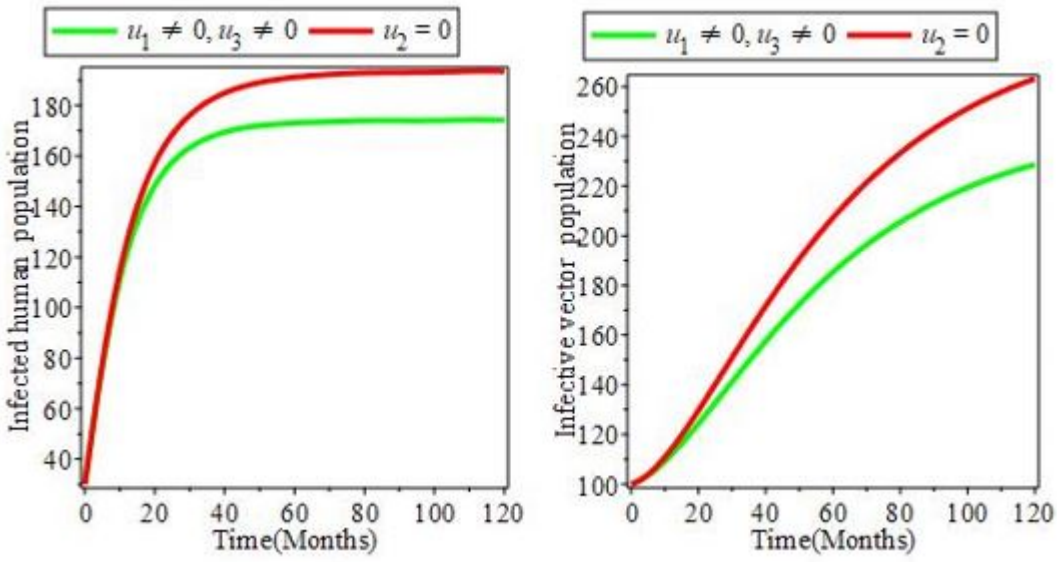


Figure 5.2: Simulation of Listeriosis model: Optimal prevention of susceptible humans and treatment of infected animals.

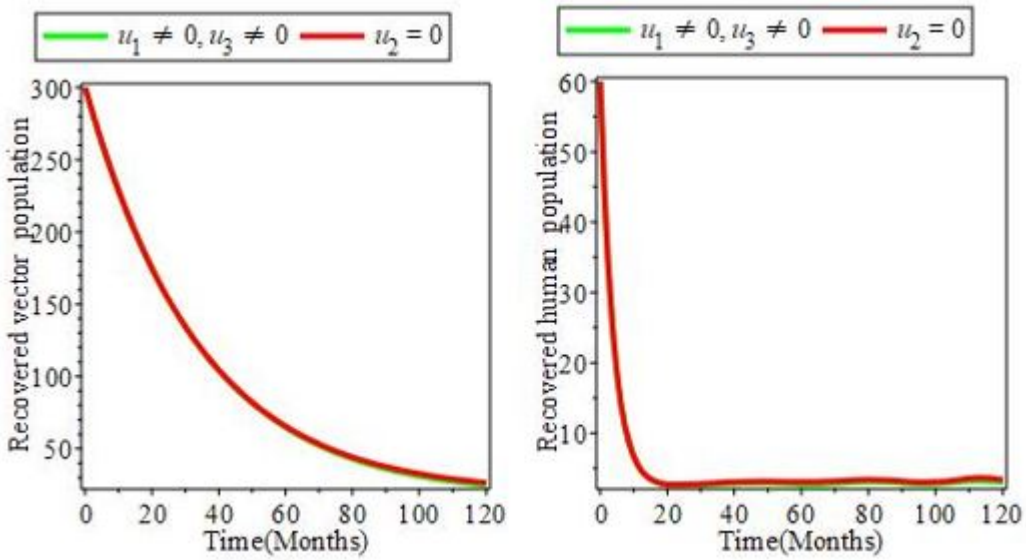


Figure 5.3: Simulation of Listeriosis model: Optimal treatment of infective vectors and preventio of susceptible humans.

## Strategy B: Optimal prevention of susceptible humans and treatment of infected humans.

The treatment control $(u_2)$of infective humans and prevention of susceptible humans, $(u_1)$ were used to optimise the objective functional while the treatment control $(u_3)$ of infected animals is set to zero. We observe that this strategy has caused a reduction in the number of infective animals $(I_v)$ and infective humans $(I_h)$ completely. This optimal strategy can best be achieved by increasing the rate of treatment of infective humans and increasing the rate of prevention of susceptible humans.

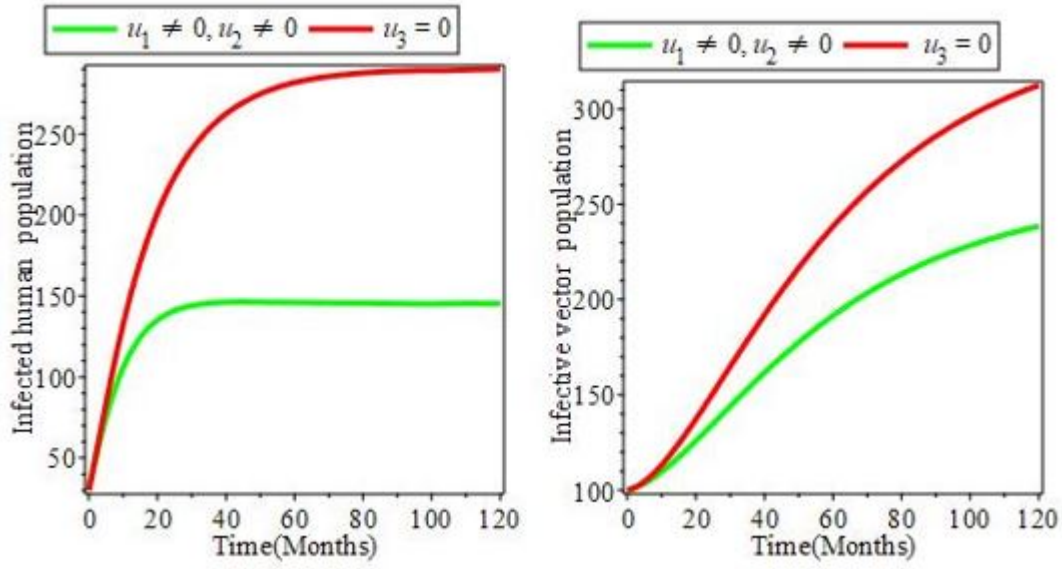


Figure 5.4: Simulation of Listeriosis model: Optimal treatment of infective humans and prevention of susceptible humans.

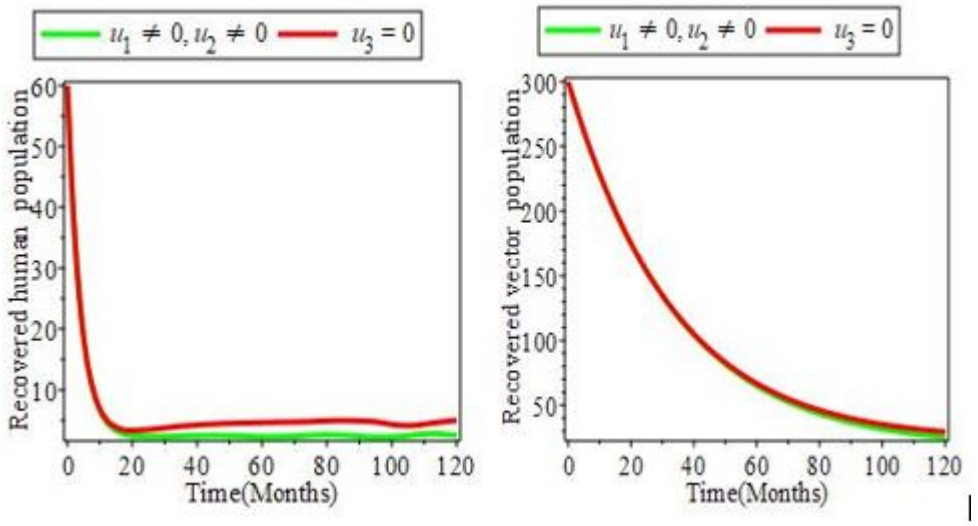


Figure 5.5: Simulation of Listeriosis model: Optimal treatment of infective humans and prevention of susceptible humans.

## Strategy C: Optimal treatment of infective vectors and treatment of infective humans.

We optimise the objective function by using treatment control of infective vectors $(u_3)$ and treatment control of infective humans $(u_2)$. The optimisation was done by setting the prevention control on humans $(u_1)$ to zero. As a result of this strategy, it can be observed that there has been a reduction in the number of infective vectors $(I_v)$ and infective humans $(I_h)$. The epidemiological implication is that the spread of Listeriosis can be controlled through regular treatment of infective vectors and the treatment of infective humans. This optimal strategy can best be achieved by treating all infective animals that are having the infections.

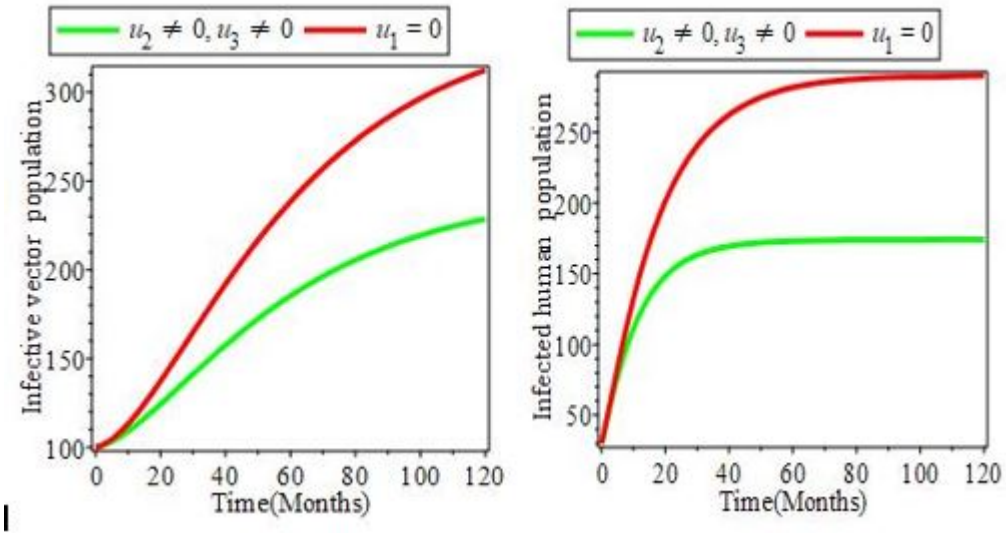


Figure 5.6: Simulation of Listeriosis model: Optimal treatment of infective vectors and treatment of infective humans.

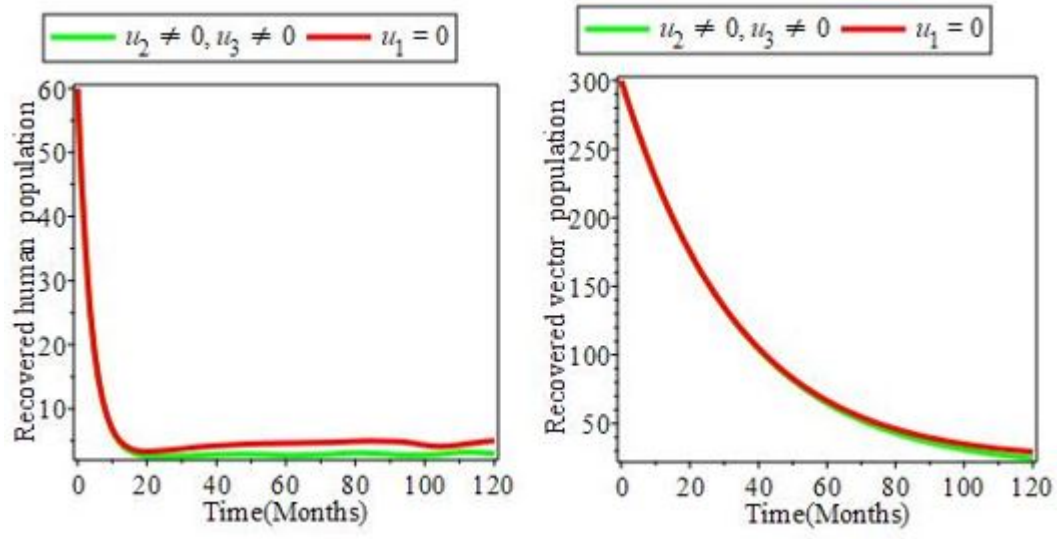


Figure 5.7: Simulation of Listeriosis model: Optimal treatment of infective vectors and treatment of infective humans.

## 5.7 Conclusion

In this paper, we formulated and analysed a deterministic model for the transmission mechanism of Listeriosis disease by the inclusion of treatment of infectious humans and treatment of infectious vectors. We determined the basic reproductive number,$(R_{hv})$,

and carried stability analysis and existence of the equilibrium points. We established from the qualitative analysis of the model that there exist multiple endemic equilibrium. In epidemiology, implication of this is that, effective control of the disease can be reached if the basic reproductive number,$(R_{hv})$, is less than unity (the critical value). We then carried out the sensitivity analysis of the basic reproduction number,$(R_{hv})$ . This analysis showed that, increasing livestock recovery rate, would cause a decrease in the basic reproduction number,$(R_{hv})$. Moreover, decreasing livestock recovery rate, would increase the basic reproductive number,$(R_{hv})$. Also, by increasing human transmission rate and livestock transmission rate, would cause an increase in the basic reproduction number,$(R_{hv})$ and by decreasing human transmission rate and livestock transmission rate, would cause a corresponding decrease in the basic reproduction number, $R_{hv}$.

The rate of Listeriosis infection can be reduced by ensuring that the rate of interaction between susceptible humans and infectious animals, $(\beta)$ is minimised. Moreover, the spread of Listeriosis infection can be curbed by reducing the rate of interaction between susceptible animals and contact with infected animals.

The qualitative analysis of optimal control was performed and the necessary conditions for the optimality of Listeriosis disease was analysed. The three most effective strategies according to our model are as follows: The combination of treatment of infectious vectors,$(I_v)$ and treatment of infectious humans,$(I_h)$, combination of prevention of susceptible humans,$(S_h)$ and the treatment of infective animals,$(I_v)$ and combination of prevention of susceptible humans,$(S_v)$ and the treatment of infectious humans,$(I_v)$.

# Chapter 6

# Co-dynamics of Anthrax and Listeriosis with Optimal Control.

## 6.1 Model Formulation

In this section, we divide the model into sub-compartments. The total vector population is represented by $N_v$, this is divided into sub-compartments that consist of susceptible animals $(S_v)$ and animals infected with anthrax $(I_v)$. The total human population,$(N_h)$ is divided into sub-compartments consisting of susceptible humans,$(S_h)$, individuals that are infected with anthrax,$(I_a)$, individuals that are infected with Listeriosis, individuals that are infected with both anthrax and Listeriosis $(I_{al})$, those that have recovered from anthrax, Listeriosis and both anthrax and Listeriosis respectively as;$(R_a)$,$(R_l)$ and $(R_{al})$. $(C_p)$ is population of carcasses of animals in the soil which may have died of Anthrax. These carcasses which have not been properly disposed have the tendency of causing infections. The total vector and human populations are represented as;

$N_h = S_h + I_a + I_l + I_{al} + R_a + R_l + R_{al}$.

$N_v = S_v + I_v$.

Where, $\pi = \dfrac{C_p v}{K + C_p}$.

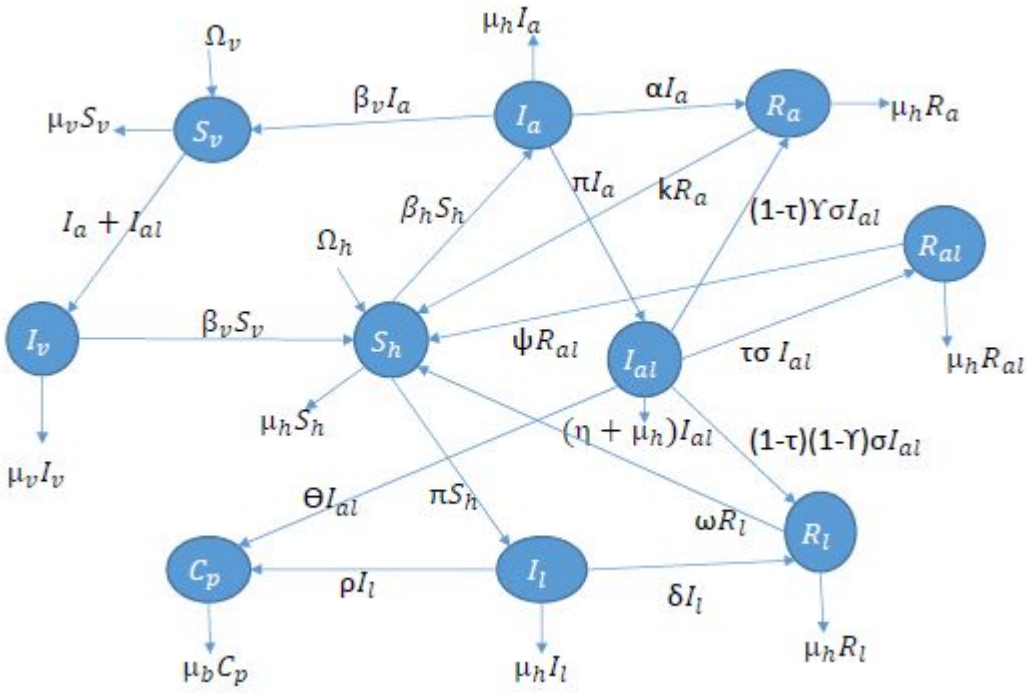


Figure 6.1: Flow chart for the co-infection model.

The concentration of carcasses and ingestion rate are denoted as $K$ and $v$ respectively. Listeriosis related death rates are $m$ and $\eta$ respectively and Anthrax related death rate are $\phi$and $n$ respectively. Waning immunity rates are given by; $\omega, k$ and $\psi$. Where $\alpha, \delta$and $\sigma$ are the recovery rates respectively and $\tau(1-\sigma)$ are the bi-infected infected persons who have recovered from Anthrax only. The natural death rates of human and vector populations are $\mu_h$ and $\mu_v$ respectively and the modification parameter is given by $\theta$. The bi-infected infected persons who have recovered from Listeriosis is denoted by $(1-\tau)(1-\sigma)$. This implies that;

$\sigma + \tau(1-\sigma) + (1-\tau)(1-\sigma) = 1.$

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= \Omega_h + kR_a + \omega R_l + \psi R_{al} - \beta_h I_v S_h - \pi S_h - \mu_h S_h \\
\frac{dI_a}{dt} &= \beta I_v S_h - \pi I_a - (\alpha + \mu_h + \phi) I_a \\
\frac{dI_l}{dt} &= \pi S_h - \beta_l I_v I_l - (\delta + \mu_h + m + \rho) I_l \\
\frac{dI_{al}}{dt} &= \beta_h I_v I_l + \pi I_a - (\sigma + \mu_h + \eta + \theta) I_{al} \\
\frac{dR_a}{dt} &= \alpha I_a - (k + \mu_h) R_a + (1 - \tau) \gamma \sigma I_{al} \\
\frac{dR_l}{dt} &= \delta I_l - (\omega + \mu_h) R_l + (1 - \tau)(1 - \gamma) \sigma I_{al} \\
\frac{dR_{al}}{dt} &= \tau \sigma I_{al} - (\psi + \mu_h) R_{al} \\
\frac{dC_p}{dt} &= \rho I_l + \theta I_{al} - \mu_b C_p \\
\frac{dS_v}{dt} &= \Omega_v - \beta_v (I_a + I_{al}) S_v - \mu_v S_v \\
\frac{dI_v}{dt} &= \beta_v (I_a + cI) S_v - \mu_v I_v
\end{aligned}\right\} \tag{6.1.1}$$

## 6.2 Analysis of Listeriosis only model

In this section, only the Listeriosis model is considered in the analysis of the transmission dynamics.

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= \Omega_h + \omega R_l - \pi S_h - \mu_h S_h \\
\frac{dI_l}{dt} &= \pi S_h - (\delta + \mu_h + m) I_l \\
\frac{dR_l}{dt} &= \delta I_l - (\omega + \mu_h) R_l \\
\frac{dC_p}{dt} &= \rho I_l - \mu_b C_p
\end{aligned}\right\} \tag{6.2.1}$$

### 6.2.1 Disease-Free Equilibrium

We obtain the disease-free equilibrium of the Listeriosis only model by setting the system of equations in equation (6.2.1) to zero. At disease-free equilibrium, there are no infections and recovery.

$\Omega_h + \omega R_l - \pi S_h - \mu_h S_h = 0$

$$S_h^* = \frac{\Omega_h}{\mu_h}$$
$$\xi_{0l} = \left(S_h^*, I_l^*, R_l^*, C_p^*\right) = \left(\frac{\Omega_h}{\mu_h}, 0, 0, 0\right).$$

### 6.2.2 Basic reproduction number

The reproduction number is referred to as the number of infections that an individual would cause in a completely susceptible population. The concept of the Next Generation Matrix would be employed in computing the basic reproduction number. Considering the following differential equations;

$$\left.\begin{aligned} \frac{dI_l}{dt} &= \pi S_h - (\delta + \mu_h + m) I_l \\ \frac{dC_p}{dt} &= \rho I_l - \mu_b C_p \end{aligned}\right\}$$

Let $f$ and $v$ be those entering and leaving the compartments respectively;

$$f = \begin{bmatrix} \pi S_h \\ \rho I_l \end{bmatrix} \text{ and } v = \begin{bmatrix} (\delta + \mu_h + m) I_l \\ \mu_b C_p \end{bmatrix}$$

Where $\pi = \dfrac{C_p v}{K + C_p}$.

Using the theorem in Van den Driessche and Watmough (2002) on the Listeriosis model in equation $(6.2.1)$ ,the basic reproduction number of the Listeriosis only model $(\Re_{0l})$, is given by:

$$\Re_{0l} = \frac{v \rho \Omega_h}{\mu_b \mu_h K (\delta + \mu_h + m)} \tag{6.2.2}$$

### 6.2.3 Existence of the disease-free equilibrium

### 6.2.4 Endemic equilibrium

The endemic equilibrium points are computed by setting the system of differential equations in the Listeriosis only model $(6.2.1)$ to zero. The endemic equilibrium points are as follows:

$$S_h^* = \frac{\Omega_h + \omega R_l^*}{\mu_h + \pi^*}, I_l^* = \frac{\pi^* S_h^*}{(\delta + \mu_h + m)}, R_l^* = \frac{\delta I_l^*}{\omega + \mu_h}, C_p^* = \frac{\rho I_l^*}{\mu_b}.$$

$$\xi_{0l} = \left(S_h^*, I_l^*, R_l^*, C_p^*\right) = \left(\frac{\Omega_h + \omega R_l^*}{\mu_h + \pi^*}, \frac{\pi^* S_h^*}{(\delta + \mu_h + m)}, \frac{\delta I_l^*}{\omega + \mu_h}, \frac{\rho I_l^*}{\mu_b}\right).$$

$$\left.\begin{aligned} S_h^* &= \frac{\Omega_h + \omega R_l^*}{\mu_h + \pi^*} \\ I_l^* &= \frac{\pi^* S_h^*}{(\delta + \mu_h + m)} \\ R_l^* &= \frac{\delta I_l^*}{\omega + \mu_h} \\ C_p^* &= \frac{\rho I_l^*}{\mu_b} \end{aligned}\right\} \tag{6.2.3}$$

### 6.2.5 Existence of the endemic equilibrium

**Lemma 4.** *The Listeriosis only model has a unique endemic equilibrium if and only if the basic reproduction number* $\Re_{0l} > 1$.

*Proof.* The Listeriosis force of infection $\left(\pi = \frac{C_p v}{K + C_p}\right)$, satisfies the polynomial;

$$P(\pi^*) = A(\pi^*)^2 + B(\pi^*) = 0 \tag{6.2.4}$$

Where; $A = \Omega_h \rho(\omega + \mu_h) + \mu_b K(m(\omega + \mu_h) + \mu_h(\delta + \mu_h + \omega))$,

and

$B = (\omega + \mu_h)(1 - R_{0l})$.

By mathematical induction, $A > 0$ and $B > 0$ whenever the basic reproduction number is less than one $(\Re_{0l} < 1)$.

This implies that $\pi^* = \frac{-B}{A} \leq 0$. In conclusion, the Listeriosis model has no endemic any time the basic reproductive number is less than one $(\Re_{0l} < 1)$. □

The analysis illustrates the impossibility of backward bifurcation in the Listeriosis model. Because there is no existence of endemic equilibrium whenever the basic reproduction number is less than one $(\Re_{0l} < 1)$.

## 6.3 Analysis of Anthrax only model

In this section, only the Anthrax model is considered in the analysis of the transmission dynamics. Considering the system of differential equations in the anthrax model only;

$$\left.\begin{aligned} \frac{dS_h}{dt} &= \Omega_h + kR_a - \beta_h I_v S_h - \mu_h S_h \\ \frac{dI_a}{dt} &= \beta I_v S_h - (\alpha + \mu_h + \phi) I_a \\ \frac{dR_a}{dt} &= \alpha I_a - (k + \mu_h) R_a \\ \frac{dS_v}{dt} &= \Omega_v - \beta_v I_a S_v - \mu_v S_v \\ \frac{dI_v}{dt} &= \beta_v I_a S_v - \mu_v I_v \end{aligned}\right\} \tag{6.3.1}$$

### 6.3.1 Disease-free equilibrium

We obtain the disease-free equilibrium of the Anthrax only model by setting the system of equations in model $(6.3.1)$ to zero. At disease-free equilibrium, there are no infections and recovery.

$\Omega_h + kR_a - \beta_h I_v S_h - \mu_h S_h = 0$

$S_h^* = \dfrac{\Omega_h}{\mu_h}.$

$\Omega_v - \beta_v I_a S_v - \mu_v S_v = 0$

$S_v^* = \dfrac{\Omega_v}{\mu_v}.$

$$\xi_{0a} = (S_h^*, I_a^*, R_a^*, S_v^*, I_v^*) = \left(\frac{\Omega_h}{\mu_h}, 0, 0, \frac{\Omega_v}{\mu_v}, 0\right). \tag{6.3.2}$$

### 6.3.2 Basic reproduction number

By employing the concept of the "Next Generation Matrix" in computing the basic reproduction number. Considering only the differential equations that causes the infections;

$$\left.\begin{aligned} \frac{dI_a}{dt} &= \beta I_v S_h - (\alpha + \mu_h + \phi) I_a \\ \frac{dI_v}{dt} &= \beta_v I_a S_v - \mu_v I_v \end{aligned}\right\}$$

Let $f$ and $v$ be those entering and leaving the compartments respectively;

$$f = \begin{bmatrix} \beta I_v S_h \\ \beta_v I_a S_v \end{bmatrix} \text{ and } v = \begin{bmatrix} (\alpha + \mu_h + \phi) I_a \\ \mu_v I_v \end{bmatrix}$$

Using the theorem in Van den Driessche and Watmough (2002) on the Anthrax model in equation $(6.3.1)$ ,the basic reproduction number of the Anthrax only model $(\Re_{0a})$, is given by:

$$\Re_{0a} = \sqrt{\frac{\Omega_h \Omega_v \beta_h \beta_v}{\mu_h \mu_v^2 (\alpha + \mu_h + \phi)}} \tag{6.3.3}$$

### 6.3.3 Stability of the disease-free equilibrium

Using the next generation operator concept in Van den Driessche and Watmough (2002) on the systems of equation in model $(6.3.1)$, the linear stability of the disease-free equlibrium $(\xi_{0a})$, can be ascertained. The disease-free equilibrium is locally asymptotically stable whenever the basic reproduction number is less than one $(\Re_{0a} < 1)$. and unstable whenever the basic reproduction number is greater than one $(\Re_{0a} > 1)$.

### 6.3.4 Endemic equilibrium

The endemic equilibrium points are computed by setting the system of differential equations in the Anthrax only model $(6.3.1)$ to zero. The endemic equilibrium points are as follows:

$$S_h = \frac{\Omega_h + kR_a^*}{\mu_h + \beta_h I_v^*}, I_a^* = \frac{\beta_v S_h^* I_v^*}{(\alpha + \mu_h + \phi)}, R_a^* = \frac{\alpha I_a^*}{k + \mu_h}, S_v^* = \frac{\Omega_v}{\mu_v + \beta_v I_a^*}, I_v^* = \frac{\beta_v S_v^* I_a^*}{\mu_v}.$$

The endemic equilibrium of the Anthrax only model is given by;

$$\xi_{0a} = \left(S_h^*, I_a^*, R_a^*, S_v^*, I_v^*\right) = \left(\frac{\Omega_h + kR_a^*}{\mu_h + \beta_h I_v^*}, \frac{\beta_v S_h^* I_v^*}{(\alpha + \mu_h + \phi)}, \frac{\alpha I_a^*}{k + \mu_h}, \frac{\Omega_v}{\mu_v + \beta_v I_a^*}, \frac{\beta_v S_v^* I_a^*}{\mu_v}.\right)$$

$$\xi_{0a} = \left( \frac{\Omega_h + kR_a^*}{\mu_h + \beta_h I_v^*}, \frac{\beta_v S_h^* I_v^*}{(\alpha + \mu_h + \phi)}, \frac{\alpha I_a^*}{k + \mu_h}, \frac{\Omega_v}{\mu_v + \beta_v I_a^*}, \frac{\beta_v S_v^* I_a^*}{\mu_v}. \right) \tag{6.3.4}$$

### 6.3.5 Existence of the endemic equilibrium

**Lemma 5.** *The Anthrax only model has a unique endemic equilibrium whenever the basic reproduction number* $(\Re_{0a})$ *is greater than one* $(\Re_{0a} > 1)$.

*Proof.* Considering the endemic equilibrium points of the Anthrax only model;
$\xi_{0a} = \left( \frac{\Omega_h + kR_a^*}{\mu_h + \beta_h I_v^*}, \frac{\beta_v S_h^* I_v^*}{(\alpha + \mu_h + \phi)}, \frac{\alpha I_a^*}{k + \mu_h}, \frac{\Omega_v}{\mu_v + \beta_v I_a^*}, \frac{\beta_v S_v^* I_a^*}{\mu_v} \right)$.
The endemic equilibrium point satisfies the given polynomial;

$$P(I_a^*) = A_1 (I_a^*)^2 + B_1 (I_a^*) = 0 \tag{6.3.5}$$

Where;

$A_1 = \beta_v (\Omega_v \beta_h (k\phi + \mu_h (\alpha + k + \phi + \mu_h)) + \mu_h (k + \mu_h)(\alpha + \phi + \mu_h)\mu_v)$

and

$B_1 = (k + \mu_h)\left(1 - R_{0a}^2\right)$.

By mathematical induction, $A_1 > 0$ and $B_1 > 0$ whenever the basic reproduction number is less than one $(\Re_{0a} < 1)$.

This implies that $I_a^* = \frac{-B_1}{A_1} \leq 0$. In conclusion, the Anthrax only model has no endemic any time the basic reproductive number is less than one $(\Re_{0a} < 1)$. □

The analysis illustrates the impossibility of backward bifurcation in the Anthrax only model. Because there is no existence of endemic equilibrium whenever the basic reproduction number is less than one $(\Re_{0a} < 1)$.

## 6.4 Anthrax-Listeriosis co-infection model

In this section, the dynamics of the Anthrax-Listeriosis co-infection model in equation (6.1.1) is considered in the analysis of the transmission dynamics.

### 6.4.1 Disease-free equilibrium

The disease-free equilibrium of the Anthrax-Listeriosis model is obtained by setting the system of equations of model (6.1.1) to zero. At disease-free equilibrium, there are no infections and recovery.

$\Omega_h + kR_a + \omega R_l + \psi R_{al} - \beta_h I_v S_h - \pi S_h - \mu_h S_h = 0$

$S_h^* = \dfrac{\Omega_h}{\mu_h}$

$\Omega_v - \beta_v \left(I_a + cI_{al}\right) S_v - \mu_v S_v = 0$

$S_v^* = \dfrac{\Omega_v}{\mu_v}$

The disease-free equilibrium is given by;

$\xi_{0al} = \left(S_h^*, I_l^*, I_a^*, I_{al}^*, R_l^*, R_a^*, R_{al}^*, C_p^*, S_v^*, I_v^*\right)$

$$\xi_{0al} = \left(\frac{\Omega_h}{\mu_h}, 0, 0, 0, 0, 0, 0, 0, \frac{\Omega_v}{\mu_v}, 0\right) \tag{6.4.1}$$

### 6.4.2 Basic reproduction number

The concept of the next generation operator method in Van den Driessche and Watmough (2002) was employed on the system of differential equations in model (6.1.1) to compute the basic reproduction number of the Anthrax-Listeriosis co-infection model. Considering the following system of differential equations;

$$\left.\begin{aligned}
\frac{dI_a}{dt} &= \beta I_v S_h - \pi I_a - (\alpha + \mu_h + \phi) I_a \\
\frac{dI_l}{dt} &= \pi S_h - \beta_l I_v I_l - (\delta + \mu_h + m + \rho) I_l \\
\frac{dI_{al}}{dt} &= \beta_h I_v I_l + \pi I_a - (\sigma + \mu_h + \eta + \theta) I_{al} \\
\frac{dC_p}{dt} &= \rho I_l + \theta I_{al} - \mu_b C_p \\
\frac{dI_v}{dt} &= \beta_v (I_a + cI) S_v - \mu_v I_v
\end{aligned}\right\}$$

Let $f$ and $v$ be those entering and leaving the compartments respectively;

$$f = \begin{bmatrix} \beta I_v S_h \\ \pi S_h \\ \beta_h I_v I_l + \pi I_a \\ \rho I_l + \theta I_{al} \\ \beta_v (I_a + cI) S_v \end{bmatrix} \text{ and } v = \begin{bmatrix} \pi I_a + (\alpha + \mu_h + \phi) I_a \\ \beta_l I_v I_l + (\delta + \mu_h + m + \rho) I_l \\ (\sigma + \mu_h + \eta + \theta) I_{al} \\ \mu_b C_p \\ \mu_v I_v \end{bmatrix}$$

By taking the jacobian matrices of $f$ and $v$ as $F$ and $V$ respectively and finding the product of $FV^{-1}$. Now computing the eigenvalues of the matrix $FV^{-1}$and taking the dominant eigenvalue. The Anthrax-Listeriosis co-infection model has a reproduction number $(\Re_{al})$ given by;

$\Re_{al} = max\{\Re_a, \Re_l\}$

Where, $\Re_a$ and $\Re_l$ are the basic reproduction numbers of Anthrax and Listeriosis respectively.

$$\Re_a = \sqrt{\frac{\Omega_h \Omega_v \beta_h \beta_v}{\mu_h \mu_v^2 (\alpha + \mu_h + \phi)}} \tag{6.4.2}$$

and

$$\Re_l = \frac{v \rho \Omega_h}{\mu_b \mu_h K} \left( \frac{(\sigma + \mu_h + \eta + \theta) + \theta (\delta + \mu_h + m)}{(\delta + \mu_h + m)(\sigma + \mu_h + \eta + \theta)} \right) \tag{6.4.3}$$

**Theorem 16.** *The disease free equilibrium* $(\xi_{0al})$ *is locally asymptotically stable whenever*

*the basic reproduction number is less than one* $(\Re_{al} < 1)$ *and unstable otherwise.*

### 6.4.3 Impact of Listeriosis on Anthrax

In this section, the impact of Listeriosis on Anthrax and the vice versa is analysed. This is done by expressing the reproduction number of one in terms of the other. By expressing the basic reproduction number of Listeriosis on Anthrax, that is expressing $\Re_l$ in terms of $\Re_a$;

From; $\Re_a = \sqrt{\dfrac{\Omega_h \Omega_v \beta_h \beta_v}{\mu_h \mu_v^2 (\alpha + \mu_h + \phi)}}$

Solving for $\mu_h$ in the above,

$$\mu_h = \frac{-G_1 \Re_a + \sqrt{G_1^2 \Re_a^2 + 4G_2}}{2\mu_v \Re_a},$$

where,

$G_1 = \mu_v (\alpha + \phi)$ and $G_2 = \Omega_h \Omega_v \beta_h \beta_v$

Also, letting;

$$\sqrt{G_1^2 \Re_a^2 + 4G_2} = G_3 \Re_a + G_4,$$

This implies;

$$\mu_h = \frac{\Re_a (G_3 - G_1) + G_4}{2\mu_v \Re_a} \tag{6.4.4}$$

By substituting $\mu_h$ into the basic reproduction number of Listeriosis $(\Re_l)$;

$$\left.\begin{aligned} \Re_l = \quad & \frac{\Re_{0l} (G_4 + (G_3 - G_1) \Re_a + 2(\sigma + \eta + \theta) \mu_v \Re_a}{G_4 + (G_3 - G_1) \Re_a + 2(\sigma + \eta + \theta) \mu_v \Re_a} \\ & + \frac{\theta (G_4 + (G_3 - G_1) \Re_a + 2(m + \delta) \mu_v \Re_a))}{G_4 + (G_3 - G_1) \Re_a + 2(\sigma + \eta + \theta) \mu_v \Re_a} \end{aligned}\right\} \tag{6.4.5}$$

where the basic reproduction number of Listeriosis only model $(R_{0l})$ is given the relation;

$$\Re_{0l} = \frac{v \rho \Omega_h}{\mu_b \mu_h K (\delta + \mu_h + m)}.$$

Now, taking the partial derivative of $\Re_l$ with respect to $\Re_a$ in equation $(6.4.5)$, gives;

$$\frac{\partial \Re_l}{\partial \Re_a} = \frac{2G_4\theta\left(m+\delta-(\sigma+\eta+\theta)\right)\mu_v\Re_{0l}}{\left[G_4+(G_3-G_1+2(\sigma+\eta+\theta)\mu_v\Re_a)\right]^2}. \tag{6.4.6}$$

If $(m+\delta) \geq (\sigma+\eta+\theta)$, the derivative $\left(\frac{\partial \Re_l}{\partial \Re_a}\right)$, is strictly positive. Two scenarios can be deduced from the derivative $\left(\frac{\partial \Re_l}{\partial \Re_a}\right)$, depending on the values of the parameters;

$\frac{\partial \Re_l}{\partial \Re_a} = 0$, and $\frac{\partial \Re_l}{\partial \Re_a} \geq 0$.

1. If $\frac{\partial \Re_l}{\partial \Re_a} = 0$, it implies that $(m+\delta) = (\sigma+\eta+\theta)$ and the epidemiological implications is that Anthrax has no significance effect on the transmission dynamics of Listeriosis.

2. If $\frac{\partial \Re_l}{\partial \Re_a} > 0$, it implies that $(m+\delta) \geq (\sigma+\eta+\theta)$, and the epidemiological implications is that an increase in Anthrax cases would result in an increase Listeriosis cases in the environment. That is Anthrax enhances Listeriosis infections in the environment.

However, by expressing the basic reproduction number of Anthrax on Listeriosis, that is expressing $\Re_a$ in terms of $\Re_l$;

$$\mu_h = \frac{H_1 - H_2\Re_l + \sqrt{H_3\Re_l^2 + H_4\Re_l + H_5}}{2\Re_l}. \tag{6.4.7}$$

where;

$H_1 = (1+\theta)\Re_{0l}$, $H_2 = (m+\delta+\sigma+\eta+\theta)$

$H_3 = (\sigma+\eta+\theta-m-\delta)$, $H_4 = 2(\theta-1)(m+\delta-\sigma-\eta-\theta)\Re_{0l}$

$H_1 = (1+\theta)^2\Re_{0l}^2$.

By letting,

$\sqrt{H_3\Re_l^2 + H_4\Re_l + H_5} = H_6\Re_l + H_7$.

It implies that;

$$\mu_h = \frac{(H_6 - H_2)\,\Re_l + H_7 + H_1}{2\Re_l}.$$

Therefore,

$$\Re_a^2 = \frac{4\Omega_h\Omega_v\beta_h\beta_v\Re_l^2}{[(H_6 - H_2)\,\Re_l + H_7 + H_1]\,[H_7 + H_1 + 2\,(\alpha+\phi)\,\Re_l + (H_6 - H_2)\,\Re_l]\,\mu_v} \quad (6.4.8)$$

Now, taking the partial derivative of $\Re_a$ with respect to $\Re_l$ in equation (6.4.8), gives;

$$\frac{\partial\Re_a}{\partial\Re_l} = \frac{4\,(H_7 + H_1)\,[H_7 + H_1 + (\alpha + \phi + H_6 - H_2)\,\Re_l]\,\Omega_h\Omega_v\beta_h\beta_v\Re_l}{[(H_6 - H_2)\,\Re_l + H_7 + H_1]^2\,[H_7 + H_1 + (2\,(\alpha+\phi) + H_6 - H_2)\,\Re_l]^2\,\mu_v} \quad (6.4.9)$$

If the partial derivative of $\Re_a$ with respect to $\Re_l$ is greater than zero, $\left(\frac{\partial\Re_a}{\partial\Re_l} > 0\right)$, the biological implication is that an increase in the number of cases of Listeriosis would result in an increase in the number of cases of Anthrax in the environment. Moreover, the the impact of Anthrax treatment on Listeriosis can also be analysed by taking the partial derivative of $\Re_a$ with respect to $\alpha$, $\left(\frac{\partial\Re_a}{\partial\alpha}\right)$.

$$\frac{\partial\Re_a}{\partial\alpha} = -\frac{\alpha}{\alpha + \phi + \mu_h}.$$

Clearly, $\Re_a$ is a decreasing function of $\alpha$, the epidemiological implication is that the treatment of Listeriosis would have an impact on the transmission dynamics of Anthrax.

### 6.4.4 Analysis of backward bifurcation

In this section, the phenomenon of backward bifurcation is carried out by employing the centre manifold theory on the system of differential equations in model (6.1.1). Bifurcation analysis was carried out by employing the centre manifold theory in Castillo-Chavez and Song (2004); Okosun and Makinde (2014). Considering the human trans-

mission rate ($\beta_h$) and $v$ as the bifurcation parameters, it implies that $\Re_a = 1$ and $\Re_l = 1$ if and only if,

$$\beta_h = \beta_h^* = \frac{\mu_h \mu_v^2 (\alpha + \phi + \mu_h)}{\Omega_h \Omega_v \beta_v},$$

and

$$v = v^* = \frac{\mu_b \mu_h K (\delta + \mu_h + m)(\sigma + \mu_h + \eta + \theta)}{\rho \Omega_h (\sigma + \mu_h + \eta + \theta + \theta (m + \delta + \mu_h))}.$$

By considering the following change of variables;

$S_h = x_1$, $I_a = x_2$, $I_l = x_3$,$I_{al} = x_4$,$R_a = x_5$,

$R_l = x_6$,$R_{al} = x_7$,$C_p = x_8$,$S_v = x_9$,$I_v = x_{10}$.

This would give the total population as;

$$N = x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7 + x_8 + x_9 + x_{10}.$$

By applying vector notation;

$$X = (x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8, x_9, x_{10})^T.$$

The Anthrax-Listeriosis co-infection model can be expressed as;

$\frac{dX}{dt} = F(X)$, where $F = (f_1, f_2, f_3, f_4, f_5, f_6, f_7, f_8, f_9, f_{10})^T$.

The following system of differential equations are obtained;

$$\left.\begin{aligned}
\frac{dx_1}{dt} &= \Omega_h + k x_5 + \omega x_6 + \psi x_7 - \beta_h x_{10} x_1 - \pi x_1 - \mu_h x_1 \\
\frac{dx_2}{dt} &= \beta_h x_{10} x_1 - \pi x_2 - (\alpha + \mu_h + \phi) x_2 \\
\frac{dx_3}{dt} &= \pi x_1 - \beta_l x_{10} x_3 - (\delta + \mu_h + m + \rho) x_3 \\
\frac{dx_4}{dt} &= \beta_l x_{10} x_3 + \pi x_2 + (\sigma + \mu_h + \eta + \theta) x_4 \\
\frac{dx_5}{dt} &= \alpha x_2 - (k + \mu_h) x_5 + (1 - \tau) \gamma \sigma x_4 \\
\frac{dx_6}{dt} &= \delta x_3 - (\omega + \mu_h) x_6 + (1 - \tau)(1 - \gamma) \sigma x_4 \\
\frac{dx_7}{dt} &= \tau \sigma x_4 - (\psi + \mu_h) x_7 \\
\frac{dx_8}{dt} &= \rho x_3 + \theta x_4 - \mu_b x_8 \\
\frac{dx_9}{dt} &= \Omega_v - \beta_v (x_2 + x_4) x_9 - \mu_v x_9 \\
\frac{dx_{10}}{dt} &= \beta_v (x_2 + x_4) x_9 - \mu_v x_{10}
\end{aligned}\right\} \quad (6.4.10)$$

Backward bifurcation is carried out by employing the centre manifold theory on the system of differential equations in model (6.1.1). This concept involves the computation of the Jacobian of the system of differential equations in (6.4.10) at the disease free equilibrium ($\xi_0$). The Jacobian matrix at disease free equilibrium is given by;

$$J(\xi_0) = \begin{bmatrix} -\mu_h & 0 & 0 & J_1 & k & \omega & \psi & J_2 & 0 & J_3 \\ 0 & -J_4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & J_3 \\ 0 & 0 & -J_5 & J_1 & 0 & 0 & 0 & J_2 & 0 & 0 \\ 0 & 0 & 0 & -J_6 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \alpha & 0 & J_7 & -J_8 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \delta & J_9 & 0 & -J_{10} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \sigma & 0 & 0 & -J_{11} & 0 & 0 & 0 \\ 0 & 0 & \rho & \theta & 0 & 0 & 0 & -\mu_b & 0 & 0 \\ 0 & -J_{12} & 0 & -J_{12} & 0 & 0 & 0 & 0 & -\mu_v & 0 \\ 0 & J_{12} & 0 & J_{12} & 0 & 0 & 0 & 0 & 0 & -\mu_v \end{bmatrix} \tag{6.4.11}$$

where;

$J_1 = \dfrac{\rho\Omega_h}{\mu_h}$, $J_2 = \dfrac{\mu_b(\delta+\mu_h+m)(\sigma+\mu_h+\eta+\theta)}{\rho(\sigma+\mu_h+\eta+\theta+\theta(\delta+\mu_h+m))}$,

$J_3 = \dfrac{\mu_v^3(\alpha+\phi+\mu_h)}{\Omega_v\beta_v}$, $J_4 = (\alpha+\phi+\mu_h)$,

$J_5 = (\delta+\mu_h+m)$, $J_6 = (\sigma+\mu_h+\eta+\theta)$, $J_7 = (1-\tau)\gamma\sigma$,

$J_8 = (k+\mu_h)$, $J_9 = (1-\tau)(1-\gamma)\sigma$, $J_{10} = (\omega+\mu_h)$,

$J_{11} = (\psi+\mu_h)$ and $J_{12} = \dfrac{\Omega_v\beta_v}{\mu_v}$.

Clearly, the Jacobian matrix at disease free equilibrium has a case of simple zero eigenvalue as well as other eigenvalues with negative real parts. This is an indication that the centre manifold theorem is applicable. By applying the centre manifold theorem in Castillo-Chavez and Song (2004), the left and right eigenvector of the Jacobian matrix

$J(\xi_0)$ is computed first. Letting the left and right eigenvector represented by:

$y = \begin{bmatrix} y_1, & y_2, & y_3, & y_4, & y_5, & y_6, & y_7, & y_8, & y_9, & y_{10} \end{bmatrix}$ and

$w = \begin{bmatrix} w_1, & w_2, & w_3, & w_4, & w_5, & w_6, & w_7, & w_8, & w_9, & w_{10} \end{bmatrix}^T$ respectively.

The following were obtained;

$$w_1 = \frac{Kw_5}{\mu_h} + \frac{w_2\mu_v^2(\alpha+\phi+\mu_h)}{\mu_h}, w_2 = \frac{\mu_v^2}{\Omega_v\beta_v},$$

$$w_3 = \quad w_4 = \quad w_6 = \quad w_7 = \quad w_8 = 0, w_5 = \frac{\alpha\mu_v^2}{\Omega_v\beta_v(k+\mu_h)},$$

$w_9 = -w_{10}, w_{10} = 1.$

and

$$y_1 = \quad y_3 = \quad y_5 = \quad y_6 = \quad y_7 = \quad y_8 = \quad y_9 = 0, y_2 = \frac{v_{10}\Omega_v\beta_v}{\mu_v(\alpha+\phi+\mu_h)},$$

$$y_2 = y_4, y_{10} = \frac{-\mu_v(\sigma+\mu_h+\eta+\theta)}{\Omega_v\beta_v}.$$

Moreover, by further simplifications, it can be shown that;

$$a = \frac{\tau w_{10}\mu_v^3(q_1)}{\Omega_v\beta_v} - 2w_{10}\beta_v\left[\frac{\mu_v^2(q_1)}{\mu_h\Omega_v\beta_v} + \frac{\alpha K\mu_v^2(q_1)}{\mu_h\Omega_v\beta_v(k+\mu_h)(\alpha+\phi+\mu_h)}\right],$$

$$q_1 = \sigma+\mu_h+\eta+\theta$$

$$b = y_2w_{10}\frac{\Omega_h}{\mu_h} > 0.$$

It can be deduced that the coefficient $b$ would always be positive. Backward bifurcation will take place in the system of differential equations in equation (6.1.1) if the coefficient $a$ is positive. In conclusion, it implies that the disease free equilibrium is not globally stable.

The diagram in Figure 6.2 shows the simulation of the model indicating the existence of backward bifurcation. This phenomenon only exists in situations where the disease free equilibrium and the endemic equilibrium coexist . The biological implication is that the idea that when the basic reproduction number is less than one, the disease can be controled is no longer a sufficient condition. The diagram in Figure 6.2 confirms the analytical results which shows that endemic equilibrium exists when the basic reproduction number is greater than unity.

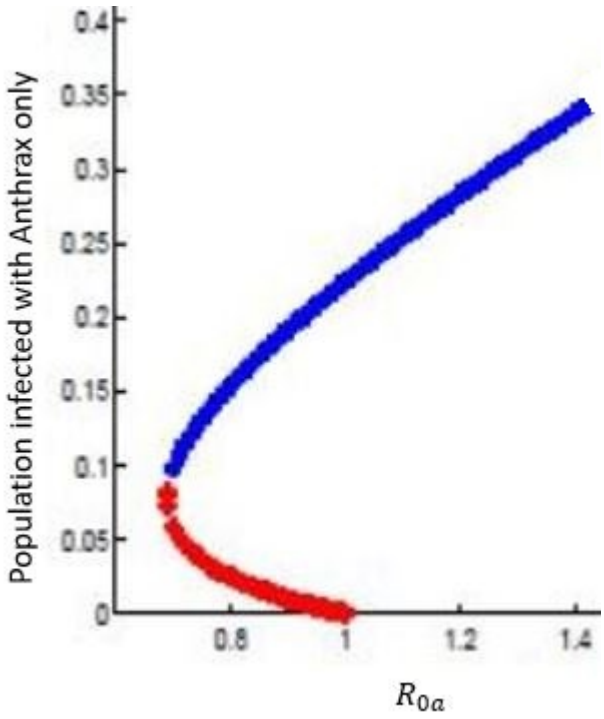


Figure 6.2: The existence of backward bifurcation.

## 6.5 Sensitivity Analysis of the Co-infection model

We performed the sensitivity analysis of the basic reproduction number of the co-infection model. The essence of sensitivity analysis is to determine the significance each parameter on the basic reproduction number. The sensitivity index of the basic reproduction number $(\Re_0)$ to a parameter $x$ is given by the relation:

$\Pi_x^{\Re_0} = \left(\frac{\partial \Re_0}{\partial x}\right)\left(\frac{x}{\Re_0}\right)$.

The sensitivity analysis of the basic reproduction number of Anthrax $\Re_{0a}$ and Listeriosis $\Re_{0a}$ were computed separately, since the basic reproduction number of the co-infection model is usually;

$\Re_0 = max\{\ \Re_{0a}\ \ ,\ \ \Re_{0l}\ \}$.

### 6.5.1 Sensitivity indices of $\Re_{0a}$.

In this section, we derive the sensitivity of the basic reproduction number of Anthrax ($\Re_{0a}$), to each of the parameters. Detailed sensitivity indices of the basic reproduction number of Anthrax ($\Re_{0a}$) as a result of evaluation from other parameter values are shown in Table 6.1. The values in Table 6.1, shows that the most sensitive parameters are the human recruitment rate, vector recruitment rate, human transmission rate and vector transmission rate. In creasing or decreasing the human recruitment rate by 10% would increase or decrease the basic reproduction number of Anthrax by 12.164%. Moreover, increasing or decreasing human and vector transmission rates by 10% would increase or decrease the basic reproduction number of Anthrax by 1.216% and 0.243% respectively.

| Parameter | Description | Sensitivity Index |
|---|---|---|
| $\Omega_h$ | Human recruitment rate | 1.2164 |
| $\Omega_v$ | Vector recruitment rate | 0.2433 |
| $\beta_h$ | Human transmission rate | 0.1216 |
| $\beta_v$ | Vector transmission rate | 0.0243 |
| $\alpha$ | Anthrax recovery rate | $-0.0037$ |
| $\mu_h$ | Human natural death rate | $-0.0122$ |
| $\mu_v$ | Vector natural death rate | $-0.0061$ |
| $\phi$ | Anthrax related death rate | $-0.0065$ |
| $\theta$ | Modification parameter | $3.42913 * 10^{-}6$ |

Table 6.1: Sensitivity indices of the basic reproduction number of Anthrax to each of the parameter values.

### 6.5.2 Sensitivity indices of $\Re_{0l}$.

In this section, we derive the sensitivity of the basic reproduction number of Listeriosis ($\Re_{0l}$), to each of the parameters. Detailed sensitivity indices of the basic reproduction number of Listeriosis ($\Re_{0l}$) as a result of evaluation from other parameter values are shown in Table 6.2. The values in Table 6.2, shows that the most sensitive parameters are the human recruitment rate, Listeriosis contribution to environment, bacteria

ingestion rate and Listeriosis related death. In creasing or decreasing the human recruitment rate by 10% would increase or decrease the basic reproduction number of Listeriosis by 0.201487%. Moreover, increasing or decreasing Listeriosis contribution to environment and bacteria ingestion rate by 10% would increase or decrease the basic reproduction number of Listeriosis.

| Parameter | Description | Sensitivity Index |
|---|---|---|
| $\Omega_h$ | Human recruitment rate | 0.0201487 |
| $\sigma$ | Co-infected human recovery rate | $-5.41441 * 10^-6$ |
| $\mu_h$ | Human natural death rate | $-0.00014638$ |
| $\eta$ | Listeriosis death rate among co-infected | $-5.41441 * 10^-6$ |
| $\theta$ | Modification parameter | $3.42913 * 10^-6$ |
| $v$ | Bacteria ingestion rate | 0.0000402975 |
| $\rho$ | Listeriosis contribution to environment | 0.0000309981 |
| $K$ | Concentration of carcasses | $-2.01487 * 10^-10$ |
| $\delta$ | Listeriosis recovery rate | $-0.0000402218$ |
| $\mu_b$ | Carcasses mortality rate | $-0.0080595$ |
| $m$ | Listeriosis related death | $-0.0000402218$ |

Table 6.2: Sensitivity indices of the basic reproduction number of Listeriosis to each of the parameter values.

## 6.6 Extension of the model to optimal control

In this section, the analysis of an optimal control is carried out to determine the impact of the five intervention schemes. The optimal control problem is derived by incorporating the following control functions into the Anthrax-Listeriosis co-infection model (6.1.1) and the introduction of an objective functional that seeks to minimise: $(u_1, u_2, u_3, u_4, u_5)$. The controls $u_1(t)$ and $u_2(t)$ denotes the efforts on preventing Anthrax and Listeriosis respectively. The controls $u_3(t)$ and $u_4(t)$ denotes the treatment of Anthrax and Listeriosis infected persons respectively. Moreover, $u_3(t)$ satisfies $0 \leq u_3 \leq f_3$ and $u_4(t)$ satisfies $0 \leq u_4 \leq f_4$ , where $f_3$ and $f_4$ are the drug efficacy use in the treatment of Anthrax and Listeriosis infected persons respectively. Also, $u_5(t)$ is the control on the treatment of co-infected persons and it satisfies $0 \leq u_5 \leq f_5$.

Where $f_5$ is the drug efficacy use in the treatment of Anthrax-Listeriosis co-infected persons. The following system of differential equations are obtained as a result of incorporating the controls in the model;

$$\left.\begin{aligned}
\frac{dS_h}{dt} &= \Omega_h + kR_a + \omega R_l + \psi R_{al} - (1-u_1)\beta_h I_v S_h - (1-u_2)\pi S_h - \mu_h S_h \\
\frac{dI_a}{dt} &= (1-u_1)\beta_h I_v S_h - (1-u_2)\pi I_a - (u_3\alpha + \mu_h + \phi) I_a \\
\frac{dI_l}{dt} &= (1-u_2)\pi S_h - (1-u_1)\beta_l I_v I_l - (u_4\delta + \mu_h + m + \rho) I_l \\
\frac{dI_{al}}{dt} &= (1-u_1)\beta_h I_v I_l + (1-u_2)\pi I_a + (u_5\sigma + \mu_h + \eta + \theta) I_{al} \\
\frac{dR_a}{dt} &= u_3\alpha I_a - (k+\mu_h) R_a + (1-\tau)\gamma u_5 \sigma I_{al} \\
\frac{dR_l}{dt} &= u_4\delta I_l - (\omega + \mu_h) R_l + (1-\tau)(1-\gamma) u_5 \sigma I_{al} \\
\frac{dR_{al}}{dt} &= \tau u_5 \sigma I_{al} - (\psi + \mu_h) R_{al} \\
\frac{dC_p}{dt} &= \rho I_l + \theta I_{al} - \mu_b C_p \\
\frac{dS_v}{dt} &= \Omega_v - (1-u_1)\beta_v (I_a + I_{al}) S_v - \mu_v S_v \\
\frac{dI_v}{dt} &= (1-u_1)\beta_v (I_a + I_{al}) S_v - \mu_v I_v
\end{aligned}\right\} \tag{6.6.1}$$

In epidemiological models, the essence of optimal control analysis is to minimise the spread or number of infections, cost of treatment and cost of preventive measures. The objective functional that can be used to achieve this is given by:

$$J(u_i) = \int_0^{t_f} \left(A_1 I_a + A_2 I_l + A_3 I_{al} + A_4 I_v + A_5 u_1^2 + A_6 u_2^2 + A_7 u_3^2 + A_8 u_4^2 + A_9 u_5^2\right) dt. \tag{6.6.2}$$

Where; $i = 1,2,3,4,5$.

subject to the system of differential equations in $(6.6.1)$.

Where, $A_1, A_2, A_3, A_4, A_5, A_6, A_7, A_8, A_9$ are the weight constants to aid balance the terms in the integral to avoid the dominance of one another. They are termed as the bal-

ancing cost factors. $A_1I_a, A_2I_l$ are the costs associated with infected persons with Anthrax and Listeriosis respectively. $A_3I_{al}, A_4I_v$ are the cost associated with co-infected persons and infected vectors respectively. $A_5u_1^2, A_6u_2^2$ are the cost associated with efforts of prevention of Anthrax and Listeriosis respectively. $A_7u_3^2, A_8u_4^2$ are the cost associated with the treatment of Anthrax and Listeriosis infected persons respectively. $A_9u_5^2$ is the cost associated with the treatment of persons infected with both Anthrax and Listeriosis simultaneously (co-infected persons).

Where $t_f$ is the final period of the intervention. This implies that $(A_1I_a, A_2I_l, A_3I_{al}, A_4I_v)$, represents a linear function for the cost associated with infections

and $\left(A_5u_1^2, A_6u_2^2, A_7u_3^2, Au_4^2, A_9u_5^2\right)$, represents a quadratic function for the cost associated with prevention and treatments.

The model control efforts is by linear combination of $u_i^2(t)$, $(i = 1,2)$ . The quadratic in nature of the control efforts are as a result of the assumption that costs are generally non-linear in nature. Moreover, the nature of the functional is chosen in line with existing literature on epidemic models. Thus, our aim is to minimise the number of infective and reduce cost of treatment. The objective is finding the optimal functions $\left(u_1^*(t), u_2^*(t), u_3^*(t), u_4^*(t)\right)$ , such that;

$$J(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*) = \{J(u_1, u_2, u_3, u_4, u_5) \mid u_1, u_2, u_3, u_4, u_5 \in \cup\} \tag{6.6.3}$$

where $\cup = \{(u_1, u_2, u_3, u_4, u_5) : u_1, u_2, u_3, u_4, u_5 measurable,$

$\left(0 \leq u_1 \leq 1, 0 \leq u_2 \leq 1, 0 \leq u_3 \leq f_2, 0 \leq u_4 \leq f_3, 0 \leq u_5 \leq f_5 \forall t \in \left[0, t_f\right]\right)\}$

are the control set.

### 6.6.1 Pontryagin's Maximum Principle

The Pontryagin's Maximum Principle provides the necessary conditions that an optimal must satisfy Fleming and Rishel (2012). The principle changes the system of

differential equations in (6.5.1) and equation (6.5.2) into minimisation problem pointwise Hamiltonian $(H)$, with respect to $(u_1, u_1, u_1, u_1, u_1)$.

$$\left.\begin{aligned} H &= A_1 I_a + A_2 I_l + A_3 I_{al} + A_4 I_v + A_5 u_1^2 + A_6 u_2^2 + A_7 u_3^2 + A_8 u_4^2 + A_9 u_5^2 \\ &+ \lambda_1 \{\Omega_h + k R_a + \omega R_l + \psi R_{al} - (1-u_1)\beta_h I_v S_h - (1-u_2)\pi S_h - \mu_h S_h\} \\ &+ \lambda_2 \{(1-u_1)\beta_h I_v S_h - (1-u_2)\pi I_a - (u_3\alpha + \mu_h + \phi) I_a\} \\ &+ \lambda_3 \{(1-u_2)\pi S_h - (1-u_1)\beta_l I_v I_l - (u_4\delta + \mu_h + m + \rho) I_l\} \\ &+ \lambda_4 \{(1-u_1)\beta_h I_v I_l + (1-u_2)\pi I_a + (u_5\sigma + \mu_h + \eta + \theta) I_{al}\} \\ &+ \lambda_5 \{u_3\alpha I_a - (k+\mu_h) R_a + (1-\tau)\gamma u_5 \sigma I_{al}\} \\ &+ \lambda_6 \{u_4\delta I_l - (\omega + \mu_h) R_l + (1-\tau)(1-\gamma) u_5 \sigma I_{al}\} \\ &+ \lambda_7 \{\tau u_5 \sigma I_{al} - (\psi + \mu_h) R_{al}\} \\ &+ \lambda_8 \{\rho I_l + \theta I_{al} - \mu_b C_p\} \\ &+ \lambda_9 \{\Omega_v - (1-u_1)\beta_v (I_a + I_{al}) S_v - \mu_v S_v\} \\ &+ \lambda_{10} \{(1-u_1)\beta_v (I_a + I_{al}) S_v - \mu_v I_v\} \end{aligned}\right\} \tag{6.6.4}$$

Where $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7, \lambda_8, \lambda_9, \lambda_{10}$ are referred to as the co-state variables (adjoint variables).

**Theorem 17.** *Given optimal controls* $\left(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*\right)$ *and solutions*

$S_h, I_a, I_l, I_{al}, R_a, R_l, R_{al}, C_p, S_v, I_v$ *of the corresponding state systems* (6.5.1)

*and* (6.5.2) *that minimise the objective functional* $J(u_1, u_2, u_3, u_4, u_5)$ *over* $\cup$.

*Then there exists adjoint variables* $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6, \lambda_7, \lambda_8, \lambda_9, \lambda_{10}$ *satisfying;*

$\frac{d\lambda_i}{dt} = -\frac{\partial H}{\partial \dot{x}(t)}$.

*where* $i = 1,2,3,4,5,6,7,8,8,9,10$ *and* $\dot{x} = S_h, I_a, I_l, I_{al}, R_a, R_l, R_{al}, C_p, S_v, I_v$ ,

*with transversality conditions;*

$\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = \lambda_5(t_f) = \lambda_6(t_f) = \lambda_7(t_f) = \lambda_8(t_f) = \lambda_9(t_f) = \lambda_{10}(t_f) = 0,$

*and ;*

$$u_1^* = min\left\{1, max\left(0, \frac{\beta_h I_v S_h\left(\lambda_2-\lambda_1\right)+\beta_l I_v I_l\left(\lambda_4-\lambda_3\right)+\beta_v S_v\left(I_a+I_{al}\right)\left(\lambda_{10}-\lambda_9\right)}{2A_5}\right)\right\}$$

$$\left.\begin{aligned} u_2^* = &\quad min\left\{1, max\left(0, \frac{\pi S_h\left(\lambda_3-\lambda_1\right)+\pi I_a\left(\lambda_4-\lambda_2\right)+\rho\left(I_l+\theta I_{al}\right)\lambda_8}{2A_6}\right)\right\} \\ u_3^* = &\quad min\left\{1, max\left(0, \frac{\alpha I_a\left(\lambda_2-\lambda_5\right)}{2A_7}\right)\right\} \\ u_4^* = &\quad min\left\{1, max\left(0, \frac{\delta I_l\left(\lambda_3-\lambda_6\right)}{2A_8}\right)\right\} \\ u_5^* = &\quad min\left\{1, max\left(0, \frac{\sigma I_{al}\left[\lambda_4+\left(1-\tau\right)\gamma\lambda_5+\left(1-\tau\right)\left(1-\gamma\right)\lambda_6-\tau\lambda_7\right]}{2A_9}\right)\right\} \end{aligned}\right\} \tag{6.6.5}$$

*Proof.* There exists an optimal control due to the convexity of the integral of the objective functional $J$ with respect to $u_1, u_2, u_3, u_4, u_5$, a priori boundedness of the state solutions and the Lipschitz property of the state system with respect to the state variables Fleming and Rishel (2012). The differential equations governing the adjoint variables are obtained by differentiating the Hamiltonian function, evaluated at the optimal control.

From the relation;

$$\frac{d\lambda_i}{dt} = -\frac{\partial H}{\partial \dot{x}\left(t\right)} \tag{6.6.6}$$

where $i = 1,2,3,4,5,6,7,8,8,9,10$ and $\dot{x}= S_h, I_a, I_l, I_{al}, R_a, R_l, R_{al}, C_p, S_v, I_v$. The system of equations obtained as a result of taking the partial derivatives of the Hamiltonian with respect to the associated state variables are the solutions of the adjoint systems. The following adjoint or co-state variables are solutions of adjoint systems obtained

below;

$$\left.\begin{aligned}
-\frac{d\lambda_1}{dt} &= \mu_h\lambda_1 + (1-u_1)\,\beta_h I_v\,(\lambda_1-\lambda_2) - (1-u_2)\left(\frac{C_p v}{K+C_p}\right)(\lambda_1-\lambda_3)\\
-\frac{d\lambda_2}{dt} &= -A_1 - u_3\alpha\lambda_5 + (1-u_2)\left(\frac{C_p v}{K+C_p}\right)(\lambda_2-\lambda_4) + (-u\alpha+\mu_h+\phi)\,\lambda_2\\
&\quad + (1-u_1)\,\beta_v S_v\,(\lambda_9-\lambda_{10})\\
-\frac{d\lambda_3}{dt} &= -A_2 + (1-u_1)\,\beta_v I_v\,(\lambda_3-\lambda_4) - u_4\delta\lambda_6 - (1-u_2)\,\rho\lambda_8 + (u_4\delta+\mu_h+m)\,\lambda_3\\
-\frac{d\lambda_4}{dt} &= -A_3 + (u_5\sigma+\mu_h+\eta+\theta)\,\lambda_4 - (1-\tau)\,\gamma u_5\sigma\lambda_5 + (1-\tau)\,(1-\gamma)\,u_5\sigma\lambda_6\\
&\quad + \tau u_5\sigma\lambda_7 + \theta\lambda_8 + (1-u_1)\,\beta_v S_v\,(\lambda_{10}-\lambda_9)\\
-\frac{d\lambda_5}{dt} &= -k\lambda_1 + (k+\mu_h)\,\lambda_5\\
-\frac{d\lambda_6}{dt} &= -\omega\lambda_1 + (\omega+\mu_h)\,\lambda_6\\
-\frac{d\lambda_7}{dt} &= -\psi\lambda_1 + (\psi+\mu_h)\,\lambda_7\\
-\frac{d\lambda_8}{dt} &= (1-u_2)\,S_h\frac{Kv}{(K+C_p)^2}\,(\lambda_2-\lambda_3) + (1-u_2)\,I_a\frac{Kv}{(K+C_p)^2}\,(\lambda_2-\lambda_4) + \mu_b\lambda_8\\
-\frac{d\lambda_9}{dt} &= (1-u_1)\,\beta_v\,(I_a+I_{al})\,(\lambda_9-\lambda_{10}) - \mu_v\lambda_9\\
-\frac{d\lambda_{10}}{dt} &= -A_4 + (1-u_1)\,\beta_h S_h\,(\lambda_1-\lambda_2) + (1-u_1)\,\beta_h I_l\,(\lambda_3-\lambda_4)
\end{aligned}\right\} \tag{6.6.7}$$

The system of equations in (6.5.7) satisfies the transversality conditions;

$\lambda_1(tf) = \lambda_2(tf) = \lambda_3(tf) = \lambda_4(tf) = \lambda_5(tf) = \lambda_6(tf) = \lambda_7(tf) = \lambda_8(tf) = \lambda_9(tf) = \lambda_{10}(tf) = 0.$

Now, combining the Pontryagin's Maximum Principle and the existence result of the optimal control (Pontryagin, 1987; Fleming and Rishel, 2012).

Moreover, the characterisation of the optimal control is obtained by solving the partial derivative of the Hamiltonian function with respect to the control sets and equating the derivatives to zero.

$$\frac{\partial H}{\partial u_i} = 0 \tag{6.6.8}$$

where; $u_i = u_i^*$, and $i = 1,2,3,\ldots,n$. The following are obtained;

$$\left.\begin{aligned}
\frac{\partial H}{\partial u_1} = 0 = \;& 2A_5u_1 + \beta_h I_v S_h(\lambda_1 - \lambda_2) + \beta_l I_v I_l(\lambda_4 - \lambda_3) + \beta_v S_v(I_a + I_{al})(\lambda_9 - \lambda_{10}) \\
\frac{\partial H}{\partial u_2} = 0 = \;& 2A_6u_2 + \pi S_h(\lambda_1 - \lambda_3) + \pi I_a(\lambda_2 - \lambda_4) - \rho(I_l + \theta I_{al})\lambda_8 \\
\frac{\partial H}{\partial u_3} = 0 = \;& 2A_7u_3 + \alpha I_a(\lambda_5 - \lambda_2) \\
\frac{\partial H}{\partial u_4} = 0 = \;& 2A_8u_4 + \delta I_l(\lambda_6 - \lambda_3) \\
\frac{\partial H}{\partial u_5} = 0 = \;& 2A_9u_5 + \sigma I_{al}[\lambda_4 + (1-\tau)\gamma\lambda_5 + (1-\tau)(1-\gamma)\lambda_6 + \tau\lambda_7]
\end{aligned}\right\} \tag{6.6.9}$$

The following are obtained by re-arranging and simplification;

$$\left.\begin{aligned}
u_1^* = \;& \frac{\beta_h I_v S_h(\lambda_2 - \lambda_1) + \beta_l I_v I_l(\lambda_4 - \lambda_3) + \beta_v S_v(I_a + I_{al})(\lambda_{10} - \lambda_9)}{2A_5} \\
u_2^* = \;& \frac{\pi S_h(\lambda_3 - \lambda_1) + \pi I_a(\lambda_4 - \lambda_2) + \rho(I_l + \theta I_{al})\lambda_8}{2A_6} \\
u_3^* = \;& \frac{\alpha I_a(\lambda_2 - \lambda_5)}{2A_7} \\
u_4^* = \;& \frac{\delta I_l(\lambda_3 - \lambda_6)}{2A_8} \\
u_5^* = \;& \frac{\sigma I_{al}[\lambda_4 + (1-\tau)\gamma\lambda_5 + (1-\tau)(1-\gamma)\lambda_6 - \tau\lambda_7]}{2A_9}
\end{aligned}\right\} \tag{6.6.10}$$

By employing the phenomenon of standard control arguments involving the bounds on the controls, it can be concluded that;

$$u_i^* = \begin{cases} 0 & if \quad \Phi_i^* \leq 0 \\ \Phi_i^* & if \quad 0 < \Phi_i^* < 1 \\ 1 & if \quad \Phi_i^* \geq 1 \end{cases} \tag{6.6.11}$$

for $i = 1,2,3,4,5$

where;

$$\left.\begin{aligned}
\Phi_1^* &= \frac{\beta_h I_v S_h (\lambda_2 - \lambda_1) + \beta_l I_v I_l (\lambda_4 - \lambda_3) + \beta_v S_v (I_a + I_{al}) (\lambda_{10} - \lambda_9)}{2A_5} \\
\Phi_2^* &= \frac{\pi S_h (\lambda_3 - \lambda_1) + \pi I_a (\lambda_4 - \lambda_2) + \rho (I_l + \theta I_{al}) \lambda_8}{2A_6} \\
\Phi_3^* &= \frac{\alpha I_a (\lambda_2 - \lambda_5)}{2A_7} \\
\Phi_4^* &= \frac{\delta I_l (\lambda_3 - \lambda_6)}{2A_8} \\
\Phi_5^* &= \frac{\sigma I_{al} [\lambda_4 + (1-\tau) \gamma \lambda_5 + (1-\tau)(1-\gamma) \lambda_6 - \tau \lambda_7]}{2A_9}
\end{aligned}\right\} \quad (6.6.12)$$

□

### 6.6.2 Numerical methods and results

In this section, the numerical solutions of the optimal system are illustrated using Range-Kutta fourth order scheme. This optimal strategy was obtained by solving the state systems, adjoints equations and the transversality conditions. The optimal problem is a two-point boundary-value problem with two separate boundary conditions at initial times $t = 0$ and final times $t = t_f$. The primary objective is to solve this optimal problem for the final time, $t_f = 120$ days. The chosen period represents the period at which preventive strategies and treatment is expected to be stopped. The numerical simulation was conducted by solving the state equations $(6.5.1)$ using Range-Kutta fourth order scheme with a guess of controls over a simulated period. Secondly, the current iteration of the state equations $(6.5.1)$, the adjoint equations and the transversality conditions are then used by a backward method. Moreover, controls are then updated by the use of a convex combination of the controls in the previous iterations as well as values from the characterizations of the system. The process is repeated and the iteration is stopped if the values of unknowns at the previous iteration are very close to those at the present iteration, Okosun et al. (2016).

The following of optimal control strategies under consideration were paired during

simulations and the best four most effective combinations were selected; Control efforts on prevention of Anthrax infections $u_1$, control efforts on prevention of Listeriosis infections $u_2$, control efforts $u_3$ and $u_4$ on treatment of Anthrax and Listeriosis infected persons respectively and the control efforts $u_5$ on the treatment of Anthrax-Listeriosis co-infected persons.

The description of the variables and parameters used in the simulation of the co-infection model are shown in Table 6.3.

| Parameter | Description | Value | Reference |
|---|---|---|---|
| $\phi$ | Anthrax death rate | 0.2 | (Health line, Dec., 2015) |
| $m$ | Listeriosis death rate | 0.2 | Adak et al., 2002. |
| $q$ | Anthrax co-infected death rate | 0.04 | assumed |
| $\eta$ | Listeriosis co-infected death rate | 0.08 | assumed |
| $\beta_h$ | Human transmission rate | 0.01 | (Mushayabasa et al., 2015) |
| $\beta_v$ | Vector transmission rate | 0.05 | assumed |
| $k$ | Anthrax waning immunity | 0.02 | assumed |
| $\mu_v$ | Vector natural death rate | 0.0004 | (Mushayabasa et al., 2015) |
| $\Omega_h$ | Human recruitment rate | 0.001 | assumed |
| $\Omega_v$ | Vector recruitment rate | 0.005 | (Mushayabasa et al., 2015) |
| $\alpha$ | Anthrax recovery rate | 0.33 | (Brookmeyer et al., 2003) |
| $\delta$ | Listeriosis recovery rate | 0.002 | assumed |
| $\psi$ | Anth.-List. waning immunity | 0.07 | assumed |
| $\rho$ | List. contr. to environment | 0.65 | assumed |
| $\sigma$ | Co-infected recovery rate | 0.005 | assumed |
| $\mu_b$ | Bacteria death rate | 0.0025 | assumed |
| $\mu_h$ | Human natural death rate | 0.2 | (Mushayabasa et al., 2015) |
| $\omega$ | Listeriosis waning immunity | 0.001 | assumed |
| $\theta$ | Modification parameter | 0.45 | assumed |
| $\varepsilon$ | Anthrax Co-infected recovery rate | 0.025 | assumed |
| $K$ | Concentration of carcasses | 10000 | (Okosun and Makinde, 2014) |
| $v$ | Bacteria ingestion rate | 0.5 | (Okosun and Makinde, 2014) |

Table 6.3: Variables and parameters of the co-infection model.

### 6.6.3 Strategy 1: Optimal prevention $(u_2)$ and treatment $(u_4)$of Listeriosis.

We optimised the objective functional by using Listeriosis prevention control of susceptible persons $(u_2)$ and Listeriosis treatment control of infected persons $(u_4)$. This is done by setting the Anthrax prevention control $(u_1)$, Anthrax treatment control $(u_3)$ and Anthrax-Listeriosis co-infection control of infected persons $(u_5)$ to zero. Figure 6.3 shows a reduction in the number of Listeriosis infected individuals but this is not as much as the case in the number of Anthrax infected individuals. However, we observe in Figure 6.4 shows a significant reduction in the number of Anthrax-Listeriosis co-infected individuals. The biological implication is that the spread of Anthrax and Listeriosis can best be eradicated through prevention of susceptible individuals and animals and the treatment of infected humans from Listeriosis. This optimal strategy of treating a larger population of infected humans that have the infections in the community and campaign on prevention can greatly impact on combating the diseases. Cases without control are indicated with black lines and cases with control are indicated with blue lines.

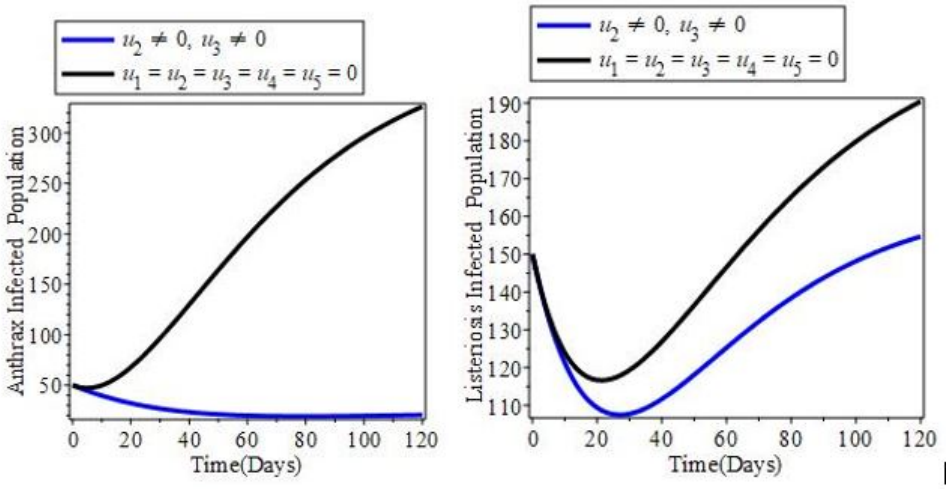


Figure 6.3: Simulation of the co-infection model showing the effects of prevention and treatment on Anthrax and Listeriosis infected population.

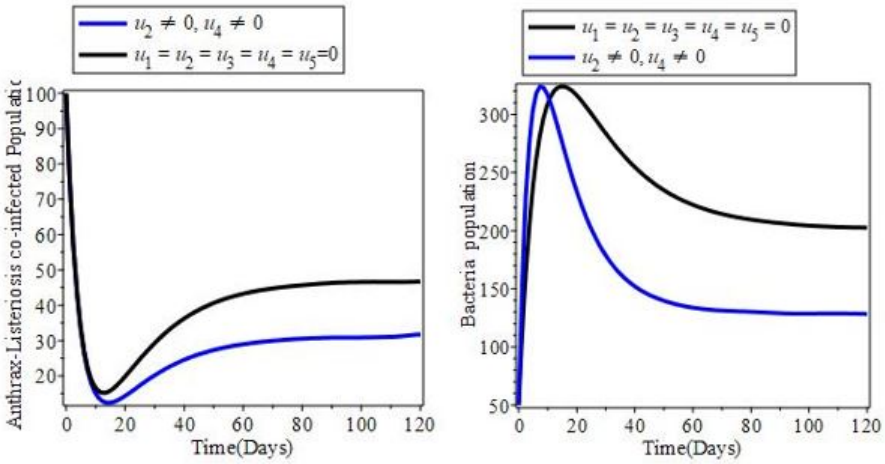


Figure 6.4: Simulation of co-infection model showing the effects of prevention and treatment on Anthrax-Listeriosis infected population and bacteria population.

### 6.6.4 Strategy 2: Optimal prevention of both Anthrax $(u_1)$ and Listeriosis $(u_2)$.

The objective functional is optimised by using Anthrax prevention control $(u_1)$ and Listeriosis prevention control $(u_2)$ of susceptible persons. This is done by setting the Anthrax treatment control of infected persons $(u_3)$, treatment control of Listeriosis infected persons $(u_4)$ and treatment control of co-infected persons $(u_5)$ to zero. Our observations in Figure 6.5 shows a sharp reduction in the number of Anthrax infected population and there is also reduction in the population of Listeriosis infected persons. There are much impact in reduction of Anthrax infected persons than Listeriosis infected persons. Moreover, Figure 6.6 shows a reduction in the number of Anthrax-Listeriosis co-infected population and a reduction in the population of bacteria. The biological implication is that the spread of Anthrax can be controlled through regular prevention susceptible individuals by educating the public on the dangers associated with Anthrax and Listeriosis. Cases without control are indicated with black lines and cases with control are indicated with blue lines.

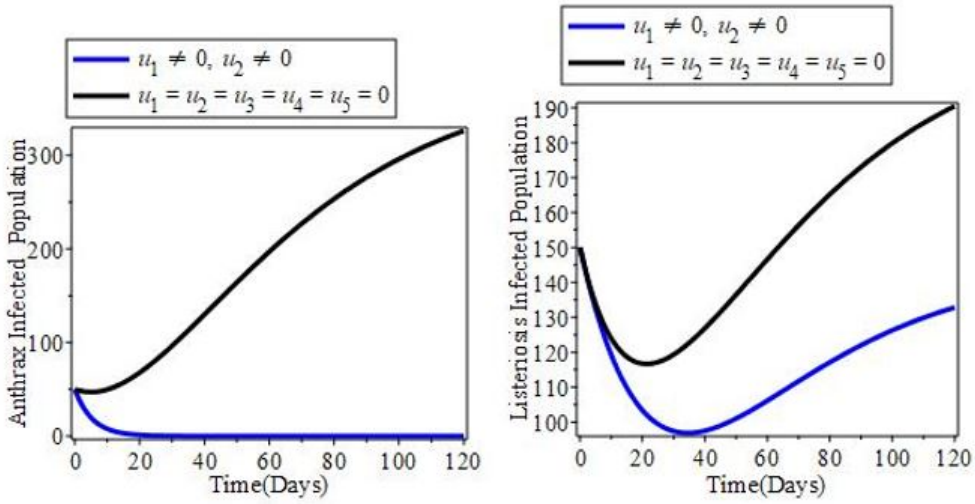


Figure 6.5: Simulation of the co-infection model showing the effects of Anthrax and Listeriosis prevention on Anthrax and Listeriosis infected population.

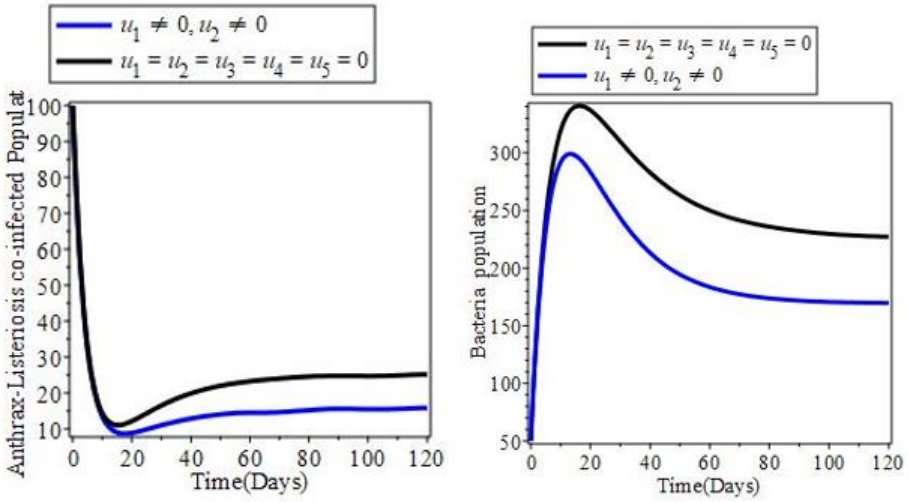


Figure 6.6: Simulation of the co-infection model showing the effects of Anthrax and Listeriosis prevention on co-infected population and bacteria population.

### 6.6.5 Strategy 3: Optimal prevention $(u_1)$and treatment $(u_3)$of Anthrax.

The objective functional is optimised by using anthrax prevention control $(u_1)$ and anthrax treatment control $(u_3)$ of infected persons. This is done by setting the Listeriosis prevention controls $(u_2)$, treatment control of Listeriosis infected persons $(u_4)$ and

treatment control of co-infected persons $(u_5)$ to zero except the Anthrax prevention control $(u_1)$ and Anthrax treatment control $(u_3)$ of infected persons. Figure 6.7 shows a sharp reduction in the number of Anthrax infected population and there is also reduction in the population of Listeriosis infected persons. Moreover, Figure 6.8 :shows a reduction in the number of Anthrax-Listeriosis co-infected population and a reduction in the population of bacteria that are responsible for the diseases in the environment. Prevention and treatment controls are responsible for the reduction in the spread of the diseases. The biological implication is that the spread of Anthrax can be controlled through regular prevention by educating the public on the dangers associated with Anthrax and the treatment of infected humans. This optimal strategy can best be achieved by treating all or an appreciable number of infected animals and humans that have the infections. Cases without control are indicated with black lines and cases with control are indicated with blue lines.

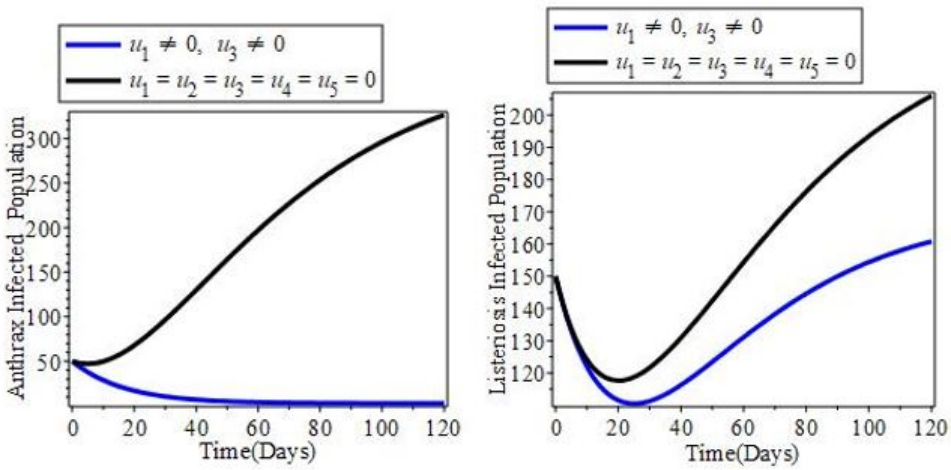


Figure 6.7: Simulation of the co-infection model showing the effects of prevention and treatment on Anthrax and Listeriosis infected population.

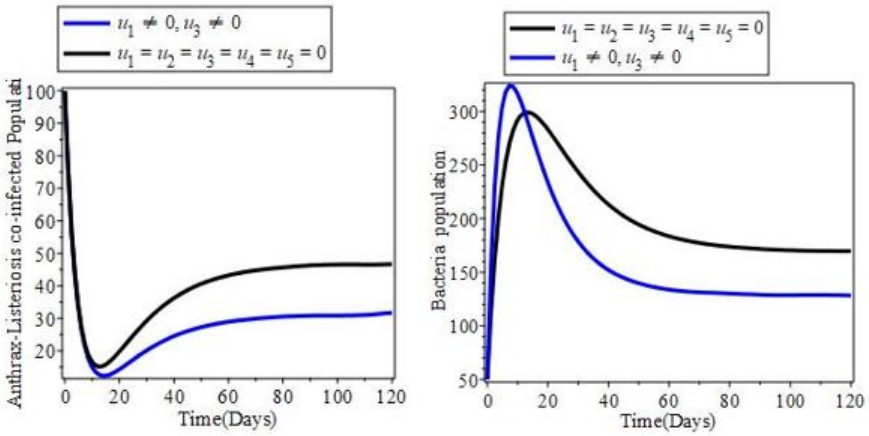


Figure 6.8: Simulation of the co-infection model showing the effects of prevention and treatment on co-infected population and bacteria population.

### 6.6.6 Strategy 4: Optimal treatment of both Anthrax $(u_3)$ and Listeriosis $(u_4)$.

The objective functional is optimised by using anthrax treatment control of infected persons $(u_3)$ and Listeriosis treatment control of infected persons $(u_4)$. This is done by setting the Anthrax prevention control $(u_1)$, Listeriosis control $(u_2)$ and treatment control of co-infected persons $(u_5)$ to zero.We observe that in Figure 6.9, there is a complete reduction in the number of Anthrax infected population and there is also reduction in the population of Listeriosis infected persons. Moreover, Figure 6.10 shows a reduction in the number of Anthrax-Listeriosis co-infected population and a reduction in the population of bacteria that are responsible for the diseases in the environment. The biological implication is that the spread of both diseases can be controlled through regular treatment of infected persons. This optimal strategy has impacted positively as the number of co-infected persons has reduced drastically. Cases without control are indicated with black lines and cases with control are indicated with blue lines.

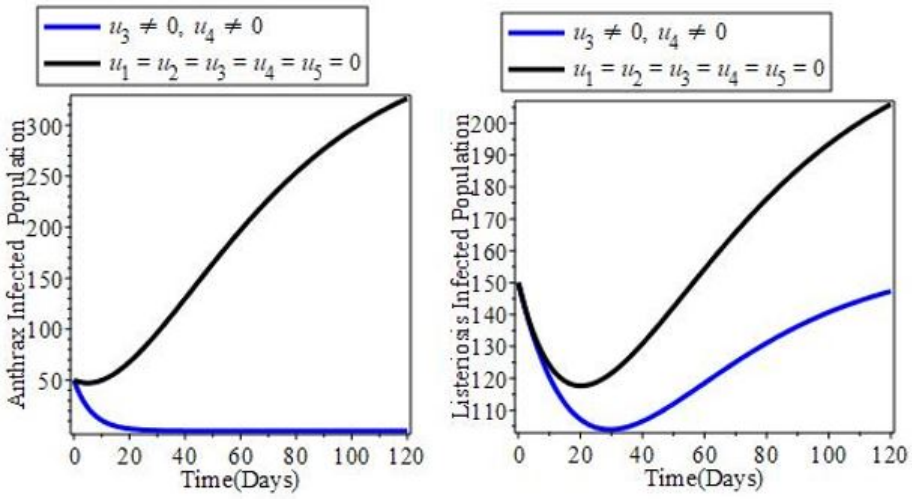


Figure 6.9: Simulation of co-infection model showing the effects of Anthrax and Listeriosis treatment on Anthrax and Listeriosis infected population.

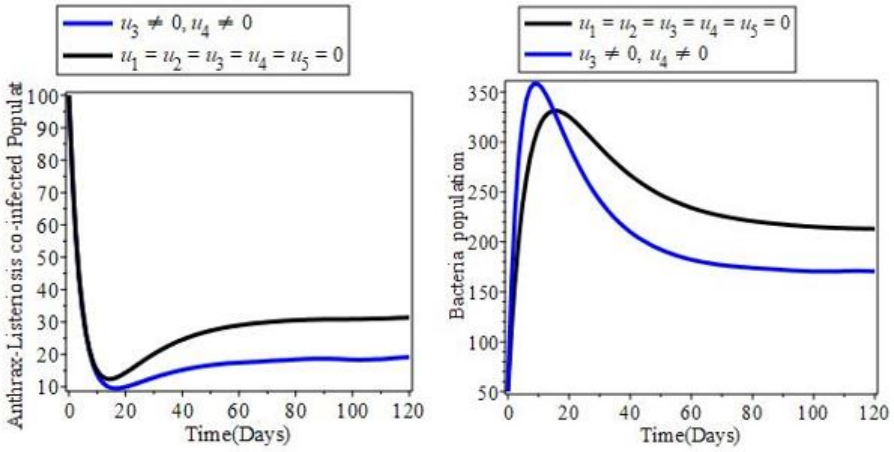


Figure 6.10: Simulation of co-infection model showing the effects of Anthrax and Listeriosis treatment on co-infected population and bacteria population.

## 6.7 Conclusion

The transmission mechanism of the formulated Anthrax-Listeriosis co-infection model which incorporated the following controls; prevention of susceptible humans, prevention of susceptible vectors, treatment of infected humans, treatment of infected vectors and treatment of Anthrax-Listeriosis co-infected humans was determined.

The best optimal control strategies for the Anthrax-Listeriosis co-infection is the combination of the optimal prevention of susceptible humans from Listeriosis infection and treatment of Listeriosis infectious humans as well as the optimal treatment of Anthrax infected humans and treatment of Listeriosis infected humans.

The deterministic model was analysed qualitatively and quantitatively for a better understanding of the transmission dynamics of Anthrax and Listeriosis co-infection. It was revealed that, the disease free equilibrium of the Anthrax model only is locally stable when the basic reproduction number is less one and a unique endemic equilibrium whenever the basic reproduction number is greater than one.

Moreover, the disease free equilibrium of the Listeriosis model only is locally stable when the basic reproduction number is less one and a unique endemic equilibrium whenever the basic reproduction number is greater than one. Model analysis also reveals that the disease free equilibrium of the Anthrax-Listeriosis co-infection model is locally stable whenever the basic reproduction number is less one.

The phenomenon of backward bifurcation was exhibited by our model. The biological implication is that the idea of the model been locally stable whenever the reproduction number is less than unity and unstable otherwise does not apply. This means that the Anthrax-Listeriosis co-infection model shows a case of co-existence of the disease free equilibrium and the endemic equilibrium whenever the basic reproduction number is less than one.

The analysis of Anthrax-Listeriosis co-infection model revealed that Anthrax infections can be attributed to increased risk of Listeriosis but the reverse is not true. However, optimal prevention and treatment of Anthrax and not keeping Listeriosis under control is not the best strategy of eradicating either of the disease.

The optimal prevention and treatments on Listeriosis would only be the effective way of eradicating Listeriosis only if Anthrax is kept under control. Anthrax infections can be attributed to the increased number of bacteria growth as shown in figure 6.8 and

figure 6.10. In the existence of co-infection, the effective strategy is to incorporate intervention strategies with Anthrax control strategies in order to control Anthrax.

# Chapter 7

# Conclusion, Recommendations and Future Research

In this research, three new mathematical models have been formulated to study the transmission mechanisms of Anthrax, Listeriosis and Anthrax-Listeriosis co-infection. All the three mathematical models have been analysed qualitatively and quantitatively. These three mathematical models are a great contribution to infectious disease modelling and applied mathematics as a whole. The proposed deterministic models, the qualitative analysis, quantitative analysis and the application of optimal control theory and analysis that were employed can best be used in the effective control of Anthrax, Listeriosis and Anthrax-Listeriosis co-infection epidemics. The major contribution in this research is the Anthrax-Listeriosis co-infection model. There have not been any study on the modelling of Anthrax-Listeriosis co-infection model. Both Anthrax and Listeriosis diseases can be categorised under zoonotic diseases and are both bacteria related infections. Hence the need to study the transmission dynamics of both diseases and the best optimal control strategy in combating the spread of the infections.

## 7.1 Summary of contributions

In this section, a summary of contributions each of the following models are presented:

1. Anthrax disease model
2. Listeriosis disease model
3. Anthrax-Listeriosis co-dynamics model

### 7.1.1 Anthrax disease model

A vaccination compartment with waning immunity was incorporated into the model. The qualitative analysis showed that the Anthrax model has two equilibrium. The disease-free equilibrium of the Anthrax model is locally asymptotically stable if the basic reproductive number is less than one, $(R_a < 1)$ and unstable if the basic reproductive number is greater than one, $(R_a > 1)$. The disease can die out of the population whenever the reproduction number is less than one. This can be achieved by tackling the parameters that would reduce the reproduction number. The basic reproductive number (rate) combines the biology of infections with the social and behaviour of the factors influencing contact rate. The basic reproductive number (rate) is the threshold parameter that governs the spread of a disease. However, sensitivity analysis revealed that decreasing $\alpha$would increase the basic reproductive number, $(R_{hv})$. Also, by increasing human contact rate, $\beta$ and animal contact rate, $\lambda$ would cause an increase in the basic reproduction number, $R_{hv}$. The Anthrax infections can be eradicated by ensuring that the both human and animal contact rates are kept constant. Moreover, the extension of the Anthrax model to optimal control theory seeks to minimise the objective functional subject to some controls variables. The best control measure in combating the Anthrax infection is prevention of susceptible humans and treatment of

infected animals in the populations. Public health policy makers should concentrate on prevention of humans and the treatment of infected animals.

### 7.1.2 Listeriosis disease model

The basic reproductive number, $(R_l)$ of the Listeriosis model was computed and analysed qualitatively. This is to determine the parameters that contributes to the spread of Listeriosis in the population. Human and animal contact rates are responsible for the spread of Listeriosis in the population. Efforts should be put in place by government and policy makers in reducing these parameters. Stability analysis and existence of the equilibrium points were conducted. It established that the Listeriosis model exhibited multiple endemic equilibrium. Sensitivity analysis of the basic reproduction number, $(R_l)$ , was performed. It was established that, increasing animal (livestock) recovery rate, there would be a decrease in the basic reproduction number $(R_l)$. Moreover, by increasing human recovery rate, there would be decrease in the reproduction number. Therefore, the spread of Listeriosis infection can be reduced treating infectious humans and animals in the population. The optimal control of Listeriosis infection was performed and the necessary conditions for the optimal of Listeriosis disease was analysed. The two most effective control strategies according to the Listeriosis model are as follows: The combination of treatment of infectious vectors $(I_v)$ and treatment of infectious humans $(I_h)$ , combination of prevention of susceptible humans $(S_h)$ and the treatment of infectious vectors $(I_v)$ . Government and health policy makers should more efforts in controlling the spread of Listeriosis by treatment of infectious humans and infectious animals.

### 7.1.3 Anthrax-Listeriosis co-infection model

Anthrax-Listeriosis co-infection model which incorporated the following controls; prevention of susceptible humans, prevention of susceptible vectors, treatment of infected

humans, treatment of infected vectors and treatment of Anthrax-Listeriosis co-infected humans was formulated.

The best optimal control strategies for the Anthrax-Listeriosis co-infection is the combination of the optimal prevention of susceptible humans from Listeriosis infection and treatment of Listeriosis infectious humans as well as the optimal treatment of Anthrax infected humans and treatment of Listeriosis infected humans.

However, optimal prevention and treatment of Anthrax and not keeping Listeriosis under control is not the best strategy for eradicating either of the disease. The optimal prevention and treatments on Listeriosis would only be the effective way of eradicating Listeriosis only if Anthrax is kept under control. Anthrax infections can be attributed to the increased number of bacteria growth in the environment. The biological implication is that, Listeriosis infection might not be attributed to increased risk of Anthrax. In the existence of co-infection, the effective strategy is to incorporate intervention strategies with Anthrax control strategies in order to control Anthrax infections.

The disease free equilibrium of the Anthrax model only and Listeriosis model only is locally asymptotically stable whenever the reproduction number is less unity and a unique endemic equilibrium whenever the reproduction number is greater than unity.

Moreover, the qualitative analysis reveals that the disease free equilibrium of the Anthrax-Listeriosis co-infection model is locally asymptotically stable whenever the reproduction number, $(\mathfrak{R}_{al})$, is less one. Anthrax-Listeriosis co-infection model exhibited the phenomenon of backward bifurcation. Biologically, the implication is that the idea of the model been locally asymptotically stable whenever the reproduction number is less than unity and unstable otherwise does not apply. The impact of Listeriosis on Anthrax infections reveals that Anthrax infections can attribute to increased risk of Listeriosis but the reverse is not the same.

## 7.2 Future Research

The three deterministic models that were formulated in this research can be extended in divers ways. The following are recommended for future research;

1. The deterministic models can be extended by employing the concept of delay differential equations. This concept can take care of period of contracting the disease and showing clinical symptoms. Delay differential equations can be employed in all the three deterministic models.

2. Epidemiological models generally dynamic in nature. Compartments can be incorporated depending on the assumptions and dynamics of the disease in question. A drug resistance compartment can be incorporated into the Anthrax disease model in further research on Anthrax disease modelling.

3. A vaccination compartment can also be incorporated into the Listeriosis disease model. The vaccination compartment can either be incorporated into the animal population or the human population.

4. The Anthrax-Listeriosis co-infection model can be extended by incorporating vaccination compartments and a drug resistance classes for both Anthrax and Listeriosis diseases. The addition of these compartments increases the complex nature of these disease dynamics.

## 7.3 List of publications

The following manuscripts have been extracted from the thesis and published in the following journals: International Journal of Mathematics and Mathematical Sciences, Global Journal of Pure and Applied Mathematics and Journal of Mathematical Theory

and Modelling. These journals are index by; Scopus, Cross Ref, Google Scholar, SCI, ISI, Index Copernicus, EBSCO, Open Access and World Cat.

1. Shaibu Osman, Oluwole Daniel Makinde, and David Mwangi Theuri. Stability analysis and modelling of Listeriosis dynamics in human and animal populations. Global Journal of Pure and Applied Mathematics, 14(1):115–137, 2018.

2. Shaibu Osman, Oluwole Daniel Makinde, David Mwangi Theuri. Mathematical Modelling of Transmission Dynamics of Anthrax in Human and Animal Population. Journal of Mathematical Theory and Modelling. 8(6):47-67, 2018.

3. Shaibu Osman, Oluwole Daniel Makinde, David Mwangi Theuri. A Mathematical Model for Co-infection of Listeriosis and Anthrax Diseases. International Journal of Mathematics and Mathematical Sciences. (ACCEPTED).

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