MATHEMATICAL ANALYSIS OF FOOT AND MOUTH DISEASE WITH OPTIMAL CONTROL: A CASE STUDY OF FMD IN NAMIBIA

By

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FACULTY OF HEALTH, NATURAL RESOURCES AND APPLIED SCIENCES,

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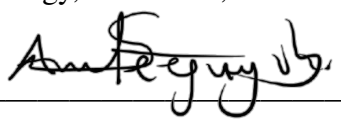
Dedication

I offer this work in loving memory of my father and brother, wishing for their souls to find everlasting tranquillity.

Certification

I certify that this project work was carried out by **Palivamwe Merolly Ndeevelo, Student number: 212013661** in the Department of Mathematics, Statistics and Actuarial Science, Namibia University of Science and Technology, Windhoek, Namibia.



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Declaration

I, **Palivamwe Merolly Ndeevelo, Student number 212013661**, hereby declare that the project titled "**Mathematical Analysis of Foot and Mouth Disease with Optimal Control: A Case Study of FMD in Namibia**" is a true reflection of my own work and that all the sources used in this study have been indicated and acknowledged by means of complete references and that this work has not been submitted for any other degree at any other institution.

_____

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(20 June 2023)

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I, **Palivamwe Merolly Ndeevelo**, being a candidate for the degree of **Master of Science in Applied Mathematics** accept the requirements of the **Namibia University of Science and Technology** to the retention and use of theses deposited in the Library and Information Services. In terms of these conditions, I agree that the thesis deposited in the Library and Information Services will be accessible for purposes of study and research, in accordance with the normal conditions established by the Librarian for the care, loan or reproduction of theses.

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Abstract

This study aims to comprehensively analyse Foot and Mouth Disease (FMD) by formulating two mathematical models specifically tailored for confined and unconfined environments in Namibia. The models composed for this research incorporate essential compartments that capture the intricate dynamics of livestock populations, including their susceptibility to FMD, latent exposure, infectiousness, and recovery. Furthermore, the models account for the implementation of optimal control measures by farmers and the disease control mechanisms employed by national institutions such as the vaccination campaign, culling and quarantining of livestock.

To ensure the stability and equilibrium of the proposed models, well-established mathematical principles such as the LaSalle Invariance principle, Lyapunov function and Routh-Hurwitz stability analysis are utilized. These methods assist in determining the equilibrium points of the models and assessing their stability properties. In addition, historical data on FMD reported cases within the country is also incorporated to enhance the accuracy and applicability of the models analyses.
The study utilises numerical simulations with an Ordinary Differential Equation (ODE) solver in Python to demonstrate the impact of various scenarios of FMD progression. Furthermore, an excel-input data sheet is created to facilitate basic analysis and to showcase the variability range resulting from modifications in FMD dynamics.

By employing a combination of mathematical modelling, stability analysis, historical data integration, and numerical simulations, this research provides significant insights into the behaviour and control of FMD in confined and unconfined environments in Namibia. The findings

contribute to the existing knowledge of FMD in Namibia and provide insights that can inform decision-making and policy formulation in combating this economically significant disease.

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Chapter 1

Introduction

The introductory section of this study presents information on the background of FMD in Namibia as a framework, reasons for conducting the study and what it entails to achieve together with its significance in controlling the disease. Additionally, a summary of the entire study is provided at the conclusion of this chapter.

1.1 Background of the Study

Mathematical analysis deals with theories of differentiation, integration, limits, measure and analytic functions that are applied to physical, economical, biological and other real-world models. Various examples of such applications can be found in the work of [9], [39], [54], [53], [59], [11], [15] whose results justified the practice of control measures against infectious diseases from the mid-17th century. These applications form the base of mathematical analysis in studying a commonly known livestock foot and mouth disease which pose serious impact on Namibia's livestock industry. According to [56], FMD is a transboundary animal infection that significantly impacts the productivity of livestock, leading to disruptions in both regional and international trade of animals and animal-based products.

Multiple mathematical models have been created to depict the spread of infectious diseases, with origins tracing back to the 20th century when Kermack and McKendrick introduced the classical Susceptible-Infectious-Recovered (SIR) model to analyse epidemics of plague and cholera in London and Bombay. According to [11], the SIR model has been widely utilized as a fundamental framework for numerous subsequent infectious disease models.

In the study conducted by [32], a basic classical SIR model was developed to investigate the

transmission of FMD in Namibia. This simplified model divided the population into three compartments, allowing for a clearer understanding of the more intricate epidemiological modelling outcomes.

Different epidemiological studies extended the classical SIR model by including demographics such as birth and death. Furthermore, extension of the SIR model framework can be applied in multiple ways such as by including seasonality to show whether infectious disease epidemic has sustained cycles or by implementing additional compartments capturing the behavioural and biomedical control interventions [41].

Analysis of extended demographic models depict information on the cycle of an infectious disease epidemic and endemic level. The distinction between epidemic models and endemic models lies in their temporal scope. Epidemic models are employed to depict the rapid spread of diseases within a time frame of less than one year. On the other hand, endemic models are utilized to investigate diseases that persist over extended periods, characterized by the continual replenishment of susceptible individuals through factors such as birth or the recovery from temporary immunity [28].

Understanding Foot and Mouth Disease

The awareness and efforts to control FMD can be traced back to several centuries ago. It was the first disease affecting cloven-hoofed ruminants for which the viral cause, FMD virus (FMDV), was demonstrated by Loeffler and Frosch [22]. FMD is attributed to a genus Aphthovirus, which belongs to the Picornaviridae family. This genus encompasses seven serotypes that are immunologically distinct: serotypes A, O, C, South African Territories (SAT-1, SAT-2, SAT-3), and Asia-1 [33]. It is important to note that these serotypes do not confer cross immunity.

Within the various serotypes, there exists a virus infection-associated antigen (VIA) that exhibits group reactivity and holds significant importance in the serological diagnosis of FMD infection. To date, the identification of over 60 subtypes of the virus and the ongoing emergence of new subtypes exemplifies the dynamic nature of the phenomenon under investigation. According to the manual of diagnostic tests and vaccines for terrestrial animals by the World Organisation for Animal Health (OIE), the ongoing generation of novel FMDV variants is a re-

sult of the persistent mutation arising from error-prone RNA replication, recombination events, and selective pressures imposed by the host. These dynamic processes contribute to the continuous evolution and diversification of the FMDV population [58].

According [12], the high contagiosity of the disease enables the rapid spread of viral infection among cloven-hoofed ruminants, including cattle, sheep, goats, African buffaloes, and swine. In the study of [5] it was recognised that cattle can sustain FMDV for a maximum of 3 years and 6 months while African buffaloes sustain the virus for up to 5 years. The study of [56], characterised FMD as a disease that primarily spreads via direct contact between animals. At the same time secondary transmission occurs via shared water points, shared pasture, or via airborne with viral spores carried by the wind.

The incubation period of FMD is a function of multiple variables, including the species of the infected cloven-hoofed ruminant, the strain of the FMDV, the route of inoculation, and the dose of the FMDV, [8]. According to [38] and [29], the reported FMD incubation period for livestock population ranges between 2 to 14 days after contact with an infectious cloven-hoofed ruminant. Empirical evidence obtained through veterinary laboratory observations demonstrates that the FMDV elicits a significant elevation in body temperature in infected animals, denoted as a high fever, with a duration typically ranging from 2 to 6 days ($T \in [2,6]$). This fever is subsequently accompanied by the appearance of vesicular lesions in the oral cavity and interdigital spaces of the hooves, leading to excessive salivation and impaired ambulation, manifesting lameness, and reduced appetite.

The infectious period for livestock affected by FMD extends for approximately 7 to 10 days. During this period, infected animals exhibit symptomatic manifestations of the disease and continue to be a source of infection. The outcome of the infection, whether recovery or mortality, is influenced by factors such as age and pre-existing immunity. It is important to note that the mortality rate associated with FMD is generally low, albeit subject to variations [38]. As indicated by [33], the estimated fatality rate for adult livestock in the context of FMD falls within the range of 0 to 5 per cent. Figure 1.1 illustrates the graphical depiction of the clinical manifestations associated with FMD.

Figure 1.1: FMD clinical signs

Surveillance of Foot and Mouth Disease

The government of the Republic of Namibia facilitates a mycobacterium surveillance strategy that was implemented through passive and active surveillance of FMD in the country. Passive surveillance involves investigating reported suspect clinical cases of livestock through ante and post-mortem examination of organs or intradermal testing. While active surveillance involves testing livestock and examination of carcasses at slaughter facilities using intradermal testing before exporting or importing stock.

According to [34], mycobacterium surveillance is considered the standard method for routine confirmation of FMD infection. However, rapid nucleic acid techniques like polymerase chain reaction (PCR) are also utilized for confirming FMD cases. The Namibian surveillance strategy covers three demarcated zones:

1. Zone 1: The FMD Infected Zone

   This geographic area covers the Zambezi region due to the periodic occurrence of FMD. As highlighted by the [25], controlling the disease in this zone poses significant chal-

lenges due to its inclusion in the Kavango Zambezi Trans-Frontier Conservation Area (KAZA). The area is inhabited by African Buffaloes, known carriers of the FMD virus, making the disease control efforts more complex.

2. Zone 2: FMD Protection Zone

   This geographic area is also known as the FMD Containment Zone due to the current outbreak within the area. The zone covers Kunene, Ohangwena, Oshikoto, Oshana, Omusati, Kavango East and West region. The Meat Board reported that this zone creates a barrier to FMD by preventing the disease from spreading into the FMD Free zone. Historically, the FMD Containment Zone was free from FMD for 40 years. But due to an open border between Namibia and Angola, animals from the two countries basically share pastures and water points, exposing the zone to FMD infection, [25].

3. Zone 3: FMD Free Zone (Commercial Area)

   This geographic area is separated from the FMD Containment zone, which includes a double stock physical barrier proof of game fence called the Veterinary Cordon Fence (VCF). The VCF cut through from Palgrave Point on the west coast of Namibia and cut through to a point on the common border-point between Namibia and Botswana, with entry and exit frontier posts along the fence. In addition to the physical barrier, the Ministry of Agriculture and Land Reforms have deployed Veterinary officers at each frontier post to disinfect necessary materials and conduct inspection on possible contaminated items that flows into the FMD Free Zone, especially during outbreaks seasons.

The northern part of the VCF comprises zones 1 and 2, that form the Northern Communal Area (NCA), while the whole southern part is composed of zone 3 alone that forms the Commercial area.

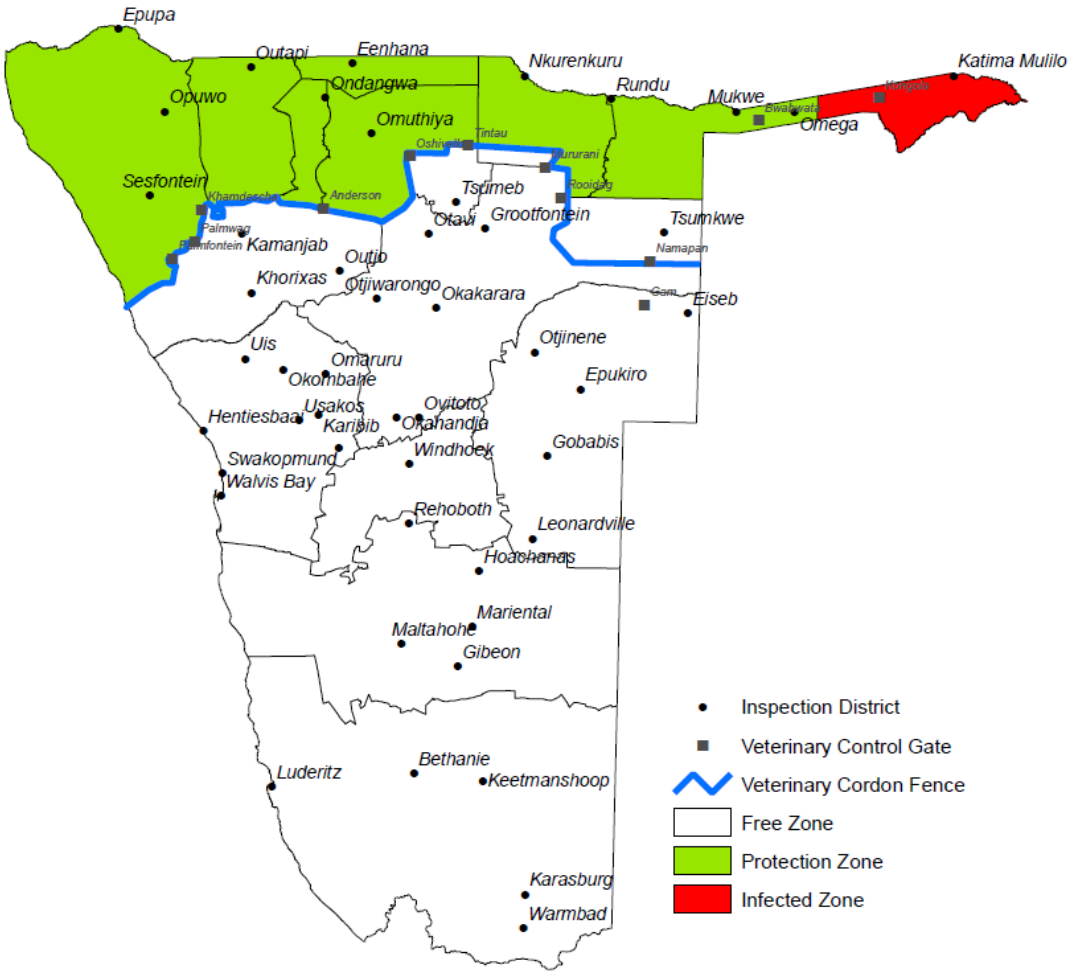

Figure 1.2: Map of Namibia FMD inspection districts and zones

According to [24], the ongoing global prevalence of FMDV infection is sustained across three continental reservoirs in Africa, Asia, and South America. These reservoirs are further divided into seven main infection pools, each encompassing multiple serotypes of the virus. Due to the predominant circulation of the virus within these regional reservoirs, viral strains have evolved and become region-specific strains. This necessitates the development of customized vaccines, particularly for type A and SAT viruses.

The global distribution of FMDV is characterized by an association with economic development, where prosperous nations have successfully eliminated the disease, while developing countries face challenges due to resource limitations and inadequate infrastructure. The attainment of FMD-free status presents significant trade opportunities for countries with potential for livestock exports, thereby incentivising investments in veterinary services and FMD control measures, [55]. However, the substantial investment required to ensure a sustainable export

flow may be unattainable or economically unfeasible, particularly for countries that are net importers of livestock and related products. Consequently, many nations do not prioritize the eradication of FMD as a primary objective.

The geographical region encompassing the reservoir of SAT 1 to 3 viruses transcends traditional political and economic boundaries. This reality has significant implications, as the FMD problem is beyond the scope of individual countries to address independently, and the responsibility is often perceived to lie with a third party. Furthermore, national efforts to enhance FMD control are impeded by the risk of cross-border infection transmission from neighbouring countries. Consequently, there has been limited progress in reducing the prevalence of FMD infection within most of the existing reservoirs over the past four decades.

The figure below (Figure 1.3) depicts the inferred national FMD status overlaid with the regional distribution of FMDV pools and the predominant serotypes of the virus (adapted from the FMD World Reference Laboratory website http://www.wrlfmd.org/).

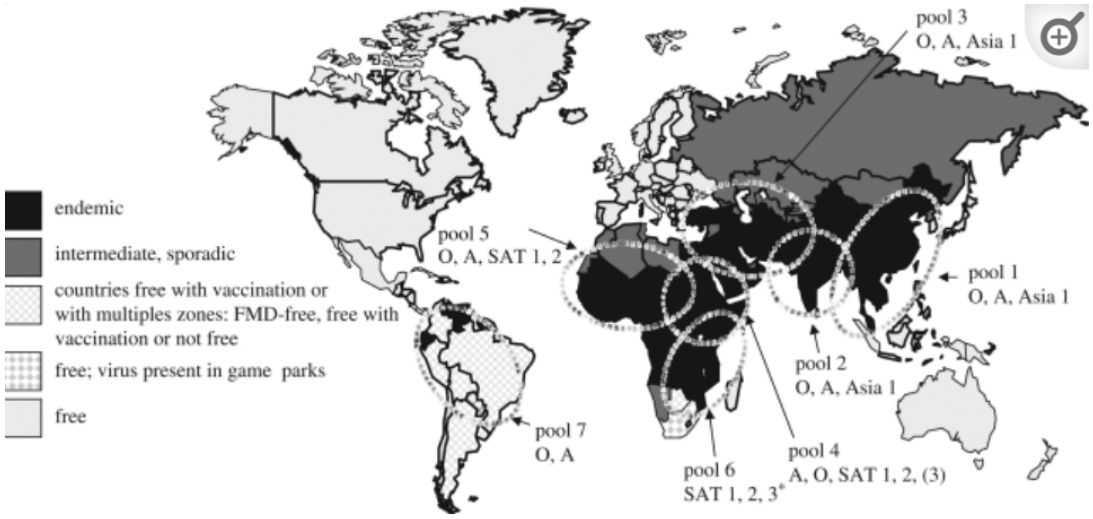

Figure 1.3: Country FMD Status Map

Control Mechanisms and Prevention of Foot and Mouth Disease

FMD prevention and control strategies aim to mitigate the spread of the disease and minimize its impact on livestock populations. These mechanisms encompass various measures and interventions to reduce the transmission of FMDV, enhance biosecurity, and manage outbreaks

effectively, [58].

According to [8], [12], [34] and [33], the essential elements of preventing and controlling FMD consist of:

1. Vaccination Programs:

   Vaccines play a crucial role in conferring immunity against specific FMDV serotypes. Vaccination campaigns target susceptible livestock populations, particularly in endemic regions or areas at high risk of FMD outbreaks.

2. Surveillance and Early Detection:

   Active surveillance systems are implemented to monitor the presence and circulation of FMDV. Early detection of FMD cases allows for prompt response and containment measures to prevent further spread.

3. Biosecurity Measures:

   Strict biosecurity protocols are essential to prevent the introduction and transmission of FMDV. These measures include quarantine procedures, restricted animal movement, proper disinfection, and hygiene practices within livestock facilities.

4. Control of Animal Movement:

   Restricting the movement of livestock, especially in outbreak-affected areas, helps contain the spread of FMD. Movement controls can involve regional restrictions, animal movement permits, and tracing systems to monitor the movement of susceptible animals.

5. Education and Awareness:

   Public awareness campaigns and educational programs aim to inform livestock owners, farmers, and other stakeholders about FMD risks, prevention measures, and the importance of early reporting of suspected cases.

6. Rapid Response and Containment:

   Timely response to FMD outbreaks is crucial to limit the disease's impact. Rapid containment measures, including culling infected and at-risk animals, implementing quarantine zones, and disinfection protocols, help prevent further disease transmission.

7. International Collaboration:

   Cooperation and information sharing between countries and international organizations are vital for effective FMD prevention and control. Collaborative efforts facilitate the exchange of knowledge, resources, and best practices to combat FMD on a global scale.

By implementing these comprehensive prevention and control mechanisms, countries can reduce the incidence and impact of FMD, safeguard livestock health, and protect the economic interests associated with the livestock industry.

According to the [58], there are two approaches for prophylaxis in controlling and preventing FMD. These two methods are outlined as follows:

Sanitary Prophylaxis

The approach of sanitary prophylaxis, as outlined by [58], includes the following measures:

1. Border animal movement control and surveillance to protect free zones.
2. Implementation of quarantine measures.
3. Slaughter of infected, recovered, and FMD-susceptible contact animals.
4. Thorough cleaning and disinfection of premises and all contaminated materials.
5. Proper disposal of carcasses and contaminated animal products within the infected area.

Medical Prophylaxis

The medical prophylaxis approach involves the use of vaccines, specifically inactivated and live attenuated vaccines. However, caution is needed with live attenuated vaccines due to the risk of reversion to virulence. The use of conventional live FMD vaccines may also hinder the detection of infection in vaccinated animals.

Traditional FMD vaccines consist of chemically inactivated cell-culture-derived preparations of a seed virus strain blended with suitable adjuvants and excipients. These vaccines can be categorized as either standard potency or higher potency vaccines.

1. Standard Potency Vaccines (commercial vaccines):

   These vaccines contain sufficient antigen and appropriate adjuvants, providing a minimum potency level of $3PD_{50}$ (50 per cent protective dose). After two initial vaccinations given 1 month apart, they provide six months of immunity. The selection of vaccine strains is based on their antigenic relationship with circulating strains, and many vaccines are multivalent to ensure broad antigenic coverage against prevailing strains.

2. Higher Potency Vaccines (emergency vaccines):

   These vaccines contain sufficient antigen and adjuvants, offering a minimum potency level of $6PD_{50}$ (50 per cent protective dose). They are recommended for vaccination in populations that have no previous exposure to FMD. These vaccines provide a wider spectrum of immunity and rapid onset of protection.

In addition to these prophylaxis methods, a progressive control pathway for Foot and Mouth Disease (PCP-FMD) has been developed by the FAO. The PCP-FMD is a framework for designing FMD control programs in countries where FMD is still endemic [12]. It aims to progressively reduce the impact of FMD and the load of FMDV. The PCP-FMD consists of several stages of control activities, as depicted in Figure 1.4. Implementation of these stages enables countries to increase their level of FMD control, leading to successful applications for OIE endorsement of a national control program vaccination or official freedom from FMD with or without vaccination, depending on the stage reached, [33].

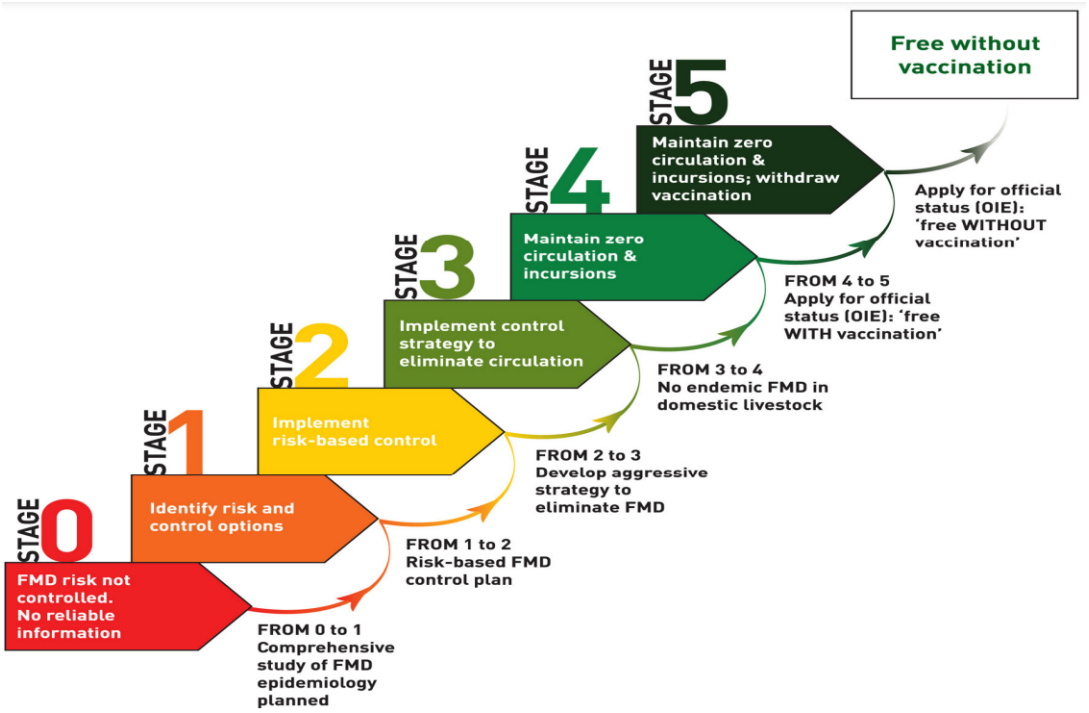

Figure 1.4: FMD control activity Stages

1.2 Statement of the Research

The nature of an FMD virus is so remarkable for its environmental resistance as Namibia continues to experience sporadic outbreaks of FMD, especially in its northern communal areas. In normal circumstances, the disease causes high morbidity and low mortality with massive economic impact of isolating infected countries from the global livestock trade market, especially when there is a failure to implement control measures in infected and exposed areas.

Namibia is among the listed FMD infected Southern African Development Community (SADC) members and it is currently being investigated on the production of FMD-free livestock commodities exported to the United Nation of America and the Republic of China [50].

To mitigate the economic and welfare impact of FMD, vaccination of susceptible livestock is an effective measure. However, it is crucial that the vaccine closely matches the specific strain and serotype responsible for FMD. Furthermore, the duration of protection provided by the vaccine is typically limited, lasting around 12 months or less, as noted by [43].

A significant challenge lies in maintaining high levels of vaccination and herd immunity within livestock populations, particularly in developing countries. This necessitates the presence of

advanced vaccine manufacturing capabilities, a robust delivery infrastructure, and a reliable system for livestock identification. These requirements make the task of sustaining widespread vaccination and achieving optimal herd immunity a complex undertaking.

Another challenge arises from the presence and growing population of African buffaloes in northern Namibia, where there is a lack of mechanisms to control their herd size. It is important to note that African buffaloes can also be affected by the FMD virus. Once the infection infiltrates this unmanaged buffalo population, controlling the disease becomes exponentially more difficult in relation to livestock.

Despite numerous comprehensive studies conducted on FMD outbreaks and other diseases in the SADC subcontinent, such as those by [29], [30], and [26], the existing biological and veterinary knowledge has not been extensively quantified to develop a complex model capable of accurately encompassing all the mechanisms of disease transmission within both confined and unconfined environments. Although there is great potential to gather a significant amount of data on the location and movement of livestock, compared to the understanding of buffalo interactions, the precision of such data is still insufficient to enable definitive predictions of FMD spread. As a result, the majority of existing FMD models rely on the traditional SIR model for analysing disease transmission.

Moreover, quantifying features such as the level of biosecurity on a farm poses a challenge, as they are not typically recorded but have a significant influence on the spread of infection. Therefore, it is crucial to rely on the knowledge and expertise of veterinary practitioners and diagnostic laboratory reports for this study. In the event of an outbreak, farmers and veterinary practitioners utilize vaccines to provide broad disease protection coverage in the unconfined environment. Conversely, in the confined environment, the control measures involve the slaughtering and disposal (burial or incineration) of infected animals. This practice is considered a drastic control mechanism aimed at eradicating the disease and is often less costly compared to vaccinating or living with FMD.

Considering these aforementioned dynamics and limitations, we develop two distinct mathematical models that capture the dynamics of FMD in Namibia. The first model extends the confined environment model to incorporate control intervention mechanisms and the interac-

tion between buffaloes and livestock that is typically observed in the unconfined environment. Subsequently, these models will be utilized in a predictive approach to assess the impact of control mechanisms and disease management in both environmental settings. Ultimately, these models will enable us to draw conclusions regarding the dynamics of the biological system at the FMD-free equilibrium point.

1.3 Study Objectives

The primary objective of this study is to develop mathematical models, in the form of ordinary differential equations (ODEs), that depict the progression of FMD in two distinct environmental settings in Namibia: the confined environment and the unconfined environment. The focus is on assessing optimal control solutions for disease management. The specific objectives of this study are as follows:

(i) Formulate mathematical models for FMD progression in both the confined and unconfined environments.

(ii) Derive the basic reproduction number (R_0) of FMD, which indicates the average number of secondary infections caused by a single infected individual.

(iii) Determine the FMD-Free Equilibrium (DFE) point, which represents the disease-free state.

(iv) Determine the FMD Endemic Equilibrium point, which represents the long-term equilibrium with a persistent presence of the disease.

(v) Determine the optimal control solution for managing FMD in each environment.

Guidelines for Objectives

These study objectives are accomplished through two modules:

1. Module 1: Mathematical Formulation and Analysis of the Confined Environment FMD Model

In this module, the progression of FMD is mathematically formulated and analysed in a closed, homogeneous population. The focus is on optimal control measures such as livestock vaccination. The study assumes no herd mixing in the confined environment and that livestock do not share pasture with FMD carriers, specifically African buffaloes.

2. Module 2: Mathematical Formulation and Analysis of the Unconfined Environment FMD Model

   This module formulates and analyse the progression of FMD in heterogeneous populations across two neighbouring locations. The study incorporates optimal control measures involving livestock quarantine and vaccination. It assumed herd mixing in the unconfined environment and knowledge that livestock share pastures with the FMD carrier.

The division of the study into two modules provides a competitive advantage by offering an asymmetric reward in understanding the dynamic progression of FMD in Namibia. The assumptions made in each module are supported by direct and sufficient evidence, particularly regarding the geographical distribution of African buffaloes along Namibia's interface.

1.4 Research Methodology

Extensive discussions of applicable methodologies of the study are detailed in chapter two of this study. The study formulated two mathematical models of FMD progression, namely the 'Susceptible, latently Exposed, Infectious and Recovered' (SEIR) model and the 'Susceptible, latently Exposed, Infectious, Quarantined, and Recovered' (SEIQR) model in attempts to systematically describe the progression of FMD amongst livestock populations in the two environmental settings.

In the absence of a memorandum of understanding (MoU) between the researcher and primary data provider, a desktop review of all the latest available secondary data or information related to FMD in Namibia was conducted and the procedure included direct observation of data from exclusive electronic media, literature, and the application of formal objective data measurement, which is more of the technical know-how of the disease amongst livestock in both confined and unconfined environments.

The data was pre-processed and analysed to avoid duplicate and missing values, following basic quality standards of data processing under the statistical environment. The study employs the LaSalle Invariance principle, Lyapunov function and Routh-Hurwitz stability analysis to determine the equilibria of both models, while the Pontryagin's maximum principle was used in finding the optimal control of the two models. The numerical simulation is conducted using ODE solver in Python which was performed on an 11th-generation Intel(R) Core(TM) i7-1185G7, 3.00GHz, 32 GB with a 64-bit operating system.

An Excel-input data tool for educational purposes was also implemented to capture numerical simulations as parameter changes. In addition, another Excel spreadsheet on livestock population for FMD distribution by district and region is provided as well. The developed simulation scripts and codes can be accessed in the appendices, while the Excel illustration tool and district data form part of the study's supplementary materials.

Equations involving a function and its derivatives are explored for the ODE model's formulation and these models encompass a collection of differential equations that depicts information about compartmental inflow and outflow of livestock. The two models of *SEIR* and *SEIQR* with a latency period between livestock becoming infectious and being infected by an FMDV during an outbreak are discussed separately in modules 1 and 2 of this study.

The latter model is designed for the unconfined environment where quarantining of livestock and herd mixing in two neighbouring locations were exercised. Some preliminary concepts, stability definitions and discussion of methodologies that describe the framework of this study are detailed in Chapter 2 under Supporting Mathematical Theories and Preliminaries Concepts section. These mathematical concepts are utilized in developing the two models and performing analyses, which will be described and demonstrated in the proceeding chapters. To distinguish them from the numbering of Chapters to Chapters, both equations and figures are assigned numbers specific to their respective domains.

1.5 Significance and Importance of the Study

This study holds significant value in the field of infectious disease research, specifically in the formulation of an infectious disease model that incorporates both behavioural and biomedical

control interventions for FMD. By including these interventions, the study aims to provide a comprehensive analysis of the disease's progression, surpassing the limitations of classical SIR models commonly used in similar studies.

The inclusion of behavioural and biomedical interventions in the formulated models enables a more realistic and nuanced analysis of FMD dynamics. This comprehensive approach allows for a better understanding of the effectiveness of control measures and provides valuable insights into the impact of these interventions on disease transmission.

One key aspect of the study is its focus on capturing information on different FMD interventions within the two environmental settings of Namibia. This expands the analysis and ensures that the findings are both significant and applicable. The precise analysis of these models is crucial, as it allows for a comprehensive assessment of the frequency, severity, and control mechanisms of FMD, while also considering potential unintended consequences.

Furthermore, this study fills an important gap in the existing literature by formulating mathematical models that capture the dynamics of FMD transmission in both confined and unconfined environmental settings of Namibia. The models developed in this study will serve as valuable tools for animal health officials in raising awareness about the threats and progression of FMD within communities. Moreover, they will support the development of effective disease eradication programs and aid in the quantitative assessment of control measures.

The findings of this study will have practical implications for disease control policy and decision-making. By providing a better understanding of FMD transmission dynamics and the effectiveness of interventions, the results can inform strategic disease control interventions, promote better decision-making processes, and track progress towards achieving FMD-free status in Namibia.

Additionally, the study contributes to the advancement of epidemiological modelling and serves as a monitoring tool to shed light on the underlying mechanisms of infectious diseases. The application of mathematical models to FMD surveillance data allows for the exploration of scientific hypotheses and the quantitative assessment of different control strategies.

Moreover, the study acknowledges the presence of African buffaloes and their significant role in FMD transmission. By considering empirical evidence and capturing the spread of FMD in

livestock, the models developed in this study provide valuable insights into the dynamics of FMD transmission in the presence of buffaloes.

Overall, the output of this study is expected to guide decision-making, improve existing theories, identify research gaps, and contribute to future epidemiological studies. By providing guidance for disease control interventions and tracking progress towards FMD-free status, this study has the potential to make a meaningful impact in the field of FMD research and control efforts in Namibia.

1.6 Limitations of the Study

While this study contributes valuable insights into the dynamics of FMD transmission in Namibia, it is important to acknowledge certain limitations that may impact the generalization and applicability of the findings.

Firstly, it should be noted that this study focuses on two distinctive models as outlined in the Methodology section. While more extended models exist in the literature, the scope of this study is limited to these specific models. The population considered in the models is based on the livestock population in the confined and unconfined environments of Namibia, as observed through consolidated data from electronic media and literature. However, it is essential to recognize that the specific characteristics of other regions or countries may differ, and caution should be exercised when extrapolating the findings to different contexts.

The analysis of FMD in this study is primarily based on the investigation of the most recent catastrophic outbreak in Namibia, relying on reported cumulative cases across various districts in commercial and communal areas. It is crucial to acknowledge that the accuracy and completeness of the reported data may vary, and the study is reliant on the availability and reliability of the data sources used.

The numerical solutions presented in the study utilize data referenced from the Namibia Meat Board and the Ministry of Agriculture, Water and Land Reforms (MAWLR). However, it is important to note that certain parameter values were estimated using historical data to address any deficiencies in the reviewed data. While efforts have been made to ensure the accuracy of the parameter values, there may still be uncertainties associated with these estimations.

Furthermore, it is important to clarify the interpretation of hyphens (-) and zeros (0) in the tables or data presented. A hyphen (-) represents a value of zero, while a zero (0) indicates insignificant values. This distinction is crucial for understanding the significance of certain parameters or variables in the models.

It is important to acknowledge the limitations related to the application of the models to FMD data. While the sets of ODEs used in this study can be applied to various infectious diseases, it is essential to consider the specific characteristics of FMD. For example, the models in this study neglect the infectivity of livestock during the latency period, and they also do not account for unreported cases. These factors may impact the accuracy of the models and their ability to fully capture the spread of FMD within the population.

Additionally, the models assume constant parameter values, which may not reflect the dynamic nature of FMD transmission and recovery rates over time. It is important to recognize that these rates may vary and evolve as the disease progresses, which could have implications for long-term simulations and predictions.

In conclusion, while this study provides valuable insights into FMD dynamics in Namibia, it is crucial to consider the limitations outlined above. Future research should aim to address these limitations and further refine the models to enhance their accuracy and applicability in capturing the complexities of FMD transmission.

1.7 Outline of the Study

This study consists of five chapters that collectively provide a comprehensive analysis of FMD dynamics in Namibia. The following outline summarizes the content of each chapter:

Chapter 1: Introduction

- Background and motivation of the study
- Overview of FMD biology and control measures
- Statement of the problem
- Objectives of the study

- Description of the applied methodology
- Significance of the study
- Limitations of the study

Chapter 2: Literature Review

- Review of relevant literature pertaining to FMD.
- Discussion of supporting mathematical theories, concepts, and formulated models of FMD and other infectious diseases that underpin the study's objectives.

Chapter 3: Analysis of FMD in the Confined Environment (Module 1)

- Formulation and analysis of a set of ordinary differential equations to examine FMD transmission in a confined environment
- Examination of the dynamics and implications of FMD spread in this setting

Chapter 4: Analysis of FMD in the Unconfined Environment (Module 2)

- Formulation and analysis of a set of ordinary differential equations to investigate FMD transmission in an unconfined environment
- Examination of the dynamics and implications of FMD spread in this setting

Chapter 5: Results, Conclusions, and Recommendations

- Summary of the study's findings and results obtained from the formulated models
- Interpretation and discussion of the implications of the findings
- Conclusion drawn from the analysis
- Recommendations for future research and disease control strategies

Through this structured approach, the study aims to provide a thorough understanding of FMD dynamics in both confined and unconfined environments in Namibia. The analysis will contribute to the existing knowledge base, inform disease control efforts, and provide guidance for

future research in this field.

This study concludes with a compilation of the references cited throughout the research and the inclusion of appendices containing the simulation routine codes utilized in the analysis.

Chapter 2

Literature Review

The objective of this chapter is to present a comprehensive review of the literature concerning model formulation theories, applications, and the dynamics of FMD models. The review encompasses various contextual information obtained from different studies on FMD dynamics, which serve as essential building blocks for this study.

Firstly, we delve into the contextual information derived from a range of studies focusing on the dynamics of FMD models. These studies offer valuable insights and serve as the cornerstone of our research. By thoroughly examining the existing literature, we develop a deeper understanding of the dynamics of FMD and its implications for modelling.

Secondly, we discuss supporting mathematical theories and preliminary concepts that are relevant to the mathematical analysis of the formulated models. Additionally, we explore mathematical models that incorporate vaccination and quarantine as control measures. This extension of the discussion is a crucial aspect of our study, as it allows us to explore more comprehensive models that account for these vital interventions.

Furthermore, this chapter outlines various methods employed in modelling FMD, along with their associated benefits, limitations, and results. Through a critical analysis of these methods, we identify gaps and limitations in the existing research, which motivate the need for this study. These identified gaps will guide our research towards addressing unexplored areas and making meaningful contributions to the field of FMD modelling.

Overall, this literature review establishes a solid foundation for our research by synthesizing the relevant theories, concepts, and findings from existing studies. It serves as a roadmap for the subsequent chapters of this study, providing the framework for framing the research problem

and selecting appropriate methodologies to achieve the objectives of this study.

2.1 Review of Formulated Mathematical Models for Infectious Diseases

In this section, we present a thorough examination of the mathematical models developed for infectious diseases, with special attention given to the influential contributions of A.G. McKendrick and W.O. Kermack in 1927. These distinguished public health physicians expanded upon the earlier research conducted by S.R. Ross, who was honoured with the second Nobel Prize in medicine in 1911 for his proposal of a differential equation model for malaria as a host-reactor disease [10].

The SIR model, developed by McKendrick and Kermack, continues to be a fundamental compartmental model in the field of infectious disease modelling. It has laid the groundwork for numerous subsequent models, establishing itself as a cornerstone in the field [57]. The SIR model comprises three compartments:

(i) The susceptible compartment (S) represents livestock individuals who are susceptible to the disease. If a susceptible individual encounters an infectious individual, they become infected and transition to the infectious compartment.

(ii) The infectious compartment (I) comprises livestock individuals who have contracted the disease and have the ability to transmit it to susceptible individuals.

(iii) The removed compartment (R) encompasses livestock individuals who have either recovered from the disease and moved into the removed compartment or have experienced natural or disease-related deaths. In most studies, the number of deaths is typically considered negligible compared to the total population. This compartment is also referred to as the recovered or resistant compartment.

The SIR model plays a fundamental role in comprehending the dynamics of diseases and has been extensively utilized to simulate the spread and control of infectious diseases. A significant contribution of McKendrick and Kermack's research was the identification and formulation of the basic reproduction number, which is elaborated on independently in section 2.3 of

this thesis. They demonstrated the criticality of the basic reproduction number in determining whether a disease will propagate or decline within a population. Moreover, their work highlighted the significance of population-level factors, including infection rates, recovery rates, and contact rates, in influencing the dynamics of disease transmission. They illustrated how modifications in these parameters can impact the progression of an epidemic and facilitate the assessment of control measures and interventions.

According to [42], the "Intermediate Quantitative Economics with Python" online resource provides valuable insights into modelling infectious diseases. The resource presents various epidemiological models, including the SIR model, which is commonly used to study the spread of infectious diseases. By utilizing Python programming, researchers can simulate and analyse the dynamics of disease transmission, such as the FMD, through differential equations. This modelling approach allows for the investigation of different scenarios and intervention strategies to better understand and control disease outbreaks.

In an investigation carried out at the Kruger National Park in South Africa, [20] expanded the SIR model by constructing a stochastic quantitative model to evaluate the annual risk of FMD transmission from buffaloes to livestock herds. The primary objective of their study was to propose improved control strategies for reducing FMD infection in the cattle population and gaining insights into the transmission dynamics between livestock and buffalo populations. According to the model results, immunizing the livestock population was identified as the most effective measure for safeguarding against FMDV. The study also revealed that FMDV transmission had a higher likelihood of occurring when livestock and buffaloes interacted within the national park, particularly through shared water points. Considering these findings, the authors recommended minimizing interaction between livestock and buffaloes in the absence of additional control measures.

Using data from the 2001 UK epidemic, [48] conducted a study that introduced a probabilistic model for FMD transmission. The main objective of their research was to investigate the

optimal implementation of reactive ring vaccination, considering the limited capacity available for vaccination of livestock. The study underscored the importance of reactive vaccination as a valuable tool for controlling future FMD epidemics and suggested that culling of vaccinated livestock was unnecessary. The optimal size of the vaccination ring was found to depend on logistical factors and exhibited robustness to changes in epidemiological parameters. Additionally, the study explored alternative approaches to reactive vaccination, such as targeting farms or herds near previously reported cases.

[30] introduced an optimal control problem in their study by developing a mathematical dynamic model specifically for FMD in Zimbabwe. Their model considered the implementation of vaccination and culling strategies targeting symptomatic and infectious non-symptomatic animals. Through simulations, they demonstrated that vaccination and the identification of infectious non-symptomatic animals were the most effective control measures during FMD outbreaks. These findings align with the conclusions of [22] and [35], emphasizing the efficacy of vaccination as the primary control measure for managing FMD outbreaks.

It is worth noting that the study by [30] acknowledged limitations related to animal movement, seasonal variation, and assumptions about FMDV transmission. Their work provided valuable insights into different control measures, although it remains unclear whether they developed separate models for the two populations and the two environmental settings.

By reviewing the formulation and structure of the SIR model, we establish a basis for the subsequent analysis and modelling efforts in our study of infectious diseases. Furthermore, various modifications and extensions of the SIR model have been proposed to capture additional complexities, such as the incorporation of vaccination and quarantine as control measures. These interventions play a crucial role in addressing the specific needs of livestock farmers in Namibia and contribute to the government's ongoing efforts to enhance the country's animal health status. By implementing these measures, Namibia aims to build confidence in the safety and quality of its livestock products in both domestic and international markets.

2.2 Supporting Mathematical Theories and Preliminaries Concepts

The terms we came across are infection rate, contact rate, adequate contact rate, simple mass action incidence rate, standard incidence, saturation incidence, basic reproduction number, threshold numbers, etc. whose definitions highlights:

An infectious disease transmitted through direct contacts. For instance, the number of livestock contacted by an FMDV infective per unit of time is called a contact rate of infection and is denoted by $P(N)$. This rate depends on total population N. Once susceptible livestock get in contact with the infective, they may be infected. If we take β as the probability of infection caused by each contact, then the function βN is referred to as the adequate contact rate, which describes the infection strength of the infective and this is usually varied on the toxicity level of the FMDV and the environment situation. Infectious diseases are mostly transmitted to susceptible population through direct contact with infective stock and this results in the mean adequate contact rate of $\beta P(N)\frac{S}{N}$, which is called the infection rate. The total new infective stock in the infectious compartment is expressed as $\beta P(N)\frac{SI}{N}$, which is called an incidence of the disease. There are three types of incidence rates used in modelling infectious diseases, viz;

(i) The standard incidence, which takes into consideration the constant contact rate. i.e. $P(N) = k$ then incidence $= \frac{\delta SI}{N}$, where $\delta = \beta k$

(ii) The bilinear or simple mass action incidence, which takes into consideration the contact rate proportional to total population size. i.e. $P(N) = kN$ then incidence $= \delta SI$, where $\delta = \beta k$ which is the transmission coefficient.

(iii) The saturation incidence, which takes into consideration the constant H for which the number of susceptible is compared to when large enough. i.e. $\frac{\delta SI}{H+S}$

In summary, thresholds are basically numbers that are capable of forecasting whether the disease will persist or not over time. In the subsections below, we provide information on the

building blocks of the two distinct, but interrelated models that are formulated and analysed separately in module 1 and 2 of this study.

2.2.1 System Stability

(i) System stability is characterized by all the roots of the characteristic equation residing in the left half of the complex plane used for graphing Laplace transforms. In this case, the system is considered stable.

(ii) Marginal stability is observed when all the roots of the system are located on the imaginary axis of the complex plane used for graphing Laplace transforms. Such a system is referred to as marginally stable.

(iii) System instability occurs when all the roots of the system lie in the right half of the complex plane used for graphing Laplace transforms. In this situation, the system is deemed unstable.

In the realm of mathematics, the Laplace transform, originally developed by the esteemed French scholar and polymath Pierre-Simon Marquis de Laplace, is an integral transformation that converts a function with a real variable into a function with a complex variable. This mathematical technique holds significant importance in the scientific community due to its ability to solve differential equations effectively. Through the application of the Laplace transform, ordinary differential equations can be converted into algebraic equations, simplifying convolution operations by replacing them with multiplication.

Now, let's examine the stability of a system by considering a non-linear time-variant system described by the equation $\frac{dy}{dx} = f(x)$, where $f : K \to \mathbb{R}$ and K is a subset of $\mathbb{R}^n$. An equilibrium point x_e in $\mathbb{R}^n$ is defined as a point where $f(x_e) = 0$. If x_e is an equilibrium point, then the trajectory $x(t) = x_e$ represents the system, which can be categorized into two stability types:

(i) Globally Asymptotically Stable (GAS): For every trajectory $x(t)$, it is guaranteed that $x(t) \to x_e$ as t approaches infinity.

(ii) Locally Asymptotically Stable (LAS): In the vicinity or at x_e, there exists a positive constant L such that if $||x(0) - x_e|| \leq L$, then $x(t) \to x_e$ as t approaches infinity.

Moreover, it is worth emphasizing that various forms of stability exist, such as uniform and exponential stability. Consequently, determining stability in any of these forms can be a formidable task, particularly when dealing with a nonlinear function f.

2.2.2 The Basic Reproduction Number R_0

The basic reproduction number, denoted as R_0 [2], [3], [4], [17], is a key epidemiological metric. It represents the average number of secondary infections generated by a typical infected livestock within a fully susceptible livestock population. This parameter holds significant importance as a threshold value for evaluating the severity of an epidemic, especially when no intervention or control measures are in place.

Put simply, this number helps us grasp how FMD behaves and whether it will eventually disappear or continue to exist. It is calculated when no vaccination, quarantine or culling of livestock is administered. When control measures are considered, they will impact R_0 to decrease and provide different perspectives on the epidemic severity status. In epidemiological models, when $R_0 = 1$, it means that one infected individual is expected to transmit the disease to exactly one susceptible individual. If $R_0 < 1$, it suggests that the disease is unlikely to cause an outbreak. However, if $R_0 > 1$, it indicates that each infected individual is likely to infect at least one susceptible individual, regardless of the environmental conditions. It is important to note that, for the purpose of this study, it is important to consider that the occurrence of an epidemic is not guaranteed solely based on R_0, as there may be additional probabilistic factors that are not accounted for in the scenarios.

The next-generation matrix method is employed to calculate R_0 and analyse the overall stability of equilibrium points in the models. This method involves computing the largest eigenvalue of the next-generation matrix, which acts as a threshold for assessing stability.

In the study by [54], the next-generation matrix method was applied to determine R_0 in a compartmental disease transmission model based on a system of ordinary differential equations

(ODEs). This method, which is relatively recent, proved to be valuable in evaluating the stability of the foot and mouth disease-free equilibrium (FMD-FE) state.

The FMD-FE state represents a scenario where the entire population consists of uninfected livestock (i.e., $S > 0$ and $E = I = R \leq 0$). By utilizing the next-generation matrix method, R_0 is obtained as the largest eigenvalue of the next-generation matrix, which separates the FMD infectious models into two rate matrices. These matrices are commonly known as matrix F, which represents the path to the infection compartment, and matrix V, which encompasses the dynamics of compartments E, I, R, and S.

The Control Reproduction Rate

The control reproduction rate, customary denoted by (R_c) is defined as the rate at which transmission occurs in the livestock population that is not entirely susceptible due to the presence of control measures intervention. R_c plays a vital role as a threshold parameter that measures the effectiveness of control measures carried out in the attempt to control the disease outbreak.

In the presence of an FMD outbreak, the actual numerical value of R_c can be used to draw some important analysis, such as the prevalence of FMD at peak, the initial growth rate of the outbreak and proportion of infected livestock. Bifurcation is defined as the changes in the qualitative behaviour of the model as parameters are varied.

For example, when control measures are induced to eliminate FMD, the model will exhibit forward bifurcation at $R_c = 1$. An example illustrating forward bifurcation is presented in figure 2.1 below, where K denote the force of FMD infection.

If $R_c < 1$, the FMD model will eventually reach the FMD-FE state, and FMD will be eradicated. On the contrary, if $R_c > 1$, it is an alarming situation, which will lead to FMD becoming endemic.

2.2.3 Routh-Hurwitz Principle

The Routh-Hurwitz principle (or criterion) is a mathematical test that provides sufficient conditions for determining the stability of linear time-invariant dynamical models or control systems. It offers a method to assess whether all the roots of the characteristic polynomial of a linear

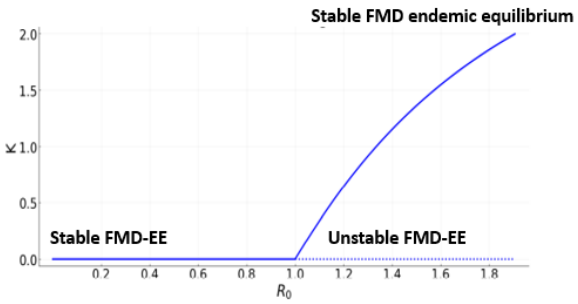

Figure 2.1: Forward bifurcation when livestock FMD death rate is 0.02

model have negative real parts [36].

In 1876, the English mathematician Edward John Routh introduced the Routh test as an efficient recursive algorithm for stability analysis. This test involves organizing the polynomial coefficients into a matrix known as the Routh array. By examining the sign patterns of specific determinants in the Routh array, one can determine the stability of the polynomial.

In 1895, the German mathematician Adolf Hurwitz independently proposed an alternative approach. He suggested arranging the coefficients of the polynomial into a square matrix called the Hurwitz matrix. Hurwitz demonstrated that the polynomial is stable if and only if all the determinants of its principal submatrices are positive.

Both procedures are equivalent, with the Routh test providing a more efficient means of computing the determinants of the Hurwitz matrix compared to direct computation.

Advantages of the Routh-Hurwitz Principle

(i) The system's stability can be easily evaluated without the necessity of solving the equation.

(ii) It is possible to determine the range of values for parameter K that guarantees stability.

(iii) The point of intersection between the root locus and the imaginary axis can also be determined.

Limitations of the Routh-Hurwitz Principle

(i) The Routh-Hurwitz criterion does not provide the exact locations of poles in the left or right half of the complex plane, where Laplace transforms are graphed.

(ii) The principle is only applicable to linear systems.

(iii) It is valid only for characteristic equations with real coefficients.

Example 2.1.

Let's examine the nth-degree characteristic polynomial with real constant coefficients:

$$P(S) = S^n + x_1 S^{n-1} + x_2 S^{n-2} + ... + x_{n-1} S + x_n$$

If all the coefficients $x_1, x_2, ..., x_n$ have the same sign and no terms are missing, the Routh-Hurwitz criterion can be applied to check the stability of the system. Otherwise, the system is considered unstable. Here are the steps to apply the Routh-Hurwitz criterion:

Step 1: Arrange all the coefficients into two rows:

$$\text{Row 1:} \quad x_1 \quad x_3 \quad x_5 \cdots; \quad \text{Row 2:} \quad x_2 \quad x_4 \quad x_6 \cdots$$

Step 2: In the next step, we combine these two rows to create the third row.

$$\text{Row 1:} \quad x_1 \quad x_3 \quad x_5 \cdots; \quad \text{Row 2:} \quad x_2 \quad x_4 \quad x_6 \cdots; \quad \text{Row 3:} \quad y_1 \quad y_2 \quad y_3 \cdots$$

Where $y_1 = -\frac{1}{x_1}(x_4 x_5 - x_3 x_6)$

$$y_2 = -\frac{1}{x_3}(x_2 x_5 - x_1 x_6); \quad \text{and} \quad y_3 = -\frac{1}{x_5}(x_1 x_4 - x_2 x_3)$$

Step 3: Next, we define the Hurwitz matrices for each value of n using the coefficients x_i for $i = 1, 2, ..., n$ from the characteristic polynomial:

$$H_1 = \begin{pmatrix} x_1 \end{pmatrix}; \quad H_2 = \begin{pmatrix} x_1 & 1 \\ x_3 & x_2 \end{pmatrix}; \quad H_3 = \begin{pmatrix} x_1 & 1 & 0 \\ x_3 & x_2 & x_1 \\ x_5 & x_4 & x_3 \end{pmatrix}$$

and

$$H_n = \begin{pmatrix} x_1 & 1 & 0 & 0 & ... & 0 \\ x_3 & x_2 & x_1 & 1 & ... & 0 \\ x_5 & x_4 & x_3 & x_2 & ... & 0 \\ . & . & . & . & ... & . \\ . & . & . & . & ... & . \\ . & . & . & . & ... & . \\ 0 & 0 & 0 & 0 & ... & x_n \end{pmatrix}$$

For a characteristic polynomial with $n = 5$, the Routh-Hurwitz criterion is applied to determine the conditions for the roots of $P(S)$ to have a negative real part. According to Table 2.1, it is required that all the coefficients are strictly positive.

Table 2.1: Routh-Hurwitz Criterion

n-size	Additional conditions	Coefficient signs
5	$(x_1x_4 - x_5)(x_1x_2x_3 - {x_3}^2 - {x_1}^2x_4) > x_5(x_1x_2 - x_3)^2 + x_1{x_5}^2$	$x_1 > 0, x_2 > 0, x_3 > 0, x_4 > 0, x_5 > 0$
4	$x_1x_2x_3 > {x_3}^2 + {x_1}^2x_4$	$x_1 > 0, x_2 > 0, x_3 > 0, x_4 > 0$
3	$x_1x_2 > x_3$	$x_1 > 0, x_2 > 0, x_3 > 0$
2	-	$x_1 > 0, x_2 > 0$
1	-	$x_1 > 0$

Example 2.2.

Let's assess the stability of the system by examining its characteristic equation:

$$x^4 + 2x^3 + 6x^2 + 4x + 1 = 0$$

Solution

The coefficients results yield:

$$\begin{pmatrix} x^4 & 1 & 6 & 1 \\ x^3 & 2 & 4 & 0 \\ x^2 & 4 & 1 & 0 \\ x^1 & 3.5 & 0 & 0 \\ x^0 & 0 & 0 & 0 \end{pmatrix}$$

$$y_1 = -\frac{1}{2}(1(4) - 2(6)) = 4; \quad y_2 = -\frac{1}{2}(1(0) - 2(1)) = 1$$

$$z_1 = -\frac{1}{4}(2(1) - 4(4)) = 3.5; \quad w_1 = -\frac{1}{3.5}(4(0) - 3.5(1)) = 1$$

And since all the coefficients in the first columns are of the same sign, the given characteristic equation has no roots with positive real parts. Hence, the system is said to be stable.

2.2.4 Lyapunov Theory

Lyapunov theory is a mathematical framework used to draw conclusions about the trajectories of a system described by the differential equation $\frac{dy}{dx} = f(x)$, without the need to explicitly determine the trajectories themselves. A typical Lyapunov theorem takes the following form:

(i) If there exists a function $V : \mathbb{R}^n \to \mathbb{R}$ that satisfies certain conditions on V and $\frac{dV}{dt}$,

(ii) Then, the trajectories of the system exhibit certain properties.

If a function V satisfying the specified conditions exists, it is referred to as a Lyapunov function (also known as Lyapunov's second method for stability), and its existence proves that the desired property holds for the trajectories. A Lyapunov function is a scalar function used to analyse the stability of an equilibrium in an ordinary differential equation (ODE). The method of Lyapunov functions is widely used to investigate the stability of nonlinear models and is considered one of the most popular approaches in this context.

In 1892, the Russian mathematician Alexander Mikhailovich Lyapunov introduced the method of Lyapunov in his work "The general problem of motion stability." This method encompassed concepts such as linearization and the direct method. The construction of Lyapunov functions is tailored to the specific characteristics of the ordinary differential equations (ODEs) under consideration. Nevertheless, this approach is widely acknowledged as the most effective method for investigating the asymptotic behaviour of solutions. In this study, Lyapunov functions are restricted to independent ODE models of the form:

$$\frac{dy_i}{dt} = f(y_i), i = 1, 2, ..., n \tag{2.1}$$

with the zero equilibrium $P \equiv 0$.

Lyapunov Stability Theorems

The Lyapunov Stability Theorems can be described as follows:

Stability Theorem in the Lyapunov Sense

If there exists a Lyapunov function $V(X)$ in the neighbourhood U of the zero solution $X = 0$ for an autonomous system, then the equilibrium point $X = 0$ is Lyapunov stable.

Asymptotic Stability Theorem

If there exists a Lyapunov function $V(X)$ with negative definite derivatives $\frac{dV}{dt} \leq 0$ for all $X \in U$ in the neighbourhood of U of the zero solution $X = 0$ for an autonomous system, then the equilibrium point $X = 0$ is asymptotically stable.

Lyapunov Instability Theorem

Assuming the existence of a continuously differentiable function $V(X)$ in the neighbourhood of U of the zero solution $X = 0$, with:

(i) $V(0) = 0$

(ii) $\frac{dV}{dt} \geq 0$

If there exist points in the neighbourhood of U where $V(X) \geq 0$, then the zero solution $X = 0$ will be considered unstable.

Example 2.3.

Let's analyse the stability of the zero solution for the following system:

$$\frac{dx}{dt} = -2x, \frac{dy}{dt} = x - y$$

Solution

Since the system has constant coefficients and is a linear homogeneous system, we can use a quadratic form as a Lyapunov function:

$$V(x) = V(x,y) = ax^2 + bb^2$$

Here, a and b are the coefficients that need to be determined, with the exception of the origin where $V(x,y)$ is zero. The function $V(x,y)$ is clearly positive everywhere, and we can calculate its total derivative. Therefore,

$$\begin{aligned}
\frac{dV}{dt} &= \frac{\partial V}{\partial x}\frac{dx}{dt} + \frac{\partial V}{\partial y}\frac{dy}{dt} \\
&= 2ax(-2x) + 2by(x-y) \\
&= -4ax^2 + 2bxy - 2by^2 \\
&= -2b[x^2(\frac{4a}{2b}) - xy + y^2] \\
&= -2b[x^2(\frac{2a}{b}) - xy + y^2]
\end{aligned}$$

If the condition mentioned earlier is satisfied, the expression within the brackets can be rewritten as the square of the difference. Therefore,

$$\frac{2a}{b} = \frac{1}{4}$$

Which can also be written as: $8a = b$ or $a = \frac{b}{8}$ We can choose suitable values such as $a = 1$ and $b = 8$, resulting in the derivative becoming:

$$\frac{dV}{dt} = -16(\frac{x^2}{4} - xy + y^2); \quad \frac{dV}{dt} = -16(\frac{x}{2} - y)^2 \leq 0$$

Therefore, we can conclude that a Lyapunov function exists for the given system, and its derivative is negative everywhere except at the origin. This implies that the system's zero solution is asymptotically stable.

Advantages of Lyapunov Functions

(i) Lyapunov functions are useful for analysing the stability and instability characteristics of equilibrium points in both linear and nonlinear systems.

(ii) The method does not rely on knowing the precise solution $x(t)$.

(iii) The approach can be employed to examine the stability of non-oscillatory equilibrium points.

Limitations of Lyapunov Functions

(i) There is no universally applicable technique for constructing Lyapunov functions.

(ii) Lyapunov functions can be formulated as quadratic forms in homogeneous autonomous systems with constant coefficients.

2.2.5 LaSalle's Invariance Principle

The Principle, also referred to as LaSalle-Krasovskii's theorem, offers a method to demonstrate asymptotic stability even when the derivative of the Lyapunov function is only negative semi-definite.

The principle was introduced by Joseph LaSalle, an American mathematician who developed stability results for both continuous and discrete cases. LaSalle's Invariance Principle represents a version of Lyapunov's theorems that focuses on invariance and limit sets. In the early 1960s, LaSalle extended the concept of Lyapunov functions by incorporating the idea of sets of limit points and the characteristic of certain sets, where a given function maps elements from one set to another. By utilizing these concepts, LaSalle was able to demonstrate a less restrictive definition of Lyapunov functions.

To accomplish research objectives, the broader applicability of LaSalle's special cases is utilized through the utilization of calculus on measure chains and linear dynamic processes, as developed by Aulbach in their curated works from 1990 [6].

Within this study, LaSalle's invariance principle is employed to establish stability outcomes for

nonlinear models of the following form:

$$\frac{dx}{dt} = f(x(t)), x(0) = x_0 \tag{2.2}$$

In the equation above, $x(t) \in \mathbb{R}^n$ represents the state variables, $f(x(t))$ denotes the vector-valued nonlinear function that characterizes the system dynamics, and x_0 is the initial condition where the equilibrium point is located at $(f(0) = 0)$.

A set $\mathfrak{I} \subset \mathbb{R}^n$ is invariant if it satisfies the following condition: $x(0) \in \mathfrak{I} \rightarrow x(t) \in \mathfrak{I} \forall t > 0$. Additionally, two types of invariant sets are defined in relation to Equation (2.2):

(i) An invariant set is considered valid for Equation (2.2) if $x(0) \in \mathfrak{I}$ implies $x(t) \in \mathfrak{I}$ for all $t \in \mathbb{R}$

(ii) A positive invariant set is considered valid for Equation (2.2) if $x(0) \in \mathfrak{I}$ implies $x(t) \in \mathfrak{I}$ for all $t \geq 0$.

LaSalle's Theorem

LaSalle's Theorem states the following principle: Consider a system characterized by equation 2.2), where Ω is a compact and positively invariant set contained within M, which is a subset of $\mathbb{R}^n$. Let $V : M \rightarrow \mathbb{R}$ be a continuously differentiable function satisfying $\frac{dV(x)}{dt} \leq 0$ for all x in Ω. Define O as the subset of Ω where $\frac{dV(x)}{dt} = 0$. Let $\mathfrak{I}$ denote the largest invariant set within O. According to LaSalle's Theorem, for any solution originating from within Ω, as time t tends to infinity, the trajectory approaches $\mathfrak{I}$. In other words, the following limit holds:

$$\lim_{t \rightarrow \infty} (inf_{z \in \mathfrak{I}} ||x(t) - z||) = 0,$$

where $\inf_{z \in \mathfrak{I}} ||x(t) - z||$ represents the distance (or minimum norm) between the trajectory $x(t)$ and the set $\mathfrak{I}$.

It is noteworthy to acknowledge the inclusive relationship among the sets in LaSalle's theorem:

$$\mathfrak{I} \subset O \subset \Omega \subset M \subset \mathbb{R}^n \tag{2.3}$$

A formal proof of the theorem demonstrates that all trajectories $x(t)$ are bounded and converge towards a positive limit set L^+ contained within $\mathfrak{I}$ as t approaches infinity. This limit set L^+ may consist of asymptotically stable equilibriums and stable limit cycles.

Systems of Equations

As previously mentioned, a significant number of mathematical models are formulated using differential equations, serving as essential components for both linear and non-linear models. Let's examine a system comprising n first-order ordinary differential equations (ODEs) expressed as follows:

$$\frac{dy}{dt} = f(y,t,\lambda), y \in G \subset \mathbb{R}^n, t \in \mathbb{R}, \lambda \in D \subset \mathbb{R}^m \tag{2.4}$$

In this system, the sets G and D represent open subsets in $\mathbb{R}^n$ and $\mathbb{R}^m$, respectively, while λ serves as a parameter. Equation (2.4) represents a collection of ordinary differential equations (ODEs), where the function $f(y,t,\lambda)$ on the right-hand side denotes a vector field.

Definition 2.1.

A system of the form described in (2.4) is classified as linearly independent if the function f explicitly depends on time t (i.e., $f = f(y)$). Conversely, if the function f does not explicitly depend on t, then (2.4) is considered a linear dependent model.

Consider the general autonomous system given by:

$$\frac{dy}{dt} = f(y), y \in \mathbb{R}^n \tag{2.5}$$

In this case, where f is independent of time t, the function in the system (2.5) comprises terms that are either unrelated to y or have a linear relationship with t. The trajectory of a solution $y(t)$ in (2.5) encompasses the collection of all points that can be attained by $y(t)$ for a given value of t. As a result, the system can exhibit either linear or nonlinear behaviour.

To construct the phase diagram of the system in $\mathbb{R}^n$, one must plot all conceivable trajectories of $y(t)$ passing through each point. Within this diagram, there exist specific points where the vector field f becomes zero. These points, known as equilibrium points, hold crucial impor-

tance in comprehending the qualitative behaviour of solutions.

In the case of an equilibrium solution for the system (2.5), denoted as $y = y^* \in \mathbb{R}^n$, where $f(y^*) = 0$, an important result follows. If the function $f(y)$ is integrable, a fundamental autonomous system can be described as:

$$\frac{dy}{dt} = f(y), y \in \mathbb{R}$$

In this scenario, the solution is given by:

$$y(t) = y(0) + \int_0^t f(v)dv, y \in \mathbb{R} \tag{2.6}$$

This solution provides a relationship between the value of $y(t)$ and the initial condition $y(0)$, incorporating the integral of the function $f(v)$ with respect to v over the interval from 0 to t.

In general, the solution for the basic autonomous system exists when the right-hand side function f is continuous. However, it is important to note that continuity conditions, as demonstrated in the example below, do not necessarily ensure the uniqueness of solutions for a nonlinear autonomous system.

Example 2.4.

Now, let's examine the initial-value problem (IVP) described in [26].

$$\frac{dy}{dt} = 3y^{\frac{2}{3}}, y(0) = 0$$

The IVP produces two solutions passing through the point $(0,0)$. These solutions are represented by $y_1(t) = t^3$ and $y_2(t) = 0$ for all t in the set of real numbers. It is worth noting that the function $f(y) = 3y^{\frac{2}{3}}$ is continuous at $y = 0$ but it is not differentiable at $y = 0$.

Definition 2.2.

The Jacobian matrix of f at the equilibrium point y^*, denoted as $Df(y^*)$, is defined as the matrix consisting of the partial derivatives of f with respect to its variables, evaluated at y^*.

$$\left[\frac{\partial f_i}{\partial y_j}\right]_y = y^* = \begin{pmatrix} \frac{\partial f_1}{\partial y_1}(y*) & \dots & \frac{\partial f_1}{\partial y_n}(y*) \\ . & . & . \\ . & . & . \\ . & . & . \\ \frac{\partial f_n}{\partial y_1}(y*) & \dots & \frac{\partial f_n}{\partial y_n}(y*) \end{pmatrix}$$

2.2.6 The Jacobian

The Jacobian matrix is a mathematical tool that represents the matrix of first-order partial derivatives of a set of functions with respect to their variables. If we have functions denoted as $f_1, f_2, ..., f_n$, which depend on variables $x_1, x_2, ..., x_n$, the Jacobian matrix is defined as follows:

$$\left|J\right| = \begin{vmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} & \dots & \frac{\partial f_1}{\partial x_n} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} & \dots & \frac{\partial f_2}{\partial x_n} \\ . & . & . & . \\ . & . & . & . \\ \frac{\partial f_n}{\partial x_1} & \frac{\partial f_n}{\partial x_2} & \dots & \frac{\partial f_n}{\partial x_n} \end{vmatrix} \tag{2.7}$$

The Jacobian determinant, which is the determinant of the Jacobian matrix, serves as a measure to assess the functional dependence between the functions $f_1, f_2, ..., f_n$. If the Jacobian determinant, denoted as $|J|$, is equal to zero, it indicates that there is functional dependence among the functions. On the other hand, if the Jacobian determinant is nonzero, it implies that there is no functional dependence between the functions.

Example 2.5.

Let us determine whether the following functions are dependent or not using the Jacobian approach.

1. $f(x,y) = x^2 + 2xy + y^2$, $g(x,y) = \ln x + \ln y$
2. $f(x,y) = x^2 e^{3y-4x}$, $g(x,y) = 2\ln x + 3y - 4x$

Solution

1.

$$|J| = \begin{vmatrix} \frac{\partial f}{\partial x} & \frac{\partial f}{\partial y} \\ \frac{\partial g}{\partial x} & \frac{\partial g}{\partial y} \end{vmatrix} = \begin{vmatrix} 2x+2y & 2x+2y \\ \frac{1}{x} & \frac{1}{y} \end{vmatrix}$$
$$= \frac{2x+2y}{y} - \frac{2x+2y}{x} = \frac{2x}{y} - \frac{2y}{x} \neq 0$$

Therefore, f and g are not dependent.

2.

$$|J| = \begin{vmatrix} \frac{\partial f}{\partial x} & \frac{\partial f}{\partial y} \\ \frac{\partial g}{\partial x} & \frac{\partial g}{\partial y} \end{vmatrix} = \begin{vmatrix} 2xe^{3y-4x} - 4x^2e^{3y-4x} & 3x^2e^{3y-4x} \\ \frac{2}{x} - 4 & 3 \end{vmatrix}$$
$$= 6xe^{3y-4x} - 12x^2e^{3y-4x} - (6xe^{3y-4x} - 12x^2e^{3y-4x}) = 0$$

Hence, there exists a relationship of functional dependence between the functions f and g.

2.2.7 Pontryagin's Maximum Principle

The Pontryagin's maximum principle is a fundamental result in optimal control theory. It was developed by Russian mathematician Lev Pontryagin in the 1950s and is widely used in various fields such as engineering and physics. The principle provides a powerful tool for solving certain types of optimal control problems.

At its core, Pontryagin's maximum principle is used to find optimal controls for a system described by a set of ordinary differential equations subject to constraints. The goal is to determine the control inputs that optimize a certain performance criterion, usually described by an objective function.

The general formulation of an optimal control problem is as follows:

Given a dynamic system described by the state variables x and control variables u, subject to a set of differential equations:

$$\frac{dx}{dt} = f(x,u)$$

where $\frac{dx}{dt}$ represents the time derivative of the state vector x.

Here we want to find an optimal control policy $u^*(t)$ over a specified time interval $[t_0, t_f]$, that minimizes or maximizes an objective function J:

$$J = \phi(x(t_f)) + \int_{t_0}^{t_f} L(x(t), u(t), t)dt$$

where $\phi(x(t_f))$ is the terminal cost, representing the cost of the state variable x at the final time t_f.

$L(x(t), u(t), t)$ is the running cost, representing the cost at each instant t.

The Pontryagin's maximum principle states that for an optimal control policy $u^*(t)$, there exist costate variables (also called adjoint variables) $\lambda(t)$ such that the following conditions are satisfied:

1. Hamiltonian Function: The Hamiltonian function H is defined as:

$$H(x(t), u(t), \lambda(t), t) = L(x(t), u(t), t) + \lambda(t)^T f(x(t), u(t))$$

2. Maximum Principle: The optimal control $u^*(t)$ maximizes the Hamiltonian H at each point in time, subject to the system dynamics:

$$u^*(t) = \arg\max H(x(t), u(t), \lambda(t), t)$$

3. Costate Equations: The costate variables $\lambda(t)$ satisfy the following differential equations, known as the costate equations:

$$\dot{\lambda} = -\frac{\partial H}{\partial x}$$

4. Terminal Condition: The terminal condition for the costate variables is given by:

$$\lambda(t_f) = \frac{\partial \phi}{\partial x}(x(t_f))$$

By solving the costate equations backward in time from the final time t_f to the initial time t_0, and combining them with the optimal control obtained from the maximum principle, we can determine the optimal control policy $u^*(t)$ that minimizes or maximizes the given objective function J.

The Pontryagin's maximum principle is a powerful and elegant tool for solving a wide range of optimal control problems and has found applications in diverse areas of science and engineering.

Chapter 3

Module 1: Mathematical Formulation and Analysis of the Confined Environment FMD Model

This chapter presents the mathematical formulation and analysis of a deterministic model for FMD in the confined environment of Namibia. The model aims to describe the dynamics of FMD within various compartments, capturing the interactions between infected and susceptible livestock.

To facilitate comprehension, a schematic diagram is provided, illustrating the flow of FMD through different compartments as infected and susceptible livestock interact.

The formulated model for the confined interface specifically focuses on a variant of FMD that disregards reinfection. Furthermore, a rigorous mathematical analysis is conducted to establish the well-posedness of the model, ensuring its biological relevance and coherence.

3.1 Mathematical Formulation of the Model

The livestock population within the district is divided into four epidemiological compartments, each representing a distinct disease status. These compartments are mutually exclusive and provide a classification framework for the animals.

The first compartment is denoted as the susceptible class (S), which includes livestock that are currently free of the disease but are susceptible to infection. The second compartment is the latently exposed class (E), consisting of animals that have been infected with the disease but have not yet displayed noticeable clinical symptoms. The third compartment is the infectious class (I), comprising animals that are infected with the disease and exhibit evident clinical

symptoms. Finally, the fourth compartment is the completely removed class (R), consisting of animals that have recovered from the disease and acquired permanent immunity to the specific viral strain.

The total livestock population (N) is expressed as the sum of individuals in each compartment:

$$N = S + E + I + R \leq K,$$

where K represents the maximum carrying capacity of livestock within the district.

The assumption is made that livestock enter the susceptible class at a constant rate denoted as α. In this class, animals can contract FMDV through direct contact with infected livestock or exposure to airborne infectious forces. The transition from the susceptible class to the latently exposed class takes place at a rate of δSI, where δ represents the probability of FMDV transmission. Furthermore, livestock experience mortality due to natural causes at a rate of ε, as well as mortality attributed to the disease at a rate of μ.

The population of latently exposed livestock decreases as individuals transition to the infected class. This transition is determined by the rate of γE, which takes into consideration both the natural death rate εE and the disease progression. The population of infected livestock is derived from the latently exposed population that has developed symptoms and become infectious at a rate of γE. This population is subsequently reduced by natural and disease-induced deaths, occurring at a rate of $(\varepsilon + \mu)I$, as well as by the transition of livestock to the recovery class at a rate of θI.

The population of recovered livestock is subject to a decrease caused by natural deaths, occurring at a rate of εR. This assumption is made in the study, where no reinfection with the same viral strain is considered.

The presented flow diagram in Figure 3.1, along with the description provided above, gives rise to the following system of nonlinear ordinary differential equations (equation 3.1). This system serves as a model for our abbreviated *SEIR* model of FMD in the confined environment for the livestock population.

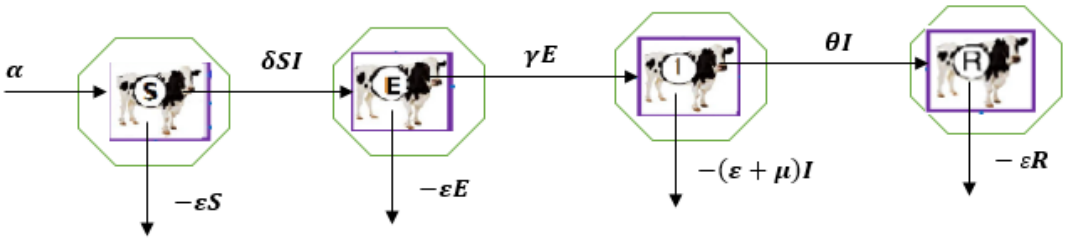

Figure 3.1: Schematic diagram depicting FMD transmission dynamics in the confined environment

$$\begin{aligned}
\frac{dS}{dt} &= \alpha - (\delta I + \varepsilon)S \\
\frac{dE}{dt} &= \delta SI - (\gamma + \varepsilon)E \\
\frac{dI}{dt} &= \gamma E - (\varepsilon + \mu + \theta)I \\
\frac{dR}{dt} &= \theta I - \varepsilon R
\end{aligned} \tag{3.1}$$

Table 3.1: Description of the *SEIR* variables

State Variables	Description
S	Livestock that are susceptible to FMDV strain infection.
E	Latently exposed livestock to FMDV strain show no symptoms and are not infectious yet.
I	Livestock that are infected with FMDV strain, showing clinical symptoms and infectious.
R	Livestock that have recovered from the FMDV strain.

3.2 Mathematical Analysis of the Confined Environment Model

Initially, the study assesses the well-posedness of the model by investigating the positivity and boundedness of the solutions for S, E, I, and R in relation to time (t). These considerations are crucial to ensure the biological significance of both the formulated environmental models in this study.

3.2.1 Positive Invariance of the SEIR Model

Given the ODE model represented by equation (3.1), it is imperative to ensure that the livestock population variables maintain non-negative values. This is crucial for establishing the epidemiological significance of the model and ensuring its biological meaningfulness. Specifically, we

aim to demonstrate that solutions of the system of equations, subject to positive initial conditions, remain positive for all $t > 0$. This condition establishes a biologically feasible region denoted by Ω, within which the model's results hold true.

To establish the positivity of solutions, we will employ a theorem and present a rigorous proof based on the literature review. By demonstrating the non-negativity of all FMD state variables, we can affirm the model's validity and its ability to provide meaningful insights into the confined environment FMD dynamics.

Theorem 3.2.1. *Positivity of Solutions: Let $S(t_0) \geq 0$, $E(t_0) \geq 0$, $I(t_0) \geq 0$, and $R(t_0) \geq 0$ represent the non-negative initial values of the FMD state variables in equation (3.1). Then, for $t \geq t_0$, the solutions $S(t)$, $E(t)$, $I(t)$, and $R(t)$ of the model satisfy $S(t) \geq 0$, $E(t) \geq 0$, $I(t) \geq 0$, and $R(t) \geq 0$.*

Proof. We begin by assuming that for $t > 0$, $N(0) \geq 0$, $S(0) \geq 0$, $E(0) \geq 0$, $I(0) \geq 0$, and $R(0) \geq 0$. To prove by contradiction, let us assume that there exists a first time t_1 such that $S(t_1) = 0$, $\frac{dS}{dt}(t_1) < 0$, and $E(t) > 0$, $I(t) > 0$, and $R(t) > 0$ for $t > t_1$. From equation (3.1), we have:

$$\frac{dS}{dt_1} = \alpha - (\delta I + \varepsilon)S(t_1)$$

Since $S(t_1) = 0$, according to our assumption, we obtain:

$$\frac{dS(t_1)}{dt} = \alpha > 0$$

However, this contradicts our assumption that $\frac{dS}{dt}(t_1) < 0$. Therefore, it must be the case that $S(t) \geq 0$ for all $t \geq 0$.

Similar reasoning applies to $E(t_2) = 0$, $\frac{dE}{dt}(t_2) < 0$, $I(t_3) = 0$, $\frac{dI}{dt}(t_3) < 0$, and $R(t_4) = 0$, $\frac{dR}{dt}(t_4) < 0$, where

$$\frac{dE(t_2)}{dt} = \delta S(t_2)I(t_2) > 0, \quad \frac{dI(t_3)}{dt} = \gamma E(t_3) > 0, \quad \frac{dR(t_4)}{dt} = \theta I(t_4) > 0$$

Hence, the solutions of the model with non-negative initial conditions remain non-negative for all $t \geq 0$. □

3.2.2 Boundedness of Solutions for the SEIR Model

Lemma 3.2.2. *By employing the methodology outlined in [45], we postulate that all solutions $S(t)$, $E(t)$, $I(t)$, and $R(t)$ are strictly positive for $t \geq 0$. Hence, it follows that these solutions are bounded for all $t \geq 0$.*

Proof. Considering the positivity of solutions in Ω, we can reduce the model (equation 3.1) to the following form:

$$\begin{aligned} \frac{dS}{dt} &= \alpha - (\delta I + \varepsilon)S \\ \frac{dE}{dt} &= \delta SI - (\gamma + \varepsilon)E \\ \frac{dI}{dt} &= \gamma E - (\varepsilon + \mu + \theta)I \end{aligned} \tag{3.2}$$

By summing the ODEs in equation (3.2), we obtain:

$$\frac{d(S+E+I)}{dt} = \alpha - (S+E+I)\varepsilon - (\mu+\theta)I \leq \alpha - (S+E+R)\varepsilon$$

By considering the supremum limit of $\frac{d(S+E+I)}{dt}$ as t approaches infinity, we obtain: $\lim_{t\to\infty} Sup[S+E+I] \leq \frac{\alpha}{\varepsilon}$ Hence, due to the positivity and upper bound of all FMD state variables by $\frac{\alpha}{\varepsilon}$, the feasible region for the confined system of ODEs is characterized as:

$$\Omega = \{(S,E,I) \in \mathbb{R}^{\mathbb{H}} : S+E+I \leq \frac{\alpha}{\varepsilon}, S > 0, E \geq 0, I \geq 0\}$$

□

3.2.3 Disease-free Equilibrium for the SEIR Model

The FMD-FE state $P_0 = (\frac{\alpha}{\varepsilon}, 0, 0)$ always exist when $I \leq I_0$. Where, I_0 is a fixed value of infectious livestock such that $0 < I \leq I_0$. That is when there is zero latently exposed and infectious livestock, the equilibrium point of the models is given by:

$$\begin{aligned} \alpha - (\delta I^* + \varepsilon)S^* &= 0 \\ \delta S^* I^* - (\gamma + \varepsilon)E^* &= 0 \\ \gamma E^* - (\varepsilon + \mu + \theta)I^* &= 0 \end{aligned} \tag{3.3}$$

The FMD-FE point of the model which is denoted by P_0 is given as

$$P_0 = (S^*, E^*, I^*) = (\frac{\alpha}{\varepsilon}, 0, 0)$$

When $I > I_0$, it indicates that the treatment rate or control measures, such as the vaccination rate, are proportional to the number of infectious livestock, unless the vaccination capacity of the herd has been reached. In that case, the treatment rate or control measures will be at their maximum vaccination capacity.

Considering the treatment or control measure considered in the confined environment as a rate function expressed as cI.

The FMD endemic equilibrium (FMD-EE) of ODEs in (3.3) will then satisfies,

$$\begin{aligned} \alpha - (\delta I^* + \varepsilon)S^* &= 0 \\ \delta S^* I^* - (\gamma + \varepsilon)E^* &= 0 \\ \gamma E^* - (\varepsilon + \mu + \theta)I^* - cI^* &= 0 \end{aligned} \tag{3.4}$$

In the SEIR model, the analysis of both the latently exposed and infectious ODEs can be used to assess the occurrence and cessation of the FMD epidemic. It is determined that the epidemic is still ongoing when the rate of change of both ODEs is greater than 0, expressed as $\frac{d(E+I)}{dt} > 0$. This implies that $\frac{dE}{dt} + \frac{dI}{dt} > 0$. From the SEIR model equation (3.2), this leads to $\delta SI - \varepsilon E - (\varepsilon + \mu + \theta)I > 0$. Considering that $I > 0$, we can infer that $\delta S - \varepsilon E - X_0 > 0$, where $X_0 = \varepsilon + \mu + \theta$. Given that $S > E$, $X_0 > 0$, $\varepsilon > 0$, and $\delta > 0$, this is equivalent to $\delta S - \varepsilon E - X_0 > 0$. Conversely, when the rate of change of both ODEs is less than 0, it indicates that FMDV is diminishing and the disease is under control, potentially coexisting with livestock for an extended period. The stability of FMD-FE is further examined in the subsequent section, focusing on the spectral radius of the next generation matrix, which determines the basic reproduction number.

3.3 The Basic Reproduction Number R_0 for the SEIR Model

The fundamental objective is to determine the average number of new FMD infections generated by a single infectious livestock in a fully susceptible population at the FMD-FE state. The

ODEs in (3.2) consistently correspond to the FMD-FE state $P_0 = (\frac{\alpha}{\varepsilon}, 0, 0)$. Let $P = (E, S, I)^T$. The ODEs in (3.2) can be reformulated as:

$$\frac{dP}{dt} = \mathscr{F}(P) - \mathscr{V}(P) \tag{3.5}$$

Here, $\mathscr{F}$ represents the rate of new infections resulting from the transition of individuals from the susceptible compartment to the latently exposed compartment or from the infectious compartment to the removed compartment. $\mathscr{V}$ represents the rate of livestock movement into or out of the infectious compartment. Utilizing this approach, we can define two matrices that capture the rate of new infection appearances in each compartment:

$$\mathscr{F}(P) = \begin{pmatrix} \delta SI \\ \alpha \\ \gamma E \end{pmatrix} \quad \text{and} \quad \mathscr{V}(P) = \begin{pmatrix} (\gamma+\varepsilon)E \\ (\delta I+\varepsilon)S \\ (\varepsilon+\mu+\theta)I \end{pmatrix}$$

At FMD-FE P_0, the Jacobian matrices of $\mathscr{F}(P)$ is given by,

$$F = \begin{pmatrix} 0 & \delta I & \delta S \\ 0 & 0 & 0 \\ \gamma & 0 & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} \gamma+\varepsilon & 0 & 0 \\ 0 & \delta I+\varepsilon & 0 \\ 0 & 0 & \varepsilon+\mu+\theta \end{pmatrix}.$$

The inverse of V is given by,

$$V^{-1} = \begin{pmatrix} \frac{1}{\gamma+\varepsilon} & 0 & 0 \\ 0 & \frac{1}{\delta I+\varepsilon} & 0 \\ 0 & 0 & \frac{1}{\varepsilon+\mu+\theta} \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} 0 & \delta I & \delta I \\ 0 & 0 & 0 \\ \gamma & 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{\gamma+\varepsilon} & 0 & 0 \\ 0 & \frac{1}{\delta I+\varepsilon} & 0 \\ 0 & 0 & \frac{1}{\varepsilon+\mu+\theta} \end{pmatrix} = \begin{pmatrix} 0 & \frac{\delta I}{\delta I+\varepsilon} & \frac{\delta I}{\varepsilon+\mu+\theta} \\ 0 & 0 & 0 \\ \frac{\gamma}{\gamma+\varepsilon} & 0 & 0 \end{pmatrix}$$

Let $a_1 = \frac{\delta I}{\delta I+\varepsilon}$ and $a_2 = \frac{\gamma}{\gamma+\varepsilon}$, and $a_3 = \frac{\delta I}{\varepsilon+\mu+\theta}$. Therefore, finding the eigenvalues of the matrix:

$$FV^{-1} - I\lambda = \begin{pmatrix} 0-\lambda & a_1 & a_3 \\ 0 & 0-\lambda & 0 \\ a_2 & 0 & 0-\lambda \end{pmatrix}$$

The characteristic equation, given by $\det(FV^{-1} - I\lambda) = -\lambda(\lambda^2 - a_1(0) + a_3(a_2\lambda)) = -\lambda^3 + a_2a_3\lambda$, leads to the basic reproduction number R_0 as the spectral radius of the next generation

matrix:

$$R_0 = \rho(FV^{-1})$$

which can be expressed as

$$\begin{aligned} R_0 &= a_2 a_3 \\ &= (\frac{\gamma}{\gamma+\varepsilon})(\frac{\delta I}{\varepsilon+\mu+\theta}) \\ &= \frac{\gamma\delta I}{(\gamma+\varepsilon)(\varepsilon+\mu+\theta)} \end{aligned} \tag{3.6}$$

Also, a unique positive solution $P^* = (S^*, E^*, I^*)$ is generated from model (3.3) when $R_0 > 1$. That is

$$S^* = \frac{\alpha}{\delta I^* + \varepsilon}$$

$$E^* = \frac{\delta S^* I^*}{\gamma+\varepsilon} = \frac{\delta(\frac{\alpha}{\delta I^*+\varepsilon})I^*}{\gamma+\varepsilon} = \frac{\alpha\delta I^*}{(\gamma+\varepsilon)(\delta I^*+\varepsilon)}$$

$$I^* = \frac{\gamma E^*}{\varepsilon+\mu+\theta-c} = \frac{\gamma(\frac{\alpha\delta I^*}{(\gamma+\varepsilon)(\delta I^*+\varepsilon)})}{\varepsilon+\mu+\theta-c} = \frac{\alpha R_0}{\varepsilon+\mu+\theta-c}$$

We say that $I^* \leq I_0$ iff $R_0 \leq \frac{\delta I_0}{\varepsilon} + 1 \triangleq K_0$. Then, P^* is an endemic equilibrium of ODEs (3.3) iff $K_0 \geq R_0 > 1$.

The theorem below summarizes the discussion to equilibria.

Theorem 3.3.1. *Let* $K_0 = \frac{\delta I_0}{\varepsilon} + 1, K_1 = 1 + \frac{\delta c I_0 - \gamma}{(\varepsilon+\mu+\theta)\varepsilon} + 2\frac{\sqrt{(\varepsilon+\mu+\theta)\gamma\delta c I_0}}{(\varepsilon+\mu+\theta)\varepsilon}$ *and* $K_2 = 1 + \frac{\delta c I_0 - \gamma}{(\varepsilon+\mu+\theta)\varepsilon} + \frac{(\varepsilon+\mu+\theta)2\delta I_0}{(\varepsilon+\mu+\theta)\varepsilon}$.

1. *The ODEs in (3.2) always have the FMD-FE state* $P_0 = (\frac{\alpha}{\varepsilon}, 0, 0)$.

2. *The FMD-EE state* $P_i = (S^*, E^*, I^*)$ *of ODEs in (3.3) exists iff* $1 < R_0 \leq K_0$.

3. *Two more FMD-EE state* $P_i = (S_i, E_i, I_i), i = 1, 2$ *of ODEs in (3.3) exists iff* $R_0 \geq K_1$ *and* $R_0 > K_2$.

Proof. To generate positive solutions from model (3.2), first we set the equations to zero to get $S = \frac{\alpha}{\delta I+\varepsilon}$, $E = \frac{\varepsilon+\mu+\theta}{\gamma} I + \frac{cI_0}{\gamma}$. Once we substitute into (3.2), we obtain

$$x_1 I^2 + x_2 I + x_3 = 0 \tag{3.7}$$

Where, $x_1 = (\varepsilon+\mu+\theta)(\gamma+\varepsilon)\delta > 0$, $x_2 = (\gamma+\varepsilon)((\varepsilon+\mu+\theta)\varepsilon+\delta cI_0) - \gamma\delta\alpha = (\gamma+\varepsilon)((\varepsilon+\mu+\theta)\varepsilon+\delta cI_0) - (\varepsilon+\mu+\theta+x_3)\varepsilon R_0)$, and $x_3 = (\gamma+\varepsilon)\varepsilon cI_0 > 0$

Let us define the discriminant of equation (3.7) as $\Delta = x_2^2 - 4x_1x_3$.

If $x_2 \geq 0$, then equation (3.7) does not have any positive solutions. Similarly, if $\Delta < 0$, then equation (3.7) does not have any real solutions. However, if $x_2 < 0$ and $\Delta \geq 0$, then equation (3.7) has two positive solutions.

$$\therefore \Delta \geq 0 = {x_2}^2 = [(\gamma+\varepsilon)((\varepsilon+\mu+\theta)\varepsilon+\delta cI_0) - (\varepsilon+\mu+\theta+x_3)\varepsilon R_0)]^2$$

and

$${x_2}^2 \geq 4\gamma\delta cI_0(\gamma-\varepsilon)^2(\varepsilon+\mu+\theta)$$

For instance

$$R_0 \leq 1 + \frac{\delta f(I_0) - \gamma c}{(\varepsilon+\mu+\theta+x_3)\varepsilon} - 2\frac{\sqrt{(\varepsilon+\mu+\theta)\gamma\delta cI_0}}{(\varepsilon+\mu+\theta+x_3)\varepsilon}$$

or

$$R_0 \geq 1 + \frac{\delta cI_0 - \gamma x_3}{(\varepsilon+\mu+\theta+x_3)\varepsilon} + 2\frac{\sqrt{(\varepsilon+\mu+\theta)\gamma\delta cI_0}}{(\varepsilon+\mu+\theta+x_3)\varepsilon} \triangleq K_1$$

It is important to note that $x_2 < 0$ can be equivalently expressed as $R_0 > 1 + \frac{\delta cI_0 - \gamma x_3}{(\varepsilon+\mu+\theta+x_3)\varepsilon}$. Thus, equation (3.7) will have two positive solutions, denoted as I_1 and I_2, if $R_0 \geq K_1$. The values of I_1 and I_2 are given by $I_1 = \frac{-x_2-\sqrt{\Delta}}{2\delta(\gamma+\varepsilon)(\varepsilon+\mu+\theta)}$ and $I_2 = \frac{-x_2+\sqrt{\Delta}}{2\delta(\gamma+\varepsilon)(\varepsilon+\mu+\theta)}$.

If we set $S_1 = \frac{\alpha}{\varepsilon+\delta I_1}$ and $S_2 = \frac{\alpha}{\varepsilon+\delta I_2}$

$E_1 = E_2 = \frac{\alpha}{\gamma+\varepsilon} - \frac{(\varepsilon+\mu+\theta+x_3)\varepsilon}{\delta\gamma}(R_0-1)$

Then $P_i = (S_i, E_i, I_i)$, where $i = 1, 2$ which are FMD-EE state of (3.7) if $I_i > I_0$.

$I_1 > I_0$ iff $-x_2 - \sqrt{\Delta} > 2\delta(\gamma+\varepsilon)(\varepsilon+\mu+\theta)I_0$

This implies that

$$x_2 + 2\delta(\gamma+\varepsilon)(\varepsilon+\mu+\theta)I_0 < 0$$

From the definition of x_2, it follows that

$$R_0 > 1 + \frac{\delta cI_0 - \gamma x_3}{(\varepsilon+\mu+\theta+x_3)\varepsilon} + \frac{(\varepsilon+\mu+\theta)2\delta I_0}{(\varepsilon+\mu+\theta+x_3)\varepsilon} \triangleq K_2$$

On the similar argument, $I_2 < I_0$ iff $R_0 < K_2$. □

Interpretation of R_0

The calculation of R_0 holds great significance in comprehending the average number of newly infected livestock arising from a single infectious animal within the context of FMD. It involves a comparison between the incidence of new infections and other population dynamics within the model.

R_0 relies on the interplay of several factors. It is determined by multiplying the birth rate α, FMD exposure rate γ, and disease transmission rate δ, which collectively contribute to the likelihood of an individual animal becoming infectious. This value is subsequently divided by the proportion of natural deaths ε. The denominator of this division is obtained by multiplying the sum of livestock deaths from natural causes and the FMD exposure rate $(\gamma+\varepsilon)$ by the sum of livestock deaths resulting from both natural and disease-related factors, in addition to the proportion of livestock exiting the infectious compartment $(\varepsilon+\mu+\theta)$.

If the numerator in the expression for R_0 (representing the rate of FMD occurrence) surpasses the denominator (representing the combined cessation rates), it indicates that the population of infectious livestock will persistently increase over time.

3.4 Sensitivity Analysis of R_0 in Confined Settings

To perform the sensitivity analysis of the basic reproduction number R_0, we can investigate the impact of small changes in each parameter on the value of R_0. This can be done by calculating the partial derivatives of R_0 with respect to each parameter.

These partial derivatives provide information about the sensitivity of R_0 to small changes in each parameter. If a partial derivative is close to zero, it indicates that a small change in that parameter will have a minimal effect on R_0. On the other hand, if a partial derivative is significantly different from zero, it suggests that a small change in that parameter will have a more substantial impact on R_0.

By calculating these partial derivatives, we can assess the sensitivity of R_0 to parameter changes and identify which parameters have the most significant influence on the basic repro-

duction number. Suppose we assume the following initial values for the parameters: $\alpha = 0.2$, $\delta = 0.3$, $\gamma = 0.4$, $\varepsilon = 0.1$. $\mu = 0.05$, and $\theta = 0.06$.

We can calculate the partial derivatives of R_0 with respect to each parameter as follows:

$$\begin{aligned}
\frac{\partial R_0}{\partial \alpha} &= 0 \\
\frac{\partial R_0}{\partial \delta} &= \frac{\gamma I}{(\gamma+\varepsilon)(\varepsilon+\mu+\theta)} \\
\frac{\partial R_0}{\partial \gamma} &= \frac{\delta I}{(\gamma+\varepsilon)(\varepsilon+\mu+\theta)} - \frac{\gamma\delta I}{(\gamma+\varepsilon)^2(\varepsilon+\mu+\theta)} \\
\frac{\partial R_0}{\partial \varepsilon} &= -\frac{\gamma\delta I}{(\gamma+\varepsilon)^2(\varepsilon+\mu+\theta)} - \frac{\gamma\delta I}{(\gamma+\varepsilon)(\varepsilon+\mu+\theta)^2} \\
\frac{\partial R_0}{\partial \mu} &= 0 \\
\frac{\partial R_0}{\partial \theta} &= 0
\end{aligned}$$

Substituting the initial values into these expressions, we get:

$$\begin{aligned}
\frac{\partial R_0}{\partial \alpha} &= 0 \\
\frac{\partial R_0}{\partial \delta} &= \frac{0.4I}{(0.4+0.1)(0.1+0.05+0.06)} \\
\frac{\partial R_0}{\partial \gamma} &= \frac{0.3I}{(0.4+0.1)(0.1+0.05+0.06)} - \frac{0.4(0.3I)}{(0.4+0.1)^2(0.1+0.05+0.06)} \\
\frac{\partial R_0}{\partial \varepsilon} &= -\frac{0.4(0.3I)}{(0.4+0.1)^2(0.1+0.05+0.06)} - \frac{0.4(0.3I)}{(0.4+0.1)(0.1+0.05+0.06)^2} \\
\frac{\partial R_0}{\partial \mu} &= 0 \\
\frac{\partial R_0}{\partial \theta} &= 0
\end{aligned}$$

Based on these calculations, we can see that the partial derivatives with respect to α, μ, and θ are all zero. This indicates that small changes in these parameters will have no effect on R_0.

On the other hand, the partial derivatives with respect to δ, γ, and ε are non-zero, indicating that changes in these parameters will have an impact on R_0.

3.5 Local Asymptotic Statibility (LAS) Analysis of SEIR FMD-FE

In the study of dynamical systems, it is often important to assess the stability of equilibrium points. While equilibrium points may not always exhibit stability, it is beneficial to categorize them based on their stability properties. To analyse the local and global stability of the equilibria, we employ the analytic approach of examining the eigenvalues of the Jacobian matrices associated with the ODEs in (3.2). This allows us to gain insights into the stability characteristics of the equilibrium points.

FMD-free equilibrium point P_0

We evaluate the Jacobian matrix at P_0 as follows;

$$J(P_0) = \begin{pmatrix} -(\delta I + \varepsilon) & 0 & \delta S \\ \delta I & -(\gamma+\varepsilon) & \delta S \\ 0 & \gamma & -(\varepsilon+\mu+\theta) \end{pmatrix} \tag{3.8}$$

With the eigenvalues $-(\delta I + \varepsilon)$, $-(\gamma+\varepsilon)$, and $-(\varepsilon+\mu+\theta)$ all being negative, it can be concluded that the FMD-FE point P_0 exhibits local asymptotic stability.

Lemma 3.5.1. *Consider the Lyapunov function $L = \gamma E + (\gamma+\varepsilon)I$ to investigate the global stability of P_0 such that*

$$\frac{dL}{dt} = \gamma\frac{dE}{dt} + (\gamma+\varepsilon)\frac{dI}{dt} = (\gamma\delta S - (\gamma+\varepsilon)(\varepsilon+\mu+\theta))I \leq (\frac{\gamma\alpha\delta}{\varepsilon} - (\gamma+\varepsilon)(\varepsilon+\mu+\theta))I$$

If $R_0 < 1$, then

$$\frac{dL}{dt} = (\gamma+\varepsilon)(\varepsilon+\mu+\theta)(R_0-1)I \leq 0$$

The maximal compact invariant set within the region $(S,E,I) \in \Omega : \frac{dL}{dt} = 0$ is denoted by P_0. By applying LaSalle's Invariance Principle, as presented in [1], we can establish the following theorem.

Theorem 3.5.2. *The FMD-FE point P_0 of the model in equation (3.2) is globally asymptotically stable within the region Ω if $R_0 \leq 1$. However, if $R_0 > 1$, then P_0 is considered unstable.*

Proof. To demonstrate the stability, we utilize the concept of a Lyapunov function, as discussed in the existing literature, by considering:

$$L_0 = y_1 E + y_2 I + y_3 E^* + y_4 I^*$$

Here, y_1, y_2, y_3, and y_4 are positive constants that need to be determined. By differentiating L_0 with respect to time t along the solutions of the model, we obtain:

$$\frac{dL_0}{dt} = y_1 \frac{dE}{dt} + y_2 \frac{dI}{dt} + y_3 \frac{dE^*}{dt} + y_4 \frac{dI^*}{dt}$$

Since $S \leq \frac{\alpha}{\varepsilon}$ at FMD-FE, we replace the derivatives $\frac{dE}{dt}$, $\frac{dI}{dt}$, $\frac{dE^*}{dt}$ and $\frac{dI^*}{dt}$ into the equation of $\frac{dL_0}{dt}$ to get,

$$\begin{aligned}
\frac{dL_0}{dt} &= y_1 \delta SI - (\gamma+\varepsilon) y_1 E + y_2 \gamma E - (\varepsilon+\mu+\theta) y_2 I + y_3 \delta S^* I^* - (\gamma+\varepsilon) y_3 E^* \\
&\quad + y_4 \gamma E^* - (\varepsilon+\mu+\theta) y_4 I^* \leq \frac{\alpha \delta y_3 I^*}{\varepsilon} - (\gamma+\varepsilon) y_3 E^* + y_4 \gamma E^* - (\varepsilon+\mu+\theta) y_4 I^* \\
&= \frac{\alpha \delta y_1 I}{\varepsilon} - (y_1 - y_2)\gamma E - \varepsilon y_1 E - (\varepsilon+\mu+\theta) y_2 I + \frac{\alpha \delta y_3 I^*}{\varepsilon} \\
&\quad - (y_3 - y_4)\gamma E^* - \varepsilon y_3 E^* - (\varepsilon+\mu+\theta) y_4 I^*
\end{aligned}$$

By collecting linear terms and setting the coefficients E, I, E^*, I^* to 0, we get,

$$\begin{aligned}
&\frac{\alpha \delta y_1}{\varepsilon} I - (\gamma+\varepsilon) y_1 E + y_2 \gamma E - (\varepsilon+\mu+\theta) y_2 I + \frac{\alpha \delta y_3}{\varepsilon} I^* \\
&\qquad - (\gamma+\varepsilon) y_3 E^* + y_4 \gamma E^* - (\varepsilon+\mu+\theta) y_4 I^* \\
&\qquad = 0
\end{aligned}$$

Solving for y_1, y_2, y_3, and y_4 yield,

$$y_1 = -\frac{\delta \alpha \varepsilon - (\varepsilon+\mu+\theta) y_4}{\gamma+\mu}, \quad y_2 = 0 \quad y_3 = -\frac{\gamma - (\varepsilon+\mu+\theta) y_4}{\gamma+\mu},$$

and if we let $y_4 = 1$ then this will give us,

$$\begin{pmatrix} y_1 \\ y_2 \\ y_3 \\ y_4 \end{pmatrix} = \begin{pmatrix} -\frac{\delta\alpha\varepsilon-(\varepsilon+\mu+\theta)y_4}{\gamma+\mu} \\ 0 \\ -\frac{\gamma-(\varepsilon+\mu+\theta)y_4}{\gamma+\mu} \\ 1 \end{pmatrix} = \frac{1}{\gamma+\mu} \begin{pmatrix} (\varepsilon+\mu+\theta)y_4 - \delta\alpha\varepsilon \\ 0 \\ (\varepsilon+\mu+\theta)y_4 - \gamma \\ \gamma+\mu \end{pmatrix},$$

So,

$$y_1 = (\varepsilon+\mu+\theta)y_4 - \delta\alpha\varepsilon, \quad y_2 = 0, \quad y_3 = (\varepsilon+\mu+\theta)y_4 - \gamma,$$

and

$$y_4 = \gamma+\mu.$$

If we factorise y_1 and y_3 this will yield,

$$y_1 = \delta\alpha\varepsilon(R_K - 1), \quad y_3 = \gamma(R_K - 1),$$

and $R_K < 1$ for y_1 and $y_3 > 0$, where

$$R_K = \frac{(\varepsilon+\mu+\theta)y_4}{\delta\alpha\varepsilon}$$

$$\begin{aligned} \Longrightarrow \frac{dL_0}{dt} &\leq (\frac{(\varepsilon+\mu+\theta)y_4}{\delta\alpha\varepsilon} - \delta\alpha\varepsilon)SI - (\varepsilon+\mu+\theta)y_4 I \\ &= \delta\alpha\varepsilon(R_K - 1)I - (\varepsilon+\mu+\theta)y_4 I \\ &(\delta\alpha\varepsilon(R_K - 1) - R_J)I \end{aligned}$$

Where

$$\begin{aligned} R_J &= (\varepsilon+\mu+\theta)y_4 \\ &\delta\alpha\varepsilon((R_K - 1) - \frac{R_J}{\delta\alpha\varepsilon})I \end{aligned}$$

Therefore,

$$\frac{dL_0}{dt} \leq -\delta\alpha\varepsilon(1 - R_0)I \Longrightarrow \frac{dL_0}{dt} \leq -Q(1 - R_0),$$

where $Q = \delta\alpha\varepsilon$ is a constant and

$$R_0 = \frac{(\varepsilon+\mu+\theta)(R_K-1)-(\varepsilon+\mu+\theta)R_K}{\delta\alpha\varepsilon}$$

If $R_0 < 1$, then $\frac{dL_0}{dt} < 0$ when $E = I = E^* = I^* = 0$. Thus, the largest compact invariant set within Ω for which $\frac{dL_0}{dt} = 0$ when $R_0 \leq 1$ is represented by the singleton containing P_0.

Therefore, applying the LaSalle Invariance Principle, we can conclude that P_0 is globally asymptotically stable when $R_0 \leq 1$. This completes the proof. □

FMD-endemic equilibrium point P^*

We evaluate the Jacobian matrix at P^* as follows;

$$\left|J(P^*)\right| = \begin{vmatrix} -\delta I^*-\varepsilon & 0 & -\delta S^* \\ \delta I^* & -(\gamma+\varepsilon) & 0 \\ 0 & \gamma & -(\varepsilon+\mu+\theta) \end{vmatrix} = \begin{vmatrix} -\varepsilon R_0 & 0 & -\frac{\alpha\delta}{\varepsilon R_0} \\ \varepsilon(R_0-1) & -(\gamma+\varepsilon) & 0 \\ 0 & \gamma & -(\varepsilon+\mu+\theta) \end{vmatrix}$$

With the characteristic polynomial of $J(P^*)$ given by

$$\lambda^3 + x_1\lambda^2 + x_2\lambda + x_3$$

where

$$x_1 = 2\varepsilon+\mu+\theta+\gamma+\varepsilon R_0, \quad x_2 = (\varepsilon R_0+\gamma+\varepsilon)(\varepsilon+\mu+\theta)+(\gamma+\varepsilon)\varepsilon R_0$$

$$\begin{aligned} x_3 &= (\gamma+\varepsilon)(\varepsilon+\mu+\theta)\varepsilon R_0 + \gamma\alpha\delta\frac{(R_0-1)}{R_0} \\ &= (\gamma+\varepsilon)(\varepsilon+\mu+\theta)2\varepsilon R_0 - (\gamma+\varepsilon)(\varepsilon+\mu+\theta)\varepsilon \end{aligned}$$

It is clear that $x_1 > 0$ and if $R_0 > 1$ then $x_3 > 0$.

$$\begin{aligned} x_1x_2 - x_3 &= (2\varepsilon+\mu+\theta+\gamma+\varepsilon R_0)((\varepsilon R_0+\gamma+\varepsilon)(\varepsilon+\mu+\theta)+(\gamma+\varepsilon)\varepsilon R_0) \\ &\quad -(\gamma+\varepsilon)(\varepsilon+\mu+\theta)2\varepsilon R_0 + (\gamma+\varepsilon)(\varepsilon+\mu+\theta)\varepsilon > 0 \end{aligned}$$

By employing the Routh-Hurwitz criteria, it can be deduced that for $R_0 > 1$, the eigenvalues of $J(P^*)$ are negative, which leads to the following results.

Lemma 3.5.3. *Assume $R_0 > 1$. Then, the FMD-EE point P^* is locally asymptotically stable.*

Proof. To establish the global stability of P^*, we consider the Lyapunov function given by

$$L = (S - S^* - S^* ln\frac{S}{S^*}) + (E - E^* - E^* ln\frac{E}{E^*}) + \frac{\gamma+\varepsilon}{\varepsilon}(I - I^* - I^* ln\frac{I}{I^*})$$

Hence,

$$\frac{dL}{dt} = (1 - \frac{S^*}{S})\frac{dS}{dt} + (1 - \frac{E^*}{E})\frac{dE}{dt} + (\frac{\gamma+\varepsilon}{\varepsilon})(1 - \frac{I^*}{I})\frac{dI}{dt}$$

By substituting the expressions of derivatives from equation (3.3) and utilizing the relation

$$\alpha = \delta S^* I^* + \varepsilon S^*$$

we obtain the following expression:

$$\begin{aligned}
\frac{dL}{dt} &= (1 - \frac{S^*}{S})((S - S^*)\varepsilon + \delta S^* I^* - \delta SI) + (1 - \frac{E^*}{E})(\delta SI \\
&\quad - (\gamma+\varepsilon)E) + (1 - \frac{I^*}{I})(\varepsilon + \mu + \theta + x_3)\frac{(\gamma+\varepsilon)I}{\varepsilon} \\
&= -\frac{(S - S^*)(S - S^*)\varepsilon}{S} + \delta S^* I^* - \delta S^* I^* \frac{S^*}{S} + \delta S^* I - \delta SI\frac{E^*}{E} + (\gamma+\varepsilon)E^* - (\gamma+\varepsilon)E\frac{I^*}{I} \\
&\quad - (\varepsilon + \mu + \theta)\frac{(\gamma+\varepsilon)I}{\varepsilon} + (\varepsilon + \mu + \theta)\frac{(\gamma+\varepsilon)I^*}{\varepsilon}
\end{aligned}$$

Since $\varepsilon E^* = (\varepsilon + \mu + \theta)I^*$ then, this implies that

$$\delta S^* I - (\varepsilon + \mu + \theta)\frac{(\gamma+\varepsilon)I}{\varepsilon} = \delta S^* I - (\gamma+\varepsilon)\frac{IE^*}{I^*} = (\delta S^* I^* - (\gamma+\varepsilon)E^*)\frac{I}{I^*} = 0$$

So for

$$\begin{aligned}
\frac{dL}{dt} &= -\frac{(S - S^*)(S - S^*)\varepsilon}{S} + 3(\gamma+\varepsilon)E^* - \delta S^* I^* \frac{S^*}{S} - \delta SI\frac{E^*}{E} - (\gamma+\varepsilon)\frac{EI^*}{I} \\
&= -\frac{(S - S^*)(S - S^*)\varepsilon}{S} + (3 - \frac{S^*}{S} - \frac{SE^*I}{S^*EI^*} - \frac{EI^*}{E^*I})(\gamma+\varepsilon)E^* \leq 0
\end{aligned}$$

Since

$$\frac{S^*}{S} + \frac{SE^*I}{S^*EI^*} + \frac{EI^*}{E^*I} - 3 \geq 0$$

, it implies that $\frac{dL}{dt} = 0$ if and only if $S = S$, $E = E$, and $I = I$. The maximal compact invariant set in $(S,E,I) \in \Omega : \frac{dL}{dt} = 0$ is the singleton P. By applying the LaSalle invariance principle, we conclude the following:

If $R_0 > 1$, the endemic equilibrium P^* is globally asymptotically stable. □

FMD-endemic equilibrium P_1 and P_2

By analysing the Jacobian matrix at P_1 and ${P_2}^*$, we get

$$\left|J(P_1)\right| = \begin{vmatrix} -\delta I_1 - \varepsilon & 0 & -\delta S_1 \\ \delta I_1 & -(\gamma+\varepsilon) & 0 \\ 0 & \gamma & -(\varepsilon+\mu+\theta) \end{vmatrix} = \begin{vmatrix} -\frac{\alpha}{S_1} & 0 & -\delta S_1 \\ \delta I_1 & -\frac{\delta S_1 I_1}{E_1} & 0 \\ 0 & \gamma & \frac{cI_0-\gamma E_1}{I_1} \end{vmatrix}$$

$$\left|J(P_2)\right| = \begin{vmatrix} -\delta I_1 - \varepsilon - (\gamma+\varepsilon) & 0 & \delta S_1 \\ \gamma & -\delta I_1 - \varepsilon - (\varepsilon+\mu+\theta) & 0 \\ 0 & \delta I_1 & -(\gamma+\varepsilon) - (\varepsilon+\mu+\theta) \end{vmatrix}$$

To determine the local stability of P_1 and P_2, the following lemma is applicable.

Lemma 3.5.4. *Consider a 3×3 real matrix D. If the trace $tr(D)$, determinant $det(D)$, and determinant $det(D_1)$ of D are all negative, then all eigenvalues of D have negative real parts.*

We can clearly get $tr(J(P_1)) < 0$

$$det(J(P_1)) = \frac{1}{E_1}(\alpha\delta\gamma E_1 I_1 S_1) < 0 \quad \text{since} \quad \gamma E_1 - cI_0 > 0$$

$$det(J(P_2)) = (-\delta I_1) - \varepsilon - (\gamma+\varepsilon)(-\delta I_1 - \varepsilon - (\varepsilon+\mu+\theta))(-(\gamma+\varepsilon) - (\varepsilon+\mu+\theta)) + \gamma\delta^2 S_1 I_1$$

One can see that

$$det(J{P_1}^2) < 0, \quad \text{if} \quad \delta^2 {I_1}^2(\gamma + 2\varepsilon\mu + \theta) > \varepsilon\delta^2 S_1 I_1$$

The same argument can be used for P_2 as well and the endemic equilibria for P_i, $i = 1,2$ are locally asymptotically stable when

$$\frac{S_i}{I_i} < \frac{2\varepsilon\mu + \theta}{\varepsilon}.$$

This approach was also applied in [53], [5], [20], [13], and [16] for local stability testing.

3.6 Optimal Control

The optimal control problem for FMD is formulated from the perspective of an epidemiologist aiming to identify an optimal controller that minimizes the number of infected livestock during an outbreak within a specified time frame.

In the considered scenario, two control measures, namely vaccination and culling, are implemented in a controlled environment. Conversely, for the unconfined environment, livestock are subjected to quarantine and vaccination as preventative measures against FMDV infection. The model presented in Chapter 4 of this study incorporates the practice of quarantining livestock between location 1 and location 2 in the unconfined environment.

3.6.1 Using both Vaccination and Culling Measures

The study showcase the anticipation reactions to the two control actions being:

(a) The use of vaccination, denoted by $v(t)$ and quantified as a fraction on the general population of livestock at the given time t. This action $v(t)$ is expected to reduce the livestock susceptible population and increase the completely removed population as $t \longrightarrow \infty$.

(b) The control action $u(t)$, which represents the utilization of culling, is applied as a fraction of the total livestock population at time t. This control action is expected to decrease the populations of latently exposed and infectious livestock while increasing the population of completely removed livestock as t approaches infinity.

The study remodels the dynamic model in equation (3.1) to capture the effects of these two control actions to produce:

$$\begin{aligned}
\frac{dS}{dt} &= \alpha - (\delta I(t) + \varepsilon + v(t))S(t) \\
\frac{dE}{dt} &= \delta S(t)I(t) - (\gamma + \varepsilon + u(t))E(t) \\
\frac{dI}{dt} &= \gamma E(t) - (\varepsilon + \mu + \theta + u(t))I(t) \\
\frac{dR}{dt} &= \theta I(t) + v(t)S(t) + (E(t) + I(t))u(t) - \varepsilon R(t)
\end{aligned} \tag{3.9}$$

Based on the overall framework of the optimal control problem described in Equation (3.9), we introduce the following objective function:

$$J(v(t),u(t)) = \int_0^n (A_1E(t) + A_2I(t) + \frac{1}{2}(A_3v^2 + A_4u^2))dt \tag{3.10}$$

The study regards the quantities of latently exposed and infectious livestock, along with the associated control actions $v(t)$ and $u(t)$, as costs to be minimized.

The weights A_1 and A_2 correspond to the importance assigned to the variables E and I, respectively. On the other hand, A_3 and A_4 represent the weights associated with the minimal control actions. The Lagrangian function $L(E,I,v(t),u(t))$ is constructed using the integrand given in Equation (3.10). Consequently, the study considers the control functions $v(t)$ and $u(t)$ as piecewise continuous functions defined within the set $W = [0, w_{max}(v,u)]$. As stated in [23], control actions defined in an additive manner with bounded coefficients are guaranteed to exist in standard optimal control theory.

The optimal control of the models can be derived using the Pontryagin's maximum principle.

Theorem 3.6.1. *The control actions in the confined environment are associated with adjoint variables $\lambda_i, i = 1,2,3,4$, which satisfy the following conditions:*

$$\begin{aligned}
\frac{d\lambda_1}{dt} &= (\delta I(t) + \varepsilon + v(t))\lambda_1(t) - \delta I(t)\lambda_2(t) - \lambda_4(t)v(t) \\
\frac{d\lambda_2}{dt} &= A_1 + (\gamma + \varepsilon + u(t))\lambda_2(t) - \lambda_3(t)\gamma - \lambda_4(t)u(t) \\
\frac{d\lambda_3}{dt} &= A_1 + (\lambda_1(t) + \lambda_2(t))(\delta S(t)) - \lambda_3(t)(\varepsilon + \mu + \theta + u(t)) \\
\frac{d\lambda_4}{dt} &= \lambda_4(t)\varepsilon
\end{aligned} \tag{3.11}$$

The adjoint variables λ_i in the confined environment satisfy the boundary conditions $\lambda_i(t) = 0$ for all $i = 1,2,3,4$. Moreover, the optimal control variables can be expressed as follows:

$$\begin{aligned}
v^*(t) &= min\{max\{0, \frac{(\lambda_4 - \lambda_1)S^*}{A_3}\}, 1\} \\
u^*(t) &= min\{max\{0, \frac{(E^* + I^*)\lambda_4 - E^*\lambda_2 - I^*\lambda_3}{2A_4}\}, 1\}
\end{aligned} \tag{3.12}$$

Proof. Let the Hamiltonian for the optimal control action of the confined environment be defined by,

$$H = A_1E + A_2I(t) + \frac{1}{2}(A_3v^2(t) + A_4u^2(t)) + (\alpha - (\delta I(t) + \varepsilon + v(t))S(t))\lambda_1 + (\delta S(t)I(t) - (\gamma + \varepsilon + u(t))E(t))\lambda_2 + (\gamma E(t) - (\varepsilon + \mu + \theta + u(t))I(t))\lambda_3 + (\theta I(t) + v(t)S(t) + (E(t) + I(t))u(t) - \varepsilon R(t))\lambda_4$$

The adjoint model is thus expressed as:

$$\begin{aligned}
\frac{d\lambda_1}{dt} &= -\frac{\partial H}{\partial S(t)} = (\delta I(t) + \varepsilon + v(t))\lambda_1 - \delta I(t)\lambda_2 - v(t) \\
\frac{d\lambda_2}{dt} &= -\frac{\partial H}{\partial E(t)} = -A_1 + (\gamma + \varepsilon + u(t))\lambda_2 - \gamma\lambda_3 - u(t)\lambda_4 \\
\frac{d\lambda_3}{dt} &= -\frac{\partial H}{\partial I(t)} = -A_2 + \delta S(\lambda_1 - \lambda_2) + (\varepsilon + \mu + \theta + u(t))\lambda_3 - (\theta + u(t))\lambda_4 \\
\frac{d\lambda_4}{dt} &= -\frac{\partial H}{\partial R(t)} = -\varepsilon(-\lambda_4)
\end{aligned} \tag{3.13}$$

which is simplified to:

$$\begin{aligned}
\frac{d\lambda_1}{dt} &= -\frac{\partial H}{\partial S(t)} = (\lambda_1 - \lambda_2)\delta I(t) - v(t) \\
\frac{d\lambda_2}{dt} &= -\frac{\partial H}{\partial E(t)} = (\lambda_2 - \lambda_3)\gamma + (\lambda_2 - \lambda_4)u(t) + \varepsilon\lambda_2 - A_1 \\
\frac{d\lambda_3}{dt} &= -\frac{\partial H}{\partial I(t)} = (\lambda_1 - \lambda_2)\delta S(t) + (\varepsilon + \mu + \theta + u(t))\lambda_3 - (\theta + u(t))\lambda_4 - A_2 \\
\frac{d\lambda_4}{dt} &= -\frac{\partial H}{\partial R(t)} = \varepsilon\lambda_4
\end{aligned} \tag{3.14}$$

The optimality conditions will then yield:

$$\begin{aligned}
\frac{\partial H}{\partial v(t)} &= A_3v(t) - S(t)\lambda_1 + S(t)\lambda_4 = 0 \Rightarrow \frac{(\lambda_4 - \lambda_1)S(t)}{A_3} \\
\frac{\partial H}{\partial u(t)} &= 2A_4u(t) - E(t)\lambda_2 - I(t)\lambda_3 + (E(t) + I(t))\lambda_4 = 0 \Rightarrow = \frac{-(E(t) + I(t))\lambda_4 + E(t)\lambda_2 + I\lambda_3}{2A_4}
\end{aligned} \tag{3.15}$$

which defines the quantity:

$$v^*(t) = \frac{(\lambda_1 - \lambda_4)S^*}{A_3}$$
$$u^*(t) = \frac{-(E^* + I^*)\lambda_4 + E^*\lambda_2 + I^*\lambda_3}{2A_4} \tag{3.16}$$

By considering the limits on the vaccination control, we obtain the following:

$$v^*(t) = \begin{cases} \frac{(\lambda_1-\lambda_4)S^*}{A_3} & \text{if} \quad 0 \leq \frac{(\lambda_1-\lambda_4)S^*}{A_3} \leq 1, \\ 0 & \text{if} \quad \frac{(\lambda_1-\lambda_4)S^*}{A_3} \leq 0, \\ 1 & \text{if} \quad \frac{(\lambda_1-\lambda_4)S^*}{A_3} \geq 1. \end{cases}$$

Which in compact notation yields,

$$v^*(t) = min\{max\{0, \frac{(\lambda_1 - \lambda_4)S^*}{A_3}\}, 1\} \tag{3.17}$$

Using the bounds for culling control, we get,

$$u^*(t) = \begin{cases} \frac{-(E^*+I^*)\lambda_4+E^*\lambda_2+I^*\lambda_3}{2A_4} & \text{if} 0 \leq \frac{-(E^*+I^*)\lambda_4+E^*\lambda_2+I^*\lambda_3}{2A_4} \leq 1, \\ 0 & \text{if} \frac{-(E^*+I^*)\lambda_4+E^*\lambda_2+I^*\lambda_3}{2A_4} \leq 0, \\ 1 & \text{if} \frac{-(E^*+I^*)\lambda_4+E^*\lambda_2+I^*\lambda_3}{2A_4} \geq 1. \end{cases}$$

Which in compact notation yields,

$$u^*(t) = min\{max\{0, \frac{-(E^* + I^*)\lambda_4 + E^*\lambda_2 + I^*\lambda_3}{2A_4}\}, 1\} \tag{3.18}$$

The following optimality system is produced by using equation (3.16) and (3.18),

$$\frac{dS}{dt} = \alpha - (\delta I(t) + \varepsilon)S(t) - min\{max\{0, \frac{(\lambda_1 - \lambda_4)S^*}{A_3}\}, 1\}S(t)$$
$$\frac{dE}{dt} = \delta S(t)I(t) - (\gamma + \varepsilon)E - min\{max\{0, \frac{-(E^* + I^*)\lambda_4 + E^*\lambda_2 + I^*\lambda_3}{2A_4}\}, 1\}E(t)$$
$$\frac{dI}{dt} = \gamma E(t) - (\varepsilon + \mu + \theta)I - min\{max\{0, \frac{-(E^* + I^*)\lambda_4 + E^*\lambda_2 + I^*\lambda_3}{2A_4}\}, 1\}I(t)$$
$$\frac{dR}{dt} = \theta I(t) + min\{max\{0, \frac{(\lambda_1 - \lambda_4)S^*}{A_3}\}, 1\}S(t) + min\{max\{0, \frac{-(E^* + I^*)\lambda_4 + E^*\lambda_2 + I^*\lambda_3}{2A_4}\}, 1\}E(t)$$
$$+ min\{max\{0, \frac{-(E^* + I^*)\lambda_4 + E^*\lambda_2 + I^*\lambda_3}{2A_4}\}, 1\}I(t) - \varepsilon R(t) \tag{3.19}$$

$$
\begin{aligned}
\frac{d\lambda_1}{dt} &= (\delta I+\varepsilon)\lambda_1(t)+min\{max\{0,\frac{(\lambda_1-\lambda_4)S^*}{A_3}\},1\}\lambda_1(t)-\delta I\lambda_2(t)-min\{max\{0,\frac{(\lambda_1-\lambda_4)S^*}{A_3}\},1\}\lambda_4(t)\\
\frac{d\lambda_2}{dt} &= A_1+(\gamma+\varepsilon)\lambda_2(t)+min\{max\{0,\frac{-(E^*+I^*)\lambda_4+E^*\lambda_2+I^*\lambda_3}{2A_4}\},1\}\lambda_2(t)\\
&\quad -\lambda_3(t)\gamma-min\{max\{0,\frac{-(E^*+I^*)\lambda_4+E^*\lambda_2+I^*\lambda_3}{2A_4}\},1\}\lambda_4(t)\\
\frac{d\lambda_3}{dt} &= A_1+(\lambda_1(t)+\lambda_2(t))(\delta S)-(\varepsilon+\mu+\theta)\lambda_3(t)\\
&\quad -min\{max\{0,\frac{-(E^*+I^*)\lambda_4+E^*\lambda_2+I^*\lambda_3}{2A_4}\},1\}\lambda_3(t)\\
\frac{d\lambda_4}{dt} &= \lambda_4(t)\varepsilon
\end{aligned}
\tag{3.20}
$$

With the initial conditions $S(0)>0, E(0)>0, I(0)>0, R(0)=0$, and the transversal conditions $\lambda_i(t)=0$, for all $i=1,2,3,4$.

Chapter 4

Module 2: Mathematical Formulation and Analysis of the FMD Model in an Unconfined Environment

This chapter builds upon the deterministic FMD mathematical model developed in Module 1 of the study. The model is further analysed and presented using a schematic diagram to depict the transmission and spread of FMD among different compartments, particularly when livestock interact between two communal locations.

The model formulated for the unconfined interface focuses on a variant based FMD whereby African buffaloes infested environment is considered since buffaloes are the host of the most reported FMDV strains.

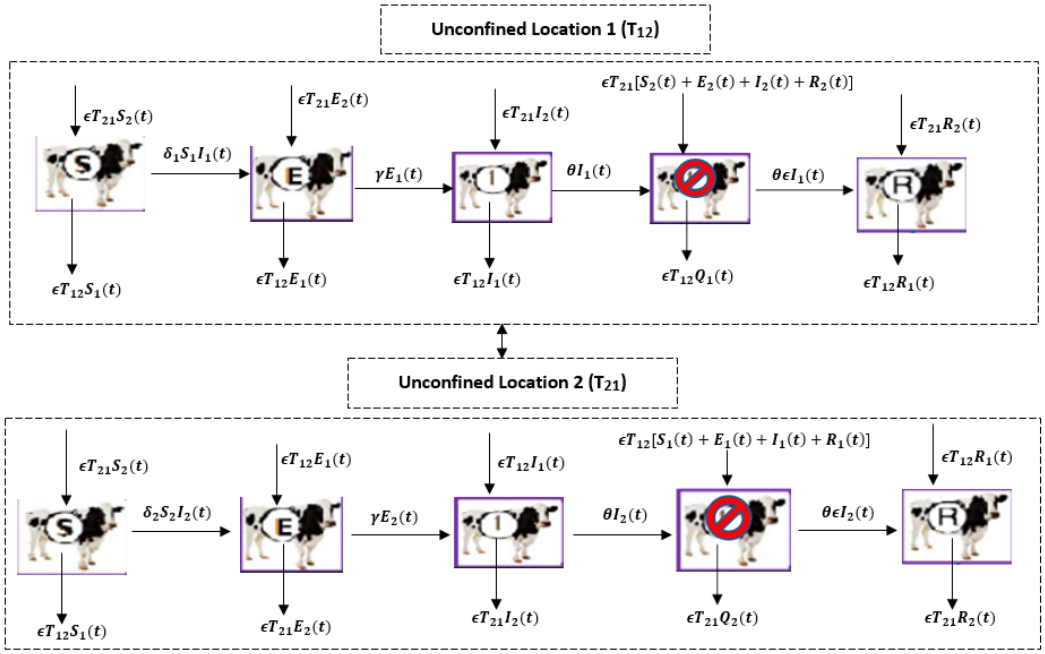

Figure 4.1: Schematic diagram depicting FMD transmission dynamics in the unconfined environment

4.1 Mathematical Formulation of the Model

The livestock population in each location is represented by the following variables at time t:

Location 1:

- Susceptible population: $S_1(t)$
- Latently exposed population: $E_1(t)$
- Infectious population: $I_1(t)$
- Completely removed population: $R_1(t)$
- Quarantined population: $Q_1(t)$

Location 2:

- Susceptible population: $S_2(t)$
- Latently exposed population: $E_2(t)$
- Infectious population: $I_2(t)$
- Completely removed population: $R_2(t)$
- Quarantined population: $Q_2(t)$

The total livestock population in each location, denoted by $N_1(t)$ and $N_2(t)$ respectively, can be expressed as the sum of the corresponding compartments:

Location 1: $N_1(t) = S_1(t) + E_1(t) + I_1(t) + R_1(t) + Q_1(t)$

Location 2: $N_2(t) = S_2(t) + E_2(t) + I_2(t) + R_2(t) + Q_2(t)$

where $N_1 + N_2 \leq K$, and K denote the interface carrying capacity of livestock in the two location.

It is assumed that livestock are recruited into the classes of location 1 and 2 at the rates, εT_{21} and εT_{12}, respectively. where ε denote the rate of livestock movement between locations 1 and 2. T_{21} and T_{12} are the probabilities of livestock in location 2 moving into location 1 and livestock in location 1 moving into location 2, respectively.

Livestock in the susceptible classes become infected with FMDV through direct contact with infectious livestock or airborne infection forces. This decrease the class population as livestock progress to the latently exposed classes of location 1 and 2 at the volume of, $\delta_1 S_1(t)I_1(t)$ and $\delta_2 S_2(t)I_2(t)$ at time t, respectively. The probability of transmission of the FMDV is put at δ_1 and δ_2, since the transmission in the two locations are not the same.

The number of latently exposed livestock decreases due to two factors. Firstly, there is a progression of livestock from the latently exposed class to the infected classes at rates $\gamma E_1(t)$ and $\gamma E_2(t)$ in locations 1 and 2, respectively. Secondly, there is movement of livestock between location 1 and 2 at rates $\varepsilon T_{12} E_1(t)$ and $\varepsilon T_{21} E_2(t)$, respectively. Here, γ represents the rate at which latently exposed livestock become infectious, and εT_{12} and εT_{21} represent the rates of movement between the locations.

The number of infected livestock is determined by the rate at which the latently exposed population becomes symptomatic and infectious. This occurs at rates $\gamma E_1(t)$ and $\gamma E_2(t)$ in locations 1 and 2, respectively.

The number of recovered livestock in each location is produced at rates $\theta E_1(t)$ and $\theta E_2(t)$, respectively. Here, θ represents the rate at which infectious livestock recover or die.

Based on the flow diagram presented in Figure 4.1 and the above description, we obtain the following system of non-linear ordinary differential equations (ODEs) that models our $S_i E_i I_i R_i Q_i$ model of FMD for the livestock population in the unconfined environment of locations $i = 1, 2$:

$$
\begin{aligned}
\frac{dS_1}{dt} &= -\delta_1 S_1(t) I_1(t) - \varepsilon T_{12} S_1(t) + \varepsilon T_{21} S_2(t) \\
\frac{dE_1}{dt} &= \delta_1 S_1(t) I_1(t) - \varepsilon T_{12} E_1(t) - \gamma E_1(t) + \varepsilon T_{21} E_2(t) \\
\frac{dI_1}{dt} &= \gamma E_1(t) + \varepsilon T_{21} I_2(t) - \theta I_1(t) - \varepsilon T_{12} I_1(t) \\
\frac{dR_1}{dt} &= \theta I_1(t) + \varepsilon T_{21} R_2(t) - \varepsilon T_{12} R_1(t) \\
\frac{dQ_1}{dt} &= \varepsilon(T_{21}(S_2(t) + E_2(t) + I_2(t) + R_2(t))) - \varepsilon(T_{12}(S_1(t) + E_1(t) + I_1(t) + R_1(t))) - \theta Q_1(t) \\
\frac{dS_2}{dt} &= -\delta_2 S_2(t) I_2(t) + \varepsilon T_{12} S_1(t) - \varepsilon T_{21} S_2(t) \\
\frac{dE_2}{dt} &= \delta_2 S_2(t) I_2(t) + \varepsilon T_{12} E_1(t) - \gamma E_2(t) - \varepsilon T_{21} E_2(t) \\
\frac{dI_2}{dt} &= \gamma E_2(t) - \varepsilon T_{21} I_2(t) - \theta I_2(t) + \varepsilon T_{12} I_1(t) \\
\frac{dR_2}{dt} &= \theta I_2(t) - \varepsilon T_{21} R_2(t) + \varepsilon T_{12} R_1(t) \\
\frac{dQ_2}{dt} &= \varepsilon(T_{12}(S_1(t) + E_1(t) + I_1(t) + R_1(t))) - \varepsilon(T_{21}(S_2(t) + E_2(t) + I_2(t) + R_2(t))) - \theta Q_2(t)
\end{aligned}
\tag{4.1}
$$

Table 4.1: Description of the $S_i E_i I_i R_i Q_i$ variables

State variable	Description
S_1	Livestock in location 1 that are susceptible to FMDV strain infection
E_1	Livestock in location 1 that are latently exposed to FMDV strain infection without showing any clinical symptoms and not infectious yet
I_1	Livestock in location 1 that are infected with FMDV strain, showing clinical symptoms and infectious
R_1	Livestock in location 1 that have recovered from the FMDV strain
Q_1	Livestock that are quarantined in location 1 facility
S_2	Livestock in location 2 that are susceptible to FMDV strain infection
E_2	Livestock in location 2 that are latently exposed to FMDV strain infection without showing any clinical symptoms and not infectious yet
I_2	Livestock in location 2 that are infected with FMDV strain, showing clinical symptoms and infectious
R_2	Livestock in location 2 that have recovered from the FMDV strain
Q_2	Livestock that are quarantined in location 2 facility

4.2 Mathematical Analysis of the Unconfined Environment Model

Firstly, to ensure the biological meaningfulness of our model, it is important to examine the well-posedness of the model. This involves investigating the positivity and boundedness of the solutions for $S_1(t)$, $S_2(t)$, $E_1(t)$, $E_2(t)$, $I_1(t)$, $I_2(t)$, $R_1(t)$, $R_2(t)$, $Q_1(t)$, and $Q_2(t)$ with respect to time (t).

4.2.1 Positive Invariance of the $S_iE_iI_iR_iQ_i$ Model

Considering the ODE model given by equation (4.1), it is crucial to demonstrate the epidemiological meaningfulness of the model by showing that all FMD state variables remain non-negative. This ensures that solutions of the system of equations, starting from positive initial conditions, remain positive for all $t > 0$. The region in which the model is biologically meaningful is referred to as the biological feasible region and is denoted as Ω_1.

Theorem 4.2.1. *Positivity of Solutions: If the initial values of the FMD state variables in equation (4.1) are non-negative, then the solutions* $S_1(t), S_2(t), E_1(t), E_2(t), I_1(t), I_2(t), R_1(t), R_2(t), Q_1(t)$ *and* $Q_2(t)$ *of the model will also be non-negative for* $t \geq 0$.

Proof. Let's consider the assumptions: for $t > 0$, $N_1(0)$ and $N_2(0) \geq 0$, $S_1(0)$ and $S_2(0) \geq 0$, $E_1(0)$ and $E_2(0) \geq 0$, $I_1(0)$ and $I_2(0) \geq 0$, $R_1(0)$ and $R_2(0) \geq 0$, and $Q_1(0)$ and $Q_2(0) \geq 0$. Alternatively, we assume by contradiction that there exists a first time t_1 satisfying $S_1(t_1) = 0$, $\frac{dS_1(t_1)}{dt} < 0$, $S_2(t_1) = 0$, $\frac{dS_2(t_1)}{dt} < 0$, $E_1(t) > 0$, $E_2(t) > 0$, $I_1(t) > 0$, $I_2(t) > 0$, $R_1(t) > 0$, $R_2(t) > 0$, $Q_1(t) > 0$, and $Q_2(t) > 0$ for $0 < t < t_1$. Using equation (4.1), we can represent $\frac{dS_1}{dt}$ and $\frac{dS_2}{dt}$ as:

$$\frac{dS_1(t_1)}{dt_1} = -\delta_1 S_1(t_1) I_1(t_1) - \varepsilon T_{12} S_1(t_1) + \varepsilon T_{21} S_2(t_1) = 0 \tag{4.2}$$

$$\frac{dS_2(t_1)}{dt_1} = -\delta_2 S_2(t_1) I_2(t_1) + \varepsilon T_{12} S_1(t_1) - \varepsilon T_{21} S_2(t_1) \tag{4.3}$$

Since $S_1(t_1) = 0$ and $E_1(t) > 0$, $I_1(t)$, and $R_1(t)$ according to our assumption, we have $\frac{dS_1(t_1)}{dt} = N_1(t_1) - (E_1(t_1) + I_1(t_1) + R_1(t_1)) > 0$. However, this contradicts our initial assump-

tion that $\frac{dS_1(t_1)}{dt} < 0$. Hence, we conclude that $S_1(t) \not< 0$, implying $S_1(t) > 0$.

Suppose there exists a time t_2 such that $E_1(t_2) = 0$, $\frac{dE_1(t_2)}{dt} < 0$, and $S_1(t) > 0$, $I_1(t) > 0$, $R_1(t) > 0$, $Q_1(t) > 0$, $S_2(t) > 0$, $E_2(t) > 0$, $I_2(t) > 0$, $R_2(t) > 0$, and $Q_2(t) > 0$ for $0 < t < t_2$. Considering the equation:

$$\frac{dE_1(t_2)}{dt_2} = \delta_1 S_1(t_2) I_1(t_2) - \gamma E_1(t_2) - \varepsilon T_{12} E_1(t_2) + \varepsilon T_{21} E_2(t_2) \tag{4.4}$$

Since the assumption states that $E_1(t_2) = 0$ and $S_1(t)$, $I_1(t)$, $R_1(t)$, $Q_1(t)$, $S_2(t)$, $E_2(t)$, $I_2(t)$, $R_2(t)$, and $Q_2(t) > 0$, it follows that $\frac{dE_1(t_2)}{dt_2} = \delta_1 S_1(t_2) I_1(t_2) > 0$. Therefore, we conclude that $E_1(t) > 0$ for all t in the interval $(0, t_2)$.

Now, let's suppose there exists a time t_3 such that $I_1(t_3) = 0$, $\frac{dI_1(t_3)}{dt_3} < 0$, and $S_1(t) > 0$, $R_1(t) > 0$, $Q_1(t) > 0$, $S_2(t) > 0$, $E_1(t) > 0$, $E_2(t) > 0$, $I_2(t) > 0$, $R_2(t) > 0$, and $Q_2(t) > 0$ for $0 < t < t_3$. Then, we have

$$\frac{dI_1(t_3)}{dt_3} = \gamma E_1(t_3) - \theta I_1(t_3) - \varepsilon T_{12} I_1(t_3) + \varepsilon T_{21} I_2(t_3) \tag{4.5}$$

Since from the assumption $I_1(t) = 0$ and $E_1(t) > 0$, then

$\frac{dI_1(t_3)}{dt_3} = \gamma E_1(t_3) + \varepsilon T_{21} I_2(t_3) > 0$

Which is a contradiction, hence $I_1(t) \not< 0$. Therefore, $I_1(t) > 0, \forall t \in (0, t_3)$.

Suppose that there exist the first time t_4 such that $R_1(t_4) = 0$, $\frac{dR_1(t_4)}{dt_4} < 0$ and $S_1(t) > 0$, $E_1(t) > 0$, $I_1(t) > 0$, $Q_1(t) > 0$, $S_2(t) > 0$, $E_1(t) > 0$, $E_2(t) > 0$, $I_2(t) > 0$, $R_2(t) > 0$, and $Q_2(t) > 0$, for $0 < t < t_4$. Now considering,

$$\frac{dR_1(t_4)}{dt_4} = \theta I_1(t_4) + \varepsilon T_{21} R_2(t_4) \tag{4.6}$$

Given the assumption that $R_1(t_4) = 0$ and $I_1(t_4) > 0$, we can evaluate $\frac{dR_1(t_4)}{dt_4} = \theta I_1(t_4) > 0$. However, this contradicts our assumption. Therefore, we conclude that $R_1(t) \leq 0$. Consequently, $R_1(t) > 0$ for all t in the interval $(0, t_4)$.

Let's assume there exists a time t_5 such that $Q_1(t_5) = 0$, $\frac{dQ_1(t_5)}{dt_5} < 0$, and $S_1(t) > 0$, $E_1(t) > 0$, $I_1(t) > 0$, $R_1(t) > 0$, $S_2(t) > 0$, $E_1(t) > 0$, $E_2(t) > 0$, $I_2(t) > 0$, $R_2(t) > 0$, and $Q_2(t) > 0$ for

$0 < t < t_5$. If we analyse the equation:

$$\frac{dQ_1(t_5)}{dt_5} = \varepsilon(T_{21}(S_2(t_5)+E_2(t_5)+I_2(t_5)+R_2(t_5))) - \varepsilon(T_{12}(S_1(t_5)+E_1(t_5)+I_1(t_5)+R_1(t_5))) - \theta Q_1(t_5) \tag{4.7}$$

From the assumption that $Q_1(t_5) = 0$ and $S_1(t)$, $E_1(t)$, $I_1(t)$, $R_1(t)$, $S_2(t)$, $E_1(t)$, $E_2(t)$, $I_2(t)$, $R_2(t)$, and $Q_2(t) > 0$, it follows that $\frac{dQ_1(t_5)}{dt_5} = \frac{dQ_1(t_5)}{dt} = \varepsilon(T_{21}(S_2(t_5)+E_2(t_5)+I_2(t_5)+R_2(t_5))) - \varepsilon(T_{12}(S_1(t_5)+E_1(t_5)+I_1(t_5)+R_1(t_5))) > 0$

This leads to a contradiction, thus indicating that $Q_1(t) \not< 0$. Consequently, we can conclude that $Q_1(t) > 0$ for all t in the interval $(0, t_5)$. A similar analysis can be applied to $S_2(t)$, $E_2(t)$, $I_2(t)$, and $Q_2(t)$, with the condition $S_2(t)$, $E_2(t)$, $S_2(t)$, $I_2(t)$, and $Q_2(t) > 0$ holding for all t in the interval $(0, t_10)$, where:

$\frac{dS_2(t_6)}{dt_6} = N_2(t_6) - (E_2(t_6) + I_2(t_6) + R_2(t_6)) > 0 > 0$

$\frac{dE_2(t_7)}{dt_7} = \delta_1 S_2(t_7) I_2(t_7) > 0$

$\frac{dI_2(t_8)}{dt_8} = \gamma E_2(t_8) > 0 > 0$

$\frac{dR_2(t_9)}{dt_9} = \theta I_2(t_9) > 0$

$\frac{dQ_2(t_10)}{dt_10} = \frac{dQ_1(t_10)}{dt_10} = \varepsilon(T_{12}(S_1(t_10)+E_1(t_10)+I_1(t_10)+R_1(t_10))) - \varepsilon(T_{21}(S_2(t_10)+E_2(t_10)+I_2(t_10)+R_2(t_10))) > 0$

Therefore, we can conclude that the model solutions, starting from non-negative initial conditions, will remain non-negative for all $t \geq 0$. □

4.2.2 Boundedness of Solutions for the $S_iE_iI_iR_iQ_i$ Model

Lemma 4.2.2. *All solutions* $S_1(t), E_1(t), I_1(t), R_1(t), Q_1(t), S_2(t), E_2(t), I_2(t), R_2(t), Q_2(t) > 0$ *remain bounded for all* $t \geq 0$.

Proof. Since we have established that the solutions in Ω_1 are positive, we can sum the differential equations in the model (equation 4.1) to obtain:

$$\frac{d(S_1 + E_1 + \cdots + Q_2)}{dt} = \frac{1}{\theta}(Q_1 + Q_2) \leq \theta(Q_1 + Q_2)$$

where $\theta \geq 1$.

By taking the limit supremum of

$$\frac{d(S_1+E_1+\cdots+Q_2)}{dt} \quad \text{as} \quad t\to\infty$$

we have

$$\lim_{t\to\infty} Sup[S_1+E_1+I_1+\cdots+Q_2] \leq \frac{1}{\theta}$$

. This implies that all the FMD state variables are positive and bounded above by $\frac{1}{\theta}$. Therefore, the feasible region for the unconfined system of ODEs is defined as:

$\Omega_1 = (S_1, E_1, I_1, R_1, Q_1, S_2, E_2, I_2, R_2, Q_2)$

Where,

$(S_1, E_1, I_1, R_1, Q_1, S_2, E_2, I_2, R_2, Q_2) \in \mathbb{R} \mid S_1+E_1+I_1+...+Q_2 \leq \frac{1}{\theta}, S_1, S_2 > 0, E_1, E_2, ..., Q_1, Q_2 \geq 0.$

□

4.2.3 Disease-free Equilibrium for the $S_iE_iI_iR_iQ_i$ Model

In the $S_iE_iI_iR_iQ_i$ model, the disease-free equilibrium state denoted by P_0 is given by $P_0 = \left(\frac{1}{\theta}, 0, 0, 0, \frac{1}{\theta}, 0, 0, 0\right)$. This equilibrium state always exists when the solutions to the right-hand side of equation (4.1) are set to 0, assuming no control measures are implemented. At this equilibrium state, both Q_1 and Q_2 have a value of 0, indicating the absence of infections and recoveries.

4.3 The Basic Reproduction Number R_0 for the $S_iE_iI_iR_iQ_i$ Model

Following the approach of [54], we employ the method of the next generation matrix to analyse the FMD-FE state. This analysis involves utilizing matrices in the form of FV^{-1}, where $\mathscr{F}$ represents the non-negative rate at which infected livestock classes generate new infections, and $\mathscr{V}$ corresponds to the non-singular average length of time that livestock spend in different

locations. Where,

$$\mathscr{F} = \begin{bmatrix} \delta_1 S_1(t) I_1(t) \\ \gamma E_1(t) \\ \delta_2 S_2(t) I_2(t) \\ \gamma E_2(t) \\ \varepsilon(T_{21}(S_2(t)+E_2(t)+I_2(t)+R_2(t))) - \varepsilon(T_{12}(S_1(t)+E_1(t)+I_1(t)+R_1(t))) \\ \varepsilon(T_{12}(S_1(t)+E_1(t)+I_1(t)+R_1(t))) - \varepsilon(T_{21}(S_2(t)+E_2(t)+I_2(t)+R_2(t))) \end{bmatrix} \tag{4.8}$$

and

$$\mathscr{V} = \begin{bmatrix} (\gamma+\varepsilon T_{12})E_1(t) - \varepsilon T_{21}E_2(t) \\ (\theta+\varepsilon T_{12})I_1(t) - \varepsilon T_{21}I_2(t) \\ (\gamma+\varepsilon T_{21})E_2(t) - \varepsilon T_{12}E_1(t) \\ (\theta+\varepsilon T_{21})I_2(t) - \varepsilon T_{12}I_1(t) \\ \theta Q_1(t) \\ \theta Q_2(t) \end{bmatrix} \tag{4.9}$$

Therefore

$$F = \begin{pmatrix} 0 & \delta_1 S_1(t) & 0 & 0 & 0 & 0 \\ \gamma & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \delta_2 S_2(t) & 0 \\ 0 & 0 & 0 & \gamma & 0 & 0 \\ -\varepsilon T_{12} & -\varepsilon T_{12} & 0 & \varepsilon T_{21} & \varepsilon T_{21} & 0 \\ \varepsilon T_{12} & \varepsilon T_{12} & 0 & -\varepsilon T_{21} & -\varepsilon T_{21} & 0 \end{pmatrix} \tag{4.10}$$

$$V = \begin{pmatrix} \gamma+\varepsilon T_{12} & 0 & 0 & -\varepsilon T_{21} & 0 & 0 \\ 0 & \theta+\varepsilon T_{12} & 0 & \gamma+\varepsilon T_{21} & -\varepsilon T_{21} & 0 \\ -\varepsilon T_{12} & 0 & 0 & 0 & 0 & 0 \\ 0 & -\varepsilon T_{21} & 0 & 0 & \theta+\varepsilon T_{21} & 0 \\ 0 & 0 & 0 & 0 & \theta & 0 \\ 0 & 0 & 0 & 0 & 0 & \theta \end{pmatrix} \tag{4.11}$$

$$V^{-1} = \begin{pmatrix} \frac{1}{\gamma+\varepsilon T_{12}} & 0 & 0 & -\frac{1}{\varepsilon T_{21}} & 0 & 0 \\ 0 & \frac{1}{\theta+\varepsilon T_{12}} & 0 & \frac{1}{\gamma+\varepsilon T_{21}} & -\frac{1}{\varepsilon T_{21}} & 0 \\ -\frac{1}{\varepsilon T_{12}} & 0 & 0 & 0 & 0 & 0 \\ 0 & -\frac{1}{\varepsilon T_{21}} & 0 & 0 & \frac{1}{\theta+\varepsilon T_{21}} & 0 \\ 0 & 0 & 0 & 0 & \frac{1}{\theta} & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{1}{\theta} \end{pmatrix} \tag{4.12}$$

$$FV^{-1} = \begin{pmatrix} 0 & \delta_1 S_1(t) & 0 & 0 & 0 & 0 \\ \gamma & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \delta_2 S_2(t) & 0 \\ 0 & 0 & 0 & \gamma & 0 & 0 \\ -\varepsilon T_{12} & -\varepsilon T_{12} & 0 & \varepsilon T_{21} & \varepsilon T_{21} & 0 \\ \varepsilon T_{12} & \varepsilon T_{12} & 0 & -\varepsilon T_{21} & -\varepsilon T_{21} & 0 \end{pmatrix} \tag{4.13}$$

$$\begin{pmatrix} \frac{1}{\gamma+\varepsilon T_{12}} & 0 & 0 & -\frac{1}{\varepsilon T_{21}} & 0 & 0 \\ 0 & \frac{1}{\theta+\varepsilon T_{12}} & 0 & \frac{1}{\gamma+\varepsilon T_{21}} & -\frac{1}{\varepsilon T_{21}} & 0 \\ -\frac{1}{\varepsilon T_{12}} & 0 & 0 & 0 & 0 & 0 \\ 0 & -\frac{1}{\varepsilon T_{21}} & 0 & 0 & \frac{1}{\theta+\varepsilon T_{21}} & 0 \\ 0 & 0 & 0 & 0 & \frac{1}{\theta} & 0 \\ 0 & 0 & 0 & 0 & 0 & \frac{1}{\theta} \end{pmatrix} \tag{4.14}$$

$$= \begin{pmatrix} 0 & -\frac{\delta_1 S_1(t)}{\theta+\varepsilon T_{12}} & 0 & \frac{\delta_1 S_1(t)}{\gamma+\varepsilon T_{21}} & -\frac{\delta_1 S_1(t)}{\varepsilon T_{21}} & 0 \\ \frac{\gamma}{\gamma+\varepsilon T_{12}} & 0 & 0 & -\frac{\gamma}{\varepsilon T_{21}} & 0 & 0 \\ 0 & 0 & 0 & 0 & -\frac{\delta_2 S_2(t)}{\theta} & 0 \\ 0 & -\frac{\gamma}{\varepsilon T_{21}} & 0 & 0 & \frac{\gamma}{\theta+\varepsilon T_{21}} & 0 \\ -\frac{\varepsilon T_{12}}{\gamma+\varepsilon T_{12}} & -(\frac{\varepsilon T_{12}}{\theta+\varepsilon T_{12}}+1) & 0 & \frac{1}{T_{21}} & \frac{T_{12}}{T_{21}}+(\frac{1}{\theta+1})\varepsilon T_{21}+\frac{\varepsilon T_{21}}{\theta} & 0 \\ \frac{\varepsilon T_{12}}{\gamma+\varepsilon T_{12}} & \frac{\varepsilon T_{12}}{\theta}+1 & 0 & -\frac{(\gamma+\varepsilon)T_{21}T_{12}+\varepsilon T_{21}}{\gamma+\varepsilon T_{21}} & -\frac{\varepsilon T_{12}}{\varepsilon T_{21}}-\frac{\varepsilon T_{21}}{\theta+\varepsilon T_{21}}-\frac{\varepsilon T_{21}}{\theta} & 0 \end{pmatrix} \tag{4.15}$$

If we let $b_1 = -\frac{\delta_1 S_1(t)}{\theta+\varepsilon T_{12}}$, $b_2 = \frac{\delta_1 S_1(t)}{\gamma+\varepsilon T_{21}}$, $b_3 = -\frac{\delta_1 S_1(t)}{\varepsilon T_{21}}$, $b_4 = \frac{\gamma}{\gamma+\varepsilon T_{12}}$, $b_5 = -\frac{\gamma}{\varepsilon T_{21}}$, $b_6 = -\frac{\delta_2 S_2(t)}{\theta}$, $b_7 = -\frac{\gamma}{\varepsilon T_{21}}$, $b_8 = \frac{\gamma}{\theta+\varepsilon T_{21}}$, $b_9 = -\frac{\varepsilon T_{12}}{\gamma+\varepsilon T_{12}}$, $b_{10} = -(\frac{\varepsilon T_{12}}{\theta+\varepsilon T_{12}}+1)$, $b_{11} = \frac{1}{T_{21}}$

$b_12 = \frac{T_{12}}{T_{21}}+(\frac{1}{\theta+1})\varepsilon T_{21}+\frac{\varepsilon T_{21}}{\theta}$, $b_{13} = \frac{\varepsilon T_{12}}{\gamma+\varepsilon T_{12}}$, $b_{14} = \frac{\varepsilon T_{12}}{\theta}+1$, $b_{15} = -\frac{(\gamma+\varepsilon)T_{21}T_{12}+\varepsilon T_{21}}{\gamma+\varepsilon T_{21}}$, and $b_{16} = -\frac{\varepsilon T_{12}}{\varepsilon T_{21}}-\frac{\varepsilon T_{21}}{\theta+\varepsilon T_{21}}-\frac{\varepsilon T_{21}}{\theta}$ Then the eigenvalues of the matrix are given by:

$$FV^{-1} - I\lambda = \begin{pmatrix} -\lambda & b_1 & 0 & b_2 & b_3 & 0 \\ b_4 & -\lambda & 0 & b_5 & 0 & 0 \\ 0 & 0 & -\lambda & 0 & b_6 & 0 \\ 0 & b_7 & 0 & -\lambda & b_8 & 0 \\ b_9 & b_{10} & 0 & b_{11} & b_{12}-\lambda & 0 \\ b_{13} & b_{14} & 0 & b_{15} & b_{16} & -\lambda \end{pmatrix} \tag{4.16}$$

with the characteristic equation expressed as:

$$\lambda^6 + b_{12}\lambda^5 + (b_{12} - b_{11}b_8)\lambda^4 + b_{16}b_{11}\lambda^3 + b_6\lambda^2 - b_{15}\lambda + b_{15}b_{12} = 0$$

The eigenvalues of FV^{-1} can be derived as $0, 0, \pm\sqrt{{b_{12}}^2 - 2(b_{16}+b_8\lambda)\lambda^2 - b_{15}}$, $\pm\sqrt{{b_{12}}^2 + 4b_6 b_{12} - b_{15}}$.

Hence, the basic reproduction number, which is the spectral radius of the NGM, is defined as $R_0 = \rho(FV^{-1})$, and it can be calculated as follows:

$R_0 = max(R_1, R_2, R_3, R_4) = max(R_2, R_4)$, where $R_1 = -\sqrt{{b_{12}}^2 - 2(b_{16} + b_8\lambda)\lambda^2 - b_{15}}$, $R_2 = \sqrt{{b_{12}}^2 - 2(b_{16} + b_8\lambda)\lambda^2 - b_{15}}$, $R_3 = -\sqrt{{b_{12}}^2 + 4b_6 b_{12} - b_{15}}$, and $R_4 = \sqrt{{b_{12}}^2 + 4b_6 b_{12} - b_{15}}$

The key distinction between the reproduction numbers $\mathscr{R}_{\in}$ and $\mathscr{R}_{\triangle}$ lies in the interaction between buffaloes and livestock. This indicates that the dominant FMDV strain in the unconfined setting is determined by the rate of mixing between buffaloes and livestock in T_{12} and T_{21}.

4.4 Sensitivity Analysis of R_0 in Unconfined Settings

To perform a sensitivity analysis of the basic reproduction number, we investigate how changes in the model parameters affect the value of R_0. This analysis helps us understand the impact of parameter variations on disease transmission and control in an unconfined environment.

If we assume a simplified model with the following baseline parameter values:

$\delta_1 = 0.5$, $\delta_2 = 0.3$, $\gamma = 0.2$, $\varepsilon = 0.1$, $T_{12} = 0.4$, $T_{21} = 0.2$, $\theta = 0.1$.

And perform a sensitivity analysis by varying each parameter while keeping other baseline parameter values fixed, we will observe the resulting changes in R_0.

Calculating R_0 using the baseline parameter values:

$R_0 = \max(R_2, R_4) = \max(\sqrt{b_{12}^2 - 2(b_{16} + b_8\lambda)\lambda^2 - b_{15}}, \sqrt{b_{12}^2 + 4b_6 b_{12} - b_{15}})$

Varying δ_1

$\delta_1 = 0.3$:

By substituting δ_1 value into the expressions for b_1, b_2, b_3, b_9, and b_{13} yield:

$b_1 = -\frac{\delta_1 S_1(t)}{\theta + \varepsilon T_{12}} = -\frac{0.3 S_1(t)}{\theta + 0.1(0.4)}$

$b_2 = \frac{\delta_1 S_1(t)}{\gamma + \varepsilon T_{21}} = \frac{0.3 S_1(t)}{0.2 + 0.1(0.2)}$

$b_3 = -\frac{\delta_1 S_1(t)}{\varepsilon T_{21}} = -\frac{0.3 S_1(t)}{0.1(0.2)}$

$b_9 = -\frac{\varepsilon T_{12}}{\gamma + \varepsilon T_{12}} = -\frac{0.1(0.4)}{0.2 + 0.1(0.4)}$

$b_{13} = \frac{\varepsilon T_{12}}{\gamma + \varepsilon T_{12}} = \frac{0.1(0.4)}{0.2 + 0.1(0.4)}$

Calculate the new R_0 value using the updated b_1, b_2, b_3, b_9, and b_{13}.

$\delta_1 = 0.5$:

By substituting δ_1 value into the expressions for b_1, b_2, b_3, b_9, and b_{13} yield:

$b_1 = -\frac{\delta_1 S_1(t)}{\theta+\varepsilon T_{12}} = -\frac{0.5S_1(t)}{\theta+0.1(0.4)}$

$b_2 = \frac{\delta_1 S_1(t)}{\gamma+\varepsilon T_{21}} = \frac{0.5S_1(t)}{0.2+0.1(0.2)}$

$b_3 = -\frac{\delta_1 S_1(t)}{\varepsilon T_2 1} = -\frac{0.5S_1(t)}{0.1(0.2)}$

$b_9 = -\frac{\varepsilon T_{12}}{\gamma+\varepsilon T_{12}} = -\frac{0.1(0.4)}{0.2+0.1(0.4)}$

$b_{13} = \frac{\varepsilon T_{12}}{\gamma+\varepsilon T_{12}} = \frac{0.1(0.4)}{0.2+0.1(0.4)}$

Calculate the new R_0 value using the updated b_1, b_2, b_3, b_9, and b_{13}.

$\delta_1 = 0.7$:

Substituting $\delta_1 = 0.7$ into the expressions for b_1, b_2, b_3, b_9, and b_{13} yield:

$b_1 = -\frac{\delta_1 S_1(t)}{\theta+\varepsilon T_{12}} = -\frac{0.7S_1(t)}{\theta+0.1(0.4)}$

$b_2 = \frac{\delta_1 S_1(t)}{\gamma+\varepsilon T_{21}} = \frac{0.7S_1(t)}{0.2+0.1(0.2)}$

$b_3 = -\frac{\delta_1 S_1(t)}{\varepsilon T_{21}} = -\frac{0.7S_1(t)}{0.1(0.2)}$

$b_9 = -\frac{\varepsilon T_{12}}{\gamma+\varepsilon T_{12}} = -\frac{0.1(0.4)}{0.2+0.1(0.4)}$

$b_{13} = \frac{\varepsilon T_{12}}{\gamma+\varepsilon T_{12}} = \frac{0.1(0.4)}{0.2+0.1(0.4)}$

Varying δ_2

$\delta_2 = 0.2$:

Substituting $\delta_2 = 0.2$ into the expressions for b_6 and b_{14} yield:

$b_6 = -\frac{\delta_2 S_2(t)}{\theta} = -\frac{0.2S_2(t)}{0.1}$

$b_{14} = \frac{\varepsilon T_{12}}{\theta} + 1 = \frac{0.1(0.4)}{0.1} + 1$

Calculate the new R_0 value using the updated b_6 and b_{14}.

$\delta_2 = 0.3$:

Calculating the new R_0 value using the baseline b_6 and b_{14} yield:

$b_6 = -\frac{\delta_2 S_2(t)}{\theta} = -\frac{0.3S_2(t)}{0.1}$

$b_{14} = \frac{\varepsilon T_{12}}{\theta} + 1 = \frac{0.1(0.4)}{0.1} + 1$

Calculate the new R_0 value using the updated b_6 and b_{14}.

$\delta_2 = 0.4$:

Calculating the new R_0 value using the baseline b_6 and b_{14} yield:

$b_6 = -\frac{\delta_2 S_2(t)}{\theta} = -\frac{0.4 S_2(t)}{0.1}$

$b_{14} = \frac{\varepsilon T_{12}}{\theta} + 1 = \frac{0.1(0.4)}{0.1} + 1$

Varying γ

$\gamma = 0.1$:

Substituting $\gamma = 0.1$ into the expressions for b_4 and b_7 yield:

$b_4 = \frac{\gamma}{\gamma + \varepsilon T_{12}} = \frac{0.1}{0.1 + 0.1(0.4)}$

$b_7 = -\frac{\gamma}{\varepsilon T_{21}} = -\frac{0.1}{0.1(0.2)}$

Calculate the new R_0 value using the updated b_4 and b_7.

$\gamma = 0.2$:

Substituting $\gamma = 0.2$ into the expressions for b_4 and b_7 yield:

$b_4 = \frac{\gamma}{\gamma + \varepsilon T_{12}} = \frac{0.2}{0.2 + 0.1(0.4)}$

$b_7 = -\frac{\gamma}{\varepsilon T_{21}} = -\frac{0.2}{0.1(0.2)}$

Calculate the new R_0 value using the updated b_4 and b_7.

$\gamma = 0.3$:

Substituting $\gamma = 0.3$ into the expressions for b_4 and b_7: $b_4 = \frac{\gamma}{\gamma + \varepsilon T_{12}} = \frac{0.3}{0.3 + 0.1(0.4)}$

$b_7 = -\frac{\gamma}{\varepsilon T_{21}} = -\frac{0.3}{0.1(0.2)}$

For the remaining parameters, R_0 will remain the same since they do not appear in the expressions for b_1, b_2, b_3, b_4, b_6, b_7, b_9, b_{13}, and b_{14}.

Performing these calculations will give us the new R_0 values for each parameter variation, allowing us to assess the sensitivity of R_0 to parameter changes.

4.5 Local Asymptotic Stability (LAS) Analysis of $S_iE_iI_iR_iQ_i$ FMD-FE

The local asymptotic stability of the FMD-FE model is determined by examining the eigenvalues of the Jacobian matrix derived from the right-hand side of the ODEs in equation (4.1). If all the eigenvalues of the Jacobian matrix are negative, the FMD-FE is locally asymptotically stable. Conversely, if any eigenvalue is positive, the FMD-FE is unstable. In this analysis, we focus on evaluating the Jacobian matrix at the FMD-FE state P_0 to assess the local stability of the model, without explicitly considering global stability since it is implied by local stability.

$$J(P_0) = \begin{pmatrix} -\varepsilon T_{12} & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -(\varepsilon T_{12}+\gamma) & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \gamma & -(\varepsilon T_{12}+\theta & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \theta & -\varepsilon T_{12} & 0 & 0 & 0 & 0 & 0 & 0 \\ -\varepsilon T_{12} & -\varepsilon T_{12} & -\varepsilon T_{12} & -\varepsilon T_{12} & -\theta & \varepsilon T_{21} & \varepsilon T_{21} & \varepsilon T_{21} & \varepsilon T_{21} & 0 \\ \varepsilon T_{12} & 0 & 0 & 0 & 0 & -\varepsilon T_{21} & 0 & 0 & 0 & 0 \\ 0 & \varepsilon T_{12} & 0 & 0 & 0 & 0 & -(\varepsilon T_{21}+\gamma) & 0 & 0 & 0 \\ 0 & 0 & \varepsilon T_{12} & 0 & 0 & 0 & \gamma & -(\varepsilon T_{21}+\theta) & 0 & 0 \\ 0 & 0 & 0 & \varepsilon T_{12} & 0 & 0 & 0 & \theta & -\varepsilon T_{21} & 0 \\ \varepsilon T_{12} & \varepsilon T_{12} & \varepsilon T_{12} & \varepsilon T_{12} & 0 & -\varepsilon T_{21} & -\varepsilon T_{21} & -\varepsilon T_{21} & -\varepsilon T_{21} & - \end{pmatrix} \tag{4.17}$$

As we have observed that $J(P_0)$ can be expressed as the difference between the matrices F and V obtained from the calculation of R_0, it has been proven that all eigenvalues of $J'(P_0)$ are negative if $\rho(FV^{-1}) < 1$. Therefore, $J(P_0)$ is locally asymptotically stable when $\mathscr{R}_\infty < 1$, $\mathscr{R}_\in < 1$, $\mathscr{R}_\ni < 1$, and $\mathscr{R}_\triangle < 1$.

4.6 Optimal Control

To minimize the number of infected livestock in the unconfined environment, this study incorporates FMD control measures, specifically the use of quarantine facilities and mass livestock vaccination programs.

4.6.1 Using both Vaccination and Quarantine Measures

Unlike the scenario of the confined settings, in this case, Q_1 and Q_2 are considered, and a proportion $v(t)S_i(t)$ of the susceptible population in each unconfined location $i = 1$ and 2 is vaccinated against FMDV infection. As a result, the dynamic model presented in equation (4.1) is modified to account for the effects of these two control actions, resulting in the following remodelled model:

$$
\begin{aligned}
\frac{dS_1}{dt} &= -\delta_1 S_1(t)I_1(t) - \varepsilon T_{12}S_1(t) + \varepsilon T_{21}S_2(t) - (S_1(t)+S_2(t))v(t) \\
\frac{dE_1}{dt} &= \delta_1 S_1(t)I_1(t) - \varepsilon T_{12}E_1(t) - \gamma E_1(t) + \varepsilon T_{21}E_2(t) \\
\frac{dI_1}{dt} &= \gamma E_1(t) + \varepsilon T_{21}I_2(t) - \theta I_1(t) - \varepsilon T_{12}I_1(t) \\
\frac{dR_1}{dt} &= \theta I_1(t) + \varepsilon T_{21}R_2(t) - \varepsilon T_{12}R_1(t) + (S_1(t)+S_2(t))v(t) \\
\frac{dQ_1}{dt} &= \varepsilon(T_{21}(S_2(t)+E_2(t)+I_2(t)+R_2(t))) - \varepsilon(T_{12}(S_1(t)+E_1(t)+I_1(t)+R_1(t))) - \theta Q_1(t) \\
\frac{dS_2}{dt} &= -\delta_2 S_2(t)I_2(t) + \varepsilon T_{12}S_1(t) - \varepsilon T_{21}S_2(t) - (S_2(t)+S_1(t))v(t) \\
\frac{dE_2}{dt} &= \delta_2 S_2(t)I_2(t) + \varepsilon T_{12}E_1(t) - \gamma E_2(t) - \varepsilon T_{21}E_2(t) \\
\frac{dI_2}{dt} &= \gamma E_2(t) - \varepsilon T_{21}I_2(t) - \theta I_2(t) + \varepsilon T_{12}I_1(t) \\
\frac{dR_2}{dt} &= \theta I_2(t) - \varepsilon T_{21}R_2(t) + \varepsilon T_{12}R_1(t) + (S_2(t)+S_1(t))v(t) \\
\frac{dQ_2}{dt} &= \varepsilon(T_{12}(S_1(t)+E_1(t)+I_1(t)+R_1(t))) - \varepsilon(T_{21}(S_2(t)+E_2(t)+I_2(t)+R_2(t))) - \theta Q_2(t)
\end{aligned}
\tag{4.18}
$$

Now we need to find the control actions $v(t)$, $Q_1(t)$, and $Q_2(t)$ that minimize the objective function $J(v(t), Q_1(t), Q_2(t))$. The specific approach for solving this problem depends on the optimization techniques used. For the purpose of this study, we used the common method known as the Pontryagin's maximum principle, which provides necessary conditions for the optimal control.

The Pontryagin's maximum principle involves introducing the Hamiltonian function, which is defined as the sum of the objective function and the inner product of the costate variables

(multipliers) and the dynamics equations. In this case, the Hamiltonian H is given by:

$$\begin{aligned} H &= A_1E_1(t) + A_2I_1(t) + A_3E_2(t) + A_4I_2(t) \\ &\quad - ((S_1(t) + S_2(t))A_5v^2(t) + (E_1(t) + I_1(t))A_6T_{12}Q_1(t) \\ &\quad + (E_2(t) + I_2(t))A_7T_{21}Q_2(t)) \end{aligned} \tag{4.18}$$

The necessary conditions for optimality are as follows.

Hamiltonian Maximization Condition:

$\frac{\partial H}{\partial v} = -(S_1(t) + S_2(t))2A_5v(t) = 0$ This condition implies that the control action $v(t)$ should be chosen such that the Hamiltonian is maximized with respect to v.

Costate Equations:

$$\begin{aligned} \frac{\partial H}{\partial S_i} &= -\frac{dS_i}{dt} \\ &= -\frac{\partial((E_1(t) + I_1(t))A_6T_{12}Q_1(t))}{\partial S_i} - \frac{\partial((E_2(t) + I_2(t))A_7T_{21}Q_2(t))}{\partial S_i} \end{aligned} \tag{4.19}$$

These equations describe the rate of change of the costate variables $S_i(t)$ ($S_1(t)$ and $S_2(t)$) with respect to time.

Transversality Conditions:

At the final time n, the costate variables should satisfy the following conditions:

$\lambda S_i(n) = \frac{\partial J}{\partial S_i(n)} = 0$ These conditions ensure that the final values of the costate variables do not affect the objective function.

Control Equations:

$$\begin{aligned}\frac{\partial H}{\partial Q_i(t)} &= -\frac{dQ_i}{dt} \\ &= -\frac{\partial((E_1(t)+I_1(t))A_6T_{12}Q_1(t))}{\partial Q_i(t)} - \frac{\partial((E_2(t)+I_2(t))A_7T_{21}Q_2(t))}{\partial Q_i(t)}\end{aligned} \tag{4.20}$$

These equations describe the rate of change of the control variables $Q_i(t)$ $Q_1(t)$ and $Q_2(t)$ with respect to time.

The numerical simulation for optimality is summarised in Chapter 5 with the following initial values:

Constants:

$A_1 = 0.5, A_2 = 0.3, A_3 = 0.4, A_4 = 0.2, A_5 = 0.1, A_6 = 0.2, A_7 = 0.3$

Parameters:

$\delta_1 = 0.4, \delta_2 = 0.3, \gamma = 0.2, T_{12} = 0.5, T_{21} = 0.6$

Initial Conditions:

$S_1(0) = 100, E_1(0) = 10, I_1(0) = 5, R_1(0) = 0, Q_1(0) = 0$

$S_2(0) = 150, E_2(0) = 5, I_2(0) = 2, R_2(0) = 0, Q_2(0) = 0$

Chapter 5

Summary of Results, Conclusions and Recommendations

This chapter provides a summary of the numerical simulations conducted to validate the predictions of the analytical results and optimal control solutions for managing FMD in the country. The dynamics of both the *SEIR* and $S_iE_iI_iR_iQ_i$ models are illustrated through the utilization of an ODE solver in Python, which allow us to observe the behaviour of FMD over time. The Python simulation code used for the simulations is provided in Appendix I and II of the study.

5.1 Numerical Simulation Results

The behaviour of FMD in Namibia was analysed using the *SEIR* and $S_iE_iI_iR_iQ_i$ models, along with their optimality systems, which were solved through numerical simulations. The optimality systems represent non-linear two-point boundary value problems with specific boundary conditions at time $t = 0$ and $t = T$. In this study, the simulations were conducted for a fixed terminal period of $T = 182$ days, equivalent to a 6-month duration. The numerical values used in the models were obtained from reliable and available data, supplemented with parameter estimations to ensure informed predictions.

Different scenarios were considered by implementing various mitigation plans at different rates, allowing for a comprehensive understanding of the behaviour of FMD as different control measures were implemented. Given the limited availability of data, secondary data sources were utilized to estimate the parameters, which are further discussed in the subsequent section. Table 5.1 provides a summary of the estimated parameter values at a specific time point. Addition-

ally, the values of FMD transmission rates (δ, δ_1, and δ_2), the average FMD latency exposure rate of livestock (γ), and the average FMD infection rate (θ) were adjusted to investigate the impact of parameter variations on the population dynamics. The models' dynamics are inter-

Table 5.1: Systems parameter values, descriptions and data sources

Parameter	Description	Value	Source
α	Livestock birth (recruitment into the confined area) rate	3.122×10^{-2}	[27]
δ	Probability of FMD transmission in the confined area	5.0×10^{-2}	[27]
δ_1	Probability of FMD transmission in location 1 of unconfined area	3.5×10^{-2}	[27], [52]
δ_2	Probability of FMD transmission in location 2 of unconfined area	3.9×10^{-2}	[27], [52]
ε	Livestock natural death rate in confined environment or probability of livestock movement between location 1 and 2 in unconfined area	0.009 or 8.0×10^{-2}	[12], [27]
μ	Livestock disease-induced death rate	1.0×10^{-2}	[12], [31], [27]
γ	Average FMD latently exposure rate of livestock	$\frac{1}{14}$	[27], [30], [12]
θ	Average FMD infection rate of livestock	$\frac{1}{18}$	[12], [31], [27]
T_{12}	Probability of livestock movement in unconfined area from location 1 to location 2	2.6×10^{-2}	[52], [31], [27]
T_{21}	Probability of livestock movement in unconfined area from location 2 to location 1	2.3×10^{-2}	[52], [31], [27]

preted graphically using Python ODEs solver and parameter values in table 5.2 but these values can be adjusted to study FMD behaviour in different settings or adjusted to reflect true values based on the availability of data. As previously highlighted, in the next section, we illustrated on how each parameter value is determined.

Data Fitting and Parameters Estimation

The study pointed out its reliance on secondary FMD datasets, which are gathered from secondary sources, viz; the Meat Board of Namibia (MBN) and the Ministry of Agriculture, Water and Land Reforms archives. The data file are contained in the additional material of the study. In addition, this data are supplemented by historical cumulative FMD cases datasets from reviewed literatures and models fitting for parameter values estimation and performing of numerical simulations. The datasets in the additional materials were compiled from the reported

Table 5.2: Cumulative FMD cases in Confined and Unconfined environment

Period	2016	2017	2018	2019	2020	2021
FMD cases	4,270	4,391	5,008	5,121	5,179	5,325

cases of livestock at risk, sick, dead, and test results from different inspection districts of the country, which is comprised of both confined and unconfined districts.

Estimation of α

Based on the demographic statistics provided by the Ministry of Agriculture, Water, and Land Reforms, the estimated value of α is approximately 3.122. This value corresponds to the average number of livestock births per day in Namibia.

Estimation of δ, δ_1, and δ_2

$\delta \approx 5 \times 10^{-2}$, $\delta_1 \approx 3.5 \times 10^{-2}$, and $\delta_2 \approx 3.9 \times 10^{-2}$ were calculated by using Meat Board of Namibia statistic to realize FMD transmission probabilities in the confined and unconfined environments. Livestock primarily contract the disease through close contact with infectious individuals. However, transmission does not occur between livestock that have recovered from FMD within the past 3 months or those that have been fully vaccinated.

Estimation of ε

$\varepsilon \approx 0.009$ is calculated by using the Ministry of Agriculture, Water, and Land Reforms statistics for natural deaths in Namibia (22,618) divided by the livestock population of the entire country (2,513,116). This quotient provided our natural death rate. In the scope of livestock movement between location 1 and 2 in the unconfined area, the probability of movement is fixed to 8.0×10^{-2}

5.1.1 *SEIR* and $S_iE_iI_iR_iQ_i$ Models Experiments

To minimize the spread of FMD infection and "flatten the curve," we conducted experiments using the *SEIR* and $S_iE_iI_iR_iQ_i$ models. Our goal was to study the behaviour of the infection curve as different parameters were varied.

In these experiments, we utilized Python code to analyse the cumulative cases and employed

the method of least square curve fitting. This approach allowed us to generate parameter values that accurately represent the data. Figure 5.1 depicts the cumulative cases as a fraction of the populations under investigation.

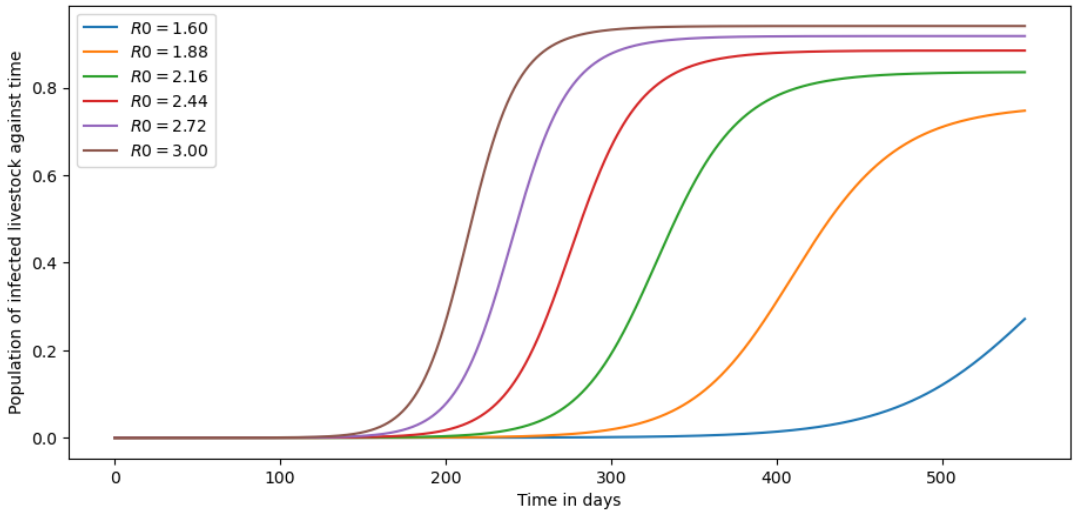

Figure 5.1: Plot of FMD cumulative cases, as the fraction of the population with varied R_0

We then experiment the FMD cases when the effective FMD transmission rate (δ, δ_1 and δ_2) is constant, followed by calculations of the time path of infected livestock when the rate is varied under different assumptions. As anticipated, reducing the effective FMD transmission

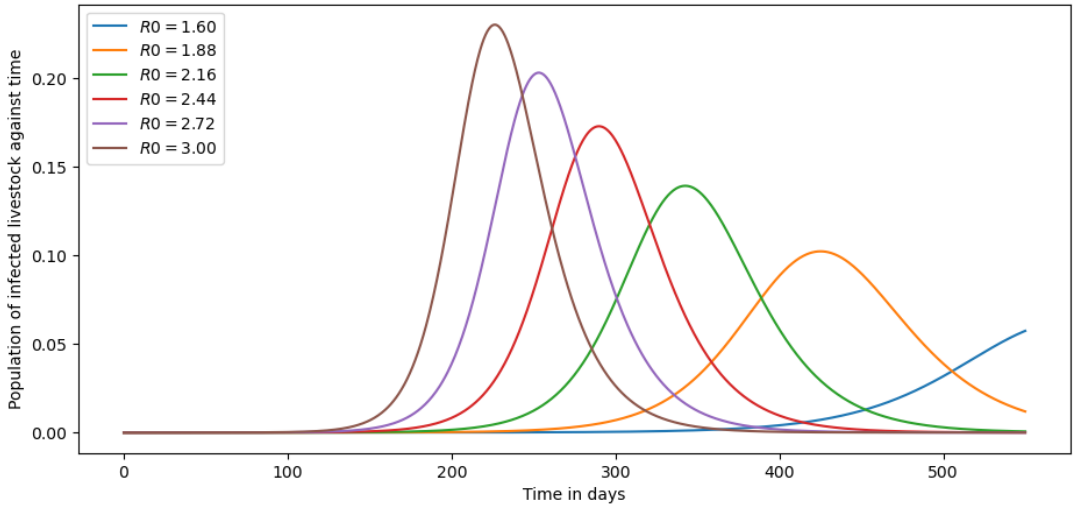

Figure 5.2: Plot of current FMD cases as the fraction of the population with varied R_0

rates leads to a decrease in the peak of current FMD cases. Figure 5.3 illustrates the impact of optimal control measures on the susceptible population. The effective FMD transmission rate starts at 3.0 and gradually decreases to 1.6. We observe a decline in the susceptible population as optimal control measures are progressively implemented. This decrease is attributed to the vaccination or culling of susceptible livestock, indicating the effectiveness of control measures. The optimal control models allow for the regulation of the rate or speed at which vaccination, quarantine, or culling measures are implemented. It is important to note that vaccination may not be effective for livestock already exposed to FMDV, resulting in their transition to the latently exposed and infectious compartments. By considering various alternative rates, such as a range of 10 to 20 per cent, the time path for the effective transmission rate can be determined.

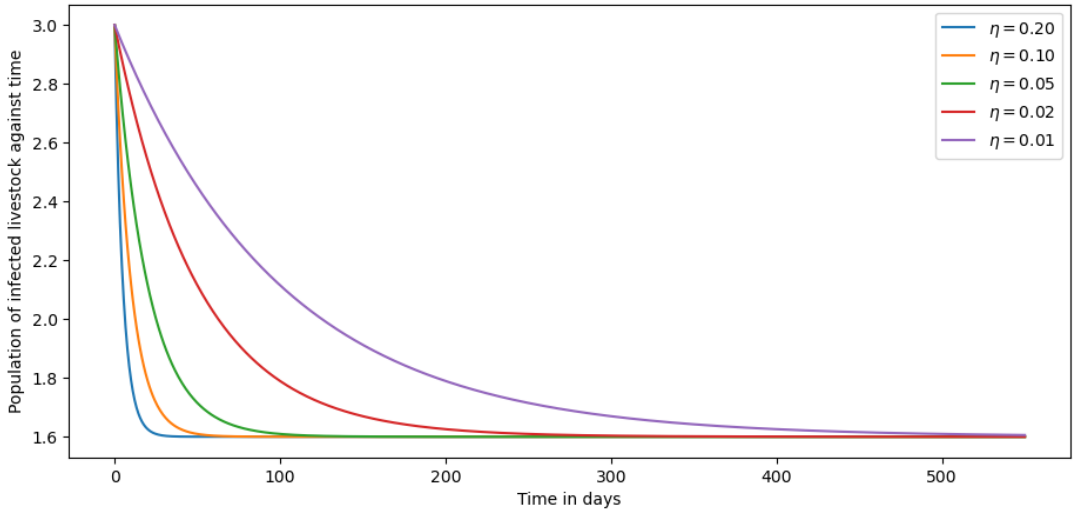

Figure 5.3: Effects of successively imposed confined FMD vaccination as the mitigation plan with alternative rates

The time path of infected livestock with these alternative rates on the current FMD cases and cumulative cases as the fraction of the population are demonstrated in figure 5.4 and 5.5, respectively.

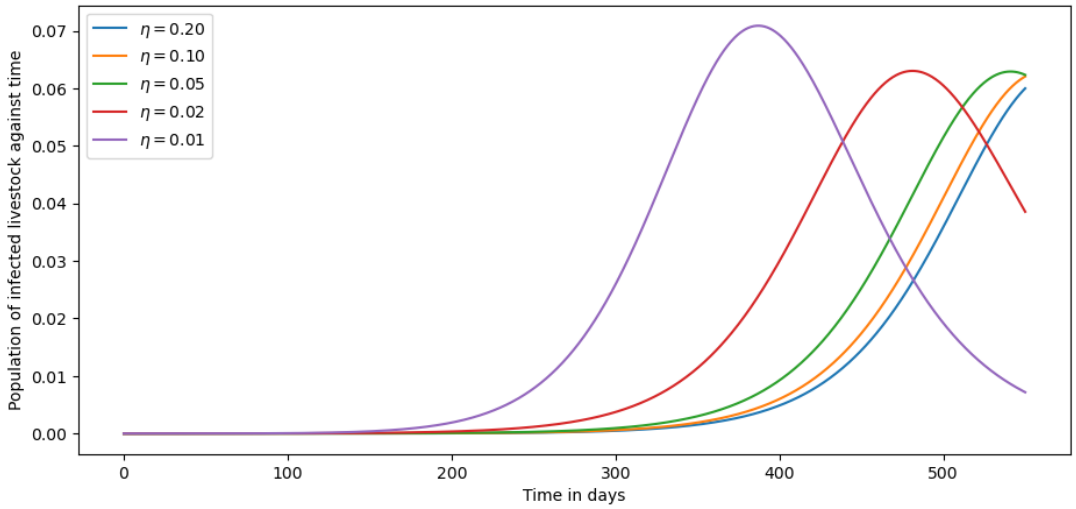

Figure 5.4: Current confined FMD cases, as the fraction of the population under successively imposed FMD mitigation plan with alternative rates

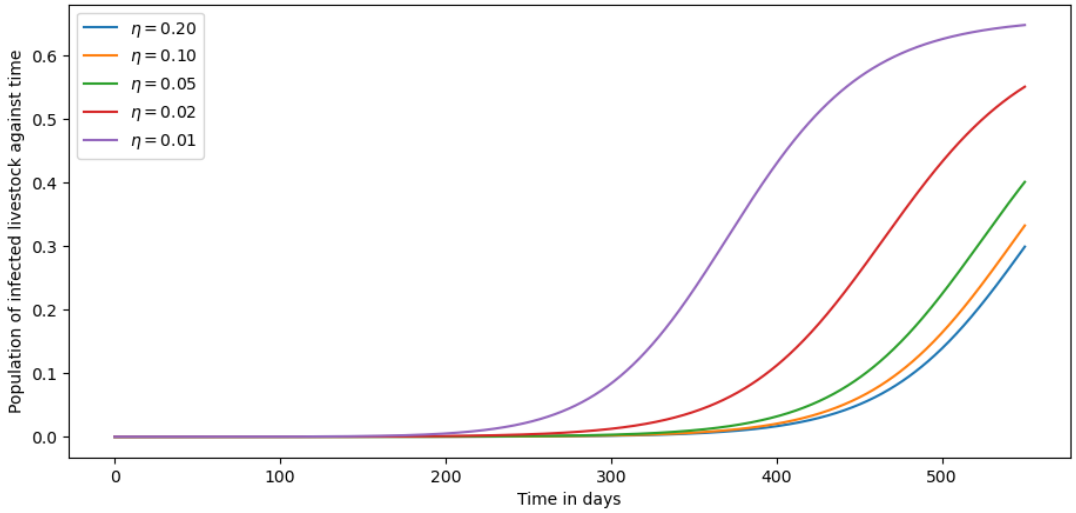

Figure 5.5: Current unconfined FMD cases, as the fraction of the population under successively imposed FMD mitigation plan with alternative rates

5.1.2 Maximising the Mitigation Plan

If we consider an optimal control scenario in which the effective FMD transmission rate is equal to 2.0 for 60 days and then equal to 0.5 for the remaining 122 days, this corresponds to control interventions in 2 months period. Secondly, if we consider an optimal control scenario in which the effective FMD transmission rate is equal to 2.0 for 122 days and then equal to 0.5 for the remaining 60 days, then this corresponds to control interventions in approximately 4 months period. These shows that, delayed intervention periods have effects in lowering FMD transmission rate. The parameters initiate the $S_iE_iI_iR_iQ_i$ model with 2500 active FMD infections and 7500 livestock already latently exposed to the virus and thus soon to be contagious. When we calculate the time path, the number of active infections are presented as follows in figure 5.6 with scenario 1 and 2 referring to confined and unconfined settings, respectively.

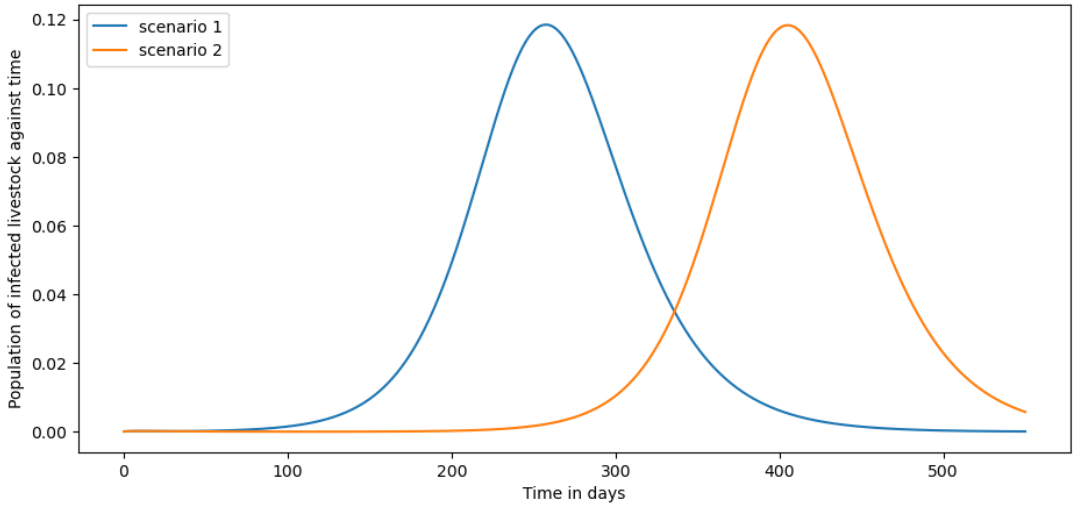

Figure 5.6: Cumulative FMD cases, as the fraction of the population under successively imposed FMD mitigation plan with alternative rates

If we assume that 1 per cent of the cases will results in FMD-induced mortality, the cumulative number of deaths will be as follows. When mitigation plans are administered, pushing

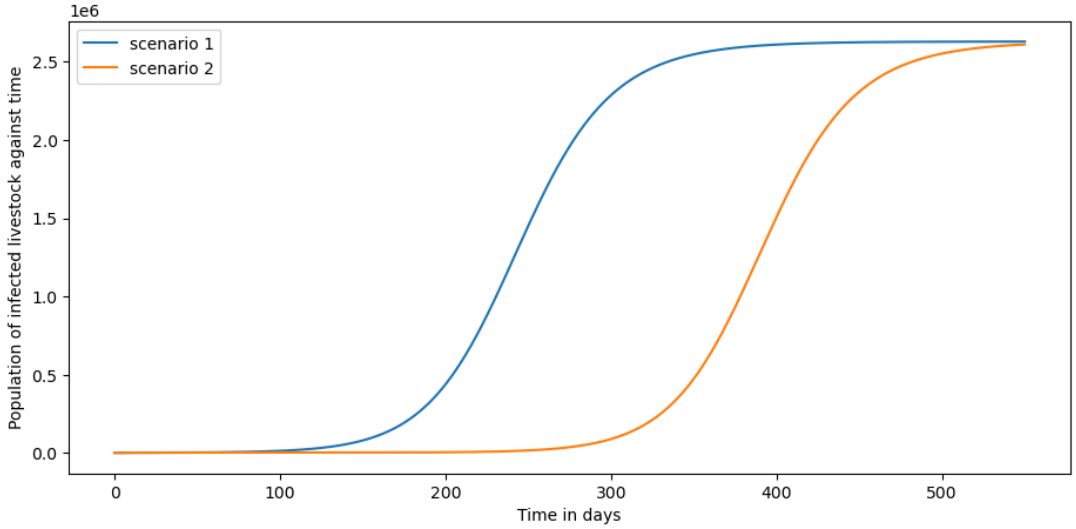

Figure 5.7: Cumulative number of deaths

the peak of the curve further may reduce the cumulative number of FMD-related deaths, as depicted in figure 5.8.

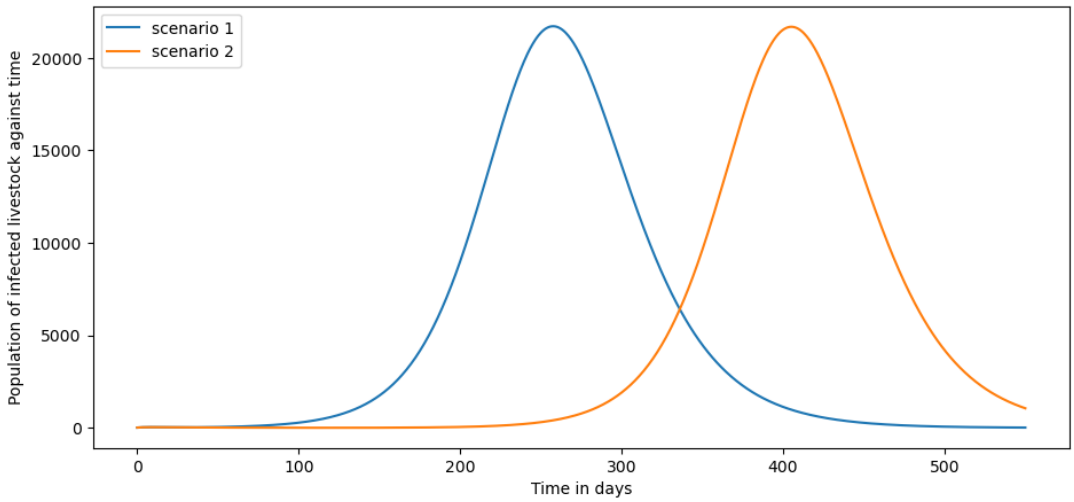

Figure 5.8: Cumulative number of deaths with mitigation plan administered

5.2 Conclusions

We developed two distinct models to analyse and manage the spread of FMD during a pandemic. We validated our models by using real-world data on FMD transmission in confined and unconfined areas. Our study demonstrates that the $SEIR$ and S_i, E_i, I_i, R_i, Q_i models can also be applied to analyse the transmission of other infectious diseases.

Through our analysis, we gained valuable insights into key factors such as the basic reproductive number R_0, which indicates the conditions under which an FMD outbreak may occur in the at-risk population. Our examination of R_0 revealed that adjusting parameters such as δ, δ_1, and δ_2.plays a crucial role in reducing infections. By decreasing the values of these parameters, the number of FMD infections in a specific environment can be reduced.

We also found that when $R_0 < 1$, the model reaches a locally asymptotically stable state known as the disease-free equilibrium. Additionally, our observations indicate that δ, δ_1, and δ_2 are important factors in determining whether R_0 is less than or greater than 1.

Based on the sensitivity analysis, the sensitivity of R_0 to parameter changes in the unconfined environment is determined by comparing the new values of R_0 obtained when varying each parameter. Here is a summary of the findings:

(i) δ_1: New values of R_0 obtained by varying δ_1 showed that changing this parameter had an impact on R_0. As δ_1 increased from 0.3 to 0.7, the new R_0 values changed, indicating

a sensitivity of R_0 to variations in δ_1.

(ii) δ_2: Varying δ_2 did not result in changes to the new R_0 values, indicating that R_0 was not sensitive to variations in δ_2.

(iii) γ: Similar to δ_2, changing γ did not affect the new R_0 values, suggesting that R_0 was not sensitive to variations in γ.

In conclusion, the sensitivity of R_0 to parameter changes depends on the specific parameter being varied. In this analysis, δ_1 was found to have an impact on R_0, while δ_2 and γ did not affect R_0 significantly. This indicates that the dominant FMDV strain in the unconfined setting, as determined by R_0, is particularly sensitive to changes in the parameter δ_1 (the rate at which infected livestock classes generate new infections), but less sensitive to variations in δ_2 (the corresponding rate for buffaloes) and γ (the rate of transition from exposed to infected state).

5.3 Recommendations

Based on the findings of this study, several recommendations can be made regarding FMD control management. The key recommendations are as follows:

1. Vaccination:

   The study emphasizes the importance of vaccination in managing FMD. It suggests that a combination of high vaccination rates and a low rate of vaccine protection loss is the most effective strategy for reducing the burden of FMD. Conversely, a low vaccination rate combined with a high rate of protection loss is the least effective strategy. While prophylactic vaccination alone may not lead to complete eradication of FMD, it can significantly contribute to burden reduction when combined with reactive vaccinations or other control measures such as reactive culling.

2. Quarantine:

   The study highlights the significance of quarantine measures in managing FMD. It reveals that a higher rate of shedding from latently exposed and infectious animals in specific locations (location 1 and 2) leads to an escalation in the burden of FMD. Conversely,

imposing restrictions on the movement of infected livestock through quarantine measures can contribute to a reduction in the burden of FMD.

In conclusion, considering the findings of this study, the following recommendations are proposed:

1. Vaccination: Implement a comprehensive vaccination strategy with high vaccination rates and minimal loss of vaccine protection to effectively reduce the burden of FMD. Consider combining prophylactic vaccination with reactive vaccinations and other control strategies like reactive culling for improved eradication outcomes.

2. Quarantine: Strengthen quarantine measures to restrict the movement of infected livestock. This will help prevent the spread of FMD and reduce its burden. Focus on locations with a high rate of shedding from latently exposed and infectious animals, such as location 1 and 2.

By implementing these recommendations, FMD control management efforts can be optimized, leading to a significant reduction in the burden of the disease. Based on the sensitivity analysis results, we recommend:

1. Further investigation on the parameter δ_1 to be made: Since the sensitivity analysis showed that R_0 is particularly sensitive to changes in δ_1, it would be beneficial to conduct more in-depth studies or gather additional data on this parameter. Understanding the factors influencing δ_1 and its potential variations can provide valuable insights into the dynamics of the disease transmission and aid in developing more effective control strategies.

2. Refining the estimation of δ_2 and γ: Although the sensitivity analysis indicated that changes in δ_2 and γ did not significantly affect R_0, it is still important to ensure accurate estimation of these parameters. Consider refining the estimation methods or obtaining more precise data for δ_2 and γ. Even if they have a limited impact on R_0, having accurate parameter estimates contributes to a more comprehensive understanding of the disease dynamics.

3. Evaluate additional factors: While the current analysis focused on the sensitivity of R_0 to specific parameters, it is important to consider other relevant factors that may influence the spread and control of FMDV. For example, factors related to vaccination strategies, movement patterns of livestock and buffaloes, or environmental conditions could play significant roles. Incorporating these factors into the model and conducting sensitivity analyses can provide a more comprehensive assessment and guide decision-making.

4. Monitoring and adjusting control measures: Regular monitoring of disease prevalence and transmission dynamics can help assess the effectiveness of control measures and identify areas for improvement. By continuously evaluating the impact of control strategies on reducing R_0, adjustments can be made to optimize interventions and minimize the spread of FMDV.

5. Collaboration with experts: Engaging with domain experts, epidemiologists, and veterinary professionals can provide valuable insights and expertise in interpreting the results of the sensitivity analysis and formulating appropriate recommendations. Their knowledge and experience can help guide further research, refine models, and develop targeted control strategies.

5.4 Future Directions

The following future extensions to the modelling and mathematical analyses presented in this thesis are recommended:

1. Sensitivity and Uncertainty Analysis

   Conduct sensitivity and uncertainty analysis on the models to examine the impact of uncertainties in parameter estimates on the numerical simulation results. This analysis will provide insights into the robustness and reliability of the model outputs, taking into account the variability in parameter values.

2. Full Models Global Asymptotic Stability Analysis

   Explore the global asymptotic stability of the endemic equilibria of the full models, ex-

tending the analysis beyond special cases. Investigate the stability properties of the models under various conditions and parameter ranges to gain a deeper understanding of the long-term behaviour of the system.

3. Bifurcations of the Periodic Solutions

   Investigate the uniqueness, stability, and bifurcations of the periodic solutions in the non-autonomous models presented in Chapter 3 and 4. Analyse how the system dynamics change as external factors or parameters vary, leading to the emergence of different periodic solutions. Understand the stability properties of these solutions and their significance in the context of the studied system.

By pursuing these future directions, further insights can be gained into the modeling framework and mathematical analyses presented in this thesis. This will contribute to a more comprehensive understanding of the system dynamics, enhance the robustness of the results, and provide a basis for future research and practical applications.

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Chapter 6

Appendix I: Confined Environment Python Code Repository

6.1 SEIR Simulation

```
import numpy as np
import matplotlib.pyplot as plt
from scipy.integrate import odeint

$def model(y, t):
S, E, I, R = y$

$alpha = 0.5
delta = 0.1
gamma = 0.3
epsilon = 0.2
mu = 0.1
theta = 0.05$

$dSdt = alpha - (delta * I + epsilon) * S
dEdt = delta * S * I - (gamma + epsilon) * E
dIdt = gamma * E - (epsilon + mu + theta) * I
dRdt = theta * I - epsilon * R

$return [dSdt, dEdt, dIdt, dRdt]$

$\# Initial conditions
S0 = 1.3e5
E0 = 0.1
```

```
I0 = 0.1
R0 = 0.0
y0 = [S0, E0, I0, R0]$

$\# Time points
t = np.linspace(0, 10, 100)$

$\# Solve the differential equations
sol = odeint(model, y0, t)$

$\# Plot the results
plt.plot(t, sol[:, 0], label='S')
plt.plot(t, sol[:, 1], label='E')
plt.plot(t, sol[:, 2], label='I')
plt.plot(t, sol[:, 3], label='R')
plt.xlabel('Time')
plt.ylabel('Population')
plt.legend()
plt.title('SEIR␣Model')
plt.show()$
```

6.2 SEIR R_0 Simulation

```
%matplotlib inline
$import matplotlib.pyplot as plt
plt.rcParams["figure.figsize"] = (11, 5) \\
\#set default figure size
import numpy as np
from numpy import exp
from scipy.integrate import odeint
pop_size = 3.3e8
   = 1 / 18
   = 1 / 5.2$

$def F(x, t, R0=1.6):
"""
Time derivative of the state vector.$
```

```
$\* x is the state vector (array_like)
\* t is time (scalar)
\* R0 is the effective transmission rate, \\
defaulting to a constant$

"""
$s, e, i = x$

$\# New exposure of susceptibles
   = R0(t) *     if callable(R0) else R0 *
ne =     * s * i$

$\# Time derivatives
ds = - ne
de = ne -     * e
di =     * e -     * i$

$return ds, de, di$

$\# initial conditions of s, e, i
i_0 = 1e-7
e_0 = 4 * i_0
s_0 = 1 - i_0 - e_0
x_0 = s_0, e_0, i_0$

$def solve_path(R0, t_vec, x_init=x_0):$
"""
$Solve for i(t) and c(t) via numerical integration,
given the time path for R0.$

"""
$G = lambda x, t: F(x, t, R0)
s_path, e_path, i_path = odeint(G, x_init, t_vec).\\
transpose()$

$c_path = 1 - s_path - e_path \\
# cumulative cases
return i_path, c_path$
```

```
$t_length = 550
grid_size = 1000
t_vec = np.linspace(0, t_length, grid_size)$

$R0_vals = np.linspace(1.6, 3.0, 6)
labels = [f'$R0 = {r:.2f}$' for r in R0_vals]
i_paths, c_paths = [], []$

$for r in R0_vals:
i_path, c_path = solve_path(r, t_vec)
i_paths.append(i_path)
c_paths.append(c_path)$

$def plot_paths(paths, labels, times=t_vec):$

$fig, ax = plt.subplots()$

$for path, label in zip(paths, labels):
ax.plot(times, path, label=label)$

$ax.legend(loc='upper left')
ax.set_xlabel('Time in days')
ax.set_ylabel('Population of infected against time')$

$plt.show()
plot_paths(i_paths, labels)$

$def plot_paths(paths, labels, times=t_vec):$

$fig, ax = plt.subplots()$

$for path, label in zip(paths, labels):
ax.plot(times, path, label=label)$

$ax.legend(loc='upper left')
ax.set_xlabel('Time in days')
ax.set_ylabel('Population of infected livestock against t

$plt.show()
```

```
plot_paths(i_paths, labels)
plot_paths(c_paths, labels)$

$def R0_mitigating(t, r0=3,    =1, r_bar=1.6):
R0 = r0 * exp(-     * t) + (1 - exp(-     * t)) * r_bar
return R0$

$ _vals = 1/5, 1/10, 1/20, 1/50, 1/100
labels = [fr'$\eta␣=␣{  :.2f}$' for    in   _vals  ]$

$fig, ax = plt.subplots()$

$for   , label in zip( _vals , labels):
ax.plot(t_vec, R0_mitigating(t_vec,   =  ), label=label)$

$ax.legend()
ax.set_xlabel('Time␣in␣days')
ax.set_ylabel('Population␣of␣infected␣livestock␣against␣t
plt.show()$

$i_paths, c_paths = [], []$

$for    in   _vals  :
R0 = lambda t: R0_mitigating(t,   =  )
i_path, c_path = solve_path(R0, t_vec)
i_paths.append(i_path)
c_paths.append(c_path)$

$plot_paths(c_paths, labels)$

$# initial conditions
i_0 = 25_000 / pop_size
e_0 = 75_000 / pop_size
s_0 = 1 - i_0 - e_0
x_0 = s_0, e_0, i_0$

$R0_paths = (lambda t: 0.5 if t < 30 else 2,
lambda t: 0.5 if t < 120 else 2)$
```

```
$labels = [f'scenario␣{i}' for i in (1, 2)]$

$i_paths, c_paths = [], []$

$for R0 in R0_paths:
i_path, c_path = solve_path(R0, t_vec, x_init=x_0)
i_paths.append(i_path)
c_paths.append(c_path)$

$plot_paths(i_paths, labels)$

$   = 0.01$

$paths = [path *    * pop_size for path in c_paths]
plot_paths(paths, labels)$

$paths = [path *    *    * pop_size for path in i_paths]
plot_paths(paths, labels)$
```

6.3 SEIR Optimal Simulation

```
import numpy as np
from scipy.integrate import solve_ivp
from scipy.optimize import minimize

$\# Define the ODE system$
def ode_system(t, y, alpha, delta, epsilon, gamma, mu, th
$S, E, I, R = y$
$dS_dt = alpha - (delta * I + epsilon) * S
dE_dt = delta * S * I - (gamma + epsilon) * E
dI_dt = gamma * E - (epsilon + mu + theta) * I
dR_dt = theta * I - epsilon * R
return [dS_dt, dE_dt, dI_dt, dR_dt]$

$\# Define the objective function for optimal control
def objective(u, t, y0, alpha, delta, epsilon, gamma, mu,
N = len(u)
T = t[-1]
```

```
dt = T / (N - 1)
y = np.zeros((N, 4))
y[0] = y0$

$for i in range(N - 1):
t_span = [t[i], t[i + 1]]
sol = solve_ivp(lambda t, y: ode_system(t, y, alpha, delta
t_span, y[i], method='RK45')
y[i + 1] = sol.y[:, -1]$

$R_final = y[-1, -1]  \# Final value of R$

$\# Define the cost function to be minimized
cost = np.sum(u ** 2) + R_final ** 2
return cost$

$\# Define the time span and initial conditions
t_span = [0, 10]
y0 = [0.9, 0.1, 0.0, 0.0]$

$\# Define the parameters
alpha = 0.2
delta = 0.3
epsilon = 0.1
gamma = 0.1
mu = 0.05
theta = 0.05$

$\# Define the time points for control
N = 100
t = np.linspace(t_span[0], t_span[1], N)$

$\# Solve the optimal control problem
u0 = np.zeros(N) \\
result = minimize(lambda u: objective(u, t, y0, alpha, de
u0, method='SLSQP')$

$\# Extract the optimal control trajectory
u_opt = result.x$
```

```
$\# Simulate the system with the optimal control \\
sol = solve_ivp(lambda t, y: ode_system(t, y, alpha, delta
t_span, y0, method='RK45')$

$\# Plot the results
import matplotlib.pyplot as plt$

$plt.figure(figsize=(10, 6))
plt.subplot(2, 1, 1)
plt.plot(sol.t, sol.y[0], label='S')
plt.plot(sol.t, sol.y[1], label='E')
plt.plot(sol.t, sol.y[2], label='I')
plt.plot(sol.t, sol.y[3], label='R')
plt.xlabel('Time')
plt.ylabel('Population')
plt.legend()$

$plt.subplot(2, 1, 2)
plt.plot(t, u_opt, label='Optimal control')
plt.xlabel('Time')
plt.ylabel('Control')
plt.legend()$

$plt.tight_layout()
plt.show()$
```

6.4 SEIQR Simulation

```
import numpy as np
from scipy.integrate import odeint
import matplotlib.pyplot as plt

$def SEIQR_model(y, t, N, delta1, delta2, \\
gamma, theta, T12, T21, epsilon): \\
S1, E1, I1, R1, Q1, S2, E2, I2, R2, Q2 = y \\
dS1dt = -delta1*S1*I1 - epsilon*T12*S1 + epsilon*T21*S2 \
dE1dt = delta1*S1*I1 - epsilon*T12*E1 - gamma*E1 + epsilo
```

```
dI1dt = gamma*E1 + epsilon*T21*I2 - theta*I1 - epsilon*T1
dR1dt = theta*I1 + epsilon*T21*R2 - epsilon*T12*R1 \\
dQ1dt = epsilon*(T21*(S2+E2+I2+R2)) - epsilon*(T12*(S1+E1
dS2dt = -delta2*S2*I2 + epsilon*T12*S1 - epsilon*T21*S2 \
dE2dt = delta2*S2*I2 + epsilon*T12*E1 - gamma*E2 - epsilo
dI2dt = gamma*E2 - epsilon*T21*I2 - theta*I2 + epsilon*T1
dR2dt = theta*I2 - epsilon*T21*R2 + epsilon*T12*R1 \\
dQ2dt = epsilon*(T12*(S1+E1+I1+R1)) - epsilon*(T21*(S2+E2
return dS1dt, dE1dt, dI1dt, dR1dt, dQ1dt, dS2dt, dE2dt, d

$N = 1000
delta1 = 0.3
delta2 = 0.2
gamma = 0.1
theta = 0.05
T12 = 0.12
T21 = 0.6
epsilon = 0.03
S1, E1, I1, R1, Q1, S2, E2, I2, R2, \\
Q2 = N-10, 10, 0, 0, 0, N-10, 0, 0, 0, 0 \\
y0 = S1, E1, I1, R1, Q1, S2, E2, I2, R2, Q2 \\
t = np.linspace(0, 100, 10000)$

$result = odeint(SEIQR_model, y0, t, \\
args=(N, delta1, delta2, gamma, theta, T12, T21, epsilon)
S1, E1, I1, R1, Q1, S2, E2, I2, R2, Q2 = result.T$

$plt.figure(figsize=[20,6])
plt.plot(t, Q1, label='Quarantined location 1')
plt.plot(t, Q2, label='Quarantined location 2')
plt.plot(t, S1, label='Susceptible location 1')
plt.plot(t, S2, label='Susceptible location 2')
plt.plot(t, E1, label='Exposed location 1')
plt.plot(t, E2, label='Exposed location 2')
plt.plot(t, I1, label='Infected location 1')
plt.plot(t, I2, label='Infected location 2')
plt.plot(t, R1, label='Recovered location 1')
plt.plot(t, R2, label='Recovered location 2')
plt.xlabel('Time (days)')
```

```
plt.ylabel('Population')
plt.title('SEIQR Model')
plt.legend(loc='best')
plt.show()$
```

6.5 SEIQR R_0 Simulation

```
import numpy as np
from scipy.linalg import eigvals

$\# Function to compute the Jacobian matrix \\
def jacobian(S1, E1, I1, R1, Q1, S2, E2, I2, R2, Q2, delta
epsilon, gamma, theta, delta2, T12, T21): \\
return np.array([
[-delta1 * I1 - epsilon * T12, 0, 0, epsilon * T21, 0, ep
[delta1 * I1 - epsilon * T12, -epsilon * T12 - gamma, 0,
[gamma * E1 - epsilon * T12, 0, -theta - epsilon * T12, e
[0, 0, theta, -epsilon * T12 - epsilon * T21, 0, 0, 0, 0,
[0, 0, -theta, 0, -theta, 0, 0, 0, 0, 0],
[epsilon * T12, epsilon * T12, 0, 0, 0, -delta2 * I2 - ep
[0, epsilon * T12, 0, 0, 0, delta2 * I2 - epsilon * T21,
[0, 0, epsilon * T21, epsilon * T21, 0, gamma * E2 - epsi
[0, 0, 0, epsilon * T21, 0, 0, theta, 0, -epsilon * R2 -
[0, 0, -theta, -theta, -theta, 0, 0, 0, 0, -theta]
])$

$\# Parameters
delta1 = 0.1
epsilon = 0.05
gamma = 0.05
theta = 0.03
delta2 = 0.15
T12 = 0.02
T21 = 0.01$

$\# Disease-free equilibrium
S1_star = 1
E1_star = 0
```

```
I1_star = 0
R1_star = 0
Q1_star = 0
S2_star = 1
E2_star = 0
I2_star = 0
R2_star = 0
Q2_star = 0$

$\# Compute the Jacobian matrix
J = jacobian(S1_star, E1_star, I1_star, R1_star, Q1_star,
S2_star, E2_star, I2_star, R2_star, Q2_star,
delta1, epsilon, gamma, theta, delta2, T12, T21)$

$\# Compute the eigenvalues$
```

6.6 SEIQR Optimal Simulation

```
import numpy as np
from scipy.integrate import solve_ivp
from scipy.optimize import minimize

$\# Define the ODE system
def ode_system(t, y, alpha, delta, \\
epsilon, gamma, mu, theta):
S, E, I, R = y
dS_dt = alpha - (delta * I + epsilon) * S
dE_dt = delta * S * I - (gamma + epsilon) * E
dI_dt = gamma * E - (epsilon + mu + theta) * I
dR_dt = theta * I - epsilon * R
return [dS_dt, dE_dt, dI_dt, dR_dt]$

$\# Define the objective function for optimal control
def objective(u, t, y0, alpha, delta, \\
epsilon, gamma, mu, theta):
N = len(u)
T = t[-1]
dt = T / (N - 1)
```

```
y = np.zeros((N, 4))
y[0] = y0$

$for i in range(N - 1):
t_span = [t[i], t[i + 1]]
sol = solve_ivp(lambda t, y: ode_system(t, y, alpha, delta
t_span, y[i], method='RK45')
y[i + 1] = sol.y[:, -1]$

$R_final = y[-1, -1]  \# Final value of R$

$\# Define the cost function to be minimized
cost = np.sum(u ** 2) + R_final ** 2
return cost$

$\# Define the time span and initial conditions
t_span = [0, 10]
y0 = [0.9, 0.1, 0.0, 0.0]$

$\# Define the parameters
alpha = 0.2
delta = 0.3
epsilon = 0.1
gamma = 0.1
mu = 0.05
theta = 0.05$

$\# Define the time points for control
N = 100
t = np.linspace(t_span[0], t_span[1], N)$

$\# Solve the optimal control problem
u0 = np.zeros(N)
result = minimize(lambda u: objective(u, t, y0, alpha, de
u0, method='SLSQP')$

$\# Extract the optimal control trajectory
u_opt = result.x$
```

```
$\# Simulate the system with the optimal control
sol = solve_ivp(lambda t, y: ode_system(t, y, alpha, delta
t_span, y0, method='RK45')$

$\# Plot the results
import matplotlib.pyplot as plt$

$plt.figure(figsize=(10, 6))
plt.subplot(2, 1, 1)
plt.plot(sol.t, sol.y[0], label='S')
plt.plot(sol.t, sol.y[1], label='E')
plt.plot(sol.t, sol.y[2], label='I')
plt.plot(sol.t, sol.y[3], label='R')
plt.xlabel('Time')
plt.ylabel('Population')
plt.legend()$

$plt.subplot(2, 1, 2)
plt.plot(t, u_opt, label='Optimal control')
plt.xlabel('Time')
plt.ylabel('Control')
plt.legend()$

$plt.tight_layout()
plt.show()$
```