

Faculty of Sciences
Department of Mathematics & Statistical Sciences

Transmission and Control of Foot and Mouth Disease in Botswana: Insights from dynamic modelling, sensitivity analysis and pair approximation

by

Kedibonye Molefe

Reg. No: 12001138

BSc (Pure and Applied Mathematics), BIUST, Botswana

A Dissertation/Thesis Submitted to the Faculty of Sciences in Partial Fulfillment of
the Requirements for the Award of the Degree of Master of Science in Pure and
Applied Mathematics of BIUST

Supervisors:

Dr John Boscoh H. Njagarah
Department of Mathematics & Statistical Sciences,
Faculty of Sciences, BIUST
E-mail: njagarahh@biust.ac.bw

Dr Notice Ringa

1. British Columbia Centre for Disease Control, Vancouver, BC, Canada,
 2. University of British Columbia, Vancouver, BC, Canada
- E-mail: notice.ringa@bccdc.ca

October 21, 2022

DECLARATION REGARDING THE WORK AND COPYRIGHT

Candidate KEDIBONYE MOLEFE

Student ID: 12001138

Thesis Titled: Transmission and Control of Foot and Mouth Disease in Botswana:
Insights from dynamic modelling, sensitivity analysis and pair approximation

I **KEDIBONYE MOLEFE**, certify that the Thesis is all my own original work and that I have not obtained a degree in this University or elsewhere on the basis of any of this work.

This dissertation/thesis is copyright material protected under the Berne Convention, the Copyright and Neighbouring Rights Act, Act. No. 8 of 2000 and other international and national enactments, in that behalf, on intellectual property. It must not be reproduced by any means, in full or in part, except for short extracts in fair dealing; for researcher private study, critical scholarly review or discourse with an acknowledgement, without the written permission of the office of the Postgraduate School, on behalf of both the author and the BIUST.

Signed: K. Molefe

Date: 21 October 2022

Primary Supervisors Dr John Boscoh H. Njagarah and Dr. Notice Ringa

I **John Boscoh H Njagarah**, hereby confirm that I have inspected the above titled thesis and, to the best of my knowledge, it is based on the original work of the candidate.

Signed: [Signature]

Date: 24/10/2022

I **Notice Ringa**, hereby confirm that I have inspected the above titled thesis and, to the best of my knowledge, it is based on the original work of the candidate.

Signed: [Signature]

Date: 24/10/2022

Abstract

Foot and Mouth disease (FMD) remains a global concern despite that many developed countries have eliminated it. This is because FMD is still endemic in some parts of the world, and it can spread around the world via several transmission routes including international trade of affected agricultural products. Botswana which experiences recurring outbreaks of FMD in some parts of the country, FMD has a major negative impact on the beef industry as its outbreaks prevent the country from gaining access to major markets such as the European Union (EU). Hence, there is a need to eliminate the disease to prevent its spread, future outbreaks and to increase control measures. In this thesis, two mathematical models for the dynamics of FMD accounting for the direct, indirect and spatial transmission are formulated and analysed. The first model is a homogeneous-mixing model of FMD with carriers. We derived the basic reproduction number, $\mathcal{R}_0$, and analysed the existence and stability of the disease-free equilibrium. The parameters used in our model were estimated from literature and sensitivity analysis of selected parameters on $\mathcal{R}_0$ as well as the full model was performed using the Latin Hypercube Sampling scheme (LHS). The sensitivity analysis results show that the parameters β_1 and β_2 , which represent direct and indirect transmission of the virus from the infected animals and environment, respectively, together with the shedding of the virus into the environment by the infected animals, have the greatest positive Partial Rank Correlation Coefficients (PRCCs) whilst the parameter for the recovery rate of the infected (α) and the increase in carrier animals (γ) have the highest negative PRCCs. If the processes described by parameters with negative PRCCs are increased, then chances of containing the FMD infections are enhanced. Our numerical simulations show that reducing the contact between susceptible animals and infected surfaces by 80% can reduce the disease burden by up to 71%. However, a combination of controls including reducing contact with infected surfaces and disinfecting leading to increased decay of the pathogen by 100 folds from the baseline value can lead to elimination of the disease. Our second model is a pair approximation model of FMD with carriers. The results show that both the symptomatic and asymptomatic (carriers) nodes in a network have the potential to aggravate spread the disease. The results also show that $\mathcal{R}_0$ is proportional to the infection rate from the carriers associated with lower recovery rates in a network. Therefore, early identifications of infected animals and their contacts in the initial stages of an outbreak followed by prompt application of spatially-oriented control measures, can help contain the disease. We recommend that, when controlling the disease, a combination of control measures be implemented if the disease is to be contained in a shorter period of time. We further suggest that cost-effectiveness analysis and optimal control of admissible controls be studied to ascertain the best combination of disease containment measures.

Dedications

I dedicate my thesis to God, the Almighty for giving me the strength and wisdom to never give up in completing this thesis. A special feeling of gratitude to my loving family and my many friends whose words of encouragement and support that had me going strong throughout this tough yet exciting journey. For my special friend Duduetsang Sengakane for the support and comfort whenever there seemed no way.



Acknowledgements

I am grateful to two of my supervisors Dr Hatson John Boscoh Njagarah and Dr Notice Ringa for their time, support, invaluable advice and patience they invested in helping me to complete this thesis. My gratitude extends to Botswana International University of Science and Technology, (BIUST) and the Faculty of Science (through Simons Foundation) for the financial support to undertake my studies at the Department of Mathematical and Statistical Sciences, BIUST. I also thank the lecturers from my department, Professor Subash Rao to mention, for always encouraging us to complete our Masters studies. Last but not least, I would like to thank BIUST for the studentship that allowed me to carry out this research work successfully.



Contents

Contents	vi
List of Figures	vi
List of Tables	vii
1 Introduction and Literature Review	1
1.1 Foot and Mouth Disease	1
1.2 Foot and Mouth Disease in Botswana	2
1.3 Literature of Mathematical Models of Foot and Mouth disease	4
1.4 Motivation of the Study	5
1.5 Aim and Objectives	6
1.6 Organisation of the Thesis	6
2 A Homogeneous-Mixing Model of FMD Model with Carriers	7
2.1 Model Formulation	7
2.2 Model Analysis	9
2.2.1 Positivity of Solutions	10
2.2.2 Boundedness of Solutions	11
2.3 FMD-Free Equilibrium and the Basic Reproduction Number, $\mathcal{R}_0$	12
2.3.1 Disease-Free Equilibrium	12
2.3.2 The Basic Reproduction Number	13
2.3.3 Endemic Equilibrium	14
2.4 Numerical Simulations	19
2.4.1 Parameter Estimation	19
2.4.2 Sensitivity Analysis	20
2.4.3 Sensitivity Analysis Based on the Full Model	24
2.4.4 Numerical Results	29
2.5 Conclusion	32
3 A Pair Approximation Model of Foot and Mouth disease with Carriers	34
3.1 Introduction	34
3.2 The Mathematical Model	34
3.2.1 Model Equations	36
3.3 Threshold Dynamics	37
3.4 Results and Discussion	40
3.5 Conclusions	41
4 Conclusion and Discussion	43

Appendix	45
A MATLAB and R Codes for Figures in Chapter 2	45
A.1 Matlab Code for the Tornado Plot, Box Plot and PRCCs Respectively in Figure 2.2a, Figure 2.2b and Table 2.4.	45
A.2 Matlab Code for the Scatter Plots in Figure 2.3	48
A.3 Matlab Code for the Sensitivity of the Full Model in Section 2.4.3.	52
A.4 R Code for the Significance of PRCCs for Sensitivity of the Full Model in Section 2.4.3.	54
A.4.1 fmdprcc text file	56
A.4.2 Python Code for Figures 2.12	56
B MATLAB Codes for figures in Chapter 3	59
B.1 Matlab Code For Figure 3.1	59
B.2 Matlab Code For Figure 3.3	59
C Derivation of Chapter 3 equations	61
C.1 Derivation of the $[SI]$ Pair	61
C.2 Derivation Of Equations Of Motion For C_{SI} and C_{SC}	62
C.2.1 Full Correlations	64
C.2.2 CLUSTERING i.e , $\phi = 0$	68

List of Figures

1.1	Botswana Foot and Mouth Disease Control Zones.	3
2.1	A compartmental representation of the model for FMD with infection from the environment.	8
2.2	Partial Rank Correlation Coefficients (PRCCs) for selected model parameters	21
2.3	Scatter plots for the four parameters with the greatest absolute values of PRCC	23
2.4	Sensitivity analysis PRCCs of parameters with respect to Exposed class (E).	24
2.5	PRCCs of model parameters for the Exposed animals at selected time ranges	24
2.6	Sensitivity analysis PRCCs of parameters with respect to pre-symptomatic population (A).	26
2.7	PRCCs of model parameters for the pre-symptomatic animals at selected time ranges	26
2.8	Sensitivity analysis PRCCs of parameters with respect to the Infected population (I).	27
2.9	PRCCs of model parameters for the symptomatic infected animal population at selected time ranges	27
2.10	Sensitivity analysis PRCCs of parameters with respect to the Carriers (C). .	28
2.11	PRCCs of model parameters for the Carrier animals at selected time ranges .	29
2.12	The trend of FMDV when $\mathcal{R}_0 < 1$ and when $\mathcal{R}_0 > 1$	30
2.13	Impact of direct contact with the FMD pathogen in the spread of FMD. . . .	31
2.14	Effect of varying contact between animals and the FMD pathogen contaminated surfaces in the spread of FMD	31
2.15	Effect of disinfecting FMD pathogen contaminated surfaces.	32
3.1	The basic reproduction number $\mathcal{R}_0$ varying the recovery rate, σ	40
3.2	Infection time series for the numbers of susceptible, exposed, infectious, carriers and recovered farms	41
3.3	Infection peak versus λ_i and λ_c	41

List of Tables

2.1	Summary of model state variables and their descriptions.	9
2.2	Symbols and description of parameters used in the model.	9
2.3	Nominal values of parameters used in the model in figure 2.1.	20
2.4	Parameter PRCC Significance and their FDR adjusted p-values	22
2.5	p-values pairwise comparison of significant parameters in Table 2.4 after FDR adjustment.	22
2.6	Parameters after FDR adjustment.	23
2.7	Exposed population parameter PRCC significance (FDR Adjusted p-values). .	25
2.8	Pre-symptomatic population parameter PRCC significance (FDR Adjusted p-values).	26
2.9	Infected population parameter PRCC significance (FDR Adjusted p-values). .	28
2.10	Carriers population parameter PRCC significance (FDR Adjusted p-values). .	29
3.1	Events affecting $[SI]$, the rates of occurrence of the events and the change they cause to $[SI]$	35
C.1	Definitions of variables $n_x(i)$, $n_{xy}(i)$, ζ_x and ζ_{xy}	61

1. Introduction and Literature Review

1.1 Foot and Mouth Disease

Foot and Mouth Disease (FMD), is a highly transmissible, contagious infectious disease affecting cloven-hoofed domestic and wild animals such as goats, sheep, cattle, pigs and buffaloes [1, 2]. The pathogen which causes FMD is an Aphthovirus which belongs to the Picornaviridae family [3]. There are 7 known serotypes of FMD virus and over 60 sub-types of this virus [4, 5]. These serotypes vary according to the geographical region and are classified as African types (STA 1, STA 2, STA 3), European types (O, A and C) and Asian types (Asia).

Vaccination against one serotype does not provide protection against other serotypes, that is, there is no universal vaccine against the disease [5]. This means that FMD vaccines must match to the type and sub-type present in the affected area. This makes it difficult to control FMD through vaccination alone. Therefore, multiple control measures may need to be adopted. Susceptible animals can be infected via direct contact with infected animals, infected animal products, exposure to fomites or through wind-borne aerosol. The FMD virus maybe present in milk and semen for up-to 4 days before the animal shows clinical signs [6]. Clinical signs include fever, blister like lesions in the mouth, on the teats, between the hooves and above the hooves. Excessive salivation, lameness, reduced milk production and decreased feed consumption are also observed [7, 8].

The FMD causing virus can survive on surfaces such as metals, transport vehicles, grazing lands, drinking points of animals and in the air [9]. This implies that an uninfected animal can acquire the virus through contact with the infected surfaces, that is, there is a possibility for the FMD virus to spread from such contaminated surfaces to an uninfected animal, a route referred to as indirect transmission. We note that there is inadequacy of studies that capture the impact of environmental contamination and its role in the transmission of FMD. Therefore, inclusion of the proportion of indirect transmission from the environment in mathematical model structures is a very important aspect as it helps us in drawing insights into its contribution to the disease dynamics.

At the moment, there is no known cure for FMD. Vaccines can protect animals against exposure to the disease but do not always prevent the animals from being infected. FMD rarely leads to death but it compromises the health and quality of products that are obtained from animals with a history of the disease. Mortality rate is high in young animals than in adult animals [5]. Control measures against FMD include isolation, culling, vaccination, public education and sanitation etiquette more specifically disinfecting the affected areas.

FMD is endemic or near-endemic in many parts of the world, particularly in developing countries, which have limited resources for disease control. It has a negative impact on the

economies of many countries because of strict rules that prohibit international trade of animal products from previously affected territories [10]. Currently, many countries are being faced with a war against the re-occurrences of FMD. Outbreaks of FMD in a specific area are usually controlled by quarantines and movement restrictions, cleansing and disinfection of affected premises, equipment and all herds on farms whether infected or not are slaughtered and disposed off safely. For instance, in the 2001 United Kingdom FMD outbreak, it was estimated that there was a total of 2030 FMD cases and as a means of controlling the disease and preventing its re-occurrence, at least 6.5 million animals were culled [11]. This caused a loss which composed of food industry and compensation for culled animals to the value summing upto 5.27 billion pounds [12, 13, 14].

1.2 Foot and Mouth Disease in Botswana

Cattle farming contributes hugely to the livelihood of Botswana and the country's overall agricultural gross domestic product (GDP). The beef sector is a core element of the economy and contributes about 80% to the GDP. With Botswana being one of the countries in Southern Africa that heavily rely on beef exports to grow its economy, the FMD epidemic has turned to be a nightmare to the country and a threat to its economy as its outbreaks prevent the country from gaining access to major markets such as the European Union (EU). These outbreaks have lead to a great loss to the country through reduced production, increased costs of FMD control as well as poor access to markets. For instance, from 2009 to 2014, it cost the government of Botswana about P127 211 668.00 to control the disease by vaccination and culling, following the outbreaks in the north and eastern parts of the country[15]. FMD is endemic in Botswana and several other countries worldwide and has been globally prevalent for centuries now despite the application of control measures. The long history of FMD in Botswana dates back to the 1930's [16]. FMD was first recorded in Botswana in the early 1930's and later eradicated in 1934, but only to reappear throughout the 1940's, 50's, 70's and 80's [15, 17], with the last reported cases in the 80's occurring in September 1980 [16, 17]. After a long time of no outbreak, in 2002, Botswana started to experience irregular FMD outbreaks even in previously FMD-free zones [17].

The disease in Botswana is caused by 3 serotypes *i.e.*, SAT1, SAT 2, and SAT 3. These serotypes are found in regions where there are wild buffaloes in the northern parts of the country, which are considered as life-long asymptomatic carriers of the FMD virus. Control of Foot and Mouth disease in Botswana is mainly premised on vaccination in FMD high-risk areas, biosecurity measures, disease surveillance, movement control and public education [18]. All these control measures follow the international standards from the World Organisation for Animal Health (OIE). Because of the re-occurrences of FMD, the key strategies used in the control of the spread of FMD during outbreaks include cordon fences, vaccination, biosecurity, movement control through disease control gates or checkpoints and surveillance. Through the cordon fences, the country is divided into different zones namely, FMD vaccination zone, red zone (found in the northern part of the country), FMD surveillance zone (areas at the interface of the FMD red zones and FMD green zones) and the FMD free/non-

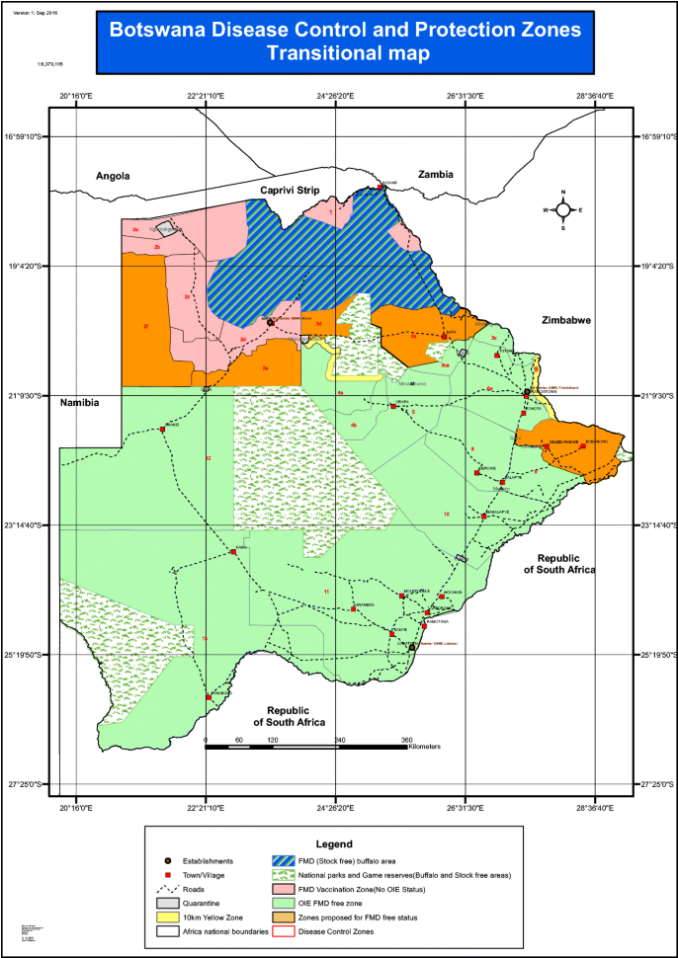


Figure 1.1: Botswana Foot and Mouth Disease Control Zones. Source: Department of veterinary service (DVS), Botswana (2017), [19].

vaccinated zone [15, 20]. The map of Botswana showing these zones is given in Figure 1.1.

1.3 Literature of Mathematical Models of Foot and Mouth disease

A number of mathematical models of FMD have been formulated and analysed to understand the dynamics of the disease. The availability of data on the 2001 United Kingdom (UK) epidemic outbreak of FMD resulted in the development of several mathematical models describing the mechanism of the disease spread as well as inform policy by employing relevant control measures that can contain the disease more effectively to prevent future outbreaks. The difference between the types of these models depends in the way they capture characteristics of this disease and the available techniques for solving such models.

Most mathematical epidemiology models are based on the classical infectious disease model developed by W.O. Kermack and A.G. McKendrick susceptible-infectious-recovered (SIR) model in 1927 [21]. This model is formulated by dividing the host population into three disease states (called compartments) of susceptible (S), infectious (I) and recovered (R) individuals. This model assume that susceptible individuals interact with infected individuals at a given infection rate, say λ which describes the force of infection. The infected individuals recover over time at a given recovery rate, say σ and acquire immunity [21]. These rates of infection and recovery are called parameters of the model.

The SIR model can be analysed to find solutions to the model (here, the numbers of states S, I and R individuals at any time, t) and studying the model threshold dynamics which are the conditions determining whether the disease will persist or die out. This basic model only accounts for infection and removed events which are sufficient to describe a simple epidemic and the threshold condition necessary for an epidemic to start. This means that endemic disease transmission or recurring epidemics are not accounted for in the SIR model. This condition cannot be ignored, as such there is need to extend the basic SIR model by considering variables and model parameters that are of interest to a given study. Going forward, we outline some selected models developed to study FMD based on past disease outbreaks. We note also that the list presented here is by no means exhaustive.

Ferguson *et al.*, (2001) [2] designed a pair approximation model that explored the impact of potentially more effective control strategies such as ring culling and ring vaccination. In their model, the authors divided the state variables into susceptible farms [S], exposed [E], infectious [I], recovered farms [R] and pairs of farms [XY] where X and Y represent disease statuses; susceptible, exposed, infectious or recovered. They performed the simulation of the model which showed that both ring culling and ring vaccination control foot and mouth disease more rapidly with ring culling predicted to be more effective compared to vaccination.

Keeling *et al.*, (2001) [22], explored the dynamics of the 2001 UK FMD outbreak using an individual farm-based stochastic model. Each farm was classified as either susceptible, incubating, infectious or slaughtered. The transmission of FMD between farms was determined

by the number and type of livestock, the distance between susceptible and infectious farms, distinction between localised spread of the disease and possibility of long-range transmission. It was determined that culling of farms neighbouring infected premises controls the disease more effectively.

In 2007, Ster and Ferguson [23] modelled the transmission of the 2001 foot and mouth epidemic in Great Britain. They developed a Markov Chain Monte Carlo (MCMC) method for estimating epidemiological parameters for a range of simple transmission models. The authors made an assumption that infectious farms were completely observed in 2001, equivalent to assuming that farms that were proactively culled but not diagnosed with FMD were not infectious, even if some were infected. The results obtained were similar to the observations in [22] as the estimated parameters showed that culling was important for the control of the 2001 FMD epidemic.

Traulsen *et al.*, (2010) [24], developed a spatial and temporal Monte-Carlo simulation model to analyse the epidemiology and control of foot and mouth disease. A stochastic simulation model with special focus on the simultaneous estimation of the airborne spread and the modelling of contacts between farms was presented. The authors investigated the influence of eleven input parameters and interactions between them were estimated. The results showed that the considered parameters as well as the interactions between them had a significant impact on the epidemic duration and the number of infected and culled farms.

In 2016, Mushayabasa [25] modelled the intrinsic dynamics of foot and mouth disease. In the paper, two models for FMD were proposed which incorporated relevant biological and ecological factors, vaccination effects and seasonal impacts during the interaction among susceptible, vaccinated, exposed, infected, carrier and recovered animals. The study results showed that vaccination alone may not be sufficient to eradicate FMD.

In this work, two mathematical models for the transmission of FMD disease are formulated and analysed. The first proposed model considers susceptible, exposed, asymptomatic and infected animals, carriers, recovered and infection from the environment as the classes for the disease progression. The details of the model are given in Chapter 2. The second model follows the pair approximation approach to study the effect of space on the spread of FMD. The details of the model and its analysis are given in Chapter 3.

1.4 Motivation of the Study

Foot and Mouth disease has a major effect on the beef industry in Botswana which contributes the larger share (about 80%) of the total contribution by the agricultural sector. FMD outbreaks prevent access to major beef export markets. The significance of this study is to highlight the effect of both direct and indirect transmission of FMD, and to identify the key process that much be addressed if future outbreaks are to be prevented. We explore characteristics of re-occurrences of single outbreaks of FMD and their dependence on the disease re-importation.

1.5 Aim and Objectives

Aim

To develop mathematical models incorporating the environment and space as factors that have impact in the dynamics of Foot and Mouth disease, including but not limited to direct and indirect transmission routes.

Objectives

- Develop a SEIR type model for FMD incorporating both direct and indirect transmission from the environment.
- Perform the model analysis for the formulated Homogeneous-Mixing model in order to determine its behaviour based on the equilibrium points, reproduction number and sensitivity analysis.
- Build a pair approximation model incorporating the spatial spread of FMD.
- Carry out mathematical analysis for the pair approximation model based on the threshold dynamics.

1.6 Organisation of the Thesis

In this thesis, we propose a mathematical framework to study the dynamics of FMD by incorporating asymptomatic carriers as one of the driving forces of the transmission dynamics. In Chapter 2, we start with the basic model represented by Ordinary Differential Equation (ODE) system with interaction among susceptible, exposed, asymptomatic, symptomatic, carriers, recovered groups and the virus infected environment. We investigate the disease threshold dynamics through the basic reproductive number and conduct the equilibrium and numerical analysis of the model. In Chapter 3, we proceed to study FMD dynamics by incorporating spatiality. We develop and study a pair approximation model of FMD where the disease pathogen is transmissible from both symptomatic infectious and asymptomatic carrier nodes to susceptible contacts on a prescribed network structure. We do this by computing the basic reproduction number for the pair approximation model, the results are then discussed based on $\mathcal{R}_0$ and appropriate conclusions drawn. In Chapter 4, we present the general conclusion to the thesis, recommendations and suggestions for future work.

2. A Homogeneous-Mixing Model of FMD Model with Carriers

2.1 Model Formulation

We present a basic mathematical model for the transmission dynamics of Foot and Mouth Disease (FMD), which spreads in endemic or near-endemic countries like Botswana. The susceptible animals can be infected through direct contact with the infected animal or indirect contact with the FMD infected surfaces (environment). In the population considered, upon direct contact with the disease pathogen, *picarnovirus*, susceptible animals (S) become exposed to the disease through contact with infected animals or surfaces infected with the virus. Upon exposure, the animals are classified as exposed (E). The exposed animals later progress to the infectious state. Once infected, animals that are pre-symptomatic and symptomatic are grouped in classes (A) and (I) respectively. It is estimated that animals exposed to FMD, depending on the FMD serotype and the host, are exposed for approximately σ^{-1} days before some become infectious and others become carriers (C). These animals also decrease in number because of FMD related mortality and some recover from the disease [2, 6]. Carrier animals remain in the carrier state for a period of 3 to 3.5 years [9]. Through indirect exposure to FMD pathogens, animals are exposed to infected environments, where the virus from infectious classes pre-symptomatic (A), infected (I) and carriers (C) is present. If S , E , A , I , C , R and W represent number of susceptible, exposed, asymptomatic, infected, carriers, recovered and infected environment compartments respectively, then at any point in time the total animal population size is given by

$$N(t) = S(t) + E(t) + A(t) + I(t) + C(t) + R(t).$$

The force of infection is assumed to follow a standard incidence. The model assumes animals join the susceptible group at the rate π by births and immigration. Every animal group in a population is reduced by natural death at a rate μ except for the infected group which has FMD related mortality at rate δ . We also assume that once an animal recovers from the disease it does so with permanent immunity. By combining the direct and indirect routes of transmission of the disease pathogen, the force of infection is given by

$$\lambda = \left(\left(\frac{\beta_1(A + \eta_1 I + \eta_2 C)}{N} \right) + \left(\frac{\beta_2 W}{K + W} \right) \right),$$

where, N is the total population, K is the FMD pathogen concentration in the environment that increases the likelihood of transmission through the indirect route to 50%, η_1 and η_2 are the rates at which infected group and carriers pass the disease pathogen relative to the asymptomatic infected animals. β_1 and β_2 are effective transmission rates which account for

the number of effective contacts and the probability that a contact results into an infection. The flow diagram for the transmission dynamics of the proposed model is represented in Figure 2.1.

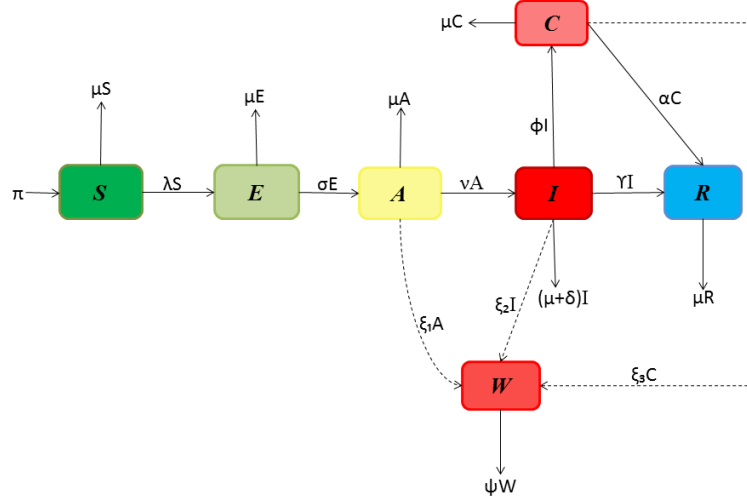


Figure 2.1: A compartmental representation of the model for FMD with infection from the environment.

Following the flow diagram, Figure 2.1, model formulation and related assumptions, the system of ordinary differential equations for the model are given by

$$\frac{dS}{dt} = \pi - (\lambda + \mu)S, \quad (2.1a)$$

$$\frac{dE}{dt} = \lambda S - Q_1 E, \quad (2.1b)$$

$$\frac{dA}{dt} = \sigma E - Q_2 A, \quad (2.1c)$$

$$\frac{dI}{dt} = \nu A - Q_3 I, \quad (2.1d)$$

$$\frac{dC}{dt} = \phi I - Q_4 C, \quad (2.1e)$$

$$\frac{dR}{dt} = \gamma I + \alpha C - \mu R, \quad (2.1f)$$

$$\frac{dW}{dt} = \xi_1 A + \xi_2 I + \xi_3 C - \psi W, \quad (2.1g)$$

where $Q_1 = \mu + \sigma$, $Q_2 = \mu + \nu$, $Q_3 = \phi + \mu + \delta + \gamma$, and $Q_4 = \alpha + \mu$.

State Variable	Meaning
S	Susceptible animals
E	Exposed animals
A	Presymptomatic animals
I	Infected animals
C	Carrier animals
R	Recovered animals
W	Contaminated surfaces/objects in the environment

Table 2.1: Summary of model state variables and their descriptions.

Parameter Symbol	Description
π	Recruitment rate into the susceptible group
μ	Natural mortality rate of animals
σ	Rate at which exposed animals become presymptomatic infectious
ν	Transition from presymptomatic to infected group
ϕ	Rate at which infected animals become carriers
γ	Recovery rate of the infected animals
α	Recovery rate of the carriers
β_1	Transmission rate directly from the infected group
β_2	Transmission rate from the environment
ψ	Virus decay into the environment
η_1	Infection rate of infected animals relative to the presymptomatic group
η_2	Infection rate of carriers relative to the presymptomatic group
ξ_1, ξ_2, ξ_3	Rates at which presymptomatic, infected and carrier groups respectively shed the disease pathogen into the environment
δ	FMD related mortality rate
K	Pathogen concentration in the environment that increases the likelihood of infection from the environment by 50%

Table 2.2: Symbols and description of parameters used in the model.

2.2 Model Analysis

The variables and parameters of the model are assumed to be positive for $t > 0$. The analysis of system (2.1) will therefore be performed in a region defined by;

$$\Omega = \{\Omega_H \times \Omega_W : \Omega_H \in \mathbb{R}_+^6, \Omega_W \in \mathbb{R}_+^1\}$$

where;

$$\Omega_H = \left\{ (S(t), E(t), A(t), I(t), C(t), R(t)) \in \mathbb{R}_+^6 \mid 0 \leq N \leq \frac{\pi}{\mu} \right\}.$$

$$\Omega_W = \left\{ W(t) \mid 0 \leq W(t) \leq \frac{(\xi_1 + \xi_2 + \xi_3)\pi}{\mu\psi} \right\}.$$

2.2.1 Positivity of Solutions

We now consider the positivity of system (2.1). Here, we prove that all the state variables, susceptible, exposed, asymptomatic, infected, carriers and the infected environment remain positive and the solutions of our system (2.1) with positive initial conditions will remain positive for all $t > 0$.

Theorem 1. *Given the initial conditions $S_0 > 0$, $E_0 \geq 0$, $A_0 \geq 0$, $I_0 \geq 0$, $C_0 \geq 0$, $R_0 \geq 0$, $W_0 \geq 0$, the solutions $S(t)$, $E(t)$, $A(t)$, $I(t)$, $C(t)$, $R(t)$, $W(t)$ are non-negative for all $t > 0$.*

This can be proven as follows;

Proof. Suppose that

$$\hat{t} = \sup\{t > 0 : S > 0, E > 0, A > 0, I > 0, C > 0, R > 0, W > 0\} \in [0, t].$$

Thus $\hat{t} > 0$, and it follows from first equation of the system (2.1) that

$$\frac{dS}{dt} = \pi - (\lambda + \mu)S$$

We thus have

$$\frac{dS}{dt} \geq -(\lambda(t) + \mu)S \geq (\hat{\lambda} + \mu)S,$$

where, $\hat{\lambda} = \max\{\lambda(t) : t \geq 0\}$.

We now solve the inequality by separation of variables and integrate both sides with respect to the corresponding variable to obtain;

$$\int_{S_0}^S \frac{dw}{w} \geq \int_0^t -(\hat{\lambda} + \mu)dz$$

so that,

$$S(t) \geq S_0 e^{-(\hat{\lambda} + \mu)t} > 0. \quad (2.2)$$

From equation (2.1b), we have

$$\begin{aligned}\frac{dE}{dt} &= \lambda S - Q_1 E \\ &\geq -Q_1 E,\end{aligned}$$

whose solution is obtained by separation of variables and integrating with respect to corresponding variables and results in

$$E(\hat{t}) \geq E_0 e^{-Q_1 \hat{t}} \geq 0. \quad (2.3)$$

For the remaining state variables, we use the same approach and obtain;

$$\begin{cases} A(t) \geq A_0 e^{-Q_2 \hat{t}} \geq 0, \\ I(t) \geq I_0 e^{-Q_3 \hat{t}} \geq 0, \\ C(t) \geq C_0 e^{-Q_4 \hat{t}} \geq 0, \\ R(t) \geq R_0 e^{-\mu \hat{t}} \geq 0, \\ W(t) \geq W_0 e^{-\psi \hat{t}} \geq 0, \end{cases} \quad (2.4)$$

for all $\hat{t} > 0$.

From equations (2.2)- (2.4), we observe that the state variable solutions of system (2.1) are non-negative provided the initial conditions are non-negative. This completes the proof. $\square$

2.2.2 Boundedness of Solutions

The total population considered in this model is not constant. To determine whether the state variables of the animal population are bounded, or enough to show that the total population is bounded using the system of equations (2.1) and the expression for the total population, the evolution equation for the change in the population is given by

$$\frac{dN}{dt} = \pi - \mu N(t) - \sigma I(t) \quad (2.5)$$

$$\leq \pi - \mu N(t). \quad (2.6)$$

The inequality (2.6) can be solved by separation of variables or using an integrating factor method to obtain

$$N \leq \frac{\pi}{\mu} + \left(N_0 - \frac{\pi}{\mu} \right) e^{-\mu t}, \quad (2.7)$$

where $N(0) = N_0$.

We note from equation (2.7) that, the $\lim_{t \rightarrow \infty} N(t) = \frac{\pi}{\mu}$. Clearly $\frac{\pi}{\mu}$ is the upper bound of N .

Therefore, we note that for $0 \leq N(0) \leq \frac{\pi}{\mu}$, we have

$$0 \leq N(t) \leq \frac{\pi}{\mu}.$$

For the environmental variable W , we have;

$$\begin{aligned} \frac{dW}{dt} &= \xi_1 A + \xi_2 I + \xi_3 C - \psi W \\ &\leq (\xi_1 + \xi_2 + \xi_3) \frac{\pi}{\mu} - \psi W, \end{aligned}$$

because $A(t)$, $I(t)$ and $C(t)$ are less than $\frac{\pi}{\mu}$ for all $t > 0$.

Applying the Gronwall inequality [26, 27], for the initial condition of the environmental variable

$$0 \leq W(0) \leq \frac{(\xi_1 + \xi_2 + \xi_3)\pi}{\mu\psi},$$

we have

$$0 \leq W(t) \leq \frac{(\xi_1 + \xi_2 + \xi_3)\pi}{\mu\psi}. \quad (2.8)$$

This shows the existence of bounded solutions. Hence, the region Ω is positively invariant under the flow induced by system (2.1). Thus, in Ω our system is well-posed hence it is adequate to study the dynamics of the model in the domain Ω .

2.3 FMD-Free Equilibrium and the Basic Reproduction Number, $\mathcal{R}_0$

2.3.1 Disease-Free Equilibrium

Let the state variables at the disease free equilibrium $\mathcal{E}_0$ be $S^*, E^*, A^*, I^*, C^*, R^*, W^*$. To determine the equilibrium solutions, we set the right-hand-side of the system of equations (2.1) to zero and obtain

$$\begin{aligned} 0 &= \pi - (\lambda^* + \mu)S^*, \\ 0 &= \lambda^* S^* - Q_1 E^*, \\ 0 &= \sigma E^* - Q_2 A^*, \\ 0 &= \nu A^* - Q_3 I^*, \\ 0 &= \phi I^* - Q_4 C^*, \\ 0 &= \gamma I^* + \alpha C^* - \mu R^*, \\ 0 &= \xi_1 A^* + \xi_2 I^* + \xi_3 C^* - \psi W^*. \end{aligned}$$

In the absence of the FMD pathogen the system (2.1) gives a FMD-free equilibrium point($\mathcal{E}_0$) given by

$$\mathcal{E}_0 = \left(S_0, E_0, A_0, I_0, C_0, R_0, W_0 \right) = \left(\frac{\pi}{\mu}, 0, 0, 0, 0, 0, 0 \right). \quad (2.9)$$

To analyse the existence of equilibrium points, we ought to use the reproduction number evaluated in terms of the model parameters. This threshold value (reproduction number) is also vital in making conclusions about the stability of the obtained equilibrium points.

2.3.2 The Basic Reproduction Number

The basic reproduction number, R_0 , is the expected number of secondary cases produced by a single infectious individual upon introduction into a completely susceptible population [28]. An epidemic outbreak is expected if on average an infected individual produces more than one new infection when introduced into a susceptible population, *i.e.*, when $R_0 > 1$ but an infection will die out if $R_0 < 1$. Here, we use the next generation matrix method outlined in [29, 30] to determine our R_0 and adopt the same matrix definitions used in [30] to avoid confusion. Taking the infected compartments to be E, A, I, C and W, the matrices for new infection terms and the transfer terms between compartments are given by

$$\mathcal{F} = \begin{pmatrix} \left(\left(\frac{\beta_1(A+\eta_1 I + \eta_2 C)}{N} \right) + \left(\frac{\beta_2 W}{K+W} \right) \right) S \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \text{ and } \mathcal{V} = \begin{pmatrix} Q_1 E \\ -\sigma E + Q_2 A \\ -\nu A + Q_3 I \\ -\phi I + Q_4 C \\ -(\xi_1 A + \xi_2 I + \xi_3 C) + \psi W \end{pmatrix}$$

Linearisation of the matrices $\mathcal{F}$ and $\mathcal{V}$ at the disease free equilibrium yields

$$F = \begin{pmatrix} 0 & \beta_1 & \beta_1 \eta_1 & \beta_1 \eta_2 & \frac{\beta_2 \pi}{K \mu} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} Q_1 & 0 & 0 & 0 & 0 \\ -\sigma & Q_2 & 0 & 0 & 0 \\ 0 & -\nu & Q_3 & 0 & 0 \\ 0 & 0 & -\phi & Q_4 & 0 \\ 0 & -\xi_1 & -\xi_2 & -\xi_3 & \psi \end{pmatrix}.$$

Mathematically, $\mathcal{R}_0$ is given as the spectral radius of the matrix FV^{-1} so that after further simplification, we obtain

$$\mathcal{R}_0 = \rho(FV^{-1}) = \mathcal{R}_0^A + \mathcal{R}_0^I + \mathcal{R}_0^C + \mathcal{R}_0^W, \quad (2.10)$$

where

$$\begin{aligned}\mathcal{R}_0^A &= \frac{\sigma\beta_1}{Q_1Q_2} = \left(\frac{\sigma}{Q_1}\right)\left(\frac{\beta_1}{Q_2}\right), \\ \mathcal{R}_0^I &= \frac{\nu\sigma\beta_1\eta_1}{Q_1Q_2Q_3} = \left(\frac{\nu}{Q_2}\right)\left(\frac{\sigma}{Q_1}\right)\left(\frac{\beta_1\eta_1}{Q_3}\right), \\ \mathcal{R}_0^C &= \frac{\nu\sigma\phi\beta_1\eta_2}{Q_1Q_2Q_3Q_4} = \left(\frac{\nu}{Q_2}\right)\left(\frac{\sigma}{Q_1}\right)\left(\frac{\phi\beta_1\eta_2}{Q_3Q_4}\right), \\ \mathcal{R}_0^W &= \frac{\beta_2\sigma(Q_3Q_4\xi_1 + \nu Q_4\xi_2 + \nu\phi\xi_3)\pi}{\mu K\psi Q_1Q_2Q_3Q_4}.\end{aligned}$$

We note that $\mathcal{R}_0$ is the sum of components of the reproduction number representing the contribution of individuals from compartments A , I , C and W respectively. It depends on several model parameters particularly, the FMD transmission rate due to contact between infected and susceptible animals as well as contact with the infected environment (*i.e* the environment infected with the virus that causes FMD).

We note that the process of determining the reproduction number by the next generation matrix method presumes local stability of the disease free equilibrium [30]. We therefore have the following theorem

Theorem 2. *The disease-free equilibrium ($\mathcal{E}_0$) of the model system (2.1) defined on the domain Ω , is locally asymptotically stable.*

2.3.3 Endemic Equilibrium

The endemic equilibrium is the state at which the disease cannot be totally eradicated in a population [31]. So we let system (2.1) have an endemic equilibrium given by;

$$\mathcal{E}_1^* = (S^{**}, E^{**}, A^{**}, I^{**}, C^{**}, R^{**}, W^{**}). \quad (2.11)$$

To determine $\mathcal{E}_1^*$, we set the left hand side of our system (2.1) to zero to obtain

$$0 = \pi - (\lambda^{**} + \mu)S^{**}, \quad (2.12a)$$

$$0 = \lambda^{**}S^{**} - Q_1E^{**}, \quad (2.12b)$$

$$0 = \sigma E^{**} - Q_2A^{**}, \quad (2.12c)$$

$$0 = \nu A^{**} - Q_3I^{**}, \quad (2.12d)$$

$$0 = \phi I^{**} - Q_4C^{**} = 0, \quad (2.12e)$$

$$0 = \gamma I^{**} + \alpha C^{**} - \mu R^{**} = 0, \quad (2.12f)$$

$$0 = \xi_1 A^{**} + \xi_2 I^{**} + \xi_3 C^{**} - \psi W^{**}, \quad (2.12g)$$

where,

$$\lambda^{**} = \frac{\beta_1(A^{**} + \eta_1 I^{**} + \eta_2 C^{**})}{S^{**} + E^{**} + A^{**} + I^{**} + C^{**} + R^{**}} + \frac{\beta_2 W^{**}}{K + W^{**}}$$

From equations (2.12c)-(2.12g), we express the appropriate steady state values in terms of A^{**} such that

$$\begin{cases} E^{**} &= \frac{Q_2}{\sigma} A^{**}, \\ I^{**} &= \frac{\phi}{Q_3} A^{**}, \\ C^{**} &= \frac{\phi\nu}{Q_3 Q_4} A^{**}, \\ R^{**} &= \Phi_1 A^{**}, \\ W^{**} &= \Phi_2 A^{**}, \end{cases}$$

where $\Phi_1 = \frac{1}{\mu} \left(\frac{\gamma\nu Q_4 + \alpha\phi\nu}{Q_3 Q_4} \right)$ and $\Phi_2 = \frac{1}{\psi} \left(\frac{\xi_1 Q_3 Q_4 + \xi_2 \nu Q_4 + \xi_3 \phi\nu}{Q_3 Q_4} \right)$.

Adding (2.12a) and (2.12b) we get

$$\begin{aligned} 0 &= \pi - \mu S^{**} - Q_1 E^{**} \\ S^{**} &= \frac{\pi}{\mu} - \frac{Q_1}{\mu} E^{**} \\ S^{**} &= \frac{\pi}{\mu} - \frac{Q_1 Q_2}{\sigma\mu} A^{**} \end{aligned}$$

The total population at the endemic equilibrium is given by

$$\begin{aligned} N^{**} &= S^{**} + E^{**} + A^{**} + I^{**} + C^{**} + R^{**} \\ &= \frac{\pi}{\mu} - \frac{Q_1 Q_2}{\sigma\mu} A^{**} + \frac{Q_2}{\sigma} A^{**} + A^{**} + \frac{\phi}{Q_3} A^{**} + \frac{\phi\nu}{Q_3 Q_4} A^{**} + \Phi_1 A^{**} \\ &= \frac{\pi}{\mu} - \frac{Q_1 Q_2}{\sigma\mu} A^{**} + \left(\frac{Q_2 Q_3 Q_4 + \sigma Q_3 Q_4 + \phi\sigma Q_4 + \phi\sigma\nu + \sigma Q_3 Q_4 \Phi_1}{\sigma Q_3 Q_4} \right) A^{**} \\ &= \frac{\pi}{\mu} - \Phi_3 A^{**}, \end{aligned}$$

where $\Phi_3 = \frac{Q_1 Q_2 Q_3 Q_4 - \mu(Q_2 Q_3 Q_4 + \sigma Q_3 Q_4 + \phi\sigma Q_4 + \phi\sigma\nu + \sigma Q_3 Q_4 \Phi_1)}{\sigma\mu Q_2 Q_3 Q_4}$.

Therefore, the total population is given by

$$N^{**} = \frac{\pi}{\mu} - \Phi_3 A^{**} \quad (2.13)$$

The force of infection at the endemic equilibrium is given by

$$\begin{aligned} \lambda^{**} &= \frac{\beta_1(A^{**} + \eta_1 \frac{\phi}{Q_3} A^{**} + \eta_2 \frac{\phi\nu}{Q_3 Q_4} A^{**})}{\frac{\pi}{\mu} - \Phi_3 A^{**}} + \frac{\beta_2 \Phi_2 A^{**}}{K + \Phi_2 A^{**}} \\ &= \frac{\beta_1 \frac{Q_3 Q_4 + \eta_1 \phi Q_4 + \eta_2 \phi\nu}{Q_3 Q_4} A^{**}}{\frac{\pi}{\mu} - \Phi_3 A^{**}} + \frac{\beta_2 \Phi_2 A^{**}}{K + \Phi_2 A^{**}} \\ &= \frac{\beta_1 \Phi_4 (K + \Phi_2 A^{**}) + \beta_2 \Phi_2 (\frac{\pi}{\mu} - \Phi_3 A^{**}) A^{**}}{(\frac{\pi}{\mu} - \Phi_3 A^{**})(K + \Phi_2 A^{**})}, \end{aligned}$$

where $\Phi_4 = \frac{Q_3 Q_4 + \eta_1 \phi Q_4 + \eta_2 \phi \nu}{Q_3 Q_4}$.

Therefore,

$$\lambda^{**} = \frac{\left[\beta_1 \Phi_4 (K + \Phi_2 A^{**}) + \beta_2 \Phi_2 \left(\frac{\pi}{\mu} - \Phi_3 A^{**} \right) \right] A^{**}}{\left(\frac{\pi}{\mu} - \Phi_3 A^{**} \right) (K + \Phi_2 A^{**})}. \quad (2.14)$$

Substituting (2.14) into (2.12b) we obtain

$$\begin{aligned} 0 &= \left[\frac{\left(\beta_1 \Phi_4 (K + \Phi_2 A^{**}) + \beta_2 \Phi_2 \left(\frac{\pi}{\mu} - \Phi_3 A^{**} \right) \right) A^{**}}{\left(\frac{\pi}{\mu} - \Phi_3 A^{**} \right) (K + \Phi_2 A^{**})} \right] \left(\frac{\pi}{\mu} - \frac{Q_1 Q_2}{\sigma \mu} A^{**} \right) - \frac{Q_1 Q_2}{\sigma} A^{**} \\ 0 &= \left[\beta_1 \Phi_4 (K + \Phi_2 A^{**}) + \beta_2 \Phi_2 \left(\frac{\pi}{\mu} - \Phi_3 A^{**} \right) \right] \left(\frac{\pi}{\mu} - \frac{Q_1 Q_2}{\sigma \mu} A^{**} \right) - \frac{Q_1 Q_2}{\sigma} \left(\frac{\pi}{\mu} - \Phi_3 A^{**} \right) (K + \Phi_2 A^{**}) \\ 0 &= \left[\beta_1 \Phi_4 K + \beta_1 \Phi_2 \Phi_4 A^{**} + \beta_2 \Phi_2 \frac{\pi}{\mu} - \beta_2 \Phi_2 \Phi_3 A^{**} \right] \left(\frac{\pi}{\mu} - \frac{Q_1 Q_2}{\sigma \mu} A^{**} \right) - \frac{Q_1 Q_2}{\sigma} \left[\frac{\pi}{\mu} K + \Phi_2 \frac{\pi}{\mu} A^{**} - \right. \\ &\quad \left. K \Phi_3 A^{**} - \Phi_2 \Phi_3 A^{**2} \right] \\ 0 &= \left[\left(\beta_1 \Phi_4 K + \beta_2 \Phi_2 \frac{\pi}{\mu} \right) + \left(\beta_1 \Phi_2 \Phi_4 - \beta_2 \Phi_2 \Phi_3 \right) A^{**} \right] \left(\frac{\pi}{\mu} - \frac{Q_1 Q_2}{\sigma \mu} A^{**} \right) - \frac{Q_1 Q_2}{\sigma} \left[\frac{\pi}{\mu} K + \left(\Phi_2 \frac{\pi}{\mu} - K \Phi_3 \right) A^{**} \right. \\ &\quad \left. - \Phi_2 \Phi_3 A^{**2} \right] \\ 0 &= \left(\beta_1 \Phi_4 K + \beta_2 \Phi_2 \frac{\pi}{\mu} \right) \frac{\pi}{\mu} - \left(\beta_1 \Phi_4 K + \beta_2 \Phi_2 \frac{\pi}{\mu} \right) \frac{Q_1 Q_2}{\sigma \mu} A^{**} + \Phi_2 \left(\beta_1 \Phi_4 - \beta_2 \Phi_3 \right) \frac{\pi}{\mu} A^{**} + \Phi_2 \left(\beta_1 \Phi_4 \right. \\ &\quad \left. - \beta_2 \Phi_3 \right) \frac{Q_1 Q_2}{\sigma \mu} A^{**} - \Phi_2 \left(\beta_1 \Phi_4 - \beta_2 \Phi_3 \right) \frac{Q_1 Q_2}{\sigma \mu} A^{**2} - \frac{Q_1 Q_2}{\sigma} \frac{\pi}{\mu} K - \frac{Q_1 Q_2}{\sigma} \left(\Phi_2 \frac{\pi}{\mu} \right. \\ &\quad \left. - K \Phi_3 \right) A^{**} + \frac{Q_1 Q_2}{\sigma} \Phi_2 \Phi_3 A^{**2} \\ 0 &= \left[\frac{Q_1 Q_2}{\sigma} \Phi_2 \Phi_3 - \Phi_2 \left(\beta_1 \Phi_4 - \beta_2 \Phi_3 \right) \frac{Q_1 Q_2}{\sigma \mu} \right] A^{**2} + \left[\Phi_2 \left(\beta_1 \Phi_4 - \beta_2 \Phi_3 \right) \frac{\pi}{\mu} - \left(\beta_1 \Phi_4 K + \beta_2 \Phi_2 \frac{\pi}{\mu} \right) \frac{Q_1 Q_2}{\sigma \mu} \right. \\ &\quad \left. - \frac{Q_1 Q_2}{\sigma \mu} \left(\Phi_2 \frac{\pi}{\mu} - K \Phi_3 \right) \right] A^{**} + \left[\left(\beta_1 \Phi_4 K + \beta_2 \Phi_2 \frac{\pi}{\mu} \right) - \frac{Q_1 Q_2}{\sigma \mu} K \right]. \end{aligned}$$

This is in the form

$$\alpha_2 A^{**2} + \alpha_1 A^{**} + \alpha_0 = 0,$$

where

$$\begin{aligned}
 \alpha_0 &= \left(\beta_1 \Phi_4 K + \beta_2 \Phi_2 \frac{\pi}{\mu} \right) - \frac{Q_1 Q_2}{\sigma \mu} K \\
 &= \frac{Q_1 Q_2 \pi}{\sigma \mu} K \left[\frac{\beta_1 \Phi_4 \sigma}{Q_1 Q_2} + \frac{\beta_2 \Phi_2 \sigma}{Q_1 Q_2 K} \frac{\pi}{\mu} - 1 \right] \\
 &= \frac{Q_1 Q_2 \pi}{\sigma \mu} K \left[\frac{\beta_1 \sigma (Q_3 Q_4 + \eta_1 \phi Q_4 + \eta \phi \nu)}{Q_1 Q_2 Q_3 Q_4} + \frac{\beta_2 (Q_3 Q_4 \xi_1 + \nu Q_4 \xi_2 + \nu \phi \xi_3)}{K \psi Q_1 Q_2 Q_3 Q_4} \frac{\pi}{\mu} - 1 \right] \\
 &= \frac{Q_1 Q_2 \pi}{\sigma \mu} K [\mathcal{R}_0 - 1],
 \end{aligned}$$

with

$$\mathcal{R}_0 = \frac{\beta_1 \sigma (Q_3 Q_4 + \eta_1 \phi Q_4 + \eta \phi \nu)}{Q_1 Q_2 Q_3 Q_4} + \frac{\beta_2 (Q_3 Q_4 \xi_1 + \nu Q_4 \xi_2 + \nu \phi \xi_3)}{K \psi Q_1 Q_2 Q_3 Q_4} \frac{\pi}{\mu},$$

$$\begin{aligned}
 \alpha_1 &= \Phi_2 \left(\beta_1 \Phi_4 - \beta_2 \Phi_3 \right) \frac{\pi}{\mu} - \left(\beta_1 \Phi_4 K + \beta_2 \Phi_2 \frac{\pi}{\mu} \right) \frac{Q_1 Q_2}{\sigma \mu} - \frac{Q_1 Q_2}{\sigma \mu} \left(\Phi_2 \frac{\pi}{\mu} - K \Phi_3 \right) \\
 &= \beta_1 \Phi_2 \Phi_4 \frac{\pi}{\mu} - \beta_2 \Phi_2 \Phi_3 \frac{\pi}{\mu} - \left(\beta_1 \Phi_4 K + \beta_2 \Phi_2 \frac{\pi}{\mu} \right) \frac{Q_1 Q_2}{\sigma \mu} - \frac{Q_1 Q_2}{\sigma \mu} \frac{\pi}{\mu} \Phi_2 + K \frac{Q_1 Q_2}{\sigma \mu} \Phi_3 \\
 &= \beta_1 \Phi_2 \Phi_4 \frac{\pi}{\mu} - \frac{Q_1 Q_2}{\sigma \mu} \frac{\pi}{\mu} \Phi_2 + K \frac{Q_1 Q_2}{\sigma \mu} \Phi_3 - \beta_2 \Phi_2 \Phi_3 \frac{\pi}{\mu} - \left(\beta_1 \Phi_4 K + \beta_2 \Phi_2 \frac{\pi}{\mu} \right) \frac{Q_1 Q_2}{\sigma \mu} \\
 &= \frac{Q_2 Q_2 \Phi_2}{\sigma} \frac{\pi}{\mu} \left(\frac{\beta_1 \Phi_4 \sigma}{Q_1 Q_2} - 1 \right) + K \frac{Q_1 Q_2}{\sigma} \Phi_3 \left(1 - \frac{\beta_2 \Phi_2 \pi}{K \mu} \right) - \left(\beta_1 \Phi_4 K + \beta_2 \Phi_2 \frac{\pi}{\mu} \right) \frac{Q_1 Q_2}{\sigma \mu}.
 \end{aligned}$$

Therefore,

$$\alpha_1 = \frac{Q_2 Q_2 \Phi_2}{\sigma} \frac{\pi}{\mu} (\mathcal{R}_{0C} - 1) + K \frac{Q_1 Q_2}{\sigma} \Phi_3 (1 - \mathcal{R}_W) - \left(\beta_1 \Phi_4 K + \beta_2 \Phi_2 \frac{\pi}{\mu} \right) \frac{Q_1 Q_2}{\sigma \mu}$$

For α_2 we have

$$\begin{aligned}
 \alpha_2 &= \Phi_2 \left(\beta_1 \Phi_4 - \beta_2 \Phi_3 \right) \frac{\pi}{\mu} - \left(\beta_1 \Phi_4 K + \beta_2 \Phi_2 \frac{\pi}{\mu} \right) \frac{Q_1 Q_2}{\sigma \mu} - \frac{Q_1 Q_2}{\sigma \mu} \left(\Phi_2 \frac{\pi}{\mu} - K \Phi_3 \right) \\
 &= \frac{Q_1 Q_2}{\sigma} \Phi_2 \left[\frac{Q_1 Q_2}{\sigma \mu} - \frac{\left(Q_2 Q_3 Q_4 + \sigma Q_3 Q_4 + \phi \sigma Q_4 + \phi \sigma \nu + \sigma Q_3 Q_4 \Phi_2 \right)}{\sigma Q_3 Q_4} \right] \\
 &\quad - \beta_1 \Phi_2 \Phi_4 \frac{Q_1 Q_2}{\sigma \mu} + \beta_2 \Phi_2 \Phi_3 \frac{Q_1 Q_2}{\sigma \mu} \\
 &= \frac{Q_1 Q_2}{\sigma} \frac{Q_1 Q_2}{\sigma \mu} \Phi_2 - \frac{Q_1 Q_2}{\sigma \mu} \Phi_2 \frac{\left(Q_2 Q_3 Q_4 + \sigma Q_3 Q_4 + \phi \sigma Q_4 + \phi \sigma \nu + \sigma Q_3 Q_4 \Phi_2 \right)}{\sigma Q_3 Q_4} - \beta_1 \Phi_2 \Phi_4 \frac{Q_1 Q_2}{\sigma \mu} \\
 &\quad + \beta_2 \Phi_2 \Phi_3 \frac{Q_1 Q_2}{\sigma \mu} \\
 &= \frac{Q_1^2 Q_2^2}{\sigma^2 \mu} \Phi_2 \left[1 - \frac{\beta_1 \Phi_4 \sigma}{Q_1 Q_2} \right] - \frac{Q_1 Q_2}{\sigma \mu} \Phi_2 \frac{\left(Q_2 Q_3 Q_4 + \sigma Q_3 Q_4 + \phi \sigma Q_4 + \phi \sigma \nu + \sigma Q_3 Q_4 \Phi_2 \right)}{\sigma Q_3 Q_4} \\
 &\quad + \beta_2 \Phi_2 \frac{Q_1 Q_2}{\sigma \mu} \left[\frac{Q_1 Q_2}{\sigma \mu} - \frac{\left(Q_2 Q_3 Q_4 + \sigma Q_3 Q_4 + \phi \sigma Q_4 + \phi \sigma \nu + \sigma Q_3 Q_4 \Phi_2 \right)}{\sigma Q_3 Q_4} \right] \\
 &= \frac{Q_1^2 Q_2^2}{\sigma^2 \mu} \Phi_2 \left[1 - \frac{\beta_1 \Phi_4 \sigma}{Q_1 Q_2} \right] + \beta_2 \Phi_2 \frac{Q_1 Q_2}{\sigma \mu} \\
 &= \frac{Q_1 Q_2 \Phi_2 \Phi_3}{\sigma} - \Phi_2 \left(\beta_1 \Phi_4 - \beta_2 \Phi_3 \right) \frac{Q_1 Q_2}{\sigma \mu} \\
 &= \frac{Q_1 Q_2}{\sigma} \Phi_2 \left[\Phi_3 + \frac{\beta_2 \Phi_3}{\mu} - \beta_1 \Phi_4 \right]
 \end{aligned}$$

Therefore,

$$\alpha_2 = \frac{Q_1 Q_2}{\sigma} \Phi_2 \left[\Phi_3 + \frac{\beta_2 \Phi_3}{\mu} - \beta_1 \Phi_4 \right].$$

We have

$$\alpha_2 A^{**2} + \alpha_1 A^{**} + \alpha_0 = 0, \mid \alpha_0 = \frac{Q_1 Q_2}{\sigma} \frac{\pi}{\mu} K (\mathcal{R}_0 - 1).$$

Cases of the roots depend on the terms α_0 , α_1 and α_2 which are given below

- (a) When $\mathcal{R}_0 < 1$, $\alpha_0 < 0$. If $\alpha_2 < 0$, then the quadratic equation will have either two positive roots or two negative roots.
- (b) When $\mathcal{R}_0 < 1$, $\alpha_0 < 0$. If $\alpha_2 > 0$, then the quadratic equation will have one positive root and one negative root.
- (c) When $\mathcal{R}_0 > 1$, $\alpha_0 > 0$. If $\alpha_2 > 0$, then the quadratic equation will have either two positive roots or two negative roots.
- (d) When $\mathcal{R}_0 > 1$, $\alpha_0 > 0$. If $\alpha_2 < 0$, then the quadratic equation will have only one positive root.

2.4 Numerical Simulations

2.4.1 Parameter Estimation

The parameters in Table 2.3 have been chosen from published literature and we estimate the unknown parameters within the specified parameter ranges based on the available biological information. The natural life expectancy of cattle is estimated to be 18-20 years [32]. This corresponds to mortality rate of 0.05 per year. Depending on the commercial system, cattle will be culled at 5-6 years on average and they can give birth within 2-3 years [33]. In regions where FMD is not endemic, the morbidity rate can approach 100% in cattle and in general the average mortality rate is low in adult animals (about 1-5%) but higher in young animals (about 20% or higher) [32]. Prior to this, In Botswana the birth rate and mortality of the cattle population have been reported to be 0.473 day^{-1} and 0.059 day^{-1} respectively [20]. According to Modisa, 2020 [34] the apparent mortality rate was $\mu = 2.39 \times 10^{-4}$ per day. The entry rate to the susceptible group will therefore be given as $\pi = \mu \times N_0$, where N_0 is the total population size which we will fix to be 16750 from the report [34].

The average time period for symptoms to appear after exposure to the virus ranges between 2 and 14 days according to the World Organisation for Animal Health (OIE) and thereof [35]. After being exposed to the virus some animals remain asymptomatic and others become symptomatic. Mardones *et al.* [36] indicate that the latent period of FMD is 3.1 to 4.8 days in cattle. Also Keeling *et al.*, [22] indicated that the latent period is 4 to 5 days. For our model parameter estimation and simulations, we consider the nominal value of $\sigma = \frac{1}{4} = 0.25 \text{ day}^{-1}$, (corresponding to 4 days) estimated from the interval (0.2000,0.3333), accounting for latent period ranging from 3 days to 5 days.

According to Grubman and Baxt [37], infected animals remain symptomatic to FMD and infectious for about 7 to 10 days before they recover or become carriers. Here, we considered an average recovery rate of symptomatic animals to be $\gamma = 0.143$ which corresponds to 7 days taken for animals to recover. The natural waning of immunity after recovery is estimated to range between 6 months to 5.5 years depending on the age and the strain of the virus [22, 38]. Our model assumes that for the modelling time considered, the immunity acquired due to infection with FMD would not have waned. For our simulation, we consider a nominal value of $\phi = 0.35$ on the interval (0.15-0.5) [39].

In a cattle population 15% to 50% of the animals may become carriers. The carrier state can last as long as upto 28 days to 3.5 years [39]. For our model, we use the value of α as 0.03571. Our parameter estimation for direct transmission of the virus is taken from a similar model in [40], where $\beta_1 = 0.33$ per day in the interval (0.21-0.57). We also explore the indirect transmission scenario, based on estimated decay rates, contaminated environments have the potential to remain infectious for up to 14 days and others have reported the survival of FMDV in environments for months upto 6 months [9, 41] which accounts to $\beta_2 = 0.0714$ for our parameter estimation. The summary of parameter values used in our model numerical simulations are given in the following table;

Parameter	Range	Nominal Value	Source	Units
π		$\mu \times N_0$	Assumed	Animals per day
β_1	(0.2100, 0.5700)	0.3300	[40]	day ⁻¹
β_2	(0.0056, 0.0714)	0.0714	[9, 41]	day ⁻¹
η_1	(0, 1)	0.5	Assumed	Relative values
η_2	(0, 1)	0.06	Assumed	Relative values
μ	-	2.39×10^{-4}	[34]	day ⁻¹
γ	(0.0714, 0.143)	0.143	[37]	day ⁻¹
σ	(0.2000, 0.3333)	0.2500	[22]	day ⁻¹
ϕ	(0.0027, 0.0056)	0.0056	[39, 42]	day ⁻¹
δ	(0.0, 0.05)	0.03	[42]	day ⁻¹
ψ	(0, 1)	0.9	Assumed	time ⁻¹
K	(50, 10^5)	100000	Assumed	day ⁻¹
α	(0.0014, 0.03571)	0.03571	[39]	day ⁻¹
ξ_1	(0.00, 1.0)	0.06	Assumed	day ⁻¹
ξ_2	(0.1, 1.0)	0.4	Assumed	day ⁻¹
ξ_3	(0.01, 1.0)	0.03	Assumed	day ⁻¹
ν	(0.15, 0.5)	0.5	[39]	day ⁻¹

Table 2.3: Nominal values of parameters used in the model in figure 2.1.

Applying the above described set of estimated parameters, we have simulated the dynamics of FMD in the following results.

2.4.2 Sensitivity Analysis

Numerical simulations help in the understanding of the behaviour of complex deterministic models. In this section, we explore the behaviour of our model using sensitivity analysis which is performed to investigate the variability in the outcome variable *i.e* the FMD threshold, $\mathcal{R}_0$, that is generated from uncertainty in estimating parameter inputs and quantify how variation in model outputs may be attributed to model inputs [43, 44]. To perform sensitivity analysis on parameters of our model, we used the Latin Hypercube Sampling (LHS) scheme as described in [43]. The LHS scheme enables us to simultaneously sample the parameter space of the input variables to generate outputs [45, 46]. In the implementation of this scheme, 1000 simulations were carried out for each execution. Here, we compare two sensitivity analysis approaches of the model parameters to the model output. For our first analysis, we used MATLAB to calculate the resulting Partial Rank Correlation Coefficients (PRCCs) and a tornado plot of the PRCCs produced indicating the importance of each parameter's contribution to the variability in the time to eradication of the infection.

The PRCCs indicate the degree of effect each varied parameter has on $\mathcal{R}_0$ [43]. The sign of the PRCCs identifies the specific qualitative relationship between the input and output variable. If the PRCC has a positive sign, it indicates that when the value of that parameter increases, the number of cases will also increase and the negative PRCC indicates that the cases can be contained when the ethical processes described by that specific parameter are enhanced [43]. The results of sensitivity analysis are indicated in Figure 2.2 which shows a Tornado plot for the PRCCs for the parameters in Table 2.3. Figure 2.2 shows that both direct and indirect transmission of the virus from the environment together with the shedding of the virus into the environment by the infected animals have the greatest positive PRCCs.

This shows that they have the potential of worsening the FMD epidemic when increased. The recovery rate of infected and carrier animals, α and γ respectively, with the highest negative PRCCs have the greatest potential in helping contain the infection when enhanced. This shows they have a negative influence on $\mathcal{R}_0$ as such fewer future number of FMD cases will be recorded. We thereby note that reducing both the direct and indirect infection of the virus through strategies such as culling and quarantine of infected or carrier animals as well as disinfecting the affected areas, equipments and also personnel sanitation etiquette and movement restrictions across zones through cordon fences and disease control gates might play a vital role in containing the spread of the virus. In addition, increasing the recovery rate of carriers through treatment of the affected animals is associated with reducing the disease outbreak.

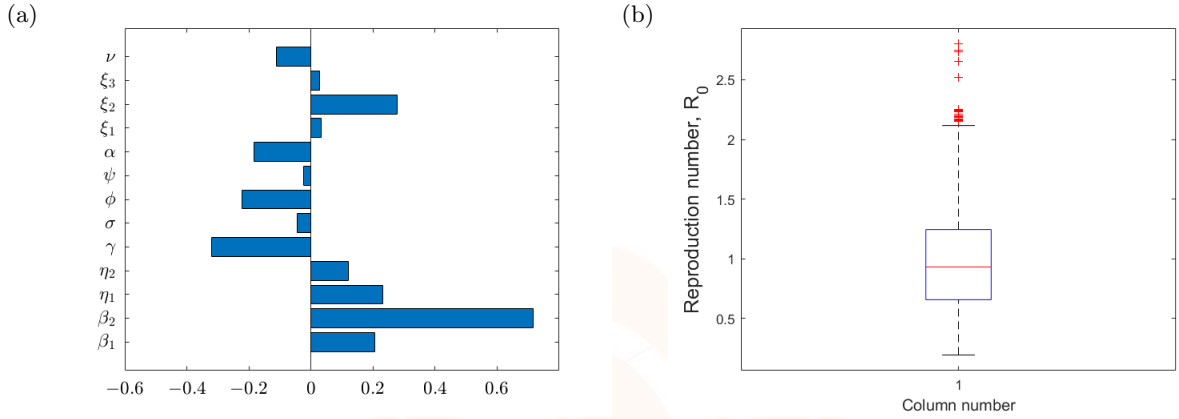


Figure 2.2: Partial Rank Correlation Coefficients (PRCCs) for a selected range of model parameters in Table 2.3.

Figure 2.2b shows the box-plot of our reproduction number, $\mathcal{R}_0$. Using the plot, the five number summary recorded for $\mathcal{R}_0$ is the minimum of approximately 0.2, the lower quartile is approximately 0.6, the median is around 0.91 and the third/upper quartile is about 1.24, with the upper adjacent of approximately 2.083. From the values displayed in the box plot, we obtained approximately 26 outliers. From the results, it can be interpreted that when certain combinations of parameters are combined, $\mathcal{R}_0$ values can rise significantly, indicating a potential worsening of the epidemic. Likewise, in some cases, $\mathcal{R}_0$ can be reduced to levels below one through several combinations of processes, which would enable curtailing of the epidemic.

As Blower and Dowlatabadi, 1994 [43] pointed out, some model parameters can have insignificant PRCC magnitudes which can still produce considerable changes in disease burden. Therefore, to determine the most important parameters that control or worsen the prevalence of FMD, we use Fisher's Transformation $\rho(r) = 0.5 \log(\frac{1+r}{1-r})$ to convert the skewed distribution to a normal distribution and calculate the p-value of each parameter based on the PRCC. [43]. We note that the calculated PRCCs are bounded within the range $[-1, 1]$. We used 'R Software' to calculate the p-values for each parameter. The PRCCs for the parameters together with their corresponding p-values are indicated in Table 2.4.

Parameter	PRCC	p-value	Significance
β_1	0.20570198	1.252e-10	TRUE
β_2	0.71564797	0.000e+00	TRUE
η_1	0.23055777	5.607e-13	TRUE
η_2	0.12128317	2.123e-04	TRUE
γ	-0.31897099	0.000e+00	TRUE
σ	-0.04518318	2.027e-01	FALSE
ϕ	-0.22242444	3.258e-12	TRUE
ψ	-0.02320610	4.663e-01	FALSE
α	-0.18402950	9.563e-09	TRUE
ξ_1	0.03349203	3.463e-01	FALSE
ξ_2	0.27821911	0.000e+00	TRUE
ξ_3	0.1469	7.404e-06	TRUE
ν	-0.11076021	6.964e-04	TRUE

Table 2.4: Parameter PRCC Significance and their FDR adjusted p-values

We perform pairwise comparisons of important parameters with p-values which are less than 0.05, to determine which pairs of parameters differ significantly. The calculated p-values after False Discovery Rate (FDR) adjustment are given in Table 2.4. From Table 2.4, we observe that parameters β_1 , β_2 , η_1 , η_2 , γ , α , ξ_2 , ξ_3 and ν are significant when compared to other parameters. Based on the pairwise FDR adjusted p-values in Table 2.5, we summarise our results in Table 2.6, where “TRUE” indicates that the parameters being compared are significantly different and “FALSE” indicates that there is no significant difference between the pair of parameters under comparison. We observe that all the parameters are significantly different except for $\beta_1 - \eta_1$, $\beta_1 - \eta_2$, $\beta_1 - \xi_2$, $\phi - \alpha$, $\alpha - \nu$ relationship some of which may not be significantly related.

	β_1	β_2	η_1	η_2	γ	ϕ	α	ξ_2	ν
β_1		0	0.5625	0.0628	0	0	0	0.09809	2.054 e-12
β_2			0	0	0	0	0	0	0
η_1				0.01518	0	0	0	0.2732	2.779 e-14
η_2					0	1.998e-14	1.275e-11	0.0003826	3.454e-07
γ						0.02477	0.001811	0	1.636e-06
ϕ							0.3847	0	0.01377
α								0	0.1051
ξ_2									0
ν									

Table 2.5: p-values pairwise comparison of significant parameters in Table 2.4 after FDR adjustment.

	β_1	β_2	η_1	η_2	γ	ϕ	α	ξ_2	ν
β_1		TRUE	FALSE	FALSE	TRUE	TRUE	TRUE	FALSE	TRUE
β_2			TRUE	TRUE	TRUE	TRUE	TRUE	TRUE	TRUE
η_1				TRUE	TRUE	TRUE	TRUE	FALSE	TRUE
η_2						TRUE	TRUE	TRUE	TRUE
γ						TRUE	TRUE	TRUE	TRUE
ϕ							FALSE	TRUE	TRUE
α								TRUE	FALSE
ξ_2									TRUE
ν									

Table 2.6: Parameters after FDR adjustment.

For parameters that have significant positive and negative PRRCs, we investigated the existence of a monotone relationship with $\mathcal{R}_0$ while keeping other parameters constant. So to check the existence of a monotone relationship with $\mathcal{R}_0$, we choose parameters that have the highest absolute values of PRCCs, i.e., β_1 , β_2 , γ . Their monotone trend is shown in Figure 2.3. As observed in Figure 2.3, $\mathcal{R}_0$ is monotone increasing with an increase in both the direct and indirect transmission of the disease pathogen from the environment and infected animals, β_1 and β_2 respectively. The scatter plots of β_1 and β_2 show an increase in $\mathcal{R}_0$ which shows that transmission from both the environment and infected animals have a strong influence on the FMD epidemic. However, the scatter plot for the recovery rate of the infected animals shows a decrease in $\mathcal{R}_0$. This gives a picture that if more animals recover from the disease the epidemic maybe contained. A slightly decreasing trend was observed for shedding rate of the virus by infected animals, ξ_2 . This shows that these parameters are correlated to $\mathcal{R}_0$.

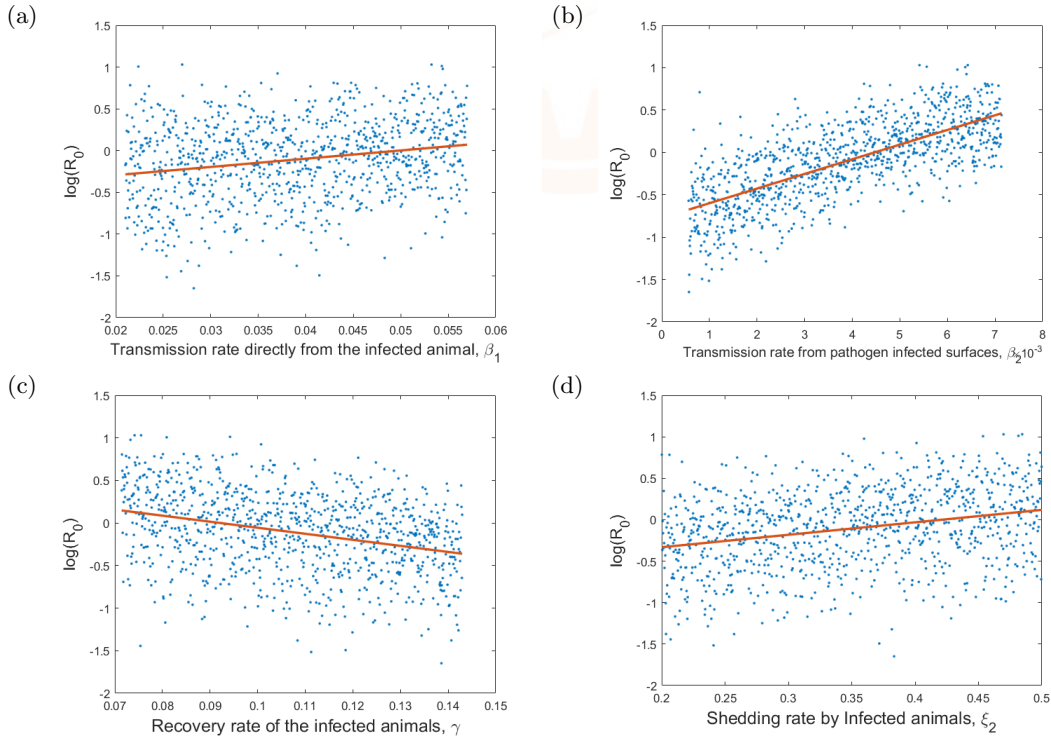


Figure 2.3: Scatter plots for the four parameters with the greatest absolute values of PRCC, obtained using parameter values in Table 2.3.

2.4.3 Sensitivity Analysis Based on the Full Model

We apply the same methodology described in Marino *et al.* [44] to perform a time-varying sensitivity analysis of the model parameters based on the entire model system of equations (2.1). PRCCs were calculated for all the varied parameters at different stages in the disease progression. To analyse the influence of specific state variables on the spread of disease at indicative time points, we extracted PRCCs at $T = 10$ days, $T = 100$ days, and $T = 250$ days. Based on the extracted PRCCs, Fisher Transformation was used to transform the possibly skewed distribution into a normal distribution, and then the p-values for the parameters were calculated [43]. A PRCC p-value greater than 0.05 indicates that a parameter is not significant; otherwise, it is significant. The resulting time varying PRCCs of the full model output for the given input values for specific state variables together with the corresponding p-values are summarised in the figures and tables below.

Sensitivity PRCCs of Parameters for the Exposed Animals

The sensitivity analysis results with respect to the Exposed population are presented in Figure 2.4, the tornado plot for PRCCs at selected time points are summarised in Figure 2.5, and the p -values together with indication of significance presented in Table 2.7

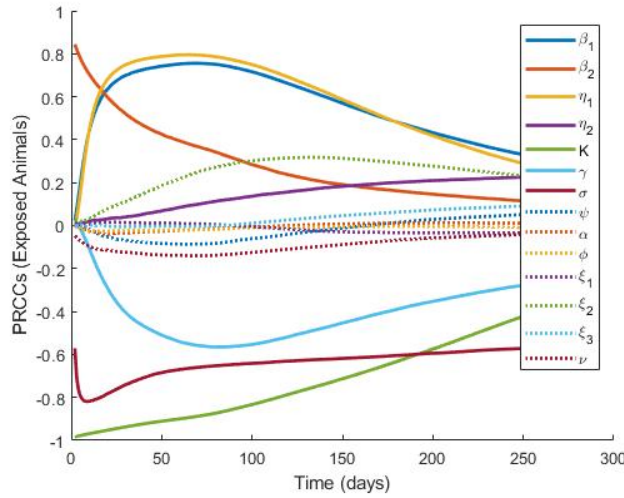


Figure 2.4: Sensitivity analysis PRCCs of parameters with respect to Exposed class (E).

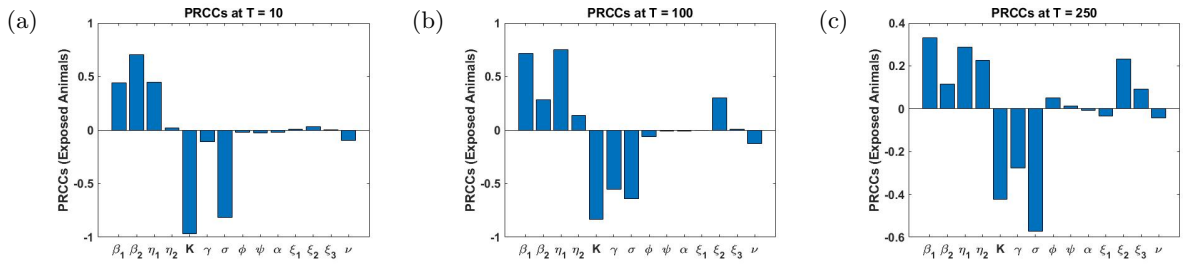


Figure 2.5: PRCCs of model parameters on the Exposed population at $T = 10$ days (Figure 2.5a), $T = 100$ days (Figure 2.5b) and $T = 250$ days (Figure 2.5c).

Parameter	$T = 10$ days			$T = 100$ days			$T = 250$ days		
	PRCC	p-value	Significance	PRCC	p-value	Significance	PRCC	p-value	Significance
β_1	0.4425	0.000000000	TRUE	0.7162	0.000e+00	TRUE	0.3299	0.000e+00	TRUE
β_2	0.7047	0.000000000	TRUE	0.7162	0.000e+00	TRUE	0.3299	0.000e+00	TRUE
η_1	0.4461	0.000000000	TRUE	0.7496	0.000e+00	TRUE	0.2885	0.000e+00	TRUE
η_2	0.0217	0.631262773	FALSE	0.1365	2.873e-05	TRUE	0.2261	1.061e-12	TRUE
K	-0.9686	0.0000000	TRUE	-0.8330	0.000e+00	TRUE	-0.4217	0.000e+00	TRUE
γ	-0.1081	0.0006634	TRUE	-0.5536	0.000e+00	TRUE	-0.2778	0.000e+00	TRUE
σ	-0.8179	0.0000000	TRUE	-0.6413	0.000e+00	TRUE	-0.5719	0.000e+00	TRUE
ϕ	-0.0177	0.5787000	FALSE	-0.0606	7.981e-02	FALSE	0.0513	1.502e-01	FALSE
ψ	-0.0273	0.3917000	FALSE	-0.0068	8.853e-01	FALSE	0.0119	7.635e-01	FALSE
α	-0.0233	0.4648000	FALSE	-0.0102	8.738e-01	FALSE	-0.0078	8.067e-01	FALSE
ξ_1	0.0067	0.8335000	FALSE	-0.0046	8.853e-01	FALSE	-0.0339	3.353e-01	FALSE
ξ_2	0.0328	0.3034000	FALSE	0.3017	0.000e+00	TRUE	0.2321	2.818e-13	TRUE
ξ_3	0.0026	0.9350000	FALSE	0.0111	8.738e-01	FALSE	0.0913	6.346e-03	TRUE
ν	-0.0954	0.0026850	TRUE	-0.1249	1.275e-04	TRUE	-0.0417	2.426e-01	FALSE

Table 2.7: Exposed population parameter PRCC significance (FDR Adjusted p-values).

Figure 2.4 shows the PRCCs of model parameters over time for changes in the exposed population. Using $T = 10$ days, $T = 100$ days, and $T = 250$ days, we selected the PRCCs and summarized them in Table 2.5. For the selected time ranges, the PRCCs and their associated p-values are shown in Table 2.7. We see in Figure 2.4 and Table 2.5 that the parameters β_1 , β_2 , η_1 , γ , σ , K and ν are sensitive to the growth of the exposed population. We note that some of the parameters observed to be significantly sensitive to changes in the exposed population are not directly associated with its dynamic equation (2.1b). The parameters β_1 , β_2 and η_1 have a positive correlation with the exposed population. This means that if we increase the transmission rate directly from the infected groups (β_1), the transmission rate of the infection from the contaminated environment (β_2), and η_1 the relative transmission of the disease from the class I compared to class A . We observe from Table 2.7 that the infection rate of carriers relative to the presymptomatic group (η_2) seems not to be significantly sensitive at the initial stages of the interaction and becomes significantly sensitive in the later stages of the disease progression (around the steady state). The parameters ϕ , ψ , α and ξ_1 are not significant throughout the course of the disease while parameters ξ_2 , ξ_3 and ν have differing levels of sensitivity with respect to the exposed class during the course of the disease progression (see Table 2.7). With reference to Table 2.7, we observed that the exposed class is significantly sensitive to changes in ν (the progression rate from A to I) in the early stages of the disease. However, in the later stages of the disease dynamics (see PRCC and p-values for time points $T = 10$, $T = 100$ and $T = 250$ days) the influence of the changes in ν on the exposed class is not significant.

Sensitivity PRCCs of Parameters on Pre-symptomatic Animals

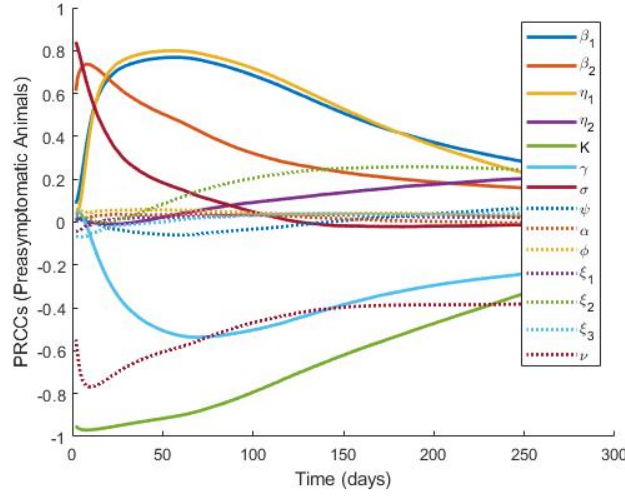
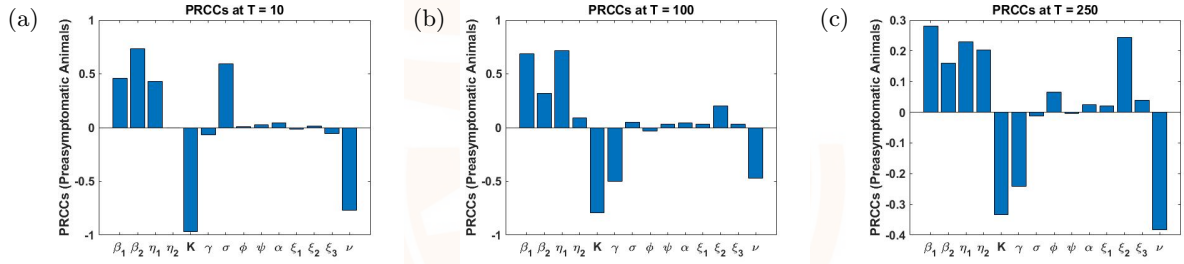


Figure 2.6: Sensitivity analysis PRCCs of parameters with respect to pre-symptomatic population (A).

Figure 2.7: PRCCs of model parameters on the pre-symptomatic population at (2.7a) $T = 10$ days, (2.7b) $T = 100$ days, and (2.7c) $T = 250$ days.

Parameter	$T = 10$ days			$T = 100$ days			$T = 250$ days		
	PRCC	p-value	Significant	PRCC	p-value	Significant	PRCC	p-value	Significance
β_1	0.4589	0.00000	TRUE	0.6845	0.000e+00	TRUE	0.2815	0.000e+00	TRUE
β_2	0.7338	0.00000	TRUE	0.3207	0.000e+00	TRUE	0.1592	8.286e-07	TRUE
η_1	0.4319	0.00000	TRUE	0.7169	0.000e+00	TRUE	0.2297	5.124e-13	TRUE
η_2	-0.0026	0.93500	FALSE	0.0914	7.068e-03	TRUE	0.2038	1.790e-10	TRUE
K	-0.9691	0.00000	TRUE	-0.7934	0.000e+00	TRUE	-0.3336	0.000e+00	TRUE
γ	-0.0644	0.08616	FALSE	-0.5029	0.000e+00	TRUE	-0.2415	3.046e-14	TRUE
σ	0.5940	0.00000	TRUE	0.0472	2.153e-01	FALSE	-0.0125	7.484e-01	FALSE
ϕ	0.0105	0.79890	FALSE	-0.0322	3.153e-01	FALSE	0.0513	1.502e-01	FALSE
ψ	-0.0273	0.39170	FALSE	0.0333	3.153e-01	FALSE	-0.0037	9.076e-01	FALSE
α	0.0460	0.23140	FALSE	0.0424	2.565e-01	FALSE	0.0257	5.346e-01	FALSE
ξ_1	-0.0140	0.79890	FALSE	-0.0328	3.153e-01	FALSE	0.0210	5.950e-01	FALSE
ξ_2	0.0123	0.79890	FALSE	0.2045	1.537e-10	FALSE	0.2431	2.487e-14	FALSE
ξ_3	-0.0551	0.14630	FALSE	0.0320	3.153e-01	FALSE	0.0390	3.093e-01	FALSE
ν	-0.7683	0.00000	TRUE	-0.4684	0.000e+00	TRUE	-0.3818	0.000e+00	TRUE

Table 2.8: Pre-symptomatic population parameter PRCC significance (FDR Adjusted p-values).

Figure 2.6 illustrates the time variable PRCCs for model parameters with respect to changes in the pre-symptomatic population. Using $T = 10$ days, $T = 100$ days, and $T = 250$ days, we selected the PRCCs and summarized them in Table 2.8. From Figures 2.6 and 2.7, and Table 2.8, we observe that the parameters β_1 , β_2 , η_1 , K and ν are more sensitive to changes in the presymptomatic animal population over a continuous time such that, gradual increase of β_1 , β_2 , η_1 will lead to an increase in pre-symptomatic animals while increasing ν will result in the decrease in pre-symptomatic animals. From Table 2.8 at the initial point of the changes in the disease, the progression of infection rate (σ) from the exposed group to the class A is significantly sensitive in the early stages and becomes less sensitive in the later stages of disease progression. In addition, we observed that the parameters η_1 and γ are not significantly sensitive in the early states (see at $T = 10$ days) but become more sensitive to changes in A later on (see PRCCs at $T = 100$ days and $T = 250$ days).

Sensitivity PRCCs of Parameters on Symptomatic Infected Animals

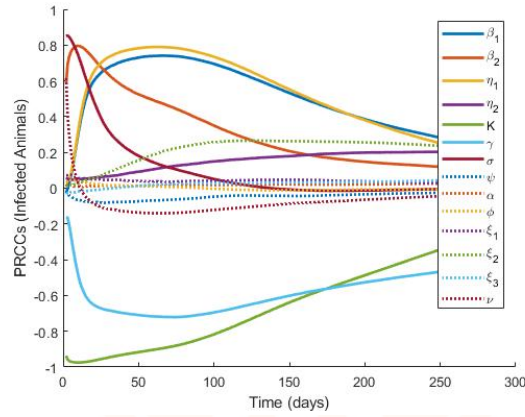


Figure 2.8: Sensitivity analysis PRCCs of parameters with respect to the Infected population (I).

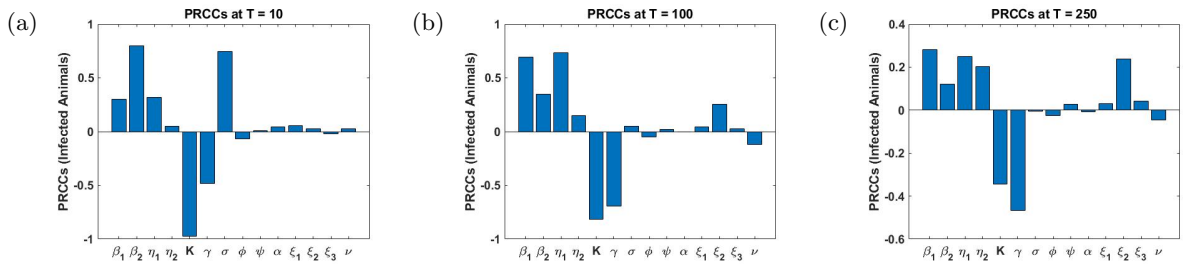


Figure 2.9: PRCCs of model parameters on the Infected population at (2.9a) $T = 10$ days, (2.9b) $T = 100$ days and (2.9c) $T = 250$ days.

Parameter	$T = 10$ days			$T = 100$ days			$T = 250$ days		
	PRCC	P-value	Significant	PRCC	P-value	Significant	PRCC	P-value	Significance
β_1	0.3020	0.00000	TRUE	0.6949	0.000e+00	TRUE	0.2817	0.000e+00	TRUE
β_2	0.7954	0.00000	TRUE	0.3500	0.000e+00	TRUE	0.1197	3.227e-04	TRUE
η_1	0.3213	0.00000	TRUE	0.7346	0.000e+00	TRUE	0.2503	3.886e-15	TRUE
η_2	0.0481	0.20380	FALSE	0.1497	4.458e-06	TRUE	0.2026	2.707e-10	TRUE
K	-0.9748	0.00000	TRUE	-0.8173	0.000e+00	TRUE	-0.3435	0.000e+00	TRUE
γ	-0.4848	0.00000	TRUE	-0.6950	0.000e+00	TRUE	-0.4671	0.000e+00	TRUE
σ	0.7429	0.00000	TRUE	0.0511	1.690e-01	FALSE	-0.0056	8.606e-01	FALSE
ϕ	-0.0646	0.08487	FALSE	-0.0473	1.926e-01	FALSE	-0.0252	5.007e-01	FALSE
ψ	0.0085	0.78970	FALSE	0.0179	6.186e-01	FALSE	0.0258	5.007e-01	FALSE
α	0.0416	0.26830	FALSE	-0.0032	9.200e-01	FALSE	-0.0082	8.583e-01	FALSE
ξ_1	0.0568	0.13030	FALSE	0.0413	2.480e-01	FALSE	0.0288	5.007e-01	FALSE
ξ_2	0.0252	0.50070	FALSE	0.2573	5.181e-16	TRUE	0.2367	1.057e-13	TRUE
ξ_3	-0.0180	0.61630	FALSE	0.0277	4.489e-01	FALSE	0.0432	2.724e-01	FALSE
ν	0.0273	0.49850	TRUE	-0.1216	2.212e-04	TRUE	-0.0449	2.724e-01	FALSE

Table 2.9: Infected population parameter PRCC significance (FDR Adjusted p-values).

The time varying PRCCs of model parameters on changes in infected animals are indicated in Figure 2.8. The selected PRCCs at $T = 10$ days, $T = 100$ days and $T = 250$ days are summarised in Table 2.9. The PRCCs together with the corresponding p-values are summarised in Table 2.9. We observe that the change in I is more sensitive to changes in parameters β_1 , β_2 , η_1 , K and γ . The aforementioned parameters have the highest potential of influencing the spread of the disease. For the transition parameter from presymptomatic, class (A) to infected animals (I), ν and rate at which the infected animals shed the virus to the environment, ξ_2 which are directly associated with infected class (see Equation (2.1d)), the results show that they are significantly sensitive in the early stages of the disease progression but not significant in the later stages of disease (see PRCCs at $T = 250$ days) as shown in Table 2.9. The parameter η_2 is observed to significantly influence changes in population of compartment I in the early stages (see PRCCs at $T = 10$ days) and then become significantly sensitive as the disease progresses.

Sensitivity PRCCs of Parameters on the Carrier Animals

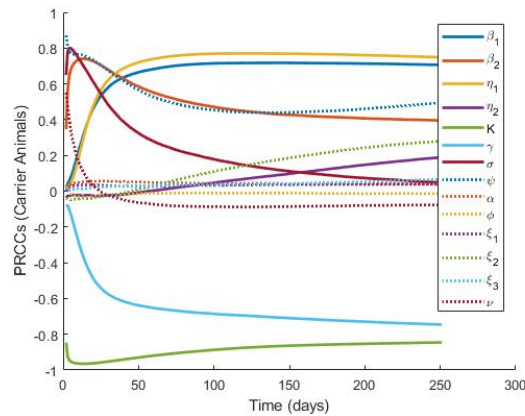


Figure 2.10: Sensitivity analysis PRCCs of parameters with respect to the Carriers (C).

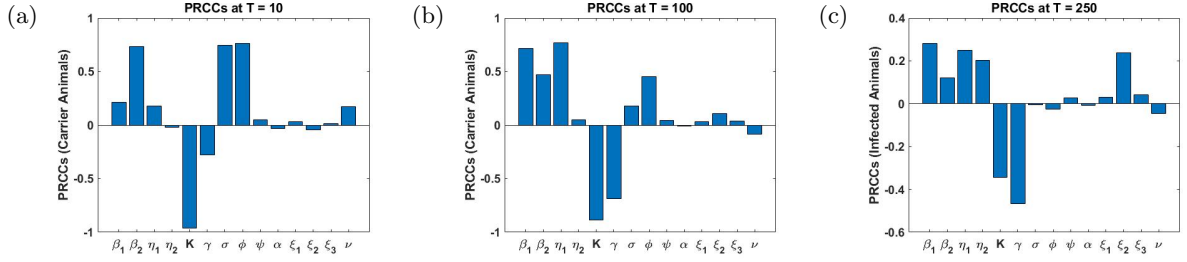


Figure 2.11: PRCCs of model parameters on the Carriers at (2.11a) $T = 10$ days, (2.11b) $T = 100$ days and (2.11c) $T = 250$ days.

Parameter	$T = 10$ days			$T = 100$ days			$T = 250$ days		
	PRCC	p-value	Significance	PRCC	p-value	Significance	PRCC	p-value	Significance
β_1	0.2155	1.523e-11	TRUE	0.7144	0.000e+00	TRUE	0.7061	0.000e+00	TRUE
β_2	0.7345	0.000e+00	TRUE	0.4712	0.000e+00	TRUE	0.3950	0.000e+00	TRUE
η_1	0.1769	4.090e-08	TRUE	0.7688	0.000e+00	TRUE	0.7490	0.000e+00	TRUE
η_2	-0.0216	5.363e-01	FALSE	0.0470	1.961e-01	FALSE	0.1892	3.300e-09	TRUE
K	-0.9637	0.000e+00	TRUE	-0.8873	0.000e+00	TRUE	-0.8457	0.000e+00	TRUE
γ	-0.2772	0.000e+00	TRUE	0.1784	3.086e-08	TRUE	-0.7458	0.000e+00	TRUE
σ	0.7462	0.000e+00	TRUE	-0.1363	5.915e-05	TRUE	0.0481	1.668e-01	FALSE
ϕ	0.7648	0.000e+00	TRUE	0.4532	0.000e+00	TRUE	0.4940	0.000e+00	TRUE
ψ	0.0470	2.179e-01	FALSE	0.0423	2.345e-01	FALSE	0.0399	2.392e-01	FALSE
α	-0.0308	3.894e-01	FALSE	-0.0109	7.324e-01	FALSE	-0.0138	6.651e-01	FALSE
ξ_1	0.0331	3.805e-01	FALSE	0.0321	3.379e-01	FALSE	0.0389	2.392e-01	FALSE
ξ_2	-0.0444	2.288e-01	FALSE	0.1094	9.974e-04	TRUE	0.2801	0.000e+00	TRUE
ξ_3	0.0138	6.651e-01	FALSE	0.0367	2.910e-01	FALSE	0.0670	4.942e-02	TRUE
ν	0.1720	8.835e-08	TRUE	-0.0869	9.767e-03	TRUE	-0.0761	2.608e-02	TRUE

Table 2.10: Carriers population parameter PRCC significance (FDR Adjusted p-values).

The time variable PRCCs of model parameters on changes in Carrier animals population are indicated in Figure 2.10. We selected the PRCCs at specific time points (that is, $T = 10$ days, $T = 100$ days and $T = 250$ days) and summarised them in Table 2.11. The PRCCs together with their corresponding p-values at the aforementioned time points are displayed in Table 2.10. From Figure 2.10 and Table 2.11, we observe that the parameters β_1 , β_2 , η_1 , γ , ϕ and K are significantly sensitive to the growth of the carrier animal population. The parameters η_1 , σ , ξ_2 and ξ_3 show varying levels of sensitivity during the progression of the disease as observed from Table 2.10. We note that accelerating the recovery rate of the infected and carrier animals, γ and α respectively is associated with low disease burden. Therefore, any process that enhances such process is essential in curtailing the spread of the disease.

2.4.4 Numerical Results

In this section, we present the numerical solutions of the FMD model (2.1). The nominal values of the parameters used in the simulations are given in Table 2.3. A reproduction number, $\mathcal{R}_0$, remains a sharp threshold for disease dynamics. When $\mathcal{R}_0 < 1$, FMD virus will be contained before being generalised to an outbreak. Therefore, the disease will consequently be eradicated from the animal population as shown in Figure 2.12a, since the graphs of all

the animal groups with the potential to spread the disease shows a significant decline to negligible values. When $\mathcal{R}_0 > 1$, the virus will spread in the population and sustain an outbreak. Therefore, the disease will persist in the population as illustrated in Figure 2.12b. When $\mathcal{R}_0$ is greater than 1, symptomatic, asymptomatic and carrier animal population would be sufficient to sustain an outbreak as the graphs show that disease will spread in the cattle population (see Figure 2.12b).

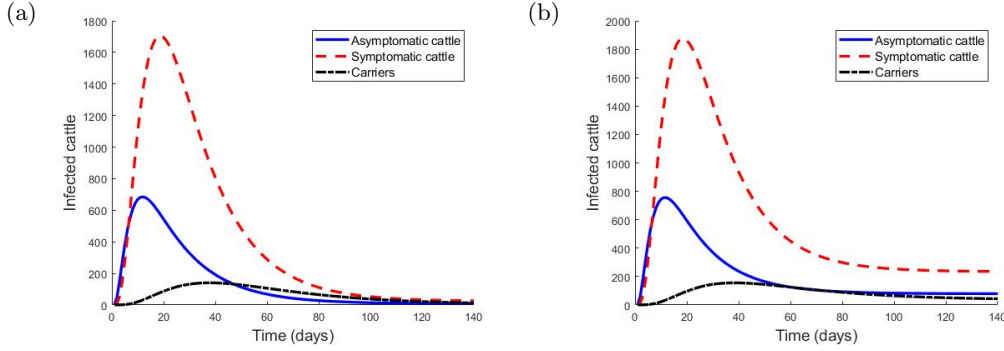


Figure 2.12: The trend of FMDV (a) when $\mathcal{R}_0 = 0.9128 < 1$ and (b) trajectory when $\mathcal{R}_0 = 1.3994 > 1$

Effect of Varying Contact Rate Between Animals

To investigate the effect of direct contact rate, β_1 , we varied the values of contact rate right at the start of the outbreak (around $t = 0$, see Figure 2.13a) and with implementation of controls 10 days after the outbreak (see Figure 2.13b). The graphs representing the significant effects of β_1 are given in Figure 2.13. The results show that all cases are characterised by an initial increase in number of infected cases, reaching peak values followed by a significant decline. The decline is presumed to be due to self-limitation of the disease resulting from the reduction in the infection probability as the numbers of susceptible animals reduced. With the focus on direct contact between animals only, we did not notice a significant difference in the number of infected cases when the controls are implemented right at the start of the outbreak or about 10 days later. We note however, that the implementation of control measures such as isolation, quarantines, and movement restrictions to reduce contact between infected cattle and susceptible cattle (see Figure 2.13) is associated with a decline in peak values of the infected animals. The decrease in the number of either susceptible or infected cattle reduces the likelihood of contact which reduces the probability of new infection generations.

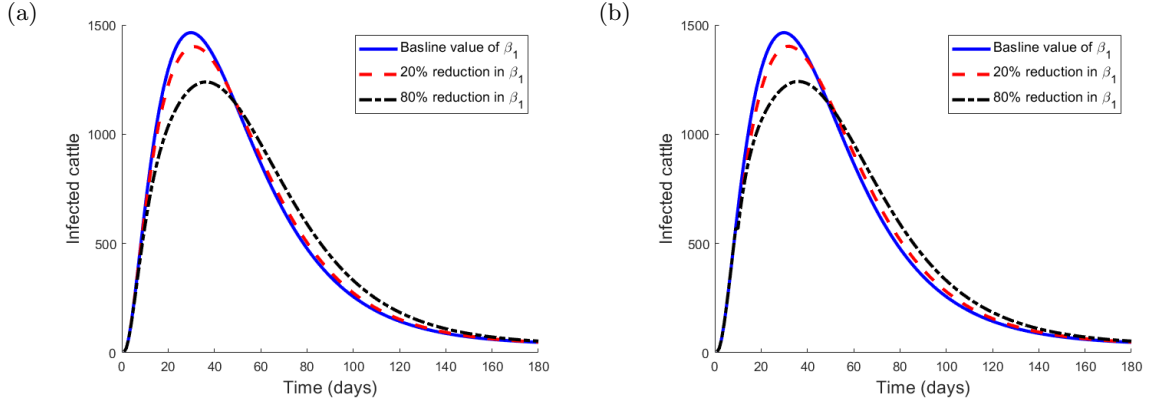


Figure 2.13: Impact of direct contact with the FMD pathogen in the spread of FMD.

Influence of Contact Between Animals and the FMD Pathogen Contaminated Surfaces

The changes on the effect of contact between animals and infected surfaces are given in Figure 2.14. Cleaning and disinfection are important control measures to reduce the FMD pathogen load on the surfaces and prevent disease spread. Disinfectants should be used to decontaminate the FMD affected farms, including but not limited to persons, vehicles and fomites entering and leaving the farm. It is observed that if we implement these control measures with an aim of 80% reduction in contact rate with the contaminated surfaces at the start of an outbreak (see Figure 2.14a), there is approximately a 71% decrease in the peak values reached by the infected class. When we compare these results with those in Figure 2.14b where the control interventions are implemented several days after an outbreak, we see that it will take more time to contain the disease as more disease case loads will be recorded. We caution that, delayed implementation of controls may result in a significant disease burden most especially during large outbreaks.

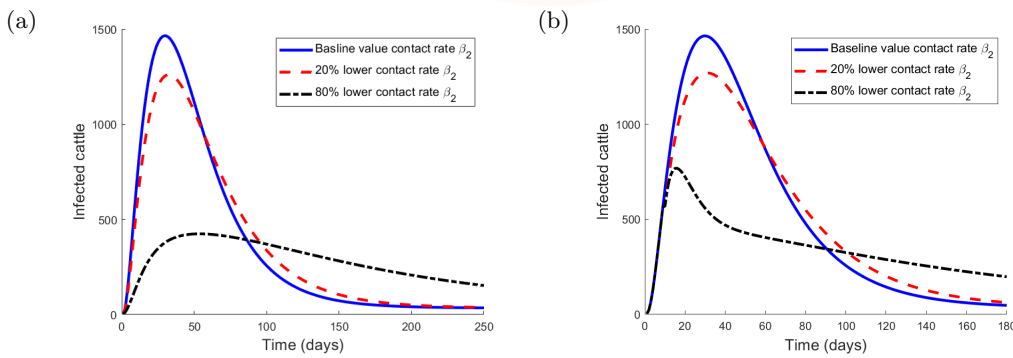


Figure 2.14: Effect of contact between animals and the FMD pathogen contaminated surfaces in the spread of FMD: control at the start of an outbreak (Figure 2.14a) and control several days after there's an outbreak (Figure 2.14b).

Importance of combining control measures

To investigate the effect of implementing a combination of controls, we study the trends of combined controls, increase virus decay from the environment (achieved by improved sanita-

tion etiquette and disinfecting contaminated surfaces) and reduction of contact rate between animals and contaminated surfaces. From Figure 2.15, it is observed that an implementation of both these control measures somewhere near the peak values, days after an outbreak, will cause a significant decline to a relative equilibrium. If we apply these controls with an aim of 80% reduction in contact rate and increase the virus decay by a factor of 100, we observe that the FMD disease case load is completely at zero. So, in the event that FMD infected cases become increasingly high, disinfection of contaminated surfaces can be implemented in order to reduce contact with the FMD pathogen.

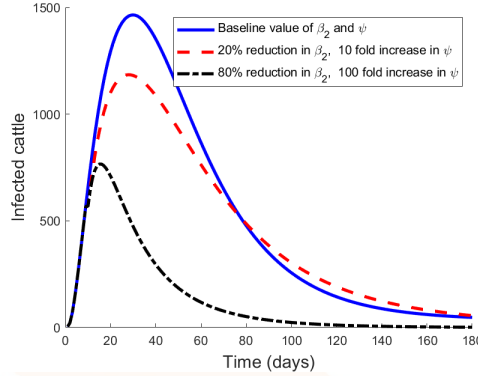


Figure 2.15: Effect of disinfecting FMD pathogen contaminated surfaces.

2.5 Conclusion

We presented a mathematical model of the spread and control of foot and mouth disease with carriers through direct transmission due to contact with the infected animal and indirect transmission due to contact with the infected environment. In this dynamical model we assumed an endemic or near endemic situation like Botswana. The model basic properties, that is, positivity of solutions, stability of the steady states and reproduction number were analysed. Positivity and boundedness of the solutions were proved to ensure that the model is well-posed. The equilibrium points of the system were obtained and their existence and stability discussed in terms of the basic reproduction number. Sensitivity analysis of the threshold (reproduction) number on the model parameters was performed to identify the important parameters that have influence in the spread of FMD. By applying the Latin Hypercube sampling scheme on sensitivity based on $\mathcal{R}_0$, we observed that if the disease is to be contained, processes described by increasing the recovery rate of the infected and carrier animals, γ and α respectively and minimal drooling of the FMD pathogen into the environment by symptomatic animals have the potential in slowing the epidemic when enhanced. When observing the effect of parameters based on the full model, we notice that the spread of FMD is aggravated by the most sensitive parameters β_1 , β_2 , η_1 , K , ν and γ which have shown that they are sensitive to the spread of foot and mouth disease over a continuous time. When observing the effect of some parameters under numerical analysis we notice that in order to fight the outbreaks of FMD there is need to reduce the contact rates, β_1 and β_2 , relative infection rates η_1 and η_2 and pathogen concentration in the environment, K . We

have observed that the implementation of combined control strategies will mean that the disease can be contained in a shorter time or period compared to the case when only one control mechanism is adopted.



3. A Pair Approximation Model of Foot and Mouth disease with Carriers

3.1 Introduction

In this chapter, we develop and study a pair approximation (PA) model that incorporates spatial transmission of foot and mouth disease. PA models explore spatial effects by employing pairs of connected individuals on a network as state variables and considering that events such as transmission of a disease can occur only between nodes that share edges. The state variables of a PA model are singletons $[X]$, which represent, for instance, the numbers of susceptible or infectious nodes, and pairs $[XY]$, which are the numbers of connected state X and state Y pairs on the network. The following description of PA models was obtained from [47, 48]. In PA models, equations of motion for singletons involves pairs, equations of motion for pairs contain triples $[XYZ]$, e.t.c. Therefore, in order to obtain a closed system of equations this hierarchy is truncated by techniques referred to as moment closure approximations (MCAs) [49]. When closure is done at the level of pairs (such that triples are approximated using pairs and singletons), then the process is called a pair approximation and have a pair approximation model. There exist varying pair closures, each one making a specific assumption about the statistical distributions of neighbourhoods in a network. If the disease spreads on a network in which the disease states of neighbours of a given node are conditionally independent, that is, there are no triangles such that in a triple $X - Y - Z$, both X and Z are neighbours of Y , but they are not connected themselves and n is the number of contacts, the ordinary pair approximation (OPA) is applied, which is given by Equation (3.1).

$$[XYZ] \approx \frac{n-1}{n} \frac{[XY][YZ]}{[Y]}. \quad (3.1)$$

If on the other hand, there is a proportion ϕ of triples that form triangles on the network, then the triangular pair approximation (TPA) is applied, and it is given by Equation (3.2).

$$[XYZ] \approx \frac{n-1}{n} \frac{[XY][YZ]}{[Y]} \left((1-\phi) + \phi \frac{N}{n} \frac{[XZ]}{[X][Y]} \right). \quad (3.2)$$

3.2 The Mathematical Model

We develop a PA model of FMD with carriers where the disease states are susceptible (S), followed by exposed but not infectious (E), then infectious (I), the carriers (C) and lastly the recovered (R). Thus, we study an SEICR model. We note here that the model analysed in this chapter is a reduced model from the one presented in Chapter 2, where the pre-symptomatic

class is eliminated as well as the contribution of the pathogen infected environment. The model parameters are transmission of disease from state S to state I individuals at a rate λ_i , transmission of disease from state S to state C individuals at a rate λ_c , transition from state E to state I at a rate ν , transition from state I to state C at a rate ρ , recovery rate σ , natural immunity waning at a rate ω . We illustrate the derivation of the equations of motion for the SEICR pair approximation model by deriving the equation of motion for $[SI]$ using an approach also used in references [50, 48].

In moment closure approximations, the dynamics of a state variable $g(t)$ is determined by summing over all events affecting the state variable. Thus, we have

$$\frac{dg(t)}{dt} = \sum_{\epsilon \in \text{events}} r(\epsilon) \Delta g(\epsilon), \quad (3.3)$$

where $r(\epsilon)$ is the rate of event ϵ and $\Delta g(\epsilon)$ is the change this event causes in $g(t)$. The equation (3.3) is called a master equation. The events affecting $[SI]$, the rates at which they occur and the change they cause to $[SI]$, are presented in Table 3.1.

Event	Rate	Change caused in $S - I$ pair
Infection of state S individual by state I neighbor within an $S - I$ pair	λ_i	destruction, $SI \mapsto EI$
Infection from the left, of state S individual by state I neighbor within an $I - S - I$ triple	λ_i	destruction, $SI \mapsto EI$
Infection from the left, of state S individual by state C neighbor within a $C - S - I$ triple	λ_c	destruction, $SI \mapsto EI$
Transition from state E to state I within an $S - E$ pair	ν	creation, $SE \mapsto SI$
Transition from state I to state C within an $S - I$ pair	ρ	destruction, $SI \mapsto SC$
Transition from state R to state S within an $I - R$ pair	ω	creation, $IR \mapsto SI$

Table 3.1: Events affecting $[SI]$, the rates of occurrence of the events and the change they cause to $[SI]$.

We have given an example of our pair approximation, SEICR (susceptible (S), exposed but not infectious (E), infectious (I), the carriers (C) and the recovered (R)) model derivation in Appendix CC.1 which gives the equation of motion for the number of susceptible-infectious ($[SI]$) pairs. After simplifications the equation of motion for $[SI]$ is given as

$$\frac{d[SI]}{dt} = -\lambda_i[SI] - \lambda_i[ISI] - \lambda_c[CSI] + \nu[SE] - \rho[SI] + \omega[IR].$$

3.2.1 Model Equations

The full model is given by the system of equations as follows:

$$\frac{d[S]}{dt} = -\lambda_i[SI] - \lambda_c[SC] + \omega[R], \quad (3.4a)$$

$$\frac{d[E]}{dt} = \lambda_i[SI] + \lambda_c[SC] - \nu[E], \quad (3.4b)$$

$$\frac{d[I]}{dt} = \nu[E] - \rho[I], \quad (3.4c)$$

$$\frac{d[C]}{dt} = \rho[I] - \sigma[C], \quad (3.4d)$$

$$\frac{d[R]}{dt} = \sigma[C] - \omega[R], \quad (3.4e)$$

$$\frac{d[SS]}{dt} = -2\lambda_i[SSI] - 2\lambda_c[SSC] + 2\omega[SR], \quad (3.4f)$$

$$\frac{d[SE]}{dt} = \lambda_i[SSI] - \lambda_i[ISE] + \lambda_c[SSC] - \lambda_c[CSE] - \nu[SE] + \omega[ER], \quad (3.4g)$$

$$\frac{d[SI]}{dt} = -\lambda_i[SI] - \lambda_i[ISI] - \lambda_c[CSI] + \nu[SE] - \rho[SI] + \omega[IR], \quad (3.4h)$$

$$\frac{d[SC]}{dt} = -\lambda_i[ISC] - \lambda_c[SC] - \lambda_c[CSC] + \rho[SI] - \sigma[SC] + \omega[CR], \quad (3.4i)$$

$$\frac{d[SR]}{dt} = -\lambda_i[ISR] - \lambda_c[CSR] + \sigma[SC] - \omega[SR] + \omega[RR], \quad (3.4j)$$

$$\frac{d[EE]}{dt} = 2\lambda_i[ISE] + 2\lambda_c[CSE] - 2\nu[EE], \quad (3.4k)$$

$$\frac{d[EI]}{dt} = \lambda_i[SI] + \lambda_i[ISI] + \lambda_c[CSI] + \nu[EE] - \nu[EI] - \rho[EI], \quad (3.4l)$$

$$\frac{d[EC]}{dt} = \lambda_i[ISC] + \lambda_c[SC] + \lambda_c[CSC] - \nu[EC] + \rho[EI] - \sigma[EC], \quad (3.4m)$$

$$\frac{d[ER]}{dt} = \lambda_i[ISR] + \lambda_c[CSR] - \nu[ER] + \sigma[EC] - \omega[ER], \quad (3.4n)$$

$$\frac{d[II]}{dt} = 2\nu[EI] - 2\rho[II], \quad (3.4o)$$

$$\frac{d[IC]}{dt} = \nu[EC] + \rho[II] - \rho[IC] - \sigma[IC], \quad (3.4p)$$

$$\frac{d[IR]}{dt} = \nu[ER] - \rho[IR] + \sigma[IC] - \omega[IR], \quad (3.4q)$$

$$\frac{d[CC]}{dt} = 2\rho[IC] - 2\sigma[CC], \quad (3.4r)$$

$$\frac{d[CR]}{dt} = \rho[IR] + \sigma[CC] - \sigma[CR] - \omega[CR], \quad (3.4s)$$

$$\frac{d[RR]}{dt} = 2\sigma[CR] - 2\omega[RR]. \quad (3.4t)$$

The factor 2 in the equations of motion for same-status pairs in the model, comes from the counting convention in pair approximations. For instance, $[SS]$ denotes twice the number of susceptible-susceptible ($S-S$) pairs. The model also obeys standard pair approximation

constraints in static networks, namely

$$\sum_X [X] = N \quad \text{and} \quad \sum_Y [XY] = n[X], \quad (3.5)$$

where n is the average neighbourhood size of each individual in the network and N is the total population size. In this study, we close equations (3.4) by using the OPA, given by equation (3.1) to approximate triples into lower-order moments.

Associated with pair approximations, is the concept of correlations functions. The correlation between farms with disease states X and Y is given by

$$C_{XY} = \frac{N}{n} \frac{[XY]}{[X][Y]}. \quad (3.6)$$

As addressed in the following sections of this chapter, the correlation functions can also be used to study threshold dynamics. The conditions $C_{XY} < 1$, $C_{XY} = 1$ and $C_{XY} > 1$ represent avoidance, random mixing and aggregation, respectively, of contacts with disease states X and Y . As shown in Equation (3.6), the number of pairs $[XY]$ can be expressed as a function corresponding correlations C_{XY} . For this reason, moment closure approximation models, such as the pair approximation model in this study, are also often called correlation models.

3.3 Threshold Dynamics

Below, we derive formulations that represent the threshold dynamics of a disease outbreak described by equations (3.4). These dynamics involve conditions that support or deter the occurrence of a disease outbreak. To capture the initial state of an outbreak, we derive expressions of the basic reproduction number, denoted by R_0 , corresponding to Equations (3.4). The basic reproduction number is defined as the expected number of secondary cases produced by a single infectious individual or animal in a completely susceptible population [51, 52, 53]. In this chapter, we apply a widely-adopted convention that the disease will spread if $\mathcal{R}_0 > 1$ and it would fail to take off if $\mathcal{R}_0 < 1$ [53].

At the initial stages of an outbreak, the disease is likely to spread if the condition $\frac{d([E]+[I]+[C])}{dt} > 0$ holds. Thus, the threshold dynamics of the disease described by Equations (3.4), can be represented by the inequality $\frac{\lambda_i[SI]+\lambda_c[SC]}{\sigma[C]} > 1$. In pair approximations, the left hand side of this inequality is in fact the general expression of R_0 for Equations (3.4). Thus,

$$R_0 = \frac{\lambda_i[SI] + \lambda_c[SC]}{\sigma[C]}. \quad (3.7)$$

Substituting Equation (3.6) into Equation (3.7) gives

$$R_0 = \frac{\lambda_i}{\sigma} \frac{n}{N} [S][I] C_{SI} + \frac{\lambda_c}{\sigma} \frac{n}{N} [S] C_{SC}. \quad (3.8)$$

Note that the basic reproduction number is described by the dynamics of the disease at the

beginning of an outbreak when there are very few state I and even fewer state C farms, and almost the entire population is susceptible. Thus, at this stage the approximation $[S] \approx N$ hold. Imposing this approximation onto Equation (3.8) gives an approximated expression of R_0 given by

$$R_0 \approx \frac{\lambda_i n}{\sigma} \frac{[I]}{[C]} C_{SI} + \frac{\lambda_c n}{\sigma} C_{SC}. \quad (3.9)$$

We use a notion from pair approximations that at the initial stages of outbreak, the correlation functions C_{SI} and C_{SC} reach some local critical values C_{SI}^* and C_{SC}^* , respectively, which play a role in determining the possibility of the spread of an outbreak. Thus, if we further assume that initially we have $\frac{[I]}{[C]} = k_2$, where k_2 is a constant, then we can rewrite Equation (3.9) as

$$R_0 \approx \frac{\lambda_i n}{\sigma} k_2 C_{SI}^* + \frac{\lambda_c n}{\sigma} C_{SC}^*. \quad (3.10)$$

The expressions for C_{SI}^* and C_{SC}^* , which we derive below, are obtained by solving the equations

$$\frac{d}{dt} C_{SI} = 0 \quad (3.11)$$

and

$$\frac{d}{dt} C_{SC} = 0, \quad (3.12)$$

respectively. We show in Appendix C, section C.2 that the equations of motion for C_{SI} and C_{SC} are

$$\frac{d}{dt} C_{SI} = \frac{N}{n} \left(\frac{1}{[S][I]} \frac{d}{dt} [SI] + \frac{[SI]}{[S][I]} \left(-\frac{1}{[I]} \frac{d}{dt} [I] - \frac{1}{[S]} \frac{d}{dt} [S] \right) \right) \quad (3.13)$$

and

$$\frac{d}{dt} C_{SC} = \frac{N}{n} \left(\frac{1}{[S][C]} \frac{d}{dt} [SC] + \frac{[SC]}{[S][C]} \left(-\frac{1}{[C]} \frac{d}{dt} [C] - \frac{1}{[S]} \frac{d}{dt} [S] \right) \right) \quad (3.14)$$

respectively. When we substitute the equations of motion for $[SI]$, $[SC]$, $[I]$ and $[C]$ from equations (3.4), into Equations (3.13) and (3.14), and use the OPA, i.e. Equation (3.1), to approximate triples into lower order moments, and furthermore, equate Equations (3.13) and (3.14) to zeroes, we obtain, respectively, the expressions

$$\begin{aligned} -\lambda_i C_{SI} - \lambda_i (n-1) \frac{[I]}{N} C_{SI}^2 - \lambda_c (n-1) \frac{[C]}{N} C_{SI} C_{SC} + \nu \frac{[E]}{[I]} C_{SE} + \omega \frac{[R]}{[S]} C_{IR} - \nu \frac{[E]}{[I]} C_{SI} \\ + \lambda_i n \frac{[I]}{N} C_{SI}^2 + \lambda_c n \frac{[C]}{N} C_{SI} C_{SC} - \omega \frac{[R]}{[S]} C_{SI} \approx 0 \end{aligned} \quad (3.15)$$

and

$$\begin{aligned}
 -\lambda_c C_{SC} - \lambda_c(n-1) \frac{[C]}{N} C_{SC}^2 - \lambda_i(n-1) \frac{[I]}{N} C_{SI} C_{SC} + \rho \frac{[I]}{[C]} C_{SI} + \omega \frac{[R]}{[S]} C_{CR} - \rho \frac{[I]}{[C]} C_{SC} \\
 + \lambda_c n \frac{[C]}{N} C_{SC}^2 + \lambda_i n \frac{[I]}{N} C_{SI} C_{SC} - \omega \frac{[R]}{[S]} C_{SC} \approx 0. \quad (3.16)
 \end{aligned}$$

We simplify these expressions by considering a large population, i.e. $N \rightarrow \infty$. Note almost the entire population is susceptible at the beginning of an outbreak, i.e. $[S] \approx N$. Therefore, the term $\lambda_i(n-1) \frac{[I]}{N} C_{SI}^2$ in Equation (3.15) can be simplified to zero, i.e.

$$\lambda_i(n-1) \frac{[I]}{N} C_{SI}^2 = \lambda_i(n-1) \frac{[I]}{N} \frac{N^2}{n^2} \frac{[SI]^2}{[S]^2 [I]^2} \approx \lambda_i(n-1) \frac{[SI]^2}{N n^2 [I]} = \frac{O(1)}{O(\infty)} \approx 0.$$

Similarly, the terms $\lambda_i n \frac{[C]}{N} C_{SI}^2$, $\lambda_c(n-1) \frac{[C]}{N} C_{SC}^2$ and $\lambda_c n \frac{[C]}{N} C_{SC}^2$ in Equations (3.15) and (3.16) can be approximated to **zeroes** at the beginning of an outbreak. Furthermore, the same argument can be used to show that initially $\frac{[C]}{N} C_{SI} C_{SC} \approx 0$, $\frac{[I]}{N} C_{SI} C_{SC} \approx 0$, $\frac{[R]}{[S]} C_{SI} \approx 0$ and $\frac{[R]}{[S]} C_{SC} \approx 0$. Therefore, Equations (3.15) and (3.16) can be simplified to

$$-\lambda_i C_{SI} + \nu k_1 C_{SE} + \omega k_4 C_{IR} - \nu k_1 C_{SI} \approx 0 \quad (3.17)$$

and

$$-\lambda_c C_{SC} + \rho k_2 C_{SI} + \omega k_4 C_{CR} - \rho k_2 C_{SC} \approx 0, \quad (3.18)$$

respectively, where for simplicity we assume that initially, we have $\frac{[E]}{[I]} = k_1$, $\frac{[C]}{[R]} = k_3$ and $\frac{[R]}{[S]} = k_4$, where k_1 , k_3 and k_4 are constants. We can conclude, based on Equations (3.17) and (3.18), that the local critical values of C_{SI} and C_{SC} at the beginning of an outbreak are given by the expressions

$$C_{SI}^* \approx \frac{\nu k_1 C_{SE}^* + \omega k_4 C_{IR}^*}{\lambda_i + \nu k_1} \quad (3.19)$$

and

$$C_{SC}^* \approx \frac{\rho k_2 C_{SI}^* + \omega k_4 C_{CR}^*}{\lambda_c + \rho k_2}. \quad (3.20)$$

Substituting Equations (3.19) and (3.20) into Equation (3.10) gives an approximation of the basic reproduction number, namely

$$R_0 \approx \frac{\lambda_i n}{\sigma} k_2 \frac{\nu k_1 C_{SE}^* + \omega k_4 C_{IR}^*}{\lambda_i + \nu k_1} + \frac{\lambda_c n}{\sigma} \rho k_2 \frac{\nu k_1 C_{SE}^* + \omega k_4 C_{IR}^*}{\lambda_c + \rho k_2} + \omega k_4 C_{CR}^*. \quad (3.21)$$

According to the theory of pair approximations, to obtain an explicit expression for R_0 at this stage, we need to further derive critical values C_{SE}^* , C_{IR}^* and C_{CR}^* , which are found by solving the equations $\frac{d}{dt} C_{SE} = 0$, $\frac{d}{dt} C_{IR} = 0$ and $\frac{d}{dt} C_{CR} = 0$, respectively. Equations of motion for these correlations will contain other correlations functions C_{XY} , where X and Y

are disease states, whose equations also need to be evaluated. This procedure will yield a system of equations of motion for correlation functions corresponding to each pair $X - Y$ in Equations (3.4). **The derivation of this full model correlations is presented in Appendix C.2.1.**

However, in the Results section below, we fix the quantities k_l , where $l = 1, 2, 3, 4$ and the values C_{SE}^* , C_{IR}^* and C_{CR}^* , and explore, without loss of generality, the impact of model parameters on R_0 using Equation (3.21).

3.4 Results and Discussion

The simulation results in this section are based on our model given by Equations (3.4). Unless stated otherwise, we consider a population distributed on a toroidal network with $N = 400$ nodes (individual farms) such that each node has $n = 4$ neighbours. We also assume that at the initial stage of an outbreak there is 1 infectious node and all other nodes are susceptible, i.e. initially, we have $[S] = 399$, $[I] = 1$, $[SS] = 796$, $[SI] = 4$, and all other state variables in Equations (3.4) are zeroes.

The number of secondary infections resulting from an infectious contact (i.e. $\mathcal{R}_0$), increases with the rate of effective contact with carriers and this is more apparent when the recovery rate is low than when it is high (Figure 3.1). This happens because as the number of carriers, who can pass on the disease causing pathogen, reduces due to high values of the recovery rate, the number of contacts leading to disease transmission decreases.

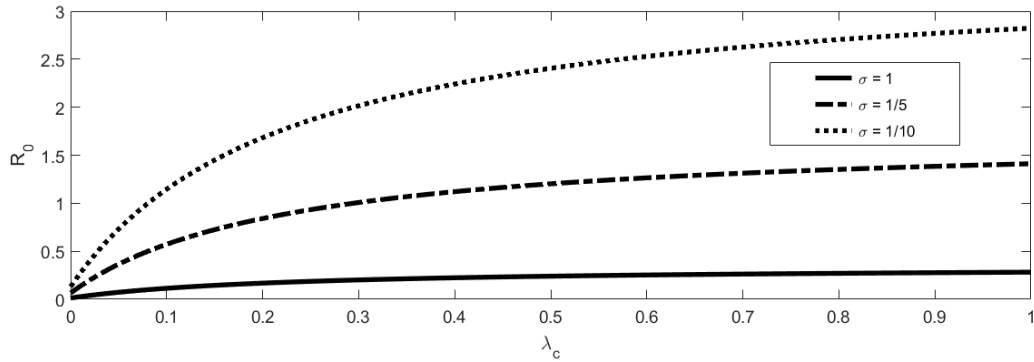


Figure 3.1: The basic reproduction number $\mathcal{R}_0$ given by equation (3.21), as a function of infection rate from carriers λ_c , for different recovery rates, σ . Other estimated constants are $\nu = 1/4$, $\rho = 1/4$, $\sigma = 1/10$, $\lambda_i = 0.01$, $n = 4$, $k_1 = 0.1$, $k_2 = 0.9$, $k_3 = 0.9$, $k_4 = 0.1$, $C_{SE} = 0.5$, $C_{IR} = 0.5$ and $C_{CR} = 0.5$.

For a prescribed parameter regime, within some period of time after the onset of an outbreak (e.g. day 55 in Figure 3.2), all previously susceptible animals would have been exposed to the disease and there would be no new infections. As expected, at this point the number of infected individuals starts to decrease. Also, as expected the graphs for other infection classes namely the exposed and the carriers, mimic the behavior of the graph for the number of infected classes.

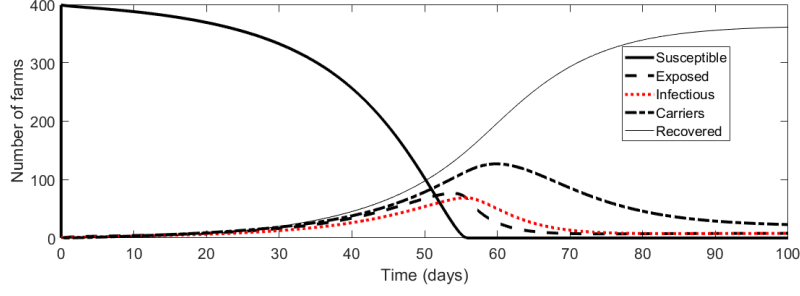


Figure 3.2: Time series for the numbers of susceptible, exposed, infectious, carriers and recovered farms as described by equations (3.4), where the model parameters are $\lambda_i = 0.5$, $\lambda_c = 0.5$, $\nu = 1/4$, $\rho = 1/4$ and $\sigma = 1/10$.

The infection peak increases with the disease transmission rates from both the infectious and the disease carriers (Figure 3.3). For the given parameter regime, it appears that both forms of disease transmission have similar effect on the infection peak. This result signifies the need to explore further, the impacts of carriers of the dynamics of FMD.

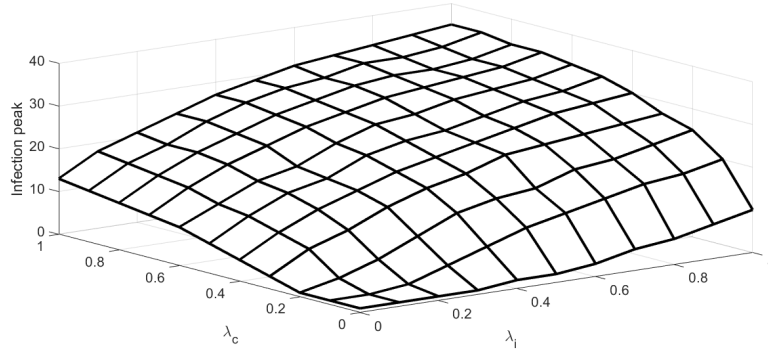


Figure 3.3: Infection peak for equations (3.4) versus λ_i and λ_c , where other model parameters are $\nu = 1/4$, $\rho = 1/4$ and $\sigma = 1/10$.

3.5 Conclusions

We developed and studied the control of a heterogeneous-mixing pair approximation model of FMD where the disease pathogen, which belongs to the picanovirus family of viruses, is transmissible from both symptomatic infectious and asymptomatic carrier nodes to susceptible contacts on a prescribed network structure. We explored the impact of infection rate from carriers (λ_c) and recovery rate (σ) on the reproduction number of which the results shows that $\mathcal{R}_0$ increases with effective contact with carriers associated with lower recovery rates. We also explored the effect of transmission rate from the infected, (λ_i) and transmission rate from the carriers, (λ_c) on the infection peak and observed that if these two parameters are increased there will be more cases of FMD in farms as such control strategies of FMD need to be applied. At biologically plausible parameter values, regardless of the underlying network of disease propagation, the optimal disease control strategy involves prevention of disease importation to susceptible populations, early detection of infected premises and rapid

destruction on both infectious and carrier nodes and rapid eradication of high-risk premises and farms at the onset of an outbreak. Moreover, we found that the clamping effect of highly clustered networks prevents a global epidemic from growing because they localize the transmission of disease and make it easier to control it. We conclude that more spatial models of FMD with carriers and other qualitative properties but relatively tractable need to be developed.



4. Conclusion and Discussion

This chapter will conclude the study by summarising the main findings and conclusions of the FMD models developed in this thesis. This thesis aimed at developing models that incorporated the carriers, environment and space as factors that have impact in the dynamics of Foot and Mouth Disease. We investigated the effect of contact with the disease pathogen in both models and found that contact with FMD pathogen is directly proportional to the disease spread.

In this study we presented a dynamical mathematical model with carriers in Chapter 2 which captures the spread of FMD through direct transmission due to contact with the infected animal and indirect transmission due to contact with the infected environment. The model basic properties, positivity and boundedness of solutions were analysed to ensure that the model is well posed. The numerical results show that whenever $\mathcal{R}_0 < 1$ the disease will die out and persist in a population whenever $\mathcal{R}_0 > 1$. This show that FMD can be contained when the reproduction number is less than unity. We have found through sensitivity analysis of the reproduction number that if the disease is to be contained processes described by increasing the recovery rate of the infected and carrier animals and minimal drooling of the FMD pathogen into the environment by symptomatic animals has to be enhanced. Also, under sensitivity analysis based on the full model we found that the most sensitive parameters β_1 , β_2 , η_1 , K , ν and γ aggravates the spread of Foot and Mouth disease.

Chapter 2 was reduced in Chapter 3 where the presymptomatic class was eliminated as well as the contribution of the pathogen infected environment. Chapter 3 studied a heterogeneous-mixing pair approximation model of FMD where the disease pathogen is transmissible from both symptomatic and asymptomatic carrier nodes to susceptible contacts on a prescribed network structure. We investigated the input of parameters, infection rate from carriers (λ_c) and recovery rate (σ) on the reproduction number. The results show that $\mathcal{R}_0$ increases with effective contact with carriers associated with lower recovery rates. We also explored the effect of transmission rate from the infected (λ_i) and carriers (λ_c) on the infection peak. Our results show that if these two parameters are increased there will be more cases of FMD in farms which will call for FMD control strategies. The findings also indicate that the clamping effect of highly clustered networks prevents a global epidemic from growing by localising the transmission of the disease making it easier to control it.

We acknowledge the optimal control strategies on FMD studies therefore, in future work optimal control studies on FMD can be explored with raw data collected from experiments or data sampled from places of interest, for example, the northern part of Botswana or Bobirwa region which are associated with common outbreaks of FMD. It is important to undertake these models as lessons learnt are flexible and it is likely that the next outbreak will have the same epidemiological characteristics. Therefore modelling a wide range of scenarios of FMD spread and impact will help to calculate the optimal control strategies for

each scenario.



A. MATLAB and R Codes for Figures in Chapter 2

A.1 Matlab Code for the Tornado Plot, Box Plot and PRCCs Respectively in Figure 2.2a, Figure 2.2b and Table 2.4.

```
1 clear ;
2 % Calling program to generated PRCC for LHS; call the LHS program
   which
3 % generates the sample; all input variables are included in the
   LHS program
4 % and output of the program is the matrix CC from Blower's
   technique paper
5
6 LHS; % call the LHS program
7 b = size(latin_output);
8 c = length(latin_output);
9
10 num = b(2);
11
12 % delclare initial parameters
13
14 rank_outcome = zeros(1000,1);
15 rank = zeros(1000,10);
16 outcome = zeros(1000,100);
17 parameters = zeros(1000,10);
18 CC = zeros(10, 10);
19 lengthofmatrix = b(2);
20 % read in data from LHS; program creates matrices outcome and
21 % parameters that are used to calculate the PRCCs
22 % variables are then ranked and results are put into
   rank_outcome
23 % matrix which is fed into create_rank_matrix which creates a
   matrix of the ranks of each
24 % parameter for each simulation; the CC matrix then created in
   the last
25 % program
26
27 [parameters , outcome] = read_in_data(N, num, latin_output);
```

```

28     [rank_outcome] = create_outcome_rank(N, num, outcome);
29     [rank, ranks] = create_rank_matrix(N, num, parameters, rank,
    rank_outcome);
30     [CC] = make_c_matrix(N, num, rank);
31     RCCMatrix = [CC];
32     Prcclist = RCCMatrix(:,16)
33
34
35     set(0, 'defaulttextinterpreter', 'tex');
36     fig11 = figure(11);
37     barh(CC(1:length(CC)-1,length(CC)))
38
39     set(gca, 'YTick', 1:16);
40     [hx,hy] = format_ticks(gca,...
41         {'$-0.6$', '$-0.4$', '$-0.2$', '$0$', '$0.2$', '$0.4$', '$0.6$', '$0
    .8$'},...
42         {'$\beta_1$', '$\beta_2$', '$\eta_1$', '$\eta_2$', '$\mu$', '$\
    gamma$', '$\sigma$', '$\phi$', '$\delta$', '$\psi$', 'K', '$\
    alpha$', '$\xi_1$', '$\xi_2$', '$\xi_3$', '$\nu$'},...
43         -0.6:0.2:0.8, [], 0, 0, [], ...
44         'FontSize', 14, 'FontWeight', 'Bold');

1 function [R_C] = calculation(para)
2
3 n= 2;
4 N0 = 16750; % estimated total population of the Hubei Province
5 mu = 0.000239; % the estimated life expectancy of the province is
    76.79 years
6 Pi = mu*N0;
7 K = 100000;
8 delta = 0.0023135710;
9 for i=1:1000;
10     beta1(i)=para(i,1);
11     beta2(i)=para(i,2);
12     eta1(i)=para(i,3);
13     eta2(i)=para(i,4);
14     gamma(i)=para(i,5);
15     sigma(i)=para(i,6);
16     phi(i)=para(i,7);
17     psi(i)=para(i,8);
18     alpha(i)=para(i,9);
19     xi1(i)=para(i,10);
20     xi2(i)=para(i,11);

```

```
21     xi3(i)=para(i,12);
22     nu(i)=para(i,13);
23
24
25     %     xi(i)=para(i,12);
26     %     k1(i) = (mu+theta(i)+alpha(i));
27     %     k2(i) = (mu+gamma(i)+delta);
28     %     aa(i) = eta(i).*(1-h(i))+phi(i).*(1-rho(i)).*h(i);
29     %     bb(i) = (1-eta(i)).*(1-h(i))+(1-phi(i)).*(1-rho(i)).*h(i);
30     %
31     %     R01(i) = beta1(i).*((aa(i)./k1(i)).*(nu + (theta(i)./k2(i)))
32         + (bb(i)./k2(i)));
33     %     R02(i) = (beta2(i)*Pi./(mu*K*Psi(i))).*((aa(i)./k1(i)).*(
34         epsilon(i)+(theta(i).*xi(i)./k2(i)))+(xi(i)*bb(i)./k2(i)));
35     %     R_C(i) = R01(i) + R02(i)
36     Q1(i) = mu + sigma(i);
37     Q2(i) = mu + nu(i);
38     Q3(i) = mu + phi(i) + delta + gamma(i);
39     Q4(i) = alpha(i) + mu;
40
41     R01(i) = (sigma(i).*beta1(i))./(Q1(i).*Q2(i));
42     R02(i) = (nu(i).*sigma(i).*beta1(i).*eta1(i))./(Q1(i).*Q2(i).*Q3(
43         i)));
44     R03(i) = (nu(i).*sigma(i).*phi(i).*beta1(i).*eta2(i))./(Q1(i).*Q2
45         (i).*Q3(i).*Q4(i)));
46     R04(i) = (beta2(i).*sigma(i).*(Q3(i).*Q4(i).*xi3(i)+nu(i).*Q4(i)
47         .*xi2(i)+nu(i).*phi(i).*xi3(i)).*Pi)/(K.*phi(i).*mu.*Q1(i).*Q2
48         (i).*Q3(i).*Q4(i)));
49     R_C(i)=(R01(i) + R02(i) + R03(i) + R04(i));
50 end
```

A.2 Matlab Code for the Scatter Plots in Figure 2.3

```

1 % I have to run LHS first , then define a new matrix C to be para.
2 n= 2;
3 N0 = 16750; % estimated total population of the Hubei Province
4 mu = 0.000239; % the estimated life expectancy of the province is
   76.79 years
5 Pi = mu*N0;
6 K = 100000;
7 para;
8 delta = 0.0023135710;
9 for i=1:1000;
10     beta1(i)=para(i,1);
11     beta2(i)=para(i,2);
12     eta1(i)=para(i,3);
13     eta2(i)=para(i,4);
14     gamma(i)=para(i,5);
15     sigma(i)=para(i,6);
16     phi(i)=para(i,7);
17     psi(i)=para(i,8);
18     alpha(i)=para(i,9);
19     xi1(i)=para(i,10);
20     xi2(i)=para(i,11);
21     xi3(i)=para(i,12);
22     nu(i)=para(i,13);
23
24
25 %     xi(i)=para(i,12);
26 %     k1(i) = (mu+theta(i)+alpha(i));
27 %     k2(i) = (mu+gamma(i)+delta);
28 %     aa(i) = eta(i).*(1-h(i))+phi(i).*(1-rho(i)).*h(i);
29 %     bb(i) = (1-eta(i)).*(1-h(i))+(1-phi(i)).*(1-rho(i)).*h(i);
30 %
31 %     R01(i) = beta1(i).*((aa(i)./k1(i)).*(nu + (theta(i)./k2(i)))
   + (bb(i)./k2(i)));
32 %     R02(i) = (beta2(i)*Pi./(mu*K*Psi(i))).*((aa(i)./k1(i)).*(
   epsilon(i)+(theta(i).*xi(i)./k2(i)))+(xi(i)*bb(i)./k2(i)));
33 %     R_C(i) = R01(i) + R02(i)
34 Q1(i) = mu + sigma(i);
35 Q2(i) = mu + nu(i);
36 Q3(i) = mu + phi(i) + delta + gamma(i);
37 Q4(i) = alpha(i) + mu;

```

```

38
39 R01(i) = (sigma(i).*beta1(i))./(Q1(i).*Q2(i));
40 R02(i) = (nu(i).*sigma(i).*beta1(i).*eta1(i))./(Q1(i).*Q2(i).*Q3(
    i)));
41 R03(i) = (nu(i).*sigma(i).*phi(i).*beta1(i).*eta2(i))./(Q1(i).*Q2
    (i).*Q3(i).*Q4(i)));
42 R04(i) = (beta2(i).*sigma(i).*(Q3(i).*Q4(i).*xi3(i)+nu(i).*Q4(i)
    .*xi2(i)+nu(i).*phi(i).*xi3(i)).*Pi)/(K.*phi(i).*mu.*Q1(i).*Q2
    (i).*Q3(i).*Q4(i)));
43 R_C(i)=(R01(i) + R02(i) + R03(i) + R04(i));
44
45 end
46
47 figure(1)
48 beta1;
49 Repnum = log(R_C);
50 pbeta1 = polyfit(beta1,Repnum,1);
51 R0beta1yfit = polyval(pbeta1,beta1);
52 plot(beta1,Repnum,'.')
53 hold on
54 plot(beta1,R0beta1yfit,'LineWidth',2)
55 xlabel('Transmission rate directly from the infected animal, \
    beta_1','FontSize',14)
56 ylabel('log(R_0)','FontSize',14)
57
58 figure(2)
59 beta2;
60 Repnum = log(R_C);
61 pbeta2 = polyfit(beta2,Repnum,1);
62 R0beta2yfit = polyval(pbeta2,beta2);
63 plot(beta2,Repnum,'.')
64 hold on
65 plot(beta2,R0beta2yfit,'LineWidth',2)
66 xlabel('Transmission rate from pathogen infected surfaces, \beta_2
    ','FontSize',12)
67 ylabel('log(R_0)','FontSize',14)
68
69 figure(3)
70 gamma;
71 Repnum = log(R_C);
72 pgamma = polyfit(gamma,Repnum,1);
73 R0gammayfit = polyval(pgamma,gamma);

```

```
74 plot(gamma,Repnum, '. ')
75 hold on
76 plot(gamma,R0gammayfit, 'LineWidth',2)
77 xlabel('Recovery rate of the infected animals, \gamma','FontSize',15)
78 ylabel('log(R_0)', 'FontSize',14)
79
80 figure(4)
81 xi2;
82 Repnum = log(R_C);
83 pxi2 = polyfit(xi2,Repnum,1);
84 R0xi2yfit = polyval(pxi2,xi2);
85 plot(xi2,Repnum, '. ')
86 hold on
87 plot(xi2,R0xi2yfit, 'LineWidth',2)
88 xlabel('Shedding rate by Infected animals, \xi_2','FontSize',15)
89 ylabel('log(R_0)', 'FontSize',14)
90
91
92 %v=0;
93
94 % figure(1)
95 % plot(beta1, log(R_C), '.', beta1, v)
96 % xlabel('Transmission rate directly from the infected animal, \beta_1','FontSize',15)
97 % ylabel('log(R_0)', 'FontSize',11)
98 %
99 % figure(2)
100 % plot(beta2, log(R_C), '.', beta2, v)
101 % xlabel('Transmission rate from the pathogen infected surfaces, \beta_2','FontSize',15)
102 % ylabel('log(R_0)', 'FontSize',11)
103
104 % figure(3)
105 % plot(gamma, log(R_C), '.', gamma, v)
106 % xlabel('Recovery rate of the infected animals, \gamma','FontSize',15)
107 % ylabel('log(R_0)', 'FontSize',15)
108
109 % figure(4)
110 % plot(xi2, log(R_C), '.', xi2, v)
111 % xlabel('Shedding rate by Infected animals, \xi_2','FontSize',15)
```

```

112 % ylabel('log(R_0)', 'FontSize', 15)
113 % figure(5)
114 % plot(psi, log(R_C), '.', psi, v)
115 % xlabel('Recruitment rate of midges, \Pi_m', 'FontSize', 15)
116 % ylabel('log(R_0)', 'FontSize', 15)
117
118 % figure(6)
119 % plot(betab, log(R_C), '.', betab, v)
120 % xlabel('Proportion of asymptomatic animals, \theta', 'FontSize', 15)
121 % ylabel('log(R_0)', 'FontSize', 15)
122 %
123 %
124 %figure(9)
125 %boxplot(R_C)
126 %axis([0.5 1.5 0 4])
127 %ylabel('Reproduction number, {R}_{0}', 'FontSize', 15)
128 %xlabel('Column number', 'FontSize', 12)
129 %
130 % close (figure(10))
131 % figure(10)
132 % hold on
133 % for i=1:10:1000
134 %     for j=1:10:1000
135 %         meanR_C(i, j)= (mean(betaI)./(1./overalpha(i)+d)).*(lambda
            ./d)+(((1./overalpha(i)).*(1./ (mean(overdelta))).*mean(p).*mean
            (gammaQ).*mean(betaR))./(((1./overalpha(i))+d).*(1./ (mean(
            overdelta)))+d)).*(1./oversigmaR(j))+d))).*(lambda./d);
136 % if meanR_C(i, j)<1
137 %     plot(overalpha(i), oversigmaR(j), '.b')
138 % else
139 %     plot(overalpha(i), oversigmaR(j), '.r')
140 % end
141 %
142 %     end
143 % end
144 % xlabel('average time of infection before treatment')
145 % ylabel('average time until switching treatments')
146 %
147 % [X, Y]=meshgrid(overalpha, oversigmaR);
148 % Z= (mean(betaI)./(1./X+d)).*(lambda./d)+(((1./X).*(1./ (mean(
            overdelta))).*mean(p).*mean(gammaQ).*mean(betaR))./(((1./X)+d)

```

```
.*(1./((mean(overdelta)))+d).*((1./Y)+d)).*(lambda./d);  
149 % figure(11)  
150 % mesh(X,Y,Z)  
151 % hold on  
152 % mesh(X,Y,X./X)
```

A.3 Matlab Code for the Sensitivity of the Full Model in Section 2.4.3.

The same code was used for the considered state variables.

```
1 clear all;  
2 close all;  
3  
4 %% Sample size N  
5 runs=1000;  
6  
7 %% LHS MATRIX %%  
8 Parameter_settings_LHS;  
9  
10  
11 beta1_LHS=LHS_Call(0.1244, beta1, 0.2924, 0 ,runs, 'unif'); %  
    baseline = 10  
12 beta2_LHS=LHS_Call(0.016, beta2, 0.0314, 0 ,runs, 'unif'); %  
    baseline = 10  
13 eta1_LHS=LHS_Call(0.2, eta1, 0.8, 0 ,runs, 'unif'); % baseline = 10  
14 eta2_LHS=LHS_Call(0.1, eta2, 0.45, 0 ,runs, 'unif'); % baseline =  
    10  
15 K_LHS=LHS_Call(100000, K, 10000000, 0 ,runs, 'unif'); % baseline =  
    10  
16 gamma_LHS=LHS_Call(0.1, gamma, 0.2, 0 ,runs, 'unif'); % baseline =  
    10  
17 sigma_LHS=LHS_Call(0.2000, sigma, 0.3333, 0 ,runs, 'unif'); %  
    baseline = 10  
18 sigma_LHS=LHS_Call(0.18000, sigma, 0.67, 0 ,runs, 'unif'); %  
    baseline = 10  
19 phi_LHS=LHS_Call(0.0027, phi, 0.0056, 0 ,runs, 'unif'); % baseline  
    = 10  
20 psi_LHS=LHS_Call(0.2, psi, 0.5, 0 ,runs, 'unif'); % baseline = 10  
21 alpha_LHS=LHS_Call(0.00078, alpha, 0.00083, 0 ,runs, 'unif'); %  
    baseline = 10  
22 xi1_LHS=LHS_Call(0.01, xi1, 0.22, 0 ,runs, 'unif'); % baseline = 10  
23 xi2_LHS=LHS_Call(0.01, xi2, 0.55, 0 ,runs, 'unif'); % baseline = 10
```

```

24 xi3_LHS=LHS_Call(0.01, xi3, 0.21, 0, runs, 'unif'); % baseline = 10
25 nu_LHS=LHS_Call(1.15, nu, 2.3, 0, runs, 'unif'); % baseline = 10
26
27
28 %% LHS MATRIX and PARAMETER LABELS
29 LHSmatrix=[beta1_LHS beta2_LHS eta1_LHS eta2_LHS K_LHS gamma_LHS
    sigma_LHS phi_LHS psi_LHS alpha_LHS xi1_LHS xi2_LHS xi3_LHS
    nu_LHS];
30
31 for x=1:runs %Run solution x times choosing different values
32     f=@ODE_LHS;
33     x
34     LHSmatrix(x,:)
35     [t,y]=ode15s(@(t,y) f(t,y,LHSmatrix,x,runs),tspan,y0,[]);
36     D=[t y]; % [time y]
37
38     %% Save only the outputs at the time points of interest [
        time_points]:
39     %% MORE EFFICIENT
40     T_lhs(:,x)=D(time_points+1,1);
41     S_lhs(:,x)=D(time_points+1,2);
42     E_lhs(:,x)=D(time_points+1,3);
43     A_lhs(:,x)=D(time_points+1,4);
44     I_lhs(:,x)=D(time_points+1,5);
45     C_lhs(:,x)=D(time_points+1,6);
46     R_lhs(:,x)=D(time_points+1,7);
47     W_lhs(:,x)=D(time_points+1,8);
48
49 end
50 %% Save the workspace
51 save Model_LHS.mat;
52 % CALCULATE PRCC
53 [prcc1 sign sign_label]=PRCC(LHSmatrix, S_lhs, 1:length(time_points)
    ,PRCC_var,0.05);
54
55 [prcc2 sign sign_label]=PRCC(LHSmatrix, E_lhs, 1:length(time_points)
    ,PRCC_var,0.05);
56 %PRCCPLOT(LHSmatrix, V_lhs, 2, PRCC_var, y_var_label(3))%save
    model1_LHS.mat;
57
58 % PRCCs for the Presymptomatics class

```

```

59 [prcc3 sign sign_label]=PRCC(LHSmatrix,A_lhs,1:length(time_points)
    ,PRCC_var,0.05);
60
61 [prcc4 sign sign_label]=PRCC(LHSmatrix,I_lhs,1:length(time_points)
    ,PRCC_var,0.05);
62
63 [prcc5 sign sign_label]=PRCC(LHSmatrix,C_lhs,1:length(time_points)
    ,PRCC_var,0.05);
64
65 figure(1)
66 set(gca,'linestyleorder',{ '-',':','-.','—','*','+'}, 'nextplot','
    add')
67 plot(prcc5,'linewidth',2)
68 legend('\beta_1','\beta_2','\eta_1','\eta_2','K','\gamma','\sigma'
    ,'\psi','\alpha','\phi','\xi_1','\xi_2','\xi_3','\nu')
69 xlabel('Time (days)'), ylabel('PRCCs (Carrier Animals)')
70 %CALCULATE PRCC
71 figure(2)
72 bar(prcc5(10,:));
73 set(gca,'XTickLabel',PRCC_var,'XTick',[1:14],'FontSize',14,'
    FontWeight','Bold'), title('PRCCs at T = 10');
74 ylabel('PRCCs (Carrier Animals)')
75
76 figure(3)
77 bar(prcc5(100,:));
78 set(gca,'XTickLabel',PRCC_var,'XTick',[1:14],'FontSize',14,'
    FontWeight','Bold'), title('PRCCs at T = 100');
79 ylabel('PRCCs (Carrier Animals)')
80
81 figure(4)
82 bar(prcc5(250,:));
83 set(gca,'XTickLabel',PRCC_var,'XTick',[1:14],'FontSize',14,'
    FontWeight','Bold'), title('PRCCs at T = 250');
84 ylabel('PRCCs (Carrier Animals)')
85
86 prcc5(10,:) '
87 prcc5(100,:) '
88 prcc5(250,:) '

```

A.4 R Code for the Significance of PRCCs for Sensitivity of the Full Model in Section 2.4.3.

```
1
2 #pvalfile <- read.table(file="covid19prccs.txt", header=T)  #
  file from Matlab
3 pvalfile <- read.table(file="fmdprcc.txt", header=T)  # file from
  Matlab
4 #pvalfile <- read.table(file="hbvprccsnew.txt", header=T)  # file
  from Matlab
5 #pvalfile <- read.table(file="prcc.txt", header=T)  # file from
  Matlab
6 source("prccomp.R")  # Source the
  function prcc
7
8 ## Sample size if common
9 N <- 1000
10
11 parcorr <- pvalfile$PRCC  # PRCC from Matlab
12 vars <- pvalfile$Variable  # Variable names
13 ns <- rep(N, length(parcorr))  # Sample sizes
14
15
16 ## Run PRCC comparisons using default alpha = 0.05
17 ## No FDR adjustment to choose important parameters
18 prcc(parcorr, ns, var.names = vars, FDR = F)
19
20
21 ## Run PRCC comparisons using alpha = 0.01
22 ## No FDR adjustment to choose important parameters
23 prcc(parcorr, ns, var.names = vars, FDR = F, alpha = 0.01)
24
25
26 ## Run PRCC comparisons using default alpha = 0.05
27 ## FDR adjustment to choose important parameters
28 prcc(parcorr, ns, var.names = vars, FDR = T)
29
30
31 prcc(parcorr, ns, var.names = vars, FDR = TRUE, round4 = FALSE)
32
33
34 ## Run PRCC comparisons using default alpha = 0.05
35 ## FDR adjustment (default) to choose important parameters
36 ## No variable names provided (uses order as names)
37 prcc(parcorr, ns)
```

A.4.1 fmdprcc text file

Variables	PRCC
beta1	0.5069
beta2	0.4525
eta1	0.1829
eta2	0.1253
gamma	-0.4947
sigma	0.0548
phi	-0.0463
psi	0.0143
alpha	-0.0696
xi1	0.0299
xi2	0.3533
xi3	0.1469
nu	0.1101

A.4.2 Python Code for Figures 2.12

```

1 from __future__ import division
2 from scipy import *
3 import numpy as n
4 import pylab
5 import scipy.integrate as integrate
6 from itertools import cycle
7 lines = ["-", "--", "-.", ":"]
8 linecycler = cycle(lines)
9
10 beta1 = 0.33; beta2 = 0.0714; eta1 = 0.05; eta2 = 0.06; mu =
    0.000239; gamma = 0.143; alpha = 0.03571; sigma = 0.2500; phi =
    0.0056; delta = 0.02; xi1 = 0.005; xi2 = 0.4; xi3 = 0.002; nu
    = 0.5; K = 20000; pi = mu*16750
11 Q1 = mu + sigma
12 Q2 = mu + nu
13 Q3 = mu + phi + delta + gamma
14 Q4 = alpha + mu
15
16 def dS(S, E, A, I, C, R, W):
17     N = S + E + A + I + C + R
18     Lambda = beta1*((A + eta1*I + eta2*C)/N) + (beta2*W)/(K+W)
19     return pi - Lambda*S - mu*S
20 def dE(S, E, A, I, C, R, W):
21     N = S + E + A + I + C + R

```

```

22  Lambda = beta1*((A + eta1*I + eta2*C)/N)+ (beta2*W)/(K+W)
23  return Lambda*S - Q1*E
24  def dA(E, A):
25  return sigma*E - Q2*A
26  def dI(A, I):
27  return nu*A - Q3*I
28  def dC(I, C):
29  return phi*I - Q4*C
30  def dR(I, C, R):
31  return gamma*I + alpha*C - mu*R
32  def dW(E, A, I, C, R, W):
33  return xi1*A + xi2*I +xi3*C- phi*W
34  def derivs(state, t):
35
36  S, E, A, I, C, R, W = state
37  deltaS = dS(S, E, A, I, C, R, W)
38  deltaE = dE(S, E, A, I, C, R, W)
39  deltaA = dA(E, A)
40  deltaI = dI(A, I)
41  deltaC = dC(I, C)
42  deltaR = dR(I, C, R)
43  deltaW = dW(E, A, I, C, R, W)
44  return deltaS, deltaE, deltaA, deltaI, deltaC, deltaR, deltaW
45
46  S0 = 10000
47  E0 = 5
48  A0 = 1
49  I0 = 2
50  C0 = 1
51  R0 = 0
52  W0 = 5000
53
54
55  Tfinal = 120
56  t = n.arange(0.0, Tfinal, 0.01)
57
58  y0 = [S0,E0,A0,I0,C0,R0,W0]
59
60  y = integrate.odeint(derivs, y0, t)
61  S = y[:,0]
62  E = y[:,1]
63  A = y[:,2]

```

```

64 I = y[:,3]
65 C = y[:,4]
66 R = y[:,5]
67 W = y[:,6]
68
69
70
71 ##### =====incidence plot to be considered
    =====
72 ##### Calculation of the reproduction number
73 R01 = (sigma*beta1)/(Q1*Q2)
74 R02 = (nu*sigma*beta1*eta1)/(Q1*Q2*Q3)
75 R03 = (nu*sigma*phi*beta1*eta2)/(Q1*Q2*Q3*Q4)
76 R04 = (S*beta2*sigma*(Q3*Q4*xi3+nu*Q4*xi2+nu*phi*xi3))/(K*phi*Q1*
    Q2*Q3*Q4)
77 R0 = R01 + R02 + R03 + R04
78
79 print "The reproduction number is\n=", R0
80 pylab.figure(3)
81 #pylab.plot(t, E, 'r--',lw =1.2,label='Infected environments')
82 pylab.plot(t, A, 'g',lw =1.2,label='Asymtomatic cattle')
83 pylab.plot(t, I, 'b--',lw =1.2,label='Symptomatic cattle')
84 pylab.plot(t, C, 'k-',lw =1.2,label='Carriers')
85
86 pylab.xlabel('Time (days)')
87 pylab.ylabel('Infected cattle')
88 pylab.legend(loc="upper right")
89 pylab.xlim(0,Tfinal)
90 pylab.grid()
91 pylab.legend(loc="upper right")
92 pylab.savefig('R0above1.png', dpi=150)
93
94 pylab.show()

```

B. MATLAB Codes for figures in Chapter 3

B.1 Matlab Code For Figure 3.1

```
1 lambda_c= (0:0.01:1)';
2 nu = 1/4; % period of time in E class
3 rho = 1/4; % time in I class
4 sigma=1/10; % time in C class
5 omega = 1/180; %time in class
6 lambda_i = 0.01;
7 n = 4;
8
9 k_1 = 0.1;
10 k_2 = 0.9;
11 k_3 = 0.9;
12 k_4 = 0.1;
13
14 C_SE = 0.5;
15 C_IR = 0.5;
16 C_CR = 0.5;
17
18 C_SI = (nu.*k_1.*C_SE + omega.*k_4.*C_IR)./(lambda_i + nu.*k_1);
19
20 C_SC = (rho.*k_2.*C_SI + omega.*k_4.*C_CR)./(lambda_c + rho.*k_2);
21
22 R_zero = (lambda_i.*n.*k_2./sigma).*C_SI + (lambda_c.*n./sigma).*
    C_SC;
23
24 %mesh(lambda_i ,lambda_c ,R_zero)
25
26 plot(lambda_c ,R_zero , 'g—', 'LineWidth', 4)
27 xlabel( '\lambda_c ')
28 ylabel( 'R_0 ')
29
30 hold on
```

B.2 Matlab Code For Figure 3.3

```

1  [lambda_i,lambda_c]= meshgrid(0:0.1:1,0:0.1:1);
2
3  % Infection Peak vs. lambda_i and lambda_c
4
5  P= [1  1  1  1  2  2  3  5  6  8 10;
6      1  1  2  5  8 11 13 15 17 18 20;
7      1  3  6 10 14 16 17 20 21 23 25;
8      3  8 11 15 18 20 23 24 25 26 27;
9      5 10 14 17 20 22 24 26 28 29 30;
10     7 12 16 18 22 24 25 27 29 30 32;
11     9 13 17 19 23 26 27 29 30 31 33;
12    10 15 19 22 25 27 29 30 31 32 34;
13    11 16 20 23 26 28 30 31 31 32 34;
14    12 17 20 24 27 29 30 32 32 33 35;
15    13 18 21 24 27 29 31 32 33 34 35];
16
17  mesh(lambda_i,lambda_c,P)
18
19  xlabel('\lambda_i')
20  ylabel('\lambda_c')
21  zlabel('Infection peak')

```

C. Derivation of Chapter 3 equations

Appendix C

C.1 Derivation of the $[SI]$ Pair

The derivation of the equation of motion for $[SI]$ requires us to define the network configuration-based variables $n_x(i)$, $n_{xy}(i)$, ζ_x and ζ_{xy} , which are described in Table C.1.

Variable	Definition
$n_x(i)$	number of state i neighbours of a node x
$n_{xy}(i)$	number of state i neighbours of a node x which has node y as a neighbour
ζ_x	disease state of node x
ζ_{xy}	disease state of an edge involving x and y

Table C.1: Definitions of variables $n_x(i)$, $n_{xy}(i)$, ζ_x and ζ_{xy} .

Using the notations in Table C.1, and considering all the events affecting $[SI]$, which are listed in Table 3.1, we write the master equation for $[SI]$ as

$$\begin{aligned} \frac{d[SI]}{dt} = & \sum_{\zeta_x=S} \lambda_i(n_x(I))(-1) + \sum_{\zeta_{xy}=SI} \lambda_i(n_{xy}(I))(-1) + \sum_{\zeta_{xy}=SI} \lambda_c(n_{xy}(C))(-1) + \sum_{\zeta_x=E} \nu(n_x(S))(+1) \\ & + \sum_{\zeta_x=I} \rho(n_x(S))(-1) + \sum_{\zeta_x=R} \omega(n_x(I))(+). \end{aligned} \quad (\text{C.1})$$

The *positive* $+$ and *negative* $-$ signs in Equation (C.1) indicate *creation* and *destruction* of the $S - I$ pair, respectively. Next, we replace quantities $n_x(S)$, $n_x(I)$, $n_{xy}(I)$, $n_{xy}(C)$ and $n_x(E)$ by their corresponding population-averaged values (means) plus the stochastic fluctuations of those quantities from the means at the nodes x and pairs xy .

Let $n(i|j)$ be the population-averaged value of $n_x(i)$ when $\zeta_x = j$ and let $n(i|jk)$ be the population-averaged value of $n_{xy}(i)$ when $\zeta_{xy} = jk$. For example, here when $\zeta_{xy} = SI$ then $n_{xy}(I)$ will be replaced by $n(I|SI) + \theta(I|SI)$ where $\theta_{xy}(I|SI)$ represents the stochastic fluctuation of the averaged value from the mean. Thus, Equation (C.1) transforms to the equation

$$\begin{aligned} \frac{d[SI]}{dt} = & - \sum_{\zeta_x=S} \lambda_i \left(n(I|S) + \theta_x(I|S) \right) - \sum_{\zeta_{xy}=SI} \lambda_i \left(n(I|SI) + \theta_{xy}(I|SI) \right) - \sum_{\zeta_{xy}=SI} \lambda_c \left(n(C|SI) + \theta_{xy}(C|SI) \right) \\ & + \sum_{\zeta_x=E} \nu \left(n(S|E) + \theta_x(S|E) \right) - \sum_{\zeta_x=I} \rho \left(n(S|I) + \theta_x(S|I) \right) + \sum_{\zeta_x=R} \omega \left(n(I|R) + \theta_x(I|R) \right). \end{aligned} \quad (\text{C.2})$$

To simplify Equation (C.2) we take out constants such as $n(I|SI)$ and the model parameters out of the sums, employ the fact that fluctuation terms such as $\sum_{\zeta_x=S} \rho_x(I|S)$ are zero by definition. Thus, Equation (C.2) simplifies to

$$\begin{aligned} \frac{d[SI]}{dt} = & -\lambda_i[S]n(I|S) - \lambda_i[SI]n(I|SI) - \lambda_c[SI]n(C|SI) + \nu[E]n(S|E) - \rho[I]n(S|I) \\ & + \omega[R]n(I|R). \end{aligned} \quad (C.3)$$

Finally, we apply to Equation (C.3), the identities $n(i|j) = \frac{[ij]}{[j]}$ and $n(i|jk) = \frac{[ijk]}{[jk]}$, which hold in all static networks, and simplify it to write the equation of motion for $[SI]$ as

$$\frac{d[SI]}{dt} = -\lambda_i[SI] - \lambda_i[ISI] - \lambda_c[CSI] + \nu[SE] - \rho[SI] + \omega[IR].$$

C.2 Derivation Of Equations Of Motion For C_{SI} and C_{SC}

The correlation between susceptible and infectious farms and the correlation between Susceptible and carriers is given by

$$C_{SI} = \frac{N}{n} \frac{[SI]}{[S][I]} \quad \text{and} \quad C_{SC} = \frac{N}{n} \frac{[SC]}{[S][C]}$$

respectively.

The derivative of the correlation between Susceptible and Infectious, $S - I$ is given by

$$\begin{aligned} \frac{d}{dt} C_{SI} &= \frac{d}{dt} \frac{N}{n} \frac{[SI]}{[S][I]}, \\ &= \frac{N}{n} \frac{d}{dt} \frac{[SI]}{[S][I]}. \end{aligned}$$

Applying the derivative quotient rule we get

$$\begin{aligned} \frac{d}{dt} C_{SI} &= \frac{N}{n} \left(\frac{[S][I] \frac{d}{dt} [SI] - [SI] \frac{d}{dt} [S][I]}{([S][I])^2} \right), \\ &= \frac{N}{n} \left(\frac{[S][I] \frac{d}{dt} [SI]}{([S][I])^2} - \frac{[SI] \frac{d}{dt} [S][I]}{([S][I])^2} \right). \end{aligned}$$

Simplifying and applying the product rule we get

$$\frac{d}{dt} C_{SI} = \frac{N}{n} \left(\frac{1}{[S][I]} \frac{d}{dt} [SI] - \frac{[SI]}{([S][I])^2} ([S] \frac{d}{dt} [I] + [I] \frac{d}{dt} [S]) \right).$$

This simplifies to

$$\frac{d}{dt} C_{SI} = \frac{N}{n} \left(\frac{1}{[S][I]} \frac{d}{dt} [SI] - \frac{[SI]}{([S][I])} \left(\frac{1}{[I]} \frac{d}{dt} [I] + \frac{1}{[S]} \frac{d}{dt} [S] \right) \right).$$

This is equivalent to

$$\frac{d}{dt}C_{SI} = \frac{N}{n} \left(\frac{1}{[S][I]} \frac{d}{dt}[SI] + \frac{[SI]}{([S][I])} \left(-\frac{1}{[I]} \frac{d}{dt}[I] - \frac{1}{[S]} \frac{d}{dt}[S] \right) \right).$$

Thus the derivative of the correlation between susceptible and infectious farms is given by

$$\frac{d}{dt}C_{SI} = \frac{N}{n} \frac{1}{[S][I]} \frac{d}{dt}[SI] + \frac{N}{n} \frac{[SI]}{([S][I])} \left(-\frac{1}{[I]} \frac{d}{dt}[I] - \frac{1}{[S]} \frac{d}{dt}[S] \right).$$

which is equivalent to

$$\frac{d}{dt}C_{SI} = \frac{N}{n} \frac{1}{[S][I]} \frac{d}{dt}[SI] + C_{SI} \left(-\frac{1}{[I]} \frac{d}{dt}[I] - \frac{1}{[S]} \frac{d}{dt}[S] \right).$$

The correlation between Susceptible and Carriers, $S - C$ farms is derived the same way. The derivation is illustrated below

$$\begin{aligned} \frac{d}{dt}C_{SC} &= \frac{d}{dt} \frac{N}{n} \frac{[SC]}{[S][C]} \\ &= \frac{N}{n} \frac{d}{dt} \frac{[SC]}{[S][C]} \end{aligned}$$

Applying the derivative quotient rule we get

$$\begin{aligned} \frac{d}{dt}C_{SC} &= \frac{N}{n} \left(\frac{[S][C] \frac{d}{dt}[SC] - [SC] \frac{d}{dt}[S][C]}{([S][C])^2} \right), \\ &= \frac{N}{n} \left(\frac{[S][C] \frac{d}{dt}[SC]}{([S][C])^2} - \frac{[SC] \frac{d}{dt}[S][C]}{([S][C])^2} \right). \end{aligned}$$

Simplifying and applying the product rule we get

$$\frac{d}{dt}C_{SC} = \frac{N}{n} \left(\frac{1}{[S][C]} \frac{d}{dt}[SC] - \frac{[SC]}{([S][C])^2} ([S] \frac{d}{dt}[C] + [C] \frac{d}{dt}[S]) \right).$$

This simplifies to

$$\frac{d}{dt}C_{SC} = \frac{N}{n} \left(\frac{1}{[S][C]} \frac{d}{dt}[SC] - \frac{[SC]}{([S][C])} \left(\frac{1}{[C]} \frac{d}{dt}[C] + \frac{1}{[S]} \frac{d}{dt}[S] \right) \right).$$

This is equivalent to

$$\frac{d}{dt}C_{SC} = \frac{N}{n} \left(\frac{1}{[S][I]} \frac{d}{dt}[SC] + \frac{[SC]}{([S][C])} \left(-\frac{1}{[C]} \frac{d}{dt}[C] - \frac{1}{[S]} \frac{d}{dt}[S] \right) \right).$$

when there are few infected individuals and almost the entire population is susceptible, i.e. $[S] \approx N$, then the terms involving $\frac{1}{N}$ goes to zero, so the equations (C.4), (C.5) and (C.6) becomes

$$\omega \frac{[R]}{[S]} C_{ER} - \omega \frac{[R]}{[S]} C_{SE} = 0, \quad (\text{C.7})$$

$$\nu [E] C_{ER} + \sigma \frac{[C]}{[R]} C_{IC} + \sigma \frac{[C]}{[R]} C_{IR} + \nu [E] C_{ER} + \sigma \frac{[C]}{[R]} C_{IC} + \sigma \frac{[C]}{[R]} C_{IR} = 0, \quad (\text{C.8})$$

$$\sigma \frac{[C]}{[R]} C_{CC} + \rho \frac{[I]}{[C]} C_{IR} - \sigma \frac{[C]}{[R]} C_{CR} - \rho \frac{[I]}{[C]} C_{CR} = 0. \quad (\text{C.9})$$

respectively.

We assume that at the initial stage of an infection we have $k_1 = \frac{[R]}{[S]}$, $k_2 = \frac{[C]}{[R]}$ and $k_3 = \frac{[I]}{[C]}$ so that equations (C.7), (C.8) and (C.9) respectively simplifies to

$$k_1 C_{ER} - \omega k_1 C_{SE} = 0,$$

$$2\nu [E] C_{ER} + 2\sigma k_2 C_{IC} + 2\sigma k_2 C_{IR} = 0,$$

$$k_2 C_{CC} + \rho k_3 C_{IR} - \sigma k_2 C_{CR} - \rho k_3 C_{CR} = 0.$$

So that C_{SE}^* , C_{IR}^* and C_{CR}^* becomes

$$C_{SE}^* = \frac{\omega k_1 C_{ER}}{\omega k_1},$$

$$C_{IR}^* = -\frac{2\nu [E] C_{ER} + 2\sigma k_2 C_{IC}}{2\sigma k_2},$$

$$C_{CR}^* = \frac{\sigma k_2 C_{CC} + \rho k_3 C_{IR}}{\sigma k_2 + \rho k_3}.$$

We need to derive the equations of motion for the correlations C_{SS} , C_{ER} , C_{IC} and C_{CC}

and they are as follows

$$\begin{aligned} \frac{d}{dt}C_{SS} = & -2\lambda_i(n-1)\frac{[I]}{N}C_{SS}C_{SI} - 2\lambda_c(n-1)\frac{[C]}{N}C_{SS}C_{SC} + 2\omega\frac{[R]}{[S]}C_{SR} + 2\lambda_in\frac{[I]}{N}C_{SS}C_{SI} \\ & + 2\lambda_cn\frac{[C]}{N}C_{SS}C_{SC} - 2\omega\frac{[R]}{[S]}C_{SS}, \end{aligned} \quad (\text{C.10})$$

$$\begin{aligned} \frac{d}{dt}C_{ER} = & \lambda_i(n-1)\frac{[S]}{N}\frac{[I]}{[E]}C_{SR}C_{SI} + \lambda_c(n-1)\frac{[S]}{N}\frac{[C]}{[E]}C_{SR}C_{SC} - \nu C_{ER} + \sigma\frac{[C]}{[R]}C_{EC} + \omega C_{ER} - \omega C_{ER} \\ & - \sigma\frac{[C]}{[R]}C_{ER} - \lambda_in\frac{[S]}{N}\frac{[I]}{[E]}C_{SI}C_{ER} - \lambda_cn\frac{[S]}{N}\frac{[C]}{[E]}C_{SC}C_{ER} + \nu C_{ER}, \end{aligned} \quad (\text{C.11})$$

$$\frac{d}{dt}C_{IC} = \nu\frac{[E]}{[I]}C_{EC} + \rho\frac{[I]}{[C]}C_{II} - \rho C_{IC} - \sigma C_{IC} - \rho\frac{[I]}{[C]}C_{IC} + \sigma C_{IC} - \nu\frac{[E]}{[I]}C_{IC} + \rho\frac{[I]}{[C]}C_{IC}, \quad (\text{C.12})$$

$$\frac{d}{dt}C_{CC} = 2\rho\frac{[I]}{[C]}C_{IC} - 2\sigma C_{CC} + \sigma C_{CC} - \rho\frac{[I]}{[C]} + \sigma C_{CC}. \quad (\text{C.13})$$

We cancel out the like terms and we assume N is large at the beginning of an infection so that the equations (C.10), (C.11), (C.12) and (C.13) becomes

$$\frac{d}{dt}C_{SS} = 2\omega\frac{[R]}{[S]}C_{SR} - 2\omega\frac{[R]}{[S]}C_{SS},$$

$$\frac{d}{dt}C_{ER} = \sigma\frac{[C]}{[R]}C_{EC} - \sigma\frac{[C]}{[R]}C_{ER},$$

$$\frac{d}{dt}C_{IC} = \nu\frac{[E]}{[I]}C_{EC} + \rho\frac{[I]}{[C]}C_{II} - \rho C_{IC} - \nu\frac{[E]}{[I]}C_{IC},$$

$$\frac{d}{dt}C_{CC} = 0.$$

We furthermore need to derive the equations of motion for the correlations C_{SR} , C_{EC} and C_{II} and they are as follows

$$\frac{d}{dt}C_{SR} = -\lambda_i(n-1)\frac{[I]}{N}C_{SR}C_{SI} - \lambda_c(n-1)\frac{[C]}{N}C_{SR}C_{SC} + \sigma\frac{[C]}{[R]}C_{SC} - \omega C_{SR} + \omega\frac{[R]}{[S]}C_{RR} + \lambda_in\frac{[I]}{N}C_{SR}C_{SI} \quad (C.14)$$

$$+ \lambda_cn\frac{[C]}{N}C_{SR}C_{SC} - \omega\frac{[R]}{[S]}C_{SR} - \sigma\frac{[C]}{[R]}C_{SR} + \omega C_{SR},$$

$$\frac{d}{dt}C_{EC} = \lambda_i(n-1)\frac{[S]}{N}\frac{[I]}{[E]}C_{SC}C_{SI} + \lambda_c\frac{[S]}{[E]}C_{SC} + \lambda_c(n-1)\frac{[S]}{N}\frac{[C]}{[E]}C_{SC}^2 - \nu C_{EC} + \rho\frac{[I]}{[C]}C_{EI} - \sigma C_{EC} \quad (C.15)$$

$$- \rho\frac{[I]}{[C]}C_{EC} - \lambda_in\frac{[S]}{N}\frac{[I]}{[E]}C_{EC}C_{SI} - \lambda_cn\frac{[S]}{N}\frac{[C]}{[E]}C_{EC}C_{SC} + \nu C_{EC},$$

$$\frac{d}{dt}C_{II} = 2\nu\frac{[E]}{[I]}C_{EI} - 2\rho C_{II} - \nu\frac{[E]}{[I]}C_{II} + \rho C_{II} - \nu\frac{[E]}{[I]}C_{II} + \rho C_{II}. \quad (C.16)$$

We cancel out the like terms so that from equations (C.14), (C.15) and (C.16) we get

$$\frac{d}{dt}C_{SR} = \lambda_i\frac{[I]}{N}C_{SR}C_{SI} - \lambda_c\frac{[C]}{N}C_{SR}C_{SC} + \sigma\frac{[C]}{[R]}C_{SC} + \omega\frac{[R]}{[S]}C_{RR} - \omega\frac{[R]}{[S]}C_{SR} - \sigma\frac{[C]}{[R]}C_{SR},$$

$$\frac{d}{dt}C_{EC} = \lambda_i(n-1)\frac{[S]}{N}\frac{[I]}{[E]}C_{SC}C_{SI} + \lambda_c\frac{[S]}{[E]}C_{SC} + \lambda_c(n-1)\frac{[S]}{N}\frac{[C]}{[E]}C_{SC}^2 + \rho\frac{[I]}{[C]}C_{EI} - \rho\frac{[I]}{[C]}C_{EC} \\ - \lambda_in\frac{[S]}{N}\frac{[I]}{[E]}C_{EC}C_{SI} - \lambda_cn\frac{[S]}{N}\frac{[C]}{[E]}C_{EC}C_{SC},$$

$$\frac{d}{dt}C_{II} = 0.$$

We furthermore need to derive the equations of motion for the correlations C_{EI} and C_{RR} and they are as follows

$$\frac{d}{dt}C_{EI} = \lambda_i\frac{[S]}{[E]}C_{SI} + \lambda_i(n-1)\frac{[S]}{N}\frac{[I]}{N}C_{SI}^2 + \lambda_c(n-1)\frac{[S]}{N}\frac{[C]}{[E]}C_{SI}C_{SC} + \nu\frac{[E]}{[I]}C_{EE} - \nu C_{EI} \quad (C.17)$$

$$- \rho C_{EI} - \lambda_i\frac{[S]}{N}\frac{[I]}{[E]}C_{EI}C_{SI} + \lambda_c\frac{[S]}{N}\frac{[C]}{[E]}C_{EI}C_{SI} - \omega\frac{[R]}{[E]}C_{EI} - \nu\frac{[E]}{[I]}C_{EI} + \rho C_{EI},$$

$$\frac{d}{dt}C_{RR} = -2\omega C_{RR} + 2\sigma\frac{[C]}{[R]}C_{CR} - \sigma\frac{[C]}{[R]}C_{RR} + \omega C_{RR} - \sigma\frac{[C]}{[R]}C_{RR} + \omega C_{RR}. \quad (C.18)$$

We cancel out the like terms from equations (C.17) and (C.18) and get

$$\begin{aligned} \frac{d}{dt}C_{EI} &= \lambda_i \frac{[S]}{[E]} C_{SI} + \lambda_i(n-1) \frac{[S]}{N} \frac{[I]}{N} C_{SI}^2 + \lambda_c(n-1) \frac{[S]}{N} \frac{[C]}{[E]} C_{SI} C_{SC} + \nu \frac{[E]}{[I]} C_{EE} - \nu C_{EI} \\ &\quad - \lambda_i \frac{[S]}{N} \frac{[I]}{[E]} C_{EI} C_{SI} + \lambda_c \frac{[S]}{N} \frac{[C]}{[E]} C_{EI} C_{SI} - \omega \frac{[R]}{[E]} C_{EI} - \nu \frac{[E]}{[I]} C_{EI}, \end{aligned}$$

$$\frac{d}{dt}C_{RR} = 2\sigma \frac{[C]}{[R]} C_{CR} - 2\sigma \frac{[C]}{[R]} C_{RR}$$

We furthermore need to derive the equations of motion for the correlations C_{EE} and C_{CR} and they are as follows

$$\begin{aligned} \frac{d}{dt}C_{EE} &= 2\lambda_i(n-1) \frac{[S]}{N} \frac{[I]}{[E]} C_{SE} C_{SI} + 2\lambda_c(n-1) \frac{[S]}{N} \frac{[C]}{[E]} C_{SE} C_{SC} - 2\nu C_{EE} - \lambda_i \frac{[S]}{N} \frac{[I]}{[E]} C_{EE} C_{SI} \\ &\quad (C.19) \end{aligned}$$

$$\begin{aligned} &\quad - \lambda_c \frac{[S]}{N} \frac{[C]}{[E]} C_{EE} C_{SI} + \nu C_{EE} - \lambda_i \frac{[S]}{N} \frac{[I]}{[E]} C_{EE} C_{SI} - \lambda_c \frac{[S]}{N} \frac{[C]}{[E]} C_{EE} C_{SI} + \nu C_{EE}, \\ &\quad (C.20) \end{aligned}$$

$$\begin{aligned} \frac{d}{dt}C_{CR} &= \sigma \frac{[C]}{[R]} C_{CC} + \rho C_{CR} + \rho \frac{[I]}{[C]} C_{IR} - \sigma C_{CR} - \omega C_{CR} - \rho \frac{[I]}{[C]} + \sigma C_{CR} - \sigma \frac{[C]}{[R]} C_{CR} + \omega C_{CR}. \\ &\quad (C.21) \end{aligned}$$

From equations (C.19) and (C.21) we cancel out the like terms and get

$$\begin{aligned} \frac{d}{dt}C_{EE} &= 2\lambda_i(n-1) \frac{[S]}{N} \frac{[I]}{[E]} C_{SE} C_{SI} + 2\lambda_c(n-1) \frac{[S]}{N} \frac{[C]}{[E]} C_{SE} C_{SC} - 2\lambda_i \frac{[S]}{N} \frac{[I]}{[E]} C_{EE} C_{SI} \\ &\quad - 2\lambda_c \frac{[S]}{N} \frac{[C]}{[E]} C_{EE} C_{SI}, \end{aligned}$$

$$\frac{d}{dt}C_{CR} = \rho C_{CR} + \rho \frac{[I]}{[C]} C_{IR} - \rho \frac{[I]}{[C]} C_{CR}.$$

C.2.2 CLUSTERING i.e , $\phi = 0$

$$\begin{aligned} 0 &= -\lambda_i C_{SI} + \lambda_i(n-1) \frac{[I]}{N} C_{SI}^2 - \lambda_c(n-1) \frac{[C]}{N} C_{SI} C_{SC} + \nu \frac{[E]}{[I]} C_{SE} + \omega \frac{[R]}{[S]} C_{IR} - \nu \frac{[E]}{[I]} C_{SI} + \lambda_i \frac{[I]}{N} C_{SI}^2 \\ &\quad + \lambda_c n \frac{[C]}{N} C_{SI} C_{SC} - \omega \frac{[R]}{[S]} C_{SI}. \end{aligned}$$

and

$$\begin{aligned}
 0 = & -\lambda_c C_{SC} - \lambda_c(n-1) \frac{[S]}{N} C_{SC}^2 - \lambda_c \frac{[I]}{N} C_{SI} C_{SC} + \rho \frac{[I]}{[C]} C_{SI} + \omega \frac{[R]}{[S]} C_{CR} - \rho \frac{[I]}{[C]} C_{SC} + \lambda_c n \frac{[S]}{N} C_{SC}^2 \\
 & + \lambda_c \frac{[I]}{N} C_{SI} C_{SC} - \omega \frac{[R]}{[S]} C_{SC}.
 \end{aligned}$$



Bibliography

- [1] U. Wernery and J. Kinne, Foot and Mouth disease and similar virus infections in camelids: A review, *Rev. sci. tech. O. int. Epiz.*, 31(3):907-918, 2012.
- [2] N. M. Ferguson, C.A. Donnelly and R.M. Anderson. The Foot and Mouth epidemic in Great Britain: pattern of spread and impact of interventions, *Science*, 292:1155-1160, 2001, doi: 10.1126/science.1061020.
- [3] G. J. Belsham, S. M. Jamal and A. B. Tner. Rescue of Foot and Mouth Disease viruses that are pathogenic for cattle from preserved viral rna samples, *PLoS ONE*, 6(1):1-10, 2011.
- [4] N. M. Rweyamamu, Foot and mouth disease control strategies in Africa, *Preventative Veterinary Medicine*, 2:329-340, 1984.
- [5] NADIS, Animal Health Skills, <https://www.nadis.org.uk/disease-a-z/cattle/foot-and-mouth-disease/>.
- [6] OIE, Foot & Mouth disease; Accessed on August 2018, <https://www.oie.int/en/animal-health-in-the-world/animal-diseases/Foot-and-mouth-disease/>.
- [7] E. K. Baipoledi, G. Matlho, M. Letshwenyo, M. Chimbombi, E. K. Adom, M. V.Raborokgwe and J.M.K. Hyera. Re-emergence of Foot and Mouth disease in Botswana. *The Veterinary Journal*, 168:93-99, 2004.
- [8] A. N. Rae, C. Nixon and P. Gardiner, Foot-and-Mouth disease and trade restrictions: Latin America access to Pacific Rim beef. *The Australian Journal of Agriculture and Resource Economics*, 43(4), 479-500, 1999.
- [9] G. E. Cottral, Persistence of Foot and Mouth disease Virus in animals, their products and the environment, *Bull Off Int Epizoot.*, 1969 Mar-Apr;71(3-4):549-68, PMID: 4324721.
- [10] M. J. Otte, R. Nuget and A. McLeod, Transboundary Animal Diseases: Assesment of socio-economic impacts and institutonal responses, *Food and Agriculture Organisation*, February 2004.
- [11] M. J. Tildesley, R. Deardon, N. J. Savill, P. R. Bessell, S. P. Brooks , M. E.J Woolhouse, B. T Grenfell & M. J Keeling, Accuracy of models for the 2001 foot-and-mouth epidemic, *Proc. R. Soc. B.*, 275: 1459-1468, 2008.
- [12] M. J. Grubman and B. Baxt, Foot and mouth Disease, *Clin Microbiol Rev.*, 17(2): 465-493, 2004, doi: 10.1128/CMR.17.2.465-493.2004.
- [13] S. M. Ali, Meat: The opium of the 21st Century, *kobo.com*, Brewen, Germany, pg 106, ISBN 978-3-7386709-4 (2015).

- [14] J. Gloster, H. Champion, J. Sorensen, T. Mikkelsen, D. Ryall, P. Astrup and A. Donaldson, Airborne transmission of Foot-and-Mouth disease virus from Burnside Farm, Heddon-on-the-Wall, Northumberland, during the 2001 epidemic in the United Kingdom, *The Veterinary Record*, (2003), 525-533.
- [15] P. D. Letebele, Control of foot and mouth disease by department of veterinary services, ministry of Agricultural development and food security, *Performance Audit, Report No.3*, 2018.
- [16] P. D. Letebele, Review Of Foot and Mouth Disease Control Strategies in Botswana, Department of Veterinary Services in Collaboration with Botswana Vaccine Institute, June 2012.
- [17] M. Mokopasetso and N. Derah, Recent outbreaks of Foot and Mouth Disease in Botswana and Zimbabwe, *Special issue*, 2005.
- [18] Control of Foot and Mouth disease by Department of Veterinary Services-FENCE Strategy, *Performance Audit*, Report No.3 of 2018.
- [19] C. Masole, O. I. Ayuya and J .C. Moreki, Determinants of adoption of alternative response to Foot and Mouth disease: micro-level evidence of smallholder pastoralist in north East District, Botswana, *Trop Anim Health Prod* 51, 373-382 (2019), <https://doi.org/10.1007/s11250-018-1698-0>.
- [20] B. S. Mguni, Annual Survey Report 2017, Department of Agricultural Research, Statistics and policy Development, *Statistics Botswana*, ISBN: 978-99968-2-073-1, 2019.
- [21] W. O. Kermack and A. G. McKendrick, A contribution to the mathematical theory of epidemics, *Proc, R.Soc.115*, pp 700-721, (1927).
- [22] M. J. Keeling, M. J. Woolhouse, D. J. Shaw, L. Matthews, M. Chase-Topping, D.T Haydon, S. J. Cornell, J. Kappey, J. Wilesmith and B. T. Granfell, Dynamics of the 2001 UK Foot and Mouth disease: stochastic dispersal in a heterogeneous landscape, *Science*, 294(5543):813-817, 2001.
- [23] S. I. Chis, N. M. Ferguson, Transmission Parameters of the 2001 Foot and Mouth Epidemic in Great Britain, *PLoS ONE* 2(6): e502.,(2007) <https://doi.org/10.1371/journal.pone.0000502>
- [24] I. Traulsen, G. Rave and J. Krieter, Sensitivity analysis of a stochastic simulation model for Foot and Mouth disease, *Leibniz Institute for Farm Animal Biology, Dummerstorf, Germany*, ISSN 0003-9438, 2010, doi: 10.5194/aab-53-529-2010.
- [25] S. Mushayabasa, Modeling the intrinsic dynamics of Foot and Mouth disease, *Mathematical Biosciences and engineering* Vol 13, 2, pp. 425-442, 2016, doi: 10.3934/mbe.2015010.
- [26] S. Busenberg and K. Cooke Vertically transmitted disease: Models and dynamics, 23. *Springer-Verlay*, 1993.

- [27] A. M. Stuart and A. R. Humphries, Dynamical systems and numerical analysis, Cambridge: *Cambridge University Press*, 1998.
- [28] O. Diekmann, J. A. P. Heesterbeek and J. A. J. Metz, On the definition and the computation of the basic reproduction ratio R_0 in models for the infectious diseases in heterogeneous populations, *J. Math. Biol.* 28(1990), 365.
- [29] O. Diekmann and J. A. P. Heesterbeek, Mathematical epidemiology of infectious diseases: Wiley series in mathematical and computational biology, *Wiley, West Sussex*, England, 2000.
- [30] P. van den Driessche and J. Watmough, Reproduction numbers and Sub-threshold, endemic equilibria for compartmental models of disease transmission, *Math. Biosci.* 180(2002), pp 29-48.
- [31] K. A. Ugwa, I. A. Agwu, N. A. Agbanyim, Mathematical analysis of the endemic equilibrium of the transmission dynamics Of Tuberculosis, *International journal of scientific & technology research volume 2*, Issue 12, Dec 2013, ISSN 2277-8616.
- [32] N. Mohd, W. Steenveld and H. Hogeveen, The average culling rate of Dutch dairy herds over the years 2007 to 2010 and its association with herd reproduction performance and health, *Journal of dairy Research*, 1-8, 2013.
- [33] Compassion in World Farming, The life of: dairy cows, *ciwf.org*, page 1, August 2012.
- [34] E. Modisa, Foot and Mouth Disease, Ministry of Agriculture Veterinary Services, Gaborone, Botswana, *Print Close*, OIE, October 2020.
- [35] S. Mushayabasa, C. P. Bhunu and M. Dhlamini, Impact of vaccination and culling on controlling Foot and Mouth disease: a mathematical modeling approach, *World of Journal Vaccines*, 1:156-161, 2011.
- [36] F. Mardones, A. Perez, J. Sanchez, M. Alkhamis, and T. Carpenter, Parameterization of the duration of infection stages of serotype O Foot-and-Mouth disease virus: an analytical review and meta-analysis with application to simulation models, *Vet Res*, 41(4):45, 2010.
- [37] M. J. Grubman and B. Baxt, Foot-and-Mouth disease, *Clinical Microbiology Reviews*, 17(2):465-493, 2004.
- [38] T. R. Doel, Natural and vaccine induced immunity to Foot and Mouth disease: the prospects for improved vaccines, *Rev. sci. tech. Off. int. Epiz.* 15(3):883-911, 1996.
- [39] S. Alexandersen, Z. Zhang and A. I. Donaldson, Aspects of the persistence of foot-and-mouth disease virus in animals-the carrier problem, *Microbes Infect.*, 4:1099-1110, 2002.
- [40] B. Tadesse, W. Molla, A. Mengistu & W. T. Jemberu, Transmission dynamics of Foot and Mouth disease in selected outbreak areas of Northwest Ethiopia. *Epidemiology and infection*, 147, e189, (2019). <https://doi.org/10.1017/S0950268819000803>.

- [41] L. M. Bartley, C. A. Donnelly, R.M. Anderson, Review of foot-and mouth disease virus survival in animal excretions and on fomites, *Vet Rec* 151:667-669, 2002, doi:10.1136/vr.151.22.667.
- [42] F. Aftosa, *Foot and Mouth Disease*, [http://www.cfsph.iastate.edu/Factsheets/pdfs/foot and mouth disease.pdf](http://www.cfsph.iastate.edu/Factsheets/pdfs/foot_and_mouth_disease.pdf), Accessed September 2014.
- [43] S. M. Blower and H. Dowlatabadi, Sensitivity and uncertainty analysis of complex models of disease transmission: an HIV Model, as an Example, *International Statistical Review*, Vol.62, No.2(Aug., 1994), pp.229-243.
- [44] S. Marino, I. Hogue, C. Ray and D. Kirschner, A methodology for performing global uncertainty and sensitivity analysis in systems biology, *J Theor Biol*, 254:178-196, (2008), doi:10.1016/j.jtbi.2008.04.011.
- [45] L. P. Swiler and G. D. Wyss, A User's Guide to Sandia's Latin Hypercube Sampling Software: LHS UNIX Library/Standalone Version, 2004.
- [46] A. Hoare, D. G. Regan and D. P. Wilson, Sampling and statistical analyses tools (SaSAT) for computational modelling, *Math Biosci*, 5(2008), 10.1186/1742-468-5-4.
- [47] A. Rizzo, M. Frasca, and M. Porfiri. Effect of individual behavior on epidemic spreading in activity-driven networks, *Physical Review E*, 90(042801), 2014.
- [48] C.T. Bauch and A.P. Galvani, Using network models to approximate spatial point-process models, *Math Biosci*, 184:101-114, 2003.
- [49] N. Ringa, Controlling transmission of infectious diseases in spatially structured populations by culling, vaccination and non-pharmaceutical interventions, *The University of Guelph*, Canada, November 2014.
- [50] M.J. Keeling. The effects of local spatial structure on epidemiological invasions, *Proceedings of The Royal Society of London*, B 22(266):859-867, 1999.
- [51] H.W. Hethcote. The mathematics of infectious diseases, *Society for Industrial and Applied Mathematics*, 42(4):599-653, 2000.
- [52] J. M. Heffernan, R. J. Smith and L.M. Wahl, Perspectives on the basic reproduction ratio. *Journal of the Royal Society*, 2(4):281-293, 2005.
- [53] P. H. T. Schimit and L. H. A. Monteiro, On estimating the basic reproduction number in distinct stages of a contagious disease spreading. *Ecological Modelling*, 240(2012):156-160, 2012.
- [54] J. Arino and J. Watmough, Current Trends in Mathematical Epidemiology, *Bull Math Biol*, 81, 4311-4312 (2019), <https://doi.org/10.1007/s11538-019-00672-3>.
- [55] M. J. Keeling, M. E. J. Woolhouse, R. M. May, G.Davies, and B.T. Grenfel, Modeling vaccination strategies against Foot and Mouth disease, *Nature*, 421:136-142, 2003.