A simulation model for Rift Valley fever transmission

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other university.

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To those who preceded, *Gachohi* and *Ekirah*, my dear parents, and to those who followed, *Lorna* and *Linah Mwangi*, my dear daughters.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF PLATES

ABSTRACT

Rift Valley fever (RVF) is a mosquito-borne viral disease of animals and humans that occurs throughout sub-Saharan Africa, Egypt, and the Arabian Peninsula. The disease is associated with enormous burdens on human and veterinary health, socio-economics and disease management. The RVF outbreaks are preceded by an interaction of a set of conditions and events. These include both biotic and abiotic factors that interact in a complex manner and at different spatial scales. This array of factors constrains a good understanding of the epidemiology of RVF. This thesis presents a study on RVF simulation modelling to understand the epidemiology of the disease. Specifically, the study aims to: (1) determine the key processes that influence the transmission dynamics of RVF in Kenya; (2) estimate the impacts generated following a RVF outbreak; (3) assess the role of RVF herd immunity patterns in influencing the occurrence of an outbreak; and (4) evaluate RVF control strategies when implemented at different stages of RVF risk.

The simulation model comprised of two hosts (cattle and sheep) and two vectors (*Aedes* and *Culex* mosquito species). The model integrated livestock host population dynamics, vector population dynamics, and vector-host transmission dynamics. Changes in the population of vectors in the model were driven by rainfall estimates obtained from the Tropical Rainfall Measuring Mission (TRMM) for Ijara Sub-county which was the study site. Simulations were implemented for 1200 days. Outputs generated by the model included: (1) incidence of RVFV infection in vectors and

hosts; (2) time to the peak incidence of RVFV in vectors and hosts; and (3) the duration of outbreaks. Following the predicted outbreak, further transmissions were prevented and simulations ran for five years to assess the post-outbreak evolution of host population and herd immunity dynamics. The impact of vaccinating 25%, 50% or 75% of the host population was assessed by simulating vaccinations at different stages of RVF risk borrowed from the 2006/7 pre-outbreak period and identified in a decision-support tool for prevention and control of RVF in the Greater Horn of Africa. The three different stages included (i) issuance of RVF early warning representing a lead time of 11 weeks based on the recent outbreak in 2006/7 in Kenya, (ii) onset of heavy rains with a lead time of 6 weeks, and (iii) at the outbreak onset. This study also assessed the possibility of RVF control by focusing against one host species by vaccinating 50% of cattle or sheep, 6 weeks to the outbreak. The impact of interventions was measured by estimating the area under incidence curve (AUC). Larva control was implemented at the outbreak onset by increasing basal mortality by 50% or 100% for different periods of time. The model was also used to evaluate integrated control measures, e.g. a combination of low coverage of 25% vaccination and the moderate increase in the larval mortality rate – 50% for 105 days which spanned the entire outbreak period.

The model predicted elevated RVF virus (RVFV) activity during the wet seasons as well as a full-blown RVF outbreak following periods with excessive, persistent and prolonged precipitation. During the predicted full-blown outbreak, *Aedes* species

lasted for a total of 93 days with two peaks at day 29 and day 73 after the initial emergence of the adults. *Culex* species lasted for 157 days with a peak at 69 days after initial emergence. Rift Valley fever virus incidence peaked in *Culex* species at 0.36%. The hosts' outbreak curves had a characteristic shape – RVFV activity commenced gradually ahead of the rapid amplification of the virus transmission processes due to an upsurge in *Culex* mosquito population. The predicted mean peak incidence of RVFV in cattle was 14%; this occurred on day 80 following initial transmissions across simulations. The predicted incidence in sheep peaked at 35% on the same day. The predicted duration of the full-blown outbreak in hosts was 100 days [range 80, 112] for both cattle and sheep.

The results of the model showed that by the end of the full-blown outbreak (day 1152), cattle and sheep populations declined to an average of 76% [range 67%, 91%] and 51% [range 39%, 64%] of their pre-outbreak populations respectively, due to RVF-induced mortality. Cattle population recovered fully approximately 3-4 years (around day 1188) after the outbreak [range 85%, 109%]. At this time (after 1188 days), the sheep population was predicted at 69% [range 55%, 88%] of the pre-outbreak population. Five years after the outbreak, the populations were, on average, 102% [range 95%, 108%] and 85% [range 66%, 104%] of the pre-outbreak populations in cattle and sheep, respectively.

The model predicted that by the end of the outbreak, 89% of cattle [range 80%, 96%] and 94% of sheep [range 65%, 99%] would be in the immune/recovered/removed state that is refractory to RVFV infection. Five years later in the simulation, these herd immunity levels were shown to decline to 6% [range 4%, 8%] in cattle and 0.3% [range 0.07%, 0.5%] in sheep. The rate of decline was intensely higher in sheep than cattle. The period it took for the herd immunity to decline to negligible levels closely mirrored (1) the predicted time it took for the populations to recover to pre-outbreak levels, and (2) the average inter-epidemic period in Kenya.

According to the model predictions, vaccinating 25% of the host population at any stage of risk did not prevent full-blown outbreaks but was associated with marginal reductions in AUC of between 16 and 37% across the two host species. Vaccinating 50% or 75% of the host population at any stage of risk appeared to have major impacts particularly with substantial reductions in AUC of between 62 and 89% across the two host species. On targeting either of the host species, protection appeared to be species-specific, i.e., there are few benefits derived in the species that remained unvaccinated.

According to the model predictions, increasing larval mortality by 50% at daily intervals from the onset of the full-blown outbreak appeared to provide a temporary protection that was lost as soon as the control was relaxed. Increasing larval mortality by 100% at daily interval was predicted to be effective only if it was sustained for more than 60 days.

The thesis viewed the simulation model as a framework that could be used for predicting RVF outbreaks and understanding complex mechanisms that produce RVF outbreaks and generating hypotheses on RVF epidemiology. This thesis identified gaps in the quantification of parameters, particularly those related to transmission, and highlighted how field observational studies and small-scale transmission experiments could be used to estimate these parameters.

The simulation model results seemed to agree with anecdotal evidence that suggest that herd immunity plays an important role in modifying the length of RVF inter-epidemic intervals given that the risk of an outbreak intensifies when the herd immunity is low in presence of suitable climatic indices. A better understanding of the role these patterns play in the epidemiology of RVF is critical to refine existing control strategies, for instance, in evaluation of (1) effectiveness of preventive vaccination strategies, (2) cost-effectiveness of vaccination campaigns, and (3) in the investigation of the relationship between the average inter-outbreak period, population turn-over (exit and entry rates) and population recovery patterns.

The results further suggested that targeted vaccination could be effective in mitigating the impacts of RVF outbreaks. However, challenges associated with disease prediction, availability, administration and delivery of vaccines need to be addressed. The predictions also suggested that the timing of an intervention, the level of coverage and the duration of implementation are key considerations for using larvicides for

RVF control. Analyses on integrated control strategies such as increased larval mortality by 50% at daily intervals from the onset and lasting the entire phase of the outbreak and vaccinating 25% of the hosts were predicted to be highly effective in preventing the occurrence of a full-blown outbreak.

In conclusion, the results of this model demonstrated an advance to ecological understanding of RVF transmission dynamics and provided a framework for analyzing the impacts of RVF outbreaks and its interventions. The predicted outputs will contribute greatly to the disease control policies in Kenya and elsewhere.

CHAPTER 1

1.0 GENERAL INTRODUCTION

1.1 Background

Rift Valley fever (RVF) is a mosquito-borne infectious disease of cattle, sheep, goats and camels. The disease is currently enzootic in sub-Saharan Africa (SSA), Egypt (Bishop *et al.,* 1980) and the Arabian Peninsula (Al-Azraqi *et al.,* 2012). Wild animals are also susceptible to the disease (Evans *et al.,* 2008). Rift Valley fever is also a zoonosis. Human transmission principally occurs through intensive contact with blood, tissues and fluids from infected animals or due to the bites from infected female mosquitoes (Anyangu *et al.,* 2010). The disease is caused by RVF virus (RVFV) of the genus Phlebovirus and family *Bunyaviridae*. The virus is transmitted between hosts through the bite of a female mosquito; it is also thought that direct transmission between infectious and susceptible hosts occurs via body fluids and secretions in the course of the outbreaks. The virus has been isolated from greater than 30 species of mosquitoes from at least 6 genera (*Aedes, Culex, Anopheles, Eretmapodites*, *Mansonia* and *Coquillettidia*) (reviewed by Bird *et al.*, 2009).

Rift Valley fever virus was first isolated and disease characterized in 1931 following an outbreak of a hitherto unknown disease that killed approximately 4,700 lambs and ewes on a single farm along the shores of Lake Naivasha in the Rift Valley region of Kenya over a 4-week period (reviewed by Bird *et al.,* 2009). However, Kenya had

previously reported a RVF-like disease in livestock in 1912 (Kitchen, 1934). Since that time, RVFV has been associated with devastating epidemics. A prominent feature of the outbreaks is the generation of huge public health and economic impacts. Moreover, the episodic nature of the disease and the rapid evolution of outbreaks create exceptional challenges for its mitigation and control by rapidly overwhelming the capacities of veterinary and medical communities. Due to these past experiences, there is a need for accurate forecasting of RVF outbreaks and carrying out efficient and timely control measures in case of an outbreak.

The impact of the multiple hosts and vectors on RVF transmission is not clear. Rift Valley fever is also associated with environmental heterogeneity involving particular rainfall patterns that generate outbreaks, multiple landscapes and local factors such as soil types and local processes that influence transmission. Socio-economic factors include herd-level and community-level processes that affect livestock management decisions, such as demographics, livestock trade, livestock movements and mixing patterns that could in turn influence the occurrence of RVF outbreaks. In such a scenario, RVF epidemiology in general and transmission dynamics in particular, are not fully understood (Pepin *et al.,* 2010; Métras *et al.,* 2011). Insufficient epidemiological knowledge may make it difficult to determine when and how to apply the existing control measures such as vaccination, vector control, movement control, or quarantine.

This study was therefore designed to apply a computer-based simulation model to predict the occurrence of RVF outbreaks in Kenya which has been broadly defined as "*the process of designing a model of a real system and conducting experiments with this model with the purpose of either understanding the behaviour of the system or of evaluating various strategies (within the limits imposed by the criterion or a set of a criteria) for the operation of the system*" (Shannon, 1975). The model simulated RVFV transmission dynamics with the purpose of advancing RVF epidemiology by tracking multiple processes and factors thought to produce the disease outbreaks. The model was then used to evaluate disease control measures. The model was based upon host population dynamics, host movements in space, vector population dynamics driven by rainfall and ecological factors and explicit transmission dynamics between the hosts and vectors.

1.2 Objectives of the study

The overall objective of the study was to develop a RVF simulation model for predicting the risk of occurrence and impacts of RVF in Ijara sub-county in the northeastern Kenya. The specific objectives were:

1. To determine the key processes and factors that influence the transmission dynamics of RVF in northeastern Kenya,
2. To estimate the impacts of RVF outbreaks on livestock productions (mortality burdens and population recovery patterns),

3. To assess the role of RVF herd immunity patterns in influencing the occurrence of an outbreak,
4. To assess single and integrated RVF control strategies and their potential success in controlling RVF incidence in livestock at different stages of RVF risk.

1.3 Thesis structure

Chapter 2 of this thesis is a literature review of the hypothetical and evidenced-based RVF knowledge and information from past works. Literature on the epidemiology of the disease including aetiology, transmission, occurrence, distribution, clinical manifestation, diagnosis, impacts, disease prevention and control is reviewed. The review pays more emphasis on the risk factors associated with the occurrence of RVF in general and the associated parameters used to run the model.

Chapter 3 offers the foundation of the study in terms of general materials and methods. Work on community-based survey as a source of model parameters is briefly introduced. A large part of the chapter deals with the model description and structure. The model description is based on a set of rules and assumptions including the number and types of parameters used.

Chapter 4 describes in detail how information collected using participatory epidemiological methods in a community-based participatory research were used to inform both RVF disease modelling parameters and knowledge synthesis.

Chapter 5 describes in detail the RVF simulation model, model outcomes and a comprehensive discussion of model outcomes and behaviour. These are in turn mapped back to the theoretical and practical understanding expressed in the literature review. This chapter identifies the parameters with scant knowledge, particularly those concerning transmission terms.

Chapter 6 assesses the evolution of population recovery for 5 years post-outbreak. In conjunction with population recovery, herd immunity dynamics are assessed as well. The long-term dynamics of these two population indices are used to answer the question on whether they can synchronize RVFV transmission patterns in presence of favourable factors for production of RVF outbreak.

Chapter 7 applies the model in predicting the effect of RVF interventions and their potential success in controlling RVF incidence in support of decision-making on outbreak epidemic preparedness, response and control.

Chapters 8 and 9 outline the main findings of the thesis work and a general discussion of how the model predictions have advanced the existing knowledge of RVF and how

the knowledge can be used for improved disease control. Specifically, Chapter 9 summarizes the conclusions of the study and proposes interesting scientific questions and issues arising from the work.

CHAPTER 2

2.0 LITERATURE REVIEW

2.1 Rift Valley fever - the disease

2.1.1 Aetiology

Rift Valley fever is caused by RVF virus (RVFV) which belongs to the genus Phlebovirus, family *Bunyaviridae* (Swanepoel and Coetzer, 2004). Most mammals including domestic and wildlife are differentially susceptible to the infection by the virus. Humans are susceptible to the virus as well. The virus is an enveloped ribonucleic acid (RNA) virus whose genome is composed of three segments designated L, M and S of negative polarity. Molecular studies show that the genome is temporally and geographically stable (Bird *et al.,* 2007; Bird *et al.,* 2008; Nderitu *et al.,* 2011).

2.1.2 Rift Valley fever ecology

Mosquitoes are the principal vectors of RVFV. Mosquitoes naturally have two principle stages of life. The aquatic stage, comprising eggs, larvae and pupa, is entirely dependent on water. The adult stage depends generally on the environment – the flora for resting and the fauna as source of food in form of blood meals. Rift Valley fever, like other mosquito-borne diseases, is, therefore, intricately linked to rainfall as the source of water for breeding. Indeed, majority of the recorded RVF outbreaks have been preceded by exceptionally heavy rainfall which generates pools and or extensive flooded areas. These in turn results in large increases in the mosquito populations

(Anyamba *et al.,* 2009). Thus, past outbreaks of RVF in the Greater Horn of Africa (the greater Somalia, Kenya, Sudan and Tanzania) have been associated with cyclical patterns of the El Niño/Southern Oscillation (ENSO) phenomenon which results in elevated and widespread rainfall (Anyamba *et al.,* 2009). The reason behind association of RVF and elevated and persistent rainfall is thought to be the breeding ecology of the incriminated mosquito species. *Aedes* species (such as *Aedes mcintoshi*, the vector associated with RVFV transmission in Kenya (Linthicum *et al.,* 1985), have the potential for vertical transmission (pathogen passed from infected adults to their offspring via eggs) (Romoser *et al.,* 2011). These species lay their eggs on edges of breeding pools where they resist desiccation and hatch only when more than six days of dry conditions are followed by inundation of the breeding pools edges by rainfall event(s) (Vignolles *et al.,* 2009). Since a proportion of the eggs are infected, a number of adult mosquitoes emerge as infected. These infected mosquitoes initiate transmission to livestock hosts during blood meal feeding. *Aedes* species, therefore, have long been hypothesized to be linked with RVF endemic maintenance mechanisms.

If rainfall persists, flooding ensues. Standing flooded water collect organic "green" material that favours massive colonization by secondary vectors particularly *Culex* and *Anopheles* mosquito species. These species lay the eggs on water and, therefore, their populations expand rapidly in presence of flooding. Accordingly, they are thought to amplify the RVFV transmissions in livestock previously initiated by *Aedes* mosquito

species. Consequently, a full-blown outbreak ensues. Thus, these species of mosquitoes are referred to as ‘‘epidemic/amplifying’’ vectors.

2.1.3 Occurrence and distribution of Rift Valley fever

2.1.3.1 Occurrence and distribution of Rift Valley fever in Kenya

The historical occurrence and distribution of RVF in Kenya has been described in details recently (Murithi *et al.,* 2010). A RVF-like disease was first reported in Kenya in 1912 (Kitchen, 1934). However, RVFV was first isolated following an explosive outbreak of sudden deaths and abortions (over a 4-week period) of approximately 4,700 lambs and ewes on a single farm along the shores of Lake Naivasha in the Rift Valley of Kenya in 1931 (Daubney *et al.,* 1931). Between 1912 and 1950, the disease was confined to the former Nakuru District where Lake Naivasha is situated. Between 1951 and 1955, RVF was reported in the former eight districts in the then Rift Valley province. Subsequently, between 1961 and 1964 there was a persistent epidemic that spread to over 30% of the districts across six out of eight former provinces in Kenya. In total, between 1951 and 2007, 11 national RVF epidemics were recorded with an average inter-epidemic period of 3.6 years [range 1, 7 years] (Murithi *et al.,* 2010). Of all the epidemics, the 2006/7outbreak was the most extensive affecting thousands of animals in 29 of 69 former administrative districts across six of the eight former provinces (Munyua *et al.,* 2010). Intriguingly, the former Western and Nyanza provinces, located on the southwestern region of the country, had never reported RVF outbreaks by 2007 (Murithi *et al.,* 2010).

2.1.3.2 Occurrence and distribution outside Kenya

Rift Valley fever infection has been identified in approximately 30 countries in Africa and the Arabian Peninsula (Figure 2.1). Following the initial disease characterization in Kenya in 1931, a severe epidemic in South Africa occurred during which an estimated 100,000 sheep died and 500,000 ewes aborted (Swanepoel and Coetzer, 2004). Up to 1977, the disease was restricted to sub-Saharan Africa (SSA). However, during that year (1977), the virus was detected along the Nile River and delta in Egypt where it caused a massive epidemic in people and livestock (Meegan, 1979). The geographic distribution of RVF progressively expanded to West Africa in 1987 (Nabeth *et al.,* 2001), to Madagascar in 1990/1 (Morvan *et al.,* 1992) and to the Arabian Peninsula in 2000 (Al-Azraqi *et al.,* 2012). A large epidemic occurred in 2006/7 in the Horn of Africa, first in Kenya, Tanzania and Somalia (Nderitu *et al.,* 2011) then in Sudan (Adam *et al.,* 2010). Outbreaks were reported in Madagascar in 2008 (Chevalier *et al.,* 2011) and South Africa in 2010 (Métras *et al.,* 2013). Figure 2.1 shows the geographic distribution of RVFV in RVF endemic countries. Countries in which epidemics are known to have occurred are indicated in red with the date of each outbreak. Countries with evidence of low-level endemic activity (antibody prevalence or occasional RVFV isolation) are indicated in pink. Countries with no evidence of RVF occurrence are indicated in white.

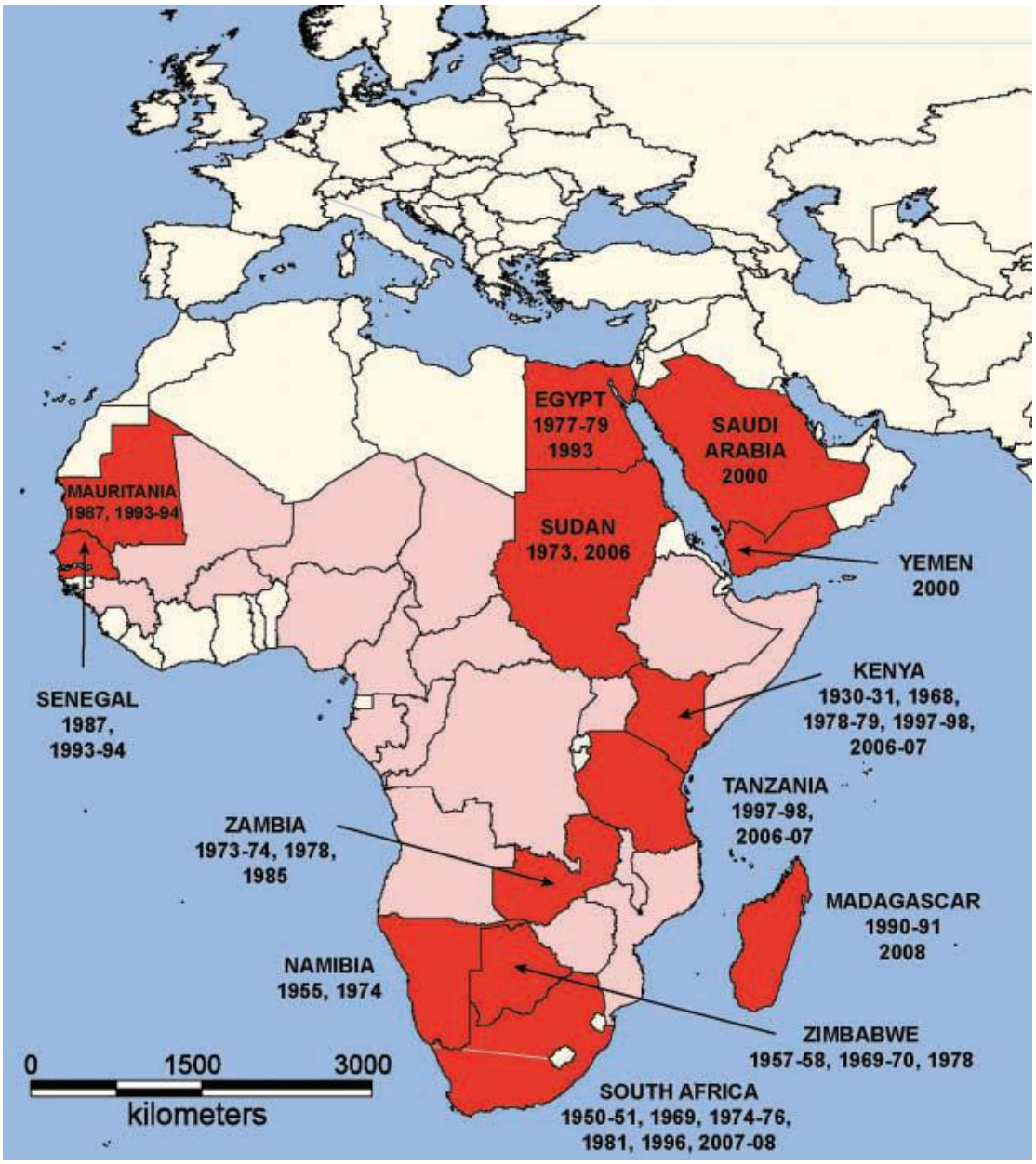


Figure 2.1 Geographic distribution of RVFV in RVF endemic areas (Source: Bird *et al.*, 2009).

2.1.4. Transmission of Rift Valley fever virus

Rift Valley fever virus may be transmitted via various routes:

Vertical transmission to mosquito progeny

Laboratory demonstration of trans-ovarial transmission in *Aedes mcintoshi* was reported recently (Romoser *et al.*, 2011). These findings support the hypothesis that *Aedes mcintoshi* is involved in the endemic maintenance of RVFV by vertical transmission. However, there are few studies (field or experimental) that have investigated the vertical transmission rate (a measure of the average number of infected progeny per infected female). During the 2006/7 RVF outbreak, infection rates of between 0.65 and 10.65 per 1,000 mosquitoes were estimated among *Aedes* species across diverse sites in Kenya (Sang *et al.,* 2010) which translates to approximately 1%. The transmission experiment highlighted earlier on (Romoser *et al.*, 2011) demonstrated low vertical infection rates (11.4%, 4/35 mosquitoes) following virus injection into the hemocoel (Romoser *et al.*, 2011).

Mosquito bite

Rift Valley fever virus is principally transmitted to ruminant hosts through a bite from an infected mosquito (Bird *et al.,* 2009). Humans can also get infected from infectious bites – *Aedes* and *Culex* mosquito bites were reported to play an important role in the transmission of RVFV in 2000 outbreak in Yemen and Saudi Arabia that resulted in approximately 2,000 human infections and 250 deaths (Madani *et al.,* 2003). Mosquitoes get infected following a mosquito blood meal from an infected host. The

ingested virus passes into the mid gut where it replicates before infecting different organs in the mosquito including the reproductive system in *Aedes* species (Romoser *et al.,* 2011). At the end of the extrinsic incubation period, the salivary glands are infected and the virus can be transmitted during a subsequent blood meal.

Direct contact between animals and humans

There is no evidence that incriminates transmission of RVFV infection between animals through direct contact with infected animal tissues, bodily fluids and fomites. Direct transmission is, however, possible because susceptible animals get exposed to contaminated excretions, aborted foetal materials and placental membranes which contain large numbers of virus particles (Pepin *et al.,* 2010). The virus particles can either contaminate the local environment directly or infect animals in close contact (Pepin *et al.,* 2010). In addition, *in vitro* experiments have demonstrated the possibility of persistence of RVFV in the environment for long periods of time (storage of RVF-infected tissue culture fluids at 4^{o}C for up to 30 days without loss of infectivity or antigenicity is possible) (Craig *et al.,* 1967). Humans get infected by RVFV mainly through intensive contact with acutely infected animals, or by handling infected tissues - indeed, many historical outbreaks of RVF in South Africa were initially detected as illnesses among veterinarians and their assistants after they performed necropsies on infected animals (Bird *et al.,* 2009).

Aerosol route in humans

Human RVFV infections may follow as a result of aerosol transmission during the handling of aborted foetal materials or the slaughtering of infected livestock (Bird *et al.,* 2009). This route of infection has been described among slaughterhouse and laboratory workers (Pepin *et al.,* 2010). Exposing mice to aerosols containing RVFV can cause infection (Brown *et al.,* 1981). There are no reports of aerosol RVFV transmission among livestock.

Ingestion of infected eggs by larva

Romoser *et al.* (2011) have further hypothesized of an exogenous source of infection via ingestion of infected eggs by mosquito larvae and other organisms (and possibly livestock). This, if proved, has potentially significant epidemiological implications in the RVFV transmission during the course of an outbreak.

Influence of the mode of transmission

Pepin *et al.* (2010) speculate that the relative importance of each mode of transmission varies according to the stage of the epidemic – i.e. in the initial stages, the mosquito bites predominates while direct contact may play a big role later in the course of an epidemic. Other authors maintain that the bites of infected mosquitoes predominate over the course of an outbreak regardless of the stage of the outbreak (Bird *et al.,* 2009). It is not clear whether the success of a natural infection in livestock is dependent on the transmission route. Furthermore, it is difficult to quantify the

epidemiological significance of the different modes of transmission under field conditions. Knowledge gaps on route-specific RVFV transmission properties can be addressed by the design of transmission experiments. One such recent experiment concluded that different routes of infection determine the pathogenesis of RVF by influencing the pattern in which the virus spreads in the host and the organs it targets (Le Coupanec *et al.,* 2013).

2.1.5 Natural infection in animals and humans

2.1.5.1 Clinical presentations

A detailed description of the clinical picture in naturally-infected animals is given by Swanepoel and Coetzer, (2004). Following experimental infection, the incubation period lasts for a few hours to a few days and is dependent on the inoculation dose, the virus strain, the route of inoculation, the age of each animal and the animal species tested (Swanepoel and Coetzer, 2004). Natural RVF disease is typified by sudden onset of high fever (41^{o}C) among young animals. The fever is accompanied by acute prostration, collapse and death. Livestock RVF epidemics usually manifest as sweeping "abortion storms". Abortions may be accompanied by dystocia and some teratology. Disease in adults is also characterized by peracute to acute disease associated with anorexia, nasal discharge and diarrhoea. Other signs include lachrymal discharges, salivation, vomiting, lymphadenitis, colic and jaundice (Swanepoel and Coetzer, 2004). The affected animals are highly viraemic (approximately 1.0 x 10^{6}

plaque forming units (PFUs)/mL to 1.0 x 10^8 PFUs/mL) for about 10 days (Bird *et al.*, 2009).

Livestock species and age within species shows marked biological heterogeneity in terms of disease outcomes (Swanepoel and Coetzer, 2004). Thus, young lambs (<1 month old) are highly susceptible to RVFV infection, with case fatality rates (CFR) reaching 90 to 100%. Adult sheep are less susceptible to infection, with CFR of approximately 10 to 30%. However, abortion rates can be high (90 to 100%). Neonatal (<1 month old) calves are less susceptible than neonatal lambs with CFR ranging between 10 and 70%. Adult cattle are more resistant than adult sheep with CFR of approximately 5 to 10%. Although goats are highly susceptible to infection, they appear to be more refractory to severe disease than sheep (Bird *et al.,* 2009). Camels are the least susceptible, in most cases exhibiting abortions only (Swanepoel and Coetzer, 2004).

The majority of human infections result in a mild to moderate self-limiting febrile illness of short duration. However, in a small percentage (~1 to 2%) of patients, the disease can progress to more serious complications, including acute hepatitis, encephalitis, retinitis, or a hemorrhagic syndrome, with a hospitalized CFR of ~10 to 20% (Bird *et al.,* 2009).

2.1.5.2 Viraemia development and general immune response

Rift Valley fever virus has a high propensity for development of significant viraemia in sheep, goats and cattle (1.0×10^6 to 1.0×10^8 PFUs/mL of blood) (Bird *et al.,* 2009). The vertebrate hosts are viraemic for only 2–7 days (Pepin *et al.,* 2010) implying that they are unlikely to serve as long-term reservoir of the virus. Viraemia development and intensity appears to be age- and species-dependent. For instance, viraemia in lambs that are less than one week old is detectable within 16 hours of infection that has been initiated with small doses of the virus, and persists for the duration of infection that mostly ends fatally within 36-42 hours (European Food Safety Authority, EFSA, 2005). In older ruminants, viraemia develops more slowly becoming detectable 1 - 2 days post infection (EFSA, 2005). In adult vertebrate hosts, viraemia is most intense on the second to fifth day (EFSA, 2005).

Following RVFV infection, a robust adaptive immune response is developed, with the production of detectable neutralizing antibodies from the 4th – 8th day after infection (Morrill *et al.,* 1987). These antibodies are accompanied by the production of Immunoglobulin (Ig) M and IgG antibodies. As in other infections, the detection of RVF IgM antibodies denotes recent RVFV infection. Immunoglobulin M antibodies do not persist beyond the 50th to 90th day in the majority of cases after infection (Bird *et al.,* 2009; Pepin *et al.,* 2010). Figure 2.2 illustrates a generalized time course of viraemia and antibody response against RVFV in livestock and its bearing on diagnostic testing (discussed in the section on Diagnosis" below).

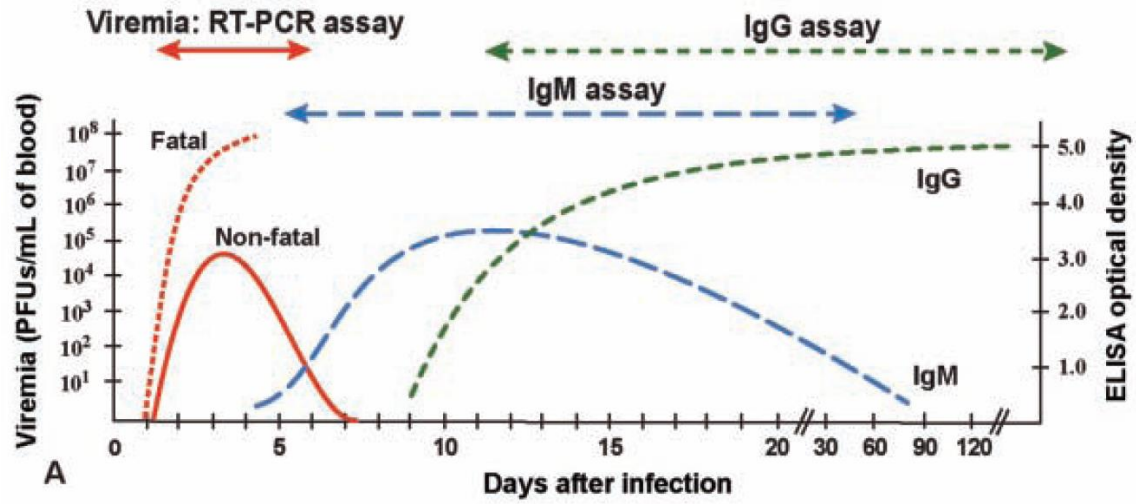


Figure 2.2: Generalized time course of viraemia and antibody response against RVFV in livestock. Note that viraemia levels attained determine the prognosis of a case (Source: Bird *et al.,* 2009).

2.1.6 Rift Valley fever public health and economic impacts

The public health impact of RVF is experienced through human and animal morbidity and mortality. The episodic nature of the disease, and the rapid evolution of outbreaks, normally overwhelms medical and veterinary infrastructures in the countries affected which, in most cases, lack both capacity and institutional memory to cope (Bird *et al.*, 2009). As an example, during the recent 2006/7 epidemic that occurred in Kenya, of 700 suspected cases, 392 met probable or confirmed case definitions (Nguku *et al.*, 2010). The case fatality ratio was 1.8 (95% Confidence Interval [CI] 1.3–3.8). Sero-surveys suggested an attack rate up to 13% of residents in heavily affected areas. There were up to 180,000 infected mildly ill or asymptomatic people within highly affected areas in Kenya (Nguku *et al.*, 2010).

In addition to animal morbidity and mortality and abortions, a RVF outbreak can have wide-ranging impacts on the livestock production sector and other segments of the livestock economy. Rich and Wanyoike (2010) highlighted production impacts, employment losses (particularly for casual labour), and a reduction in operating capital among slaughterhouses and butchers that slowed the recovery of the livestock sector once the disease had abated. On a macroeconomic basis, these authors estimated that the 2006/7 RVF outbreak led to losses of over Ksh 2.1 billion (US$32 million) on the Kenyan economy, based on its negative impacts on agriculture and other sectors as well.

Trade and livelihood related impacts are experienced once the outbreak is confirmed. Gachohi *et al.,* (2012) reported that movement control and market closures were the main response measures implemented by the Kenyan Department of Veterinary Services (DVS) to manage the 2006/7 RVF outbreak particularly in areas that had cases in both livestock and humans. This mainly affects pastoral and agro-pastoral systems where livestock is a key asset that fulfills multiple economic, social and risk management priorities. International livestock trade is affected as well. For instance, the 1997/8 RVF outbreak was associated with significant economic impact due to a ban on livestock exports from the Greater Horn of Africa (Little *et al.,* 2001).

2.2 Rift Valley fever - epidemiology

2.2.1 Risk factors for Rift Valley fever occurrence

The risk factors for RVF occurrence are described under three topics: biological, environmental and socio-economic factors.

2.2.1.1 Biological risk factors for Rift Valley fever

Livestock age and species

This review has already highlighted host-related risk factors including age and species as animal-level risk factors for RVF occurrence. Young animals of any species are highly susceptible relative to adult animals. Studies carried out following an outbreak reported lower seroprevalence in young animals compared to adult animals (Lancelot *et al.,* 1990; Thiongane *et al.,* 1991; Zeller *et al.,* 1995; Chevalier *et al.,* 2011). This can be explained by three reasons: (1) the low number of survivors in the young age category following an outbreak, and (2) replacement of susceptible animals through births, and (iii) adults will have had a longer period to experience an exposure.

A gradient of susceptibility to RVF-induced mortality is evident with sheep and goats being the most susceptible, followed by cattle and camels in that order. However, studies carried out in West Africa following an outbreak reported similar seroprevalence values in sheep and goats (Guillaud *et al.,* 1988; Lancelot *et al.,* 1990; Thiongane *et al.,* 1991).

In contrast to the dramatic high fatality observed among young ruminant animals during epidemics, children and neonatal infants seem to be less affected by the disease (Madani *et al.,* 2003). Further studies should elucidate whether the underlying difference in susceptibility of young animals with that observed in humans are as a result of a lack of exposure or whether there are true species-specific differences in susceptibility.

Studies report similar RVF incidence values across age groups within a species and across species (sheep, goats and cattle) (Lancelot *et al.,* 1990). Similar incidence values implies comparable force of infection (the per capita risk of a susceptible host being infected) which is a function of several transmission parameters: (i) vector biting rate, (ii) probability of transmission from an infectious mosquito to a susceptible host given that a contact between the two occurs, (iii) vector: host ratio, (iv) vector blood meal index (a function of host preference) and (v) RVFV prevalence in the vector. It is unlikely for a multi-host population to commonly share these transmission drivers. With this consideration, the incidence values are likely to be inaccurate.

Sex of the host animal

Female pregnant animals are at a higher risk of additional RVF burden as a pregnancy gets terminated at any stage once RVFV infection is established in the female host. Abortion rates follow the species susceptibility gradient – it nearly reaches 100% in sheep, followed by goats through to cattle and camels (Bird *et al.,* 2009). A similar

scenario as that found in children versus neonatal ruminant mortalities is observed in pregnant women versus pregnant ruminants, i.e. in contrast to the massive abortion storms observed among ruminant animals, pregnant women were less likely to be affected by the disease (Madani *et al.*, 2003). Likewise, studies are required to find out the basis of these differences.

Immune responses by the host

Immune status is an additional biological factor that determines whether an infection is successful or not. Infection with RVFV is hypothesized to induce lifelong neutralizing immunity (Pepin *et al.*, 2010). A threshold of immunity that is fully protective has not been well characterized. Extensive knowledge regarding natural RVFV immunology is lacking and requires further detailed studies, for instance in relation to, the inoculation dose, the virus strain, the route of inoculation, the competence of vectors in transmitting RVFV, and animal-level factors.

Vectors of Rift Valley fever virus

Unlike majority of arboviruses (arthropod-borne viruses) which are transmitted by a narrow range of vectors, RVFV has the potential to get adapted to a remarkable range of vectors, including ticks and a variety of flies (Pepin *et al.*, 2010). The minimum infection rates (MIR), based on the numbers of isolations per 1000 adult female mosquitoes, support the epidemiological importance of mosquitoes as competent RVFV vectors (Pepin *et al.*, 2010). Species with high MIRs for RVFV in adult female

mosquitoes sampled in the wild include *Aedes mcintoshi* in Kenya (83.3/1000) *Aedes dentatus* in Zimbabwe (43.5) and *Culex theileri* in Zimbabwe (9.7/1000) (Pepin *et al.,* 2010). In experimental assessment of competence of vectors, the vector competence index (VCI) is used (Jupp and Kemp, 1993). The VCI integrates infection and transmission rates into a single statistic. Species with high VCIs for RVFV in adult female mosquitoes sampled in the wild include *Culex theileri* in South Africa (0.22-0.53) *Culex pipiens* in Egypt (0.05-0.91) and *Aedes palpalis* in Central African Republic (0.46) (Pepin *et al.,* 2010).

Rift Valley fever virus has been isolated from certain member species of the mosquito genera; *Anopheles, Eretmapodites, Coquillettidia* and *Mansonia* implicating them as vectors of RVF. However, vector competence experiments demonstrated that they are nearly incapable of transmission to hosts (Pepin *et al.,* 2010). Specifically, *Aedes vexans arabiensis* were implicated in large outbreaks in West Africa (Zeller *et al.,* 1997) and Saudi Arabia in 2000 (Jupp *et al.,* 2002). The epidemic/amplifying secondary vectors in Saudi Arabia in 2000 were *Culex poicilipes* (Diallo *et al.,* 2000) and *Culex tritaeniorhynchus* (Jupp *et al.,* 2002).

Entomologic studies in Kenya during the 2006/7 RVF outbreak reported, 77 pools of mosquitoes representing 10 species tested positive for RVFV: *Aedes mcintoshi/circumluteolus* (26 pools), *Aedes ochraceus* (23 pools), *Mansonia uniformis* (15 pools); *Culex poicilipes, Culex bitaeniorhynchus* (3 pools each); *Anopheles*

squamosus, Mansonia africana (2 pools each); *Culex quinquefasciatus, Culex univittatus, Aedes pembaensis* (1 pool each) (Sang *et al.,* 2010). Although these species achieved threshold susceptibility to RVFV, their competence for onward transmission was not elucidated.

2.2.1.2 Environmental risk factors for Rift Valley fever

Mosquito population dynamics are inextricably connected to the environmental variables. This section describes how the temporal dynamics of vector and RVFV interact with environmental variables to enable transmission. The spatially defined focus of transmission may be characterized by climate, elevation, vegetation and hydrology. For instance, rainfall is critical in providing suitable breeding habitats for mosquitoes (Anyamba *et al.,* 2009). Temperature is a key driver of mosquito and RVFV life history traits that combine to determine transmission intensity (Turell *et al.,* 1985). These factors may affect RVF transmission intensity at different scales. Environmental factors will be covered at two scales – local processes of virus transmission and large-scale ecological risk factors.

Local processes of RVFV transmission

Rift Valley fever transmission in Africa and the Arabian Peninsula is characterized by varied landscapes. The result is a generation of foci of transmission. These foci may be defined by remote sensing and statistical tools (Soti *et al.,* 2013). Table 2.1 summarizes the literature that reports local factors that influence RVFV transmission.

The main factors related to the local processes of RVFV transmission are water-related variables such as water bodies' surface area and distribution, previous occurrence of RVF in an area, soil type and hydrology, landscape with flat topology and shallow depressions that easily support flooding, vegetation density index, local bio-ecosystem factors, local rainfall patterns and proximity to wildlife (Table 2.1).

Large-scale ecological risk factors

Table 2.2 summarizes the different aspects of climate and large-scale ecological variability and their relationships to RVF outbreaks. Large-scale ecological risk factors of RVF occurrence mainly include indicators of climate variability such as sea-surface temperature (SST) patterns, cloud cover, rainfall, and ecological indicators (primarily vegetation) on a global scale (Anyamba *et al.*, 2009). All the documented moderate or large RVF outbreaks that have occurred in the Horn of Africa (Figure 2.3) between 1950 and 2007 have been associated with ENSO-associated above-normal and widespread rainfall.

For instance, during the September 2006 to November 2006 period, anomalous warming of SSTs (>1°C) in the eastern-central Pacific region and the concurrent anomalous warming of SSTs (>0.5°C) in the western equatorial Indian Ocean region generated warm ENSO conditions. These conditions enhanced precipitation over the central and eastern Pacific and the Western Indian Ocean (WIO) extending into the Horn of Africa (Anyamba *et al.,* 2009). These rains resulted in excess rainfall amounts

of >400 mm during the same period in some locations (Figure 2.4). A combination of elevated SSTs and subsequent elevated rainfall and the persistence of greener-than-normal conditions over a 3-month period in the RVF endemic region can be used to identify areas with ideal ecological conditions for mosquito vector emergence and survival. This knowledge has been used in the design and implementation of an early warning system (EWS) (Anyamba *et al.*, 2009).

Table 2.1: Local factors that influence RVFV transmission by country/regional/continental spatial scale

Spatial scale	Local factor	Key result/interpretation	References
Kenya; Tanzania	Previous occurrence of RVF -- the probability of an area being involved in a national epidemic was higher in areas that had previously reported disease compared to areas that had no prior disease activity	• Once introduced into certain permissive ecologies, the RVFV becomes enzootic	Murithi *et al.*, 2010; Sindato *et al.*, 2014
Africa	Previous occurrence of RVF -- areas with high seroprevalence were those having experienced previous outbreaks	• Areas with low seroprevalence considered in the context of trade as a potential risk for export of infected animals.	Clements *et al.*, 2007a
Kenya; Tanzania	Soil type -- RVF case areas were more likely than non-case areas to have soil types that retain surface moisture.	• Soil type may influence flooding, drainage and potentially the ability for infected *Aedes* egg stages (which remain in the soil) to remain infectious in the ground until heavy flooding at which time maturation of egg stages and mass breeding occurs • Soil type data may add specificity to climate-based forecasting models for RVF.	Munyua *et al.*, 2010; Nguku *et al.*, 2010; Sindato *et al.*, 2014
Kenya	Flooding	• Flooding is followed by presence of mosquito swarms and transmissions – mean interval between the onset of heavy rains and appearance of mosquito swarms was 23 days. • Mean interval between first appearance of mosquito swarms and first suspected RVF case in livestock was 16 days	Jost *et al.*, 2010
Kenya, Somalia, Tanzania	Topology	• Flat topology of the area and water retaining soil types support flooding, dense bush cover, and high *Aedes* mosquito populations, • All these factors facilitate higher adult survival through availability of breeding sites, resting sites and blood meal sources	World Health Organization (WHO) 1998.

Eastern and Southern Africa	Landscape - shallow depressions in the general topography, with water-saturated soil overlaying a poorly porous stratum that produces flooding	• Heightened risk for RVF transmission if infected *Aedes* eggs present	Whitlow, 1984.
Eastern and Southern Africa	Landscape - suitable habitats for *Aedes* species breeding found in shallow depressions in the flood-plains of rivers when floodwaters overflow the river-banks	• Heightened risk for RVF transmission if infected *Aedes* eggs present	Pepin *et al.*, 2010
Senegal	Vegetation density index around water ponds positively correlated with RVFV serologic incidence in hosts	• Risk of RVFV transmission higher in the vicinity of ponds surrounded by a dense vegetation cover that may provide sheltered habitats for mosquitoes	Soti *et al.*, 2013
Senegal	Water surface area and water bodies distribution	• Sequel: spatial heterogeneity in RVFV transmission	Chevalier *et al.*, 2005
Senegal	Average total monthly rainfall during December to February is one of the most important spatial predictor of risk of positive RVF serologic status	• Identifying lower Senegal basin at risk, • Southern Mauritania and Southern Senegal more at risk	Clements *et al.*, 2007b
Madagascar	Existence of a sylvatic cycle between mosquitoes and wild reservoirs (including rodents) living in the forest	• The sylvatic cycle could explain the persistence and the re-emergence of the virus in the area adjacent to the forest	Chevalier *et al.*, 2011
West Africa	Local bioclimatic zone Prevalence is higher in Guinean bioclimatic zone - compared with Sudanian zone for cattle - compared with Sudanian and Sahelian zones for small ruminants	• Guinean zone is a wetter area compared to the Sudanian or Sahelian zones leading to an expected higher RVF transmission if vectors are present	Zeller *et al.*, 1995
Tanzania	Local ecosystem -- RVF occurrence between 1930 and 2007 associated with the eastern Rift Valley ecosystem	• Suitable ecological features necessary for livestock keeping and survival of RVFV include: bimodal rainfall pattern, soils with high moisture retention capacity, uncontrolled livestock movements	Sindato *et al.*, 2014
Senegal	Without animal migration from outside the system, within-Ferlo (Senegal) virus persistence was possible if cattle moved between ponds and if rainfall did not occur at the same time at all ponds	• Theoretical transmission scenarios	Favier *et al.*, 2006
General	RVFV endemicity -- the RVFV can persist if there is a high contact rate between hosts and mosquitoes	• Theoretical transmission scenarios	Gaff *et al.*, 2007

Kenya, Somali, Tanzania	Presence of different lineages of RVFV, both within the same outbreak foci and across geographically distant outbreak foci during the 2006–2007 RVF outbreaks.	• Findings support the concept of re-emergence of resident populations of endemic viruses in each outbreak foci, probably via either spontaneous hatching of infected *Aedes* mosquito larvae or expansion of a resident virus that was maintained through low-level cycling among vertebrates and possibly humans.	Nderitu *et al.,* 2011
Kenya; Tanzania	Wildlife	• Wildlife may be reservoirs for RVFV during inter-epidemic period and may play a role in amplifying the virus during epidemics.	Evans *et al.,* 2008; Sindato *et al.,* 2014; Boiro *et al.,* 1987; Pretorius *et al.,* 1987.
Senegal	Hydrology – integrating a parameterized hydrological model that simulated daily water variations of mosquito breeding sites with mosquito population models capable of reproducing the major trends of population dynamics of the two main vectors of RVFV in Senegal, *Aedes vexans* and *Culex poicilipes.*	• Provided mechanistic insights to explain why RVF reported outbreaks in Northern Senegal are not directly associated with rainfall as it is the case in East Africa. • RVF occurs during years of concurrent occurrence of both species in high densities. • These occur when abundant rains occur at regular intervals throughout the rainy season.	Soti *et al.,* 2012
West Africa	Rainfall patterns suitable for emergence of *Aedes vexans* mosquitoes	• The amount of water from a single rainfall event must reach at least of 10 mm • A rainfall event delivering more than 10 mm, must occur after a 6-day period without rain, • A rainfall event delivering more than 40 mm must occur after a 6-day period with less than 30 mm of rain.	Vignolles *et al.,* 2009

Table 2.2: Large-scale ecological risk factors that influence RVFV transmission by country/regional/continental spatial scale

Spatial scale	Large-scale ecological risk factor	Key result/Interpretation	Reference
Kenya, Somalia, Tanzania	Rainfall: Southern Oscillation Index (SOI) and *El Nino*/Southern Oscillation (ENSO)-related variations in precipitation The SOI is an atmospheric indicator of the phase and amplitude of ENSO.	• Rainfall increases the number and sizes of mosquito breeding sites – this leads to an increase in the survival of aquatic stages of mosquitoes, a corresponding increase in the emergence rate of new adults, and a higher egg-laying rate • Most RVF outbreaks in the Horn of Africa that have occurred during the negative phase of the SOI are associated with ENSO warm events. • Documented moderate or large RVF outbreaks in the Horn of Africa over the last 60 years linked to ENSO-associated above normal and widespread rainfall (Figure 2.3)*.	Anyamba *et al.*, 2009
Kenya, Somalia, Tanzania	Large-scale green vegetation development (measured by satellite-derived time series vegetation measurements of photosynthetic activity (normalized difference vegetation index (NDVI)) associated with periods of elevated and widespread rainfall	• Green vegetation provides resting and sheltered sites for adult mosquitoes. • Developing indicator for RVFV activity using remote sensing and mosquito abundance data	Linthicum *et al.*, 1987.
General	Temperature	• Temperature influences mosquito and pathogen life history traits that combine to determine transmission intensity, including mosquito development rate, biting rate, and development rate.	Depinay *et al.*, 2004.
General	Temperature	• Higher temperatures decrease the incubation period of RVFV in mosquitoes	Turell *et al.*, 1985
Regional scale	Disease spread through infected windborne vectors	• Regional scale: importance of RVFV spread by wind	Sellers *et al.*, 1982

*Not all RVF outbreaks are associated with ENSO warm events: a 1989 Kenyan local RVF outbreak was associated with local heavy rainfall at the focus of the outbreak (Anyamba *et al*., 2009)

Table 2.3: Socio-economic factors that influence RVFV transmission by country/regional/continental spatial scale

Spatial scale	Socio-economic factor	Interpretation	Reference
Senegal	Temporary human and livestock habitation (night pens) around water ponds	• Host-seeking RVF nocturnal mosquito vectors serve as risk for RVFV transmission	Pin-Diop *et al.*, 2007
Madagascar	Intra-country livestock movement and trade	• Cattle movement and trade may contribute to introduction of RVFV in an area	Chevalier *et al.*, 2011
East African countries, Arabian Peninsula	Inter-country livestock movement and trade	• Cattle movement and trade may contribute to introduction of RVFV in an area	Pepin *et al.*, 2010
Egypt, Yemen, Saudi Arabia	Anthropogenic factors related to agriculture – development of irrigation dams	• May encourage reproduction of certain *Culex* mosquitoes; impact on floodwater *Aedes* however, seems less likely, • May alter vector biodiversity and abundance driving RVF emergence and transmission, • May alter frequency and intensity of interactions between hosts and vectors driving RVF emergence and transmission • Increase local endemic prevalence without impacting on the frequency of epidemics. • The intensity of epidemics, however, may be expanded as in the Mauritanian outbreak	Wilson, 1994; Pepin *et al.*, 2010
Egypt	Movements of infected livestock as a potential pathway for RVFV introduction into a disease free area, for example, in Egypt in 1977	• On a regional scale, the importance of RVFV spread by animal movements through trade suggested	Sellers *et al.*, 1982.
Saudi Arabia/ Yemen	Trade and movement of sheep from Eastern Africa to Saudi Arabia or in Yemen during festive periods identified as a risk for the introduction of RVFV -- it appears from the genomic data that the origins of this outbreak were closely linked to the large 1997–1998 East African epidemic/epidemic.	• Ban of livestock trade as an option for preventing disease spread whenever exporting countries are identified as being in a ‘‘pre-epidemic/epidemic’’ suggested	Davies 2006.
West Africa	Movement of livestock	• At least 5 introductions of RVFV took place in Senegal and Mauritania from distant African	Soumaré *et al.*, 2012.

		regions. • Barkedji in Senegal possibly a hub associated with the three distinct entries of RVFV in West Africa.	
Inter-continental level	Introduction of RVFV via illegal importation of viraemic animals and contaminated products coming from RVF epidemic areas identified as a threat for Europe	• Intercontinental scale: importance animal movements and contaminated products through trade suggested from risk assessments	EFSA, 2005
Madagascar	Movement of infected livestock and or infected mosquitoes - the most recent Madagascar outbreak (2008/9) was caused by a virus likely arriving in the country sometime between 2003 and 2008 and that this outbreak may be an extension of the 2006–2007 East African outbreak.	• RVFV outbreaks in Madagascar result not from emergence from enzootic cycles within the country but from recurrent virus introductions from the East African mainland	Carroll *et al.*, 2011
Senegal	Small ruminants population turn-over	• Following the 1987 RVF outbreak, antibody seroprevalence dropped from 71.7% in 1988 to 23.9 % in 1989.	Thiongane *et al.*, 1991.

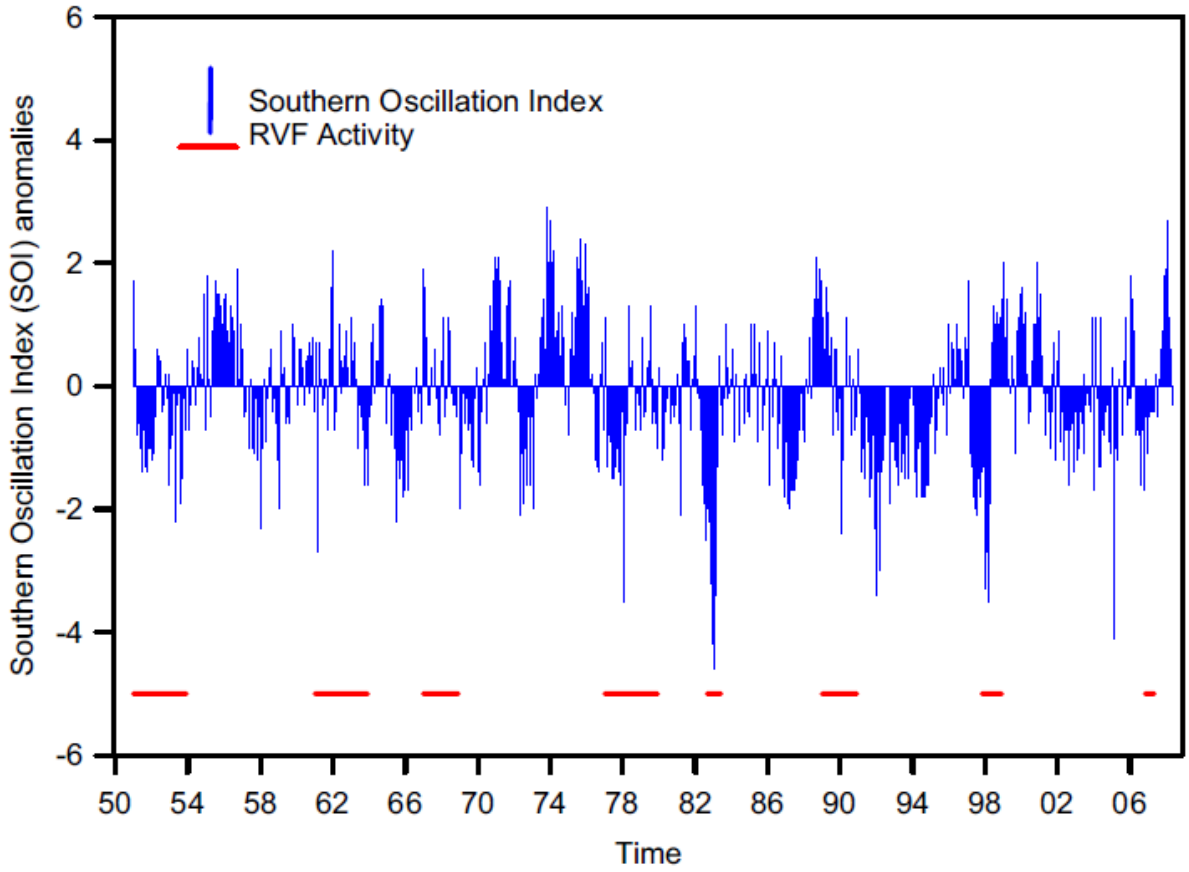


Figure 2.3: Time series of monthly Southern Oscillation Index (SOI) with periods of approximate heightened RVF activity (red horizontal bars) from 1950 to 2008. SOI values are shown as standard deviation with reference to the 1951–1980 base periods (Source: Anyamba *et al.*, 2009).

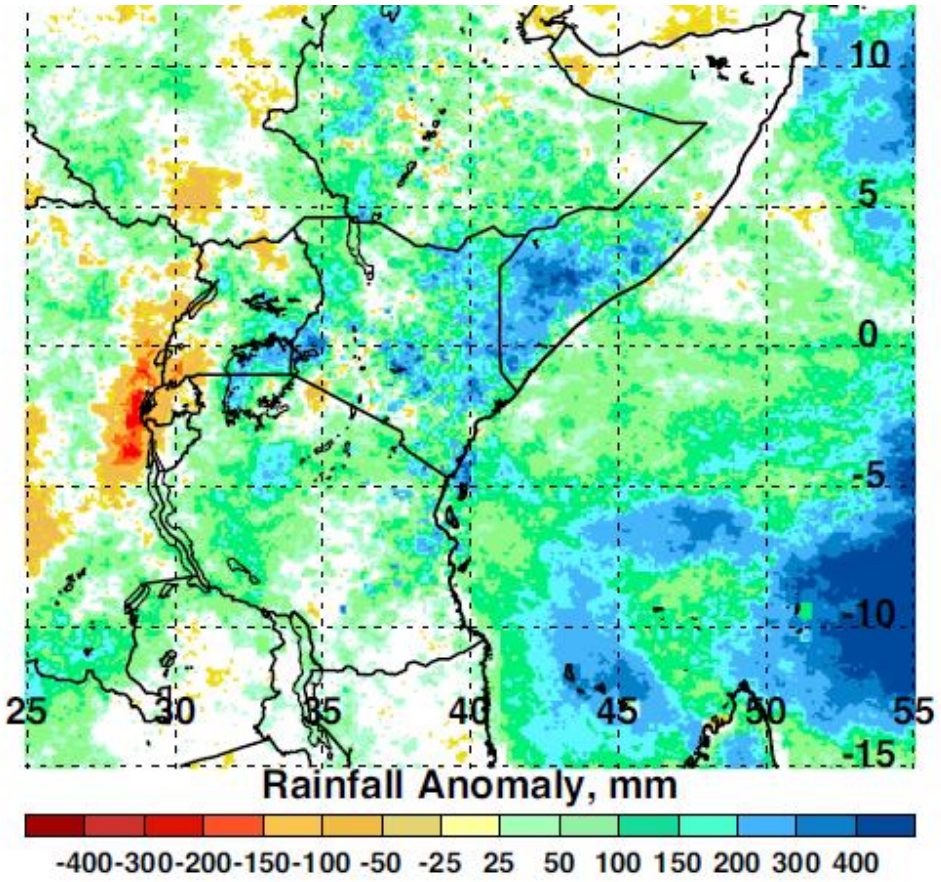


Figure 2.4: Seasonal rainfall anomalies in millimeters for the Horn of Africa from September to November 2006. The anomalies are computed as deviations from the long-term seasonal mean for the period 1995–2006 (Source: Anyamba *et al.,* 2009).

2.2.1.3 Socio-economic factors

Socio-economic factors include herd-level and community-level processes that affect livestock management decisions, such as demographics, livestock trade, livestock movements and mixing patterns. Anthropogenic factors related to agriculture alter ecosystem diversity that could in turn influence the occurrence of RVF outbreaks. Table 2.3 summarizes the different socio-economic aspects and their relationships with RVF outbreaks.

2.3 Progress in modelling for Rift Valley fever

Good progress has been made on RVF modelling and prediction using statistical and dynamical models (Métras *et al.,* 2011). Statistical models have been used to identify socio-ecological factors associated with RVF exposure in domestic livestock (Chevalier *et al.,* 2011) and to predict the risk of outbreak particularly in eastern Africa (Anyamba *et al.,* 2009). Dynamic systems models, on the other hand, have been used to identify processes that promote RVF endemicity (Favier *et al.,* 2006). Gaff *et al.* (2007) developed a mathematical model for the spread of RVF that combines frequency incidence of disease transmission between two vector species (*Aedes* and *Culex* mosquitoes) and one livestock host. Other models that have been published include a network-based meta-population model used to simulate the distribution of RVF outbreak in South Africa (Xue *et al.,* 2012) and a dynamic model used to assess vertical transmission of RVFV in floodwater *Aedes* species and inter-outbreak persistence (Chitnis *et al.,* 2013). Recently, Chamchod *et al.* (2014) proposed a mathematical model to investigate the epidemic and endemic transmission of RVFV among ruminants. These models have given less attention to two important factors that influence RVFV transmission patterns - climate particularly rainfall, and livestock population dynamics.

2.4 Model parameters and parameterization

Parameters are generally all quantities that are used to describe and run a model. Parameters need not to be constant, but all their values need to be decided before the model runs. Parameters include the following:

1. Boundary parameters which describe the values along the spatial and temporal boundaries of a system.
2. Constants which take on constant values in a particular model run and are always the same from one run to another
3. Forcing functions which are parameters that describe the effect of the outside world upon the system. They may change in time or space, but they do not respond to changes within the system, e.g., rainfall and temperature

There may be a number of ways to source model parameters – literature review and empirical studies. Table 2.4 lists host module parameters related to expected and RVF-induced abortion obtained from data collected by participatory techniques from the livestock keepers in the study area immediately after the 2006/7 RVF outbreak (Jost *et al.,* 2010). Table 2.5 illustrates parameters related to *Aedes* and *Culex* species population dynamics.

Since the core of this thesis is on transmission of a mosquito-borne pathogen, a detailed description of transmission-related parameters will be offered. Ronald Ross and George Macdonald are acknowledged as the pioneers in the development of mathematical models of mosquito-borne pathogen transmission (Smith *et al.,* 2012).

Table 2.4: Host parameters based on participatory epidemiological assessment of the Rift Valley fever outbreak in Kenya in 2006/7

Parameter	**Symbol**	**Value**	**Source**
Probability of expected abortion in cattle	Ab_c	0 - 0.001526*	Jost *et al.*, 2010
Probability of expected abortion in sheep	Ab_s	0.000365 - 0.000807*	Jost *et al.*, 2010
Probability of RVF-induced abortion in cattle	Ab_{cRVF}	0.063 – 0.5*	Jost *et al.*, 2010
Probability of RVF-induced abortion in sheep	*AbsRVF*	0.556 – 0.811*	Jost *et al.*, 2010

*uniform distribution was used when running the model

Table 2.5: Vector parameters based on published literature

Parameter	**Symbol**	**Value**	**Source**
Buried *Aedes* eggs hatching rate	H_A	0.33	Fischer *et al.*, 2011
Aedes larva daily mortality rate	μ_{Al}	0.2	Hawley, 1988
Aedes pupa development rate	E_A	0.2	Paula *et al.*, 2013
Aedes pupa daily mortality rate	μAp	0.1	Rueda *et al.*, 1990
Aedes adult daily mortality rate	μAa	0.1	Muir and Kay, 1998
Average number of *Aedes* eggs laid per day by one mosquito	S_A	10	Otero *et al.*, 2006†
Aedes lifespan	*d2*	3-60	Gaff *et al.*, 2007
Aedes eggs development rate to buried eggs	J_A	0.167	Vignolles *et al.*, 2009
Culex eggs hatching rate	H_C	0.33	Clements, 1992
Culex larva daily per capita mortality rate	μ_{Cl}	0.2	Unavailable
Culex larva development rate	P_C	0.1	Clements, 1992
Culex pupa development rate	E_C	0.2	Gokhale *et al.*, 2013
Culex pupa daily mortality rate	μC_p	0.1	Unavailable
Culex adult daily mortality rate	μC_a	0.1	Jones *et al.*, 2012
Average number of *Culex* eggs laid per day by one mosquito	S_C	40	Wong *et al.*, 2011¥
Culex lifespan	d_3	3-60	Gaff *et al.*, 2007

Where the source of parameter has been indicated unavailable, the arbitrary figure was used

†An adult female *Aedes* lays 63 eggs every 3 days, so it is assumed to lay 20 eggs per day. Assuming a sex ratio of 1:1, and because only females are modeled, only 10 eggs are laid per day in the model.

¥An adult female *Culex* lays between 200 and 300 eggs every 3 days, so we assumed an average lay 80 eggs per day. Assuming a sex ratio of 1:1, and because only females are modeled, only 40 eggs are laid per day in the model.

The structure of these models is based on a set of assumptions. Progressive refinement of these assumptions has since played a central role in development of research on mosquito-borne pathogen transmission and the development of strategies for mosquito-borne disease prevention and control. The following is a list of parameters that commonly define vector-borne pathogen transmission models as borrowed from the Ross-Macdonald theory of malaria transmission:

i. The population density of mosquitoes and hosts to obtain the number of vectors per host.
ii. The proportion of infected mosquitoes and hosts that are infectious
iii. The probability that a mosquito becomes infected after biting an infected host
iv. Proportion of blood meals taken by a mosquito from a host
v. Infected, but not yet infectious mosquitoes
vi. The proportion of bites by infectious mosquitoes that infect a host
vii. Host blood feeding rate (the proportion of mosquitoes that feed on a host each day)
viii. Mosquito survival (either as the probability of surviving one day, or the instantaneous death rate)
ix. The pathogens' hosts latent period, often referred to as the ''intrinsic incubation period''
x. The pathogen's mosquito latent period, often called the ''extrinsic incubation period
xi. The number of days from infection to infectiousness in the host (latent period)

xii. The number of days from infection to infectiousness in the mosquito

xiii. The recovery period from infection in hosts

xiv. The average lifespan of a mosquito

Table 2.6 quantifies these parameters from the literature.

Table 2.6: Transmission parameters based on published literature

Parameter	Symbol	Value	Source
Aedes biting rate	G_A	0.33	Canyon *et al.*, 1999
Culex biting rate	G_C	0.33	Durand *et al.*, 2010
Probability of infected mosquito producing infection in a host	b_C	0.001–0.54	Chitnis *et al.*, 2013
Proportion of *Aedes* blood meals obtained from cattle	BM_{AC}	0.0005	Unavailable*
Proportion of *Aedes* blood meals obtained from sheep	BM_{AS}	0.0005	Unavailable*
Proportion of *Culex* blood meals obtained from cattle	BM_{CC}	0.5	Unavailable*
Proportion of *Culex* blood meals obtained from sheep	BM_{CS}	0.5	Unavailable*
Adequate contact rate: *Aedes* to livestock	β_{12}	0.0021- 0.2762	Gaff *et al.*, 2007
Adequate contact rate: livestock to *Aedes*	β_{21}	0.0021- 0.2429	Gaff *et al.*, 2007
Adequate contact rate: livestock to *Culex*	β_{23}	0.0000 - 0.3200	Gaff *et al.*, 2007
Adequate contact rate: *Culex* to livestock	β_{32}	0.0000 - 0.0960	Gaff *et al.*, 2007
Latent period in *Aedes* species	L_{Ae}	1 day	Turell *et al.*, 1985
Latent period in *Culex* species	LCl	3 days	Turell *et al.*, 1985
Probability of infected blood meal giving infection in *Aedes* spp	b_{Ae}	0.38-0.86	Turell *et al.*, 1985
Probability of infected blood meal giving infection in *Culex* spp	b_{Cl}	0.30-0.89	Turell *et al.*, 1985
Probability of an infected cow moving to the latent stage	Θ	0.3-0.6	Chitnis *et al.*, 2013
Probability of an infected cow moving to the infectious stage	$1\text{-}\theta$	0.4-0.7	Chitnis *et al.*, 2013
Latent period in hosts	L_C *or* L_S	1 to 6 days	Turell *et al.*, 1985; Gaff *et al.*, 2007
Infectious period in hosts	i_C *or* i_S	3 to 10 days	Bird *et al.*, 2009; Pepin *et al.*, 2010
The maximum number of mosquito bites a cow can sustain per unit time	Σh	0.1-50	Chitnis *et al.*, 2013
Probability of RVF-induced mortality in neonate cattle	m_{NCRVF}	0.2 to 0.7	Bird *et al.*, 2009
Probability of RVF-induced mortality in weaner cattle	m_{WCRVF}	0.05 to 0.1	Unavailable*
Probability of RVF-induced mortality in yearling cattle	m_{YCRVF}	0.02 to 0.1	Unavailable*
Probability of RVF-induced mortality in adult cattle	m_{ACRVF}	0.01 to 0.05	Bird *et al.*, 2009
Probability of RVF-induced mortality in neonate sheep	m_{NSRVF}	0.7 to 1	Bird *et al.*, 2009
Probability of RVF-induced mortality in weaner sheep	m_{WSRVF}	0.05 to 0.2	Unavailable*
Probability of RVF-induced mortality in growing sheep	m_{GSRVF}	0.01 to 0.2	Unavailable*
Probability of RVF-induced mortality in adult sheep	m_{ASRVF}	0.01 to 0.1	Bird *et al.*, 2009

*Arbitrary values used where parameter values were unavailable

Two important and measurable transmission quantities can be computed from these parameters: (1) the force of infection and (2) the basic reproduction number. The force of infection (FoI) is the per-capita risk of a susceptible host being infected (Reiner Jr *et al.,* 2014). The FoI is a product of the adequate contact rate and the proportion of infected hosts that are infectious. The adequate contact rate, on the other hand, is the rate at which contact between an infective and a susceptible individual occurs and the probability that such contact will lead to an infection. This parameter (adequate contact rate) is extremely difficult to determine directly. The adequate contact rate can be disaggregated to its components which are: the vector: host ratio, host blood feeding rate, fraction of blood meals on hosts and probability of transmission of infection from an infectious mosquito/host to a susceptible host/mosquito given that a contact between the two occurs (Smith *et al.,* 2012). Disaggregation is more intuitive biologically, but mathematically more complex because of the need to quantify each of the component parameters.

The basic reproductive number, R_0, quantifies the inherent ability of an infectious agent to perpetuate itself in a host population. In the simplest case of a homogeneously mixing population, R_0 is defined as the expected number of secondary infections deriving from a single index case in a "totally susceptible" population (Anderson and May, 1991). R_0 is, therefore, a measure of the success of pathogen propagation into a population; if $R_0>1$, an outbreak is possible if the pathogen is introduced, whereas if $R_0<1$, propagation will fail. R_0 is a quantity that integrates all factors that determine

whether a pathogen can establish or not, in a weighted way as a product of two terms (Smith *et al.*, 2012):

$$madb_h * \frac{p^n ab_m}{-\ln p}$$

Where "*m*" is the mosquito-host ratio, "*a*" is the biting rate of a female mosquito, "*d*" is the duration of infectiousness in hosts; "*p*" is the daily survival probability of mosquitoes, and "*n*" is the duration of the extrinsic incubation period. The transmission parameters "*bm*" and "*bh*" quantify the probability of transmission from an infectious mosquito to a susceptible host and from an infectious host back to a mosquito, respectively. In total, the first term, "*m a d bh*", quantifies the number of mosquitoes expected to acquire infection from each infectious host. The second term

$$\frac{p^n ab_m}{-\ln p}$$

represents the probability that a mosquito, once infected, will transmit the agent to a susceptible host. This expression is often referred to as the "Ross-Macdonald expression" (Smith *et al.*, 2012). The basic reproduction number also indicates the amount of effort needed to control a disease in an area. This is because, in a susceptible population, each individual infectious host initially infects R_0 new individuals on average. Therefore, any intervention must prevent at least R_0–1 out of every R_0 infections to result in a reproduction number $R_0 \leq 1$ and control the infection.

That is, the critical efficacy of interventions in reducing transmission must be $\frac{R_0 - 1}{R_0} = 1 - \frac{1}{R_0}$.

2.5 Diagnosis

Clinical diagnosis in the absence of hemorrhagic or specific organ manifestations is non-specific and, therefore, definitive diagnosis of RVFV depends mainly on reliable laboratory tests. However, RVF may be suspected in animals when there is a sudden clinical picture of large sweeping abortion storms and significant mortality in adult livestock with newborn animal mortality approaching 100%. If these pointers are accompanied by a febrile illness with headache and myalgia in humans, further suspicion is raised. In the laboratory, diagnosis of RVF is carried out using the following techniques (1) virus isolation (Anderson *et al.,* 1989), (2) antigen detection (Meegan *et al.,* 1989), (3) nucleic acid amplification techniques (Ibrahim *et al.,* 1997), and (4) detection of specific antibodies (Swanepoel *et al.,* 1986).

2.6 Prevention and control

2.6.1 Vaccines

Following the initial isolation of RVFV in 1931, various vaccines against RVFV have been developed. There are two existing animal vaccines against RVFV - live-attenuated vaccines (SmithBurn, Clone 13 and MP-12) and inactivated vaccines. The first vaccine for RVF was developed in South Africa by attenuation of a field isolate (Entebbe isolate - Smithburn) by serial passages in mouse brains (Pepin *et al.,* 2010).

The vaccine is live and induces early and long-term immunity after a single injection (Pepin *et al.,* 2010). The use of the live vaccine is restricted – it is reported to induce certain teratogenic effects, abortions and stillbirths (Kamal, 2009). Rift Valley fever virus Clone 13 (CL13) is a safe and efficacious natural live attenuated RVFV mutant, which was isolated from a non-fatal human case of RVF (Office International des Epizooties, OIE, 2008). A recent randomized controlled field trial designed to assess the immunogenicity and safety of CL 13 found out that the mutant vaccine induces high levels of protective antibodies in sheep and goats (>90%) and moderate levels in cattle (65%) (Njenga *et al.,* 2015). The vaccine was deemed safe as none of the vaccinated animals developed evidence of RVF disease upon challenge including teratology (Njenga *et al.,* 2015). In addition, only 1 out of 120 pregnant animals had an abortion that was not associated with the RVF disease (Njenga *et al.,* 2015). The MP-12 vaccine was developed, via chemical mutagenesis of the RVFV, out of the need for a highly attenuated and safe RVF vaccine (Vialat *et al.,* 1997). The MP-12 is under development as both a human and veterinary vaccine (Ikegami and Makino, 2009).

Formalin-inactivated vaccines, though safe, have the disadvantage of cumbersome application in the field - they require 3 initial inoculations over a period of 1 to 2 months followed by annual booster inoculations due to its short duration of protective immunity (Barnard, 1979).

Apart from safety and efficacy issues in RVF vaccines, additional limiting factors in RVF immunization include (1) the reliance on a cold chain that challenges the efficient storage and delivery in low resource settings (Daouam *et al.*, 2014), (2) shorter vaccine shelf-life relative to the period between RVF outbreaks, and (3) harsh terrain that present logistical nightmares particularly when it floods (Consultative Group for RVF Decision Support, 2010). Research into new and improved vaccines in terms of safety, efficacy, thermo-stability, and longer shelf-life is needed for effective control of RVF using this strategy (Ikegami and Makino, 2009).

2.6.2 Vector control

Vector control programs principally include adult mosquito control and/or immature mosquito (primarily larva) control. Adult mosquito control is useful for a quick knockdown of adults, taking into consideration, their feeding and resting times and places. Strategies for vector control include directly targeting flying or resting adults with either thermal fogging or ultra-low volume (ULV) spraying, or by targeting resting adults through barrier spraying of vegetation or artificial substrates (Anyamba et al., 2010). Adult control can reduce RVFV transmission to animals and humans through reductions of mosquito-host contacts through reducing the number of progeny produced. Larval mosquito control reduces the adult emergence rate whether used prior to or after flooding. Control of larval mosquitoes can be achieved by applying insecticide to water habitats where mosquitoes develop. In flooded areas such as that occurs during RVF outbreaks, larval control can be achieved by spraying insecticides

by use of airplanes and helicopters (Anyamba *et al.*, 2010). There are no reports of effectiveness of vector control on RVF transmission patterns. However, immature control products, known as insect growth regulators (IGRs) such as methoprene in sustained release Altosid™ Pellets (Wellmark International, Schaumberg, IL), have been demonstrated to be effective in controlling both *Aedes* and *Culex* vectors of RVFV, even when placed into breeding habitats several months before flooding (Anyamba *et al.,* 2010).

2.6.3 Movement control

After confirmation of RVF outbreak in Kenya in 2006, the Department of Veterinary Services in Kenya implemented measures geared towards preventing further spread of RVFV through animal movement restrictions, closure of livestock markets and slaughter bans (Gachohi *et al.*, 2012). Risk assessments and related approaches such as pathway assessment and ranking have incriminated vector and animal movements as possible routes of RVF introduction and spread (Métras *et al.*, 2011). Genetic evidence of virus movements across Africa (Bird *et al.,* 2007) and from the East African mainland to Madagascar Island (Carrol *et al.,* 2011) has been reported. Animal surveillance should be implemented if animals are being moved, for different reasons, from established enzootic areas.

2.6.4 Integrated control

Integrated disease control involves use of at least two control methods in an optimal combination. Rift Valley fever integrated control has been successfully applied during the 1977–1979 epidemics in Egypt along the Nile River. The Israel government commenced with widespread vaccination and testing program in the Sinai Peninsula where greater than 1.2 million doses of inactivated RVFV vaccine were used. At the same time, movement control and destruction of infected animals and intensive vector control measures throughout the Sinai Peninsula and in the Gaza Strip were applied. These integrated measures successfully prevented the spread of RVFV northward into Israel (Klopfer-Orgad *et al.*, 1981).

CHAPTER 3

3.0 GENERAL MATERIALS AND METHODS

This chapter has two main sections: Community-based participatory research survey and the simulation model description.

3.1 Community-based participatory research survey

This section provides details on the study site and a general overview of the methods used in collection of the participatory data in the study site.

3.1.1 The study site

The study used Ijara sub-county situated in Garissa County (Figure 3.1). The sub-county was curved out of the then Garissa District in 2000. The area was selected because it is a key RVF hotspot in the country which often experiences RVF outbreaks. Indeed, since 1961, Ijara sub-county has experienced at least 4 RVF outbreaks in the years: 1961, 1962, 1997-98 and 2006-07 (Murithi *et al.,* 2010). In addition, a number of studies and intensive surveillance on the disease have been carried out there (Jost *et al.,* 2010; Munyua *et al.,* 2010). The sub-county lies approximately between latitude 10 7`S and 20 3`S and longitude 400 4`E and 410 32`E and covers an area of 9,642 km2 (Figure 3.1). The area is arid to semi-arid and it is inhabited by the Somali pastoralists who practice transhumance nomadism for their livelihoods. Approximately one quarter of the sub-county on the eastern side

bordering Somalia is covered by the Boni forest; the forest is an important resource for the local pastoralists who use it as the dry season grazing area.

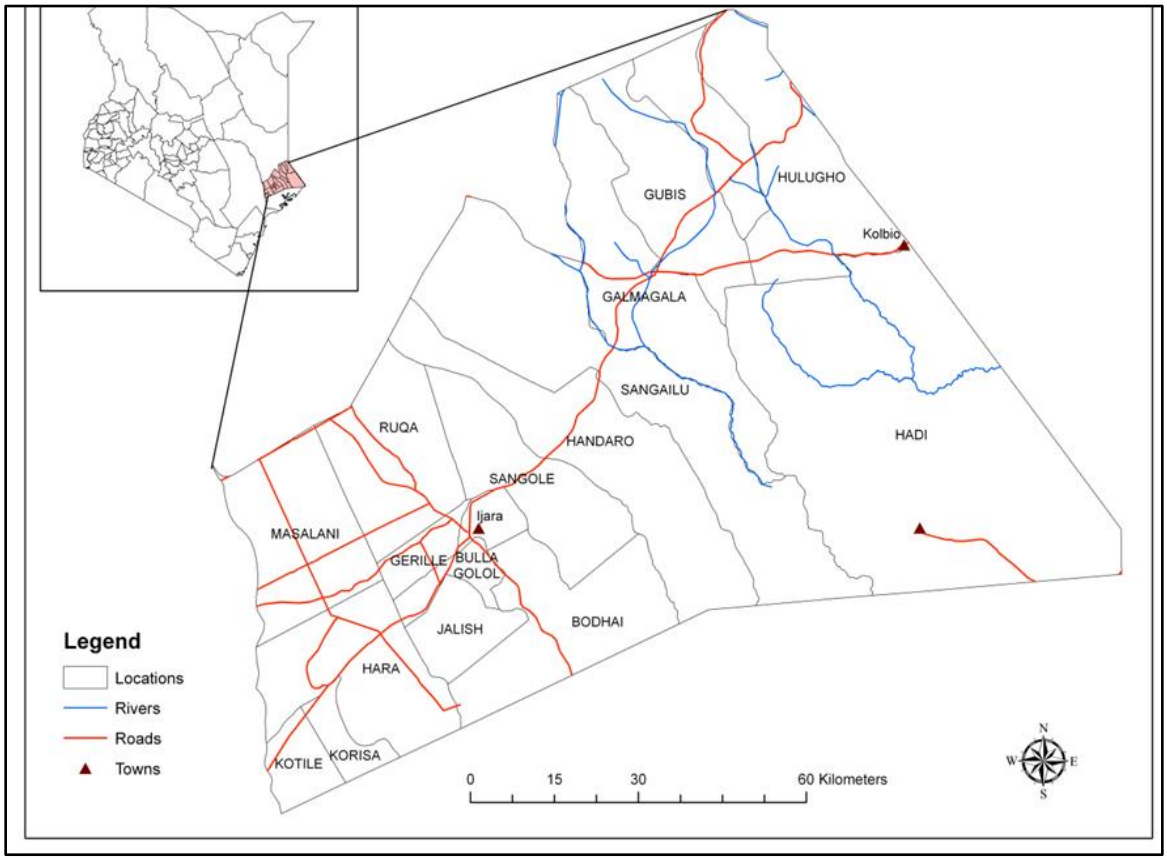


Figure 3.1: Map of Ijara Sub-county showing administrative locations, physical features and its location in Kenya.

The vegetation in the rest of the sub-county comprises of acacia shrubs, star and elephant grasses and is used mainly as the wet season grazing area. The altitude ranges between 0 and 90 metres above sea level and the topography is generally flat with scattered undulating plains. A large part of the sub-county is covered by black cotton and alluvial soils with lesser areas covered with sandy soils towards the coastal border. The western boundary of the sub-county is marked by the Tana River; its riverine

vegetation also serve as an additional dry season grazing area particularly for the small stock and cattle from the adjacent villages (GoK, 2009).

Ijara sub-county experiences low bimodal rainfall whose density ranges between 750 and 1000 mm per annum. Long rains occur between March and May while short rains occur between October and December. Temperatures range between 15 and 38^0C, though they tend to remain high throughout the year. Over 90% of the land in the sub-county is either trust or government land that is used by the local communities for pastoralism. The carrying capacity of the land is 15.5 tropical livestock units (TLUs)/hectare. The population size of cattle, sheep and goats was estimated at 352,617, 323,676 and 348,648 respectively in 2012 (sub-county Veterinary office, annual unpublished report, 2012).

3.1.2. Community-based participatory data collection

Participatory appraisals were held between August 2012 and February 2013 to collect information on livestock demographics and movement patterns. A sub-location, the smallest administrative area with a human population of 4,000 – 5,000 was used as the sampling unit. A total of 27 sub-locations were selected using a two-stage stratified random sampling technique from a sampling frame that comprised 40 sub-locations. A division was used as a stratifying variable. The sub-locations were proportionately selected based on the number of sub-locations per division. The total number of sub-locations per division and the number that were selected, in proportion to the number

of sub-locations per division, are outlined in Table 3.1. All divisions (n=6) were eligible for sampling.

Table 3.1: Total number and selected sub-locations by division in Ijara sub-county, August 2012 to February 2013

Division	Total number of sublocations	Number of selected sub-locations
Sangailu	8	4
Ijara	10	7
Masalani	13	11
Korisa	2	1
Kotile	5	3
Bodhai	2	1

One site within a sub-location was purposefully selected for an interview if it had a majority of households clustered in a small area. Each meeting comprised of at least 10 (mainly the local pastoralists and community leaders). These meetings were convened with the help of the community animal health workers and the local administrator, which in most cases was the Assistant Chief/Chief of the area. Each session ran between 1 and 2 hours and interviews were conducted using the local Somali language with the help of a translator. Interviews were guided by a checklist of open-ended questions (Appendix 1). Meeting sites were geo-referenced after the interview using the Arc 1960 Geographic Coordinate System. Figure 3.2 shows the distribution of these sites within the sub-county.

Participatory epidemiological (PE) techniques used in the surveys included semi-structured interviews, proportional piling and participatory mapping. These techniques have been described by Catley and Mariner (2002) and used in a pastoral ecosystem in

Kenya (Bett *et al.*, 2009). Table 3.2 outlines the specific information gathered using each of these methods.

Semi-structured interviews

Semi-structured interview is a guided interview where only some of the questions are predetermined and new questions come up during the interview. A checklist (Appendix 1), rather than a questionnaire, of important points was used.

Proportional piling

Proportional piling is a scoring technique used to determine perceptions on the relative importance, abundance or frequency of a list of items. It uses a set of counters (e.g. beans, pebbles, etc.) that are piled against a given item and then counted to determine relative percentages or proportions (Catley and Mariner, 2002). This survey used a total of 100 beans for all the exercises conducted.

Participatory mapping and timelines

Participatory mapping is a visualization method in PE that provides any spatial information of interest but particularly on livestock distribution, movement, interactions, diseases and disease vectors.

Table 3.2: A summary of the type of information collected using each of the three PE techniques during participatory surveys conducted in Ijara sub-county, August 2012 to February 2013

Participatory technique	**Information gathered**
Semi-structured interviews	Types of livestock species kept Classification of age categories Age at first breeding Interval between parturition and subsequent heat Frequency of repeat breeding Frequency of twinning Determining the age ranges in each age category Lifespan, by sex Cattle herd and sheep/goat flock sizes
Proportional piling	Relative abundance of livestock species Proportion of pregnancies carried to term (% of abortions) Mortality and case fatalities by age group and season Proportion of animals sold and slaughtered by season Relative incidence and case fatality rates of livestock diseases
Participatory mapping and timelines	Location of settlements and seasonal grazing sites Livestock movement patterns between July 2011 and July 2012

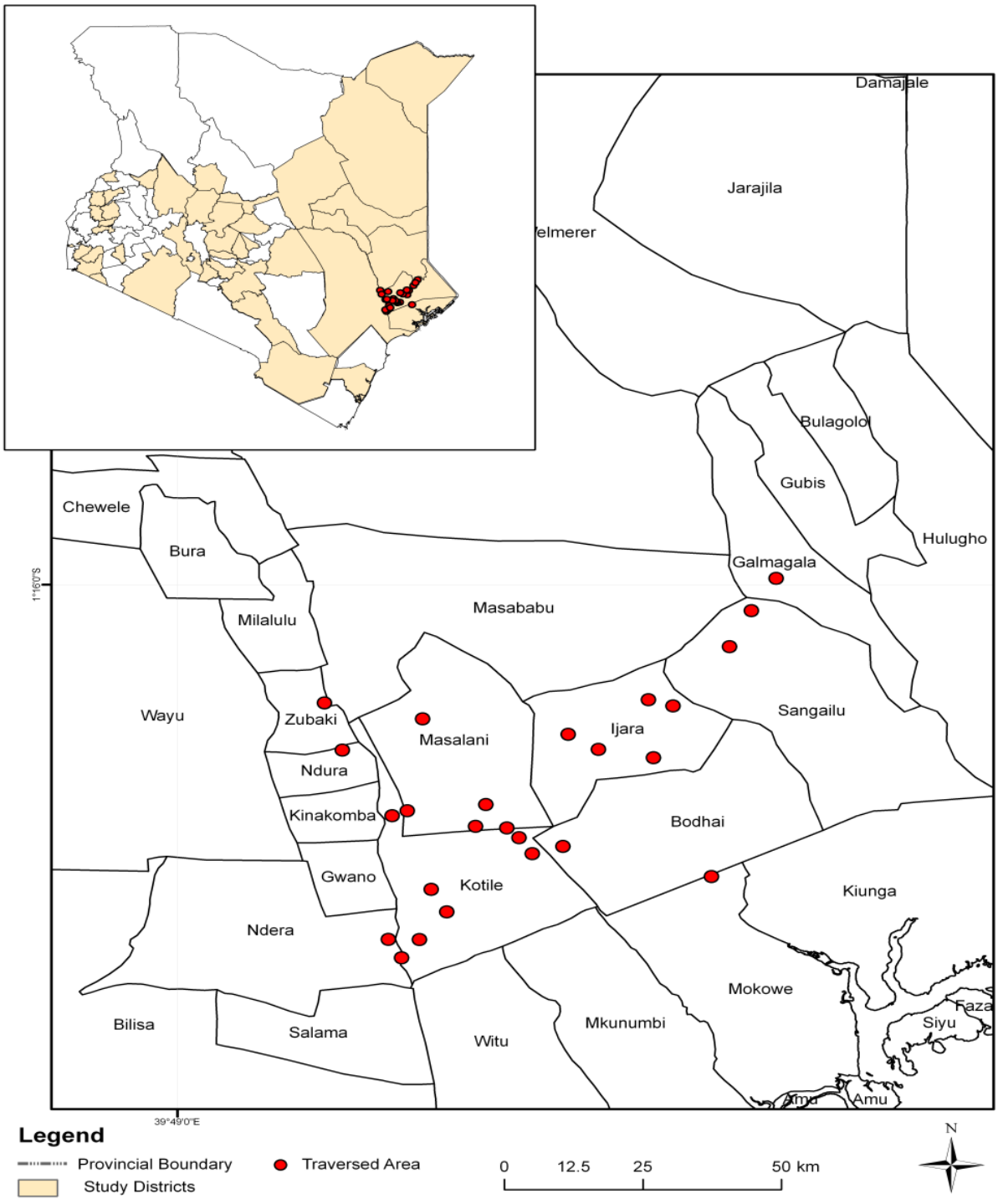


Figure 3.2: Map of Ijara sub-county showing the locations of villages surveyed in the study.

3.2 Model description

3.2.1 Overview of the model

The model contains host and vector modules implemented in a spatial landscape made up of 10,000 square grid cells each measuring 500mx500m, representing an area of 2,500km^2. Hosts were represented as individuals while the vector population was modeled using difference equations. The vectors' population growth used probability functions that utilized daily rainfall obtained from Tropical Rainfall Measuring Mission (TRMM). The TRMM is a joint project between the National Aeronautics and Space Administration (NASA) and the Japan Aerospace Exploratory Agency (JAXA) unveiled in November 1997 to monitor tropical rainfall (Kummerow *et al.,* 2000). All the model processes were programmed using C++ language in Borland Builder 6.0. The model ran in discrete time steps, with each step simulating all the processes that took place within a day. One run was implemented to run for 1200 days. This was the period in which data on daily precipitation and RVF cases in livestock that were used to generate the functions was available. This period included the recent 2006/7 outbreak in the study area.

In developing the model, the following assumptions were made:

1. One time step denoted a day. The model had two modules – host and vector modules. The host module comprised of two host species (cattle and sheep) and was implemented using an individual-based approach. The vector module

comprised of two mosquito species (*Aedes* and *Culex* spp) and was implemented using difference equations.

2. The model was developed based on data and some of the knowledge that had been gathered from Ijara Sub-county, Kenya. The area is an RVF endemic site and was one of the epicenters during the last two outbreaks (1997/1998 and 2006/2007). Rainfall data used in the model were extracted from Tropical Rainfall Measuring Mission (TRMM) based on the GPS coordinates for 17 high risk sites in the area for the period June 2006 to June 2007 to include the outbreak period between November 2006 and April 2007.
3. The ratio of cattle to sheep was 1:2. This was based on livestock census data collected in 2012 which estimated the populations of cattle, sheep and goats at 352,617, 323,676 and 348,648 respectively in the target area (District Veterinary office, annual report, 2012). Sheep and goat populations were combined and represented as sheep. Hosts were classified into four age groups (young, weaner, yearling and adult groups) while vectors were classified into eggs, larvae, pupae and adults. In modeling the population dynamics, hosts and vectors were subject to constant daily mortality rates.
4. RVFV transmission is thought to involve primary and secondary vectors. Primary vectors, which mainly comprise of floodwater *Aedes mcinthoshi*, are believed to act as reservoirs for RVFV as infected mosquitoes can transmit the virus transovarially. Trans-ovarial transmission of the virus in infected *Aedes* species ensures that a proportion of mosquitoes emerges as infected adults and

can, therefore, initiate transmission in livestock as they take their blood meals. Secondary vectors, on the other hand, include *Culex* species, *Mansonia* species, other mosquito species and certain biting flies. The secondary vectors lay their eggs directly on water, and therefore, require stagnant water bodies for breeding. Such breeding environments always develop in flat or shallow depressions following increased precipitation and persistent flooding. The secondary vectors get infected when they feed on infectious livestock. When large populations of susceptible livestock are available, RVFV transmission is amplified by the secondary vectors as they take their blood meals. The model tracked all these processes including the primary and secondary RVFV transmission events by *Aedes* spp and *Culex* spp, respectively. Trans-ovarial transmission of the virus in *Aedes* species was not modeled explicitly. In addition, *Culex* spp. was assumed to represent all the secondary vectors of RVFV.

5. In modeling mosquito infection dynamics, the vector population was divided into susceptible, exposed and infectious segments (S-E-I model). Susceptible vectors represented the proportion that can become infected if they ingest blood from an infectious host. Exposed vectors were infected with the virus but not yet capable of transmitting the virus to a susceptible host until a latency period had elapsed. Infectious vectors were capable of transmitting the virus to a susceptible host and infectious vectors remained infected for life. Super infections were ignored.

6. In modeling host infection dynamics, the individual-based epidemiological modeling was based on the following assumptions: (1) individual hosts were different; (2) individuals interacted with each other locally; (3) individuals were mobile; and (4) the environment for individuals was heterogeneous.
7. In modeling individual host infection states, a host could be either in the susceptible, exposed, infectious and recovered segments (S-E-I-R model). The susceptible state represented the state in which the host could become infected if an infectious vector fed on a host. The exposed state represented the state in which the host was infected with the virus but not yet capable of transmitting the virus for a defined period of time, i.e. the latent period. The infectious state represented the state in which the host was capable of transmitting the virus to a susceptible vector. Infectious hosts suffered an additional RVF-induced mortality but if they recovered from the infection, they remained immune.
8. Infectiousness was assumed to be constant during the infectious periods in hosts. Super infections in the hosts were ignored.
9. In the model, the susceptibility to RVFV of the two host species considered was assumed to be constant. However, in parameterizing RVF-induced mortality, the case fatality rates for the young animals were differentiated from those of the adults, yearlings' weaners and young ones.
10. The duration of the latent periods in both host species was assumed to be similar.

11. The duration of the infectious periods in both host species was assumed to be similar.
12. *Aedes* mosquito spp can draw blood meals from each host at equal proportions.
13. *Culex* mosquito spp can draw blood meals from each host at equal proportions.

3.2.2 The model landscape

Grid cells were used to permit the representation of spatial heterogeneities in the model through the variation of (i) the locations of vector breeding sites, and (ii) host movement patterns associated with transhumance pastoralism where animals are moved depending on pasture and water availability. For the purposes of the analyses, the grid was randomly populated with two kinds of mosquito breeding sites: (i) a total of 50 breeding sites for *Aedes* and *Culex* species and (ii) 3000 sites for *Culex* species. More *Culex* species sites were included in the model to mimic flooding conditions and generate larger *Culex* population than *Aedes* population.

3.2.3 The host module

Two hosts – cattle and sheep – were considered in the model. Sheep represented the highly susceptible species and cattle the moderately susceptible species. As the outcome of the disease in sheep and goats is not markedly different, the sheep in the model represents goats. This avoided complicating the model with three host species. In essence, the census population of sheep and goats were combined to one species. The host module simulated the hosts' (i) population dynamics, (ii) their movement

patterns across the grid cells, and (iii) their RVFV exposure patterns (specifically from infectious vectors). The host module was driven by static and dynamic rules that track essential ecological processes that influence RVFV transmission based on the input parameters illustrated in the Chapter 2.

Static rules and module initialization

Species: hosts were classified into two species -- cattle and sheep -- and both were represented in the model as individuals.

Age: each host was initially allocated age in days (see below); they were further classified into four age categories that included neonates, weanlings, growers and adults based on the allocated ages as per population structures obtained from empirical data collected during participatory epidemiology survey in the study site (Figure 3.3).

Sex: the sex of a host was defined according to host structure obtained from the empirical data collected during participatory epidemiology survey in the study site (findings detailed in Chapter 4). The model was initialized with a female to male ratio of 7:3 in cattle and 6:4 in sheep respectively.

Physical location: hosts occupied explicit locations on the grid (Plate 3.1.). Herds/flocks were randomly distributed on the grid. The model was initialized with 100 herds each comprising 30 cattle and 100 flocks each comprising 60 sheep. This

approximately scaled down the actual livestock population census of Ijara sub-county (refer to the section on "Introduction and study site" on livestock census) by 100.

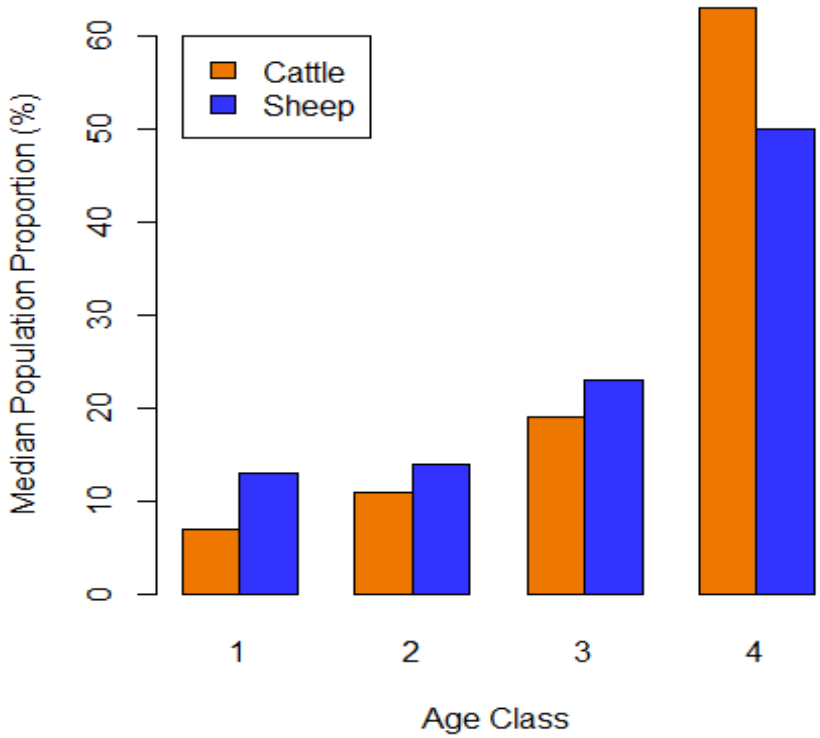


Figure 3.3: Median proportions of the hosts' age classes (1-neonates, 2-weanlings, 3-growers and 4-adults) by species. The age ranges for each class in cattle are: neonates (0 to 4 months), weanlings (5 months to 1 year), growers (1 to 2 years) and adults (>2 years) while in sheep are: neonates (0 to 2 months), weanlings (3 months to 6 months), growers (7 months to 1 year) and adults (>1 year).

Infection status: at the end of each day, a host was classified into one of the four successive states depending on RVFV exposure status. These states were: (i) susceptible - a host that had not been exposed to the virus and, therefore, had a chance of contracting an infection following exposure, (ii) exposed - a host that had an infection but not yet capable of transmitting the virus, (iii) infectious - an infected host that was capable of transmitting the virus, and (iv) recovered – a host that had

recovered from the infection and attained a life-long immunity. Infectious bites on hosts in the exposed and infectious stages did not result to superinfections and they, therefore, got “wasted”. Similarly, any infectious mosquito bites on recovered hosts got "wasted". All hosts were assumed to be susceptible at the start of simulations and at the time of entry through births.

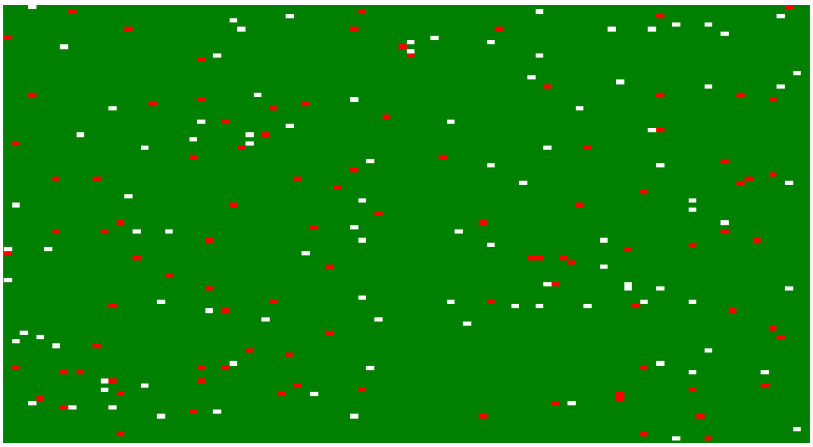


Plate 3.1: A snapshot of the model grid visualizing physical random locations of hosts on a particular day. (The red spots represent 100 cattle herds while the white spots represent 100 sheep flocks)**.**

Reproduction status: At the beginning of a simulation, each female animal of breeding age (see below) was randomly assigned to each of the three reproductive categories with a probability of 0.33. The categories included non-pregnant, pregnant and perinatal. The dynamic rules controlling reproduction are detailed below.

Dynamic rules

Entry of hosts into the population

New hosts were introduced into the simulation through births only. The model tracked the entire reproduction cycle beginning with conception, gestation and perinatal period. This tracking allowed for realistic prediction of the frequency of births. *Rules:* Female cattle and sheep could not breed before they have fully matured and attained their respective breeding ages: cattle – 2 years and sheep - 8 months – according to the data obtained though participatory epidemiology techniques in the study site (Chapter 4). Non-pregnant hosts were open to conceive any day if conception rules were met. Pregnant hosts were subject to a gestation counter (see below). Once the gestation period was completed, the host gave birth to a young one. Hosts in the perinatal category were subject to a perinatal counter (see below). Once the perinatal period was accomplished, the host became open to conceive any day if conception rules were met. Rift Valley fever-diseased hosts could not conceive during exposed or infectious periods.

Conception probabilities (Table 3.3.) were simply derived from inter-parturition intervals calculated as follows: cattle have an average gestation period of 285 days and a calving to conception period (perinatal period) of 180 days (according to data collected during participatory epidemiology survey in the study site) (Chapter 4): thus, the probability of conception (*CpCo*) was (1/ (285+180)); sheep, on the other hand, have an average gestation period of 150 days and a lambing to conception period (perinatal period) of approximately 90 days; thus, the probability of conception (*CpSo*) was (1/ (150+90)). This study further assumed that the actual conception

probability (*CpC* for cattle and *CpS* for sheep) were globally density-dependent on a carrying capacity (*CCC* for cattle and *CCS* for sheep) (Table 3.3.) and obeyed the following relation:

Cattle: $CpC = CpCo * \exp(1-(\text{current cattle population}/CCC))$ (Equation 1)

Sheep: $CpS = CpSo * \exp(1-(\text{current sheep population}/CCS))$ (Equation 2)

Table 3.3: Host conception and carrying capacity parameters

Parameter	**Symbol**	**Value**	**Source**
Cattle conception probability	*CpCo*	0.00215	This study
Sheep conception probability	*CpSo*	0.00417	This study
Cattle carrying capacity	*CCC*	3000	arbitrary
Sheep carrying capacity	*CCS*	6000	arbitrary

It followed that, when the number of hosts of a given species was less than the carrying capacity, the conception probability was higher than the natural probability and *vice versa*. New born hosts were added to the dam's herd/flock and assigned age 1 day and randomly classified as being either a male or a female with a probability of 0.5. Following birth, the dam entered the calving to conception period (perinatal period) during which it nursed the young one. Upon completion of this period, the host became open for the subsequent conception.

Aging of host

Each host's age was incremented by 1 day. Following attainment of the specified ages for each age class (Figure 3.3), the host made a transition to the subsequent age class. The age ranges for each class in cattle were: neonates (0 to 4 months), weanlings (5 months to 1 year), growers (1 to 2 years) and adults (>2 years) while in sheep are:

neonates (0 to 2 months), weanlings (3 months to 6 months), growers (7 months to 1 year) and adults (>1 year).

Exits of the host from the population

Hosts exited from the simulation depending on their age, species and sex. *Rules:* For simplicity, only adult cattle older than 3 years and adult sheep older than 1 year exited from the simulation. This assumption allowed the attainment of a stable population with approximately similar age structure as the one shown in Figure 3.3. Following the study area's socio-economic trends (from participatory epidemiology techniques), the exit probability of male hosts was assumed to be double those of female hosts for both livestock species. This concept reflected the higher turnover of male animals attributable to slaughter and sale offtakes. In addition, sheep had higher population turnover associated with higher fecundity rate, off-take, replacement rate and shorter lifespan relative to cattle and, therefore, their exit probability was reasonably higher. In addition, male and female cattle were not allowed to remain in the simulation beyond 5 and 8 years of age, respectively. Male and female sheep were disallowed to remain in the simulation beyond 4 and 6 years of age, respectively. This information was obtained from empirical data collected during participatory epidemiology survey in the study site (Chapter 4). The population dynamics model was initially run for five years to verify that the population structure was stable before transmission module was permitted to run.

Abortions by the hosts

Not all successful conceptions were carried to the full term of pregnancy. Abortion can occur at some expected background frequency (due to inter-current infections or other environmental stresses) or at an increased frequency following the occurrence of RVF outbreak (RVF-induced abortions). The frequency of RVF-induced abortion was expected to be higher in sheep than cattle because this livestock species is more susceptible to the disease. *Rules*: Pregnant cattle and ewes could experience abortion at any stage of pregnancy with probabilities Ab_c and Ab_s, respectively (Table 2.4 in Chapter 2). Infectious RVF-infected cattle and sheep aborted at any stage of pregnancy with probabilities Ab_{cRVF} and Ab_{sRVF} respectively (Table 2.4 in Chapter 2). The abortion related parameters used in the model were obtained from data collected by participatory techniques from the livestock keepers in the study area immediately after the 2006/7 RVF outbreak (Jost *et al.*, 2010).

Movement patterns by the hosts

Host movement was modelled explicitly by generating a series of coordinate positions in the grid that mimicked the movement of hosts. The spatial-temporal seasonal movement patterns were elucidated from a participatory mapping survey in the study area (Chapter 4). *Rules*: Cattle herds covered a daily random distance range of between 0.5 and 10km. During these movements, the destination site selected could or could not have been a mosquito breeding site. Host vector contacts leading to potential transmission of the virus occurred when susceptible hosts randomly selected a

mosquito breeding site holding infectious mosquitoes and/or when infectious hosts reached a mosquito breeding site holding susceptible mosquitoes. Sheep flock movement patterns were simulated in a similar manner. Sheep moved a random distance range of between 0.5 and 4.5km a day. Appendix 2 shows the summary code implemented for the rules described in the host module.

3.2.4 The vector module

This module simulated vectors' (i) population dynamics in a life-stage structured compartmental model using difference equations, and (ii) RVFV exposure patterns from infected hosts. For each mosquito species, the population dynamics of both aquatic (immature) and adult stages were simulated explicitly using different probability functions that were dependent on rainfall. The daily rainfall estimates were obtained from TRMM processed for 17 areas in the study site during the 1200 days in which data on RVF cases in livestock were available. The daily precipitation estimates over all the sites were averaged to obtain a single mean value that was used to generate the probability functions for each mosquito vector species.

3.2.4.1 Aedes species population dynamics

The model ran in discrete time steps of one day where $Eg_{brd(t)}$, $Lv_{(t)}$, $Pp_{(t)}$ and $Ad_{(t)}$ denoted the number of *Aedes* species per life stage, i.e. buried eggs in the soil, larvae, pupa and adults, respectively. As stated earlier on, it was assumed that there are 50 breeding sites for *Aedes* species in the grid. In each of the 50 breeding sites for *Aedes*

species in the grid, 160 "clean" *Aedes* eggs (non-infected with RVFV) and 40 "infected" *Aedes* eggs (infected with RVFV) were deposited in the soil. The infected eggs arbitrarily constituted 20% of all buried eggs. This proportion was borrowed from field studies in Rajasthan, India, that found that up to 20% of *Aedes aegypti* and *Aedes albopictus* larvae tested positive for dengue virus (Angel and Joshi, 2008). The first step in the breeding process was the hatching of buried eggs to larvae when conditions become suitable. The complete set of the difference equations that execute population dynamics, via mortality and development to the subsequent life stage, was given by:

$$Lv_{(t+1)} = Lv_{(t)} + (Eg_{brd(t)*} H_A) - (Lv_{(t)}* \mu_{Al}) - (Lv_{(t)}* E_A);$$

$$Pp_{(t+1)} = Pp_{(t)} + (Lv_{(t)}* E_A) - (Pp_{(t)}*\mu Ap) - (Pp_{(t)}*F_A);$$

$$Ad_{(t+1)} = Ad_{(t)} + (Pp_{(t)}* F_A) - (Ad_{(t)}* \mu Aa);$$

$$Eg_{brd(t+1)} = Eg_{brd(t)} + (Ad_{(t)*}S_A)*J_{A;} \qquad \text{(Equation 3)}$$

Table 2.5 (in Chapter 2) illustrates parameters related to *Aedes* species. Hatching of buried *Aedes* eggs used a fuzzy logic approach. The reasoning behind using fuzzy logic approach was as follows: *Aedes* adult mosquitoes lay their eggs along the edges of breeding sites where they mature and hatch only when more than six days of dry conditions are followed by total inundation from a rainfall event (Vignolles *et al.*, 2009). At the beginning of a rainy season, *Aedes* mosquito population quickly grows. However, if rains become persistent with extensive flooding over time, *Aedes* populations decline due to the unavailability of suitable breeding ecological niche, that

is, lack of dry conditions for egg maturation. There can be, therefore, a second peak in *Aedes* mosquito densities at the end of the rainy season particularly if there is a gap in rainfall for several days (Chitnis *et al.,* 2013). Considering these breeding characteristics, a simple fuzzy distribution model comparable to that implemented by Emert *et al.* (2011) was implemented. However, Emert *et al.* (2011) applied cumulative rainfall as input of oviposition in their malaria transmission study.

In the RVF model, accumulated rainfall was used as an input for hatching of buried *Aedes* eggs. The principle works as follows: (1) none or a small number of *Aedes* eggs hatch under small amounts of rainfall (Vignolles *et al.,* 2009), (2) total inundation of breeding sites with water leads to a very high hatching rate of the eggs (Linthicum *et al.,* 1983), and (3) there is a decline of adult numbers once extensive flooding persist. A study by Linthicum *et al.* (1983) on temporal emergence of primary (*Aedes*) and secondary (*Culex*) species is evidence of this principle. The fuzzy logic model, therefore, distinguished between dry unsuitable conditions (threshold $\cup 1$), a most suitable condition (S), and unsuitable conditions due to very high rainfall and flooding (threshold $\cup 2$). The fuzzy distribution model computed proportions between 0 (unsuitable conditions, $\cup 1$ and $\cup 2$) and 1 (most suitable condition, S). Several scenarios representing 3, 7, 14 and 21 days accumulated daily rainfall obtained from TRMM for the study area with the different threshold parameters for each scenario were generated. A 21-day cumulative rainfall ($R\Sigma 21d$) with $\cup 1 = 0$, S = 5 and $\cup 2 = 8$ generated a reasonable function that linked with the function that propelled

secondary (*Culex* species – see below) vectors. The fuzzy suitability (*f*) of $R\Sigma 21d$ was computed by means of a sigmoidal curve as follows (Emert *et al.*, 2011):

if $U_1 < R\Sigma 21d < S$

$$(f)\ R\Sigma 21d = 1 - \cos^2\left(\frac{R\sum 21d - \bigcup_1}{S - \bigcup_1}\frac{\Pi}{2}\right)$$

else, if $S < R\Sigma 21d < \bigcup_2$

$$(f)\ R\Sigma 21d = cos^2\left(\frac{R\Sigma 21d - S}{\bigcup_2 - S}\frac{\Pi}{2}\right)$$

else

$(f)\ R\Sigma 10d = 0.$ (Equation 5)

The number of hatching buried eggs which formed the basis of the modelled *Aedes* population was determined by the multiplication of the hatching rate with the respective value of the fuzzy function as follows:

$Lv_{(t+1)} = Lv(t) - (Lv(t)^* \mu_{Al}) - (Lv(t)^* E_A)^* \{(Eg_{brd}(t)^* H_A)^* (f)\ R\Sigma 21d\ \}$; (Equation 6)

Aedes eggs have high desiccation resistance and can survive dry conditions in a dormant state for months to years (Linthicum *et al.*, 1983; Linthicum *et al.*, 1985) though the actual mortality rate of the buried eggs is unknown. In the model, a density-dependent function that capped the daily numbers of buried eggs equal to the initial value was inserted. This was done to ensure that the eggs that hatch, at any particular time, were dependent on the value of the fuzzy function alone. Movement of

hosts into a site with adult *Aedes* species increased chances of the vector successfully obtaining a blood meal required for oviposition. As these sites harbored both "clean" and "infected" *Aedes* mosquitoes, transmission of RVFV was possible (see details in transmission module below).

3.2.4.2. Culex species population dynamics

Normally, *Culex* species population grows following extensive and persistent flooding. This scenario was mimicked in the model by randomly populating the grid with 3000 grid cells each with 5000 *Culex* eggs. Reports in the literature indicate that the population densities of this and other secondary vectors increases tremendously when precipitation and flooding persists for more than 21 days (Linthicum *et al.*, 1983). To generate large populations of *Culex* species in the model, the distribution of rainfall (from TRMM) in the sites that were affected by RVF in the 2006/7 over a one year period (July 2006 to June 2007) was analyzed in an attempt to identify a rainfall pattern that best represented the high risk period that fell between November 2006 and February 2007. Rainfall patterns examined included:

- Running cumulative values over 7, 14, 21 and 28 days
- Cumulative number of wet days, where a wet day was day i when the cumulative rain (for each of the scenarios identified above) exceeded 2, 4, 6, 8 or 10 mm.

Thus, a total of 4 x 5 scenarios representing cumulative rainfall values by cumulative number of wet days were generated. A dummy variable indicating presence/absence of

an outbreak was also derived and used as an outcome variable in a logistic regression model that had cumulative rainfall and the number of wet days as predictors. The model that gave the best fit (determined by the least log likelihood estimate) was used to generate probability values for defining the suitability of environmental conditions for *Culex* species development, and hence the amplification of RVFV transmission. The logistic regression model structure was as follows:

$$\ln\left(\frac{P}{1-P}\right) = \beta_o + \beta_1 x_1 + \beta_1{}^2 x_1 + \beta_2 x_2 + \beta_2{}^2 x_2 . \qquad \text{(Equation 7)}$$

These parameters are described in Table 3.4.

Table 3.4: Logistic regression model parameters used to grow *Culex* species mosquitoes

Description	**Symbol**	**Value**
Logistic model constant	β_o	-8.810176
Coefficient for the 28-day cumulative rainfall variable	β_1	0.5235267
Coefficient for the 28-day cumulative rainfall variable squared	$\beta_1{}^2$	-0.0181538
Daily value for the 28-day cumulative rainfall	x_1	Daily value from data
Coefficient for the counter variable	β_2	0.1695463
Coefficient for the counter variable squared	$\beta_2{}^2$	-0.0010245
Daily value of the counter variable	x_2	Daily value from data

The probability estimates (*p*) used to weight the number of *Culex* eggs that hatch in a grid cell in a day in the simulation model was derived as follows (Dohoo *et al.*, 2003):

$$\frac{e^{\left(\beta_o + \beta_1 x_1 + \beta_2{}^2 x_1 + \beta_2 x_2 + \beta_2{}^2 x_2\right)}}{1 + e^{\left(\beta_o + \beta_1 x_1 + \beta_2{}^2 x_1 + \beta_2 x_2 + \beta_2{}^2 x_2\right)}} \qquad \text{(Equation 8)}$$

The complete set of difference equations that executed population dynamics taking account of mortality during each stage and development to the subsequent life stage was given by:

$$Eg_{(t+1)} = Eg_{(t)} + (Ad_{(t)*}S_C) - (Eg_{(t)*}H_C)$$

$$Lv_{(t+1)} = Lv_{(t)} + (Eg_{(t)}*H_C) - (Lv_{(t)*}\mu_{Cl}) - (Lv_{(t)*}P_C);$$

$$Pp_{(t+1)} = Pp_{(t)} + (Lv_{(t)}*P_C) - (Pp_{(t)}*\mu Cp) - (Pp_{(t)}*E_C);$$

$$Ad_{(t+1)} = Ad(t) + (Pp(t)*E_C) - (Ad(t)*\mu C_a); \quad \text{(Equation 9)}$$

The number of hatching eggs which formed the basis of the modelled *Culex* population was determined by the multiplication of the hatching rate with the daily predicted probability (p) estimated by the above logistic regression model as follows:

$$Eg_{(t+1)} = Eg_{(t)} + (Ad_{(t)*}S_C) - \{(Eg_{(t)*}H_C)*p\} \quad \text{(Equation 10)}$$

Naturally, there is no vertical transmission of RVFV in *Culex* mosquitoes and, therefore, the model was initialized with "clean" (susceptible) *Culex* mosquitoes alone. Infection of *Culex* mosquitoes in the model was entirely as a result of movement of RVFV-infected hosts into a site with adult "clean" (susceptible) *Culex* species upon successfully obtaining a blood meal. Ingestion of a blood meal was required for oviposition to occur. To prevent uncontrollable population explosion, a density-dependent function was incorporated in the egg laying stage. These parameters are described in Table 2.5 in Chapter 2.

3.2.5. The Rift Valley fever virus transmission module

Vector to host transmission

The probability of a host becoming infected following a bite by an infectious mosquito was computed from the force of infection computed as a product of:

1. *Vector biting rate*, estimated as an inverse of the feeding interval in a species (G_A or G_C) (Table 2.5 in Chapter 2).
2. *Host infectivity* i.e. probability of infected mosquito producing an infection in a host following a bite: Data on age- and host-species specific infectivity was unavailable. A single host infectivity parameter for all ages and species was used (Table 2.6 in Chapter 2).
3. *Vector-host ratio*: this was a daily model-generated parameter computed by dividing the population of a given vector species by a given host species.
4. *Vector blood meal index* is a measure of the proportion of blood meals obtained by a given vector species from a specific host species. The values of these parameters were not available in literature. For the purposes of these analyses, vectors were assumed to obtain the same proportion of blood meals from the two host species, i.e. no host preference was assumed. *Aedes* species tend to remain in the immediate vicinity of the larval habitats and only feed during the day, at dusk and at dawn (Pepin *et al.,* 2010). Linthicum *et al.* (1985) reported that the overall mean distance travelled by female *Aedes lineatopennis* in the 44 days after emergence was 0 – 150 metres only. On the other hand, the more nocturnal *Culex* species are more likely to disperse to

find vertebrate hosts to feed on, leading to extensive dissemination of RVFV (Pepin *et al,* 2010). Subra (1981) in an extensive account of the biology of *Culex pipiens quinquefasciatus*, a competent vector of RVFV in Africa (Pepin *et al,* 2010), reported minimum flight ranges of 500-600m and more frequently around 1km and a maximum of 8km in Réunion Island. For these reasons, the proportion of blood meals obtained by *Aedes* species from domestic hosts was assumed to be much smaller relative to that obtained by *Culex* species, (Table 2.6 in Chapter 2), that is, more *Aedes* blood meals were assumed to be distributed among RVF non-competent hosts.

5. Rift Valley fever virus prevalence in the vector: this is a daily estimate of the proportion of infectious vectors for a given species in the population.

The composite force of infection for a given host was simply the sum of the force of infection derived from each vector species as follows:

Force of infection to cattle = (*Aedes* biting rate*cattle infectivity**Aedes*:cattle ratio**Aedes* blood meal proportion from cattle* RVFV prevalence in *Aedes*) + (*Culex* biting rate*cattle infectivity**Culex*:cattle ratio* *Culex* blood meal proportion from cattle* RVFV prevalence in *Culex*).

NB: The first term in the equation was the force of infection from infectious *Aedes* population whereas the second term was the force of infection from infectious *Culex* population.

Force of infection to sheep = (*Aedes* biting rate* sheep infectivity**Aedes*:sheep ratio**Aedes* blood meal proportion from sheep * RVFV prevalence in *Aedes*) + (*Culex* biting rate* sheep infectivity**Culex*:sheep ratio* *Culex* blood meal proportion from sheep * RVFV prevalence in *Culex*).

NB: The first term in the equation was the force of infection from infectious *Aedes* population whereas the second term was the force of infection from infectious *Culex* population.

The composite force of infection was then simply converted into a probability scale using the following equation:

Probability = 1-(exponential (-composite force of infection)) (Equation 11)

Host infection aging

Host infection aging code served as a counter that calculated the cumulative number of days a host has been in a given infection stage. For example, for an individual host, following a successful exposure to the infection, the aging process for the latent period commenced with the increment of number of days since exposure by 1 day; this calculation was effected at the end of each day. The host transited to the infectious stage when the command returned an equivalent number of days as the latent period (L_C and L_S for cattle and sheep respectively, Table 2.6 in Chapter 2). The same process was repeated when the host was in the infectious stage and the host transited to the recovered stage when the infectious period (i_C and i_S for cattle and sheep respectively,

Table 2.6 in Chapter 2) elapsed. These periods were assumed to take similar durations in sheep and cattle. Infectiousness in hosts was assumed to be constant during the entire infectious period. Hosts suffered RVF-specific mortality during the infectious period. This mortality depended on the age and the species of the host (Table 2.6 in Chapter 2). The end of the infectious period marked the beginning of immune phase that continued until the host died or the simulation was terminated. Immune hosts did not contribute to the transmission of the virus.

Host to vector transmission

The force of infection for the host-to-vector transmission of the virus was a product of:

1. *Vector biting rate*
2. *Vector infectivity* – this is assumed to vary by species (Table 2.6)
3. *Vector blood meal index*.
4. *RVFV prevalence in the host*: the proportion of infectious hosts in the population.

The overall daily force of infection for each vector species was the sum of the host specific force of infection as follows.

Force of infection to *Aedes* = (*Aedes* biting rate* *Aedes* infectivity**Aedes* blood meal proportion from cattle* RVFV prevalence in cattle) + (*Aedes* biting rate* *Aedes* infectivity* *Aedes* blood meal proportion from sheep* RVFV prevalence in sheep)

NB: The first term in the equation was the force of infection from infectious cattle population whereas the second term was the force of infection from infectious sheep population.

Force of infection to *Culex* = (*Culex* biting rate* *Culex* infectivity* *Culex* blood meal proportion from cattle* RVFV prevalence in cattle) + (*Culex* biting rate* *Culex* infectivity* *Culex* blood meal proportion from sheep* RVFV prevalence in sheep)

NB: The first term in the equation is the force of infection from infectious cattle population whereas the second term is the force of infection from infectious sheep population.

Following a successful exposure to the virus, vectors transited to the exposed state (Table 2.6 in Chapter 2). The virus underwent biological development and as soon as it infected the mouth parts, the infected mosquito was capable of transmitting the virus to the susceptible hosts. Infected vectors remained so for life.

CHAPTER 4

4.0 A COMMUNITY-BASED PARTICIPATORY STUDY TO ESTIMATE PARAMETERS FOR THE RIFT VALLEY FEVER MODEL

4.1 Introduction

Pastoral communities possess a wealth of knowledge on livestock management and health due to their strong dependency on livestock for livelihoods. The knowledge includes good clinical diagnostic skills and awareness of modes of disease transmission, among others (Catley and Mariner, 2002). Awareness of existence of this local livestock knowledge by veterinary epidemiologists led to integration of participatory epidemiological methods (PE) to obtain local intelligence on the various topical issues including measures of disease frequency (Catley and Mariner, 2002). Participatory Epidemiology is the systematic use of participatory approaches and methods to improve understanding of diseases and options for disease control (Catley and Mariner, 2002).

Participatory methods in veterinary epidemiology have found use in animal health surveys, needs assessment and action plans (Bett *et al.,* 2009) and disease modeling (Mariner *et al.,* 2005, Mariner *et al.,* 2006), among other uses (Catley and Mariner, 2002). The use of community-based participatory approaches in informing disease modeling emanates from the need to provide expert opinion on the realities on the ground. In addition, recommendations for modeled disease control measures should be grounded in the knowledge of the participants who are the potential beneficiaries of

the proposed interventions. Models of Rinderpest and Contagious Bovine Pleuropneumonia transmission dynamics have been developed partly using data obtained through participatory research in South Sudan (Mariner *et al.,* 2005, Mariner *et al.,* 2006). Retrospective assessments of the recent 2006/7 RVF outbreak in Ijara sub-county using participatory epidemiological techniques provided useful information for model development and/ or validation and which can contribute to surveillance and early warning systems (Jost *et al.,* 2010). Examples of this useful information include relative incidence of RVF and its impacts on livelihoods, RVF outbreak incidence, case fatality and mortality rates and the time intervals between key epidemiological events that preceded the outbreak.

This study was designed to collect data on livestock population dynamics in Ijara sub-county, Kenya to partly inform disease modeling. These included host demographics, particularly those defining rates of entry and exit into the herd and seasonal movement patterns. This information was used as parameters in the RVF simulation model described in Chapter 5.

4.2. Materials and Methods

4.2.1 Data collection

Data were collected using participatory techniques. Details on data collection were given in Chapter 3.

4.2.1.1 Identification and scoring of livestock species by number

To determine the relative proportions of livestock species kept, participants were first asked to list the type of livestock species commonly kept in their area. The responses given were listed on a flip chart. The next step involved scoring them based on their number using a proportional piling technique (see Chapter 3). Circles were drawn alongside each species. The participants were then given 100 beans to distribute to the listed species based on the relative abundance of the livestock species, assuming that 100 beans represented the population of livestock in the area. Livestock species that had the highest population got a bigger pile of beans and vice versa. The piles were counted when all the participants had settled on the distribution provided. They were also asked to give reasons that supported the results observed – e.g. why a particular species was perceived as having the highest/lowest population sizes.

4.2.1.2 Identification and scoring of livestock age structures

In this exercise, participants were first asked to list the local names of age categories for cattle, sheep and goats. Alongside each name, the participants were asked to mention the age ranges of the age categories. The next step involved scoring them based on their number using a proportional piling technique as described above. The piles were further disaggregated down to sex level for each age category.

4.2.1.3 Animal offtakes

Proportional piling technique, as described above, was carried out to determine the number of animals sold or slaughtered in Ijara sub-county by species and seasons between July 2011 and July 2012.

4.2.1.4 Reproduction parameters

Proportional piling technique, as described above, was carried out to estimate several reproduction parameters. These parameters included proportion of repeat breeders, proportion of animals giving birth to twins and proportion of pregnancies that terminate prematurely. For instance, on the proportion of abortions/pregnancies carried to term, participants were given 100 beans to represent animals that were pregnant. They were asked to divide the beans into two: the number of animals that was expected to carry their pregnancies to term verses the number that would abort.

4.2.1.5 Livestock diseases incidence and case fatality rates

The participants were first requested to mention the diseases acquired by each of the livestock species kept over the 1-year period leading to the time of the survey (July 2011 and July 2012). These diseases were listed on a flip chart. The participants mostly used the local disease names or syndromes to identify the diseases. These names were either translated on site by community animal health workers or at the local veterinary office. The participants were then asked to rank cattle diseases in terms of impact on livelihoods. For the three top-ranked diseases (and RVF if not

ranked amongst the top 3), proportional piling technique was carried out to determine incidence and case fatality rates (CFR) for the year preceding the survey (and for RVF, incidence and CFR during the 2006/7 outbreak for each of the three species – cattle, sheep and goats). Briefly, for each disease, the participants were asked to pile 100 beans on two circles on the flip chart representing animals that were healthy and sick from the target diseases. From the proportion that became sick, the participants were asked to pile the proportion of animals that died out of the disease and the proportion that recovered.

4.2.1.6 Herd/flock sizes, reproduction parameters, lifespans, and wildlife species found in the area

Information on herd/flock sizes, age at first breeding, interval between parturition and subsequent heat lifespans, and wildlife species found in the area was collected using semi-structured interviews as explained in Chapter 3.

4.2.1.7 Participatory mapping

Participants were guided to develop maps of their areas indicating human settlements, grazing sites, watering points, roads and service centers e.g. towns. These maps were used to facilitate discussions on a variety of socio-economic activities including livestock grazing patterns. Timelines were used together with the maps to identify locations where livestock were situated, on a monthly basis, over the period July 2011 to July 2012. Timelines on livestock movements/locations were developed in a reverse

order starting with identification of the sites where livestock were in July 2012, and the earliest time (month) when these animals were taken there. This approach was repeated until the full period specified above (July 2011 to July 2012) was covered. Mapping of the livestock movement patterns was done by species (specifically cattle, sheep and goats).

4.2.1.8 Grazing distances

For a selected number of focus groups (n=10), grazing distances were estimated. One member of the group was asked to accompany this thesis author to the sites the herders take the animals for grazing. The grazing distance between villages and the grazing sites were estimated using the Global Positioning System (GPS) handset.

4.2.1.9 Data management

All data obtained were entered into a database designed using Microsoft Excel® and analyzed in STATA 11 using non-parametric statistical tests. Medians and their respective 10th and 90th percentile ranges were estimated.

Data on livestock movement patterns obtained from the participatory mapping exercises were entered into a database designed using Microsoft Excel® as well. The data variables formulated included:

i. Sub-location

ii. GPS coordinates of the interview sites and other locations that had been used for grazing over the year
iii. Livestock species
iv. Month/year
v. Indicator variable which when used together with the month/year specifies whether a given livestock species was just arriving at a given grazing site, had been there for some time or was being moved out to other sites with more pasture/water.
vi. Monthly mean Normalized Difference Vegetation Index (NDVI) data

Monthly mean NDVI data for all the geo-referenced sites for the study period were obtained from SPOT VEGETATION®, filtered and merged with the movement data obtained from the map. The mean Normalized Difference Vegetation Index is a simple numerical index or indicator that provides a standardized method of comparing vegetation greenness between satellite images. Normally, higher index values are associated with high levels of healthy vegetation cover whereas low figures denote little to no vegetation cover. Statistical analyses were carried out to determine mean NDVI values for periods when livestock were being moved out of their recent grazing sites due to lack of pastures (lack of vegetation). Up to 1000 bootstrap samples were generated from the sample and used to estimate 95% confidence intervals (95% CI) for the mean NDVI values for each site at the time when animals were being moved out from these areas. These analyses were carried out in STATA 11 and the results

represented as thresholds for livestock movement from specific sites. Movement patterns for sheep and goats were combined since these livestock species were often moved to similar locations.

4.3 Results

4.3.1 Types of livestock kept and herd/flock sizes

All focus groups listed goats, sheep, cattle, donkeys and chicken as the livestock species kept in their areas. Table 4.1 shows the results of scoring of types of livestock species kept by abundance. Goats and sheep formed the largest proportion of the livestock in the area and donkeys the least (Table 4.1). The median cattle herd sizes and sheep flock sizes and the respective 10th and 90th percentiles were 50 (30, 100) and 100 (60, 200).

Table 4.1: Types of livestock species kept and their relative population sizes determined using median percentage scores (with 10th and 90th percentiles) in Ijara Sub-county, Kenya August 2012 to February 2013.

Livestock species (n=22)*	Median	10th and 90th percentiles*
Goats	40	(21, 47.5)
Cattle	27.5	(21.5, 44.5)
Sheep	21	(13, 27.5)
Chicken	6	(2.5, 17.5)
Donkeys	4	(2.5, 6.5)

Medians proportions represent the middle value when numbers are put in ascending or descending order; this column therefore does not necessarily have to add up to 100%.
*Number of villages where this information was collected.

4.3.2. Age structure of livestock

Table 4.2 shows the proportional categorization of age categories of cattle and sheep in the population. These categories are disaggregated further by sex. Most participants identified at least 4 livestock age categories for each species; these included:

Cattle: *Dalan* (0-4 months), *Ashirow* (5-12 months), *Sarar* (13-36 months) and *Hauwechi* (adults);

Goats: *Dalan* (0-2 months), *Sarar* (3-5 months), *Asan* (6-12 months) and *Riya* (adults), and,

Sheep: *Maqal* (0-2 month), *Saben* (3-4 months), *Laah* (5-12 months) and *Hauwechi* (adults).

In both species, the adult population constituted the highest proportion though adult cattle proportion was higher than adult sheep proportion. A notable feature in both species was that subsequent age categories had less male animals relative to female animals, particularly in cattle (Table 4.2).

4.3.3. Lifespans and animal exits

Table 4.3 shows the lifespans of different classes of livestock kept for different livelihood purposes. Cattle and sheep/goats exited the herds as early as 1.5 years and 1 year after birth, respectively, with reported wide age ranges (Table 4.3).

Table 4.4 shows median percentages (10th and 90th percentiles) of animals sold or slaughtered in Ijara Sub-county by seasons during the year preceding this study (July 2011 to July 2012). Of the three species, sheep and cattle appear to experience the highest and the lowest rate of exit respectively through slaughter and sales (Table 4.4). Generally, exit rates (considering lifespans and offtakes) for sheep/goats were substantially higher relative to those of cattle (Tables 4.4 and 4.5).

4.3.4. Reproduction parameters

Female sheep and goats commenced breeding much earlier relative to female cattle depending on season (Table 4.5). Similarly and expectedly, the interval between parturition and subsequent heat was longer in cattle relative to sheep and was species-dependent (Table 4.5). Although goats were more likely to experience repeat breeding (due to failure to conceive or due to early embryonic death), they were more likely to give birth to twins compared to sheep and cattle (Table 4.6). Goats were reported to experience baseline abortions compared to sheep and cattle (Table 4.6). Abortions, regardless of species, were more likely to occur in dry season compared to wet season (Table 4.6).

4.3.5. Relative incidence of diseases

Participants mentioned African animal trypanosomosis (*Gendi*), Rift Valley fever (*Sandik*), foot-and-mouth disease (*FMD*) (Habeb), contagious bovine pleuropneumonia (CBPP) (*Sanap*), contagious caprine pleuropneumonia (CCPP) (*Gesdor*), gastro-Intestinal helminthes, anthrax, black quarter and lumpy skin disease (LSD) as the main diseases experienced in livestock in the area. African animal trypanosomiasis (22 villages), CBPP (14 villages) and CCPP (10 villages) were more likely to be ranked amongst the top three in terms of impact on livelihoods (Table 4.7). Other diseases that were mentioned frequently were RVF, FMD and tick-borne diseases (Table 4.7). Almost all livestock were reported to be affected by African animal trypanosomiasis during the previous year preceding the study (Table 4.8). The

incidence of CCPP was reportedly higher than for CBPP (Table 4.8). The incidence of RVF was reported highest in sheep and lowest in cattle. Indeed, some participants reported that RVF did not affect cattle in their villages (Table 4.8). Rift Valley fever case fatality rates (CFR) were reported to be highest in sheep compared to goats and cattle (Table 4.8). Whereas the incidence of African animal trypanosomiasis (all species affected) was the highest, the CFR for this disease was reported the lowest compared to the other diseases (Table 4.8). Case fatality rates in CBPP and CCPP (though affecting cattle and sheep respectively) were not substantially different (Table 4.8).

Table 4.2: Median percentage of age categories in the population and the percentage by sex within age category in cattle and sheep population in Ijara sub-county, Kenya, August 2013 to February 2014.

	Cattle (n=7)*								**Sheep (n=6)***							
Age category	Neonates		Weanlings		Growers		Adults		Neonates		Weanlings		Growers		Adults	
Age	0 to 4 months		5 months to 1 year		1 to 2 years		>2 years		0 to 2 months		3 months to 6 months		7 months to 1 year		>1 year	
Sex	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M
Proportion (%) by sex within age category	54	46	60	40	71	29	84	16	47	53	54	46	73	27	79	21
Proportion (%) in the population	7		11		19		63		13		14		23		50	

NB: F: female; M: male. For each age category, the proportions add up to a 100. The proportions of all age categories in a species add up to a 100. *Number of villages where this information was collected.

Table 4.3: Median lifespan age (with 10th and 90th percentiles) of cattle, sheep and goats population in Ijara sub-county, Kenya, August 2013 to February 2014.

Livestock species	**Age category**	**Age in years**
Cattle (n=7)*	Bull calves destined for sale/slaughter	5 [1.5, 6.5]
	Breeder bulls for breeding	10 [7, 12]
	Cow for breeding and milk production	10 [7.5, 12]
Sheep/goats (n=6)*	Lambs/kids destined for sale/slaughter	3 [1, 6]
	Breeder rams for breeding	5 [3.5, 6]
	Ewe/doe for breeding and milk production؏	6.5 [5, 8]

*Number of villages where this information was collected. ؏ Does alone are used for milk production

Table 4.4: Median percentages (10th and 90th percentiles) of animals sold or slaughtered in Ijara sub-county by seasons (July 2011 to July 2012), August 2013 to February 2014.

Livestock species	**Sales (%)**		**Slaughter (%)**	
	Wet season	Dry season	Wet season	Dry season
Cattle (n=7)*	4.5 (0, 20)	6 (2, 15)	2 (1, 3)	0 (0, 2)
Goats (n=6)*	8 (5, 17.5)	15 (4, 21)	4 (0, 17.5)	5 (0, 10)
Sheep (n=6)*	10 (4, 20)	19 (10, 30)	6 (4, 10)	4 (3, 14)

*Number of villages where this information was collected.

Table 4.5: Reproduction parameters estimated from participatory exercises in Ijara sub-county, August 2013 to February 2014.

Livestock species	**Age at first breeding in months (n=22)***				**Interval between parturition and subsequent heat in months (n=22)***	
	Females		Males			
	Wet season	Dry season	Wet season	Dry season	Wet season	Dry season
Cattle	24 (36, 48)	48(48,60)	42 (42, 60)	48 (48, 60)	6 (1, 12)	12 (12, 24)
Goats	7 (12, 30)	12 (18, 24)	6 (24, 30)	30 (12, 36)	3 (2, 5)	6 (3, 12)
Sheep	7.5 (6, 24)	12 (8, 18)	6 (12, 24)	10 (12, 24)	2 (1, 3)	5 (2, 12)

*Number of villages where this information was collected

Table 4.6: Additional reproduction parameters estimated from participatory exercises in Ijara sub-county, August 2013 to February 2014.

Livestock species	**Proportion of repeat breeders (n=6)***	**Proportion of animals giving birth to twins (n=15)***	**Proportion of pregnancies that are expected to terminate prematurely (abortions) (n=21)***	
			Wet season	Dry season
Cattle	0.1 (0.0, 0.3)	0.0 (0, 0.001)	0.2 (0.0, 0.4)	0.3 (0.2, 0.6)
Goats	0.35 (0.2, 0.6)	0.3 (0.1, 0.5)	0.3 (0.2, 0.5)	0.5 (0.2, 0.6)
Sheep	0.0 (0.0, 0.2)	0.1 (0.0, 0.3)	0.1 (0.0, 0.5)	0.3 (0.1, 0.5)

*Number of villages where this information was collected

Table 4.7: Frequency of ranking of top three diseases across all villages in Ijara sub-county, August 2013 to February 2014.

Disease	Rank 1	Rank 2	Rank 3
African Animal Trypanosomiasis	20	2	-
Contagious Bovine Pleuropneumonia (CBPP)	1	8	5
Contagious Caprine Pleuropneumonia (CCPP)	1	4	5
Rift Valley fever (RVF)	4	1	2
Foot-and-Mouth Disease (FMD)	-	2	5
Tick-borne diseases	-	2	2
Other diseases	-	7	7

Table 4.8: Relative incidence and case fatality rate (CFR) scores (with 10th and 90th percentiles) of the three most important diseases of livestock observed in the previous year (July 2011 to July 2012) and RVF (2006/7) in Ijara sub-county, Kenya, August 2013 to February 2014.

Disease	Incidence	Case fatality rate
African Animal Trypanosomiasis	100 [74, 100]	19 [8, 38]
Contagious Bovine Pleuropneumonia (CBPP)	38 [25, 75]	36 [19, 90]
Contagious Caprine Pleuropneumonia (CCPP)	65 [39, 84]	42 [27, 64]
Rift Valley fever in cattle	14 [0, 54]	25 [0, 55.4]
Rift Valley fever in sheep	42 [82, 100]	84 [61, 97]
Rift Valley fever in goats	39 [21,84]	46 [24, 83]

4.3.6. Livestock movement patterns and grazing distances

The overall NDVI mean for the study period (July 2011 and July 2012) was 0.42 (95% CI: 0.38 – 0.46). At the time when sheep/goats and cattle were being moved out of a grazing site, mean NDVI values were estimated to be 0.15 (95% CI: 0.08 – 0.22) and 0.27 (95% CI: 0.14 – 0.40) respectively. Tables 4.9 and 4.10 show the monthly mean NDVI estimates for the areas where livestock were grazed in during the period considered for these analyses. The median distances (and their 10th and 90th percentiles) travelled by cattle and sheep in kilometers were 10 (4.5, 12) and 3.5 (2.5, 7.5) respectively. Plate 4.1 shows an example of a map indicating migration patterns

of livestock in Hara sublocation, Ijara sub-county developed during one of the community-based participatory surveys.

4.3.7. Wildlife species in Ijara sub-county

The participants listed buffalo, rodents, mongoose, giraffe, topi, baboons, antelopes, dik dik, wild dogs, lions, warthog, leopard, waterbucks, hyena, cheetah, lesser kudu as the wildlife found in the area.

Table 4.9: Monthly NDVI for the areas used to graze sheep and goats by four different grazing communities in Ijara sub-county over the period July 2011 to July 2012

Month	Warende Goga→Shelu Plain→Bodhai			Abalatiro→Warawesa →Gababa			Bodhai→Shelu Plain		Atheweiyno →Warawesa	
July 2011	-0.03	0.92	0.92	0.92	0.92	0.92	0.92	0.92	0.92	0.92
August 2011	0.92	0.74	0.61	-0.09	0.9	0.2	0.61	0.74	0.81	0.9
September 2011	0.86	0.74	0.13	0.92	0.76	0.05	0.13	0.74	0.77	0.76
October 2011	0.24	0.46	0.55	0.34	0.22	0.68	0.55	0.46	0.28	0.22
November 2011	0.65	0.9	0.11	0.1	0.91	0.16	0.11	0.9	0.05	0.91
December 2011	0.74	0.46	0.15	0.85	0.8	0.25	0.15	0.46	-0.1	0.8
January 2012	0.52	0.04	0.12	0.39	0.38	0.24	0.12	0.04	0.46	0.38
February 2012	0.17	0.92	0.71	0.18	0.11	0.81	0.71	0.92	0.12	0.11
March 2012	-0.03	0.81	0.42	0.01	-0.04	0.48	0.42	0.81	-0.09	-0.04
April 2012	-0.05	0.86	0.26	-0.03	0.16	0.37	0.26	0.86	0.92	0.16
May 2012	0.12	0.82	0.68	0.05	0.39	0.52	0.68	0.82	-0.1	0.39
June 2012	0.19	0.71	-0.09	-0.03	0.14	0.73	-0.09	0.71	0.85	0.14
July 2012	0.02	0.68	0.4	0.92	0.07	0.56	0.4	0.68	0.81	0.07

Grey shading indicates areas where sheep and goats were in a given month. Negative NDVI values correspond to water, low positive to slightly negative values correspond to bare soil while values ranging from 0.3 to 0.8 correspond to dense vegetation.

Table 4.10: Monthly NDVI for the areas used to graze cattle by four different grazing communities in Ijara Sub-county over the period July 2011 to July 2012

Month	Boni→Korisa		Boni→Haji Mohamed		Boni→Gababa→Kitele			Boni→Falema →Bura	
July 2011	0.22	0.92	0.22	0.92	0.22	0.92	0.92	0.22	0.92
August 2011	0.22	0.85	0.22	0.9	0.22	0.2	-0.05	0.22	0.86
September 2011	0.12	0.86	0.12	0.76	0.12	0.05	-0.04	0.12	0.86
October 2011	0.34	0.13	0.34	0.05	0.34	0.68	0.45	0.34	0.26
November 2011	0.26	0.42	0.26	0.52	0.26	0.16	0.15	0.26	0.67
December 2011	0.66	0.26	0.66	0.36	0.66	0.25	0.08	0.66	0.56
January 2012	0.66	0.01	0.66	0.14	0.66	0.24	0.77	0.66	0.38
February 2012	0.32	-0.1	0.32	-0.03	0.32	0.81	0.48	0.32	0.08
March 2012	0.38	0.88	0.38	0.92	0.38	0.48	0.16	0.38	-0.04
April 2012	0.27	0.84	0.27	0.88	0.27	0.37	0.1	0.27	0.92
May 2012	0.08	-0.05	0.08	-0.1	0.08	0.52	0.15	0.08	0.05
June 2012	0.44	-0.1	0.44	-0.01	0.44	0.73	0.22	0.44	0.23
July 2012	0.4	0.87	0.4	0.85	0.4	0.56	0.07	0.4	0.01

Grey shading indicates areas cattle were in a given month. Negative NDVI values correspond to water, low positive to slightly negative values correspond to bare soil while values ranging from 0.3 to 0.8 correspond to dense vegetation.

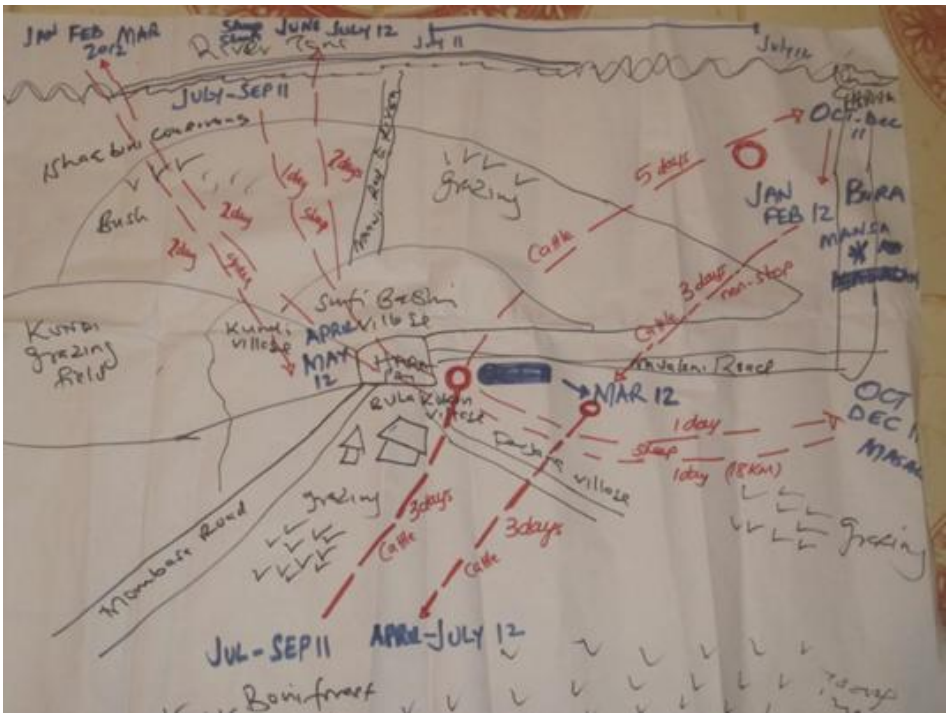


Plate 4.1: A map indicating migration patterns of livestock in Hara sublocation, Ijara sub-county developed during one of the community-based participatory survey.

4.4 Discussion

Results from participatory surveys demonstrated that the local communities had a good knowledge on livestock production and the epidemiology and history of key livestock diseases and associated events in their area and zoonotic diseases that can impact on their livelihoods and health. Participatory epidemiology addresses some of the challenges of conventional epidemiological methods, particularly those that require formal/probability sampling designs in sparse populations in extensive settlements (Bett *et al.*, 2009). This study used three main methods of participatory data collection: (1) informal interviewing using semi-structured interviews with focus-group discussions, (2) ranking and scoring including simple ranking and proportional piling, (3) visualization including mapping and timelines; these have been described

by Catley and Mariner (2002). These techniques have been employed previously, in combination with quantitative techniques, to develop epidemiological models of disease transmission (Mariner *et al.,* 2005, Mariner *et al.,* 2006).

This study further used participatory epidemiological surveys to identify types of livestock species being kept in the area as well as their relative population sizes. This information was used to determine relative populations of hosts (cattle and sheep) used in the model. These data were validated with livestock census data from the local veterinary office which indicate a sheep-cattle population ratio of 2:1. It is normally hypothesized that there is a huge variability in the susceptibility of the various animal species to RVFV infection. Sheep and goats are thought to amplify RVFV transmissions given the development of high viraemia titres during outbreaks (Bird *et al.,* 2009). The participatory study, thus, contributed in elucidating the disease ecological mechanisms emanating livestock population structure that can influence RVF transmission dynamics.

Results from this study support the widely acknowledged concept of population dynamics variability among cattle, sheep and goats through offtake rates (sales, slaughters and mortalities). Available official statistics on these processes in pastoral and small holder production systems are often not reliable because sales are usually made for subsistence needs and so they do not get reported. The study findings corroborate the generally held view that pastoral livestock, particularly the small

ruminants, have a very high turn-over rates. The high offtake rates negatively affect the persistence of a herd immunity that often arises either from natural infection or vaccination. In a disease context, host population demographics are known to play important roles in the dynamics of infectious diseases in humans (Finkenstädt *et al.*, 1998; Cummings *et al.*, 2009). The role that variability in demographic aspects plays on dynamics of infectious diseases in animals is not known. This thesis used PE data to attempt to answer the question on why a single RVF outbreak is always observed in presence of multiple hosts that have wide variation in population turnover in Chapter 6.

Females comprise a large proportion of the adult populations given the reported high offtake rates in males in both cattle and sheep. This sex structure enhances the impacts of RVF through RVF-induced abortions. Massive abortions during outbreaks are expected to impact heavily on post-outbreak population recovery patterns. This assessment is covered in Chapter 6 of this thesis as well.

African animal trypanosomiasis, CBPP and CCPP were perceived to have negative impacts on livestock production in Ijara Sub-county. African animal trypanosomiasis was reported to be associated with high incidence throughout the year due to herders grazing patterns in Ijara sub-county. Approximately one quarter of the sub-county on the eastern part is covered by the Boni Forest. The forest is used as a dry season grazing site. Forested habitats promote tsetse flies (the vectors of trypanosomiasis)

population growth (Rogers *et al.,* 1996). However, the estimated CFR for trypanosomiasis was low due to the herders' knowledge on the clinical presentation of the disease, thereby, frequently administering both chemoprophylaxis and chemotherapeutic agents on the cattle. Whereas the lower CFR for trypanosomiasis was attributed to regular and frequent purchase of drugs against the disease, thereby reducing mortality burdens, the impacts of CBPP and CCPP were attributed to unavailability of reliable treatments leading to high CFR.

It is interesting to note that pastoralists perceived RVF as a disease of sheep relative to goats and cattle in accordance with formal knowledge (Bird *et al.,* 2009). As the interest of the study was RVF, only after ranking and scoring the top three diseases for incidence and CFR was RVF introduced in the discussion. This avoided any bias towards any particular disease. In addition, the separation into healthy and sick livestock and further disaggregation of the sick into those that died and those that recovered elicited lengthy discussions amongst the participants that led to the accurate capture of their perceptions. Epidemiological assessment of 2006/7 in the Somali ecosystem showed that the Somali pastoralists are reasonably knowledgeable at recognizing symptoms of RVF and risk factors such as heavy rainfall and mosquito swarms (Jost *et al.,* 2010). The Somali pastoralists principally depend on their livestock for their livelihoods and, therefore, are expected to possess a wealth of knowledge concerning the constraints facing their livestock.

This study revealed that Somali pastoralists practice transhumance pastoralism that ensures frequent and extensive livestock movements in structured patterns. This is a strategy used by the pastoralists to cope or manage climate variability where animals are moved from areas with dwindling pasture and water to areas where these resources are plenty. The survey established that the movement patterns were dependent on environmental conditions and the type of animals kept. An analysis of these patterns against NDVI estimates from this study (as a proxy for weather/seasonal variability) indicated that there is a tendency of increased movement during periods of low NDVI. Small ruminants have a higher NDVI threshold for movement than cattle. This is mostly attributed to their potential for browsing on a variety of shrubs that can withstand drier conditions for a longer time relative to normal pasture. These results need to be, however, interpreted with caution as low NDVI estimates might not always imply increased livestock movement. This is because NDVI estimates measure the amount of greenness or green forage that is present in an area rather than pasture availability. Nevertheless, these results are encouraging in that they produced unique information relatively quickly and at low cost. Worden (2007) used a similar strategy to analyze livestock movement dynamics in the greater Amboseli ecosystem in Kenya. There is a huge potential in benefitting from cattle mobility data, for instance, data on space–time dynamics of cattle mobility among pastoralists has been linked to space–time dynamics of RVF in Ijara sub-county (Owange *et al.*, 2014).

Approximately one quarter of Ijara sub-county is covered by the Boni forest. A section of the forest, the Boni National Reserve, is under the management of the Kenya Wildlife Service as a protected conservation area. Participants in the PE study were able to identify various wildlife species found in the sub-county. Interestingly, a previous extensive study reported prevalence of antibodies against RVFV in Kenyan wildlife including some from Ijara and Garissa areas (Evans *et al.,* 2008). Specimens from African buffalo, black rhino, lesser kudu, impala, African elephant, kongoni, and waterbuck had detectable neutralizing antibodies against RVFV. High RVFV sero-prevalence (>15%) was reported in black rhinos and certain ruminants (kudu, impala, buffalo, and waterbuck). High titres were also reported in animals born during the inter-epidemic period (1999–2006). However, all lions, giraffes, plains zebras, and warthogs tested negative. Sixteen out of 19 (84%) of the ruminant (gerenuk, waterbuck, and eland) specimens collected during the 2006/7 outbreak had RVFV-neutralizing titres ≥1:80. Although these data provided evidence that wild ruminants are infected by RVFV, there is no proof that these wild animals play a role in the virus maintenance between outbreaks and/or virus amplification just prior to a full-blown outbreak. However, bats and rodents are suspected to be reservoirs of RVFV in Senegal (Boiro *et al., 1*987) and South Africa (Pretorius *et al.,* 1987) respectively. Due to the high humidity expected in dense forests favourable to mosquito breeding, the existence of an endemic sylvatic cycle between mosquitoes and wild reservoirs living in a forest cannot be ruled out. However, the pastoralists did not have knowledge of any role that wildlife may have in RVF endemicity or epidemicity.

Anyamba *et al.* (2010) puts forward a hypothesis – that movement of viraemic animals to other ecological zones in the course of RVF outbreaks amplifies outbreaks especially if these areas have large populations of *Culex* mosquitoes that play a role in creating secondary RVF transmission foci. This hypothesis, if empirically proved true, may have epidemiological implications as recently, a sero-survey of cattle in Ijara sub-county reported that the highest RVFV circulation was detected after herds pass through the Boni forest (Owange *et al.,* 2014). These animals may amplify outbreaks if they transit or arrive in areas that have large populations of *Culex* mosquitoes. In light of this, this thesis further hypothesizes that movements of animals between dry and wet seasonal areas might be playing some role in linking domestic and sylvatic transmission cycles of RVFV.

Participatory epidemiology is still evolving. Previously, these approaches were used in the analysis of animal disease problems (Bett *et al.,* 2009), post-outbreak epidemiological assessments (Jost *et al.,* 2010) and in the design, implementation and evaluation of disease control and eradication programmes (Mariner *et al.,* 2012) among others. This study adapted the application of PE to inform useful model parameters particularly those related to host demographics. The study provided unique qualitative/semi-quantitative and quantitative information at very low cost. Further, the study revealed that interventions aimed at African animal trypanosomiasis, CBPP and CCPP were likely to have a positive impact on the livelihoods of pastoralists in Ijara sub-county. Participatory disease surveillance that recognizes the local rich

livestock knowledge as being consistent with formal knowledge is expected to be potentially more sensitive and useful in integrated disease surveillance and research systems.

CHAPTER 5

5.0 A SIMULATION MODEL FOR THE RIFT VALLEY FEVER TRANSMISSION IN IJARA SUB-COUNTY, KENYA

5.1 Introduction

One of the many challenges of RVF epidemiology is the understanding of the conditions and factors associated with the occurrence of RVF and how they interact to produce full-blown outbreaks. Consequently, prediction of RVF occurrence and the design of timely and effective interventions remains a challenge (Gachohi *et al.*, 2012). Disease simulation modelling is a powerful methodology that explicitly incorporates the key processes in a disease system in a model. However, although simulation modelling presents a huge opportunity of advancing disease dynamics understanding, it requires a good understanding of disease ecology and availability of data. Through mimicking complex systems, simulation models can be experimented upon in ways that would be impossible, too costly or unethical to do in natural systems.

Nevertheless, knowledge on RVF occurrence, impacts, surveillance and control strategies has improved over time through the use of different modelling strategies (Métras *et al.,* 2011). For instance, risk factor analyses were used to identify socio-ecological risk factors associated with RVF exposure in domestic livestock (Chevalier *et al.,* 2011). Recently, there has been a progressive interest in developing RVF simulation models. However, these models seem to focus on understanding of RVFV

persistence in the environment (Favier *et al.,* 2006; Gaff *et al.,* 2007; Niu *et al.,* 2012; Chitnis *et al.,* 2013; Chamchod *et al.,* 2014). Whereas these models have led to both qualitatively and quantitatively empirically relevant insights, they do not adequately describe mechanisms that may, in addition, be key drivers of RVF transmission dynamics. These include but not limited to multi-host population structuring, rainfall patterns favourable for RVFV occurrence, spatial vector-host contact rate heterogeneity, socio-economic processes that influence host population dynamics and seasonal host movement patterns. These drivers have been recognized in RVF-endemic areas in Africa (Chevalier *et al.,* 2011; Soti *et al.,* 2012; Sumaye *et al.,* 2013).

This chapter describes the development of a RVF simulation model with the aim of understanding the key ecological processes that influence the transmission dynamics of the disease. The model builds on the previously highlighted modelling work in the literature review. The key unique highlights of the model were (1) representation of the multi-host species as unique individuals and vectors as population segments in simulating their population dynamics, (2) use of probability functions derived from daily satellite-based rainfall to temporally simulate vector population dynamics, and (3) spatial heterogeneity of contacts between hosts and vectors facilitated by hosts' movements that are linked to static vector populations. Thus, the study addressed certain previous recommendations, quoted verbatim "….*progress in understanding and combating zoonoses requires a new generation of models that address a broader*

set of pathogen life histories and integrates across host species and scientific disciplines" (Lloyd-Smith *et al.,* 2009).

5.2 Materials and methods

5.2.1. Rift Valley fever model structure

The structure of the model is described in detail in Chapter 3. This section summarizes the known and hypothesized components and processes that influence RVF transmission. All these processes took place in the grid framework.

A grid cell could or could not have been a mosquito breeding site. In a breeding site for the floodwater *Aedes mcinthoshi*, water is a prerequisite for hatching of eggs. However, if water is unavailable, the eggs can resist desiccation and persist for long periods (Pepin *et al.,* 2010) (Figure 5.1). Hatching into larva ensues following subsequent flooding of these habitats. This breeding ecology was implemented in the model using a fuzzy distribution model adapted from Emert *et al.* (2011). The aquatic life cycle was completed upon adult emergence from pupa (Figure 5.1). Because of the transovarial transmission of the virus in infected *Aedes* species, a proportion of mosquitoes emerged as infected adults and could, therefore, initiate transmission as they took their blood meals. If the grid cell was a breeding site for secondary vectors, increased precipitation and flooding were necessary for the amplification of the population. These mosquito species were represented by *Culex* species in the model. *Culex* species population emergence was simulated by using a logistic probability

function generated from a statistical logistic regression model. The vector module executed the population dynamics of these vectors (both aquatic and adult stages) using simple difference equations (Chapter 3). These processes are illustrated in Figure 5.1.

Figure 5.2 shows the framework used to develop the host module. Details are contained in Chapter 3. Rift Valley fever virus transmission can occur when herds/flocks move to mosquito breeding sites. When bitten by an infectious mosquito, a host had a daily probability of becoming infected based on the daily force of infection as described in Chapter 3. An exposed host transited from a susceptible to the latent state. Such a host could become infectious after a latency period. A susceptible mosquito that fed on such a host could have a chance of being infected. During the infectious phase, the host may either die or recover from the disease. It was assumed that hosts that recovered remained immune to the virus for the rest of their life (Figure 5.2).

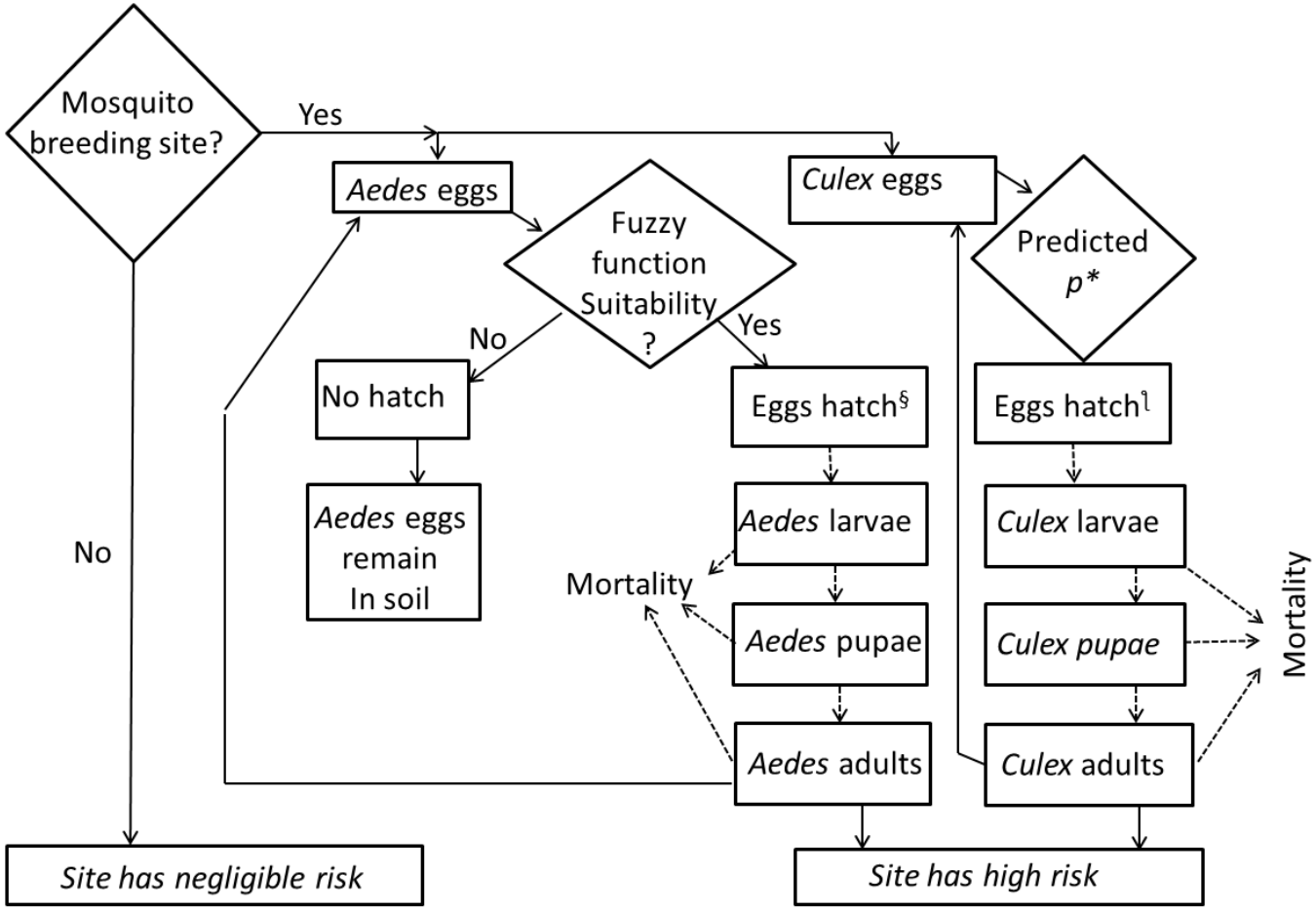


Figure 5.1: Flow diagram representing daily processes that drive vector population dynamics and the level of risk at a breeding site in the model. Eggs hatch § denotes multiplying the number of *Aedes* eggs with respective daily value of the fuzzy function. Eggs hatch ≀ denotes multiplying the number of *Culex* eggs with respective daily predicted *p** value (for details refer to Chapter 3).

In summary, the status of each grid cell in the landscape was, therefore, determined by three events: the first determined whether a grid cell is a mosquito breeding site, and the second, the respective mosquito densities determined by the different probability functions that controlled mosquito growth, and third, visitation of the cell by a herd/flock. A grid cell, therefore, had negligible risk if it was not a mosquito breeding site and *vice versa*.

5.2.2. Data sources

Information obtained from literature, particularly on vector ecology and population dynamics, and empirical data collected from participatory epidemiological studies were used to parameterize the model. Parameters defining host demographics, particularly those defining rates and ages of exit (culling and lifespan) and seasonal patterns of movement were collected through participatory studies that involved pastoralists and their herders in focus group discussions (Chapter 4).

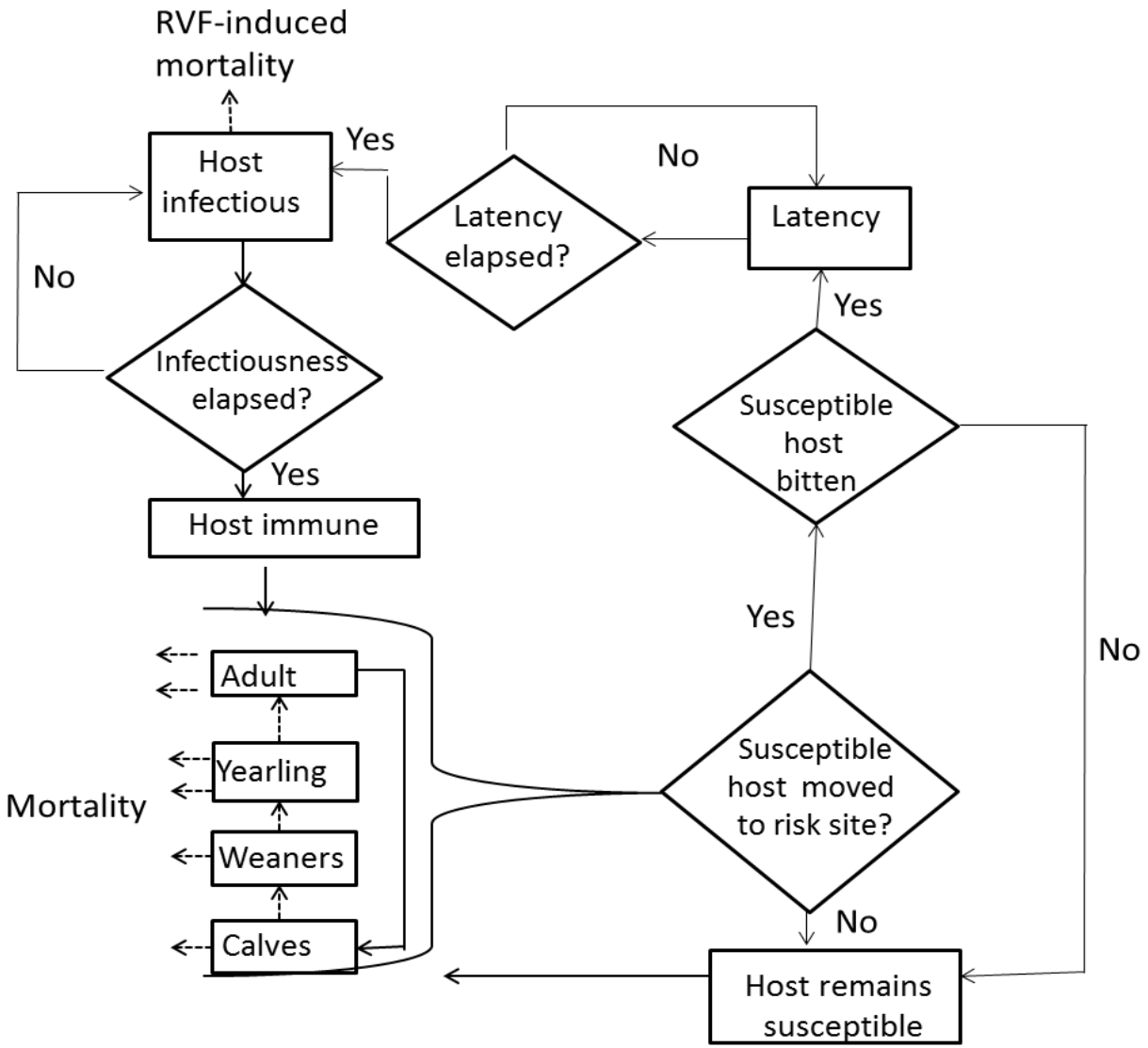


Figure 5.2: Flow diagram representing the individual host infection process and host population dynamics

5.2.3. Model analyses

A total of 1000 simulations were generated from the default model and their means computed and presented graphically using STATA 11. The outcomes generated included (1) incidence of RVFV infection in vectors and hosts, (2) time to the peak incidence of RVFV in vectors and hosts, and (3) the duration of outbreaks. These runs consisted of all transmission events independent of the amount of rain. To evaluate the impacts of the herd immunity, all transient RVFV transmission events that preceded the main outbreak were prevented and an additional 1000 simulations run on an entirely susceptible population. The comparison between the resultant incidences curves were analyzed by computing the area under the curves (AUC). The AUC integrated several components of a curve into one statistic: outbreak persistence time, peak incidence and outbreak size.

5.3. Results

5.3.1. Simulation of mosquito population dynamics

The model successfully simulated, using the probability functions, linkages between rainfall variability and density of mosquitoes (both primary and secondary vectors of RVFV). Figure 5.3 shows the temporal relationship generated between cumulative precipitation and the respective vector: host ratio (obtained from dividing the total number of mosquitoes (for each species) by the total number of hosts (both species)). These outputs support empirical observations that show that the vector: host ratio increases with precipitation. However, the model expectedly predicted that the vector:

host ratio peaks lagged behind those of cumulative precipitation. Given that the vector: host ratio is a critical factor of the force of infection, heavy precipitation increased this ratio (more vectors per host per unit time) and subsequently elevated the risk of RVFV transmission.

The model predicted several periods when the vector: host ratio was substantial (Figure 5.3). One period had sustained precipitation as evidenced by high cumulative values (between day 1000 and 1100 (Figure 5.3)). Other periods that had low vector: host ratios had short-lived precipitation events that were not able to support the amplification of mosquito populations to appreciable levels (Figure 5.3).

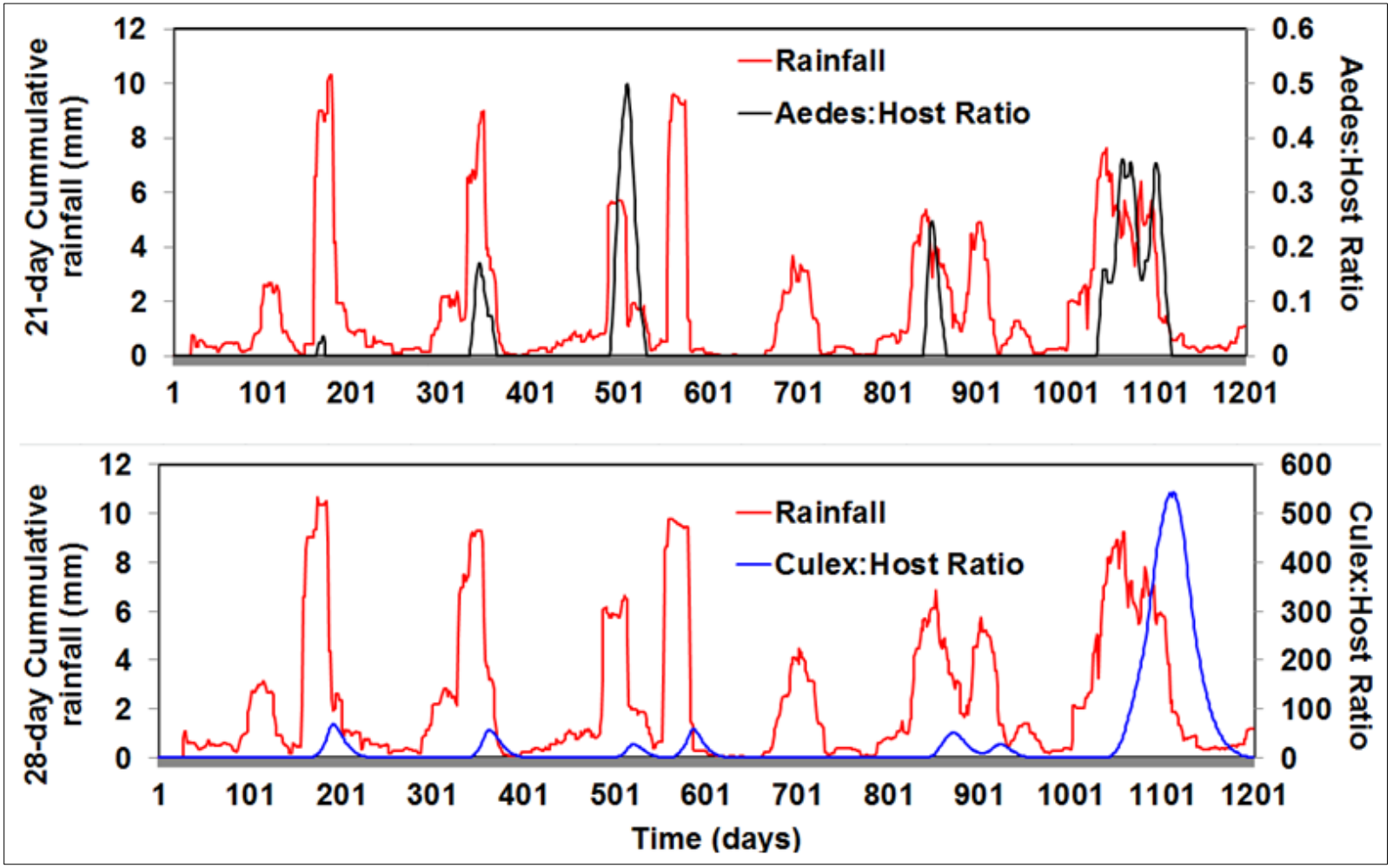


Figure 5.3: Predicted temporal relationship between precipitation and vector host ratios.

5.3.2. Infection dynamics in vectors and hosts

RVFV transmission was initiated when infected *Aedes* eggs hatch and develop to emerge as adults. The adults subsequently took their blood meals from susceptible hosts. The infection was initialized with 20% of buried eggs being infected. *Aedes* species lasted for a total of 93 days with two peaks at day 29 and day 73 post initial emergences of the adults. *Culex* species lasted for 157 days with a peak at 69 days after initial emergence. Transmissions to *Culex* species by the viraemic hosts began between 44 and 69 days after the initial transmission of RVFV to livestock by *Aedes* species and lasted for an average of 19 days (range 14, 25) across simulation runs. RVFV incidence peaked in this species at 0.36% (Figure 5.4).

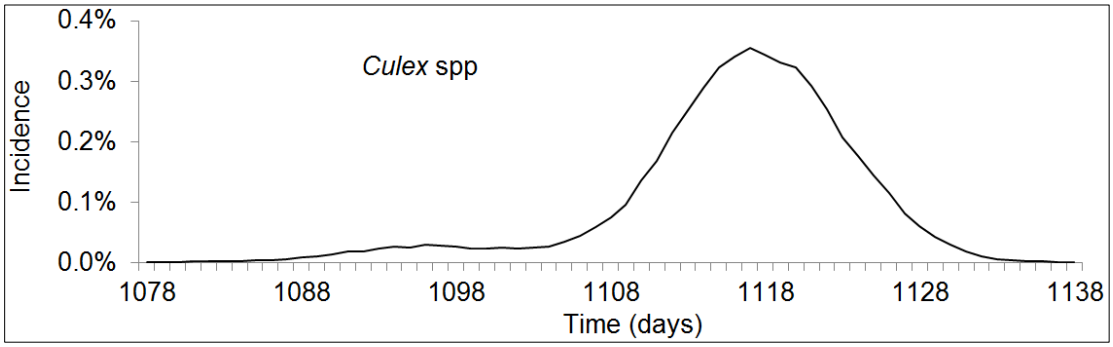


Figure 5.4: Simulated incidence of RVFV in *Culex* species during the period of the simulated outbreak between days 1078 and 1138 across simulations.

Predicted RVFV incidence in hosts is shown in Figure 5.5. These predictions show four transient RVFV transmission events associated with seasonal rains and one main outbreak associated with heavy and persistent precipitation (that occurred between days 1037 and 1152). In general, seasonal transmission events failed to result in full-blown outbreaks given that no amplification of population of *Culex* species occurred (compare with Figure 5.3). The outbreak curve had a characteristic shape – RVFV

activity had a slow onset that quickly gains momentum to a full-blown outbreak (Figure 5.5). The predicted mean peak incidence of RVFV in cattle was 14.1% on day 81 following initial transmissions. The incidence in sheep peaked on the same day at 35.2%. The predicted duration of the outbreak was an average of 100 days (range 80, 111) in both host species.

Figure 5.6 shows the evolution of herd immunity in both hosts. The seasonal/inter-annual transmissions boosted herd immunity over time. The high herd immunity levels attained at end of the outbreak are described and discussed in detail in chapter 6.

Figure 5.7 shows the outbreak curve resulting from preventing seasonal transmissions that occur before the full-blown outbreak (compare to Figure 5.5). The slow-onset characteristic shape in Figure 5.5 disappeared and RVFV activity had a more rapid onset (Figure 5.7). The predicted mean peak incidence of RVFV in cattle was 17.5% on day 55 following initial transmissions. The incidence in sheep peaked two days later (day 57 following initial transmissions) at 25.4%.

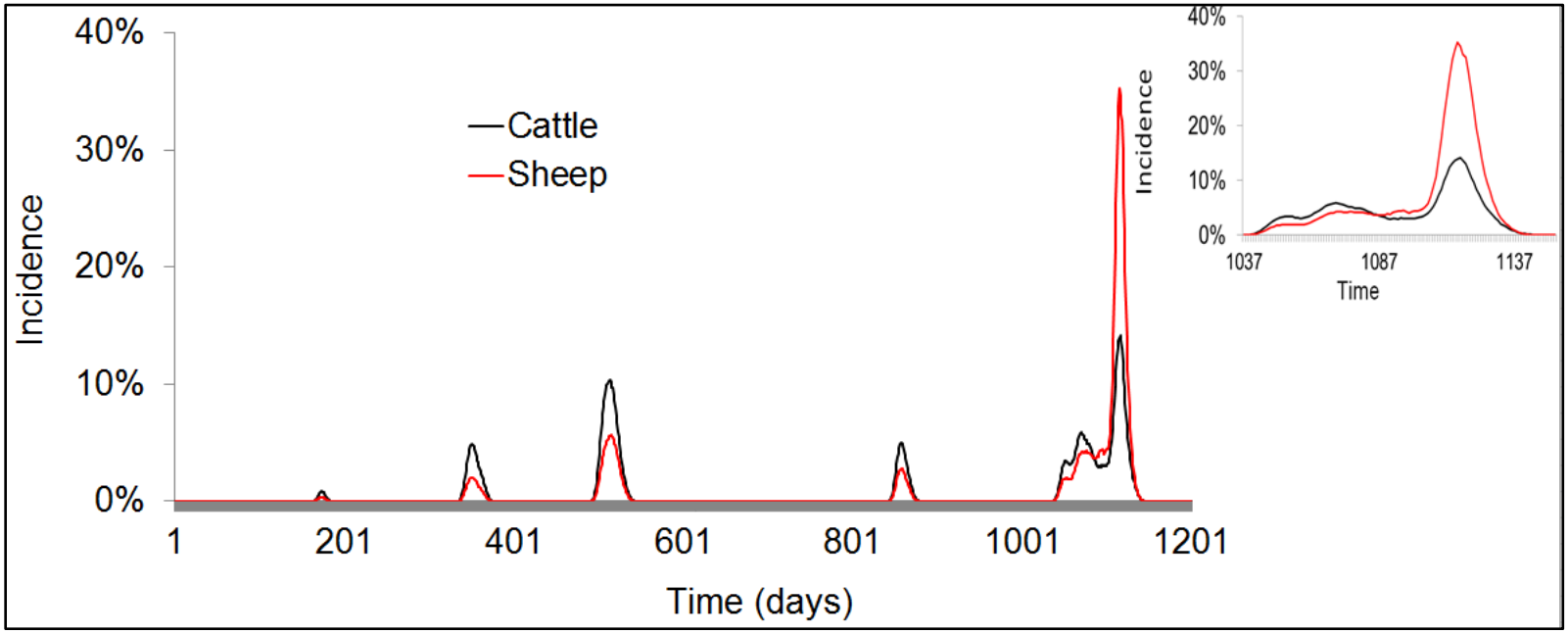


Figure 5.5: Simulated incidence of RVFV in hosts over the study period of 1200 days. The inset graph is a magnification of the outbreak period between days 1037 and 1152.

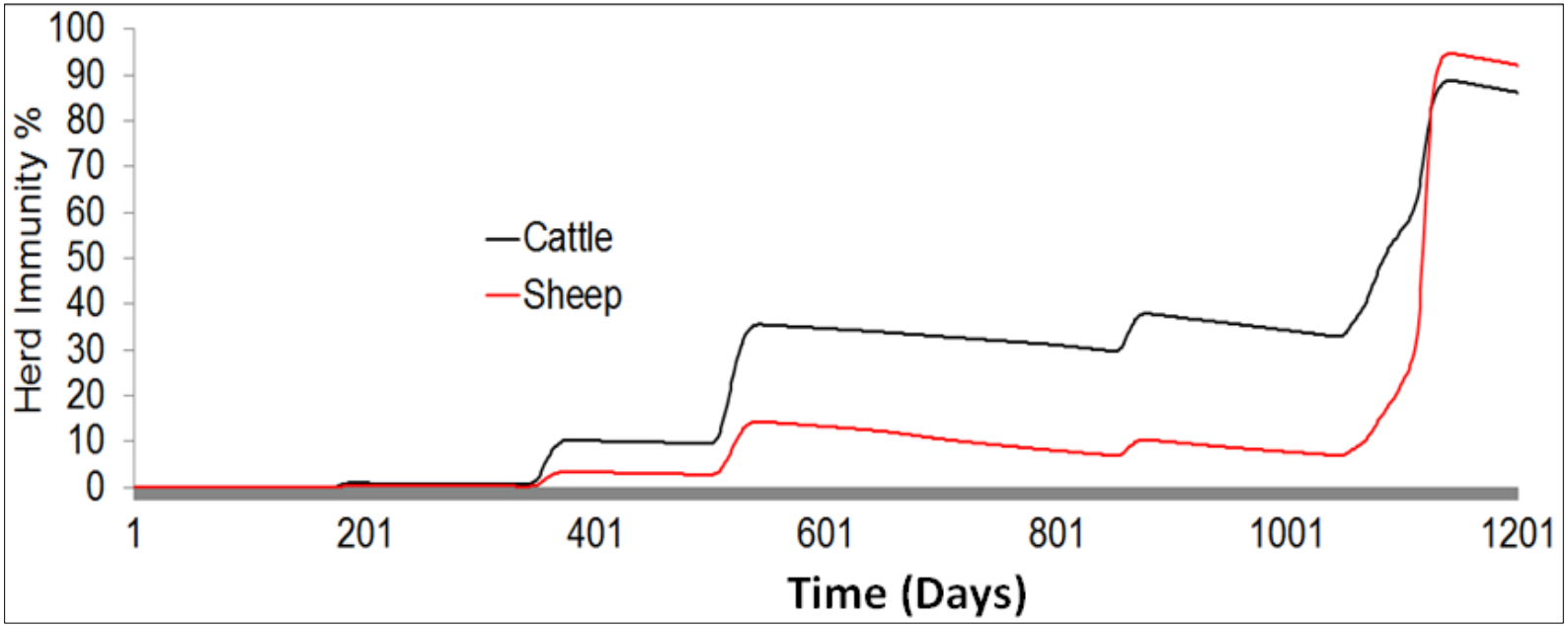


Figure 5.6: Predicted evolution of RVF herd immunity in hosts over 1200 days.
Note the slight boosts in immunity corresponding to seasonal precipitation and increases in vector host ratio in Figure 5.3 and incidence in hosts in Figure 5.5.

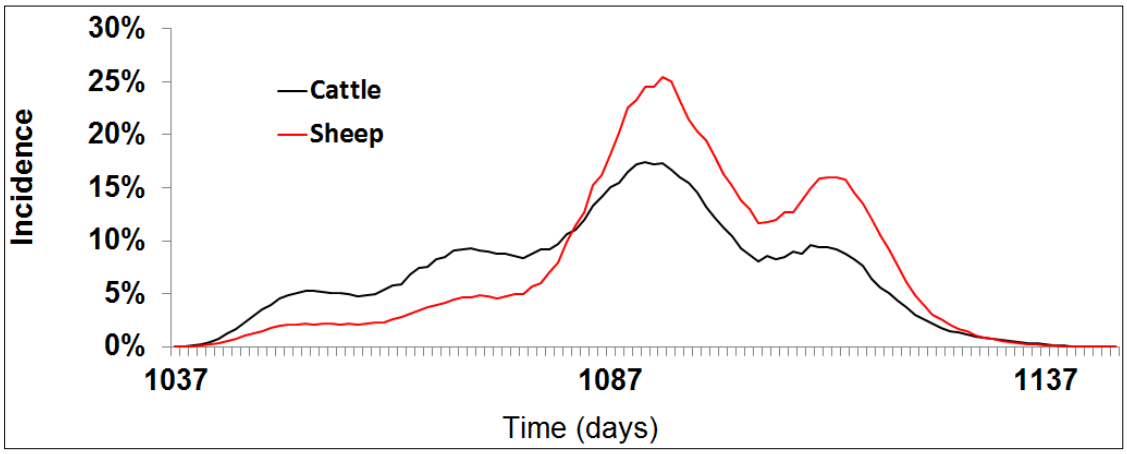


Figure 5.7: Simulated incidence of RVFV in hosts following prevention of inter-annual transmissions that occur before the full-blown outbreak.

The computed areas under incidence curves (AUC) in Figure 5.7 were higher than those in Figure 5.7. Results obtained reveal a reduction of AUCs in Figure 5.7 of 34% and 6% in cattle and sheep respectively. The higher AUC resulting from preventing seasonal transmissions (accompanied by earlier peaking of incidence of 26 and 24 days in cattle and sheep respectively) revealed the importance of seasonal transmissions in boosting herd immunity and consequently reducing disease incidence.

5.4. Discussion

A generic model that combined precipitation patterns, mosquito population dynamics and host demographics to simulate RVFV transmission was developed. The model predicted elevated RVFV activity during the wet seasons as well as a full-blown RVF outbreak following periods with excessive and persistent precipitation. Elevated and persistent rainfall is a risk factor for RVF outbreaks -- all the 11 reported RVF outbreaks in Kenya occurred in years when the average annual rainfall increased by

more than 50% in the affected areas (Murithi *et al.,* 2010). Previously, RVF monitoring and prediction systems have successfully utilized climate (rainfall variability) and environmental cues for forecasting future disease risks owing to their high predictive ability (Anyamba *et al.,* 2010).

In the current model, daily rainfall estimated from TRMM was used in the generation of probability functions that propelled vector emergence and abundance. The TRMM estimate for rainfall data has been found useful in predicting and simulating mosquito population dynamics and mosquito-borne disease risk (Adimi *et al.,* 2010). Reports of evaluation and comparison of the temporal characteristics of the daily TRMM rainfall estimate with that of the ground rainfall data in Ijara sub-county were lacking. Such evaluations have yielded mixed results at different time and spatial scales in Kenya and elsewhere (Nicholson *et al.,* 2003; Li *et al.,* 2012). Nevertheless, the TRMM precipitation data was able to temporally predict the growth and abundance of the two main mosquito species involved in RVFV transmission. However, rainfall from adjacent sub-counties could result in run-offs that could end up in the area of interest. The run-off water could improve water moisture and lead to hatching of buried eggs. In this way, the model results and outputs on the ground would be different. Future model refinements will increase the precipitation catchment areas to include this scenario.

The outbreak curve had a characteristic shape, that is, RVFV activity had a slow onset that quickly gained momentum to a full-blown outbreak. Outbreak investigations and case reporting have not been carried out to determine the incidence of RVF in the field. Thus, natural incidence curves that can effectively validate the model incidence outcomes are lacking. Nevertheless, empirically, the first suspected RVF cases in livestock in Ijara were reported in the month of October 2006 (Jost *et al.,* 2010) and cases peaked in December 2006 (Munyua *et al.,* 2010). These observations, qualitatively, imply a similar slow onset followed, over time, by an exponential-like curve.

The novelty of the vector module is in the utilization of separate probability distributions from daily precipitation that ensured temporal succession of primary and secondary vector population growths that is normally experienced during RVF outbreaks. Unlike the model of Chitnis *et al* (2013) the model from this study ignores trans-ovarial transmission dynamics (i.e. transmission of RVFV to *Aedes* eggs) and its implications on the generation of an outbreak. Therefore, detailed dynamics of *Aedes* mosquitoes were excluded. In this study, the vector module focused more on the integrated role of the vector population dynamics and rainfall variability in predicting outbreaks which is discussed below.

Adult *Aedes* mosquito emergence events were dependent on water (rainfall) that inundated breeding habitats (Linthicum *et al.,* 1985). This study simulated spatio-

temporal distribution of *Aedes* species density based on cumulative rainfall (over 1200 days) using a fuzzy distribution model similar to that employed by Emert *et al.* (2011). Probability values from the fuzzy distribution model (driven by levels of cumulative rainfall) were used to force hatching of *Aedes* eggs. The model set the rate of hatching at a very low rate when the amounts of rainfall are low but inundation of the breeding sites led to an increase in the hatching rate which then dropped sharply once flooding persisted; this pattern follows observations made by Linthicum *et al.* (1983) and Vignolles *et al.* (2009). There are suggestions that there can be a second peak in *Aedes* mosquito densities at the end of the rainy season if there is a gap in rainfall for several days (Chitnis *et al.*, 2013). The nonlinear fuzzy function is very sensitive to the amount of rainfall; consequently, the simulation model reproduced the second peak. Despite this assumption's qualitative nature, it seemed more rational rather than assuming and using a simple linear function of rainfall. Vignolles *et al.* (2009) pointed out the requirements for *Aedes vexans* hatching in West Africa. Empirical studies are needed in East Africa to accurately quantify the amount of rainfall regimes (and how they interact with soil infiltration rates (Nguku *et al.*, 2010) required for hatching.

The statistical logistic function that propelled *Culex* species population dynamics was based on empirical studies that reported that the mosquito breeding sites were colonized by massive swarms of *Culex* (and other mosquito species as well) if they remained flooded for at least 28-42 days (Linthicum *et al.*, 1983). Additionally, livestock keepers in the study area reported a mean average of 23 days between the

start of heavy rains and the appearance of mosquito swarms during the 2006/7 outbreak (Jost *et al.,* 2010), though most likely these included both primary and the secondary species. The model accurately captured these temporal relationships between cumulative rainfall and secondary mosquito species emergence. Generation of parameter estimates from statistical inferential models to simulate transmissions that match actual outbreaks has been carried out in foot-and-mouth Disease (FMD) studies (Chis Ster *et al.,* 2009). It is encouraging to note that the two independent functions (fuzzy model and statistical logistic function) used to generate the two vector population species separately simulated a single outbreak that temporally matched the 2006/7 RVF outbreak in the study area.

Hosts were represented in the model as individuals in an attempt to capture some of the host heterogeneities that influence RVFV transmission. Individual-based models (IBMs) use a bottom-up approach where agents are considered as the primary components of a system (Grimm, 1999). Individual-based modeling is a form of systems dynamics modeling that represents a system from the perspective of its constituent hosts. In the model, the host carries out behaviour appropriate for the RVF epidemiological system using a set of rules – e.g. aging, reproduction, movement, culling, infection, etc. The approach is complemented by more realistic assumptions that include (Grimm, 1999): (a) individuals are intrinsically different, (b) the contacts occur with only a restricted number of other individuals at a given time, (c) the spatial distribution of individuals is complex, for instance, livestock are normally clustered in

herds/flocks, (d) individuals are mobile, and (e) the environment for the individuals is heterogeneous, meaning that the contact structure in the population is complex. The aggregate of individual behaviour over time produces system-level "emergent" phenomena. In outbreak management, IBM models are adequate in the initial phases of outbreaks, in situations when the population size is small (Green *et al.,* 2006) and at the end of outbreaks (Keeling, 2005). The initial phases of an outbreak are particularly important for disease control measures because it is practical and easier to change the course of the outbreak. On the other hand, in population-based compartmental modeling that divides a population into compartments depending on the infection status, i.e. susceptible, exposed, infectious and recovered (SEIR) (Anderson and May, 1991), it is possible to have fractions of individuals in a state when one is dealing with small populations. This may lead to unrealistic outcomes, for example, endemic patterns relying on very small densities of individuals, normally referred to as "atto-foxes" (Mollison, 1991). An additional constraint in population-based compartmental modeling is that transition rates do not allow for demographic stochasticity induced by small populations (Camacho *et al.*, 2011).

The IBM used in this study was, therefore, able to capture dynamic complexity to a greater extent in systems as experienced in RVF epidemiological system, for instance, differences in infection mortality probability at the species and age level. Besides, this framework provides a natural description of a system, for example, it is more natural to describe how hosts get infected through movement in a vector breeding site than to

come up with the equations that govern the movements of the hosts. Individual-based modelling is flexible from a number of dimensions - for example, it is easy to add more individuals, it is easy to tune the complexity of the agents, for instance, behavior and rules of interactions and the ability to change levels of description and aggregation (clusters of herd/flocks etc.). In this way, this study used IBM as a virtual "laboratory" where different types of interventions were tested (Chapter 7).

The current model predicted a higher infection incidence in sheep than cattle despite the use of similar host infectivity parameter. The use of a similar host infectivity parameter on two host species results in a lower force of infection in the species with higher population number, i.e. sheep due to the larger denominator in computing infection prevalence (see Chapter 3). In this case, the higher RVF mortality in sheep could have enhanced the force of infection through the dramatic reduction of the sheep population as the outbreak progressed. West Nile virus modelling work has reported that host mortality intensifies transmission during an outbreak by concentrating vector mosquitoes on the remaining hosts (Foppa and Spielman, 2007). The question of whether the same mechanism applies to RVF in sheep remains open for investigation. Species-based parameters on host infectivity to RVFV following an infectious bite are not available. Transmission experiments (discussed below) are needed to quantify the species-specific and age-dependent probabilities of transmission of RVFV.

The results of the analyses also demonstrated that seasonal/inter-annual transmissions boost herd immunity over time. Predicted seasonal transmissions that occurred during the wet seasons were associated with the emergence of few infected floodwater *Aedes* species only. These events did not result in full-blown outbreaks given that flooding was not sustained and, therefore, secondary vectors did not develop to appreciable levels. These predictions were supported by empirical studies that have been done in Kenya (Bird *et al.,* 2008; Lichoti *et al.,* 2014; Owange *et al.,* 2014), Madagascar (Chevalier *et al.,* 2011) and Tanzania (Sumaye *et al.,* 2013) that demonstrate limited RVFV activity in the wet seasons. These seasonal transmissions might be responsible for sustaining herd immunity over time especially when there are no external shocks associated with droughts, migration and tribal animosities.

Unlike previous models that have used a composite term for adequate contact rates between hosts and vectors (Gaff *et al.,* 2007; Niu *et al.,* 2010), this study disaggregated the adequate contact rate (or the probability of contact) into its individual components. The components included the vector biting rate, the vector and host infectivity (probability of successful infection in vectors and hosts respectively), blood meal index and vector host ratio (Smith *et al.,* 2012). Although the host module was individual-based, the force of infection, which was the per capita risk of a susceptible host being infected, was computed as a global variable, i.e., the product of probability of contact and the prevalence of infection (in hosts/vectors – refer to Chapter 3). Moreover, it is more plausible to regard the force of infection as time-

varying due to seasonal variability in mosquito densities (Reiner Jr *et al.,* 2014). This study chose this regime to tailor the complexity of the model to the type of calibration data that can be obtained in the future through field studies or transmission experiments.

The vector biting rate (frequency of feeding) was set as a constant. It is known that the frequency of mosquito feeding increases with temperature which has additional impacts on pathogen transmission dynamics (Emert *et al.,* 2011). This study ignored the effects of temperature and concentrated on the well characterized influence of rainfall on the occurrence of RVF outbreaks (Anyamba *et al.,* 2010). Given that RVF is limited to tropical climates that favour year-round presence of mosquitoes, this study hypothesized that water availability in breeding sites may play a more dominant role in the occurrence of RVF transmissions relative to temperature. Although the temperature tends to remain high and constant throughout the year in Ijara sub-county, future model refinements should incorporate not only the effects of temperature on vector population dynamics but also on the extrinsic incubation periods of RVFV in vectors (Ba *et al.,* 2005).

Parameters on host infectivity were not available. Information from the literature suggests that host infectivity depends on livestock age and species. For instance, viraemia becomes demonstrable in neonate lambs a few hours post-infection with small doses of RVFV, and persists for the duration of infection that ends fatally within

36-42 hours (EFSA, 2005). In older ruminants, viraemia becomes demonstrable 1-2 days post infection and persists for up to seventh day (EFSA, 2005). Maximum titers recorded have been 10^{10} Mouse Intraperitoneal 50% Lethal Dose (MIPLD50/ml) in lambs, 10^{7} in sheep and calves, 10^{8} in kids and 10^{5} in goats (EFSA, 2005). This limited data on infectivity between different species defines one of the important parameter quantification gaps. Information on transmission between different ages and species, when available, will inform future modelling work necessary for better understanding of RVFV transmission patterns in multiple species – for instance, how diversity of host species may buffer or amplify RVF outbreaks. Additionally, these data would unravel the relationship between susceptibility to RVFV and infectiousness among host species; for instance, in FMD, cattle are the most susceptible species whereas pigs are the most infectious (Cox and Barnett, 2009). Such information, if available for RVFV, may greatly contribute in the design of control strategies. Thus, for modelling of RVF transmission in a framework such as adopted in this study, within-group transmission experiments with a single and mixed host species are directly relevant and useful.

Inclusion of space in the model made it necessary to model movement patterns of hosts and heterogeneity of contacts between vectors and hosts. In the model, mobile herds/flocks connect static mosquito subpopulations in space. This assumption seemed reasonable given that in comparison to mosquitoes, herds/flocks moved more frequently and over large spatial scales (Butt, 2010). Nonetheless, within a grid cell,

two assumptions applied: first, the distribution of vectors over the susceptible host species was homogeneous implying that a host species had equal chances of being bitten by a vector. At the cell level, the vector-host transmission rate was, therefore, determined by the proportion of infectious vectors and the proportion of the visiting host population that was susceptible (frequency-dependent transmission). Between the grid cells, movements of hosts ensured dissemination of RVFV, establishing new foci of infection throughout the space. Such a structure is distinct from a single homogeneously mixing population commonly applied in other RVF models (Gaff *et al.*, 2007, Niu *et al.*, 2012, Chitnis *et al.*, 2013, Chamchod *et al.*, 2014). In this study, the model implemented random movements of the herds/flocks. Future model refinements will incorporate the recognized highly structured movement patterns practiced by pastoralists (Butt, 2010) as well as those offered during the participatory survey (Chapter 4). This model also assumed non-preference biting for the susceptible host species. Other models of mosquito-borne pathogens indicated that host preference-induced contact heterogeneity was a key factor in driving vector-borne pathogen outbreaks in multi-species host communities (Simpson *et al.*, 2011). Feeding preference of RVF vectors has not been documented yet, though on-going projects are gathering this information in the study site. Future improvements of the model will incorporate possible feeding preferences by vectors particularly when quantified in relation to the host abundance (feeding index).

In this study, the vector: host ratio, which describes the per capita number of vectors per host, was an important variable in vector-borne pathogen transmission (Smith *et al.,* 2012). Seasonal variation of the ratio in the model was responsible for RVFV amplification in hosts during the outbreak. This was more biologically intuitive as mosquito bites increase as a function of vector: host ratio. Normally, this ratio should reach a threshold level, i.e. a maximum number of mosquito bites a host can sustain per unit time. Chitnis *et al.* (2013) assumed human values for cattle (range, 1 to 50) in defining this threshold. Given the initial parameters, the current model computed a peak ratio of 500 during the outbreak. The model will in future be refined to a much lower ratio for greater accuracy.

Infectious and latent periods data were available in the literature (Pepin *et al.,* 2010); however, constant infectiousness in hosts was assumed in the current model during the infectious period. Ideally, it is plausible to assume infectiousness levels that vary over time during the infectious period. Although no clear evidence of relationship between viraemia levels and infectiousness has been documented, one approach in modelling infectiousness would be to represent it as a function of viraemia, by for instance, simplifying it in a linear relationship. However, there is great variation in the clinical profile of RVF cases. Moreover, the relative infectiousness of asymptomatic, mild, moderate and severe cases in hosts is not documented. This study assumed constant infectiousness as the best starting point before these data becomes available.

The current model assumed that all the RVFV transmissions were vector-borne. However, other modes of RVFV transmission described earlier -- such as aerosol (LaBeaud *et al.,* 2008) mechanical (Hoch *et al.,* 1985) and ingestion of infected larva (Romoser *et al.,* 2011) — are thought to play a role in the transmission of the disease. The importance of these additional routes of transmission has not been assessed; this study hypothesized that they may not change the overall patterns of RVF transmission.

CHAPTER 6

6.0 PREDICTED HOST POPULATION RECOVERY AND HERD IMMUNITY PATTERNS FOLLOWING A SIMULATED RIFT VALLEY FEVER OUTBREAK

6.1. Introduction

The impact of RVF outbreaks on livestock dynamics is evident during the course of an outbreak through RVF-induced mortality particularly in neonatal animals and RVF-induced abortions (Bird *et al.,* 2009). These impacts are expected to disturb population age-structure in at least two ways: (1) inadequate replacement of breeding stock leading to delayed population recovery (Chamchod *et al.,* 2014), and, (2) prolonged calving to conception interval in females associated with expected dystocia and retained afterbirths following RVF-induced abortions (Noakes *et al.,* 2001). These impacts are largely felt in pastoral and agro-pastoral systems where livestock is a key asset that fulfills multiple economic, social and risk management priorities.

The proportion of livestock that survives a RVF infection is immune to reinfection. A measure of the level of population-immunity (or, more commonly, herd-immunity) is the proportion of the population that is immune from further infection. The significance of herd immunity lies in the reduction of the number of the susceptible segment in the population which in turn effectively reduces the efficiency with which a pathogen is transmitted between hosts. Population recovery, through recruitment of susceptible animals, expectedly, reduces the herd immunity.

Host population demographics, particularly the rate of recruitment of susceptible hosts via births are a key basis for long-term recurrence of infectious diseases (Earn *et al.*, 2000). For instance, the long-term cycling of sylvatic dengue virus has been hypothesized to be driven by population turnover and decline in herd immunity in non-human primates (Vasilakis *et al.*, 2011). Reports on post-RVF outbreak population recovery patterns and associated cycling of herd immunity are lacking. The objective of this study was to determine the relationship between post-RVF outbreak host demographic and herd immunity patterns in a 2-host population. The two hosts (cattle and sheep) are, expectedly, characterized by different recruitment rates (through births) and different exit rates (through offtakes, culling and lifespan). The study also attempted to assess how herd immunity patterns may influence RVF transmission dynamics. The study further assessed whether hosts with different population turnover may experience outbreaks of RVF at different periods when observed as isolated populations given different patterns of herd immunity and suitable climatic indices.

6.2. Materials and Methods

6.2.1. Introduction

This chapter applied the model described in Chapter 3 and 5. Following the predicted outbreak, further transmissions are prevented and simulations run for five years to assess the evolution of host population and immunity dynamics. The purpose of this assessment was to determine (1) the time it takes for the host population to recover to

their carrying capacity, (2) the time it takes for the herd immunity to decline to levels sufficient for generation of an outbreak, and (3) qualitatively whether it is possible for hosts with different demographics (entry and exit rates) to experience outbreaks of RVF at different periods when analyzed as isolated populations. A total of 1000 simulations were used for these analyses.

6.2.2. Data management and simulation

Upon the termination of transmissions for each of the host species, the population was analyzed as a proportion (%) of their carrying capacity population. On the same day of termination of transmissions, the herd immunity was determined by dividing the current number of immune hosts of a given species with total current number of hosts for that species. This procedure was repeated after every subsequent year (365 days) for 5 years. All data were analyzed using STATA 11. Results in text are given as mean and the range of values (minimum and maximum). Graphic results utilize box and whisker plots.

6.3. Results

The model simulated levels of mortality for each host species. At the end of the large outbreak (day 1152 (Figure 5.5., in Chapter 5)), cattle and sheep populations declined to an average of 76% (range 67%, 91%) and 51% (range 39%, 64%) of their carrying capacity populations respectively. Figure 6.1 shows the evolution of hosts' population dynamics during post-outbreak period in sheep and cattle. Cattle population fully

recovered to their pre-outbreak populations on average 3-4 years (on day 1259) following the outbreak. At this time (on day 1259 after the end of outbreak), the sheep population was still on the recovery tangent; it was predicted that it would have achieved 71% (range 56%, 89%) of the pre-outbreak population at this time. At the end of five years following the outbreak, the populations were on average 102% (range 95%, 108%) and 86% (range 66%, 104%) of the pre-outbreak populations in cattle and sheep respectively across simulations.

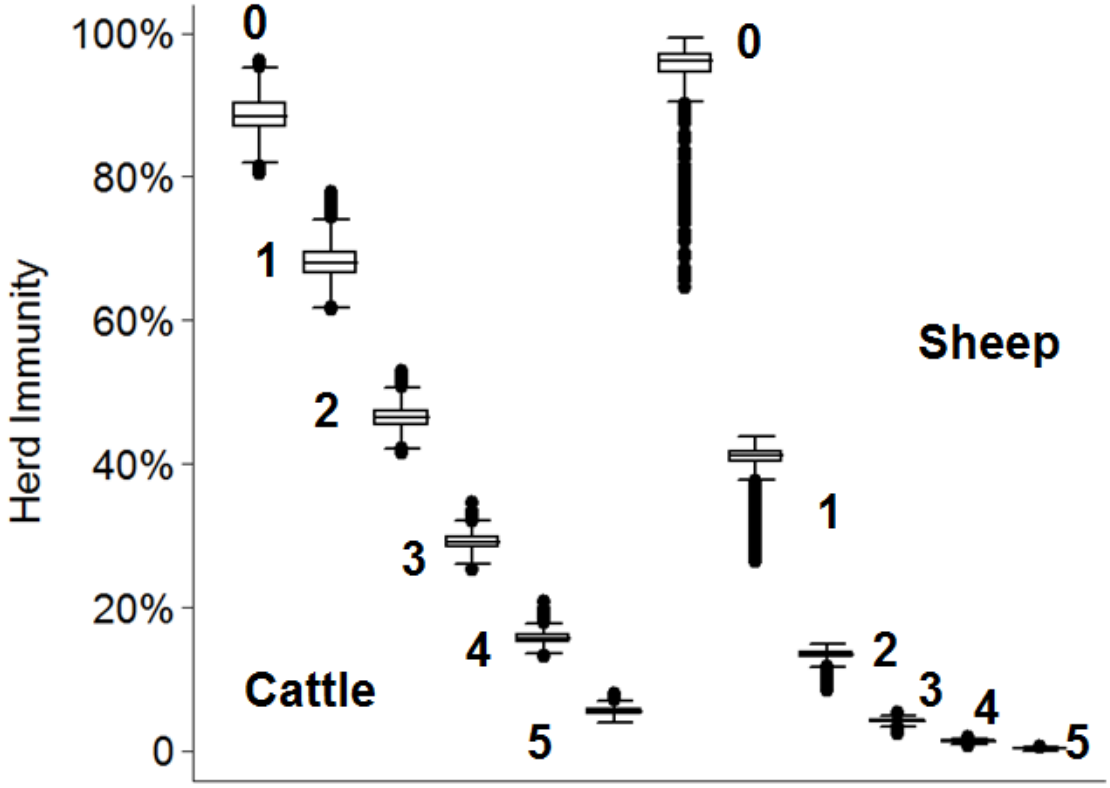


Figure 6.1: A box-and-whisker-plot showing the evolution of hosts' population dynamics during post-outbreak period. Key: The serial numbers denote time in years as follows: 0 -- end of outbreak; 1 -- 1 year after the outbreak; 2 -- 2 years after the outbreak; 3 -- 3 years after the outbreak; 4 -- 4 years after the outbreak; 5 -- 5 years after the outbreak. For observations in the time point analyzed, the thick line inside the box denotes the median, the box encloses 50% of the observations and the whiskers show the lower and upper 25% of the predicted observations.

Out of 1000 simulations (which can be taken as stochastic outcomes of 1000 host populations), 21 simulations in cattle and 982 simulations in sheep failed to recover fully 5 years post outbreak. This implied that the probability of cattle and sheep population recovering to carrying capacity 5 years after the outbreak was 98% and 2% respectively.

High herd immunity levels were attained just at end of the outbreak (89% in cattle [range 81%, 96%] and 94% in sheep [range 65%, 99%]). Five years later, the herd immunity levels decline to 6% [range 4%, 8%] in cattle and 0.3% [range 0.07%, 0.5%] in sheep (Figure 6.2). The rate of decline was intensely higher in sheep than cattle.

Figure 6.3 shows the evolution of herd immunity for both species for 3000 days and the predicted average time interval between attainment of 50% herd immunity and decline down to 50% herd immunity in cattle and sheep following the predicted outbreak. This time interval in cattle was 731 days and 328 days in sheep (Figure 6.3). Other time intervals computed in a similar fashion are shown in Table 6.1. The model predicted that over time, it took approximately more than double the time it took for herd immunity to decline to a certain level in cattle compared to sheep (Table 6.1). This implied, for example, that if herd immunity of <50% was the threshold required for the generation of a full-blown outbreak, and given the presence of RVFV infected mosquitoes, an outbreak in sheep could occur one year earlier relative to cattle when viewed as isolated systems.

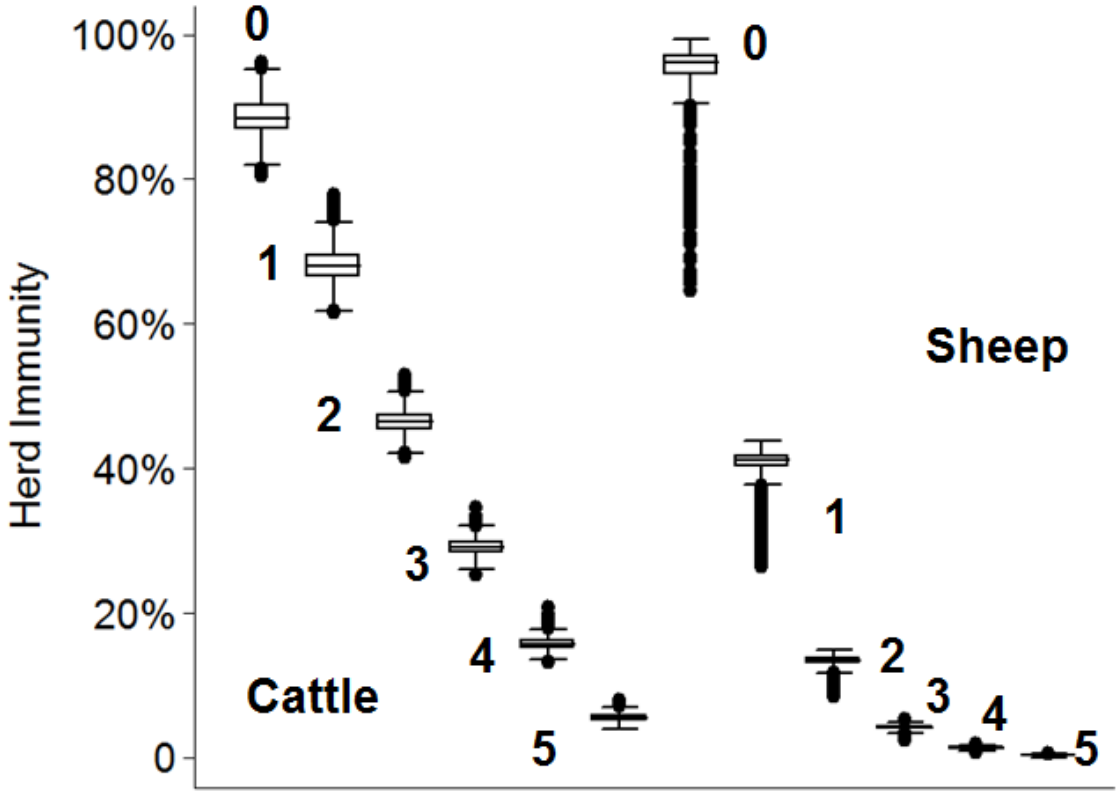


Figure 6.2: A box-and-whisker-plot showing the evolution of herd immunity dynamics during the post-outbreak period. Key: The serial numbers denote time in years as follows: 0 -- end of outbreak; 1 -- 1 year after the outbreak; 2 -- 2 years after the outbreak; 3 -- 3 years after the outbreak; 4 -- 4 years after the outbreak; 5 -- 5 years after the outbreak. For observations in the time point analyzed, the thick line inside the box denotes the median, the box encloses 50% of the observations and the whiskers show the lower and upper 25% of the predicted observations.

Table 6.1: Predicted time intervals (in days) between the attainment and loss of different levels of herd immunity in both hosts following the predicted outbreak

Herd immunity (%)	Cattle	Sheep
40	937	404
50	731	328
60	528	263
70	370	211
80	222	164
89	21	112

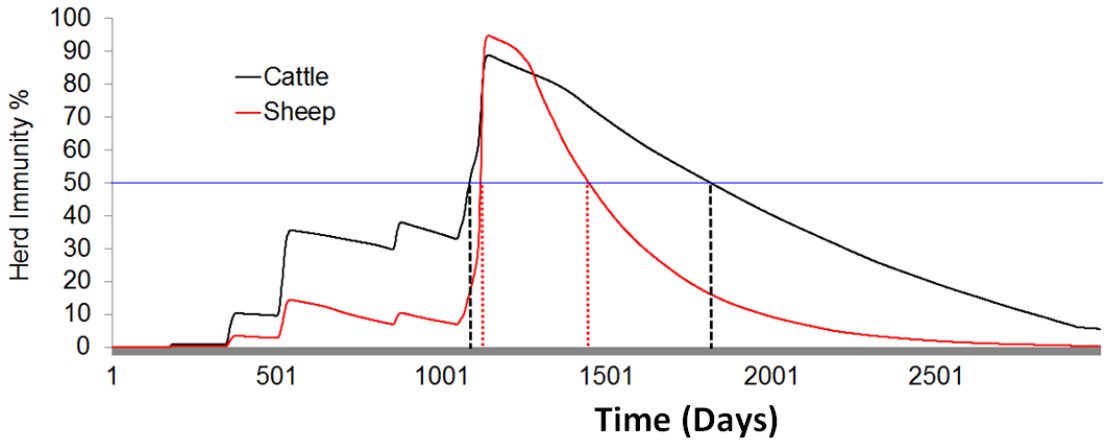


Figure 6.3: Predicted evolution of RVF herd immunity in hosts over 3000 days and predicted time interval between the attainment of and loss of down to 50% immunity in both hosts. The intervals are shown as black dots (cattle) and red dots (sheep).

6.4 Discussion

The RVF transmission simulation model was applied to predict host demographic and herd immunity patterns following the full-blown outbreak to assess the time it took for population to recover to carrying capacity by species and for the immune host population to decline given the variation in population turnover between the species. The predictions highlighted are solely due to RVF effects and does not include socio-economic interventions such as buying new breeding ewes following the predicted outbreak.

These information provided insights into whether herd immunity dynamics corresponded to the long inter-outbreak period observed in RVF and whether the different host species may experience outbreaks of RVF at different periods when analyzed as isolated populations. The study predictions suggested that the presence of dramatic variability in population recovery patterns among cattle and sheep owing to

differences in host species demographics. The study also showed that the host population recovery patterns accompanied by loss of herd immunity can synchronize RVF incidence patterns. The results further showed that given favourable climate conditions, RVF outbreaks may theoretically be experienced at different times when multiple host communities are considered as isolated populations. Empirical studies may be required to authenticate these findings.

This study assumed that infection with RVFV induced life-long immunity. The assumption was reasonable considering that RVFV antibodies neutralizing activity in the human and animal body confers immunity for life (Paweska *et al.,* 2005). The model predicted high herd immunity levels following the outbreak in animals that got infected but survived. These predictions were supported by observations made by Wilson (1994) that suggest that herd immunity levels of more than two-thirds can be achieved after a major RVF outbreak. Other reports suggest that 70-80% herd immunity is attained after a major RVF outbreak as well (Thiongane *et al.,* 1991; Chevalier *et al.,* 2004). These levels subsequently decline with time with the rate of decline being more apparent in sheep than in cattle. These predictions agree with findings in the Senegal River basin where following the 1987 RVF outbreak, the sheep population antibody seroprevalence dropped substantially from 72% to 24% in Dagana Sub-county between 1988 and 1989 (Thiongane *et al.,* 1991). This is because sheep have higher population turn-over rates than cattle due to their high fecundity, offtake, replacement rate and shorter lifespan. In cattle, lower birth rates relative to

sheep results in slow flow of susceptible individuals into the population while their longer lifespan increase the longevity of immune individuals. In absence of transmissions following the outbreak in the model, the herd immunity declines to negligible levels after a period of three to five years across the species. This period predicted by the model closely mirrors the predicted time it takes for the populations to recover to pre-outbreak levels/carrying capacity (discussed below) and the average inter-epidemic period in Kenya which has been estimated to be 3.6 years (range 1–7 years) (Murithi *et al.,* 2010). The findings from this study seemed to agree with anecdotal evidence that suggested that herd immunity plays an important role in modifying the length of RVF outbreak intervals given that the risk of an outbreak intensifies when the herd immunity is low and this is supported by the presence of suitable climatic indices. In West Africa, Ndione *et al.* (2003) attributed RVF outbreaks to loss of herd immunity over time (5–7-year inter-outbreak period in Senegal) that also corresponds closely to the time it takes for the renewal of a domestic herd of ruminants. Considering the assumption of life-long immunity in hosts, the observed relationship (between herd immunity and population recovery) is as a result of supply of susceptible hosts through births or purchases and not due to waning of immunity in individual hosts as occurs in other infections, for instance FMD (Ringa and Bauch, 2014). A better understanding of the role that these patterns play in the epidemiology of RVF is critical to refine existing control strategies, for instance, in evaluation of effectiveness of preventive vaccination strategies, cost-

effectiveness of vaccination campaigns, and effectiveness of focusing control against only one host species only.

Expectedly, a RVF outbreak consequence is a reduction in host population numbers associated with abortions, dramatic perinatal mortality and moderate mortality in adult livestock (Bird *et al.,* 2009). The model simulated RVF-induced reductions in host populations that depended on host specific mortality parameters. Thus, mortality in sheep severely reduced their population relative to cattle. The model was applied to assess the post-outbreak herd/flock recovery patterns as a critical RVF impact on livelihoods of livestock keepers. Recovery rate in sheep was predicted to be lower than that of sheep. This observation is possible considering the greater mortality among lambs, the loss of a greater number of pregnancies in breeding ewes during the outbreak that delay recruitment of lambs compared to cattle, and the higher population turnover associated with higher off-takes relative to cattle. The Food and Agriculture Organization (FAO), for example, estimates a 1.1% annual growth rate for cattle and 0.2% growth for small ruminants populations in Ethiopia (Pantuliano and Wekesa, 2008). Off-takes for cattle were estimated at 8%, while that for sheep and goats were put at an average of 37% per annum in Ethiopia (Pantuliano and Wekesa, 2008). Although the model did not incorporate the entire host entry and exit sources, the reproductive component of the host is modeled mechanistically. Thus, reproductive events, for instance, conception, depended on changes in herd dynamics making the model to be more realistic. Although these insights were based on simulations, there

was substantial additional value in providing empirical proof of the observed quantitative phenomena and to better understand the extent to which RVF-induced mortality influences host demography. The proof would have implications for post-outbreak livestock population numbers management policy by for instance, intervening by helping livestock keepers replace breeding females during recovery.

Host demography through birth rate has been shown to directly affect the inter-epidemic periods in measles (Finkenstädt *et al.*, 1998) and dengue viral infection (Cummings *et al.*, 2009). Additional sources of population turn-over variability are exit rates and lifespan. Rift Valley fever virus infects multiple host species with different population entry and exit rates. In the model, these are represented by cattle and sheep. A high proportion of the population that is immune increases the likelihood that an infectious mosquito will feed on an immune individual. Consequently, this reduces the force of infection in the host population. With different rates of decline in herd immunity between hosts, it is possible for certain hosts to experience outbreaks of disease at different periodicities when observed as isolated populations. This appears the case in RVF as sheep herd immunity declined to 50% of herd immunity in less than a year and to 40% in less than two years. Considering that the average inter-epidemic period in Kenya has been estimated to be 3.6 years (range 1–7 years) (Murithi *et al.*, 2010), outbreaks are possible given favourable climatic indices. However, this model implemented a multi-host population, and at any given time, the average herd immunity was expected to lie between that of sheep and cattle. The latter

implies that this would reduce the overall force of infection. This is one ecological condition where an increase in the diversity of host species may buffer infectious disease outbreaks. There are no reports of RVF outbreaks being dominated by a single species in a multi-host population. This could be due to the fact that the cycling of ENSO phenomenon which results in elevated and widespread rainfall associated with RVF outbreaks (Anyamba *et al.*, 2010) take longer than the decline in herd immunity in all host species. However, with the global climate change, the frequency and severity of RVF outbreaks are expected to increase in the Horn of Africa (Martin *et al.*, 2008). A possible consequence of the latter scenario would be a host species dominating an outbreak relative to another. The insights generated by the model predictions have the potential for designing targeted disease ecological-related control strategies.

CHAPTER 7

7.0 EVALUATION OF THE EFFECTIVENESS OF RIFT VALLEY FEVER CONTROL MEASURES USING THE SIMULATION MODEL

7.1. Introduction

The rapid evolution of RVF outbreaks generates exceptional challenges in its mitigation and control. A decision-support tool for prevention and control of RVF in the Greater Horn of Africa (Consultative Group for RVF Decision Support (RVF DST), 2010) identified a series of events that indicates increasing risk of an RVF outbreak and matches interventions to each event. The basis of the tool is that occurrence of certain natural events are indicative of increasing risk of an outbreak. The tool identifies actions that should be implemented in tandem with this evolving risk profile. Examples of these events are heavy rains, flooding and occurrence of mosquito swarms while examples of actions are livestock vaccination and vector control.

Vaccination against RVF in livestock is recommended to commence and end before the occurrence of a full-blown outbreak. This is because during an outbreak, there is possibility of mechanical spread of the virus through vaccination needles and transmission by mosquitoes when the live attenuated vaccines are used (Turell and Rossi, 1991). During an outbreak, the area is already flooded and this presents huge accessibility constraints. Pre-outbreak vaccination of livestock also presents a challenge: the time interval between ordering RVF vaccine and attainment of herd

immunity has been approximated to be 141 days. This time interval suggests that the RVF alert would need to be given at least 5 months in advance. The best prospective predictions of RVF occurrence based on satellite measurements of global and regional climate indices, so far, has been with lead times of 2–4 months before the outbreak (Anyamba *et al.,* 2010). In addition, the Smithburn vaccine has a shelf-life of approximately 4 years (RVF DST, 2010), while the interval between outbreaks in Kenya is 3.6 years (range 1-7 years) (Murithi *et al.,* 2010) making vaccine stocking difficult to implement due to expiry concerns. There are no field studies that have evaluated the effectiveness of RVF vaccination strategies.

Considering these challenges, this study applied the model described in Chapters 3 and 5 to assess the effectiveness of disease control strategies when applied singly or in an integrated manner at different stages of risk as identified in the decision-support tool (RVF DST, 2010). The objective was to support the decision-making on outbreak preparedness, response and control. The control strategies evaluated included vaccination and larva control.

7.2. Materials and methods

7.2.1. Animal vaccinations

To accurately assess the effectiveness of the control strategies, all seasonal transmissions that occurred prior to the full-blown outbreak (Figure 5.5. in Chapter 5) were prevented. All assessments in this Chapter, hence, commence with an entirely

susceptible population. Twenty five percent, 50% and 75% of each host species population in the model are vaccinated at different time points. Three time points representing the different stages of RVF risk were used for this study: (1) issuance of RVF early warning based on heavy rainfall forecasts by Kenya's national meteorological service representing a lead time of 11 weeks based on the recent outbreak in 2006/7, (2) onset of heavy rains with a lead time of 6 weeks, and (3) occurrence of mosquito swarms and first RVF cases in livestock at RVF outbreak onset.

A constant number of hosts (150 cattle and 300 sheep in the model, representing 15,000 cattle and 30,000 sheep in the field) were vaccinated daily until the targeted herd immunity (25%, 50% or 75%) was achieved. The assumption was that one technician can vaccinate 1,000 cattle or 2,000 sheep in a day. Two teams each comprising of 16 personnel were sent out daily to vaccinate. This information was sourced from Ijara sub-county Veterinary Office and subsequently implemented in the model to reflect realism. In this way, it took 5 days, 10 days and 15 days to achieve 25%, 50% and 75% population immunity. This study also assessed the possibility of RVF control by focusing against one host species by vaccinating 50% of cattle or sheep 6 weeks to the outbreak. The impact was measured by estimating the area under incidence curves (AUC). The AUC integrated several components of a curve into one statistic: outbreak persistence time, peak incidence and outbreak size. The results were presented graphically. A total of 1000 simulations were used for these analyses.

7.2.2. Larva control

The model was also applied to assess the effectiveness of larva control when applied alone. One time point was used: occurrence of mosquito swarms and first RVF cases in livestock at the onset of outbreak. A one-off constant increment in larvae mortality above the mortality rate in the model (0.2 per day) by 50% or 100% is implemented daily for either 30, 45, 60, 75, 90 or 105 days to mimic larva control. The first five scenarios (i.e. either 30, 45, 60, 75 or 90 days) represented situations where interventions began but were relaxed after the respective periods. The last scenario (105 days) mimicked larva control during the entire period of the outbreak. The results were presented graphically.

7.2.3. Integrated control

Integrated disease control involves use of at least two control methods in an optimal combination. Two interventions, i.e. vaccination and larva control were selected. The lowest level in each intervention, i.e. 25% vaccination and an increment in larvae mortality by 50% for 105 days which spans the entire outbreak period were assessed. This approach mimicked the integrated control measures carried out successfully during the 1977–1979 epidemic in Egypt along the Nile River where the Israeli government commenced with widespread vaccination and subsequently applied intensive vector control measures throughout the Sinai Peninsula and in the Gaza Strip. These integrated measures successfully prevented the spread of RVFV northward into Israel (Klopfer-Orgad *et al.*, 1981).

7.3. Results

7.3.1. Population coverages at different stages of Rift Valley fever risk

Table 7.1 shows the percentage reductions in AUC upon vaccinating 25%, 50% and 75% of the host population at different stages of RVF risk based on events preceding the 2006/7 outbreak Figure 7.1 shows the graphical results of the same. Note that the default incidence curves (illustrated as No intervention in Figure 7.1) for both cattle and sheep resulted from an entirely susceptible population.

Vaccinating 25% of the host population at any stage of risk did not prevent full-blown outbreaks (Figure 7.1) but was associated with marginal reductions in AUC (Table 7.1). Vaccinating 50% of the host population appeared to have major impacts particularly at any stage of risk. Vaccinating earlier on (11 or 6 weeks to the outbreak) led to impacts that were species-dependent – higher impacts realized in cattle population relative to sheep population. Vaccinating 75% of the host population had the greatest impact regardless of timing or species. In especially the 25% scenario, presence of herd immunity delayed the timing of peak transmissions.

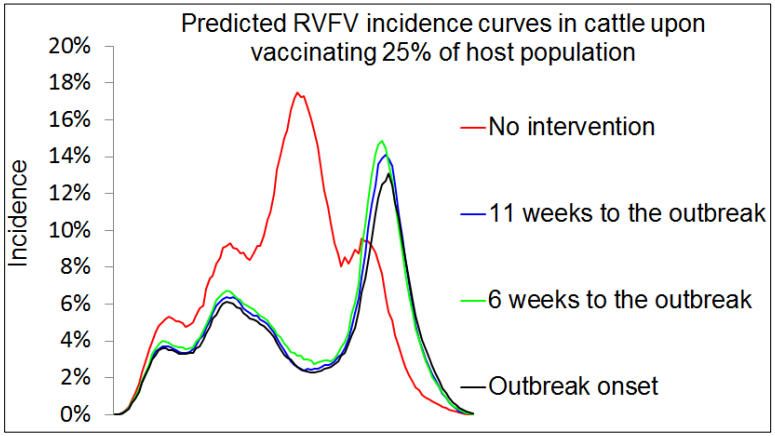
7.3.2. Targeting host species

Table 7.2 shows the percentage reductions in AUC upon vaccinating 50% of cattle or sheep, 6 weeks to the outbreak. Figure 7.2 shows the graphical results of the same. Several interesting findings were revealed: (1) Protection appeared to be species-specific, i.e. there were few benefits derived in the species that remained

unvaccinated; however cattle benefited more from vaccinating sheep alone than sheep from vaccinating cattle alone, and impacts in a host species were less when hosts species are singularly vaccinated compared to when both species were simultaneously vaccinated, as shown in Table 7.2 (50% 6 weeks to the outbreak) were less than those shown in Table 7.1 (50% 6 weeks to the outbreak).

Table 7.1: Predicted impacts of different vaccination coverages targeting 25%, 50% and 75% of the host population at different stages of RVF risk based on events preceding the 2006/7 outbreak

Vaccination coverage	**Lead time to outbreak (weeks)**	**Percentage reduction in area under incidence curve**	
		Cattle	Sheep
25%	11	34	16
	6	27	13
	0	37	25
50%	11	64	62
	6	67	69
	0	69	73
75%	11	85	86
	6	86	88
	0	87	89



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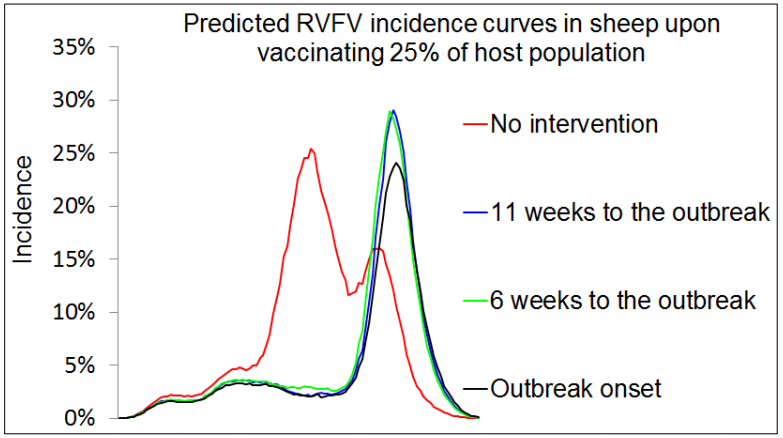

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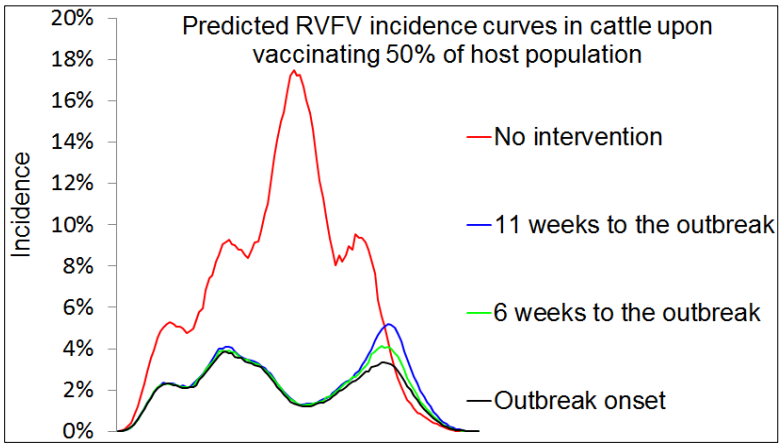

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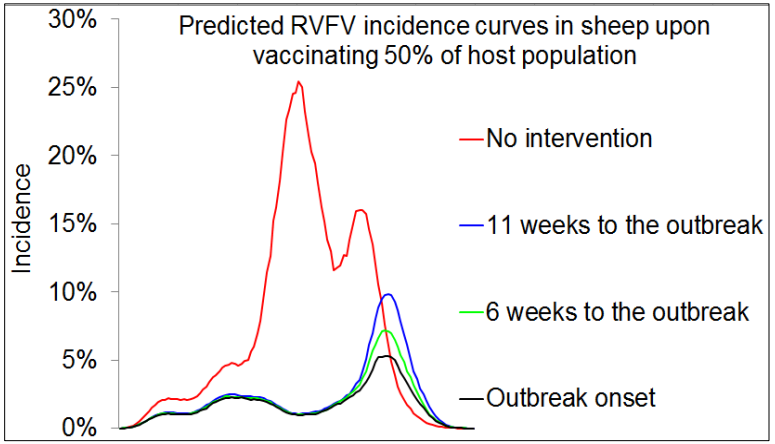

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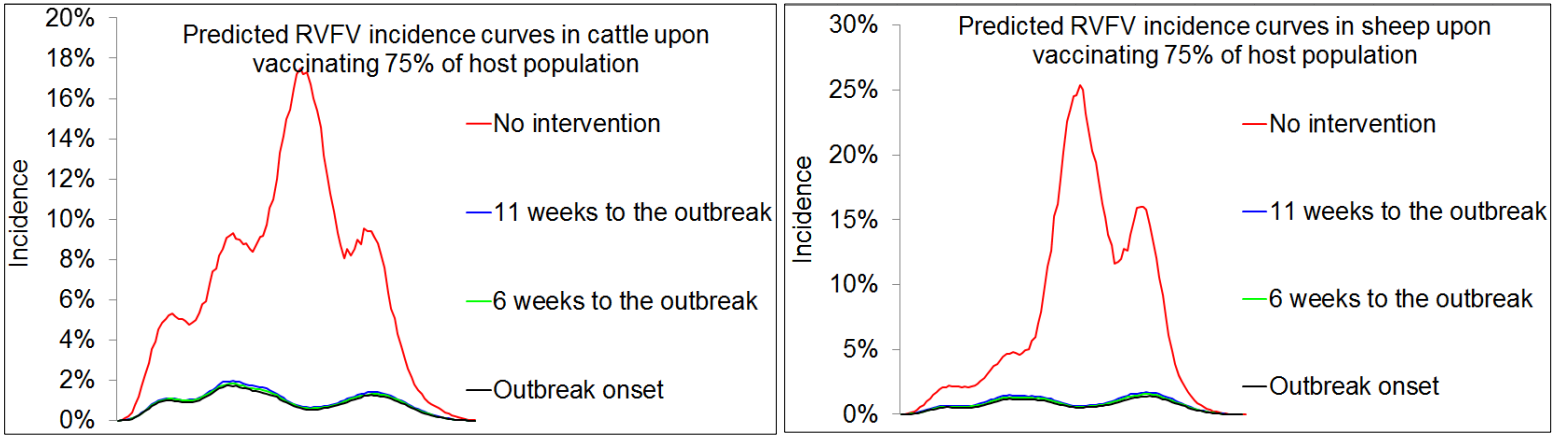

Figure 7.1: Predicted incidence curves in cattle (A, C and E) and sheep (B, D and F) upon vaccinating 25% (A and B), 50% (C and D) and 75% (E and F) of the host population at different stages of RVF risk based on events preceding the 2006/7 outbreak.

Table 7.2: Predicted impacts of vaccination targeting host species by vaccinating 50% of either cattle or sheep 6 weeks to the outbreak

	Percentage reduction in area under incidence curve in	
Vaccination coverage	Cattle	Sheep
Cattle alone	56	0
Sheep alone	10	45

7.3.3. Larva control

Increasing larval mortality by 50% daily following commencement of transmissions (day 0 of the outbreak) did not prevent a full-blown outbreak for all periods assessed including the entire outbreak period (Figure 7.3). In all instances, an outbreak flared-up once the control was relaxed, i.e. the period of application corresponded with the delay in the peak of transmissions (Figure 7.3). The peak of transmission was also higher than the baseline curve. This was attributed to favourable conditions for breeding resulting from persistent flooding mosquito challenge as time progressed leading to higher rate of emergence of adults.

Increasing larval mortality by 100% daily following commencement of transmissions (day 0 of the outbreak) was predicted to be effective in preventing a full-blown outbreak but only if sustained for >60days (Figure 7.4).

7.3.4. Integrated control

Increasing larval mortality by 50% daily following commencement of transmissions (day 0 of the outbreak) lasting the entire phase of the outbreak in combination with a herd immunity of 25% was predicted to be highly effective in preventing the

occurrence of a full-blown outbreak (Figure 7.5). Each of these interventions failed to prevent the occurrence of an outbreak when applied singularly (Figure 7.1 A and B and 7.3). Though transmissions were hugely interrupted, the herd immunity did not rise beyond 40-50% at the end of the outbreak.

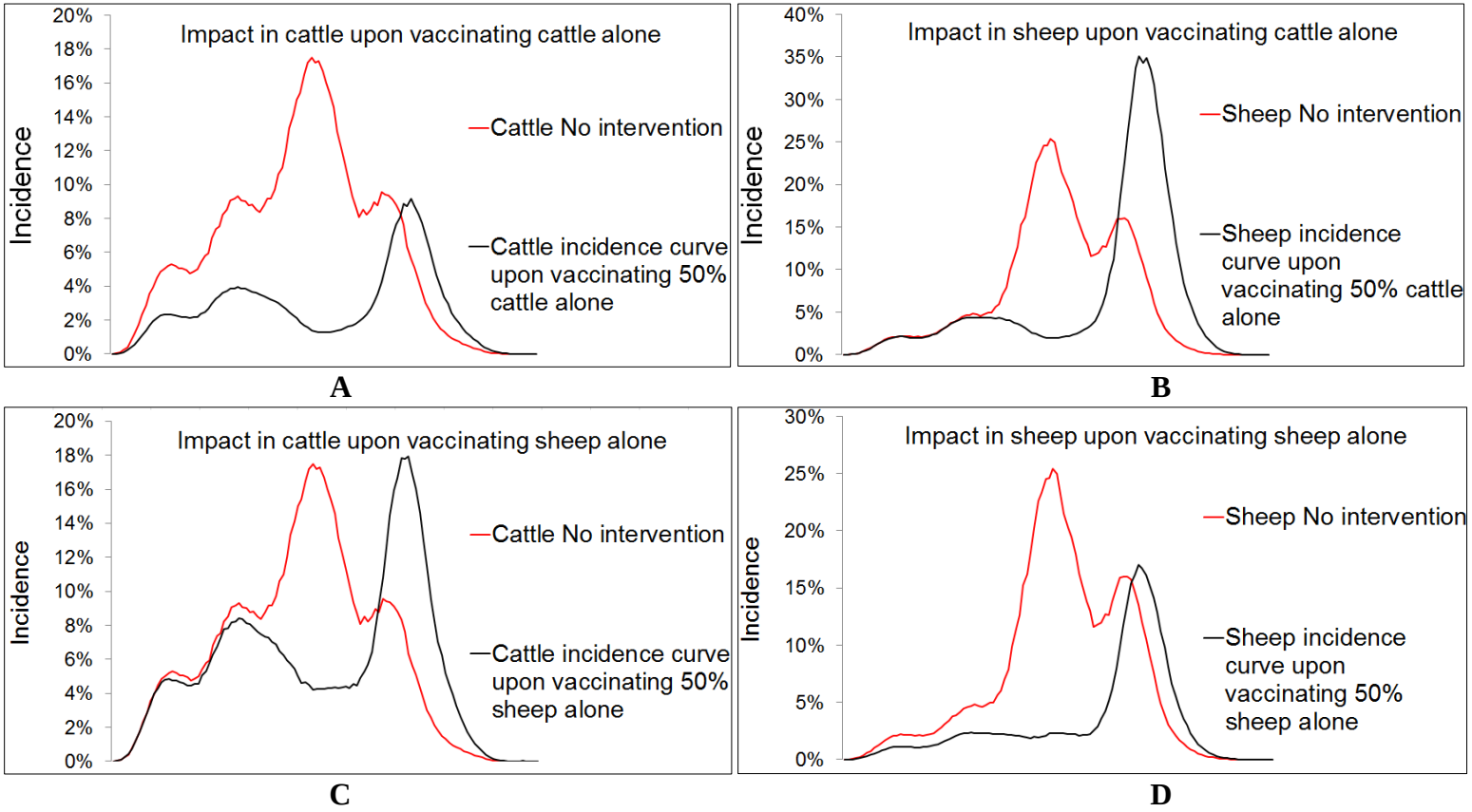

Figure 7.2: Predicted incidence curves of RVF upon vaccinating cattle alone (A and B) and sheep alone (C and D).

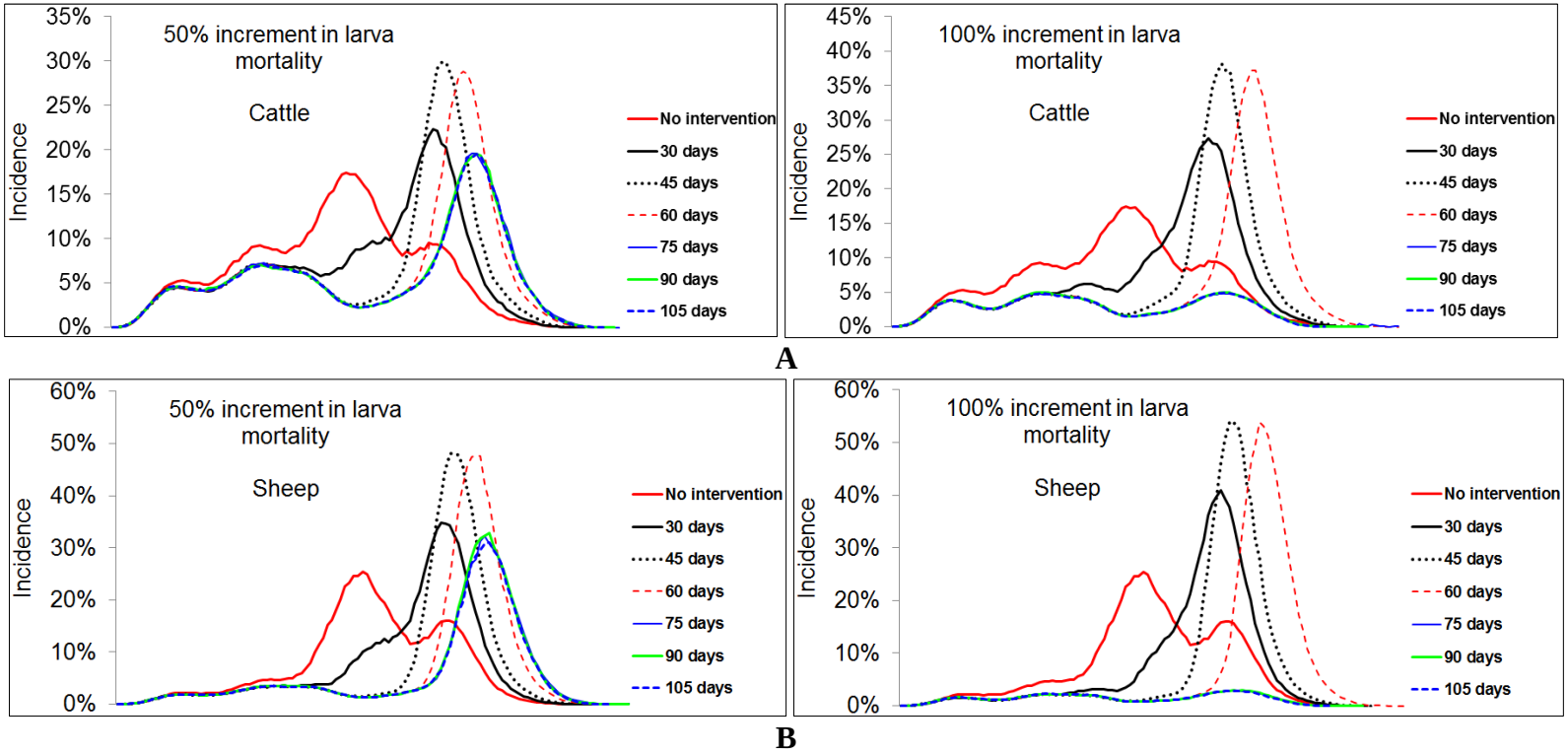

Figure 7.3: Predicted impacts on RVF incidence in cattle (A) and sheep (B) following larva control

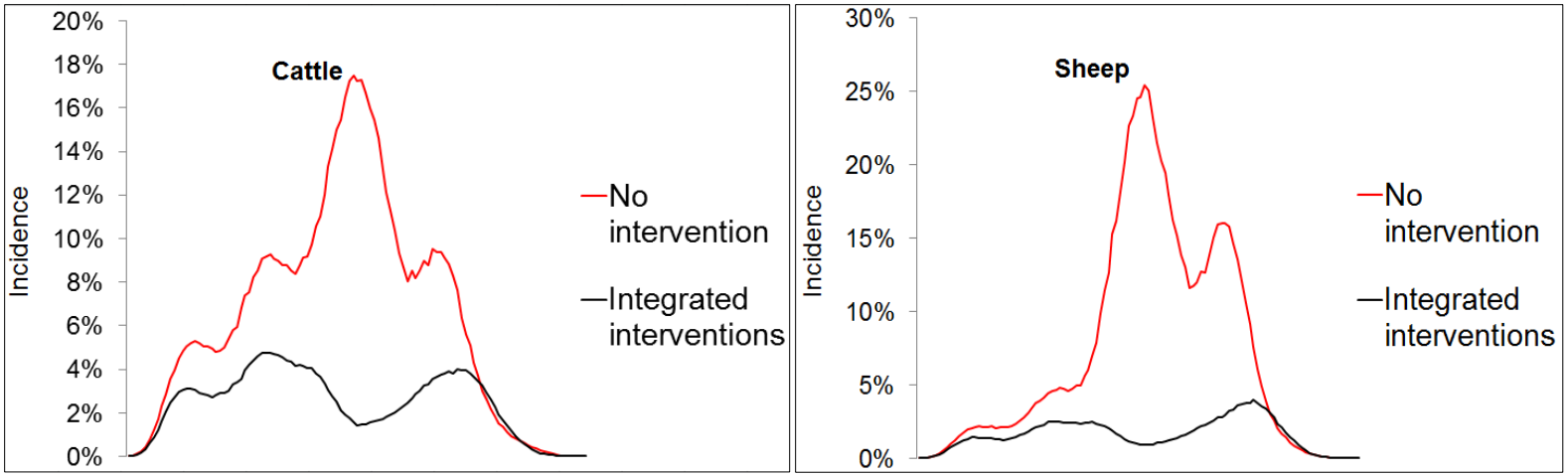

Figure 7.4: Predicted impacts in cattle (A) and sheep (B) following integrated interventions - larva control by increasing larva mortality by 50% for 105 days in a population with 25% herd immunity at the commencement of the outbreak

7.4. Discussion

Simulation models have proved to be useful tools in helping the planning of control strategies of mosquito-borne diseases (Ooi *et al.,* 2006; Burattini *et al.,* 2008; Chao *et al.,* 2012). This study applied the RVF simulation model in the evaluation of impacts of intervention strategies when implemented singularly or in an integrated manner to assess their potential success in controlling RVF incidence in livestock at different stages of RVF risk. Analyses of the predictions revealed that targeted vaccination can be effective in mitigating the impacts of RVF outbreaks. However, this depends on vaccination coverage - vaccination was predicted to be effective only when at least approximately 50% of herd immunity is present prior to the outbreak. On the other hand, an increase in base larval mortality by 50% failed to prevent the occurrence of an outbreak even when applied throughout the course of the outbreak. Increasing the base larval mortality by 100% was predicted to prevent the occurrence of an outbreak only when sustained application >60 days is ensured. This implied that mosquito challenge intensified during the period <60 days this period basically due to the amplification of population of secondary vectors. Interestingly, integrating the two interventions that failed to prevent outbreaks when applied singularly (25% vaccination coverage or an increase in base larval mortality by 50%) diminished the outbreak size effectively.

Previously, vaccination against RVF in the Greater Horn of Africa has been understood to be extremely challenging to an extent that some experts consider it as

impossibility (RVF DST, 2010). This is due to unavailability of vaccines during the time they are required arising from (a) short-expiry periods by vaccine stocks relative to inter-outbreak periods, and (b) short prospecting times of predictions of RVF occurrence (RVF DST, 2010). Findings from this study are expected to contribute to the way forward towards these propositions (discussed below).

This study predicted that starting with a population with 50% herd immunity for both hosts, 6-11 weeks to the outbreak was adequate in preventing a full-blown outbreak. However, mounting vaccination campaigns that can achieve this level of herd immunity is challenging in terms of disease control resources. For the population in Ijara sub-county, the model assumed two teams each comprising of 16 personnel each vaccinating 1000 cattle and 2000 sheep/goats daily for 10 days. The RVF DST recommended vaccination in livestock in "hot spots", particularly those that become non-accessible when rains commence (RVF DST, 2010). Commencing with a population with 25% herd immunity in both hosts in the population was inadequate in preventing a full-blown outbreak. These predictions agree with findings by Gachohi *et al.* (2012) that during the 2006/7 RVF outbreak in Kenya, vaccination coverage achieved was too low to be effective (estimated coverage ranged from 3% to 18% in cattle, 3% to 56% in sheep, 1% to 25% in goats and 2% to 4% in camels). Indeed, model predictions from this study reveal that vaccinating either of the host species alone was inadequate to prevent a full-blown outbreak in the unvaccinated host species. This was attributed to lower herd immunity achieved by targeting the single

host populations. Vaccinating 50% of cattle alone, for example, achieve 17% herd immunity in the population whereas vaccinating 50% of sheep alone achieve 33% herd immunity in the population. Vaccinating 50% of both species achieve 50% herd immunity. Correspondingly, proportional reductions in AUC are consistent with these findings. One way to overcome vaccination challenges around the time an outbreak is looming is to conduct annual/biannual vaccination exercises that will regularly boost herd immunity over time such that considering the 50% threshold predicted to prevent a full-blown outbreak, only a "top-up" exercise would be required in case RVF risk is heightened. Using these predictions, for the example, if a population's herd immunity is 25% (with its likelihood of generating an outbreak), boosting it to 50% (and avoid generating an outbreak) demands less effort and resources.

The results in this chapter were, however, based on the assumption of similar host infectivity values between cattle and sheep and similar host preference in taking up of blood meals by vectors. These two parameters are unlikely to be similar in the field. Dissimilar values are likely to generate different values of force of infection. In such a scenario, one host species may dominate the transmission terms (Simpson *et al.*, 2011). In such a case, it may be possible to control the disease by focusing vaccination against this species. Unfortunately, with limited data, it's difficult to offer concrete conclusions about such propositions. Nevertheless, the study revealed additional benefits in cattle by vaccinating sheep relative to the benefits sheep receive by vaccinating cattle.

Normally, sheep are associated with higher RVF-induced mortality relative to cattle. Previous modelling strategies reported that host mortality may intensify transmission, both by concentrating vector mosquitoes on remaining hosts and by preventing the accumulation of herd immunity (Foppa and Spielman, 2007). With regard to these observations, and assuming the asymmetrical force of infection favourable to cattle, this study hypothesized that vaccination be targeted towards sheep. However, sheep and goats are associated with high population turn-over, meaning that for herd immunity to be sustained in the population, regular vaccination exercises are required. The uncertainty of the assumptions upon which these arguments are built and the overwhelming lack of knowledge of transmission terms make acquisition of relevant field data on these biological processes a top research priority.

Vector control is a key strategy in combating mosquito-borne diseases and is the only tool available for preventing transmission in diseases in which no vaccine, prophylaxis, or therapeutic agents are available, for instance, dengue (Burattini *et al.*, 2008). The results of this study predicted that only sustained larva control for over 60 days daily could effectively control an RVF outbreak and even then, the basal larval mortality should be increased by 100% (from 0.2 to 0.4). Application of larvicides for shorter periods or using formulations that kill 30% of them (increasing basal mortality from 0.2 to 0.3 by 50%) had little effect on RVFV transmission. Intuitively, the turnover of mosquitoes is very high and consequently, the mosquito population was

restored rapidly and the population became quickly re-infected by the infected livestock.

Control of mosquito larva can be achieved only by applying larvicides to water habitats where mosquitoes develop. Normally, the period during which a RVF outbreak occurs is characterized by extensive areas of standing water. Because of the expansiveness of the flooded areas such as Ijara sub-county, this exercise can only be accomplished by airplanes and/or helicopters making it costly. In field studies, similar to the model predictions, larvicide products known as insect growth regulators (IGRs) such as methoprene in sustained release Altosid™ Pellets (Wellmark International, Schaumberg, IL) were found to be effective in controlling both *Aedes* and *Culex* vectors of RVFV and, moreover, even when placed into standing water several months before flooding (Logan *et al.,* 1990). Sustained release products control mosquitoes for an extended period of time (1–2 months) without retreatment (Anyamba *et al.,* 2012) and could find suitable use during RVF outbreaks in areas such as Ijara sub-county.

Recent field innovations seem to overcome the application of larvicides in expansive flooded areas such as Ijara sub-county. Devine *et al.* (2009) exploited adult mosquitoes as vehicles of larvicide transfer from resting sites to oviposition sites where larva reside. A series of field trials carried out in Peru demonstrated that setting of a juvenile hormone analogue (JHA) dissemination stations in just 3–5% of the

available resting sites resulted in almost complete coverage of sentinel aquatic habitats, achieving mortality in 95–100% of the larval cohorts of *Aedes aegypti* developing at those sites. This is a promising approach that can be designed and implemented prior to amplification of secondary vector populations which are associated with RVFV amplification in livestock.

Integrating vaccination and vector strategies was predicted to be more effective than either interventions implemented alone. This is an interesting and encouraging finding considering the resource and time constraints normally experienced during outbreaks. As mounting serious vaccination campaigns is difficult once outbreak begins due to accessibility constraints, efforts may be shifted to suppressing adult emergence through sustained larva control. This integration can be targeted in known hotspots to improve the effectiveness and efficiency of disease control and optimize interventions as well. This scenario is similar to that adopted in Integrated Vector Management (IVM) in Malaria control that is based on a rational decision-making process for the optimal use of resources for vector control (WHO, 2008). Successful implementation of IVM is dependent on (a) integration of non-chemical and chemical vector control methods and their integration with other disease-control measures, (b) evidence-based decision making using methods based on sound knowledge of factors influencing local vector biology, and (c) disease transmission knowledge among other factors (Beier *et al.*, 2008). A drawback of this model prediction related to integrating vaccination and vector strategies is that though transmissions are hugely interrupted, the herd

immunity does not rise beyond 40-50% at the end of the outbreak implying that the population would become susceptible sooner in absence of sustained vaccination.

Logistic difficulties present immense challenges in implementing the tested interventions particularly in RVF endemic areas that are in remote rangelands and are inaccessible during heavy rains. However, challenges associated with prediction of the outbreak, availability and delivery of vaccines and larvicides need to be addressed. If confirmed by empirical studies, these findings have important implications for the implementation of risk-based RVF interventions. Consequently, cost-effectiveness analysis (CEA) should be integrated with these studies to prioritize these interventions.

CHAPTER 8

8.0 GENERAL DISCUSSION

From this study, the individual-based modeling (IBM) approach in the host module successfully modelled the complexity in the host RVF epidemiological component. A disadvantage of IBM in simulating the behavior of all of the hosts is that it can be extremely computational intensive and, therefore, time consuming (Grimm *et al.*, 1999). For this study, running one simulation for 1200 days took approximately 15 minutes while running the simulation for 3000 days took 26 minutes. Although computing power is still increasing at a remarkable speed, the high computational requirements of IBM remain a challenge when it comes to modeling large systems. The choice of the model structure (IBM) approach in the host module and the explicit inclusion of space successfully allowed macro-level disease ecological patterns to emerge from explicitly described micro-level behaviors, interactions, and movements of the hosts in a spatially heterogeneous framework.

Through careful design and methodology, this study demonstrated resource-mediated grazing movement strategies that pastoralists employ to counter environmental variability. For the pastoralists from Ijara sub-county, judicious movement patterns of sheep and goats and cattle is dependent on environmental conditions and the type of animals kept. When analyzed against NDVI estimates, these patterns revealed the tendency of increased movement during periods of low NDVI. Community-based surveys using participatory epidemiological methods are a low-cost approach

adaptable to collection of parameters necessary in disease transmission modelling. Somali pastoralists from Ijara sub-county possess rich livestock and disease knowledge. They were able to describe RVF incidence and case fatality rate (CFR) patterns across different livestock species consistent with the formal knowledge, similar to Jost *et al.*, 2010, five years after the occurrence of the outbreak.

The model successfully simulated, using independent probability functions, linkages between rainfall variability and density of mosquitoes (both primary and secondary vectors of RVFV). Although the vector: host ratio increased with precipitation, the peaks of the ratio, expectedly, lagged behind those of cumulative precipitation. The model predicted elevated RVFV activity during the wet seasons (dependent on amount of rain) as well as a full-blown RVF outbreak following periods with excessive and persistent precipitation. The shapes of the incidence curves varied depending on whether the population was entirely susceptible or a proportion of the population was immune at the beginning of the outbreak. The two curves, across host species, had similar outbreak persistence times (the time to outbreak fade-out). However, they differed in time to the peak incidence and the number of transmissions (outbreak size). The host and *Culex* species outbreak curve had a characteristic shape – a slow onset that quickly rose to a full-blown outbreak. The predicted mean peak incidence of RVFV in cattle was approximately half that of sheep. However, the curves (for cattle and sheep) peaked almost at the same time and the outbreak lasted the same duration in both host species. Transmission events that occurred periodically during the wet

season were predicted to boost herd immunity. The simulation model described in this study has potential for better understanding of factors contributing to RVF endemicity and epidemics as well as planning and optimizing RVF control, including integrated interventions. This model could also be applied to other vector-borne viral infections that are majorly weather dependent such as chikungunya viral infection.

Based on the results of this study, population recovery patterns following the mortality impacts of RVF differed between cattle and sheep. Cattle population fully recovered to pre-outbreak levels earlier than sheep. Indeed, at the end of 5 years, the probability of cattle and sheep population recovering to carrying capacity is estimated to be 98% and 2% respectively. In general, prior to the outbreak, the seasonal/inter-annual transmissions boost herd immunity over time. High herd immunity levels were attained in both host species just at end of the outbreak. Following the prevention of any transmissions after the outbreak for five years, the herd immunity levels declined to negligible levels in both hosts though the decline was intensely higher in sheep relative to cattle. This period predicted by the model closely mirrored (a) the predicted time it took for the populations to recover to pre-outbreak levels/carrying capacity and (b) the average inter-epidemic period in Kenya which has been estimated to be 3.6 years (range 1–7 years) (Murithi *et al.,* 2010). There is a potential of incorporating this model (that predicts herd immunity dynamics) to climatic models (that predicts climatic indices alone) for greater outbreak forecasting accuracy.

The results of the study showed that vaccinating 25% of cattle and sheep at any stage of RVF risk was not effective in preventing RVF outbreaks. However, vaccinating at least 50% of both cattle and sheep at any stage of RVF risk was predicted to be effective in preventing large RVF outbreaks. To exert a significant effect on RVFV transmission, the model predicted sustained source reduction of larva at mosquito breeding sites through increasing their mortality by 100% of basal mortality for at least 60 days since the commencement of transmissions. Integrated control, by combining 25% herd immunity and sustained source reduction of larva at mosquito breeding sites through increasing their mortality by only 50% of basal mortality for the entire outbreak period, was adequate for preventing an outbreak. This has important implications for the implementation of risk-based outbreak prediction response vaccination campaigns.

CHAPTER 9

9.0 CONCLUSIONS AND RECOMMENDATIONS

9.1 Conclusions

This thesis draws the following conclusions:

1. The model successfully dissected the complexity of mechanisms that can produce RVF outbreaks. Its main strength lies in incorporation of multi-hosts and multi-vector population dynamics, coupling the hosts and vectors with transmission terms, the explicit spatial structure and the link with climate.
2. The model outcomes provide valuable insights into the dynamics of the spread of RVF epidemics. The study generated qualitative predictions and empirically-testable hypotheses about the fundamental role that hosts, vectors, environmental factors and socio-ecological factors play in the production of RVF outbreaks.
3. The model was applied to predict the occurrence and impacts of RVF and in evaluating single and integrated disease management tools and their potential success in controlling RVF incidence in livestock populations.
4. The model assumptions, findings and predictions are open for empirical inquiry.
5. The model was presented as a tool with which researchers and public health policy makers can carry out "*what-if*" type of analyses to guide research in the field and transmission experiments.

9.2 Recommendations

From the foregoing, this thesis recommended the following:

1. This study revealed that animal health constraints that include diseases such as African Animal Trypanosomiasis, CBPP, CCPP and RVF existed in Ijara sub-county. Interventions aimed at controlling these diseases are likely to have a positive impact on the livelihoods of Ijara sub-county pastoralists.
2. Evaluation of satellite-based precipitation products in areas endemic to RVF and other mosquito-borne diseases whose dynamics are heavily influenced by precipitation is recommended for accurate predictions of mosquito population dynamics and infection risk.
3. Models of RVF spread are in most cases hypothetical because validation is difficult due to lack of empirical data. To obtain incidence data, disease reporting systems need to be strengthened and should involve communities (most likely via community animal health workers) as well. New strategies for model validation are, therefore, needed. A starting point is to challenge the models with accurately collected seasonal RVF outbreak data.
4. This study has identified many areas of information gaps particularly those related to transmission terms. Due to data constraints, RVF modelling has largely assumed quantitative parameter information from other vector-borne diseases or as subjective estimates. Experimental and field studies should be designed and implemented to play the following roles (1) when combined with modelling, they can guide model construction and improve on previous,

provisional model assumptions, and (2) quantify the specifics of the transmission process.

5. This thesis evaluated the effectiveness of mosquito source reduction through mass larviciding. Its effective use may also be limited by lack of data on the relative productivity of specific habitats and the consequent need to seek out, identify, and treat all potential sites. Intensive and innovative entomologic research on new technologies for vector control is urgently required. This thesis proposes and recommends research on development of genetically modified *Aedes* mosquitoes that may interrupt vertical transmission of RVFV into the ovaries thereby preventing emergence of RVFV-infected adult mosquitoes. For the effective implementation of any of these interventions, the primary challenge is in realizing sufficient coverage of the insect population (vector control given local constraints on financial and human resources). This entails conducting detailed cost-benefit analyses to support decision making.

6. Finally, this thesis came up with interesting scientific questions and issues (from literature review, from the modeling process and model predictions) that are open for empirical inquiry and which can contribute to development of more refined simulation models. This thesis recommends that research funds be committed towards answering the following research questions:

a. Questions and issues related environmental factors

i. What are the rainfall patterns (ENSO-related or not) favourable for RVFV amplification in the Greater Horn of Africa?

ii. How can spatially defined foci of RVFV transmission be characterized by abiotic factors such as vegetation as well as by climate, latitude, elevation, and hydrology?

iii. Particular soil types appear to influence the spatial occurrence of RVF outbreaks. What are the characteristics of these soils that demarcate this influence? Is it water retention properties that favour flooding and/or biochemical properties that favour temporal viability of eggs?

iv. What role does wildlife play in the persistence of RVFV between outbreaks and during the early phases of an outbreak? Is there a sylvatic endemic maintenance of RVFV as occurs in Dengue fever and Yellow fever, for example and what constitutes the sylvatic endemicity?

b. Questions and issues related to vectors

i. Vectors of RVF have legendary been characterized as primary (represented by *Aedes* species) and secondary (represented by *Culex* species). Field studies report that RVF occurs during years when both species are present simultaneously in high densities. Ecological factors (extensive flooding) are thought to limit the populations of primary vectors. These knowledge needs to

be empirically proved to answer questions such as: can the primary vectors alone drive RVF full-blown outbreaks, or in other words, though the vector competence index (VCI) of certain *Culex* species is high in the laboratory, are the infections found in them during field outbreaks out of vector competence or are they incidental findings?

ii. RVF vector host preferences (in terms of blood feeding) have not been characterized. If the preferences do exist, how do they drive transmission of RVFV in a community of several host species?

iii. What are the vertical transmission rates in *Aedes* mosquitoes? How can this mechanism be interrupted to prevent the emergence of infected adults?

iv. How important is vertical transmission in *Aedes* mosquitoes during the outbreak and for the persistence of RVFV between outbreaks?

v. What is the lifespan of buried *Aedes* eggs? Do they contribute to virus persistence by allowing replenishment of aged eggs in the soils during the annual wet seasons?

vi. Do areas that experience RVF outbreaks experience spatially-heterogeneous local mosquito abundance patterns?

c. Questions and issues related to hosts

i. Susceptibility to RVFV infection by species and age within species is not known although it can be inferred from viraemia development data. Currently,

the assumption is that susceptibility to RVF-induced mortality corresponds to susceptibility of the animal to RVFV. How accurate is this?

ii. In a multi-host community, how do RVF transmission dynamics in a host species affect transmission dynamics in other host species? In other words, are there host species that dominate the transmission dynamics, either through host preference by vectors or through their abundance in the population or even through higher virus shedding?

iii. What is proportion of asymptomatic RVF cases in livestock? How is the viraemia development in the asymptomatic RVF cases segment? What is their epidemiological significance in the buffering of RVFV spread during an outbreak?

iv. How does infectiousness in livestock hosts vary with time during the infectious period?

v. What is the relationship between viraemia and infectiousness in the different host species?

vi. Are there threshold virus particles that must be introduced through successful biting by mosquito vectors to produce long-lasting immunity in hosts?

d. Questions and issues related to socio-economic factors

i. What is role of animal movements, for whatever reason, in introducing and spreading of RVFV in an area?

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Appendix 1: Rift Valley fever field data collection checklist

Introductions and reason for the visit (familiariaze with livestock keeping practices in the area)

Village map

Livestock species kept

Proportional abundance

Contribution to livelihoods

Herd structure

Age categories

Age names

Proportional abundance

Age at first breeding

Interval between parturition and subsequent heat

Frequency of repeat breeding

Frequency of twinning

Lifespan, by sex

Cattle herd and sheep/goat flock sizes

Challenges of livestock keeping

Diseases acquired by the three major livestock species kept over the last year and historically - test whether RVF comes up (literature says Somali community calls it sandik)

Impacts of major livestock diseases

Epidemiological indicators

Diseases syndrome/clinical signs in livestock

Occurrence

Indicators associated with its occurrence – vectors/weather/

Prevention and control in livestock

Method of transmission to people

Diseases syndrome/clinical signs in people

Prevention and control in people

Movement patterns over the one past year by sex

Question and answer session – community empowerment

Thanking the participants

Appendix 2: Summary code

This section includes the summary code implemented for the rules described in the host module (Chapter 3). The codes were implemented in C++ programming language in the following sequence:

Aging rules

Add the age of host by 1 day in each time step

Conception rules

if a female host is mature, then this host may conceive with a daily conception probability

Expected abortion rules

if a female host is pregnant, then this host experiences abortion with a daily expected abortion probability

then the host becomes open for new conception

RVF-induced abortion rules

if a female host is pregnant, if the host experiences RVF infection, then this host experiences abortion with a daily RVF-induced abortion probability

then the host becomes open for new conception

Parturition rules

if Pregnancy period> Gestation period, then a new born host is born and allocated sex status with a probability of 0.5

if Nursing period>PeriNatal period, then the host becomes open for new conception

Transmission rules

if a susceptible host moves to a site with infectious mosquitoes, the host becomes infected with a probability computed from the force of infection

then the infected host enters the latent state

if period spent in latency>Latent period, host enters the infectious state

if period spent in infectious state>Infectious period and the host is alive, the host enters the immune state

An immune host is not susceptible to further RVF infection

Host exit rules

if host is in the RVF infectious state, this host may die with a daily age-dependent RVF probability

if host is attains a certain age dependent on species and sex, this host is removed from the simulation

Movement rules

Hosts move in the grid as herd/flocks randomly

get the current position{x position, y position}

if herd movement distance is a random integer between -10 and 10, if flock movement distance is a random integer between -4 and 4, then update {x position, y position}using random movement distances.