SPATIAL EPIDEMIOLOGY AND PREDICTIVE MODELLING OF RIFT VALLEY FEVER IN GARISSA COUNTY, KENYA

By

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DECLARATION

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hereby declare that this is my original work that has not been presented wholly or partly for the award of any degree or academic honors elsewhere

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DEDICATION

To my entire family, Dad Bonventure Odeyo, Mum Betty Amakove Odeyo for their committed parenthood, Brothers Archduke and Alex, Sister Linet for support and encouragement in my academic endeavours. To my Late grandparents Elias Malomba Obuyu and Maria Abungu Olweyo who believed in my passion for excellence.

"All models are wrong, but some are useful"

(George.E.P.Box, Statistician, 1919-2013)

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LIST OF ABBREVIATIONS

ACZ	Agroclimatic Zone
AFI	Acute Febrile Illnesses
AUC	Area Under Curve
BRT	Boosted Regression Trees
CDC	Centers for Disease Control
CI	Confidence Interval
DEM	Digital Elevation Model
DVS	Directorate of Veterinary Services
ELISA	Enzyme-Linked Immunosorbent Assay
ENSO	El Niño/Southern Oscillation
EVI	Enhanced Vegetation Index
EWS	Early Warning System
FAO	Food and Agricultural Organization
FGD	Focus Group Discussion
GIS	Geographical Information Systems
GPS	Global Positioning System
IgG	Immuno Globulin G
IgM	Immuno Globulin M
ILRI	International Livestock Research Institute
INLA	Integrated Nested Laplace Approximation
KAP	Knowledge, Attitude and Practices

KEMRI	Kenya Medical Research Institute
MAM	March- April- May
MODIS	Moderate-resolution Imaging Spectroradiometer
NDVI	Normalised difference vegetation index
NGO	Non-Governmental Organizations
OD	Optical Density
OIE	Office des Epizooties-World Organization for Animal Health
OND	October – November- December
OR	Odds Ratio
RNA	Ribonucleic Acid
ROC	Receiver Operating Characteristic
RVF	Rift Valley Fever
RVFV	Rift Valley Fever Virus
SDM	Species Distribution Modelling
VNT	Virus Neutralization Test
WHO	World Health Organization

ABSTRACT

Rift Valley fever (RVF) is an emerging arboviral zoonotic disease of domesticated livestock that causes disease in humans and has significant socio-economic impacts. In domestic ruminants, RVF causes abortions in females and high mortality rates in new-borns. In humans, the disease begins with mild to acute febrile illness, and may progress to a severe haemorrhagic syndrome. Kenya has experienced two major outbreaks in the last 20 years; the 1997 outbreak that resulted in 89,000 human infections and 170 human deaths reported in Garissa and Southern Somali, and the 2006-2007 outbreak that resulted in livestock deaths estimated at US$10 million in economic loss, and additional production losses related to abortions and decline in milk production estimated at US$77,000.

Outbreaks of RVF in Garissa have been associated with high rainfall and flooding due to drastic climate variability, and the introduction of the virus associated with livestock movement and trade with neighbouring countries have enhanced RVF endemicity. The lack of preparedness of local communities which includes lack of knowledge on cause, risks and symptoms, poor attitude and practices in undertaking effective management increases their vulnerability to the disease outbreaks. Limited resources in health and livestock sectors have hampered routine serological monitoring of RVF virus activity to guide mitigation strategies. The lack of adaptable tools for risk communication of impending disease outbreaks lead to delayed response and control of RVF outbreaks in Garissa.

To address the above challenges a study was conducted in Garissa with the goal to investigate the spatial distribution and risk of Rift Valley Fever in Garissa using model-based approaches in prediction of outbreaks in response to climate variability. This was specifically achieved by evaluation of the knowledge, attitude and practices (KAP) of communities living in Garissa County on RVF outbreaks; determination of RVF seroprevalence in cattle, sheep, and goats during an interepidemic period and investigation of the spatial risk distribution and development of risk maps as part of an early warning system (EWS) tools.

A systematic review of existing literature highlighting RVF epidemiology with a local and global perspective emphasising on descriptive epidemiology, spatial and temporal distribution, molecular epidemiology, serological surveillance and control measures was done at the beginning of the study. This was followed by a two-week reconnaissance survey that was conducted in 2012 to identify the study area, select the target human and animal populations which was crucial in designing the study and acquisition of secondary datasets. Participatory epidemiology was used where 275 local participants were selected and engaged through face to face interviews, key informant interviews and focus group discussions.

Descriptive statistics were used to characterise levels of knowledge, attitudes and practices while logistic regression analyses were conducted to identify predictors of knowledge and practices. In July 2013, a cross-sectional survey was conducted where 370 ruminants were sampled from eight RVF prone areas of Garissa to determine the seroprevalence of RVF. Rift Valley fever virus (RVFV) antibodies were detected using a multispecies competitive enzyme-linked immunosorbent assay (c-ELISA) for specific detection of RVFV IgG antibodies. Mixed logistic regression models were used to determine the association between RVF seropositivity and species, sex, age, and location of the animals.

In order to determine the influence of environmental, climatic and demographic drivers on the spatial distribution and predict the risk in of RVF occurrence in Garissa, the relationship between these predictor variables and seroprevalence of the ruminants was analyzed using species distribution modelling (SDM) approaches. A robust machine learning technique (*Boosted Regression Trees (BRT)* and a Bayesian hierarchal geostatistical model (Integrated Nested Laplace Approximation (INLA) were used to analyse spatial distribution of Rift Valley fever seropositivity. The predictive power of all models was evaluated, validated to determine the level of agreement in accurately predicting the spatial pattern and risk of Rift Valley fever.

Two hundred and seventy-five people participated in the KAP survey, all (100%) of the 214 males (78%) and 61 females (22%) had heard of RVF, majority of males (61.7%) had high knowledge of RVF, while 82% of females had low knowledge. Results from the logistic regression analyses show that males had a fourfold likelihood (Odds Ratio-OR= 4.25, 95%CI 1.99-9.06) of being knowledgeable about RVF than females. Stormy abortions were identified as the most recognizable clinical sign in animals by 71.6% of the participants, while 50.2% of participants indicated high fever as common sign in humans. Increasing age and conversely lack of formal education were strongly associated with high levels of knowledge. The relationship between the overall knowledge of RVF and the respondents gender was statistically significant (χ^2=36.23, df=1, p-value <0.001). RVF was controlled mainly through livestock vaccinations and avoiding consumption of animal products.

The serological survey detected a high overall seroprevalence of 27.6% (95% CI [23–32.1]) of RVF in 370 (271 goats, 87 sheep, and 12 cattle) ruminants. Sheep, cattle, and goats had seroprevalences of 32.2% (95% CI [20.6–31]), 33.3% (95% CI [6.7–60]), and 25.8% (95% CI [22.4–42]), respectively. Seropositivity in male species was 31.8% (95% CI [22.2–31.8]), whereas that of females was 27% (95% CI [18.1–45.6]). Animals greater than 1year-old had an 18-fold likelihood to be seropositive than animals less than 1 year, OR 18.24 (95% CI 5.26-116.4),

The spatial model, BRT predicted approximately 16,810 km^2 of very high risk (predicted probability of 0.70), which is 70% of the total area of Garissa County. High precipitation (35%), high human and livestock density (27%) and elevated temperatures (17 %) were the most important variables to predict high risk for RVF occurrence. The BRT model predicted the highest risk (>0.5-1.0) in the north-western parts of Garissa, areas adjacent to the Tana River with widespread foci of medium to low risk (<0.3), central parts and around perennial water bodies.

The predictive performance of BRT model was high AUC of ROC score of (0.7 ±0.001 s.d). INLA predicted overall medium risk (<0.3) (mean of the spatial component), with small areas (those close to observed data locations) having very high risk (>0.5-1.0). The predictive performance of INLA was found to be very high with AUC of ROC score of 0.9 ±0.001 s.d). There was a significant positive correlation and good model agreement between INLA/RF (global correlation, r =0.44) in predicting the serologic status of RVF in Garissa.

The community had high knowledge on RVF symptoms and transmission and recognized vaccination as the main prevention strategy. Assessment of knowledge and practices of a population is a first step for planning public health and veterinary intervention before and during RVF outbreaks in Garissa. Despite the overall high seroprevalence of RVF in all ruminants, older animals had high likelihood of being seropositive due to prolonged exposure.

The endemicity of RVF in Garissa may be enhanced by movement of live (infected) animals to Garissa livestock market from Somalia and may be responsible for re-introduction of disease. Seropositive animals tended to aggregate near wetlands indicating spatial dependency of these cases in north western, central and southern parts of Garissa.

This is the first study in Kenya that has used logistic regression and geostatistical models to investigate predictive factors associated with RVF prevalence in livestock, using actual serological data. It has provided predictive model-based risk maps for Garissa, at a high spatial resolution by exploring the underlying spatial processes and displayed high risk incidence areas. The generated predictive risk maps might be suggestive for areas to be targeted for RVF sentinel surveillance and intervention, this is useful for policy decision-makers to prioritize intervention areas for cost-effective and optimal resources allocation for RVF prevention and control.

The findings of this study contribute to the overall understanding of the risk factors that predispose communities and their livestock to potential RVF outbreaks. It also provides baseline serological status of the disease and precisely predicts where the next likely outbreaks will occur which is very useful in assisting strategic, targeted and cost-effective preparedness and implementation of control measures.

CHAPTER ONE

1.0 GENERAL INTRODUCTION

Rift valley fever (RVF) is an arthropod-borne zoonosis caused by a phlebovirus that is potential global threat to domestic animals and humans. Outbreaks in Kenya and East Africa have led to substantial economic losses due to massive abortion in livestock, ban on livestock trade and human death. RVFV was first isolated and characterized in 1931 during an epizootic of fatal hepatic necrosis and abortion in sheep (Daubney *et al*., 1931).

The RVF epidemics are closely linked to the occurrence of the warm phase of the El Niño/Southern Oscillation (ENSO) phenomenon that lead to heavy rainfall and flooding (Anyamba *et al*., 2001). Flooding of low altitude areas with depressions *dambos* lead to hatching of eggs of the *Aedes* mosquitoes and the subsequent adults transmit the virus to animals. When *Aedes* mosquitoes infect domestic animals with RVF, virus amplification occurs in these vertebrate hosts, leading to propagation into various *Culex* species that are capable of transmitting the virus to a wider area beyond the area of the original outbreak (Anyamba *et al*., 2010).

The 1997-1998 RVF outbreaks in Kenya caused 170 human deaths in Garissa, which was the epicenter of outbreak (Woods, *et al*. 2002). A total of 478 human cases were also reported in Kenya and southern Somalia (Centers for Disease and Prevention ,1998). The 2006-2007 epidemic period led to more than 30,000 livestock and 700 human cases and 158 human deaths (Munyua, *et al*. 2010; Nguku, *et al*. 2010).

The previous RVF outbreaks have led to significant socioeconomic and public health impacts which include disruption (quarantine) and closure of livestock markets hence affecting trans-boundary livestock trade, closure of schools, food safety and security uncertainties, financial impact to livestock keepers, strain of the veterinary and medical and general environmental hazard due to carcass disposal (Woods, *et al*. 2002). During the 2006-2007 outbreak, the total economic loss due to livestock deaths was estimated at US$10 million, loss due to milk production and abortions was approximately US$77,000. Undisclosed losses in failure to replenish animal stocks due to stillbirths and abortions was significant at over 20% reduction (Rich and Wanyoike, 2010).

1.1 Statement of the problem

Despite these outbreaks of RVF in Garissa, few attempts have been made to determine knowledge, attitude and practices on RVF by the affected community. Lack of low levels of knowledge on RVF causes, symptoms and management has led to delayed health seeking behaviour, poor preparedness and control. In Kenya, the effects of gender, occupation, education and incomes have been demonstrated to influence the levels of knowledge, attitudes and practices on RVF prevention and control. The lack of knowledge on causation, risk and RVF transmission can lead to sustained transmission and high burden of RVF in vulnerable populations who continue to handle, consume animal and animal products from uninspected sick and dead animals (Anyangu *et al*., 2010; Abdi *et al*., 2015). In Garissa, a number of serological surveys have been conducted with focus on epidemics (LaBeaud, *et al*. 2008; Nguku, *et al*. 2010) but limited research has been done to determine RVF virus transmission patterns during the interepidemic periods (Gray, *et al*. 2015; Muiruri, *et al*. 2015).

In Africa, outbreaks of RVF have been predicted using transmission dynamics models climatic and environmental indicators (Leedale, *et al.*, 2016). Prospective spatiotemporal and mathematical models have used vectors and livestock to flag areas at high risk of RVFV transmission based on key environmental indicators in endemic areas of Africa and Arabian Peninsula (Abdo-Salem *et al*., 2006; Britch *et al*., 2013; Metras *et al*., 2015).

1.2 Justification

There is an urgent need, therefore, for raising public knowledge and awareness on RVF causation, transmission risks as well as to improve the attitude on preventive and control measures to enhance their preparedness and response to future RVF outbreaks. There is further need to establish the serological status of ruminants in Garissa and predict the spatial distribution pattern of RVF occurrence for identification of high risk areas that will be targeted for cost effective control strategies and provide an early warning systems framework for wider application to other animal diseases.

1.3 Objectives

Overall Objective

To determine the Spatial epidemiology and predictive modelling of Rift Valley fever in Garissa County, Kenya.

Specific objectives

1. To evaluate the community's knowledge and practices during Rift Valley fever outbreaks in Garissa County.
2. To determine Rift Valley fever seroprevalence in cattle, sheep, and goats during an interepidemic period in Garissa County.
3. To investigate the spatial distribution of Rift Valley fever occurrence in Garissa County
4. To develop predictive risk maps for Rift Valley fever in Garissa County

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Rift Valley fever

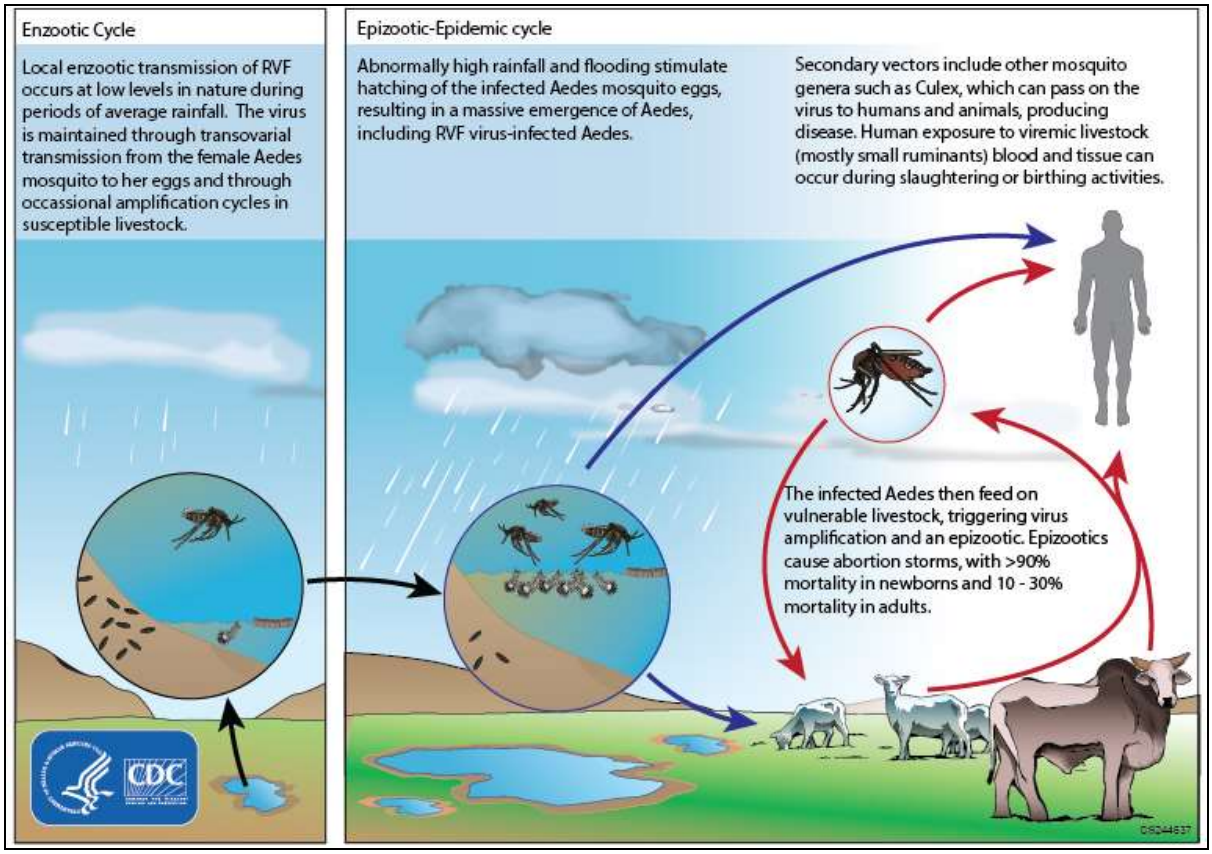
Rift valley fever (RVF) is an arthropod-borne viral zoonosis with a potential global threat to domestic animals and humans. RVF outbreak was reported among sheep in Kenya 1912 and 1913, but the virus it was first isolated and characterized in 1931 during an epizootic of fatal hepatic necrosis and abortion in sheep. Major epidemics have occurred throughout Africa and recently Arabian Peninsula, Egypt (1977), Kenya (1997–1998, 2006-2007), Saudi Arabia (2000–2001) and Yemen (2000–2001), Sudan (2007) and Mauritania (2010) (Daubney *et al*., 1931, Meegan 1979, Hoogstraal *et al*., 1979, Woods *et al*. 2002, Jost *et al*., 2010, Abdo-Salem *et al*., 2006, Aradaib *et al*., 2013, Sow *et al*., 2014).

The RVF virus (RVFV) is the causative agent that belongs to the genus *Phlebovirus* in the family *Bunyaviridae*. The virus is primarily transmitted to vertebrate hosts by the bite of infected mosquitoes in *Aedes* and *Culex* genera, other biting insects are potential secondary- mechanical vectors; *Mansonia, Anopheles, Culicoides* spp (Davies and Martin 2003). The RVFV genome contains tripartite RNA segments designated large (L), medium (M), and small (S) contained in a spherical (80–120 nm in diameter) lipid bilayer. The S-segment encodes N and NSs genes in an ambisense manner, the M-segment. NSm (NSm2), 78 kD (NSm1), Gn and Gc genes, and the L-segment, the RNA-dependent RNA polymerase (L) gene (Ikegami and Makino 2011)

2.2 Rift Valley fever Cycle and climate teleconnection

The RVF epizootics and epidemics are closely linked to the occurrence of the warm phase of the El Niño/Southern Oscillation (ENSO) phenomenon and elevated Indian Ocean temperatures that lead to heavy rainfall and flooding of habitats known as "*dambos*," which contain transovarially infected *Aedes* mosquito eggs (Logan *et al*., 1991), persistent rainfall lead to flooding of the *dambos* leading to hatching of the eggs of the *Aedes* mosquitoes and the subsequent adults transmit the virus to small domestic ruminants (sheep, goats) then to large ruminants (cattle, camels) and wild ruminants (buffalo). These depressions also serve as good habitats for eggs of *Culex* mosquitos which is responsible for the secondary phase of virus amplification leading to propagation and transmission of the virus to a wider area beyond the area of the original outbreaks (Linthicum *et al*., 1999), details shown in **Figure 1**

The ability of the infective *Aedes vexans* mosquito eggs to remain viable during prolonged drought provides the conditions for epizootics to start once the soil where these eggs are located is flooded for long enough to allow hatching of the infective larvae, presence of susceptible ruminant species for virus amplification (Anyamba *et al*., 2001, Anyamba *et al*., 2010). Between epidemics the virus is believed to be maintained through vertical transmission in *Aedes* spp and circulates at very low incidence without noticeable clinical manifestation in both humans and animals (Davies and Martin, 2003; WHO,2008).



(*Source CDC* https://www.cdc.gov/vhf/rvf/resources/virus-ecology.html)

Figure 1: Life cycle and transmission dynamics of Rift Valley fever virus

2.3 Rift Valley fever clinical signs

RVFV infection causes serious disease in both animal and human populations, resulting in significant agricultural, economic and public health consequences. RVF a notifiable disease that predominantly affects domestic animals (cattle, goats, sheep and camels); African buffalo (*syncerus caffer*), black rhino, lesser kudu, African elephant, Kongoni, and waterbuck and humans (Evans *et al*., 2008; Adeyeye *et al*., 2011). In livestock, the disease has characteristic high mortality (100 % in neonatal and 10-20 % among adults) and high abortion rates in infected pregnant animals (Coetzer, 1981).

In humans RVFV causes a mild, acute febrile illness with fever, malaise, and myalgia, a minority of human cases are complicated by retinitis (10%), encephalitis (8%), and haemorrhagic fever (1%) with significant risk of related morbidity and mortality (LaBeaud *et al*., 2011). About 1-20% of patients develop ocular complications, including retinitis, leading to scotomata, and other visual disturbances. In humans there are complications of haemorrhagic fever, retinitis, blindness and encephalitis may occur in 1-2 % of affected individuals with a case fatality ratio of approximately 10-20 % (Madani *et al*., 2003).

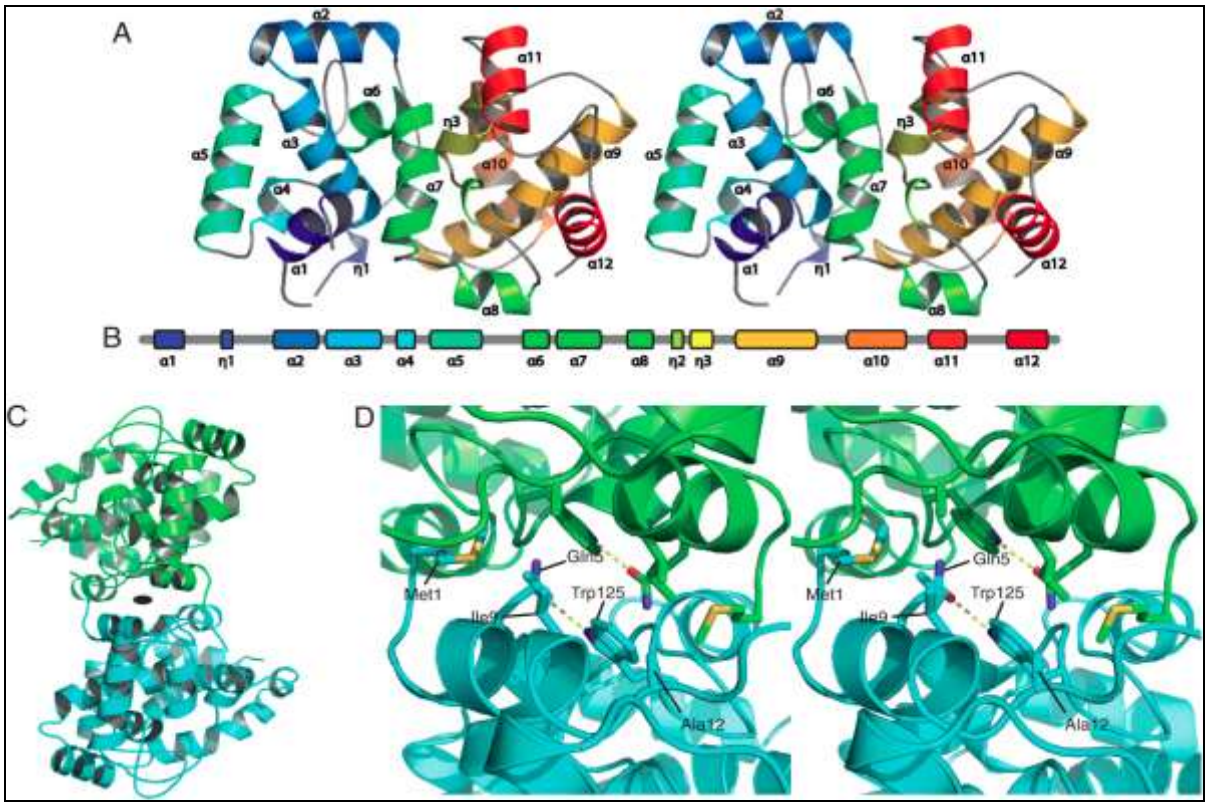
2.4 Public health impacts of Rift Valley fever outbreaks

RVFV is an OIE high-impact transboundary pathogen and a United States Department of Agriculture (USDA) and Centers for Disease Control and Prevention (CDC) overlap Category A select agent, requiring mandatory reporting to the OIE and other governmental organizations if cases are detected (OIE, 2014). It can cause high mortality and morbidity, potentially resulting in a major impact on public health. The lack of prophylactic and therapeutic measures, the transmission by many species of mosquitoes and the significant threat to livestock associated with RVFV make this pathogen a serious public health concern not only for endemic, developing countries, but also for many non-endemic developed countries due to the possibility of bioterrorist attack (Bouloy, 2009)

2.5 Molecular biology of Rift Valley fever virus

Rift Valley fever virus is a negative sense single stranded RNA virus with a tripartite genome consisting of small (S), medium (M), and large (L)segments. The L segment encodes the viral RNA-dependent RNA polymerase, and the M segment encodes at least two non-structural proteins of unknown function, collectively referred to as NSm and the structural glycoproteins Gn and Gc. The L and M genome segments are of negative-sense polarity, whereas the S genome segment is of ambisense polarity. Cryoelectron tomography has recently revealed that RVFV, once thought to be pleomorphic, has, an icosahedral structure, with a T=12 triangulation number. Among viruses, this type of structure is only known to occur in Uukuniemi virus, a related phlebovirus (Freiberg *et al*., 2008)

RVF virions are spherical, consisting of an envelope and a ribonucleocapsid (RNP) Virions measure 80–120 nm in diameter. The viral envelope is covered by 122 capsomers, consisting of heterodimers of the Gn and Gc glycoproteins on an icosahedral lattice. The surface capsomers form 110 cylinder-shaped hexamers and 12 pentamers (Huiskonen *et al*., 2009) **Figure 2**. Envelope surface projections 9 nm long form distinctive spikes that cover the surface and are embedded in a 7 nm lipid bilayer. The envelope surrounds 3 RNPs corresponding to the S, M and L genome segments. The RNP of bunyaviruses is filamentous, with a length of 200–3000 nm and a width of 10– 12 nm. The ribonucleocapsid is thought to have a pan-handle-like structure, due to complementary sequences at the genome termini. The N proteins form ring-like hexamers with an external diameter of 100nm and the viral RNA is believed to bind to its cavity (Raymond *et al*., 2010, Ferron *et al*., 2011).



Adapted from (Raymond *et al*., 2010)

Figure 2: Molecular structure of Rift Valley fever virus (RVFV)

Explanation of structure

(**A**) Polypeptide fold. The stereo ribbon diagram is colored as a rainbow from blue at the N terminus to red at the C terminus with loops in gray. Helix α7, (vertical) in the center of the image, links the N lobe at the left and the C lobe at the right. (**B**) Diagram of helical secondary structure in the RVFN polypeptide. Colors are matched to A. (**C**) RVFV N dimer. In this view along the dimer axis, monomers are in green and cyan and the twofold axis is indicated by an ellipse. (**D**) Details of the dimer interface. The subunits are colored as in C, side chains with dimer contacts are shown in stick form in the stereo view. Hydrogen bonds are shown as dashed lines.

2.5.1 Genetic diversity and identification of lineages in Kenya

Kenya has encountered RVF cyclic outbreaks for the past 80 years, phylogenetic analysis indicate the circulation of multiple lineages B, C, K and L, with C being isolated from outbreaks in Zimbabwe (1978), Madagascar (1991), Saudi Arabia (2000–2001) and South Africa (2008–2009). However there was a similarity in isolates of 1977, 1983 and the (1997-1998, 2006-2007) outbreaks in Kenya. The isolation of viruses falling in the lineage K may indicate virus introduction through vaccination using live vaccine (Grobbelaar *et al*., 2011)

Genomic analysis of over 3000 animal specimens collected from over 80% of Kenyan districts during the 2006-2007 outbreak demonstrated concurrent circulation and genetic reassortment of multiple virus lineages in 31 RVFV isolates. The 2006/2007 outbreak viruses had the same ancestry as the 1997/1998 East African strains. A wider geographical viral spread determined by serologic analysis revealed almost 10% infection in all the districts leading to isolation of 31 viral specimens covered all genome segments (Bird *et al*., 2008).

In East Africa phylogenetic analysis of 16 RVF viruses isolated from humans, livestock, and mosquitoes during the 2006–2007 outbreak revealed 3 distinct lineages, which in comparison had clustered similarity to the Kenyan isolates of 1980, 1998 and the Saudi Arabia isolate of 2000. This strongly suggest the possibility of autochthonous virus reemergence and spontaneous release of resident virus maintained inter-epidemically in desiccated *Aedes* spp eggs which hatch during flooding (Nderitu *et al*., 2011).

During the Kenyan 2006-2007 RVF outbreak virus isolates were analyzed for genetic diversity in three outbreak regions. They included KEN/Gar 001/06, KEN/Gar 002/06, KEN/Gar 004/06, and KEN/Gar008/06 from Garissa, KEN/Kil 006/07 and KEN/Mal 032/07(Kilifi) and KEN/Bar 032/07, KEN/Bar 035/07 (Baringo) Districts. The eight human isolates had between 96.6% and 99.6% nucleotide sequence identity with each other across the M segment of the genome. The gene segment analyzed for these viruses also had a similarly high homology with the RVF strains involved in the 1996–1997 RVF outbreak in Kenya and 2000 outbreak in Saudi Arabia (Nguku *et al*., 2010).

2.5.2 Diagnosis of Rift Valley fever

Serological analysis is routinely used for epidemiological surveillance and control programmess of RVF in human and animal populations. It involves collecting of blood and extracting sera before actual laboratory analysis. In Kenya Enzyme-Linked Immunosorbent Assays (ELISA) have been previously used with greater success in detection of RVF during interepidemic period (Lichoti *et al*., 2014; Owange *et al*., 2014).

This however has setbacks like health risk to laboratory personnel due to accidental exposure, restrictions for utilization outside endemic areas or inability to distinguish between exposure and active infections. Variuos methods have been developed to overcome such shortcomings, notably sandwich and capture ELISAs (both based on inactivated antigen) for detection of IgG and IgM antibody to Rift Valley fever virus in bovine, caprine and ovine sera (Paweska *et al*., 2003).

In Kenya a sentinel seroepidemiological surveillance was conducted during interepidemic periods (IEPs) of 2009- 2012. Serum samples from livestock and humans Ijara, Naivasha and Marigat were analyzed using the inhibition enzyme-linked immunoassay kit for the detection of antibody (both IgG and IgM) to Rift Valley fever virus. The positive serum samples for RVFV virus-specific antibodies were then tested for IgM antibodies using the IgM capture enzyme-linked immunoassay. There was evidence of RVFV circulation in livestock during the IEP in Ijara and Marigat where previous outbreaks had been reported. Despite that there were no detectable human cases, the use of serological analysis demonstrated IEP transmission of RVFV and seroconversion in livestock (Lichoti *et al*., 2014).

A seroepidemiological survey on Rift Valley fever (RVF) among small ruminants and their close human contacts in Makkah, Saudi Arabia utilised a RVF competition multi-species enzyme-linked immunosorbent assay (ELISA) for detecting anti-RVF virus immunoglobulin G (IgG)/immunoglobulin M (IgM) antibodies and an RVF IgM-specific ELISA. A seroprevalnce of 16.8% was detected in 500 sheep and goats tested using the competition ELISA but no IgM antibodies were detected while 9% of persons in close contact tested seropositive in the RVF competition ELISA. The human-linked syndromic surveillance is a time and cost saving method in resource limited settings (Mohamed *et al*., 2014).

Rapid diagnosis and screening of RVFV requires safer, more sensitive and time saving diagnostic methods that does not necessarily require manipulation of infectious material (blood samples). In order to quantify small RNA segments a real-time detection reverse transcription (RT)-PCR using TaqMan technology has been developed, it specifically targets nonstructural protein-coding regions (Garcia *et.al*., 2001). The primary screening for RVF has been demonstrated by europen laboratories ring trial to evaluate the efficacy of Rift Valley fever virus (RVFV) ELISAs. Five types of ELISAs, two of which were specific for IgM antibodies, were evaluated on sera were derived from cattle or sheep and originated from RVF endemic areas, there was a high (>90%) agreement of two commercially available ELISAs with the virus neutralization test(VNT) (Kortekaas *et al.*, 2013).

A combination of diagnsotic tests has been used in human cases where a wider genetic analysis and clinical characterization on patient sera for RVF infections was conducted by reverse transcription-polymerase chain reaction (RT-PCR), serology for RVFV antigens by indirect immunofluorescence assay (ELISA) and virus isolation. The RT-PCR assay was an excellent complement to the antigen and antibody ELISA detection systems for rapid diagnosis of RVF during the 2000-01Rift Valley fever outbreak in Saudi Arabia and Yemen (Shoemaker *et al*., 2002).

An epidemiological, clinical, and laboratory characterization of the involved 683 patients hospitalized with laboratory-confirmed Rift Valley fever in Saudi Arabia in 2000-01. The use of ELISAs to detect RVF virus antigen and specific IgM in patient serum or blood samples, further detection of viral RNA in serum or blood specimens using RT-PCR, and RVF-specific immunohistochemical testing of a liver biopsy specimens demonstrated the improved diagnosis of RVF (Madani *et al*., 2003).

The detection of RVFV in wildlife in Kenya was conducted on 1008 sera from 16 different species of wildlife , the presence of RVFV-specific antibodies was tested by by indirect enzyme-linked immunosorbent assay (I-ELISA) for detection of RVF-specific IgG, further Virus neutralization test (VNT) was conducted during the during the 1999–2005 interepidemic period. A RVFV antibody prevalence of (>15%) was observed in black rhinos and ruminants (kudu, impala, buffalo, and waterbuck) with the highest titres (up to 1:1280) observed mostly in buffalo, including those animals born during the interepidemic period. This use of combination of these diagnostic methods shed light on role played by various wildlife species in the maintenance and transmission cycle of RVFV when there are outbreaks (Evans *et al*., 2008).

2.6 Spatial-temporal epidemiology and Predictive modelling of Rift Valley fever

Earlier predictive studies used satellite derived normalized differential vegetative index (NDVI) and other environmental variables to assess the potential for RVFV activity in two ecologically distinct but enzootic areas of Nairobi and Naivasha in Kenya. Monthly rainfall estimates and adult mosquitoes were collected to evaluate the potential viral activity factor statistic from NDVI. There was positive correlation between NDVI and rainfall in both ecological zones leading to high mosquito population levels and hence high likelihood of RVF occurrence (Linthicum *et al*., 1987).

Previous monitoring and risk mapping system of RVF has been effective in assessing the potential spatial and temporal distribution of the disease in Africa, this has led to precise prediction to the 2006-2007 outbreaks in the Horn of Africa. Due to the rapid expansion of the geographic range of RVF a remotely sensed early warning system for RVF vectors using mosquito surveillance data and climate data is promising to assist in planning control strategies (Linthicum *et al*., 2007).

The first prospective prediction of RVF virus circulation was modelled using the 2006-2007 East African outbreak data. Spatiotemporal analysis using climatic and environmental variables were used in combination with vector surveillance data to predict potential outbreaks in Africa with suitable areas of eminent epidemics identified with a lead time of 3 months (Anyamba *et al*., 2010). Time series analysis of NDVI from 1997 to 1998 identified localized areas that received anomalous rainfall, hence led to conditions associated with the emergence of RVFV vectors resulting in outbreaks. This has been supported by recent studies that improved methods can enable accurate prediction in in lead times of 2–4 months (Linthicum *et al*., 1999, Anyamba *et al*., 2001)

A large-scale continental estimate of RVF prevalence in Africa using serological data has been explored by a spatially explicit Bayesian logistic-regression model. There was a correlation that associated high-prevalence clusters in areas that had previously experienced epidemics including Kenya's North-Eastern region and Somalia. This study forms a framework for estimating the seroprevalance where no accurate serological data are available (Clements *et al*., 2007).

Using knowledge driven spatial modelling, RVF endemicity suitability maps for Africa have been also developed by Clements *et al*. (2006). Most of Sub-Saharan Africa (SSA) had high predicted suitability of RVF occurrence; moderate suitability was predicted for Morocco, Algeria and Tunisia while the whole of the Sahara Desert was unsuitable. This was corroborated with overlay of observed serological prevalence for suitability for RVF in Senegal, thus providing wider applications where serological data is available (Clements *et al*., 2006).

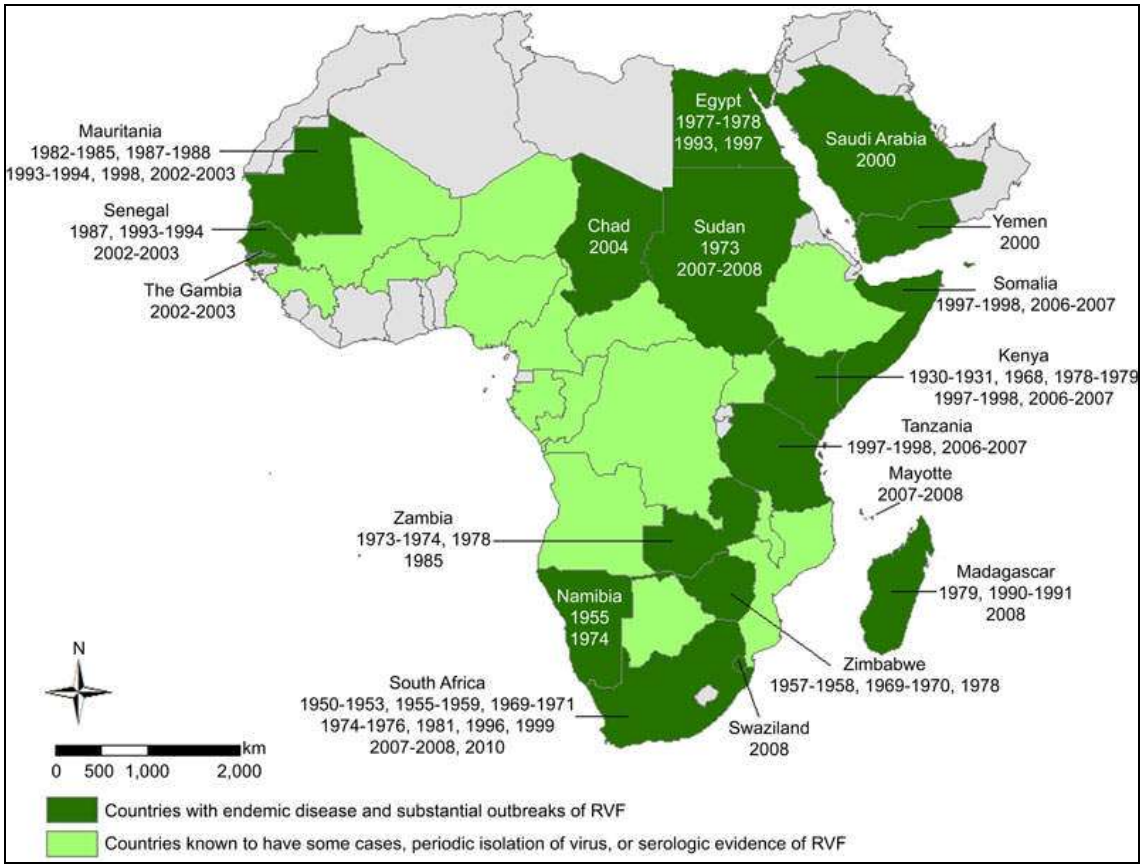
Retrospective seroepidemiological studies using wildlife data correlate well with spatial predictions and the epidemiological sequence of RVFV transmission providing a future window of improving RVF transmission risk models (Britch *et al*., 2013). Sindato *et al*., (2014) in Tanzania examined the distribution of RVF outbreaks from 1930 to 2007. There was observed heterogeneity in outbreaks and increased likelihood of occurrence in areas receiving rainfall above 400mm and that had clay or loam soils (Sindato *et al*., 2014).

Spatial analysis of non-clinical RVF cases in Tanzania indicated the existence of multiple ruminant hosts that were potential reservoirs of RVFV during inter-epidemic period and increased likelihood of outbreaks in animals located at elevations less than 1000m (Sindato *et al*., 2013). RVF forecasting models and early warning systems have been developed to enable national authorities to implement measures to avert impending outbreaks. In Kenya RVF prediction and preparedness of outbreaks relies mainly on climatic forecasting databases that uses monitoring and risk mapping system of satellite measurements (Anyamba *et al*., 2001).

In Kenya, Hightower *et al*. (2012) utilized geo-referenced locations of human RVF cases during the 2006-2007 outbreak combined with geological and climatological attributes to estimate incidence of RVF. A correlation of altitude and disease outbreak was evident with areas at ≤1,100 meters consistently having epidemics (Hightower *et al.*,2012). This finding was in agreement with an earlier Tanzanian study that indicated high intra-village seroprevalence of IgG in domestic and wild ruminants and higher risk at low altitudes (Balkhy & Memish, 2003)

2.7 Spatial distribution and global burden of RVF

The epidemic focus of RVFV was contained in Kenya in 1912 until three decades later, before spreading to neighbouring Tanzania in the late 1940s. Intensive outbreaks in Southern Africa in the 1950s were evident in South Africa, Namibia, Zimbabwe and Zambia forming secondary epidemic foci (Swanepoel, 1981, Davies *et al*., 1992, Sindato *et al*., 2014). The proximity of the Arabian Peninsula to the Horn of Africa and associated livestock trade may be responsible for the geographical spread of the virus to Saudi Arabia and Yemen (Ahmad, 2000, Shoemaker *et al*., 2002, Abdo-Salem *et al*., 2006, Bird *et al*., 2009) (**Figure 3**).



Adapted from (Bird *et al*., 2009)

Figure 3: Spatial distribution of RVF in Africa and Arabian Peninsula by 2011

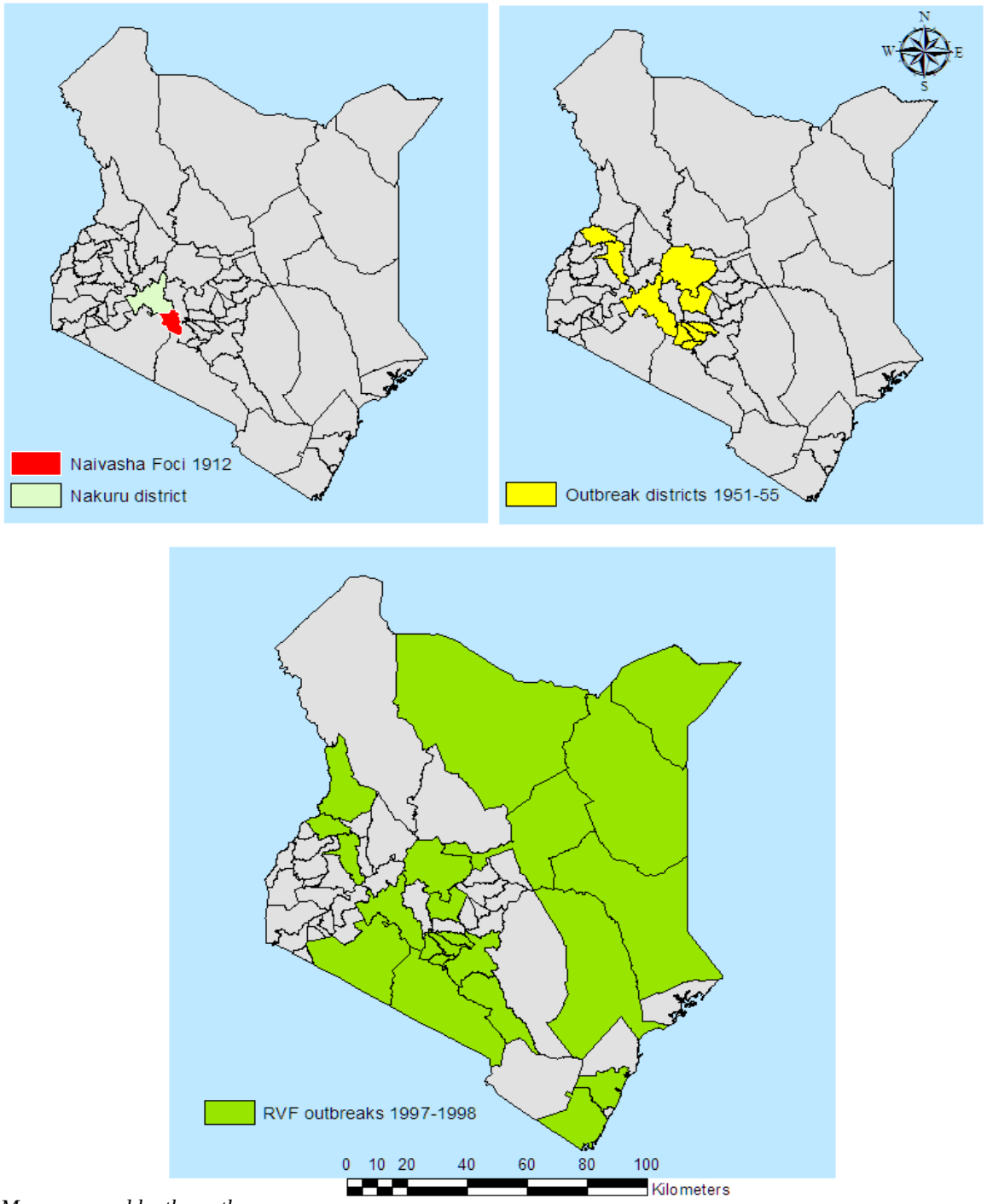
An epidemiologic shift was evident in the West African pocket in the late 1980s, and may have been associated with climate variability, leading to aggressive emergence and dispersal of competent mosquito vectors of *Aedes* and *Culex* species to the large ruminant populations in Mauritania and Senegal (Wilson *et al*., 1994, Zeller *et al*., 1997, Sow *et al*., 2014). Southern Africa and West Africa have reported the longest RVF outbreak periods with South Africa and Mauritania sustaining longer outbreaks compared to the rest of the Horn of Africa (Pienaar and Thompson, 2013).

The South African epizootic of 1951 led to deaths of over 100,000 sheep and half a million livestock abortions (Coetzer *et al*., 1994). In Egypt, a notable human epidemic was reported in 1977 causing an estimated 600 deaths and significant livestock abortions and mortalities, it may have been associated with introduction of the virus through livestock trade from the Horn of Africa and aggressive emergence of mosquitoes from the flooded Nile River (Meegan, 1979). An additional 45 RVF cases were reported in farmers in Seedy Salim district and 17 human deaths were confirmed in the Egyptian Kafr Al-Sheikh governorate (Centers for Disease Control and Prevention, 2003).

In 2006-2007 the outbreak that affected Kenya, Somalia and Tanzania led to substantial losses of livestock and almost 700 human deaths (Bird *et al*., 2008, Anyangu *et al*., 2010, Munyua *et al*., 2010, Murithi *et al*., 2011). In 2000, sustained heavy rainfall in the Arabian Peninsula led to flooding and the first outbreak of RVF in Saudi Arabia and Yemen (Ahmad, 2000) which resulted in over 200,000 human infections with an estimated 250 human deaths and thousands of livestock deaths (Centers for Disease and Prevention, 2000, Balkhy and Memish, 2003, Abdo-Salem *et al*., 2006).

2.7.1 Spatial distribution of RVF in Kenya

RVF was first reported in Kenya's Rift Valley at Naivasha in 1912, subsequent outbreaks have occurred at cyclic intervals of 5-15 year more recently in 2006/2007. The clinical disease and virus activity has occurred extensively in the country with a number of epizootics over the years. Data available at the Kenya department of veterinary services indicates that earlier notable outbreaks occurred in 1936, 1944, 1951, 1960/63, 1967/68, 1978/79 in the country with more significant outbreaks in 1951-55 and the widely reported 1997-1998 outbreak and 2006-2007 in North Eastern Kenya, this spread to Somalia (Munyua *et al*., 2010, Murithi *et al*., 2011, World Health Organization, 2007) (**Figure 4 & 5**)



Map prepared by the author

Data reanalysed from (Murithi *et al*., 2011)

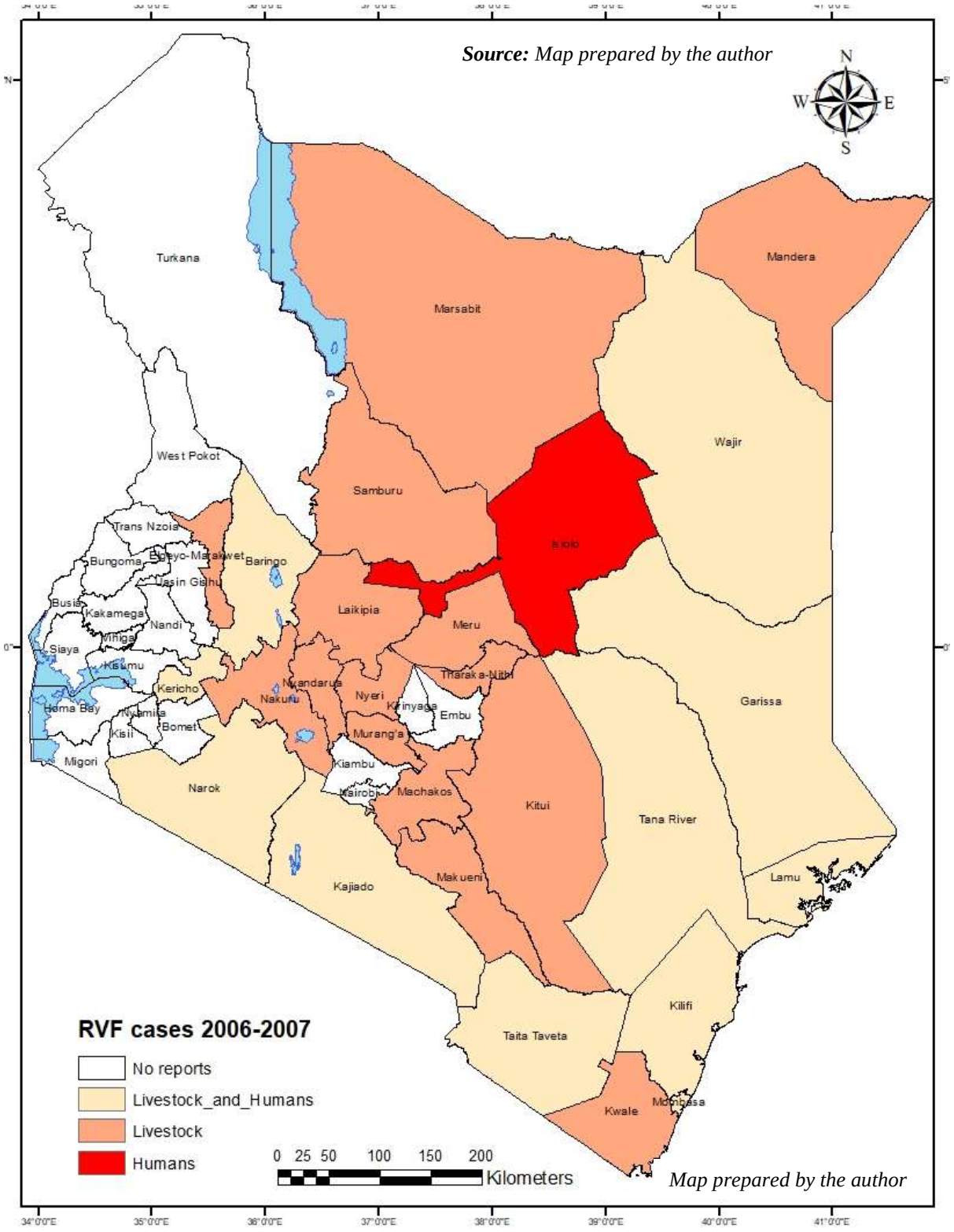
Figure 4: Spatial and temporal distribution of RVF outbreaks in Kenya 1912- 1998

2.8 Epidemiological risk factors and socioeconomics of RVF in Kenya

Human and animal prevalence studies focus on description of risk factors for outbreak using odds ratios (OR) as a measure of association of factors in prevalence studies. Majority of the studies examine human-animal contact or consumption of animal products. Risk factors associated with human infections include touching or disposing aborted foetuses, assisting in animal birthing or direct fluid contact by slaughtering sick animals (Nicholas *et al.,* 2014).

During the 2006 inter-epidemic period in Kenya, a randomized household cluster survey was conducted in two RVF outbreak foci areas among 248 individuals and there was increased risk for males working as herders, older people living in rural areas and those involved in disposing aborted foetuses or being exposed to mosquitoes and animals (LaBeaud *et al*., 2008). In addition, a cross-sectional serological survey was conducted during the 2006- 2007 outbreak that indicated increased risk of infection was associated with consuming or handling products from sick animals, contact with livestock as herdsmen and handling of aborted fetus, milking, skinning, slaughtering, sleeping with animals, touching blood, and caring for animals during birthing (Anyangu *et al*., 2010)

The most recent Kenyan Rift Valley fever outbreak occurred during El Niño rains from November 2006 through April 2007; resultant flooding led to increase in mosquito populations. In three months RVF cases were reported in 29 of the 69 districts (now counties) in Kenya, with the largest number of human cases coming from Garissa, Kilifi, and Baringo counties (Munyua *et al*., 2010). (**Figure 5**)



(Data reanalysed from Munyua *et al*., (2006)

Figure 5: Spatial distribution of RVF in livestock and humans during the 2006/7 outbreak in Kenyan counties.

An RVF epidemic in 18 districts lasting about five months claimed 158 lives of the 700 human cases from late 2006 to end of first quarter of 2007. Over 85% of the 340 confirmed and probable cases were reported from the four districts of Garissa (107, 31%), Baringo (83, 24%), Ijara (75, 22%), and Kilifi (33, 10%) (Munyua *et al*., 2010). Of 72 cases (42, 58% male) with occupation history available, 25 (35%) were herdsmen, 20 (28%) were housewives, 12 (17%) were farmers, and 12 (17%) were students. There was a history of consumption or handling of products from sick animals in 39 57% of these cases with majority associated with milk collection, cooking, and slaughtering (Nguku *et al.*, 2010)

In East Africa, high risk areas for RVFV activity are identified based on ecological suitability for vector survival, historical presence of virus or proximity to known infected areas, and areas experiencing increased rainfall and flooding. High incidence has been reported in areas having soils with poor drainage, flat landforms with low altitudes below 500 m. The soil types associated with increased RVF incidence were solonetz, calcisols, solonchaks, and planosols. RVF incidence was higher in areas having soils with both extremely slow and very slow drainage (Hightower *et al*., 2012)

2.8.1 Socio-economic burden and public health impacts of RVF in Kenya

The significant socioeconomic and public health impacts attributed to RVF outbreaks are qualitative losses that include disruption (quarantine) and closure of livestock markets hence affecting trans-boundary livestock trade, closure of schools, food safety uncertainties, financial impact to livestock keepers, strain of the veterinary and medical and general environmental hazard due to carcass disposal (Woods *et al*., 2002)

In late 1997 heavy rainfall led to RVF epidemic in humans in Garissa, Kenya and Southern Somali with estimated 89,000 human infections. Severe febrile illness was confirmed in 77 persons and 170 hemorrhagic fever-associated deaths were reported in 202 susceptible persons in Garissa only, 478 human deaths were reported in both Kenya and southern Somalia (Woods *et al*., 2002) . Since no outbreak investigation studies were conducted beyond Garissa, the national estimate burden may have been underestimated (LaBeaud *et al*., 2007)

Economic losses attributable to RVF has been found to be substantial due to value chain impacts on livestock producers, traders, slaughterhouses and butchers. These include; poor livestock sales, quarantines, mortalities, abortions. However most studies quantify partial costs and losses failing to measure mid or long term impacts, public health burden or RVF intervention strategies (Peyre *et al*., 2015)

A value chain analysis was conducted in Garissa and Ijara districts of Kenya to describe the extent of losses attributable to the 2006-2007 RVF outbreak, this was projected at a regional and national level, macro-level impacts using RVF outbreak as a shock event to livestock producers, traders, butchers and end point consumers. Total economic loss due to livestock deaths was estimated at US$10 million, loss due to milk production and predicted abortions was approximately US$77,000. Undisclosed losses in failure to replenish animal stocks due to stillbirths and abortions was significant at over 20% reduction (Rich and Wanyoike, 2010)

Further local level impacts included quarantines, foregone revenue due to failure to sell animals, pastoralist dropouts to other commercial activities, occupation loss of livestock traders and brokers, prolonged closure of slaughterhouses and butcheries led to estimated US$2000 and US$6000 monthly loss. The national level impacts on basis of marketed off take rates and that the potential marketed value of cattle declined by 2.3% and an estimated 1% decline in the value of dairy and goat/sheep production and a 1% decline in the overall value of meat (Rich and Wanyoike, 2010)

2.9 Control measures of Rift Valley fever outbreaks in Kenya

Vaccination programs targeting livestock during non-epidemic periods or as an early countermeasure against nascent outbreaks could therefore eliminate one of the main sources of animal and human infection and limit the overall scope of epidemics. Vaccination is a key element in breaking the chain of human epidemics, and could lead to control of this significant public health threat (Bird and Nichol, 2012; Dungu *et al*., 2013). Currently RVF infections in endemic areas of Kenya is controlled by conferment of lifelong immunity through vaccination of animals using the RiftVax®, an attenuated strain of RVFV that has been reported to cause abortions, stillbirths and neonatal deaths in sheep and goats teratogenesis has been reported in ewes, cows and goats. Abortion and stillbirths have been associated with in-utero transmission of replicating vaccine virus to the foetus causing its death and termination of pregnancy (von Teichman *et al*., 2011).

Measures to control mosquitoes during outbreaks are effective by targeted pyrethroid spraying and destruction of the mosquito breeding sites. Dipping of cattle with pyrethroid derivatives gets rid not only of ticks but also other biting insects, which play an important role in the transmission of RVF. Where appropriate, individuals should wear protective clothing, such as long-sleeve shirts and pair of trousers, use bed nets and insect repellent and avoid outdoor activity at peak biting times of the vector species (Sindato *et al*., 2011)

Monath in 2013 outlined a one health approach strategy of controlling zoonotic diseases including RVF by vaccination of livestock. The triad of frameworks proposed models that focus on animal immunization for economic viability as they are integral in disease transmission cycle and efforts should be geared towards production of low cost veterinary vaccines or dual vaccines that can protect both animals and humans against RVF. Despite regulatory and economic challenges, the next generation RVF vaccines should target both animals and humans (Monath, 2013; Kortekaas, 2014).

2.9.1 Vector Surveillance, Risk Mapping for Control of RVF outbreaks

It's imperative to understand the distribution and types of competent vectors involved in transmission of Rift Valley Fever in Kenya to implement effective vector control strategies. An entomological surveillance during the 2006-2007 outbreaks in Kenya demonstrated that up to 10 mosquito species mainly in *Aedes* and *Culex* spp tested positive for RVFV and may serve as potential vectors (Sang *et al.*, 2010). Blood meal analysis indicate that *Ae. ochraceu*s and *Ma. Uniformis* may have been involved in RVFV transmission in Garissa and Baringo in 2007/2007 outbreaks (Lutomiah *et al*., 2014). Spatial analysis indicate that competent RVF vectors may be geographically restricted to some regions with possible spread to other habitats directly influencing the epidemiologic dynamics of RVF (Mwangangi *et al*., 2012).

CHAPTER THREE

KNOWLEDGE AND PRACTICES ON RIFT VALLEY FEVER OUTBREAKS IN GARISSA COUNTY, KENYA.

3.0 Introduction

Knowledge, Attitude and Practice (KAP) surveys employ qualitative and quantitative methods to offer insight of communities' ability to document, recollect and act on existing information for decision making in management of diseases. Most of the practices are aligned to perceptions and beliefs of the community hence improving prevention and control of diseases (Abdi *et al*., 2015). The epidemiological assessment of Knowledge, attitude and practices to RVF outbreaks has been conducted previously in Kenya and Tanzania to document the lessons learned by affected communities and assist in decision making and preparedness and response plans for future RVF outbreaks (Jost *et al*., 2010).

Despite the recurrent outbreaks in Garissa and other areas in East Africa, few attempts have been made to document the community preparedness, understanding of causation, transmission and control of RVF outbreaks (Abdi *et al*., 2015, Shabani *et al*., 2015, Ng'ang'a *et al*., 2016, Affognon *et al*., 2017) but there is still an existing gap on associations of gender, education and incomes on the level of knowledge, attitudes and practices to RVF. The lack of knowledge on causation, risk and RVF transmission has led to high burden of RVF in vulnerable populations who continue to consume animal and animal products from uninspected sick and dead animals (Anyangu *et al*., 2010).

There is urgent need for raising public awareness of the risk factors of RVF infection as well as the protective measures as first line of public health intervention to reduce the burden of infection in humans and animals (Shabani *et al*., 2015). There is an emphasis on increasing the knowledge and awareness of livestock keepers in effective design of early warning systems for prompt outbreak response to RVF (El Rehima *et al*., 2011). The aim of this study was to assess the knowledge of residents in Garissa in regard to Rift Valley fever causes, symptoms, modes of transmission and control practices.

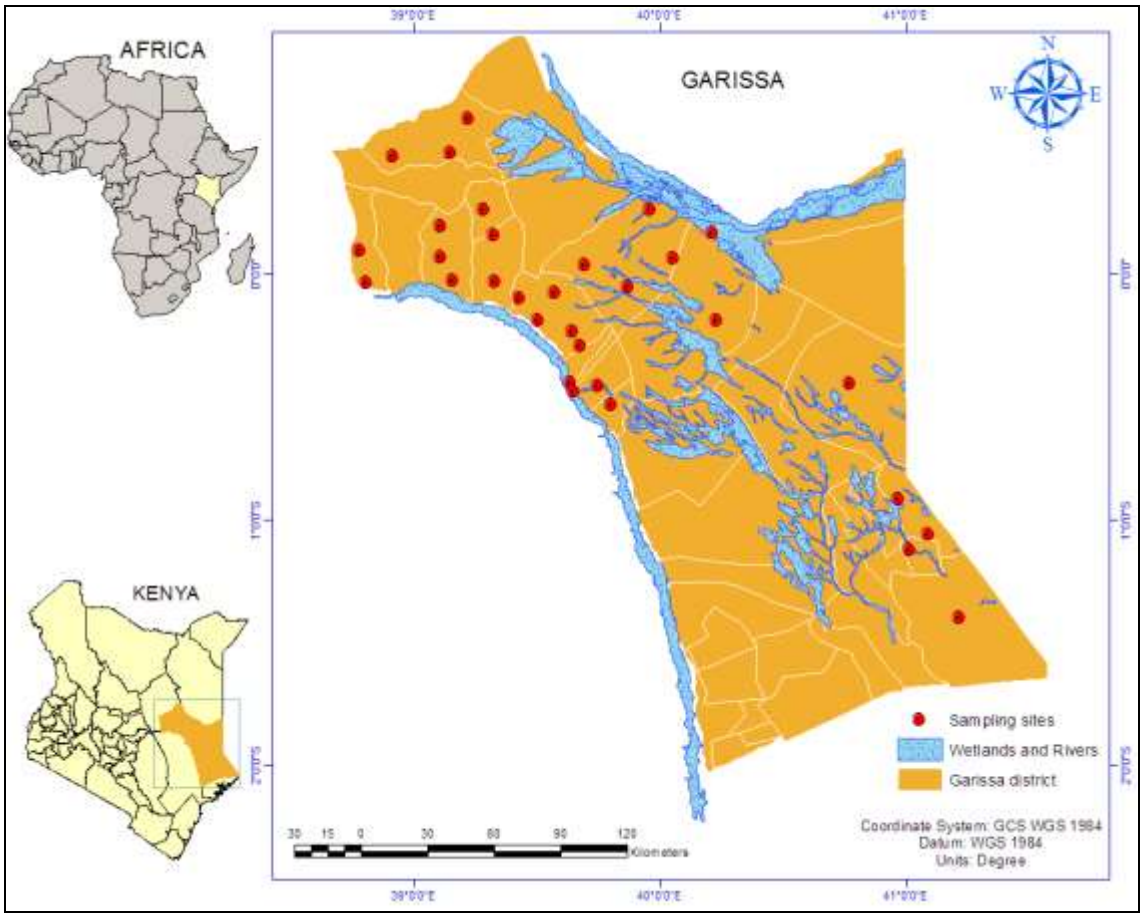
3.1 Methods

3.1.1 Description of area of study

The study was carried out in eight subcounties of Garissa county in semi-arid North Eastern Kenya, Garissa county covers approximately 33,620km^2 where pastoral farming is mainly practiced by an estimated 623,060 persons owning 1,358,007 livestock (Kenya National Bureau of Statistics, 2010) (**Figure 6**). Field surveys were conducted in Central Garissa, Dadaab, Hulugho, Jarajila, Mbalambala, Sankuri, Danyere, Shant-abak divisions, this was approximately six (6) years after the 2006-2007 outbreak; Garissa county is in Agroclimatic zone (ACZ) V-VI (Arid and Semi-Arid) that experiences two rainy seasons, long rains (March- April- May- MAM) and short rains (October-November- December OND) with annual averages of 300-600 mm and diurnal temperature ranges of 20- 38°C having an altitude ranging from 70- 400 m above sea level. Solonchaks are the dominant soils in the slightly sodic soils with luvisols, lixisols and arenosols (Hightower *et al*., 2012).

3.1.2 Study design

A cross-sectional household survey was conducted in March 2013 to pretest and select of households and participants in areas where outbreaks were previously reported; proper data collection including key informant interviews (KII) and FGDs were also done in two weeks of March 2014. Households were identified and stratified based on convenience of accessibility, using cluster sampling of human populations residing in the selected areas, most participants were included on the basis that they were pastoralists (having lived and kept livestock for more than ten years) and were present during the 2006-2007 outbreaks. The primary sampling unit (PSU) was a *"bulla";* this is a cluster of homesteads that comprises of 10 to 15 nuclear family units with their livestock, ten bullas were selected for this study.



Source: *Map prepared by the author*

Figure 6: Map of Garissa county indicating the study sampling sites

3.1.3 Study population and sampling

Individuals aged eighteen years and above living in the study area for more than one year before the commencement of study were recruited and consented using written and oral consent. Participating households were sampled conveniently according to approaches described by LaBeaud *et al*., (2008), while where no persons were found (non-participating households) a substitution was done using additional, randomly selected households as described by Shabani *et al*, (2015). The convenient sampling was based on accessibility of the bullas, proximity to grazing and watering areas and security of research personnel.

Households were identified and stratified based on convenience of accessibility, using cluster sampling of human populations residing in the selected areas, participants were conveniently selected and mainly included pastoralists who had lived and kept livestock for more than ten years and were present during the 2006-2007 outbreaks. The community unit of engagement was a *bulla;* this is a cluster of homesteads that comprises of 10 to 15 units comprising of nuclear families with their livestock. Using the above inclusion criteria and methods proposed earlier by (Kansiime *et al*., 2014)

3.1.3 Data collection: Qualitative and Quantitative methods

Twenty-five individuals were involved in pre-testing of the semi structured questionnaires before the commencement of data collection. The semi-structured questionnaire was pretested in 20 households of Shimbirye, Shanta Abak, Garissa Township and Fafi subcounties to check consistence and validity of the questions. The questionnaire was modified on the basis of the result of the pre-test. The participants demographic and educational backgrounds were assessed and were specifically engaged through face to face interviews using a semi-structured questionnaire which covered knowledge on causes of RVF and climate change, number and species of livestock kept (species, breeds), effects of RVF

outbreaks on livestock and human health, income lost due to livestock deaths and livelihood constraints. The intervention strategies used in response to RVF outbreaks, access and distance from water sources, source of restock animals after loss due to disease and source of information for preparedness of outbreaks. An investigation at the major livestock market focused on determination income sources from livestock sales, lost revenue due to disease outbreaks and disruption of livestock markets during the 2006-2007 outbreaks. The questionnaire was in English but whenever necessary it was translated to Swahili or Somali by interpreters (**Appendix 1**).

Focus Group Discussions

Thirty participants (20 men and 10 women) were selected according to age, gender and occupation, these individuals did not participate in the pretest interviews. There was need to create homogeneity in the group to help participants feel more comfortable expressing their opinions. FGDs were conducted to explore individual's knowledge and practices in regard to RVF emergence and climate change coping and adaptation mechanisms. A single focus group had at least 5 participants and lasted for at least 30 minutes using the structured questionnaire (**Appendix 2 and Appendix 5**). *Probe questions* were used to introduce participants to the discussion topic (RVF), and make them feel more comfortable sharing their opinion within the group, *Follow-up questions* were used to delve further into the discussion topic and understand the participants' opinions with eventual *exit questions* to ensure

Key Informant Interviews

In order to investigate the impacts of previous RVF outbreaks on community and the role of stakeholders in preparedness and control, expert opinion was sought by administering questionnaires during face-to-face interviews with 24 individuals in animal and human health sectors who are routinely involved in zoonotic surveillance and implementation of control strategies. The experts included community based animal health workers, community health workers, animal health assistants, NGO workers, nurses, clinical officers, veterinary and medical officers. (**Appendix 3 and Appendix 4**).

Evaluation of Knowledge and Practices

To assess the importance of RVF in relation to other livestock diseases, groups of four participants with the guidance of a facilitator who provided an in-depth knowledge of most common and significant signs associated with RVF outbreaks. In-depth interviews collected descriptions of the clinical presentation of RVF in humans and livestock. Knowledge was measured based on ability to recognize disease, cluster of symptoms and transmission patterns of RVF. Perceived risks and attitudes were measured on a likert scale and cross-tabulation analysis of each item was dichotomized into (1) strongly disagree/disagree/unsure and (2) strongly agree/agree. Practice was measured on respondents' ability to implement recommended control and preventative strategies.

A score of 1 was assigned if the respondent had heard of RVF and 0 if the answer was incorrect. A score of 2 was assigned if the respondent was able to mention 3 or more symptoms of RVF in animals or humans, a score of 1 if a respondent mentioned 1–2 signs and a score of zero if the answer was not provided or incorrect. A similar scoring method was used for the questions on symptoms of RVF in humans and preventive measures against RVF. If all answers were correct, the total score would be 3 for RVF knowledge and practice. A respondent was categorized as knowledgeable or having good practice about RVF if he/she obtained a 50 % cut-off point. Cumulative scores were obtained for individuals and means were used for classification/ranking of knowledge and practice.

3.2 Statistical analysis

Bivariate analysis was performed to explore associations between overall knowledge and independent variables such as age, sex, education level and occupation. Associations were considered to be statistically significant if they achieved a $p < 0.05$. Multiple logistic regression models were fitted to estimate independent associations between knowledge and predictor (demographic) variables. Variables were included in multivariable model if the level of significance achieved at the bivariate analyses stage was $p < 0.2$ or were known potential cofounders or factors associated with knowledge from previous studies (Abdi *et al*., 2015). A backward stepwise method was used in order to build the final model. To investigate the effects of demographic characteristics on the overall knowledge of RVF signs and symptoms, knowledge of RVF against demographic characteristics (gender, age, education and income) were also modelled.

3.3 Results

3.3.1 Socio-demographic characteristics of participants

A total of 275 respondents were sampled from 31 households, 5 government offices, 3 hospitals and 2 livestock markets in Garissa County (**Figure 7**) and out of this, 78% (214/275) were males and 22% (61/275) were females. Majority (42.9%) of the respondents had a secondary level of education, primary (23.6%), tertiary (16.7%) and none (16.7%) respectively. The average age of the respondents was 35.1±0.62 years and ranged from 19 yrs to 79 yrs. 38.5% (**Figure 8**), of those sampled were pastoralists followed by NGO workers (21%), teachers (10.5%) and others (30%). The average monthly income ranged from Ksh.0 to Ksh. 120,000 with mean of Ksh. 20,869 ± 1104 per month. Majority of household heads were male 65%, while 30% were females, the remaining 5% were a male relative to the household head. Most of the respondents were pastoralists (38.5%) and 68.0% of these had temporary residence at the time of the study (**Table 1 & Table 2**).

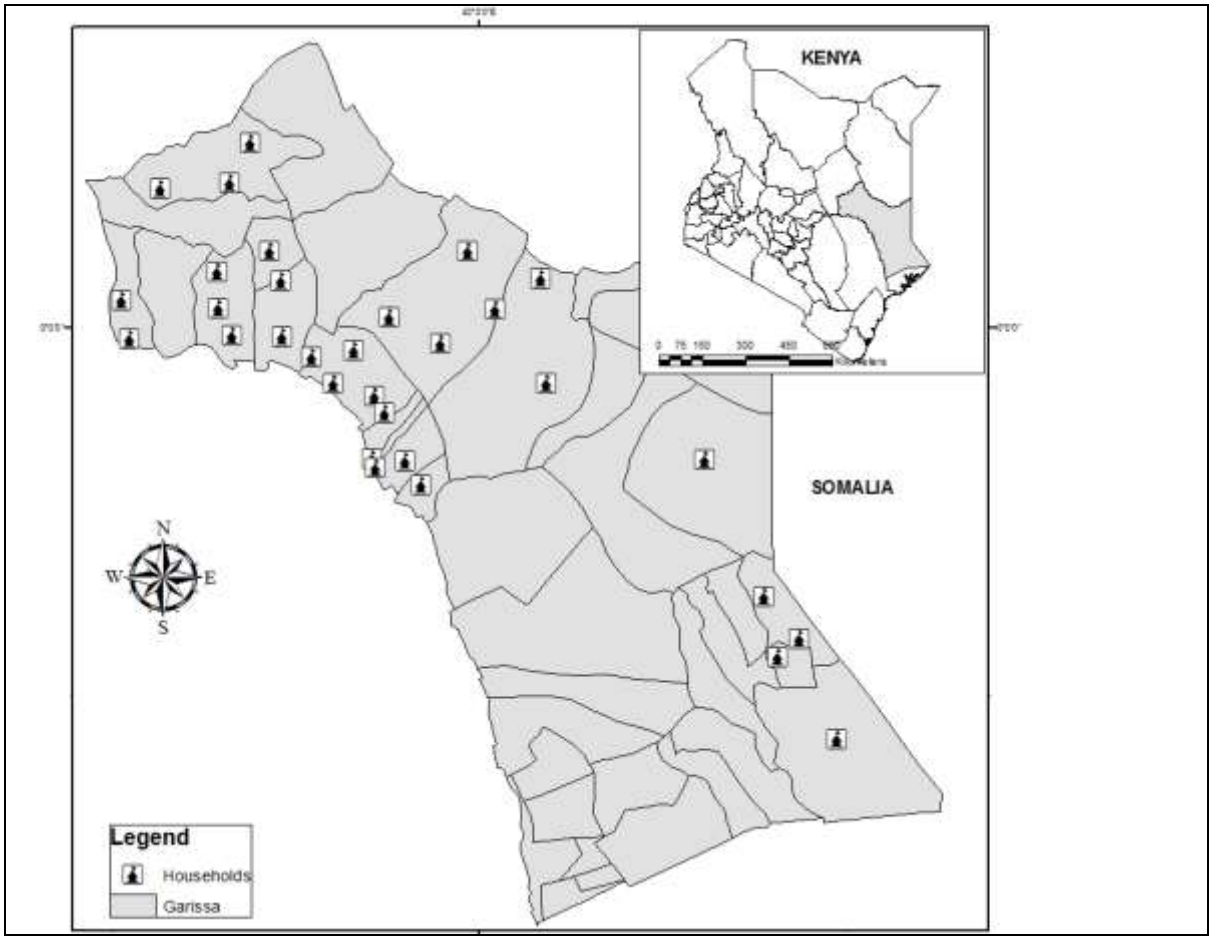


Figure 7: Map of Garissa indicating households for knowledge and practices assessment

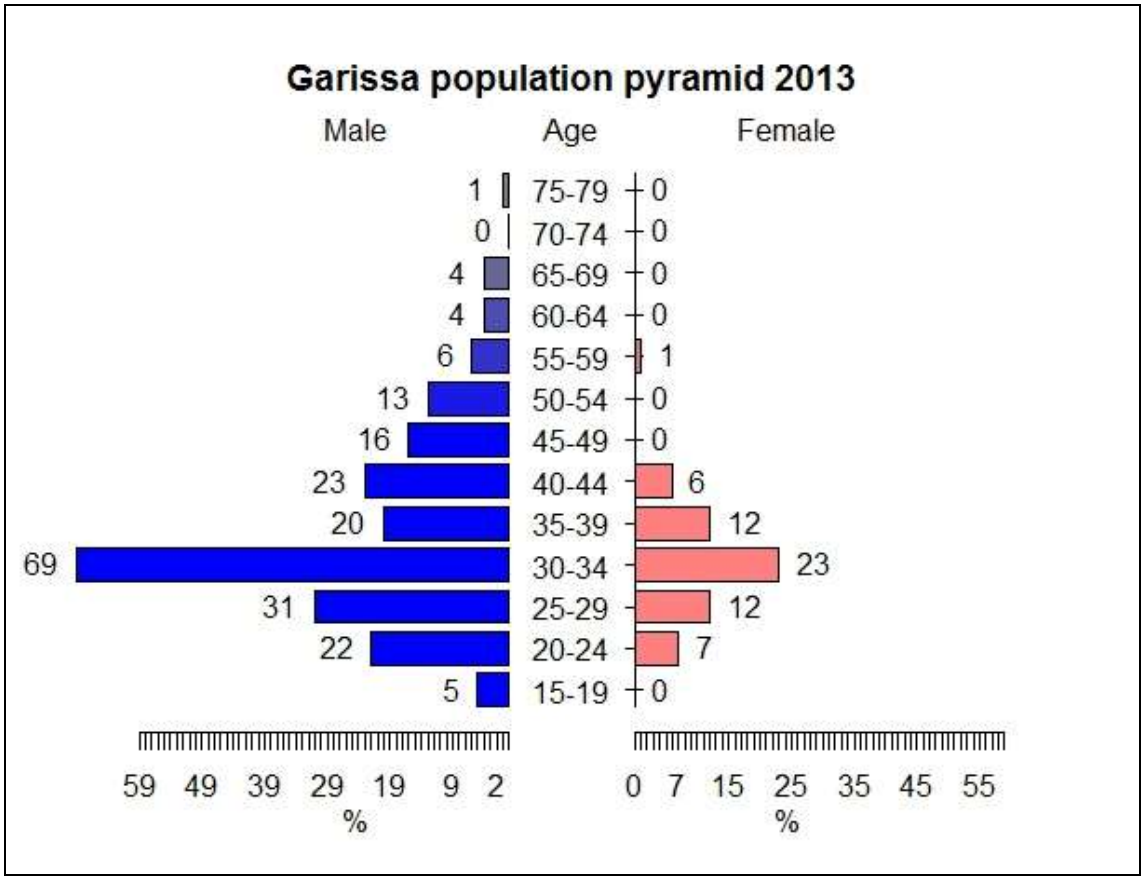


Figure 8: Population pyramid describing the demographics of study participants

Table 1: Demographic characteristics of study participants

Characteristic	frequencies (n= 275)	Percentages (%)
Sex		
Male	214	77.8
Female	61	22.2
Age group in years		
<20	5	1.8
20–24	29	10.5
25–29	43	15.6
30–34	92	33.5
35–39	32	11.6
40–44	29	10.5
45-49	16	5.8
>50	29	10.5
Educational level		
Primary level *	65	23.6
Secondary level	118	42.9
Post-secondary level	46	16.7
None	46	16.7
Residence status		
Permanent	88	32.0
Temporary	187	68.0
Income status (Ksh)		0.0
1000 – 5000	44	16.0
5000-10,000	52	18.9
10,000-20000	83	30.2
>20,000	96	34.9
Occupation		
Pastoralist	106	38.5
NGOs	81	29.5
Teachers	29	10.5
Administrators	14	5.1
Para veterinary	13	4.7
Animal traders	12	4.4
Veterinarian	7	2.5
Medical	4	1.5
Student	4	1.5
Others	5	1.8

3.3.2 Identification of climatic and non-climatic factors in RVF outbreaks

A seasonal calendar was developed during the FGDs, this was important for the identification of causative factors of climate change and related diseases including RVF. Three groups of participants were tasked to the regular cycles or patterns of activities within a community for up to 13 months. The purpose of the activity was to correlate disease outcome (RVF) with climatic factors; rainfall, temperature, humidity and other interventions. Four major seasons were identified and classified chronologically in the local *Somali* language; *Jilal* (short drought), *Guu* (long rains), *Hagar* (prolonged drought) and *Deyr* (short rains). The amounts of rainfall directly influenced the availability of water and pastures and hence the pricing of livestock. Routine RVF vaccinations were strategically conducted in previous RVF hotspots prior to *Guu* (long rains) as an anticipatory preventive mechanism of RVF outbreak. The prediction of rain or drought on the pattern of constellations, a constellation of stars that resembled specific animals was associated with heavy rains, whereas the indefinite shapes spelled long droughts.

3.3.3 Socio-demographic characteristics influence on overall knowledge of RVF

All respondents (100%) had heard of RVF referred to as *sandik* in the local language (*somali*). The overall knowledge on RVF was good with 185 respondents (74%) recognizing more than half of animal clinical symptoms (scored >50%). Majority of the respondents 71.6% and 69.8% recognized stormy abortions and high mortality of newborn animals respectively. Less than half of the respondents mentioned ocular nasal discharges (39.3%) and jaundice (33.1%). RVF in humans, high fever and haemorrhagic diarrhoea were the most recognized signs at 50.2% and 37.8% respectively (**Table 2**). The recognition of RVF symptoms was evenly distributed among respondents in different divisions of the county, with highest levels in Shanta Abak (**Table 3**).

Table 2: Knowledge proportion of respondents on RVF in Garissa

Factor/variable	Pastoralists and animal traders (%)	NGO workers (%)	Teachers (%)	Veterinary professionals (%)	Medical professionals (%)	Others (%)	Average knowledge (N=275, %)
Demographics	118 (42.9)	81(29.5)	29 (10.5)	20 (7.3)	4 (1.5)	23(8.4)	23(8.4)
1.Have you ever heard about RVF	118 (100)	81(100)	29 (100)	20 (100)	4 (100)	23(100)	275(100)
2. Cause and Transmission Animals and humans							
Contact with another person or animal	100(84.7)	55(67.9)	15(51.7)	20 (100)	4 (100)	18(78.3)	212(77)
Bite by mosquito	45(38.1)	60(74.1)	10(34.5)	0(0)	0(0)	5(21.7)	120(43.6)
Eating meat of dead or sick animals	78(66.1)	81(100)	20(69.0)	20 (100)	4 (100)	21(91.3)	224(81.4)
Touching or contacting animal fluids or aborted foetus	56(47.5)	74(91.4)	18(62.1)	20 (100)	4 (100)	18(78.3)	190(69.0)
3. Symptoms in animals							
Stormy abortions	105(89.0)	40(49.4)	22(75.9)	20 (100)	0(0)	17(73.9)	204(74.2)
High Mortality	118(100)	80(98.8)	27(93.1)	20 (100)	0(0)	15(65.2)	260(94.5)
High fever	110(93.2)	60(74.1)	23(79.3)	20 (100)	0(0)	20(87.0)	233(84.7)
Haemorrhagic diarrhoea	80(67.8)	54(66.7)	16(55.2)	20 (100)	0(0)	16(69.6)	186(67.6)
Ocular-nasal discharge	104(88.1)	38(46.9)	24(82.8)	20 (100)	0(0)	14(60.9)	200(72.7)
Jaundice	86(72.9)	40(49.4)	10(34.5)	20 (100)	0(0)	10(43.5)	166(60.3)
4. **Symptoms in humans**							
High fever	118(100)	70(86.4)	25(86.2)	10 (50)	4 (100)	6(26.1)	233(84.7)
Headache	107(90.7)	65(80.2)	20(69.0)	5(25)	4 (100)	18(78.3)	218(79.3)
Joint and muscle pain	104(88.1)	42(51.9)	24(82.8)	6(30)	2(50)	12(52.2)	190(69.0)
Haemorrhage	110(93.2)	30(37.0)	28(96.6)	2(10)	2(50)	16(69.6)	188(68.4)
5. Animal Preventive measures							
Vaccination	118(100)	71(87.7)	27(93.1)	20 (100)	2(50)	20(87.0)	258(93.8)
Selling of animals	60(50.8)	40(49.4)	12(41.4)	10 (50)	0(0)	22(95.7)	144(52.3)
6. Human Preventive measures							
Thorough cooking of meat	118(100)	67(82.7)	26(89.7)	5(25)	0 (0)	14(60.9)	230(83.6)
Avoid eating dead/sick animals	118(100)	81(100)	27(93.1)	20 (100)	4 (100)	16(69.6)	266(96.7)
Use of protective gear when slaughtering animals	95(805)	70(86.4)	21(72.4)	20 (100)	4 (100)	20(87.0)	230(83.6)
Avoid contact with aborted foetus/dead animal	82(69.2)	81(100)	24(82.8)	20 (100)	4 (100)	21(91.3)	232(84.3)

Table 3: Knowledge and recognition of RVF animal clinical signs according to area

Animal Clinical Signs	Daadab (%)	Danyere (%)	Township (%)	Hulugho (%)	Shanta Abak (%)
Storm abortions	46	53	25	54	89
High Mortality	55	65	44	52	78
High fever	69	72	79	64	82
Diarrhea (Hemorrhagic)	15	10	37	33	40
Ocular-nasal discharge	48	50	56	53	60
Jaundice	36	14	29	43	47

3.3.4 Influence of education and gender on knowledge of RVF

Majority of the male respondents (61.7%) had a high knowledge on RVF while a higher proportion (82%) of female respondents had low knowledge of RVF. The relationship between the overall knowledge of RVF and the respondents gender was statistically significant (χ^2=36.23, df=1, p-value <0.001). There was a strong correlation between level of education and knowledge of disease (Pearson's correlation coefficient r^2 = 0.6). The analysis of knowledge score showed that out of a maximum of 6 points, the scores of the participants ranged from 0 to 6 with a mean of 3.50±0.11 and median of 4 indicating a normal distribution of knowledge among all respondents.

Male respondents were four times more likely to be knowledgeable about RVF than their female counterparts (OR= 4.25, 95%CI 1.99-9.06). The odds of having good knowledge on RVF was found to improve with increasing in age of the respondents (b=0.061, z=3.82, p-value=0.000). In contrast, respondents who had secondary education were 33.5% less likely to be knowledgeable than those who had no formal education. However, the level of income did not have any significant influence on knowledge of respondents (p = 0.095) (**Table 4**)

Table 5: Association between RVF knowledge and (education, gender)

Variables	Levels	Estimates	OR	Z	P-value	95% CI of OR	
						Lower	Upper
Gender	Male	1.4467	4.25	3.74	<0.01	1.99	9.06
	Female*	-	-	-	-		
	Age	0.0613	1.06	3.82	<0.01	1.03	1.20
Education	None*	-	-	-	-	-	-
	Primary	-0.1746	0.8398	-0.37	0.712	0.3320	2.1239
	Secondary	-1.0937	0.3350	-2.46	<0.01	0.1403	0.800
	Tertiary	-0.9736	0.3777	-1.63	0.103	0.1172	1.2177
	Income	-0.0000	0.9999	-1.67	0.095	0.9999	1.000

The level of education had significant influence on the overall level of knowledge of RVF (χ^2=29.45, d.f=3, p =0.000). Majority (78.3%) of respondents with no formal education had high knowledge of RVF while in contrast a lower proportion (66.2%) of respondents who had primary education had high knowledge of RVF and less than 50% of the respondents who had secondary and tertiary education had high knowledge of RVF (**Table 5**)

Table 6: Relationship between level of education and knowledge of Rift Valley fever

Knowledge of RVF	Level of education							
	None		Primary		Secondary		Tertiary	
	n	%	n	%	n	%	n	%
Low	10	21.7	22	33.8	70	59.3	30	65.2
High	36	78.3	43	66.2	48	40.7	16	34.8
Total	46		65		118		46	

3.3.5 Practices regarding Rift Valley fever prevention and control

The majority (60%) of respondents recognized vaccination as the most effective way of controlling RVF and other livestock diseases. The risk factor assessment revealed preventive practices during outbreaks which included: avoidance of consumption of animal products (raw milk 50% and meat (64%) from sick animals, avoiding handling the aborted foetus (45%) and avoiding sheltering of humans and animals in the house (15 %). Mosquito control was practiced by 17% of respondents by burning of medicinal herbs for smoking of houses to reduce the number of mosquitoes and hence biting and transmission of RVF. Regarding disposal of carcasses as a preventive strategy, the slaughtering of sick animals suspected of RVF was avoided by 40.88% and burial of dead animals was practiced by 60% of pastoralists. The majority of respondents (92.4%) identified that cooking meat thoroughly before consumption could reduce the risk of RVF infection. As a mechanism to evade heavy rainfall and eventual flooding and mosquito emergence, traditional astrologists used the position of stars to predict rains thereby enabling 56% of the pastoralists to migrate away from the high-risk areas across the border to fall back grazing areas. As an anticipatory mechanism to avoid economic losses during RVF outbreaks, there was increased livestock sales in 75% of pastoralists and livestock sellers prior to the 2006-2007 RVF outbreaks.

3.4 Discussion

The assessment of knowledge and practices of community in response to RVF outbreaks in Garissa revealed that all the respondents had heard about RVF, as it was the epicentre of the previous (1997/1998 and 2006/2007) RVF outbreaks in Kenya (Nanyingi *et al*., 2015). Despite the high general knowledge, there was lack or extremely low level of knowledge on specific clinical signs in animals and humans by medical professionals, high fever was a common sign recognised in both humans and animals.

The community understanding the RVF transmission routes and risk factors for infection is first step to effective implementation of prevention and control strategies during an outbreak. There was a consensus across the different groups of participants that contact with sick animals or people, contact with fluids or foetus from sick animals and consumption of meat from dead or sick animals increased risk for infection (Anyangu, *et al*., 2010). However, most respondents had the low knowledge of on the role of mosquito bite as vector in the transmission of RVF, this was previously reported in Ijara (Abdi *et al*., 2015) (Table 3).

The high recognition of clinical signs by somali pastoralists concurs with finding of recent studies in neighbouring areas of Ijara (Abdi *et al*., 2015) and an earlier comparative assessment of the 2006/2007 RVF outbreak in Kenya and Tanzania that indicated that the Somali pastoralists in Kenya could provide more accurate and detailed clinical descriptions of RVF, than their Maasai counterparts in Tanzania (Jost *et al*., 2010). This may be attributed to effective delivery of control and prevention educational messages after RVF outbreaks and good institutional memory of the pastoralists.

The low level of knowledge by medical professionals specifically to signs in animals and preventative measures in animals and humans could be due lack of continuous medical training hence a necessity for capacity building in one health and zoonotic diseases. High fever and hemorrhage were identified as the main signs in humans, followed by joint and muscle pains. RVF cases in human present from mild self-limiting illness to severe hemorrhagic phase, the patients developing hemorrhage have a high case fatality rate of 10-20 % (Madani *et al*., 2003).

Majority of the pastoralists has a positive attitude and good practices towards the control of RVF from the information mainly obtained from community meetings, radio, humanitarian workers and health/veterinary workers. They reckoned that RVF led to substantial impact on public health and economy due to livestock deaths, decreased livestock sales and ban on consumption of meat and livestock products. Majority of respondents recognized that consuming unsafe milk or uninspected meat may pose a risk for RVF transmission in humans and hence proper cooking and avoidance of consumption of carcasses of dead animals was practiced (Shabani *et al*., 2015).

The findings of this study should be interpreted in light of limitations of using semi-structured questionnaire based survey. The assessment was conducted six years after last outbreak and mostly in areas that experienced previous RVF outbreaks hence the findings may be generalized due to recall bias. Despite these challenges the approach is useful in providing baseline information in prevention and control of future RVF outbreaks.

CHAPTER FOUR

SEROEPIDEMIOLOGIC SURVEILLANCE OF RIFT VALLEY FEVER IN GARISSA

4.0 Introduction

Rift Valley fever seroepidemiological surveillance allow the early detection of the virus and provides the first indications for the transition from endemic to epidemic cycle, however it provides insight of the infection status of animals for a short window of duration of viremia. There is need for routine longitudinal monitoring of the antibody prevalence in susceptible species in endemic areas using sentinel herds (Kortekaas *et al.*, 2013).

During the initial stages of RVF infection, rapid diagnosis can be made by quantitative real-time polymerase chain reaction (RT-PCR) to detect viremic animals. Economical and appropriate tools for diagnosis and surveillance of RVF include; Enzyme-linked immunosorbent assays (ELISA) and virus neutralization tests (VNT) which are highly recommended for antibody detection, where Immunoglobulin M and IgG indicates recent and historical exposure, respectively (Bird *et al*., 2008; Paweska *et al*., 2005).

While most RVF serological surveys in Eastern Africa focus on epidemics (Woods *et al*., 2002, World Health Organization, 2007, LaBeaud *et al.*, 2008, Nguku *et al.*, 2010), limited research has been done to determine RVF virus transmission patterns during the interepidemic periods (King *et al.*, 2010, Muiruri *et al*., 2015, Gray *et al*., 2015). The objective of this study was to determine levels of RVF virus exposure in goats, sheep and cattle in Garissa County, during an inter-epidemic period.

4.1 Methods

4.1.1 Study area

Refer to description in Chapter 3 and Figure 6.

4.1.2 Study design and sample size determination

A cross-sectional study design was used and the sample size was determined based on methods for estimating a proportion of diseased animals that have a defined precision in entire animal population (Dohoo and Martin , 2009) with a *priori* RVFV seroprevalence (P) of 50%, maximum allowable error of 10% (P= 50 ±10) and confidence level of 95%, the required sample size was estimated to be 384 animals.

4.1.3 Selection of the sites and animals

Eight areas in the County that were affected by the 2006-2007 RVF outbreaks were purposively selected for the survey. These were Danyere, Kone, Sankuri, Korakora, Bouralgi, Disso, Yumbis and Hulugho areas. A total of 300 villages from these areas by using a probability proportionate to size approach but only 30 of these villages were finally selected conveniently based on their suitability for mosquito breeding, presence of artificial animal watering points and high livestock populations. Herds that had been vaccinated against RVF were excluded from the study. These herds were identified with the help of the local veterinarians and animal technicians. Locations of all the sampled herds and water bodies were recorded using a global positioning system (GPS) receiver coordinates. Cattle, sheep and goats were sampled excluding camels, this was due to camel owners traditional believes that putting camels in prolonged recumbency may lead to bloating and death, hence they were uncooperative to allow sampling. The strenuous nature of restraining cattle led to extremely smaller sample sizes.

4.1.4 Serological sampling and testing

Five (5) ml of whole blood was collected from 415 animals by jugular venipuncture into plain vacutainer tubes and transported to the Garissa laboratory and kept at room temperature for 20 minutes. The sample size increased from the initial 384 to cater for accidental spillages, 45 samples were discarded due to leakages and compromise in quality during transportation leaving 370 viable samples. Centrifugation was done for 10 minutes at 3,000 rpm. Sera was recovered as aliquots into cryovials and stored at -80°C until testing at KEMRI laboratories. The presence of RVFV antibodies was investigated using a commercial indirect competitive ELISA (cELISA) (ID Screen® *IDVet Innovative Diagnostics, Grabels, France*). Briefly, 50µl of pre-diluted serum samples and controls (positive and negative) were added in the wells of the coated plate and 50 µl of RVF sample dilution buffer added to each well containing the controls or samples. Each plate was then covered with an adhesive cover plate and incubated for one hour at 37°C. Three washes were performed with wash solution before 100 µl of conjugate was added and incubated for 30 minutes at 21°C. The three wash steps were repeated and 100 µl of substrate added to each well and incubated for 15 minutes at 21°C, then 100 µl of stop solution was added. The results were read within 30 minutes after stopping the reaction at 450 nm on a microplate reader (*Biokit, ELX800-USA*). Validation of the test was done when the mean value of the negative control O.D (ODNC) > 0.7 and positive control (ODPC) was <30% of the ODNC (ODPC/ ODNC <0.3). Seropositivity was detectable as suspect or negative (S/N %) value of ≤ 40% (Ellis *et al*., 2014). Samples that had S/N > 50% were considered negative for total RVF antibodies. The sensitivity and specificity of the test was 98% and 100%, respectively (Kortekaas *et al.,* 2012).

4.2 Statistical analysis

Univariable logistic regression analysis was used to determine the association between the putative risk factors and the serostatus for RVF for each animal. The effects of the exposure variables on the distribution of the outcome variable while controlling for other covariates was estimated. Variables for which an association ($p \leq 0.2$) was detected were included as predictors in a mixed effect logistic regression model. The factors meeting this criterion were species, age, sex, location and formed the maximum saturated model. By using a backward stepwise elimination process, an assessment of the factors and their interactions and retained in the model only when $p \leq 0.05$. The final fitted individual models were evaluated by including location (sampling site) as a random effect to adjust for possible clustering of RVF seropositivity within herds. Intra-cluster correlation coefficient (ρ) describing the degree of similarity among seropositive animals in each location was estimated. Adjusted odds ratios (OR) for seropositivity were estimated using a "*lme4"* package in R. All analysis were performed using R statistical software version 3.1.3 (R Development CoreTeam, 2016).

4.3 Results

4.3.1 Cross-sectional survey

Seropositivity for 370 samples was analyzed as stratified by location, species and age as presented in (**Table 6 and Table 9**).

Table 7: Distribution of animals sampled by area, species and age

Study area	**Species**	**Number sampled**		**Age**	
		Male	**Female**	**≤1year**	**>1year**
Bouralgi	Cattle	0	0	0	0
	Goats	0	14	2	12
	Sheep	2	9	3	8
Danyere	Cattle	0	0	0	0
	Goats	1	27	0	28
	Sheep	2	14	0	16
Disso	Cattle	0	0	0	0
	Goats	2	17	10	9
	Sheep	1	15	4	12
Hulugho	Cattle	0	0	0	0
	Goats	1	12	0	13
	Sheep	3	13	3	13
Kone	Cattle	0	0	0	0
	Goats	9	100	25	84
	Sheep	3	12	1	14
Korakora	Cattle	2	10	6	6
	Goats	0	19	0	19
	Sheep	1	5	0	6
Sankuri	Cattle	0	0	0	0
	Goats	12	26	11	27
	Sheep	0	0	0	0
Yumbis	Cattle	0	0	0	0
	Goats	3	28	7	24
	Sheep	2	5	0	7
Total		44	326	72	298

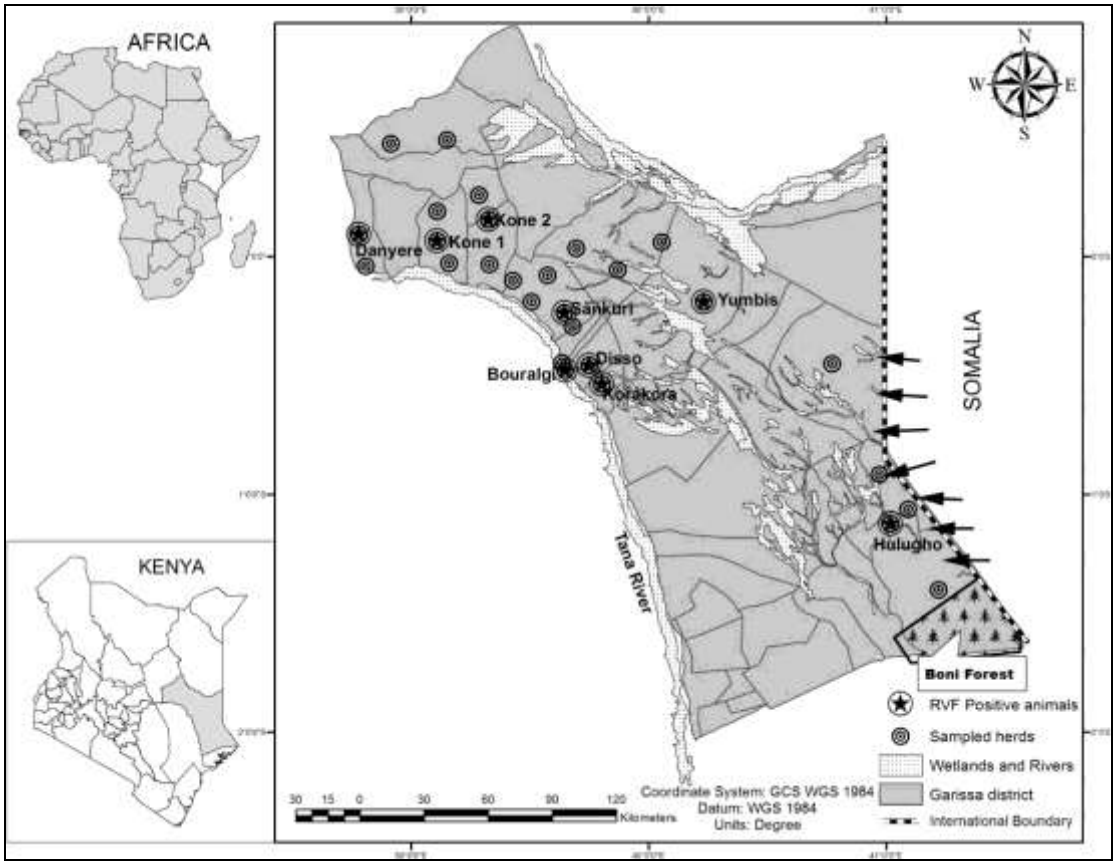
4.3.2 Seroprevalence by location, sex and species

The overall RVFV antibody seroprevalence was 27.6% (95% CI 23-32.1). The seropositivity for cattle, sheep and goats was 33.3% (4/12), 32.2 % (28/87) and 25.8% (70/271) respectively. A unique local maximum seroprevalence of 76.9% (10/13) was recorded in goats from Hulugho in the southern part and 45.5% (5/11) in sheep from Bouralgi in the west-central part (**Table 7**). The variance between locations from the logistic regression model was 0.09 for 370 animals and the intracluster correlation coefficient (ICC) ρ(rho) of 0.02 was estimated within areas.

Table 8: Rift Valley fever seroprevalence by the study area and species

	Goats			**Sheep**			**Cattle**		
Area	n	SP (%)	95% C.I	n	SP (%)	95% C.I	n	SP (%)	95% C.I
Bouralgi	14	50	23.8-76.2	11	45.5	16-74.9	_	_	_
Danyere	28	35.7	18-53.5	16	37.5	13.8-61.2	_	_	_
Disso	19	5.3	4.3-15.3	16	12.5	3.7-28.7	_	_	_
Hulugho	13	76.9	54-99.8	16	31.2	8.5-54	_	_	_
Kone	109	16.5	9.5-23.5	15	40	15.2-64.8	_	_	_
Korakora	19	36.8	15.2-58.5	6	16.7	13.2-46.5	12	33.3	16.7- 46
Sankuri	38	21.1	8.1-34	_	_	_	_	_	_
Yumbis	31	29	13.1-45	7	42.9	6.2-79.5	_	_	_

**SP = Seroprevalence, CI= Confidence Interval



(Nanyingi *et al*., 2016)

Figure 9: Spatial distribution of all sampled and seropositive herds in Garissa

The overall seroprevalence for all male species was 31.8% (95% CI 18.1-45.6) and females 27% (95% CI 22.2-31.8). Female goats had seroprevalence of 26.3% (95% CI 20.8-31.9) while males had 21.4% (95% CI 6.2-36.6), 30.1% (95% CI 19.6-40.7). Goats > 1 year had seroprevalence of 31.9% (95% CI 25.7-38.2) while sheep > 1 year had 35.5 (95% CI 24.8-46.3). Sheep ≤ 1 year had prevalence of 9.1% (95% CI -7.9-26.1) compared to goats 1.8% (95% CI -1.7-5.3) as indicated in (**Table 8**).

Table 9: Rift Valley fever seroprevalence in sheep and goats by age and sex

			Sampled	Positive	SP (C.I)
Goats	sex	Female	243	64	26.3 (20.8-31.9)
		Male	28	6	21.4 (6.2-36.6)
	Age	>1 year	216	69	31.9 (25.7- 38.2)
		≤1year	55	1	1.8 (-1.7-5.3)
Sheep	sex	Female	73	22	30.1(19.6-40.7)
		Male	14	6	42.6 (16.9-68.8)
	Age	>1 year	76	27	35.5 (24.8-46.3)
		≤ 1 year	11	1	9.1(-7.9-26.1)

**SP = Seroprevalence, CI= Confidence Interval

4.3.3 Host factors influence on seropositivity

A logistic regression model with location as a random effect was used to investigate the association between RVFV antibody prevalence and host factors (age and sex). Due to lack of accurate animal demographics and to control for confounding, age was categorized as ≤1 year and >1 year. Seropositivity increased with advanced age, animals >1-year-old had an 18-fold likelihood to be seropositive than animals ≤1 year, OR 18.24 (95% CI 5.26-116.4), p = (0.0001) (**Table 9**).

Table 10: Effect of sex, species and age on RVFV seropositivity in Garissa

		RVF Seroprevalence		
Variable	Levels	OR	95%CI	p value
Sex	Female	1*	-	-
	Male	1.17	0.55-2.48	0.65
Species	Caprine	1*	_	-
	Bovine	1.07	0.55-15.87	0.19
	Ovine	1.05	0.58-1.88	0.86
Age	≤1 year	1*	-	-
	>1 year	18.91	5.51-120.17	< 0.0001†††

OR= *Odds Ratio,* CI= *Confidence Interval*, *= *Reference level*, † = *Significance level*

4.4 Discussion

RVF outbreaks have been reported in Garissa in 1997/1998 and 2006/2007, The 1997–1998 RVF outbreaks in Kenya caused 170 human deaths in Garissa, which was the epicenter of the outbreak (Woods *et al*. 2002). A total of 478 human cases were also reported in North Eastern Kenya and southern Somalia (Centers for Disease and Prevention ,1998). During the 2006–2007 epidemic period, more than 30,000 livestock and 700 human cases and 158 human deaths were reported in Kenya (World Health Organization, 2007, Munyua *et al*. 2010, Nguku *et al*. 2010).

Serological surveys have been previously conducted in Garissa and neighbouring areas to determine RVFV circulation in livestock and humans. In Ijara, a sentinel livestock surveillance was conducted between 2009–2012 among sheep and goats, there was an overall decrease in seropositivity from 5.3% to 3.6% with no significant difference in seropositivity between the animal types (Lichoti *et al*., 2014). Another longitudinal study was conducted on six herds, each comprising of 700–1000 cattle in Ijara between 2012 and 2013, a seropositivity of 13.1% was reported in cattle sero-surveyed by inhibition ELISA test while 1.4% was positive for IgM ELISA test indicating active infection (Owange *et al*., 2014).

In 2011, a seroepidemiological survey on RVF among 500 small ruminants and their close human contacts was conducted in Saudi Arabia (Mohamed *et al*., 2014). In total, 84 (16.8%) of sheep and goats tested positive for IgG indicating previous exposure to RVFV while 9% of humans tested seropositive. This is attributed to livestock importation and migration within Saudi Arabia, which may be applicable to Garissa.

A human RVF seroprevalence study was conducted in Bodhei Village in Lamu County, this forested area is in proximity to the epidemic prone Garissa, 219 humans had an (18%) overall seroprevalence for anti-RVFV with adults having 28%, and children 3%; ($P < 0.001$), confirming that significant RVFV transmission occurs outside of recognized high-risk areas during the interepidemic periods (Muiruri *et al*., 2015).Future seroepidemiological studies should consider designing syndromic surveillance mechanisms for cost-effective prevention and control of outbreaks.

The passive surveillance for RVFV may not highly effective in detecting new epidemic threats in disease endemic areas. A human-livestock linked cross-sectional seroepidemiological study was conducted from July 2010 to June 2012 to examine the evidence for circulation of Rift Valley fever virus (RVFV) among herders in Western and Eastern parts of Kenya including Garissa County. In Garissa of the 230 participants who were enrolled 36 (15.7%) screened positive for IgG antibodies, most of seropositive cases were relatively young, confirming that indeed some human RVFV infections may be occurring during interepidemic periods (Gray *et al*., 2015).

Virus neutralization test (VN), IgG and IgM enzyme linked immunosorbent assay (ELISA) were used in an RVF serological study in five districts of Zambezia Province, Mozambique. It was demonstrated that RVFV-specific antibodies were continuously present in of sheep and goats, suggesting the circulation of RVFV during inter-epidemic periods, there was a seven-fold (OR = 7.3) likelihood of being seropositive in older compared to younger animals, which was also observed in the current study (Fafetine *et al*., 2013).

CHAPTER FIVE

SPATIAL EPIDEMIOLOGY OF RIFT VALLEY FEVER IN GARISSA

5.0 Introduction

Spatial epidemiology focuses on the description and analysis of geographic variations in infectious diseases with respect to demographic, environmental, behavioural, socioeconomic and genetic risk factors (Elliott and Wartenberg, 2004). Spatial and temporal distribution of infectious diseases including RVF is driven by an interplay of climate variation, presence of competent vectors and complex ecological processes that result in strong spatial patterns due to pathogen dispersal, spatial restriction of vectors or reservoirs for pathogens or aggregation of susceptible hosts (Ostfeld *et al*., 2005). RVF epidemics have been predicted using advances in geographical information systems (GIS) and remote sensing (RS) technology that can model the transmission dynamics using climatic and environmental indicators (Leedale *et al*., 2016). Prospective spatiotemporal and mathematical models have used vectors and livestock to flag areas at highest risk of RVF virus transmission based on key environmental indicators in endemic areas of Africa and Arabian Peninsula (Britch *et al*., 2013, Metras *et al*., 2015, Abdo-Salem *et al*., 2006).

Ecological niche models (ENMs) also known as Species distribution models (SDMs) are a class of methods that use disease occurrence data in conjunction with environmental data to make a correlative model of the environmental conditions that meet the disease ecological requirements and predict the relative suitability of habitat. Species distribution models (SDMs) like Boosted regression trees (BRT) use regression techniques to identify the correlative associations of disease occurrence to a suite of explanatory and spatially extensive variables (Anderson *et al*., 2006).

The BRT algorithm builds an initial regression tree and then improves upon it in a progressive stage-wise manner (boosting) repetitively to minimize variation in the responses at each stage (Ashby *et al*., 2017). The Integrated Nested Laplace Approximation (INLA) is used for Bayesian inference that offers a highly flexible modelling environment that produces SDM-type spatial predictions that additively account for 'random' effects, such as sampling bias (Karagiannis-Voules *et al*., 2013). Recently INLA has been has successfully been used to predict both continental and small-scale risks of RVF at spatial and temporal scale by determining the influence of environmental and climatic drivers on RVF seroprevalence in livestock and humans (Redding *et al*., 2017, Bett *et al*., 2017).

Logistic regression models have been previously used to predict risk factors for RVF occurrence, these are based on disease presence data and other environmental and climatic covariates (Munyua *et al*., 2016; Gikungu *et al.*, 2016). Vector suitability and occurrence of RVF using INLA has been predicted in irrigated and flooded areas of Eastern Kenya (Bett *et al*., 2017). Most studies however do not exclusively integrate animal and human populations hence cannot account for the host viral intensification, amplification and spillage of infections.

The aim of this study was to determine the influence of underlying environmental, host and climatic drivers to the spatial risk of RVF outbreaks in Garissa and also make space sensitive predictions to better direct surveillance resources at the county level. This study compared the predictive performance and agreement of a non-spatial SDM method (BRT) to a spatially-explicit Bayesian SDM method (INLA) using a small-scale area that can form a framework for wider area application to RVF and other zoonotic diseases in Kenya.

5.1 Methods

5.1.1 Study Area

Refer to description in Chapter 3 and Figure 6.

5.1.2 Rift Valley fever data

RVF occurrence data were collected for the month of July 2013 in a cross-sectional serological survey in Garissa. A total of 415 ruminants (cattle, sheep and goats) were sampled in 31 locations georeferenced locations. Seropositivity for 370 of the samples was determined by IgG ELISA where 103 animals tested positive for RVFV, despite that several animals were positive in the same location only one record was used for each location, leaving 16 positives as presence points (Nanyingi *et al*., 2016). Any location that had one or more cases of RVF seropositive animals was coded as having disease "presence", while a set of randomly selected points were generated and were coded as disease "pseudo-absence" (PA), these were included in all models.

5.1.3 Explanatory variables: Data extraction for spatial modelling

Remote sensed climatic and environmental layers used in modelling included: monthly rainfall estimates, precipitation, elevation, enhanced vegetation index (EVI), soil types and euclidean distance to rivers and water, human population density and animal population density (sheep and goats). The stepwise extraction procedure is detailed in **Appendix 6** and sources of data are summarised in (**Table 10**).

Table 11: Climatic, environmental and demographic predictors

Input covariate	**Time Period**	**Spatial Resolution**	**Source (All data used is open source)**
Rainfall	2013-2014	6 km^2	http://chg.geog.ucsb.edu/data/chirps
Temperature	2013-2014	1km^2	https://webfiles.york.ac.uk/KITE/AfriClim/
EVI	Fixed-time	250 m^2	https://earthexplorer.usgs.gov
Soil types	Fixed-time	1km^2	http://data.ilri.org/geoportal
Distance to rivers and waterbodies	Fixed-time	1km^2	http://data.ilri.org/geoportal
Digital Elevation Model (DEM)	Fixed-time	90 m^2	https://earthexplorer.usgs.gov
Human population	2014	100 m^2	http://www.worldpop.org.uk
Goat and sheep densities	2014	1km^2	http://www.livestock.geo-wiki.org

5.2 Spatial modelling

5.2.1 Boosted Regression Trees (BRT)

Using Gradient Boosting Machines (GBM) (Elith *et al.*, 2008) and the provided functions ('raster', 'sp', 'gbm' and 'dismo' libraries) in the statistical package R (*https://www.r-project.org*), different BRT models were run using all 9 explanatory variables against RVF (presence /pseudo absence). BRT stochasticity is defined by the bag fraction (bf), this is the percentage of data randomly selected at each step (the proportion of data to be used in each run). The learning rate(*lr*) determines the contribution of each tree to the growing model. A low learning rate, is preferable and it implies a larger number of trees, is advised. The tree complexity(*tc*) represents the number of nodes in a tree and the number of interactions (Elith *et al.*, 2008). This BRT model was accordingly fitted using a *tr* of 5, *bf* of 0.75 and a *lr* of 0.0001 to build an average of 1000 trees. Predictive error was measured as the Bernoulli residual deviance between the predicted values of the model and the observed values of the test data.

Model evaluation and validation

The model used 90% randomly selected dataset for model calibration while 10% was used for validation. To evaluate the predictive power of BRT, the model accuracy and performance was validated using the area under the receiver operating characteristic curve (AUC of ROC). Values of AUC approaching one (1) indicate a well-performing model while an AUC equal to 0.5 indicates the model performs no better than random prediction and are tested statistically with a z-score (Z) and standard error (SE) estimates. AUCs were interpreted in conjunction with measures of omission and commission calculated using the summated 10 best models (Elith *et al.*, 2008).

5.2.2 Bayesian geostastical modelling

A bayesian hierarchical explicit spatial model was performed, where model parameters were estimated via INLA fitted in R (*R-INLA*) and a homonymous R-package (www.r-inla.org). The analysis employed methods proposed by Rue *et al*., (2009), and formulated by the equation below:

$$n_{i=}\beta_{O^2} + \sum_{y=1}^{Y} \beta_y x_y + f(z_1) \quad (1)$$

Where:

The seroprevalence data, *yi* was a binary variable, 1 representing a positive test result and 0 otherwise, in this analysis, the observed presence of RVF seropositivity (+ve) and the randomly generated pseudo negative (-ve) were assumed to have a binomial distribution. ηi is the linear predictor linked to the original scale of the outcome *yi* through a link function, β_0 is a scalar representing the intercept, βy represent the values of the coefficients quantifying the linear effect of covariates *xy*, and *f* (*zi*) is a function used to account for the spatial random effect.

Specific predictor covariates considered included rainfall, temperature, EVI, distance to rivers and waterbodies, elevation, human and livestock population. A Stochastic Partial Differential Equations approach (SPDE) was used to fit a Gaussian random effect to account for spatial autocorrelation, disease clumping or clustering tendency and sampling bias in different locations with different livestock species and densities (Lindgren *et al*., 2011). The posterior distributions of the model parameters were generated by the model. These quantify the uncertainty in the values of the unknown model parameters at 95% credible interval (CI), and it is used to determine the significance of all covariates. All analyses were performed in R version 3.3.2 software **(**R Development CoreTeam, 2016).

(*Details on BRT and R INLA models' formulation is provided in* (**Appendix 7**).

5.2.3 Spatial probability risk categorization

Risk maps predicted by the models were generated by creating a spatial range of RVF occurrence, the raster layers generated in R were imported in ArcMap and using the symbology tool the predicted risk probability for all the model outputs was categorized into five classes; very low (0–0.1), low (>0.1–0.2), medium (>0.2–0.4), high (>0.4–0.5), and very high (>0.5) in ArcGIS software v.10.5 (Environmental Systems Research Institute (ESRI), 2016).

5.3 Results

5.3.1 Boosted regression trees (BRT)

The map in **Figure 10,** illustrates the predicted spatial pattern of the RVF prevalence across Garissa county as modelled by BRT. The model predicted high probability (>0.5-1.0) of RVF occurrence in the north-western part of Garissa. There was moderate to low prevalence in the central parts but this increased again towards the southern parts. The areas adjacent to the Tana River on the western border of Garissa had very high probability (>0.5-1.0) of seropositivity compared to the central parts of Garissa (<0.3). The localized areas of high prevalence are associated with presence of perennial water bodies that attract animal and human aggregation and vector abundance, these areas have potential for virus amplification that can lead to outbreaks.

The BRT model was performed using 51% (n=16) of all points for seropositive areas for testing. The predictive performance was found high for the ensemble prediction map after the 100 iterations resulted in a AUC of ROC score of (0.7 ±0.001 s.d). These predictions were represented in the probability risk map of RVF where distinct spatial patterns of different probabilities of RVF risk were identified (**Figure 10).** BRT predicted approximately 16,810 km2 of very high suitable habitat (predicted risk probability of 0.7), which is 70% of the total area of Garissa County. There is a high predicted risk along the entire southern border of the county, as it is bordered by the larger Tana river thereby providing conducive mosquito breeding sites for RVF mosquitoes.

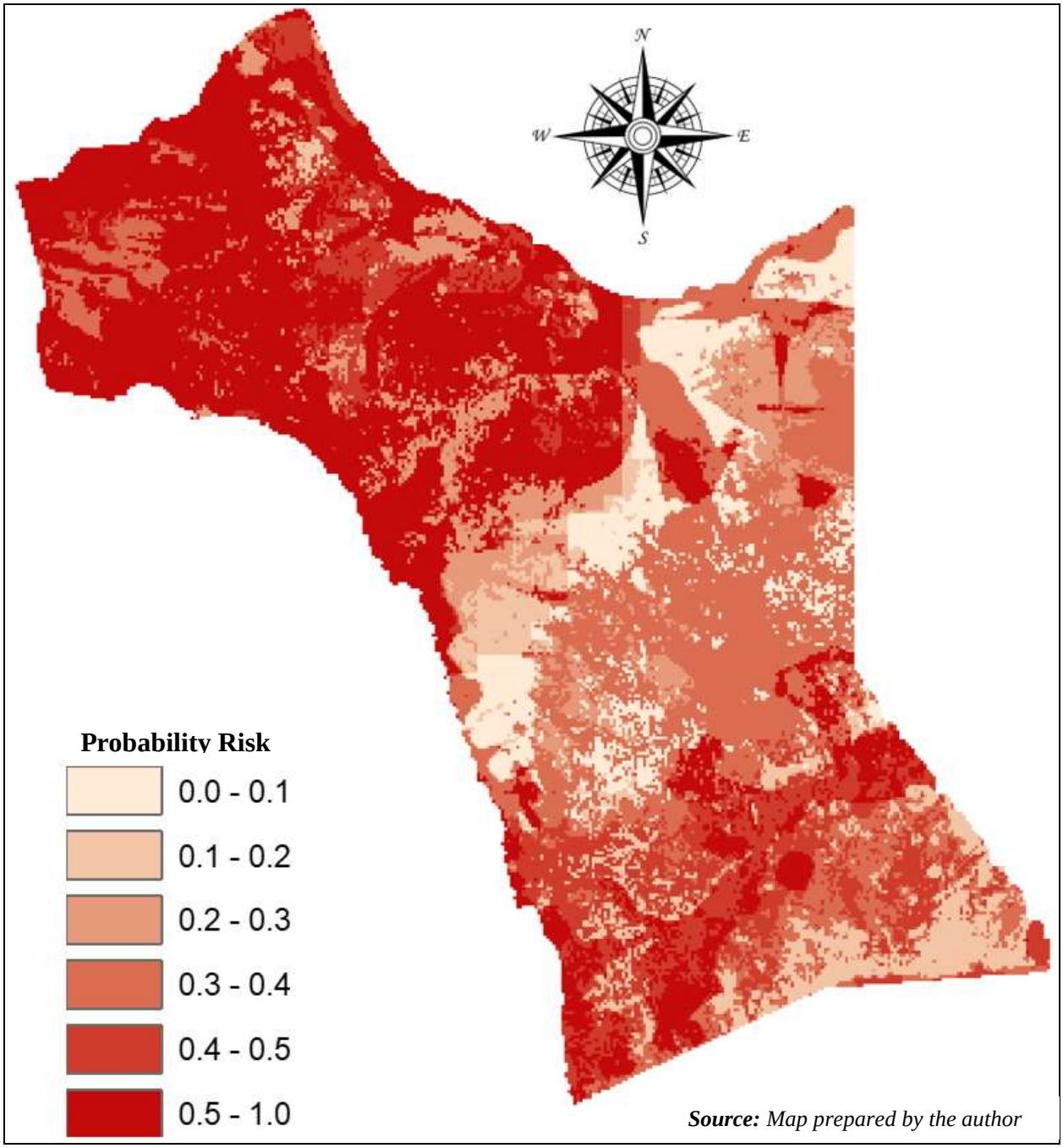


Figure 10: Probability risk of RVF predicted prevalence based on BRT

Relative importance of variables to the BRT model

The relative importance of the predictors in the BRT model that contributed to the risk of RVF serological status was identified according to (Friedman, 2002). The relative importance is based on the number of times a variable is selected for splitting, weighted by the squared improvement and averaged over all trees. The relative importance of each variable is then scaled so that the sum adds to 100 as percentages. A higher percentage of a variable indicates a stronger relative importance of this variable on the response. Parameter reduction of the full predictor set resulted in a simplified set of 9 significant predictors to the spatial risk of RVF occurrence (**Figure 11**).

It was observed that the high human population in a grid cell substantially contributed to the models with a relative importance of 35 %, with a nearly linear increasing association with the occurrence of RVF. Sheep population was the second most important predictor of the RVF occurrence (relative importance of 27%). High precipitation and temperature had relative importance of 17 % and 10% respectively. The soil type has a significant contribution to the RVF occurrence at (relative importance of 5%). Finally, vegetation index and distance from water bodies had equal but the least relative importance 3%. Despite sheep population higher influence, the goat density did not demonstrate significant contribution to predict the RVF seropositivity with relative influence of <5%.

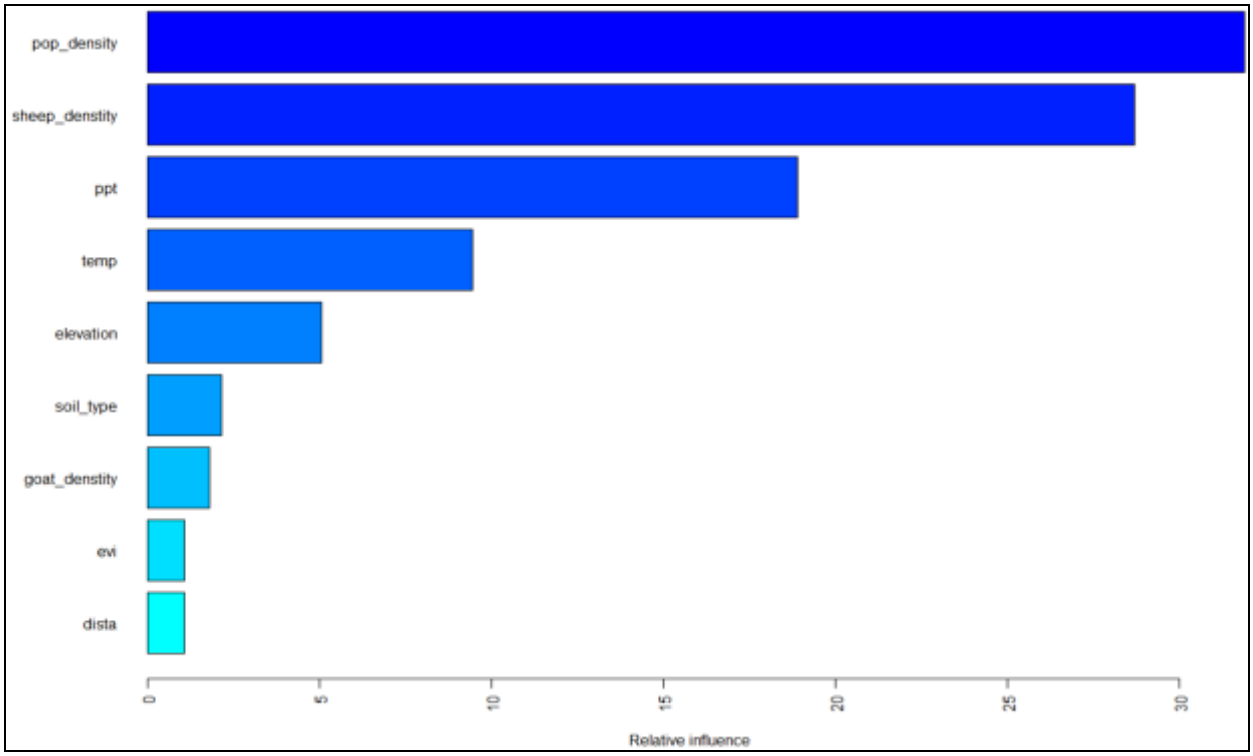


Figure 11: Relative influence of predictors on RVF prevalence as predicted by BRT

Legend

Pop-density- human population density	**Evi**- enhanced vegetative index
Ppt – precipitation	**Dista**- distance from rivers and water bodies
Temp – temperature	

5.3.2 INLA (Integrated Nested Laplace Approximation)

The map in **Figure 12** shows consistent high risk in the north-western parts of Garissa, which decreases to medium risk (>0.2–0.4) towards the central parts. There are interspersed foci of high risk most notably in central to eastern parts near perennial water bodies and around south-eastern areas of Garissa, which borders Boni forest. The proximity to the forest may contribute to increase in vegetation cover (EVI) and hence mosquito density. The western border of Somalia had the lowest predicted risk (<0.1). The map shows that most of the study area had medium risk (the overall mean of the spatial component), with small areas (those close to observed data locations) having increased risk. The predictive performance of INLA was found to be very high with AUC of ROC score of 0.9 ±0.001 s.d).

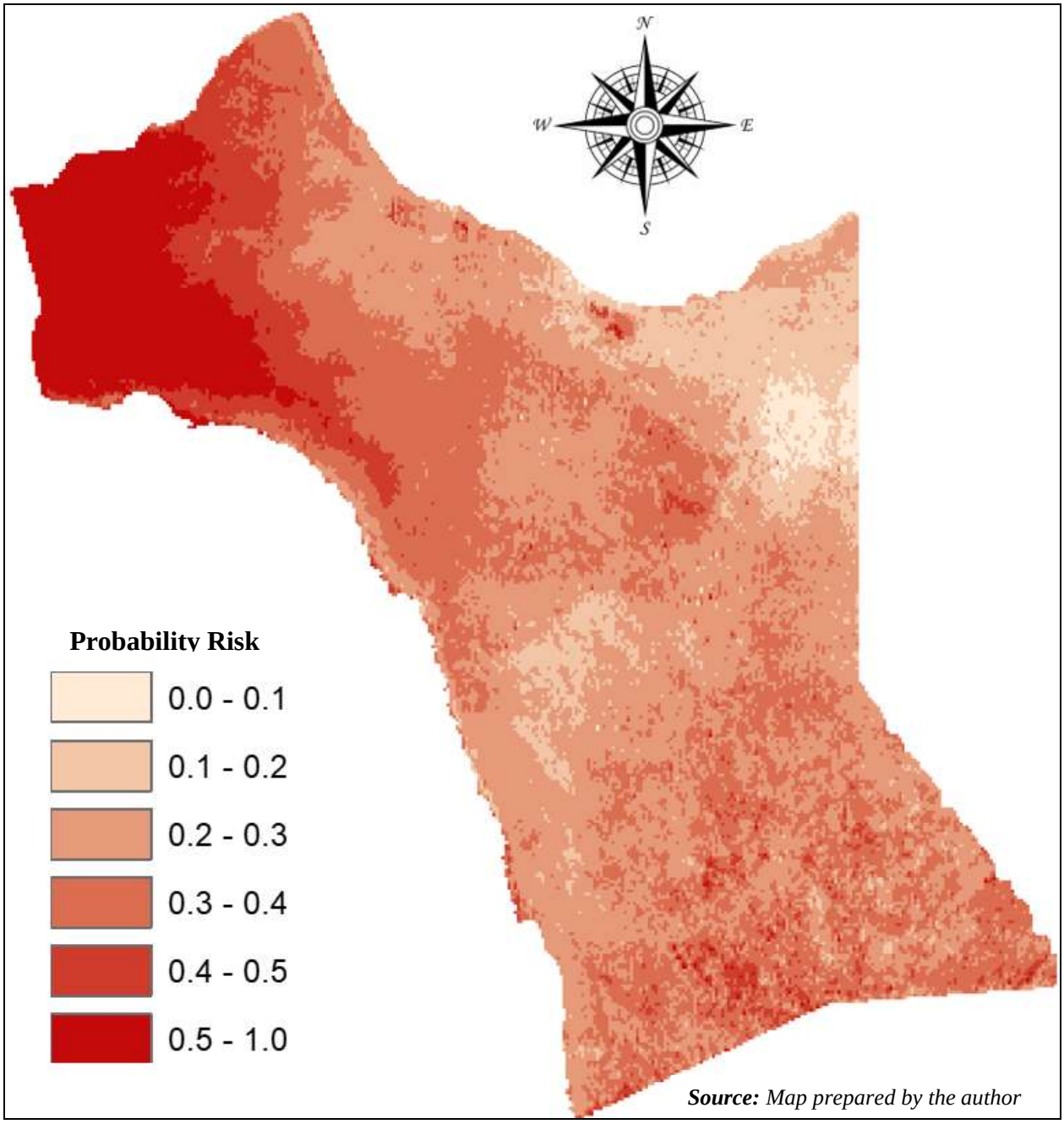


Figure 12: Probability risk of RVF prevalence distribution based on INLA

5.3.3 Models agreement on spatial predictions.

Pearson's correlation coefficient (PCC) was used to measure how closely predictions agreed between the two methods. Overall, BRT predicted a broader distribution of suitable areas of occurrence compared to INLA. However, relative suitability of habitats was consistent between models: areas of highest probability identified by BRT were also the areas of selected by INLA. There was a significant positive correlation between INLA/BRT (global correlation, r =0.44) in predicting the serologic status of RVF in Garissa, hence good model agreement. Habitats with the highest probability of RVF occurrence were found near areas with large human and animal population (**Figure 13**)

Both modelling techniques selected similar variables as the most important factors driving RVF prevalence distribution. Agreement between model predictions was moderately positively correlated (r <0.5) when evaluated over the whole county, this may be due different responses of each algorithm in extreme environmental interactions and downscaled spatial extents.

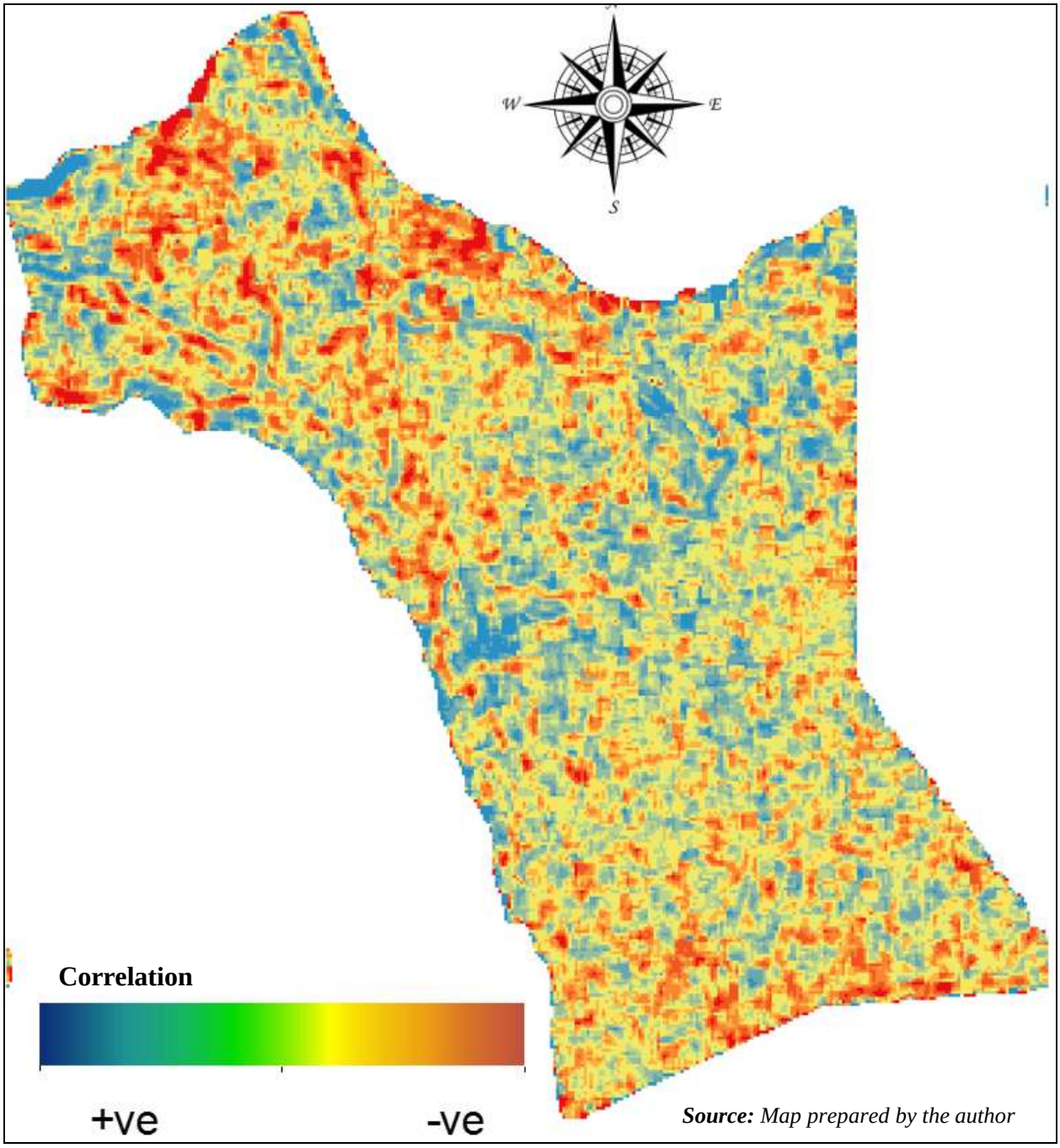


Figure 13: Localized correlation of RVF probability risk by BRT and INLA.

5.4 Discussion

This study contributes to the expanding knowledge and application of spatial epidemiology in the prediction of RVF risk, these may assist in prioritization of areas of disease control by targeted vaccination strategies. Its novelty is inclusion of human and animal demographics and hydrological profiles of a small-scale endemic area for RVF outbreaks. The predictive maps of the current study indicate that the northwest parts of Garissa are at the highest risk of future RVF outbreaks and can be integrated into early warning systems.

Spatial epidemiology and ecological niche modelling (ENM) have been successfully used unravelling the effects of climatic and environmental factors on the expanding geographical risk of RVF vectors in Kenya and Saudi Arabia (Ochieng *et al*., 2016; Sallam *et al*., 2013). Maximum entropy (Maxent) and boosted regression tree (BRT) models using environmental predictors, human population density, hydrological data, and vegetation indices have been used to predict the occurrence of RVF vectors in Middle East and North Africa (Conley *et al*., 2014).

In Kenya, RVF outbreaks have been previously predicted using occurrence data from 1951-2007, where the risk of exposure and outcome of outbreaks was determined by examining the ecological and climatic drivers. The risk of RVF was positively associated with high precipitation, persistent Normalized Difference Vegetation Index (NDVI), low altitude and impervious soils (Munyua *et al*., 2016).

Spatially explicit risk maps for the risk of RVF outbreaks in eastern and central Kenya been created by identifying ecological factors. Using generalized linear modelling (GLM) the influence of ecological variables to RVF occurrence was assessed, these included NDVI, evapotranspiration (ET), livestock density, elevation and soils. The most significant drivers for RVF occurrence in Tana River, Garissa, Isiolo, and Lamu counties were high livestock density, presence of green vegetation and slow evapotranspiration (Mosmotai *et al*., 2016).

A dynamic risk based model for Rift Valley fever outbreaks was developed for Garissa, Murang'a and Kwale counties in Kenya Using logistic regression. It was based on historical RVF outbreaks and climatic and environmental data (rainfall, temperature, relative humidity, normalised difference vegetation index and sea surface temperature). Predictors were investigated in a three-month lag period except NDVI which a four-month lag period was considered. Rainfall, minimum and NDVI were the most significant predictors of RVF outbreaks in the three counties (Gikungu *et al.*, 2016).

Geostastical modelling has been recently used in a cross-sectional study that was conducted in pastoral areas of Eastern Kenya to investigate the influence of irrigation on risk of RVF outbreaks and other zoonotic pathogens. Livestock and wildlife population trends were analysed, followed by a Bayesian model (R-INLA) to analyse the relationship between RVF mosquito vectors and seroprevalence data. The seroprevalences of RVFV was higher in the irrigated compared to the pastoral areas hence indicating the role of flooding vector survival and emergence. There was evidence that land use/land cover changes directly affected the distribution of the zoonotic diseases including Rift Valley fever (Bett *et al*., 2017)

CHAPTER SIX

GENERAL DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

6.1 Discussion

This study aimed to determine the spatial epidemiology and predict the risk of RVF in Garissa County, Kenya. It specifically assessed the knowledge, attitude and practices of communities living in Garissa. It also determined the seroprevalence of RVF in cattle, sheep and goats and finally developed predictive RVF risk maps for areas of potential outbreaks using species distribution modelling. The research focused on efforts to increase the adaptive capacity of pastoral livestock farmers to management of RVF, information on indigenous knowledge, attitude and practices in livestock disease management in response to climate change was collected and analyzed. The community had high levels of knowledge and practice in detection and control of RVF.

This study demonstrates that RVFV-specific antibodies are continuously present in at least a low percentage of sheep and goats in Garissa. It strongly suggests the circulation of RVFV during inter-epidemic periods without the manifestation of the typical clinical signs in livestock. The predictive models based on disease prevalence and climatic parameters flagged out high risk areas of RVF occurrence as part of an early warning system. This is a small-scale cross-sectional study based on a replicable triad approach of (*field -lab -computational modelling*) that provides an epidemiological framework for studying RVF and other zoonotic diseases in Kenya.

6.1.1 Knowledge and practices

This research assessed the community's' knowledge and practices of RVF during an interepidemic period in Garissa, Kenya. It targeted both low and high-risk populations, of whom 185/275 (74%) had high knowledge on RVF symptoms and transmission while 60% recognized vaccination as the main prevention strategy. All the participants 275 (100%) had heard about RVF (commonly known as '*sandik'* in somali), The findings indicated that all the study population had good knowledge of RVF which is in agreement with a previous study in the same geographical area (Abdi *et al.,* 2015*)* and in Tanzania (Shabani *et al*., 2015). While good preventive practices during RVF outbreaks were reported to in this study, a qualitative study carried out in neighbouring Ijara and Isiolo districts to assess lay perceptions of risk factors for RVF indicated low knowledge on the disease transmission dynamics to humans with poor understanding of consumption and behavioural risk factors (Ng'ang'a *et al.,* 2016, Affognon *et al*., 2017).

Despite the high knowledge on causation and transmission of RVF including mosquito bites, some respondents (30%) often confused the symptoms of RVF (fever, joint paints) with malaria and instituted immediate self-medication with anti-malarials and analgesics (Chipwaza *et al*., 2014). It is imperative that during diagnosis of fever clinicians consider malaria and other acute febrile illnesses (AFI) or fevers of unknown origins (FUO) as differentials for RVF and other arboviral infections like dengue fever (DF), chikungunya virus which have been isolated from AFI patients in the same study region (Ochieng *et al.,* 2015)

The understanding of causative factors (climatic and non-climatic) that lead to the re-emergence and spread of RVF among animal and human populations in Garissa calls for the need for capacity building of key stakeholder for prevention and control of the disease (Consultative Group for RVF Decision Support, 2010). During the interepidemic periods recognition of concurrent animal-human symptoms like sudden fever and hemorrhages should be handled with caution and used as an early warning indicator of RVF outbreaks (Consultative Group for RVF Decision Support, 2010), but more evidence of RVF subclinical circulation and genetic analysis is required for enhanced public health and veterinary surveillance (Nakoune *et al*., 2016).

The findings of this study on knowledge and attitudes underscore the significance of increased awareness of a pastoral community to RVF and other climate sensitive-vector borne diseases. It highlights the significance of indigenous knowledge and use of traditional medicines to manage RVF, these strategies can be combined with targeted livestock vaccination strategies to significantly lessen risk of transmission and burden of RVF. The seasonal calendar explored the seasonal changes in human and livestock diseases, water and forage availability which is vital for policies aimed at designing strategic and effective RVF control practices.

6.1.2 Seroprevalence

This study reported the presence of RVFV IgG antibodies in domestic ruminants from Garissa County in Kenya, six years after the 2006-2007 outbreak. While the overall seroprevalence of RVF in sheep, cattle and goats in this study area was 27.6% , an earlier study in the same and neighbouring areas of Ijara reported high seropositivity of about 70% in small ruminants, this may be attributed to differences in time of sampling and number of animals sampled (Lichoti *et al*., 2014).

Garissa has suitable ecological conditions forming a suitable niche for mosquito survival and hence virus persistence in the environment (Woods *et al.*, 2002). It has forested areas like Boni, with a rich hydrological network of Tana river and wetlands or *dambos*, less pervious soil types and vast flat areas that form floodplains during prolonged rainy seasons, this provides conducive mosquito breeding grounds and a large ruminant population provides hosts for potential virus amplification (Hightower *et al.*, 2012).

The spatial distribution of seropositivity across the study sites was sparse with observed aggregation near perennial water bodies or temporary watering points indicating spatial dependency in north western, central and southern parts of Garissa (Nanyingi *et al*., 2016). Longitudinal studies in Garissa indicated circulation of RVFV that was likely related with livestock migration to forested areas of Boni (Lichoti *et al*., 2014, Owange *et al*., 2014, Arum *et al.*, 2015).

High RVF seroprevalence has been demonstrated in humans living in Garissa and the neighboring Lamu county and the findings of this study confirm the high prevalence of RVFV in livestock serve which may serve as surrogate indicators for disease in humans (Muiruri *et al*., 2015, Gray *et al*., 2015). Garissa is the main route of livestock trade into Kenya from Somalia by trekking of live animals RVFV may be introduced to previously uninfected areas leading to the creation of an endemic foci. (**Figure 5**), this has been observed in Sahrawi territories and the Comoros islands where RVF outbreaks have been associated with transboundary livestock trade (Di Nardo *et al*., 2014, Roger *et al*., 2014)

The role of sex and age in RVF seropositivity has been examined. In Madagascar, IgG antibodies were significantly higher in males than in females in both cattle and small ruminants, there was an observed increase in seropositivity with the age of the animals ($p<0.0001$) (Jeanmaire *et al*., 2011). However, the current study in Garissa did not detect any significant difference in seroprevalence according to sex for all animal species ($p = 0.68$) despite the overall prevalence in male animals being 42.6% (CI 16.9-68.8) compared to females 30.1% (CI 19.6- 40.7).

In 2010, a cross-sectional survey was conducted in 313 sheep and 449 goats in Mozambique, Using an IgG ELISA the overall seroprevalence of sheep and goats was much higher in females than in males but on further multiple logistic regression analysis the effect of sex was confounded by age as majority of older animals were female goats. older animals had a seven-fold likelihood of being seropositive than young animals (OR = 7.3; p,0.001) (Fafetine *et al*., 2013).

6.1.3 Spatial risk modelling

This is the first study in Kenya to use logistic regression and spatially explicit geostastical modelling to investigate the interaction between predictive factors (environmental, climatic and demographic) associated with RVF prevalence in domestic ruminants in a high-risk area. The study provided predictive model-based risk maps for Rift Valley fever in Garissa, at a high spatial resolution (1×1 km) by exploring the underlying spatial processes and displayed high risk incidence areas. The use of both machine learning and Bayesian geostatistical models fitted on prevalence data to identify environmental, climatic and demographic predictors of RVF spatial risk distribution is novel and informative where data is sparse due to infrequent surveillance. These methods have been successfully used to predict the geographic risk of other infectious diseases including dengue fever and Avian Influenza (HPAI) H5N1 (Elith *et al*., 2008, Martin *et al*., 2011, Ashby *et al.*, 2017)

Using the BRT algorithm, high precipitation, high human and livestock density and elevated temperatures were most influential predictors of high risk of RVF occurrence. This concurs with a RVF dynamic risk model in Kenya that provided a lead-time of three months before outbreaks (Gikungu *et al.*, 2016). In Tana River County, Kenya, irrigated areas have also been shown to have the highest influence on occurrence of RVF since they provide conducive breeding habitat for mosquito vectors for RVF (Bett *et al*., 2017). Similarly, human population density, irrigation and rainfall have been found to be the main drivers of RVF cases in Africa (Redding *et al*., 2017). However the study observed that soil type had low influence on occurrence of RVF despite previous studies that associated four types of soils (solonetz, calcisols, solonchaks, and planosols) with high risk of RVF in Garissa (Hightower *et al*., 2012)

The BRT models performed well in predicting the risk of RVF occurrence, however it may have also displayed a degree of over-fitting especially in the northern parts of the study area. The BRT analysis has proven useful in a wide range of epidemiological studies by use of remotely-sensed imagery classification for other infectious diseases such as Lassa fever, Ebola, Crimean-Congo haemorrhagic Fever and Dengue Fever (Messina *et al.*, 2015, Mylne *et al*., 2015, Pigott *et al*., 2014) .

The spatial distribution by INLA model may reflect a very small range of spatial correlation due to the changes in demographic and environmental covariates. The predictions close to observed data locations were based on the covariates plus the spatial random-effect but predictions in all other locations were only based solely on the covariates. The spatial variation of the incidence of a diseases can help us to detect areas where the disease is particularly prevalent, which may lead to the detection of previously unknown risk factors (Bivand *et al.*, 2013).

INLA is widely used for Bayesian inference compared to Markov chain Monte Carlo (MCMC) since it is computationally efficient, fast, flexible and the outputs are more easily interpretable for non-experts' implementation. INLA has the potential to account for spatial autocorrelation while maintaining strong predictive power and inferential performance with spatially biased data and compared to BRT (Beguin *et al.*, 2012).

The current study underscores the importance of species distribution modelling in ecologically identifying factors related to transmission and outcome of RVF. Regression models are powerful tools for selecting relevant predictors and modelling complex interactions, while boosting avoids misclassification problems inherent in regression models like random forests. Thus, the comparisons of models performance may lead to greater confidence and specificity in predictions of disease distribution (Strobl *et al*., 2009).

Visual inspection and matching of the produced risk maps to historical occurrence of RVF in the entire study area may be suggestive that humans and animals in or near seropositive areas were at the highest risk of RVF infection, indicating a persistent endemic foci due to reintroduction of the virus from neighbouring Somalia (Britch *et al*., 2013, Nanyingi *et al*., 2016). However, the probability of autochthonous RVF re-emergence in Garissa cannot be ruled out, which underscores the need for stochastic host-vector model risk modelling approaches to explain the vertical and horizontal transmission that may be spatiotemporally dependent (Pedro *et al*., 2016).

The developments in Bayesian geostatistics (INLA) will enable analyses of surveillance data in almost ‘‘real’’ time and risk maps can be automatically updated thereby reducing the time from field data collection to reporting. These models may be useful in delineating the contribution of variables that may have necessarily contributed to determining RVFV ecological niche.

This study attempts to explain the expanding geographical range of RVF outbreaks in Garissa, while the cyclic (10-15years) occurrence can be further strengthened by using host-vector stochastic modelling. The predictions may partially concur with findings from other studies that rainfall is one of the most important factor that triggers outbreaks in the East African region (Pedro *et al*., 2016). Similarly process-based models have been utilized using climate data to predict geographical changes in RVF outbreak susceptibility that is mainly influenced by climate change and local livestock serological status (Leedale *et al*., 2016).

Despite that both models showed strong agreement in selection of areas with the highest probability of RVF occurrence with (BRT AUC 0.7 and INLA 0.9), the outputs of these models must be regarded as preliminary and absolute predictions should be interpreted with caution considering that that the number of seropositive cases used in the analysis were very few and localized in some areas which could have resulted in overfitting (Metras *et al*., 2015).

Presence-only models used in this study rely on the assumptions that RVF seroprevalence is equally detectable across Garissa, they also treat densely and sparsely populated areas the same hence generalizing the higher probability of occurrence and detectability of RVFV (Conley *et al*., 2014). Despite these limitations, this modelling framework will act as a springboard for further research to better understand the spatial epidemiology of RVF in Kenya and East Africa.

6.2 Conclusions

- There was high overall knowledge on Rift Valley fever causes, symptoms but limited knowledge on specific risk factors, there were good practices regarding prevention and control which was highly influenced by the level of education, occupation and gender.

- RVFV-specific antibodies presence in livestock strongly suggests the circulation of RVFV during inter-epidemic periods without the manifestation of the typical clinical signs.

- The predictive maps identified areas with high human and animal populations being at highest risk for occurrence of Rift Valley fever, which concurred with historical spatial patterns of outbreaks in Garissa.

6.3 Recommendations

This research provides the following recommendations:

1. There is need to address the knowledge gap in community's specific understanding of predisposing environmental and behavioural risk factors to RVF outbreaks through collaborative one health programs.

2. Routine monitoring of RVF status by sentinel livestock surveillance should be conducted in the mapped *hotspot* areas of Garissa during the interepidemic period for early outbreak detection.

3. The predicted *hotspots* for RVF occurrence should be targeted as central points of livestock vaccinations for strategic and cost-effective prevention of future RVF outbreaks in Garissa.

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APPENDICES

Appendix 1: KAP Questionnaire

A. General Household information

A1. Date of interview: …… A2. Interviewer: ……

A3. District: …….. A4. Division: ……

A5. Location: ……A6. Household GPS reading:

N…… E…… A7. Household number: ……

A8. Respondent: Head of household Other □ Specify: ……

A9. Name: ……

A10. Gender Male □ Female □ A11. Age: ……

A12. Level of education: None □ Primary □ Secondary □ College □

A13. Number of people in the household Adults: □ Children: ……..

A14. Average Monthly Economic in Ksh: □ 500 -5000, □ 500 -15000, □ 15000 - 50000, □ >50000

B. Knowledge, Attitude and Practice in response to Climate Change

B1. What is the main cause of climate change? □ Lack of rainfall □High temperatures

B2. How many animals (cattle/sheep/goats/camels) do you have: □1 -50 □50 -100 □>500 Specify……..

B3 How many have died due to high temperatures and low rainfall

No.……

B4. Which species of animals are severely affected by effects of harsh climate?

……

B5. What conditions /diseases affecting livestock in order of frequency (most frequent to least frequent) have you encountered during the harsh climatic period?

1. _____
2. _____
3. _____

B6. Whom do you receive intervention when animals fall sick?

□ Veterinarian □ AHA □ CBAHW □ Neighbour

B7. How far in distance do you seek assistance when animals fall sick?

1. Near (within 2 kilometers) human settlements □ 2. Far > 2km □ 3. Both

B8. What are the major effects of climate change on the livestock production?

B9. What have you done already to cope, adapt to or mitigate effects of climate change?

Specify …….

B10. What kind of support do you receive from either government or NGOs during the harsh climate periods?

1. Fodder □ Water □ Stocking replacements □

   other……..

B11. How often does it rain in a years (Months)?

……

B12. Do you have Livestock Insurance cover?

1. Yes □ 2. No □

C. Livestock Climate Sensitivity information

C1. Is the grazing area?

2. Near (within 2 kilometers) human settlements □ 2. Far > 2km □ 3. Both

C2. Is the Source of water for animals?

1. River/ streams □ 2 Boreholes □ 3. Dams/ pans □ 4. Other, specify

C3. What is the distance of water source from human settlements and animal watering points?

1. Near (within 2 kilometers) □ 2. Far (more than 2 kilometers) □

C4. (a) How many animals access the water point at any given time?

C5. What do you do if there is a lack of water/drought? _____

C6. Are you a resident of this area? □ Yes □ No, if Yes foe how long

Permanently □ Temporarily □

C7. From where do you acquire new stock?

1. Locally □ 2. Adjacent districts □ 3. Transboundary □ 4 Other specify C8. Do you experience stock theft and how do you cope with it in harsh climatic conditions?

C8. Is there a "disaster management plan" in place in your village/settlement?

C9. How would you like to receive information about Climate Change and adaptation methods?

C10. Do you have anything you would like to add about any climate change issues?

RESPONDENTS CONSENT AGREEMENT:

I …… Hereby agree to participate in this study with my full consent and conscious and declare that to the best of my Knowledge the information that I have provided is true, accurate and complete.

Signature / Thumb print..... Date ...../201….

Appendix 2: Schedule for RVF Focus Group Discussions

Socio-demographics

FGD No:

Profile of Group:

Village: Location: Sub-location: County:

General themes to probe

Livelihood practices

- Different means of livelihoods utilizing the environment and the different categories of people (by gender, social status, socio-economic standing in the community) involved in these means of livelihoods.
- Changes in livelihood practices over the years.
- Gender roles and responsibilities in the identified forms of livelihoods.
- Seasonal variations in roles and responsibilities by socio-demographic characteristics related to livelihood activities
- Livestock systems and Land use over the years.

Vector borne disease in relation to Livestock and human health

- Most common Livestock and human VBDs in the community
- Linkage of VBDs (Probe on RVF) with Climate change.
- Perceptions on risk factors for VBDs (Probe on RVF).
- Knowledge and perceptions about VBDs (Probe on RVF) symptoms and treatment.
- Practices related to VBDs (Probe on RVF).

- Health seeking behaviour of people suspecting VBDs (Probe on RVF).
- Methods (both conventional and indigenous) for identifying VBDs (Probe on RVF).
- Impact of VBDs (Probe on RVF) on individuals, families, communities and their livelihoods
- Knowledge of factors associated with transmission, spread, control methods, effects of control of VBDs (Probe RVF).

Control of RVF

- Knowledge of existing adaptation strategies for RVF ***(Probe 1: on RVF. Probe 2: Indigenous and non-indigenous strategies, their strengths & weaknesses).***
- Perceptions about the existing disease control measures and their impacts on the RVF and the ecosystem.
- Impact of the control measures on the various community livelihoods.

Thank you – Asante

Appendix 3: Schedule for RVF Key Informants Interview

a) Biographical data

- Name
- Location
- Sub-location
- Village
- Age
- Sex
- Marital status
- Education background
- Position in the community
- Occupation
- Religion

c) Community Attitude and Perceptions Towards Rift Valley Fever

- What are the common vectors borne diseases in this community? (Probe for knowledge concerning VBDs)
- What are the perceived causes of these vector borne diseases (Probe for RVF)?
- Who is more likely to get vector borne diseases (Probe for RVF)?
- What activities expose people to risk of RVF infection)?

d) Management and Control of RVF

- How do you manage VBDs in this community? (Probe 1: RVF Probe 2: For both indigenous and conventional)
- How much if any do you think these different management services cost?
- How can people deal with this problem in your area?
- What kinds of measures have been taken over the years to date, to control RVF in the county? (Probe 1: government strategies Probe 2: Community/local strategies. Probe 3: Their strengths and weaknesses Probe 4. Strategies affordable to the communities).
- What kinds of indigenous early warning systems exist in this community?
- What is the role of the community in the control and management of VBDs (Probe for RVF)
- What are the challenges faced by the stakeholders in the fight against VBDs? (Probe for RVF).

Thank you- Asante

Appendix 4: Informed Consent (1- KII)

Information sheet for the individuals participating in the research

FOR CONDUCTING INTERVIEWS (KEY INFORMANT INTERVIEWS/ IN-DEPTH INTERVIEWS)

Name of Organization: University of Nairobi, Department of Public Health Pharmacology and Toxicology

Title of Project:

"Spatial predictive modelling of Rift Valley Fever in response to climate change in Garissa, Kenya"

Source of Funding: Colorado State University (CSU)

The University of Nairobi and the CSU Fort Collins US, under LCCRSP, are undertaking a research on Spatio-temporal predictive modelling of Rift Valley Fever in response to climate change in Garissa, Kenya

Purpose of the research:

Climate change is a global concern and its impacts are known to affect among other things the occurrence of vector borne diseases such as Rift valley fever. Changes in climate leads to changes in the environment and this can in turn affect the occurrence and spread of RVF. RVF has serious consequences not only on the affected individuals but also on their livestock and livelihoods and the development of the country. An understanding of how these changes and the different roles and responsibilities played by communities in preparedness and management of the spread of RVF could provide information which can be used to make appropriate management (early warning systems) and control methods to reduce the occurrence. Therefore, we need to have a better understanding of the role played by climate

change on the spread of RVF to help in developing early warning systems for improving the management and control of RVF and other climate sensitive vector-borne diseases.

We would therefore like to find out what you know about vector-borne diseases such Rift valley fever among others, in relation to the above mentioned and related issues.

Procedures: To find answers to some of these questions, we invite you to take part in this research project. If you accept, you will be required to take part in an interview where we will ask you questions concerning your knowledge, perceptions on and experiences with **RVF** in this community, spread and extent, the relationship of livelihood practices and the community response. Your understanding of climate change and relationship to the occurrence and spread of RVF, factors influencing RVF occurrence and spread, community knowledge and perceptions about the disease, the community management and control and existing adaptation strategies.

You are being invited to take part in this interview because we feel that your experience as a veterinarian/medical personnel/teacher/government or NGO personnel/opinion leader in the community can contribute much to this discussion. During this discussion, however, we would like you to give us your opinion on the questions that we will pose to you, based on your personal experiences and your experience within the community. If you do not wish to answer any of the questions, you may say so, and keep quiet. The interview will take place at a convenient venue yet to be identified and no one else but the research team will be present during this discussion. Additionally, the information recorded is considered confidential. The expected duration of the discussions is approximately 45 minutes.

Risks and discomforts: There is a slight risk that you may share some personal or confidential information with the research team by chance, or that you may feel uncomfortable talking about some of the topics. However, we do not wish this to happen, and you may refuse to answer any question, if you feel they are personal.

Benefits: There will be no direct benefits to you. But your participation is likely to help us to make better decisions concerning management and control of RVF

Incentives: You will not be provided any incentive to take part in the research.

Confidentiality: The information that we collect from this research project will be kept confidential and will only be used for research purposes. Information about you that will be collected from the study will be stored in a file, which will not have your name on it, but a number assigned to it. Which number belongs to which name will be kept under lock and key, and will not be disclosed to anyone else except the research team. We will contact you first, to book an appointment for the discussion and second, to inform you about the date and venue to share with you the findings of the study.

Right to refuse or withdraw: You do not have to take part in this research if you do not wish to do so, and this will not affect you or your relationship with our organization in any way.

Who to contact: This proposal has been reviewed and approved by University of Nairobi Ethical Review committee, which is a committee whose task is to make sure that research participants are protected from harm.

If you have any questions you may ask them now or later. If you wish to ask queries later, you may contact the following:

Dr. Mark Nanyingi (Principal Investigator); Mobile phone No: 0721117845

Dr. Gerald Muchemi (Project supervisor): Mobile phone No: 0722357381

Appendix 5: Informed Consent (2- FGD)

Information sheet for the individuals participating in the research

FOR CONDUCTING FOCUS GROUP DISCUSSIONS

Name of Organization: University of Nairobi, Department of Public Health Pharmacology and Toxicology

Title of Project:

"Spatial predictive modelling of Rift Valley Fever in response to climate change in Garissa, Kenya"

Procedures: To find answers to some of these questions, we **invite** you to take part in this research project. If you accept, you will be required to take part in a discussion with between 5-10 other persons with similar experiences. One of us will lead the discussions and will be assisted by another member of the research team who will be taking notes.

Who to contact: This proposal has been reviewed and approved by the UON Research ethics committee, which is a committee whose task is to make sure that research participants are protected from harm. If you have any questions you may ask them now or later. If you wish to ask queries later, you may contact the following:

Dr. Mark Nanyingi (Principal Investigator)

Mobile phone No: 0721117845

OR

Dr. Gerald Muchemi (Project supervisor)

Mobile phone No: 0722357381

CONSENT FOR INTERVIEWS AND FOCUS GROUP DISCUSSIONS

"I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions I have been asked have been answered to my satisfaction. I consent voluntarily to participate in this study and understand that I have the right to withdraw from the discussion at any time with no consequences. I also consent to the interview notes of our discussion being written down". (Where written consent may not be possible, verbal consent will be sought with approval from local administrators)

Informant's Name_____ Signature_____

Date _____ Place _____

Witness (Name) _____ Signature_____

Date _____ Place _____

INFORMED CONSENT FORM

I,…….., ID.No……,

from……..(village and county)

being of 18 years or older and having full legal capacity to consent for my child/ children (named below), have been informed about the study entitled:

Title: "*Spatial predictive modelling of Rift Valley Fever in response to climate change in Garissa, Kenya"***,** headed by the Study Investigator Dr. Mark Nanyingi Tel: **0721117845**

The nature, duration, purpose, voluntary nature and inconveniences or hazards that may reasonably be expected have been fully explained to me. I have understood the information regarding the study, and what will happen. I have been given the opportunity to ask questions concerning this study and these (if any) have been answered to my satisfaction.

I understand that I may at any time during the study, withdraw the consent in the best interest of my children without any loss or penalty. My refusal of the subject to participate will involve no penalty or loss of benefits to which my family are otherwise entitled. Tick (√) only one box per individual

Participants' name	Age (yrs)	I **do** consent	I **do not** consent
1.			
2.			
3.			
4.			

Parents' signature or left thumb print:…….

Date…….

Witness: I hereby confirm that the study has been explained to the parent. All questions (if any) have also been answered to her satisfaction, and she, of her own free will, has consented for her child/ children to take part in the study.

Name of witness			
Signature of witness		Date:	

Name of person explaining the study:

……

Appendix 6: Data extraction for Rift Valley fever spatial modelling

Animal sampling

Serologic data for RVF were sampled with assistance from staff based at the Garissa regional Veterinary from different sites and different herds. In total 370 samples from 30 herds were used in seroprevalence analysis as ***(detailed in chapter 5).*** The geographical locations of the seropositive herds formed the presence data that was used in the spatial modelling (**Figure 6**)

Rainfall and Temperature

Monthly rainfall estimates for Garissa from July 2013-December 2014 were extracted from the Climate Hazards Group InfraRed Precipitation (CHIRPS) a quasi-global high-resolution rainfall dataset that has spatial and temporal global coverage from 1981 to present (http://chg.geog.ucsb.edu/data/chirps). CHIRPS is archived at Geo-spatial CLIMatological (GeoCLIM) (http://wiki.chg.ucsb.edu/wiki/GeoCLIM). CHIRPS incorporates 0.05° resolution satellite imagery with in-situ station data to create gridded rainfall time series for trend analysis. CHIRPS was developed to support the United States Agency for International Development Famine Early Warning Systems Network (FEWS NET) (Funk *et al*., 2015).

Monthly temperature estimates were extracted from AFRICLIM database(https://www.york.ac.uk/environment/research/kite/resources/). Version 3.0 of the database spans ten general circulation models (GCMs), downscaled using five regional climate models (RCMs) and four contemporary baselines, under two representative concentration pathways of the IPCC-AR5 (RCP4.5 and RCP8.5) (Platts *et al*., 2015)

Enhanced Vegetation Index (EVI)

Remotely-sensed enhanced vegetation index (EVI) was extracted from Moderate-resolution Imaging Spectroradiometer (MODIS) data sets were sourced from the National Aeronautics and Space Administration (NASA) (http://modis.gsfc.nasa.gov). The maximum- value composited EVI with spatial and temporal resolution of 1 km and 16 days. The EVI has been considered a modified NDVI with improved sensitivity to high biomass regions and improved vegetation monitoring capability through a de-coupling of the canopy background signal and a reduction in atmospheric influences (Matsushita *et al*., 2007).

Digital Elevation Model (DEM)

The Digital Elevation Model (DEM) describing the altitude of the study area was derived from global data explorer of the USGS (https://earthexplorer.usgs.gov/). The country level elevation was obtained from an interpolated DEM that had been processed further by ILRI GIS unit (http://www.ilri.org/GIS). These data on elevation for Garissa district was compared to the clipped shapefile from the country level as acquired by ILRI from Shuttle Radar Topography Mission (SRTM) at a 3 arc second spatial resolution $1km^2$ http://srtm.usgs.gov/ .

Soil types

Soil types raster was obtained from ILRI GIS database http://data.ilri.org/geoportal. This is extracted from Africa Soil Information Service (AfSIS) a globally integrated large-scale, research-based project maintained by Earth institute, Columbia http://africasoils.net/ that develops a practical, timely, and cost-effective soil health surveillance service to map soil conditions. Archived digital soil maps for drainage were downloaded at 250m resolution for Africa and downscaled to Kenya then Garissa. The exploratory soil map and ACZ map of Kenya is based on classification by FAO **(**FAO, 2014). Thirteen soil types were classified in Garissa with only four (solonetz, calcisols, solonchaks, and planosols) being used for modelling based on previous studies (Hightower *et al*., 2012).

Human population

Human population density for 2013-2014 was obtained as Gridded Population of the World, from "*WorldPop"* which depicts the spatial relationship of global human populations and the environment (2000-2020) (http://www.worldpop.org.uk). WorldPop population distribution datasets have been used in applications around the World, covering the fields of epidemiology, health metrics and impact assessments, amongst others. The output datasets depict population counts and densities for multiple years per 100x100m grid cells for individual countries, and per 1x1km grid cells for continents.

Livestock populations

Livestock population densities (sheep and goats) from "*Livestock Geo-Wiki"*, a portal for global maps of livestock distributions and production (http://www.livestock.geo-wiki.org), its multi-partner collaboration between ILRI, FAO and the Université Libre de Bruxelles (ULB-LUBIES), that provides global maps of livestock distributions and production systems, we focused on the small ruminants because they are involved in the primary amplification of RVF before it spreads to humans and other animals, we excluded cattle due to extremely small sample size. Before the analysis, all raster layers were resampled to a spatial resolution of $1km^2$ and clipped to the extent of the study area. All analysis was done using ArcView 10.5. For all the layers in derived from satellite imagery, gap-filling algorithms were used to correct anomalies caused by cloud cover. The pixel values of the all predictor variables were extracted for each RVF positive location and geoprocessed before spatial modelling (Weiss *et al*., 2014).

Appendix 7: Models formulation

R INLA

Model formulation

Let Y_{it} be the number of RVF positives for Garissa i at year t. We assume that the Y_{it}'s are generated by a negative binomial distribution, i.e. $Y_{it} \sim NB(\mu_{it}, k)$ with mean μ_{it} and dispersion parameter k. The linear predictor $\eta_{it} = \log(\mu_{it}) = \log(P_i) + X_{it}^T \beta + w_i + e_t$ includes an offset term for the population P_i, the vector X_{it}^T of covariates, spatially and temporally structured random effects w_i and e_t, respectively. Consider that the vector of w_i arises from a multivariate normal distribution $w \sim MVN(0, \Sigma)$ with Matérn covariance function between locations i, j that is, $\Sigma_{ij} = \frac{\sigma^2 (\kappa d_{ij})^{\nu} K_{\nu}(\kappa d_{ij})}{\Gamma(\nu) 2^{\nu-1}}$, where σ^2 is the spatial process variance, d_{ij} is the distance between the centroids of i, j, κ is a scaling parameter, ν is a smoothing parameter fixed to 1 in our application and K_{ν} is the modified Bessel function of second kind and order ν. The Matérn specification of the covariance matrix implies that the spatial range r, that is the distance at which spatial correlation becomes negligible (i.e., < 10%) is $r = \frac{\sqrt{8}}{\kappa}$. a stationary autoregressive AR (1) process for e_t is adopted such that, $e_t \sim N(\rho e_{t-1}, \tau_2^{\,2})$ for $t > 1$ and $e_1 \sim N(0, \tau_1^{\,2})$, where $\tau_1^{\,2} = \tau_2^{\,2} / (1 - \rho^2)$ and ρ the auto-correlation parameter, constraint in the interval $(-1, 1)$.

Bayesian model formulation is completed by specifying prior distributions for the remaining parameters and five hyperparameters. In particular, we choose $\log$ - gamma priors for τ_2^{-2}, σ^{-2}, r and k parametrized in the log scale, that is, $\log\left(\tau_2^{-2}\right)$, $\log\left(\sigma^{-2}\right) \sim \log Ga(1,0.0005)$, $\log(k) \sim \log Ga(1,1)$, $\log(r) \sim \log Ga(1,0.01)$. A normal prior distribution is used for ρ, re-parametrized in order to be defined in $\Re$, that is $\log\left(\frac{1+\rho}{1-\rho}\right) \sim N(0,6.66)$. Normal priors $N(0,0.001)$ were also assigned for the regression coefficients and a vague normal one for the intercept.

Bayesian inference using SPDE

Bayesian inference estimates the marginal (or full conditional) posterior distributions $p(\phi_j \mid y) = \int p(\phi_j \mid \theta, y)\, p(\theta \mid y) d\theta$ of the elements of the parameter vector $\phi = (\beta, w, e)^T$, where θ is the vector of hyperparameters and y are the data. Geostatistical models often rely on Markov chain Monte Carlo (MCMC) simulation to estimate $p(\phi_j \mid y)$. Hence Σ is approximated by the covariance matrix Q^{-1} of the Gaussian Markov random field (GMRF), which provides directly the inverse of Q, overcoming a computationally intensive matrix operation. The spatial process representation is based on a partition of the study region into a set of non-intersecting triangles.

INLA can be used for fast Bayesian inference. INLA approximates the above integral by $\hat{p}(\phi_j \mid y) = \sum_k \hat{p}(\phi_j \mid \theta_l, y)\hat{p}(\theta_l \mid y)\omega_l$. $\hat{p}(\theta_k \mid y)$ is calculated from the Laplace approximation of $p(\theta \mid y)$, that is $\hat{p}(\theta \mid y) \propto \left.\frac{p(\phi, \theta \mid y)}{\hat{p}_G(\phi \mid \theta, y)}\right|_{\phi=\phi_M}$, where $\hat{p}_G(\phi \mid \theta, y)$ is the Gaussian approximation of $p(\phi \mid \theta, y)$ and ϕ_M is the mode of $p(\phi \mid \theta, y)$. $\hat{p}(\phi_j \mid \theta_l, y)$ is also calculated from a Laplace approximation of $p(\phi_j \mid \theta, y)$ and ω_l are weights associated with θ_l. The prediction of the spatial random effect on a grid of locations is performed by projecting the triangular random effects on the grid and calculating a weighted sum of the values at the vertices. Estimates of the total number of cases across the whole county can be obtained by summing pixel-level predictions. The INLA package does not provide directly variation measures for joint distributions and therefore, it cannot estimate the variance of the above quantities. However, it can estimate the variance of linear combinations of η_{it} for a given time point t (e.g. 2010). Using the Taylor expansion, the variance of the total predicted cases is given by: $Var\left(\sum_i \exp(\eta_{it})\right) \approx Var\left(\sum_i \exp(E(\eta_{it}))\eta_{it}\right)$ where the weights $\exp(E(\eta_{it}))$ of the linear combination are the point predictions at pixel i. INLA can estimate the right part of the above equation in a second model fit, which includes the prediction grid with missing values in the response. Additional linear combinations were defined to calculate the variance of the cases per division in a similar manner.

INLA implementation

The data file contained standardized continuous predictors and the dummy (0/1) variables of the categorical ones. We assigned a missing value to the response of a randomly selected set of 20% of the data (test data). The response was predicted for these points and used to calculate cross-validatory measures.

The R package "maps" was used to define the boundaries of Garissa that was triangulated. The inla.mesh.create.helper (), inla.spde2.matern () functions, of the INLA package, were applied to construct the domain (mesh) and define the covariance function of the spatial process. The inla () was called to perform approximate Bayesian inference and obtain summaries for the coefficients and the hyper-parameters. The grid for prediction was constructed with the inla.mesh.projector (). Inla.mesh.project () projected the mean of the latent spatial effect on the grid. Using ArcMap 10.5, covariate values and the population data were extracted at the grid points, which were later, read in R. The mean of the linear predictor was calculated and summarized over the divisions to approximate the predicted cases. Finally, a second inla () call enabled the estimation of the variance of the cases aggregated over the whole county.

Boosted Regression Trees

Formulation

$$f(x) = \sum_{m} f_{m(X)} = \sum_{m} \beta_{m} b(x;\gamma_m)$$

where

fx is the linear predictor linked to the original scale of the outcome function, β_m is a scalar representing the intercept, *βy* represent the values of the coefficients quantifying the linear effect of covariates *xy*. The functions $b(x;\gamma_m)$ represent the individual trees, with γ_m defining the split variables, their values at each node, and the predicted values (Friedman *et al*., 2001). The β_m represent weights given to the nodes of each tree in the collection and determine how predictions from the individual trees are combined.

Estimation of the parameters of additive models depends on the functional form of *f* and can be difficult. Forward stagewise fitting simplifies the problem by estimating β_m and Y_m sequentially from m = 1 to n.

Gradient boosting involves a two-step approximation of the loss function; the first step estimates Y_m using a least squares regression tree, and the second estimates β_m.

Appendix 8: Publications

The respective chapters of this thesis have fully or partially generated the following peer reviewed publications (as attached):

1. **Nanyingi, M.O.,** Munyua, P., Kiama, S.G., Muchemi, G.M., Thumbi, S.M., Bitek, A.O., Bett, B., Muriithi, R.M. and Njenga, M.K. (2015). A systematic review of Rift Valley Fever epidemiology 1931-2014. *Infect Ecol Epidemiol*, 5, 28024.
2. **Nanyingi, M.O.,** Muchemi, G.M., Thumbi, S.M., Ade, F., Onyango, C.O., Kiama, S.G. and Bett, B.(2016). Seroepidemiological Survey of Rift Valley Fever Virus in Ruminants in Garissa, Kenya. *Vector Borne Zoonotic Dis*. 17(2), pp.141-146 .

Manuscripts under preparation

1. Knowledge and Practices on Rift Valley fever outbreaks in Garissa county, Kenya.
2. Spatial predictive modelling of Rift Valley Fever risk in Garissa, Kenya**.**

During the course of this study, several fruitful collaborations have also led to the following publications. (These are however not discussed within this Thesis)

1. Ochieng, A.O., **Nanyingi, M.**, Kipruto, E., Ondiba, I.O., Amimo, F.A., Oludhe, C., Olago, D.O., Nyamongo, I.K. and Estambale, B.A. (2016). Ecological niche modelling of Rift Valley fever virus vectors in Baringo, Kenya. *Infect Ecol Epidemiol.* Nov 17; 6:32323
2. Munyua, P., Bitek, A., Osoro, E., Pieracci, E.G., Muema, J., Mwatondo, A., Kungu, M., **Nanyingi, M.**, Gharpure, R., Njenga, K. and Thumbi SM. Prioritization of Zoonotic Diseases in Kenya, 2015 *PLoS One*. 2016 Aug 24;11(8): e0161576.