A simulation model for Rift Valley fever transmission

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A thesis submitted in fulfilment of the requirements for the degree of

Doctor of Philosophy (Veterinary Epidemiology)

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University of Nairobi

November, 2015
DECLARATION

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

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ABSTRACT

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

The simulation model comprised of two hosts (cattle and sheep) and two vectors (Aedes and Culex mosquito species). The model integrated livestock host population dynamics, vector population dynamics, and vector-host transmission dynamics. Changes in the population of vectors in the model were driven by rainfall estimates obtained from the Tropical Rainfall Measuring Mission (TRMM) for Ijara Sub-county which was the study site. Simulations were implemented for 1200 days. Outputs generated by the model included: (1) incidence of RVFV infection in vectors and
hosts; (2) time to the peak incidence of RVFV in vectors and hosts; and (3) the duration of outbreaks. Following the predicted outbreak, further transmissions were prevented and simulations ran for five years to assess the post-outbreak evolution of host population and herd immunity dynamics. The impact of vaccinating 25%, 50% or 75% of the host population was assessed by simulating vaccinations at different stages of RVF risk borrowed from the 2006/7 pre-outbreak period and identified in a decision-support tool for prevention and control of RVF in the Greater Horn of Africa. The three different stages included (i) issuance of RVF early warning representing a lead time of 11 weeks based on the recent outbreak in 2006/7 in Kenya, (ii) onset of heavy rains with a lead time of 6 weeks, and (iii) at the outbreak onset. This study also assessed the possibility of RVF control by focusing against one host species by vaccinating 50% of cattle or sheep, 6 weeks to the outbreak. The impact of interventions was measured by estimating the area under incidence curve (AUC). Larva control was implemented at the outbreak onset by increasing basal mortality by 50% or 100% for different periods of time. The model was also used to evaluate integrated control measures, e.g. a combination of low coverage of 25% vaccination and the moderate increase in the larval mortality rate – 50% for 105 days which spanned the entire outbreak period.

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

The results of the model showed that by the end of the full-blown outbreak (day 1152), cattle and sheep populations declined to an average of 76% [range 67%, 91%] and 51% [range 39%, 64%] of their pre-outbreak populations respectively, due to RVF-induced mortality. Cattle population recovered fully approximately 3-4 years (around day 1188) after the outbreak [range 85%, 109%]. At this time (after 1188 days), the sheep population was predicted at 69% [range 55%, 88%] of the pre-outbreak population. Five years after the outbreak, the populations were, on average, 102% [range 95%, 108%] and 85% [range 66%, 104%] of the pre-outbreak populations in cattle and sheep, respectively.
The model predicted that by the end of the outbreak, 89% of cattle [range 80%, 96%] and 94% of sheep [range 65%, 99%] would be in the immune/recovered/removed state that is refractory to RVFV infection. Five years later in the simulation, these herd immunity levels were shown to decline to 6% [range 4%, 8%] in cattle and 0.3% [range 0.07%, 0.5%] in sheep. The rate of decline was intensely higher in sheep than cattle. The period it took for the herd immunity to decline to negligible levels closely mirrored (1) the predicted time it took for the populations to recover to pre-outbreak levels, and (2) the average inter-epidemic period in Kenya.

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

According to the model predictions, increasing larval mortality by 50% at daily intervals from the onset of the full-blown outbreak appeared to provide a temporary protection that was lost as soon as the control was relaxed. Increasing larval mortality by 100% at daily interval was predicted to be effective only if it was sustained for more than 60 days.
The thesis viewed the simulation model as a framework that could be used for predicting RVF outbreaks and understanding complex mechanisms that produce RVF outbreaks and generating hypotheses on RVF epidemiology. This thesis identified gaps in the quantification of parameters, particularly those related to transmission, and highlighted how field observational studies and small-scale transmission experiments could be used to estimate these parameters.

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

The results further suggested that targeted vaccination could be effective in mitigating the impacts of RVF outbreaks. However, challenges associated with disease prediction, availability, administration and delivery of vaccines need to be addressed. The predictions also suggested that the timing of an intervention, the level of coverage and the duration of implementation are key considerations for using larvicides for
RVF control. Analyses on integrated control strategies such as increased larval mortality by 50% at daily intervals from the onset and lasting the entire phase of the outbreak and vaccinating 25% of the hosts were predicted to be highly effective in preventing the occurrence of a full-blown outbreak.

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