Development of a dynamic model for the emergence of Lassa fever in West Africa

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Contents

List of Figures

List of Tables

A dissertation submitted in partial fulfillment of the requirements for the degree of **Doctor of Philosophy**

Declaration

I certify that:

- The thesis being submitted for examination is my own account of my own research;
- My research has been conducted ethically;
- Where I have drawn on the work, ideas and results of others this has been appropriately cited in the thesis;
- Where any collaboration has taken place with other researchers, I have clearly stated in the thesis my own personal contribution;
- The entirety of the work described in the thesis has been undertaken subsequent to my registration for the higher degree for which I am submitting for examination;
- The thesis submitted is within the required word limit as specified by the RVC.

Abstract

Endemic zoonotic infectious diseases represent a large proportion of preventable morbidity and mortality across much of the world. The potential for endemic zoonotic infectious diseases to undergo range expansion, increasing the number of individuals at risk of infection is of significant concern.

Spillover events of zoonoses into human populations typically occur at a local scale. Sustained human-to-human transmission following spillover can result in epidemics and pandemics of diseases originating from animal reservoirs.

Understanding the locations at greatest risk of spillover events is of particular interest to strengthen local public health responses in endemic regions to outbreaks. Additionally, identifying potential locations of spillover of zoonoses is imperative for efforts to prevent pandemics of pathogens of zoonotic origin.

Studies assessing locations at greatest risk typically rely upon large consolidated databases of host presence and absence data alongside datasets on host-pathogen associations. Here, I have shown that these datasets suffer from spatial and temporal sampling biases. I produce a synthesised dataset of rodent trapping studies to mitigate some of these biases by providing high-resolution rodent detection and non-detection data alongside spatio-temporal host-pathogen associations.

Understanding the interplay between different rodent species in a host-pathogen system is important to understand the hazard of zoonotic spillover events. Here, I have reported on a rodent sampling study in a Lassa Fever endemic region to describe the association of species detection and land use type accounting for imperfect detection.

Within these different land use types species contact each other at different rates. This has implications for the transmission of pathogens within these settings. Here, I have described the contact patterns between individuals of different species and the prevalence of antibodies to our target pathogen to model potential transmission networks.

Finally I use the data produced in Chapters 3 and 4 to model the hazard of zoonotic spillover in Eastern Sierra Leone. I adopt a BART to produce a multi-species distribution model to predict the occupancy of different species across the region and information on antibody prevalence to model the occurrence of the pathogen of interest.

List of Acronyms

Placeholder

Acknowledgements

Placeholder

1 Introduction

1.1 Theoretical framework

1.1.1 Rodent trapping study design

1.1.2 Data exploration and visualisation

1.1.3 Statistical modelling

1.2 Aims and objectives of the thesis

1.2.1 Aim

1.2.2 Objectives

1.3 Chapter overview

- **Chapter 2:** Background information is given. This information helps motivate future chapters and may be useful for non-subject area experts.
- **Chapter 3:** This chapter presents a study conducted to synthesise rodent trapping data from West Africa. Focussing on a comparison to consolidated data sources on rodent host species ranges, presence-absence data and host-pathogen associations. The spatial biases of rodent trapping data are explored and data is presented in a suitable format for other researchers to incorporate in their analyses to mitigate bias from other data sources.
- **Chapter 4:** This chapter presents data from a two year rodent trapping study implemented as part of this thesis. This chapter focusses on rodent detection in different land use types. A model of occurrence by land use type is produced accounting for imperfect detection in observations of rodents.
- **Chapter 5:** This chapter presents data on rodent antibody prevalence to *Lassa mammarenavirus* from samples obtained as part of the two year rodent trapping study. The prevalence of antibodies to this virus are described at species and land use level. Contact networks between individuals of different species are reconstructed to investigate potential transmission networks.
- **Chapter 6:** This chapter consolidates data from the two previous chapters to produce a hazard map of *Lassa mammarenavirus* spillover in Eastern Sierra Leone.
- **Chapter 7:** Results from all previous Chapters are summarised and discussed as a whole. The strengths and weaknesses of the analysis in this thesis are outlined. Further work is outlined.

1.4 Thesis output

This thesis has produced: peer reviewed papers; preprints; talks at academic conferences and a dashboard for exploring relevant data. These outputs are detailed in the following section.

1.4.1 Peer reviewed papers

- Simons D., Attfield L., Jones K., Watson-Jones D., Kock R. *Rodent trapping studies as an overlooked information source for understanding endemic and novel zoonotic spillover*, PLOSNTD, 2023, ...
- Simons D. *Lassa fever cases suffer from severe under-reporting based on reported fatalities*, International Health, 2023, ...

1.4.2 Papers under review

- ...

1.4.3 Software

1.4.3.1 Interactive tools

- **Explore Rodent Trapping Studies in West Africa**: Developed to showcase the data extracted and synthesised in the Rodent trapping studies as an overlooked information source for understanding endemic and novel zoonotic spillover article. Link: https://diddrog11.shinyapps.io/scoping_review_app/

1.4.4 Talks

- **Planetary Health Alliance**
- **EEID 2022**
- **Transmissable Vaccines 2023**

1.5 Summary

- This chapter provides an introduction to rodent borne zoonotic infectious diseases and Lassa Fever. It then motivates the remainder of this thesis.
- An outline of the theoretical framework used throughout this thesis is given.
- The aims and objectives of this thesis are detailed.
- An overview of the chapters is provided.

- Finally the dissemination of this work so far is summarised, broken down into peer reviewed output, preprints, software output, and talks given at academic conferences.

2 Background

2.1 Zoonotic infectious diseases

2.1.1 Surveillance of endemic zoonoses

2.1.2 Predicting changing zoonotic spillover risk

2.1.3 Rodent borne zoonotic infectious diseases

2.1.4 Sampling rodent distributions

2.2 *Lassa mammarenavirus* and Lassa Fever

2.2.1 *Lassa mammarenvirus* epidemiology

2.2.2 Lassa Fever epidemiology

2.2.3 Lassa Fever treatment

2.2.4 Lassa Fever in Sierra Leone

2.3 Rodent hosts of *Lassa mammarenavirus*

2.3.1 Heterogeneity of rodent occurrence

2.3.2 Heterogeneity of rodent abundance

2.4 Systems approaches to endemic zoonoses

2.5 Summary

3 Rodent trapping studies as an overlooked information source for understanding endemic and novel zoonotic spillover

3.1 Summary

3.2 Abstract

3.3 Introduction

3.4 Methods

3.4.1 Data sources

3.4.1.1 Host and pathogen trapping data

3.4.2 Analysis

3.4.2.1 What is the extent of spatial bias in the rodent trapping data?

3.4.2.2 Are rodent trapping derived host-pathogen associations present in a consolidated zoonoses dataset?

3.5 Results

3.5.1 What is the extent of spatial bias in the rodent trapping data?

3.5.2 Are rodent trapping derived host-pathogen associations present in a consolidated zoonoses dataset?

3.5.3 What is the spatial extent of pathogen testing within a host's range?

3.6 Discussion

4 Small mammal species community structures vary importantly by land-use type in a Lassa fever endemic region of Sierra Leone.

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5 Reconstructing rodent contact networks to understand potential routes of *Lassa mammarenavirus* transmission.

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6 Model chapter.

7 Discussion chapter.