Understanding and predicting effects of global environmental change on zoonotic disease

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I, Rory James Gibb, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, these are indicated in the thesis. The contributions of coauthors to specific chapters are described in full in the thesis outline.

Abstract

Global environmental change is increasingly recognized to influence risk of numerous zoonotic (animal-borne) infectious diseases. There is a fast-growing body of research into climate change effects on zoonotic risks, but broad-scale studies have rarely investigated how climate interacts with other key drivers, in particular land use change. Here, I evaluate effects of land use and climate on zoonotic disease risk, both generally and in a case study disease, by integrating multiple data types (ecological, epidemiological, satellite) and tools from biodiversity science, spatiotemporal epidemiology and land use modelling. First, I compile and analyse a global database of local species communities and their pathogens, and show that ecological communities in anthropogenic land uses globally are increasingly dominated by zoonotic host species, including mammalian reservoirs of globally-significant zoonoses, and that these trends are likely mediated by species traits. Second, I examine interacting effects of land, climate and socioeconomic factors on Lassa fever (LF), a neglected rodent-borne viral zoonosis that is a significant public health concern in West Africa, focusing on disease risk projection at both short (interannual) and long (multi-decadal) time horizons. In an epidemiological analysis of case surveillance time series from Nigeria, I show that present-day human LF incidence is associated with climate, agriculture and poverty, that periodic surges in LF cases are predicted by seasonal climate-vegetation dynamics, and that recent emergence trends are most likely underpinned by improving surveillance. At longer timescales, I then couple a mechanistic disease risk model with a dynamic land change model and climate projections, to show that different economic and climate policy futures (Shared Socioeconomic Pathways) may result in markedly different outcomes for LF risk and burden by 2030 and 2050 across West Africa. Finally, I synthesise the implications of these results for our understanding of the global change ecology of zoonotic disease, the epidemiology and control of LF, and for broader Planetary Health perspectives on managing zoonotic risks.

Impact statement

Zoonotic diseases (diseases with an animal reservoir) are a growing threat to global public health. Human-induced environmental changes are reshaping ecological communities and changing human patterns of contact with wildlife, and in turn driving the spillover, emergence and spread of zoonoses. This thesis applies tools and concepts from biodiversity modelling, risk modelling and epidemiology to understand how human pressures affect the risks of zoonotic disease spillover, both in general and for a case study disease (Lassa fever in West Africa). This is a highly topical area, given the SARS-CoV-2 pandemic and recent severe epidemics of other zoonoses including Zika and Ebola. Consequently the subject matter and findings will be of significant interest for academic research and policy audiences in ecology, public health and land use policy, as well as being of broader public interest.

From an ecological science perspective, the thesis provides significant and novel insights into the global change ecology and drivers of zoonotic disease, that contribute to recent debates around how best to manage landscapes to reduce disease risk. For example, Chapter 2 enhances our understanding of the global generality and predictability of the effects of land use on zoonotic host communities, and from a policy perspective suggests that lower use-intensity landscapes may often assist in reducing zoonotic hazards and preserving biodiversity. This work has recently been accepted for publication in *Nature*. All of the analyses in this thesis have also involved developing methodological innovations that are applicable more broadly (see discussion in Chapter 6), including several statistical approaches to control for biases in research effort, and the incorporation of dynamic land use models into disease risk modelling.

The findings from Chapters 3 to 5 will contribute significantly to public health efforts to prevent and control Lassa fever, a high-burden priority disease in West Africa. Chapter 3 is the first substantial review of the eco-epidemiology of Lassa fever, was published in 2017 in *Pathogens & Global Health*, and identifies and outlines key knowledge gaps and research priorities. Chapters 4 and 5 address some of these gaps, and will contribute directly to control of Lassa fever via an ongoing collaboration with the Nigeria Centre for Disease Control (NCDC). Chapter 4 identifies important areas of Nigeria for enhancing disease surveillance, shows that recent high case surges are likely to have been driven by improving surveillance, and shows the potential scope for an early-warning system to prioritise clinical resources ahead of seasonal peaks in infection risk. The long-term ecosystem perspective of Chapter 5 goes on to identify key regions of West Africa (including north Nigeria) that are expected to experience significant increases in Lassa fever risk in the coming decades. These results are timely, as several Lassa fever vaccine candidates are currently in development, and the efficacy of vaccine trials and vaccination campaigns will depend on improving our understanding of at-risk populations.

Finally, the published research from this thesis will contribute to enhancing public understanding of the environmental context of zoonoses, which is especially important in light of the COVID-19 pandemic.

Acknowledgements

Three-and-a-half years later, and a heartfelt thank you to my advisors who have been consistent sources of support though the many challenges of doctoral research. Kate Jones, for all the opportunities, encouragement, and reminders to stay focused on the bigger picture. Dave Redding, for endless crunching of ideas and statistical troubleshooting. Tim Newbold, for many thoughtful discussions of methods, maths and ecological context. Thanks also to Richard Pearson, for acting as my thesis chair.

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A note on reproducibility and data access

Data and code (where not freely available online) used in the analysis chapters are provided in the accompanying linked repositories, and full lists of all data sources are provided in the appendices for each chapter. Repository links are included in the end notes for each chapter.

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Thesis outline of contents and collaborators

Chapter 1
Introduction.
This chapter synthesises current knowledge of the interacting effects of land use and climate change on zoonotic disease risk and incidence. Some of the material from this introduction and the discussion (Chapter 6) is published in an *Analysis* article at *BMJ* under the title *"Ecosystem perspectives are needed to manage zoonotic disease risks in a changing climate"*.

Chapter 2
Global effects of land use on local zoonotic host diversity.
In this chapter, I conduct a global-scale analysis of the effects of human land modification on local zoonotic host community diversity and composition. The work was conducted in collaboration with David W. Redding, Kai Qing Chin, Tim Newbold, Christl A. Donnelly, Tim Blackburn and Kate E. Jones. The study was conceived by myself and DWR, I designed and conducted all analyses with statistical advice from CAD, preliminary analyses (using the EID2 pathogens database only) were conducted by KQC and DWR during the former's master's degree, and all authors contributed to the paper. This work was published in *Nature* under the title *'Zoonotic host diversity increases in human-dominated ecosystems'*. An earlier version of these results was published as a meeting abstract in *Lancet Planetary Health* (Gibb et al., 2018), and I have presented this chapter at the 2018 Planetary Health Meeting (Edinburgh), 2018 International Statistical Ecology Conference (St. Andrews), 2018 ISS Symposium on Health and Climate Change (Istituto Superiore di Sanita, Rome) and the British Ecological Society Annual Meeting 2018. Additional thanks to L. Enright, A. Etard, L. Franklinos, R. Freeman, R. Lowe and R. Pearson for discussion and comments.

Chapter 3
Understanding the ecology, epidemiology and drivers of Lassa fever in West Africa.
In this chapter, I review and synthesise current knowledge of the ecology, epidemiology and distribution of Lassa fever, a rodent-borne disease endemic to West Africa, to identify knowledge and data gaps for later chapters. This work was conducted in collaboration with Lina M. Moses (Tulane University), DWR and KEJ. I undertook the literature review and wrote the paper with feedback from all coauthors. The Lassa fever case dataset was originally collated by LMM with contributions from Kelsey Confreda, and updated and analysed by myself. This chapter was published in July 2017 in the journal *Pathogens and Global Health* under the title *'Understanding the cryptic nature of Lassa fever in West Africa'* (Gibb et al., 2017), and the typeset published paper is provided in Appendix 4. Additional thanks to J. Koninga, D. Grant, A. Kamara, A.B. Gogra, M. Lahai, M. Leach and D. Rogers.

Chapter 4
Climate, land use and reporting effort shape the present day distribution and dynamics of Lassa fever in Nigeria.
In this chapter, I conduct a spatiotemporal epidemiological analysis of the climatic, ecological and socioeconomic drivers of acute human Lassa fever in Nigeria. This work was a multi-institution collaboration with the Lassa Fever Technical Working Group at the Nigeria Centre for Disease Control (NCDC), initiated during a large seasonal surge in LF cases during 2018. The

collaborators were DWR and KEJ (UCL), Lauren Enright and CAD (Imperial College London), Ibrahim Abubakar (Institute for Global Health), Chioma Dan-Nwafor, Elsie Ilori, Yashe Rimamdeyati Usman, Saliu Oladele, Michael O. Amedu, Akanimo Iniobong, Ipadeola Oladipupo and Chikwe Ihekweazu (all NCDC and affiliated organisations). The data were collected and collated by collaborators at NCDC. I jointly led and designed the study with DWR, and I led and conducted all the analysis, data processing and modelling, and wrote the chapter (and manuscript) with input from all coauthors. This work is currently in review at *Nature Communications* under the title *'Spatiotemporal analysis of surveillance data enables climate-based forecasting of Lassa fever'*. I presented results from this chapter at the 2019 Lassa Fever International Conference in Abuja, Nigeria.

Chapter 5

The nexus of future agricultural and socioeconomic change and Lassa fever risk in West Africa.

In this chapter, I analyse the effects on integrated agricultural, socioeconomic and climatic pathways on LF risk across West Africa, using a dynamic land change model and a process-based disease risk model. I conceived, developed and conducted all analyses with additional advice from Piero Visconti and LMM, and technical support from Tamás Krisztin (who conducted land use downscaling) and Henry Ferguson-Gow. This chapter significantly expands on preliminary concepts I developed during a Master's research project (2015, UCL) that applied a simpler disease model to a single climate-land cover scenario. Most of the work was undertaken during a summer short fellowship in the Ecosystems Services & Management program at the International Institute for Applied Systems Analysis (IIASA), which was funded by a IIASA YSSP grant from NERC. An earlier version of this chapter was submitted as a report to IIASA. Additional thanks to F. Gaupp, A. Palazzo and M. Gidden for discussion and ideas.

Chapter 6

Discussion and synthesis.

In this chapter I evaluate the key findings and methodological contributions of the thesis, and assess future research priorities, with a focus on understanding the global change ecology of zoonotic disease, and the scope for Planetary Health approaches to zoonoses.

List of main text figures and tables.

Supplementary figures and tables for all chapters are included in Appendices 1-3.

Chapter 1:
Introduction.

1.1. Understanding the effects of environmental change and biodiversity loss on human health and wellbeing: a whole-systems challenge.

We are living through an era of profound and global environmental change. As recent debates around defining the Anthropocene have emphasised, human societies have been reshaping the Earth system over thousands of years (Lewis and Maslin, 2015). However, these impacts have drastically accelerated since the mid-20th century, as rising energy use has driven exponential growth in fossil fuel emissions (IPCC, 2018), and as globalising economies have placed increasing demands on ecosystems for sustenance and profit, leading to widespread deforestation, agricultural expansion, urbanisation, and biodiversity losses (Díaz et al., 2019; Foley et al., 2005; Grimm et al., 2008; MA, 2005). This century's defining challenge is to understand and address the impacts of these changes on the health and wellbeing of human and non-human life. Globally, many metrics of human health (e.g. longevity, child mortality) have on average improved significantly in the last 50 years as a consequence of economic development (Whitmee et al., 2015). Yet these improvements are unequally distributed, and aggregate statistics mask stark inequalities across regions and countries, for example in terms of poverty, food security, child mortality and infectious disease burdens (Osgood-Zimmerman et al., 2018; Weiss et al., 2019, 2018). Many economically marginalised people, especially in developing countries, are directly dependent on ecosystems for their livelihoods and sustenance, making them particularly susceptible to the impacts of natural hazards (e.g. drought, extreme weather events, disease outbreaks) (Peduzzi et al., 2009). Ongoing climate change and ecological degradation are likely to only further exacerbate these vulnerabilities (Cardona et al., 2012).

Biodiversity loss and biodiversity change, and their effects on ecosystem structure and function, are critical aspects of the environment-health nexus (Cardinale et al., 2012; Isbell et al., 2017). Current discourses around biodiversity conservation recognise the intrinsic value of non-human nature, while also emphasising the fundamental material contributions of ecosystems to human wellbeing (Díaz et al., 2015; Mace, 2014). The landmark Millennium Ecosystem Assessment in 2005 conceptualised these contributions as *ecosystem services* (ES) mediating stocks and flows of goods (e.g. food, timber) and services (e.g. carbon sequestration, pollination) to people (MA, 2005). The Intergovernmental Panel on Biodiversity and Ecosystem Services (IPBES) has expanded this concept to *nature's contributions to people*, incorporating

indigenous knowledges and more diverse cultural perspectives on nature (Díaz et al., 2018). These frameworks emphasise that ecosystems provide both direct and indirect benefits to human populations. Conversely, the processes that erode biodiversity and ecosystem function – most significantly land use change, climate change, and industrial and agrochemical pollution – can negatively impact many dimensions of human health, including food and water security, exposure to natural hazards (e.g. climatic extremes, infectious disease), and mental health and wellbeing (Myers et al., 2013; Sandifer et al., 2015; Watts et al., 2019). Land use and related pressures in particular (e.g. agriculture, plantations, roads, extractive industry, urbanisation) are a dominant ecological force globally: ~75% of the earth's terrestrial surface is experiencing detectable human impacts (Venter et al., 2016), and natural vegetation is increasingly fragmented and pockmarked through a matrix of human-dominated habitat (Fahrig, 2003; Taubert et al., 2018). These trends are ongoing, with deforestation, agricultural and urban expansion expected to continue throughout this century (Hurtt et al., 2011; Popp et al., 2017; Seto et al., 2012). Resulting declines in biodiversity and ecosystem services will likely have complex, multifactorial effects on health and wellbeing (Cardinale et al., 2012; Isbell et al., 2017; Myers et al., 2013).

Measuring and predicting the interacting effects of biodiversity change and other anthropogenic processes (e.g. climate change, deforestation) on human health is therefore a critical challenge spanning ecology, epidemiology and public health (Myers et al., 2013). Although a wealth of research has identified relationships between biodiversity loss and declines in ecosystem service provision (e.g. pollination, carbon sequestration) (Isbell et al., 2017, 2011; Tilman et al., 2014), there is far less evidence of clear causal links between such changes and downstream public health outcomes. The challenge of attributing causality is a reflection of underlying system complexity. For instance, although deforestation for agriculture may provide immediate local nutritional and/or economic benefits to health, these benefits can mask underlying negative effects of ecological degradation, that may also manifest over longer timescales (e.g. due to extinction debts or lagged climate change) (MacDonald and Mordecai, 2019; Wearn et al., 2012). Such effects are also increasingly spatially displaced, for example by globalised trade, which extracts nature's benefits (e.g. agricultural products, timber, groundwater) away from sites of ecosystem degradation, often in the global South, towards richer economies in the global North (Bergmann and Holmberg, 2016; Dalin et al., 2017; Tsing, 2005; Wallace et al., 2016). Such spatial inequalities both drive and obscure the negative health outcomes of environmental change. Populations and regions on the frontiers of ecosystem degradation and informal urbanisation generally experience the greatest exposure and vulnerability to natural hazards (e.g. extreme weather, endemic disease risk), but are also

systematically under-researched and under-resourced (Baeza et al., 2017; Barrett et al., 2011; Nixon, 2013; Sachs et al., 2009; Titley et al., 2017).

We therefore need to develop a fuller understanding of the pathways through which biodiversity change and ecosystem degradation, and their upstream drivers (e.g. food demand, trade, global inequality), can lead to positive or negative health outcomes. Such knowledge will be critical to developing and targeting interventions, either aimed at mitigating changing risks or at adapting to them (Cardona et al., 2012). For instance, land use decisions invariably involve trade-offs and synergies between different health-relevant ecosystem services, such as food and water security, disease risk and biodiversity conservation (Bateman et al., 2013, 2011; Howe et al., 2014). Historically, a focus on provisioning services and for-profit extraction (e.g. crop and timber production) has driven the rapid, unsustainable global expansion of plantation ecosystems, leading to massive biodiversity losses and erosion of locally- and globally-important regulating services (e.g. carbon sequestration, pollination) (Foley et al., 2005; Gibbs et al., 2010; Newbold et al., 2016a, 2015). More sustainable approaches are needed, to both conserve natural systems and reduce human exposure to the hazardous effects of biodiversity loss. Achieving these outcomes sustainably and equitably requires systems-based perspectives that recognise the complex interdependencies and trade-offs between human, wildlife and ecosystem health (Carpenter et al., 2009; Nicholson et al., 2009; Ostrom, 2007). Such complexities are acknowledged in interdisciplinary science-policy frameworks such as EcoHealth, One Health and Planetary Health (Galaz et al., 2015; Kingsley and Taylor, 2016; Whitmee et al., 2015), and to some degree in global governance targets such as the UN Sustainable Development Goals (SDGs) (Scharlemann et al., 2016). Nonetheless, the siloed nature of institutional and disciplinary perspectives means that operationalising more holistic management of ecosystems for people and nature remains challenging. For example, the SDG framework includes some discrete conservation-related targets, but does not articulate the fundamental extent to which socioeconomic goals – including global health and poverty alleviation – depend on preserving functional and resilient ecosystems.

1.2. Zoonotic and vector-borne disease risk and emergence: a neglected ecosystem disservice.

One key aspect of health that can be rapidly affected by anthropogenic environmental change is the risk and burden of infectious disease, and especially zoonotic (animal-borne) and vector-borne infections (Kilpatrick and Randolph, 2012; Lloyd-Smith et al., 2009; Patz et al., 2004). These are human-infectious pathogens whose transmission cycles involve animal reservoir hosts and/or arthropod vectors (e.g. mosquitoes, ticks) (Taylor et al., 2001). Globally,

zoonoses are a massive burden on public health and economies. For example, endemic diseases that typically arise from zoonotic (animal-to-human) transmission (e.g. leptospirosis, leishmaniasis, brucellosis, Lyme disease, zoonotic malaria, trypanosomiasis) have been estimated to cause around 1 billion human infections per year, mainly in the tropics (Halliday et al., 2015a; Karesh et al., 2012). Many originate from wildlife, although domesticated animals are also intermediate or reservoir hosts of many infections (Gortazar et al., 2014; Robinson et al., 2016; Wiethoelter et al., 2015). Crucially, animal-borne infections appear to be on the rise globally, have comprised around 60% of newly emerging human pathogens since 1950 (Jones et al., 2008), and have been responsible for almost all of the most severe epidemics and pandemics of recent decades (e.g. COVID-19, SARS, novel influenzas, dengue, Ebola, Zika). The economic costs of such large outbreaks can be extremely severe. For example, the economic burden of the 2013-15 West African Ebola epidemic may have been as high as $54 billion USD (Huber et al., 2018). At the time of writing, ~4 million cases of COVID-19 have so far been confirmed globally, which has destabilised economies, overwhelmed health systems, and led to social distancing measures being imposed on ~50% of the global population (Andersen et al., 2020; Cash and Patel, 2020).

Zoonotic disease risk and emergence are inherently socio-ecological and environmental problems, since multi-host disease systems involve complex interactions among people, animals, pathogens and landscapes (Karesh et al., 2012; Lloyd-Smith et al., 2009; Patz et al., 2005). Consequently, reservoir host, vector and pathogen geographies, and their relationships to environmental factors such as climate and vegetation, underpin distributions of human zoonotic disease risk (Murray et al., 2018, 2015; Peterson, 2008). In turn, environmental change and ecosystem degradation can play significant roles in driving cross-species transmission (*'spillover'*) risks from animals to humans. Anthropogenic landscapes such as cropland, pasture and plantations can significantly influence disease risks, for example by altering host, vector and pathogen communities, and/or altering landscape structure in ways that affect contact rates (e.g. fragmentation, hydrology, resource provisioning) (Burkett-Cadena and Vittor, 2018; Cox and Gaston, 2018; Faust et al., 2018; Murray and Daszak, 2013; Ostfeld et al., 2000; Suzán et al., 2015; Young et al., 2014). Climatic factors such as temperature, humidity, rainfall and vegetation seasonality can impact disease systems via numerous pathways, including by limiting environmental suitability for hosts and pathogens (i.e. climatic niches) (Murray et al., 2018; Pulliam, 2000), driving reservoir population dynamics (Fichet-Calvet et al., 2008; Tian et al., 2017) and affecting host, vector and pathogen reproduction and physiology (Lafferty, 2009; Mordecai et al., 2017, 2013a).

Such environmental and ecological forcings of disease systems shape spatial and temporal distributions of *zoonotic hazard* (i.e. the latent potential for pathogen spillover to humans) (Figure 1.1). But significantly, socio-ecological changes simultaneously modulate the other components of risk, *exposure* (i.e. opportunities for contact and transmission) and *vulnerability* (i.e. potential for adverse impacts caused by infection, either individually or at population-level) (Figure 1.1) (Hosseini et al., 2017). These changes can exacerbate disease risks directly (e.g. by increasing human-wildlife-livestock contact rates) or indirectly (e.g. via climate-driven impacts on food security, nutrition and susceptibility to infection), or could dampen risks, for example via improvements in sanitation and housing through urban planning or poverty alleviation. Such interactions are crucial to understanding and managing risks, since exposure and vulnerability are generally the key factors determining the severity of natural hazard impacts (e.g. extreme weather events, drought) on individuals and populations (Cardona et al., 2012; Hagenlocher and Castro, 2015). For example, although *Leptospira* bacteria are found in urban rodent populations worldwide, the vast majority of leptospirosis burden globally is concentrated in poor and informal urban settlements with inadequate sanitation and consequent high exposure levels (Torgerson et al., 2015).

Future pathways of socioeconomic and environmental change will therefore likely lead to complex outcomes and trade-offs in terms of zoonotic disease and other contributors to health (e.g. agricultural production and food security) (Carpenter et al., 2009; Garchitorena et al., 2017; Ngonghala et al., 2017a; Rohr et al., 2019). Approaches addressing zoonotic and vector-borne disease management within such a multifunctional ecosystems context – rather than as distinct problems to be addressed individually – are being successfully explored for some diseases (e.g. Daszak, 2019; Sokolow, 2015; Sokolow et al., 2019). Yet zoonoses have generally been neglected in global change assessments, despite disease regulation being considered a key regulating service (MA, 2005; Marco et al., 2020; UK National Ecosystem Assesment, 2011). This problem is not simply of ecological interest, but also limits our ability to address current and emerging vulnerabilities. Zoonoses have often been framed in Global North sciences in terms of biosecurity and novel pandemic risk, sometimes even for pathogens with scant evidence of sustained human-to-human transmission (Holmes et al., 2018; Morse et al., 2012; Pigott et al., 2017; Wilkinson, 2016). Such systemic risks are clearly important, but a focus on pandemics alone is not sufficient: sustained human-to-human transmissibility is relatively rare among zoonotic pathogens (Wertheim et al., 2012), and the highest disease burdens are generally suffered by structurally vulnerable populations in endemic areas (Cleaveland et al., 2017; Dzingirai et al., 2016; Halliday et al., 2015a).

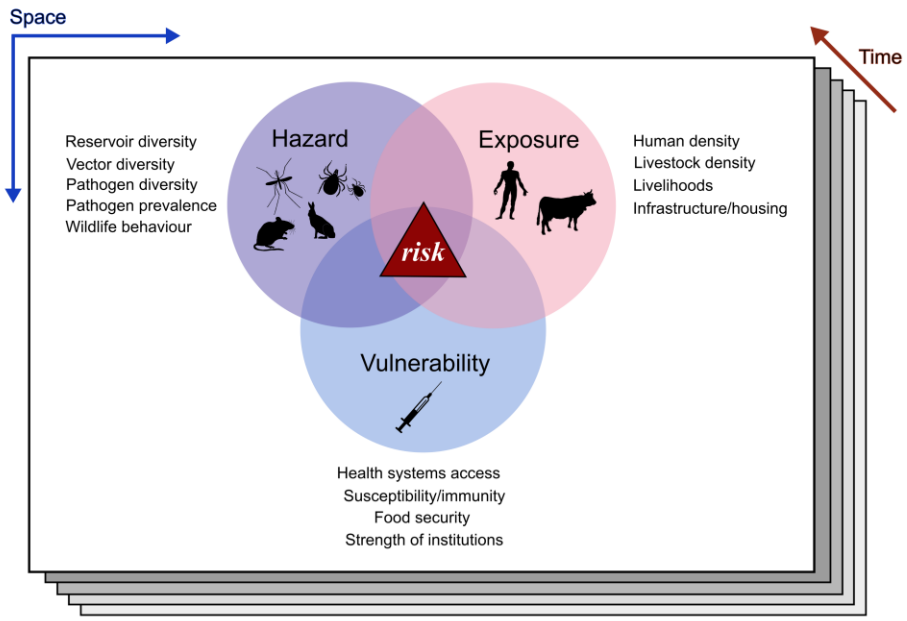

Figure 1.1. Components of zoonotic and vector-borne disease risk over space and time. Risk is classically defined as the product of hazard, exposure and vulnerability (Cardona et al., 2012; Peduzzi et al., 2009). This schematic shows examples of contributors to hazard, exposure and vulnerability for zoonotic disease systems, although these vary between diseases and contexts. Environmental and socio-ecological changes over space (blue arrows) and time (red arrows) (e.g. seasonality, climate change, land use, urbanisation and other socioeconomic factors) can impact one or multiple of these components simultaneously, leading to complex and dynamic emergent landscapes of disease risk. These effects could be synergistic (e.g. land change both favouring high reservoir host abundance and high human-wildlife contact) or antagonistic (e.g. land change favouring high vector abundance but improving food security and reducing disease susceptibility).

Several regions are at the convergence of already-high zoonotic and vector-borne disease incidence, rapid land use and climatic change, growing populations, and existing socioeconomic vulnerabilities (e.g. West and Central Africa, tropical South America, Southeast Asia). Land use and climate change processes are themselves linked by feedbacks; for example, regional warming can negatively impact crop yields leading to further agricultural land expansion. Reconciling potential trade-offs between food and water security, disease risks and conservation will therefore be critical challenges facing decision-makers in these regions (Palazzo et al., 2017), and interventions will likely involve some combination of mitigation (e.g. vaccination, land use policy) and adaptation measures (e.g. health systems and surveillance capacity building) (Campbell-Lendrum et al., 2015; Ihekweazu and Abubakar, 2017). To date, predictive models at policy-relevant scales have mainly focused on climate change alone, for example using climate model ensemble outputs to project future transmission potential (e.g. Caminade et al., 2014; Messina et al., 2015). Better accounting for multiple drivers could enable zoonotic hazards and risks to be more fully integrated into the socioeconomic and climate

scenario frameworks used for assessment and decision-making around other systemic risks arising from global change (e.g. food security, extreme weather) (Gaupp et al., 2019; Palazzo et al., 2017; Redding et al., 2016; Riahi et al., 2015; Rosa et al., 2017; Willenbockel, 2015). Doing so, however, will require developing a clearer understanding of the processes that drive emergent disease risks in changing environments (Figure 1.1).

1.3. Challenges and knowledge gaps for understanding and predicting land use and climate change effects on zoonotic disease risks.

Until recently there have been relatively few integrated efforts to quantify net zoonotic disease risks within global change and sustainable development contexts. In part, this is likely a consequence of disciplinary and institutional divides. The dynamics, drivers and spillover of zoonoses from wildlife reservoir populations have been studied in detail in their own fields (e.g. disease ecology, EcoHealth) (Plowright et al., 2017). Epidemiology and public health research has instead tended to focus on modelling, mapping and short-term (e.g. interannual) forecasting at policy-relevant scales, usually for priority diseases (e.g. malaria, dengue) and often without incorporating much ecological information (Caminade et al., 2014; Feachem et al., 2019; Hay et al., 2013; Lowe et al., 2016; Messina et al., 2015). However, such disciplinary boundaries are shifting with increasing research focus on operationalising One Health perspectives (Bardosh et al., 2017b; Leach et al., 2017; Scoones et al., 2017), the development of large platforms such as the Lancet Commissions and Planetary Health (Watts et al., 2016; Whitmee et al., 2015), and multisectoral epidemic preparedness initiatives such as PANDORA (https://www.pandora-id.net/) that integrate zoonotic ecology and surveillance, institutional capacity building, epidemiology and clinical work.

Perhaps more problematic is the formidable challenge of quantifying and predicting the effects of environmental and ecosystem change on disease risks. The system complexity that drives pathogen transmission in changing environments – involving multi-scale feedbacks between reservoir, vector and human populations, landscape structure, climate and socioeconomic factors (Figure 1.2) – makes causal relationships difficult to identify (Kraemer et al., 2019; Plowright et al., 2008). This problem is compounded by imperfect or biased observation, especially for neglected and emerging diseases. Reservoir and maintenance communities and their geographical distributions are often poorly characterised, even for many priority wildlife-borne zoonoses (e.g. Ebola, Crimean-Congo haemorrhagic fever) (Murray et al., 2018). Disease surveillance in humans has been historically patchy and is often geographically skewed towards known hotspots and/or regions with stronger health infrastructure. The result

is that we have poor baseline understanding of the present day incidence, burden and geographical distribution of numerous zoonoses, which may often be significantly underestimated, particularly when non-specific febrile diseases can be misdiagnosed as ubiquitous infections (e.g. malaria) (Gire et al., 2012; Halliday et al., 2015a). These knowledge gaps both harm present-day disease control efforts, and confound inference of spatial patterns, trends, and environmentally-driven emergence (Campbell-Lendrum et al., 2015). For example, top-down correlative mapping approaches (i.e. regressing reported case locations against environmental predictors) are often used to project zoonotic transmission potential to novel climates and locations. Yet if applied without sufficient caution, such models often replicate underlying reporting biases (Peterson et al., 2014) and generally assume linear and non-hierarchical relationships between predictor variables that may act upon different components of risk (Figure 1.1) so can be poorly generalizable to novel conditions (Washburne et al., 2019). For example, Ebola models would have significantly underestimated risk in West Africa prior to the catastrophic 2013-15 epidemic (Pigott et al., 2014), while successive Lassa fever mapping exercises have consistently underpredicted risk across large areas of Africa where the disease has subsequently been found (Fichet-Calvet and Rogers, 2009; Mylne et al., 2015).

Addressing these problems requires clearer understanding of the ecological factors that drive true (and observed) zoonotic transmission risk over space and time, and in changing ecosystems (Figure 1.2) (Murray et al., 2018; Plowright et al., 2017). For example, there is compelling evidence that anthropogenic landscapes are commonly associated with increased zoonotic disease risks at the local (i.e. eco-epidemiological) scale (Brearley et al., 2013; Gottdenker et al., 2014; Shah et al., 2019), but it is unclear whether this trend is underpinned by consistent and predictable ecological processes. For some better-studied diseases clear causal pathways have been identified, including bat-livestock interactions for Nipah and Hendra viruses (Plowright et al., 2011; Pulliam et al., 2012), reservoir community change for Lyme disease, hantavirus and West Nile virus in North America (Kilpatrick, 2011; Kilpatrick et al., 2017a; Luis et al., 2018; Ostfeld et al., 2000; Ostfeld and LoGiudice, 2003), and forest-agriculture ecotones for *Plasmodium knowlesi* in southeast Asia (Fornace et al., 2019, 2016). However, funding for long-term research is often difficult to access and maintain, so the evidence for most diseases and contexts instead comes from short-term observational studies that measure broad 'snapshot' indicators of pathogen transmission intensity, such as vector abundance or host serology (Gottdenker et al., 2014), which are often insufficient to elucidate underlying drivers. The evidence base for impacts of ecosystem disturbance and biodiversity on disease risk thus often appears to be contradictory, system-specific and scale-dependent (Halliday and Rohr, 2019; Hosseini et al., 2017; Keesing et al., 2010; Wood et al., 2017).

Recent years have seen significant efforts towards developing a more general theory and evidence base for ecological drivers of disease risk, but these have often focused more on species and community characteristics than on environmental drivers of change (Stephens et al., 2016; Suzán et al., 2015). For example, species-level macroecological analyses are providing insights into the traits and processes that influence reservoir host status and pathogen sharing (Albery et al., 2020; Brierley et al., 2015; Cooper et al., 2012a; Luis et al., 2015; Stephens et al., 2016) and highlighting putative reservoir species for targeted surveillance (e.g. Babayan et al., 2018; Han et al., 2015; Olival et al., 2017; Wardeh et al., 2020). Meanwhile, community-level research has been dominated by understanding whether community diversity has consistent buffering effects on pathogen transmission rates (i.e. dilution effects) (Faust et al., 2017; Johnson et al., 2013; Keesing et al., 2010; LoGiudice et al., 2003). Although such effects appear to be common in nature (Civitello et al., 2015), poor understanding of their idiosyncrasies has prompted contentious debates about the operational usefulness of such an idealised model (Randolph and Dobson, 2012; Rohr et al., 2020; Salkeld et al., 2013; Wood et al., 2017; Young et al., 2013). Indeed, given that species turnover and homogenisation (rather than absolute richness loss) appear to be dominant features of biodiversity responses to human pressures (Blowes et al., 2019; Gonzalez et al., 2016; Newbold et al., 2018), understanding specific drivers and processes of local community disassembly and turnover is likely to be more useful than a focus on biodiversity per se (e.g. species richness) (Johnson et al., 2015; Joseph et al., 2013; Suzán et al., 2015). For example, disease risk in real-world systems often appears to be most strongly influenced by the abundances of one or a few key reservoir (i.e. maintenance) host species (Fichet-Calvet et al., 2007; Morand et al., 2019; Young et al., 2014), which may respond in predictable ways to local habitat and climatic factors (Titcomb et al., 2017; Young et al., 2017). Yet we have a poor understanding of whether pressures such as agricultural intensification and climate change have global, directional effects on reservoir and vector communities and distributions (i.e. on zoonotic hazard; Figure 1.2) in ways that could impact emergent patterns and trends of zoonotic disease risk.

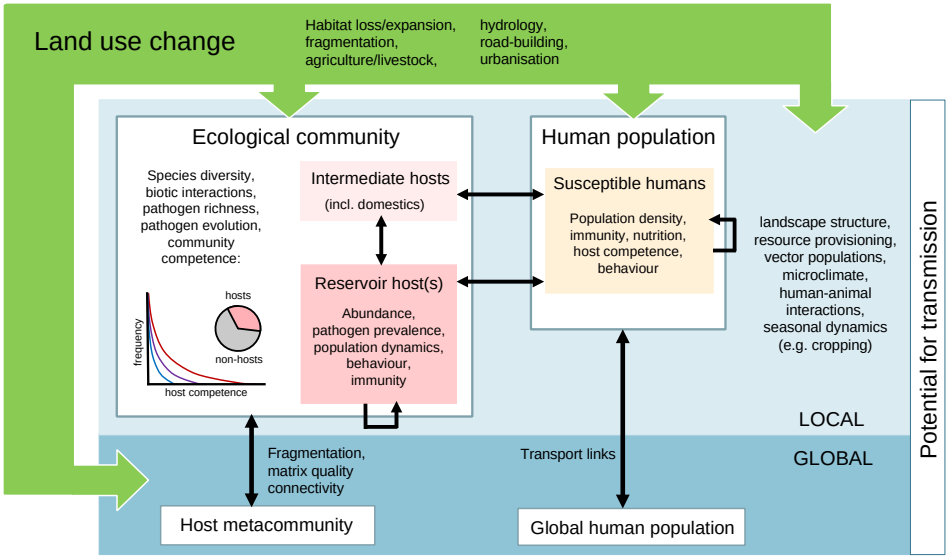

Figure 1.2: The effects of land use on zoonotic pathogen transmission. Pathogen transmission between potential hosts shown as black arrows. Land use change (green driver) acts on both the composition of the ecological community (white boxes), and on environmental features that influence contact and transmission both locally (light blue box) and at broader geographical scales (dark blue box). These processes occur within a broader system context also influenced by additional environmental (e.g. climatic), socioeconomic and demographic factors.

1.4. Opportunities for ecological process perspectives on components and pathways of zoonotic spillover risk: thesis aims and objectives.

Changing zoonotic disease risks under future environmental forcings will be multi-driver, multi-factorial and will emerge from the interplay of ecological hazard, exposure and vulnerability (Figure 1.1). As discussed above, our understanding of the complexities of these interactions is patchy, and it is unclear how effective regression-based models fitted to present-day disease data will be for projecting to novel future conditions (a consistent challenge in ecological and biodiversity forecasting; Evans et al., 2013). Some potential routes forward are offered by process-based perspectives on components of risk (Figure 1.1) and recent conceptual developments that have unpacked the complexities of cross-species transmission.

In particular, Plowright *et al.* (2017) usefully conceptualise zoonotic spillover as a path-dependent phenomenon: in order for spillover and human disease to successfully occur at a given place and time, a series of conditions must be simultaneously met, which include those relating to ecology (e.g. reservoir host presence and abundance; pathogen presence within reservoir), host-pathogen interactions (e.g. reservoir competence, human and host immune responses, pathogen shedding), pathogen biology (e.g. persistence in the environment,

adaptations to successfully infect and replicate within a human host) and opportunities for exposure and transmission (e.g. landscape structure, competent vector abundance). Their model provides a more concrete theoretical basis for the evolution, emergence and spread of novel human infections than previous, more descriptive attempts (e.g. Wolfe et al., 2007). It also provides a clear and operationalizable conceptual framework within which to explicitly analyse (or hierarchically model) the environmental and socio-ecological dependencies of key components of zoonotic spillover risk (i.e. hazard, exposure, vulnerability), either generally or for specific disease systems (Becker et al., 2019; Washburne et al., 2019). Indeed, several recent modelling studies have highlighted the improved benefits afforded by incorporating pathogen-specific transmission processes into ecological risk models (Childs et al., 2019; Perez-Saez et al., 2015; Redding et al., 2019; Redding et al., 2016). For example, a recent analysis of present and future Ebola risk in Africa showed markedly different geographical distributions of spillover potential (at human-bat interfaces) and potential for large epidemics following spillover (driven by human-human contact rates and socioeconomic factors) (Redding et al., 2019). Similarly, incorporating existing vaccination coverage (i.e. vulnerability) significantly improves spatial predictions of present-day yellow fever outbreak risk in Brazil (Childs et al., 2019).

In this thesis, I use a risk components-based framework (Figure 1.1) as a conceptual model for understanding and predicting effects of land use and climate change on zoonotic disease, both in general and for a case study of Lassa fever in West Africa (McCormick et al., 1987b). Land use change is a key driver of zoonotic disease in many systems but whether this occurs through general and predictable processes has been unclear and intensely-debated (Keesing et al., 2010; Rohr et al., 2020). In Chapter 2, I use a comparative, empirical approach to address the question of whether anthropogenic land uses (secondary, managed and urban ecosystems) have globally consistent effects on a key component of zoonotic hazard: the diversity and taxonomic composition of zoonotic host communities (inset box, Figure 1.2). To do this, I compile and combine a large database of host-pathogen relationships with a global database of local ecological communities (6801 sites from 184 published studies globally). I aim to answer the question: does human land modification have consistent and predictable effects on the diversity and community composition of zoonotic reservoir host taxa, and if so, is there evidence that these effects may be related to species traits that facilitate host status?

Hierarchical, mechanistic ecological models offer the potential to better link zoonotic disease risks to global environmental change projections, and to evaluate the potential risk trade-offs associated with future different land use, climate and socioeconomic pathways (Riahi et al., 2015). However, data and research gaps have hindered our ability to quantify the present-

day environmental dynamics of many neglected zoonoses (Gire et al., 2012; Wilkinson, 2017) and thus to parameterise more complex models, limiting capacities to forecast disease risk either in the short-term (interannual) or the long-term (decadal). In this thesis I focus on understanding and addressing some of these gaps for a case study disease, Lassa fever, a rodent-borne viral haemorrhagic fever that is generally considered to be a significant contributor to the burden of disease in rural West Africa (Andersen et al., 2015; McCormick et al., 1987b). Historically biased surveillance has led to poor baseline knowledge of the disease's incidence, geographical distribution and drivers (Wilkinson, 2017, 2016). Localised evidence from endemic areas suggests that Lassa risk may be seasonal and climatically-dependent (Lo Iacono et al., 2016; Shaffer et al., 2014), and its association with rural livelihoods suggests that widespread expansion of agriculture in West Africa (Sultan and Gaetani, 2016) may substantially increase risk in the coming decades. A recent modelling study suggested that projected climate change under the HadGEM-3 model may favour increased Lassa incidence by 2070, but did not explicitly examine how different agricultural pathways may interact with these climatic shifts to determine realised risk (Redding et al., 2016). Lassa fever is now an increasing priority on the global health agenda following several large case surges in recent years, and significant funding is being channelled into vaccine and diagnostic development (Emperador et al., 2019; Purushotham et al., 2019; Rottingen et al., 2017). Given that Lassa is an endemic, spillover-driven disease, better ecological understanding of its distribution, drivers and dynamics is needed to better target control measures towards vulnerable communities.

In Chapter 3 I synthesise current knowledge on the ecology and epidemiology of Lassa fever, and ask: what is the current evidence of the ecological factors linked to Lassa transmission and what are the key knowledge gaps from the perspective of improving our ability to predict and forecast risk? Then, in Chapter 4, I conduct an in-depth spatiotemporal epidemiological analysis of the first long-term human case surveillance dataset for Lassa fever, as part of a collaborative study with the Nigeria Centre for Disease Control (NCDC). Here, I explicitly analyse the roles of surveillance effort and environment in shaping current understanding of Lassa incidence in Nigeria and, controlling for effort, examine the seasonal and spatial dynamics and drivers of disease risk. In Chapter 5, I use knowledge, parameters and methods obtained from the previous chapters to extend an ecological risk model for Lassa fever to explicitly incorporate effects of land use on zoonotic hazard and exposure. I combine this model with a dynamic land model and socioeconomic scenarios to explore the nexus of agricultural and socioeconomic change and Lassa risk in West Africa in the coming decades. Finally, in Chapter 6 I synthesise and discuss the key insights and findings from the thesis, and propose critical future research directions and policy relevance.

Chapter 2:
Global effects of land use on local zoonotic host diversity.

In this chapter, I combine a global biodiversity database with comprehensive host-pathogen interactions data, to conduct a global-scale analysis of the present-day effects of human land modification (secondary, managed and urban ecosystems) on local zoonotic host diversity and community composition.

2.1. Abstract

Land use change (e.g. agriculture, urbanization) is widely recognised to influence zoonotic disease risk and emergence in humans. but whether this is underpinned by predictable ecological changes remains unclear and has been intensely debated. In particular, it has been widely hypothesised that systematic differences in species' resilience to anthropogenic impacts, linked to traits, life-histories and phylogeny, might result in habitat disturbance causing predictable changes in the diversity and species composition of potential zoonotic hosts. Here, I analyse 6801 ecological assemblages and 376 host species worldwide to show that land use has global and systematic effects on local zoonotic host communities. Controlling for research effort and survey methods, known wildlife hosts of human-shared pathogens and parasites comprise a significantly greater proportion of site-level species richness (18%–72% increase) and total abundance (21%–144% increase) in intensively-used secondary, human-managed and urban ecosystems than in nearby undisturbed habitats. This effect varies in magnitude among mammalian and avian taxonomic orders. In particular, rodent, bat and passerine bird zoonotic host species increasingly dominate disturbed assemblages, which may be one factor underpinning the global importance of these taxa as zoonotic disease reservoirs. Crucially, I further show that mammal species that harbour more pathogens overall (either human-shared or non-human shared) are more likely to occur in managed ecosystems, suggesting that my overall results may be mediated by ecological or life-history traits that influence both host status and human-tolerance. These results suggest that global changes in mode and intensity of land use are creating growing interfaces between people, livestock and wildlife reservoirs of zoonotic disease, and highlight the need to prioritise wildlife and human disease surveillance in agriculturally intensifying and urbanising habitats.

2.2. Introduction

Anthropogenic environmental change impacts many dimensions of human health and wellbeing, including the incidence and emergence of zoonotic and vector-borne diseases (Myers et al., 2013). Although large-scale research into environmental drivers of disease has mostly focused on climate, there is growing consensus that land use change (conversion of natural habitats to agricultural, urban or otherwise anthropogenic ecosystems) is a globally-significant mediator of human infection risk and disease emergence (Gottdenker et al., 2014; Keesing et al., 2010). Land use change directly and indirectly drives biodiversity loss, turnover and homogenisation (including through biological invasions and rare species losses) (Newbold et al., 2018, 2015), modifies landscape structure in ways that modulate epidemiological processes (e.g. fragmentation (Faust et al., 2018), resource provisioning (Becker et al., 2018)) and can increase human-wildlife contact (e.g. via agricultural practices or hunting) (Myers et al., 2013). These processes interact to influence transmission dynamics in reservoir and vector communities and ultimately spillover risk to humans (Plowright et al., 2017; Shah et al., 2019), with land use change implicated in driving both endemic (e.g. trypanosomiasis (Gottdenker et al., 2012), malaria (Fornace et al., 2016)) and epidemic (e.g. Nipah (Pulliam et al., 2012), West Nile (Kilpatrick, 2011)) zoonoses. However, the complexity of these systems (Figure 1.2) has made it difficult to identify whether land use has consistent effects on the ecological factors underpinning zoonotic disease risk (Gottdenker et al., 2014), a critical knowledge gap given the extensive global land change anticipated this century (Popp et al., 2017).

Although there is broad evidence for regulatory effects of local species diversity on pathogen transmission (Civitello et al., 2015), such effects are not universal: higher disease risk in depauperate assemblages has been observed for some disease systems (e.g. *Borrelia* (LoGiudice et al., 2003), West Nile (Kilpatrick, 2011), *Ribeiroia* (Johnson et al., 2013)) but not others. One ecological factor underlying these inconsistencies may be differences in host species sensitivity to human pressures (Ostfeld and LoGiudice, 2003). It is often proposed that more effective zoonotic host species might be generally more likely to persist in disturbed ecosystems, since certain trait profiles (e.g. 'fast' life-histories, higher population densities) correlate to both reservoir status and reduced extirpation risk in several vertebrate taxa (Johnson et al., 2015; Purvis et al., 2000). Alternatively, any such tendencies might be taxonomically or geographically idiosyncratic: for example, mammals that are more closely phylogenetically-related to humans are more likely to be zoonotic reservoirs (Olival et al., 2017), but may also be highly variable in their sensitivity to human impacts (Purvis et al., 2000). Reservoir host responses to disturbance have been investigated in certain taxa (e.g. primates

(Young et al., 2013)) and disease systems (Gottdenker et al., 2012; LoGiudice et al., 2003), but to date there has been no comprehensive analysis of the effects of land use on zoonotic host diversity and species composition.

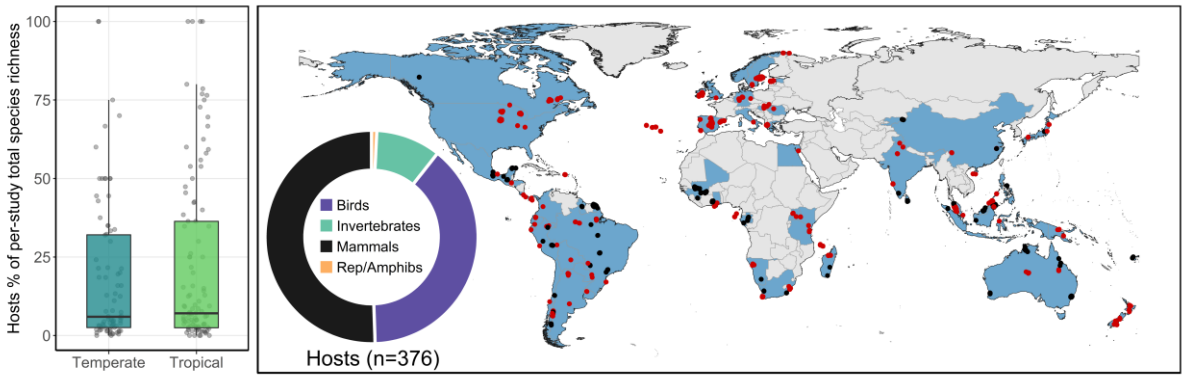

Figure 2.1: Combined ecological communities and zoonotic host species dataset. Points show the geographical locations of surveyed assemblages (n=6801 sites), with mammal survey locations coloured black and all other sites in red, and countries containing sites shaded in blue. Inset chart shows the taxonomic distribution of hosts of human-shared pathogens (birds, invertebrates, mammals, reptiles and amphibians; see Methods). Boxplots and points show, for each study, host species richness as a percentage of the total per-study sampled richness, split across temperate and tropical biomes (n=184 studies; boxes show median and interquartile range, whiskers show values within 1.5*IQR from quartiles).

2.3. Results and Discussion

Here, I use a global dataset of 6801 ecological assemblages derived from the Projecting Responses of Ecological Diversity in Changing Terrestrial Systems (PREDICTS) biodiversity database, to test whether land use has systematic effects on the zoonotic potential of local wildlife communities. I identified records of wildlife hosts of known human pathogens and endoparasites (henceforth *'pathogens'*) within PREDICTS using a comprehensive host-pathogen associations database, and classified species as zoonotic hosts (henceforth *'hosts'*) based on evidence of association with at least one human-shared pathogen (Methods). PREDICTS compiles >3.2 million species records from 666 studies that sampled biodiversity across land use gradients, enabling global comparisons of local assemblages in primary vegetation (minimally-disturbed baseline) to nearby secondary (recovering from past disturbance), managed (cropland, pasture, plantation) and urban sites, of varying use intensities (here, minimal or substantial-use), sampled using the same protocols (Hudson et al., 2017). I identified records of 376 host species in a dataset of 6801 survey sites from 184 studies across 6 continents, with a taxonomic distribution broadly representative of known zoonotic host diversity (Figure 2.1, Table S2.1, Table S2.2; Methods). I compared host responses to land use to

those of all other species at the same locations (*'non-hosts'*, approximating the response of background biodiversity; n=6512 species), using Bayesian mixed-effects models to control for study methods and sampling design (Methods). Pathogen detection is sensitive to research effort, such that some poorly studied species might be misclassified as non-hosts. I account for this uncertainty in the models using a bootstrap approach, with each iteration transitioning a proportion of non-host species to host status, with species-level transition rates determined by both publication effort and taxonomic order (Text S2.1, Figure 2.2a-e). In each bootstrap model the total number of host species in the dataset was increased by median 32% (range 24-40%, Figure 2.2f), and all parameter estimates are obtained across each full bootstrap ensemble (by calculating from posterior samples; Methods).

I first estimated the effects of land use type and intensity on two community metrics: site-level host species richness (number of host species; related to potential pathogen richness) and host total abundance (total number of host individuals; a more epidemiologically-relevant metric related to opportunities for transmission) (Lloyd-Smith et al., 2009). Both host richness and total abundance either persist or increase in response to land use, against a background of consistent declines in all other (non-host) species in human-dominated habitats (Figure 2.3a-b). Together these changes lead to hosts comprising an increasing proportion of ecological assemblages in secondary, managed and urban land (Figure 2.3c-d, Tables S2.3-S2.5). Notably, land use intensity has clear positive effects on community zoonotic potential both within and between land use types, with largest increases in substantial-use secondary and managed (posterior median: +18-21% host proportion richness, +21-26% proportion abundance) and urban sites (+62-72% proportion richness, +136-144% proportion abundance; but with higher uncertainty due to sparser sampling). These results are robust to testing for sensitivity to random study-level variability (Figure S2.1a), geographical biases in data coverage (Hudson et al., 2017) (Figure S2.1b), and strictness of host status definition (Figure S2.2). The last of these is crucial to understanding disease risk, since species capable of being infected by a given pathogen may not contribute substantially to transmission dynamics or zoonotic spillover risk. I therefore repeated analyses for mammals only (the major reservoirs of zoonoses globally) with reservoir status strictly-defined as an association with at least one zoonotic agent (aetiologic agent of a specific human disease with a known animal reservoir), based on pathogen detection, isolation or confirmed reservoir status (143 host species, 2026 sites, 63 studies). Overall trends remain consistent, although with notably stronger effects on host proportion of total abundance (+42-52% in secondary and managed land), and weaker effects on host richness that may reflect underlying variability in responses between mammal taxa (Figure S2.2).

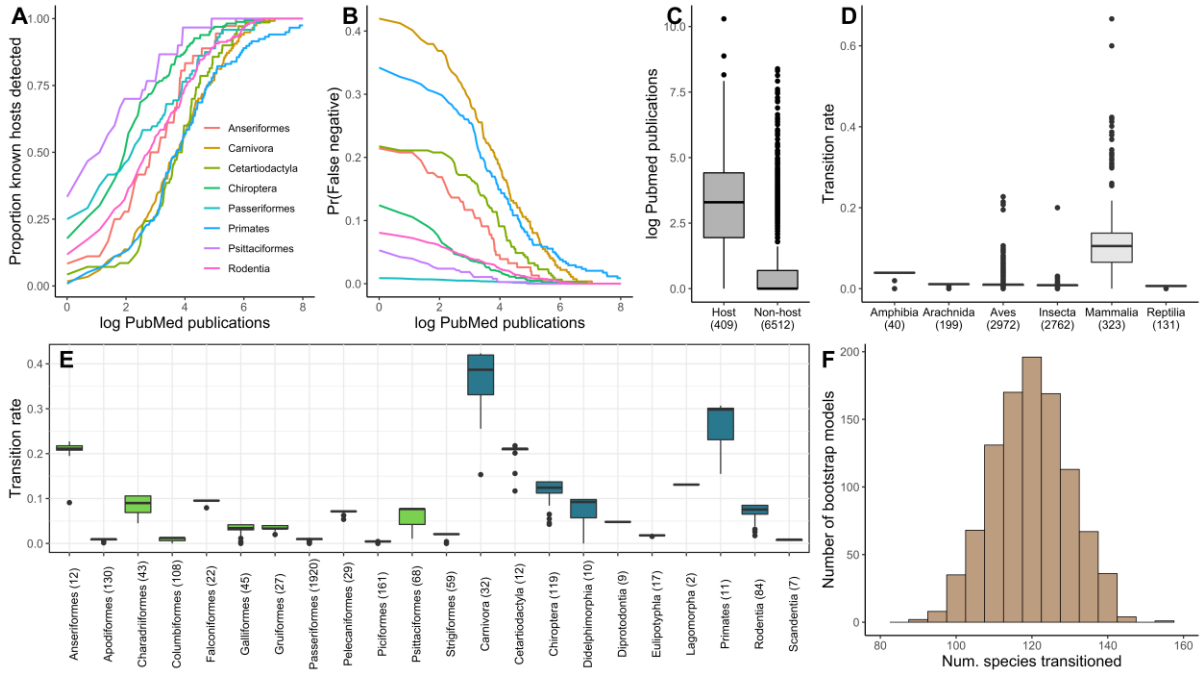

Figure 2.2: Approximating research effort bias for non-host species within the PREDICTS dataset. For all non-host species, I approximated the likelihood of false classification given research effort (i.e. probability of being a host, but not detected), based on the distribution of publication effort across known zoonotic hosts within the same taxonomic order (Text S2.1). Line graphs show, for several orders, the cumulative curve of publication counts for known zoonotic hosts (A; shown on log-scale), and approximated false classification probability, which declines and asymptotes with increasing levels of research effort (B) (line colours denote taxonomic order). Boxplots show the distribution of PubMed publications for all host and non-host species in PREDICTS (C), and false classification probabilities (used as bootstrap transition rates) for all non-hosts per taxonomic class in PREDICTS (D), and per key mammalian and avian order (E) (bracketed numbers denote number of non-host species per-group; boxes show median and interquartile range, whiskers show values within 1.5*IQR from quartile). Histogram shows the number of non-host species transitioned to host status for each of 1000 bootstrapped models of the full dataset (E; median 121, 95% quantile range 102–142).

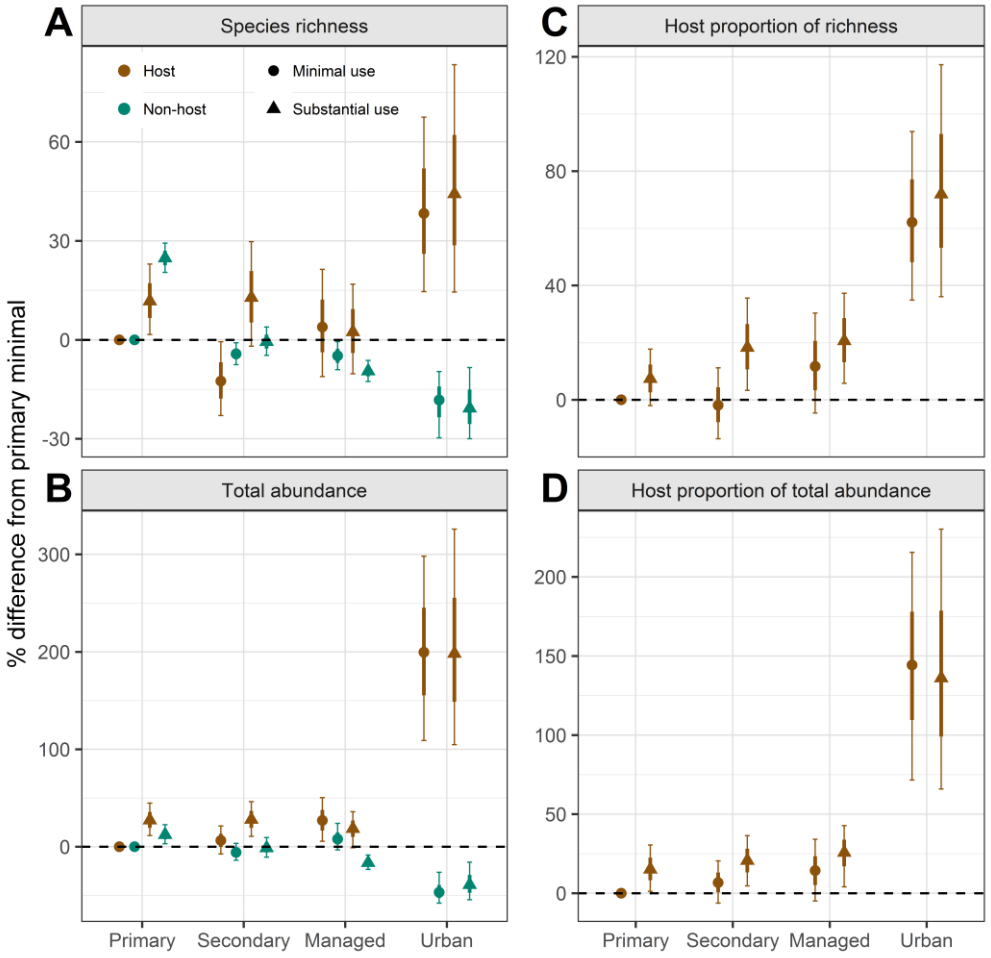

Figure 2.3: Effects of land use on site-level host species richness and total abundance. Points, wide and narrow error bars show modelled percentage difference in diversity metrics (posterior marginal median, 67% and 95% quantile ranges respectively, across 1000 bootstrap models) relative to a baseline of primary land under minimal use (dashed line) (n=6801 sites: primary (1423 and 1457 for minimal and substantial use, respectively), secondary (1044, 629), managed (565, 1314), urban (136, 233)). Models are of species richness (A) and total abundance (B) of host species and of all other (non-host) species, and of hosts as a proportion of total site-level richness and abundance (C-D). Point shape denotes land use intensity (minimal or substantial) and colour denotes host (brown) or non-host (green). All posterior estimates were calculated across an ensemble of 1000 bootstrapped models, each with a proportion of non-hosts probabilistically transitioned to host status (median 121, range 90–150; Figure 2.2f) to account for variability in species-level research effort (Methods, Text S2.1). Models also included fixed effects for human population density and random effects for study methods and biome (Methods). Parameter estimates represent averaged effect sizes across multiple studies with differing survey methods and taxonomic focus, so do not have an absolute numerical interpretation.

To examine the possibility of such taxonomic variability in host responses to land use, I separately analysed mean land use effects on species-level occurrence and abundance of zoonotic host (strictly-defined) and non-host species, for several mammalian (Carnivora, Cetartiodactyla, Chiroptera, Primates, Rodentia) and avian orders (Passeriformes, Psittaciformes) that are well-sampled in PREDICTS and harbour the majority of known zoonoses (Methods). I again used bootstrapping to account for host status uncertainty, and predicted abundance change using a hurdle model-based approach to account for zero-inflation (combining separately-fitted occurrence and zero-truncated abundance models; Figure S2.3). Within most orders, non-host species tend to decline more strongly in response to land disturbance than host species, but with substantial between-order variation in the direction and clarity of effects (Figure 2.4, Table S2.6). Notably, within passerine birds, bats and rodents, hosts and non-hosts show clear divergent responses to land use, with host species abundances on average increasing (+14-96% Passeriformes, +45% Chiroptera, +52% Rodentia) while non-host abundances decline (-28-43% Passeriformes, -13% Chiroptera, -53% Rodentia) in human-dominated relative to primary sites (Figure 2.4). Although such a tendency has been observed in some disease systems, these results suggest this is a more general phenomenon in these taxa, which may contribute to numerous documented links between anthropogenic ecosystems and bat-, rodent- and bird-borne emerging infections (e.g. corona-, henipa-, arena- and flaviviruses, *Borrelia* spp.) (Kilpatrick, 2011; LoGiudice et al., 2003; Pulliam et al., 2012). In contrast, primate and carnivore host responses are not clearly distinguishable from overall species declines in these orders, consistent with past studies that found no consistent links between land disturbance and disease in primates (Young et al., 2013) and highlighting the importance of ecotonal or edge habitats as human-primate epidemiological interfaces (Fornace et al., 2016; Goldberg et al., 2008) (although sparser urban sampling means that the urban adaptations of certain primates, such as macaques, are likely underrepresented).

The differing responses of host and non-host species may be mediated by covariance between traits influencing both host status and human-tolerance (Joseph et al., 2013), but could also reflect histories of human-wildlife contact and coevolution of shared pathogens (Plowright et al., 2017). If the former is the case I hypothesised that harbouring a higher number of pathogens overall (richness of either zoonotic or non-zoonotic pathogens; a metric often correlated to species traits (Kamiya et al., 2014)), would be associated with more positive species responses to land use. I tested this across all mammals in the dataset (due to more complete pathogen data availability than for other taxa; 546 species, 1950 sites), here controlling for species-level differences in research effort by analysing residual pathogen richness not explained by publication effort (Methods, Figure S2.4). I find that increasing

pathogen richness positively predicts species' probability of occurrence in managed but not primary sites, a result that is consistent for either human-shared or non-human-shared pathogens (no documented infection of either people or domestic animals; Figure 2.5, Table S2.7). For human-shared pathogens, the strength of this relationship (slope parameter) is significantly larger in managed sites than in both primary and secondary land, and for non-human-shared pathogens the strength of this relationship is larger in both managed and secondary sites than in primary land (Figure 2.5d-f; slopes for primary land not significantly different from 0). This result suggests that the net increase in zoonotic host diversity in disturbed sites is at least partly trait-mediated: in particular, species traits associated with a faster pace-of-life are often correlated both with reservoir status and infection outcomes (Johnson et al., 2012; Joseph et al., 2013) (potentially owing to life-history trade-offs between reproductive rate and immune investment (Lee et al., 2008)) and with population resilience to anthropogenic pressures (Purvis et al., 2000). A trait-mediated explanation is also supported by my finding that differential host and non-host species responses to land use are most clearly detected when comparing across large clades with a wide diversity of life-histories, such as rodents, passerines and, notably, mammals overall (Figure S2.3). In contrast, generally longer-lived, large-bodied clades (e.g. primates, carnivores) show more idiosyncratic or negative responses to landscape disturbance (Figure 2.4).

Overall, my results indicate that the homogenising impacts of land use on biodiversity globally (Newbold et al., 2018) have produced systematic changes to local zoonotic host communities, which may be one factor underpinning links between human-disturbed ecosystems and disease emergence. By leveraging site-level survey data, these analyses reflect community changes at the epidemiologically-relevant local landscape scale (Pieter T J Johnson et al., 2015), negating the need to ignore community interactions or generalise ecological processes to coarser spatial scales (a typical limitation of global studies that can confound or mask biodiversity-disease relationships (Rohr et al., 2020)). These results reflect zoonotic potential, since proximity to reservoir hosts is not necessarily sufficient for zoonotic spillover (Hosseini et al., 2017), and emergent disease risk will depend on contextual factors (e.g. pathogen prevalence, intermediate host/vector populations, landscape structure, human socioeconomics) that may synergistically or antagonistically affect contact and transmission dynamics (Plowright et al., 2017). Nonetheless, land use also predictably impacts other factors that can amplify within- and cross-species transmission (Brearley et al., 2013) (e.g. resource provisioning (Becker et al., 2018), vector diversity (Burkett-Cadena and Vittor, 2018)), and increases potential for human-wildlife contact (Shah et al., 2019): for example, human populations are consistently higher at disturbed sites in this dataset (Figure S2.5). Global

expansions of agricultural and urban land forecast for the coming decades, predominantly in low- and middle-income countries (Popp et al., 2017), thus have the potential to create growing risk interfaces for zoonotic pathogen exposure. In particular, the large effect sizes but sparser data availability for urban ecosystems (especially for mammals; Figure S2.2) highlight a key knowledge gap for anticipating urbanisation effects on public health and biodiversity. My findings therefore strongly support calls to enhance proactive human and animal surveillance within agricultural, pastoral and urbanising ecosystems (Hassell et al., 2016; Holmes et al., 2018), and highlight the need to incorporate disease-related costs into future land use and conservation planning.

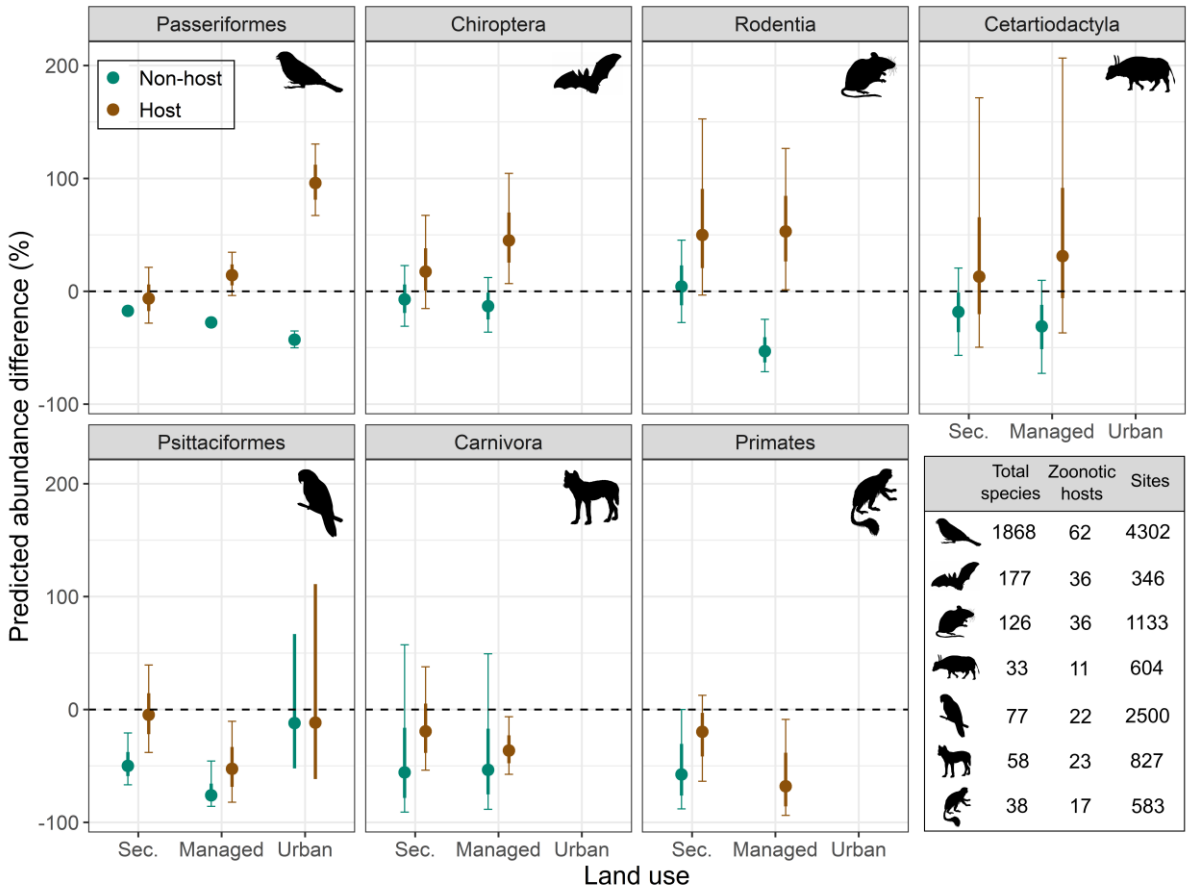

Figure 2.4: Effects of land use on species abundance of mammalian and avian zoonotic hosts and non-hosts. Points, wide and narrow error bars show average difference in species abundance (posterior median, 67% and 95% quantile ranges respectively, across 500 bootstrap models) in secondary (Sec.), managed and urban sites relative to a primary land baseline (dashed line), across all host (brown) and non-host (green) species in each mammalian or avian order. For mammals, zoonotic host status was defined strictly (direct pathogen detection, isolation or confirmed reservoir status), and urban sites were excluded owing to sparse urban sampling (only 2 studies; additionally, no non-host primates were recorded in managed land, and urban 95% quantile range for Psittaciformes is not shown due to high uncertainty). Abundance differences were predicted using a hurdle model approach (by combining estimates from separately-fitted occurrence and zero-truncated abundance models; see Figure S2.3, Table S2.6, Methods). The inset table shows per-order numbers of species in the dataset (between 8% and 35% of total described species in each order), known zoonotic hosts (prior to bootstrap), and sampled sites.

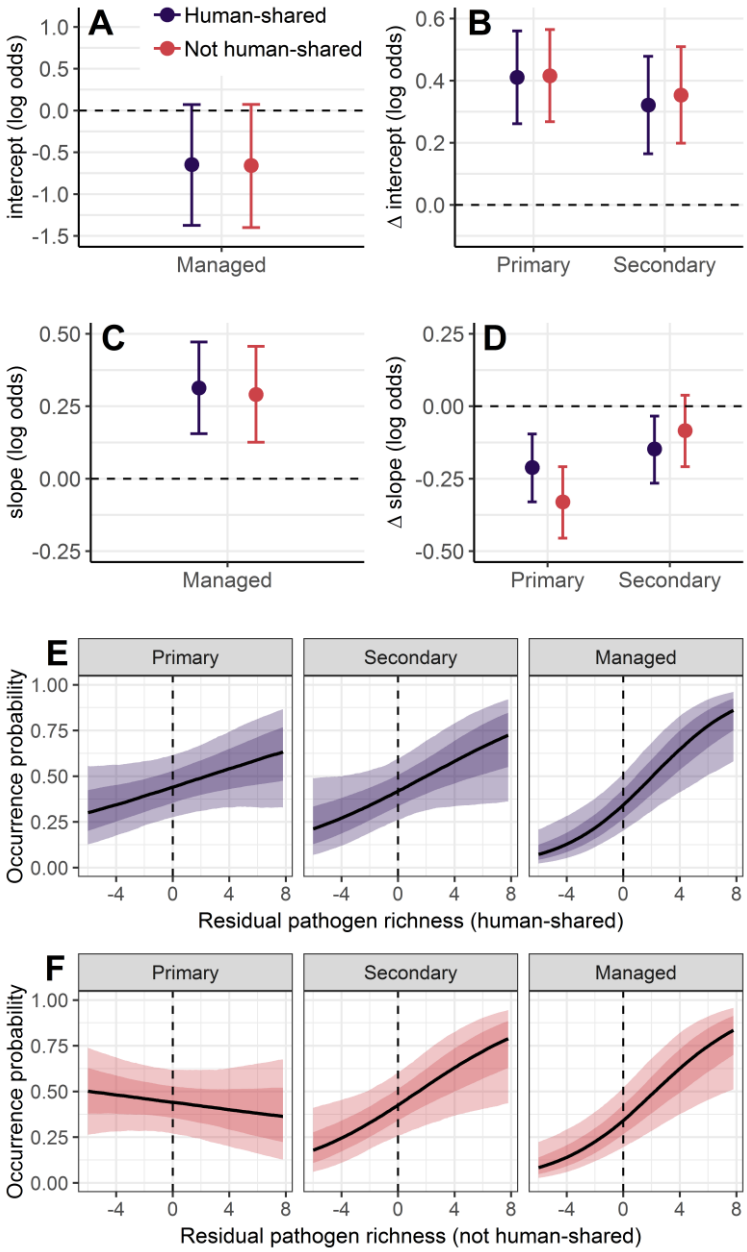

Figure 2.5: Effects of land use on the relationship between mammal species pathogen richness and occurrence probability. Points and error bars show the intercept (A-B) and slope parameters (C-D) of the relationship between residual pathogen richness (scaled to mean 0, sd 1) and mammal species occurrence probability on the linear predictor (log-odds) scale (median ± 95% credible interval). Intercept parameters represent the average occurrence probability of a species with residual pathogen richness of 0 (i.e. with average pathogen richness given research effort and taxonomy), and slope parameters represent the change in occurrence probability for one scaled unit (standard deviation) increase in residual pathogen richness (Figure S2.4). Intercept and slope parameters for primary and secondary land measure the differences relative to managed land (i.e. delta-intercept or delta-slope; B, D). Plotted lines show these relationships on the probability scale (E-F), showing the median (black line), 67% (dark shading) and 95% (light shading) credible interval, based on 000 samples from the approximated joint posterior. Full model summaries and results of sensitivity analyses are in Table S2.7.

2.4. Materials and Methods

I combined a global database of ecological assemblages (Projecting Responses of Ecological Diversity In Changing Terrestrial Systems, PREDICTS) (Hudson et al., 2017) with data on host-pathogen and host-parasite associations, to create a global, spatially-explicit dataset of local zoonotic host diversity. I define pathogens and parasites (henceforth *'pathogens'*) as including bacteria, viruses, protozoa, helminths and fungi (excluding ectoparasites). PREDICTS contains species records compiled from 666 published studies that sampled local biodiversity across land use type and intensity gradients, allowing global space-for-time analysis of land use effects on local species assemblages (i.e. comparison between sites with natural vegetation considered to be a baseline). I analysed relative differences in wildlife host community metrics (zoonotic host species richness and abundance) between undisturbed (primary) land and nearby sites under varying degrees of anthropogenic disturbance. I subsequently conducted further analyses to examine how host species responses to land use vary across different mammalian and avian orders, and to test whether mammal pathogen richness (including both human and non-human pathogens) covaries with tolerance to land use.

2.4.1. Datasets

Ecological community and land use data. Each of the >3.2 million records in PREDICTS is a per-species, per-site measure of either occurrence (including absences) or abundance, alongside metadata on site location, land use type and use intensity. The database provides as representative a sample as possible of local biodiversity responses to human pressure, containing 47,000 species in a taxonomic distribution broadly proportional to the numbers of described species in major terrestrial taxonomic groups (Hudson et al., 2017). I first pre-processed PREDICTS following previous studies (Newbold et al., 2015): records collected during multiple sampling events at one survey site (e.g. multiple transects) were combined into a single site record, and for studies whose methods were sensitive to sampling effort (e.g. area sampled), species abundances were adjusted to standardise sampling effort across all sites within each study, by assuming a linear relationship between sampling effort and recorded abundance measures (both following (Newbold et al., 2015)). My analyses of species occurrence and richness are therefore based on discrete count data, whereas abundances are pseudo-continuous (counts adjusted for survey effort). Due to the multi-source structure of PREDICTS (multiple studies with differing methods and scope), the absolute species richness and abundance measures are non-comparable between studies (Hudson et al., 2017), so these analyses necessarily measure relative differences across land use classes.

Host-pathogen association data. I compiled animal host-pathogen associations from several source databases, to provide as comprehensive a dataset as possible of zoonotic host species and their pathogens: the Enhanced Infectious Diseases (EID2) database (Wardeh et al., 2015); the Global Mammal Parasite Database v2.0 (GMPD2) which collates records of parasites of cetartiodactyls, carnivores and primates(Stephens et al., 2017); Plourde *et al*.'s reservoir hosts database (Plourde et al., 2017) ; Olival *et al*.'s mammal-virus associations database (Olival et al., 2017); and Han *et al.*'s rodent zoonotic reservoirs database (Han et al., 2015) augmented with pathogen data from the Global Infectious Disease and Epidemiology Network (GIDEON) (Table S2.8). I harmonised species names across all databases, excluding instances where either hosts or pathogens could not be classified to species level. To prevent erroneous matches due to misspelling or taxonomic revision, all host species synonyms were accessed from Catalogue Of Life using 'taxize' v.0.8.9 (Chamberlain and Szocs, 2013). Combined, the dataset contained 20,382 associations between 3883 animal host species and 5694 pathogen species.

Each source database applies different methods and taxonomic scope. EID2 defines associations broadly, based on evidence of a cargo species being found in association with a carrier (host) species, rather than strict evidence of a pathogenic relationship or reservoir status (Wardeh et al., 2015). The other 4 databases were developed using targeted searches of literature and/or surveillance reports, focus mainly on mammals, and provide more specific information on strength of evidence for host status (either serology, pathogen detection/isolation, and/or evidence of acting as reservoir for cross-species transmission). I therefore harmonised definitions of host-pathogen associations across the full combined database. Across all animal taxa I broadly defined associations based on any documented evidence (cargo-carrier or stronger, i.e. including all datasets). Additionally, for mammals only (due to more comprehensive pathogen data availability), I was able to define two further tiers based on progressively stronger evidence: firstly, serological or stronger evidence of infection, and secondly, either direct pathogen detection, isolation or reservoir status. Across all pathogens, I also harmonised definitions of zoonotic status. Each pathogen was classified as *human-shared* if recorded as infecting humans within either one of the source host-pathogen databases or an external human pathogens list collated from multiple sources (Table S2.8). Because the source datasets contain some organisms that infect humans and animals rarely or opportunistically, or that may not strictly be zoonotic (e.g. pathogens with an environmental or anthroponotic reservoir), pathogens were also more specifically defined as *zoonotic agents* (aetiologic agent of a specific human disease with a known animal reservoir) if classed as such in GIDEON, Wertheim *et al.*'s Atlas of Human Infectious Diseases (Wertheim et al., 2012) or Taylor *et al*.'s human pathogens database (Taylor et al., 2001).

Combined datasets of hosts and land use. I combined PREDICTS with the compiled host-pathogen database by matching records by species binomial, and each species record was given a binary classification of 'host' or 'non-host' of human-shared pathogens. I adopted a two-tiered definition of host status, to examine the impact of making more or less conservative assumptions about the likelihood of a species contributing to pathogen transmission dynamics and spillover to humans. Firstly, I defined host status broadly: as any species with an association with at least one human-shared pathogen (as defined above), which for mammals must be based on serological or stronger evidence of infection (henceforth referred to as the *'full dataset'*). 177 studies in PREDICTS contained host species matches (190 mammals, 146 birds, 1 reptile, 2 amphibians, 37 invertebrates, listed in Table S2.1). Secondly, since mammals are the predominant reservoirs of both endemic and emerging zoonotic infections due to their phylogenetic proximity to humans (Han et al., 2016; Rottingen et al., 2017), I also defined mammal species as zoonotic reservoir hosts based on stricter criteria: an association with at least one zoonotic agent (as defined above) which must be based on direct pathogen detection, isolation or confirmed reservoir status (henceforth referred to as *'mammal reservoirs subset'*). Within PREDICTS, 63 studies contained host matches based on this narrower definition (143 mammal reservoir hosts; Table S2.1).

Prior to analysis, I filtered PREDICTS to include only studies that sampled taxa relevant to zoonotic transmission, since the full database includes many studies with a different taxonomic scope (e.g. plants or non-vector invertebrates) (Hudson et al., 2017). I retained all studies that sampled any mammal or bird species, as these groups are the main reservoir hosts of zoonoses. For all other taxa, given that zoonoses and their hosts occur globally, I made the more conservative assumption that studies with no sampled hosts represent false absences (i.e. resulting from study aims and methodology) rather than true absences (i.e. no hosts are present), and only included studies with at least one host match in one sampled site in community models. This resulted in a final dataset of 530,161 records from 6801 sites in 184 studies (full dataset) and 51,801 records from 2066 sites within 66 studies (mammal reservoirs dataset; including mammal studies only) (Figure 2.1). Some host records were of arthropod vectors, but as these are a small proportion of records (around 2%; Table S2.1) I generically refer to all matched species as *'hosts'*. By matching on species binomial I assume that pathogens are equally likely to occur anywhere within their hosts' geographical range; evidence from terrestrial mammal orders suggests that this assumption is reasonable globally (Cooper et al., 2012a; Harris and Dunn, 2010). Although overlooking geographical variation in pathogen occurrence, pathogen geographical distributions are poorly understood and subject to change, making it difficult to define geographical constraints on host status.

I aggregated land use classes in PREDICTS to ensure a more even distribution of sampled sites. I assigned each survey site's land use type to one of four categories: primary vegetation, secondary vegetation, managed ecosystems (plantation forest, pasture and cropland) and urban. Land use intensity was assigned to either minimal, substantial (combining light and intense use), or cannot decide (the latter were excluded from models). Original use intensity definitions (Newbold et al., 2015) reflect gradation of potential human impacts within land use types; for example urban sites range from minimal (villages, large managed green spaces) to high intensity (impervious with few green areas). Land use categories simplify complex landscape processes, so this aggregation might mask subtle differences in disturbance mode and intensity. However, although some local studies have found differences in zoonotic host abundance and pathogen prevalence between different management regimes (Young et al., 2017), there was no *a priori* reason to hypothesise differences between managed ecosystem types globally. Study regions were categorised as temperate or tropical, following (Newbold et al., 2016b).

2.4.2. Statistical analysis

Accounting for species-level differences in pathogen discovery effort. The probability of identifying zoonotic pathogens within a species is strongly influenced by effort, meaning that poorly-studied species could be falsely classified as non-hosts. Since research effort might also positively correlate with species' abundance in anthropogenic landscapes, accounting for this uncertainty is crucial. In statistical models I therefore consider host status (and derived metrics such as host richness) to be an uncertain variable, by assuming that all known hosts in the dataset are true hosts (true positives), and that non-hosts comprise a mixture of true non-hosts and an unknown number of misclassified species. I propagate this uncertainty into all model estimates using a bootstrapping approach, in which each iteration transitions a proportion of non-host species to host status with a probability influenced by research effort and taxonomic group (with poorly-researched species in taxonomic orders known to host more zoonoses having the highest transition rates; Figure 2.2, Text S2.1).

I estimate disease-related research effort using species publication counts extracted from the PubMed biomedical database (1950–2018) for every species within the dataset (n=7285; Figure 2.2c), following other studies in disease macroecology in which publication effort often explains much of the variation in response variables (Cooper et al., 2012b; Olival et al., 2017). Across 100 randomly-sampled mammal species from PREDICTS, PubMed publication counts were highly correlated to those from Web of Science and Google Scholar (both Pearson *r*

= 0.93), indicating robustness to choice of publications database. Using publication counts directly to index species misclassification probability is problematic, since the relationship between publication effort and host status is both nonlinear (e.g. due to positive feedback, where pathogen detection drives increasing research towards a species or taxon) and taxon-specific (e.g. because some taxa are more intensely targeted for surveillance). I therefore calculate a trait-free approximation of false classification probability for non-host species (detailed in Text S2.1) by assuming, first, that a species' relative likelihood of being a zoonotic host is proportional to the number of known hosts in the same taxonomic order (i.e. a poorly-studied primate is more likely to be a zoonotic host than a poorly-studied moth), and second, that confidence in non-host status accrues and saturates with increasing publication effort (following the cumulative curve of publication effort for known hosts within the same order; Figure 2.2a-b). Therefore, under-researched mammals, followed by birds, have the highest estimated false classification probabilities, but with substantial variation among mammalian and avian orders (Figure 2.2d-e).

Since data constraints prevent direct observation of how host detections accrue with discovery effort, this trait-free approximation leverages current knowledge of the distribution of zoonotic hosts and publication effort across broad taxonomic groups, and thus might over- or underestimate absolute host potential in any particular species. For example, because species traits and research effort are autocorrelated, the assumption that all non-host species per taxonomic group are equally likely to host zoonoses may conservatively overestimate host potential in less-researched species: many ecological traits that make species more likely to be poorly-studied (e.g. lower population density, smaller range size (Ducatez and Lefebvre, 2014; González-Suárez et al., 2012)) would often be expected to reduce their relative importance in multi-host pathogen systems (Paull et al., 2012). Nonetheless, my approach is sufficient to address the study's main confounding factor, i.e. the potential for biased distribution of research across land use types and biomes globally.

Community models of host species richness and total abundance. All modelling was conducted using mixed-effects regression in a Bayesian inference framework (Integrated Nested Laplace Approximation (INLA) (Lindgren and Rue, 2010; Rue et al., 2009). I aggregated ecological communities data to site-level by calculating the per-site species richness (number of species) and total abundance (total number of sampled individuals, adjusted for survey effort) of host and non-host species. Land use type and intensity were combined into a categorical variable with 8 factor levels (type+intensity, for 4 types and 2 intensity levels). During model selection I considered fixed effects for land use and log-transformed 2015 human population density

extracted from CIESIN (because synanthropic species diversity might respond to changes in human population density independently of land use; Figure S2.5). All models included random intercept for study to account for between-study variation, and I additionally considered random intercepts for spatial block within study (to account for the local spatial arrangement of sites), site ID (to account for overdispersion caused by site-level differences) (Newbold et al., 2015) and biome (as defined in PREDICTS).

I modelled the effects of land use on the richness and total abundance of host and non-host species separately, using a Poisson likelihood (log-link) to model species richness (discrete counts). Since abundance data were continuous following adjustment for survey effort, I followed other PREDICTS studies (Newbold et al., 2015) and modelled log-transformed abundance with a Gaussian likelihood; log-transformation both reduces overdispersion and harmonises interpretation of the fixed effects with the species richness models (i.e. both measure relative changes in geometric mean diversity from primary land under minimal use). I also modelled the effects of land use on host richness and abundance as a proportion of overall site-level sampled species richness or abundance, by including log total species richness as an offset in Poisson models, and log total abundance as a continuous fixed effect (effectively an offset) in abundance models.

For each response variable I first selected among candidate model structures, comparing all combinations of random effects with all fixed effects included, and subsequently comparing all possible fixed effects combinations using the best-fitting random effects structure. In all cases I selected among models using the Bayesian pointwise diagnostic metric Watanabe-Akaike Information Criterion (WAIC) (Hooten and Hobbs, 2015) (Tables S2.3-S2.4). The final models were subsequently checked for fit and adherence to model assumptions, including testing for spatial autocorrelation in residuals (Figure S2.6). I then bootstrapped each final model for 1000 iterations to incorporate research effort. For each iteration, each non-host species was randomly transitioned to host status as a Bernoulli trial with success probability p equal to estimated false negative probability (as described above; Text S2.1, Figure 2.2), all community response variables were recalculated, the model was fitted and 2500 samples were drawn from the approximated joint posterior distribution. I then calculated posterior marginal parameter estimates (median and quantile ranges) across all samples from the bootstrap ensemble (Figure 2.3, Table S2.5). Between 90 and 150 non-host species (median 121) were selected to transition per iteration, increasing the total number of hosts by 24–40% (median 32%; Figure 2.2f). Because study coverage is heterogeneous globally, I subjected the full model ensembles to random and geographical cross-validation (Figure S2.1). I also conducted the

same modelling procedure using only the strictly-defined mammal reservoirs subset (Figure S2.2).

Species-level estimates of land use effects on mammalian and avian zoonotic hosts. Because aggregate community diversity metrics may mask important variation between taxonomic groups, I separately modelled the average effects of land use type on the occupancy and abundance of all hosts and non-hosts of zoonotic agents within five mammalian (Carnivora, Cetartiodactyla, Chiroptera, Primates, Rodentia) and two avian orders (Passeriformes, Psittaciformes). For mammals I defined zoonotic host status strictly (pathogen detection, isolation or confirmed reservoir status, as described above) and excluded urban sites due to sparse urban sampling for mammals in PREDICTS (only 2 studies). All models included an interaction term between land use type and zoonotic host status (host or non-host) and random intercepts for each species-study combination and for taxonomic family (to account for gross phylogenetic differences). I again accounted for variable research effort per species as described above, fitting 500 models per order, and calculating posterior marginal estimates across samples drawn from the whole ensemble (Table S2.6).

Abundance data were overdispersed and zero-inflated due to the high proportion of absence records (i.e. sites where species were not found despite being sampled for). I therefore used a hurdle model-based approach (Zuur et al., 2010) to estimate effects of land use on abundance, by separately fitting occurrence models (presence-absence; binomial likelihood, logit-link) to the complete dataset for each mammalian order, and zero-truncated abundance models (ZTA, log-abundance with Gaussian likelihood) to the dataset with absences removed (Figure S2.3). Mean differences in abundance across land uses are then calculated as the product of the proportional differences in predicted occurrence probability and ZTA relative to primary land (Zuur et al., 2010). I used posterior samples from paired occurrence (transformed to probability scale) and ZTA models (transformed to linear scale) to calculate a distribution of hurdle predictions separately for each bootstrap iteration (i.e. with the same non-hosts reclassified). I then summarised predicted changes per land use type across samples from the entire bootstrap ensemble (median and quantile ranges; Figure 2.4). Due to the complex nested structure of PREDICTS, the hurdle predictions assume independence between occurrence and ZTA processes (Zuur et al., 2010), so do not formally account for the possibility of covariance at random effects (species or family) level. For clarity, I therefore also show the contributions of each separate model for each order (Figure S2.3, Table S2.6). In most orders, and when fitting models across all mammal species, land use often appears to act most consistently on species

occurrence, with more variable effects on ZTA, suggesting that the independence assumption may be broadly reasonable at this global and cross-taxa scale.

Relationship between pathogen richness and responses to land use across mammal species. Pathogen richness (the number of pathogens hosted by a species) is a widely-analysed trait in disease macroecology, with both overall pathogen richness, shared pathogen richness (i.e. number of pathogens shared between focal species) and zoonotic pathogen richness often correlated to species traits such as intrinsic population density, life history strategy and geographic range size (Dallas et al., 2018; Johnson et al., 2012; Kamiya et al., 2014; Olival et al., 2017). If human-disturbed landscapes systematically select for species trait profiles that facilitate host status, we might expect to observe positive responses to land use in species with higher richness of either human-shared or non human-shared pathogens (Young et al., 2013). I tested this hypothesis for mammals, due to availability of much more comprehensive pathogen data than for other taxa, by analysing the relationship between species pathogen richness and probability of occurrence across three land use types (primary, secondary and managed; urban sites excluded due to limited sampling).

Within the subset of PREDICTS studies that sampled for mammals, containing 26,569 records of 546 mammal species (1950 sites, 66 studies), I used the host-pathogen association dataset to calculate, firstly, each mammal species' richness of human-shared pathogens, and secondly its richness of pathogens with no evidence of infecting either humans or domestic animals (*'non human-shared'*), defining associations based on serological evidence or stronger. Of the 546 mammals, 190 species had at least one known human-shared pathogen (human-shared pathogen richness mean 1.92, sd 6.07) and 96 species had at least one non human-shared pathogen (non human-shared pathogen richness mean 0.81, sd 4.16). I account for research effort differently than in the binary host status models above, since pathogen richness is a continuous variable that is influenced by magnitude of effort (i.e. more effort would be expected to increase the number of detected pathogens; Figure S2.4b). Therefore, I account for effort by estimating per-species residual pathogen richness not explained by publication effort (i.e. the difference between observed pathogen richness and expected pathogen richness given publication effort and taxonomic group). To do this, I modelled the effect of publication effort on pathogen richness (discrete counts) separately for human-shared and non human-shared pathogens, using a Poisson likelihood with a continuous fixed effect of log-publications and random intercepts and slopes for each mammalian Order and Family (to account for broad taxonomic differences in host-pathogen ecology between orders (Olival et al., 2017)). I fitted the model to data from all mammal species in the host-pathogen database (n=780) and predicted

expected mean pathogen richness for all mammals in PREDICTS. We calculated residuals from observed values for these species (Figure S2.4), which I expect represent trait-mediated variation, given the evidence that mammal pathogen richness covaries with species traits after accounting for phylogeny and research effort (Olival et al., 2017).

I then modelled the relationship between residual pathogen richness (scaled to mean 0, sd 1) and species probability of occurrence across land use types, separately for human-shared and non-human-shared pathogens (Figure 2.5). Species occurrence was modelled using a binomial (logit-link) likelihood, with fixed effects for the interaction between residual pathogen richness and land use type, and random intercepts for species, order, study and spatial block within study. As with prior analyses, models were checked for fit and adherence to assumptions. Pathogen surveillance in animals is often focused on species of zoonotic concern, meaning that pathogen inventories (especially of non-human-shared pathogens) may be more complete for some taxonomic groups than others. I therefore tested model sensitivity to separately fitting models containing, firstly, only species from the four most comprehensively-sampled mammalian orders for parasites and pathogens (Primates, Cetartiodactyla, Perissodactyla and Carnivora; the focal taxa of the Global Mammal Parasite Database (Stephens et al., 2017)), and secondly, species from all other mammal orders. I also tested for sensitivity to uncertainty in the publications-pathogen richness relationship, by separately fitting the land use model to 400 sets of residuals derived using posterior samples from the fitted publication effort model (Figure S2.4g-h), and summarising parameters across the full ensemble. Fixed effects directions and strength of evidence were consistent across all models (Table S2.7). Data processing and analyses were conducted in R v. 3.4.1 (R Core Team, 2017), with model inference conducted using R-INLA (http://r.inla.org) (Lindgren and Rue, 2010; Rue et al., 2009).

2.4.3. Data availability

All code and data used in this chapter (where not freely available online) are archived at Figshare (doi: 10.6084/m9.figshare.7624289), and data sources are fully listed in Table S2.8.

Chapter 3:
Understanding the ecology, epidemiology and environmental drivers of Lassa fever in West Africa.

The rest of the thesis focuses on a case study disease, Lassa fever, a rodent-borne viral haemorrhagic fever that is a growing public health concern in West Africa. In this chapter, I review and synthesise the current state of knowledge on the ecology, epidemiology and surveillance of Lassa fever, to ask: what is the current evidence of the ecological factors linked to LF transmission, and what are the key knowledge gaps from the perspective of improving our ability to forecast disease risk and design interventions?

3.1. Abstract

Lassa fever (LF), a rodent-borne viral haemorrhagic fever, is gaining recognition as an important endemic disease with severe impacts on some of West Africa's poorest communities. Despite growing attention from global health institutions and several recent, high-profile surges in human cases, our knowledge of LF ecology, epidemiology and distribution is limited. This is a barrier to both short-term disease forecasting and prevention, and longer-term prediction of how future environmental changes in West Africa may affect Lassa virus (LASV) transmission dynamics between the rodent reservoir host (*Mastomys natalensis*) and people. Here, I synthesise current knowledge of LF ecology and epidemiology to show that extrapolations from past research have produced an incomplete picture of the disease's true incidence and distribution, with negative consequences for policy planning, medical treatment and management interventions. Although the recent increase in LF case reports is likely an artefact of improved diagnostics and surveillance, recent studies indicate that socio-ecological changes in West Africa may drive increases in LF burden this century. Future research to understand this cryptic disease should focus on understanding its geographical distribution, disease burden and spatial and seasonal drivers, with the aim of improving the integration of LF into public policy and disease control strategies.

3.2. Introduction

Lassa fever is an acute and occasionally severe rodent-borne viral haemorrhagic fever, with cases in humans geographically constrained to sub-Saharan West Africa. Discovered in 1969, Lassa fever (LF) is endemic to much of rural Nigeria and the countries of the Mano River Union (Sierra Leone, Guinea and Liberia; MRU) (Richmond and Baglole, 2003). International interest in Lassa virus (LASV) has often focused on global health security, since its long incubation period (usually 7-10 days) makes it one of the most commonly exported viral haemorrhagic fevers (VHFs) to countries outside its endemic range (Brosh-Nissimov, 2016). As a result, LASV is now classified as a Select Agent by the US Federal Select Agent Program, requiring Biosafety Level-4 conditions for laboratory study (US Department of Health and Human Services, 2016). In contrast, its contribution to the burden of disease in West Africa has historically been under-appreciated, despite suggestions that it causes considerable annual morbidity and mortality in some of Africa's poorest communities (McCormick et al., 1987b; Richmond and Baglole, 2003). Awareness of LF as a public health issue is increasing, especially following the 2013-16 Ebola virus disease (EVD) epidemic in the MRU, which has galvanized national and international agencies' attempts to improve the prediction of and response to disease outbreaks in West Africa. In 2015, the World Health Organisation listed LF among priority diseases requiring urgent research and development attention (WHO, 2017a). In response, LASV was made a priority for vaccine development funding by the multi-agency Coalition for Epidemic Preparedness Innovations (CEPI), alongside several other emerging viruses (Rottingen et al., 2017).

Despite growing interest in LF, our knowledge of its ecology, epidemiology and distribution in West Africa is limited. For decades, disease surveillance has piggy-backed on biomedical research projects based in districts where LF is already recognized as a problem. However, previous seroprevalence studies have suggested high numbers of undiagnosed infections in non-endemic areas (Akoua-Koffi et al., 2006; Emmerich et al., 2006; Sogoba et al., 2016) and, in recent years, official incidence reports have seen a substantial increase in the number and geographical extent of cases, which suggests that the true incidence and spatial distribution of the disease may be underestimated (Figure 3.1). Since this chapter was originally written and published in 2017 (Gibb et al., 2017), several sequential years of very high reported caseloads in Nigeria across increasingly large areas of the country (2018-2020; see Chapter 4), have raised further questions about the true extent of LF incidence and burden (Dan-Nwafor et al., 2019; Elsie A. Ilori et al., 2019). This lack of understanding is a barrier to effective

interventions and policy, such as the targeting of future vaccines towards communities at greatest risk, prioritization in health planning and assessments of global health security.

In this chapter, I therefore synthesize current knowledge of the ecology and epidemiology of LF to address several questions with relevance for disease management. Firstly, what are the key knowledge gaps and research priorities with implications for LF control and prevention? Secondly, what is the current understanding of the distribution of LASV in West Africa, and what are the possible reasons for the recent geographical expansion in LF case reports? Thirdly, how might projected socio-ecological changes impact the incidence and distribution of LF in the coming decades? Much of West Africa is experiencing rapid demographic and environmental shifts that may profoundly affect the transmission dynamics of many important zoonotic diseases (Wallace et al., 2014; Wilkinson, 2016). Within LF-endemic countries these changes are occurring in societal contexts of high levels of poverty, recent civil conflict, and poor access to healthcare, which increase the complexity of prevention and management of LF and other diseases such as malaria, cholera, yellow fever and EVD (Bardosh et al., 2016; Kelly et al., 2013). There is thus a clear need for better integrated knowledge of the drivers of cross-species LASV transmission, to facilitate disease forecasting and inform interventions that will reduce infection risk in affected communities (Scoones et al., 2017; Wilkinson, 2016).

3.3. Disease and diagnosis

In humans LASV causes a wide spectrum of disease manifestations, ranging from asymptomatic infections to acute and severe disease. Onset of acute LF is gradual and nonspecific, often beginning with intermittent fever and malaise followed by myalgia, sore throat, facial oedema and severe headache (Bausch et al., 2001; McCormick et al., 1987a). Recovery begins eight to ten days after onset, while fatal cases progress to shock, organ failure and death, sometimes with haemorrhagic manifestations (see (Yun and Walker, 2012) for a recent review of the pathogenesis of LF). However, haemorrhagic signs are often absent, and less common in LF compared to New World arenaviral fevers (Bausch et al., 2001; McCormick et al., 1987a; Paessler and Walker, 2013). Pregnancy is generally recognized as a risk factor associated with increased LF-related mortality (Price et al., 1988; Shaffer et al., 2014). Permanent or temporary sensorineural hearing loss is a common sequela, affecting up to an estimated 25% of all convalescent LF patients (Cummins et al., 1990). Most LASV infections are mild or subclinical; sampled human populations with high LASV seroprevalence and seroconversion rates often report much lower incidence of LF-like febrile disease, suggesting

regular viral exposure but relatively few acute cases (Bausch et al., 2001; Kernéis et al., 2009; McCormick et al., 1987b; O'Hearn et al., 2016; Sogoba et al., 2016). The reasons for this variation in pathogenesis are unknown, although proposed mechanisms include variation in LASV strain virulence (Bowen et al., 2000; Sogoba et al., 2016, 2012), and differences in genetic susceptibility to LASV infection between human populations (Andersen et al., 2012). At the time of writing (2017) there is currently no available LF vaccine, and although several candidate vaccines have been developed to various stages, no human trials have occurred to date (Grant-Klein et al., 2011; Zapata et al., 2014). However, this may change in the near future with the recent prioritisation of LASV by CEPI alongside ongoing research into LF vaccine design (Hastie et al., 2017; Rottingen et al., 2017).

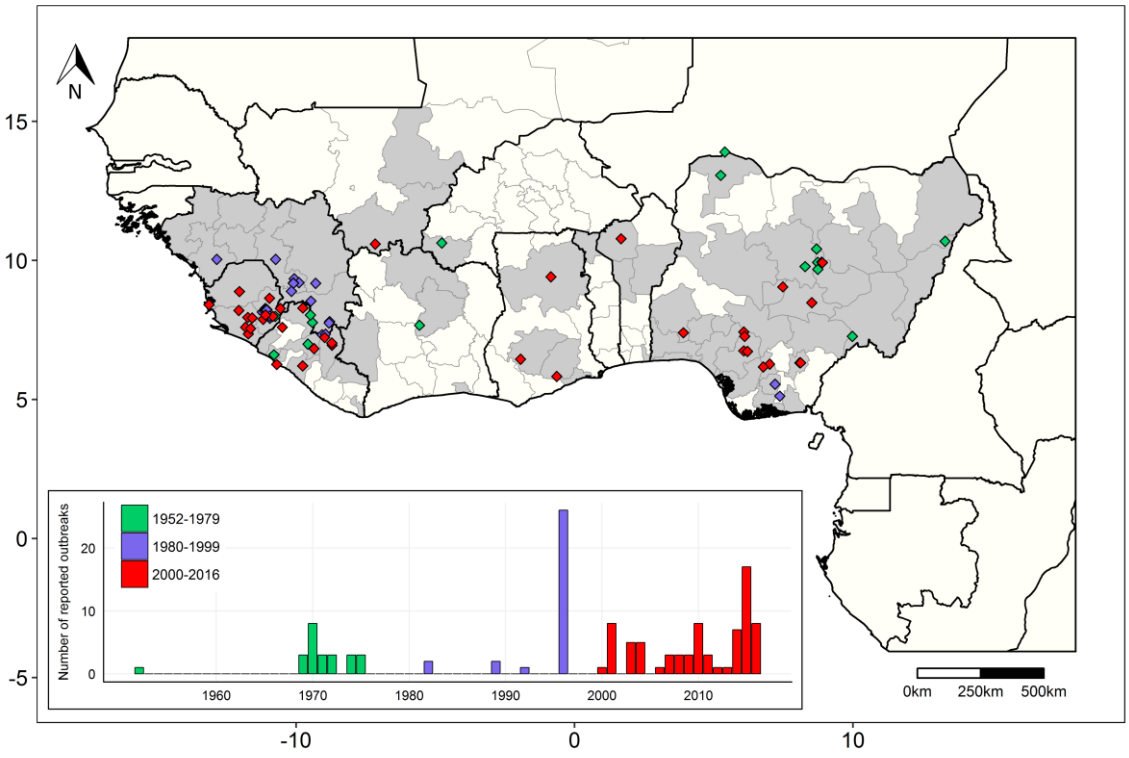

Figure 3.1: The known distribution and reported history of Lassa fever and Lassa virus in West Africa. Points on the map represent human LF outbreak reports in West Africa (both suspected and confirmed) from 1952-2016 with a confirmed geographical locality (n=102) (colored per time period). Each point represents a separately reported cluster of cases from either a research publication or surveillance report, which may span multiple years of surveillance. Grey shading represents sub-national administrative regions with evidence of LASV or a LASV-like arenavirus in either humans or rodents. Inset shows a bar chart of per-year LF outbreak reports (both with and without a confirmed geographical locality, n=129), with each denoted by its reported start year. The full dataset with additional information on data sources and evidence criteria is provided in supplementary data for this chapter.

One major barrier to LF research is the difficulty of diagnosis based on clinical signs and symptoms alone. Early-stage LF presents similarly to other febrile illnesses (e.g. malaria, typhoid fever, EVD) (Bausch et al., 2001), and LF is often only suspected after development of haemorrhagic symptoms in the late stages of disease. Milder cases in the community therefore often go unrecognized and unreported, with only severely ill people referred for LF testing and treatment (Shaffer et al., 2014). Most health facilities in West Africa have limited access to laboratory testing to confirm diagnosis of LF (Schroeder and Amukele, 2014), which requires either viral detection by RT-PCR, antibody or antigen detection by enzyme-linked immunosorbent assay (ELISA), or viral isolation (recently reviewed in (Raabe and Koehler, 2017)). The lack of easily-accessible diagnostics for LF has implications for medical treatment since it may delay the commencement of ribavirin therapy, which is most effective when administered during early stage disease (McCormick et al., 1986; Shaffer et al., 2014). Lack of diagnostics has also resulted in under-reporting of LF cases, and a geographical bias in LF detections nearby to established laboratories, such as the dedicated Lassa Fever Ward at Kenema General Hospital, Sierra Leone (KGH) and the Institute of Lassa Fever Research and Control at Irrua Specialist Teaching Hospital, Nigeria (Asogun et al., 2012; Gire et al., 2012; Khan et al., 2008).

The consequence of under-reporting has been to confound understanding of the incidence, geographical distribution and mortality of LF. Annual case estimates are often cited as 100,000-300,000 LASV infections and around 5000 deaths per year across West Africa, but these are extrapolations from one longitudinal study in Sierra Leone in the 1980s (McCormick et al., 1987b), and have not been subsequently adjusted for population increases or improvements in diagnostic sensitivity and specificity. Other studies have confirmed that LF is a significant contributor to infectious disease burden in hyper-endemic areas of Nigeria and the MRU (Bausch et al., 2001; O'Hearn et al., 2016), but its incidence across West Africa remains poorly understood. Under-reporting of milder cases may also be one reason for the marked contrast in reported case fatality rates between community and clinic, which vary from 2% in the community to over 60% in hospital settings (Bausch et al., 2001; McCormick et al., 1987a; Shaffer et al., 2014). Despite growing interest in LF from a public health perspective, these knowledge gaps have to date precluded formal quantitative assessments of the total burden of LF and LF-associated sequelae. With diagnostic tests improving, longitudinal studies are needed throughout tropical West Africa to characterise the spectrum of infection severity and assess the disease's true incidence and burden. This would be an important step towards shifting the global health narrative often associated with LF away from biosecurity (Wilkinson, 2016), and

towards a more nuanced understanding of LF as a neglected endemic disease and significant public health concern.

3.4. Ecology, epidemiology and transmission of Lassa virus

3.4.1. Reservoir host ecology and epidemiology

Lassa virus is a single-stranded RNA virus (Family: *Arenaviridae*) which, similarly to most other arenaviruses, is primarily associated with a single rodent reservoir host species. The LASV reservoir host, the Natal multimammate rat *Mastomys natalensis* (Monath et al., 1974), is one of the most widespread rodent species in sub-Saharan Africa (Granjon, 2016) and its presence is a major spatial predictor of human LF risk (Redding et al., 2016). In West Africa, *M. natalensis* is abundant in rural human homes, surrounding agricultural fields and gardens, occurring at much lower densities in forested and urban areas (Borremans et al., 2011; Demby et al., 2001; Fichet-Calvet et al., 2008, 2007; Makundi et al., 2007). The high likelihood of human-host contact results in regular spillover and endemic disease in rural areas where LASV is maintained in the rodent population (Figure 3.2), which is in contrast with many VHFs that occur in sporadic outbreaks such as EVD and yellow fever. LF is primarily a rural disease, with very few cases originating from large urban areas (Richmond and Baglole, 2003). This may be due to the low abundance of *M. natalensis* in heavily built-up environments, possibly because of competitive interactions with invasive rodent communities (especially *Rattus rattus* and *Mus musculus*) and increased use of concrete for houses and streets in urban areas (Demby et al., 2001; Garba et al., 2014).

There has been extensive research into *Mastomys natalensis* population ecology, motivated by the species' status as both major agricultural pest and reservoir of several important human diseases, including plague (*Yersinia pestis*), bartonellosis (*Bartonella spp.*), leishmaniasis (*Leishmania* spp.) and leptospirosis (*Leptospira* spp.) (Halliday et al., 2015b; Katakweba et al., 2012; McCauley et al., 2015). However, the ecology and epidemiology of LASV in *M. natalensis* is complex and not well understood. Most evidence comes from long-term research projects in Guinea (West Africa), where LASV is endemic, and Tanzania (East Africa), where *M. natalensis* populations host other arenaviruses including Morogoro virus (MORV) and Gairo virus (GAIV) (Borremans et al., 2011; Fichet-Calvet et al., 2016, 2007; Gryseels et al., 2015). The latter two viruses are closely related to LASV but non-pathogenic to humans, and as such are potentially useful model systems for understanding arenavirus ecology in this species. In both regions, *M. natalensis* shows seasonal population dynamics that are linked to trends in

rainfall. Although capable of breeding all year round, the rainy season is associated with higher fecundity and peaks in recruitment, which may be linked to crop maturation and increased food availability, and population crashes often occur in the dry season (Fichet-Calvet et al., 2008; Makundi et al., 2007). These dynamics appear to be less strongly pronounced in studies from Guinea, where *M. natalensis* is found at highest densities inside houses and in proximal cultivated areas (Fichet-Calvet et al., 2007) than in many trapping studies conducted in Tanzanian agricultural and mosaic landscapes (Makundi et al., 2007). Evidence from both laboratory and field studies suggests that LASV, MORV and GAIV are minimally pathogenic in *M. natalensis*, consistent with long-term coevolution for persistence in strongly fluctuating reservoir host populations (Mariën et al., 2017b; Walker et al., 1975).

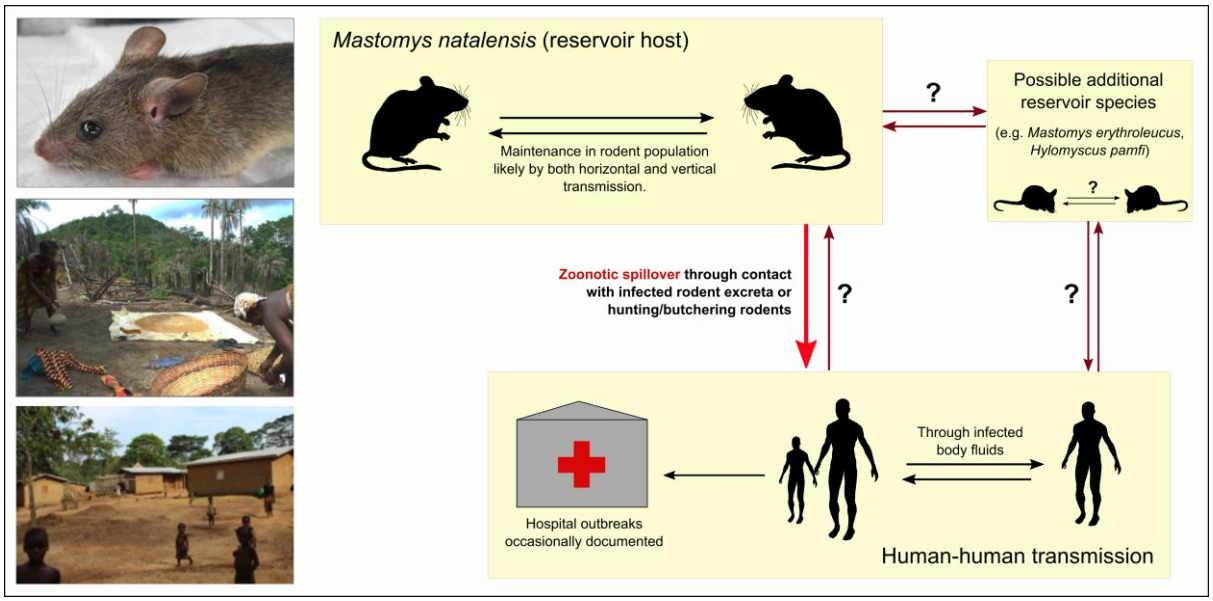

Figure 3.2: Transmission ecology of Lassa virus in rodents and humans. The primary reservoir host, the Natal multimammate rat (*Mastomys natalensis,* pictured top left), is a synanthropic species that is widespread throughout rural sub-Saharan West Africa. Other putative rodent reservoir species have been identified, but there is currently little data on LASV prevalence within these populations or routes of transmission to people. It is unknown whether and how often human-to-rodent transmission occurs (photographs © A. Wilkinson).

The mechanisms of LASV transmission in wild rodent populations are unclear. Several studies have proposed an important role of LASV transmission from mothers to offspring (vertical transmission). For example, *Mastomys* neonates experimentally infected with LASV or MORV develop chronic infections with persistent viral shedding (Borremans et al., 2015; Walker et al., 1975). However, although laboratory studies can shed light on the biological plausibility of transmission mechanisms, their capacity to adequately represent predominant and critical modes of transmission under natural conditions may be more limited (Mariën et al., 2017a). Field research suggests that the main mode of LASV and MORV transmission in wild rodents is

between individuals of the same generation (horizontal transmission), leading to short duration infection with transient viral shedding (Fichet-Calvet et al., 2008). Evidence for horizontal transmission includes a positive relationship between age and viral antigen prevalence (an indicator of active infection) in juvenile rats (Fichet-Calvet et al., 2008), and also positive correlations between rodent age and antibody seroprevalence, indicating increasing likelihood of exposure with age (Demby et al., 2001; Fichet-Calvet et al., 2014; Mariën et al., 2017b). Horizontal transmission routes are poorly understood, but there is indirect evidence for a role of rodent behaviour. For example, seroprevalence data from Tanzania suggest that MORV transmission may be density-independent (Borremans et al., 2011) and that sexual behaviour may be involved in GAIV transmission (Mariën et al., 2017b).

Overall, the current evidence suggests that most transmission in wild rodents is horizontal, but that a smaller amount of vertical transmission (leading to chronic infections) may contribute to viral persistence in the population (Borremans et al., 2011; Fichet-Calvet et al., 2014, 2008). The highest proportion of live LASV and MORV infections (indicated by presence of viral RNA or antigen) is often found in young animals (Borremans et al., 2011; Fichet-Calvet et al., 2008), suggesting that the rapid influx of susceptible juveniles during rainy season peaks in recruitment may be a driver of documented seasonal fluctuations in rodent LASV seroprevalence (Demby et al., 2001; Fichet-Calvet et al., 2007). Understanding these dynamics is not merely of ecological interest, since trends in rodent LASV prevalence may drive spatiotemporal variation in the force of zoonotic infection to humans. Uncertainty regarding LASV transmission in rodent populations is a key knowledge gap that could inform, for example, optimal rodent control and LF prevention regimes in endemic areas.

One factor that may limit the usefulness of MORV and GAIV as ecological models for LASV is their seemingly low host plasticity. To date both viruses have only been found in *M. natalensis* and are non-pathogenic to humans (Gryseels et al., 2017). In contrast, evidence of LASV infections is regularly detected in other rodents, including *R. rattus* and *M. musculus*, although these appear to be transient hosts (Demby et al., 2001). The picture of LASV ecology has also been complicated by the recent identification of two other putative LASV reservoir hosts, *Hylomyscus pamfi* and *Mastomys erythroleucus* (Olayemi et al., 2016a). LASV-seropositive *M. erythroleucus* have been trapped in regions where *M. natalensis* is absent but seropositivity is documented in humans, suggesting that this species may be involved in zoonotic transmission (Olayemi et al., 2016a). This highlights the need for further work to fully understand the spectrum of reservoir and transient hosts, and identify where other species than *M. natalensis* may be involved in LASV persistence in the reservoir community.

3.4.2. Zoonotic transmission dynamics and human epidemiology

The routes of LASV zoonotic spillover are poorly understood. Similarly to other arenaviruses and hantaviruses, human LASV infections are thought to mostly occur via contact with infected rodent excreta, such as through contaminated food and inhalation of aerosols from dried urine or droppings (Figure 3.2) (McCormick et al., 1987b; Ter Meulen et al., 1996). Most contact probably occurs in houses, gardens and fields, where rodent densities are highest (Bonwitt et al., 2017a; Dzingirai et al., 2016; Grant et al., 2016). However, the routes of LASV infection have not been definitively established; for example, to date there has been no testing of environmental samples to identify highest risk rodent-human interfaces (e.g. houses, fields) and to understand the conditions that facilitate persistence of LASV in the external environment. Hunting and butchering of rodents has been shown to be associated with increased risk of LF-like febrile disease (Ter Meulen et al., 1996), although the evidence remains inconclusive, with other studies finding no significant relationship between rodent hunting and butchering and LASV IgG prevalence (Kernéis et al., 2009). The relative risk of infection through butchering may also be affected by preferences for eating particular rodent species. For example, in areas of Sierra Leone, rodents captured from fields, where *M. natalensis* often occurs at lower densities, are more likely to be butchered and eaten than rodents captured in villages (Bonwitt et al., 2016). It is also unknown what modes of contact, such as direct contact with rodent blood or inhalation of urine-contaminated dust particles, are associated with higher risk of virus transmission. Several social factors are also associated with LF risk, including housing quality, evidence of rodent burrows in houses, and high human densities in homes (Bonner et al., 2007).

Like many endemic tropical diseases, LASV spillover dynamics emerge from complex interactions between multiple human and environmental factors (Grant et al., 2016). In rodents such factors may include seasonal population and viral transmission dynamics (Demby et al., 2001; Fichet-Calvet et al., 2008; Makundi et al., 2007) and behaviour such as consumption of food in people's homes (Fichet-Calvet et al., 2007), and in people may include variation in rodent consumption (Bonwitt et al., 2016), land use practices (Grant et al., 2016; Kamara et al., 2015) and age and gender-related exposure risk (Grant et al., 2016; Shaffer et al., 2014). This complexity presents challenges for risk forecasting and planning interventions, since local social-ecological system dynamics may vary across tropical West Africa. There is strong evidence of seasonal patterns in infection risk, with hospitalized cases peaking during the dry season (Bausch et al., 2001; Lo Iacono et al., 2016; McCormick et al., 1987b; Shaffer et al., 2014), but the drivers of these peaks remain poorly understood. Rainfall is associated with LF risk (Fichet-Calvet and Rogers, 2009), which may relate to the link between rainfall and *M. natalensis*

recruitment and population density (Makundi et al., 2007). In Sierra Leone there is evidence that dry season land use practices, such as soil perturbation, burning of fields to prepare for planting, wetland cultivation and rodent pest management, may bring people into closer contact with rodents (Grant et al., 2016; Kamara et al., 2015; Lo Iacono et al., 2016). Human-reservoir contact rates may also vary due to seasonal movement of rodents into homes and gardens to seek stored food, but the evidence of seasonal differences in *M. natalensis* abundance between villages and fields is inconclusive (Demby et al., 2001; Fichet-Calvet et al., 2007). Seasonal and spatial variation in human activities such as rodent butchering and farming may also drive peaks in zoonotic transmission (Bonwitt et al., 2016; Scoones et al., 2017), but this needs more investigation. There is an urgent need for further combined ecological and social science research into the drivers of LASV spillover dynamics (e.g. (Grant et al., 2016; Lo Iacono et al., 2016; Scoones et al., 2017)) throughout West Africa. This is required to both improve early-warning LF forecasts, for example by identifying key environmental drivers (e.g. high rainfall and other climatic fluctuations) that are strongly predictive of future outbreaks, and to identify high-risk human-rodent interactions that are suitable for targeted interventions to reduce risk.

Human-to-human LASV transmission can occur via contact with infected bodily fluids, and nosocomial transmission has been documented (Monath et al., 1973; Troup et al., 1970). However, recent research supports the long-held hypothesis that a majority of LF cases are acquired from rodents rather than people. Epidemiological modelling of LF admissions data from KGH showed that around 20% of hospitalized cases were attributable to human-to-human transmission (Lo Iacono et al., 2015), although genomic evidence from LASV isolates from hospital patients in Sierra Leone and Nigeria suggests that human-to-human infections are much rarer (Andersen et al., 2015). This discrepancy may be related to the apparent role of super-spreaders in driving many of the human-to-human cases in the KGH data (Lo Iacono et al., 2015). Teasing apart human- from rodent-acquired infections in affected communities is difficult, since in both cases transmission occurs in similar settings (e.g. in the home, on farms). Better knowledge of this gap, such as the factors that increase transmission risk between people and the drivers of super-spreading events, could improve efforts to manage LF in community settings. Interestingly, the long persistence of viruria (3-9 weeks) during the post-recovery phase of human disease also suggests a possible mechanism by which human-to-rodent transmission could contribute to community maintenance of LASV (Lo Iacono et al., 2015), although this has not been investigated.

3.5. Distribution and phylogeography of Lassa virus

The geographical distribution of Lassa fever is unusual in that it appears to be non-contiguous, with confirmed LF cases until recently confined almost entirely to areas of Nigeria, Sierra Leone, Guinea and Liberia (Figure 3.1). The countries in-between have historically been considered non-endemic for LF, despite serological evidence of LASV or a cross-reactive arenavirus in rodents and/or humans in Mali, Cote d'Ivoire, Ghana and Burkina Faso (Figure 3.1) (Richmond and Baglole, 2003). However, evidence is growing to support a substantially expanded endemic range of LASV, with human LF outbreaks recently confirmed in southern Mali, Togo, Burkina Faso, Ghana, Benin and Cote d'Ivoire (Dzotsi et al., 2012; Manning et al., 2015; Safronetz et al., 2010; Sogoba et al., 2012), and serosurveys showing LASV circulation at up to 50% prevalence in *M. natalensis* populations in southern Mali (Safronetz et al., 2013).

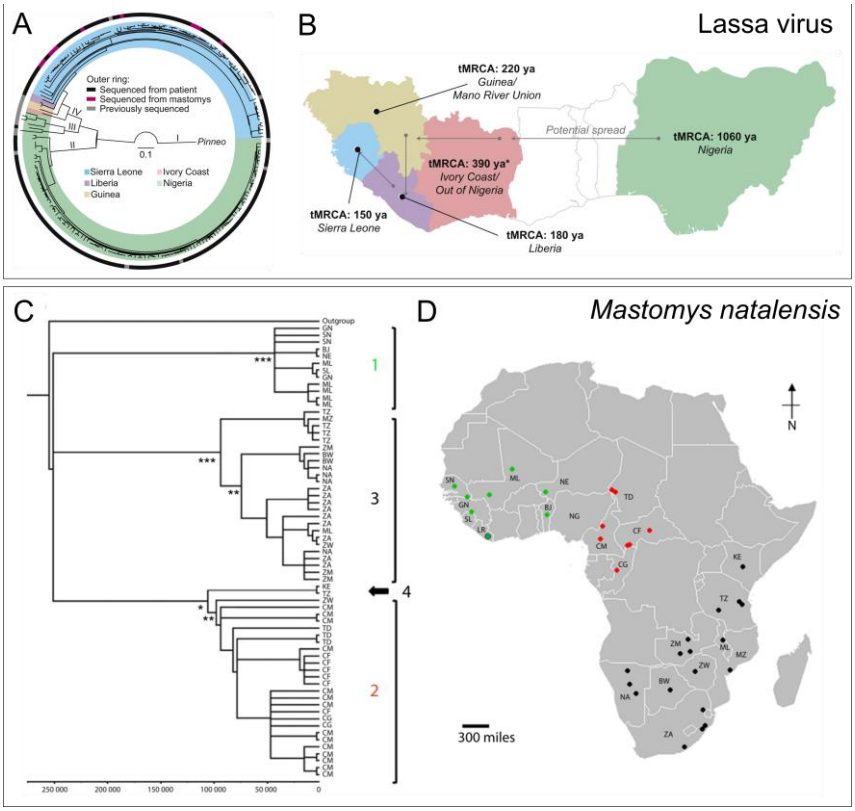

Figure 3.3: Phylogeography of Lassa virus and its reservoir host Mastomys natalensis. (A) Phylogeny of Lassa virus isolates from humans and rodents, and (B) reconstructed LASV evolutionary history across West Africa. (C) Cytochrome *b* phylogenetic tree of *M. natalensis* sampled from across the species' full range of sub-Saharan Africa, and (D) the geographical distribution of samples. *M. natalensis* in West Africa form a separate clade from the rest of the continent (clade 1, shown in green). LASV appears to only occur in this western clade. (A-B reproduced from (Andersen et al., 2015), with permission from Elsevier. C-D reproduced from (Redding et al., 2016), © 2016 The Authors, under CC BY 4.0 license https://creativecommons.org/licenses/by/4.0/).

Three distinct LASV lineages currently circulate in Nigeria (lineages I-III) and another (lineage IV) in the MRU area (Andersen et al., 2015) (Figure 3.3a), and a recently proposed lineage V is formed of isolates from Mali and Cote d'Ivoire (Manning et al., 2015). Current phylogeographic evidence suggests that this complex of extant LASV strains originated in Nigeria approximately 1060 years ago and spread to neighbouring countries between 300 and 500 years ago, before arriving last in the Mano River Union (MRU) area around 150 years ago (Andersen et al., 2015; Bowen et al., 2000) (Figure 3.3b). Another putative Nigerian strain, related to lineages I, II and III, was recently isolated from proposed reservoir host species *H. pamfi,* providing further evidence that LASV appears to be more widespread and ecologically complex than previously thought (Olayemi et al., 2016a).

Knowledge of the true spatial distribution of LASV in rodents across West Africa is confounded by the same problems that impair understanding of LF incidence, i.e. limited access to accurate diagnostics and poor surveillance and monitoring. Surveillance for LASV in rodents has been biased towards known LF-endemic countries, and a lower awareness of LF outside these regions means that past human outbreaks elsewhere may have often gone undiagnosed (Peterson et al., 2014). Several past risk maps produced for LF (seen in (Fichet-Calvet and Rogers, 2009) and (Mylne et al., 2015)) probably misrepresent the true LASV distribution, since this geographical reporting bias is often not accounted for during statistical modelling (Peterson et al., 2014). This problem is compounded by both poor access to diagnostic facilities in more remote areas and the potential for detection errors in serological assays. Multiple arenaviruses have been identified in *M. natalensis* and other rodents in West and Central Africa, and although LASV assay specificity has improved in recent years, cross-reactivity with other closely-related viruses can lead to false positive detections (Coulibaly-N'Golo et al., 2011; Emonet et al., 2006; Fichet-Calvet et al., 2014). Such uncertainty is likely to apply particularly to older records, for example an arenavirus identified as LASV was reported in several Central African countries in the 1980s (Richmond and Baglole, 2003), but the lack of subsequent detections of LASV or LF outside West Africa suggests these may have been erroneous. False negatives in detection and diagnosis are also possible because of the high genetic diversity among extant LASV strains. LASV is unusually diverse across its range (up to 27% nucleotide and 14.8% amino acid divergence in the nucleoprotein (NP) gene) compared to other VHF agents such as EBOV (Andersen et al., 2015; Bowen et al., 2000; Leski et al., 2015), prompting recent proposals that LASV might best be defined as a species complex (Olayemi et al., 2016a).

Other possible reasons for the larger geographical distribution of LASV than of reported human LF may be variations in either the genetic resistance of human populations or the

pathogenicity of LASV strains. Such mechanisms might be responsible for the apparent lack of LF in certain regions (such as southern Mali) where substantial rates of human and rodent seroprevalence have been documented (Sogoba et al., 2016). Recent large genomic studies have provided some evidence to support this hypothesis. For example, evidence has been found of positive selection on genes biologically linked to LASV infection in the Yoruba people of Nigeria, suggesting some degree of evolved resistance (Andersen et al., 2012). An extensive study of LASV isolates from humans and rodents across West Africa reported higher values for viral traits associated with virulence in isolates from Sierra Leone compared to those from Nigeria, which the authors suggested could contribute to the higher case fatality rates recorded in Sierra Leone (Andersen et al., 2015). The difference in fatality rates could instead be due to socioeconomic (e.g. poverty, nutritional status) or clinical factors (Andersen et al., 2015), but such variation in pathogenicity is plausible given the high genetic diversity of the LASV complex.

Perhaps more difficult to explain, but relevant to disease prevention, are heterogeneities in LASV distribution in rodent populations at both large and local geographical scales. In LF-endemic areas there is large variation in LASV infection prevalence in *M. natalensis* between neighbouring villages, and sometimes even between houses within a village (Demby et al., 2001; Fichet-Calvet et al., 2014). Population genetic studies suggest that this may be due to the species' limited dispersal range (Gryseels et al., 2017, 2016; Russo et al., 2016), but there is also evidence of regular human-mediated movement of LASV and/or infected rodents over longer distances (Fichet-Calvet et al., 2016; Lalis et al., 2013; Leski et al., 2015), suggesting that road transport networks have the potential to facilitate virus dispersal to LASV-free areas. However, the current prevalence and genetic diversity of LASV in *M. natalensis* populations remains unknown for most of West Africa. Future research is needed to address these data gaps and evaluate epidemiological connectivity between rodent subpopulations at both local (within-country) and regional scales, similarly to recent work on fruit bat (*Eidolon helvum*) hosts of henipaviruses and Lagos bat virus (Peel et al., 2013).

Another key question concerns the geographical limits of the LASV distribution. Despite *M. natalensis* occurring throughout sub-Saharan Africa, laboratory-confirmed LF cases have only ever been recorded in West Africa (west of the Nigeria-Cameroon border). Phylogeographic evidence suggests that West African *M. natalensis* forms a distinct clade from the rest of the continent, with LASV having apparently evolved in this western clade (Colangelo et al., 2013; Redding et al., 2016) (Figure 3.3b). It is unknown whether the limited LASV distribution is due to biological factors (e.g. host resistance to infection, coinfection dynamics with other arenaviruses) or geographical barriers to host dispersal (the Sahara Desert to the North and the

Cameroonian highlands to the East). In particular, it is unclear whether variation in LASV reservoir host competence exists in different African *M. natalensis* populations, and how this may affect the distribution of LF. A recent study in Tanzania found strong spatial segregation of MORV and GAIV infection across an apparently geographically contiguous Natal multimammate rat population (Gryseels et al., 2017). This segregation appears to be a result of host-virus coevolution, with the study results showing that MORV and GAIV are each restricted to a separate matrilineal subclade of *M. natalensis*. These results suggest that genetic variation in host competence between different *M. natalensis* subclades might restrict LASV to western clade animals (Gryseels et al., 2017); if this were the case, then future range expansions of LASV beyond West Africa would be unlikely. However, as discussed above, LASV shows much greater host plasticity than MORV and GAIV, meaning that this remains an open question. Extensive testing of both human and rodent populations is needed along the eastern boundaries of the known LF distribution (eastern Nigeria and the border with Cameroon), in order to elucidate the role of resistance and coinfection on the spatial distribution of the disease. Unpicking these factors will be key to determining whether projected climate and land use change could drive an eastward range expansion and emergence of LF elsewhere in Africa, and thereby designing appropriate preventative measures.

3.6. Forecasting Lassa fever risk and responses to environmental change

Trends in LF during this decade have followed a pattern typical of an emerging pathogen, with a notable increase in suspected and confirmed LF outbreaks across a growing area of West Africa (Figure 3.1) (Dzotsi et al., 2012; Safronetz et al., 2010; Shaffer et al., 2014; WHO, 2017b). Sources of case reports have also shifted from mainly research publications to disease surveillance reports. Most recently, since this chapter was published (Gibb et al., 2017), over the period of 2018 to 2020 Nigeria reported its highest ever seasonal incidences of LF, with cases detected in most states (see Chapter 4). Rather than a phase shift in LASV ecology, this apparent long-term trend of emergence is most likely a function of increasing surveillance for LF and other VHFs in West Africa under both public health and biosecurity agendas. For example, the accuracy of LASV diagnostic tools and accessibility of suitable laboratory facilities across West Africa have improved over the last decade (Shaffer et al., 2014; Wilkinson, 2016). There is also increasing political will and institutional funding for VHF surveillance in Africa, with the roll-out of disease surveillance policy frameworks such as the WHO International Health Regulations (IHR2005) and Integrated Disease Surveillance and Response (IDSR), and especially following the severity and slow global response to the 2013-2016 EVD epidemic in West Africa (Coltart et al., 2017). As a result, a fuller picture of the endemic distribution of LF

and LASV has started to emerge (Figure 3.1), although the recent case surges in Nigeria have also focused attention on the potential environmental factors that may be driving seasonal and geographical trends in LF incidence (see Chapter 4 of this thesis).

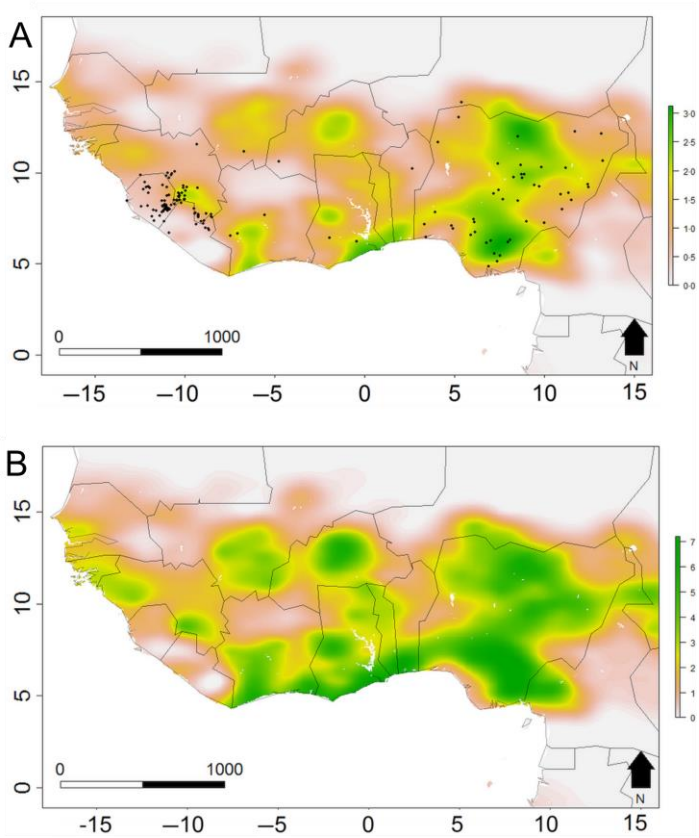

Figure 3.4: Present and predicted future distribution of Lassa fever risk in West Africa, estimated from environmental-mechanistic models. Colour scales show predicted annual LASV spillover events per grid cell for (A) present day and (B) 2070 under a projected scenario of human population growth, climate and land cover change. Annual LASV spillover events are predicted using a spatially-explicit epidemiological model parameterized with *M. natalensis* distribution and human population data, reported in (Redding et al., 2016). (Figure reproduced from (Redding et al., 2016), © 2016 The Authors, under CC BY 4.0 license https://creativecommons.org/licenses/by/4.0/).

Indeed, although the current broadening geographical range of reported LF is unlikely to be a true range expansion, regional environmental changes may impact LF ecology and epidemiology in several ways (Figure 3.4). West Africa has experienced profound environmental, socioeconomic and demographic shifts in recent decades, including population growth, land use change (including deforestation, mining and commercial agricultural expansion), bushmeat extraction, urbanization and growing transport connectivity (Norris et al., 2010; Wilkinson, 2016). The region is also forecast to experience strong climate change effects, impacting crop yields alongside other important ecosystem services (Roudier et al., 2011). Such

anthropogenic processes are thought to be major drivers of zoonotic and vector-borne disease (Patz et al., 2004). Ecological niche modelling has identified key environmental variables correlated with LF outbreaks, in particular rainfall, human population density and rice yields (Fichet-Calvet and Rogers, 2009; Redding et al., 2016). Some future climate projections for West Africa involve warmer temperatures and increased rainfall, which are predicted to increase the climatic suitability for *M. natalensis* across much of the region (Redding et al., 2016). Most land use forecasts predict extensive cultivated land expansion, both for subsistence and commercial export agriculture (e.g. oil palm) (Ahmed et al., 2016; Wilkinson, 2016). This could drive increases in human LASV exposure by expanding suitable habitat for *M. natalensis*, facilitating the spread of LASV between geographically separate rodent populations, or (as suggested by Chapter 2 of this thesis) driving shifts in ecological community composition towards higher densities of generalist small mammals (including *Mastomys*) in more intensively managed land (i.e. dilution-like effects) (Bordes et al., 2015; Keesing et al., 2010). Such land use homogenization has been hypothesized as a driver of EBOV emergence in West Africa (Wallace et al., 2014). Alternatively, it has been proposed that expansion of mechanized commercial agriculture might reduce *M. natalensis* populations (Massawe et al., 2007), thereby decreasing LASV exposure, but at the cost of reducing community access to land for subsistence farming (Moses et al., 2012). A useful but challenging future step with policy relevance would be to evaluate the trade-offs associated with different land use futures, incorporating zoonotic disease burden alongside other ecosystem services with poverty, human health and conservation relevance (Kilpatrick et al., 2017b). These are questions I explore further in Chapter 5.

The ability to predict the effects of these environmental drivers depends on unpicking how different anthropogenic processes impact viral transmission. Prospective field-based studies into the ecology and epidemiology of LASV in human-dominated ecosystems, including longitudinal monitoring of rodents and humans over months and years, are required to elucidate the spatial and seasonal dynamics of disease with less detection bias. The environmental and behavioral routes of rodent-to-human LASV transmission can be identified through community-based studies. Ecological and epidemiological modelling is also required to evaluate the impacts of different drivers on transmission, inform disease management and enable forecasting. For example, LF was recently used as a case study system for novel, One Health-informed modelling approaches (Grant et al., 2016; Scoones et al., 2017). A recent study developed a theoretical framework, based on a generalization of Poisson processes, to jointly model zoonotic spillover and onward human-to-human transmission, in order to evaluate the effects of biological, ecological and social parameters on transmission outcomes (Lo Iacono et

al., 2016). Modelling Kenema General Hospital LF data as a case study, their results again suggested that seasonal variation in infection risk may underpin the observed distribution of hospitalized cases. Another recent analysis developed a large-scale, spatially-explicit compartmental model to evaluate the impacts of future climate, land-use and socioeconomic scenarios on human LASV infections (Figure 3.4a) (Redding et al., 2016). Their results suggested that projected climate change (from one general circulation model) and population growth may lead to a doubling of LASV infections by 2070 (Figure 3.4b). Such studies make many simplifying assumptions, and given the gaps in knowledge of the present-day LASV ecology and distribution, any resulting predictions involve large amounts of uncertainty. Nonetheless, the advantage of such process-based frameworks is in enabling diverse information to be incorporated into model parameters, including both biological (e.g. host abundance, immunity, infection prevalence) and socio-ecological factors (e.g. land use practices, rodent consumption, age-related variation in exposure risk, human movement) (Buckee et al., 2017; Perez-Saez et al., 2016; Stensgaard et al., 2016). This creates the potential to move away from small-scale and correlative risk mapping towards a predictive system dynamics approach that considers zoonotic disease dynamics as a function of multiple interacting environmental and social drivers. In Chapter 5, I further develop these methods with a focus on mechanistic representation of land use drivers of LF, in order to conduct a scenario-based analysis of the nexus of agriculture, socioeconomics and LF risk across West Africa.

Recent multidisciplinary case studies of LF in Sierra Leone have emphasized that such integrated knowledge can inform interventions to reduce exposure to the viral reservoir, such as land management practices, food storage and rodent control (Grant et al., 2016; Wilkinson, 2016). LF is potentially a good model system for operationalizing and assessing the outcomes of such a One Health-informed approach, since it is tractable to study; its single primary host species and high prevalence in rodent populations make ongoing monitoring more practically viable than for most other VHFs. There is potential for insights into LF management to be applied to ecologically similar rodent-borne viruses such as New World arenaviruses and hantaviruses (Charrel and de Lamballerie, 2010; Yan et al., 2007). However, as a mainly single host system, it is unclear whether insights into LF may be as relevant to more complex disease systems with multiple reservoir, amplifying host or vector species which each respond differently to environmental drivers (e.g. yellow fever, EBOV, chikungunya) (Alexander et al., 2012). Since LASV is much less transmissible between people than viruses such as EBOV, it may also be less useful as an epidemiological model for epidemic VHFs, where single spillover events can lead to extended chains of human-human transmission.

3.7. Summary and outstanding questions

In this review I have shown that past biases in LF research have produced an incomplete picture of the disease's true incidence and distribution in West Africa, with consequences for medical treatment and disease management. We therefore close by emphasizing several critical knowledge gaps that must be filled to improve LF prevention and forecasting. These are: (1) Establishing the true spatial and seasonal distribution of LASV in rodent populations across West Africa, and how these correlate with observed spatiotemporal trends in human LF infections (both acute and asymptomatic). This will require longitudinal studies of LASV seroprevalence in people and rodents throughout the predicted geographic range of the virus, alongside improved disease monitoring of at-risk human populations inside and outside the known LF-endemic range. (2) Unpicking the mechanisms of zoonotic LASV transmission, including behaviors and local practices (e.g. housing, land use, rodent consumption) that enhance infection risk. (3) Identifying geographical variation and genetic correlates of LASV strain virulence and human and rodent susceptibility to LASV infection. Are certain virus lineages more pathogenic than others, and does innate resistance to infection vary across human and rodent subpopulations in West Africa, and how do these affect understanding of who is most at risk? (4) Identifying the barriers (biological, geographical and/or ecological) that limit LASV to *M. natalensis* populations in West and Central Africa.

The growing attention on LF by global health institutions, such as its recent prioritization for vaccine development, is a positive trend, especially given the consistent impacts of the disease on many districts that were also severely affected by the 2013-16 Ebola epidemic. Nonetheless, a continued shift in institutional understanding is required towards treating LF as a high-burden neglected disease rather than an epidemic threat. The situation should be improved by ongoing improvements in diagnostics and surveillance, which may provide the data required for a more robust assessment of the true burden of LF on communities in West Africa. Simultaneously, further unpicking the complex ecological drivers of LASV dynamics (see Chapter 4) will enable improved forecasting and targeted medical and environmental interventions.

Supplementary data

The dataset and sources for spatial distribution and history of Lassa fever and Lassa virus in West Africa (used to produce Figure 3.1) are hosted on Figshare (https://figshare.com/s/0ac8547b7147e400c140).

Chapter 4:

Climate, land use and reporting effort shape the distribution and dynamics of Lassa fever in Nigeria.

In this chapter I conduct an in-depth spatiotemporal epidemiological analysis of systematic, multi-year Lassa fever surveillance data (Nigeria 2012-2019), to identify the climatic and socio-ecological correlates of observed Lassa fever incidence, assess the scope for short-term forecasting in endemic hotspots, and evaluate the importance of reporting effort in driving observed incidence trends in recent years. These analyses were conducted as part of a collaboration with the Nigeria Centre for Disease Control, and coauthors and contributors are listed in the thesis outline.

4.1. Abstract

Lassa fever (LF) is an acute rodent-borne viral haemorrhagic fever that is a longstanding public health concern in West Africa and increasingly a global health priority. Recent molecular studies have confirmed the fundamental role of the rodent host (*Mastomys natalensis*) in driving human infections, but LF control and prevention efforts remain hampered by a limited baseline understanding of the disease's true incidence, geographical distribution and underlying drivers. Here, through analysing 8 years of weekly case reports (2012-2019) from 774 local government authorities (LGAs) across Nigeria, I identify the geographical correlates of LF incidence, and show that endemic LF occurs in predictable, seasonal surges linked to rainfall and vegetation dynamics. District-level annual occurrence and incidence are associated with rainfall, poverty, agriculture, urbanisation and housing, although LF's patchy distribution is mainly explained by reporting effort, suggesting that many infections are still going undetected. Seasonal climate dynamics and reporting effort are together sufficient to explain recent temporal trends in known endemic areas, including the sharp uptick in 2018-19, with high out-of-sample predictive accuracy. These temporal models provide a basis for forecasting LF incidence surges up to two months in advance, and suggest the scope for developing an early-warning system for public health planning.

4.2. Introduction

In 2018 and 2019, Nigeria recorded its ever annual incidence rates of Lassa fever (633 confirmed cases in 2018 and 810 in 2019, across 28 states), prompting national and international healthcare mobilisation and raising concerns of an ongoing, systematic emergence of LF nationally (Ipadeola et al., 2020). Lassa virus (LASV; Arenaviridae, Order: Bunyavirales) is a WHO-listed priority pathogen and a major focus of international vaccine development funding (Rottingen et al., 2017) and, although often framed as a global health threat, LF is foremost a neglected endemic zoonosis. A significant majority of cases – including those from recent years in Nigeria (Siddle et al., 2018) – are thought to arise directly from spillover from the LASV reservoir host, the widespread synanthropic rodent *Mastomys natalensis* (Andersen et al., 2015; Elsie A Ilori et al., 2019; Lo Iacono et al., 2015). Evidence of correspondence between human case surges and seasonal rainfall patterns suggests that LF is a climate-sensitive disease (Fichet-Calvet and Rogers, 2009), whose incidence may be increasing with regional climatic change (Redding et al., 2016). The present-day incidence and burden, however, remain poorly defined, because LASV surveillance has historically been opportunistic and focused towards known endemic districts (Gibb et al., 2017), and often-cited annual case estimates (of up to 300,000) are consequently based on only limited serological evidence from a handful of early studies (Bausch et al., 2001; McCormick et al., 1987b). This, alongside LF's nonspecific presentation, means that many mild or subclinical infections are thought to go undetected (Sogoba et al., 2016; Wilkinson, 2016). The patchy understanding of LF's true annual incidence and drivers both hinders disease control (Akpede et al., 2018) and provides limited contextual understanding of whether the recent massive surges in reported cases result from improvements in surveillance or a true emergence trend (Gire et al., 2012). To address this gap, I conducted the first spatiotemporal epidemiological analysis of acute human Lassa fever, using systematically-collected case data from 8 years of surveillance in Nigeria.

4.3. Results and Discussion

The dataset, collated by the Nigeria Centre for Disease Control (NCDC), consists of weekly epidemiological reports of acute human LF cases collected by all 774 local government authorities (LGAs) across Nigeria between January 2012 and December 2019 (Figure 4.1). Throughout the study period, 161 LGAs from 32 of 35 states reported cases, with a mean annual total of 276 (± 102 s.e.m.) confirmed cases, though with evidence of pronounced spatial and temporal clustering. For example, most cases (75%) are reported from just 3 of the 36 Nigerian states (Edo, Ondo and Ebonyi), and there is consistent evidence of seasonality in all areas across

the reporting period, with the exception of 2014-15, when a lull in recorded cases was coincident in timing with the West African Ebola epidemic (Figure 4.1). Annual dry season peaks of LF cases typically occur in January, which is confirming past hospital admissions data from Nigeria (Akpede et al., 2019; Asogun et al., 2012) and Sierra Leone (Shaffer et al., 2014), with some secondary peaks evident in early March and, increasingly, a lower number of cases detected throughout the year (Figure 4.1). Both overall temporal trends and cumulative case curves suggest that 2018 and 2019 appear markedly different from previous years, with very high peaks in confirmed cases extending from January into March, and high suspected case reporting continuing throughout 2019 (Figure 4.1, Figure S4.1).

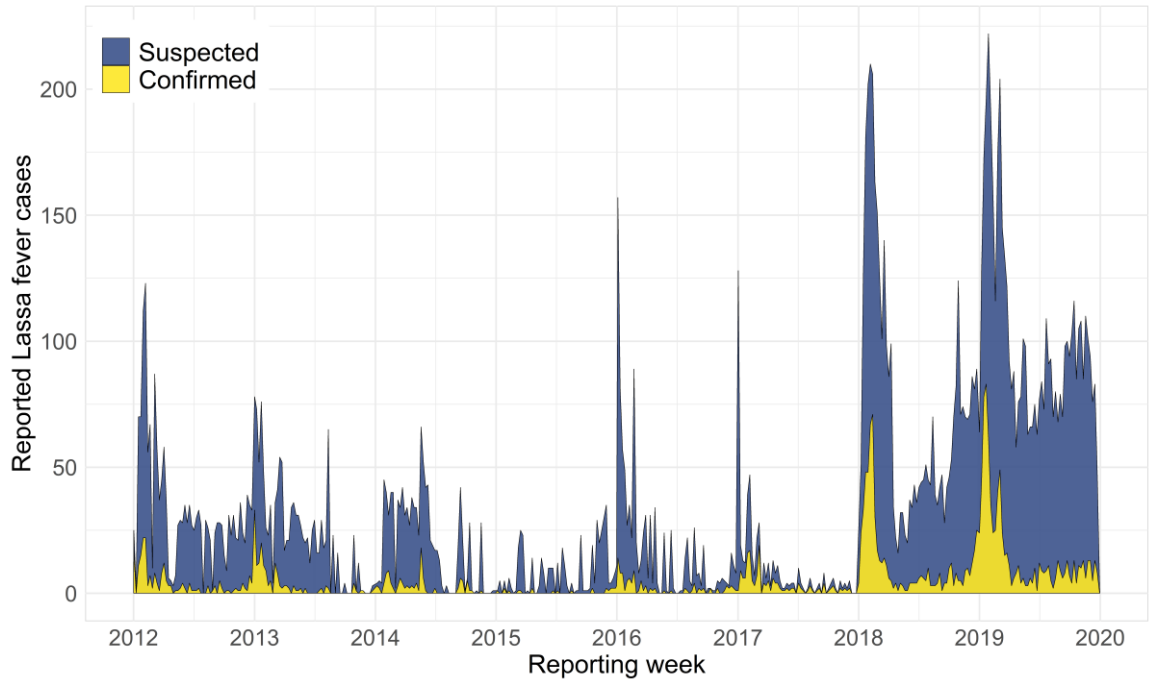

Figure 4.1: Temporal trends in country-wide Lassa fever reporting and incidence from 2012 to 2018. Polygon height shows the weekly total cases reported across Nigeria, with colour denoting the proportion of cases that were laboratory-confirmed (yellow) or suspected (blue). The full case time series was compiled from two reporting regimes at the Nigeria Centre for Disease Control: Weekly Epidemiological Reports 2012 to 2016, and Lassa Fever Technical Working Group Situation Reports 2017 to 2019 (with case reports followed-up to ensure more accurate counts; datasets shown separately in Figure S4.1). Full description of case definitions and reporting protocols is provided in Methods.

Improvements to country-wide surveillance could, however, be driving any apparent increase in both the incidence and geographical extent of LF in Nigeria. For instance, during the 2012-2019 monitoring period, within-country LF surveillance and response was strengthened under NCDC co-ordination, with a dedicated NCDC Technical Working Group (LFTWG)

established in 2016, the opening of three additional LF diagnostic laboratories in 2017-19 (to a total of five; Figure 2), the ongoing roll-out of country-wide intensive training on LF surveillance, clinical case management and diagnosis (Table S4.1) (Ilori et al., 2019), and the deployment of a mobile phone-based reporting system to 18 states during 2017 (NCDC, 2016) (Methods). The result of these improvements is apparent in the smoother case accumulation curves in 2018-19 than observed previously (Figure S4.1), as well as the notable, marked increase in the geographical extent of LF case reports over time. From 2012 to 2015 most reported cases originated from Esan Central in Edo State, the location of Nigeria's longest-established LF diagnostic laboratory and treatment centre at Irrua Specialist Teaching Hospital (ISTH) (Asogun et al., 2012) (Figure 4.2). The geographical extent of suspected and confirmed case reports rapidly expanded across Nigeria from 2016, with a contemporaneous decline in cases from Esan Central (Figure 4.2). This process can be seen clearly in LGAs surrounding Esan Central (Figure 4.2, inset) and may reflect increasingly precise attribution of the true geographical origin of cases.

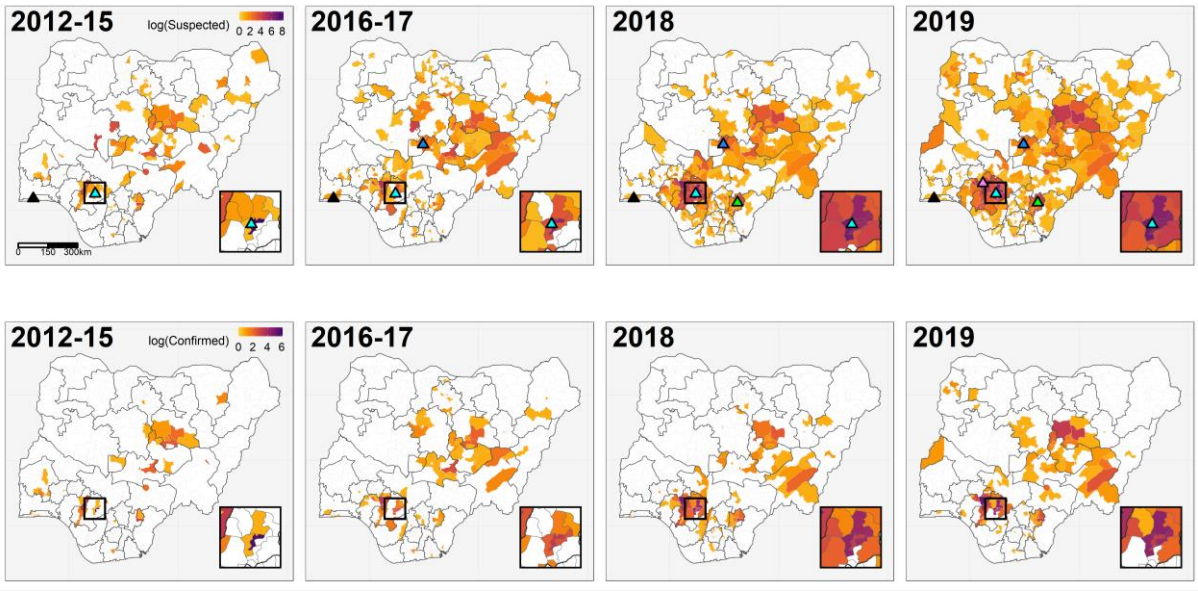

Figure 4.2: Spatiotemporal trends in Lassa fever surveillance, confirmed cases, and diagnostic laboratory capacity across Nigeria. Maps show, on the natural log scale, the total reported Lassa fever cases (suspected and confirmed; top row) and laboratory-confirmed cases only (bottom row) in each local government authority during the specified year(s). Triangles in the top row show the locations of laboratories with Lassa fever diagnostic capacity. Irrua Specialist Teaching Hospital (Edo, established 2008; inset box, pale blue) and Lagos University Teaching Hospital (Lagos, southwest; black) were both operational since before 2012. Three further laboratories became operational during the study period: Abuja National Reference Laboratory in 2017 (FCT Abuja, north-central; dark blue), Federal Teaching Hospital Abakaliki in 2018 (Ebonyi, southeast; green), and Federal Medical Centre Owo in 2019 (Ondo, south, purple).

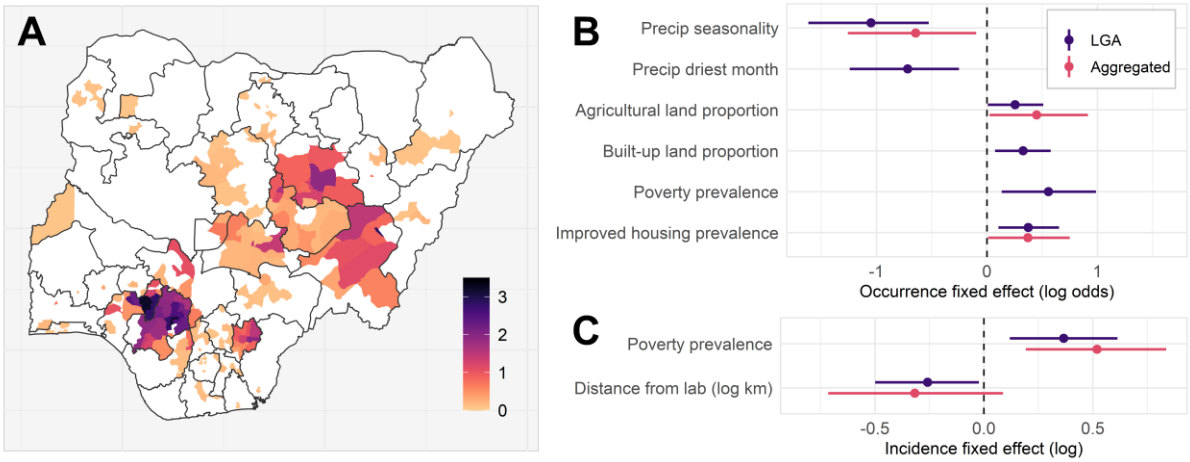

Figure 4.3: Spatial distribution and correlates of Lassa fever annual occurrence and incidence (2016-19) at local government authority-level across Nigeria. Map shows model predicted incidence-given-presence (A; cases per 100,000 persons in LGAs with >0 confirmed cases, visualised on the natural log scale), with LGAs with no confirmed cases shown in white. Points and error-bars show socio-ecological fixed effects parameter estimates (posterior mean and 95% credible interval) for best-fitting models of Lassa fever occurrence (B; log odds scale) and incidence-given-presence (C, log scale), fitted to data at either LGA-level (shown in purple) or at lower spatial resolution (130 aggregated districts, shown in pink; Methods, Figure S4.4). Models included fixed and random effects for socio-ecological predictors, reporting effort, State and Year and showed good out-of-sample posterior predictive performance (Methods, Figure S4.3). Some parameters were not included in the best occurrence model at aggregated district level (urban proportion, poverty and precip driest month), suggesting that these act on LF occurrence at more localised scales.

To determine the influence of climatic and socio-ecological factors on the geographical distribution of LF risk, I examined the spatial correlates of annual LF confirmed case occurrence and incidence from 2016 to 2019 (i.e. following the expansion of systematic surveillance) using Bayesian hierarchical models. I adopt a hurdle model-based approach to limit confounding effects of zero-inflation, so separately model annual occurrence across Nigeria (n=774 LGAs across 4 years; binomial likelihood) and incidence-given-presence in LGAs with 1 or more confirmed cases (n=161 across 4 years; case counts modelled as a negative binomial process with log human population as an offset) (Figure 4.3). In both models I incorporate local changes in surveillance over space and time using an index of annual suspected case reporting effort (Methods, Figure S4.2), along with 2 further spatially-structured fixed and random effects (State-level random effects, log distance from LF diagnostic lab; Table S4.2). Full models with socio-ecological covariates improved model fit compared to reporting-only null models, accounted for all spatial signal in the data, and were robust to cross-validation and predictive checks (Methods, Figure 4.4, Figure S4.3).

I find that LF occurrence is predicted by climatic factors (medium-to-high precipitation with fewer seasonal extremes) and increasing agricultural land use, which may synergistically affect both reservoir host population sizes and contact with people, as well as several socioeconomic factors that likely jointly influence effective human rodent-contact, healthcare access and LF awareness (Figure 4.3b). These include strong positive relationships with local poverty and proximity to LF diagnostic centre, and counter-intuitive positive relationships with urbanisation and improved housing. The latter relationships may be indexing other ecological (e.g. rodent synanthropy) or reporting processes (e.g. greater awareness and medical access in urban centres) not accounted for by other predictors. The limits of the endemic area of LF appear to be defined, therefore, by the interface of suitable environmental conditions for the reservoir host and socioeconomic conditions that facilitate human-rodent contact, principally rainfed agricultural systems. Notably, after accounting for State-level differences and spatiotemporal reporting effort, incidence within non-zero LGAs is predicted only by poverty (Figure 4.3c), suggesting that socioeconomic factors regulating human exposure are an important driver of relative risk in environmentally-suitable areas. Public programmes aimed at poverty alleviation may therefore have a positive impact on reducing LF incidence.

These results are consistent when modelling at lower spatial resolution (130 aggregated districts; Figure S4.4), although with weaker or absent effects of urbanisation and poverty on disease occurrence (suggesting these may act on detection or risk at more localised scales; Figure 4.3b). Projecting occurrence model fixed effects spatially (Figure 4.4) suggests that large contiguous areas of Nigeria are environmentally suitable for LF transmission, and that underreporting may be highest in northern and eastern states. Some of these areas appear to have low reporting effort for LF, and represent key places to target increased surveillance (e.g. Oyo, Osun, Ogun and Kogi states). However, LF's patchy spatial distribution (Figure 4.3a) and the extremely high incidence in some endemic hotspots (particularly in the south) are mainly explained by reporting effort and random effects, and are poorly predicted by socio-ecological effects alone (Figure 4.4c). One interpretation of these results is that the current observed geographical distribution of LF is predominantly shaped by surveillance effort, and that undetected cases are much more ubiquitous than currently recognised; this is feasible given the widespread nature of *M. natalensis*, and indeed is supported by the year-on-year expansion of the endemic area in Nigeria as surveillance continues to be rolled-out. Alternatively, since LASV prevalence in rodents can vary widely over small geographical scales (e.g. between neighbouring villages) (Fichet-Calvet et al., 2014), it is also possible that LF risk is highly discontinuous and localised, for unknown reasons. To identify underreported areas and target interventions, therefore, future surveys outside known endemic foci are urgently needed to

understand unmeasured social or environmental factors influencing risk (e.g. high public and clinical awareness, agricultural practices (Fichet-Calvet et al., 2008) or LASV hyperendemicity in rodents (Olayemi et al., 2018, 2016b)).

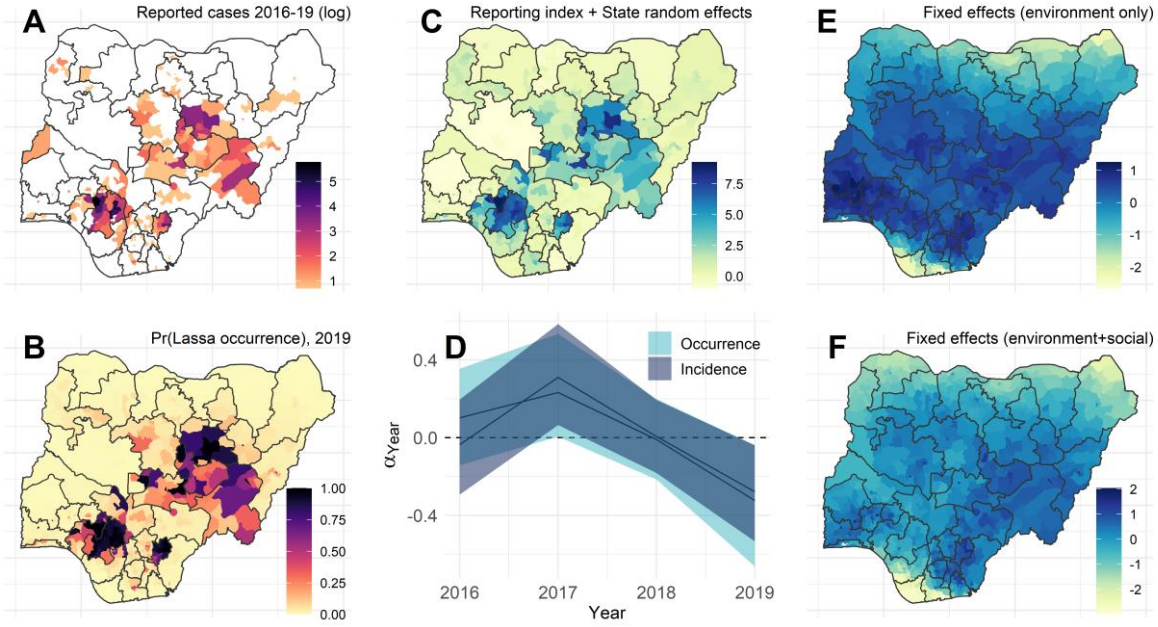

Figure 4.4: Components of the spatial models of Lassa fever occurrence and incidence across Nigeria. Total cases across the entire modelling period are displayed (A), showing case counts in LGAs with >0 cases reported as a colour scale (natural log scale) and LGAs with no reported cases in white. Model-fitted probability of LF occurrence is shown for 2019 (B). The other plots show marginal effects of occurrence model components on the linear predictor scale (log-odds for occurrence; log for incidence). Spatial reporting-based and random effects are shown for 2019 (C), and effects of year on both occurrence and incidence are small after accounting for reporting effort (D; relatively higher random intercept in 2017 because of low suspected case counts during that year). Contributions of fixed effects to the linear predictor are projected assuming consistent detection effort (E-F, log-odds scale), for both environmental-only (climate and agriculture; E) and combined socioeconomic and environmental effects (F).

Understanding and predicting LF seasonal risk dynamics is critical to inform disease prevention, control and forecasting within known endemic areas. I therefore analysed the spatiotemporal climatic predictors of weekly incidence (2012-2019) in two endemic foci with distinct seasonal climates and agro-ecologies (Figure S4.5), in southern (Edo and Ondo; 68% of all reported cases) and northern Nigeria (Bauchi, Plateau and Taraba; 12% of all cases). Within each area I modelled weekly incidence in 5 approximately equal-area districts (aggregated clusters of LGAs; Methods) as a negative binomial process, accounting for baseline between-district differences and surveillance increases over space and time using reporting-based and

district-level random effects (as above). To investigate effects of contemporaneous and lagged environmental conditions on seasonal LF dynamics, I considered temporally-explicit, lagged fixed effects for local precipitation, air temperature and vegetation greenness (Enhanced Vegetation Index; EVI) (Figure S4.5, Methods). The best models for each area significantly improved fit compared to detection-only models (Methods) and accurately reproduced observed case counts in out-of-sample predictive simulation tests (i.e. >95% of observations falling within the 95% posterior predictive interval; Figure 4.5, Figure 4.6, Figure S4.6-S4.7). Notably, in both north and south Nigeria, seasonal LF peaks are strongly associated with increasing rainfall at 90-50 days prior to reporting week and with lower vegetation during the period of infection (0-60 days prior to reporting) (Figure 4.5c). Additional effects of air temperature in the northern endemic area (Figure 4.6c) may be due to the significantly wider seasonal temperature fluctuations than in the south (Figure S4.5). Separately projecting environmental and non-environmental (reporting and year random effect) components over time shows that linear combinations of lagged climatic effects, interacting with annual changes in reporting, are sufficient to explain LF periodicity (distance between peaks) and trends (relative height of peaks) in both regions (Figure 4.5a-b, Figure 4.6a-b). Notably, climatic factors drive substantial intra- and interannual variability in predicted amplitude of dry season peaks (up to 6-fold relative change in incidence in the south, and 12-fold in the north). These results suggest that environmental factors may have contributed to the very low LF incidence in 2014-15, and that the very large case surges in 2018-19 likely resulted mainly from a step change in surveillance and/or other unmeasured factors (since these years were climatically similar to 2016-17; Figure 4.5b, Figure 4.6b).

Taken together, these results provide evidence for an important role of climate in explaining LF occurrence and incidence patterns. The consistent interaction between lagged rainfall and vegetation dynamics across two agro-ecologically different regions in Nigeria strongly suggests a role of reservoir host population ecology. Indeed, rainy season peaks are similarly predictive of subsequent *M. natalensis* population surges and crop damage in East Africa (Leirs et al., 1996). Temporal variation in rodent and human LASV infections may be driven by seasonal and interannual rodent population dynamics (putatively linked to climate-driven cycles in resource availability and land use (Massawe et al., 2007)) or human agricultural and food storage practices (Gibb et al., 2017), all of which are important targets for future research. For example, declines in vegetation during the weeks preceding transmission could lead to synchronous food-seeking behaviour in rodents (as natural food availability reduces) and human behaviour changes relating to harvest and crop processing.

The high out-of-sample predictive accuracy of the temporal models suggests that, provided reporting effort is adequately accounted for, lagged climate variables could enable advance forecasting of LF peaks within known endemic areas (Ballester et al., 2016). Predictive simulation of incidence beyond the study period (to 1st March 2020, fixing non-environmental effects at 2019 levels) successfully captures the higher peak in 2020 (when comparing to preliminary State-level case counts; Figure 4.5a, Figure 4.6a), although 2020 observed case numbers in northern districts tend to exceed posterior mean predicted values, potentially due to further improvements in surveillance sensitivity. Simplified, lag-only models that can project 2 months in advance (i.e. using only climate at >60 days lag) are also sufficient to capture the relative amplitude and timing of seasonal peaks, including 2020 (Figure S4.7), suggesting that this approach could provide the basis for developing a forecast system in LF-endemic areas. Such early-warning approaches are increasingly used for vector-borne disease control (e.g. dengue (Lowe et al., 2016)) but are rare for directly-transmitted zoonoses. This dataset is a relatively short time series (n=8 years) and improving these models year-on-year with new surveillance data, and including more precise data on agricultural practices, should assist in further clarifying predictors of large case surges and improving forecast accuracy. Nonetheless, these findings have implications for disease control and targeting LASV surveillance in rodents and humans to environmentally-suitable areas where LF is apparently absent, and demonstrate the critical role of improvements in systematic human case surveillance across West Africa (Akpede et al., 2019; Shaffer et al., 2014), as setting the basis for future control of this high priority disease.

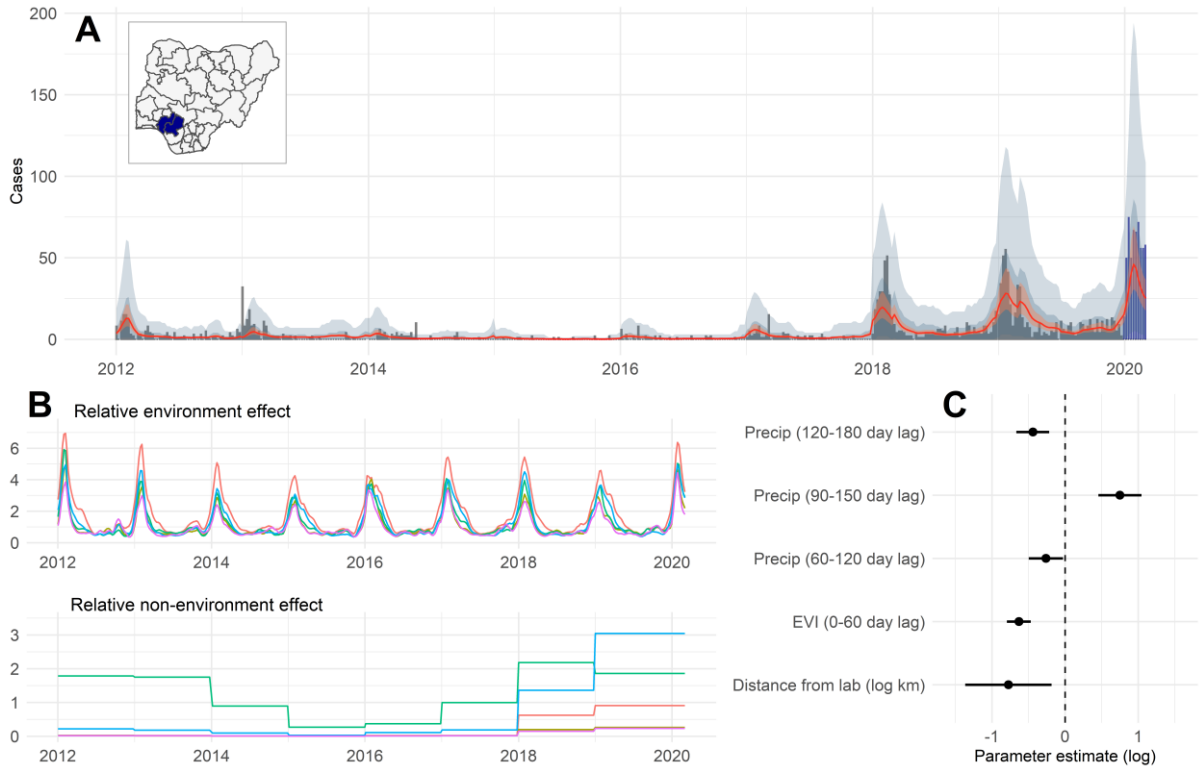

Figure 4.5. Modelled temporal dynamics and drivers of confirmed Lassa fever cases in Edo and Ondo States (southern endemic area). Case time series (A) shows observed and out-of-sample (OOS) predicted weekly case counts, summed across 5 aggregate districts in Edo and Ondo States (inset map). Time series graph shows observed counts from 2012 to 2019 (grey bars), OOS posterior median and 95% credible interval (red line and ribbon) and OOS 67% (dark grey shading) and 95% (light grey shading) posterior predictive intervals (A). OOS predictions were made within sequential two-month windows across the full time series at district-level (i.e. observation-level; Figure S4.6). Dark blue bars show preliminary 2020 weekly case counts for comparison (not included in model fitting), and predictions for 2020 assume non-environmental effects at 2019 levels (Methods). The marginal mean effects of environmental (precipitation, EVI) and non-environmental model components (reporting index, lab distance, year-level random effects) are shown separately for each district (B). These denote proportion change in confirmed cases over time, so are not interpretable on the absolute scale. Model fixed effects for precipitation, EVI and lab distance are shown on the linear predictor (log) scale (C; mean+95% credible interval). Models for Northern endemic districts (Bauchi, Plateau, Taraba) have similar fixed effects and predictive ability, but different environmental dynamics (Figure 4.6).

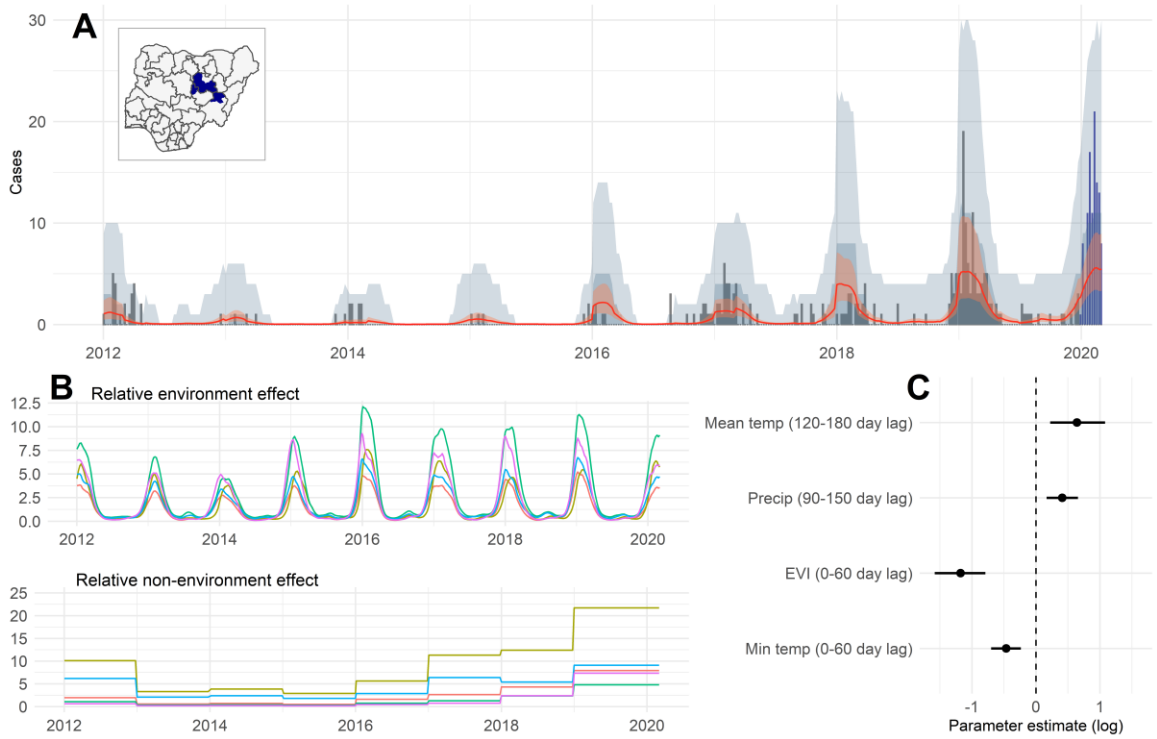

Figure 4.6. Modelled temporal dynamics and drivers of confirmed Lassa fever cases in Bauchi, Plateau and Taraba states (northern endemic area). Case time series (A) shows summed observed and out-of-sample (OOS) predicted weekly case counts, modelled across 5 aggregate districts in Bauchi, Plateau and Taraba States (inset map). Relative environmental effects are shown separately for each district (B), and fixed effects are shown on the log scale (C; mean+95% credible interval). See descriptions in Figure 4.5 legend.

4.4. Materials and Methods

4.4.1. Lassa fever human case surveillance data

I analyse weekly reported counts of suspected and confirmed human cases and deaths attributed to Lassa fever (LF) (as defined in Table S4.1), between 1st January 2012 and 30th December 2019, from across the entire of Nigeria. The weekly counts were reported from 774 local government authorities (LGAs) in 36 Federal States and the Federal Capital Territory, under Integrated Disease Surveillance and Response (IDSR) protocols, and collated by the Nigeria Centre for Disease Control (NCDC). All suspected cases, confirmed cases and deaths from notifiable infectious diseases (including viral haemorrhagic fevers; VHFs) are reported weekly to the LGA Disease Surveillance and Notification Officer (DSNO) and State Epidemiologist. IDSR routine data on priority diseases are collected from inpatient and

outpatient registers in health facilities, and forwarded to each LGA's DSNO using SMS or paper form. Subsequently, individual LGA DSNOs collate and forward the data to their respective State Epidemiologist, also by SMS and paper form, for weekly and monthly reporting respectively to NCDC. From mid-2017 onwards, data entry in 18 states has been conducted using a mobile-phone based electronic reporting system called mSERS, with the data entered using a customised Excel spreadsheet that is used to manually key into NCDC-compatible spreadsheets. Data from this surveillance regime (*'Weekly Epidemiological Reports'*; WER) were collated by epidemiologists at NCDC throughout the period 2012 to March 2018 (Figure S4.1).

Throughout the study period, within-country LF surveillance and response has been strengthened under NCDC coordination. LGAs are now required to notify immediately any suspected case to the state level, which in turn reports to NCDC within 24 hours, and also sends a cumulative weekly report of all reported cases. A dedicated, multi-sectoral NCDC LF Technical Working Group (LFTWG) was set up in 2016 with the responsibility of coordinating all LF preparedness and response activities across states. Further capacity building occurred in 2017 to 2019, with the opening of three additional LF diagnostic laboratories in Abuja (Federal Capital Territory), Abakaliki (Ebonyi State) and Owo (Ondo State) (to a total of five; Figure 4.2) and the roll-out of intensive country-wide training on surveillance, clinical case management and diagnosis. Due to the rapid expansion in test capacity, the definition of a suspected case in our data has changed over the surveillance period: from 2012 to 2016, suspected cases include probable cases that were not lab-tested, whereas from 2017 to 2019, all suspected cases were tested and confirmed to be negative.

In addition to the Weekly Epidemiological Reports data, since 2017 LF case reporting data has also been collated by the LF TWG and used to inform the weekly NCDC LF Situation Reports (*SitRep data*; https://ncdc.gov.ng/diseases/sitreps). This regime includes post-hoc follow-ups to ensure more accurate case counts, so our analyses use WER-derived case data from 2012 to 2016, and SitRep-derived case data from 2017 to 2019 (see Figure 4.1 for full time series). A visual comparison of the data from each separate time series, including the overlap period (2017 to March 2018) is provided in Figure S4.1, and all statistical models considered random intercepts for the different surveillance regimes. Where other analyses of recent Nigeria LF incidence have been more spatially and temporally restricted (Akhmetzhanov et al., 2019; Zhao et al., 2019), the extended monitoring period and fine spatial granularity of these data provide the opportunity for a detailed empirical perspective on the local drivers of LF at country-wide scale, and their relationship to changes in reporting effort.

4.4.2. Data summaries, mapping and processing.

I visualised temporal and seasonal trends in suspected and confirmed LF cases within and between years, for both surveillance datasets. Weekly case counts were aggregated to country-level and visualised as both annual case accumulation curves, and aggregated weekly case totals (Figure 4.1, Figure S4.1). I also mapped annual counts of suspected and confirmed cases across Nigeria at the LGA-level to examine spatial changes in reporting over the surveillance period (Figure 4.2).

Since analyses of aggregated district data are sensitive to differences in scale and shape of aggregation (the modifiable areal unit problem (Gotway and Young, 2002)), I also aggregated all LGAs across Nigeria into 130 composite districts with a more even distribution of geographical areas, using distance-based hierarchical clustering on LGA centroids (implemented using 'hclust' in R), with the constraint that each new cluster must contain only LGAs from within the same state (to preserve potentially important state-level differences in surveillance regime). Weekly and annual suspected and confirmed LF case totals were then calculated for each aggregated district. I used these spatially aggregated districts to both test for the effects of scale on spatial drivers of LF occurrence and incidence, and as the spatial unit for modelling the seasonal climatic and environmental drivers of LF incidence in endemic districts (see '*4.3.3. Statistical analysis*').

4.4.3. Statistical analysis

I analyse the full case time series (Figure 4.1) to characterise the spatio-temporal incidence and drivers of Lassa fever in Nigeria, while controlling for year-on-year increases and expansions of surveillance effort. All data processing was conducted in R v.3.4.1 with the packages R-INLA (Lindgren and Rue, 2010), raster (Hijmans, 2016) and velox (Hunziker, 2017). Statistical modelling was conducted using hierarchical regression in a Bayesian inference framework (Integrated Nested Laplace Approximation (INLA)), which provides fast, stable and accurate posterior approximation for complex, spatially-structured regression models (Lindgren and Rue, 2010; Rue et al., 2009), and has been shown to outperform alternative methods for modelling environmental phenomena with evidence of spatially biased reporting (Redding et al., 2017).

Quantifying spatio-temporal trends in surveillance effort. Surveillance effort for Lassa fever has expanded significantly across Nigeria during the study period, characterised by higher case

counts within known endemic areas, an increase in reporting throughout the year, and a marked geographical expansion in case reports (Figures 4.1-4.2, Figure S4.1). Accounting for these changes is critical to avoid conflating apparent increases in incidence (due to improved surveillance) with true increases in incidence due to environmental factors. I therefore used data on spatiotemporal trends in suspected-only (i.e. *not* confirmed) case reports to proxy for per-LGA, per-year reporting effort. Clinical criteria for suspected LF cases are broad due to the disease's non-specific febrile presentation (see definitions in Table S4.1), so suspected case reporting should reasonably reflect relative differences in index of suspicion for the disease, while being less sensitive to true spatial and interannual differences in incidence than confirmed case reports (as seen in Figure 4.2). However, suspected case counts are overdispersed and heterogeneous geographically, meaning that absolute counts are an inappropriate measure for comparing relative changes in effort between LGAs in different areas of Nigeria. For example, although high numbers of cases have consistently been reported in hyper-endemic states such as Edo, the relative increases in case reports have been similar or greater in many northern areas with lower absolute case counts (Figure 4.2). Absolute annual counts also do not capture changes in the temporal dimension of reporting within endemic states (i.e. reporting increasingly occurring throughout the year, rather than solely during the dry season; Figure 4.1).

I therefore derived a bounded (0 to 1) index of relative reporting effort, defined as the probability of reporting at least 1 suspected case per month within a given year (i.e. annual suspected case reporting probability across 12 monthly 'trials' per year). This is sufficient to capture both geographical expansion of reporting to areas formerly considered non-endemic (Figure 4.2), and temporal expansion of reporting in known endemic hotspots (Figure 4.1). I estimated this quantity using binomial regression (logit link) to account for geographical and temporal dependencies in reporting effort across Nigeria, with temporal effects for Year (both nationally and separately per-LGA, each modelled as a first-order random walk) and spatial effects for LGA and State (both independent and identically-distributed random intercepts). Inference was conducted in R-INLA, separately for both LGAs and for spatially aggregated districts (as described above). I extracted the posterior median fitted values per-state, per-LGA to use as a covariate in subsequent models (hereafter termed *'Reporting Index'*). Geographical distribution and temporal trends in Reporting Index are visualised in Figure S4.2. Since suspected and confirmed case reporting are spatially highly correlated (Figure 4.2), this metric may conservatively overestimate reporting signal in spatial models (discussed further below), but nonetheless provides a data-driven proxy for the influence of changing awareness on spatial case patterns.

Identifying the spatial socio-ecological correlates of annual Lassa fever occurrence and incidence. I modelled annual LF incidence at country-wide scale to identify the spatial, socio-ecological correlates of disease across Nigeria. I used annual confirmed case counts per-LGA across the last 4 years of surveillance (2016 to 2019) as a measure of LF incidence, since these years followed the establishment of updated systematic surveillance protocols and the associated geographical expansion of suspected case reports (Figure 4.2), and so are likely to more fully represent the true underlying distribution of LF across Nigeria. In total, 161 LGAs reported confirmed LF cases from 2016 to 2019, with the majority of cases reported from a much smaller subset (75% from 18 LGAs), and 613 LGAs reported no confirmed LF cases (total=774 LGAs; median 0 cases, mean 2.21, range 0—321). This overdispersed and zero-inflated distribution presents a challenge for fitting to incidence counts, so I instead adopt a two-stage hurdle model-based approach, and separately model LF occurrence in all LGAs (presence-absence) and incidence-given-presence (i.e. within LGAs that have reported at least 1 confirmed case within the time period, n=161). This both ensures that fitted models adhere to distributional assumptions, and also enables a clearer separation of the contributions of different socio-ecological factors to disease occurrence and to total case numbers in endemic areas.

I modelled annual presence-absence per-LGA using a binomial error distribution (logit link) and confirmed case counts in non-zero LGAs as a negative binomial distribution (log link), with log-transformed human population included as an offset (thereby modelling the effect of covariates on per-person LF incidence). I considered the same suite of random and fixed effects in both occurrence and incidence models. I considered seven geographically and temporally-structured covariates to account for spatiotemporal trends in surveillance effort, as follows: Reporting Index (as derived above) as a linear covariate; a state-level random intercept and correlated random slope of Reporting Index, to account for gross between-state differences in LF endemicity and clinical and public awareness; a temporal effect of Year, modelled as a first-order random walk to account for between-year dependency; a random intercept for surveillance regime; and two distance-based linear covariates as proxies for LF awareness and healthcare access (log mean Euclidean distance from nearest LF diagnostic laboratory, and log mean distance to nearest hospital (Maina et al., 2019)). I additionally considered fixed effects for covariates that could influence *Mastomys natalensis* bioclimatic niche through precipitation (mean precipitation of the driest month, mean precipitation of the wettest month, precipitation seasonality; all extracted and calculated from CHIRPS Africa daily precipitation rasters for the monitoring period (Funk et al., 2015)) and temperature (annual mean air temperature and air temperature seasonality; extracted and calculated from NOAA daily temperature rasters), habitat preferences (proportion of land under agricultural use), and socioeconomic factors that

could influence human-rodent contact and disease detection (human population density within LGA; proportion urban, i.e. built-up, land cover within the LGA; proportion of the population living in poverty; proportion of the population living in improved housing). I considered both linear and quadratic terms for temperature and rainfall because past studies of *M. natalensis* distribution suggest that these responses may be nonlinear (Fichet-Calvet and Rogers, 2009; Redding et al., 2016). Prior to modelling I examined all covariates for collinearity and removed covariates that were highly collinear with one or more other others (Pearson correlation coefficient >0.8). Continuous covariates not log-transformed were scaled (to mean 0, sd 1) prior to model fitting, and all fixed effects were assigned uninformative Gaussian prior distributions (mean 0, precision 0.001). The full suite of covariates tested across all analyses, data sources and associated hypotheses are described in Table S4.5.

I conducted model inference and selection in R-INLA, and evaluated model fit for both occurrence and incidence models using Deviance Information Criterion (DIC) (Gelman et al., 2014). I conducted model selection on fixed-effects with the full random effects structure included, evaluating the contribution of covariates to model fit by removing each covariate in turn from the full model (all fixed and random effects) and examining the effect on DIC (Hooten and Hobbs, 2015), and excluding covariates that did not improve predictive ability by a threshold of at least 2 DIC units. Most of the spatial variation was explained by Reporting Index-based effects (Figure 4.4), as expected given the metric's conservative nature (see above). Including socio-ecological fixed effects nonetheless consistently improved model fit when compared to either random effects-only (Year and State; occurrence ΔDIC=-107.5; incidence ΔDIC=-24) or random and reporting effects models (occurrence ΔDIC=-8; incidence ΔDIC=-5). All posterior parameter distributions and residuals were examined for fit and adherence to distributional assumptions. Testing for residual spatial autocorrelation using Moran's *I* showed that all spatial signal was accounted for by both the occurrence (Moran's *I* statistic=-3.02 , p=0.7) and incidence models (I=-1.25, p=0.9). I further evaluated the fit and predictive ability of the full models (all effects) using random 8-fold cross-validation and out-of-sample posterior predictive simulation (Figure S4.3). I also conducted geographically-structured cross-validation, in turn fitting separate models holding out all LGAs from each of 12 States that have either high (Bauchi, Ebonyi, Edo, Nasarawa, Ondo, Plateau, Taraba) or low (Kogi, Delta, Kano, Enugu, Imo) documented incidence. Posterior predictive checks revealed good predictive ability for both occurrence and incidence models, although with a tendency to under-predict occurrence in early years, and fixed-effects direction and magnitude were robust in all geographical hold-out models (Figure S4.3).

To test for sensitivity to aggregation scale, I additionally conducted all spatial modelling at a lower spatial resolution, by fitting occurrence and incidence models to data at 130 aggregated districts (as described above). Confirmed LF case totals were calculated for each district, socio-ecological covariates were extracted, and model fitting, selection and evaluation was again conducted following the above described protocol (Figure 4.3b, Figure S4.4, Table S4.2).

Temporal drivers of Lassa fever cases in high-incidence areas. A growing body of data from clinical records (Asogun et al., 2012; Lo Iacono et al., 2015; Shaffer et al., 2014), ethnographic and social science research (Bonwitt et al., 2017b; Kelly and Marí Sáez, 2018) and rodent population and serological monitoring (Fichet-Calvet et al., 2007; Makundi et al., 2007) suggests that LF is a potentially climate-sensitive endemic disease, with temporal trends in human and rodent infection hypothesised to be associated with seasonal cycles in rodent population ecology and human land use and food storage practices (see Chapter 3). I therefore developed spatiotemporal models to quantify the climatic and environmental conditions associated with LF risk dynamics (weekly case counts) across the full duration of surveillance (2012 to 2019). A handful of LGAs have reported the majority of cases in Nigeria, and low and/or variable surveillance effort outside these areas could confound inference of temporal environmental drivers. Here, I therefore fit models to only data from known endemic areas with case reporting records that span the entire monitoring period, which occur in two main foci: the southern hyper-endemic cluster in Edo and Ondo States, and the northern cluster spanning Bauchi, Plateau and Taraba States (which in total account for 80% of total confirmed cases over the monitoring period; Figure 4.3a). These areas are distinct from each other in terms of climate (Figure S4.5) and agro-ecology, sociocultural factors and livelihoods (FEWSNET, 2018) so to avoid potential confounding effects of unmeasured factors, I model the two areas separately using the same protocol (as described below). This approach also provides the benefit of a comparison of key temporal environmental correlates in different socio-ecological settings. Within each area (henceforth referred to as Southern and Northern endemic areas) I fit models to LF time series from 5 spatially aggregated districts (clusters of LGAs as derived above): spatial aggregation better harmonises the resolution of disease data with climatic data, and reduces potential noise associated with uncertain attribution of the true LGA of origin for cases in the early part of the time series (especially in Southern states; see Figure 4.2).

In each endemic area, I modelled weekly case counts per-district (n=5 districts over 8 years; total 2090 observations per model) as a negative binomial process (log link) to account for seasonal overdispersion, with inference again conducted using R-INLA. I used a similar suite

of temporally-variant fixed and random effects as in the spatial model to account for temporal differences in baseline incidence and reporting effort: Reporting Index as a linear covariate (Figure S4.2), a district-level random intercept and correlated random slope of Reporting Index; a temporal effect of Year to account for unique characteristics of each year not explained by environment (modelled as a first-order random walk), and a linear covariate for distance from Lassa fever diagnostic lab. We did not include any of the temporally-invariant covariates included in the spatial incidence models, since the smaller number of districts (5 per endemic area) provides low comparative power to detect clear effects of these on baseline temporal incidence.

To investigate the potential impacts of seasonal and interannual environmental variation on LF incidence, I tested for the current and lagged effects of three environmental covariates: precipitation, air temperature, and vegetation greenness (measured using Enhanced Vegetation Index; EVI). I considered five different time lags (from 0 to 5 month starting points) to account for, firstly, the time lag between LASV infection event and hospital attendance and, secondly, any possible temporally-lagged effects of seasonal environmental cycles on *M. natalensis* population ecology, behaviour and LASV seroprevalence (Fichet-Calvet et al., 2007). Precipitation data were obtained from CHIRPS (Climate Hazards Infrared Precipitation with Stations) daily Africa precipitation rasters (January 2011—March 2020); this dataset is based on combining sparse weather station data with satellite observations and interpolation techniques, and is specifically designed to support accurate hydrologic forecasts in areas with poor weather station coverage (such as tropical West Africa) (Funk et al., 2015). Air temperature daily minimum and maximum rasters were obtained from NOAA and averaged to calculate daily mean temperature, and EVI was obtained from processing 16-day composite layers from NASA (excluding all grid cells with unreliable observations due to cloud cover and linearly interpolating between observations to give daily values; Table S4.5). For all covariates, I extracted the mean value across all cells within each district per day. Then, across a two-month window for each lag value (0-60, 30-90, 60-120, 90-150 and 120-180 days prior to reporting date), I calculated the mean of precipitation, EVI, and mean (Tmean), minimum (Tmin) and maximum daily temperature (Tmax). Environmental dynamics for the entire surveillance period in each endemic area are visualised in Figure S4.5, and show consistent differences in terms of gross temperature, rainfall and vegetation regimes,

For each endemic area, I fitted a non-environmental null model including only reporting-based and random effects (henceforth *'reporting-only model'*). I then conducted model selection to determine the combination of environmental covariates that best explain weekly

incidence, again selecting among models using DIC (Lowe et al., 2018). Uninformative priors were set for all parameters and hyperparameters, and best model parameter estimates were robust to systematically varying these. I selected for two best models: one considering environment at all timelags including contemporaneous to reporting (*'full model'*) and one considering only environment at >60 day lag prior to reporting to test forecasting ability (*'forecast model'*). Both environmental models explained significantly more of the variation in data relative to reporting-only models, although full models performed slightly better (Southern full ΔDIC=-201.8, forecast ΔDIC=-148.6; Northern full ΔDIC=-173.9, forecast ΔDIC=-145.4). To validate predictive ability I then conducted out-of-sample (OOS) posterior predictive simulation using a two-month holdout window across the full time series. For holdout models I excluded all observations from each sequential two-month window, re-fitted the model, drew 2500 parameter samples from the approximated joint posterior, then used these to (1) calculate OOS posterior mean and intervals and (2) simulate the OOS negative binomial predictive distribution (i.e. the range of plausible expected case counts given the model). I then calculated and visualised the proportion of observed values falling within 67% and 95% OOS predictive intervals as a measure of predictive ability, overall and over time (Figure S4.6). Finally, I predicted posterior mean and predictive intervals for the 2020 Lassa fever season (using environmental data up to March 2020) from the models fitted to the full time series. I compared these predictions to 2020 preliminary statewide confirmed case counts compiled for the NCDC Situation Reports, holding reporting covariates and random effects to the same level as 2019 (i.e. predictions for 2020 assume the same reporting effort; Figure 4.5, Figure 4.6, Figure S4.7). Because these are preliminary data they are unsuitable for model fitting, but provide a useful future out-of-sample test for forecasting ability.

Data and code availability

Nigeria case data are used under a data sharing agreement with the Nigeria Centre for Disease Control, and code and data will be released on publication of this chapter. Sources for all freely-available environmental datasets are described in Table S4.5.

Chapter 5:

The nexus of future agricultural and socioeconomic change and Lassa fever risk in West Africa.

Building on insights into key Lassa fever drivers from the previous chapter, this chapter focuses on medium-to-long term forecasting, applying a process-based risk modelling approach and dynamic land change model, to evaluate how different agricultural change pathways may differentially impact trends in Lassa fever risk across West Africa. This chapter's goal is to move towards evaluating zoonotic disease risk within the same quantitative framework as other ecosystem outputs with health relevance (e.g. food security via crop yields, water security), i.e. as a nexus issue subject to synergies and trade-offs.

5.1. Abstract

Expanding and intensifying agricultural systems are important loci of trade-offs among environmental constituents of health and sustainable development (e.g. food and water security, disease risk, biodiversity). Zoonotic infectious disease burdens are a crucial, but under-evaluated, component of this environment-health nexus. Here, I use a systems-based modelling approach to evaluate impacts of agricultural change in West Africa on Lassa fever (LF), an environmentally-driven rodent-borne zoonosis and growing public health concern. I simulate effects of 3 spatially-explicit agricultural, socioeconomic and climatic pathways on LF risk trends to 2070 (SSP-RCPs, from low- to high climate impacts), using a dynamic economic land use change model and a process-based model of viral spillover risk at the human-rodent interface. Population increases and climate change generally predict net increases in exposure risk in most LF-endemic countries in the coming decades. Critically, however, I show that between-scenario differences in projected land use either significantly amplify or dampen these risk increases in many countries (e.g. Liberia, Sierra Leone, southern Nigeria), with clear divergences between different socioeconomic pathways by 2050. Notably, slower agricultural expansion and preservation of forested areas under a higher-equity, lower-impact scenario (SSP1-RCP2.6) buffer predicted risk in many areas, suggesting potential for policy interventions to facilitate synergies between disease mitigation, poverty alleviation and ecosystem conservation. Conversely, some regions show consistently increasing risk trends across most future scenario pathways (e.g. northern Nigeria, Liberia, Guinea), highlighting priorities for health capacity building and surveillance. This systems-informed approach can inform disease surveillance, public health initiatives (e.g. vaccination) and evaluation of medium- to long-term consequences of future policy pathways for zoonotic disease risk and burden.

5.2. Introduction

A defining global challenge this century, as emphasised by policy frameworks such as the UN Sustainable Development Goals, is to maintain food and water security for the world's populations, while simultaneously improving human health and sustaining biodiversity (and its associated ecological functions on which health and wellbeing depend) (Carpenter et al., 2009; Díaz et al., 2015; Whitmee et al., 2015). Human-managed landscapes are key loci of potential synergies and trade-offs between these agendas, since agricultural expansion and intensification are needed to meet food production requirements, but also drive biodiversity losses and erosion of ecosystem services vital to health (Cardinale et al., 2012). Infectious diseases, and in particular zoonotic and vector-borne infections (Lloyd-Smith et al., 2009), are a critical facet of the environment-health nexus. Expansions of anthropogenic landscapes have been linked globally to general increases in zoonotic reservoir populations (see my analyses in Chapter 2), increasing prevalence of many zoonotic pathogens in wildlife (Civitello et al., 2015; LoGiudice et al., 2003) and intensified rates of human-reservoir-vector contact (Hassell et al., 2019; Pulliam et al., 2012). Consequently, agricultural systems show elevated human risks of numerous endemic and epidemic diseases (Halstead et al., 2018; Jones et al., 2013; Shah et al., 2019) and increased probabilities of zoonotic disease emergence (Allen et al., 2017; Keesing et al., 2010). Simultaneously, theoretical models show the potential for disease- and agriculture-linked 'poverty traps' characterised by chronic disease burdens coupled with economic and food insecurity (Ngonghala et al., 2017b), which may in future be exacerbated by climate stresses on crop yields and nutrition.

Evaluating how future agricultural trends may impact zoonotic disease risks in vulnerable regions is therefore of critical importance for identifying potential trade-offs between disease risks and food production (Rohr et al., 2019), and for anticipating the long-term public health consequences of alternative environmental policy pathways (Watts et al., 2016; Whitmee et al., 2015). Such knowledge can inform local and regional climate adaptation; for example, identifying regions with increasing hazard for important zoonoses can support targeting interventions to reduce population vulnerability (e.g. health systems strengthening, vaccination campaigns) or regulate reservoir host or vector populations (via traditional or ecological control methods) (Campbell-Lendrum et al., 2015; Sokolow et al., 2019). However, to date predictive disease modelling at policy-relevant scales has focused on future climate effects (mainly for vector-borne diseases such as malaria and arboviruses; Caminade et al., 2014; Mordecai et al., 2017; Ryan et al., 2019), with fewer efforts to incorporate interactions with other key system processes that structure human-wildlife epidemiological interfaces, in

particular the type and intensity of land use (Franklinos et al., 2019; Hassell et al., 2016). This is likely to be an important omission for many wildlife-borne zoonoses (see Chapter 2).

The impacts of environmental change are unequally distributed: many of the world's most economically-vulnerable regions have among the highest present-day rates of deforestation, agricultural expansion and zoonotic disease burden, and climate change is generally expected to exacerbate these vulnerabilities (Cardona et al., 2012). West Africa is a particularly important example, as a hotspot for numerous zoonoses (O'Hearn et al., 2016) and with complex legacies of colonialism, conflict and weak health systems that have left many countries structurally vulnerable to infectious disease (such as the catastrophic 2013-16 Ebola epidemic; Bardosh et al., 2016). Much of the population of West Africa is heavily dependent on rainfed and subsistence agriculture for food security (Sultan and Gaetani, 2016), and is experiencing significant agricultural expansion and pressures on land systems due to effects of global trade policies (Wallace et al., 2016), increasing populations, and declining crop yields under climate change (Palazzo et al., 2017; Sultan and Gaetani, 2016). Consequently, cropland area in West Africa approximately doubled between 1976 and 2013, and alternative socioeconomic and climatic pathways imply markedly different regional futures in terms of food security, poverty, and agricultural land expansion trends (Palazzo et al., 2017).

One disease likely to be affected by these trends is Lassa fever (LF), an acute rodent-borne viral haemorrhagic fever caused by the Lassa arenavirus (LASV). Following decades of sparse surveillance, LF is now increasingly recognised as a widespread endemic disease arising mainly from zoonotic spillover (rodent-to-human transmission) (Asogun et al., 2012; Shaffer et al., 2014; Siddle et al., 2018; Wilkinson, 2016), and a significant contributor to disease burden in rural communities (with past extrapolations of up to 300,000 cases and 5000 deaths annually; McCormick et al., 1987). Symptomatic cases and serological evidence of exposure are now regularly identified in most sub-Saharan West African countries (Gibb et al., 2017), and for several years observed incidence has been increasing year-on-year in Nigeria (see Chapter 4). Consequently, LF is a WHO priority disease and target for accelerated vaccine development, and understanding the drivers and distribution of LF risk is an increasing priority for disease control (Dan-Nwafor et al., 2019). Importantly, LF is an environmentally-sensitive disease, and is closely linked to the distribution and population ecology of the synanthropic rodent reservoir host *Mastomys natalensis* (Chapter 3). Geographical trends in disease risk and incidence, both locally and at large-scales, are predicted by socio-ecological factors affecting rodent populations and human-rodent contact, including agriculture, rainfall and poverty, and seasonal case surges are linked to rainfall and vegetation dynamics (see Chapter 4). LF spillover risk is likely to be

sensitive to future environmental shifts in the coming decades; a recent modelling study suggested that climatic changes (under the HadGem3 climate model) may lead to significant geographical expansion of incidence by 2070, however only examined a single heuristic land use scenario (Redding et al., 2016). Land use can locally increase or dampen disease risks across large areas of otherwise contiguous climatic suitability, meaning that different agricultural pathways in the coming decades – especially in already LF hyperendemic areas (e.g. south Nigeria, Sierra Leone) – could have markedly different effects on disease risk.

Land use change processes are dynamically shaped by economic and climatic feedbacks at multiple scales: for example, changes in demand, trade policy or crop yields (e.g. due to climate impacts) can accelerate or reduce agricultural expansion and deforestation rates. Dynamic economic-environmental assessment models (Harfoot et al., 2014) are increasingly used to capture these feedbacks and evaluate how different future socioeconomic assumptions may affect global and regional land use trends (Leclère et al., 2017, 2014; Prestele et al., 2016). Outputs from these models provide an opportunity to examine the sensitivity of zoonoses to plausible, multi-driver scenarios of global change, within the broader science-policy framework used in climate mitigation and adaptation research (SSP-RCP-SPAs; Kebede et al., 2018; Riahi et al., 2015). Recent studies have used harmonised future global land use realisations developed for the SSP-RCPs in biodiversity (Newbold et al., 2015) and disease modelling (Carlson et al., 2020), but each emissions scenario was quantified using different assessment models so their comparability is unclear (Hurtt et al., 2011). In this study, I therefore use a single dynamic regional land change model and an econometric downscaling model to spatially project land change trends across West Africa for 3 socioeconomic-climatic scenarios to 2030, 2050 and 2070. I evaluate how these agricultural pathways interact with climatic and socioeconomic change to impact projected LF risk using an ecological spillover risk model, accounting for uncertainty in future climate (across 4 general circulation models; GCMs) and spatial patterns of land use change (from GLOBIOM). I aim, firstly, to evaluate the degree to which projected land changes may either dampen or increase the effects of climate change on LF risk across West Africa, particularly in known endemic countries. Secondly, I aim to identify whether particular regions are consistently projected to become more suitable for LF across all emissions and land use pathways, as these may be priorities for expanding clinical and public health efforts to reduce the burden of LF.

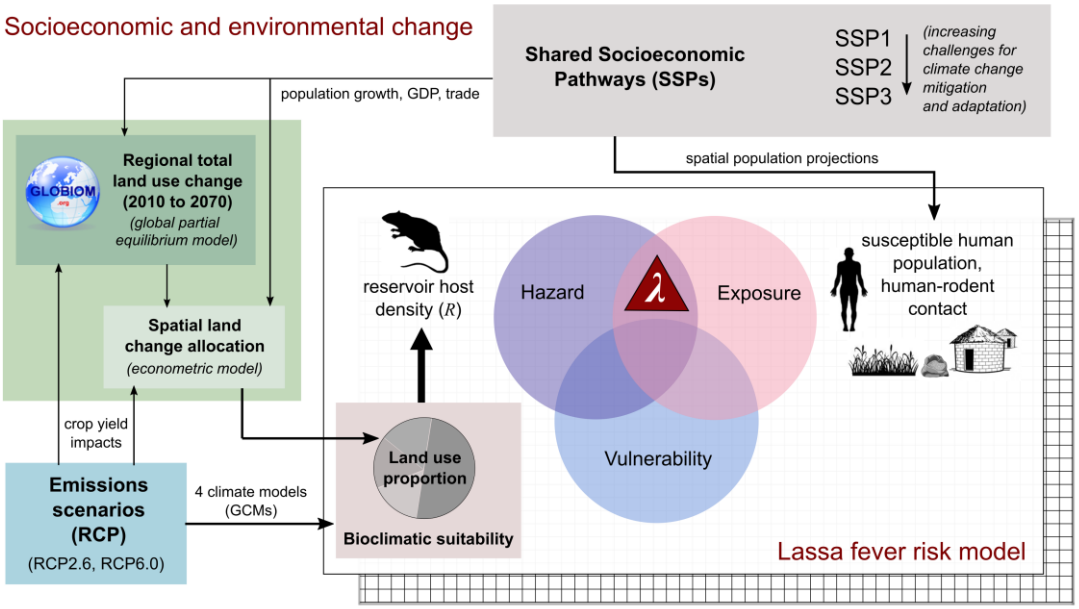

Figure 5.1: Modelling framework for effects of socioeconomic, agricultural and climate change on Lassa fever risk. Lassa fever spillover risk (estimated cases per year λ; shown as red triangle) is projected per grid-cell using a process-based model (white box) incorporating ecological hazard, i.e. reservoir host density R, and exposure (see Methods; vulnerability not explicitly included). The model is projected across 3 future scenarios to 2070 (Table 5.1) based on quantified socioeconomic projections under different Shared Socioeconomic Pathways (grey box) and climate change projections under different Representative Concentration Pathways (blue box). Land use change in West Africa is dynamically modelled and spatially allocated using SSP-RCP inputs into the Global Biosphere Management Model (GLOBIOM; green box). Black arrows represent data outputs and inputs, i.e. model linkages.

5.3. Materials and Methods

5.3.1. Quantifying future agricultural and environmental pathways for West Africa

I developed spatially-explicit regional scenarios within the Shared Socioeconomic Pathways (SSP) framework (Figure 5.1). The SSPs are future narratives of global change structured along axes of institutional challenges for climate mitigation and adaptation, whose global and regional implications for numerous future socio-environmental factors have been extensively studied and quantified (e.g. population, economic development, land use, GHG emissions) (Palazzo et al., 2017; Popp et al., 2017; Riahi et al., 2015). I coupled each of 3 SSPs with a plausible climate forcing trajectory (representative concentration pathway; RCP) given socioeconomic and mitigation policy assumptions: SSP1-2.6 (low challenges for mitigation/adaptation, low climate impacts, lowest population growth), SSP2-6.0 (medium challenges and medium-high climate change, a 'middle-of-the-road' pathway), and SSP3-6.0

(high challenges, medium-high climate change, highest population growth). SSP2 and SSP3 were matched with the same climate forcing scenario (RCP 6.0) to compare differences in LF risk under the same climate assumptions but different socioeconomic assumptions. The key global and regional features of the scenarios are described in Table 5.1. It is important to emphasise that the SSPs are different narratives of the future, and as such their quantified socioeconomic and land use outcomes are not predictions of future change, but are model-based projections of plausible changes under the assumptions of each scenario narrative (Riahi et al., 2015).

Regional simulation of land change dynamics. I simulated global land-cover-land-use (LCLU) dynamics to 2070 for each SSP-RCP scenario using GLOBIOM, an economic model that has been used extensively to evaluate global and regional changes in land use, crop productivity, food security, bioenergy and deforestation (Havlík et al., 2014; Leclère et al., 2014; Meijl et al., 2018; Palazzo et al., 2017). GLOBIOM is a global, dynamic, partial equilibrium model of the agricultural, forestry and bioenergy sectors, which is parameterised using economic, geospatial and biophysical data. The model simulates the competition for land across 30 global economic regions under socioeconomic (e.g. population growth, productivity), climate mitigation policy (e.g. deforestation/afforestation policies), trade, and biophysical (e.g. crop growth and livestock parameters, carbon stock) drivers, and outputs regional aggregate projections of land use change and intensification, crop, livestock and timber production, and greenhouse gas emissions (Fricko et al., 2017). For each SSP-RCP scenario (Table 5.2), I used GLOBIOM to project decadal land change totals globally, and extract projections for our focal region of West Africa (Figure S5.1). Full model documentation is provided in (Fricko et al., 2017; Havlík et al., 2014; Leclère et al., 2017), so I only provide an overview here.

Briefly, land resource and supply side activities (e.g. crop and timber production) are represented within local simulation units (variable-sized clusters of 5 arc-minute grid cells that share similar biophysical characteristics), which represent 6 land cover classes (natural forest, managed forest, other natural vegetation, grassland, cropland, and short rotation biofuel plantations) and 18 agricultural crops, as well as forest products and livestock. The model is run in recursive, decadal timesteps from the baseline year of 2000, and driven by regional input data on socioeconomic parameters for each SSP scenario (e.g. population growth, GDP growth). At each timestep economic equilibrium is optimised across the 30 economic regions, to maximise the sum of consumer and producer surplus. With each timestep, changes in domestic demand for land outputs (e.g. crops) within each region are met either by changing import/export quantities, or through land use expansion (e.g. regional amount of cropland increases) and/or intensification (e.g. regional cropland amount stays the same but is

reallocated to increase productivity). Land changes represented in the model include transitions from natural vegetation to cropland and managed forest, and reversion from cropland to non-forested natural vegetation, but do not include reforestation. Climate change effects are included as RCP-specific impacts on potential crop yields, calculated from projections in (Leclère et al., 2014).

Table 5.1: Key features of the socioeconomic and climatic scenarios (RCP-SSPs).

SSP	RCP	SSP socioeconomic narrative	Climate mitigation policy features	Agricultural and land use features	Population by 2050 (West Africa)	Population economic vulnerability
SSP1	2.6	Sustainability: increasing global, regional and local institutional cooperation to reduce environmental degradation, invest in education and health in low- and middle income countries (LMICs) and reduce within- and between-country inequality. Gradual transition towards emphasis on human well-being rather than economic growth. Moderate international trade.	Rapid global cooperation on emissions mitigation from 2020, with high regulation of emissions from land use (via carbon pricing).	Rapid technological improvements in agricultural productivity shared across countries, helping to close yield gaps in LMICs. Strong regulation of land change (e.g. deforestation) to reduce environmental trade-offs. Food traded globally.	600m	Low
SSP2	6.0	Middle-of-the-road: social, economic and technological trends do not shift from historical patterns. Institutions make gradual progress on reducing environmental degradation, fossil fuel emissions and inequality, but these are geographically variable. Persistent inequality. Moderate international trade.	Intermediate cooperation on emissions mitigation from 2040, with intermediate regulation of emissions from land use.	Medium pace of technological improvements in agricultural productivity. Medium regulation of land change with slow declines in rate of deforestation. Food traded globally, but still mostly within regions.	700m	Medium
SSP3	6.0	Regional rivalry: an increasing focus on domestic and regional issues at the expense of global cooperation, exacerbated by weak institutions and barriers to global trade. Declining investments in technology and education. Low regulation of environmental degradation and slow overall economic growth. Persistent or worsening inequality, especially in LMICs. Low international trade.	Fragmented cooperation on from 2040, with faster transition within high-income countries, and limited regulation of emissions from land use.	Slow improvements in agricultural productivity in LMICs. Limited regulation of land change, resulting in ongoing deforestation. Reduced global trade flows for agricultural goods, resulting in increased reliance on domestic or regional production.	817m	High

Spatial downscaling of land change projections. The regional aggregate land change totals calculated in GLOBIOM must then be spatially downscaled to individual simulation units (clusters of 5 arc-minute grid cells). To do this, I employed a recently-developed Bayesian econometric land use change model (Leclère et al., 2017), calibrated using West Africa-specific data on recent land use change and its drivers (Leclère et al., 2017). The model is documented in (Krisztin et al., 2015; Leclère et al., 2017), so I only provide an overview here. Briefly, land use change within each 5 arc-minute cell is modelled as a multinomial logit process. Farmers within each simulation unit are represented as rational actors that, at each 10-year timestep *t*, seek to maximise return by allocating grid cells to different land classes (cropland, grassland, forest, managed forest, other natural vegetation). Allocation choices are dependent on land allocation at timestep *t–1*, farmers' socioeconomic characteristics, geophysical properties of the land, the costs and profits associated with each land class, and spatial dependency with neighbouring simulation units (to account for the fact that land use change is a highly spatially-dependent process).

The model was parameterised by fitting to regional data on observed land use change for one timestep (2000 to 2010), with parameters estimated for the dependency on socioeconomic (e.g. population, distance to market), agricultural (e.g. average wood and crop yields) and geophysical (e.g. altitude, soil type, temperature) variables (Krisztin et al., 2015; Leclère et al., 2017). To downscale future GLOBIOM projections across West Africa, the parameterised model was used to spatially allocate total projected changes of each land class at each timestep (Figure S5.1) across a 5 arc-minute raster, from a baseline composite of the year 2000 ESA-CCI land cover map and Global Forest Model (G4M) natural/managed forest map. Spatial allocation is driven by specific socioeconomic (e.g. population (Riahi et al., 2015)) and climatic variables (climate effects on crop yields (Leclère et al., 2014)) for each SSP-RCP scenario (Figure 5.1). This process is recursive (i.e. each subsequent timestep *t* depends on downscaled allocation at *t–1*), and due to the Bayesian nature of the econometric model, can be used to generate a posterior distribution of future LCLU allocation pathways across West Africa (Figure S5.2). I simulated 100 spatially-downscaled land use allocations from this posterior for each SSP-RCP scenario, with which to propagate this uncertainty into disease models. Although these LCLU scenarios therefore incorporate uncertainty in spatial allocation of GLOBIOM's regional totals, they notably do not account for other potential sources of variability in land use futures, for example between GLOBIOM and other land use models that are based on different frameworks and assumptions (Alexander et al., 2017; Prestele et al., 2016). Because GLOBIOM combines both bushland and desert as 'other natural vegetation', in downscaled LCLU maps I

reclassified to desert all 'other natural vegetation' falling in cells classified as desert in the 2010 ESA-CCI satellite data.

Climate change projections. I generated projected downscaled bioclimatic variables for 2030, 2050 and 2070 under RCPs 2.6 and 6.0, from each of 4 general circulation models (GCMs) to account for climate model uncertainty. I used bias-corrected daily projections of minimum temperature, maximum temperature and precipitation from 4 GCMs from the ISIMIP (Warszawski et al., 2014) database (GFDL-ESM2M, HadGEM2-ES, IPSL-CM5A-LR and MIROC5) to generate annual bioclimatic variables for all years from 1979 to 2060, following methods described in (Fordham et al., 2011). For each GCM, bioclimatic anomalies were calculated for each future year (2020 to 2060) relative to the modelled baseline of 1979-2013 (the same time period as the CHELSA dataset). These anomalies were then added to CHELSA bioclimatic variables (1979-2013) to generate fine-scale annual future bioclimatic variables, which were spatially interpolated using a smoothing spline (to reduce edge-effects caused by downscaling lower-resolution GCM projections) and aggregated to 5 arc-minutes. Finally, these were used to derive, for each RCP and GCM, future bioclimatic variables for three time epochs, 2030 (mean 2021-2040), 2050 (mean 2041-2060) and 2070 (mean 2061-2080) (Table S5.1).

Human population and socioeconomic data. I used freely-available gridded projections of per-country future human population density for each SSP, which were spatially-downscaled following the scenario assumptions on key socioeconomic processes (e.g. migration, economic development, urbanisation). Data and downscaling methods are described in (Jones and O'Neill, 2016).

5.3.2. Structure and parameterisation of Lassa fever risk model

In this study, LF spillover risk is conceptualised as the intersection of ecological hazard (reservoir host populations), human exposure, and population vulnerability, following the classical definition of risk that is commonly used for natural hazards modelling under climate change (Cardona et al., 2012; see Chapter 1). To evaluate hazard and human exposure risk across future agricultural pathways, I developed a spatially-explicit mechanistic LF zoonotic transmission risk model incorporating reservoir host ecology and human socioeconomics (Figure 5.1), by adapting the model framework of Redding *et al.* (2016, 2019). An earlier version of this model was used to estimate LF incidence to 2070 using a single climate model, but used only one heuristic land cover change pathway, and only modelled land use effects on reservoir occurrence, rather than relative abundance or density. Given the land use focus of the study, I

restructured and extended the model to explicitly account for effects of different land use classes on reservoir relative abundance (a more epidemiologically-relevant metric), by inferring parameters from a meta-analytic dataset (similar to the approach in Chapter 2). The model structure is described in full below, and visually summarised in (Figure 5.1).

Model of Lassa fever zoonotic hazard and transmission risk. Annual LF spillovers (X_i) within each 5 arc-minute grid cell *i* are considered to follow a Poisson process (following the generalised spillover framework of Lo Iacono et al., 2016)

$$X_i \sim Pois(\lambda_i) \quad (1)$$

where parameter λ_i describes the mean number of LF spillovers per time interval (here, one year). I define λ_i as *risk* for LF transmission, which is determined by exposure intensity function

$$\lambda_i = \beta \log(H_i)(R_i Pr_i) \quad (2)$$

where H_i is the human population density, R_i is the estimated reservoir host population density, Pr_i is the prevalence of LASV in the reservoir host population, and β is the transmission coefficient that defines the probability of infection per scaled human-reservoir contact per timestep. I assume that human-rodent contact density scales logarithmically with human population density (see discussion in '*Scaling of human-rodent contact density*').

I define $R_i Pr_i$ (infectious reservoir host population density) as the *ecological hazard* for LF transmission. Although recent studies have isolated LASV from several rodent species (Olayemi et al., 2016a), the significance of their contribution to natural transmission dynamics remains unclear, whereas extensive evidence supports the Natal multimammate rat (*Mastomys natalensis*) being the dominant reservoir for human LF. Here, I therefore focus on *M. natalensis*, although the model could be extended to include multiple reservoir hosts. Reservoir population density R_i is determined by the interaction between land cover-land use (LCLU) and climate as follows:

$$R_i = c_i \eta_i \quad (3)$$

where c_i is the local bioclimatic suitability for reservoir host presence, which is modelled as a function of *n* climatic variables:

$$c_i = f(\text{Bioclim}_{i,1} \ldots \text{Bioclim}_{i,n}) \in \{1, 0\} \quad (4)$$

and η_i is the local predicted reservoir host relative density, which is modelled as:

$$\eta_i = \alpha_{NF}NF_i + \alpha_{Bu}Bu_i + \alpha_{Gr}Gr_i + \alpha_{Cr}Cr_i + \alpha_{MF}MF_i + \alpha_{Urb}Urb_i \quad (5)$$

where α are parameters describing the relative density of *M. natalensis* across the different LCLU types (Table 5.2), multiplied by the proportion cover of each LCLU type within grid cell i (natural forest NF; bushland Bu; grassland Gr; cropland Cr; managed forest MF; urban Urb; these categories are used as they map to land use classes in GLOBIOM). This approach treats reservoir density as a hierarchical process, with α parameters controlling density in areas that are considered climatically suitable (i.e. with a value of 1), and therefore assuming that land use acts on density independently of climate (see Discussion). To run the model requires parameter estimates for the above formulae, which are described in the following sections and summarised in Table 5.2.

Estimation of reservoir host bioclimatic suitability. I inferred per-grid cell bioclimatic suitability for *M. natalensis* (c_i) as a function of 8 bioclimatic variables using an ensemble of binomial (presence/absence) ecological niche models fitted to geolocated occurrences for West African *M. natalensis* (Figure S5.3a), following Redding *et al.* (2016). I collated occurrences from Global Biodiversity Information Facility and the scientific literature (GBIF, 2018) (Table S5.1), filtered to remove ambiguous species classifications and points with low spatial accuracy (≥3 decimal places lat-lon), and thinned to reduce spatial autocorrelation (removing duplicates within the same 0.5-degree resolution grid cell), following data cleaning best-practice guidelines for niche modelling (Araújo et al., 2019). For each point (n=239) I extracted data on 8 bioclimatic variables from the CHELSA climatologies dataset (Karger et al., 2017a) that we expect to be relevant to *M. natalensis* suitability given past studies of the species' ecology (Fichet-Calvet et al., 2007) and the correlates of LF risk (Chapter 4; Fichet-Calvet et al. 2009): mean annual temperature, temperature seasonality, mean temperature of the wettest quarter, mean temperature of the driest quarter, annual total precipitation, precipitation seasonality, mean precipitation of the driest quarter, mean precipitation of the wettest quarter (Table S5.1).

I fitted an ensemble of niche models using three modelling methods (generalised linear model GLM; generalised additive model GAM; boosted regression trees BRT), to account for structural uncertainty in performance of different model types (Araújo et al., 2019; Visconti et al., 2016). For each method I fitted 25 models by combining occurrences with 5 separate sets of random pseudoabsence points across West Africa (400 each for GLM and GAM; 200 for BRT (Barbet-Massin et al., 2012)) and 5-fold partitioning each dataset into a training (80% of data)

and test dataset (20% of data) to evaluate predictive performance. Model predictive performance on test data was consistently medium-to-high (all models AUC >0.73; mean AUC for GLM 0.79, for GAM 0.84, for BRT 0.85). Suitable-unsuitable threshold for each model (to convert to a binary prediction of suitability) was calculated as the value that maximises the sum of sensitivity and specificity (Liu et al., 2016, 2005). For each model I projected and thresholded present-day bioclimatic suitability at 5 arc-minute grid-cell level across West Africa using CHELSA climate data (Karger et al., 2017b). For future climates, I projected and thresholded all models using future bioclimatic variables derived from general circulation models (see above section '*Climate change projections*') (Table S5.1).

Estimation of parameters for reservoir host density across land cover-land use classes. I statistically inferred parameters describing local *Mastomys natalensis* density responses to LCLU using a meta-analytic approach (following the PREDICTS project (Newbold et al., 2015)). I collated site-level *M. natalensis* abundance and density estimates from published surveys of small mammal diversity across land use type and intensity gradients, from across a broadly climatically suitable area of sub-Saharan Africa (17 peer-reviewed and grey literature studies from Sierra Leone, Ghana, Nigeria, Guinea, Ethiopia and Tanzania; Supp. Table 2). The criteria for study inclusion followed (Hudson et al., 2017), requiring that land use type must be clearly described for each site, and that individual site-level numerical estimates must be provided either in effort-insensitive form (i.e. density) or alongside per-site survey effort (trap nights). For studies where trapping effort varied across sites, abundance estimates within studies were adjusted assuming a linear relationship between sampling effort and recorded abundance, following (Newbold et al., 2015). For studies that sampled the same site longitudinally, I calculated the mean of multiple samples within each year (i.e. across seasons). I classified site-level land use type into five broad classes based on source descriptions: natural forest, managed forest (including agricultural and timber plantations), bushland, grassland and cropland (to match classifications in GLOBIOM). The full dataset contains 125 estimates from 17 studies (Table S5.2).

I estimated posterior parameter distributions for relative rodent density as a function of LCLU type using Bayesian mixed-effects models, inferred using Integrated Nested Laplace Approximation (INLA) (Lindgren and Rue, 2010). Site-level estimates were log-transformed and modelled using a Gaussian likelihood, with land use type as a categorical fixed effect, and random intercepts for study and site (following the same modelling approach as in Chapter 2). Natural forest was set as the intercept, so fixed effects estimates for other land classes measure average divergences in relative density from natural forest (whose α_{NF} is fixed at 1) (Table 5.1;

Figure S5.3b). Posterior parameter estimates were exponentiated to the linear scale before running disease risk models (Table 5.2). Insufficient urban gradient studies were available to empirically evaluate the relationship between *M. natalensis* density and built-up urban land, so this parameter was fixed at 1 (i.e. baseline suitability) to reflect evidence that the species is often absent or found at low density in highly built-up areas (as discussed in Chapter 3) (Garba et al., 2014; Gibb et al., 2017). Fixed effects estimates were robust to study-level (random k-fold) and geographical (biome-level) cross-validation (Figure S5.3c). I assume that the relationship between LCLU and *M. natalensis* is constant across the species' geographical range, since the dataset's relatively small size precludes empirical evaluation of potential geographical variability (e.g. due to nonlinear land use-climate interactions (Newbold et al., 2019)). I discuss the potential implications of this assumption in the Discussion.

Lassa virus prevalence in reservoir. Presence and prevalence of infection within the zoonotic reservoir are critical components driving the force of zoonotic infection to humans (Plowright et al., 2017). However, the lack of data on reservoir LASV presence and prevalence outside well-surveyed hyperendemic locales (e.g. Guinea (Fichet-Calvet et al., 2016, 2014, 2007)) makes it unfeasible to collate numeric estimates at regional scale, and to define broad-scale constraints on LASV reservoir prevalence. Therefore, here I assume that *Pr* is homogeneous within reservoir populations across West Africa, which despite overlooking localised spatiotemporal variability in infection prevalence, is broadly reasonable given evidence of widespread human and rodent exposure to LASV across the region (Gibb et al., 2017; Nimo-Paintsil et al., 2019). Indeed, as shown in Chapter 4, several successive years of systematic and expanding surveillance in Nigeria have indicated that human exposures to LF occur country-wide. As further data become available in future (e.g. from systematic rodent monitoring), this assumption could be relaxed to improve differentiation of spatial and/or seasonal trends in infection risk (Lo Iacono et al., 2016).

Scaling of human-rodent contact density. The scaling of contact rates with susceptible and infectious host density is a critical component of modelling pathogen transmission, and simple density-dependent (mass-action) scaling does not effectively describe transmission dynamics across numerous host-pathogen systems, including those involving arenaviruses and *M. natalensis* (Borremans et al., 2017; McCallum et al., 2001). For zoonotic transmission, estimating the functional form of contact rate scaling with changing reservoir (rodent) and target host population densities (human) is extremely challenging, due to the numerous factors that may influence contact processes and an overall lack of data on human-rodent interactions. Earlier studies using this environmental-mechanistic framework scaled species-wide estimates of

average absolute reservoir population density by climatic suitability and then approximated human-reservoir contact rates using an ideal free gas model (Redding et al., 2016); however, this was not feasible to implement here because the land use parameters in our model reflect relative (rather than absolute) abundance. I therefore assume that human-rodent contact rates are linearly correlated to model-predicted rodent relative density (since rodent model parameters are estimated directly from baited trapping data), and logarithmically to human density (i.e. contact density = $R_i \log(H_i)$). Consequently, contact rates (and projected LF risk) asymptote with increasing human density, which is consistent with evidence that human-rodent contact rates do not significantly change along urban-rural gradients in Thailand (Suwannarong and Chapman, 2015), and do not appear strongly correlated to specific socioeconomic factors (e.g. wealth) in LF-endemic areas of Sierra Leone (Bonwitt et al., 2017b, 2016). Further empirical data on drivers of human-rodent interactions across environmental gradients are a key knowledge gap for improving parameterisation, and in the meantime one future direction will be to analyse the sensitivity of results to different scaling assumptions of contact density.

Spillover rate. The force of infection parameter in epidemiological models (Mccallum et al., 2017) governs the rate at which susceptible individuals transition into an infected state. Here, β (spillover rate) describes this phenomenon, as the estimated mean number of new acute cases per-scaled human-rodent contact per-year (Table S5.2), under the simplifying assumptions that all rodents are equally likely to be infected and shed virus (see '*Lassa virus prevalence in reservoir*'). Data on more localised drivers of LASV exposure are sparse, and although my findings in Chapter 4 show that district-level LF incidence is correlated to socioeconomic factors (in particular poverty), identifying the isolated effects of these factors on incidence is challenging given the confounding effects of research effort and other covariates (see Figure 4.4). Here, I therefore assume that this parameter is homogeneous across West Africa, although other factors (poverty, housing quality, agricultural practices) likely stratify human-rodent contact rates across spatial and economic axes. I statistically estimated β from incidence estimates (total acute human cases 2016-18) collated from Situation Reports of reported LF cases from 123 endemic districts in Nigeria (Ilori et al., 2019). I modelled case incidence in a Bayesian mixed-effects framework (INLA), following procedures described in Chapter 4. To summarise, within each district d, mean human-rodent contact density ($\mu R_d \log(\mu H_d)$) was calculated from mean human density (μH_d extracted from CIESIN Gridded Population of the World 2015; GPW) and mean predicted rodent density (μR_d projected at 5 arc-minutes across ESA-CCI LCLU 2010 and niche model ensemble) across all grid cells falling within the district. I then modelled case counts per district as a negative binomial process (n=123), with human-rodent contact-density included as an offset so that intercept parameter measures the posterior

mean (± 95% credible interval) cases per scaled contact over 3 years. This is then divided by 3 to give an annual estimate (β). Because LF surveillance in Nigeria is geographically biased towards certain areas (Ilori et al., 2019), I included a continuous spatially-structured random intercept in the model (Gaussian random field with Matérn covariance function, fitted using a stochastic partial differential equations approach) to control for spatial autocorrelation in case counts. The modelling approach is described in Chapter 4.

Table 5.2: Parameter values, data sources and estimation methods for process-based Lassa fever risk model.

Parameter type	Parameter name	Description	Mean	95% CI (if applicable)	Estimation method	Source
Land use-land cover effects on reservoir density	α_{NF}	Reservoir relative density in natural forest (mixed-effects model intercept so fixed at 1)	1	n/a	Bayesian mixed-effects model	Meta-analytic dataset of *M. natalensis* abundance and density estimates across land use gradients (n=125 estimates from 17 studies)
	α_{Bu}	Reservoir relative density in bushland	3.75	2.41 – 5.88		
	α_{Gr}	Reservoir relative density in grassland	3.65	2.36 – 5.57		
	α_{Cr}	Reservoir relative density in cropland	7.22	4.74 – 10.93		
	α_{MF}	Reservoir relative density in managed forest	1.61	0.84 – 3.15		
	α_{Urb}	Reservoir relative density in built-up lands	1	n/a	Fixed at 1 (baseline suitability)	
Reservoir bioclimatic suitability	c	Per-grid-cell predicted reservoir suitability as a function of 8 bioclimatic variables (thresholded to binary 1/0)	n/a	n/a	Ensemble of 75 distribution models inferred using three methods (GLM, GAM, BRT)	*M. natalensis* geolocated occurrences from published literature and GBIF (n=239)
Lassa virus prevalence (within-reservoir)	Pr	Estimated prevalence of LASV in *M. natalensis* in specific grid-cell	1	n/a	Not estimated; fixed at spatially uniform due to low data availability.	n/a
Exposure rate	β	Infections per rodent-log(human) contact per year, assuming spatially uniform LASV prevalence in rodents	0.129	0.081 – 0.201	Spatially-explicit Bayesian mixed effects model of district-level LF incidence data (2016-18; n=123 districts).	Nigeria Centre for Disease Control Situation Reports

5.3.3. Present-day projection and evaluation of Lassa fever risk model

I projected the LF model under present-day environmental and socioeconomic conditions using 5 arc-minute datasets on land-cover-land-use (ESA-CCI 2010), bioclimatic variables (CHELSA 1979-2013) and human population density (Gridded Population of the World 2010) (Table S5.1). ESA-CCI land cover was reclassified to follow the same LCLU scheme as GLOBIOM (Leclère et al., 2017) and aggregated to 5 arc-minutes by calculating the proportion of each LCLU class. To propagate parametric uncertainty in reservoir climate and LCLU responses into LF risk projections, I ran the model for 1000 iterations of randomly-drawn land use parameters (samples from joint model posterior) and climate (single thresholded distribution model) parameters, and calculate summary metrics of hazard (R_i) and risk (λ_i) (mean and relative uncertainty, i.e. st.dev/sqrt(mean)) per-grid cell (Figure 5.2, Figure S5.4). I evaluated model predictive performance under present-day conditions by comparing projected mean risk at known geographical locations of human LASV exposure (1990-2019) to the background distribution of projected risk across West Africa (following approaches of Redding *et al.*, 2016). I defined LASV exposure as either acute LF disease or serological evidence of infection between 1990 and 2019, and compiled a dataset of geolocated point occurrences (see Chapter 3, Figure 3.1) and district-level acute case records from Nigeria (Ilori et al., 2019) (Figure 5.2, Table S5.1). To account for uncertainty in location of infection event, I extracted mean projected risk within a surrounding 15km radius buffer (for geolocated points) or across the entire district polygon (for districts) (Figure S5.4c). These were compared to risk at 500 randomly-drawn background points across the broadly climatically suitable area of West Africa (mean predicted bioclimatic suitability >0.025 across present-day niche model ensemble). I compared four model specifications to evaluate the impact on predictive ability of explicitly including different environmental drivers: constant hazard (rodent density held constant at its mean across West Africa, i.e. spatial variability in risk driven only by human density); climate hazard (hazard is driven only by climatic suitability, i.e. rodent density is held constant across all land classes); land use hazard (hazard is driven only by land use effects on rodent abundance); and full model (hazard driven by both land use and climate) (Figure S5.4b, S5.5).

5.3.4. Projection of Lassa fever risk across future agricultural and socioeconomic scenarios

I used the gridded datasets of future SSP-RCP pathways of agricultural, climatic and socioeconomic change (as developed above) as input data for the LF risk model, and projected LF hazard (R_i) and exposure (λ_i) for each of 3 SSP-RCP scenarios and 4 time epochs (2010 baseline, 2030, 2050 and 2070). Here, I focused on propagating uncertainty in projected

environmental change (rather than disease model parametric uncertainty) into LF projections, so fixed rodent land use (α) parameters constant at their mean (Figure S5.3b) and use mean bioclimatic suitability (c_i) across the full niche model ensemble for each RCP-GCM-year combination. Within-scenario variance in hazard and exposure is therefore driven only by differences in LCLU spatial allocations and in climate between GCMs. I calculated and summarised hazard (R_i) and exposure (λ_i) for all LCLU-climate combinations (400, i.e. 4 GCMs · 100 LCLU samples) for each model run. Since the environmental and socioeconomic components of each scenario are integrated (i.e. LCLU depends on both climatic and socioeconomic assumptions), it is not possible to estimate how each driver would act truly independently of the others. However, to compare the effects of land change on risk trends between scenarios, I also separately ran submodels in which (1) only human population changes (i.e. only exposure changes, with no environmental change effects on hazard) and (2) human population and climate change (i.e. changes in hazard only driven by climate with no change in LCLU) (following a similar approach to Redding *et al.,* 2016). The differences between these submodels and the full trend projections indicates the effect of land use.

5.4. Results and Discussion

5.4.1. Evaluating Lassa fever model performance under present-day conditions.

Spatially projecting LF under present day conditions shows a wide, heterogeneous distribution of hazard and exposure across sub-Saharan West Africa (Figure 5.2). The full model including both LCLU and climate improves discriminative ability relative to simpler models assuming null effects of either or both environmental factors, both broadly across West Africa (Figure S5.4a-b) and within most endemic countries (Figure S5.5). Propagating parametric uncertainty in the rodent model into projections (across 1000 randomly-drawn sets of climate and LCLU parameters) shows that prediction uncertainty is highest in north Nigeria, potentially because of sparse reservoir occurrence data in this region (Figure S5.4c, Figure S5.3a). These results suggest that large-scale habitat and land use patterns broadly structure LF risk across climatically-suitable West Africa (a finding that is consistent with my Nigeria-specific results in Chapter 4; see Figure 4.3). By presenting barriers to dispersal, current land use patterns might also influence LASV's highly spatially-clustered phylogeography (for example, between north and south Nigeria; Andersen et al., 2015). However, the model overestimates potential LF risk relative to observed human exposure in some areas (much of Mali, Burkina Faso and central Nigeria; the southwest Nigeria–Benin border region; Cote d'Ivoire). These discrepancies indicate research priorities for understanding present and future LF burden, since it is unclear

whether they represent false absences from patchy surveillance, or true absences due to ecological (e.g. lack of LASV in *M. natalensis*, competitive exclusion by other rodents) or virological factors (e.g. lower LASV strain virulence (Andersen et al., 2015)), or socioeconomic factors (e.g. poverty, agricultural practices) that influence population exposure and vulnerability (Figure 5.1).

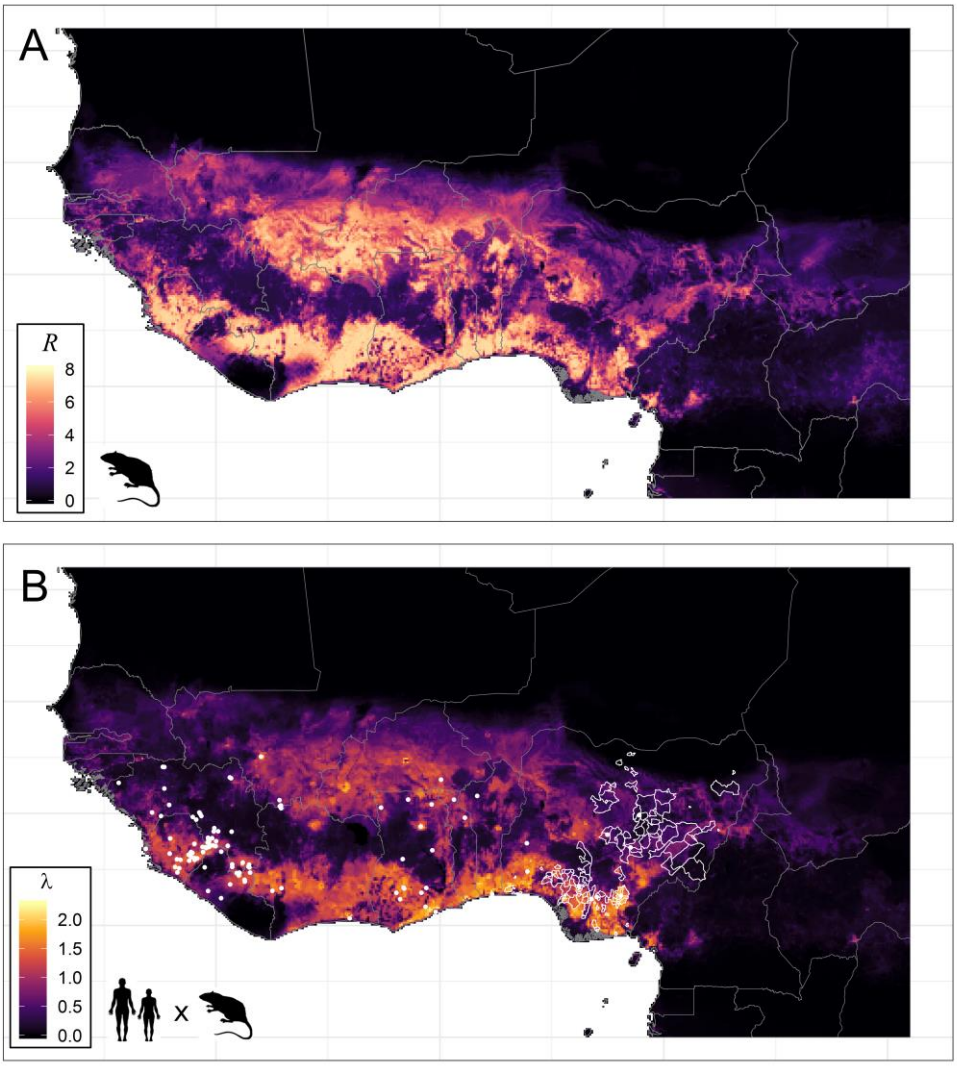

Figure 5.2: Modelled distribution of Lassa fever ecological hazard and risk under present-day conditions. Maps show projected ecological hazard for zoonotic LF transmission (A: potential relative density of reservoir host *Mastomys natalensis* per 5 arc-minute grid cell, R_i) and projected LF risk (λ_i; estimated annual human cases per grid cell, assuming homogeneity of both within-reservoir LASV prevalence and spillover rate) with present-day land use, climate and human population. Overlaid white points and polygons in (B) are known locations of recent confirmed human LASV exposure (either acute disease or seroprevalence from 1990 to 2019) at either specified locations (points) or administrative districts (polygons). The full environmental model with hazard driven by both land use and climate accurately reproduces the observed distribution of risk relative to alternative, simpler models (Figure S5.4b).

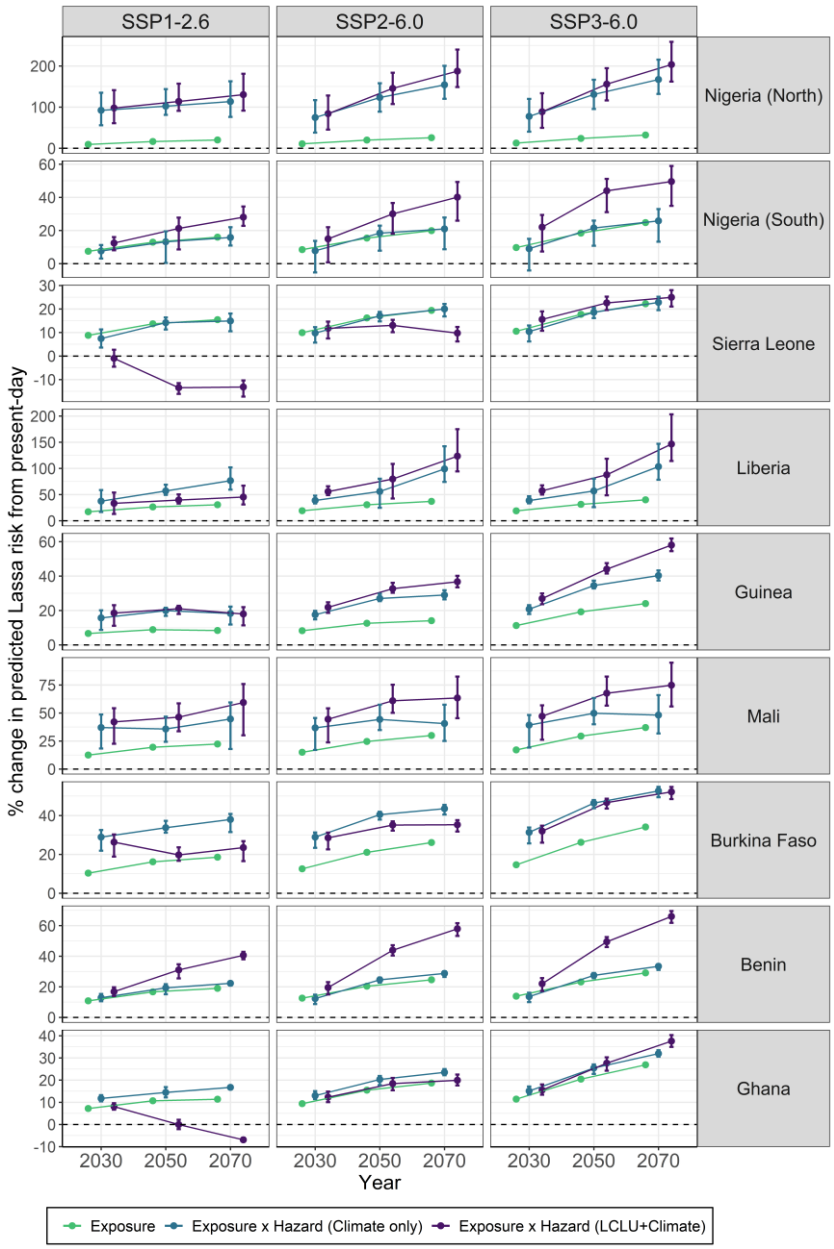

Figure 5.3: Effects of land use, climate and population change on projected Lassa fever trends in endemic countries. Points and errorbars show the % change in mean LF risk (λ_i) across all grid cells within each country, from a 2010 baseline to 2030, 2050 and 2070 (mean, 5th and 95th percentiles across all LCLU-climate combinations per scenario). Panels show, for each country (rows) and scenario (columns), the overall projected trend in LF risk including all drivers (purple) in comparison to submodels where either only human population changes (i.e. exposure only) or only human population and climate change (i.e. change in hazard driven only by climate, with LCLU held at present-day values). The difference between submodels indicates the relative contribution of different drivers to changes in risk: in particular, the difference between climate-driven and full trends indicates whether land use significantly impacts expected climate-driven trends. Overall country-level trends in risk are also visualised for clear comparison between-scenarios in Figure S5.6. Trends are shown for LF-endemic (Nigeria, Sierra Leone, Liberia, Guinea) and sporadically endemic countries (Mali, Burkina Faso, Benin, Ghana), with Nigeria partitioned into north and south due to its large size and agro-ecological diversity.

5.4.2. Quantified pathways of agricultural and socioeconomic change in West Africa.

In all socioeconomic scenarios, GLOBIOM projects substantial regional expansion of agriculture and managed forest area (timber plantations) by 2050 (Figure S5.1), with very similar trajectories for SSP2 and SSP3 (~40% and rising cropland expansion by 2050 and rapid declines in natural vegetation). In contrast, in SSP1-2.6 natural forests are conserved, cropland expands slowly and stabilises by 2050 (at ~30% expansion), and managed forests expand more rapidly. Under spatially-explicit downscaling based on the econometric model, expansions of cropland and losses of natural vegetation are widely distributed across the region, but are particularly concentrated in the savannah regions of Nigeria, Benin, Cote d'Ivoire and southern Mali (visualised for SSP2-6.0 in Figure S5.2).

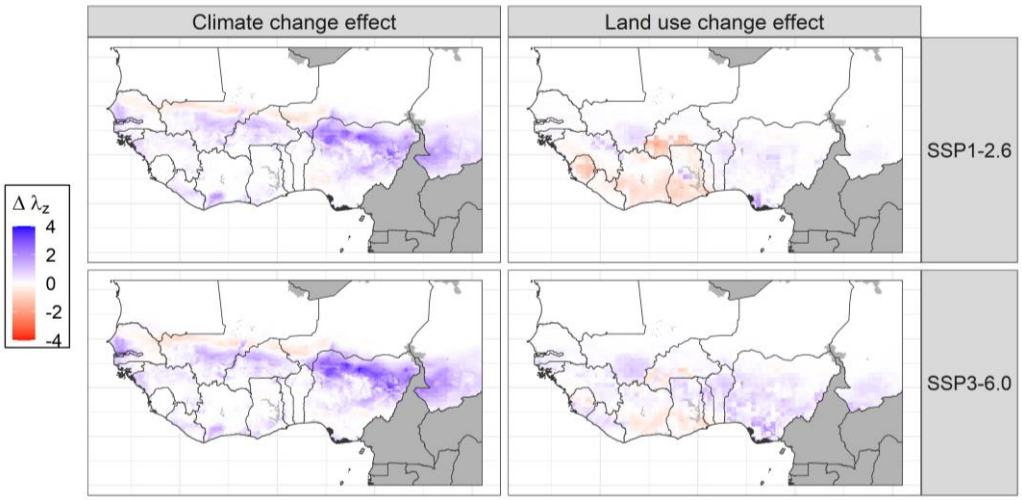

Figure 5.4: Geographical distribution of land use and climate change effects on Lassa fever risk in West Africa in 2050. Maps show, for 2050, the geographical distribution of climate and land use change effects on predicted mean LF risk per grid cell ($\Delta\lambda_i$). Climate effects are calculated as the difference between exposure-only and exposure-climate submodels (i.e. between light and dark green trends in Figure 5.3). Land use effects are calculated as the difference between all-drivers and exposure-climate submodels (i.e. between dark green and purple trends in Figure 5.3), and denote where projected land changes lead to either increased or decreased risk relative to a climate-only model. Colour scale denotes either net increases (blue) or decreases (red) in ecological risk for LF.

5.4.3. Future trends in Lassa fever risk across socioeconomic scenarios and agricultural pathways.

For all scenarios, per-country mean LF risk is projected to increase in the coming decades across almost all LF-endemic countries (purple trend lines in Figure 5.3; also Figure S5.6). Significant increases are observed by 2030 across most countries and scenarios, with notably large increases in northern Nigeria (85-100%), where the disease is now being

increasingly detected (Ilori et al., 2019), and Liberia (29-50%). By fitting submodels that separately examine the contributions of exposure (human population change) and hazards (climate only, and climate and land use), I find that much of this overall upward trend results from increasing exposure due to population growth (from ~307m regionally in 2010 to between 600m (SSP1) and 817m (SSP3) by 2050; light green trend lines in Figure 5.3). Consistent with Redding *et al.* (2016), climate change generally acts to further increase risks, although these effects are minimal in already suitable climates for *M. natelensis* (e.g. Sierra Leone, south Nigeria) and largest further north where species range expansions are projected to occur (e.g. north Nigeria, Guinea, Burkina Faso, Mali; dark green trend lines in Figure 5.3). Crucially, however, projected land use change either amplifies or dampens these increases, depending on countries and scenarios (Figure 5.3-5.4). Consistent rates of cropland expansion from now to 2070 under SSPs 2-3 (Figure S5.1-S5.2) continually increase mean risk of LF transmission across most countries, and notably strongly in Nigeria, Liberia, Guinea and Benin (Figure 5.3). In contrast, under SSP1, natural forest preservation, decelerating rates of agricultural expansion and increases in managed forest are projected to cause human-reservoir contact and LF risk to asymptote or decline in many areas (e.g. Liberia, Sierra Leone, Burkina Faso, Ghana) relative to climate change-only submodels (Figure 5.3-5.4; Figure S5.5-S5.6). The variance in risk driven by uncertainty in econometric model spatial allocation of LCLU is low (generally under 5%), relative to the variance driven by disagreement between climate GCMs (Figure 5.3). However, although it is important to stress that this variability does not account for other salient sources of structural uncertainty in land change projections (e.g. between different integrated assessment models) (Alexander et al., 2017; Prestele et al., 2016).

In contrast to the heterogeneous effects of land use, there is general agreement among climate GCMs that expansion of climatic suitability for *M. natalensis* will generally increase LF hazard by 2030 even under the lowest climate impacts pathway (RCP2.6) (Figure 5.3). These climate-driven increases are particularly concentrated in the central-to-eastern Sahel, and are the main driver of the very increases in LF risk projected for northern Nigeria (Figure 5.3-5.4, Figure S5.6). This result is consistent with climate model intercomparison studies indicating that this subregion will experience higher overall precipitation and longer monsoon seasons in the coming decades (Sultan and Gaetani, 2016), both of which are known to influence *M. natalensis* population dynamics and resulting force of zoonotic infection to humans (Fichet-Calvet et al., 2008, 2007; Marien et al., 2019). In contrast, climate change is projected to drive relatively minimal increases in risk in southern, already endemic areas (e.g. Sierra Leone, south Nigeria), where land use change is the main driver of changing hazards. However, because the climatic impacts on LF in our model are limited to changes in bioclimatic suitability for *M.*

natalensis presence, these results do not account for how more subtle climatic changes in already-suitable areas (e.g. changes in seasonal rainfall affecting rodent population dynamics) could impact dynamics and intensity of human LF incidence (see Chapter 4).

These magnitude and geographical distribution of these projected risk trends will be sensitive to several key assumptions in the disease model. In particular, the assumption of log-linear human-rodent contact density (see Methods) means that the effects of human population growth on exposure (Figure 5.3; green trend lines) are reduced relative to, for example, assuming mass-action (where exposure would scale linearly with human population increases). Similarly, although human-rodent contact rates may in reality vary significantly between land use types, crop types and agro-ecologies (e.g. due to differences in spatial or seasonal behaviour), we assume modes of contact are consistent across land uses due to a lack of data. Filling these data gaps will be a priority for finer differentiation of disease risks.

5.4.4. Implications for understanding effects of land use policy on disease risks.

By considering both land use change and zoonotic risk as emergent from multiple, interacting social and environmental processes, these analyses highlight the importance of a systems-based, multi-driver perspective to understanding global change effects on zoonotic disease. Land use trajectories arising from alternative socioeconomic and climatic assumptions (population, trade, climate effects on crop yields; Table 5.1) have markedly different effects on projected LF risk (Figure 5.3-5.4), whereas considering climate change effects on reservoir suitability alone would predict either stable or increasing risk in most countries from now to 2050 (Figure 5.3). Notably, projected land trends in the more globally-equitable, sustainability-focused SSP1 scenario (preservation of natural forest, stabilizing agricultural expansion due to yield intensification and trade openness) reduce net environmental risk in many areas (Figure 5.4), indicating the potential for synergies between poverty alleviation, biodiversity conservation, and disease risk mitigation. Conversely, although SSP2-6.0 and SSP3-6.0 involve very similar agricultural trajectories which largely amplify LF hazard (Figure 5.4, Figure S5.1), more rapid population growth in SSP3 leads to larger risk increases due to higher exposure (Figure 5.3). Importantly, the SSPs' different socioeconomic narratives (from increasing equity in SSP1 to high poverty and regional fragmentation in SSP3 (Riahi et al., 2015)) also suggest that the highest environmental risk scenario (SSP3) is also the most likely to exacerbate economic vulnerability to disease impacts. I do not explicitly include a vulnerability component of risk in these models (Figure 5.1), because of the challenges of clearly defining vulnerability indices for a relatively data-deficient disease such as LF (Cardona et al., 2012). In future, incorporating

spatially-explicit vulnerability metrics (e.g. based on poverty or inequality; Rao et al., 2019) would provide further insights into this important question.

Significantly, even within low-impact emissions pathways, by 2030 climate and land change are consistently projected to intensify LF transmission potential in certain regions of West Africa, particularly north-west and north-central Nigeria and southern Mali (Figure 5.5). Since surveillance for LF in West Africa remains very patchy, and the disease's present-day burden is poorly defined (see '*Evaluating Lassa fever model performance under present-day conditions*'), this is important from the perspective of strengthening health system capacities for LF detection and treatment in areas where communities may be exposed to increasing risk. Clinical diagnosis for early-stage LF is complicated by the disease's nonspecific presentation (resembling malaria and other common febrile illnesses), and rapid diagnosis can significantly improve the efficacy of treatment and patient outcomes (Emperador et al., 2019; Wilkinson, 2017). As well as targeting areas of discrepancy between our present-day models and observed exposure (Figure 5.2b), enhancement of systematic human and rodent surveillance at these potential emergence frontiers (Figure 5.5) – as has recently occurred in Nigeria (Chapter 4) – would be valuable for both public health and understanding incidence of this cryptic disease.

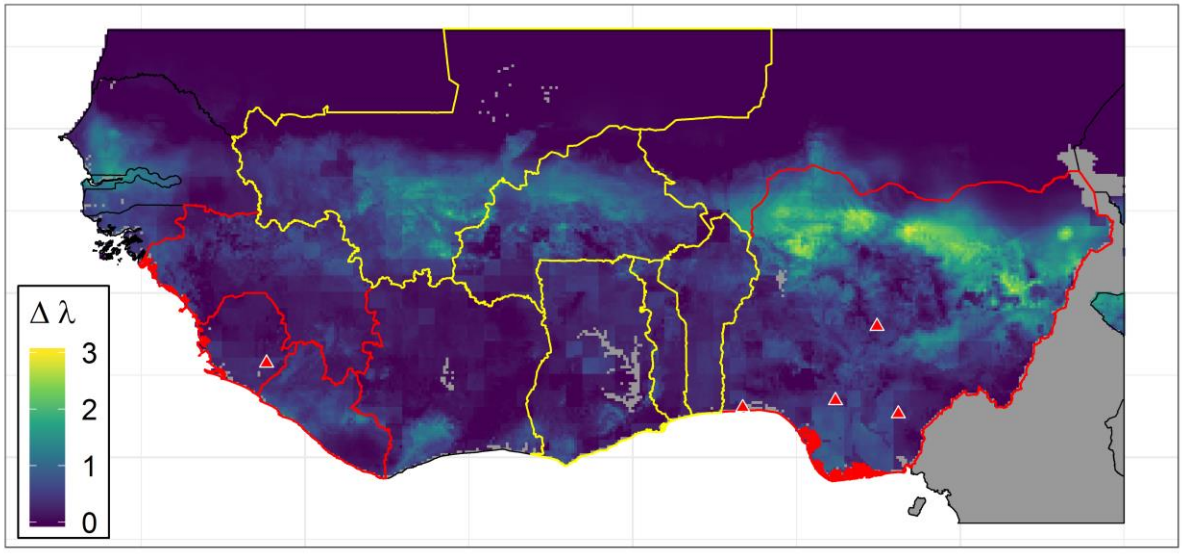

Figure 5.5: Multi-scenario projected change in Lassa fever risk to 2030, and priorities for surveillance and diagnostic capacity building. Map colour scale shows the mean projected change in Lassa fever risk per-grid cell from 2010 to 2030 (mean $\Delta\lambda_i$ across all LCLU-climate combinations) across all 3 SSP-RCP scenarios. Country outlines denote currently endemic (red) or sporadic (yellow) reported acute LF cases. Red points show current locations of laboratories with LF diagnostic capacity in Nigeria and Sierra Leone. On average, LF risk is projected to stay stable or increase across all SSP-RCPs, with environmentally-driven increases in areas of currently low surveillance capacity and high population vulnerability (north Nigeria, southern Mali, Liberia).

More broadly, this study represents a step towards incorporating disease risks more explicitly into the frameworks used to quantify biodiversity, health and ecosystem services trade-offs under global change (Díaz et al., 2019). Projecting disease risk trends to 2030 and 2050, as well as 2070, intentionally connects these analyses more immediately to near-term public health policy and development targets (e.g. the Sustainable Development Goals). Notably, shorter time-horizons see relatively little environmental differentiation between SSP-RCP scenarios, although scenario pathways begin to clearly diverge by 2050 (Figures 5.3-5.4, Figure S5.6), most notably in the LF-hyperendemic Mano River Union (Liberia, Sierra Leone, Guinea) where forest preservation under SSP1 significantly dampens risk compared to higher-impact pathways. Current global climate trajectories are, however, closer to RCP6.0 than RCP2.6, and the steady increases in risks in SSP2-3 suggest that the consequences of ongoing socioeconomic and environmental trends for disease risks may not become fully apparent for decades (Barnett et al., 2015; Rosenbloom et al., 2019). This study's use of a single land change model (GLOBIOM) does present its own limitations for evaluating these trajectories of agricultural change, as different integrated assessment models based on different assumptions show considerable disagreement about global trends in land use this century (Alexander et al., 2017). A useful future step would be to extend this approach to compare projections among multiple land use models (as I have done for climate by using 4 GCMs). Indeed, although this study has focused on Lassa fever, there would be value in extending this risk components-based approach to multiple diseases in zoonosis-vulnerable regions such as West Africa. Multi-disease comparison studies leveraging multiple climate and land use change models could provide a fuller picture of future global change effects on disease burden, and facilitate geographical health systems prioritization and land use planning.

Data and code availability

All data sources are listed in full in Table S5.1. Code for these analyses are in progress and hosted on GitHub (https://github.com/rorygibb/lassa_globiom).

Chapter 6:
Discussion and synthesis.

The unfolding crises caused by the SARS-CoV-2 pandemic have once again focused global attention on the threats posed by zoonoses, and to the role of anthropogenic processes in driving pathogen spillover and onward spread. This problem is at essence ecological, leading to significant efforts in ecology to predict novel disease emergence (Morse et al., 2012; Olival et al., 2017) and identify general relationships influencing disease risk (Keesing et al., 2010; see Chapter 1). Yet, as emphasised by debates around the dilution effect, operationalising these bodies of knowledge for public health and epidemic prevention has proven extremely difficult. In part, this is likely because emerging epidemics and pandemics (e.g. SARS, COVID-19 or Ebola) arise from chance combinations of biological, ecological and social circumstances that are inherently challenging to predict. Indeed, although zoonoses (and especially viruses) are often studied through the lens of pandemic prediction (Carlson, 2020; Pigott et al., 2017), it may well be impossible to predict where and when the next spillover of a novel pandemic virus will occur. For example, much of the public discussion around COVID-19 has focused on the circumstances of the original spillover event(s) (which may or may not have involved a market in Wuhan) (Andersen et al., 2020) yet, while such precise contextual knowledge is important, it will not now assist in controlling the human-to-human spread of the virus, and is unlikely to match the exact future circumstances that would give rise to yet another SARSr-CoV epidemic. What is needed are broader perspectives on the social-ecological pressures that are exacerbating local zoonotic hazards and exposures, and thereby creating conditions of increasing vulnerability to both endemic disease burden (Halliday et al., 2015a; Ngonghala et al., 2014) and severe and destabilising epidemics (Morse et al., 2012).

The research presented in this thesis has taken a multi-driver, process-based perspective on the effects of these pressures on the hazard, risk and incidence of zoonotic diseases, both in a general pan-disease context (Chapter 2) and for a case study of Lassa fever in West Africa (Chapters 3 to 5). In Chapter 2 I showed that land use has global and systematic effects on local zoonotic host community diversity. Among the key findings of this study was the importance of human-managed landscapes in facilitating increased abundances of rodent reservoir hosts of zoonotic pathogens and parasites (up to 52% increase; Figure 2.4). Understanding the relationship between future expansions of agricultural landscapes (Popp et al., 2017) and rodent-borne diseases risks is crucial in vulnerable, fast-changing areas, of which Lassa fever in West Africa is a particularly pertinent case study. In a review of existing

knowledge on the eco-epidemiology of Lassa fever (Chapter 3), I argued that improving control for LF will require more clearly identifying the disease's current distribution and drivers, and their relationship to changes in reporting effort (Figure 3.1). I was able to address some of these gaps by analysing the first long-term, systematic surveillance dataset for LF, collected over 8 years in Nigeria, and identifying clear environmental dependencies of human LF risk (Chapter 4). Looking forward, I then examined the consequences of different future agricultural pathways for LF regionally, and found that, while climate changes across all emissions pathways are expected to expand the at-risk area of LF, land use changes have potential to either exacerbate or dampen these risks (Chapter 5).

In this synthesis chapter, I discuss the contributions of these studies to broader knowledge, and highlight outstanding questions. First, I discuss methodological innovations and challenges, and propose how the approaches I have developed could be extended to improve modelling of zoonotic risks in the future. Secondly, I discuss how my results contribute to our understanding of land use and climate change effects on zoonotic risk, and specifically on the epidemiology and control of Lassa fever. Finally, I offer a broader perspective on zoonotic disease as an environmental nexus issue within a Planetary Health context, and discuss how disease risks may interact with other climate-linked vulnerabilities to affect human health.

6.1. Methodological developments, challenges and future directions

One of the most consistent confounders to understanding the ecological processes driving zoonotic disease risks is the existence of systematic biases in host-pathogen and disease data, as well as in biodiversity data more broadly (see Chapter 1). Accounting for these data and surveillance biases has been a consistent challenge throughout in this thesis, which I have addressed using hierarchical or mechanistic modelling approaches to approximate either data-generating or ecological process. In Chapter 2 I developed a novel bootstrapping method to propagate species-level uncertainty in zoonotic reservoir host status into community-level models of host diversity (Figure 2.2, Text S2.1). This method effectively simulates how improved sampling of poorly-studied 'non-host' species could impact estimates of the responses of host diversity to land use. Importantly, this approach more clearly showed the importance of land use intensity in driving increases in host richness and abundance (Figure 2.3). This kind of method could be usefully applied more broadly in host-pathogen macroecology, especially when analysing metrics (e.g. network statistics) that are likely to be strongly influenced by missing data (Gomez et al., 2013; Luis et al., 2015). In future, applying simulation-based approaches similar to those developed here – i.e. explicitly informed by prior biological knowledge and

proxies for measurement uncertainty (Text S2.1) – could assist in evaluating how improved sampling of poorly-studied species may affect inferred host-pathogen interaction networks.

Similarly, in Chapter 4, explicitly accounting for ongoing expansions in surveillance (Figure 4.2) was crucial to identifying the relative effects of environment and reporting on the distribution and dynamics of Lassa fever in Nigeria. To do this, I used suspected (negative) case reports at district-level as a proxy for surveillance sensitivity over space and time, and derived a statistical index of suspected case reporting effort (Figure S4.2). When included as a covariate in spatio-temporal incidence models, this allowed me to disentangle the effects of interannual surveillance changes on overall incidence, from the effects of lagged rainfall and vegetation (Figure 4.5-4.6). High out-of-sample predictive ability in Nigeria suggests that short-term forecasting of climate-driven disease dynamics in endemic areas is feasible, although the time-series is still fairly short (8 years); future year-on-year evaluations of predictive performance would assist in understanding the scope for an early warning system for public health decision support (Ballester et al., 2016; Lowe et al., 2016). Importantly from a public health perspective, my analyses also showed that 2018 and 2019 were climatically similar to prior years, and suggested that the unprecedentedly large seasonal surges in LF during 2018 and 2019 were most likely the result of improved surveillance. Nonetheless, because the reporting index is based on suspected case data for the same disease it is still fairly conservative, with the potential to overestimate the importance of effort relative to environmental factors (particularly spatially; see caveats in Section 4.4.3). Indeed, this complexity of statistical accounting for surveillance effort, and some apparently counterintuitive fixed effects results (e.g. for improved housing; see Figure 4.3), highlight the limitations of such a correlative, linear modelling-based approach to inferring the dynamics of zoonoses – that it is not possible to clearly infer mechanistic relationships between predictor covariates and components of risk (Figure 1.1). Such caveats caution against using the models in Chapter 4 to project risk more broadly across West Africa, or at long future timescales.

Some authors have argued that correlative modelling and mapping approaches are still often the most conservative approach to projection of future disease risks, in the absence of detailed biological knowledge to parameterize mechanistic models (Messina 2015). However, for neglected zoonoses with poor data coverage (such as Lassa fever), there are clearly benefits to more ecologically-informed approaches that leverage existing knowledge of the species involved in transmission cycles, their responses to environment, and the drivers of spillover (Murray et al., 2018; Peterson, 2008). Innovations in mechanistic modelling of spillover offer insights into how these processes scale up to broader patterns in human disease, but in the past

have either focused mainly on climate (Mordecai et al., 2017; Ryan et al., 2019), have treated host ecology as a latent variable (Lo Iacono et al., 2016), or adopted relatively simple representations of land use (e.g. effects on host occurrence within distribution models; Redding et al., 2016). The study presented in Chapter 5 focused on incorporating ecological mechanisms and scenarios of land use change into future disease projections, and thus required specifically parameterising the effects of land use on local hazard (i.e. reservoir host density). To do this, I restructured the environmental-mechanistic framework of Redding *et al.* (2016) to include parameters for the relationships between different land use types and *Mastomys natalensis* relative abundance (a more epidemiologically-relevant metric than occurrence), inferred using a similar meta-analytic approach to Chapter 2 (Figure S5.3).

Using this approach, I found that including land use effects on reservoir host abundance improved predictions of present-day LF distribution compared to a climate-only model (Figure S5.2), which supports Chapter 4's findings that Lassa incidence in Nigeria is associated with agriculture (Figure 4.3). Due to data constraints the parameterization was relatively simple, assuming that land use acts on host populations independently of climate rather than interactively; against this assumption, there is recent evidence that species responses to land use change may depend on proximity to thermal tolerance limits (Williams and Newbold, 2020). Such spatial complexities of interacting climate-land use effects on reservoir host communities may be crucial in shaping future hazards and, along with pathogen-specific parameters (e.g. effects of temperature on transmission rates), would be an useful next step towards further improving the ecological component of these models. However, inferring such relationships statistically would require large datasets of geolocated species abundances across the full range of present-day climatic niche space (Isaac et al., 2020), or doing so using process-based niche models would require species-level physiological information (e.g. thermal tolerances) (Kearney and Porter, 2009). Such data are available for some important mosquito vectors (Mordecai et al., 2013b, 2017), but rarely exist for reservoir host species and communities. The approach I developed here represents a step in that direction, by leveraging available species-level data from ecological gradient studies (Chapter 5).

Similar approaches could be extended to other zoonotic diseases for which sufficient host species occurrence and gradient-based abundance data are available. However, an ongoing challenge will be evaluation of predictive performance, selection of appropriate model complexity, and testing under what conditions such models may perform well or badly (Getz et al., 2018). In Chapter 5 I evaluated risk prediction ability by comparing estimated risk (here, hazard and exposure) at known historical LF case occurrence locations to background points

(following Redding et al., 2016), which is a compromise given a lack of incidence data for West Africa. Case occurrence is however a coarse proxy for realized risk, and one useful future research direction would be to systematically evaluate the performance of this kind of statistical-mechanistic disease model for predicting not only occurrence, but also relative incidence. For example, a recent study applying a similar model for yellow fever showed significant promise in recovering observed spatial and temporal disease trends in Brazil (Childs et al., 2019). Ideally a broader structured evaluation would include comparison across multiple zoonotic disease systems with different characteristics, for example in terms of transmission route (e.g. vector-borne versus directly-transmitted) or reservoir communities (e.g. small mammals, birds, or primates). Such systematic tests would be challenging for African zoonoses due to very patchy human case data, but could feasibly be carried out elsewhere globally. For instance, many South American countries are experiencing rapid environmental changes and have significant zoonotic disease burdens, but in many cases have had historically stronger health and disease reporting systems.

6.2. Contributions to understanding the global change ecology of zoonotic spillover risk

Although the debates around diversity-disease relationships have often been framed around biodiversity loss, two decades of disease ecology research have above all emphasised that *how* local ecological communities change under anthropogenic pressures is crucial to determining the consequences for disease risk (whether zoonotic or in wildlife) (Pieter T J Johnson et al., 2015; Joseph et al., 2013; Keesing et al., 2006; Ostfeld and LoGiudice, 2003). For example, under a null expectation that species extirpation risk is random with respect to host status (Ostfeld and LoGiudice, 2003), we would expect local host diversity to correlate positively with overall community diversity, and thus for pathogen transmission rates to generally be higher in more biodiverse, undisturbed communities (i.e. so-called 'amplification effects') (Faust et al., 2017; Joseph et al., 2013). Indeed, research and policy narratives around zoonotic emergence risk have often leveraged such a conceptual model, by characterising humans as agents of incursion into natural landscapes (e.g. via hunting), or contact at ecotonal interfaces (e.g. forest edges), as crucial drivers of emergence and outbreak risk. When novel outbreaks do occur, such narratives can lead to local communities being blamed for causing spillover through supposedly risky extractive or cultural practices (e.g. wildlife hunting, consumption and trade) (Bonwitt et al., 2018), with less focus on the wider ecological and economic context that creates zoonotic hazards.

Chapter 2 instead shows that the currently-dominant global pressure on terrestrial biodiversity – land use change – plays a complex and nuanced role in shaping reservoir host communities and human-wildlife interfaces. My results suggest that species losses are *not* random with respect to host status, and that reservoir host communities respond in systematic ways to anthropogenic land use intensity, leading to overall increases in community zoonotic potential (Figure 2.3) but also taxonomic differentiation (with human-dominated landscapes increasingly dominated by passerine, bat and rodent hosts; Figure 2.4). This finding is consistent with evidence from system-specific studies; for example, dilution-like effects (i.e. higher disease risk) in defaunated or agricultural systems have almost always been documented in either rodent-borne (e.g. hantaviruses, Bartonella, Lyme disease, rickettsias) or avian zoonoses (e.g. West Nile virus) (Kilpatrick et al., 2006; Ostfeld et al., 2000; Suzán et al., 2009; Young et al., 2014). In contrast, primate-borne diseases are often associated with ecotonal or mosaic landscapes (i.e. areas where primate hosts persist at sufficiently high abundances) (e.g. Goldberg et al., 2008). Such nuances certainly matter for evaluating who, where, and what kinds of landscapes, are at greater risk for some pathogens and not others (Plowright et al., 2017). Thus, although global land changes are having general, directional effects on overall zoonotic hazard and human exposure potential (Figure 1.1) – which may be one factor behind increasing emergence rates of zoonoses globally (Allen et al., 2017; Jones et al., 2008) – taxon- or pathogen-specific approaches are still necessary to understand how particular diseases may be affected by current and future environmental change (as I showed in Chapter 5).

My findings in this thesis raise a number of pressing questions that are crucial to better understanding the global change ecology of zoonotic disease risk. Firstly, what are the species-level ecological and biological traits mediating shifts towards higher zoonotic potential in human-dominated landscapes? My analyses were necessarily restricted to known hosts of known zoonoses, yet both binary 'host' status and pathogen richness are coarse representations of underlying continuous trait distributions, and could arguably provide less insight into the potential for novel pathogen emergence from as-yet-unknown host species. Further insights into disease emergence risk could come from linking my approach – focused on responses to environmental change – with traits- and network-based methods focused on identifying species with potentially reservoir-like characteristics (Albery et al., 2020; Gomez et al., 2013; Han et al., 2015). For example, my findings in Chapter 2 are broadly consistent with the hypothesis for a role of life history traits; species with a faster pace-of-life often show greater population resilience to anthropogenic pressures (Purvis et al., 2000) and lower investment in adaptive immunity due to a trade-off with growth and reproduction (Hawley and Altizer, 2011). Further research into the macroecology of adaptive immunity (Becker et al., 2020), and how immune

traits (e.g. white blood cell counts) covary with local extirpation risk across the mammalian and avian tree of life, could provide more detailed insights into these relationships. This will include understanding exceptions to broad patterns. For example, bats (Order: Chiroptera) show clear divergent responses to land use between host and non-host species, yet are unusually long-lived for their body size, and have distinctive immune system traits thought to be linked to coping with the energetic stresses of powered flight (Brook and Dobson, 2015). Notably, in bats extinction risk is correlated to wing morphology (Jones et al., 2003; Jung and Threlfall, 2018), such that longer-distance flyers are more tolerant to disturbance, indicating a possible role of movement ecology in shaping the patterns we observe (Figure 2.4).

Another important future research direction concerns the role of landscape characteristics in mediating zoonotic hazard. The importance of land use intensity (Figure 2.3) suggests that human-dominated agricultural and plantation systems are key foci of disease risk (Gottdenker et al., 2014; Shah et al., 2019), and that incursion or edge-based models of risk may be more relevant to certain types of infections (e.g. primate-borne) than others. This raises broader questions around how to structure and manage such landscapes so as to ensure food security, preserve biodiversity and deliver co-benefits by regulating reservoir host populations (i.e. the 'ecosystem service' of disease regulation). For example, how does landscape structure surrounding agricultural or urban sites (e.g. degree of fragmentation, forest cover, vegetation heterogeneity) affect the zoonotic potential of communities, and across what spatial scales? To what extent are the trends we observe driven by community filtering (i.e. hosts in anthropogenic sites are a nested subset of primary vegetation species) versus species turnover (i.e. hosts are novel synanthropic colonisers from elsewhere), and how might such metacommunity dynamics affect the potential for zoonotic pathogen persistence and spread across fragmented landscapes (McCallum and Dobson, 2002; Suzán et al., 2015; White et al., 2018)? Do the diversity and abundance of important arthropod vector genera (e.g. *Aedes*, *Culex* and *Anopheles* mosquitoes; *Ixodes* ticks) follow similar predictable community shifts in response to land use (Burkett-Cadena and Vittor, 2018), and how does this affect general patterns of spillover potential? In the context of Lassa fever, what kinds of agricultural and land management practices could assist in naturally regulating *M. natalensis* populations in order to dampen seasonal surges in spillover risk (Figure 4.5-4.6), and/or reducing human-rodent contact during those highest-risk periods? Is it feasible to design land management strategies to reduce disease hazards that account for the long-term perturbations of climate change (Chapter 5; Albert et al., 2017)?

Such questions have until recently rarely been addressed in a disease ecology context (although see Sokolow et al., 2019), unlike in the ecosystem services and multifunctionality domains where they are ubiquitous (and, for example, focus on understanding how economically-important pollinator populations are maintained in cropland habitat) (Cardinale et al., 2012; Vanbergen and Initiative, 2013). Yet they have urgent relevance to current debates in the biodiversity and environmental policy communities about the relative value of 'land sparing' versus 'land sharing' approaches to human-wildlife coexistence (Kremen, 2015). For example, narratives around zoonotic risk that focus mainly on exposure processes (e.g. spillover from hunting in wild landscapes; edge-based models; Faust et al., 2018) might advocate for the benefits of land sparing with minimal human-wildlife contact. Yet in contrast, my results provide some support for the notion that lower-intensity landscapes managed for wildlife *and* people (i.e. land sharing) might often be an overall better strategy for reducing net hazard across multiple zoonoses, alongside maintaining other vital ecosystem services (Isbell et al., 2017). With the ongoing development of the IPBES platform (Díaz et al., 2019), including stakeholder-developed scenarios for nature and people (Rosa et al., 2017), it is a timely moment for infectious disease hazards to be better incorporated into decision-making around biodiversity and human wellbeing. Chapter 5 presented a single-disease case study showing the importance of accounting for landscape change in future projection for Lassa fever. Further development and systematic evaluation of these kinds of models could provide one route towards spatial analyses of net zoonotic risks (i.e. across multiple diseases) and potential trade-offs with agricultural production under present and future climatic and socioeconomic conditions (similar to those conducted for other ecosystem services such as carbon storage and sequestration; Gibbs et al., 2010; West et al., 2010). Improving our understanding of this crucial question will also require better characterising the links between changing ecological hazards and realised risk of multiple zoonoses (i.e. disease occurrence, incidence and burden), for example by leveraging long-term time-series of biodiversity monitoring and disease surveillance data collected in fast-changing regions (e.g. the Brazilian Amazon).

6.3. Contributions to understanding the epidemiology and control of Lassa fever

As recently as 2017, when I began working on this thesis, Lassa fever was neglected in comparison to other many emerging viruses (Chapter 3). Since then, the funding of LF vaccine development by the Coalition for Epidemic Preparedness Innovations (CEPI), alongside recent high-profile case surges in Nigeria, has led to an abrupt rise in international public health attention on LF. Much of the recent research on Lassa virus has focused on vaccine and diagnostic development (Purushotham et al., 2019), with few recent published studies on the

ecology of the disease. Yet the growing evidence that LF cases arise mainly from zoonotic spillover (Elsie A Ilori et al., 2019; Siddle et al., 2018) emphasises that understanding LASV ecology will be crucial to targeting disease control and prevention (Mari Saez et al., 2018). For example, for a spillover-driven pathogen with such a widespread rodent reservoir, protecting human populations via vaccines would effectively require universal roll-out (or roll-out to high risk demographic groups) in areas where LASV is known to be endemic in *M. natalensis* populations. Yet our understanding of such risk hotspots continues to be extremely limited (a factor that is also likely to impact the design of field trials of vaccine efficacy). Therefore, one of the crucial questions I identified in Chapter 3, and addressed in part in Chapter 4, is the extent to which surveillance effort shapes our current understanding of LF's endemic area, and whether LASV could be ubiquitous but unobserved in *M. natalensis* across much of West Africa.

When analysing the first systematic, multi-year surveillance dataset for LF, I found that the main factors explaining disease occurrence and incidence in Nigeria were indeed related to reporting effort (Figures 4.4-4.6). Notably, the sharp increase in incidence in 2018-2019 appears to have been mainly driven by the Nigeria Centre for Disease Control's ongoing roll-out of systematic surveillance. Indeed, the socio-ecological conditions associated with LF occurrence and incidence (rainfall, agriculture, poverty) occur across much of Nigeria (Figure 4.4), suggesting either that the heterogeneity of observed LF incidence is explained by factors that we are unable to measure yet (e.g. LASV hyperendemicity in rodents), or that LF may be much more widespread than currently observed. In support of the latter hypothesis, successive surveillance years in Nigeria (most recently 2020) have continued to see ongoing expansion of the known endemic area. Given that most LASV infections are believed to be mild or asymptomatic (McCormick et al., 1987b), and that case fatality rates are lowest in hyperendemic hotspots (suggesting a bias towards detecting only the most severe cases elsewhere) (Akpede et al., 2019; Ilori et al., 2019), it appears highly likely that a very large number of infections are continuing to go undetected. Other recent evidence similarly suggests a significant number of undetected infections elsewhere in West Africa where the disease is not considered endemic (Nimo-Paintsil et al., 2019). Future human surveillance should therefore continue to target areas that are predicted to be environmentally suitable based on both empirical (Chapter 4) and mechanistic modelling (Chapter 5), to better characterise the distribution of the disease. But there is also a clear need to develop systematic rodent monitoring programmes to better characterise geographical and seasonal variations in rodent LASV seroprevalence in Nigeria (and more broadly), and how these vary along the broad axes of risk (climatic, agricultural, poverty) identified in this study. Establishing such baseline knowledge is especially important

that future climatic and socio-ecological changes are projected to drive net increases in LF risk in Nigeria across all future scenario pathways (Chapter 5).

The analyses in Chapter 4 also provide the first detailed empirical insight into the environmental and socio-ecological correlates of LF incidence. Until now, studies have been restricted to occurrence-based niche models (based on datasets such as Figure 3.1) which, although suggesting a role of rainfall in characterising the broad distribution of LF risk, were unable to identify finer-scale processes (Fichet-Calvet and Rogers, 2009; Mylne et al., 2015). Chapter 4 provides strong evidence that rainfall dynamics are key determinants of the risk of LF spillover, over space and also seasonally within endemic areas. This relationship is likely to be mediated by reservoir host population ecology, with *M. natalensis* showing seasonal, rainfall-linked population dynamics, with population growth during the rainy season (as food availability increases) followed by crashes during the dry season (Chapter 3). Notably, in endemic areas of Nigeria, LF risk effectively follows the curve of seasonal rainfall at a 3-5 months lag (Figures 4.5-4.6); the lag between rodent population growth and peak in spillover intensity may be due to lags in LASV infection peak in the rodent population, and/or behavioural or physiological consequences of the onset of the dry season. Supporting the latter hypothesis, declines in vegetation greenness around the time of infection are consistently important in predicting peaks, suggesting that increased infection risk might be associated with elevated human-rodent contact (as rodents seek stored food in and around human habitation) (Fichet-Calvet et al., 2007) and/or physiological stress and increases in viral shedding as food availability declines (as hypothesised in some bat species; Kessler et al., 2018). Notably, comparing seasonal incidence dynamics between southern and northern endemic areas does suggest that climate is a limiting factor on *M. natalensis* populations and Lassa fever incidence; human cases occur year-round in the south (where rainfall and vegetation are consistently higher; Figure S4.5) but are much more sporadic between surges in the north (Figures 4.5 and 4.6).

Importantly, these findings in Chapter 4 in turn provided empirical support for some key assumptions and decisions in the environmental-mechanistic model I implemented in Chapter 5 – these include supporting the rationale for including more explicit land use parameters, the use of use of climate niche models to estimate limits to *M. natalensis* suitability, and the assumption that LASV is found in *M. natalensis* throughout West Africa. My global change analyses indicate a more complex future picture of LF risk than was suggested in Redding *et al.*'s (2016) original study that proposed this modelling framework and projected risks in 2070 using a single general circulation model. I found that different climate and

socioeconomic futures result in markedly different projected agricultural pathways for West Africa (Figure S5.1), and that these may either dampen or amplify projected risks in different areas (Figure 5.3; see full discussion in Chapter 5). It is important to again emphasise that these results are projections (rather than future predictions) under the assumptions of a single land change model (GLOBIOM), and thus are inherently uncertain (Prestele et al., 2016). Nonetheless, the findings offer some specific conclusions form a public health perspective: that both climatically suitable areas currently undergoing land changes, and human-dominated agricultural landscapes experiencing increasing precipitation trends, are likely to be high risk for future LF emergence. In particular, although there is significant disagreement among general circulation models about future climate trends across much of West Africa, there is general consensus that precipitation will significantly increase in the central-eastern Sahel (Sultan and Gaetani, 2016). My results suggest that this will lead to consistent increases in LF risk in northern Nigeria regardless of the climate mitigation scenario (Figure 5.3-5.5); this is a region that is already highly agricultural, where *M. natalensis* and LASV are already known to be present, and with high levels of poverty and existing vulnerabilities. Strengthening health systems to improve detection, early diagnosis and treatment of LF in areas like this should be a critical facet of adaptation to increasing disease risks.

Simultaneously, leveraging both ongoing human surveillance and rolling out rodent surveys would assist in further assessing the scope for a seasonal early-warning system for the timing and amplitude of peaks in different regions (Chapter 4). With near real-time meteorological data increasingly available, such a system could provide public health decision support for disease prevention (e.g. advance warning of high risk periods) or treatment (e.g. by increasing clinical suspicion for LF to ensure appropriate, early treatment of probable cases) (Campbell-Lendrum et al., 2015). In particular, marked differences in baseline incidence between adjacent districts in Nigeria highlight the need for comparative socio-ecological systems studies between apparently LF hyper- and hypo-endemic areas, to identify the reasons why seasonal surges appear more dampened in some areas than others. Focusing on the seasonal interaction of landscape characteristics, rodent population dynamics and behaviour, and seasonal human practices (e.g. agriculture) would assist in better understanding the ecology of this neglected disease, while providing crucial mechanistic information to inform more accurate short-term and long-term forecasting.

6.4. Towards nexus-based approaches to adaptation to changing zoonotic disease risks

There is increasing recognition of the threats that zoonotic and vector-borne diseases pose to global public health in a changing climate (Watts et al., 2019). Although novel pandemics are an ongoing concern (as emphasised by SARS-CoV-2), the majority of zoonotic disease burden is endemic and falls on poorer populations in low- and middle-income countries. Like other natural hazards, pathogens both exploit and amplify these existing vulnerabilities: many endemic infections are diseases of poverty, linked to living closely alongside domestic animals and synanthropic wildlife (Bonwitt et al., 2017b; Halliday et al., 2015a; Kelly and Marí Sáez, 2018) and exacerbated by food and healthcare insecurities that can lead to vicious cycles of poverty and disease (Garchitorena et al., 2017; Ngonghala et al., 2017a). There is a general consensus that climate change impacts – for example, on agriculture, water, sanitation, and exposure to extreme weather – will most severely impact on those already-vulnerable populations (Cardona et al., 2012). Global climate change mitigation to ensure a low-emissions, low-warming future will be fundamental to reducing these impacts (IPCC, 2018). Simultaneously, mitigation of land use change impacts urgently requires broader, systems-based analyses of the upstream drivers (i.e. economic and trade pressures from richer Global North economies) that are driving deforestation, plantation expansion, and increasing disease hazards in vulnerable regions (Marques et al., 2018; Wallace et al., 2015; Wallace and Wallace, 2016). However, given that international mitigation targets and agreements are not proceeding quickly enough to prevent significant levels of warming, local and national-level adaptation strategies will be increasingly crucial to limit the negative consequences of climate change for health and wellbeing (Moss et al., 2010; Watts et al., 2019).

Increasingly, such challenges to adaptation are framed and analysed as nexus issues, asking: how can natural resources and food systems be managed to balance trade-offs and support sustainable, healthy livelihoods, that are also as resilient as possible to the effects of climate change (e.g. Pastor et al., 2019)? Similar questions are increasingly prevalent within biodiversity conservation, such as how best to design protected area and habitat networks that are robust to climate impacts (Albert et al., 2017). My findings throughout this thesis suggest there would be a great deal of value in including quantitative analyses of disease risks in assessments of future environment-health trade-offs. Indeed, the concept of the 'unhealthy landscape' has been used to describe forms of land use that amplify multiple health hazards (Patz et al., 2004), and such issues increasingly intersect both with IPBES's work to preserve biodiversity and ecosystem services (Díaz et al., 2019), interest in nature-based solutions, and urgent conversations about environmental and climate justice. Broad-scale ecological modelling

approaches such as those applied in Chapter 5, as well as more general indicators of zoonotic hazard (Chapter 2, Section 6.2), could support this work by evaluating disease hazard and risk consequences of proposed future land use changes, and thus better understand the nexus of land use, climate, food security and zoonotic disease risk.

Importantly, Planetary Health and resilience-based perspectives that are grounded in stakeholder objectives and in addressing emerging vulnerabilities can inform the kinds of questions that zoonotic disease modellers could and should be asking. To usefully support environmental and public health decisions for climate adaptation, future risk modelling needs to move beyond static correlative mapping of how transmission potential is expected to change under different emissions scenarios, and towards process-based approaches that enable testing of the effects of more localised social and ecological interventions on projected spatial and/or temporal risk patterns (Ihekweazu and Abubakar, 2017). Mathematical or hybrid statistical-mechanistic approaches based on components of risk for multiple zoonoses (Figure 1.1) – as I have applied in this thesis for one case study disease – could provide a useful toolkit for supporting adaptation policy in public health (e.g. health systems and surveillance strengthening, community-based participatory approaches) or environment domains (e.g. land use and agricultural policy). These kinds of questions include: Where are future expansions or increases in ecological hazard (i.e. reservoir and vector population potential) predicted to intersect with existing or increasing social vulnerabilities to infectious disease? Where are the consensus areas of increasing hazard and vulnerability across all future emissions trajectories and climate models (Chapter 5), and thus likely to be priorities for strengthening health systems and improving surveillance? How should geographical roll-out of vaccine campaigns for spillover-driven zoonoses (e.g. Lassa fever) be designed to prioritise the most vulnerable populations? How can agricultural and land use planning strategies ensure both future resilience of food security and economies to expected climate impacts (e.g. expansion or intensification of agriculture in environmentally suitable areas) while minimising associated disease hazards? Is there potential for spatial land use synergies between biodiversity conservation commitments, food security and disease risk mitigation, and how resilient are these synergies (and trade-offs) to within- and between-scenario climate uncertainty?

From the ecological modelling side, moving towards addressing such questions will require robust evaluation of model predictive performance and uncertainty (both structural within disease models, and scenario-based). Risk process modelling approaches nonetheless provide a clearer framework for quantifying and communicating different sources of uncertainty to decisionmakers than correlation-based mapping approaches (which, for example,

conflate hazard and exposure; Figure 4.3). Moving beyond the global Shared Socioeconomic Pathways (Chapter 5) towards national or regional stakeholder-developed environmental scenario pathways (as were recently developed for West Africa; Palazzo et al., 2017, 2016) could also provide more context-sensitive and useful frameworks for policymakers to evaluate and act on disease risks in an environment-health context. Nonetheless, ecological change perspectives, while necessary for many diseases, will not be sufficient to address these challenges. Recent public health assessments of future vector-borne disease risks have identified poor baseline knowledge of current disease distribution and burden as a crucial barrier to future adaptation (Campbell-Lendrum et al., 2015). As outlined in Chapters 1 and 3, this is also the case for most zoonoses. As shown by the Nigeria Centre for Disease Control's recent prioritisation of LF, rolling out epidemiological surveillance is crucial (Holmes et al., 2018), and can rapidly and significantly improve baseline understanding of dynamics, drivers and distribution for priority infections (Chapter 4). Simultaneously, what is urgently needed is better understanding of socioeconomic vulnerabilities to disease and their sensitivity to environmental changes, and how these play out both for specific diseases and more generally (Bardosh et al., 2016, 2017a; Dzingirai et al., 2016; Grant et al., 2016). Traditional public health infectious disease interventions generally target population exposure and vulnerability, and such interventions in the present will still be among the most effective means of adapting to increasing disease hazards (Cardona et al., 2012). The quantitative work in this thesis has focused mainly on hazards and exposure, but also understanding the effects of interventions to reduce vulnerabilities (e.g. health systems strengthening, poverty alleviation, urban planning, vaccine campaigns) will ultimately be crucial to intervening to reduce emerging spillover and epidemic risks under rapid global change.

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Appendices

Appendix 1: Supplementary figures and data for Chapter 2.

This appendix provides supplementary figures, tables and information on data sources for the analyses conducted in Chapter 2, *'Global effects of land use on local zoonotic host diversity'.* The items contained in this appendix are:

Text S2.1: Approximating research effort bias for non-host species within PREDICTS. I use a bootstrapping approach to propagate species-level uncertainty in zoonotic host status into community models. Each iteration transitions a proportion of non-hosts into host status, with species transitioned at a rate equal to their approximated likelihood of being a false classification (i.e. a host, but not detected) given research effort (PubMed publication count 1950-2018) and taxonomic group. I calculate a trait-free approximation of false classification rate for each non-host species in PREDICTS, by leveraging information on the distribution of publication counts for currently known zoonotic hosts within the same taxonomic order.

Specifically, I consider 'non-hosts' to be a mixture of true and false classifications, and that false classification probability is influenced by (1) π, the probability of being a host, and (2) ρ_m, the probability of a zoonotic pathogen being detected in a host species after m publications. Data constraints mean that neither of these parameters is directly estimable; for example, true zoonotic host status is influenced by phylogeny, ecological and life-history traits, which are the focus of ongoing research beyond the scope of this study (Olival et al., 2017). I therefore approximate these quantities as follows:

Firstly, I assume that π (relative probability of a species being a zoonotic host) is proportional to the number of currently known hosts in the same order i, such that:

$$\pi_i = \frac{\text{Number of hosts in order } i}{\text{Total number of species in order } i}$$

This may under-or over-estimate true host potential at individual species level; for example, since low research effort is often associated with traits that predict lower competence in multi-host systems (e.g. low population densities(Ducatez and Lefebvre, 2014; González-Suárez et al., 2012)), it is possible that averaging across entire orders may tend to overestimate host potential in poorly researched species. Nonetheless, this approach is sufficient to capture current understanding of broad cross-taxa differences in host potential (e.g. that primates in general are more likely to host zoonoses than insects).

Secondly, I assume that ρ_m (the probability of a zoonotic pathogen being detected in a host) accrues and saturates with increasing m (number of publications). This process cannot be observed directly due to the snapshot nature of publication counts. Therefore, for each publication count value x I approximate $\rho_{m,i}$ as $\text{P}(m \leq x)$ across all currently known hosts within the same taxonomic group i (i.e. the cumulative distribution; Extended Data 2a). Although a simplification, this is sufficient to describe how publication effort is distributed for known hosts across taxonomic groups (e.g. that 50% of known rodent hosts have 15 or fewer publications).

I can then approximate the false classification rate (FCR: the probability of being a host and *not* detected) for a species in taxonomic order i and with publication count m, as:

$$\text{FCR} = \text{P}(\text{False classification} \mid m, i) = \pi_i * (1 - \rho_{m,i})$$

I use species-specific FCR estimates as transition rates in land use model bootstrapping (with each non-host species transitioned as a Bernoulli trial with p = FCR; Methods, Extended Data 2b-

e). For mammals and birds, I calculate these estimates using input data for all extant species and orders (species lists via IUCN, and host status extracted from our host-pathogen database). For all other taxa, because they comprise a relatively small number of hosts in our dataset, I calculate these estimates using only species within PREDICTS as input data (assuming a representative sample). For taxonomic orders that contain no known host species, I fix π at 0.01 (i.e. species transition at a base rate of 1 in 100 bootstraps) and calculate ρ_m at the next-lowest taxonomic level (Class).

Figure S2.1: Random (study-level) and geographical cross-validation of community models (full dataset). I tested the sensitivity of fixed effects estimates to both random and geographically-structured (biome-level) subsampling. For random tests I fitted 8 hold-out models, excluding all sites from 12.5% of studies at a time (mean 12.5% of total sites excluded per model, range 4%-19%; results in A). For geographical tests I fitted 14 hold-out models, with each excluding all sites from one biome (mean 7% of sites excluded per model, range 0.07%-32%; results in B). Points and error bars show posterior marginal parameter distributions for each hold-out model (median and 95% quantile range, with colour denoting hold-out group or biome), calculated across samples from 500 bootstrap iterations per-model to account for variable research effort across species. Directionality and evidence for fixed-effects estimates are robust to both tests, suggesting that my results are not driven by data from any particular subset of studies or regions. Urban parameters are however the most sensitive to exclusion of data, likely due to the relatively sparse representation of urban vertebrate diversity in the PREDICTS database (17 studies in the full dataset).

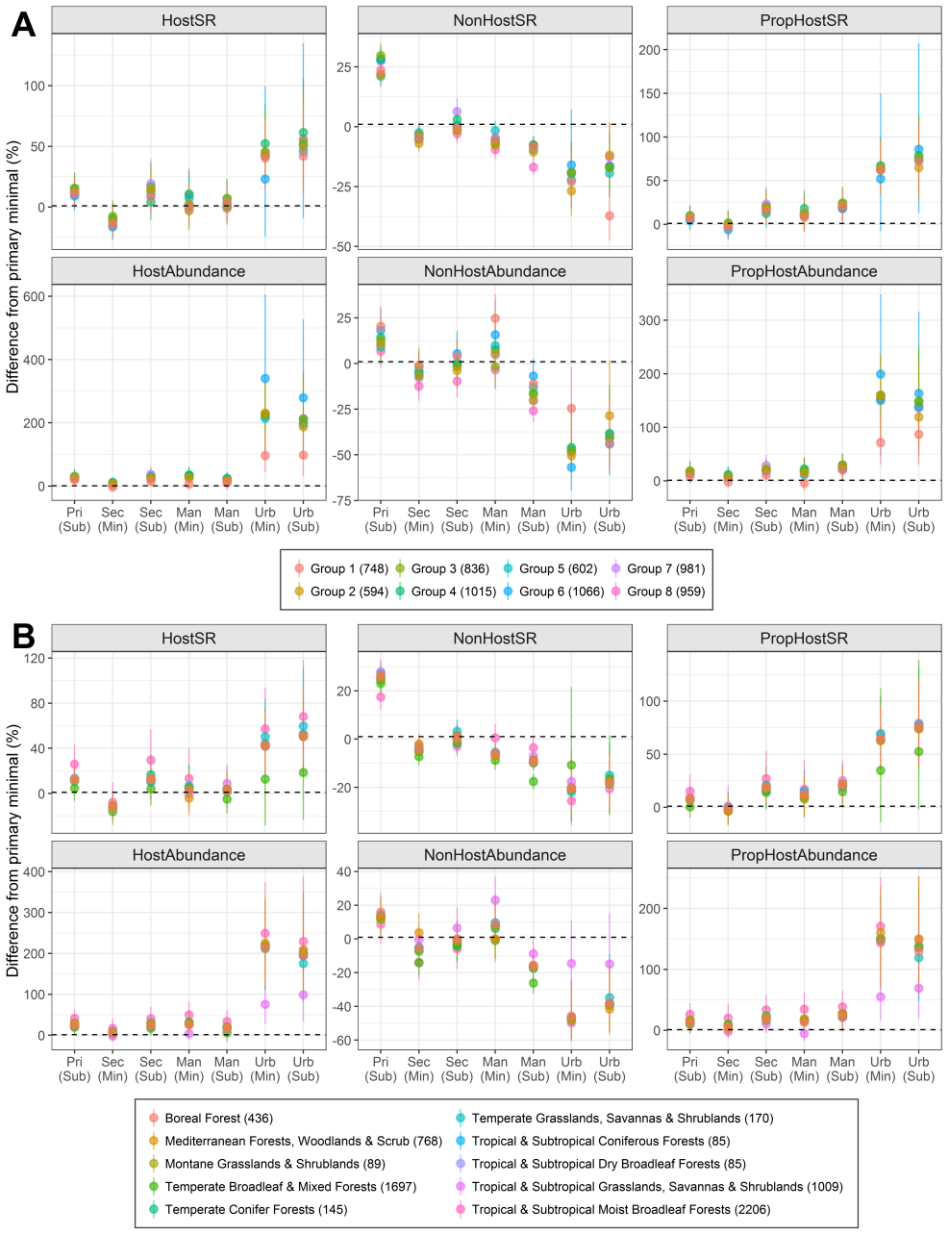

Figure S2.2: Effects of land use on site-level mammalian reservoir host species richness and total abundance. Points, wide and narrow error bars show differences in diversity metrics from primary minimal use baseline (posterior marginal median, 67% and 95% quantile ranges respectively, across 1000 bootstrap models). Models are of species richness (A) and total abundance (B) of reservoir host and all other (non-host) species, and of hosts as a proportion of site-level richness (C) and total abundance (D). For managed and urban sites, use intensities were combined to improve evenness of sampling (n=2026 sites from 63 studies: primary (589 and 572 for minimal and substantial use respectively), secondary (144, 257), managed (348) and urban (116)). Posterior estimates were calculated across an ensemble of 1000 bootstrapped models (median 51, range 38–62 non-hosts transitioned to host status, i.e. increasing host number by 28–46%) (Methods). Urban sites results show the same trend as the full dataset (Figure 2.3), but are not visualised due to wide uncertainty: 88.7% (-2.1, 252.3) proportion richness, 307% (78.8, 500.7) proportion abundance (posterior median and 95% quantile range; see Table S2.5). Point shape indicates use intensity (minimal, substantial or both combined) and colour indicates host (brown) or non-host (green). Reservoir species are listed in Supp. Table 1 (mammal species listed as 'Detection/reservoir' in the 'Evidence of host status' column).

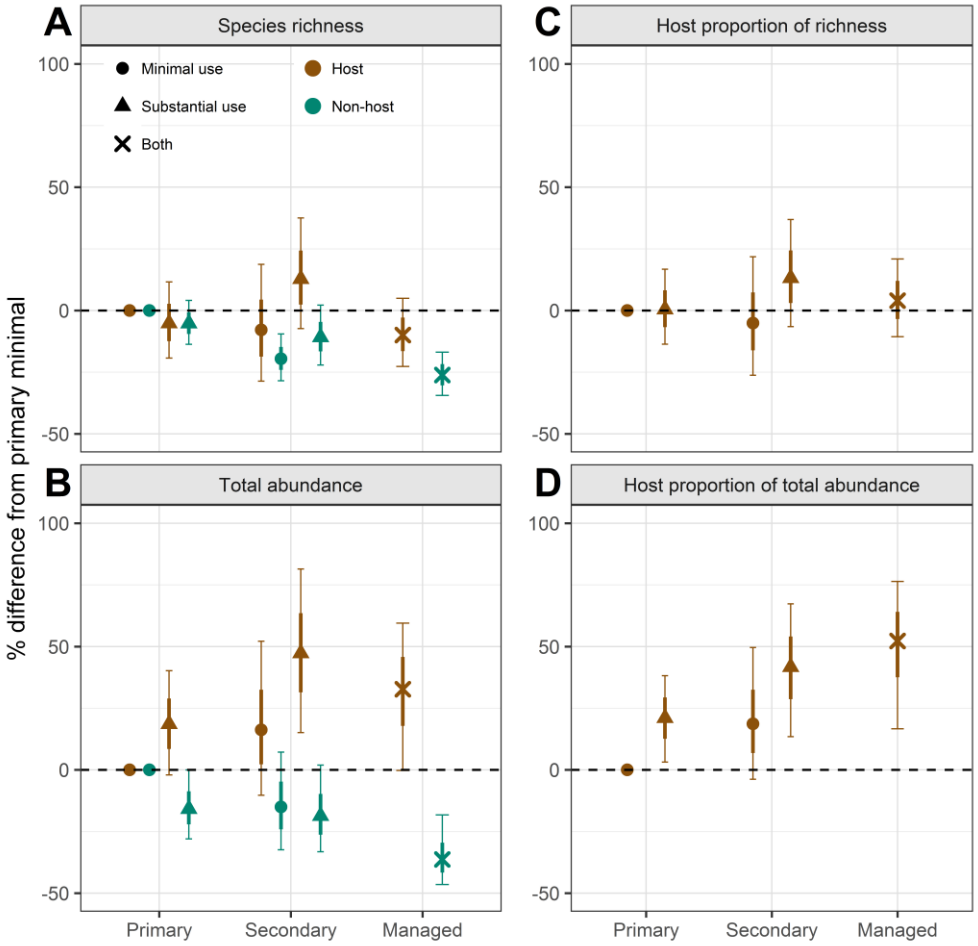

Figure S2.3: Effects of land use on occurrence and zero-truncated abundance (abundance given presence) of mammalian and avian hosts and non-hosts of zoonotic agents. Each row of three plots shows the results of species-level modelling for each of 5 mammalian and 2 avian orders, and for mammals overall. Points, wide and narrow error bars show average difference in species occurrence probability (left column) and zero-truncated abundance (ZTA; middle column) (posterior median, 67% and 95% quantile ranges across 500 and 750 bootstrap iterations, for each order and all mammals respectively). Differences are shown in secondary (Sec), managed and urban sites relative to a primary land baseline (dashed line), across all host (brown) and non-host (green) species. Histograms show, for each taxonomic group, the distribution of host species counts across all bootstrap models (i.e. after reclassifying non-hosts) compared to current number of known hosts (red vertical line), and the total number of species included in models (brackets in plot title). Estimates from occupancy and ZTA models (Table S2.6) were combined, assuming independence of processes, to give the hurdle predictions in Figure 2.4. Mammal reservoir status was defined based on strict criteria (pathogen detection or isolation), and the full list of host species included in these estimates is provided in Table S2.1 (scored '1' in the' zoonotic agent host' column).

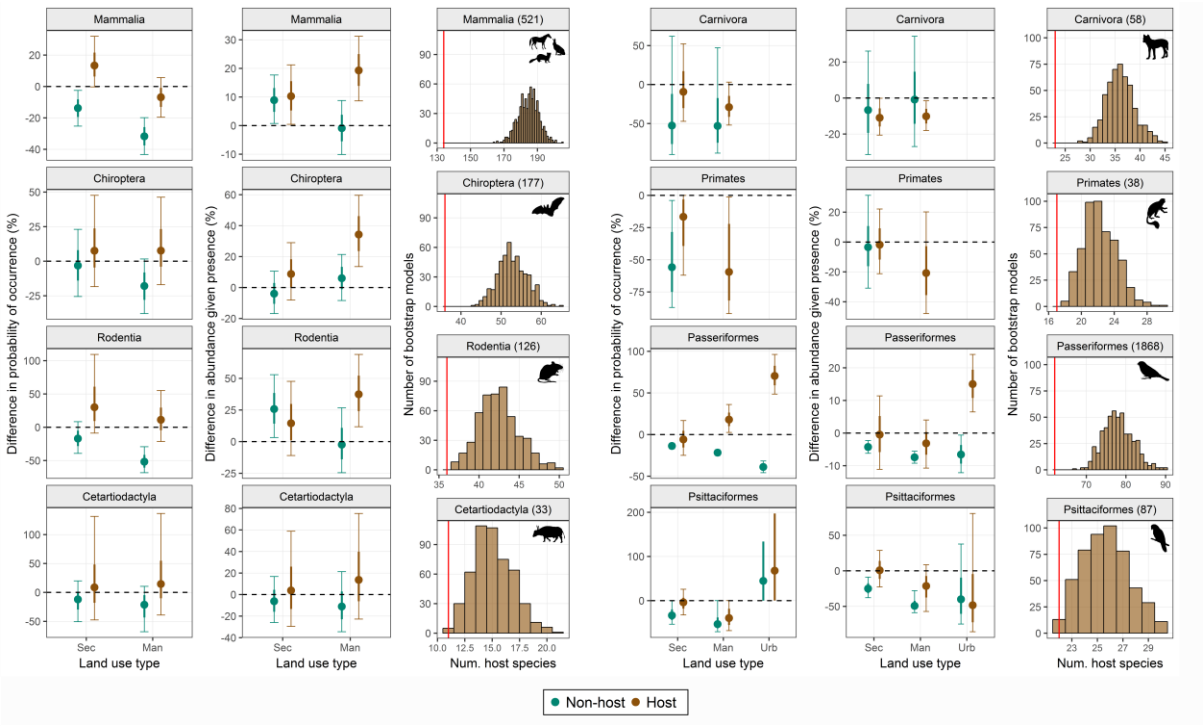

Figure S2.4: Residual human-shared and non-human-shared pathogen richness across mammals. Distribution of human and non human-shared pathogen richness (A) and relationship to publication counts (B-C) are shown for mammals in our host-pathogen association dataset (n=780 species; points represent species shaded by Order, associations defined on serological or stronger evidence). Observed versus fitted plots (D-E) show where observed deviates from expected pathogen richness given log-publications and taxonomic group (Poisson likelihood with random intercepts and slopes for Order and Family; slope estimates for log-publications are similar for both human and non human-shared pathogens, β of 0.298 and 0.248 respectively). I used the fitted models to predict expected pathogen richness for mammals in PREDICTS (n=546) and derived residuals from observed values (shown in F), which were used in land use models (Figure 2.5). Calculating per-species residual quantile ranges across 2500 posterior parameter samples shows that within-species residual variance is generally small relative to residual size (G-H, points and error-bars show posterior median, 67% and 95% intervals, scaled to unit variance), and land use model results are robust to including this uncertainty (Chapter 2 Methods, Table S2.7).

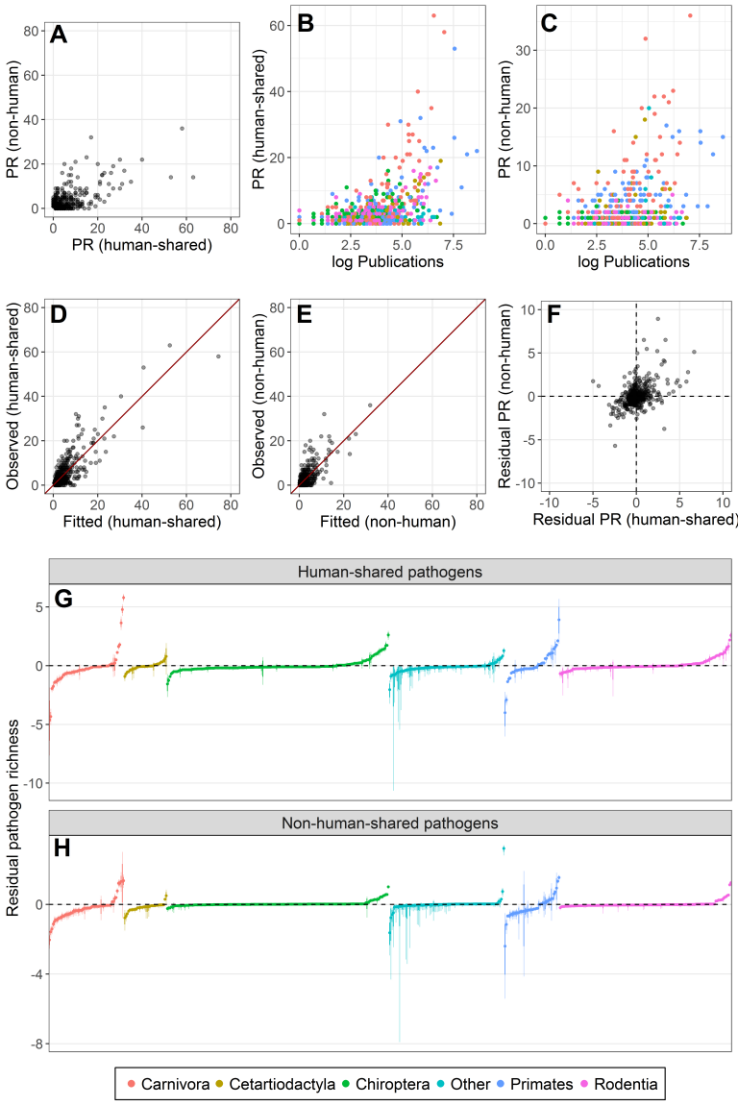

Figure S2.5: Differences in human population density between land use types, for all sites within the full dataset. Points and boxplots show the distribution of log-transformed human population density, separated by land use type and intensity, across all sites included in community models (n=6801; points represent individual sites; boxes coloured by land use type; numbers denote the number of sites in each category). Human population density estimates were extracted from CIESEN Gridded Population of the World 4, for 2005, the median year of studies included in the dataset. Per-site log human density estimates were considered as fixed effects in community models of host diversity, since human-tolerant or synanthropic species might respond to human population change independently of land use (see Methods).

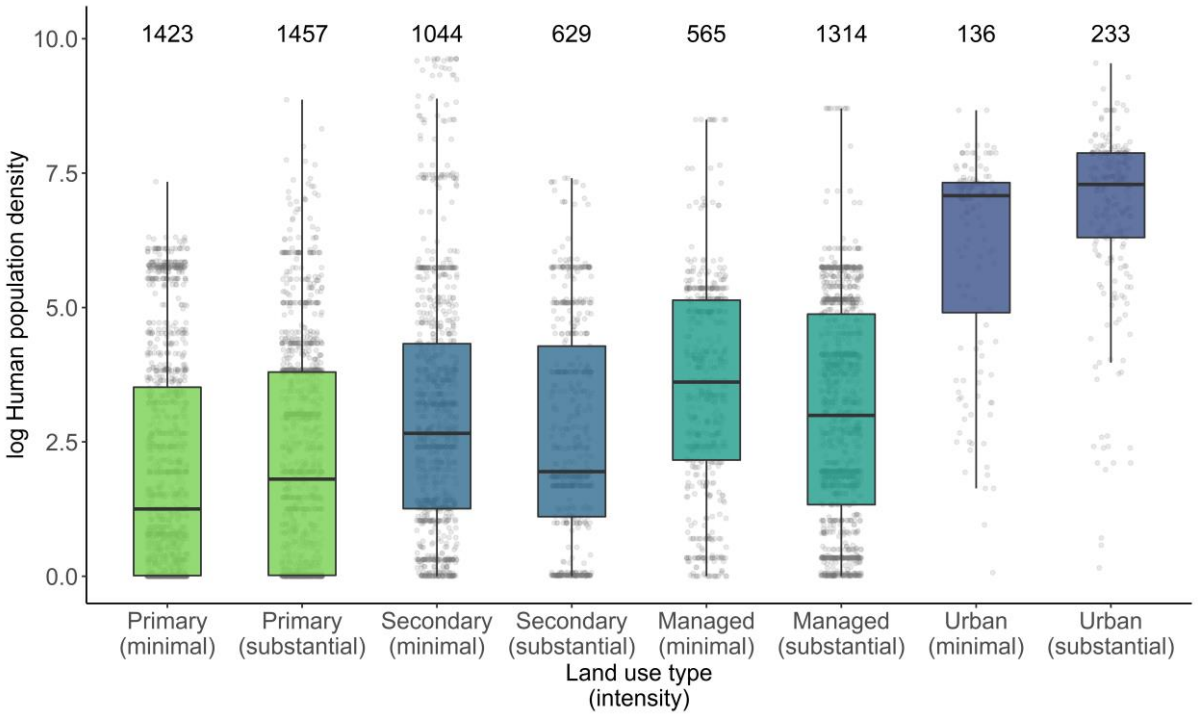

Figure S2.6: Diagnostic plots for all community models (full dataset and mammal reservoirs subset). Species richness counts were modelled with a Poisson likelihood, and abundance (adjusted counts) were log-transformed and modelled with a Gaussian likelihood (see Methods). Plot titles refer to model response variables: species richness (SR), total abundance (Abundance), for hosts, non-hosts, and for hosts as a proportion of the community (Prop). Points in (A) show observed data against model-fitted values, and the red line shows the expectation if observed equals fitted. I also tested for spatial autocorrelation of residuals across all sites within each study, with histograms (B) showing the distribution of per-study Moran's *I* *p*-values (indicating significance of spatial autocorrelation among sites within that study) for each model. Numbers in brackets are the percentage of studies that contained significant spatial autocorrelation ($p<0.05$, shown as a red line). Overall, spatial autocorrelation was fairly low across the dataset (statistically significant in 14%-30% of studies across the different models, with maximum 26% for models with host metrics as response variables). Residuals and statistics were derived from a single fitted model including community mean false classification probability as a linear covariate to account for research effort (with known hosts given a false classification probability of 0), rather than the full bootstrap ensemble.

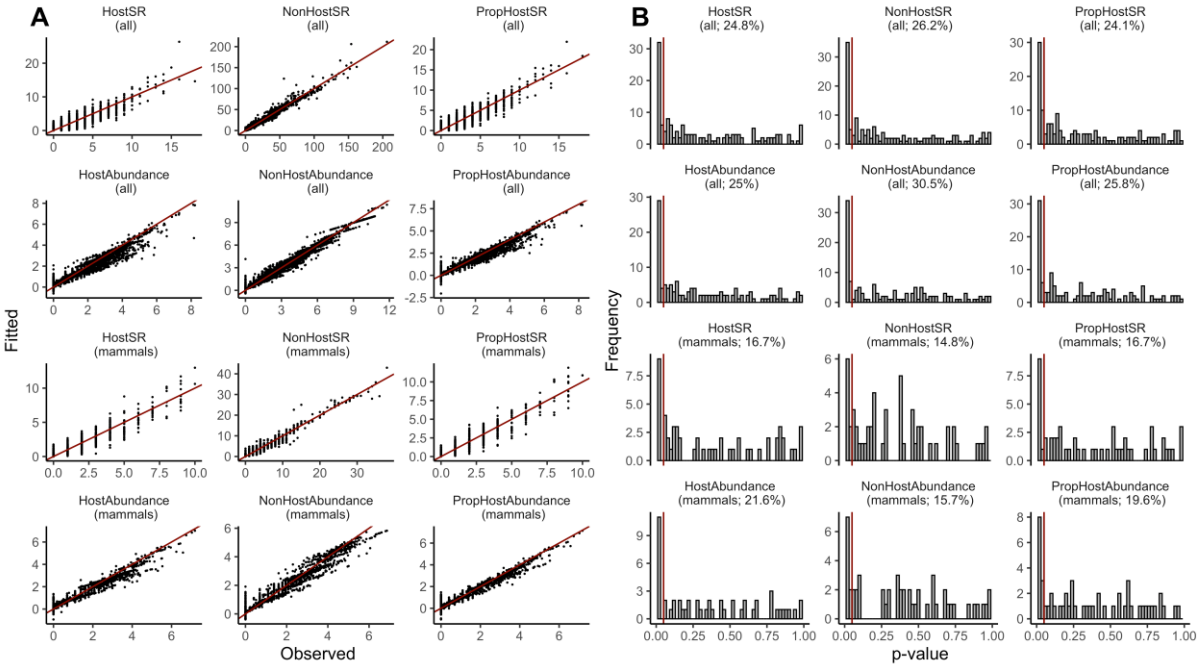

Table S2.1: Hosts of human-shared parasites and pathogens with corresponding records in the PREDICTS database (n=376). The table lists all animal species in the PREDICTS database that have evidence of an association with at least one human-shared pathogen or parasite, and includes summary information on each species' known associated pathogen diversity, pathogen richness (of both human-shared and non human-shared pathogens) and host-pathogen data sources. The 'evidence of host status' column denotes the strength of evidence for assigned host status: either cargo-carrier (broadest), serological, or pathogen detection/isolation (strongest). Species associated with at least one zoonotic agent (aetiologic agent of a specific human disease with animal reservoir) are scored '1' in the 'zoonotic agent host' column (for mammals this association is based on serological or stronger evidence). 'Num studies' and 'Num sites' columns indicate the amount of sampling for each species in PREDICTS. Full details of definitions and data sources are provided in Methods. A more comprehensive version of this table (including pathogen species names), and a table of all non-host species included in this study, is provided in in the data repository.

Host binomial	Class	Order	Human-shared pathogen diversity	Evidence of host status	Zoonotic agent host	Pathogen richness (human-shared)	Pathogen richness (not human/ domestic-shared)	Data sources	Num studies	Num sites
Lithobates catesbeianus	Amphibia	Anura	bacteria/rickettsia	Cargo-carrier	0	3	11	EID2	1	61
Litoria caerulea	Amphibia	Anura	helminth	Cargo-carrier	1	1	1	EID2	2	200
Oribatula tibialis	Arachnida	Sarcoptiformes	fungi	Cargo-carrier	0	1	1	EID2	3	110
Steganacarus magnus	Arachnida	Sarcoptiformes	fungi	Cargo-carrier	0	1	1	EID2	1	20
Accipiter cooperii	Aves	Accipitriformes	virus	Cargo-carrier	1	1	3	EID2	1	300
Accipiter gentilis	Aves	Accipitriformes	virus	Cargo-carrier	1	1	0	EID2	1	124
Accipiter gularis	Aves	Accipitriformes	virus	Cargo-carrier	1	1	0	EID2	3	82
Accipiter trivirgatus	Aves	Accipitriformes	virus	Cargo-carrier	1	1	0	EID2	2	76
Buteo buteo	Aves	Accipitriformes	virus	Cargo-carrier	1	1	2	EID2	7	841
Buteo jamaicensis	Aves	Accipitriformes	virus	Cargo-carrier	1	1	2	EID2	4	428
Buteo lagopus	Aves	Accipitriformes	virus	Cargo-carrier	1	1	0	EID2	1	21
Buteo lineatus	Aves	Accipitriformes	virus	Cargo-carrier	1	1	1	EID2	1	300
Milvus migrans	Aves	Accipitriformes	virus	Cargo-carrier	1	1	0	EID2	7	596
Pandion haliaetus	Aves	Accipitriformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	2	85
Aix sponsa	Aves	Anseriformes	virus	Cargo-carrier	1	2	0	EID2	1	300
Alopochen aegyptiaca	Aves	Anseriformes	virus	Cargo-carrier	1	1	0	EID2	4	757
Anas capensis	Aves	Anseriformes	virus	Cargo-carrier	1	1	0	EID2	1	39
Anas querquedula	Aves	Anseriformes	virus	Cargo-carrier	1	2	1	EID2	1	42
Anas superciliosa	Aves	Anseriformes	virus	Cargo-carrier	1	1	0	EID2	2	183
Dendrocygna viduata	Aves	Anseriformes	virus	Cargo-carrier	1	1	0	EID2	1	360
Netta peposaca	Aves	Anseriformes	virus	Cargo-carrier	1	1	0	EID2	1	360
Upupa epops	Aves	Bucerotiformes	bacteria/rickettsia	Cargo-carrier	0	1	0	EID2	7	391
Podargus strigoides	Aves	Caprimulgiformes	protozoa	Cargo-carrier	1	1	0	EID2	3	232
Dromaius novaehollandiae	Aves	Casuariiformes	virus	Cargo-carrier	1	2	5	EID2	2	61
Burhinus oedicnemus	Aves	Charadriiformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	2	237

Chroicocephalus ridibundus	Aves	Charadriiformes	helminth, virus	Cargo-carrier	1	3	1	EID2	1	42
Larus delawarensis	Aves	Charadriiformes	bacteria/rickettsia, virus	Cargo-carrier	1	2	3	EID2	1	300
Larus dominicanus	Aves	Charadriiformes	protozoa, virus	Cargo-carrier	1	2	0	EID2	1	6
Limosa limosa	Aves	Charadriiformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	2	49
Tringa totanus	Aves	Charadriiformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	2	49
Ciconia ciconia	Aves	Ciconiiformes	bacteria/rickettsia, virus, fungi	Cargo-carrier	1	3	1	EID2	3	321
Geotrygon montana	Aves	Columbiformes	virus	Cargo-carrier	1	1	0	EID2	10	163
Streptopelia orientalis	Aves	Columbiformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	7	216
Zenaida macroura	Aves	Columbiformes	virus	Cargo-carrier	1	4	1	EID2	1	300
Piaya minuta	Aves	Cuculiformes	virus	Cargo-carrier	1	1	0	EID2	1	150
Falco naumanni	Aves	Falconiformes	bacteria/rickettsia, virus	Cargo-carrier	1	2	0	EID2	1	39
Falco peregrinus	Aves	Falconiformes	virus	Cargo-carrier	1	1	2	EID2	2	250
Falco sparverius	Aves	Falconiformes	virus	Cargo-carrier	1	1	0	EID2	6	799
Falco tinnunculus	Aves	Falconiformes	virus, helminth	Cargo-carrier	1	2	1	EID2	3	90
Alectoris chukar	Aves	Galliformes	virus	Cargo-carrier	1	1	0	EID2	2	52
Bonasa umbellus	Aves	Galliformes	virus	Cargo-carrier	1	1	0	EID2	1	300
Lophura leucomelanos	Aves	Galliformes	virus	Cargo-carrier	1	1	0	EID2	2	8
Lophura nycthemera	Aves	Galliformes	virus	Cargo-carrier	1	1	0	EID2	2	50
Perdix perdix	Aves	Galliformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	1	42
Fulica atra	Aves	Gruiformes	protozoa, virus	Cargo-carrier	1	2	0	EID2	1	42
Gallicrex cinerea	Aves	Gruiformes	virus	Cargo-carrier	1	1	0	EID2	1	3
Agelaius phoeniceus	Aves	Passeriformes	virus	Cargo-carrier	1	1	1	EID2	1	300
Anthus campestris	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	1	42
Bombycilla cedrorum	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	4	582
Carduelis carduelis	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	7	355
Catharus fuscescens	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	4	537
Catharus guttatus	Aves	Passeriformes	virus	Cargo-carrier	1	1	1	EID2	4	297
Catharus ustulatus	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	5	175
Chloris chloris	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	1	1	EID2	7	375
Coloeus monedula	Aves	Passeriformes	virus, bacteria/rickettsia	Cargo-carrier	1	3	0	EID2	2	248
Conopophaga aurita	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	3	53
Contopus sordidulus	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	1	67
Corvus brachyrhynchos	Aves	Passeriformes	virus	Cargo-carrier	1	2	0	EID2	1	300
Corvus cornix	Aves	Passeriformes	bacteria/rickettsia, virus	Cargo-carrier	1	2	1	EID2	1	42
Corvus corone	Aves	Passeriformes	virus	Cargo-carrier	1	1	3	EID2	2	232
Corvus frugilegus	Aves	Passeriformes	virus	Cargo-carrier	1	2	2	EID2	1	42
Corvus splendens	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	6	182
Cyanocitta cristata	Aves	Passeriformes	virus	Cargo-carrier	1	2	0	EID2	2	315
Cyanopica cyanus	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	2	0	EID2	1	48
Diuca diuca	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	2	56
Emberiza cioides	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	4	84

Empidonax alnorum	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	2	315
Garrulus glandarius	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	10	524
Geothlypis tolmiei	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	1	79
Grallina cyanoleuca	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	4	235
Haemorhous mexicanus	Aves	Passeriformes	virus	Cargo-carrier	1	1	2	EID2	2	302
Hirundo rustica	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	10	733
Hypocnemis cantator	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	6	91
Hypsipetes amaurotis	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	2	0	EID2	3	42
Icteria virens	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	2	379
Isleria hauxwelli	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	2	62
Lanius schach	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	4	148
Leiothrix argentauris	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	1	6
Leiothrix lutea	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	2	44
Lonchura striata	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	7	163
Melospiza melodia	Aves	Passeriformes	virus	Cargo-carrier	1	2	0	EID2	2	315
Microeca fascinans	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	3	232
Mimus polyglottos	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	1	40
Molothrus ater	Aves	Passeriformes	virus	Cargo-carrier	1	1	1	EID2	3	522
Motacilla alba	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	5	155
Myiobius barbatus	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	7	162
Parkesia noveboracensis	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	1	79
Parus major	Aves	Passeriformes	virus	Cargo-carrier	1	1	1	EID2	14	605
Passer domesticus	Aves	Passeriformes	virus, protozoa	Cargo-carrier	1	5	4	EID2, Plourde	11	1100
Passer montanus	Aves	Passeriformes	bacteria/rickettsia, virus	Cargo-carrier	1	3	0	EID2	7	370
Passerella iliaca	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	1	60
Passerina cyanea	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	4	601
Pica pica	Aves	Passeriformes	virus	Cargo-carrier	1	2	1	EID2	2	248
Poecile montanus	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	5	196
Poephila personata	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	1	171
Querula purpurata	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	1	3
Quiscalus quiscula	Aves	Passeriformes	virus	Cargo-carrier	1	3	1	EID2	1	300
Regulus satrapa	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	1	60
Rhipidura fuliginosa	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	0	1	0	EID2	4	220
Saltator maximus	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	8	276
Sialia sialis	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	7	7	EID2	2	379
Spodiopsar cineraceus	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	2	0	EID2	1	42
Spodiopsar sericeus	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	1	42
Sturnus vulgaris	Aves	Passeriformes	virus, bacteria/rickettsia	Cargo-carrier	1	3	2	EID2	6	434
Taeniopygia guttata	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	4	1	EID2	2	61
Turdus amaurochalinus	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	5	372
Turdus merula	Aves	Passeriformes	bacteria/rickettsia, virus	Cargo-carrier	1	6	5	EID2, Plourde	10	449

Turdus migratorius	Aves	Passeriformes	virus	Cargo-carrier	1	2	1	EID2	5	597
Turdus philomelos	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	1	1	1	EID2, Plourde	6	157
Vireo griseus	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	1	79
Vireo olivaceus	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	15	1162
Willisornis poecilinotus	Aves	Passeriformes	virus	Cargo-carrier	1	1	0	EID2	6	91
Zosterops japonicus	Aves	Passeriformes	bacteria/rickettsia, virus	Cargo-carrier	1	2	0	EID2	6	88
Zosterops lateralis	Aves	Passeriformes	bacteria/rickettsia	Cargo-carrier	0	1	1	EID2	3	78
Ardea alba	Aves	Pelecaniformes	virus	Cargo-carrier	1	1	1	EID2	5	524
Ardea cinerea	Aves	Pelecaniformes	helminth, virus	Cargo-carrier	1	2	2	EID2	3	155
Bubulcus ibis	Aves	Pelecaniformes	virus	Cargo-carrier	1	1	0	EID2	13	1930
Butorides virescens	Aves	Pelecaniformes	virus	Cargo-carrier	1	3	1	EID2	4	486
Egretta garzetta	Aves	Pelecaniformes	bacteria/rickettsia, virus	Cargo-carrier	1	2	1	EID2, Plourde	5	308
Nycticorax nycticorax	Aves	Pelecaniformes	virus	Cargo-carrier	1	1	2	EID2, Plourde	1	3
Threskiornis aethiopicus	Aves	Pelecaniformes	virus	Cargo-carrier	1	1	0	EID2	3	701
Colaptes auratus	Aves	Piciformes	virus	Cargo-carrier	1	2	0	EID2	3	439
Dendrocopos major	Aves	Piciformes	virus	Cargo-carrier	1	1	0	EID2	7	482
Picoides pubescens	Aves	Piciformes	bacteria/rickettsia	Cargo-carrier	1	1	1	EID2	1	300
Amazona aestiva	Aves	Psittaciformes	virus, bacteria/rickettsia	Cargo-carrier	1	2	1	EID2	2	7
Amazona farinosa	Aves	Psittaciformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	3	27
Ara ararauna	Aves	Psittaciformes	virus	Cargo-carrier	1	1	0	EID2	3	55
Ara chloropterus	Aves	Psittaciformes	virus	Cargo-carrier	1	1	0	EID2	2	15
Aratinga acuticaudata	Aves	Psittaciformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	1	3
Aratinga pertinax	Aves	Psittaciformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	3	21
Cacatua alba	Aves	Psittaciformes	virus, fungi	Cargo-carrier	1	2	0	EID2	1	3
Deroptyus accipitrinus	Aves	Psittaciformes	virus	Cargo-carrier	1	1	0	EID2	2	15
Eclectus roratus	Aves	Psittaciformes	virus, fungi	Cargo-carrier	1	2	0	EID2	3	20
Eolophus roseicapilla	Aves	Psittaciformes	virus	Cargo-carrier	1	1	0	EID2	3	232
Lorius lory	Aves	Psittaciformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	3	20
Pionites melanocephalus	Aves	Psittaciformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	3	27
Pionus fuscus	Aves	Psittaciformes	virus	Cargo-carrier	1	1	0	EID2	3	27
Pionus maximiliani	Aves	Psittaciformes	virus	Cargo-carrier	1	1	0	EID2	3	9
Pionus menstruus	Aves	Psittaciformes	virus	Cargo-carrier	1	1	0	EID2	4	94
Poicephalus gulielmi	Aves	Psittaciformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	1	16
Poicephalus meyeri	Aves	Psittaciformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	2	662
Primolius auricollis	Aves	Psittaciformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	1	4
Probosciger aterrimus	Aves	Psittaciformes	virus	Cargo-carrier	1	1	0	EID2	3	20
Psittacula krameri	Aves	Psittaciformes	protozoa	Cargo-carrier	1	1	1	EID2	3	66
Psittacus erithacus	Aves	Psittaciformes	virus, bacteria/rickettsia	Cargo-carrier	1	2	2	EID2	3	114
Trichoglossus haematodus	Aves	Psittaciformes	bacteria/rickettsia	Cargo-carrier	1	1	1	EID2	7	255
Rhea americana	Aves	Rheiformes	protozoa	Cargo-carrier	1	1	0	EID2	1	5
Asio otus	Aves	Strigiformes	bacteria/rickettsia, virus	Cargo-carrier	1	2	0	EID2	2	318

Athene noctua	Aves	Strigiformes	bacteria/rickettsia, virus	Cargo-carrier	1	2	0	EID2	2	318
Otus scops	Aves	Strigiformes	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	2	318
Arion lusitanicus	Gastropoda		bacteria/rickettsia	Cargo-carrier	1	5	4	EID2	1	92
Helix pomatia	Gastropoda	Stylommatophora	bacteria/rickettsia	Cargo-carrier	1	4	5	EID2	1	34
Macrotermes michaelseni	Insecta	Blattodea	bacteria/rickettsia	Cargo-carrier	1	2	1	EID2	1	10
Alphitobius diaperinus	Insecta	Coleoptera	bacteria/rickettsia	Cargo-carrier	1	1	0	EID2	1	30
Brassicogethes aeneus	Insecta	Coleoptera	fungi	Cargo-carrier	0	1	1	EID2	3	187
Costelytra zealandica	Insecta	Coleoptera	bacteria/rickettsia	Cargo-carrier	1	5	2	EID2	3	38
Dendroctonus rufipennis	Insecta	Coleoptera	fungi, bacteria/rickettsia	Cargo-carrier	1	4	10	EID2	1	80
Dryocoetes autographus	Insecta	Coleoptera	fungi	Cargo-carrier	0	2	6	EID2	3	187
Harmonia axyridis	Insecta	Coleoptera	bacteria/rickettsia	Cargo-carrier	1	3	1	EID2	1	8
Hylurgus ligniperda	Insecta	Coleoptera	fungi	Cargo-carrier	0	4	1	EID2	1	5
Ips pini	Insecta	Coleoptera	fungi	Cargo-carrier	0	1	4	EID2	1	80
Orthotomicus erosus	Insecta	Coleoptera	fungi	Cargo-carrier	0	3	7	EID2	1	5
Sitona discoideus	Insecta	Coleoptera	fungi	Cargo-carrier	0	1	0	EID2	2	160
Tenebrio molitor	Insecta	Coleoptera	helminth	Cargo-carrier	1	1	3	EID2, Plourde	1	27
Aedes aegypti	Insecta	Diptera	bacteria/rickettsia, virus, helminth	Cargo-carrier	1	7	4	EID2	1	7
Anopheles triannulatus	Insecta	Diptera	virus	Cargo-carrier	1	1	0	EID2	1	7
Culex coronator	Insecta	Diptera	virus	Cargo-carrier	1	2	1	EID2	1	7
Culex portesi	Insecta	Diptera	virus	Cargo-carrier	1	2	0	EID2	1	7
Culex quinquefasciatus	Insecta	Diptera	bacteria/rickettsia, virus	Cargo-carrier	1	53	33	EID2	1	7
Drosophila melanogaster	Insecta	Diptera	bacteria/rickettsia	Cargo-carrier	1	1	5	EID2	3	13
Psorophora ferox	Insecta	Diptera	virus	Cargo-carrier	1	2	1	EID2	1	7
Acyrthosiphon pisum	Insecta	Hemiptera	fungi	Cargo-carrier	0	1	3	EID2	2	168
Toxoptera aurantii	Insecta	Hemiptera	bacteria/rickettsia	Cargo-carrier	0	1	1	EID2	1	152
Apis cerana	Insecta	Hymenoptera	bacteria/rickettsia	Cargo-carrier	1	10	2	EID2	1	6
Solenopsis invicta	Insecta	Hymenoptera	bacteria/rickettsia	Cargo-carrier	1	11	1	EID2	1	12
Vespa crabro	Insecta	Hymenoptera	fungi	Cargo-carrier	0	1	0	EID2	1	8
Archips fumiferana	Insecta	Lepidoptera	bacteria/rickettsia, fungi	Cargo-carrier	1	5	2	EID2	1	26
Hyphantria cunea	Insecta	Lepidoptera	fungi	Cargo-carrier	0	1	0	EID2	3	170
Lymantria dispar	Insecta	Lepidoptera	bacteria/rickettsia	Cargo-carrier	1	8	5	EID2	1	80
Manduca sexta	Insecta	Lepidoptera	bacteria/rickettsia	Cargo-carrier	1	2	0	EID2	1	26
Ostrinia nubilalis	Insecta	Lepidoptera	fungi, bacteria/rickettsia	Cargo-carrier	1	5	8	EID2	2	90
Pieris brassicae	Insecta	Lepidoptera	bacteria/rickettsia	Cargo-carrier	0	1	1	EID2	10	314
Pieris rapae	Insecta	Lepidoptera	fungi	Cargo-carrier	0	2	1	EID2	14	371
Plutella xylostella	Insecta	Lepidoptera	bacteria/rickettsia	Cargo-carrier	1	4	4	EID2	1	26
Spodoptera frugiperda	Insecta	Lepidoptera	bacteria/rickettsia	Cargo-carrier	0	1	1	EID2	1	80
Atilax paludinosus	Mammalia	Carnivora	virus	Detection/ reservoir	1	1	0	EID2, GMPD2, Olival	3	180
Canis lupus	Mammalia	Carnivora	fungi, bacteria/rickettsia, helminth, virus, protozoa, others	Detection/ reservoir	1	262	15	EID2, GMPD2, Olival, Plourde	2	252

Canis mesomelas	Mammalia	Carnivora	virus, bacteria/rickettsia	Detection/ reservoir	1	4	3	EID2, GMPD2, Olival	1	84
Cerdocyon thous	Mammalia	Carnivora	virus, helminth, protozoa	Detection/ reservoir	1	8	3	EID2, GMPD2, Olival	2	45
Conepatus chinga	Mammalia	Carnivora	helminth, protozoa	Detection/ reservoir	1	2	0	GMPD2	1	138
Crocuta crocuta	Mammalia	Carnivora	virus, bacteria/rickettsia, helminth	Detection/ reservoir	1	6	2	EID2, GMPD2, Olival	1	86
Leopardus geoffroyi	Mammalia	Carnivora	helminth, virus, protozoa	Detection/ reservoir	1	5	5	GMPD2, Olival, Plourde	1	138
Leopardus pardalis	Mammalia	Carnivora	helminth, virus, bacteria/rickettsia, protozoa	Detection/ reservoir	1	13	8	EID2, GMPD2, Olival, Plourde	3	40
Lutra lutra	Mammalia	Carnivora	bacteria/rickettsia, virus, helminth, protozoa	Detection/ reservoir	1	27	20	EID2, GMPD2, Olival	1	9
Lycalopex culpaeus	Mammalia	Carnivora	helminth	Detection/ reservoir	1	5	2	GMPD2	1	138
Martes foina	Mammalia	Carnivora	protozoa, virus, helminth, bacteria/rickettsia	Detection/ reservoir	1	12	10	EID2, GMPD2, Olival	1	46
Mellivora capensis	Mammalia	Carnivora	virus	Detection/ reservoir	1	1	0	Olival	1	86
Nasua narica	Mammalia	Carnivora	bacteria/rickettsia, virus	Detection/ reservoir	1	2	1	GMPD2, Olival	1	28
Nasua nasua	Mammalia	Carnivora	helminth, protozoa	Detection/ reservoir	1	2	1	EID2, GMPD2, Plourde	3	49
Panthera onca	Mammalia	Carnivora	virus, helminth, bacteria/rickettsia, protozoa	Detection/ reservoir	1	5	0	EID2, GMPD2, Plourde	2	35
Panthera pardus	Mammalia	Carnivora	virus, protozoa, helminth	Detection/ reservoir	1	6	0	EID2, GMPD2, Olival	5	125
Potos flavus	Mammalia	Carnivora	virus	Serological	1	3	0	EID2, Olival	1	40
Procyon lotor	Mammalia	Carnivora	virus, bacteria/rickettsia, helminth, protozoa, fungi	Detection/ reservoir	1	64	86	EID2, GMPD2, Olival, Plourde	1	28
Puma concolor	Mammalia	Carnivora	helminth, virus, bacteria/rickettsia, protozoa	Detection/ reservoir	1	25	12	EID2, GMPD2, Olival, Plourde	3	171
Puma yagouaroundi	Mammalia	Carnivora	helminth, bacteria/rickettsia	Detection/ reservoir	1	2	0	EID2, Plourde	1	28
Speothos venaticus	Mammalia	Carnivora	helminth	Detection/ reservoir	1	1	0	Plourde	1	7
Urocyon cinereoargenteus	Mammalia	Carnivora	helminth, bacteria/rickettsia, virus, protozoa	Detection/ reservoir	1	30	9	EID2, GMPD2, Olival	1	28
Ursus arctos	Mammalia	Carnivora	bacteria/rickettsia, virus, helminth, protozoa	Detection/ reservoir	1	15	8	EID2, GMPD2, Olival, Plourde	1	46
Vulpes vulpes	Mammalia	Carnivora	bacteria/rickettsia, helminth, virus, protozoa, others	Detection/ reservoir	1	65	38	EID2, GMPD2, Olival, Plourde	1	46
Axis axis	Mammalia	Cetartiodactyla	virus, helminth	Detection/ reservoir	1	4	3	GMPD2, Olival	1	9
Capra ibex	Mammalia	Cetartiodactyla	bacteria/rickettsia, protozoa, helminth	Detection/ reservoir	1	16	4	EID2, GMPD2, Olival	1	46
Cephalophus callipygus	Mammalia	Cetartiodactyla	virus	Detection/ reservoir	1	1	0	Olival	1	86
Cephalophus dorsalis	Mammalia	Cetartiodactyla	virus, protozoa	Detection/ reservoir	1	2	0	GMPD2, Olival	3	160
Connochaetes taurinus	Mammalia	Cetartiodactyla	bacteria/rickettsia, virus, helminth, protozoa	Detection/ reservoir	1	11	7	EID2, GMPD2, Olival	1	84
Muntiacus muntjak	Mammalia	Cetartiodactyla	virus	Serological	1	1	1	GMPD2, Olival	1	9

Odocoileus virginianus	Mammalia	Cetartiodactyla	bacteria/rickettsia, protozoa, virus, helminth	Detection/ reservoir	1	33	22	EID2, GMPD2, Olival, Plourde	2	32
Ovis ammon	Mammalia	Cetartiodactyla	helminth, virus, protozoa	Detection/ reservoir	1	3	0	GMPD2	1	46
Pecari tajacu	Mammalia	Cetartiodactyla	virus, protozoa	Serological	0	3	1	EID2, GMPD2	7	119
Philantomba monticola	Mammalia	Cetartiodactyla	virus, helminth, protozoa	Detection/ reservoir	1	4	3	EID2, GMPD2, Olival	3	175
Rusa unicolor	Mammalia	Cetartiodactyla	virus, bacteria/rickettsia, helminth	Detection/ reservoir	1	5	4	EID2, GMPD2, Olival	2	221
Sylvicapra grimmia	Mammalia	Cetartiodactyla	virus, helminth	Serological	1	10	9	EID2, GMPD2, Olival	1	84
Syncerus caffer	Mammalia	Cetartiodactyla	bacteria/rickettsia, virus, helminth, protozoa	Detection/ reservoir	1	14	7	EID2, GMPD2, Olival	3	180
Taurotragus oryx	Mammalia	Cetartiodactyla	bacteria/rickettsia, virus, helminth, protozoa	Serological	1	8	5	GMPD2	1	84
Tragelaphus scriptus	Mammalia	Cetartiodactyla	bacteria/rickettsia, virus, protozoa, helminth	Serological	1	4	7	GMPD2, Olival	2	94
Tragelaphus spekii	Mammalia	Cetartiodactyla	virus, protozoa	Detection/ reservoir	1	2	0	EID2, GMPD2	1	86
Anoura geoffroyi	Mammalia	Chiroptera	virus	Serological	1	6	2	Olival	2	10
Artibeus cinereus	Mammalia	Chiroptera	virus	Serological	1	4	0	Olival	1	3
Artibeus jamaicensis	Mammalia	Chiroptera	virus	Detection/ reservoir	1	13	1	EID2, Olival	4	74
Artibeus lituratus	Mammalia	Chiroptera	virus	Detection/ reservoir	1	16	2	EID2, Olival	6	92
Artibeus phaeotis	Mammalia	Chiroptera	virus	Detection/ reservoir	1	6	0	Olival	3	28
Artibeus planirostris	Mammalia	Chiroptera	virus, protozoa	Detection/ reservoir	1	3	0	EID2, Olival	2	18
Artibeus toltecus	Mammalia	Chiroptera	virus	Detection/ reservoir	1	2	0	Olival	2	20
Carollia brevicauda	Mammalia	Chiroptera	virus, bacteria/rickettsia	Detection/ reservoir	1	4	0	EID2, Olival	5	84
Carollia perspicillata	Mammalia	Chiroptera	virus, protozoa	Detection/ reservoir	1	13	3	EID2, Olival	5	84
Chrotopterus auritus	Mammalia	Chiroptera	virus, protozoa	Detection/ reservoir	1	2	0	EID2, Olival	5	82
Cynomops planirostris	Mammalia	Chiroptera	virus	Serological	1	1	0	Olival	1	1
Cynopterus brachyotis	Mammalia	Chiroptera	virus	Detection/ reservoir	1	4	4	Olival	3	25
Cynopterus sphinx	Mammalia	Chiroptera	virus	Detection/ reservoir	1	4	0	Olival	1	2
Desmodus rotundus	Mammalia	Chiroptera	fungi, virus, bacteria/rickettsia	Detection/ reservoir	1	10	2	EID2, Olival	6	90
Diclidurus albus	Mammalia	Chiroptera	virus	Detection/ reservoir	1	1	0	Olival	1	46
Diphylla ecaudata	Mammalia	Chiroptera	virus	Detection/ reservoir	1	1	0	EID2, Olival	1	8
Eonycteris spelaea	Mammalia	Chiroptera	virus	Detection/ reservoir	1	3	2	Olival	2	19
Eptesicus brasiliensis	Mammalia	Chiroptera	virus	Detection/ reservoir	1	1	1	EID2, Olival	1	15
Eptesicus furinalis	Mammalia	Chiroptera	virus	Detection/ reservoir	1	1	0	EID2, Olival	1	8
Eumops auripendulus	Mammalia	Chiroptera	virus	Detection/ reservoir	1	1	0	EID2, Olival	1	46
Glossophaga commissarisi	Mammalia	Chiroptera	virus	Serological	1	1	0	Olival	1	8
Glossophaga soricina	Mammalia	Chiroptera	virus, bacteria/rickettsia	Detection/ reservoir	1	10	0	EID2, Olival	6	92
Hipposideros armiger	Mammalia	Chiroptera	virus	Detection/ reservoir	1	2	0	Olival	1	2
Hipposideros bicolor	Mammalia	Chiroptera	virus	Serological	1	1	0	Olival	1	6
Lasiurus ega	Mammalia	Chiroptera	virus	Detection/ reservoir	1	1	0	EID2, Olival, Plourde	1	8

Lophostoma silvicolum	Mammalia	Chiroptera	virus	Serological	1	2	0	Olival	3	62
Megaderma lyra	Mammalia	Chiroptera	virus	Serological	1	1	0	Olival	1	2
Micronycteris megalotis	Mammalia	Chiroptera	virus	Serological	1	1	0	Olival	3	59
Miniopterus schreibersii	Mammalia	Chiroptera	virus	Detection/ reservoir	1	7	3	EID2, Olival	2	119
Molossus molossus	Mammalia	Chiroptera	fungi, virus	Detection/ reservoir	1	8	1	EID2, Olival	2	61
Molossus rufus	Mammalia	Chiroptera	virus	Detection/ reservoir	1	6	2	EID2, Olival	1	8
Mormoops megalophylla	Mammalia	Chiroptera	virus	Serological	1	2	1	Olival	1	12
Myotis californicus	Mammalia	Chiroptera	virus	Detection/ reservoir	1	1	0	EID2, Olival	1	12
Myotis macrodactylus	Mammalia	Chiroptera	virus	Serological	1	1	0	Olival	1	20
Myotis nattereri	Mammalia	Chiroptera	virus	Detection/ reservoir	1	2	1	EID2, Olival	1	20
Myotis nigricans	Mammalia	Chiroptera	virus, protozoa	Detection/ reservoir	1	4	1	EID2, Olival	1	15
Myotis riparius	Mammalia	Chiroptera	virus	Detection/ reservoir	1	1	0	EID2, Olival	2	17
Natalus stramineus	Mammalia	Chiroptera	virus	Detection/ reservoir	1	1	0	Olival	2	20
Philetor brachypterus	Mammalia	Chiroptera	virus	Serological	1	1	0	Olival	2	23
Phyllostomus discolor	Mammalia	Chiroptera	virus, protozoa	Serological	1	3	1	EID2, Olival	4	76
Phyllostomus hastatus	Mammalia	Chiroptera	virus, bacteria/rickettsia, protozoa	Detection/ reservoir	1	12	2	EID2, Olival	3	64
Platyrrhinus helleri	Mammalia	Chiroptera	virus	Serological	1	4	0	Olival	4	76
Pteronotus davyi	Mammalia	Chiroptera	fungi, virus	Detection/ reservoir	1	7	1	EID2, Olival	2	20
Pteronotus parnellii	Mammalia	Chiroptera	virus	Serological	1	6	3	EID2, Olival	4	69
Pteropus alecto	Mammalia	Chiroptera	virus	Detection/ reservoir	1	9	0	EID2, Olival, Plourde	1	168
Pteropus scapulatus	Mammalia	Chiroptera	virus	Detection/ reservoir	1	7	0	EID2, Olival, Plourde	1	168
Rousettus amplexicaudatus	Mammalia	Chiroptera	virus	Serological	1	2	0	Olival	3	25
Saccolaimus flaviventris	Mammalia	Chiroptera	virus	Detection/ reservoir	1	1	0	EID2, Olival, Plourde	2	281
Scotophilus kuhlii	Mammalia	Chiroptera	virus	Detection/ reservoir	1	5	1	EID2, Olival	1	2
Sturnira lilium	Mammalia	Chiroptera	bacteria/rickettsia, virus	Serological	1	12	3	EID2, Olival	6	92
Sturnira ludovici	Mammalia	Chiroptera	virus	Serological	1	1	0	Olival	1	8
Sturnira tildae	Mammalia	Chiroptera	bacteria/rickettsia, virus	Serological	1	2	0	EID2, Olival	3	64
Tonatia bidens	Mammalia	Chiroptera	virus, protozoa	Serological	1	2	0	EID2, Olival	1	46
Uroderma bilobatum	Mammalia	Chiroptera	virus, bacteria/rickettsia	Detection/ reservoir	1	6	2	EID2, Olival	4	76
Vampyrodes caraccioli	Mammalia	Chiroptera	virus	Serological	1	2	0	Olival	1	1
Vespertilio sinensis	Mammalia	Chiroptera	virus	Detection/ reservoir	1	1	0	Olival	1	20
Cabassous centralis	Mammalia	Cingulata	virus	Serological	1	1	0	Olival	1	28
Dasypus novemcinctus	Mammalia	Cingulata	virus, protozoa, bacteria/rickettsia, fungi	Detection/ reservoir	1	8	1	EID2, Olival, Plourde	4	103
Didelphis albiventris	Mammalia	Didelphimorphia	bacteria/rickettsia, protozoa	Detection/ reservoir	1	4	1	EID2, Plourde	4	56
Philander opossum	Mammalia	Didelphimorphia	bacteria/rickettsia, virus, protozoa	Serological	1	7	2	EID2, Olival	2	31
Macropus agilis	Mammalia	Diprotodontia	virus	Detection/ reservoir	1	3	7	EID2, Olival, Plourde	1	168
Macropus giganteus	Mammalia	Diprotodontia	protozoa, virus	Detection/ reservoir	1	5	10	EID2, Olival	3	64
Macropus robustus	Mammalia	Diprotodontia	virus	Serological	1	1	6	EID2, Olival	1	29

Trichosurus vulpecula	Mammalia	Diprotodontia	virus	Detection/ reservoir	1	2	1	EID2, Olival, Plourde	4	236
Procavia capensis	Mammalia	Hyracoidea	protozoa	Detection/ reservoir	1	3	0	EID2, Plourde	1	84
Lepus americanus	Mammalia	Lagomorpha	virus	Detection/ reservoir	1	4	0	EID2, Olival, Plourde	1	100
Lepus europaeus	Mammalia	Lagomorpha	bacteria/rickettsia, virus	Detection/ reservoir	1	4	3	EID2, Olival, Plourde	1	138
Lepus saxatilis	Mammalia	Lagomorpha	virus	Serological	1	1	0	Olival	1	84
Sylvilagus brasiliensis	Mammalia	Lagomorpha	virus	Serological	1	2	0	Olival	4	57
Ceratotherium simum	Mammalia	Perissodactyla	virus, bacteria/rickettsia, protozoa	Serological	1	5	8	EID2, GMPD2, Olival	1	84
Equus quagga	Mammalia	Perissodactyla	bacteria/rickettsia, virus, helminth	Detection/ reservoir	1	8	12	EID2, GMPD2	1	84
Myrmecophaga tridactyla	Mammalia	Pilosa	virus	Serological	0	2	0	EID2, Olival	2	12
Tamandua tetradactyla	Mammalia	Pilosa	protozoa, virus	Detection/ reservoir	1	6	0	EID2, Olival, Plourde	2	47
Allochrocebus solatus	Mammalia	Primates	virus	Serological	0	1	1	EID2, Olival	1	86
Alouatta belzebul	Mammalia	Primates	virus	Serological	1	2	5	GMPD2	1	2
Ateles chamek	Mammalia	Primates	protozoa, helminth	Detection/ reservoir	1	2	3	GMPD2	1	7
Ateles paniscus	Mammalia	Primates	protozoa, virus, bacteria/rickettsia	Detection/ reservoir	1	6	7	GMPD2, Olival	3	49
Cebus albifrons	Mammalia	Primates	bacteria/rickettsia, protozoa	Serological	1	3	8	EID2, GMPD2	1	7
Cercopithecus mitis	Mammalia	Primates	protozoa, helminth, virus	Detection/ reservoir	1	15	6	EID2, GMPD2, Olival	2	49
Cercopithecus mona	Mammalia	Primates	helminth, virus	Detection/ reservoir	1	9	2	EID2, GMPD2, Olival	1	10
Cercopithecus petaurista	Mammalia	Primates	virus	Serological	1	1	1	GMPD2, Olival	1	10
Chiropotes satanas	Mammalia	Primates	protozoa	Detection/ reservoir	1	1	4	GMPD2	1	2
Chlorocebus aethiops	Mammalia	Primates	virus, helminth, protozoa	Detection/ reservoir	1	23	15	EID2, GMPD2, Olival	1	84
Colobus polykomos	Mammalia	Primates	helminth, bacteria/rickettsia, virus	Detection/ reservoir	1	4	2	GMPD2, Olival	1	10
Gorilla gorilla	Mammalia	Primates	bacteria/rickettsia, protozoa, helminth, virus	Detection/ reservoir	1	35	26	EID2, GMPD2, Olival	1	86
Leontocebus fuscicollis	Mammalia	Primates	fungi, helminth, protozoa	Detection/ reservoir	1	4	13	EID2, GMPD2	1	7
Leontopithecus chrysomelas	Mammalia	Primates	virus, protozoa	Serological	1	3	0	GMPD2, Olival	1	40
Macaca fascicularis	Mammalia	Primates	helminth, bacteria/rickettsia, virus, protozoa, fungi	Detection/ reservoir	1	32	22	EID2, GMPD2, Olival, Plourde	1	212
Macaca nemestrina	Mammalia	Primates	virus, bacteria/rickettsia, protozoa, fungi	Detection/ reservoir	1	9	11	EID2, GMPD2, Olival, Plourde	1	212
Macaca radiata	Mammalia	Primates	virus	Detection/ reservoir	1	7	6	EID2, GMPD2, Olival	1	9
Macaca silenus	Mammalia	Primates	virus	Serological	0	1	0	EID2, GMPD2, Olival	1	9
Mandrillus sphinx	Mammalia	Primates	protozoa, helminth, virus, bacteria/rickettsia	Detection/ reservoir	1	17	11	EID2, GMPD2, Olival	1	86
Pan troglodytes	Mammalia	Primates	helminth, bacteria/rickettsia, protozoa, virus	Detection/ reservoir	1	72	25	EID2, GMPD2, Olival, Plourde	2	96
Pithecia pithecia	Mammalia	Primates	protozoa, virus, fungi	Serological	1	6	3	EID2, GMPD2, Olival	1	35

Pongo pygmaeus	Mammalia	Primates	protozoa, virus, helminth	Detection/ reservoir	1	25	5	EID2, GMPD2, Olival	3	74
Saguinus midas	Mammalia	Primates	virus, protozoa, fungi	Detection/ reservoir	1	5	9	EID2, GMPD2, Olival	1	35
Saimiri boliviensis	Mammalia	Primates	protozoa	Detection/ reservoir	1	3	9	EID2, GMPD2	1	7
Saimiri sciureus	Mammalia	Primates	protozoa, virus, fungi	Detection/ reservoir	1	11	29	EID2, GMPD2, Olival	1	35
Sapajus apella	Mammalia	Primates	protozoa, virus	Detection/ reservoir	1	14	9	EID2, GMPD2, Olival	5	86
Varecia variegata	Mammalia	Primates	virus, protozoa	Serological	1	3	1	EID2, GMPD2, Olival	1	6
Elephas maximus	Mammalia	Proboscidea	bacteria/rickettsia, virus, fungi	Detection/ reservoir	1	4	3	EID2, Olival	1	9
Loxodonta africana	Mammalia	Proboscidea	virus	Detection/ reservoir	1	4	1	EID2, Olival	1	10
Abrothrix longipilis	Mammalia	Rodentia	virus	Detection/ reservoir	1	1	0	EID2, Olival	1	32
Abrothrix olivaceus	Mammalia	Rodentia	virus	Serological	1	1	0	Olival	2	44
Akodon montensis	Mammalia	Rodentia	virus, helminth, protozoa	Detection/ reservoir	1	5	1	EID2, Olival, Han	1	16
Apodemus agrarius	Mammalia	Rodentia	bacteria/rickettsia, protozoa, virus, helminth	Detection/ reservoir	1	24	7	EID2, Olival, Han, Plourde	1	14
Atherurus africanus	Mammalia	Rodentia	protozoa	Detection/ reservoir	1	1	2	EID2, Han	2	96
Calomys callidus	Mammalia	Rodentia	virus	Detection/ reservoir	1	1	0	Han	1	5
Calomys tener	Mammalia	Rodentia	virus	Detection/ reservoir	1	2	0	Olival, Han	2	46
Cricetomys gambianus	Mammalia	Rodentia	bacteria/rickettsia, virus, protozoa	Detection/ reservoir	1	5	2	Olival, Han	1	107
Cuniculus paca	Mammalia	Rodentia	helminth, protozoa, virus	Detection/ reservoir	1	5	0	Olival, Plourde	3	70
Dasyprocta leporina	Mammalia	Rodentia	virus, helminth, protozoa	Detection/ reservoir	1	7	0	EID2, Olival, Han, Plourde	4	51
Dasyprocta punctata	Mammalia	Rodentia	helminth, virus	Detection/ reservoir	1	4	1	EID2, Olival, Plourde	1	28
Desmodillus auricularis	Mammalia	Rodentia	virus	Detection/ reservoir	1	1	0	EID2, Olival	2	22
Eothenomys melanogaster	Mammalia	Rodentia	bacteria/rickettsia	Detection/ reservoir	1	1	0	Han	1	14
Funambulus tristriatus	Mammalia	Rodentia	virus	Serological	1	1	0	Olival	1	9
Gerbilliscus kempii	Mammalia	Rodentia	virus	Detection/ reservoir	1	1	4	Olival	1	107
Gerbilliscus leucogaster	Mammalia	Rodentia	virus	Serological	1	1	0	Olival	1	2
Hydrochoerus hydrochaeris	Mammalia	Rodentia	helminth, virus	Detection/ reservoir	1	2	1	EID2, Olival, Plourde	1	5
Hydromys chrysogaster	Mammalia	Rodentia	virus	Detection/ reservoir	1	2	0	Olival	1	168
Hylaeamys megacephalus	Mammalia	Rodentia	virus, protozoa	Detection/ reservoir	1	9	2	EID2, Olival, Han	1	5
Hystrix africaeaustralis	Mammalia	Rodentia	virus	Serological	1	1	0	Olival	1	84
Lemniscomys striatus	Mammalia	Rodentia	virus	Detection/ reservoir	1	3	2	EID2, Olival	1	107
Leopoldamys edwardsi	Mammalia	Rodentia	bacteria/rickettsia	Detection/ reservoir	1	1	0	Han	1	14
Loxodontomys micropus	Mammalia	Rodentia	virus	Detection/ reservoir	1	1	0	EID2, Olival, Han	1	32
Mastomys erythroleucus	Mammalia	Rodentia	virus, protozoa	Detection/ reservoir	1	4	1	Olival, Han	1	107
Mastomys natalensis	Mammalia	Rodentia	virus, bacteria/rickettsia, protozoa	Detection/ reservoir	1	9	5	EID2, Olival, Han, Plourde	1	107

Micaelamys namaquensis	Mammalia	Rodentia	virus	Serological	1	2	0	Olival	2	22
Microtus pennsylvanicus	Mammalia	Rodentia	protozoa, virus, helminth	Detection/ reservoir	1	7	5	EID2, Olival, Han, Plourde	1	15
Myodes gapperi	Mammalia	Rodentia	bacteria/rickettsia, virus	Detection/ reservoir	1	3	1	EID2, Olival	1	100
Myodes rutilus	Mammalia	Rodentia	bacteria/rickettsia, protozoa, virus, helminth	Detection/ reservoir	1	13	3	EID2, Olival, Plourde	1	15
Neacomys spinosus	Mammalia	Rodentia	virus	Detection/ reservoir	1	2	1	Olival, Han	1	3
Necromys lasiurus	Mammalia	Rodentia	virus, protozoa, bacteria/rickettsia	Detection/ reservoir	1	5	0	EID2, Olival, Han, Plourde	3	51
Niviventer confucianus	Mammalia	Rodentia	bacteria/rickettsia, protozoa, virus	Detection/ reservoir	1	5	0	EID2, Olival, Han	1	14
Octodon degus	Mammalia	Rodentia	protozoa	Detection/ reservoir	1	2	0	EID2, Han	1	12
Oecomys bicolor	Mammalia	Rodentia	virus	Serological	0	1	1	EID2, Olival	2	8
Oligoryzomys chacoensis	Mammalia	Rodentia	virus, protozoa	Detection/ reservoir	1	3	0	EID2, Olival, Han	1	5
Oligoryzomys flavescens	Mammalia	Rodentia	virus	Detection/ reservoir	1	5	0	EID2, Olival, Han, Plourde	1	30
Oligoryzomys fornesi	Mammalia	Rodentia	virus	Detection/ reservoir	1	4	0	EID2, Olival, Han	1	5
Oligoryzomys longicaudatus	Mammalia	Rodentia	virus	Detection/ reservoir	1	3	0	EID2, Olival, Han, Plourde	2	44
Oligoryzomys nigripes	Mammalia	Rodentia	virus	Detection/ reservoir	1	5	0	EID2, Olival, Han, Plourde	2	46
Peromyscus maniculatus	Mammalia	Rodentia	bacteria/rickettsia, virus, protozoa	Detection/ reservoir	1	13	2	EID2, Olival, Han, Plourde	1	15
Phyllotis darwini	Mammalia	Rodentia	virus, protozoa	Detection/ reservoir	1	2	0	Olival, Han	1	12
Rattus exulans	Mammalia	Rodentia	helminth, virus, bacteria/rickettsia	Detection/ reservoir	1	8	0	Olival, Han	1	6
Rattus tanezumi	Mammalia	Rodentia	helminth, bacteria/rickettsia, protozoa, virus	Detection/ reservoir	1	4	0	EID2, Olival, Han	1	14
Rattus tiomanicus	Mammalia	Rodentia	helminth, bacteria/rickettsia	Detection/ reservoir	1	3	1	EID2, Olival, Han	1	6
Rhabdomys pumilio	Mammalia	Rodentia	virus, helminth	Detection/ reservoir	1	2	0	Olival, Han	2	22
Rhipidomys leucodactylus	Mammalia	Rodentia	protozoa	Detection/ reservoir	1	1	0	Han	1	3
Thryonomys swinderianus	Mammalia	Rodentia	virus	Detection/ reservoir	1	1	0	Olival	1	10
Xerus erythropus	Mammalia	Rodentia	virus	Detection/ reservoir	1	1	1	Olival	1	107
Iguana iguana	Reptilia	Squamata	bacteria/rickettsia, protozoa	Cargo-carrier	1	3	4	EID2	1	162

Table S2.2: Summary of PREDICTS studies included in community analyses (full dataset). The number of studies, sites, total sampled species diversity and geographical regions are listed for each original and aggregated land use class. This dataset contains 658,806 records from 8448 sites within 195 studies (see Methods). Sites with a land use intensity classification of 'cannot decide' (n=1647 sites) were excluded prior to community modelling, resulting in a final dataset of 6801 sites included in full community models.

Land use type (original)	Use intensity (original)	Land use type (aggregated)	Use intensity (aggregated)	Num studies	Num sites	Num unique species	Geographical regions	Taxonomic range
Primary vegetation	Minimal	Primary	Minimal	109	1423	4605	Asia, Americas, Oceania, Africa, Europe	Aves, Insecta, Mammalia, Reptilia, Amphibia, Arachnida, Chilopoda, Diplopoda
Primary vegetation	Light	Primary	Substantial	59	1050	2357	Americas, Asia, Africa, Oceania, Europe	Insecta, Aves, Mammalia, Reptilia, Amphibia, Malacostraca
Primary vegetation	Intense	Primary	Substantial	23	407	1236	Asia, Africa, Oceania, Americas, Europe	Aves, Reptilia, Amphibia, Mammalia, Insecta
Primary vegetation	Cannot decide	Primary	Cannot decide	7	111	529	Asia, Americas, Africa	Aves, Mammalia
Young secondary vegetation	Minimal	Secondary	Minimal	29	272	2039	Europe, Americas, Oceania, Asia, Africa	Insecta, Arachnida, Aves, Mammalia, Reptilia, Amphibia
Young secondary vegetation	Light	Secondary	Substantial	11	62	1070	Europe, Africa, Americas, Asia	Insecta, Aves, Mammalia
Young secondary vegetation	Intense	Secondary	Substantial	10	214	908	Europe, Africa, Oceania, Americas, Asia	Insecta, Mammalia, Aves, Reptilia, Amphibia
Young secondary vegetation	Cannot decide	Secondary	Cannot decide	9	99	379	Asia, Europe, Americas, Africa	Aves, Insecta, Mammalia
Intermediate secondary vegetation	Minimal	Secondary	Minimal	34	238	1995	Europe, Asia, Americas, Oceania, Africa	Arachnida, Aves, Mammalia, Reptilia, Insecta
Intermediate secondary vegetation	Light	Secondary	Substantial	13	109	1103	Americas, Africa, Europe, Asia	Aves, Mammalia, Insecta

Intermediate secondary vegetation	Intense	Secondary	Substantial	5	23	316	Oceania, Americas, Asia	Aves, Reptilia, Amphibia, Mammalia
Intermediate secondary vegetation	Cannot decide	Secondary	Cannot decide	5	63	218	Asia, Europe, Americas, Oceania	Aves, Mammalia
Mature secondary vegetation	Minimal	Secondary	Minimal	21	143	1406	Europe, Oceania, Asia, Africa, Americas	Gastropoda, Insecta, Arachnida, Mammalia, Aves
Mature secondary vegetation	Light	Secondary	Substantial	7	154	527	Americas, Asia	Aves, Mammalia, Insecta
Mature secondary vegetation	Intense	Secondary	Substantial	2	6	4	Asia	Mammalia
Mature secondary vegetation	Cannot decide	Secondary	Cannot decide	3	57	140	Asia, Africa	Aves, Mammalia
Secondary vegetation (indeterminate age)	Minimal	Secondary	Minimal	16	391	1123	Oceania, Europe, Africa, Asia, Americas	Insecta, Aves, Amphibia, Mammalia, Reptilia, Arachnida, Chilopoda, Diplopoda
Secondary vegetation (indeterminate age)	Light	Secondary	Substantial	8	40	289	Oceania, Asia, Americas, Africa	Insecta, Aves, Mammalia, Amphibia
Secondary vegetation (indeterminate age)	Intense	Secondary	Substantial	2	21	14	Americas, Africa	Mammalia
Secondary vegetation (indeterminate age)	Cannot decide	Secondary	Cannot decide	10	118	375	Asia, Africa, Europe, Americas	Insecta, Aves, Mammalia
Plantation forest	Minimal	Managed	Minimal	19	181	1332	Americas, Europe, Africa, Asia	Aves, Mammalia, Insecta, Arachnida
Plantation forest	Light	Managed	Substantial	22	584	1017	Asia, Americas, Africa, Europe, Oceania	Aves, Mammalia, Insecta
Plantation forest	Intense	Managed	Substantial	13	162	694	Americas, Asia, Africa, Oceania, Europe	Mammalia, Aves, Insecta
Plantation forest	Cannot decide	Managed	Cannot decide	9	52	506	Asia, Europe, Americas	Insecta, Aves, Mammalia

Pasture	Minimal	Managed	Minimal	16	182	1486	Europe, Africa, Americas, Oceania	Insecta, Mammalia, Aves, Amphibia, Arachnida, Chilopoda, Diplopoda
Pasture	Light	Managed	Substantial	24	268	1298	Europe, Oceania, Americas, Africa	Insecta, Aves, Mammalia, Reptilia, Amphibia, Arachnida, Chilopoda, Diplopoda
Pasture	Intense	Managed	Substantial	7	35	149	Europe, Oceania, Asia, Americas	Insecta, Aves, Mammalia
Pasture	Cannot decide	Managed	Cannot decide	14	594	640	Asia, Americas, Europe, Oceania, Africa	Aves, Insecta, Mammalia
Cropland	Minimal	Managed	Minimal	18	202	1061	Asia, Africa, Oceania, Europe, Americas	Aves, Insecta, Mammalia, Arachnida
Cropland	Light	Managed	Substantial	7	56	779	Africa, Oceania, Asia, Europe, Americas	Aves, Reptilia, Amphibia, Mammalia, Arachnida
Cropland	Intense	Managed	Substantial	5	209	259	Africa, Europe, Asia	Aves, Arachnida, Mammalia
Cropland	Cannot decide	Managed	Cannot decide	9	537	497	Asia, Americas, Europe, Africa	Insecta, Aves, Mammalia
Urban	Minimal	Urban	Minimal	10	136	922	Europe, Americas, Oceania, Asia, Africa	Insecta, Aves, Gastropoda, Amphibia, Mammalia
Urban	Light	Urban	Substantial	10	177	439	Europe, Americas, Oceania, Asia	Insecta, Aves, Gastropoda, Amphibia, Mammalia
Urban	Intense	Urban	Substantial	8	56	470	Europe, Americas, Asia, Oceania	Insecta, Aves, Gastropoda, Mammalia
Urban	Cannot decide	Urban	Cannot decide	2	16	150	Europe, Americas	Gastropoda, Aves

Table S2.3: Structure of Bayesian mixed-effects models of host richness and total abundance (full dataset). The table details the structure of the best models of the full dataset (main text, Figure 2). Best models were selected based on minimising Watanabe-Akaike Information Criterion (WAIC) while adhering to model assumptions. Fixed effects were composite land use+intensity (LUI; 8 level factor), research effort (average confidence in assigned host status across all species: either mean for richness models, or community-weighted mean for abundance models) and, for proportion host abundance log-transformed total site-level abundance (log(TotalAbundance); effectively acting as an offset). For proportional host richness models, log(TotalSR) was included as an offset. Random effects considered were for study (SS), spatial block nested within study (SSB), site (SSBS) and Biome. Species richness (count data) was modelled using a Poisson likelihood, and total abundance (continuous adjusted counts) was log-transformed and modelled using a Gaussian likelihood with a precision (inverse of variance) hyperprior (log-gamma; shape 0.5, scale 0.1). All fixed effects were assigned an uninformative Gaussian prior (mean 0, precision 0.01), and all random intercepts were modelled as iid Gaussian variables with a precision hyperprior (log-gamma with shape 0.1, scale 0.1). Fixed-effects estimates were robust to systematically varying priors and hyperpriors. Sites from studies that only sampled species occurrence were excluded from abundance models (n=708 sites). Following model selection, each model was bootstrapped with transitioning of non-hosts to host status, to account for variable research effort across species (Methods).

Model name	Response variable	Likelihood	Fixed effects	Random intercepts (iid)	Num sites
Host richness	HostSR	Poisson	LUI	SS, SSB	6801
Non-host richness	NonHostSR	Poisson	LUI	SS, SSB	6801
Proportion host richness	HostSR with log(TotalSR) as offset	Poisson	LUI	SS, SSB	6801
Host total abundance	log(HostAbundance+1)	Gaussian	LUI, LogHumanDensity	SS, SSB, SSBS	6093
Non-host total abundance	log(NonHostAbundance+1)	Gaussian	LUI, LogHumanDensity	SS, SSB, SSBS, Biome	6093
Proportion host total abundance	log(HostAbundance+1)	Gaussian	LUI, log(TotalAbundance+1), LogHumanDensity	SS, SSB, SSBS, Biome	6093

Table S2.4: Structure of Bayesian mixed-effects models of mammal host richness and total abundance (mammal reservoirs subset). I conducted a separate model selection procedure for models of the mammal reservoirs subset, following the same methodology and with the same model structure specifications and priors as the full dataset models (Table S2.3). Sites from studies that only sampled species occurrence were excluded from abundance models (n=103 sites).

Model name	Response variable	Likelihood	Fixed effects	Random intercepts (iid)	Num sites
Host richness	HostSR	Poisson	LUI	SS, SSB	2026
Non-host richness	NonhostSR	Poisson	LUI	SS, SSB	2026
Proportion host richness	HostSR with log(TotalSR) included as offset	Poisson	LUI	SS, SSB	2026
Host abundance	log(HostAbundance+1)	Gaussian	LUI	SS, SSB, SSBS	1963
Non-host abundance	log(NonHostAbundance+1)	Gaussian	LUI	SS, SSB, SSBS	1963
Proportion host abundance	log(HostAbundance+1)	Gaussian	LUI, log(TotalAbundance+1)	SS, SSB, SSBS	1963

Table S2.5: Fixed-effects posterior estimates from community models. Table shows posterior marginal fixed effects estimates for community models, calculated across 1000 bootstrap iterations per model (posterior median, 67% quantile range, and 95% quantile range). Results are shown for both the full dataset (Figure 2.3) and the mammal reservoirs dataset (Figure S2.2). All land use parameters (type_intensity) are for categorical covariates, with the intercept representing primary land under minimal use, and other parameters are continuous linear covariates (log human density, log total abundance). Estimates are on the linear predictor (log) scale, and therefore represent change in log-response relative to a primary land under minimal use baseline (categorical predictors) or change in the log-response caused by a unit change in the predictor (continuous predictors) while holding all other predictors constant. Fitted model intercepts represent averages across all studies with differing methodologies and taxonomic focus; these do not have a direct ecological interpretation.

Dataset	Response variable	Parameter	Posterior median	67% quantile range	95% quantile range
Full dataset	HostSR	Intercept	-0.092	-0.224, 0.036	-0.364, 0.164
		Primary_Substantial	0.111	0.064, 0.158	0.016, 0.207
		Secondary_Minimal	-0.133	-0.196, -0.071	-0.261, -0.006
		Secondary_Substantial	0.12	0.051, 0.189	-0.02, 0.261
		Managed_Minimal	0.038	-0.039, 0.115	-0.118, 0.193
		Managed_Substantial	0.024	-0.041, 0.089	-0.108, 0.156
		Urban_Minimal	0.325	0.232, 0.418	0.137, 0.516
		Urban_Substantial	0.366	0.252, 0.483	0.135, 0.607
	NonHostSR	Intercept	1.973	1.848, 2.097	1.717, 2.225
		Primary_Substantial	0.221	0.204, 0.239	0.186, 0.257
		Secondary_Minimal	-0.044	-0.061, -0.027	-0.078, -0.009
		Secondary_Substantial	-0.006	-0.027, 0.016	-0.048, 0.038
		Managed_Minimal	-0.049	-0.072, -0.027	-0.095, -0.006
		Managed_Substantial	-0.1	-0.117, -0.082	-0.135, -0.064
		Urban_Minimal	-0.202	-0.267, -0.152	-0.352, -0.101
		Urban_Substantial	-0.232	-0.295, -0.163	-0.356, -0.088
	PropHostSR	Intercept	-2.692	-2.829, -2.558	-2.975, -2.424
		Primary_Substantial	0.071	0.026, 0.116	-0.021, 0.163
		Secondary_Minimal	-0.019	-0.081, 0.043	-0.146, 0.106
		Secondary_Substantial	0.168	0.101, 0.235	0.032, 0.304
		Managed_Minimal	0.111	0.033, 0.187	-0.047, 0.265
		Managed_Substantial	0.187	0.123, 0.251	0.056, 0.317
		Urban_Minimal	0.483	0.393, 0.572	0.299, 0.662
		Urban_Substantial	0.542	0.426, 0.657	0.308, 0.776
	HostAbundance	Intercept	1.466	1.326, 1.608	1.182, 1.755
		Primary_Substantial	0.241	0.177, 0.305	0.108, 0.37
		Secondary_Minimal	0.062	-0.003, 0.125	-0.077, 0.193
		Secondary_Substantial	0.246	0.177, 0.313	0.102, 0.381
		Managed_Minimal	0.239	0.154, 0.32	0.055, 0.408
		Managed_Substantial	0.17	0.097, 0.238	-0.01, 0.307
		Urban_Minimal	1.097	0.937, 1.239	0.737, 1.382
		Urban_Substantial	1.093	0.911, 1.268	0.717, 1.449
		LogHumanDensity	0.01	-0.003, 0.024	-0.018, 0.04

	NonHostAbundance	Intercept	3.504	3.299, 3.708	3.083, 3.92
		Primary_Substantial	0.117	0.074, 0.159	0.03, 0.204
		Secondary_Minimal	-0.059	-0.104, -0.014	-0.149, 0.033
		Secondary_Substantial	-0.012	-0.062, 0.038	-0.113, 0.09
		Managed_Minimal	0.077	0.022, 0.138	-0.033, 0.215
		Managed_Substantial	-0.179	-0.221, -0.136	-0.264, -0.089
		Urban_Minimal	-0.629	-0.747, -0.5	-0.865, -0.304
		Urban_Substantial	-0.494	-0.639, -0.342	-0.785, -0.172
		LogHumanDensity	-0.003	-0.014, 0.008	-0.025, 0.019
	PropHostAbundance	Intercept	-0.702	-0.886, -0.525	-1.092, -0.337
		Primary_Substantial	0.141	0.079, 0.203	0.011, 0.266
		Secondary_Minimal	0.065	0.005, 0.123	-0.065, 0.186
		Secondary_Substantial	0.188	0.124, 0.248	0.045, 0.31
		Managed_Minimal	0.134	0.05, 0.21	-0.051, 0.293
		Managed_Substantial	0.229	0.157, 0.292	0.039, 0.356
		Urban_Minimal	0.893	0.74, 1.022	0.54, 1.149
		Urban_Substantial	0.859	0.688, 1.025	0.506, 1.195
		LogHumanDensity	0.012	0, 0.025	-0.014, 0.039
		logTotalAbund	0.548	0.525, 0.579	0.505, 0.627
Mammal reservoirs	HostSR	Intercept	0.055	-0.147, 0.248	-0.367, 0.442
		Primary_Substantial	-0.053	-0.133, 0.027	-0.214, 0.11
		Secondary_Minimal	-0.082	-0.207, 0.043	-0.337, 0.171
		Secondary_Substantial	0.12	0.023, 0.218	-0.076, 0.319
		Managed	-0.105	-0.18, -0.029	-0.257, 0.049
		Urban	0.436	0.127, 0.737	-0.189, 1.037
	NonHostSR	Intercept	0.848	0.618, 1.072	0.366, 1.301
		Primary_Substantial	-0.054	-0.1, -0.008	-0.148, 0.04
		Secondary_Minimal	-0.218	-0.276, -0.16	-0.336, -0.1
		Secondary_Substantial	-0.114	-0.181, -0.047	-0.25, 0.022
		Managed	-0.303	-0.362, -0.245	-0.422, -0.185
		Urban	-0.296	-0.491, -0.102	-0.702, 0.104
	PropHostSR	Intercept	-1.765	-1.946, -1.594	-2.145, -1.421
		Primary_Substantial	0.004	-0.07, 0.079	-0.147, 0.155
		Secondary_Minimal	-0.052	-0.176, 0.071	-0.304, 0.197
		Secondary_Substantial	0.124	0.03, 0.218	-0.068, 0.314
		Managed	0.039	-0.035, 0.113	-0.112, 0.19
		Urban	0.635	0.312, 0.948	-0.021, 1.259
	HostAbundance	Intercept	1.6	1.37, 1.831	1.131, 2.074
		Primary_Substantial	0.171	0.082, 0.254	-0.021, 0.338
		Secondary_Minimal	0.15	0.022, 0.281	-0.108, 0.42
		Secondary_Substantial	0.387	0.273, 0.492	0.141, 0.596
		Managed	0.283	0.164, 0.377	-0.002, 0.467
		Urban	1.697	1.346, 1.943	0.847, 2.179
	NonHostAbundance	Intercept	2.42	2.198, 2.642	1.965, 2.873
		Primary_Substantial	-0.172	-0.25, -0.091	-0.328, 0
		Secondary_Minimal	-0.163	-0.276, -0.049	-0.391, 0.069
		Secondary_Substantial	-0.207	-0.305, -0.102	-0.404, 0.019
		Managed	-0.451	-0.539, -0.35	-0.625, -0.202

		Urban	-1.192	-1.4, -0.946	-1.609, -0.452
	PropHostAbundance	Intercept	-0.308	-0.483, -0.133	-0.67, 0.051
		Primary_Substantial	0.191	0.119, 0.257	0.031, 0.323
		Secondary_Minimal	0.171	0.066, 0.281	-0.039, 0.403
		Secondary_Substantial	0.349	0.252, 0.432	0.127, 0.515
		Managed	0.42	0.319, 0.495	0.154, 0.568
		Urban	1.406	1.102, 1.605	0.582, 1.793
		logTotalAbund	0.635	0.608, 0.667	0.583, 0.708

Table S2.6: Fixed-effects posterior distributions from order-level models (occurrence and zero-truncated abundance). I fitted separate occurrence (binomial logit-link) and zero-truncated abundance (log-link) models to estimate the average effect of land use across all species within taxonomic subsets (order-level within mammals and birds). Models included a fixed-effects interaction term between land use type and host status, except for Primates where separate models were fitted for hosts and non-hosts due to lack of non-hosts in managed land. As with community models, each model was fitted using a bootstrap approach to account for research effort, with each iteration transitioning a proportion of non-hosts to host status (Chapter 2 Methods, Figure 2.2, Figure S2.3). Table shows summary posterior fixed effects estimates (median and 95% quantile range) calculated across posterior samples drawn from 500 bootstrapped models (2500 per model), along with number of studies and sites per order, the total number of species included, the mean number of non-hosts reclassified to 'host' for each model iteration, and the mean number of host species per model iteration. Estimates are on the linear predictor (link) scale, and are shown transformed to the natural scale in Figure S2.3.

Class	Order	Parameter	Occurrence (log odds) (posterior median and 95% interval)	Zero-truncated abundance (log) (posterior median and 95% interval)	Studies	Sites	Total species	Mean re-classified	Mean num host species (boot-strap)
Aves	Passeriformes	Intercept	-0.698 (-1.088, -0.304)	1.451 (1.272, 1.629)	78	4302	1868	16.05	78.05
Aves	Passeriformes	LandUseTypeManaged	-0.349 (-0.396, -0.303)	-0.077 (-0.097, -0.057)					
Aves	Passeriformes	LandUseTypeSecondary	-0.214 (-0.264, -0.165)	-0.044 (-0.064, -0.023)					
Aves	Passeriformes	LandUseTypeUrban	-0.671 (-0.804, -0.542)	-0.068 (-0.129, -0.006)					
Aves	Passeriformes	IsHost	-0.16 (-0.45, 0.136)	0.017 (-0.093, 0.128)					
Aves	Passeriformes	LandUseTypeManaged:IsHost	0.596 (0.373, 0.811)	0.045 (-0.041, 0.12)					
Aves	Passeriformes	LandUseTypeSecondary:IsHost	0.128 (-0.194, 0.449)	0.039 (-0.077, 0.154)					
Aves	Passeriformes	LandUseTypeUrban:IsHost	1.567 (1.323, 1.779)	0.208 (0.109, 0.305)					
Aves	Psittaciformes	Intercept	-0.58 (-9.083, 8.517)	1.9 (-6.581, 8.792)	41	2500	87	3.97	25.97
Aves	Psittaciformes	LandUseTypeManaged	-1.049 (-1.408, -0.699)	-0.678 (-0.89, -0.328)					
Aves	Psittaciformes	LandUseTypeSecondary	-0.61 (-0.922, -0.301)	-0.288 (-0.476, -0.094)					
Aves	Psittaciformes	LandUseTypeUrban	0.888 (-0.883, 2.702)	-0.511 (-1.38, 0.319)					
Aves	Psittaciformes	IsHost	0.05 (-0.642, 0.72)	-0.043 (-0.324, 0.268)					
Aves	Psittaciformes	LandUseTypeManaged:IsHost	0.28 (-0.473, 1.007)	0.451 (-0.478, 0.841)					
Aves	Psittaciformes	LandUseTypeSecondary:IsHost	0.514 (-0.04, 1.051)	0.298 (-0.062, 0.604)					
Aves	Psittaciformes	LandUseTypeUrban:IsHost	0.558 (-2.171, 3.346)	-0.152 (-1.376, 1.084)					
Mammalia	All	Intercept	-0.428 (-1.174, 0.312)	1.141 (0.89, 1.386)	63	1886	521	50.60	184.60
Mammalia	All	LandUseTypeManaged	-0.578 (-0.79, -0.364)	-0.009 (-0.107, 0.084)					
Mammalia	All	LandUseTypeSecondary	-0.239 (-0.436, -0.041)	0.085 (0.007, 0.163)					
Mammalia	All	IsHost	0.259 (-0.107, 0.622)	0.228 (0.09, 0.367)					
Mammalia	All	LandUseTypeManaged:IsHost	0.447 (0.102, 0.785)	0.185 (0.046, 0.333)					
Mammalia	All	LandUseTypeSecondary:IsHost	0.493 (0.143, 0.84)	0.012 (-0.113, 0.141)					
Mammalia	Carnivora	Intercept	-2.173 (-3.64, -0.577)	0.948 (0.609, 1.282)	15	827	58	12.86	35.86
Mammalia	Carnivora	LandUseTypeManaged	-0.835 (-2.286, 0.431)	-0.009 (-0.315, 0.295)					
Mammalia	Carnivora	LandUseTypeSecondary	-0.825 (-2.439, 0.542)	-0.07 (-0.377, 0.232)					
Mammalia	Carnivora	IsHost	-0.062 (-1.179, 1.05)	0.024 (-0.18, 0.231)					
Mammalia	Carnivora	LandUseTypeManaged:IsHost	0.455 (-0.891, 1.961)	-0.099 (-0.408, 0.214)					
Mammalia	Carnivora	LandUseTypeSecondary:IsHost	0.717 (-0.839, 2.49)	-0.046 (-0.358, 0.271)					
Mammalia	Cetartiodactyla	Intercept	0.619 (-0.936, 2.33)	1.362 (0.832, 1.893)	15	604	33	4.07	15.07
Mammalia	Cetartiodactyla	LandUseTypeManaged	-0.623 (-1.884, 0.287)	-0.117 (-0.424, 0.193)					
Mammalia	Cetartiodactyla	LandUseTypeSecondary	-0.375 (-1.329, 0.496)	-0.064 (-0.301, 0.155)					
Mammalia	Cetartiodactyla	IsHost	-0.653 (-2.089, 0.799)	0.004 (-0.263, 0.273)					
Mammalia	Cetartiodactyla	LandUseTypeManaged:IsHost	1.052 (-0.644, 2.782)	0.255 (-0.263, 0.745)					
Mammalia	Cetartiodactyla	LandUseTypeSecondary:IsHost	0.631 (-1.046, 2.287)	0.111 (-0.348, 0.554)					
Mammalia	Chiroptera	Intercept	-0.787 (-2.43, 0.903)	1.044 (0.59, 1.481)	13	346	177	16.81	52.81

Mammalia	Chiroptera	LandUseTypeManaged	-0.297 (-0.619, 0.024)	0.059 (-0.088, 0.194)					
Mammalia	Chiroptera	LandUseTypeSecondary	-0.052 (-0.405, 0.3)	-0.041 (-0.184, 0.101)					
Mammalia	Chiroptera	IsHost	0.397 (-0.176, 0.958)	0.362 (0.105, 0.621)					
Mammalia	Chiroptera	LandUseTypeManaged:IsHost	0.446 (-0.152, 1.038)	0.235 (0.002, 0.491)					
Mammalia	Chiroptera	LandUseTypeSecondary:IsHost	0.199 (-0.432, 0.822)	0.124 (-0.107, 0.361)					
Mammalia	Primates	Host_Intercept	1.848 (-0.709, 6.713)	1.737 (0.901, 2.509)	16	583	38	5.54	22.54
Mammalia	Primates	Host_Secondary	-1.005 (-1.847, -0.132)	-0.018 (-0.239, 0.2)					
Mammalia	Primates	Host_Managed	-2.539 (-3.645, -1.415)	-0.233 (-0.653, 0.183)					
Mammalia	Primates	Non-host_Intercept	0.052 (-3.045, 3.058)	1.083 (0.02, 2.136)					
Mammalia	Primates	Non-host_Secondary	-1.394 (-2.595, -0.222)	-0.036 (-0.37, 0.272)					
Mammalia	Primates	Non-host_Managed							
Mammalia	Rodentia	Intercept	-0.816 (-2.186, 0.436)	1.402 (0.941, 1.885)	31	1133	126	6.49	42.49
Mammalia	Rodentia	LandUseTypeManaged	-0.96 (-1.387, -0.513)	-0.025 (-0.282, 0.237)					
Mammalia	Rodentia	LandUseTypeSecondary	-0.271 (-0.657, 0.116)	0.229 (0.032, 0.425)					
Mammalia	Rodentia	IsHost	0.401 (-0.427, 1.256)	-0.006 (-0.314, 0.304)					
Mammalia	Rodentia	LandUseTypeManaged:IsHost	1.168 (0.283, 1.871)	0.343 (-0.001, 0.676)					
Mammalia	Rodentia	LandUseTypeSecondary:IsHost	0.81 (-0.048, 1.683)	-0.095 (-0.418, 0.24)					

Table S2.7: Fixed-effects posterior estimates from mammal pathogen richness models. Table summarises continuous fixed effects parameter estimates from human-shared and non human-shared pathogen richness models, with species occurrence (binomial logit-link) modelled as an interaction between residual pathogen richness (scaled to mean 0, sd 1) and land use type. Both models included random intercepts for species, order, study and spatial block within study. Fixed effects were assigned an uninformative Gaussian prior (mean 0, precision 0.01), and all random intercepts were modelled as Gaussian variables with a precision hyperprior (log-gamma with shape 0.1, scale 0.1). Managed land was specified as the base factor in models, so 'Intercept' and 'PathRich' are respectively the intercept and slope parameter for managed sites, and estimates for primary and secondary lands measure the differences in either intercept or slope from the base factor. All estimates are shown as median and 95% credible interval of posterior density, on the link (log-odds) scale. Estimates are shown from the full model, and from three further sensitivity analyses: the summary posterior across 400 bootstrapped models fitted to different posterior samples of residual pathogen richness (to test for sensitivity to uncertainty in the relationship between publication effort and pathogen richness), and for the full model either excluding all orders in the Global Mammal Parasite Database, or including only the orders from the Global Mammal Parasite Database (Chapter 2 Methods).

Model	Parameter	Type	Full model estimate (median ± 95 CI)	Bootstrapped posterior estimate (400 models)	Estimate excl. GMPD orders	Estimate only GMPD orders
Human-shared	Intercept	intercept	-0.647 (-1.375, 0.071)	-0.663 (-1.393, 0.058)	-0.496 (-1.242, 0.225)	-1.437 (-3.923, 1.043)
Human-shared	PathRich	continuous	0.313 (0.155, 0.471)	0.294 (0.1, 0.475)	0.697 (0.444, 0.955)	0.152 (-0.078, 0.383)
Human-shared	LU_Primary	categorical	0.41 (0.261, 0.56)	0.408 (0.258, 0.559)	0.258 (0.092, 0.425)	1.052 (0.691, 1.425)
Human-shared	LU_Secondary	categorical	0.321 (0.164, 0.478)	0.326 (0.168, 0.483)	0.261 (0.085, 0.438)	0.433 (0.085, 0.783)
Human-shared	LU_Primary:PathRich	continuous (interaction)	-0.212 (-0.33, -0.096)	-0.196 (-0.327, -0.065)	-0.386 (-0.597, -0.177)	-0.23 (-0.393, -0.071)
Human-shared	LU_Secondary:PathRich	continuous (interaction)	-0.148 (-0.266, -0.034)	-0.136 (-0.265, -0.004)	-0.226 (-0.453, -0.001)	-0.132 (-0.281, 0.006)
Non-human	Intercept	intercept	-0.659 (-1.401, 0.072)	-0.679 (-1.421, 0.051)	-0.59 (-1.344, 0.13)	-1.265 (-3.753, 1.224)
Non-human	PathRich	continuous	0.29 (0.125, 0.456)	0.264 (0.015, 0.497)	0.45 (0.159, 0.743)	0.203 (-0.013, 0.418)
Non-human	LU_Primary	categorical	0.416 (0.267, 0.564)	0.413 (0.262, 0.566)	0.329 (0.16, 0.498)	0.917 (0.59, 1.251)
Non-human	LU_Secondary	categorical	0.353 (0.198, 0.509)	0.352 (0.196, 0.507)	0.299 (0.122, 0.476)	0.549 (0.212, 0.891)
Non-human	LU_Primary:PathRich	continuous (interaction)	-0.33 (-0.455, -0.209)	-0.297 (-0.488, -0.095)	-0.66 (-0.894, -0.432)	-0.196 (-0.35, -0.044)
Non-human	LU_Secondary:PathRich	continuous (interaction)	-0.084 (-0.209, 0.037)	-0.058 (-0.263, 0.131)	-0.18 (-0.361, -0.01)	0.007 (-0.183, 0.195)

Table S2.8: Biodiversity, environmental and host-pathogen data sources. Data processing is described in Methods, and code and compiled datasets where not freely available online (e.g. human pathogens list as described below) are provided in the data repository for this chapter.

Variable/dataset name	Original format	Data source	Reference
Georeferenced species records	Occurrence and abundance per-site, nested within source studies.	Projecting Responses of Ecological Diversity in Changing Terrestrial Systems (PREDICTS).	(Hudson et al., 2016)
Land use type	Categorical: either primary, young secondary, intermediate secondary, mature secondary, cropland, pasture, plantation forest, urban.	PREDICTS database. Sites classified based on description in source paper.	(Hudson et al., 2016)
Land use intensity	Categorical: either minimal, light, intense, or cannot decide.	PREDICTS database. Sites classified based on source paper description.	(Hudson et al., 2016)
Enhanced Infectious Diseases database (EID2)	Database of cargo-carrier (host-parasite) interactions, inferred from web-based sources	EID2 database of host-parasite and related species interactions.	(Wardeh et al., 2015)
Global Mammal Parasite Database 2.0	Database of host species-parasite species associations for primates, ungulates and carnivores, collated from the scientific literature	Global Mammal Parasite Database 2.0	(Stephens et al., 2017)
Mammal viruses database	Database of all known host-virus associations for all mammals, including zoonotic status, collated from the scientific literature	Olival *et al.*'s mammal virus analysis.	(Olival et al., 2017)
Reservoir hosts database	Database of pathogen-reservoir host associations for 330 disease systems, collated from the scientific literature.	Plourde *et al.*'s reservoir host database and analysis.	(Plourde et al., 2017)
Rodent reservoirs database	Database of zoonotic reservoir status for all rodent species, with pathogen information collated from Global Infectious Disease and Epidemiology Network (GIDEON)	Han *et al.*'s analysis of zoonotic rodent reservoir traits.	(Han et al., 2015)

Human pathogens list (broad)	List of all known human pathogens/parasites collated from web and literature sources, used for cross-referencing against host datasets.	Taylor *et al*.'s human pathogens list ; DNA Pathogen Frequencies; Bode Science Center; Jones *et al*. emerging pathogens; extracted March 2017.	(Jones et al., 2008; Taylor et al., 2001)
Zoonotic agents list (strict)	All human pathogens cross referenced against web and literature lists of zoonotic agents (recognised aetiological agent of a specific human disease with an animal reservoir).	Global Infectious Disease and Epidemiology Network (GIDEON); Atlas of Human Infectious Diseases (2012); Taylor *et al* (2001).	(Taylor et al., 2001; Wertheim et al., 2012)
Disease-related research effort	Number of PubMed entries per-species, 1950-2017	Extracted from PubMed online database, August 2018.	PubMed
Human population density (2015)	Global, ~1km grid cells	Gridded Population of the World v4 (CIESIN 2015).	CIESIN

Appendix 2:

Supplementary figures and data for Chapter 4.

This appendix provides supplementary figures, tables and information on data sources for the analyses conducted in Chapter 4, *'Climate, land use and reporting effort shape the present day distribution and dynamics of Lassa fever in Nigeria'.* The items contained in this appendix are:

Figure S4.1: Lassa fever case time series from Nigeria Centre for Disease Control reporting regimes. Graphs summarise weekly surveillance data aggregated across all local government authorities (LGAs), from January 2012 to December 2019, and show the differences between two surveillance regimes. Bar plots show monthly total cases from the long-term Weekly Epidemiological Reports (top) and more recent Situation Reports (bottom) regime, with bar heights representing the total LF cases from all epidemiological weeks starting during a given month, split into suspected (grey) and confirmed (black) cases. Weekly case accumulation curves per-surveillance regime, per-year show total reported cases (including both suspected and confirmed; top graphs) and confirmed only (bottom graphs). LF trends during the overlap period between the two regimes are similar (January 2017 to March 2018) but the SitRep data (based on the most current reporting regime and including post-hoc follow-ups to ensure accurate counts) more clearly show the very large increase in both suspected and confirmed case reports in 2018. The full time series used in analyses (Figure 4.1) includes W.E.R. data from 2012 to 2016, and SitRep data from 2017 to 2019.

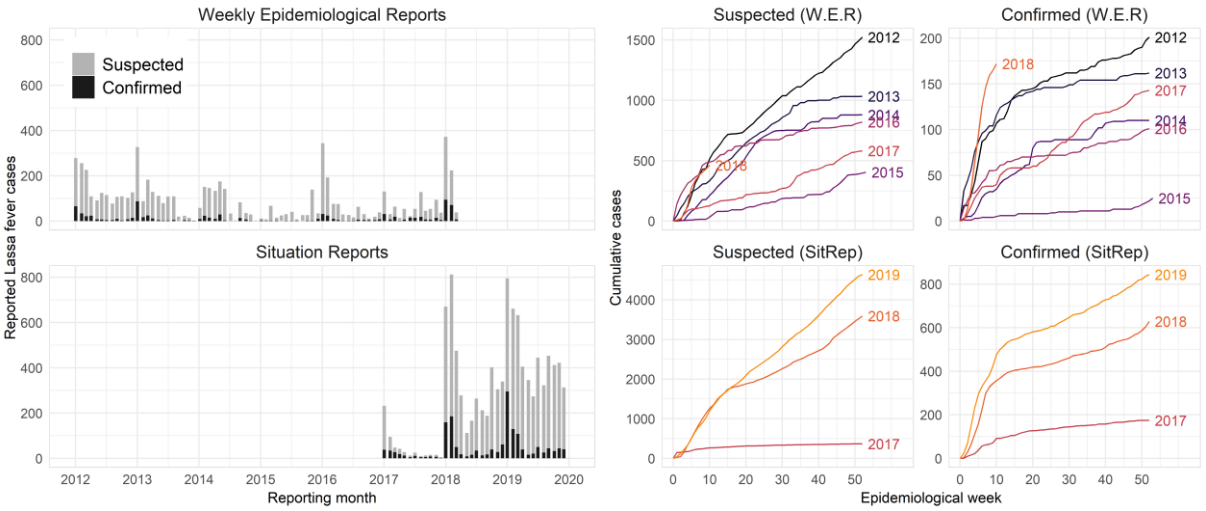

Figure S4.2: Spatiotemporal indices of suspected Lassa fever case reporting effort across Nigeria. We used annual suspected (but not confirmed) case counts as a proxy for of relative reporting effort per-LGA per-year, and statistically derived a bounded (0 to 1) index of relative suspected case reporting effort to account for these changes over space and time (Methods). Maps show, for the time period of spatial modelling (A; 2016 to 2019), Reporting Index values for each LGA, which denote the probability of at least 1 suspected case being reported per month within a given year (i.e. reporting probability across 12 monthly 'trials' per year). Trend lines (B) show annual Reporting Index values for each spatially aggregated district used in temporal modelling (cluster of LGAs; see Methods, Figure S4.4), within a subset of 25 states ordered by total LF incidence (highest to lowest). Notable here are the consistently high Reporting Index values for the Esan area of Edo State (top left graph), where Irrua Specialist Teaching Hospital is located (Figure 4.2).

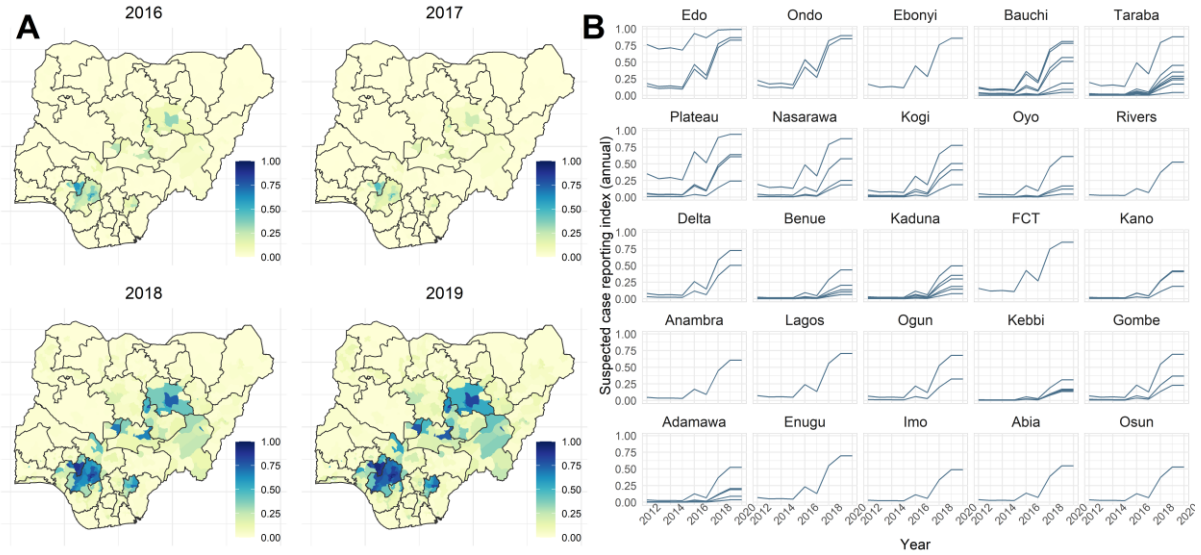

Figure S4.3: Components of the spatial models of Lassa fever occurrence and incidence across Nigeria. We conducted both random (8-fold) and geographically-structured cross-validation of the spatial models of LF incidence. For random cross-validation, we used 2500 samples drawn from each holdout model's joint posterior to simulate out-of-sample (OOS) posterior predictive distribution for occurrence (A; binomial simulation) and incidence-given-presence models (B; negative binomial simulation). Barplots for occurrence models (A) show, across all LGAs per year (shown in rows) the binned probability of observed values (either absences, left column; or presences, right column) occurring in the posterior predictive distribution, with higher values indicating better predictive ability. The model tends to underpredict presence of LF during earlier years (when reporting was lower) but performs well in 2018-2019 (bottom rows). Barplots for incidence models (B) visually show, for each State with >0 cases, the proportion of total observed values across all years falling within (green) and outside (blue) the 67% and 95% posterior predictive intervals. States are ordered by total case counts (left to right). The direction and magnitude of fixed-effects (mean ± 95% credible interval) was also robust to geographically-structured cross-validation (C), which involved in turn excluding all LGAs from each of 12 Lassa-endemic and non-endemic states (ordered by total case counts, top to bottom), indicating that the results were not overly influenced by data from any one locality.

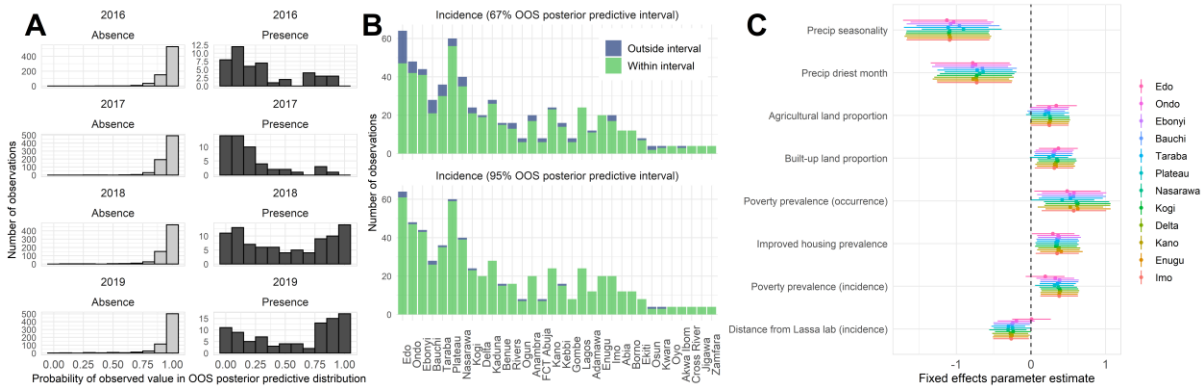

Figure S4.4: Fitted spatial models of Lassa fever occurrence and incidence for spatially-aggregated districts. Analyses of areal data can be confounded by differences in scale and shape of aggregated districts, and local government authority (LGA) geographical areas in Nigeria are highly skewed and vary over >3 orders of magnitude (median 713km^2, mean 1175km^2, range 4 – 11255km^2). To examine the effects of scale on inferences, we repeated all spatial modelling after aggregating LGAs into 130 composite districts, subject to the constraints of state boundaries, producing a more even area distribution (median 6826km^2, mean 6998km^2, range 1641 – 14677km^2). Maps show fitted values for 2019 from the spatial models of occurrence (A) and incidence-given-presence (B; with districts with no confirmed LF cases shown in white), which after model selection included the same random effects and very similar socio-ecological fixed effects to the LGA-level model (Figure 4.3). Model parameter estimates are provided in Extended Data Table 1.

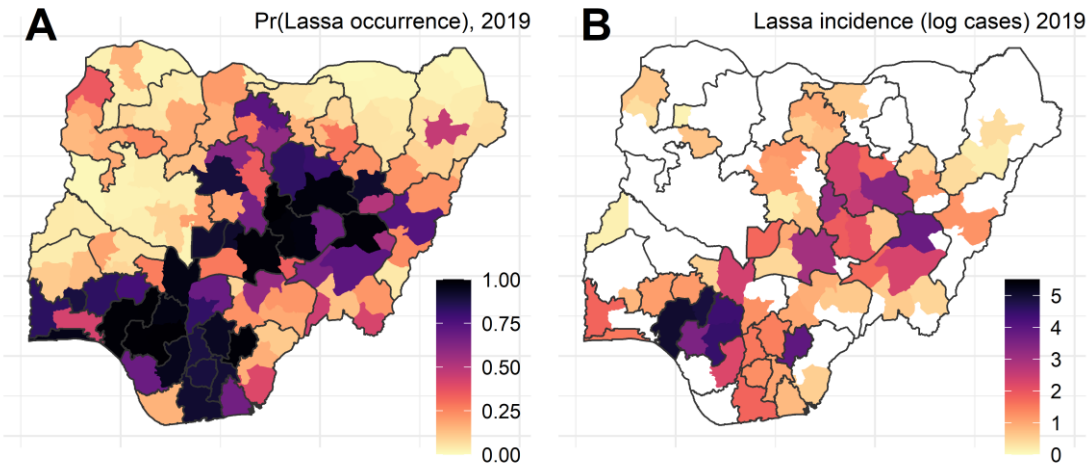

Figure S4.5: Seasonal and interannual climate and vegetation dynamics in Lassa-endemic regions of south and north Nigeria. Graphs show, for south (left column) and north (right column) Lassa-endemic areas, district-level weekly mean environmental (temperature, precipitation) and vegetation values across a 60-day window prior to reporting week (i.e. at time of transmission occurring). Lines and error-bars show the mean and range of weekly values, across all aggregated districts included in temporal models (5 per region). Temperature estimates are daily mean (Tmean; blue) and minimum (Tmin), derived from CPC interpolated air temperature layers from NOAA. Precipitation estimates are daily mean rainfall, derived from modelled daily rainfall layers from CHIRPS Africa. Vegetation estimates are daily mean Enhanced Vegetation Index (EVI), derived from processed and linearly interpolated 16-day interval EVI rasters from NASA. EVI values below a ~0.2 threshold (dotted line) indicate a lack of dense green vegetation.

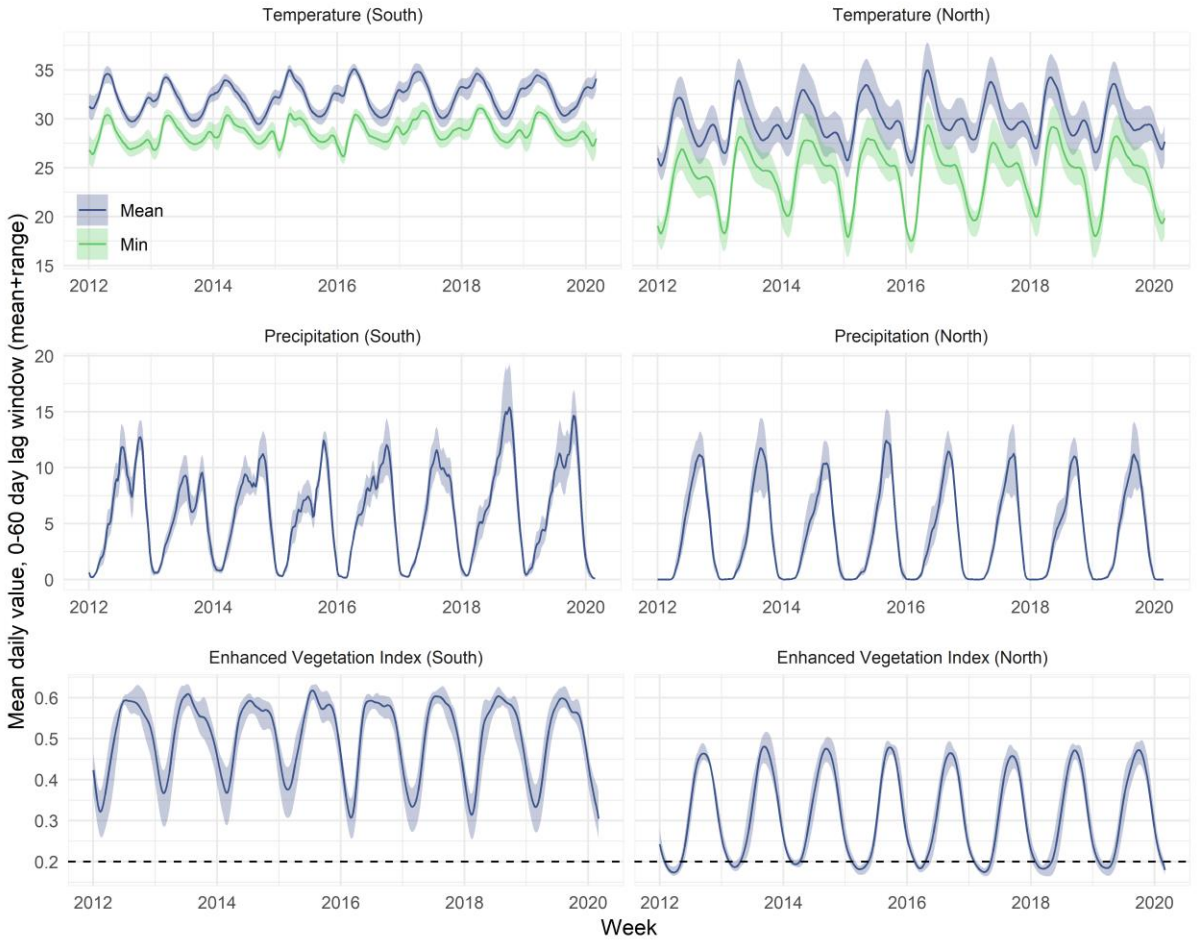

Figure S4.6: Observation-level out-of-sample trends and posterior predictive checks for temporal models of Lassa fever incidence. Trend graphs show, for each aggregated district included in models of the Southern (A) and Northern (B) endemic areas, the weekly observed confirmed LF cases (grey bars), out-of-sample posterior median and 95% credible interval (red line and ribbon), and OOS 67% and 95% simulated posterior predictive intervals (Methods). Plot names refer to the State, and local government authorities within the district in brackets. Blue barplots show the weekly predictive accuracy for the Southern (C) and Northern (D) models, shown as the proportion of weekly observations (5 per week) falling outside the 67% (top plot) and 95% (bottom plot) posterior predictive intervals (i.e. the proportion of observations predicted less successfully). Overall OOS predictive ability for the entire surveillance period was very good for both the Southern (92.6% of observations falling within the 67% predictive interval, and 98.3% within the 95% interval) and Northern models (95% of observations within 67% interval and 98.7% within the 95% interval).

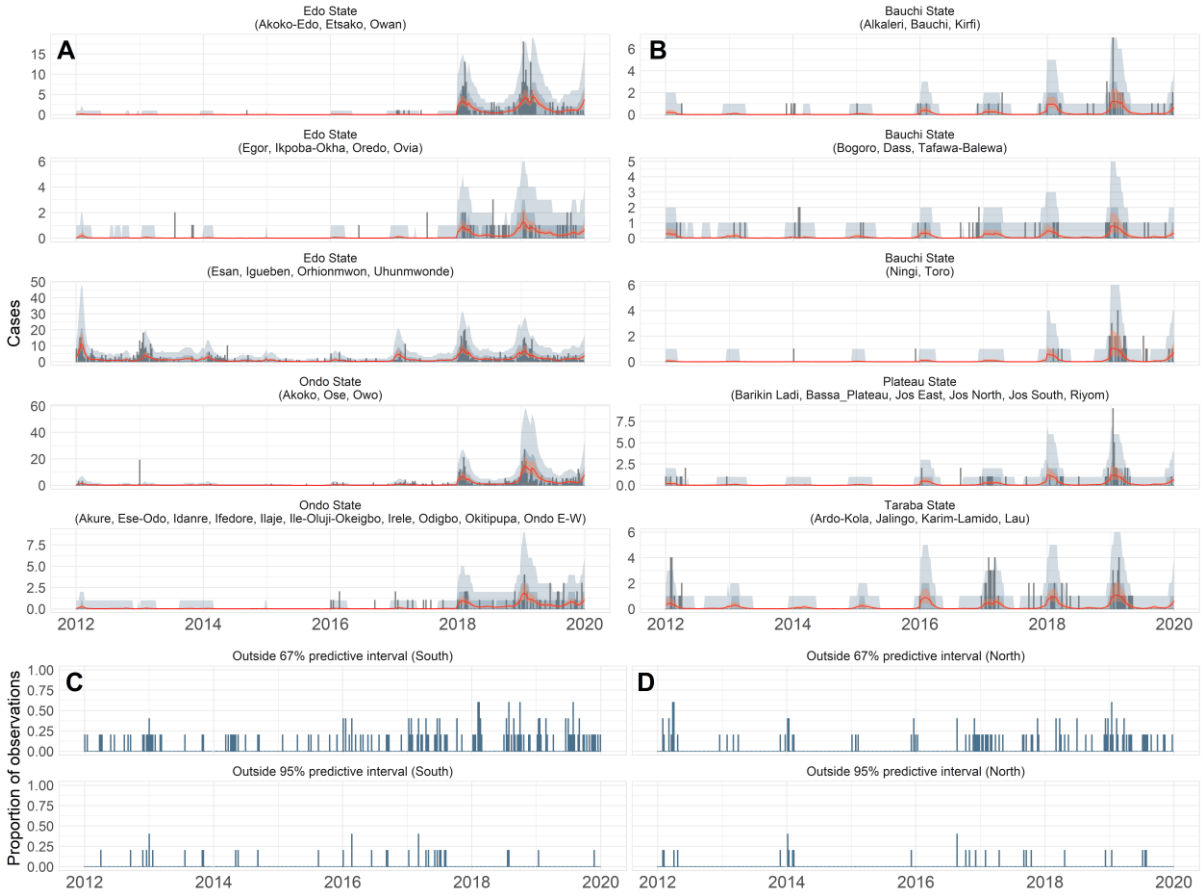

Figure S4.7: Out-of-sample predictions and 2020 forecasts for endemic States using lag-only environmental models. Trend graphs show, for each State included in temporal models, the weekly observed confirmed LF cases (grey bars), out-of-sample posterior median and 95% credible interval (red line and ribbon), OOS 67% and 95% simulated posterior predictive intervals, and preliminary weekly State-level case counts for 2020 (blue bars; not used to fit the models) (Methods). Predictions were made using separate southern (Edo, Ondo) and northern (Bauchi, Plateau, Taraba) forecast models that included lagged environmental effects to facilitate forecasting (i.e. only including covariates at >60-day lag; Methods), and 2020 predictions assume 2019 levels of reporting effort. Predicted dynamics are less regular than the full models (due to exclusion of 0-60 day vegetation and temperature effects) but forecast ability for 2012-2019 is very similar (South 91.7% of observations within 67% predictive interval, 98.1% within 95% interval; North 95.2% of observations within 67% predictive interval, 98.6% within 95% interval). Models are sufficient to capture the timing and relative peak height of different years, particularly in highest-incidence states, and to forecast the 2020 surge. One exception for 2020 is clear underprediction in Taraba State, which may be due to substantially increased State-level reporting effort in 2020(*Nigeria Centre for Disease Control, Lassa fever Situation Report, 12 April 2020*, 2020), and/or a mismatch between district-level predictions (which are only for the far north of the State; Figure 4.6) and State-level preliminary counts.

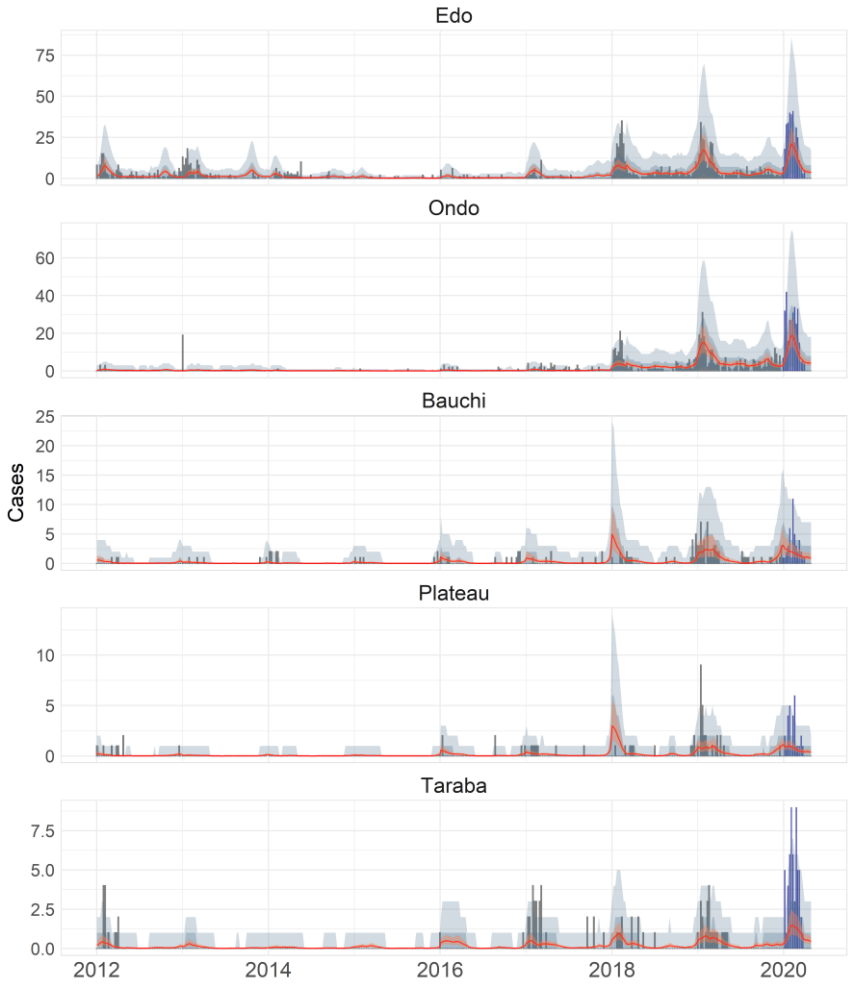

Table S4.1: Clinical definitions used for diagnosis of suspected and confirmed Lassa fever cases. Clinical definitions and criteria are listed in weekly Nigeria Centre for Disease Control Lassa fever Situation Reports(*Nigeria Centre for Disease Control, Lassa fever Situation Report, 12 April 2020*, 2020).

Term	Primary Criterion	Secondary Criterion
Alert case	Any person who has an unexplained fever (i.e. Malaria and other likely causes of fever have been ruled out), with or without bleeding OR Any person who died after an unexplained severe illness with fever and bleeding	
Suspected case	An illness of gradual onset with one or more of the following: malaise, fever, headache, sore throat, cough, nausea, vomiting, diarrhoea, myalgia (muscle pain), central chest pain or retrosternal pain, hearing loss and either:	**a.** History of contact with excreta or urine of rodents OR **b.** History of contact with a probable or confirmed Lassa fever case within a period of 21 days of onset of symptoms OR Any person with inexplicable bleeding/ haemorrhaging
Confirmed case	Any suspected case with laboratory confirmation (PCR, virus isolation).	
Deaths	Cases that die either as suspected or confirmed cases.	
Alert threshold	A single suspected case of Lassa fever.	
Outbreak threshold	A single confirmed case of Lassa fever. Clinicians should have a high index of suspicion when managing febrile illnesses; especially cases with:	a. A history of non-response to antimalarials or antibiotics. b. A compatible history of travel to an endemic area or an area with an ongoing outbreak, contact with a confirmed case of Lassa fever, negative thick blood film for malaria parasite are suggestive. c. Signs of haemorrhage and shock which is strongly suggestive, but these signs often appear late in the illness.

Table S4.2: Parameter estimates from the spatial models of Lassa fever occurrence and incidence. Tables show posterior marginal fixed effects parameter and hyperparameter estimates (median and 95% credible interval) from spatial models of annual Lassa fever occurrence and incidence-given-presence at local government authority level (occurrence n=774 LGAs over 4 years; incidence-given-presence n=161 LGAs over 4 years) and at aggregated district level (occurrence n=130 districts over 4 years; incidence-given-presence n=61 districts over 4 years). Occurrence was modelled using a binomial error distribution to estimates are on the log-odds scale, and incidence with a negative binomial (log link) so estimates are on the natural logarithmic scale. All non-logged covariates were scaled (mean 0, sd 1) prior to model fitting (Methods).

Spatial unit	Response variable	Num obs	Type	Parameter	Median	CI_0.025	CI_0.975
LGA	Occurrence	3096	fixed effect	Intercept	-3.770	-4.198	-3.394
			fixed effect	Reporting index (annual)	9.374	7.766	11.208
			fixed effect	Precip seasonality	-1.049	-1.616	-0.527
			fixed effect	Precip driest month	-0.717	-1.241	-0.253
			fixed effect	Built-up land proportion	0.327	0.074	0.577
			fixed effect	Agricultural land proportion	0.255	0.008	0.510
			fixed effect	Poverty prevalence	0.557	0.134	0.987
			fixed effect	Improved housing prevalence	0.374	0.103	0.652
			hyperparam	Precision for Year random walk (1/sd)	34.178	5.561	293.286
			hyperparam	Precision for State iid random intercept (1/sd)	1.338	0.680	2.563
			hyperparam	Precision for State-Reporting Index random slope (1/sd)	1.494	0.245	6.653
			hyperparam	Correlation coefficient for State random intercept and slope (rho)	-0.653	-0.926	-0.043
LGA	Incidence	644	fixed effect	Intercept	-12.356	-13.615	-11.070
			fixed effect	Distance from Lassa lab (log km)	-0.258	-0.499	-0.023
			fixed effect	Reporting index (annual)	4.907	3.845	5.918
			fixed effect	Poverty prevalence	0.366	0.119	0.614
			hyperparam	Size for negative binomial obs (1/overdispersion)	0.858	0.672	1.104
			hyperparam	Precision for Year random walk (1/sd)	22.457	4.410	123.719
			hyperparam	Precision for State iid random intercept (1/sd)	3.882	1.692	8.974
			hyperparam	Precision for State-Reporting Index random slope (1/sd)	1.848	0.344	7.521
			hyperparam	Correlation coefficient for State random intercept and slope (rho)	0.218	-0.535	0.757
District	Occurrence	520	fixed effect	Intercept	-2.539	-3.098	-2.047
			fixed effect	Reporting index (annual)	6.184	4.470	8.027
			fixed effect	Precip seasonality	-0.645	-1.258	-0.097
			fixed effect	Agricultural land proportion	0.450	0.024	0.914
			fixed effect	Improved housing prevalence	0.370	0.011	0.750

			hyperparam	Precision for State iid random intercept (1/sd)	1.664	0.653	4.540
			hyperparam	Precision for State-Reporting Index random slope (1/sd)	1.605	0.313	7.794
			hyperparam	Correlation coefficient for State random intercept and slope (rho)	0.646	-0.015	0.912
District	Incidence	244	fixed effect	Intercept	-13.155	-15.453	-10.908
			fixed effect	Distance from Lassa lab (log km)	-0.317	-0.715	0.088
			fixed effect	Reporting index (annual)	2.801	1.604	3.884
			fixed effect	Poverty prevalence	0.520	0.193	0.837
			hyperparam	Size for negative binomial obs (1/overdispersion)	1.258	0.886	1.800
			hyperparam	Precision for State iid random intercept (1/sd)	1.597	0.752	3.523
			hyperparam	Precision for State-Reporting Index random slope (1/sd)	1.076	0.268	3.939
			hyperparam	Correlation coefficient for State random intercept and slope (rho)	0.655	-0.045	0.896

Table S4.3: Parameter estimates from the temporal models of Lassa fever incidence in endemic areas. Tables show posterior marginal fixed effects parameter and hyperparameter estimates (median and 95% credible interval) from spatiotemporal models of Lassa fever incidence at district level (South and North, for full models and forecast models that included only environment at >60 day lag). Weekly case counts (n=2090 per model) were modelled using a negative binomial error distribution (log-link) so estimates are on the natural logarithmic scale, and all non-logged covariates were scaled (mean 0, sd 1) prior to model fitting (Methods).

Region	Model	Parameter	Type	Median	CI_0.025	CI_0.975
South	Full	Intercept	fixed effect	-14.005	-17.456	-10.025
		Distance from Lassa lab (log km)	fixed effect	-0.775	-1.367	-0.184
		Reporting index (annual)	fixed effect	2.629	-0.995	5.066
		Precip mean daily (120-180 day lag)	fixed effect	-0.441	-0.667	-0.218
		Precip mean daily (90-150 day lag)	fixed effect	0.749	0.455	1.046
		Precip mean daily (60-120 day lag)	fixed effect	-0.262	-0.496	-0.028
		EVI mean daily (0-60 day lag)	fixed effect	-0.632	-0.797	-0.469
		Size for negative binomial obs (1/overdispersion)	hyperparam	1.135	0.903	1.435
		Precision for Year random walk (1/sd)	hyperparam	2.486	0.973	6.3
		Precision for District iid random intercept (1/sd)	hyperparam	0.234	0.05	1.07
		Precision for District-Reporting Index iid random slope (1/sd)	hyperparam	0.274	0.057	1.279
		Correlation coefficient for District random intercept and slope (rho)	hyperparam	-0.944	-0.992	-0.665
South	Forecast	Intercept	fixed effect	-14.549	-18.041	-10.529
		Distance from Lassa lab (log km)	fixed effect	-0.658	-1.275	-0.047
		Reporting index (annual)	fixed effect	2.814	-0.845	5.198
		Precip mean daily (120-180 day lag)	fixed effect	-0.052	-0.26	0.154
		Precip mean daily (90-150 day lag)	fixed effect	0.975	0.677	1.278
		Precip mean daily (60-120 day lag)	fixed effect	-0.808	-1.004	-0.613
		Size for negative binomial obs (1/overdispersion)	hyperparam	0.977	0.787	1.22
		Precision for District iid random intercept (1/sd)	hyperparam	0.261	0.052	1.308
		Precision for District-Reporting Index iid random slope (1/sd)	hyperparam	0.305	0.059	1.573
		Correlation coefficient for District random intercept and slope (rho)	hyperparam	-0.922	-0.989	-0.529
		Precision for Year random walk (1/sd)	hyperparam	2.399	0.944	6.007
North	Full	Intercept	fixed effect	-17.537	-18.839	-16.289
		Reporting index (annual)	fixed effect	1.852	-0.358	4.173
		Precip mean daily (90-150 day lag)	fixed effect	0.411	0.167	0.658
		Tmean mean daily (120-180 day lag)	fixed effect	0.641	0.223	1.081
		Tmin mean daily (0-60 day lag)	fixed effect	-0.464	-0.7	-0.234
		EVI mean daily (0-60 day lag)	fixed effect	-1.177	-1.58	-0.789

		Size for negative binomial obs (1/overdispersion)	hyperparam	1.274	0.728	2.423
		Precision for District iid random intercept (1/sd)	hyperparam	0.787	0.221	2.448
		Precision for District-Reporting Index iid random slope (1/sd)	hyperparam	0.501	0.094	2.364
		Correlation coefficient for District random intercept and slope (rho)	hyperparam	-0.819	-0.964	-0.339
		Precision for Year random walk (1/sd)	hyperparam	6.538	1.92	26.272
North	Forecast	Intercept	fixed effect	-17.335	-18.642	-16.087
		Reporting index (annual)	fixed effect	1.498	-0.716	3.767
		Precip mean daily (90-150 day lag)	fixed effect	1.59	1.3	1.898
		Precip mean daily (60-120 day lag)	fixed effect	-1.503	-1.891	-1.133
		Tmean mean daily (120-180 day lag)	fixed effect	0.431	0.112	0.756
		Tmin mean daily (60-120 day lag)	fixed effect	-0.567	-0.823	-0.327
		Size for negative binomial obs (1/overdispersion)	hyperparam	0.879	0.547	1.487
		Precision for District iid random intercept (1/sd)	hyperparam	0.792	0.218	2.52
		Precision for District-Reporting Index iid random slope (1/sd)	hyperparam	0.556	0.101	2.66
		Correlation coefficient for District random intercept and slope (rho)	hyperparam	-0.842	-0.969	-0.396
		Precision for Year random walk (1/sd)	hyperparam	5.519	1.717	20.027

Table S4.4: Lassa fever-endemic districts included in the temporal models. The table shows the name and state of each spatially aggregated district included in temporal incidence models, the local government authorities (LGAs) within each district and the total number of confirmed cases detected across all years of surveillance. Cases from 2012-2016 are from the Weekly Epidemiological Reports regime, and from 2017-2018 are from the NCDC Situation Reports surveillance regime.

District	State	LGAs	Cases total (2012-2019)	Cases 2017-2019
South_1	Edo	Akoko-Edo, Etsako Central, Etsako East, Etsako West, Owan East, Owan West	215	208
South_2	Edo	Egor, Ikpoba-Okha, Oredo, Ovia North East, Ovia South West	49	42
South_3	Edo	Esan Central, Esan North East, Esan South East, Esan West, Igueben, Orhionmwon, Uhunmwonde	722	340
South_4	Ondo	Akoko North East, Akoko North West, Akoko South East, Akoko South West, Ose, Owo	456	386
South_5	Ondo	Akure North, Akure South, Ese-Odo, Idanre, Ifedore, Ilaje, Ile-Oluji-Okeigbo, Irele, Odigbo, Okitipupa, Ondo East, Ondo West	65	51
North_1	Plateau	Barikin Ladi, Bassa_Plateau, Jos East, Jos North, Jos South, Riyom	59	38
North_2	Taraba	Ardo-Kola, Jalingo, Karim-Lamido, Lau	76	34
North_3	Bauchi	Alkaleri, Bauchi, Kirfi	48	33
North_4	Bauchi	Bogoro, Dass, Tafawa-Balewa	40	16
North_5	Bauchi	Ningi, Toro	32	30

Table S4.5: Data sources for all covariates included in analyses. The table includes the sources and rationale (hypothesis) for inclusion of covariates in spatial and spatiotemporal models of Lassa fever incidence across Nigeria. Modelling is described in full in Methods.

Covariate	Type	Units	Time period	Rationale	Data source	Model
Mean distance from laboratory with LF diagnostic capacity (log-transformed)	continuous	km	Annual	Lassa fever detections were historically geographically biased towards areas near to diagnostic laboratories (e.g. Irrua Specialist Teaching Hospital; Gibb et al 2017)	Derived from diagnostic laboratory locations (via NCDC)	Spatial, temporal
Mean distance to nearest hospital (log-transformed)	continuous	km	2015	Proxy for public access to larger/regional healthcare facilities with links to state-level surveillance infrastructure	Maina *et al.*, 2019 (Maina et al., 2019)	Spatial
State ID	categorical	n/a	n/a	State-level differences in LF surveillance and awareness may influence sensitivity of reporting	n/a	Spatial
Air temperature (annual mean and seasonality)	continuous	degrees C	2011-2019, annual	Temperature may affect the environmental suitability for *M. natalensis* and/or viral transmission (e.g. through affecting persistence in the environment).	Derived from daily temperature averages from NOAA CPC Precipitation https://www.esrl.noaa.gov/psd/data/gridded/data.cpc.globaltemp.html	Spatial
Precipitation (mean wettest month, mean driest month)	continuous	mm	2011-19, annual	Evidence of links between *M. natalensis* population ecology and rainfall seasonality, and past evidence that human LF is linked to areas of high rainfall (Gibb et al., 2017)	Derived from daily Africa precipitation rasters from CHIRPS (Climate Hazards Infrared Precipitation with Stations) (Funk et al., 2015)	Spatial
Precipitation annual seasonality (coefficient of variation)	continuous	mm	2011-19, monthly	Evidence of links between *M. natalensis* population ecology and rainfall seasonality, and past evidence that human LF is linked to areas of high rainfall (Gibb et al., 2017)	Derived from daily Africa precipitation rasters from CHIRPS (Funk et al., 2015)	Spatial

Mean precipitation in 60-day window (starting 0, 30, 60, 90, 120 day lag prior to reporting week)	continuous	mm	2011-20, weekly	Evidence that *M. natalensis* population densities and patterns of human exposure may be linked to rainfall patterns (Gibb et al., 2017)	Derived from smoothed daily Africa precipitation rasters from CHIRPS (Funk et al., 2015)	Temporal
Mean, min and max air temperature in 60-day window (starting 0, 30, 60, 90, 120 day lag prior to reporting week)	continuous	degrees C	2011-20, weekly	*M. natalensis* population densities, viral persistence and patterns of human exposure may be linked to climatic patterns (Gibb et al., 2017)	Derived from smoothed daily Tmin and Tmax temperature layers from NOAA	Temporal
Mean EVI in 60-day window (starting 0, 30, 60, 90, 120 day lag prior to reporting week)	continuous	EVI	2011-20, weekly	Evidence that *M. natalensis* population densities and patterns of human exposure may be linked to climatically-driven vegetation dynamics (i.e. due to seasonal resource availability) (Gibb et al., 2017)	Derived from processed and smoothed 16-day EVI layers from NASA	Temporal
Urban land cover	continuous	proportion district area	2015	May impact both *M. natalensis* densities (which are often lower in highly urbanised environments) and human access to healthcare facilitites (i.e. detection probability)	ESA-CCI Land Cover 2015 300m raster (data for a single year as low change in proportion cover during surveillance period) https://www.esa-landcover-cci.org	Spatial
Agricultural land cover	continuous	proportion district area	2015	*M. natalensis* densities often observed to be highest in agricultural settings (Fichet-Calvet et al., 2007; Massawe et al., 2007) and cropping and crop preparation practices are a hypothesised driver of human-rodent contact (Gibb et al., 2017)	ESA-CCI Land Cover 2015 (data for a single year as relatively low change in proportion cover during surveillance period) https://www.esa-landcover-cci.org/	Spatial
Total human population (log transformed)	continuous	number of people	2012-2020, annual	Controlling for effects of increased human population on potential for LASV exposure.	WorldPop	Spatial, temporal

Proportion of LGA population living in poverty (<$1.25 per day)	continuous	proportion district population	2010	Evidence that human LASV exposure may often be linked to ability to store food in rodent-proof containers and ability to rodent-proof housing (Bonwitt et al., 2017b; Mari Saez et al., 2018)	WorldPop	Spatial
Proportion of population in locales with improved housing	continuous	proportion district population	2015	Evidence that human LASV exposure may be linked to ability to rodent-proof housing (Mari Saez et al., 2018)	Derived from Malaria Atlas Project modelled data on prevalence of improved housing(Tusting et al., 2019) (5km^2 resolution) and human population layers (WorldPop)	Spatial

Appendix 3:

Supplementary figures and data for Chapter 5.

This appendix provides supplementary figures, tables and information on data sources for the analyses conducted in Chapter 5, *'The nexus of future agricultural and socioeconomic change and Lassa fever risk in West Africa'.* The items contained in this appendix are:

Figure S5.1: Projected future land cover-land use trends in West Africa from the Global Biosphere Management Model. Lines show regional aggregate projected changes in total area (thousands km^2) of 5 LCLU classes from 2010 to 2070, simulated using GLOBIOM under the socioeconomic and climatic assumptions of 3 SSP-RCP scenarios (denoted by line colour). An example of spatially-downscaled projections of these regional totals is shown in Figure S5.2.

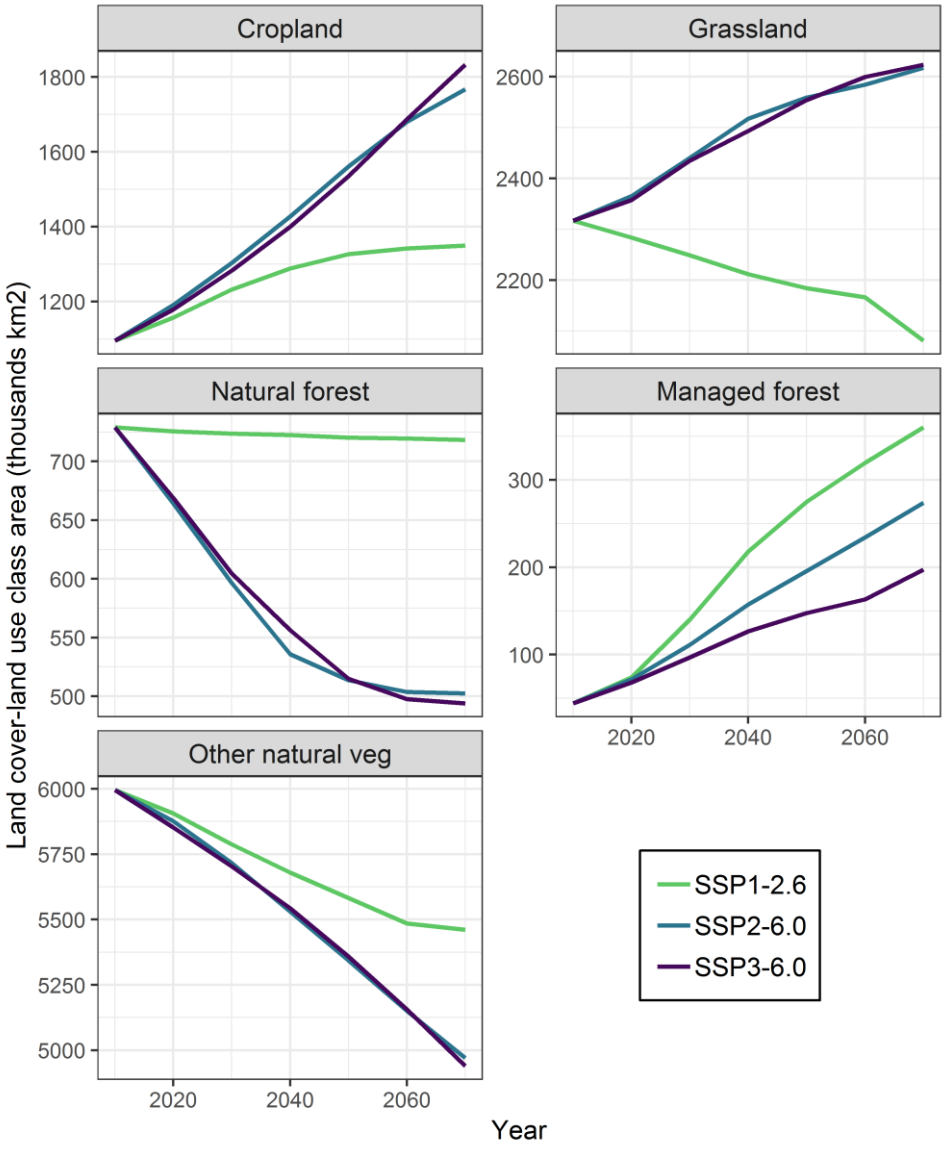

Figure S5.2: Spatially-explicit projections of land cover-land use change from 2010 to 2050 under SSP2-RCP6.0. Maps show spatially-downscaled regional LCLU aggregate totals from GLOBIOM (Supp. Figure 1) projected at 5 arc-minutes using a Bayesian econometric downscaling model from a baseline of year 2000. Columns show proportion cover per 5 arc-minute grid cell for 5 LCLU types in 2010 (A), and mean proportion change in cover of each LCLU type from 2010 to 2050 under SSP2-6.0 (B) across 100 spatial allocations of future land change (see Methods). In this scenario, large-scale losses of natural forest and other natural vegetation to cropland are projected for Liberia, Benin, Mali, Guinea, and Nigeria, while expansion of managed (timber) forests and cropland losses are projected for southern Ghana, Sierra Leone, and Cote d'Ivoire.

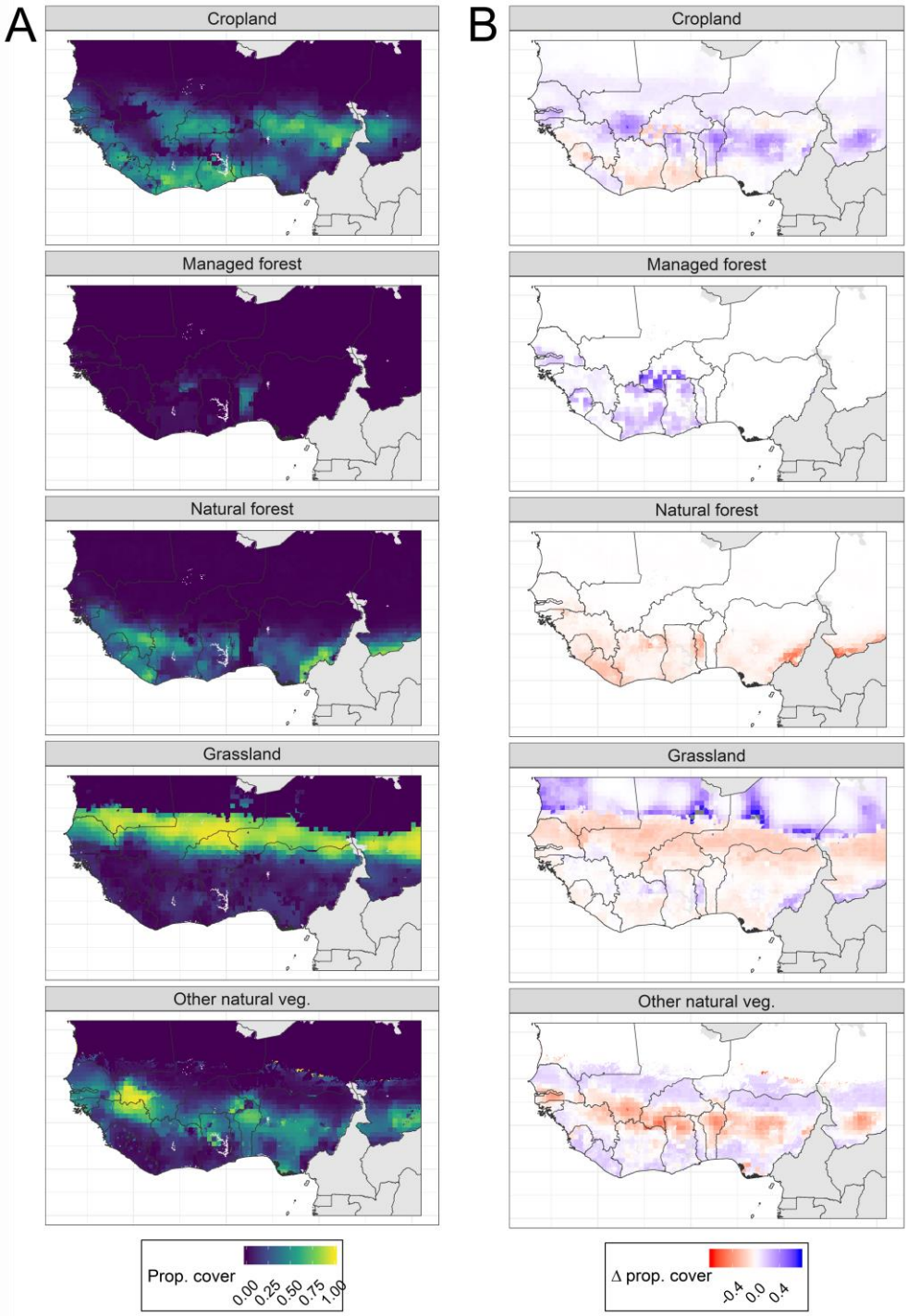

Figure S5.3: Model structure and parameter estimation for West African *Mastomys natalensis* occurrence and abundance (ecological hazard) model. Bioclimatic suitability for the reservoir host (*c*) was estimated from an ensemble of thresholded niche models (A; map colour scale shows the proportion of 75 models that predict suitability in present-day) fitted to occurrence points from GBIF and literature (overlaid on A; n=239 points). Land-cover-land-use effects on relative rodent density (*R*) were estimated using a Bayesian meta-analytic model of local abundance and density estimates (B; n=125 from 17 studies; points and error bars show fitted posterior mean and 95% credible interval). LCLU parameter estimates were robust to cross-validation at level of biome (not shown) and study (C; random 8fold). Coloured points show posterior means from 8 fitted models, each randomly excluding 1/8 of studies. Crosses and error bars show mean and s.e.m calculated across all posterior means.

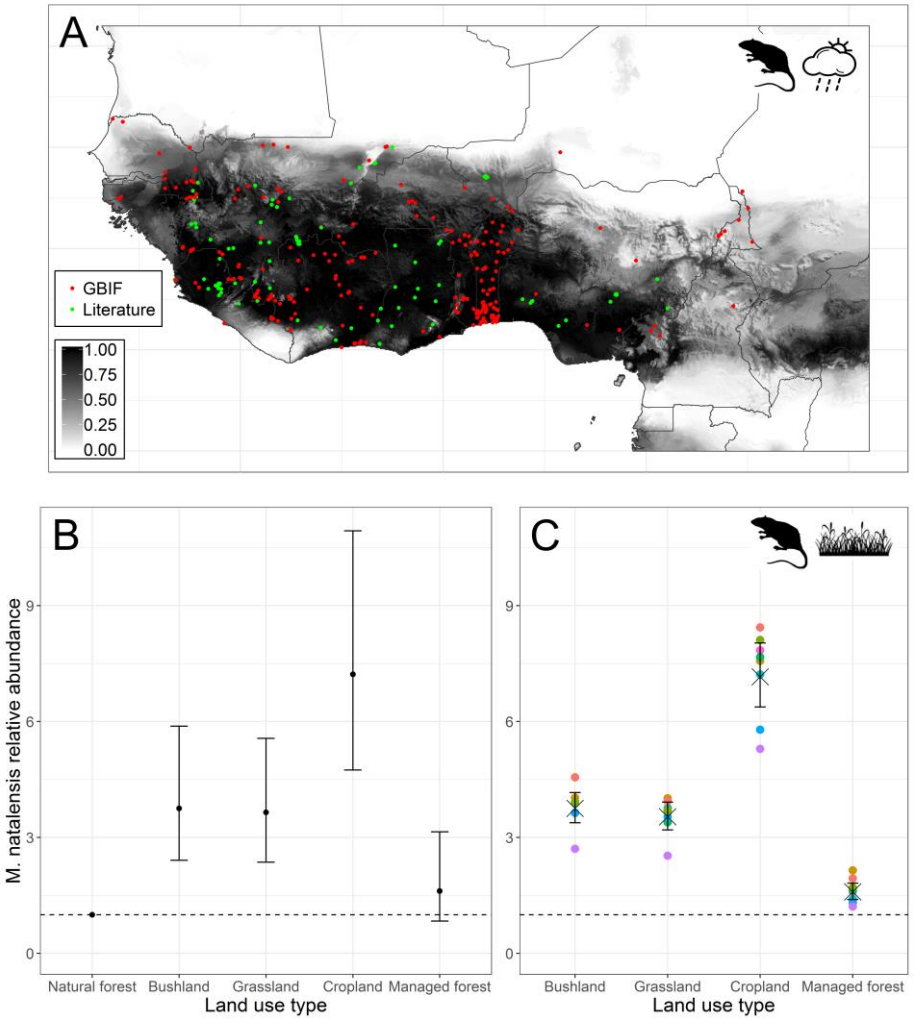

Figure S5.4: Predictive performance of hazard-exposure model of LASV transmission risk under present-day conditions. I compared performance of different risk model specifications by extracting modelled risk (λ_i) from known locations and districts of human LASV exposure (A; see Methods). Mean risk λ_i was calculated as the mean across 1000 random combinations of LCLU and climate parameters, i.e. incorporating parametric uncertainty in disease model. Risk was compared (B) between LF exposure locations (dark green boxplots) and 500 background points across climatically suitable West Africa (light green boxplots) for the full model shown in A (LU+Clim), and for models assuming risk is driven solely by human population (EnvNull), solely by climate effects on rodents (Clim) and solely by land use effects on rodents (LU). I calculated per-grid cell relative uncertainty in λ_i (RU = st.dev / sqrt(mean), i.e. large values indicate large variance relative to mean, across 1000 parameter combinations) to visualise effects of parametric uncertainty on spatial risk projections (C), which is highest in northern Nigeria, likely as a consequence of sparse rodent sampling.

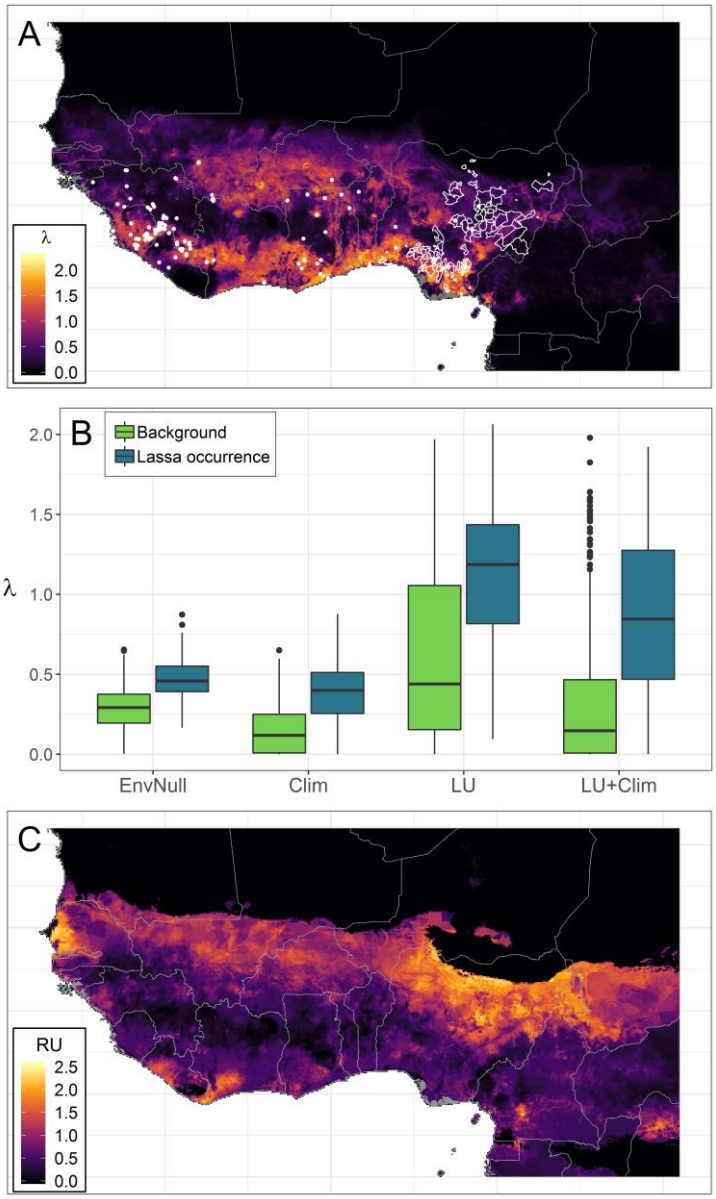

Figure S5.5: Per-country predictive performance of Lassa fever model under present-day conditions. Boxplots show per-country comparison of predicted risk at LF locations and background points within LF-endemic countries (Nigeria, SL, Liberia, Guinea) and countries with sporadic acute LF cases and documented population exposure (Ghana, Mali, Benin, Burkina Faso, Togo). Comparisons were conducted using the same procedure as in (Figure S5.4). Results indicate that LCLU is particularly useful at discriminating risk in endemic countries that are consistently climatically suitable (Sierra Leone, Guinea), and that countries with higher variability in climatic suitability the combination of both appears to be discriminatory (e.g. Liberia, Mali, Burkina Faso). The model appears to perform less well in Nigeria, which may be due to higher model uncertainty in predictions in this country (Figure S5.4c) and/or discrepancies in systematic surveillance effort across areas broadly predicted to be suitable (see Chapter 4).

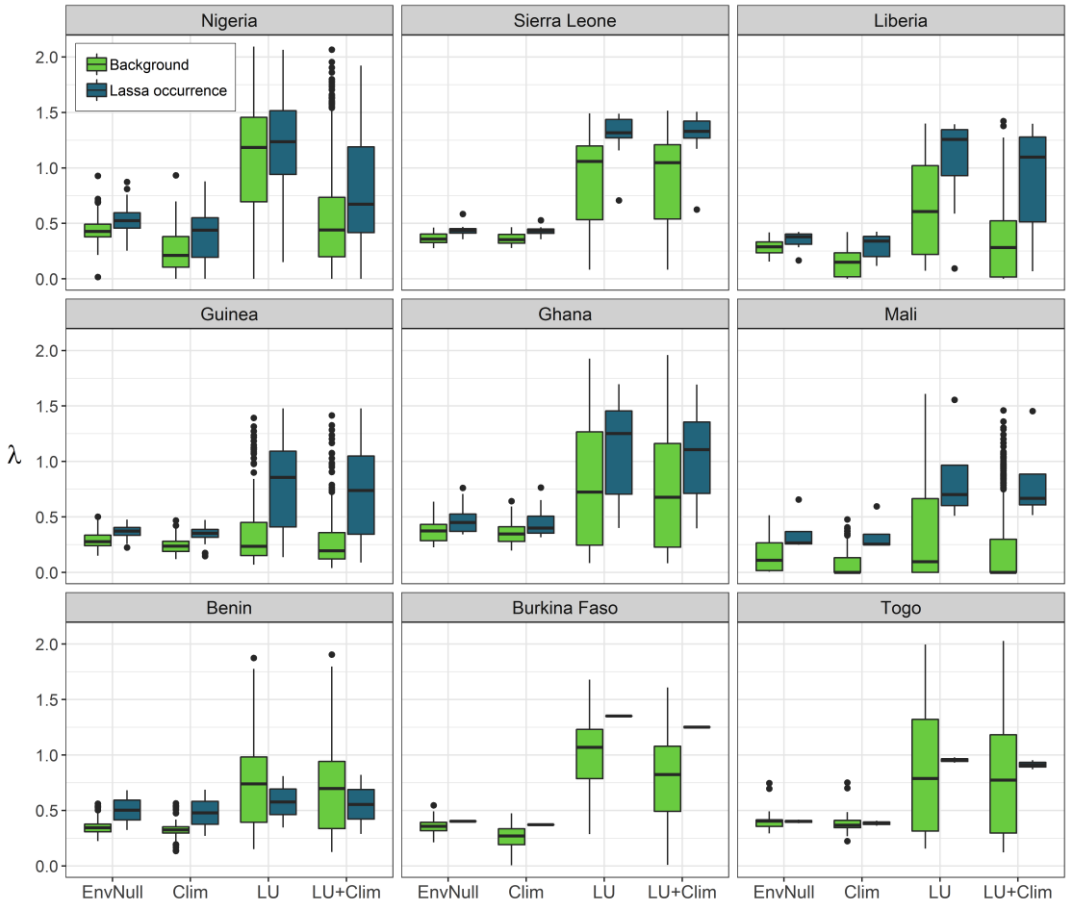

Figure S5.6: Country-level projected trends in mean LF risk across future SSP-RCP scenarios. Connected points and error bars show percentage change in mean LF risk (λ) across all grid cells within each country, from a 2010 baseline to 2030, 2050 and 2070. Points and errorbars show mean, 5th and 95th percentiles, calculated across all 400 combinations of potential climate and land use per-scenario (4 climate models x 100 LCLU allocations; i.e. uncertainty related to future environmental change). Colour denotes SSP-RCP scenario pathway. Changes are shown for LF-endemic (Nigeria, Sierra Leone, Liberia, Guinea) and sporadically endemic countries (Mali, Burkina Faso, Benin, Ghana), with Nigeria partitioned into north and south due to its large size and agro-ecological diversity. The effects of different social and environmental drivers on these overall changes are shown in Figure 5.3.

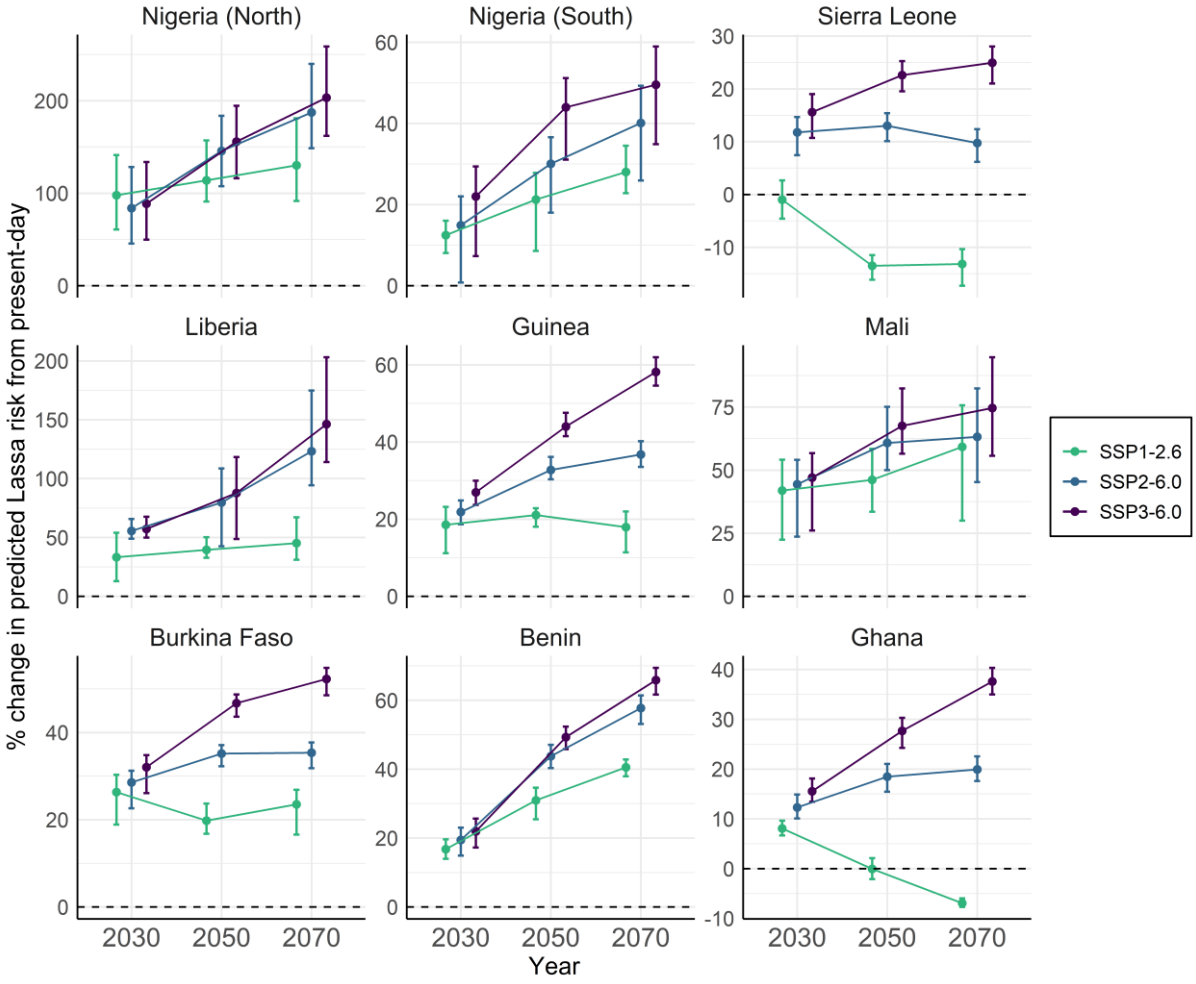

Table S5.1: List of all data sources. The table describes and provides sources for all the datasets used in this study. All code and data, where not freely available online, are provided in the accompanying Figshare repository.

Data type	Time era	Spatial resolution (original)	Description of data	Source	Reference / url
Reservoir host occurrence	1990-2018	n/a	Geolocated occurrence points for *Mastomys natalensis*, collated from Global Biodiversity Information Facility and the published literature, and filtered for taxonomic and spatial accuracy (n=239).	Global Biodiversity Information Facility and published literature.	
Reservoir host abundance	1975-2018	n/a	Local abundance and density estimates for *Mastomys natalensis* across sampled land-cover-land-use gradients across sub-Saharan Africa (17 studies, 125 estimates).	Published literature (Supp. Table 2).	
Lassa virus exposure and acute case locations	1990-2019	n/a	Geolocated records of human exposure to Lassa virus (either acute disease or seroprevalence) collated from published literature, ProMed and surveillance reports.	Gibb et al, 2017 (supplemented to 2019)	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5694855/
Lassa fever incidence	2016-2018	District level	Annual counts of acute Lassa fever cases across Nigeria, for years 2016 to 2018.	Nigeria Centre for Disease Control (Situation Reports)	https://ncdc.gov.ng/diseases/sitreps
Bioclimatic variables	Present (1979-2013)	0.0083 degrees	Gridded present-day bioclimatic variables: bio01 annual mean temperature, bio04 temperature seasonality, bio08 mean temperature of the wettest quarter, bio09 mean temperature of the driest quarter, bio12 annual total precipitation, bio15 precipitation seasonality, bio16 mean precipitation of the wettest quarter, bio17 mean precipitation of the driest quarter.	CHELSA (Climatologies at High Resolution for the Earth's Land Surface Areas)	http://chelsa-climate.org/
	2030 (2021-2040)	0.041 degrees	Gridded bioclimatic variables derived across years 2021-2040, and spatially-projected using CHELSA as present-day baseline climate. Climates calculated separately for each of four bias-corrected GCMs (GFDL-ESM2M, HADGEM2-ES, IPSL-CM5A-LR , MIROC5) and for RCPs 2.6 and 6.0. See full description of processing in Methods.	ISIMIP (Inter-Sectoral Model Intercomparison Project) database of annual, bias-corrected GCM projections.	https://esg.pik-potsdam.de/projects/isimip/
	2050 (2041-2060)	0.041 degrees	As above but for years 2041-2060.	ISIMIP (Inter-Sectoral Model Intercomparison Project) database of annual, bias-corrected GCM projections.	https://esg.pik-potsdam.de/projects/isimip/

Land-cover land-use (remotely-sensed; ESA-CCI)	Present (2010)		Land-cover land-use for 2010 (present-day baseline) from the European Space Agency Climate Change Initiative (ESA-CCI) land cover data product. Native LCLU classes reclassified into broad type classifications (see Methods).	ESA-CCI Land Cover	https://www.esa-landcover-cci.org/
Land-cover land-use (modelled)	Decadal from 2010 to 2070	0.083 degrees	Per-grid cell decadal projections of proportion cover of 7 LCLU types (cropland, grassland, other natural vegetation, managed forest, short rotation plantations, natural forest, built-up) using 2010 ESA as baseline. Derived from spatially-downscaling total regional projections of LCLU change (from GLOBIOM) using Bayesian econometric model.	Global Biosphere Management Model (GLOBIOM)	
Human population density	Present (2010)	0.041 degrees	Gridded human density estimates from CIESIN for the year 2010.	CIESIN Gridded Population of the World v4	https://sedac.ciesin.columbia.edu/data/collection/gpw-v4
	Future (2030, 2050, 2070)	0.083 degrees	Gridded human density estimates from SSPs database, spatially-downscaled for each SSP scenario.	Jones and O'Neill et al, 2016.	https://iopscience.iop.org/article/10.1088/1748-9326/11/8/084003/meta

Table S5.2: Data sources for *Mastomys natalensis* relative abundance database. Table lists published ecological surveys that contain data on abundance and/or density of *M. natalensis* across land use gradients, which were used in estimating rodent relative density parameters (Figure S5.3b-c).

Study	Country	Region	Survey year(s)	Land use types	Sites	Reference
Angelici2005	Nigeria	Edo State	1996-2001	Natural forest, Cropland, Bushland, Village	6	(Angelici and Luiselli, 2005)
Bantihum2015	Ethiopia	Awi, Ankara, Northwest Ethiopia	2011	Natural forest, Bushland, Grassland, Cropland	4	(Bantihun and Bekele, 2015)
Chekol2012	Ethiopia	Beshangul Gumuz Regional State	2012	Natural forest, Managed forest, Bushland, Grassland, Cropland	5	(Chekol et al., 2012)
Dakito2014	Ethiopia	Chebera Churchura National Park	2010-2011	Natural forest, Grassland, Bushland, Cropland	7	(Datiko and Bekele, 2014)
Dakito2007	Ethiopia	Nechisar National Park	2005-2006	Natural forest, Bushland, Cropland	6	(Datiko et al., 2007)
Gbogbo2017	Ghana	Accra	2014	Village, Cropland, Bushland	3	(Gbogbo et al., 2017)
Gryseels2016	Tanzania	Morogoro	2012	Cropland, Bushland, Grassland, Natural forest	12	(Gryseels et al., 2017)
Happold1975	Nigeria	Southwest	1967	Natural forest, Grassland, Bushland	23	(Happold, 1975)
Iyawe1988	Nigeria	Southwest Benin	1984-1985	Natural forest, Bushland, Cropland, Plantation forest	4	(Iyawe, 1988)
Jeffrey1977	Ghana	Western	1970	Managed forest, Bushland, Cropland, Village, Natural forest	8	(Jeffrey, 1977)
Macaulay2015	Tanzania	Northern Tanzania (forest/agriculture boundary)	2011	Natural forest, Cropland	6	(McCauley et al., 2015)
Mohammed2017	Ethiopia	Afar State, near Dubti Town	2013	Cropland, Bushland	4	(Mohammed et al., 2017)
Yeboah1984	Ghana	Eastern	1981-1982	Cropland, Natural forest	2	(Yeboah, 1984)
Konecny2009	Senegal	Southern Sudano-Sahelian	2005-2007	Grassland, Cropland	4	(Konecny et al., 2009)
Ryan2000	Ghana	Coastal southern Ghana	1997	Bushland, Grassland, Plantation forest	5	(Ryan and Attuquayefio, 2000)
Marien2018	Guinea	Faranah	2015	Village, Cropland, Bushland, Grassland	2	(Mariën et al., 2018)
Makundi2007	Tanzania	Central	2001	Cropland, Managed forest	4	(Makundi et al., 2007)

Appendix 4:

Typeset publications based on thesis work.

1. Gibb R., Redding D.W., Chin K.Q., Donnelly, C.A., Blackburn T.M., Newbold T., Jones K.E. (2020). Zoonotic host diversity increases in human-dominated ecosystems. *Nature* 584, 398-402. https://www.nature.com/articles/s41586-020-2562-8
2. Gibb R., Franklinos L.H.V., Redding D.W., Jones K.E. (2020). Ecosystem perspectives are needed to manage zoonotic disease risks in a changing climate. *BM*J 371 m3389. https://www.bmj.com/content/371/bmj.m3389.full
3. Gibb R., Moses L.M., Redding D.W., Jones K.E (2017). Understanding the cryptic nature of Lassa fever in West Africa. *Pathogens & Global Health* 111 (6) 276-288. https://doi.org/10.1080/20477724.2017.1369643
4. Gibb R., Redding D.W., Chin K.Q., Blackburn T.M., Newbold T., Jones K.E. (2018). Effects of land use on zoonotic host communities: a global correlative analysis. *Lancet Planetary Health* Meeting Abstracts, 2018 S2. http://dx.doi.org/10.1016/S2542-5196(18)30087-1