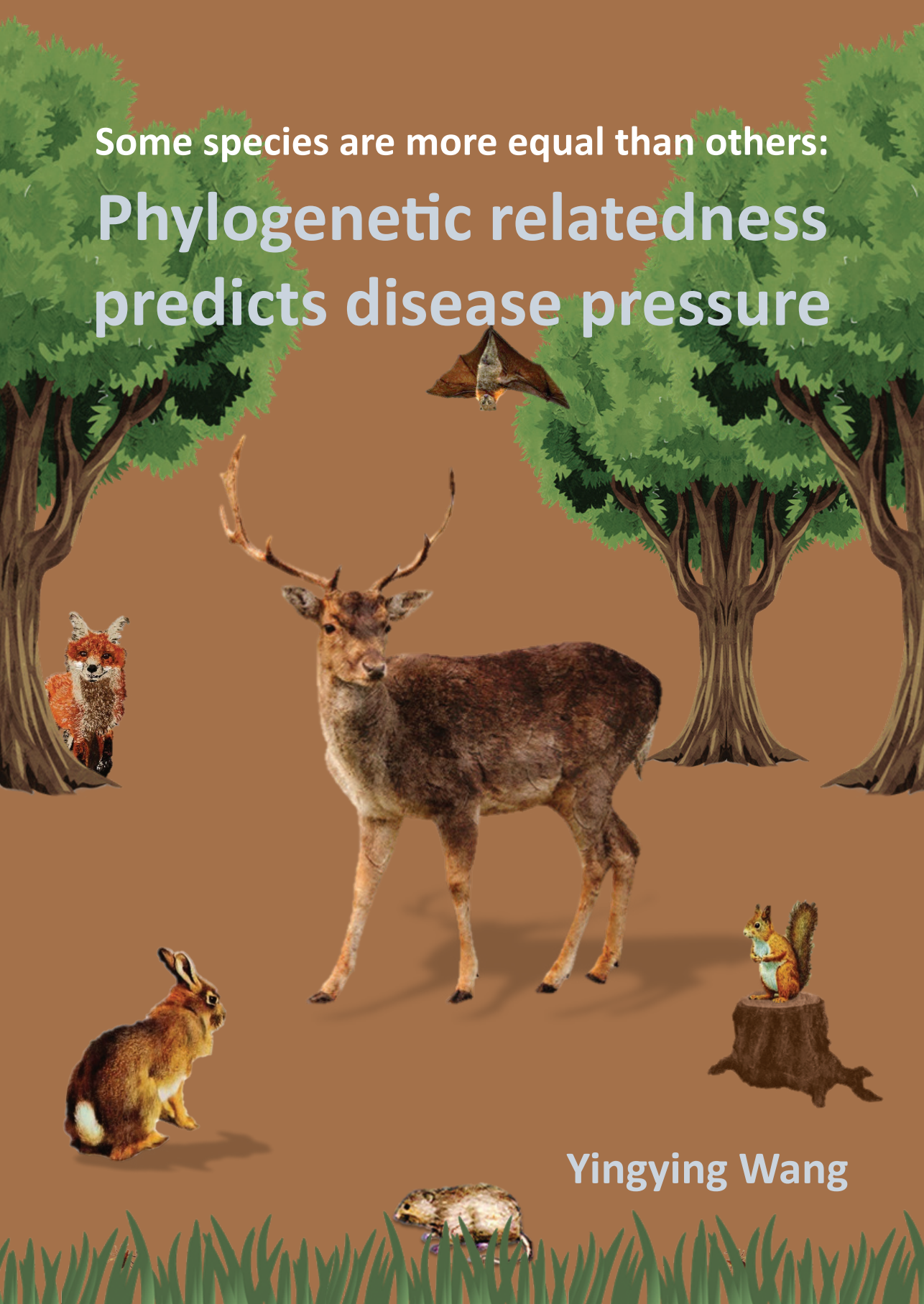
Some species are more equal than others:

Phylogenetic relatedness predicts disease pressure



Yingying Wang

Propositions

1. Phylogenetic relatedness of host assemblages is more important than species richness in influencing disease risk.
   (this thesis)

2. A constant species richness does not entail a constant disease risk.
   (this thesis)

3. In an outbred population, one is safer staying in close confines with a sick mother-in-law than with a sick mother.

4. Publicly reported databases are not trustable as the absence of a disease report is not evidence of the absence of that disease.

5. Transferring knowledge to people who need it is more important than producing knowledge.

6. The success of a PhD project is built on good supervisor management.

Propositions belonging to the thesis, entitled

Some species are more equal than others:
Phylogenetic relatedness predicts disease pressure

Yingying Wang

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Some species are more equal than others:

Phylogenetic relatedness predicts disease pressure

Yingying Wang

Thesis

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Contents

CHAPTER 1

General introduction

Human health and biodiversity

Infectious diseases remain one of the leading factors of human mortality, and there are around 17 million deaths per year because of infectious disease globally (WHO 2014). Infectious diseases continue to threaten human health and cause enormous economic losses (Fisher *et al.* 2013; Smith *et al.* 2014). For example, during the outbreak of Ebola in West Africa, 28,638 humans were infected, of which 11,316 died. The epidemic also caused around US$2.2 billion losses during the two-year period after the first reported death. Global emerging infectious disease events have increased significantly over the last decades (Jones *et al.* 2008). The increase in infectious disease risk has been mostly attributed to increasing external pressure (e.g., from human population growth, land use change, climate changes) on ecosystems. A clearer understanding of the mechanisms behind this increase in disease risk will be useful for disease prevention and management.

More than half of infectious diseases originate in animals, mostly wildlife (Wolfe *et al.* 2007). Examples include plague, rabies, brucellosis, and Lyme disease (Centre for Disease Control and Prevention). Lyme disease is caused by the spirochete *Borrelia burgdorferi* and can be transmitted by Ixodes scapularis ticks in the USA (Steere *et al.* 1978) and *Ixodes ricinus* ticks in Europe (Lindgren & Jaenson 2006). Lyme disease can spillover from wildlife (e.g., the white-footed mouse *Peromyscus leucopus*, the key reservoir host in the USA, and the bank vole *Myodes glareolus* and the wood mouse *Apodemus sylvaticus* in Europe) to humans when infected ticks feed on a human (Barbour *et al.* 1993). Like Lyme disease, many infectious diseases can be maintained and transmitted by multiple wildlife host species that vary in their competence to pathogens (Woolhouse *et al.* 2001; Jones *et al.* 2008). Biodiversity (e.g., the number of species and the wildlife assemblage composition) can influence the transmission of those diseases (Ostfeld & Keesing 2012) and can therefore affect the disease risk for humans. The direction of these so-called "disease-diversity relationships," however, is inconsistent in the literature; negative relationship (i.e., the dilution effect), positive relationship (i.e., the amplification effect), and an absence of a relationship have all been previously reported (Civitello *et al.* 2015; Huang *et al.* 2016; Ostfeld *et al.* 2018).

The dilution effect

A negative relationship between biodiversity and disease risk is called the dilution effect (LoGiudice *et al.* 2003; Keesing *et al.* 2006; Huang *et al.* 2013a, 2015; McCallum *et al.* 2015). The dilution effect is thought to work via several mechanisms, which generally involve changes in species richness (Keesing *et al.* 2006). Two example mechanisms are "encounter reduction" and "susceptible host regulation." Encounter reduction occurs when an increasing species richness leads to a decrease in the encounter rates between susceptible and infected individuals. For example, the new species can cause the home ranges of the established

species to contract. Susceptible host regulation occurs when an increasing species richness leads to a reduction in the density of susceptible species. This process can work via predator and prey interactions, for example (Hofmeester *et al.* 2017).

The dilution effect has been reported for many diseases. LoGiudice *et al.* (2003) showed that higher host species richness can decrease Lyme disease risk. Similarly, higher avian biodiversity reduced West Nile virus infection risk (Swaddle & Calos 2008). The dilution effect has also been detected in studies of hantaviruses (Clay *et al.* 2009; Suzán *et al.* 2009), Schistosomiasis (Johnson *et al.* 2009), and *Batrachochytrium dendrobatidis* and *Ribeiroia ondatrae* (Searle *et al.* 2011; Johnson *et al.* 2013). A recent meta-analysis by Civitello *et al.* (2015) that considered many types of parasites found support for lower disease risk in species-rich host communities.

The dilution effect debate

While evidence exists supporting the existence of a dilution effect, its generality is not without debate. This debate increased after publication of a study on Lyme disease by Allan *et al.* (2003). In the Lyme disease system, a tick vector and a spirochete microparasite (*Borrelia*) are generalists (Keirans *et al.* 1996) that are maintained by multiple vertebrate hosts (Barbour *et al.* 1993). Allan et al (2003) found a negative correlation between *Borrelia* infection prevalence in ticks and forest fragment size, and the authors hypothesised that this resulted from a reduction of species richness in the smaller fragments.

In the years since, many studies have argued that the dilution effect is not universal. In a meta-analysis by Salkeld *et al.* (2013), the dilution effect was not found to be general. A publication bias (i.e., one that resulted in the publication of more papers supporting the dilution effect) may have driven conclusions about the generality of the dilution effect (Salkeld *et al.* 2013). Wood *et al.* (2014) studied sixty-nine human parasites and concluded that the dilution occurred in only 12% of them. Even the most well-known dilution effect example, Lyme disease, exhibits some conflicting results. The dilution effect appears to operate for Lyme disease in North America (e.g., LoGiudice *et al.* 2008a; Keesing *et al.* 2009; Levi *et al.* 2016) but not in Europe (Hofmeester *et al.* 2016).

The generality of the dilution effect can also be complicated or even counteracted by other mechanisms related to other disease-diversity relationships (e.g., positive ones). In some cases, an “amplification effect” may be at work. With an amplification effect, increased disease risk is associated with increasing species richness, which may go hand-in-hand with a larger diversity of pathogens thereby facilitating disease risk (Wood *et al.* 2014).

Box 1 Glossary.

Biodiversity: the variety of plants and animals in an area. In many publications and the current work, biodiversity is used as shorthand for the diversity of mammal species in an area.
Alpha diversity: the local measure of biodiversity, e.g., the number of different species (species richness) in a local assemblage. In many publications also notated as "S" for species richness
Beta diversity: the similarity in diversity of species between assemblages.
Functional diversity: the range of functional traits in an assemblage of species (e.g., body mass of mammal species).
Phylogenetic diversity: a measure of biodiversity based on differences in evolutionary history among species.
Pathogens: organisms (e.g., bacteria and viruses) that live in or on other organisms (i.e., hosts) at the expense of the host organism, sometimes causing disease.
Species competence: the ability of a species to host and transmit pathogens.
Density-dependent transmission: transmission that is a function of the density of the host species.
Frequency-dependent transmission: transmission that is a function of the relative abundance of the host species.
Community R0: community-level basic reproduction ratio R0, which is the dominant eigenvalue of the next-generation matrix. Community R0 is calculated to determine the number of secondary cases resulting from an infection (Dobson 2004). A disease can enter and persist in the assemblage when community R0 >1 (Chen *et al.* 2015).
Total disease burden: the number of different diseases within a local assemblage of hosts, i.e., disease richness.
Disease risk: in the current work and in other published studies, defined variously as community R0, presence/absence of disease, total disease burden, number of cases of a certain disease, or geographic range of a certain disease, depending on the particular research question and analysis.
Dilution effect: a hypothesized negative relationship between species richness and disease risk.

What is driving the uncertainty surrounding disease-diversity relationships?

There are three requirements that need to be met for a dilution effect to occur (Keesing *et al.* 2006; Young *et al.* 2013; Huang *et al.* 2016). First, species competence to a pathogen should differ among host species. Second, species with a low competence and species that are incompetent reduce the overall pathogen transmission. Third, in relatively species-poor

assemblages, competent host species dominate the assemblage. The first requirement that species vary in competence is commonly accepted (Kilpatrick *et al.* 2006; Johnson *et al.* 2013; Huang *et al.* 2016), so it will not be discussed further here. The other two requirements, however,
are still debated (Joseph *et al.* 2013; Salkeld *et al.* 2013; Young *et al.* 2013). A range of issues add to the challenge of understanding the generality of these two requirements of the dilution effect. These complicating factors include the identity effect, the different ways to quantify disease risk (Huang *et al.* 2016), the scale of observation, and the different types of transmission.

The second requirement

That species with low competence reduce pathogen transmission is an important requirement of the dilution effect. This can happen, for example, through the two mechanisms described above (encounter reduction and susceptible host regulation; Keesing *et al.* 2006). However, this requirement is not always met in every situation. Sometimes species with low competence actually increase disease risk (or have no effect) as a result of the identity effect, the different ways to quantify disease risk, and the scale of observation.

First, the identity effect relates to the presence of one or more particular species that play a disproportionate role in a disease system. In some scenarios, a species with a low competence for a pathogen could still amplify disease risk if it is an important host for vectors or a regulator of competent hosts (LoGiudice *et al.* 2002; Hofmeester *et al.* 2016). For instance, the presence of deer (which are not competent hosts of *Borellia*; Barbour *al.* 1993; LoGiudice *et al.* 2002) increase the risk of Lyme disease by serving as reproductive hosts of ticks (Wood & Lafferty, 2013; Wood *et al.* 2014).

Second, disease risk can be measured in different ways, and the chosen variable can affect interpretations. Many empirical studies have quantified disease risk as infection prevalence (Ostfeld *et al.* 2001; Schmidt & Ostfeld 2001; Dizney & Ruedas 2009). Considering that the disease risk to humans depends on the density of infected animals, other studies have focused on this variable (either hosts or vectors, e.g., density of infected nymphal ticks; Wood & Lafferty 2013). Infection prevalence and the density of infected animals can respond in different direction when species with low competence are present (i.e., species richness increase; Huang *et al.* 2015). For instance, Roche *et al.* (2012) found that high species richness reduced the overall infection prevalence but increased the total number of infected individuals (because the total number of hosts increased).

Third, the extent to which species with low pathogen competence can reduce pathogen transmission is scale-dependent (Wood & Lafferty 2013; Kilpatrick *et al.* 2017). Host-pathogen interactions can be influenced by biotic and abiotic factors, including those

related to assemblages composition, species distribution and movement, and climate. All of these can act at different scales (Hunter 2003; LoGiudice *et al.* 2003; Cross *et al.* 2005). At a local scale, biotic interactions (e.g., those driving encounter reduction; Keesing *et al.* 2006) are assumed to be most influential (Cohen *et al.* 2016). Thus, the effect of species with low pathogen competence on pathogen transmission is expected to be strongest at relatively small scales. When studied at larger scales involving more species, even those with low competence, this relationship may be undetectable.

The third requirement

The last requirement of the dilution effect is that competent host species dominate in species poor assemblages (Johnson *et al.* 2012; Huang *et al.* 2013). Such a scenario can result from a negative relationship between host competence and local extinction risk, which can be explained by two ecological theories.

The first theory, the parasite adaptation theory, suggests that parasites tend to adapt to common hosts. Common species also normally have higher population densities and lower extirpation risks (Lively & Dybdahl 2000). Ostfeld *et al.* (2014) tested the parasite adaptation theory and found that common species tend to be more competent.

The second theory, life history theory, suggests that life history traits closely relate to host competence (Lee 2006; Johnson *et al.* 2012) and local extinction risk (MacArthur & Wilson 1967; Caro 1998; Woodroffe & Ginsberg 1998; Huang *et al.* 2013a). Specifically, species with a fast pace of life (i.e., those species that have short lifespans, short development periods, small body sizes, and large population sizes) are more susceptible to pathogens because they invest less resources in the immune system (Johnson *et al.* 2012). These species are less likely to go extinct compared to slower-living ones because their fast rates of reproduction and growth allow them to quickly recover from disturbances (MacArthur & Wilson 1967; Arcy & Keating 2002; Tomiya 2013).

In summary, a negative relationship between local extinction risk and pathogen competence is one of the fundamental mechanisms underlying the generality of the dilution effect (Huang *et al.* 2013a; McCallum 2015). When biodiversity loss occurs, common and fast-living species are less likely go locally extinct; thus, disease risk is expected to increase since these species are also predicted to be more competent for pathogens (i.e., dilution effect). However, the direction and consistency of the relationship between local extinction risk and pathogen competence is unclear (Randolph & Dobson 2012).

Some studies have documented a negative relationship between local extinction risk and pathogen competence. For example, Johnson *et al.* (2012) studied *Ribeiroia ondatrae* infection in 13 species of amphibian hosts and found that short-lived species (i.e., low

extinction risk) are more likely to become infected (i.e., high competence). Huang *et al.* (2013) studied the relation between species life-history traits and species competence in a vector-borne disease system and found that large-bodied species (i.e., high extinction risk) had low competence for several pathogens.

Other studies have shown the reverse relationship. This reversal is grounded in a different relationship between life history traits and extinction. Large species may actually be less susceptible to changes in environmental conditions (i.e., lower extinction risks; Hilbers *et al.* 2017), because populations of large-bodied mammals decline less quickly than those of small-bodied mammals (Cardillo *et al.* 2005). Although large-bodied species often have low reproduction rates, which decrease their ability to recover to their former population sizes before disturbance, those species also need only a small population size to persist (Hilbers *et al.* 2017). Moreover, large-bodied species are more resistant to habitat loss because they often have a large home range and can search for food in larger areas, while for small-bodied species, habitat loss is the greatest threat because they already have restricted home ranges (Geldmann *et al.* 2013). As a consequence of the uncertainty of the relationship between life history and extinction risk, it remains challenging to say whether small-bodied species (i.e., high competence) or large-bodied species (i.e., low competence) are more likely to remain in a local assemblage. Therefore, it is equally challenging to say whether disease risk will increase (i.e., dilution effect) or decrease (i.e., amplification effect).

Disease transmission type

In addition to the two debated requirements above that influence the generality of the dilution effect, the direction of the relationship between species richness and disease risk also depends on the type of disease transmission (i.e., density vs. frequency dependence; Dobson 2004). Some theoretical work suggests that a dilution effect is more likely with frequency-dependent diseases (Rudolf & Antonovics 2005) and that an amplification effect is more likely with density-dependent diseases (Searle *et al.* 2011; Joseph *et al.* 2013). However, in reality, diseases are often not transmitted strictly in one way (i.e., density *or* frequency dependent). Lyme disease transmission, for example, is often described as frequency dependent, but the encounter rate between ticks and competent hosts can be density dependent since more rodents equate to higher encounter rates between the rodents and ticks.

Current knowledge gaps

As discussed above, many uncertainties surround the direction and mechanisms of relationships between disease risk and species richness: species vary in their competence to pathogens, species have different extinction risks, etc. These uncertainties relate to two important knowledge gaps that must be addressed: 1) which measure of biodiversity

is most useful for understanding disease-diversity relationships and 2) how are these relationships affected by the level of biological organization (e.g., species vs. assemblage) under consideration?

Most studies of the dilution effect have focussed on species richness. However, important differences in species are overlooked when simply counting the number of species. Taking the differences among species (e.g., in physiology or ecology; Lepš *et al.* 2001) into account when measuring biodiversity can deepen the understanding of disease-diversity relationships.

Some differences in species competence and extinction risk closely relate to species life history traits (MacArthur & Wilson 1967; Caro 1998; Woodroffe & Ginsberg 1998; Lee 2006; Johnson *et al.* 2012; Huang *et al.* 2013a). Functional diversity, which incorporates differences of life history traits (i.e., body mass; Balvanera *et al.* 2006), is better than species richness in explaining variation in disease risk (Chen & Zhou 2015). Moreover, phylogeny can be important. Species that are more related are more likely to share some relevant characteristics (e.g., reservoir competence, vector competence, local density, extinction risk, life history, etc.; Webb *et al.* 2002; Huang *et al.* 2013; Olival *et al.* 2017). Thus, phylogenetic relatedness can influence disease transmission: when species are closely related, the susceptibility of those species to the same pathogens is thought to be similar (Webb *et al.* 2002; Olival *et al.* 2017). Yet only a few studies of disease-diversity relationships have accounted for this aspect of biodiversity (Liu *et al.* 2016; Wang *et al.* 2019). Likewise, the role of spatial differences between host species assemblages (β-diversity) is poorly understood (in contrast to α-diversity, i.e., species richness).

The second knowledge gap relates to the level of biological organisation under investigation and its influence on disease-diversity relationships (Kilpatrick *et al.* 2017). In natural systems, pathogen-host interactions are often complex. Pathogens normally can be maintained and transmitted by multiple species, and one species can support multiple different pathogens. For this reason, studying a single host species or a single pathogen or disease is often inadequate. For example, with such an approach, detecting how biodiversity affects the total disease burden for mammal assemblages and humans is impossible (Kilpatrick *et al.* 2017). Measuring overall disease risk (i.e., multiple pathogens or diseases) in an assemblage of mammals that vary in their competence is expected to provide new insights. More specifically, data on disease richness can help to deepen the understanding of the effect of biodiversity on overall disease risk in animal assemblages.

Overall, these knowledge gaps highlight a lack of clarity about disease-diversity relationships and point to the need for future investigations. Other biodiversity metrics, such as functional diversity, phylogenetic diversity, and β-diversity, may be more important than

species richness in shaping disease risk. Incorporating functional diversity and phylogenetic diversity into future studies may provide new insights into why the correlation between species richness and disease risk is sometimes negative (i.e., a dilution effect) and sometimes positive (i.e., an amplification effect). Incorporating β-diversity into studies of disease ecology may serve as a new tool to understand the geographic expansion of some diseases, such as Lyme disease. Furthermore, focusing on higher levels of biological organization (i.e., moving beyond focal host species and single pathogens) will help when evaluating the role of biodiversity in protecting animal and human health.

Objectives

Habitat loss and climate change are changing biodiversity by increasing species extinction, by reducing the abundance or relative abundance of species, or by influencing species distribution (i.e., range shifts). Those changes in biodiversity can affect disease risk associated with local assemblages, for example, by influencing encounter rates among species (Fig. 1.1). Understanding the mechanisms underlying the influence of biodiversity changes on disease risk is critically important. The main aim of this thesis is to advance the understanding of diversity–disease relationships. I specifically focused on disease risk at the community level (i.e., assemblages of wildlife species). Moreover, considering the shortcoming of the current understanding of disease-diversity relationships, I considered other metrics of both biodiversity (e.g., evenness, functional diversity, β diversity and phylogenetic diversity) and disease risk (e.g., community R0 and total disease burden; Fig. 1.1).
The following were my objectives.

1. To quantify disease risk at local assemblages level based on the spatial and temporal differences in their species composition, and to predict how disease risk changes along with predicted changes in biodiversity under habitat loss and climate change (Chapter 2)
2. To quantify the impact of phylogenetic diversity on disease occurrence and the total disease burden (Chapter 3)
3. To study the effect of phylogenetic diversity on disease risk and of scale-dependency on the disease-diversity relationship (Chapter 4)
4. To study the range expansion of infectious disease as a function of β diversity and landscape connectivity (Chapter 5)

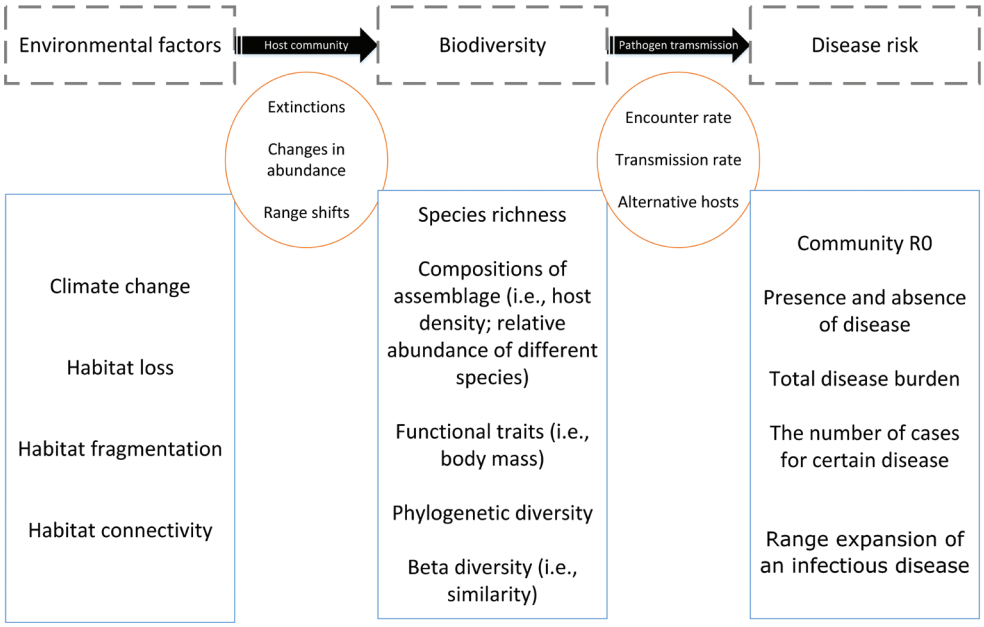

Figure 1.1 Environmental factors can influence biodiversity via ecological mechanisms, and biodiversity can impact disease risk via disease transmission mechanisms (black rectangles). Black arrows indicate "Ecological mechanisms" and "Pathogen transmission mechanisms". Contents in the orange circles indicate the way of influence; contents in blue rectangles indicate measurement for different dimensions.

Thesis outline

In **Chapter 2**, I model the effects of predicted environmental changes and habitat loss on disease risks of local assemblages based on changes in mammal assemblages (i.e., richness, evenness, and functional diversity). The composition of mammal assemblages could affect local disease risk because the majority of emerging infectious disease originate from wildlife, particularly mammal species (Wolfe *et al.* 2007). I predict when and where assemblages would experience an increase in disease risks and investigate the mechanisms underlying those changes. I also explore how disease risk changes in assemblages with constant species richness as previous studies focus more on the effects of species losses or gains to study the relationships between biodiversity and disease risk. Disease risk may change due to changes in the composition of mammal assemblage that does not involve species loss. Additionally, I compare the relative importance of effects of species richness, evenness and functional diversity on disease risk.

In **Chapter 3**, different measurement of disease risk may respond differently to species richness, and make it difficult to test the generality of the dilution effect. I consider two ways to measure disease risks, including the occurrence of individual disease and the total disease burden. Given that most studies on diversity-disease relationships did not consider the effect of phylogenetic relationship between species within local assemblages. I also study the role of phylogenetic relationships on the occurrence of certain disease and the total disease burden separately. I first study the effect of species richness and phylogenetic relationship within the local assemblage on disease occurrences by using the occurrence of 19 livestock disease in Africa. I then study the effect of species richness, phylogenetic diversity on disease richness (i.e., the total disease burden). I am able to compare the relative importance of species richness and phylogenetic structure in shaping disease pattern, and also to test the responses of disease occurrences and total disease burden to differences in species richness and phylogenetic structure.

In **Chapter 4**, using Lyme disease as a model system, we studied the effect of mammal host species richness and host relatedness on the number of reported Lyme disease cases in people. In addition, most studies of the disease diversity relationships are conducted at a single spatial scale, though the ecological process is often scale-dependent. I also take into consideration the possibility of scale-dependency of the disease-diversity relationships. I apply the analysis at both larger and smaller spatial scales (i.e., at both the state and county level). I make and test the following predictions: 1) the number of Lyme disease cases is negatively related to host species richness 2) host species relatedness is a better predictor than host species richness, and 3) the dilution effect occurs at county level, and amplification effect occurs at state scale (i.e., scale dependence).

In **Chapter 5**, I aim to understand how diseases spread over time and across the landscape, which is critical for managing disease outbreaks. In addition, although α-diversity (i.e., species richness) has received great attention in understanding patterns in Lyme disease prevalence, there is a serious knowledge gap for the impact of β-diversity (i.e., spatial differences in the similarity between host species assemblages). Moreover, in the processes of the expansion of the disease, factors do not work alone, their interactions are likely to greatly affect the expansion, more than when only considering these factors in isolation. I study how interactions between severity of diseased neighbours (i.e., the number of Lyme cases), the susceptibility of a disease-free county (i.e., the similarity in host assemblage structure), and their interactions with habitat connectivity, influence the probability that the status of a county changes from disease-free to infected.

Finally, in **Chapter 6**, I present a synthesis and discuss the results of all previous chapters and relate the results of this thesis to a broader ecological context.

CHAPTER 2

Mammal assemblage composition predicts global patterns in emerging disease risk

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Abstract

The majority of emerging infectious disease originate from wildlife, particularly mammals, so changes in distribution and composition of mammal assemblages could change local disease risk. Several studies have focused on the impacts of biodiversity on disease risk from the aspects of biodiversity loss. However, disease risk may change due to changes in the composition of mammal assemblage that does not involve species loss. Here we use predicted global species distributions and their abundances in 2015, and 2035 to asses changes in disease risk under two different climate change scenarios. We quantify disease risk, using the community level basic reproductive ratio R0, for pathogens with either density-dependent or frequency-dependent transmission. We found that hotspots of disease risk for density-dependent diseases are concentrated in tropical and northern temperate regions; this is consistent with date from published emerging disease events. Crucially, we were able to predict where and how disease risk changed over time. Changes in community/assemblage evenness substantially and constantly affect risk for both density and frequency dependent diseases. Our results suggest that disease risk predictions based on species losses or gains strongly underestimate the impacts of assemblage on disease risks, changes in assemblage-level evenness can substantially affect disease risk before species loss occurs.

Introduction

Habitat destruction and climate change have led to global biodiversity decline (Millennium Ecosystem Assessment. 2005). Worldwide, populations of many species are declining, increasing numbers of species are under threat (Butchart *et al.* 2010), and health conditions of the ecosystem can deteriorate as a result (Cardinale *et al.* 2012). As changes in diversity link to disease risk from spill-over of pathogens circulating in local mammal and bird communities (Ostfeld 2009; Ostfeld & Keesing 2012), understanding how disease risk will change under global biodiversity change has become increasingly important.

Many disease risk studies, especially ones at the assemblage level, use species loss to predict disease risk dynamics (Ostfeld 2009). They suggest species loss promotes an increasing disease risk in local communities. The possible mechanism is that large-bodied and long-lived species often extirpate first; those species often invest more in immune defences compared with small-bodied species (Johnson *et al.* 2012; Joseph *et al.* 2013). Disease risks then increase as a result of the loss of these large species that are more resistant to pathogens.

However, the relationships between species richness and disease risks are still controversial (Salkeld *et al.* 2013; Huang *et al.* 2016), as, e.g., disease risk will respond differently based on transmission type (density-dependent transmission versus frequency-dependent transmission; Box 2.1). A positive relationship between disease risk and species richness is more likely to occur under the density-dependent transmission. In the case of a generalist pathogen to which all hosts are susceptible, an increasing species diversity supplies more hosts for the pathogen, and an increase in host abundance results in an increase in contact rate, hence facilitating disease transmission. However, when the transmission is frequency-dependent, disease risk may be lower with increasing host richness, as the contact rate of hosts that have a large competence (i.e., the ability to obtain and transmit disease), can be diluted by the increases of in species richness (Keesing *et al.* 2010).

Box 2.1 Two types of mechanisms are distinguished in transmission.

Density-dependent transmission: transmission is a function of density of infected hosts and the density of susceptible hosts (Huang *et al.* 2013)

Frequency-dependent transmission: transmission is a function of the frequency (proportion of the population) of infected individuals and susceptible hosts in a population rather than density (Rudolf *et al.* 2005).

Despite the assumption of species richness as a primary factor of disease risk dynamics, the composition of ecological assemblages can also affect disease risks (Keesing *et al.* 2006; LoGiudice *et al.* 2008b). Theoretically, changes in the composition of mammal assemblage can lead to a decrease or increase in disease risks of mammal assemblages through changes in relative population densities of different species. The direction and strength of this relationship depend on (a) per capita contribution of different species to disease risk, and (b) different responses of population density of species to environmental changes. Specifically, the competence of a species to a general pathogen is related to other life history traits, like longevity and body mass (Huang *et al.* 2013a). Large-bodied species generally have stronger immunological defences than small-bodied species and are less likely to be infected (Johnson *et al.* 2012; Joseph *et al.* 2013). Thus, when communities have relatively more large-bodied species, disease risks would be lower. Responses of the population of species to environmental changes also link to life history traits. Population densities of small-bodied species are more sensitive to environmental changes (Sinclair 2003). When habitat conditions become better or habitat size becomes larger, populations of especially small species can respond quickly (Cardillo *et al.* 2005). In such cases, the assemblage would experience an increase in disease risk due to increase in abundance of small species.

Diversity can be mainly characterized in three ways (Ostfeld & Keesing 2012; Tucker & Cadotte 2013): (a) the number of different species (e.g. species richness which is mentioned above), (b) the relative abundance of different species (e.g. the composition measured by species evenness), (c) the number of species in different classes on the basis of functional diversity (Lepš *et al.* 2001). In this study, we analysed diversity via these three approaches. Given the possible impact of functional traits on disease risk of local assemblage though, few studies consider the effect of functional diversity on disease risk (but see; Chen & Zhou 2015). To measure functional diversity, i.e. the distribution of functional traits in the system (Balvanera *et al.* 2006), we quantified functional richness (the extent of complementarity among species traits; Petchey 2002), and functional evenness (i.e. the regularity of distribution of functional trait; Mouillot *et al.* 2005).

In addition, local mammal assemblages experience changes in composition through changes in population densities before species loss occurs (Gaston & Fuller 2007; Hillebrand *et al.* 2008). This raises questions: What direction will disease risk change in ways that do not involve changes in species richness? Understanding the mechanisms underlying the influence of mammal assemblage changes on disease risk is critically important for predicting disease risk at an early stage.

In this study, we evaluate the importance of effects of predicted environmental change and habitat loss on disease risks of local communities based on changes in mammal assemblages (i.e. richness, evenness, and functional diversity), we modelled where and

when communities experience increases in disease risks and studied the mechanisms underlying those changes. With projected mammals distributions, communities experience increased, decreased, or constant species richness. We first studied the potential driver at the global level. We also explored how disease risk changes in communities with constant species richness as previous studies focus more on effects of species loss or gain to detect the effect of composition change of diversity on disease risk that does not involve changes in richness. For the first time, we identify specific areas that have increased disease risks on a global scale based on the projected mammal assemblage changes. Compare the effects of diversity that measured in three ways, our study highlights the substantial effect of species evenness and gives more insight into how mammal assemblage composition influences disease risk.

Methods

To examine how mammal assemblage composition affects community R0 and how community R0 would change according to the changes of mammal assemblage composition in the future, we constructed models of species range and abundance individually for 4,466 mammal species, both now (2015) and in the future (2035). Different future models were created for two socioeconomic and climate scenarios of shared socioeconomic pathways (SSPs; O'Neill *et al.* 2014). For each time period/scenario, we aggregated the predicted species abundance and analysed the composition of the implied ecological communities. We used a mathematical model, with parameters drawn from the literature, to estimate community R0 for these communities, and then we assessed the relative importance of different factors on the change in community R0 from the present to the two future scenarios.

Species abundance data

We used species distribution and abundance projections of 4,466 mammal species with a resolution of 0.5^0 at the global level. These distributions were derived from species distribution ranges filtered according to species-specific habitat preferences and modelled according to scenarios of shared socioeconomic pathways (SSPs; O'Neill *et al.* 2014) that integrated a combination of climate model projections, socioeconomic conditions, and possible climate policies. We considered two extreme scenarios for 2035. The first, SSP1, models low challenges for mitigation and adaptation (i.e., low population growth, proactive environmental protection, and low vulnerability to climate change). The second, SSP3, models high challenges for mitigation and adaptation (i.e., high population growth, reactive environmental protection, and vulnerability to climate change vary regionally). Population sizes within suitable habitat classes were estimated per species per grid cell, using population density models based on trait information (body mass and diet) and local environmental conditions (primary productivity and climatic conditions), with taxonomic

information included as random effects (Santini *et al.* 2018). A mammal assemblage was constructed for each of the grid cells at each time point, taking into account the differences in the average density per species.

Climate data

The climatic conditions of SSP1 and SSP3 in 2035 were derived from three IPCC RCP AR5 climate scenarios (3, 4.5, and 8.5 watt/m^2 of radiative forcing), respectively compatible with 0.4-1.6, 0.9-2.0, 1.4-2.6 average degree warming with respect to the 1986-2005 average. For each scenario, the median value of 14 bioclimatic variables was calculated (Appendix 2: Table A2.1) across 17 General Circulation Models (GCMs, Appendix 2: Table A2.2). The rationale for this is to account for the large uncertainties between different GCMs in climate change projections (Rowlands *et al.* 2012). Projecting species responses for each of the individual GCMs is computationally impractical; however, the observed trends very closely tracked the ensemble median (Amecay Juárez *et al.* 2013). The median bioclimatic variable layers were derived for two time points: 2015 and 2035. For consistency with the standard procedure used to prepare present bioclimatic variables and to reduce the influence of outliers, each year was calculated as an average over a 30-year period, i.e. 2000-2030 for 2015, and 2020-2050 for 2030.

Bioclimatic envelope models

We estimated climate change effects on species distribution by fitting bioclimatic envelopes at 30' resolution for 3031 terrestrial mammal species. For another 2,033 species, we assumed constant ranges over time. We made this assumption because their current range was either too small to sample at least 30 presence points for fitting bioclimatic envelope models or their range almost entirely occupied an entire land mass, and therefore we could not draw sufficient pseudo-absence points to fit these models. Furthermore, 598 species were excluded from the analysis, as there were no range maps available so that the species could not be modelled. We used two statistical models, Generalized Linear Models and Generalized Additive Models (Merow *et al.* 2014; Beaumont *et al.* 2016), with the R package BIOMOD2 (Thuiller *et al.* 2009) to fit current bioclimatic envelopes and to project these envelopes for both SSP1 and SSP3. We allowed the algorithm to fit up to a 3rd order polynomial of each variable in the GLM and to fit cubic splines at each knot in the GAM.

We obtained the presence points to fit the models by systematically sampling one point location at each 30' resolution grid cell within the current species current range (IUCN 2015). This method of modelling bioclimatic envelopes allows robust projections of species responses to climate changes (Lawler *et al.* 2009; Visconti *et al.* 2016; Newbold 2018). To avoid creating pseudo-absences in areas of potentially suitable climate falling outside the reach of the species, pseudo-absence points were obtained by systematically sampling areas outside the current species' current range but within the same continents/islands and

the same biogeographic region (prediction extent). We drew a random sample of pseudo absences equal to the minimum between 80% of unoccupied grid-cells within the prediction extent, and 1000 pseudo-absences, for each model thousand pseudo- and their contribution to model calibration was weighted in order to reach a prevalence in the training dataset of 0.5. This pseudo-absence draw was performed five times. For each draw, we repeated three times a bootstrapping procedure by keeping 80% of the data to calibrate the model and using the remaining 20% for validation (Newbold 2018). Therefore, we had 30 models in total for each species, year and climatic scenario from the combination of two statistical models (GLM, GAM), five pseudo-absences draws, and three input data resamples. We binarised the probabilistic models using the probability thresholds that maximised the True Skill Statistic (TSS; Allouche *et al.* 2006), which is equal to sensitivity (true presence rate) plus specificity (true absences rate) minus 1. TSS varies from -1 to 1 with 0, meaning a predictive capacity close to random and values >0.5 and >0.8 are generally recognized as indicating good and very good predictive capacity respectively. For each species, year, and climatic scenario, we combined all bioclimatic envelope models with a TSS>0.8 (obtained from the bootstrapping procedure) by taking the ensemble mode value (between predicted presence and absence) for each grid cell. This ensured that the final mode was the consensus of only high-performing models.

Habitat suitability models

We used data from the IUCN Red List on the land cover and altitudinal preferences of species and their sensitivity to human disturbance. We applied these data to a land-cover classification under each scenario using the IUCN Global Mammal Assessment habitat suitability models (Rondinini *et al.* 2011; Visconti *et al.* 2011, 2016) to quantify the Extent of Suitable Habitat (ESH) for each species within a species' Extent Of Occupancy (EOO). The variables considered were the land-cover and land-use type. Each combination of land-cover and land-use were scored as either suitable or not according to IUCN expert opinion (Rondinini *et al.* 2011; Visconti *et al.* 2011, 2016); only grid cells with suitable habitat were used in further analyses. In total, we had 4,466 species of terrestrial mammals for which range data and habitat preferences were available to produce Habitat Suitability Models. For the 3,031 species for which bioclimatic envelopes were possible, we took the conservative assumption that species were not able to colonise newly suitable habitat that was not in the list of current suitable habitat types for each of the species.

Population abundance predictions

We predicted species population abundance within suitable habitat using population density models presented in (Santini *et al.* 2018). These mixed-effects models fitted on 7,561 density estimates are based on trait information (body mass and diet) and local environmental conditions (primary productivity and climatic conditions), with taxonomic information included as random effects to account for taxonomic relatedness and average

differences in population density from the intercept in different taxonomic groups. Among all models tested in (Santini *et al.* 2018), we used the best models in terms of predictive performance as measured by the minimum absolute error, namely:

$$D \sim BM + Diet + NPP + NPP^2 + P_{wq} + P_{wq}^2 + P_{cv} + P_{cv}^2$$

Where: D = log10 population density; BM = log10 body mass; Diet = Diet category (Herbivores, Omnivores, Carnivores); NPP = log10 Net Primary Productivity; P_{wq} = Precipitation of the warmest quarter; P_{cv} = Precipitation seasonality.

As in Santini *et al.* (2018), we used body mass and diet categories from (Wilman *et al.* 2014). The original models in Santini *et al.* (2018) were fitted on NPP (Imhoff *et al.* 2004), and precipitation of the warmest quarter and precipitation seasonality were from (Hijmans *et al.* 2005). In order to reproject these models to calculate future species' densities, we refitted the models using NPP from IMAGE (Stehfes *et al.* 2014), climatic variables described in Appendix 2: Table A2.1, and their future projections under SSP1 and SSP3 for 2035. In addition to the fixed effect component of the model, the predictions were based on random effects that modelled deviations from the intercept for taxonomic orders, families and species hierarchically. When a taxonomic level for a species was not present in the models, the respective random effect was set to zero. We predicted species population density per species in each grid cell per time step and SSP scenario; we multiplied density values by the predicted extent of suitable habitat to obtain an estimate of population abundance per grid cell.

Calculation of community R0

Two types of mechanisms are distinguished in pathogen transmission. With density dependence, transmission of the pathogen depends on the densities of infected and susceptible hosts. With frequency dependence, transmission of the pathogen depends on the proportion of the abundance (i.e., the frequency) of infected and susceptible hosts (Rudolf & Antonovics 2005).

For each local mammal assemblage (i.e., the species assemblage in a 0.5°), the basic reproduction ratio R0 was calculated to measure the probability that a generalist pathogen can invade or persist in a particular host assemblage (Dobson 2004). R0 was calculated from the dominant eigenvalue of the next-generation matrix (G):

$$G = \begin{bmatrix} \frac{\beta_{ii} p_{ii}}{d_i + v_i + \sigma_i} & \cdots & \frac{\beta_{ij} p_{ij}}{d_i + v_i + \sigma_i} \\ \vdots & \ddots & \vdots \\ \frac{\beta_{ji} p_{ji}}{d_j + v_j + \sigma_j} & \cdots & \frac{\beta_{jj} p_{jj}}{d_j + v_j + \sigma_j} \end{bmatrix}$$

For density-dependent diseases, p_{ij} is determined by the absolute abundance of species; for frequency-dependent diseases, p_{ij} is determined by the relative abundance of the species. A pathogen can invade and persist in a local host assemblage when R0 >1. We used allometric relationships between all parameters and body mass to generate the required parameters for the calculation of R0 in our mammal assemblages (Dobson 2004; Table 2.1). Intraspecific basic reproduction ratios ($R0_i$), which represent the competence of a species to a pathogen (Dobson 2004), were generated from a right-skewed truncated gamma distribution (κ = 0.5, ϑ = 1.5; Dobson 2004). We then calculated an $R0_i$ value for each species by assuming body mass is negatively related to intraspecific $R0_i$ (Roche *et al.* 2012), so that smaller species were more competent to the pathogen than larger ones. The negative relationship between species body mass and intraspecific $R0_i$ arise from two alternative mechanisms (Joseph *et al.* 2013; Huang *et al.* 2016). First, short-lived (usually relatively small) species invest less in their immune systems (Hillebrand *et al.* 2008). Second, pathogens evolve to infect the common species (which are also usually relatively small) in response to selective pressures associated with the loss of hosts during assemblage disassembly (Han *et al.* 2015). In fact, this negative association between body mass of species and species competence has been reported in many different pathogen systems, such as for Lyme disease (Previtali *et al.* 2012), West Nile virus (Huang *et al.* 2013a), *Ribeiroia ondatrae* (Johnson *et al.* 2012), and *Trypanosoma cruzi* (Calzada & Saldan 2012).

Statistical analyses

We used General Linear Models (GLM) to understand which factors were primarily responsible for changes in community R0 (ΔR0) under different scenarios (i.e., SSP1 and SSP3; Appendix 2: Table A2.3). For diversity, we included original species richness (SR), which is the number of different species within local assemblage in 2015; original species evenness (EV), which is Shannon's evenness index in 2015, was calculated as:

$$H' = -\sum_{i=1}^{S} \frac{n_i}{N} \ln \frac{n_i}{N},$$

Where n_i is the abundance of species *i*, *S* is the total number of species, and *N* is the number of individuals of all species. We also considered the and the original percentage of large species (PL), which is the percentage of abundance of species with body mass large than three kilograms (Wood & Lafferty 2013). Here, we choose body mass as the trait, which is generally considered important to disease transmission (Hillebrand *et al.* 2008). Through a trait-based approach, we calculated functional richness (Frich) and functional evenness (F_{ev}). We also included the change in each of these variables: ΔSR, ΔEV, ΔPL, ΔF_{rich}, and ΔF_{ev} from 2015 to 2035. We quantified changes in assemblage composition over time, such as changes in species richness (ΔSR) as $\Delta SR = \ln(SR_{2035}/SR_{2015})$. Changes in R0 over time were

calculated similarly: $\Delta R = \ln(R0_{2035} / R0_{2015})$. To compare the effect sizes of different predictors, we standardised all explanatory variables (mean = 0 and standard deviation = 1). In these GLMs, we included diversity indices, functional diversity indices, changes in both types of indices over time, and all two-way interactions between a given index and its change.

Validation of the model

To valid our predicted disease pattern, we compared our disease pattern with the risk of emerging infectious diseases (EID) risk originate in wildlife after correction for human population density and reporting effort (Allen *et al.* 2017; Appendix 2: Table A2.4). We test the relationship using the General linear mixed model (GLMM) with state as a random factor.

Sensitivity analysis

We tested the sensitivity of community R0 values to changes in interspecific transmission scaling coefficient (Appendix 2: Table A2.5).

Table 2.1 Model parameters, definitions, and values.

Parameter	Definition	Value
bi	Per capita birth rate	0.6*body mass^-0.27+0.4*body mass^-0.26
di	Per capita death rate	0.4*body mass^-0.26
vi	Disease-induced mortality	(m-1) *di*
m	Virulence term	1.5
r	Recovery scaling term	10
σi	Recovery term	*rdi*
βii	Intraspecific transmission rate	*R0i*(*di*+ *vi*+ *σi*)/ abundance
βij	Interspecific transmission rate	*Cij*(*βii*+ *βij*)/2
Cij	Interspecific transmission scaling coefficient	0.05

Source: (Dobson 2004; Joseph *et al.* 2013)

Results

Biodiversity changes

We analysed 6247 grid cells or mammal assemblages in total. Changes in species richness varied, depending on the climate change scenario. More assemblages showed an increased in species richness under scenario SSP1 than under scenario SSP3 (Fig. 2.1). The majority (59%) of assemblages increased in species richness under SSP1. However, species richness per grid cell was constant in the majority of communities modelled under SSP3.

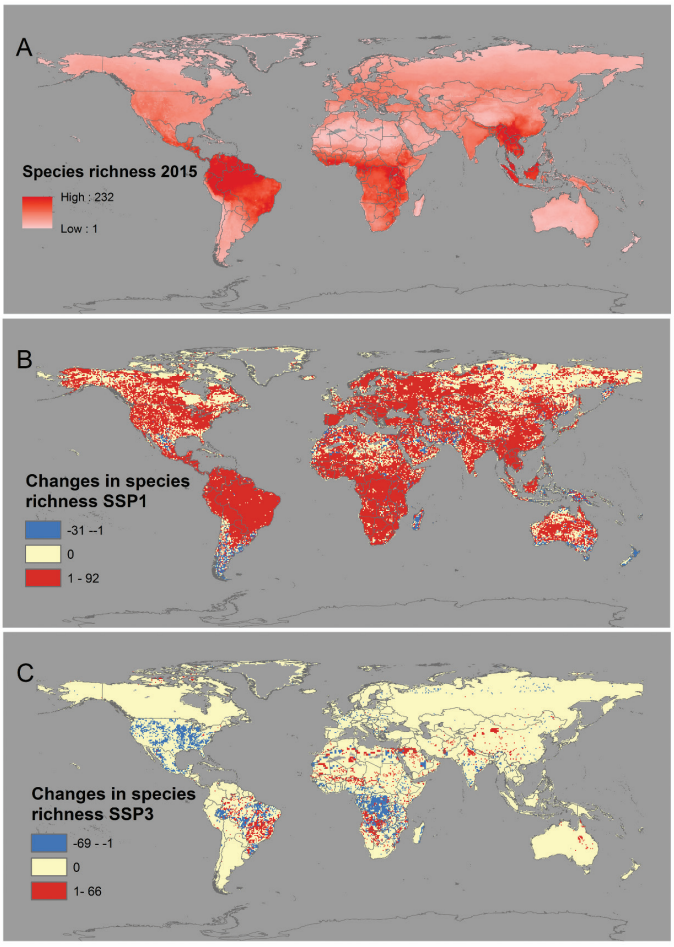

Figure 2.1 Species richness in 2015 (A) and changes in species richness from 2015 to 2035 under climate change scenario SSP1 (B) and SSP3 (C). Changes in species richness were quantified as species richness in 2035 minus species richness in 2015. Red indicates increased species richness; blue indicates decreased species richness decrease; yellow indicates constant species richness.

Global patterns of disease risk

Community R0 varies geographically for density-dependent diseases and frequency dependent diseases (Fig. 2.2). For density-dependent diseases, disease risk hotspots are typically found in tropical and north temperate regions. Hotspots of disease risk in the United States and Europe are consistent with the observed patterns in emerging infectious diseases events over the period of 1940 to 2004 (Jones *et al.* 2008). Predicted diseases patterns in our study were consistent with the risk of emerging infectious diseases (EID) as reported by Allen *et al.* (2017), and the observed EID risk increased with increasing community R0, explaining 66.9% of the variation in EID risk (Linear Mixed Model, with continent as random factor; Fig. 2.3). For frequency dependent diseases, Northern parts of Alaska and Canada, Greenland, Madagascar, and the area around the Himalayas were characterised by higher disease risk than other parts of the globe.

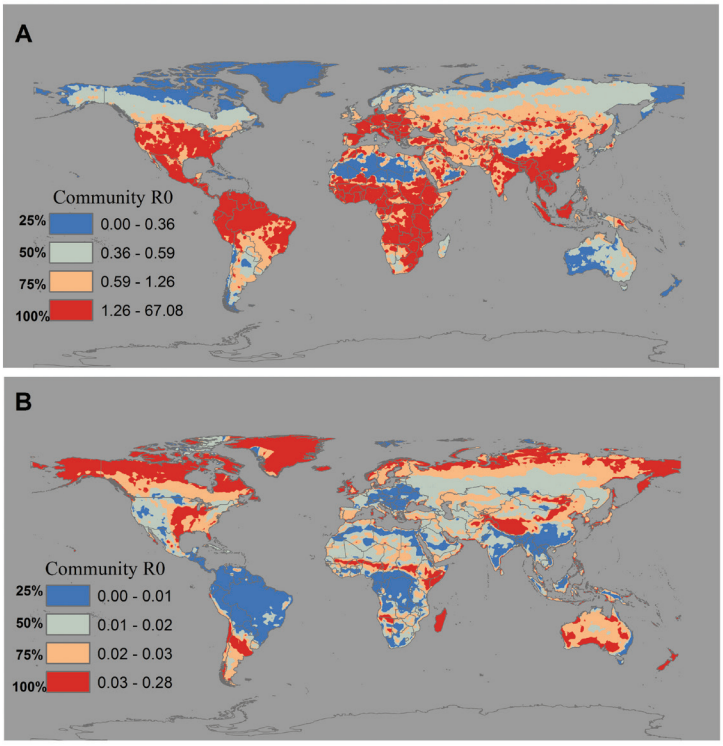

Figure 2.2 Spatial differences in the predicted community R0 with quantiles for density-dependent (A) and frequency-dependent diseases (B) in 2015.

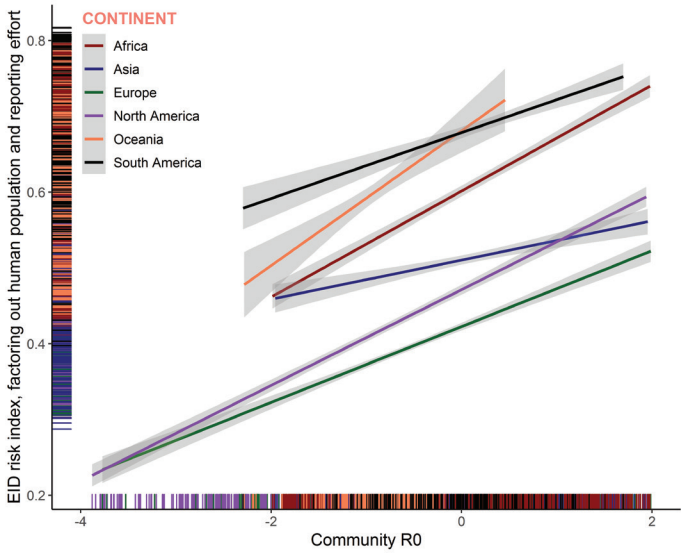

Figure 2.3 Relationships (linear regression ± 95% CLs) between predicted community R0 and reported EID risk per continent with marginal rugs.

Changes in community R0 of mammal assemblages

Community R0 changed from 2015 to 2035 (Fig. 2.4). For density-dependent diseases, areas in eastern South America, the middle part of Africa, and south part of Asia had increasing community R0; for frequency-dependent diseases, the middle part of Africa and southern part of Asia had increasing community R0.

Comparing changes in community R0 under two scenarios, for density-dependent diseases, more areas had increased disease risk in SSP1 (models low challenges for mitigation and adaptation) than that of SSP3 (models high challenges for mitigation and adaptation). However, for frequency dependent diseases, more areas had increased disease risk in SSP3.

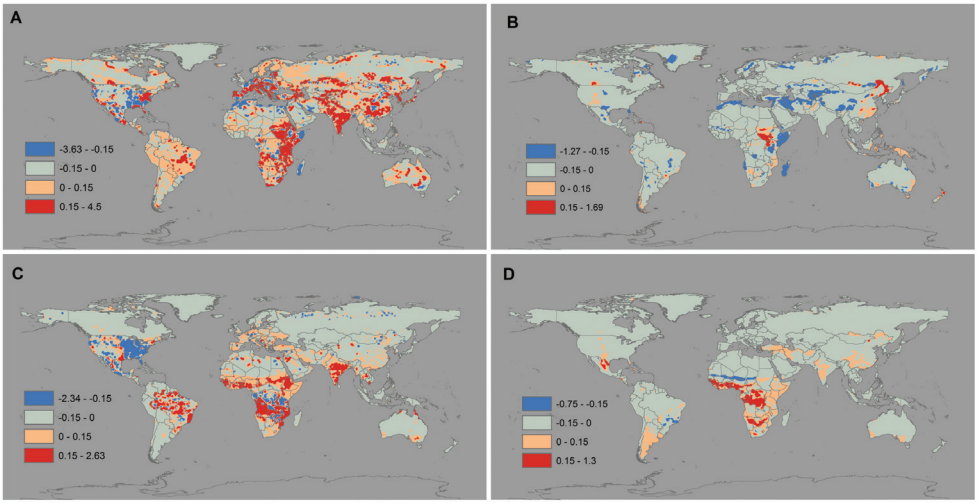

Figure 2.4 Changes in community R0 for density-dependent diseases and frequency-dependent diseases under scenario SSP1 and SSP3 from 2015-2035. Changes in community R0 [$\ln(R0_{2035}/R0_{2015})$] for density-dependent diseases under SSP1 (A) and SSP3 (C). Changes in community R0 [$\ln(R0_{2035}/R0_{2015})$] for frequency-dependent diseases under SSP1 (B) and SSP3 (D).

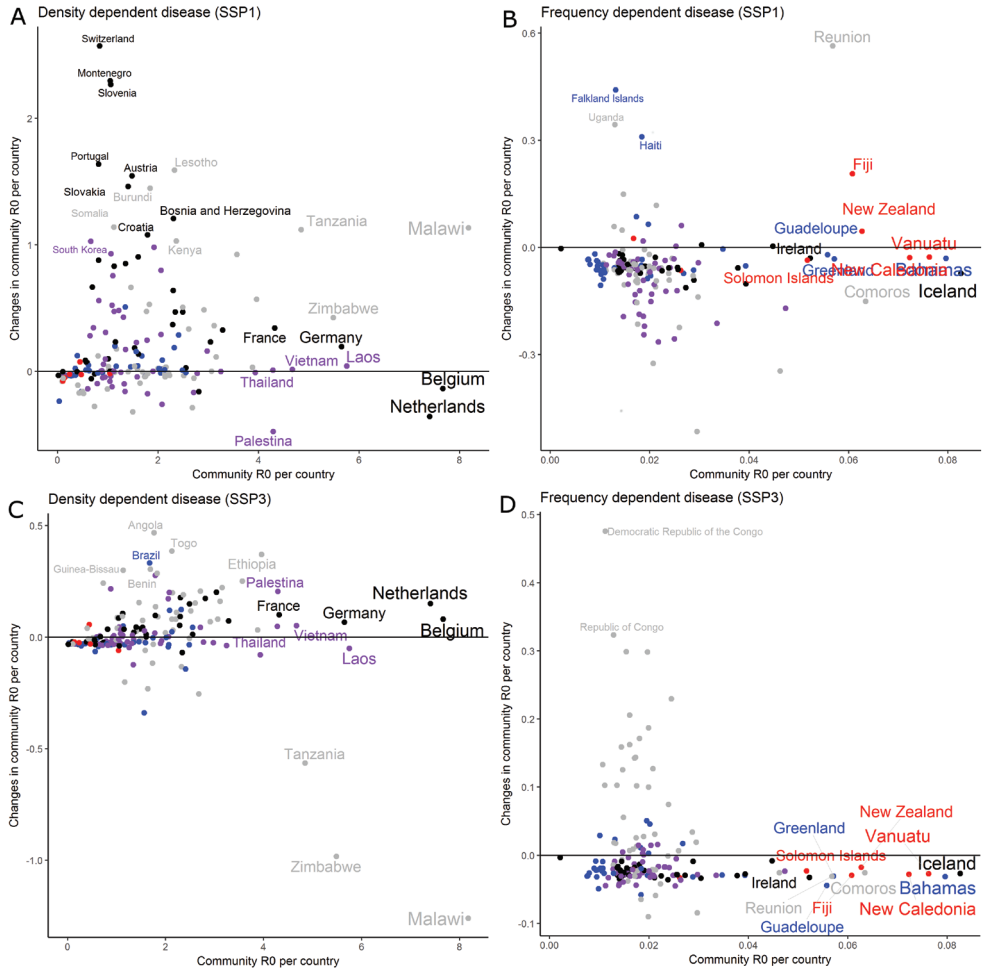

Figure 2.5 Country level disease risk and changes in disease risk. X axis- community R0 (absolute value of disease risk); Y axis- changes in disease risk increase (above line) or decrease (below line). change R0=ln(R0-2035/ R0-2015). Black: Europe; grey: Africa; purple: Asia; red: Oceania; blue: North America.

Community R0 and changes in R0 vary among countries (Fig. 2.5). For the absolute value of disease risk, Malawi, Belgium and the Netherlands have a relatively higher risk of density-dependent diseases than other countries (Fig. 2.5-A, C). Disease risk for Malawi increased around three times from 2015 to 2035, but Belgium and the Netherlands experienced a decline in disease risks for density-dependent diseases. Switzerland and Montenegro and Slovenia increased more than five times in disease risk from 2015 to 2035, although their original disease risk in 2015 is low. For frequency-dependent diseases, Iceland and Bahamas

had a relatively higher risk, whereas Reunion and the Democratic Republic of Congo had the largest increase in disease risk from 2015 to 2035 (Fig. 2.5 -B, D).

Potential drivers of changes in disease risk

To better understand what drives changes in disease risk (community R0) of assemblages at a global level, we analysed the role of original assemblage structure, changes in assemblage structure, and their interactions at the global level (Fig. 2.6, red dots) as well as areas with no changes in species richness (Fig. 2.6, blue dots). Our results showed that variables describing changes in assemblage structure are more important in determining changes in disease risk than variables describing the original assemblage structure.

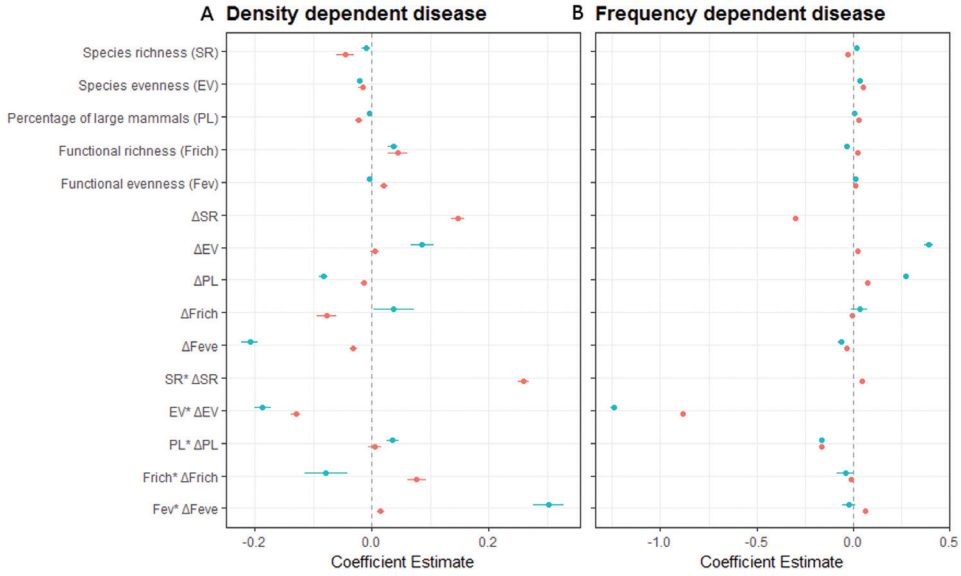

Figure 2.6 Effects of predictors on changes in community R0 for density-dependent diseases (a) and frequency-dependent diseases (b). Red: results from all communities; blue: results from a subset with only those communities with constant species richness. Estimated coefficients from multivariate analysis (n = 61,821). Posterior medians with 95% confidence intervals are shown. Coefficients with 95% confidence intervals that do not overlap with zero are significant in the model. The coefficients also illustrate the effect size of these standardised variables.

The interaction between original species evenness and change in species evenness was a constant and important factor affecting changes in disease risk. Analysing only a subset of all communities, including only areas where there are no changes in total species richness, also original species evenness and changes in evenness were the most important predictors for changes in disease risk (Fig. 2.6). This evenness effect was detected for both density-dependent diseases (Fig. 2.7-B) and frequency-dependent diseases (Fig. 2.8-B). At high levels of evenness, additional increases in evenness resulted in strong decreases in disease risk for both density-dependent and frequency-dependent diseases.

The interaction between original species richness and changes in species richness had a significant effect on changes in disease risk (Fig. 2.6) for both density-dependent disease and frequency dependent disease in the global model, but this effect differed between density-dependent and frequency-dependent transmission. For density-dependent diseases, the interaction between original species richness and change in species richness had the largest effect size (Fig. 2.6); increasing species richness promotes disease risk when original species richness was low, while reducing disease risk when original species richness was high (Fig. 2.7-B). For frequency-dependent diseases, both increases and decreases at relatively high levels of original species richness led to decreased disease risk (Fig. 2.8-A).

The interaction between the original percentage of large mammals and change in the percentage of large mammals influenced the risk of frequency dependent diseases (Fig. 2.6-B, Fig. 2.8-D). For communities originally composed of fewer large mammals, adding more large species led to a decrease in disease risk, and for communities composed of a large percentage of large mammals, losing large species led to an increase in disease risk.

The interaction between original functional evenness and change in functional evenness was an important factor in changing disease risk for both density-dependent and frequency-dependent diseases (Fig. 2.5, Fig. 2.7-D, Fig. 2.8-C). Only at high levels of functional evenness, a decrease in functional evenness resulted in strong increases in disease risk for densities dependent diseases, while for frequency dependent diseases, an increase in functional evenness led to a strong decrease in disease risk.

The interaction of functional richness and changes in functional richness had a significant effect on changes in risk in only density-dependent diseases, whereas it had no effect on changes in disease risk of frequency-dependent disease (Fig. 2.6). At intermediate levels of original functional richness, the additional increase in functional richness had the strongest effect: an increase in functional richness decreased disease risk.

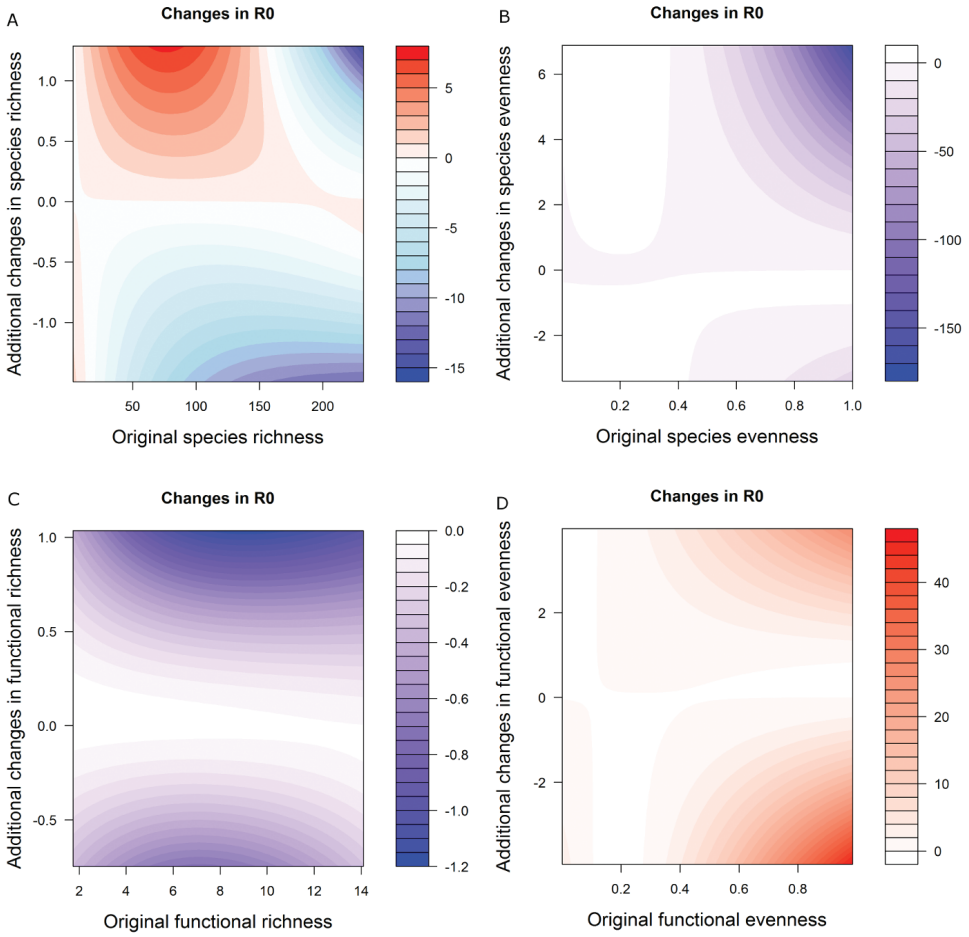

Figure 2.7 Surface maps showing interaction effects between initial values of a predictor x-axis) and changes of that predictor (y-axis) on changes of community R0 for density-dependent diseases. Colour and colour intensity indicate changes in R0: blue indicates decreased disease risk; red indicates increased disease risk.

Furthermore, when analysing only those communities in which species richness remained constant (Fig 2.6, blue dots), the interaction between original evenness and changes in evenness explained most variation in changes of risk for frequency-dependent diseases. The interaction between functional richness and change in functional richness was the most important factor for density-dependent diseases. For both types of diseases, these interaction effects were qualitatively similar to those from the complete analysis (described above).

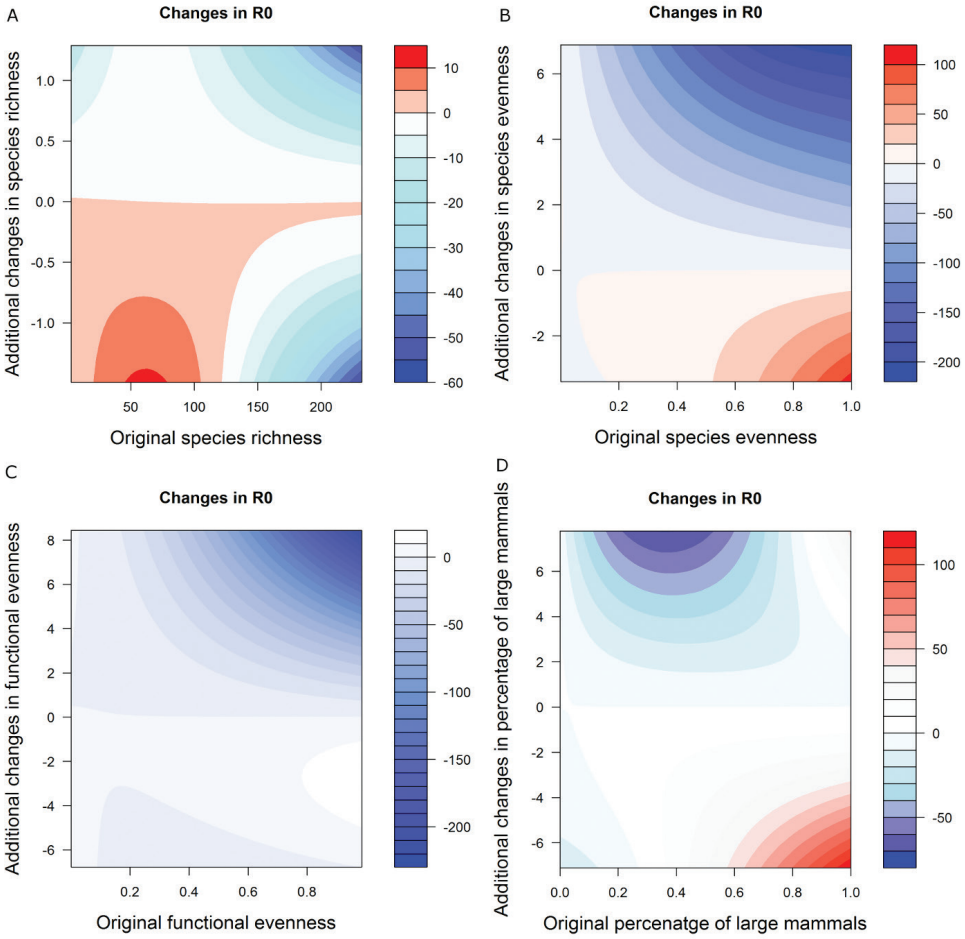

Figure 2.8 Surface maps showing interaction effects between initial values of a predictor (x-axis) and changes of that predictor (y-axis) on changes of community R0 for frequency-dependent disease. Colour and colour intensity indicate changes in R0: blue indicates decreased disease risk; red indicates increased disease risk.

Discussion

Global patterns of density-dependent disease risk and frequency-dependent disease risk

We calculated community R0 values of mammal assemblages to explore spatial patterns of disease risk for generalists pathogens with either density or frequency-dependent transmission. These R0 values, as a measure for pathogen invasion or persistence, showed clear biogeographic patterns at a global scale. Our results suggest that the current risk for

density-dependent diseases is high in developing countries in tropical regions, a result that is consistent with the results from Allen *et al.* (2017), who analysed global hotspots of emerging zoonotic diseases (EIDs) based on observed EID events. In addition, our results showed high disease risks in some developed countries in Europe and North America, e.g., Italy, Germany, France, Spain, and large parts of the contiguous United States, which is also consistent with studies of Jones *et al.* (2008). Allen *et al.* (2017) attribute the high disease risk in urban areas to reporting bias, but in our analyses, Europe and America had high disease risks due to the relatively high disease competence of the local mammal assemblages, as they had relatively more small species that are expected to be more competent for generalist pathogens (Han *et al.* 2015).

Changes in disease risk of mammal assemblages

With density-dependent transmission, more areas had an increased disease risk under scenario SSP1 (i.e., low population growth, proactive environmental protection, and low vulnerability to climate change) than scenario SSP3 (i.e., high population growth, reactive environmental protection, and vulnerability to climate changes vary regionally). The reason is that changes in disease risk for density-dependent diseases are more sensitive to changes in abundance of small species (Dobson 2004). Small species normally have large population sizes with high growth rates compared with larger species, and in this case, grow faster and expand their distribution when environmental conditions are suitable under SSP1.

Under SSP3, frequency-dependent diseases had more areas with increased disease risk, because disease risk of frequency-dependent diseases is more sensitive to the abundance of larger species (Dobson 2004). Large species with slower growth rate are more likely to go locally extinct when external conditions are not suitable under SSP3.

Drivers of changes in disease risk

Many studies have analysed the relationships between species loss and disease risks. Some studies have suggested that high biodiversity protects people from infectious diseases and that species loss would increase disease risk (Ostfeld 2009; Kilpatrick *et al.* 2017). The generalizability of these results, however, are disputed (Salkeld *et al.* 2013). We analysed the combined effect of predicted global patterns in changes in species distributions, combining both gains and losses of species. In terms of species loss, changes in disease risks are not only generated by losing species but the interaction between original species richness and changes in species richness. Disease-diversity relationships are context-specific since disease risk is determined by the competence of species that are present locally. This uncertain effects of interaction between original species richness and changes in species richness can be explained by an idiosyncratic pattern of species gains and losses that differs among mammal assemblages: sometimes competent hosts are predominantly lost which

lead to a decrease in risk, sometimes incompetent hosts are added which also lead to decrease in risk.
In addition, consistent with Dobson (2004) *and* Rudolf and Antonovics (2005), the effect of the interaction between original species richness and changes in species richness differed for diseases characterised by density-dependent or frequency-dependent transmission. For density-dependent diseases, adding host could result in an increase in transmission risk owing to increased population densities (Dobson 2004), when the original species richness is relatively low. Only when the added species decreased the abundance of the competent host, adding host decrease disease risk (Keesing *et al.* 2006a). For frequency-dependent diseases, adding hosts can reduce disease risk because adding host decrease the encounter rate between infected individuals and susceptible ones (Keesing *et al.* 2006). On the other hand, increasing the contact rate between susceptible and infected individuals can be caused by losing a non-competent host.
Changes in the interaction of original evenness and additional changes in evenness substantially affected changes in disease risks. When original evenness is relatively high, communities that become more even will experience a decrease in disease risks for both densities dependent and frequency dependent diseases. This can be explained by changes in the local densities of the different species in the mammal assemblage, as small species have relatively higher densities than larger species. An increase in evenness can be caused by a decrease in small species or an increase in large species, which both reduce disease risk as small species are more competent to pathogens than larger species.

Compared with the effect of species richness and its changes, the effect of evenness and changes in evenness is more constant, which is in agreement with earlier findings (Chen & Zhou 2015). Evenness contains not only the number of species but also the distribution of species' abundances, which is positivity correlated to contact rates among hosts (Ostfeld & Keesing 2012).

The effect of functional diversity was larger in density-dependent diseases. The interaction of functional evenness and changes of functional evenness was the most important factor when there was no change in species richness. This result highlights the importance of the distribution of functional traits (i.e. body mass) in the assemblage, which is closely related to the species' disease competence. With high original functional evenness, an additional decrease in functional evenness increases disease risk. The decrease in functional evenness can be caused by an increase in the number of small-bodied species or decrease large-bodied species, both increasing disease risk.

Our analyses show that the current spatial patterns in outbreaks of emerging infectious diseases are correlated with the mammal community structure in these areas. Local communities that have relatively more species with smaller body masses seem to be more

prone to outbreaks of these EIDs, which can be explained by the relatively higher competence of smaller species for generalist pathogens. Many studies on the relationship between diversity and diseases focussed on species loss (Ostfeld & LoGiudice 2003; Ostfeld 2009; Wood & Lafferty 2013; McCallum 2015), whereas in this study we showed that substantial changes in disease risk could occur without losing any species, which can have important implications for understanding and predicting disease risk dynamics. Hence, understanding the changes in the relative abundance of competent and incompetent hosts is pivotal for the prediction of changes in disease risk. So it is therefore urgent to focus beyond species richness, as focusing on species loss (local extinction) may underestimate the true changes in disease risk that have already occurred due to changes in species' distribution. We suggest ecologists monitor more subtle changes in wildlife community composition and to look beyond local extinction.

Appendix 2

Table A2.1 Bioclimatic variables used in the species distribution models.

WorldClim code	Variable name
BIO1	Annual Mean Temperature
BIO2	Mean Diurnal Range (Mean of monthly (max temp - min temp))
BIO4	Temperature Seasonality (standard deviation *100)
BIO7	Temperature Annual Range (BIO5-BIO6)
BIO8	Mean Temperature of Wettest Quarter
BIO9	Mean Temperature of Driest Quarter
BIO10	Mean Temperature of Warmest Quarter
BIO11	Mean Temperature of Coldest Quarter
BIO12	Annual Precipitation
BIO15	Precipitation Seasonality (Coefficient of Variation)
BIO16	Precipitation of Wettest Quarter
BIO17	Precipitation of Driest Quarter
BIO18	Precipitation of Warmest Quarter
BIO19	Precipitation of Coldest Quarter

Table A2.2 Seventeen general circulation models used in the analyses.

Abbreviation	General Circulation Model
cccma-cgcm31	Coupled Global Climate Model (CGCM3)
ccsr-miroc32hi	MIROC3.2 (hires)
ccsr-miroc32med	MIROC3.2 (medres)
cnrm-cm3	CNRM-CM3
csiro-mk30	CSIRO Mark 3.0
gfdl-cm20	CM2.0 – AOGCM
gfdl-cm21	CM2.1 – AOGCM
giss-modeleh	GISS ModelE-H
iap-fgoals10g	FGOALS1.0_g
inm-cm30	INMCM3.0
ipsl-cm4	IPSL-CM4
mpi-echam5	ECHAM5/MPI-OM
mri-cgcm232a	MRI-CGCM2.3.2
ncar-ccsm30	Community Climate System Model - version 3.0 (CCSM3)
ncar-pcm1	Parallel Climate Model (PCM)
ukmo-hadcm3	HadCM3
ukmo-hadgem1	Hadley Centre Global Environmental Model - version 1 (HadGEM1)

Table A2.3 Hypotheses and explanatory variables tested for explaining patterns in community R0 and changes thereof over time.

Category	Explanatory variable	Abbreviation	Hypothesis
Diversity	Species richness	SR	For density-dependent diseases, ↑SR means more potential hosts for pathogens and thereby ↑R0. For frequency-dependent diseases, ↑SR means diluted contact between competent species and thereby ↓R0 (Keesing *et al.* 2006).
	Species evenness	EV	Typically the abundance of small mammals is relatively larger than the abundance of large mammals. Thus, with ↑EV the relative abundance of small species would decrease and thereby ↓R0.
	Percentage of large mammals	PL	Species with a large body mass are less competent hosts to general pathogens compared with small-bodied species. Thus, a ↓PL means ↑R0.
Functional diversity	Functional richness of the body mass distribution	Frich	Species traits like body mass are related to host competence. Small species are expected to be more competent hosts. Thus, ↑Frich means a higher diversity in body masses (so decreasing the relative contribution of species with a small body mass) and thereby ↓R0.
	Functional evenness of the body mass distribution	Fev	A decrease in species with a small body mass or an increase in species with large body mass would mean ↑Fev and thereby ↓R0.

Table A2.4 Proportion of explained variance (marginal and conditional R^2) of emerging infectious disease (EID) events by community R0.

	Marginal R^2	Conditional R^2
Africa	0.34	/
Asia	0.05	/
Europe	0.25	/
North America	0.50	/
Oceania	0.15	/
South America	0.14	/
Global	0.30	0.67

Table A2.5 Proportion of explained variance (marginal and conditional R^2) by community R0 under different interspecific transmission scaling coefficients, *Cij*. The highlighted one is the one we used in the main result.

Cij value	Marginal R^2	Conditional R^2
0.0525	0.25	0.65
0.05	**0.30**	**0.67**
0.0475	0.24	0.65
0.01	0.12	0.61
0.001	0.06	0.56

CHAPTER 3

Phylogenetic structure of wildlife assemblages shapes patterns of infectious livestock diseases in Africa

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Abstract

The majority of emerging infectious disease originate from wildlife, particularly mammals, so changes in distribution and composition of mammal assemblages could change local disease risk. Several studies have focused on the impacts of biodiversity on disease risk from the aspects of biodiversity loss. However, disease risk may change due to changes in the composition of mammal assemblage that does not involve species loss. Here we use predicted global species distributions and their abundances in 2015, and 2035 to asses changes in disease risk under two different climate change scenarios. We quantify disease risk, using the community level basic reproductive ratio R0, for pathogens with either density-dependent or frequency-dependent transmission. We found that hotspots of disease risk for density-dependent diseases are concentrated in tropical and northern temperate regions; this is consistent with date from published emerging disease events. Crucially, we were able to predict where and how disease risk changed over time. Changes in community/assemblage evenness substantially and constantly affect risk for both density and frequency dependent diseases. Our results suggest that disease risk predictions based on species losses or gains strongly underestimate the impacts of assemblage on disease risks, changes in assemblage-level evenness can substantially affect disease risk before species loss occurs.

Introduction

Many pathogens can infect multiple species that vary in their ability to transmit pathogens due to differences in contact rates, susceptibility, and infectiousness (Huang *et al.* 2016; VanderWaal & Ezenwa 2016). Consequently, the diversity and composition of wildlife communities can considerably influence pathogen transmission dynamics (Ezenwa *et al.* 2006; Keesing *et al.* 2006; Joseph *et al.* 2013; Huang *et al.* 2016). Changes in host species diversity in assemblages or communities can, in theory, lead to either a 'dilution effect' or an amplification effect by altering the abundance of competent species, the rates of contact among these species, or both (Keesing *et al.* 2006). The dilution effect that high host species diversity reduces the risk of pathogen transmission can occur when incompetent species in higher-diversity communities either control the densities of competent species or the contact rates between competent species or between potential hosts and vectors (Keesing *et al.* 2006). The dilution effect has been reported in many different pathogens (Civitello *et al.* 2015; Huang *et al.* 2017), and the effect has even been labelled as a general ecosystem service of biodiversity (Bonds *et al.* 2012; Ostfeld & Keesing 2012). However, the generality of the dilution effect is disputed (Randolph & Dobson 2012; Salkeld *et al.* 2013; Wood *et al.* 2017). Assessing and understanding the relationships between host species diversity and disease risk (i.e., diversity-disease relationships) is important for predicting disease dynamics in the context of global biodiversity decline (Ostfeld & Keesing 2012; Johnson *et al.* 2015; Huang *et al.* 2016).

Most studies on the diversity-disease relationships have focused on host species richness. Although this metric is commonly used by community ecologists, this metric conveys no information about evolutionary relatedness. However, relatedness is important in disease transmission: greater evolutionary relatedness within a host assemblage means that its members are more likely to be susceptible to infection by the same pathogens (Webb *et al.* 2002; Gilbert & Webb 2007; Olival *et al.* 2017). This relationship arises from the conservatism of species' physiological traits (e.g., immunological mechanisms) that regulate host-pathogen interactions (Webb *et al.* 2002; Huang *et al.* 2013a; Olival *et al.* 2017). Consequently, the phylogenetic structure of host assemblages may influence host-pathogen interactions. To date, the role of phylogenetic structure has been mostly studied in the context of host sharing and host shifts of pathogens (Davies & Pedersen 2008; Streicker *et al.* 2010). In light of the connections highlighted above, surprisingly few studies have investigated the effects of host phylogenetic structure on disease transmission risk (Parker *et al.* 2015; Liu *et al.* 2016; Fountain-Jones *et al.* 2018).

Measures of phylogenetic diversity, an aspect of phylogenetic structure, deserve more attention in examinations of diversity-disease relationships. Phylogenetic diversity can be decomposed into two distinct components (Tucker *et al.* 2016): 1) phylogenetic richness (the

sum of accumulated phylogenetic differences among taxa), which is generally measured as Faith's index (PD) which sums the branch lengths connecting all species in an assemblage, and 2) phylogenetic divergence (the average phylogenetic difference between pairs of taxa), which is generally measured as the mean pairwise phylogenetic distance (MPD). Because these two phylogenetic diversity metrics can be influenced by species richness, standardised Faith's index (PD.Z) and MPD (MPD.Z) are commonly used to show the net phylogenetic information independent of species richness (Swenson 2014). MPD.Z is a net relatedness index (Kellar *et al.* 2015), and PD.Z can be used to determine whether an assemblage is phylogenetically overdispersed (positive PD.Z) or clustered (negative PD.Z) across terminal tips (Kellar *et al.* 2015; Mazel *et al.* 2016). However, a higher PD.Z also means that more phylogenetic information is present in an assemblage, correcting for differences in species richness. Disease risk is expected to increase with increasing PD.Z because phylogenetically richer assemblages are more likely to include one or more highly competent host species that makes an above-average contribution to disease transmission (i.e., an 'identity effect'). Disease risk is expected to decrease with increasing MPD.Z because pathogens can transmit more easily between closely related species. Until now, the relationships between net phylogenetic information and disease risk have rarely been tested (Liu *et al.* 2016), even though the general concept of diversity-disease relationships remain contentious in disease ecology.

Most studies on diversity-disease relationships have focused on individual pathogens. However, this approach overlooks the potential importance of total disease burden, that is the total number (or richness) of manifest diseases in an assemblage or community (Kilpatrick *et al.* 2017). Some studies have provided evidence for the 'diversity begets diversity' hypothesis, which generally links the diversity of pathogens (and not manifest diseases) to the diversity of species (Hechinger & Lafferty 2005; Johnson *et al.* 2015, 2016). However, pathogen diversity does not necessarily equal disease richness (Kilpatrick *et al.* 2017). For example, the complex effects of host species diversity on the risk of specific diseases (i.e., via dilution or identity effects) can complicate the relationship between host species diversity and disease richness. In addition, a species can be infected with multiple pathogens and show symptoms of a single disease or of no disease at all. Such patterns can result from different interactions among co-infecting pathogens. These interactions can be positive (e.g., immunosuppression by one pathogen facilitates infection by another), negative (e.g., competition among different pathogens), or neutral (Hawley & Altizer 2011; Kilpatrick *et al.* 2017). So far, only a few studies, which were carried out at the level of a country, have linked species diversity and disease richness, and these have shown mixed results (Guernier *et al.* 2004; Bonds *et al.* 2012; Morand *et al.* 2014). However, the coarse spatial scale of these studies presents challenges for establishing causality (Kilpatrick *et al.* 2017). Investigations at finer spatial scales may be useful in helping resolve this conflict (Kilpatrick *et al.* 2017).

One class of diseases that has wide ranging effects is infectious livestock diseases. These diseases cause huge economic losses and threaten the health of animals globally (Tomley & Shirley 2009; Wiethoelter *et al.* 2015). Since many livestock diseases (e.g., bovine tuberculosis and anthrax) also impact wild animals, they pose a threat to wildlife conservation (Tomley & Shirley 2009; Huang *et al.* 2013b). Studies on the transmission dynamics of livestock diseases in the developing world are scarce (Perry *et al.* 2013); additional research is needed to quantify the risk factors associated with these diseases. This task is particularly urgent for African countries because infectious diseases considerably impair the livestock economy, which in most cases represents a large part of the overall economy (Perry *et al.* 2013).

Many environmental factors, both abiotic and biotic, can influence the transmission of infectious livestock diseases (Perry *et al.* 2013). Climatic conditions have been well studied and are commonly linked to disease risk due to their influence on wildlife and vector distributions and pathogen survival (Guernier *et al.* 2004). Among biotic factors, livestock host density is of particular importance: high density of livestock hosts likely increases contact between infectious and susceptible individuals and facilitates disease transmission, thereby promoting disease risk (Graham *et al.* 2008). By interacting with livestock either directly (e.g., via shared resources) or indirectly (e.g., via vectors), wild animals can play important roles in livestock disease transmission (Huang *et al.* 2013b; Jones *et al.* 2013; Wiethoelter *et al.* 2015). For example, the presence of African buffalo (*Syncerus caffer*), which is a maintenance host of bovine tuberculosis (caused by *Mycobacterium bovis*), had a positive effect on the outbreak risk of bovine tuberculosis in domestic cattle (Corner 2006; Huang *et al.* 2014). Moreover, Africa is home to a large number of mammal species (Olff *et al.* 2002), and many of these species share parasites with livestock (Corner 2006).

In this study, we tested the extent to which three wildlife assemblage variables account for the variations in 1) the regional occurrence of 19 livestock diseases and 2) the total burden of these diseases (i.e., disease richness). Depending on the analysis, we also included other variables, including two livestock-related variables and several abiotic covariates. We tested several hypotheses (Table 3.1 and 3.2).

Table 3.1 Expected overall effects (positive (+), negative (–), either (+/–)) of wildlife assemblage explanatory variables (wild ungulate and carnivore species richness, phylogenetic structure) on two disease risk variables (disease occurrence and disease richness) and the hypothesised underlying mechanisms with direction.

	Disease occurrence (Risk for a single disease)	Disease richness (Total number of diseases)
Wild ungulate and carnivore species richness	(+/–) *identity effect (+) or dilution effect (-)*	(+/–) *identity effect (+) or dilution effect (-)* *'diversity begets diversity' (+)*
Standardised phylogenetic richness	(+) *identity effect (+)*	(+) *identity effect (+) or 'diversity begets diversity' (+)*
Standardised phylogenetic divergence	(–)	(–)

For disease occurrence, we predicted a positive correlation with standardised phylogenetic richness (PD.Z) due to the identity effect and a negative correlation with standardised phylogenetic divergence (MPD.Z) because pathogens can more easily transmit between closely related species. Wildlife host species richness may have either a positive effect on disease occurrence because of this identity effect or a negative effect as a result of a dilution effect. Thus, the nature of the effect of species richness depends on which effect dominates. For disease richness, we also made directional hypotheses, which were similar to those for disease occurrence, but differed slightly in terms of hypothesised mechanisms (Table 3.1).

Table 3.2 Variables (with abbreviations) used in the analyses with units and directions of predicted effects (positive (+), negative (–), either (+/–), or covariates with no a priori prediction (/)). An entry of "n/a" is used to indicate when a variable has no units and when a predictor was not included in analysis.

Category	Variable	Abbreviation	Unit	Prediction	
				Disease occurrence	Disease richness
Biotic	Wild ungulate and carnivore species richness	SR	n/a	+/-	+/-
	Standardised phylogenetic richness	PD.Z	n/a	+	+
	Standardised phylogenetic divergence	MPD.Z	n/a	-	-
	Mean phylogenetic distance to livestock	MDL	n/a	-	-
	Livestock host density	LivDen	km^2	+	+
Abiotic	Mean annual temperature	TemMean	°C	n/a	/
	Mean annual precipitation	PreMean	mm	n/a	/
	Temperature seasonality	TemSeas	n/a	n/a	/
	Precipitation seasonality	PreSeas	n/a	n/a	/
Covariate	Area of administrative unit	AREA	km^2	n/a	/

This difference results from the fact that disease richness is the product of two components: the size of the pool of potential diseases and the outbreak probability (disease occurrence) of any specific disease. In contrast to disease occurrence, disease richness can be modulated via 'diversity begets diversity', i.e., more host species equates to more niche space for different pathogens (Table 3.1). In addition, we expected, for both disease occurrence and disease richness, that the effect of phylogenetic distance between wildlife and livestock host species would be negative (since pathogens can be more easily transmitted between livestock and closely related wildlife species), and that the effect of livestock host density would be positive.

Methods

Disease data and response variables

Data on livestock diseases in Africa from 2005-2015 were obtained from the World Animal Health Information System (WAHIS; http://www.oie.int/wahid) of the World Organization for Animal Health (OIE). OIE member countries, which include almost all countries of the world, have the legal obligation to regularly report the number of cases or the state (presence/absence) of all OIE-listed (i.e., "notifiable") diseases. Notifiable diseases are defined according to specific criteria that relate to international spread and impact on humans or animals (Jebara *et al.* 2012). The data we obtained included 71 diseases that infect mammals (Appendix 3: Table A3.1). Despite their legal obligations, countries differ in how they report diseases to the OIE. For example, data are sometimes reported at the country level and sometimes at the regional (e.g., administrative unit) level; data are reported either every year, every six months, or every month. We used the lowest administrative level of reporting in our analyses, and we translated outbreak data into disease presence/absence per year. Moreover, in some countries, not all administrative units consistently reported data. We treated these as missing values in our analyses.

Several conditions were considered when determining presence/absence values for each disease. In our dataset, a missing value for a given regional administrative unit can be interpreted either as a lack of information on disease presence/absence or as a true absence (i.e., the disease was not present and therefore not reported). To address this problem, for each disease we included only the administrative units with an 'outbreak history,' which means at least one outbreak of that disease was reported in at least one year during the entire study period. By processing our data in this way, we excluded the administrative units that did not demonstrate the capacity to report data to OIE (i.e., potential false absences). We assumed that missing values from regional administrative units were indicative of true absences when that particular unit reported that same disease in another year. In our analyses, we prioritized the removal of false absences because these can strongly bias results, even though such an approach could potentially result in some true absences (i.e.,

units where outbreaks were possible, but simply did not occur over the reporting period) being overlooked.

To investigate the factors related to disease occurrence, we selected only diseases that were reported for more than 5 years and with percentages of absence ranging from 15 - 85% of the total sample. Based on these criteria, we included 19 diseases in this analysis. To investigate the factors related to disease richness, we counted the number of diseases that occurred during the entire study period for each administrative unit (Fig. 3.1). We created two different datasets of disease richness to address potential problems caused by missing values; we analysed these datasets separately and examined whether the results were consistent. In the first dataset, we treated missing values of disease occurrence at the unit level as true absences only when the country to which the unit belonged demonstrated the capacity to report that specific disease. Thus, units with disease richness ranging from 0 to 16 were included (Fig. 3.1). In the second dataset, we only included units that had an occurrence of at least one disease over the entire study period. Thus, units with disease richness of zero were excluded, and only units with disease richness ranging from 1 to 16 were included. The first dataset included 961 regional administrative units in 39 countries, comprising 91% of the 1059 regional administrative units in Africa and approximately 80% of the area of the continent. The second dataset included 832 regional administrative units in 39 countries, comprising 75% of all regional administrative units in Africa.

Wildlife assemblage explanatory variables

We calculated wildlife assemblage variables using the geographical distributions of African mammals obtained from the African Mammal Databank (AMD), which includes all African ungulate and carnivore species (Boitani *et al.* 2008). We used 176 species, belonging to 16 families in 7 orders (6 orders of ungulates, one order of carnivores). We focused on ungulates and carnivores as disease dynamics are largely determined by interactions between sympatric species, and ungulates and carnivores are most phylogenetically- and ecologically-related to livestock (Kock 2005; Wiethoelter *et al.* 2015; Han *et al.* 2016). In addition, we excluded rodents from our analyses because relatively few notifiable diseases are hosted by this group (4 of 19 diseases for disease occurrence; 11 of 71 for disease richness). Based on the AMD, we first calculated wildlife species richness (SR), defined as the total number of wild ungulate and carnivore species in an administrative unit.

Using a recently published phylogenetic tree that incorporated trees from previous studies and that included 5,020 species of mammals (Rolland *et al.* 2018), we calculated two phylogenetic diversity metrics: Faith's Index, and the mean pairwise phylogenetic distance (MPD). Because both Faith's Index and MPD can be correlated with species richness (Swenson 2014), we standardised both using a null model by shuffling the tip labels of the

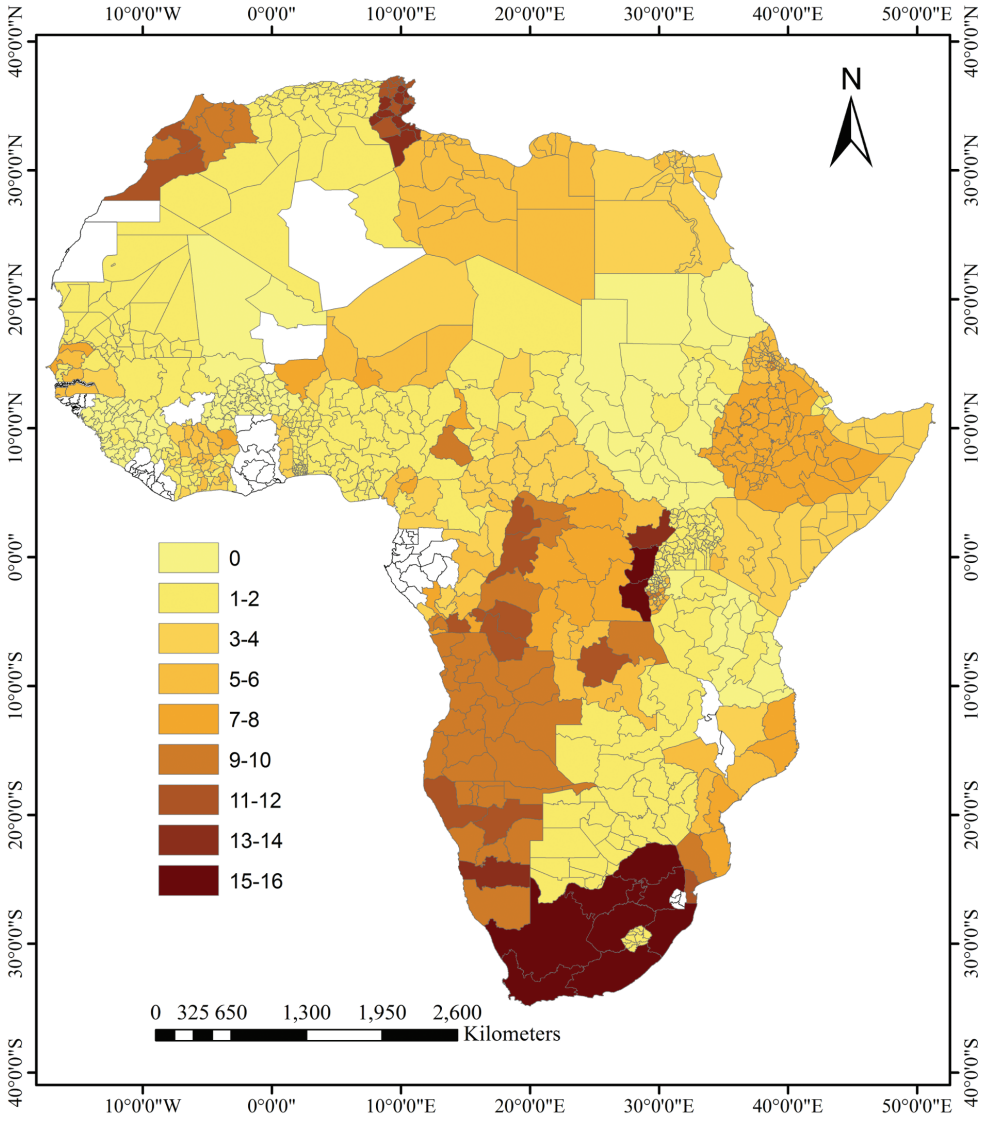

Figure 3.1 Spatial patterns of disease richness in Africa from 2005 to 2015 for each administrative unit. The map was generated using our first dataset, in which missing values about disease occurrence at the unit level were treated as true absences when the country to which the unit belonged demonstrated the capacity to report that disease. White administrative units represent missing values that do not meet these criteria.

tree. The resulting variables, standardised PD (PD.Z) and standardised MPD (MPD.Z) were independent of species richness (Swenson 2014).

Livestock explanatory variables

We calculated four livestock species-specific versions of mean distance to livestock (MDL). Each version was calculated by averaging the phylogenetic distances between a livestock species (i.e., cattle, pig, sheep or goat) and each wildlife species in a given assemblage. In disease occurrence analysis, we used the species-specific MDL for diseases with a single livestock host species, and used an average of the relevant MDL values for diseases with multiple livestock hosts. For disease richness analysis, we used an average of all four MDL values. Also for use in both analyses, we calculated livestock host density (LivDen) at the level of regional administrative unit. We used density data for cattle, pigs, sheep and goats in Africa in 2006 from the Food and Agriculture Organization of the United Nations (FAO) (Robinson *et al.* 2007). In disease occurrence analysis, we calculated LivDen by summing the density of all relevant livestock species for diseases with multiple livestock hosts, while used only that species for diseases with a single livestock host (Appendix 3: Table A3.1). For disease richness analysis, we calculated LivDen by summing all livestock species.

Abiotic covariates

In the analysis of disease richness, we also took into account several climate variables, including mean annual temperature (TemMean), mean annual precipitation (PreMean), temperature seasonality (TemSeas, among-month standard deviation*100) and precipitation seasonality (PreSeas, among-month coefficient of variation). All climate variables were derived from the WorldClim version 2.0 database (Fick & Hijmans 2017). In this analysis, we also included the area (km2) of the administrative unit.

Statistical analyses

For disease occurrence, we used a generalised linear mixed model (GLMM) with a logit link to simultaneously analyse presence/absence data for all 19 diseases. We included SR, PD.Z, MPD.Z, MDL, and LivDen as fixed variables. We also accounted for the random effects for year, country, as well as the random slope deviations for fixed factors, meaning we used a random coefficient model. Low correlations between predictors indicated little multicollinearity (Appendix 3: Table A3.2). We also found little evidence of spatial autocorrelation of the residuals using Moran's I index (Appendix 3: Table A3.3). For disease richness, we began with a linear mixed model (LMM) that included all explanatory variables (Table 3.2): SR, PD.Z, MPD.Z, MDL, and LivDen as fixed variables; TemMean, TemSeas, PreMean, PreSeas, and AREA as covariates; and country as a random factor. We then used an information theoretic approach (Akaike's Information Criterion, AICc; (Nakagawa & Freckleton 2011) to select the best models (ΔAICc < 2) from all possible models. Model averaging was used to generate parameter estimates (Nakagawa & Freckleton 2011). We tested model residuals

using *Moran's I* index and found little evidence of spatial autocorrelation (Appendix 3: Table A3.3). All analyses were conducted in R 3.4.2 with lme4 (Bates *et al.* 2015) ape (Paradis *et al.* 2004), and *MuMIn* (Barton 2015) packages.

Results

Disease occurrence

The results of our disease occurrence analysis (Table 3.3) revealed that standardised phylogenetic richness (PD.Z, OR = 1.36) had a positive overall effect on disease occurrence (Fig. 3.2), while standardised phylogenetic divergence (MPD.Z, OR = 0.89) had a negative overall effect (Fig. 3.3). In this analysis, we found no significant relationships between disease occurrence and wild ungulate and carnivore species richness (SR), mean distance to livestock (MDL), and livestock host density (LivDen).

Table 3.3 Overall effects and significance of SR, PD.Z, MPD.Z, MDL and LivDen on disease occurrence (b, model estimate coefficients; S.E., standard error).

Variables	b ± S.E.	P
SR	-0.12± 0.13	0.37
PD.Z	0.31± 0.10	<0.001
MPD.Z	-0.20± 0.10	0.04
MDL	0.17±0.06	0.27
LivDen	0.01±0.08	0.88

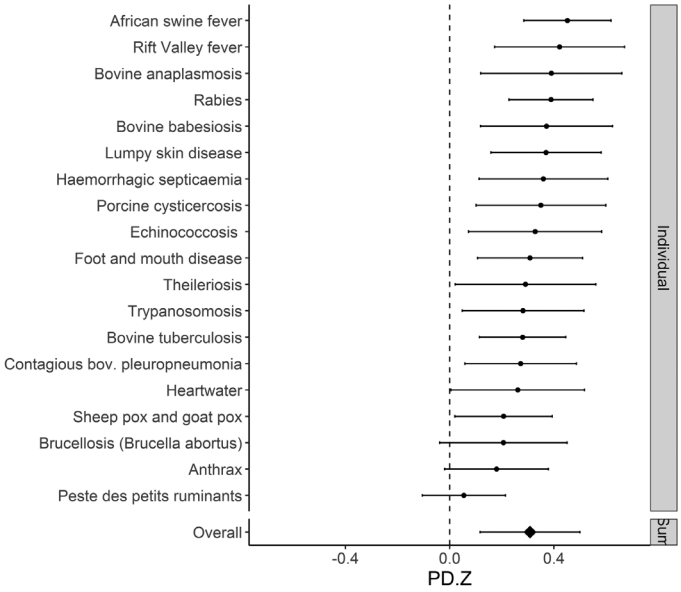

Figure 3.2 Forest plot of the effect of the standardised phylogenetic richness (PD.Z) on the occurrence of livestock diseases with 95% confidence interval for each disease (circle and bars). The average effect of all diseases is shown by the diamond.

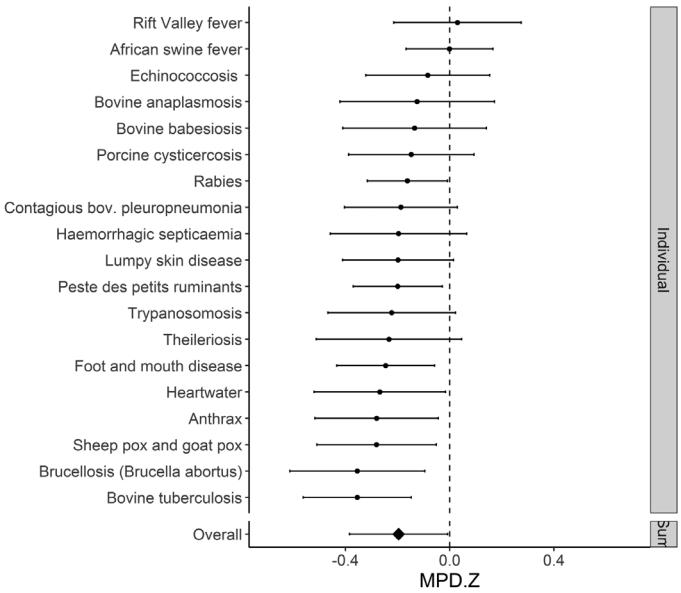

Figure 3.3 Forest plot of effect of the standardised phylogenetic divergence (MPD.Z) on the occurrence of livestock diseases with 95% confidence interval for each disease (circle and bars). The average effect of all diseases is shown by the diamond.

Disease richness

In the second analysis, two parallel approaches, which differed only in how missing values were handled (see above), gave similar results regarding which factors accounted for the variation in disease richness (Table 3.4). Wild ungulate and carnivore species richness (SR), standardised phylogenetic divergence (MPD.Z), livestock host density (LivDen), and mean annual precipitation (PreMean) were the most important factors (Table 3.4). SR and LivDen related positively to disease richness; MPD.Z and PreMean related negatively to disease richness. No other factors were identified as being important in explaining livestock disease richness.

Table 3.4 Overall results (model averaged regression coefficients (b) with their 95% confidence intervals (CI) and importance values) from disease richness analysis.

Variables	Model from data containing zeros			Model from data with no zeros		
	b ± S.E.	95% CI	Importance	b ± S.E.	95% CI	Importance
SR	0.22 ± 0.08	0.05 – 0.38	1.00	0.23 ± 0.10	0.03 – 0.43	1.00
PD.Z	0.03 ± 0.06	-0.09 – 0.14	0.08	0.02 ± 0.07	-0.11 – 0.16	0.07
MPD.Z	-0.12 ± 0.06	-0.24 – -0.01	0.90	-0.11 ± 0.07	-0.25 – -0.01	0.92
MDL	0.07 ± 0.05	-0.04 – 018	0.16	0.07 ± 0.07	-0.06 – 0.20	0.20
LivDen	0.14 ± 0.04	0.06 – 0.23	1.00	0.14 ± 0.04	0.05 – 0.24	1.00
PreMean	-0.13 ± 0.07	-0.27 – 0.01	0.89	-0.14 ± 0.07	-0.30 – 0.01	0.79
PreSeas	-0.01 ± 0.06	-0.12 – 0.10	0.08	-0.03 ± 0.07	-0.16 – 0.10	0.08
TemMean	-0.05 ± 0.07	-0.09 – 0.19	0.09	-0.02 ± 0.08	-0.14 – 0.17	0.08
TemSeas	-0.02 ± 0.12	-0.04 – 0.03	0.08	-0.04 ± 0.15	-0.33 – 0.24	0.07

Discussion

Many previous studies on the diversity-disease relationships offer support for the dilution effect (Civitello *et al.* 2015; Huang *et al.* 2017), though its generality remains a matter of debate (Randolph & Dobson 2012; Salkeld *et al.* 2013; Wood *et al.* 2014, 2017). Few of these earlier studies considered host phylogenetic diversity or focused on more than a single disease (thereby ignoring total disease burden). In our current study of 19 livestock diseases in Africa, we did not detect a significant overall relationship between wild ungulate and carnivore species richness, and regional disease occurrence. Instead, we found that disease occurrence was generally positively correlated with standardised phylogenetic richness (PD.Z) and negatively correlated with standardised phylogenetic divergence (MPD.Z). For the total disease burden, we found that disease richness was positively correlated with wild ungulate and carnivore species richness and livestock density and negatively correlated with phylogenetic divergence and mean precipitation.

For both disease occurrence and disease richness, negative correlations with standardised phylogenetic divergence suggest that assemblages composed of closely related species are more susceptible to the notifiable diseases we studied. A 'phylogenetic clade effect' may be at work. Such an effect will come about if pathogens are more easily transmitted between closely related species due, for example, to similar immunological defences or life-history traits (Huang *et al.* 2013a; Liu *et al.* 2016). In other words, assemblages composed of closely related species seem to provide favourable conditions for the spread of an infectious disease within that assemblage (Parker *et al.* 2015). Thereby, the risk of transmission to other animals, including livestock (e.g., through spillover), may be increased.

The positive correlation between PD.Z and disease occurrence might be related to the identity effect, which was first proposed to explain how biodiversity influences ecosystem functioning (Loreau & Hector 2001). In the context of the ecology of infectious diseases, key species could be determined by host competence, a species trait that is linked to phylogeny (Webb *et al.* 2002; Huang *et al.* 2013a; Olival *et al.* 2017). More phylogenetic information in an assemblage might equate to high diversity in competence. If true, phylogenetically rich assemblages would be more likely to include one or more highly competent species that makes an outsized contribution to disease transmission.

In principle, the potential identity effect may also apply to wild ungulate and carnivore species richness; however, we detected no significant correlation (positive or otherwise) between wild ungulate and carnivore species richness and disease occurrence. Some counteracting effect, for example, the dilution effect, may be to blame here (Becker *et al.* 2014; Huang *et al.* 2016). In our analyses, though, wild ungulate and carnivore species richness did correlate positively with disease richness, although the effect size was relatively small, at 1.3 over a total number of 16 diseases. Previous work in disease ecology supports the idea that 'diversity begets diversity': high species richness goes hand in hand with high pathogen richness, and ultimately high disease richness (Hechinger & Lafferty 2005; Johnson *et al.* 2015, 2016). In our analyses, the greater amount of niche space for pathogens offered by assemblages composed of many species translates to more notifiable diseases in neighbouring livestock.

In addition to wild ungulate and carnivore species richness and phylogenetic divergence, several other factors predicted disease richness. The first is livestock density, which exerted a positive influence. Previous studies have revealed positive relationships between livestock density and parasite diversity (Arneberg 2002). Higher livestock density is likely to facilitate transmission of some pathogens and facilitate disease outbreaks (Huang *et al.* 2013b, 2014). Both of these mechanisms offer insights into the positive correlation between livestock density and disease richness that we report. We were only able to use livestock density data from 2005 because data from other years were unavailable. Changes in livestock density

over time could influence relevant disease ecology relationships and may be one reason why we did not detect a significant relationship between livestock density and disease occurrence. Another significant factor is mean precipitation, which correlated negatively with disease richness. In drier areas, animals are more likely to concentrate around water sources (de Boer *et al.* 2010). Congregating in specific locations and sharing resources like water can facilitate pathogen transmission, including between wildlife and livestock, which often freely mix in African landscapes. The close association between wildlife and livestock is generally regarded as an important factor in livestock disease dynamics in Africa (Wiethoelter *et al.* 2015).

Neither disease richness nor disease occurrence correlated significantly with the mean phylogenetic distance between wildlife and livestock species. One possible explanation of this unexpected result is the low amount of variation exhibited by this phylogenetic distance index. For example, the coefficient of variation of MDLcattle was only 0.05.

Using several techniques, we endeavoured to account for reporting bias, which can be an issue with the type of data we used. For example, we compared datasets that differed in their assumptions about missing values. We also included 'country' as a random factor in an attempt to control non-independence among administrative units (e.g., in terms of veterinary service or control measures the country level). Despite much efforts we made, we must admit it is still difficult to fully account for the reporting bias. Therefore, more studies with different types (e.g., empirical, modelling, etc.) are needed to explore the role of phylogenetic structure of wildlife assemblages in the context of disease ecology. In addition, in our analyses, we did not take into account species of rodents (i.e., as potential hosts), which might also play a role driving in livestock disease outbreaks. However, excluding those livestock diseases that can also be hosted by rodents (in the analysis of disease occurrence) or including rodent species in the mammal assemblage (in the analysis of disease richness) did not meaningfully affect the results of either analysis (Appendix 3: Table A3.4). This consistency gives added confidence to the results we discuss here.

To the best of our knowledge, our study is the first to show a link between the phylogenetic structure of wildlife assemblages and disease patterns at a regional level. Specifically, our results suggest that the phylogenetic richness and divergence of the surrounding wildlife assemblage can shape patterns of livestock disease occurrence and richness in Africa. Thus, species richness alone is apparently inadequate for analyses of disease-diversity relationships, and this shortfall partly might account for current disagreements over the importance of the dilution effect. Future studies on this topic should strive to include parameters that take host phylogeny into account, in addition to the simple number of species present (i.e., species richness) in an assemblage.

Appendix 3

Table A3.1 Notifiable livestock diseases in Africa according to the World Organization for Animal Health (OIE).

Multiple species diseases, infections and infestations	Cattle diseases and infections
Anthrax	Bovine anaplasmosis
Bluetongue	Bovine babesiosis
Brucellosis (*Brucella abortus*)	Bovine genital campylobacteriosis
Brucellosis (*Brucella melitensis*)	Bovine spongiform encephalopathy
Brucellosis (*Brucella suis*)	Bovine tuberculosis
Crimean Congo haemorrhagic fever	Bovine viral diarrhoea
Epizootic haemorrhagic disease	Enzootic bovine leukosis
Equine encephalomyelitis (Eastern)	Haemorrhagic septicaemia
Foot and mouth disease	Infectious bovine rhinotracheitis/infectious pustular vulvovaginitis
Heartwater	Infection with *Mycoplasma mycoides* subsp. *mycoides* SC (Contagious bovine pleuropneumonia)
Infection with Aujeszky's disease virus	Lumpy skin disease
Infection with *Echinococcus granulosus*	Theileriosis
Infection with *Echinococcus multilocularis*	Trichomonosis
Infection with rabies virus	Trypanosomosis (tsetse-transmitted)
Infection with Rift Valley fever virus	
Infection with rinderpest virus	
Infection with *Trichinella* spp.	
Japanese encephalitis	
New world screwworm (*Cochliomyia hominivorax*)	
Old world screwworm (*Chrysomya bezziana*)	
Paratuberculosis	
Q fever	
Surra (*Trypanosoma evansi*)	
Tularemia	
West Nile fever	

Sheep and goat diseases and infections	Equine diseases and infections
Caprine arthritis/encephalitis	Contagious equine metritis
Contagious agalactia	Dourine
Contagious caprine pleuropneumonia	Equine encephalomyelitis (Western)
Infection with *Chlamydophila abortus* (Enzootic abortion of ewes, ovine chlamydiosis)	Equine infectious anaemia
Infection with peste des petits ruminants virus	Equine influenza
Maedi-visna	Equine piroplasmosis
Nairobi sheep disease	Glanders
Ovine epididymitis (*Brucella ovis*)	Infection with African horse sickness virus
Salmonellosis (*S. abortusovis*)	Infection with equid herpesvirus-1 (EHV-1)
Scrapie	Infection with equine arteritis virus
Sheep pox and goat pox	Venezuelan equine encephalomyelitis

Swine diseases and infections	Other diseases and infections
African swine fever	Camelpox
Infection with classical swine fever virus	Leishmaniosis
Nipah virus encephalitis	
Porcine cysticercosis	**Lagomorph diseases and infections**
Porcine reproductive and respiratory syndrome	
Transmissible gastroenteritis	Myxomatosis
	Rabbit haemorrhagic disease

Table A3.2 Correlation matrix among all variables.

Variable	SR	PD.Z	MPD.Z	LivDen	MDL	PreMean	PreSeas	TemMean	TemSeas	AREA
SR	---									
PD.Z	-0.35	---								
MPD.Z	-0.06	-0.49	---							
LivDen	-0.04	-0.03	0.02	---						
MDL	0.43	-0.16	-0.05	-0.11	---					
PreMean	0.11	0.04	-0.18	0.09	0.01	---				
PreSeas	0.02	-0.17	0.18	0.10	-0.08	0.07	---			
TemMean	0.06	0.02	-0.13	0.20	-0.10	0.13	-0.08	---		
TemSeas	0.26	0.13	-0.05	0.07	0.08	0.44	0.07	-0.05	---	
AREA	-0.33	0.11	-0.01	0.25	0.14	0.06	0.03	-0.16	-0.06	---
000	000	000	000	000	000	000	000	000	000	000
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000	000	000	000	000	000	000	000	000	000	000

Table A3.3 *Moran's I* of the residuals from multiple regression models to test for the presence of spatial autocorrelation.

Group	Models	Moran's I				
		(500 km)	(1000 km)	(2000 km)	(4000 km)	(8000 km)
Disease richness	First dataset	0.01	0.01	0.00	0.01	0.01
	Second dataset	0.00	0.00	0.00	0.00	0.00
Disease occurrence	African swine fever	0.00	0.00	0.00	0.00	0.00
	Anthrax	0.00	0.00	0.00	0.00	0.00
	Bovine anaplasmosis	-0.02	-0.02	-0.02	-0.02	-0.02
	Bovine babesiosis	0.00	0.00	0.00	0.00	0.00
	Bovine tuberculosis	0.01	0.01	0.01	0.01	0.01
	Brucellosis (*Brucella abortus*)	0.01	0.01	0.01	0.01	0.01
	Contagious bov. pleuropneumonia	0.00	0.00	0.01	0.00	0.00
	Echinococcosis hydatidosis	-0.01	-0.01	-0.01	-0.01	-0.01
	Foot and mouth disease	0.00	0.00	0.00	0.00	0.00
	Haemorrhagic septicaemia	0.00	0.01	0.00	0.00	0.00
	Heartwater	0.01	0.01	0.00	0.01	0.01
	Lumpy skin disease	0.01	0.00	0.00	0.00	0.00
	Peste des petits ruminants	0.00	0.00	0.00	0.00	0.00
	Porcine cysticercosis	0.02	0.02	0.02	0.02	0.02
	Rabies	0.00	0.00	0.00	0.01	0.00
	Rift Valley fever	0.00	0.00	0.00	0.00	0.00
	Sheep pox and goat pox	0.01	0.01	0.01	0.01	0.01
	Theileriosis	0.00	0.00	0.00	0.00	0.00
	Trypanosomosis	0.00	0.00	0.00	0.00	0.00

Table A3.4 Effects of predictors (standard regression coefficients) on disease occurrence and disease richness based on the new data, excluding diseases with rodent hosts, and with additional data (including the rodent distribution). * indicates significance.

Variables	Disease occurrence (removing rodent-involved disease)	Disease richness (including rodents)
Wildlife species richness (SR)	-0.08	0.09*
Standardised phylogenetic richness (PD.Z)	0.39*	0.17*
Standardised phylogenetic divergence (MPD.Z)	-0.30*	-0.28*
Mean distance to livestock (MDL)	0.12	-0.08*
Livestock density (LivDen)	-0.02	0.05*

CHAPTER 4

Host relatedness among wildlife species increases Lyme disease risk

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Zheng Y. X. Huang. Willem F. de Boer

Abstract

The effect of biodiversity change on human health is highly debated. The 'dilution effect' predicts that high vertebrate host diversity within an assemblage, often indexed by species richness, reduces disease prevalence, for example, via a reduction of the proportion of competent hosts. However, through other mechanisms, species richness may also instead increase disease risk, and this relationship is often scale dependent. The unclear relationship between species richness and disease risk necessitates a better understanding of the role of co-occurring species within the local assemblage and scale-dependency of the disease diversity relationship. For example, the probability of sharing pathogens among co-occurring species in a pool of hosts is expected to be a function of phylogenetic relationships among those hosts. Thus, host relatedness may be key to a better understanding of disease dynamics. Lyme disease is an interesting system to study the effect of host relatedness because both the agent *Borrelia burgdorferi* and its vector *Ixodes scapularis* (black-legged tick) have a wide range of host species in the United States. We studied the effect of mammal host species richness and host relatedness on Lyme disease cases. Considering the scale-dependency of disease diversity relationship, we applied the analysis at both larger and smaller spatial scales (i.e., at both the state and county levels). We also included climate and habitat fragmentation factors as covariates in our statistical analyses. We tested three predictions: 1) that the number of Lyme disease cases is negatively related to host species richness and positively related to host phylogenetic relatedness; 2) that host relatedness is a better predictor than host species richness; 3) that the effects of diversity differ between the state level and the county level (i.e., scale dependence). Our studies revealed host relatedness is a consistently important predictor of Lyme disease at both state and county level, and the effect of species richness is scale dependent. Our findings improve the understanding of the mechanisms driving infection patterns.

Introduction

In the face of global declines in biodiversity, understanding the links between biodiversity and infectious disease risk is more important than ever (Ostfeld & Keesing 2012; Pereira *et al.* 2012; Huang *et al.* 2016). Previous studies of the diversity-disease relationship mainly focussed on the effect of host species richness (Keesing *et al.* 2010; Turney *et al.* 2014; Wood *et al.* 2014). The dominant hypothesis, the dilution effect, suggests that high vertebrate host diversity within an assemblage reduces can reduce the infection risk through several mechanisms such as susceptible host regulation reduces, encounter reduction etc. (Ostfeld & Keesing 2000; Keesing *et al.* 2006). On the other hand, biodiversity may increase disease risk through many mechanisms, such as an amplification effect (Huang *et al.* 2016, 2019). The diversity-disease relationship remains debatable because of its complexity (Civitello *et al.* 2015; Huang *et al.* 2016) and its scale-dependency (Wood & Lafferty 2013; Huang *et al.* 2016). For instance, a negative relationship at a smaller spatial scale (e.g., within the forest) can change to a positive one at larger spatial scales (e.g., at landscape or regional scales; Wood & Lafferty 2013). Moreover, the dilution effect has been reported to operate for Lyme disease in North America (e.g., LoGiudice *et al.* 2008a; Keesing *et al.* 2009; Levi *et al.* 2016), but seems to be absent in Europe (Braks *et al.* 2016; Hofmeester 2019). Consequently, correlating host species richness with disease prevalence is likely insufficient for answering questions about the generality of the diversity-disease relationship. Instead, developing a better understanding of underlying mechanism is required, given that species differ in their ability to host and transmit a pathogen (LoGiudice *et al.* 2003).

Disease ecologists start to realise host phylogenetic structure (i.e., host phylogenetic relatedness) can give new insight into the important debate about disease-diversity relationships (Parker *et al.* 2015; Wang *et al.* 2019). Phylogenetic relatedness is important in disease transmission: greater evolutionary relatedness within a host assemblage means that its members are more likely to be susceptible to infection by the same pathogens (Webb *et al.* 2002; Gilbert & Webb 2007; Olival *et al.* 2017). This relationship arises from the conservatism of species' physiological traits (e.g., immunological mechanisms) that regulate host-pathogen interactions (Webb *et al.* 2002; Huang *et al.* 2013a; Olival *et al.* 2017). To date, there are only a few studies had considered the contribution of phylogenetic structure of host assemblage (Parker *et al.* 2015; Liu *et al.* 2016; Fountain-Jones *et al.* 2018; Wang *et al.* 2019), and these studies usually investigate direct-transmitted diseases, such as plant fungi disease (Parker *et al.*. 2015; Liu *et al.* 2016), avian influenza (Huang *et al.* 2019). One unresolved question is whether the effect of phylogenetic relatedness is more important than species richness in vector-borne disease; another is whether either or both species composition variables can be used in a general way to predict disease risk.

We investigated these questions using the Lyme disease system in the central and eastern United States. The etiological agent of Lyme disease is *Borrelia burgdorferi*, a spirochete that is vectored in this region of the world by *Ixodes scapularis* (black-legged tick) and maintained by multiple vertebrate hosts (Barbour *et al.* 1993). In fact, both the tick vector and the spirochete microparasite are considered generalists (Keirans *et al.* 1996). Efficient cross-species transmission of *B. burgdorferi* is a key character that has allowed the spread of Lyme disease (Hanincová *et al.* 2006). Understanding this spread and spatial differences in Lyme disease prevalence requires investigators to research potential alternative wildlife host species for the tick and the spirochete (Krasnov *et al.* 1997).

It is important to understand the role of phylogenetic relatedness of co-occurring wildlife on the number of Lyme disease cases. There are two reasons to investigate host relatedness: this variable can serve as an index of the probability that a tick encounters and successfully feeds on a new host, and the variable can serve as an index of the risk that the pathogen spills over to a new host. The encounter rate of a tick to a host is determined by the available of hosts in the assemblage (Jaenike 1990; Combes 2001). Closely related species are more likely to share the same habitat as those species have similar requirements for the environment (McCoy *et al.* 2013), so ticks can more easily feed on related alternative hosts. Successful feeding by ticks on hosts is limited by the vertebrate immune system (Barbour & Fish 1993). Since related species are expected to share some immunological characteristics (Huang *et al.* 2014), ticks can likely exploit closely related species more easily. From the point of pathogen colonization, species that are closely related are genetically and biologically more similar than distantly related ones (Harvey & Pagel 1991; Harvey 1996; Freckleton *et al.* 2002), resulting in smaller molecular, immunological barriers for cross-species transmission and establishment in new hosts (Pfenni 2000; Vienne *et al.* 2009; Longdon *et al.* 2011).

This study aims to identify patterns in Lyme disease incidence relative to the composition of co-occurring species, studying the importance of host relatedness, which may influence the presence of pathogens within an assemblage (Piesman & Sinsky 1988; LoGiudice *et al.* 2003; Wang *et al.* 2019). We also studied the scale-dependency of disease diversity relationship. To our knowledge, the effect of phylogenetic relatedness among tick hosts on disease infection prevalence has not yet been systematically investigated. Lyme disease serves as a good system for this type of investigation because the agent *B. burgdorferi* and the vector *I. scapularis* parasitise a wide range of host species. We studied the effect of species richness and host relatedness on the incidence of Lyme disease at two spatial scales; we tested whether species relatedness was a better predictor of disease risk and whether the effects of predictors are scale-dependent.

Methods

The number of Lyme disease cases in the United States was obtained from the Centers for Disease Control and Prevention (CDC; Fig. 4.1). At the state level, we used the reported number of Lyme disease cases per year for each state from 2010 to 2016 (n=285, 40 states by year combinations). At the county level, we used the reported number of Lyme disease cases per year for each county from 2000-2016 (n = 9741 unique county by year combinations). We only used data from states and counties with established or reported *I. scapularis* populations (Eisen *et al.* 2016). Since Lyme disease is in the process of spreading geographically, some reported zeros (i.e., no cases of Lyme disease detected) could represent false absences. We deleted counties where Lyme was thought to be absent in order to reduce the potential bias caused by false absences.

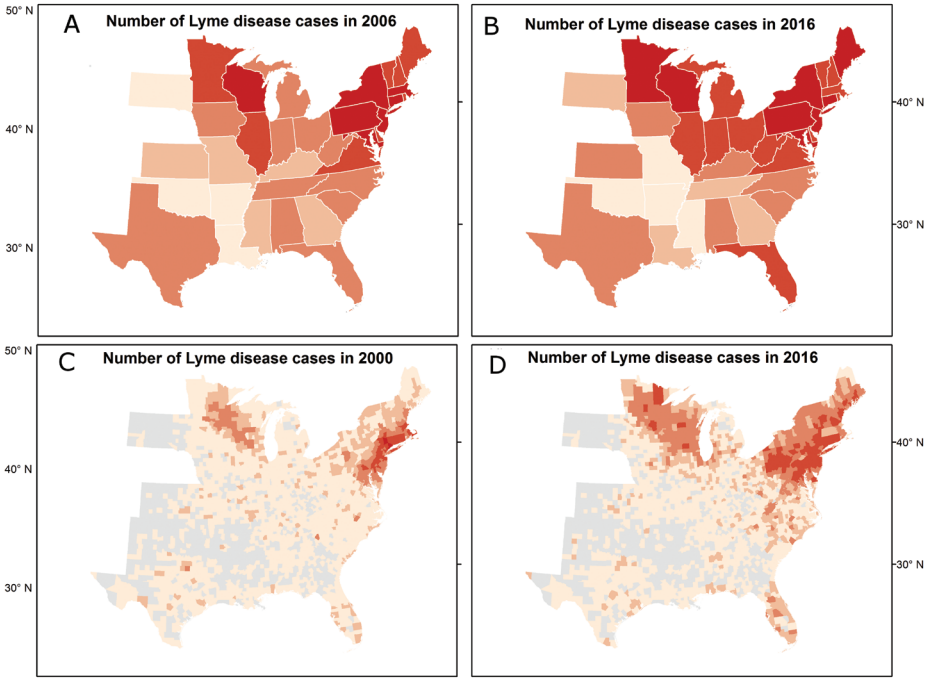

Figure 4.1 Lyme disease cases at the state level (A, B) and the county level (C, D) in the 35 states of the US with established or reported *Ixodes scapularis* populations.

The list of mammal hosts of *I. scapularis* was obtained from (Turney *et al.* 2014). To quantify the phylogenetic relatedness in different host communities, we used mean pairwise phylogenetic distance (MPD). Using the Picante package (Kembel *et al.* 2010), we calculated mean pairwise phylogenetic distance based on a phylogenetic tree that incorporated trees from previous studies and a total of 5,020 species of mammals (Rolland *et al.* 2018). Mean pairwise phylogenetic distance is hypothesised to reflect the probability that a pathogen or parasite may be shared among co-occurring hosts. Because of the potential correlation between host species richness and mean pairwise phylogenetic distance (Swenson 2014), we standardised mean pairwise phylogenetic distance using a null model by reshuffling the tip labels of the tree. The resulting standardised mean pairwise phylogenetic distance (MPD.Z) was independent of species richness (Swenson 2014; Wang *et al.* 2019).

Based on the results of a previous study on Lyme disease in the USA (Turney *et al.* 2014), we included in our statistical models six covariates that could help explain the number of Lyme disease cases. First, we included the area of deciduous or coniferous forest ("forest size") to account for the preferred habitat of *I. scapularis* (Ostfeld *et al.* 1995). Second, we included the distance of the closest border of each state and county to the closest border of Connecticut, which was identified as the place of origin of Lyme disease ("distance to source"; Barbour *et al.* 1993; Hoen *et al.* 2009). A smaller distance may positively influence the number of Lyme cases in a location (Turney *et al.* 2014). Third, we included an index of the fragmentation of preferred forest habitat ("edge density"). These first three variables were measured using ArcGIS (Version 10.5) and land cover data from the US Geological Survey (USGS; Gap Analysis Program, 2011). Since the survival of the ticks strongly depends on abiotic conditions (McCoy *et al.* 2013), we included mean annual temperature and mean annual precipitation for each state and county. These two climate variables were derived from the WorldClim version 2.0 database (Fick & Hijmans 2017). Lastly, we included the area (km^2) of the state or county.
We investigated relationships between host species diversity (species richness and MPD.Z) and the six variables described above and the number of Lyme disease cases per year (Table 4.1). Human population size was included as an offset. At the state level, we used a Poisson model with an observation-level random effect (Elston *et al.* 2001) to deal with over-dispersion of the data. At the county level, we used a negative binominal model with state as the random factor. Both models were analysed using lme4 package, and all variables were scaled using the function scale in R (version 3.5.0).

Lastly, we fitted a piecewise SEM (Lefcheck 2016) to infer the direct and indirect effects of climate, habitat condition, and host biodiversity on the number of Lyme disease cases at both the state and county levels (Appendix 4: Fig A4.1). Under this approach, we first constructed a generalised linear mixed effects model for the number of Lyme cases with SR, MPD.Z, and distance to the origin as predictor variables. We also constructed linear

mixed effects models for MPD.Z using fragmentation as a predictor and for SR using habitat (fragmentation and forest size) and climate (temperature and precipitation) variables as predictors. We report the standardised coefficient for each path from each component model. Coefficients were scaled by means and standard deviations so that comparisons can be made even if the measurements have different units. We also report marginal and conditional R^2 values, which indicate the variation explained by fixed factors only (marginal R^2) or fixed and random factors (conditional R^2). The overall fit of the piecewise SEM was evaluated using Shipley's test of d-separation. Fisher's C statistic and AIC, which were calculated with the 'piecewiseSEM' R package (Table 4.2).

Results

The number of Lyme disease cases was negatively correlated with mean pairwise phylogenetic distance (MPD.Z) at both the state and county levels (Fig. 4.2-4.4); thus, communities with relatively more closely related species had more Lyme cases. Mammalian host species richness (SR) was negatively correlated with the number of Lyme disease cases at the state level (as expected based on the dilution effect hypothesis); however, SR was positively correlated with the number of Lyme cases at the county level (Fig. 4.2-4.4). At both the state and county levels, the MPD.Z effect size was larger than the SR effect size.

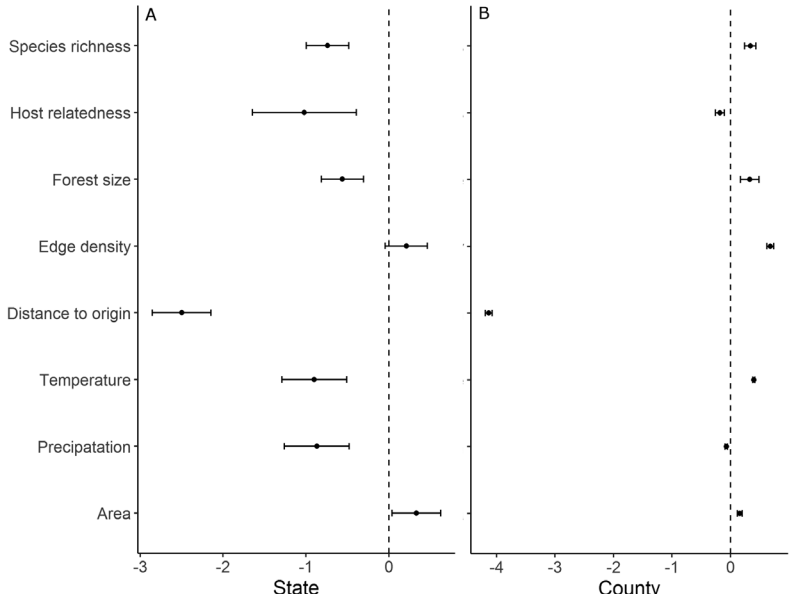

Figure 4.2 Standardised regression coefficients from GLMMs explaining variation in the number of Lyme disease cases at both the state (A) and county (B) levels.

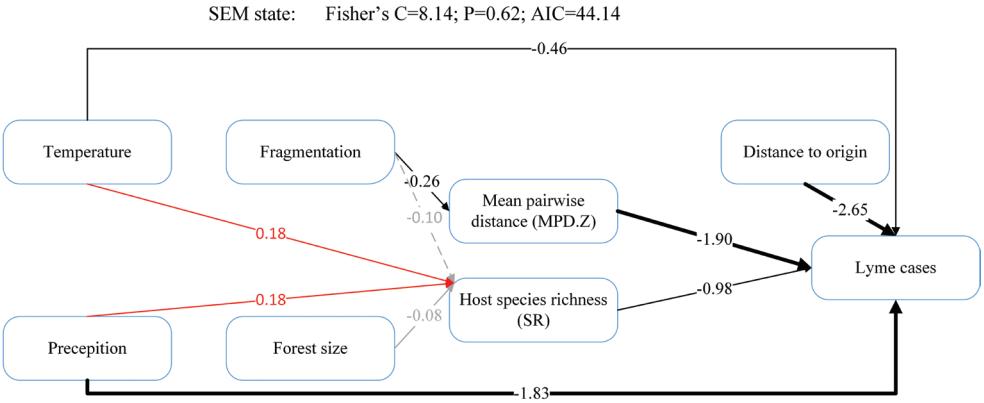

Figure 4.3 Piecewise Structural Equation Model (SEM) of climate, habitat, and biodiversity predictors of the number of Lyme cases at the state level. Solid red arrows represent positive paths (P<0.05), solid black arrows represent negative paths (P<0.05) and dotted grey arrows represent non-significant paths (P>0.05). We report the path coefficients as standardised effect.

Our SEM analyses demonstrated that the influence of fragmentation (i.e., "edge density") and forest size on the number of Lyme cases were mediated through MPD.Z and SR (Fig. 4.3, Fig. 4.4). Temperature and precipitation impacted the number of Lyme cases both directly and indirectly through species richness (Fig. 4.3, Fig. 4.4).

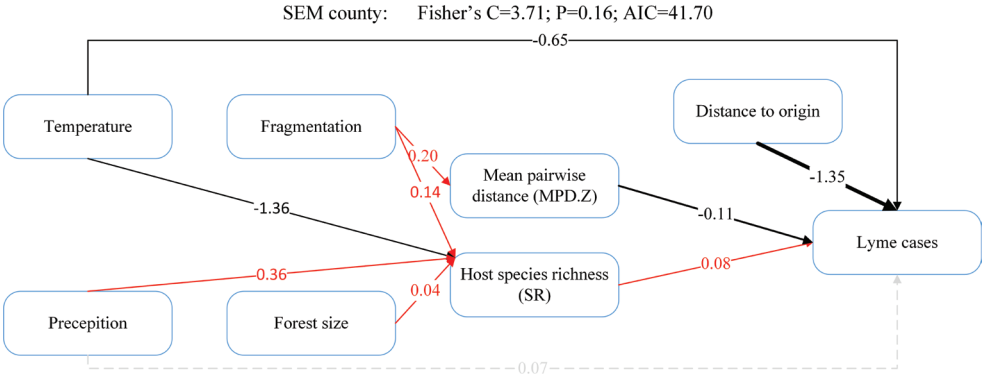

Figure 4.4 Piecewise Structural Equation Model (SEM) of climate, habitat, and biodiversity predictors of the number of Lyme cases at the county level. Solid red arrows represent positive paths (P<0.05), solid black arrows represent negative paths (P<0.05) and dotted grey arrows represent non-significant paths (P>0.05). We report the path coefficients as standardised effect sizes.

Discussion

Biodiversity affects the risk of Lyme disease for humans (LoGiudice *et al.* 2003; Wood & Lafferty 2013). Our analyses revealed a strong effect of phylogenetic relatedness on the number of Lyme cases: at both the state and county levels in the USA, mammal assemblages that are composed of species that are more phylogenetically related are associated with more reported Lyme cases. Rodents in particular and small mammals more generally are more competent than other species for ticks and tick-borne pathogens (Richter *et al.* 2004; Barbour *et al.* 2015). An assemblage with many species of rodents or small mammals is likely to be characterised by a high degree of phylogenetic relatedness (Appendix 4: Fig A4.2- A4.4) and a high risk of Lyme disease. The relationship between species richness and the number of Lyme disease is scale dependent. The effect of phylogenetic relatedness is apparently additional to the effect of species diversity (Wang *et al.* 2019).

The risk of Lyme disease to humans from aspects of phylogenetic relatedness and species richness

Two mechanisms underlying the transmission of Lyme disease to humans must be considered. First, ticks acquire the spirochete microparasite that causes Lyme during their larval or nymphal stages while feeding on infected rodents (Lane *et al.* 1991; Fig. 4.5); second, these infected ticks moult and then sometimes feed as nymphs or adults on other animals and humans, potentially infecting them (Diuk-Wasser *et al.* 2006; Fig. 4.5). Both mechanisms are mediated by the assemblage composition from both aspects of host relatedness and species richness.

With the first mechanism (Fig. 4.5), assemblage composition affects the probability that a larva feeds on a potentially infected host. From the aspect of host relatedness, close relatives of a competent host species often share the same ecological niche (McCoy *et al.* 2013), and contact rates between suitable hosts and ticks should increase. Because of the high contact rates between ticks and of those phylogenetically close relatives of the competent host, tick would increase their abundance and can complete life history easily, and which results in an increase of the number of Lyme disease cases. From the aspect of species richness, at the state level, we found that species-rich assemblages had a relatively lower risk, i.e., reported fewer Lyme disease cases. In these species-rich assemblages, relatively more non-competent hosts might dilute the densities of competent hosts (e.g., the white-footed mouse, *Peromyscus leucopus*); thus, the feeding rate of ticks on infected hosts decreases (LoGiudice *et al.* 2003). In other words, the probability that a larva feeds on a competent and infected host and becomes infected itself will be lower.

With the second mechanism, the composition of assemblage affects pathogen transmission from infected ticks to new hosts (Fig. 4.5), and the pathogen can survive in the new host,

in other words, the new hosts get infected. From the aspect of host relatedness, most tick species specially feed on phylogenetically closely related host species (Esser *et al.* 2016b). Feeding success of the vector, *I. scapularis* can be strongly limited by the immunity of its vertebrate host (*Biology of Ticks* 1993). Closely related species have similar immunological responses and thus can serve as alternative hosts (Gilbert & Webb 2007; Davies & Pedersen 2008; Losos 2008; Wiens *et al.* 2010; Longdon *et al.* 2011; Cavender-Bares & Reich 2012). In addition, as with the tick vectors, microparasites, such as the spirochete that causes Lyme disease, are also more likely to exploit host species that are phylogenetically closely related (Esser *et al.* 2016) because of shared biological traits (Jorge *et al.* 2014). When B. burgdorferi is transmitted from an infected tick to a new mammalian host (Fig. 4.5), the spirochete's survival depends on the susceptibility (and thus the immune system) of that host (Tilly *et al.* 2008). If an assemblage is composed of species that are closely related to some competent host, then many, if not all, of those related species are expected to also function as hosts, at least to some extent. More potential host species means increased transmission to and from ticks, increased parasite fitness, and ultimately, in the case of *B. burgdorferi*, increased risk of Lyme disease. From the aspect of host richness, when species richness is high, the probability of an infected nymph feeding on and transferring the pathogen to an uninfected, but competent host would be lower. Both mechanisms are associated with reduced disease risk and thus fewer cases of Lyme disease in humans.

With the second mechanism, besides the assemblage composition, the transmission of *B. burgdorferi* from infected ticks to humans (and thus the number of Lyme disease cases) depends on the contact rate between the two. This contact rate can be influenced by the size of suitable habitat and its fragmentation (Allan *et al.* 2003; Li *et al.* 2012; Ostfeld *et al.* 2018). The contact rate of ticks and humans is higher in smaller patched (Killilea *et al.* 2008; Estrada-Peña 2009), leading to an interaction that promotes Lyme disease in humans. Those small patches have a higher number of infected ticks, which make the condition even worse (Allan *et al.* 2003). Small, highly fragmented habitats generally lose many vertebrate species, especially larger ones (Blake & Karr 1987; Rosenblatt *et al.* 1999). However, rodents, which are competent hosts of *B. burgdorferi*, are more resistant to these habitat effects (Nupp & Swihart 1996). The relative abundance of a species like the white-footed mouse is often high in small patches so that the fraction of ticks feeding on this very competent host species increases. The amount of infected tick would be very high as a result. These two pathways (high contact rates and a high number of infected ticks) act together in promoting Lyme cases disease in humans.

Scale dependency of effect of species richness to Lyme disease cases

Our analyses also showed that the relationship between the number of Lyme disease cases and host species richness was scale dependent (see also: Wood & Lafferty 2013; Huang *et al.* 2016; Halliday & Rohr 2018). The negative relationship between species richness

and the number of Lyme disease cases (i.e., a dilution effect) was found at the state level, replicating the results of Turney *et al.* (2014), who used the same database but did not study the effect of host species phylogenetic relatedness. However, a positive relationship (i.e., an amplification effect) was detected when analysing the smaller county-level spatial scale. What could explain these different patterns? Even though our study includes the smallest states in the US, these political units are nevertheless relatively large (median size = 120,700 km^2). Halliday and Rohr (2018) conclude that an amplification effect of species richness is more likely to occur at larger spatial scales, where abiotic factors like climate vary sufficiently to influence species distributions (i.e., of both hosts and pathogens). However, in our study and in Trney *et al.* (2014), analyses at the state level showed an inverse relationship between species richness and the number of Lyme disease cases that is consistent with a dilution effect.

We offer two possible explanations for these results. First, the percentage of species in an assemblage that are Lyme disease hosts in general and the percentage of species in an assemblage that are rodent hosts both decreased as species richness (including host species and non-host species) increased at the state level (Appendix 4: Fig. A4.5, A4.6). Thus, increasing species richness apparently dilutes the relative abundance of hosts in these two categories, thereby leading to a reduction in the number of Lyme disease cases. Second, at these larger (state-level) spatial scales, the larger spatial heterogeneity prevents the spread of the disease by limiting the movement of host species or the contact rate among those host species, and thereby result in this negative effect of host species richness.

At county level, we found a positive relationship between species richness and the number of Lyme disease cases. Halliday and Rohr (2018) proposed that the dilution effect is more likely to occur at local scales (< 100 km^2), but in my study, counties (median size = 1,600 km^2) are larger than the smallest spatial scales (100 km^2) analysed by Halliday and Rohr (2018). In our county-level analyses, the relationship between species richness and the number of Lyme disease cases was positive overall; however, species richness had a strong nonlinear effect. A dilution effect was revealed at lower levels of species richness, while an amplification effect was revealed at higher levels of species richness (Appendix 4: Fig. A4.7, A4.8). This scale dependency within counties requires further investigation. In addition to species richness, the absolute abundances of the hosts, especially key hosts such as the white-footed mouse, might be a critical factor. In very species-poor communities, such hosts can reach very high densities (LoGiudice *et al.* 2003). This discrepancy of effect of species richness on disease risk at two spatial scales (county vs. state) raises the need for more analyses that incorporate data on the absolute and relative abundance of competent hosts species.

In summary, our analyses show that the effect of species richness on the number of Lyme cases is scale dependent, the positive effect at county scale and the negative effect at state

scale. In addition to species richness and any changes thereof, phylogenetic relationships among the mammals in an assemblage play a role in dictating disease dynamics. Communities composed of phylogenetically closely related mammal species facilitate pathogen persistence and circulation, resulting in an increase in disease risk for humans. Hence, in the future, phylogenetic relatedness must be taken into consideration when attempting to understand diversity-disease relationships.

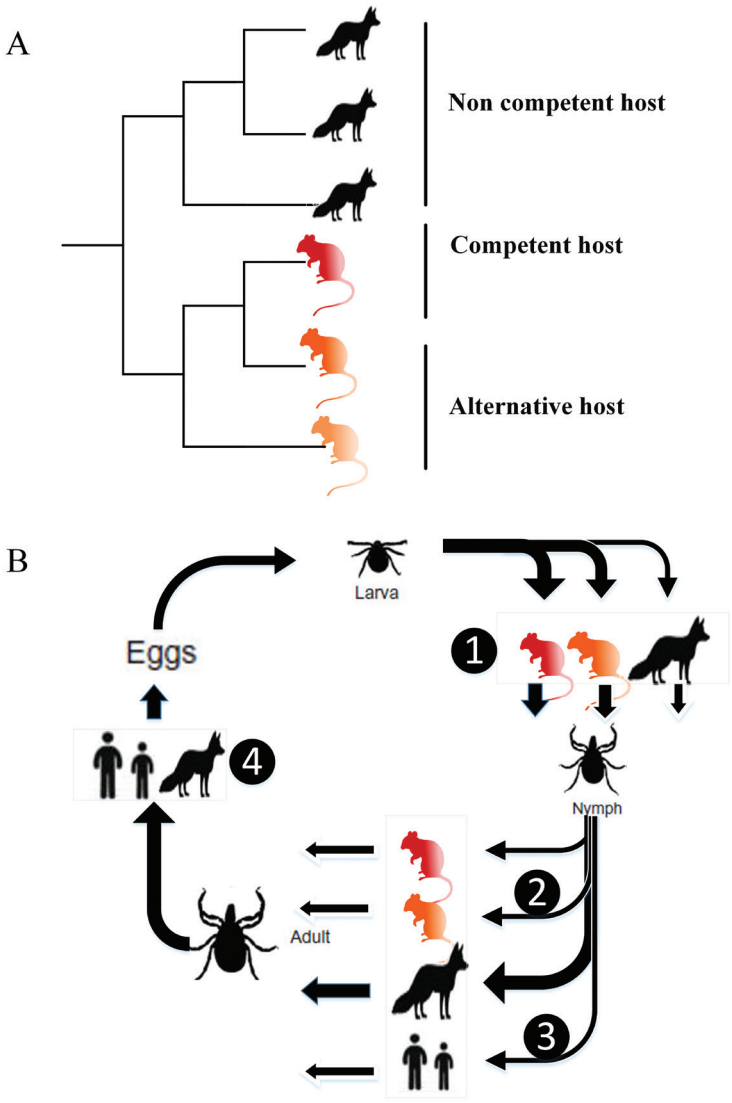

Figure 4.5 A conceptual model of assemblage and environmental factors that regulate the risk of Lyme disease. (A) A hypothetical phylogeny of host species that differ in their competence. Red indicates the highest competence for an ectoparasite vector or pathogen; yellow alternative hosts are less competent. (B) A simplified scheme of Lyme disease transmission among ticks, wild mammal hosts, and humans. Arrow thickness indicates the relative percentage of feeding to a certain host. ①: Larva feeds on the host (first blood meal); *B. burgdorferi* transmitted from infected host to tick. ②: Infected nymph feeds on small mammal (i.e., competent hosts or alternative hosts); *B. burgdorferi* transmitted from infected nymph to new host. ③: Infected nymph feeds on larger (non-competent) mammals or human. ④: Adult feeds on larger (non-competent) mammal or human.

Table 4.1 Factors included in the analyses with abbreviations, units and their predicted effects (positive (+), negative (–), either (+/–), or covariates with no a priori prediction (/)). An entry of "n/a" indicates that variable is unit-less or that no specific prediction was made or tested.

Category	Predictor	Abbreviation	Unit	predicted effects (state)	predicted effects (country)
Biotic	Host species richness	SR	n/a	+/–	+/–
	Standardised mean pairwise phylogenetic distance (host relatedness)	MPD.Z	n/a	–	–
Habitat	Forest size	CA	n/a	+	+
	Edge density	ED	n/a	+	+
Climate	Mean annual temperature	MeanTem	°C	+	+
	Mean annual precipitation	MeanPre	mm	+	+
Covariate	Area of administrative unit	AREA	km^2	n/a	n/a
	Distance to origin	DIST_C	km	n/a	n/a
Offset	Population size	pop.size		n/a	n/a

Table 4.2 Model fits of the SEMs illustrated in Figs. 4.3 and 4.4.

Model fits	Marginal R^2	Conditional R^2	Marginal R^2	Conditional R^2
Spatial scale	State	State	County	County
Lyme cases	0.72	0.72	0.39	0.61
Host relatedness (MPD.Z, standardised mean pairwise phylogenetic distance)	0.06	1.00	0.04	0.40
Host species richness (SR)	0.07	1.00	0.23	0.89

Appendix 4

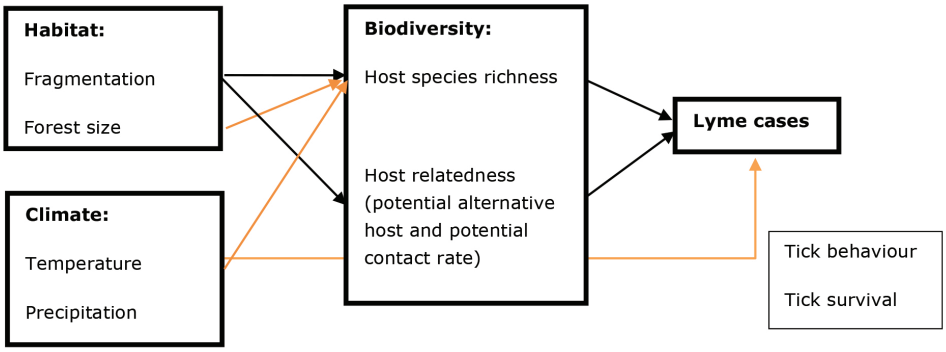

Figure A4.1 Schematic diagram showing the major factors governing spatial variation in the number of cases of Lyme disease. Red arrows represent positive paths; black arrows represent negative paths.

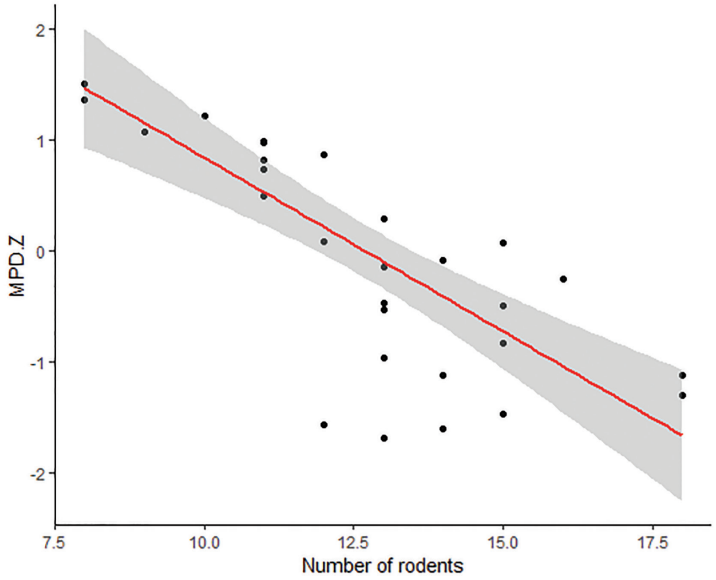

Figure A4.2 The negative relationship between the total number of rodents species in local assemblages negatively related to and host relatedness (MPD.Z) in the same community. (R^2 =0.53; Intercept= 3.98; Slope= -0.31; P <0.01).

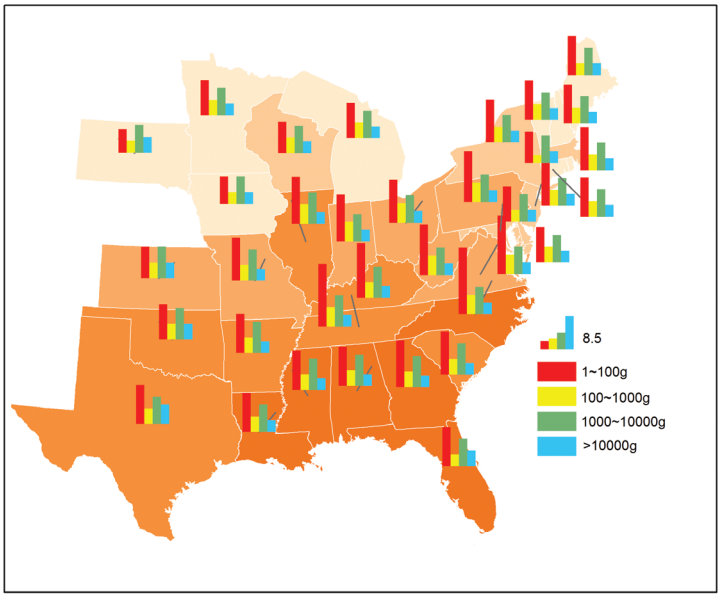

Figure A4.3 Distribution of body mass of hosts (inset bar graphs) per state and phylogenetic relatedness in host community (shading: the redder the more closely related more intense orange equates to greater relatedness) per state.

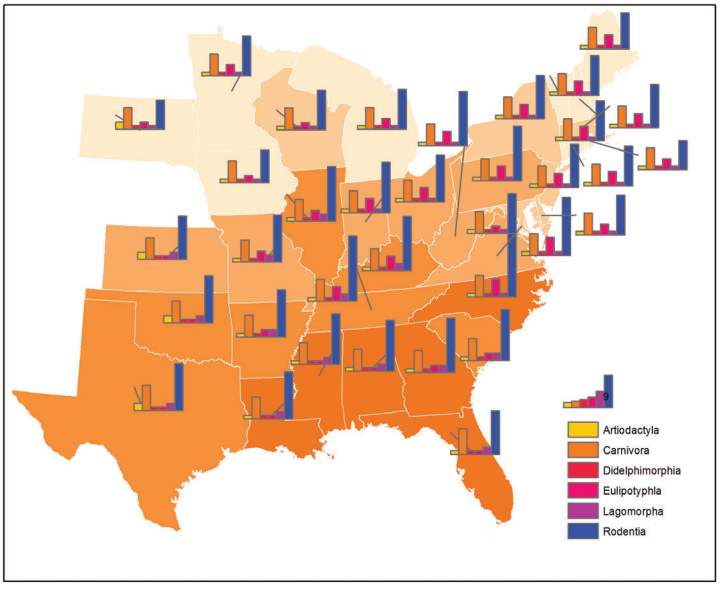

Figure A4.4 The composition of hosts per state (inset bar graphs) and phylogenetic relatedness (more intense orange equates to greater relatedness) per state(shading: the redder the more closely related).

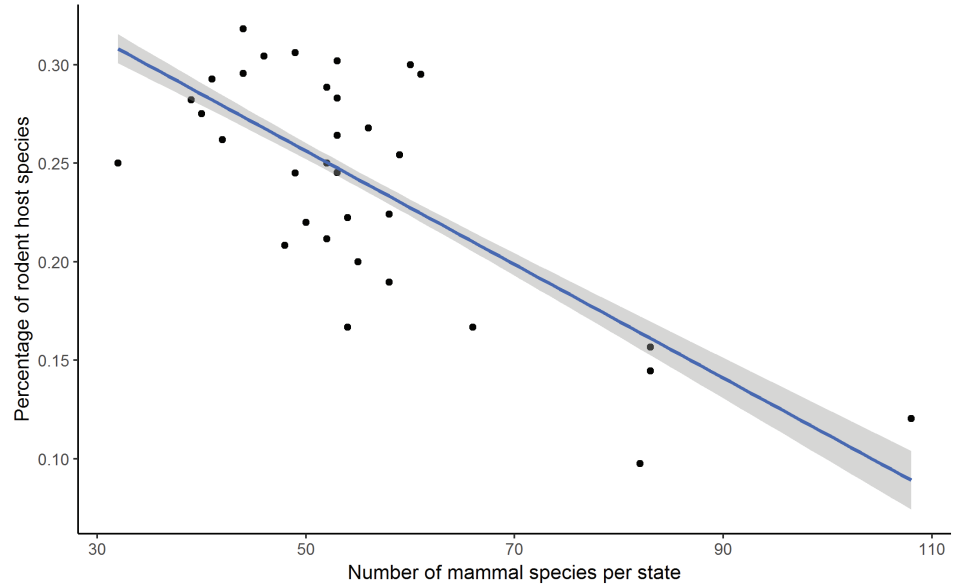

Figure A4.5 The percentage of rodent species in local assemblages is negatively related to the total number of mammal species per state (R^2 =0.53; Intercept= 0.24; Slope= -0.82; *P* <0.01).

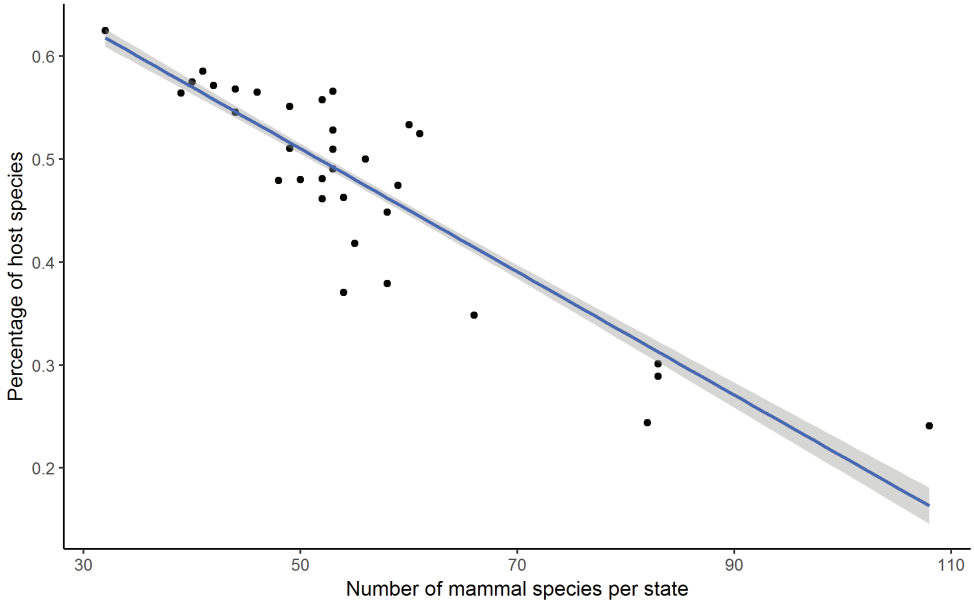

Figure A4.6 The percentage of host species over total number of mammal species in local assemblages is negatively related to the total number of mammals species per state (R^2 =0.78; Intercept= 0.48; Slope= -1.7; *P* <0.01).

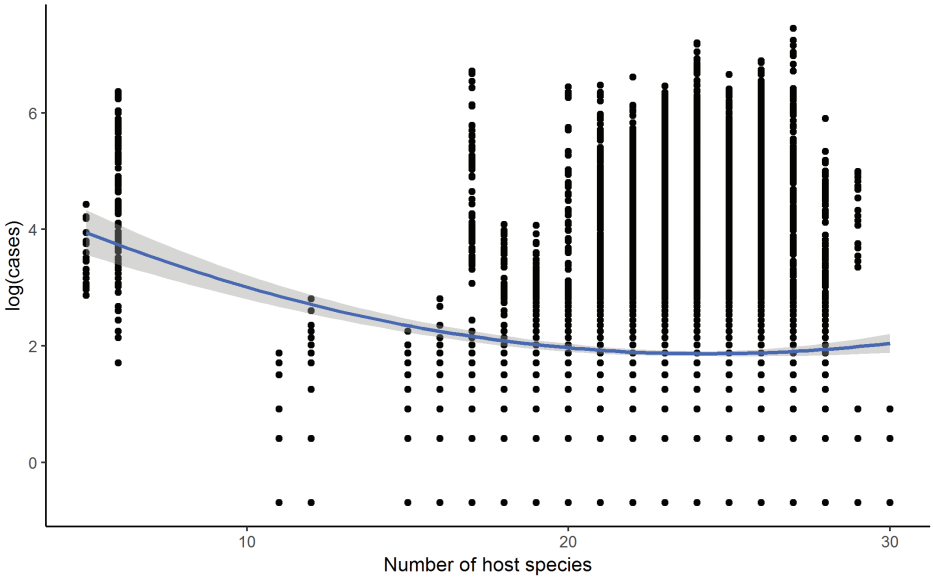

Figure A4.7 The total number of host species is related nonlinearly with the number of Lyme cases (natural log scale).

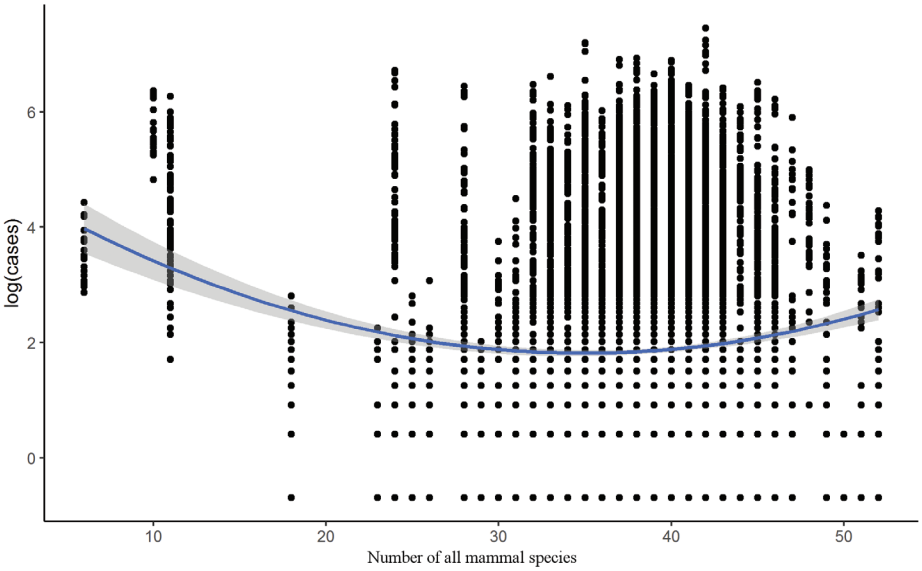

Figure A4.8 The total number of all mammal species is related nonlinearly with the number of Lyme cases (natural log scale).

CHAPTER 5

Similarity among host species assemblages and habitat connectivity shape the spatial expansion of Lyme disease

Yingying X. G. Wang, Kevin D. Matson, Yanjie Xu, Herbert H. T. Prins, Zheng Y. X. Huang. Willem F. de Boer

Abstract

Understanding the factors behind the spread of infectious diseases over time and across the landscape is critical for managing disease risk. This process of disease spread can be influenced by the suitability of disease-free areas, which can be measured by β-diversity (i.e., spatial differences in the similarity of the host species assemblage). Also, habitat connectivity affects disease spread by limiting or facilitating the movement of host and vectors. In light of the rapid expansion of Lyme disease, insights into the effect of β-diversity in combination with other ecologically germane factors are urgently required. We analysed the yearly numbers of Lyme disease cases from 2000 through 2016 from the United States at county level by examining the roles of similarity of local host assemblage (β-diversity), vegetation, habitat connectivity, and climate (i.e., temperature and humidity). Our results indicate that high β-diversity and a high degree of habitat connectivity jointly increased the probability that Lyme disease spreads from an infected county to a neighbouring disease-free county. Our results enhance the understanding of disease spread and are important for early detection and prevention of infectious disease.

Introduction

Understanding the spatial expansion of infectious disease is important in predicting the new geographic areas that would have disease presence, and of importance in disease management (Smith *et al.* 2002). The spreading rate of disease is not the same over different direction in space, which indicates the variation in spatial suitability for both host and vector (Estrada-Peña 2003). This raises a question of what factor influences the non-random spread of disease over space.

In general, the non-random expansion of disease via hosts or vectors is probably at least partly explained by characteristics of both the local and the neighbouring host assemblages (Guernier *et al.* 2004). For example, the suitability of local host assemblage (disease-free assemblage) and the intensities of infected neighbours. The suitability of the assemblage can be described by β diversity (i.e., Jaccard similarity; Dornelas *et al.* 2014), can influence the likelihood that a disease can invade a new area. The greater ecological similarity between an area that is infected and one that is uninfected means less resistance for disease spread, thus have high suitability to disease spread. Also, the intensities of infected neighbours, which can be measured by the number of reported Lyme disease cases, relate positively to the probability of transition from uninfected to infected. The reason is that high intensities of infected neighbours indicate high prevalence rates of the Lyme pathogen in ticks and hosts, which would enhance the chances that infected host or ticks invade to the disease-free county.

Range expansion of disease also depends on landscape structure variables that influence dispersal of infected hosts and vectors (Reisen 2009; Kilpatrick & Randolph 2012). Habitat connectivity can be used to understand the process of disease spread via its effect on the dispersal ability of host and vectors. For example, increasing landscape connectivity promotes outbreaks of plague among prairie dog colonies (Stapp *et al.* 2011).

More important, the three factors described above (suitability of the assemblage in a disease-free area, the intensity of infection in an area where the disease is present, and connectivity between disease-free and infected areas) likely do not work alone, for example, the effect of the intensity of infection in an area where the disease is present may depend on the connectivity level; rather, interactions are expected to influence the geographical expansion of infectious disease.

Here, we invested the effect of roles of the suitability of the assemblage in a disease-free area (i.e., the similarity of local host assemblage and infected neighbours; β-diversity) and the intensities of diseased neighbours and their two-way interactions on the spread of Lyme disease. Lyme disease is caused by *Borrelia burgdorferi* and transmitted by *Ixodes*

ticks (Steere *et al.* 1978), is recognised as an important emerging infection. Lyme disease in the United States undergoes rapid range expansions from the east coast to the southeast (Lantos *et al.* 2015). However, the rate of expansion varied within and among states. For example, some parts of states (i.e., counties) are rapidly invaded, whereas others remain disease-free for years. Not only Lyme disease but also the tick vector in expanding in range. For example, *I. scapularis* has moved northward along the eastern shores of Lake Michigan (Hamer *et al.* 2010), while also spreading across the state from west to east in Wisconsin (Lee *et al.* 2014). The large geographic range of Lyme disease and *I. scapularis* combined with the non-random spatial patterns in colonisation raise important questions about the mechanisms driving the expansion of this emerging infectious disease (Eisen *et al.* 2016).

Hence, we predict a positive relationship between the similarity in host assemblage composition between neighbouring areas that differ in their infection status (i.e., one infected and one disease free) and the probability that the disease-free area will become infected. We also predict that the intensity of infection in an area where the disease is present (i.e., the number of reported Lyme disease cases) will relate positively to the probability of transition from disease-free to infected.

In the case of Lyme disease, the dispersal and establishment in new areas of *I. scapularis* depend on the possibilities of dispersal of the tick hosts, and these possibilities of dispersal depend on both species movements and landscape characteristics. The former relates to the inherent capacities of host species to move (i.e., some species can more easily move over larger distances than other); the latter relates to parameters that help (e.g., corridors) or hinder (e.g., barriers) these movements. Because the dispersal probability of species that host *I. scapularis* partly drives the spread of Lyme disease (Watts *et al.* 2009; Walter *et al.* 2016), we predicted a positive relationship between habitat connectivity the probability of transition from disease-free to infected.

Considering the effect of the interactions, we explicitly examined the importance of two-way interactions to the transition in disease status of an area. In addition to our predictions about each individual mechanism, we predict that the probability of disease status transition is highest when higher suitability of the assemblage in a disease-free area (i.e., the similarity between disease-free area and diseased area) together with high connectivity. To our knowledge, the role of these interaction effects on disease expansion has not yet been systematically investigated. Understanding the ecological complexity underlying the spatial expansion of emerging infectious diseases will help ensure the success of programs aimed at the early detection and prevention of these diseases.

Methods

Lyme disease data

We first obtained the annual number of human Lyme disease cases in each county in the United States from 2000 until and including 2016 from the Centers for Disease Control and Prevention (CDC, Fig. 5.1). We then limited our dataset to only those counties with established or reported *I. scapularis* populations, according to Eisen *et al.* (2016). Our focus was on identifying and understanding those counties that transitioned in their Lyme disease status. Per year, we targeted only those counties that were both disease free, and that shared a border with at least one county where Lyme disease was present in that same year. We then determined, also on an annual basis, whether a disease-free county remained disease free the next year or became infected. This binomial classification served as the dependent variable in our analyses.

We described β diversity using the Jaccard similarity index, which we calculated using the function *vegdist* in vegan package in R (Oksanen *et al.* 2013). We used the list of mammal host species of *Ixodes scapularis* from Turney *et al.* (2014). The distributions of these species were then obtained from the IUCN (IUCN 2015). We also calculated forest habitat connectivity, which was calculated as the minimum percentage of forest over the two 1-km buffers on both sides of a shared border between two counties. Forest habitat connectivity was calculated using ArcGIS (Version 10.5) based on land cover data from the USGS (United States Geological Survey, Gap Analysis Program, 2011). Moreover, because the survival of ticks strongly depends on abiotic conditions (McCoy *et al.* 2013), we included mean annual temperature and mean annual precipitation as covariates in the model (Table 5.1).
All climate variables were obtained from the WorldClim version 2.0 database (Fick & Hijmans 2017).

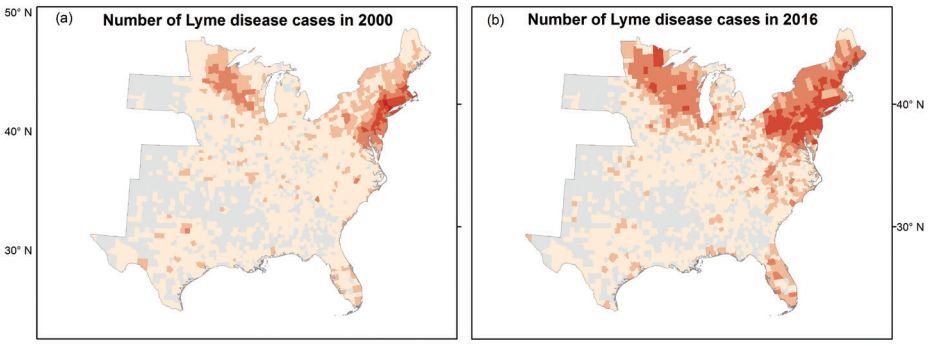

Figure 5.1 The distribution of Lyme disease cases at the county level in 2000 and 2016 in the 35 states of the United States with established or reported *Ixodes scapularis* populations.

The intensities of disease in infected neighbouring counties (i.e., the numbers of reported Lyme disease cases) were weighted using the following formula: length of the shared border between a disease-free focal county and an infected neighbour divided by the total border length of the focal clean county. Thus, an infected neighbouring county with a larger percentage of the shared border was given greater weight. Host assemblage similarity and habitat connectivity were also weighted by the percentage of the shared border between disease-free and infected counties (Table 5.1).

Data analysis

To understand the probability of Lyme infection at the county level (i.e., the transition from a disease-free county to a county with reported Lyme cases), we investigated three factors and their interactions: 1) host assemblage similarity between the disease-free and infected counties, 2) intensity of infection in the neighbouring infected county or counties, and 3) habitat connectivity between the disease-free and infected counties. Mean annual temperature and mean annual precipitation of the disease-free focal counties were included as covariates, and human population size of the disease-free focal counties was included as an offset. We used a Generalized Linear Mixed Model (GLMM) with a binominal distribution that included state and year as random factors (*lme4* package); all variables were scaled

Table 5.1 Hypotheses and explanatory variables used in influencing the spatial spread of Lyme cases in the United States.

	Explanatory variables used	Hypotheses
β diversity	The similarity of host assemblage	Counties with high similarity in hosts species with infected neighbours would have a higher disease risk.
Connectivity	Connectivity with respect to forest habitat	Counties with high connectivity with infected neighbours would have a lower risk.
Disease intensity of neighbours	Disease intensity (number of Lyme cases) of neighbouring counties	Counties close to heavily infected neighbours would have a higher risk.
Temperature	Annual mean temperature	Higher temperature and precipitation support establishment tick and contribute to the expansion of the distribution range of ticks (Gray et al. 2009; Medlock & Leach 2015)
Precipitation	Annual mean precipitation	
Shared borders	Length of shared borders with infected neighbours (km)	The similarity of host assemblage and connectivity are weighted by shared borders. Similarity values with a long shared border were given more weight.
Percentage of shared borders	Percentage of shared borders with infected neighbours over the total length of the clean county (%)	Disease intensity of neighbours is weighted by the percentage of shared borders.
Population size	Human population	Counties with high population density may have a high disease risk.

prior to their inclusion (*scale* function). Since all two-way interactions were significant, we maintained the full model and made interaction plots (*sjmisc* package). All analyses were conducted using R (version 3.5.0).

Results

A significant interaction between the intensity of infected neighbouring counties and habitat connectivity meant that intensity of infection exerted stronger effects on the probability of infection transition (from disease-free to infected) when the two counties were well connected in terms of forest habitat (Table 5.2; Fig. 5.2) compared to if they were poorly connected. Overall, the transition probability went from 20% to 90% as the border-weighted number of Lyme cases in neighbouring counties increased.

A significant interaction between host assemblage similarity and habitat connectivity meant that the Jaccard similarity index exerted stronger effects on the probability of infection transition (from disease-free to infected) when the two counties were poorly connected in terms of forest habitat (Table 5.2; Fig. 5.3) compared to if they were well connected. Overall, the transition probability was higher in areas with high habitat connectivity. As the border-weighted number of Lyme cases in neighbouring counties increased, the transition probability went from 21% to 24% in areas with low connectivity and from 26% to 27.5% in areas with high habitat connectivity.

Table 5.2 Full results (model coefficients (b) with their 95% confidence intervals (CI) and *P* values) of the Generalized Linear Mixed Model (GLMM) explaining the probability of county-level transition in disease status from Lyme disease free to Lyme disease present.

Model	b	95%CI	*P*
Weighted_ intensity of neighbors	0.21	0.17~0.24	<0.001
Weighted_connectivity	0.05	0.01~0.09	0.07
Weighted_similarity	0.06	0.02~0.10	<0.001
Weighted_ intensity of neighbors * Weighted_connectivity	0.05	0.01~0.09	0.02
Weighted_similarity * Weighted_connectivity	-0.04	-0.08~-0.01	0.03
Temperature	-0.36	-0.40~0.32	<0.001
Precipitation	0.002	-0.03~0.04	0.91

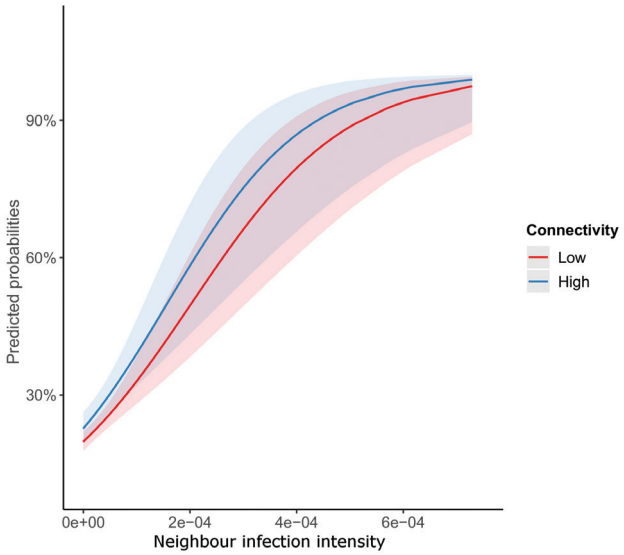

Figure 5.2 The interaction effect of the prevalence of the infected neighbouring county and the habitat connectivity on the predicted probability that a disease-free county reports the presence of Lyme disease. Red indicated low habitat connectivity; blue indicates high habitat connectivity.

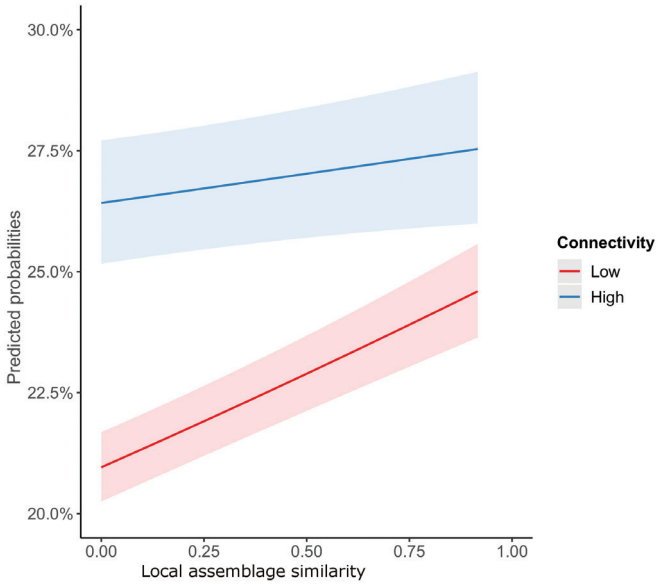

Figure 5.3 The interaction effect of the similarity in host species assemblage and habitat connectivity on the predicted probability that a disease-free county reports the presence of Lyme disease. Red indicates low habitat connectivity; blue indicates high habitat connectivity.

Discussion

The spread of Lyme disease involves the two processes: the success of dispersal and establishment of infected hosts or vectors (Altizer *et al.* 2006). For the first process, the success of dispersal is the product of dispersal potential and movement of host animal from county to county. More specific, the dispersal potential depends largely on the abundance of host and vectors and the prevalence of the Lyme pathogen in ticks and hosts (Watts *et al.* 2018). We found a significant interaction effect between the intensity of infection and habitat connectivity, which attribute to the success of dispersal of infected host and vector. In heavily infected counties, the number of ticks and the prevalence rates of the Lyme pathogen in ticks and hosts are both expected to be high. The higher number of tick and prevalence of pathogen enhanced the chances that infected host or ticks invade to the disease-free county. But the success of dispersal depends on the habitat connectivity, with higher the habitat connectivity, the effect of infection intensity is greater, increasing the probability of a transition in disease status.

For the second process, the establishment of infected hosts or vectors depends on the suitability of new areas (Watts *et al.* 2018). We found that a significant interaction between host assemblage similarity and habitat connectivity, the probability of the transition from disease-free to infected always increased with increasing similarity in host assemblage. However, the effect size of the host assemblage similarity decreased when the habitat connectivity level was relatively high. Still, high host assemblage similarity combined with high habitat connectivity had the highest predicted probability for a transition in disease status. The reason can be that higher host assemblage similarity might indicate high similarity in habitat and resource, and infected host can adapt to the new environment quickly; also for the establishment of ticks, which cannot occur without suitable hosts (Hofmeester *et al.* 2016; Watts *et al.* 2018). High similarity in host assemblage supply similar hosts and thus facilitate the establishment of vectors. In addition, for Lyme disease, the dispersal and establishment of the vector in new areas depend on the movement of hosts that vector feed on. Thus in this paper, the effect of similarity in host assemblage depends on the habitat connectivity, which affects the movement of hosts. However, the interaction effect is negative, that is to say, with well-connected habitats, the movement of hosts is facilitated, and the transition in disease status can occur even when the host assemblage similarity is not very high: host assemblage similarity is unimportant when host species can move easily across county borders. Our study showed that host species assemblage structure and habitat configuration could facilitate the range expansion of Lyme disease. Our results, therefore, provide valuable insights into the underlying mechanisms that influence the spread of diseases.

CHAPTER 6

General discussion

Biodiversity is decreasing rapidly (Dirzo *et al.* 2014). Most infectious emerging diseases originate in wildlife (Wolfe *et al.* 2007), and many of these diseases have multiple host species. Changes in biodiversity (i.e., host and non-host species) have been linked to changes in disease risk. Specifically, the emergence of those diseases often results from changes in interactions among wildlife, livestock, and people and in combination with changes in land use and climate (Alberti 2005; Alirol *et al.* 2011; Zhan *et al.* 2018). Understanding the mechanisms behind disease-diversity relationships, e.g., how disease risks change with changes in biodiversity, is critical for disease prevention and management (Keesing *et al.* 2006; Huang *et al.* 2013b; Allen *et al.* 2017).

Many studies have focused on understanding the effect species richness changes on the transmission of parasites and disease pattern (Ostfeld & Keesing 2012). In an assemblage, an increase in species richness can either decrease or increase disease risk by different mechanisms. One hypothesised disease-diversity relationship is the dilution effect, a negative relationship between biodiversity and disease risk (Schmidt & Ostfeld 2001; Keesing *et al.* 2006; Ostfeld & Keesing 2012). Some empirical studies show that as biodiversity is lost, disease risk increases (Wood *et al.* 2014; McCallum 2015). However, the generality of the dilution effect and the mechanisms behind it are still debated (Salkeld *et al.* 2013; Civitello *et al.* 2015). For example, the occurrence of dilution effect depends both on observation scale and on relationships between host extinction and host competence (Kilpatrick *et al.* 2017). Moreover, species richness can also be positively correlated to disease risk (i.e., amplification effect; Wood *et al.* 2014) because higher species richness may result in a large abundance of pathogens and thus increase disease risk (Keesing *et al.* 2010).

The objective of my thesis is to enhance the current understanding of the links between disease risk and biodiversity and how these links are influenced by changes in habitat and climate. Previous studies have focussed mainly only on species richness when exploring disease-diversity relationships (Keesing *et al.* 2006, 2010; Wood *et al.* 2014); however, biodiversity is multidimensional and can be quantified using a variety of indices (e.g., ones based on composition, functional traits, phylogenetic relationships, or β diversity). Incorporating these indices into studies of disease ecology can provide new insights into disease-diversity relationships (Chen & Zhou 2015). This study was among the first to consider essential aspects of biodiversity beyond species richness. In this final chapter, I synthesise the results of my work and discuss how they contribute to a better understanding of the ecology of disease outbreaks.

Is species richness a good indicator of disease risk?

Many studies about the dilution effect use species richness as a measure of biodiversity. It is important to study whether species richness is a good indicator. My results indicate that species richness is not always sufficient to fully understand the differences in disease risks (Table 6.1). This is supported by the following three aspects:

1. The direction of the effect of species richness on disease risk depends on the transmission type.
   In Chapter 2, I used the community-level basic reproduction ratio R0 (i.e., community R0, the probability that a pathogen can invade and persist in a local assemblage) to measure the disease risk. McCallum et al. (2015) suggested that it is how biodiversity changes, and not the biodiversity per se that affects disease risk. I therefore calculated both the original species richness and the changes in species richness and studied the interaction effect between these. My result did not support the ideas of McCallum et al. (2015). Both changes in species richness and original species richness jointly impacted disease risk. I found that for density-dependent diseases, an increase in species richness can either increase or decrease disease risk, depending on the level of original species richness (i.e., an interaction effect). For frequency-dependent diseases, changes in species richness also interacted with the original species richness. An increase in species richness decreased disease risk, but a decrease in species richness had a nonlinear effect. Disease risk increases when original species richness is low but decreases when it is high. These results indicate that the relationships between species richness and disease risk are context-specific, since disease risk is determined by the competence of the species that are present in the assemblage and the changes therein. These contrasting effects (i.e., increase or decrease in risk) can be explained by an idiosyncratic pattern of species gains and losses. For example, disease risk increases when competent hosts are lost and decreases when incompetent hosts are added.

2. The effect of species richness on disease risk depends on the measurements of disease risk.
   In Chapter 3, I studied the effects of mammal species richness on the presence/absence of diseases in 19 different livestock diseases and also on total disease burden (i.e., the number of different livestock diseases). Pathogens can spread directly from wildlife to humans or first spillover to livestock species and then to humans. The majority of cases of zoonotic pathogen spillover goes via livestock to humans (Karesh *et al.* 2012). Thus, livestock with a high disease risk poses a potential risk to humans. I found that species richness was not significantly correlated with the presence/absence of diseases (neither negative nor positive), but species richness was positively correlated with disease richness. The positive relationship between species richness and disease richness can

be explained by the theorem of "diversity begets diversity", as more mammal species supply more niches for different pathogens, which leads to more manifested diseases (Hechinger & Lafferty, 2005; Johnson *et al.* 2016).

3. The effect of species richness on disease risk depends on the spatial scale of observation.
   In Chapter 4, I studied the number of Lyme disease cases in the United States at both state scale and county scale. The negative relationship between species richness and the number of Lyme disease cases (as expected when a dilution effect operates) was found at state level. However, a positive relationship (similar to an amplification effect) was detected when analysing the data at the smaller county-level scale. These results suggest that the relationship between species richness and disease risk is scale-dependent. Halliday & Rohr (2018) concluded that a dilution effect is more likely to occur at small scale (<100 km2) where species interactions are strong and that an amplification effect is more likely to occur at regional spatial scales (> 1,000,000 km2). However, this does not necessarily conflict with my result, because my study was carried out at intermediate spatial scales (e.g., medium size of state = 120,740 km2 and medium size of county = 1,600 km2). At these intermediate scales, Halliday and Rohr (2018) assumed that both amplification and dilution effects could occur. To conclude, my results demonstrate the scale-dependency of the relationship between species richness and disease risk and suggest that multiple scales of studies are needed to fully understand disease-diversity relationships.

New insight into disease-diversity relationships

Many studies of disease-diversity relationships focus on species loss, and some propose that species loss increases disease risk (Ostfeld 2009; Kilpatrick *et al.* 2017). In my analysis (Chapter 2), I found that disease risk can still change when species richness remains constant. The reason is that, even before species loss occurs, the composition (i.e., absolute and relative densities of species) changes. The result suggests that composition and structure of wildlife assemblages are more important than species richness in affecting disease risk, which is in agreement with earlier findings (Chen & Zhou 2015). One relevant measure of assemblage composition and structure is evenness. Compared with species richness, evenness contains not only the number of species but also the relative differences in species' abundances, and these abundances are positively correlated with contact rates among hosts (Ostfeld & Keesing 2012). I also studied the influence of functional diversity in shaping disease risk. The interaction of functional evenness and changes of functional evenness was the most important factor in scenarios with constant species richness. This result highlights the importance of the distribution of functional traits, such as body mass, which is closely related to the species' disease competence (Johnson *et al.* 2012). My study thus suggests

that measurements of biodiversity that concern the structure of local assemblages and the distribution of species competences should be used in studying disease-diversity relationships.

The spatial spread of infectious diseases over time and across landscapes is also an important aspect of disease risk. My results (Chapter 5) suggests that shared characteristics of local and neighbouring animal (i.e., host) assemblages (e.g., β diversity) are important for the spread of infectious diseases. Results show a positive influence of this similarity on the spread of Lyme disease and an interaction between similarity and forest connectivity between counties. Not only the composition of the species within an assemblage affects disease risk, but also the similarities or differences between different assemblages.

I also took into account the phylogenetic relationships within local assemblages. Phylogenetic relatedness is important in disease transmission (Gilbert & Parker 2016; Wang *et al.* 2019), which is not a random process. Pathogens are more likely to transmit among closely related species compared to phylogenetically distant ones (Webb *et al.* 2002; Kuiken *et al.* 2006; Olival *et al.* 2017). For these reasons, understanding phylogenetic relationships in local assemblages can deepen our understanding of both disease risk dynamics the relationship between this risk and biodiversity. In addition, in this context, investigating phylogenetic relationships within local assemblages can help us better understand why species richness can have both positive and negative effects on disease risk.

In my analyses, especially in **Chapter 3** and **Chapter 4**, phylogenetic relatedness more consistently explains disease patterns than species richness (Table 6.1). Mean pairwise distance (MPD; note: low MPD equates to high phylogenetic relatedness) was negatively correlated with both disease presence/absence and disease richness (**Chapter 3**). In vector-borne disease systems, the effect of MPD is also consistently negatively correlated with disease risk (i.e., the number of Lyme disease cases; **Chapter 4**) at two spatial scales (county level and state level; Table 6.1). When an assemblage had a low MPD (i.e., were more phylogenetically related), more Lyme disease cases were reported.

The effect of phylogenetic relatedness suggests that if the species in an assemblage are closely related, the assemblage is expected to have a higher disease risk, both in the presence of individual diseases and in the number of different manifested diseases. With Lyme disease, assemblages composed with more closely related species have a higher number of Lyme disease cases at both county level and state level. The reason can be that those closely related species share similar life-history traits and immunological defences (Harvey 1996; Freckleton *et al.* 2002; Streicker *et al.* 2010). Higher similarity in host species leads to smaller molecular, and immunological barriers for cross-species transmission of

pathogens. With Lyme disease, this is true for both the spirochete microparasite and ticks (Longdon *et al.* 2011).

Considering the important role of host phylogenetic relatedness in multi-host systems (Wang *et al.* 2019), studying this type of relatedness can help elucidate mechanisms behind the conflicting effects of species richness on disease risk (i.e., dilution effect vs. amplification effect; Fig. 6.1). If increasing species richness is the result of additional closely related species, then phylogenetic relatedness will decline. For direct-transmitted diseases, a pathogen can spillover from one species to another more easily because those closely related species have often, to some degree, similar immunological responses and can thus serve as alternative hosts (Gilbert & Webb 2007; Longdon *et al.* 2011). Also, closely related species are more likely to co-occur at the same ecological habitat (McCoy *et al.* 2013) as they are (to some extent) ecologically similar and have similar environmental requirements. However, closely related species are also expected to strongly compete for limited resources, but this does not mean that these species cannot co-exist. Close relatives normally have divergent traits under the influence of competition (Schluter 2000), which permits their co-occurrence. Hence, the contact rates among those closely related species can be higher. Both of these two mechanisms, shared immunological responses and shared habitats, can increase disease risk. For vector-borne disease, these processes also involve vector feeding success, which can also be limited by the immunological responses of the hosts (Longdon *et al.* 2011). When a local assemblage becomes phylogenetically more diverse because of increasing species richness, both pathogens and vectors are less likely to spillover among species. As a consequence, disease risk decreases (i.e., a dilution effect occurs).

Table 6.1 Summarised effect of biodiversity on disease risk with different indicators. (+: positive effect, -:negative, /; no significant effect; Blank: not included in their studies).

Disease risk	Measure of diversity				
	Species richness	**Evenness**	**Functional evenness**	**MPD**	**β diversity (similarity among assemblages)**
Community R0 (Chapter 2)					
For density-dependent disease	Interaction effect of the original species richness and changes in species richness (+/-)	Interaction effect of the original evenness and changes in evenness (-)	Interaction effect of the original functional evenness and changes in functional evenness (+)		
For frequency-dependent disease	Interaction effect of the original species richness and changes in species richness (+/-)	Interaction effect of the original evenness and changes in species evenness (+/-)	Interaction effect of the original functional evenness and changes in functional (+)		
Disease presence and absence for 19 livestock disease (Chapter 3)	/			-	
Disease richness (Chapter 3)	+			-	
Number of cased of Lyme disease (Chapter 4)					
At country level	+			-	
At state level	-			-	
Range expansion of Lyme disease (Chapter 5)					The interaction effect of similarity and forest habitat connectivity (+)

Note: Phylogenetic relatedness is measured by the standardised mean pairwise distance (MPD.Z). The smaller the value, the closer the assemblage is phylogenetically.

Phylogenetic relatedness can also affect disease risk independently of species richness (Fig. 6.2A). Higher phylogenetic relatedness can increase disease risk because of the higher contact rates and lower immunological barriers among closely related species (including competent species; Fig. 6.2A, Scenario 1). Low host phylogenetic relatedness among species within an assemblage reduces disease risk since transmission of the pathogen to distantly related species is less likely (Fig. 6.2A, Scenario 2).

Because measurements of phylogenetic relatedness, e.g., the mean pairwise phylogenetic distance (MPD), may correlate with species richness (Swenson 2014), I used a standardised

version of MPD to study the effect purely of phylogenetic relatedness. My results strongly support that that effect is independent of that of host species richness. In summary, at assemblage level, phylogenetic structure is a better indicator for disease risk than species richness and thereby adds to our understanding of disease-diversity relationships (Parker *et al.* 2015; Wang *et al.* 2019).

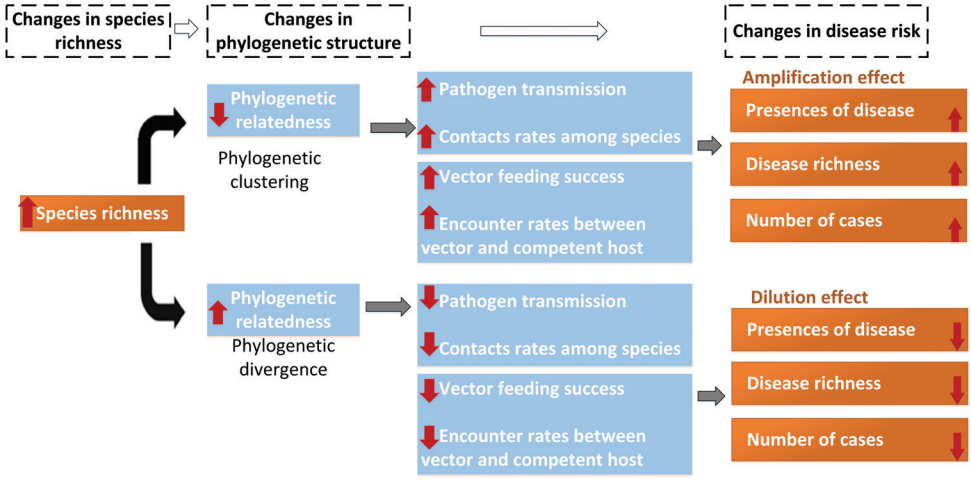

Figure 6.1 Conceptual diagram of the effect of species richness on disease risk by affecting phylogenetic relatedness within the local assemblage. When species richness increases, phylogenetic relatedness can either increase or decrease. If it decreases phylogenetic relatedness value (phylogenetic clustering), disease risk will increase because, for example, contact rates among species including competent species increase, thus amplification effect occurs; if it increases phylogenetic relatedness value (phylogenetic divergence), disease risk will decrease as transmission of pathogen to phylogenetically distant species are lee likely to occur, thus dilution effect occurs.

Analyses incorporating phylogenetic relatedness show that disease risks of assemblages are predictable with the same or different species richness. However, the question remains: how can disease risk differ if two assemblages are the same in both species richness and phylogenetic relatedness? To answer this, the relative abundance of species must be considered (Fig 6.2B). One approach is to weight the phylogenetic relatedness by abundance (i.e., species with large abundances will be given more weight). Weighting by abundance is often useful in the analyses of assemblages because species are rarely equally abundant. The distribution of abundances of different species holds important ecological information for influencing disease risk. For example, if a species that dominates in the assemblage is also a competent host for a pathogen, then this assemblage would have a higher disease

risk. Moreover, weighting phylogenetic relatedness with species abundances will add valuable information, particularly if certain species dominate the assemblage (Webb *et al.* 2002; Anderson *et al.* 2004; Mi *et al.* 2012). For example, if species with large abundances are closely related, the phylogenetic relatedness (MPD.Z weighted by abundance) would become much smaller than the unweighted value. Assemblages with dominant and related species show a clear clustering in phylogeny.

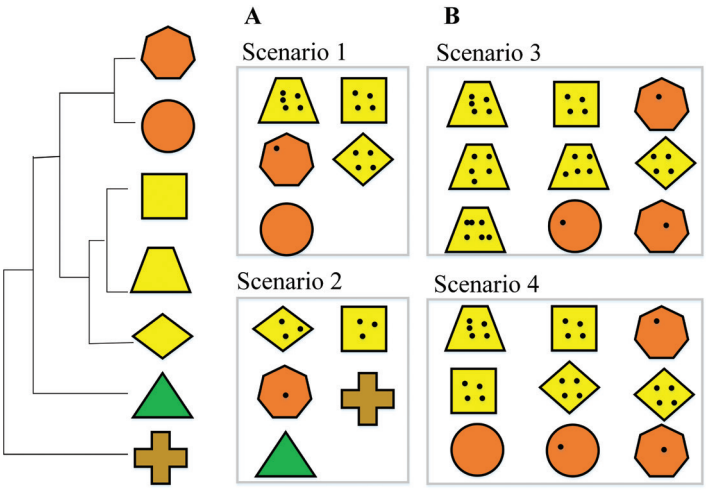

Figure 6.2 Conceptual diagram of disease risk in two hypothetical assemblages that have a different level of host phylogenetic relatedness. Left side: Phylogenetic tree of seven species. Shapes indicate different host species; the same colour indicates that species are closely related. Black spots indicate disease infection; the number of black spots indicates the intensity of the disease. (A) Scenarios 1 and 2 have the same richness but differ from each other in the level of host phylogenetic relatedness. (B) Scenarios 3 and 4 also have species richness and same the level of host phylogenetic relatedness without consideration of abundance, but 3 and 4 differ in the relative abundance of species.

Current studies overlook phylogenetic structure

Many studies of disease-diversity relationships ignore the phylogenetic structure of the assemblage under study. I reviewed the studies on disease-diversity relationships that used species richness as the measurement of host biodiversity (**Table 6.2**). I checked whether they considered the impact of abundance of the focal species, the phylogenetic structure of the different species in their study system, or both. I mainly extracted data from Civitello *et al.* (2015), where >200 effect sizes for 61 parasite species were used to test the existence of a dilution effect. They only included studies that used infection prevalence, mean parasite load, the density of infected vectors, or the percentage of diseased tissue as measurements

for disease risk. Then I summarised the direction of effect of species richness (either positive or negative). Most, but not all studies reported a dilution effect. For the same pathogen, *Anaplasma phagocytophilum*, the study of Salkeld *et al.* (2013) reported an amplification effect, but Foley et al. (2009) reported a dilution effect. The reason behind this might be that those two studies considered different focal species and "dilution" species. Only one study considered the phylogenetic structure of the host species assemblage, but it did not consider species richness (Parker et al. 2015). Only a single study (Liu et al. 2016) considered both species richness and phylogenetic structure. This study reported a negative relationship between species richness and disease risk (i.e., a dilution effect). Liu et al. (2016) also found that phylogenetic diversity, which was negatively related to disease severity, was the most important predictor. Even though some studies considered the abundance of focal species, the omission of phylogenetic relatedness from most studies and its need for inclusion is clear.

Table 6.2 Effects of species richness (positive:+, negative:–) on disease risk for different pathogens with consideration of species abundance (Yes, No) and phylogenetic relatedness (Yes, No).

Pathogen	Species richness	Abundance of focal species	Phylogenetic structure	Citation
Anaplasma phagocytophilum	+	No	No	(Salkeld et al. 2013)
Anaplasma phagocytophilum	-	No	No	(Foley et al. 2009)
Andes virus	-	No	No	(Piudo et al. 2011)
Barley/Cereal Yellow Dwarf Virus	-	No	No	(Moore et al. 2012; Lacroix et al. 2014)
Batrachochytrium dendrobatidis	-	Yes	No	(Becker et al. 2014)
Batrachochytrium dendrobatidis	-	No	No	(Venesky et al. 2014)
Bipolaris	-	No	No	(Mitchell 2002)
Borrelia burgdoferi	-	No	No	(Prusinski et al. 2006; LoGiudice et al. 2008a)
Bruchophagus	-	No	No	(Lau & Strauss 2005)
Busseola fusca	-	Yes	No	(Chabi-Olaye et al. 2005; Midega et al. 2006)
Cercospora	-	No	No	(Mitchell 2002)
Chilo	-	Yes	No	(Päts et al. 1997)
Chilo partellus	-	Yes	No	(Khan et al. 2006; Midega et al. 2006)
Colletotrichum	-	No	No	(Knops et al. 1999; Mitchell 2002)
Cryptosporidium	-	No	No	(Kilonzo et al. 2013)
Curculio elephas	-	No	No	(Soria et al. 1995)
Echinoparyphium recurvatum	-	Yes	No	(Evans & Gordon 1983; Prinz et al. 2009)
Echinostoma friedi	-	Yes	No	(Muñoz-Antoli et al. 2003)

Eimeria	-	No	No	(Rendón-Franco et al. 2014)
Erysiphe alphitoides	-	Yes	No	(Hantsch et al. 2013)
Erysiphe cichoracearum	-	No	No	(Knops et al. 1999; Mitchell 2002)
Erysiphe hypophylla	-	Yes	No	(Hantsch et al. 2013)
Escherichia coli	-	No	No	(Kilonzo et al. 2013)
Euparyphium albuferensis	-	Yes	No	(Muñoz-Antoli et al. 2003)
Giardia	-	No	No	(Kilonzo et al. 2013)
Hantaviruses (Choclo and Calabazo)	+	No	No	(Suzán et al. 2009)
Helminthosporium	-	No	No	(Mitchell 2002)
Himasthla elongata	-	Yes	No	(Thieltges et al. 2008, 2009)
Leptospira	-	No	No	(Derne et al. 2011)
Microphallus	-	Yes	No	(Kopp & Jokela 2007)
Mycosphaerella	-	No	No	(Mitchell 2002)
Parorchis acanthus	-	Yes	No	(Prinz et al. 2009)
Pectinophora gossypiella	-	Yes	No	(Schader et al. 2005)
Phyllactinia orbiculata	-	Yes	No	(Hantsch et al. 2013)
Phyllosticta	-	No	No	(Mitchell 2002)
Puccinia emaculata	-	No	No	(Mitchell 2002)
Puccinia liatridis	-	No	No	(Mitchell 2002)
Ribeiroia ondatrae	-	Yes	No	(Orlofske et al. 2012; Johnson et al. 2013)
Salmonella enterica	-	No	No	(Kilonzo et al. 2013)
Schistosoma mansoni	-	Yes	No	(Chernin 1968; Laracuente et al. 1979) (Combes & Moné 1987)
Septoria	-	No	No	(Mitchell 2002)
Septoria liatridis	-	No	No	(Knops et al. 1999; Mitchell 2002)
Septoria rudbeckiae	-	No	No	(Mitchell 2002)
Sin Nombre virus	-	No	No	(Mills 2005; Clay et al. 2009; Dizney & Ruedas 2009; Carver et al. 2011; Orrock et al. 2011)
Sin Nombre virus	+	No	No	(Skovgård & Päts 1997; Salkeld et al. 2013)
Stemborers	-	Yes	No	(Skovgård & Päts 1997)
Striga hermonthica	-	Yes	No	(Khan et al. 2006)
Trypanosoma cruzi	-	No	No	(da Xavier et al. 2012)
Uromyces lespedezae-procumbentis	-	No	No	(Knops et al. 1999; Mitchell 2002)
West Nile Virus	-	No	No	(Ezenwa et al. 2006)

Yersinia pestis	+	No	No	(Salkeld et al. 2013)
Alternaria tenuissima Ascochyta sp. Puccinia recondita Urosystis dahuricus Erysiphe graminis	-	Yes	Yes	(Liu et al. 2016)

Disease-diversity relationships are bidirectional

Biodiversity changes affect disease risk by changing the phylogenetic relatedness, as I discussed above (Fig. 6.1; Fig. 6.3). However, the role of disease in changing biodiversity is often overlooked. Thus, one frontier in the study of disease-diversity relationships is to better understand the bidirectional feedback between disease and biodiversity (Fig. 6.3).

Pathogens can influence the structure of local assemblages because species have different levels of susceptibility to pathogens. Thus, species are not affected equally (Mordecai 2011; Bagchi *et al.* 2014). For example, closely related species are likely to share pathogens, while distantly related ones are not. This might give distantly related species an advantage (i.e., rare species advantage; Liu *et al.* 2012). For other reasons, individuals within a species are also not always affected equally. For example, disease susceptibility can relate to many individual-level trains, such as age and sex (Casadevall & Pirofski 1999).

At a given point in time, the diseases circulating in an assemblage can lead to the loss of certain individuals, populations, or species. The animals that are lost are likely to be the ones most competent for the circulating disease (Daszak *et al.* 2000; Alford *et al.* 2006; Smith *et al.* 2006; Frick *et al.* 2010). This loss can increase or decrease phylogenetic relatedness in the assemblage and change transmission within and between species, which can influence the disease risk going forward (Fig. 6.4). In natural ecosystems, common species are often competent to a pathogen, and the decline of those common species can thereby lead to decreased phylogenetic relatedness, which decreases disease risk as a result.

Overall conclusions

To conclude, my study highlights the importance of composition and structure of local assemblages (i.e., evenness, functional evenness, phylogenetic relatedness) on disease risk and suggests that future studies look beyond species richness when studying disease-diversity relationships. Despite this important finding, my work also has some limitations that should be acknowledged. First of all, when using publically reported databases, reporting bias can be an issue. One particular problem is that of missing values. When possible, in my analyses I made efforts to confront this issue (e.g., adding random factors, giving more weight for data from “trustable” sources, etc.). Moreover, my correlative analyses do not

test for causal relationships. Different types of studies (e.g., empirical, modelling, etc.) are needed to explore the role of composition and structure of local assemblages in the context of disease ecology. Future studies on disease-diversity relationships should take into account phylogenetic diversity that is weighted for abundance and the bidirectional feedback between disease risk and biodiversity.

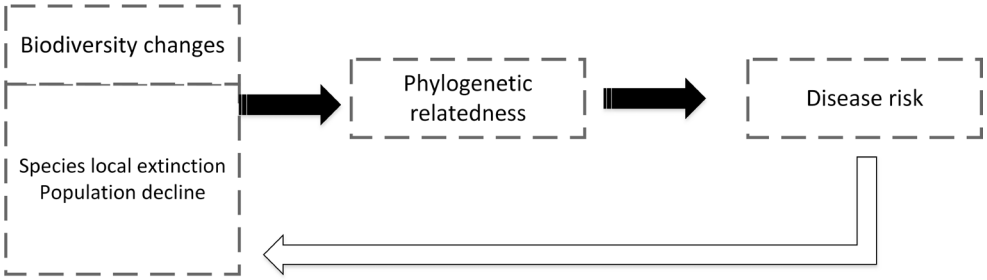

Figure 6.3 Biodiversity changes can affect disease risk by modifying phylogenetic relatedness of local assemblage (black arrow); however, disease pressure also can result in changes in biodiversity (white arrow).

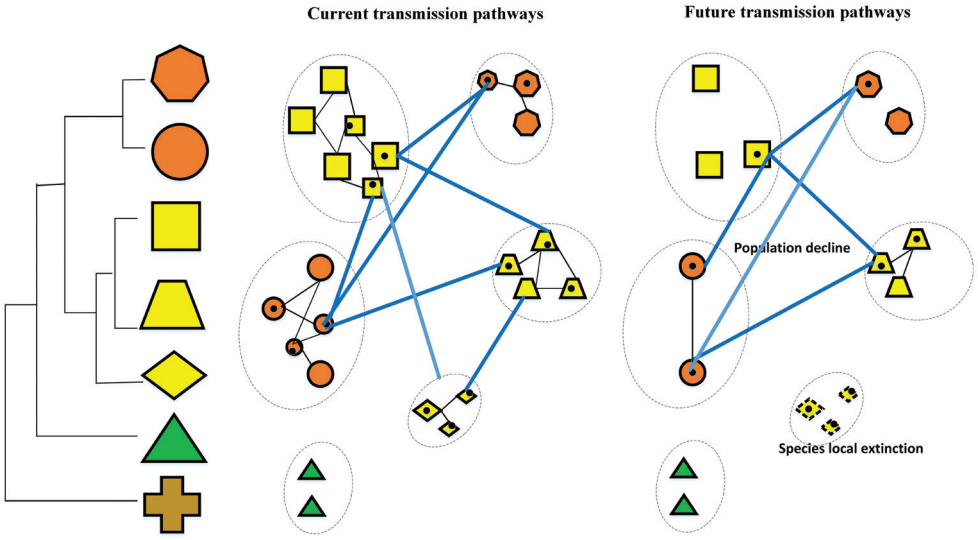

Figure 6.4 Conceptual diagram of current and future disease risk in hypothetical assemblages considering the relationships between disease and biodiversity. Left side: Phylogenetic tree of seven species. Shapes indicate different host species; shapes have dotted lines indicate species go extinct; the same colour indicates that species are closely related. Different sizes indicate individuals with different susceptibility. Black spots indicate disease infection; Black lines indicate transmission within species; blue lines indicate transmission between species.

Appendices

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Summary

Biodiversity is changing rapidly under climate changes and habitat loss. Wildlife biodiversity changes have been linked to changes in disease risk for wildlife but also for humans as most infectious zoonotic diseases originate in wildlife, especially mammals. The changes in local assemblages can affect disease transmission by affecting, for example, encounter rates among competent host species. If low-competent species go locally extinct, disease risk can increase because of high contact rates between the remaining high-competent species (i.e., a dilution effect). Although support for the dilution effect comes from both plant and animal diseases, the generality of the dilution effect and the mechanisms behind it are still uncertain.

The main objective of this thesis is to advance the understanding of the diversity-disease relationships, considering several shortcomings in the current understanding of these disease-diversity relationships. For instance, besides species richness, I also considered other metrics of biodiversity (e.g., evenness, functional diversity, and phylogeny). Moreover, I also measured disease risks in different ways (e.g., community R0 and total disease burden).

Most previous disease-diversity studies used disease prevalence as a proxy of disease risk. However, the direction of the disease-diversity relationship can change when disease risk is measured in different ways. For example, a negative relationship between biodiversity and disease risk (i.e., dilution effect) is more likely to be detected when disease risk is measured by disease prevalence, while a positive relationship is more likely to occur when using the density or number of infected individuals (Roche *et al.* 2012). So, in this thesis, I measured disease risk in various ways:

a) the community-level basic reproduction ratio R0 (i.e., community R0, the probability that a pathogen can invade and be persistent in a local assemblage), which is commonly used in theoretical studies (Dobson *et al.* 2004; Chen *et al.* 2015) (**Chapter 2**);

(b) the presences and absence of a disease, with which I was able to study the probability of occurrence of a certain disease (**Chapter 3**);

(c) the total disease burden (i.e., the number of different manifested diseases in an assemblage) (**Chapter 3**);

(d) the number of reported cases of a certain disease (**Chapter 4**).

My results indicate that the effect of species richness depends on the index used to measure disease risk, different variables used to estimate disease risk react differently to species

richness. In **Chapter 2**, based on predicted global species distributions and their abundances in 2015 and 2035, I modelled global disease risk using community R0 for diseases with density- and frequency-dependent transmission. I showed that disease risks are higher in areas with relatively more competent host species in an assemblage, a pattern that is similar to the observed global outbreaks of emerging diseases. McCallum (2015) argued that it is the loss of biodiversity, not biodiversity per se, that influence disease risk. To understand whether it is the biodiversity per se or the changes thereof that affect disease risk, I considered both the original species richness, the changes in species richness and their interactions, and the results showed that original species richness and changes in species richness jointly affect disease risk. In other words, not only the losses or gains in species richness are important but also how many species were there originally, and their interactions.

I studied the effect of species richness on (b) presence and absences of diseases in 19 livestock disease as available from databases at the World Organization for Animal Health (OIE; **Chapter 3**). I did not find a significant overall effect of species richness on disease occurrence over the studied 19 diseases (neither negative or positive; Fig. 6.1), only the effect of species richness was negative and significant for *Echinococcosis*. I measured the total disease burdens, in 71 livestock diseases that infect mammals, as available from the World Organization for Animal Health (OIE) databases from 2005 to 2015 (**Chapter 3**). The accumulated number of different manifested diseases in that decade for each administrative unit (i.e., total disease burden) was treated as a dependent variable. I found that species richness was positively related to total disease burdens. The theorem that "diversity begets diversity" supports this result, as high host species richness supplies more niches for different pathogens, which leads to more manifested diseases (Hechinger & Lafferty, 2005; Johnson *et al.* 2016). In **Chapter 4**, I used the number of Lyme disease cases in the United States, obtained from the Centre for Disease Control and Prevention (CDC) at both state scale and county scale. The negative relationship between species richness and the number of Lyme disease cases (as expected when a dilution effect operates) was found at state level. However, a positive relationship (similar to an amplification effect) was detected when analysing the smaller county-level spatial scale.

The negative relationship at state scale in my study can be explained by two reasons. First, the percentage of species in an assemblage that are host species for Lyme disease and the percentage of species in an assemblage that are rodent hosts both decreased as species richness (including host species and non-host species) increased at state level. Thus, increasing species richness dilutes the relative abundance of suitable hosts in these two categories, thereby potentially leading to a reduction in the number of Lyme disease cases. Second, at these larger (state-level) spatial scale, the larger spatial heterogeneity could prevent the spread of the disease by limiting the movement of host species or the contact

rate among those host species, and thereby result in a negative effect of host species richness.

At county level, although an overall amplification effect was detected, species richness had a strong nonlinear effect, as a negative relationship was apparent at lower levels of species richness, while a positive effect was visible at higher levels of species richness. This scale-dependency within counties requires further investigation.

I concluded that the disease-diversity relationship is scale-dependent. More studies, especially experimental ones, conducted at multiple spatial scales are certainly needed. Moreover, studies that can are directed at understanding the underlying mechanisms are also needed.

Phylogenetic relationships among host species that conserved information of host-pathogen interactions is thus a better predictor in influencing disease patterns, compared to species richness. In **Chapter 3** and **Chapter 4**, phylogenetic relatedness was proven to be negatively correlated to disease risk in both disease presence/absence analyses and disease richness analyses. The results suggest that if the species in an assemblage are closely related, the assemblage is expected to have a higher disease risk, both in the presence of certain disease and in the number of different manifested diseases. The reason can be that those closely related species share similar life-history traits and immunological defences (Streicker *et al.* 2010). Disease transmission is facilitated in an assemblage which contains more closely related species, leading to an increase in disease risk. Moreover, my results suggest that phylogenetic relatedness among host species can potentially explain why an increase in species richness sometimes increased disease risk and sometimes decreased disease risk. If increased species richness increased phylogenetic relatedness, high phylogenetic clustered assemblages may have a higher disease risk (i.e., amplification effect), because those closely related species are often abundant and competent for a shared pathogen, and pathogens spill overs can be more frequent (Gilbert & Webb 2007; Longdon *et al.* 2011). The opposite could also occur that an assemblage becomes phylogenetically dispersed, so that the transmission of a pathogen would be limited because transmission events between distantly related hosts are less likely to occur.

To conclude, my results suggest that the effect of species richness on disease risk is complex; the direction of the effect depends on the measurements of disease risk, the observation scale and the transmission type. Species phylogenetic relatedness is an important variable and generates new insight into the underlying mechanisms that drive these disease-diversity relationships.

Samenvatting

Biodiversiteit is snel aan het veranderen door klimaatsveranderingen en het verdwijnen van leefgebieden. De veranderingen in dierbiodiversiteit zijn gelinkt aan veranderingen van ziekterisico's voor wilde dieren, maar ook voor mensen, aangezien de meest besmettelijke zoönoses hun oorsprong bij wilde (zoog)dieren hebben. De veranderingen in lokale assemblages kunnen ziektetransmissie beïnvloeden door, bijvoorbeeld, de ontmoetingssnelheden tussen geschikte gastheersoorten te beïnvloeden. Als soorten met een lage competentie lokaal uitsterven, kan het ziekterisico toenemen door hoge contactsnelheden tussen de overgebleven soorten met een hoge competentie (het verdunningseffect). Alhoewel de onderbouwing voor het verdunningseffect van zowel plant- als dierziektes komen, is er nog steeds onzekerheid over de algemeenheid van het verdunningseffect en diens onderliggende mechanismen.

Het hoofddoel van dit proefschrift is om het begrip van de relaties tussen diversiteit en ziekte te vergroten, gegeven de verscheidene tekortkomingen in het huidige begrip van deze relaties. Ik neem bijvoorbeeld, naast soortenrijkdom, ook andere maten van biodiversiteit in beschouwing (bijvoorbeeld gelijkmatigheid, functionele diversiteit en fylogenie). Bovendien meet ik ook ziekterisico's op verschillende manieren (bijvoorbeeld gemeenschap R0 en totale ziektelast).

De meeste andere ziekte-diversiteit studies gebruiken ziekteprevalentie als een proxy voor ziekterisico. Echter, de richting van de ziekte-diversiteit relatie kan veranderen wanneer ziekterisico op verschillende manieren gemeten wordt. Een negatieve relatie tussen biodiversiteit en ziekterisico (verdunningseffect) is bijvoorbeeld waarschijnlijker om gedetecteerd te worden wanneer ziekterisico wordt gemeten in ziekteprevalentie, terwijl een positieve relatie waarschijnlijker is om voor te komen wanneer de dichtheid van geïnfecteerde individuen of diens aantal gebruikt wordt (Roche et al. 2012). In dit proefschrift meet ik ziekterisico dus op verschillende manieren:
a) de gemeenschapsniveau basis reproductie ratio R0 (gemeenschap R0, de kans dat een pathogeen kan binnendringen en aanhoudend kan zijn in een lokale assemblage), wat algemeen gebruikt wordt in theoretische studies (Dobson et al. 2004; Chen et al. 2015) (**Hoofdstuk 2**);

(b) de aan- en afwezigheid van een ziekte, waarmee ik in staat was om de kans op het voorkomen van een bepaalde ziekte te bestuderen (**Hoofdstuk 3**);

(c) de totale ziektelast (het aantal verschillende gemanifesteerde ziektes in een assemblage) (**Hoofdstuk 3**);

(d) het aantal gerapporteerde gevallen van een bepaalde ziekte (**Hoofdstuk 4**).

Mijn resultaten geven aan dat het effect van soortenrijkdom afhangt van de index die gebruikt wordt om ziekterisico te meten, aangezien de verschillende variabelen die gebruikt worden om het ziekterisico te schatten anders reageren op soortenrijkdom. In **Hoofdstuk 2**, gebaseerd op voorspelde mondiale soortdistributies en -aantallen in 2015 en 2035, heb ik het mondiale ziekterisico gemodelleerd met gemeenschap R0 voor ziektes met dichtheid- en frequentieafhankelijke transmissie. Ik heb laten zien dat ziekterisico's hoger zijn in gebieden met relatief meer competente gastheersoorten in een assemblage, een patroon dat vergelijkbaar is met de geobserveerde mondiale uitbraken van opkomende ziektes. McCallum (2015) beweerde dat het verlies van biodiversiteit, niet biodiversiteit zelf, ziekterisico beïnvloedt. Om te begrijpen of het biodiversiteit zelf of diens veranderingen is dat ziekterisico beïnvloedt, nam ik zowel de oorspronkelijke soortenrijkdom, de veranderingen in soortenrijkdom en de interacties in aanmerking, waar uitkwam dat oorspronkelijke soortenrijkdom en diens veranderingen samen ziekterisico beïnvloeden. Het zijn met andere woorden niet alleen de verliezen of toenames in soortenrijkdom die belangrijk zijn, maar ook hoeveel soorten er oorspronkelijk waren, inclusief de interacties.

Ik heb het effect bestudeerd van soortenrijkdom op (b) de aan- en afwezigheid van 19 veeziektes, zoals beschikbaar in databases van de Wereldorganisatie voor diergezondheid (OIE; **Hoofdstuk 3**). Ik vond geen algemeen significant effect van soortenrijkdom op het voorkomen van de 19 ziektes (niet negatief of positief, Fig. 6.1), het effect van soortenrijkdom was alleen negatief en significant voor *Echinococcosis*. Ik berekende de totale ziektelasten van 71 veeziektes die zoogdieren besmetten, zoals beschikbaar in databases van de Wereldorganisatie voor diergezondheid (OIE) van 2005 tot 2015 (**Hoofdstuk 3**). Het geaccumuleerde aantal verschillende gemanifesteerde ziektes in dat decennium voor elke administratieve eenheid (de totale ziektelast) werd als de afhankelijke variabele beschouwd. Ik kwam erachter dat soortenrijkdom positief gecorreleerd was met de totale ziektelasten. De theorie "diversiteit brengt diversiteit voort" ondersteunt dit resultaat, omdat een hoge gastheersoortenrijkdom meer niches voortbrengt voor verschillende pathogenen, wat tot meer gemanifesteerde ziektes leidt (Hechinger & Lafferty, 2005; Johnson et al. 2016). In **Hoofdstuk 4** heb ik het aantal gevallen van Lyme ziekte in de Verenigde Staten gebruikt, verkregen via het Centrum voor ziektebestrijding en -preventie (CDC) op zowel staat- als provincieschaal. De negatieve relatie tussen soortenrijkdom en het aantal gevallen van Lyme ziekte (zoals verwacht bij een verdunningseffect) werd gevonden op een staatniveau. Echter, een positieve relatie (vergelijkbaar met een amplificatie effect) werd gedetecteerd bij het analyseren van het kleinere provincieniveau.

Halliday & Rohr (2018) concludeerden dat het waarschijnlijker is dat een verdunningseffect plaatsvindt op een kleine schaal (<100 km^2), waar er sterke soortinteracties zijn; een

amplificatie effect is waarschijnlijker op regionale schalen (> 1.000.000 km^2), waar abiotische factoren zoals klimaat voldoende variëren om soortdistributies (van zowel gastheren als pathogenen) te beïnvloeden. Dit is echter niet in tegenstelling tot mijn resultaten, omdat mijn studie toegepast was op gemiddelde ruimtelijke schalen (de gemiddelde grootte van een staat was bijvoorbeeld 120.740 km^2 en van een provincie 1600 km^2). Op deze gemiddelde schalen namen Halliday en Rohr (2018) aan dat zowel het amplificatie effect als het verdunningseffect plaats kunnen vinden.

De negatieve relatie in mijn studie op een staatniveau kan verklaard worden door twee redenen. Ten eerste, het percentage van soorten in een assemblage dat gastheer voor Lyme ziekte is en het percentage van soorten in een assemblage dat knaagdier gastheer is namen beide af bij een toename van soortenrijkdom (inclusief gastheersoorten en niet-gastheersoorten) op staatniveau. Toenemende soortenrijkdom verdunt dus de relatieve aantallen van geschikte gastheren in deze twee categorieën, wat potentieel leidt tot een reductie van het aantal gevallen van Lyme ziekte. Ten tweede, op deze grotere (staatniveau) ruimtelijke schaal kan de grotere ruimtelijke heterogeniteit de verspreiding van de ziekte voorkomen door de beweging van gastheersoorten of de contactsnelheden tussen deze gastheersoorten te limiteren, wat resulteert in een negatief effect van gastheersoortenrijkdom.
Alhoewel op een provincieniveau een algemeen amplificatie effect gedetecteerd is, had soortenrijkdom een sterk niet-lineair effect, omdat een negatieve relatie zichtbaar was bij lage niveaus van soortenrijkdom, terwijl een positief effect zichtbaar was bij hoge niveaus van soortenrijkdom. Deze schaalafhankelijkheid binnen provincies heeft verder onderzoek nodig.
Ik concludeerde dat de ziekte-diversiteit relatie schaalafhankelijk is. Er zijn zeker meer studies nodig, vooral experimentele, die focussen op meerdere ruimtelijke schalen. Bovendien zijn er ook studies nodig die gericht zijn op het begrijpen van de onderliggende mechanismen.
Fylogenetische relaties tussen gastheersoorten die informatie bewaarden over gastheer-pathogeen interacties is dus een betere predictor voor het beïnvloeden van ziektepatronen vergeleken met soortenrijkdom. In **Hoofdstuk 3** en **Hoofdstuk 4** is het bewezen dat fylogenetische verwantschap negatief gecorreleerd was met ziekterisico voor zowel ziekte aanwezigheid/afwezigheid analyses en ziekterijkdom analyses. De resultaten suggereren dat als soorten in een assemblage nauw verwant zijn de assemblage een hoger ziekterisico heeft, zowel voor de aanwezigheid van een bepaalde ziekte en in het aantal verschillende gemanifesteerde ziektes. De reden kan zijn dat nauw verwante soorten vergelijkbare levensgeschiedenis kenmerken en immunologische afweermechanismen delen (Streicker et al. 2010). Ziektetransmissie wordt gefaciliteerd in een assemblage dat meer nauw verwante soorten bevat, wat tot een toename in ziekterisico leidt. Bovendien suggereren mijn resultaten dat fylogenetische verwantschap tussen gastheersoorten potentieel kan verklaren waarom een toename in soortenrijkdom soms het ziekterisico deed toenemen en soms afnemen. Als

een toegenomen soortenrijkdom fylogenetische verwantschap deed toenemen dan kunnen hoge fylogenetische geclusterde assemblages een hoger ziekterisico hebben (amplificatie effect), omdat de nauw verwante soorten vaak in overvloed aanwezig zijn en in staat zijn om pathogenen te delen en pathogene "spillovers" vaker kunnen voorkomen (Gilbert & Webb 2007; Longdon et al. 2011). Het tegenovergestelde kan ook voorkomen, dat een assemblage fylogenetisch verspreid wordt, zodat de transmissie van een pathogeen gelimiteerd wordt omdat transmissie gevallen tussen ver verwante gastheren minder waarschijnlijk zijn om voor te komen.

Kortom, mijn resultaten suggereren dat het effect van soortenrijkdom op ziekterisico complex is; de richting van het effect hangt af van de maat die gebruikt wordt om ziekterisico te meten, de schaal van observeren en het transmissietype. Fylogenetische verwantschap tussen soorten is een belangrijke variabele en genereert nieuwe inzichten over de onderliggende mechanismen die deze ziekte-diversiteit relaties aandrijven.

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Biography

Yingying Wang was born on 13th November 1989 in Shandong, China. At the early age, she started to get interested in animals. At that time, when she grew up, she wanted to be an animal keeper in the zoo. After finishing the high school, she chose to study, not surprisingly, biology at Herbei Normal University. During her four-year study of biology, she came to know about animal movements and spread of infectious disease. Her BSc thesis project was about the spatial pattern occurrence of *Ixodes persulcatus*, she did her field work in Eerguna National Natural Reserve Area situated in the China-Russia border in Inner Mongolia, China. After obtained her BSc in Biology, she moved to Nanjing University to start her MSc in Landscape Ecology. During her MSc, she specialised in land use changes with MSc thesis about effects of land use change on distribution of heavy metals in sediments and the influence mechanism in seasonal river.

After finishing her MSc, she was thrilled to hear from Dr. Willem F. de Boer that she can continue her passion for studying the distribution of animal and spread of infectious disease. After receiving scholarship from Chinese Scholarship Council, she immigrates to Netherlands for her PhD in Resource Ecology Group, Wageningen University. She officially started her PhD in August 2015 and focused on the effect of host community composition and species traits on the pattern of infectious disease. Yingying currently works as a postdoc researcher at Faculty of Mathematics and Science, Department of Biological and Environmental Science, University of Jyväskylä. Her project focuses on “Drivers of zoonotic tick-borne pathogens in natural populations”.

Publications

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*Y. Xu, Y. Si, **Y. X. G. Wang**, Y. Zhang, H. H. T. Prins, L. Cao, W. F. de Boer.* (2019). Loss of integrity in migration networks induces population decline in migratory birds *Ecological Applications*. 00:e01960 https://doi.org/10.1002/eap.1960

In advanced stage or submitted:

***Y. X. G. Wang**, K. D. Matson, H. H. T. Prins, Z. Y. X. Huang, W. F. de Boer (in revision: remote sensing-576344)* Interaction of community similarity and landscape connectivity facilitate spread of Lyme disease

*Z. Li, Z. Tang, Y. Xu, **Y. X. G. Wang**, X. Liu, P. Wang, J. Yang, Z. Duan, W. Chen, H. H. T. Prins (in revision: Environmental Science and Pollution Research-EMID:942b3d9f4497020a)* The minimum activity temperature of animals in the high-altitude ecosystem of the southwestern mountains of China

***Y. X. G. Wang**, K. D. Matson, L. Santini, P. Visconti, J. Hilbers, M. A. J. Huijbregts, Y. Xu, H. H. T. Prins, A. Dobson, T. Allen, Z. Y. X. Huang, W. F. de Boer (submitted)* Mammal assemblage composition predicts global patterns in emerging disease risk

***Y. X. G. Wang**, K. D. Matson, H. H. T. Prins, Z. Y. X. Huang, W. F. de Boer (in preparation)*
Host relatedness determine patterns of Lyme diseases.

*Jasper Eikelboom, Rascha Nuijten, **Y. X. G. Wang**, Bradley Schroder, H. H. T. Prins, (in preparation)* Legalizing international rhino horn trade: a literature review of the ongoing debate.

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PE&RC Training and Education Statement

With the training and education activities listed below the PhD candidate has complied with the requirements set by the C.T. de Wit Graduate School for Production Ecology and Resource Conservation (PE&RC) which comprises of a minimum total of 32 ECTS (= 22 weeks of activities)

Review of literature (4.5 ECTS)

- The relationship between community and disease outbreak

Writing of project proposal (4.5 ECTS)

- Infectious diseases, host community composition and species traits

Post-graduate courses (5.9 ECTS)

- Generalized Linear Models; PE&RC (2016)
- Consumer-resource interactions: in times of global environmental change; PE&RC (2018)
- Modelling population dynamics with Physiologically Structured Population Models (PSPM); PE&RC (2018)
- Dynamic models in R: programming, parameter estimation and model selection; PE&RC (2019)

Invited review of (unpublished) journal manuscript (1 ECTS)

- PLOS ONE: animal conservation (2017)

Deficiency, refresh, brush-up courses (3 ECTS)

- Ecological methods 1; Resource Ecology Group (2015)

Competence strengthening / skills courses (3.2 ECTS)

- Techniques for writing and presenting a scientific paper; PE&RC (2016)
- Writing grant proposals; WGS (2019)

PE&RC Annual meetings, seminars and the PE&RC weekend (1.5 ECTS)

- PE&RC First years weekend (2015)
- PE&RC Last years weekend (2019)

Discussion groups / local seminars / other scientific meetings (4.5 ECTS)

- R Users meeting (2017-2018)
- Landscape dynamics discussion group session (2018)
- Reading club of modelling to inform infectious disease control (2018-2019)

International symposia, workshops and conferences (4.4 ECTS)

- Current themes in ecology; Wageningen, the Netherlands (2016)
- The 12th International congress of ecology; Beijing, China (2017)
- Global one health research, the future; Wageningen, the Netherlands (2018)

Lecturing / supervision of practicals / tutorials (6 ECTS)

- Disease ecology (2016, 2017)

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