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Review

Anthropogenic Land Use Change and Infectious Diseases: A Review of the Evidence

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Abstract: Humans have altered ecosystems worldwide, and it is important to understand how this land use change impacts infectious disease transmission in humans and animals. We conducted a systematic review 305 scientific articles investigating how specific types of anthropogenic land use change influence infectious disease dynamics. We summarized findings, highlighted common themes, and drew attention to neglected areas of research. There was an increase in publications on this topic over the last 30 years spanning diseases of humans, livestock, and wildlife, including a large number of zoonotic pathogens. Most papers (66.9%) were observational, 30.8% were review or concept papers, and few studies (2.3%) were experimental in nature, with most studies focusing on vector-borne and/or multi-host pathogens. Common land use change types related to disease transmission were deforestation/forest fragmentation/habitat fragmentation, agricultural development/irrigation, and urbanization/suburbanization. In response to anthropogenic change, more than half of the studies (56.9%) documented increased pathogen transmission, 10.4% of studies observed decreased pathogen transmission, 30.4% had variable and complex pathogen responses, and 2.4% showed no detectable changes. Commonly reported mechanisms by which land use change altered infectious disease transmission included alteration of the vector, host, and pathogen niche, changes in host and vector community composition, changes in behavior or movement of vectors and/or hosts, altered spatial distribution of hosts and/or vectors, and socioeconomic factors, and environmental contamination. We discussed observed patterns in the literature and make suggestions for future research directions, emphasizing the importance of ecological and evolutionary theory to understand pathogen responses in changing landscapes.

Keywords: anthropogenic land use change, infectious diseases, literature assessment

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Introduction

Throughout the history of civilization, humans have altered their local and regional environments, and in the last century,

anthropogenic disturbance has extended on a global scale (Goudie 2000; Burney and Flannery 2005). Few areas across the earth have avoided the direct and indirect influence of humans (Goudie 2000; Burney and Flannery 2005; Foley et al. 2005). Land alterations include deforestation, rangeland expansion, urbanization/suburbanization, infrastructure development (railroad, road, power lines), hydrological alteration (dams, irrigation, canal construction), agricultural development (crops, livestock), and natural resource extraction/depletion (mining, logging, hunting) (Foley et al. 2005). Anthropogenic land use changes can negatively impact ecological integrity and biodiversity by disrupting food web structure and function, altering terrestrial and aquatic biogeochemical cycles, shifting ecosystem properties, and introducing non-native species, including pathogens (Matson et al. 1997; Tilman 1999; Foley et al. 2005). Changes in ecosystem structure and function can also modify host–pathogen interactions and lead to emergence of infectious diseases in humans, domestic animals, and wildlife (Patz et al. 2000; Foley et al. 2005; Dobson et al. 2006; Pongsiri et al. 2009; Keesing et al. 2010).

Land use change has the potential to impact disease dynamics directly and indirectly by changing the abundance, demography, behavior, movement, immune response, and contact between host species and vectors, as well as altering host community composition. There is a multitude of pathogens, types of land use conversions, and proposed mechanisms for altering infectious disease dynamics in humans and animals, and a summary of the state of the literature of this emerging field is needed in order to identify gaps in our understanding and to define future research needs. This article provides a systematic review of the growing scientific literature of relationships between land use change and infectious disease in animals and humans. Our aim is to summarize the existing literature relating to land use change and infectious disease transmission by asking the following questions: (1) What types of studies are commonly published on land use change and infectious disease transmission and what is their geographical distribution? (2) What pathogen type, transmission type, and host specificity are most studied in relation to land use change and infectious disease transmission? We expect, because disease vectors are highly sensitive to environmental change, and anthropogenic change commonly alters contact between different host species, that vector-borne as well as generalist (multi-host) pathogens will be the most common pathogen types of focus in the scientific literature. (3) What are the most commonly reported responses of pathogen transmission to land use change (increase, decrease, or no change) and are there any relationships of type of land use change to pathogen transmission responses? (4) What ecological mechanisms influence infectious disease transmission in response to land use change? (5) Are anthropogenic land use change-disease studies more likely to take place in highly productive ecosystems? We hypothesize that there will be greater evidence of land use-infectious disease relationships in highly productive ecosystems, because these regions may support increased pathogen diversity and vector and host densities, as well as higher transmission rates of infectious disease transmission.

Furthermore, we draw attention to understudied pathogen systems and landscapes, highlight common trends that occur across multiple disease systems, and provide suggestions for conceptual frameworks that help untangle mechanisms of anthropogenic drivers of infectious disease transmission in humans and wildlife. Finally, we identify research challenges and suggest future avenues of research relating to anthropogenic land use change and infectious disease.

Methods: Literature Search and Classification of Studies

A literature search using the following search term combinations was conducted in ISI Web of Science and PubMed: (land use change OR land use OR deforest* OR forest fragment*OR habitat fragment* OR habitat change OR habitat loss) AND (disease OR parasite* OR parasitism) between the earliest date of publication available in October 2012. Additional articles relating to land use change and disease were also compiled from bibliographic references of articles gathered from search engines. Irrelevant articles resulting from the search (e.g., those that were located by the search terms, but had nothing to with land use change in relation to infectious disease transmission) were discarded. Observational and experimental studies (hereafter referred to as "study" or "studies") were tallied for the following qualitative characteristics: pathogen type (pathogen species, disease caused, type of pathogen (virus, bacteria, fungus, protozoa, helminth, other), transmission type (direct, vector-borne, or trophic), host specificity (multi- or single host pathogen), target land use (agricultural development irrigation, cattle grazing, deforestation/forest fragmentation/habitat fragmentation, urbanization/suburbanization, dam building, natural resource extraction, and habitat management/land restoration), climate (temperate, tropical), anthropogenic biomes, disease response to land use change

(positive, negative, none, or complex disease responses to land use change), mechanism by which land use change influenced disease transmission (if specified). Although the original intention was to conduct a quantitative meta-analysis, the literature surveyed covered such a diversity of diseases, hosts, and landscapes, and used such a wide variety of techniques, that this initial goal was impossible. We intended to perform as broad a search as possible, but recognize that some relevant articles that did not conform to the search criteria may have been overlooked.

For observational and experimental studies, where geographic location was available, the anthropogenic biomes included in each study for a subset of descriptive and experimental studies were also tabulated using Anthromes v. 1 (Ellis and Ramankutty 2008). Anthropogenic biomes or "anthrobiomes" are landscape classifications that incorporate ecological/biome features, human use, and human population size. Data on net primary productivity (NPP) in each anthropogenic biome type calculated by Ellis and Ramankutty (2008) was compared to the number of the land use-disease studies that took place in each of the anthropogenic biomes present in the articles reviewed (Ellis and Ramankutty 2008) by a simple linear correlation test. If a study took place in more than one anthropogenic biome, then it was counted more than once, as the comparison was between study numbers and the NPP of that anthropogenic biome. Fisher exact tests evaluated associations between directionality of disease change (increased, decreased, no change) in response to land use and pathogen type, pathogen transmission mode, and type of pathogen.

Results

Trends and Patterns in the Land Use Change-Infectious Disease Literature

The literature search yielded 305 articles investigating relationships between land use change and infectious diseases. Published peer reviewed articles on land use change and diseases from the 1970s to the present increased markedly in the last decade (Fig. 1). Of the articles evaluated, 94 (30.8%) were literature reviews or "concept" papers, 204 (66.9%) were observational (longitudinal, cross sectional, or data-based models), and 7 (2.3%) involved experimental manipulation. Review and "concept" papers spanned a variety of journals in human and veterinary medicine, epidemiology, ecology, and parasitology, indicating cross-disciplinary awareness of relationships between environmental degradation and infectious disease transmission. Observational and experimental studies are summarized in a Supplementary Information (Table S1) that shows pathogen, transmission types, geographic locations, and land use changes studied in relationship to these pathogens.

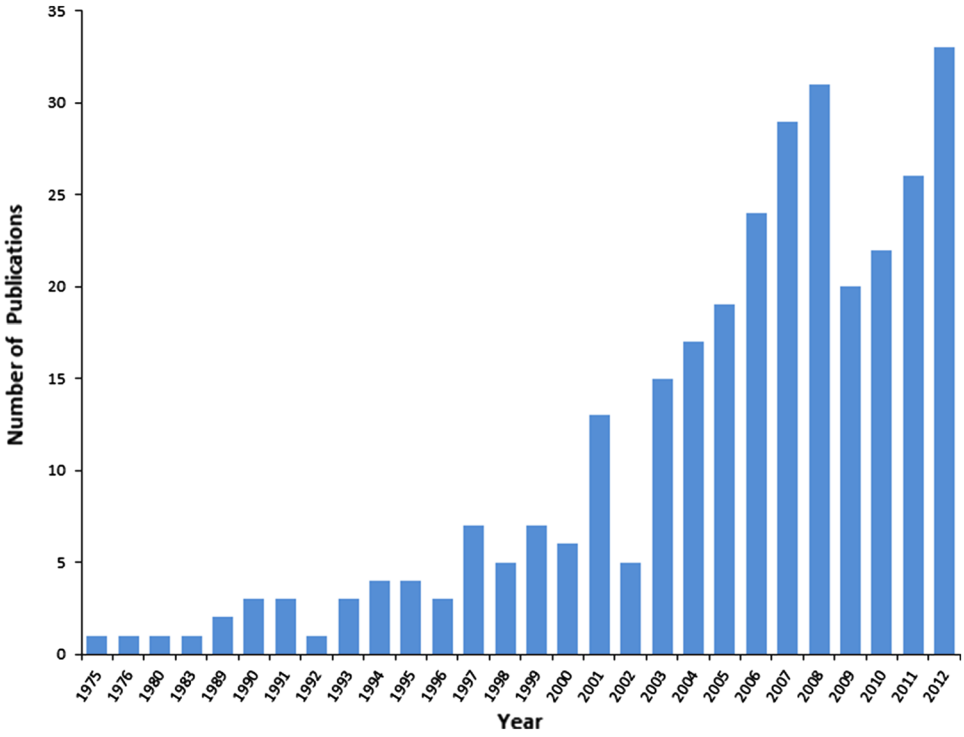

Figure 1. Number of studies of anthropogenic land use change and infectious disease, year of publication, 1975–2012.

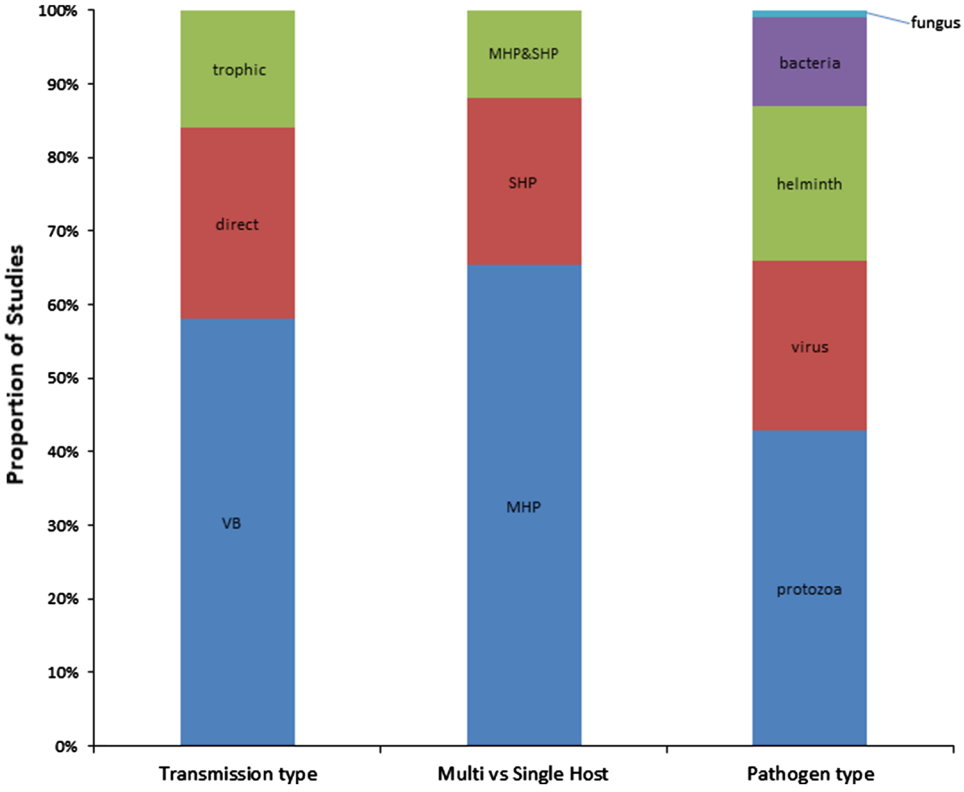

Figure 2. Transmission type (VB: vector-borne), host specialization (MHP: multi-host pathogen, SHP: single host pathogen), and pathogen type evaluated in observational and experimental studies of land use change and infectious disease (n = 211).

Studies were distributed evenly across pathogen taxa (viral, bacterial, helminth, protozoa) (Fig. 2). The diversity of pathogens within each taxa is widespread (Table 1), but some pathogens are studied with a much higher than random frequency (i.e., malaria). Most studies focused on vector-borne pathogens as opposed to direct or trophically transmitted parasites. Additionally, most pathogens studied infect multiple hosts rather than a single host. The most commonly studied pathogens in relation to land use change for observational/experimental studies were human malaria (n = 40), Old and New World leishmaniasis (n = 14), schistosomiasis (n = 11), West Nile Virus (n = 15), *Borellia burgdorferi*-Lyme disease (n = 11), and Chagas disease (n = 9). Of 204 observational and experimental studies, infectious diseases impacting humans were the primary focus of many studies (76.0%, n = 155). Just under one half (47.5%, n = 97) studied zoonoses or potential zoonoses, and 61.9% (96/155) of the diseases impacting humans were zoonoses or potential zoonoses. A large proportion of the pathogens studied in relation to land use change (approximately 80%) are also within the World Health Organization's list of neglected tropical diseases (www.who.int/zoonoses/diseases/en).

The principal land use changes studied in relation to disease transmission were deforestation/forest fragmentation/habitat fragmentation, agricultural development/irrigation, followed by urbanization/suburbanization, livestock grazing, dam building/water diversion, logging/natural resource extraction, and land restoration (Fig. 3). The geographic scope of observational and experimental studies ranged across all continents with the exception of Antarctica. However, studies from Australia/Oceania (n = 8) were much less common than other regions: North America/Central America (n = 66), Africa (n = 52), Eurasia (n = 41), and South America (n = 37). The proportion of studies from tropical (53.4%) regions was slightly greater than temperate (46.6%) regions. Studies also took place in arid environments (n = 7), arid/temperate climates (n = 4). Very few studies (n = 2) took place across a gradient of tropical, dry, and temperate climates.

We found a positive relationship between the estimated anthrobiome net primary production and the number of studies on land use change and infectious disease (Fig. 4).

Among 204 observational, experimental, or model studies that directly measured the response of pathogen infection to land use, 116 (56.9%) associate land use change with a significant increase in infectious disease prevalence, vector abundance, and/or transmission. A lower number of studies (n = 21, 10.3%) document declines in infectious disease prevalence or transmission with landscape transformation. A

Table 1. Examples of mechanisms by which anthropogenic land use change influences pathogen transmission

Pathogen	Transmission and pathogen type	Mechanism	References
Modified niche			
Malaria	Vector-borne protozoan	Increase in anopheline mosquito vectors in areas of sugar cane development observed with an increase in cattail cover in wet areas associated with cyanobacterial mats for *An. Cruciens* and decreased light for *An. Vestipennis*	Grieco et al. (2006)
		A meta-analysis of anopheline mosquito vectors of malaria show that mosquito sun preference, not niche width, associated with increased malaria vector densities in areas of deforestation and agricultural development	Yasuoka and Levins (2007)
Ehrlichiosis	Tick-borne zoonotic bacteria	Greater numbers of *E. chafeensis*-infected tick nymphs in areas of invasive honeysuckle, preferred vegetation the white-tailed deer host	Allan et al. (2010)
Bluetongue virus	Vector-borne virus of ungulates	Increased bluetonguevirus in livestock areas associated with wastewater lagoons, suitable habitats for the *Culicoides* vector	Mayo et al. (2012)
Riberoia ondatrae	Trophically (snail)-transmitted trematode of amphibians	Experimental studies link aquatic eutrophication (a common downstream result of agricultural development) with increased density of intermediate snail hosts, snail trematode production, and trematode infection intensity and reduced survivorship of amphibians	Johnson et al. (2007)
Changes in community composition			
Leishmaniasis	Vector-borne protozoan	Irrigation of desert lands led to dominance of *Phlebotomus papatisi*, a highly competent vector for visceral leishmaniasis	Eliseev et al. (1991)
Chagas disease	Vector-borne protozoan	Decreased wild mammal species richness in fragmented habitats associated with higher seroprevalence of the Chagas disease parasite in small mammal reservoir hosts	Vaz et al. (2007)
Hantavirus	Directly transmitted zoonotic virus	Hantavirus seroprevalence in mammal reservoirs increased in areas of decreased rodent diversity	Suzan et al. (2008)
Changes in spatial relationships			
Nipah virus	Directly transmitted zoonotic virus	In Malaysia, large-scale swine production facilities near mango orchards where fruit bats roost believed to be a driver of Nipah virus transmission from fruit bat reservoirs to pigs, and eventual spillover into humans	Pulliam et al. (2012)

Table 1. continued

Pathogen	Transmission and pathogen type	Mechanism	References
Change in movement or behavior of vectors and/or hosts			
Hendravirus	Directly transmitted zoonotic virus	Urban habituation of fruit bat reservoirs of henipavirus leading to increased contact between bats, humans, and domestic animals, and decreased migration potentially associated with reduced population immunity to hendravirus in urbanized bat populations	Plowright et al. (2011)
Malaria	Vector-borne protozoan	Deforestation associated with increased biting rate of anopheline (*Anopheles darlingi*) mosquito vectors of malaria	Vittor et al. (2006)
E. coli	Directly transmitted bacteria	Agricultural activity at the edge of Ugandan forest fragments inciting crop raiding behavior by primates, allowing for increased pathogen (enteric bacterial) exchange between human and non-human primates	Goldberg et al. (2008)
Socioeconomic factors			
American cutaneous leishmaniasis	Vector-borne protozoan	Poor, socially marginalized populations living closed to forests are more susceptible to cutaneous leishmaniasis infection risk in areas of deforestation	Chaves et al. (2008)
Malaria	Vector-borne protozoan	Poor socioeconomic status was among the factors associated with increased malaria risk in irrigated areas	Klinkenberg et al. (2004)
Pathogen pollution			
Toxoplasma gondii	Directly and trophically transmitted protozoan	Agricultural runoff contaminated with *Toxoplasma gondii*-infected cat feces and taken up by bivalves causes toxoplasmosis in sea otters by ingestion of *T. gondii*-contaminated bivalves.	Miller et al. (2008)
Giardia sp.	Directly transmitted protozoan	Howler monkey *Giardia* sp. prevalence in a rural area higher compared to a remote forests and villages due to increased contamination of water with livestock	Kowalewski et al. (2011)
Changes in host immunity, nutritional condition, or stress			
Lizard hemogregarine parasites	Vector-borne protozoa	In degraded oak forests, female lizards had higher parasite loads and lower body condition than lizards in undisturbed areas	Amo et al. (2007)
Avian hemoparasites	Vector-borne protozoa	Birds in urbanized areas had lower hemoparasite prevalence than those in rural areas, but higher stress hormone levels.	Fokidis et al. (2009)

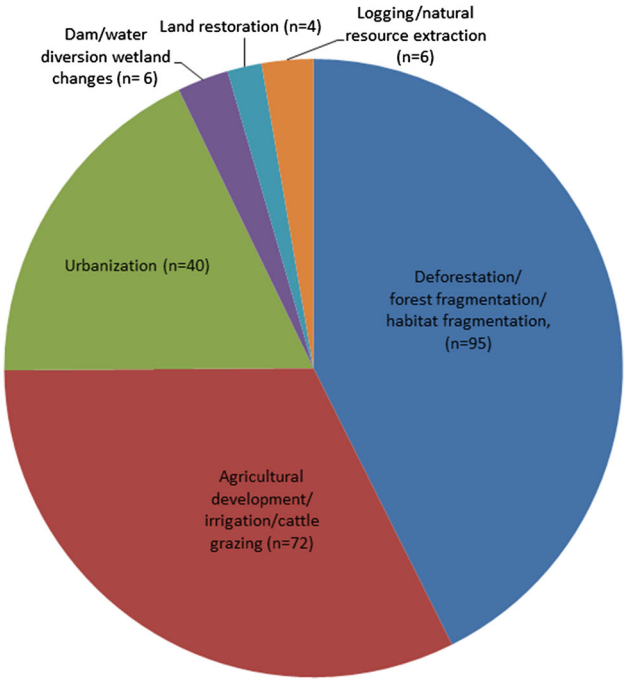

Figure 3. Types of land use change evaluated in anthropogenic land use change-infectious disease studies ($n = 211$). Many studies included more than one type of land use change.

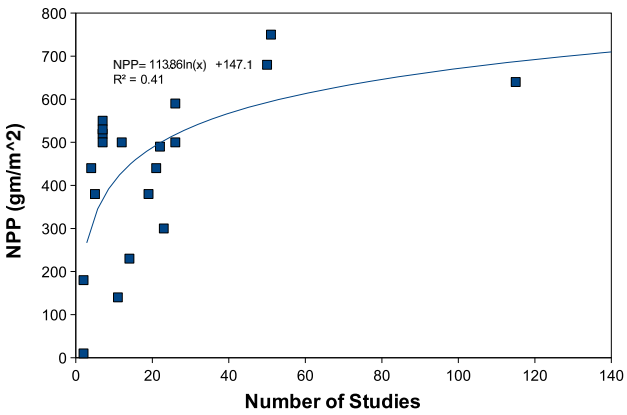

Figure 4. Relationship of net primary productivity (NPP) for a particular anthropogenic biome (Ellis and Ramankutty 2008) to the number of studies taking place in a particular anthropogenic biome.

considerable number of studies ($n = 62$, 30.4%) demonstrate variable responses (increase and decrease) to land use change resulting from complex interactions, such as changes in vector species composition between habitats, and behavioral or economic factors interacting with land use-infectious disease transmission. In four studies ($n = 5$, 2.4%), there was no significant association between land use and disease transmission. There was no significant relationship between the transmission type of the pathogen in the study and the directional response to transmission (increased, decreased, complex, no change; Fisher exact test, $P = 0.09$), or between the land use change type in a study, and the directional response to transmission (Fisher exact test, $P = 0.70$). However, there was a significant association between the pathogen type studied (bacterial, viral, protozoal, helminth-fungus was excluded from the analysis) and the directional response to transmission (Fisher exact test, $P = 0.01$), with viral and protozoan pathogens tending to increase in response to anthropogenic change.

Hypothesized Mechanisms Leading to Infectious Disease Change Following Land Conversion

Although many observational and experimental studies ($n = 81$) did not identify or address drivers of disease transmission, across our literature review we encountered at least six common mechanisms by which anthropogenic land use change was hypothesized or discussed as altering infectious disease transmission in humans and animals in observational and experimental studies. These include: (1) modified niche for the vector, host, and/or pathogen consisting of alterations in habitat architecture, microclimate, and/or resource availability ($n = 61$), (2) changes in host and vector community composition ($n = 24$), (3) altered spatial distribution of species ($n = 9$), (4) changes in behavior or movement of vectors, hosts, and/or species that interact with them ($n = 17$), and (5) socioeconomic factors altering human risk of disease transmission such as environmental contamination/pathogen pollution ($n = 6$). Occasional studies ($n = 3$) identified changes in stress levels and/or host immune status as drivers of disease transmission in response to anthropogenic disturbance. Table 1 highlights some examples of these mechanistic drivers of disease in response to land use change.

Discussion

Land Use Change and Pathogen Transmission: What the Current Evidence Suggests

Literature on Infectious Disease and Anthropogenic Land Use Change Focuses on Vector-Borne Multi-host Pathogens

Over half of the studies reviewed concerned multi-host pathogens. This observation likely reflects the fact that most animal pathogens can infect more than one host, and the applied interest in these pathogens due to their role in the

emergence of pathogens of public health, veterinary, or conservation concern. The predominance of vector-borne and trophically transmitted diseases in the literature may reflect the fact that vectors or other intermediate host populations may increase or respond more rapidly to environmental changes than primary hosts due to their much shorter generation time. In our review, the percentage of studies focusing on zoonoses (56.9%) are strikingly similar to the percentages of pathogens reported to be zoonotic: 61% of all infectious pathogens, and 60.3% of emerging infectious diseases are zoonotic (Woolhouse et al. 2001; Fenton and Pedersen 2005; Jones et al. 2008), suggesting that efforts to study zoonoses are roughly proportionate to their relative detection by humans. However, there is also considerable research interest in host-specific pathogens, such as human malaria. Also, many studies (n = 46) that investigate how diseases primarily affecting wildlife populations are influenced by anthropogenic land use change.

Anthropogenic Disturbance has Variable Effects on the Transmission of Infectious Diseases

Although over half of the studies document an increase in infectious disease transmission in response to land use change, this does not mean that most anthropogenic changes drive increased disease transmission. Bias may benefit research proposals and publications that support this finding. Oversampled pathogens (i.e., *Plasmodium*) skew trends, so that the majority of pathogens may not increase with changing landscapes. There are several examples of declines in disease transmission secondary to land use change, demonstrating a complex response of pathogens to environmental change over different spatial and temporal scales. Prevalence of *Trypanosoma cruzi*, etiologic agent of Chagas disease in humans, declined in wildlife over the course of 20 years in the Argentian Chaco, and this decline was attributed to long-term negative effects of deforestation on mammalian reservoir abundance and continued vector control campaigns (Ceballos et al. 2006). The amount and type of disturbance is also important. Partial disturbance of landscapes can result in higher human infection risk for transmission than deforested landscapes, as in the case of the zoonotic Puumala virus in Belgium (Linard et al. 2007; Tersago et al. 2008). Land use change also frequently leads to complex effects on disease transmission, especially when more than one host species is involved. For example, rice irrigation in Kenya increased mosquito vector abundance, yet lowered childhood malaria prevalence, presumptively due to zooprophylactic effects of cattle resulting from changes in mosquito feeding preference from humans to cows, which are non-competent hosts (Mutero et al. 2004). In other studies, such as Ross river virus, infectious agent transmission does not appear to respond to anthropogenic landscape change (Jardine et al. 2008).

Although studies often conclude that anthropogenic land use change increases infectious disease transmission, it is more difficult to detect if directional responses of pathogen transmission are merely context-dependent (e.g., dependent on local environmental changes), or if there are general ecological principles governing pathogen responses to environmental change, allowing for better prediction. Clearly, predicting the direction of pathogen responses to anthropogenic land use change requires an understanding of the biology and natural history of the pathogen and as well as identifying the mechanisms of disease transmission in different epidemiologic situations.

A Wide Range of Mechanisms have been Associated with Infectious Disease Responses to Anthropogenic Land Use

The most commonly studied mechanisms by which anthropogenic land use influences disease transmission are altered niches for the vector, host, or pathogen, changes in community structure (e.g., species diversity or species composition), and behavioral changes in hosts or vectors. Although relationships between vector, host, and pathogen and their niche requirement responses to land use change can be better understood within modeling and experimental contexts (Colwell and Rangel 2009), there are few studies that employ experimental and modeling approaches to understand land use change and disease transmission. Many studies also investigate how host and vector community diversity influence pathogen transmission in response to anthropogenic change. However, evaluating relationships between species diversity and disease transmission can be "value laden" most people want biodiversity to be good for their health (Dobson et al. 2006), but in some studies, biodiversity–disease relationships appear to be local and situation-dependent, with no clear directional relationships between diversity and disease transmission (Salkeld et al. 2013). Indeed, studies of biodiversity and disease have generated debate, such as the recent debate between critics (Randolph and Dobson 2012) and defenders (Ostfeld 2013) of the dilution effect, which hypothesizes that increasing species diversity leads to decreased disease

risk. Although these debates can be healthy, we suggest that advances in ecological theory (Dobson 2004) and a clear definition of the assumptions and limitations of theoretical frameworks can better guide research design and hypothesis testing to evaluate relationships between land use, community composition, and disease transmission.

Potentially important, but little studied mechanisms of infectious disease-land use change relationships include changes in host and vector behavior, nutrition, immunity, and altered co-infections or within host-communities (e.g., microbiomes) that may respond to anthropogenic change. Anthropogenic change can alter food resources for hosts and vectors, and there are complex feedbacks between host nutrition and immunity. Nutritional depletion may impair immune function and increase susceptibility to infectious diseases, and these pathogens can decrease host condition, resulting in positive feedbacks, or ''vicious circles'' between nutrition and disease transmission (Beldomenico and Begon 2010). Although supplemental wildlife feeding can boost condition for some reservoir hosts and vectors in areas of anthropogenic development, decreasing their susceptibility to infectious agents (Hines et al. 2007), these resources may cause clustering of hosts, and lead to increases in disease transmission due to greater between host contact or contact with infectious material (Sorensen et al. 2014).

Additionally, few studies evaluate how co-infection or pathogen communities infecting hosts or vectors change in response to anthropogenic land use. Because different parasites such as intestinal helminths and bacteria may interact with the immune system to increase host susceptibility to or transmission of microparasites, environmental changes that alter host exposure to one of these agents (Telfer et al. 2010), such as enteric nematodes, may also impact transmission of other co-infecting pathogens (Jolles et al. 2008; Ezenwa et al. 2010, 2012; Ezenwa and Jolles 2011; Budischak et al. 2012). Differences in diet and spatial interactions induced by land use change may impact microbiomes within host or vector populations (Ezenwa et al. 2012). Vector microbial communities (e.g., tick microbiomes) may also vary in response to environmental change and ultimately influence pathogen transmission, but this is an open area of investigation.

Lastly, different types of land use can influence how hosts, different vectors, and their pathogens can interact. For instance, in vector-borne diseases such as malaria, cattle in areas of agricultural development may have a zooprophylactic effect on malaria transmission (Mutero et al. 2004) but can increase the risk of transmission for some zoonotic tick-borne diseases (Raoult and Roux 1997). Because of the diverse mechanisms that can influence disease responses to land use change, multiple working hypotheses to evaluate relative responses of different mechanisms are important to clarify the relative importance of these mechanisms in different situations.

Highly Studied Areas are often Ecologically Productive Areas of Human Settlement

One possible explanation for this observation is that this may be related to the tendency for people to settle in high productivity areas. Because these areas tend to be preferentially for agricultural, pastoral, or forestry uses, areas of high NPP may represent true hotspots for disease transmission. Alternatively, they could simply be disproportionately well-studied areas given their proximity to human settlements, or a combination of the two. Distinguishing between these explanations for the relationship between NPP and infectious disease studies is critically important for understanding the drivers of disease emergence, and for directing future research, surveillance and pathogen discovery efforts directed toward landscape and land use types that may be hotspots for disease emergence. Additionally, ecotones in these areas may be particularly important areas for disease transmission because they facilitate inter-specific or inter-population contacts between hosts and/or vectors (Despommier et al. 2006).

Experimental Studies Investigating Land Use and Infectious Disease Transmission are Rare

The paucity of experimental studies ($n = 7$) relative to the number of review ($n = 94$) and observational studies ($n = 204$) is striking, and may reflect the relative novelty of this emerging field and/or the challenges implicit in landscape level experimental manipulations. There is almost one review or ''concept'' paper for every two original research pieces (not that ours helps this ratio). Although there is a cross-disciplinary awareness of the relationship between environmental changes and infectious disease transmission, there is a lack of experimental or analytical studies evaluating mechanistic drivers of pathogen transmission in response to land use change. Most studies use observational approaches to compare prevalence or vector

abundance over temporal (pre- and post-disturbance) or spatial (comparison of anthropogenically disturbed areas to relatively undisturbed sites) scales. Given the complex social, economic, and ecological relationships between land use change and infectious diseases, experimental approaches may fall short in providing a true understanding of why and how disease changes in response to land use. Predictive understanding of how any particular pathogen will respond to environmental change will require focused studies that consider not only shifting patterns of interspecies contacts, but also the shifts in demography, behavior, and transmission dynamics within reservoir or vector populations that accompany land use change.

Regardless, when evaluating linkages between land use change and infectious disease emergence, there are logistical difficulties in pinpointing the mechanism or mechanisms at play. Useful methods that allow for rooting out and focusing on important research questions related to causal drivers of infectious diseases driven by land use include causal diagrams of complex indirect and direct, relationships between land use and disease transmission, multiple hypothesis testing/model selection/information theory approaches, and integrated feedback between experimental studies, field studies, and computational models (“triangulation”) (Plowright et al. 2008).

Future Directions for Research

Interdisciplinary, Long-Term Data Collection: Critical for a Better Understanding of Complex Interactions Between Land Use and Infectious Diseases

Although there has been an increase in the number of studies investigating land use change and infectious disease, there are still many challenges and knowledge gaps. Anthropogenic land use change is a dynamic process. In theory, plant and animal community structure and food web relationships, as well as disease control programs or infrastructure, may be abruptly disrupted following anthropogenic disturbance, and continue to reorganize until a new equilibrium state is reached with corresponding changes in the level of disease transmission (Fig. 5). Infectious disease transmission, vector and/or reservoir abundance, diversity, spatial distribution, and infection risk may vary at different times and spatial extents post-disturbance. For example, in frontier Amazonia, increases in malaria transmission during the initial deforestation-settlement phase is followed by an eventual decline in malaria infection risk as agriculture, infrastructure, and health care improve (de Castro et al. 2006). Time since environmental disturbance may also impact disease transmission as well as control programs. For instance, malaria in areas that were initially irrigated within a 10-year period were more difficult to control by vector spraying campaigns and had higher human disease risk compared to areas that were under very long-term (30-year) irrigation (Baeza et al. 2014). Furthermore, different successional states post-deforestation also bring with them corresponding changes in dominant reservoir host and vector communities that can potentially impact transmission of zoonotic diseases. Long-term disease monitoring strategies pre-, during, and for extended periods post-disturbance can provide a more complete understanding of how disease dynamics can change relative to ecosystem state. Supporting long-term studies is financially and logistically challenging, but necessary for understanding how infectious disease transmission responds over time to anthropogenic disturbance. This is essential to avoid developing policy recommendations that are based on short term, transient effects of land use change that may over- or under-estimate linkages between land use change and disease transmission. The complexity of these systems also poses a challenge, and we encourage not only the study of exclusively human infections, but also multi-host pathogens. Finally, addressing complexity requires examination of infectious disease in the larger context of socio-political change, ideally involving collaborations among biological and social scientists.

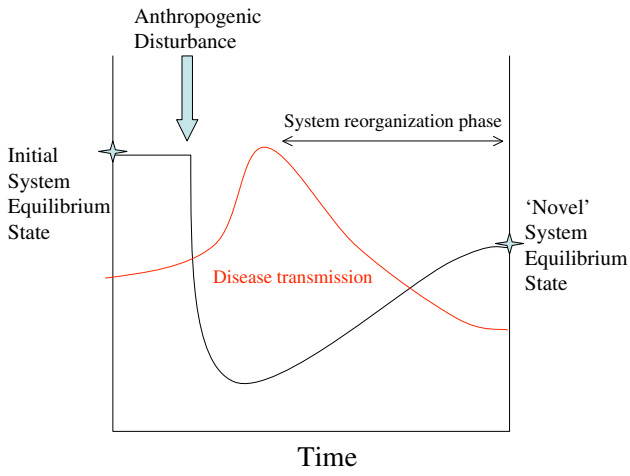

Figure 5. Conceptual model of how infectious disease transmission is a dynamic process dependent on the structure and organization of social and ecological systems.

Integrating Theoretical and Empirical Approaches for Improved Understanding, Prediction, and Prevention of Disease Transmission Driven by Land Use Change

Can we employ unified theoretical frameworks to understand which pathogen and host traits (e.g., life history) are most important in affecting shifts in disease transmission associated with anthropogenic change? Ecological theory provides conceptual frameworks for directing field studies of relationships between anthropogenic disturbance and disease transmission, and their use is emerging in infectious disease studies (Restif et al. 2012). Metapopulation, multi-host pathogen transmission, systems theory, and network theory each provide useful hypothesis-testing frameworks for understanding and predicting ways that human land use impacts infectious disease transmission and persistence. Land use change may alter spatial relationships between pathogens, hosts, and/or vectors, and metapopulation theory is useful in terms of understanding and predicting how disease may persist in these transformed landscapes (McCallum and Dobson 2002). Measuring connectivity and subsequent host or vector immigration between habitat patches may be very important in predicting the long-term persistence or fade-out of infectious disease in fragmented or degraded habitats (McCallum and Dobson 2002). Although metapopulation theory has been applied to the epidemiology of human (Xia et al. 2004) and animal (Beyer et al. 2011) infectious diseases, there are few studies that explicitly apply a metapopulation approach to evaluating relationships between land use change and disease transmission. Source–sink theoretical approaches to modeling infectious disease may also apply to pathogen-land use change relationships, as some host species or habitats that maintain and transmit infection can be considered ''sources,'' whereas other hosts or habitats that may be infected yet cannot maintain the infection nor transmit the pathogen may be considered ''sinks,'' and these ''source-sink'' relationships may change in response to environmental disturbance.

Most pathogens infect more than one host, and theoretical models of multi-host pathogen transmission and maintenance (Dobson 2004) can be applied to predictions of land use change effects on infectious disease. Multi-host models evaluate how gains and losses of particular species can lead to increased or decreased transmission. In order to predict how changes in species diversity in response to anthropogenic disturbance will affect the transmission of multi-host pathogens, it is important to identify the sources of heterogeneity and differences in life history among host species that influence their relative importance for pathogen persistence. Variation among species in susceptibility and competence, behavioral factors associated with pathogen exposures, as well as in population abundance, can influence relative transmission rates between and within species and thus the transmission consequences of species removals resulting from land use change or disease control strategies such as culling or vaccination. Pathogen dynamics within novel hosts are also important to consider, because ongoing transmission within populations of new host species (i.e., true multi-host pathogens) may require fundamentally different control strategies than constant reintroduction by cross-species transmission.

Multidisciplinary Approaches In addition to complex host networks and pathogen diversity, socioeconomic and political factors also interact with land use change to impact infectious disease transmission. Socioeconomic conditions can influence access to social services, such as vaccination, medical treatment, and vector control, causing individuals and populations to be at greater risk for diseases that respond positively to anthropogenic disturbance. El Nino Southern Oscillation (ENSO) climactic variability, poverty (lack of access to financial resources and political power), and deforestation interact to affect the risk of American cutaneous leishmaniasis in Costa Rica (Chaves et al. 2008). Therefore, multidisciplinary approaches to understanding relationships between environmental change and socioeconomic conditions are critical to effectively predict and prevent disease emergence in these complex landscapes.

Incorporation of Evolutionary Perspectives A virtually unexplored question in theory and practice is how infectious diseases may evolve in response to anthropogenic landscape transformation. Changes in host resource availability (i.e., the parasite's environment), a likely occurrence in many altered ecosystems, may shift transmission dynamics or host–pathogen interactions in ways that change pathogen virulence. For instance, fragmentation of populations with a large degree of social structure, where avirulent strains have evolved, may select for an alternate stability of a highly virulent strain (Boots and Bowers 2004). Higher densities of host species that thrive under new environmental conditions could also allow for increased virulence. These shifts in virulence could, in turn, affect the likelihood of disease emergence by cross-species

transmission or the impacts of emergence in terms of morbidity and mortality (Dennehy et al. 2006). Empirical studies that test theories of how landscape transformation can alter pathogen virulence and host shifts are important to incorporate into disease monitoring strategies in rapidly changing landscapes.

Conclusion

There is a growing body of evidence that anthropogenic land use change can directly and indirectly influence disease transmission in humans, wildlife, and domestic animals. Although there are many cases in which land use change is associated with increased disease transmission, there is a great deal of uncertainty regarding the direction, magnitude, and mechanisms of anthropogenic disturbances on infectious disease transmission and persistence. Future research programs should be transdisciplinary, incorporating ecological theory and principles and experimental methods in order to understand, predict, prevent, and manage land use change-related disease emergence.

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References

Allan BF, Dutra HP, Goessling LS, Barnett K, Chase JM, Marquis RJ, Pang G, Storch GA, Thach RE, Orrock JL (2010) Invasive honeysuckle eradication reduces tick-borne disease risk by altering host dynamics. *Proceedings of the National Academy of Sciences of the United States of America* 107(43):18523–18527

Amo L, Lopez P, Martin J (2007) Habitat deterioration affects body condition of lizards: a behavioral approach with *Iberolacerta cyreni* lizards inhabiting ski resorts. *Biological Conservation* 135(1):77–85

Baeza A, Bouma MJ, Dhiman R, Pascual M (2014) Malaria control under unstable dynamics: reactive vs. climate-based strategies. *Acta Tropica* 129:42–51

Beldomenico PM, Begon M (2010) Disease spread, susceptibility and infection intensity: vicious circles? *Trends in Ecology & Evolution* 25(1):21–27

Beyer HL, Hampson K, Lembo T, Cleaveland S, Kaare M, Haydon DT (2011) Metapopulation dynamics of rabies and the efficacy of vaccination. *Proceedings of the Royal Society B: Biological Sciences* 278(1715):2182–2190

Boots M, Bowers RG (2004) The evolution of resistance through costly acquired immunity. *Proceedings of the Royal Society B: Biological Sciences* 271(1540):715–723

Budischak SA, Jolles AE, Ezenwa VO (2012) Direct and indirect costs of co-infection in the wild: linking gastrointestinal parasite communities, host hematology, and immune function. *The International Journal for Parasitology: Parasites and Wildlife* 1:2–12

Burney DA, Flannery TF (2005) Fifty millennia of catastrophic extinctions after human contact. *Trends in Ecology & Evolution* 20(7):395–401

Ceballos LA, Cardinal MV, Vazquez-Prokopec GM, Lauricella MA, Orozco MM, Cortinas R, Schijman AG, Levin MJ, Kitron U, Gurtler RE (2006) Long-term reduction of *Trypanosoma cruzi* infection in sylvatic mammals following deforestation and sustained vector surveillance in northwestern Argentina. *Acta Tropica* 98(3):286–296

Chaves LF, Cohen JM, Pascual M, Wilson ML (2008) Social exclusion modifies climate and deforestation impacts on a vector-borne disease. *PLoS Neglected Tropical Diseases* 2(2):e176

Colwell RK, Rangel TF (2009) Hutchinson's duality: the once and future niche. *Proceedings of the National Academy of Sciences of the United States of America* 106(Suppl 2):19651–19658

de Castro MC, Monte-Mor RL, Sawyer DO, Singer BH (2006) Malaria risk on the Amazon frontier. *Proceedings of the National Academy of Sciences of the United States of America* 103(7):2452–2457

Dennehy JJ, Friedenberg NA, Holt RD, Turner PE (2006) Viral ecology and the maintenance of novel host use. *The American Naturalist* 167(3):429–439

Despommier D, Ellis BR, Wilcox BA (2006) The role of ecotones in emerging infectious diseases. *EcoHealth* 3(4):281–289

Dobson A (2004) Population dynamics of pathogens with multiple host species. *The American Naturalist* 164(Suppl 5):S64–S78

Dobson A, Cattadori I, Holt RD, Ostfeld RS, Keesing F, Krichbaum K, Rohr JR, Perkins SE, Hudson PJ (2006) Sacred cows and sympathetic squirrels: the importance of biological diversity to human health. *PLoS Medicine* 3(6):e231

Eliseev LN, Strelkova MV, Zherikhina II (1991) The characteristics of the epidemic activation of a natural focus of zoonotic cutaneous leishmaniasis in places with a sympatric dissemination of Leishmania major, *L. turanica* and *L. gerbilli*. *Meditsinskaia Parazitologiia I Parazitarnye Bolezni* 3:24–29

Ellis EC, Ramankutty N (2008) Putting people in the map: anthropogenic biomes of the world. *Frontiers in Ecology and the Environment* 6(8):439–447

Ezenwa VO, Jolles AE (2011) From host immunity to pathogen invasion: the effects of helminth coinfection on the dynamics of microparasites. *Integrative and Comparative Biology* 51(4):540–551

Ezenwa VO, Etienne RS, Luikart G, Beja-Pereira A, Jolles A (2010) Hidden consequences of living in a wormy world: nematode-induced immune suppression facilitates tuberculosis invasion in African buffalo. *The American Naturalist* 176(5):613–624

Ezenwa VO, Gerardo NM, Inouye DW, Medina M, Xavier JB (2012) Microbiology. Animal behavior and the microbiome. *Science* 338(6104):198–199

Fenton A, Pedersen AB (2005) Community epidemiology framework for classifying disease threats. *Emerging Infectious Diseases* 11(12):1815

Fokidis HB, Orchinik M, Deviche P (2009) Corticosterone and corticosteroid binding globulin in birds: relation to urbanization in a desert city. *General and Comparative Endocrinology* 160(3):259–270

Foley JA, Defries R, Asner GP, Barford C, Bonan G, Carpenter SR, Chapin FS, Coe MT, Daily GC, Gibbs HK, Helkowski JH, Holloway T, Howard EA, Kucharik CJ, Monfreda C, Patz JA, Prentice IC, Ramankutty N, Snyder PK (2005) Global consequences of land use. *Science* 309(5734):570–574

Goldberg TL, Gillespie TR, Rwego IB, Estoff EL, Chapman CA (2008) Forest fragmentation as cause of bacterial transmission among nonhuman primates, humans, and livestock, Uganda. *Emerging Infectious Diseases* 14(9):1375–1382

Goudie A (2000) *The Human Impact on the Natural Environment, 5th ed.*, Cambridge: The MIT Press

Grieco JP, Johnson S, Achee NL, Masuoka P, Pope K, Rejmankova E, Vanzie E, Andre R, Roberts D (2006) Distribution of *Anopheles albimanus*, *Anopheles vestitipennis*, and *Anopheles crucians* associated with land use in northern Belize. *Journal of Medical Entomology* 43(3):614–622

Hines AM, Ezenwa VO, Cross P, Rogerson JD (2007) Effects of supplemental feeding on gastrointestinal parasite infection in elk (*Cervus elaphus*): preliminary observations. *Veterinary Parasitology* 148(3–4):350–355

Jardine A, Speldewinde P, Lindsay MD, Cook A, Johansen CA, Weinstein P (2008) Is there an association between dryland salinity and Ross River virus disease in southwestern Australia? *EcoHealth* 5(1):58–68

Johnson PT, Chase JM, Dosch KL, Hartson RB, Gross JA, Larson DJ, Sutherland DR, Carpenter SR (2007) Aquatic eutrophication promotes pathogenic infection in amphibians. *Proceedings of the National Academy of Sciences of the United States of America* 104(40):15781–15786

Jolles AE, Ezenwa VO, Etienne RS, Turner WC, Olff H (2008) Interactions between macroparasites and microparasites drive infection patterns in free-ranging African buffalo. *Ecology* 89(8):2239–2250

Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, Daszak P (2008) Global trends in emerging infectious diseases. *Nature* 451(7181):990–993

Keesing F, Belden LK, Daszak P, Dobson A, Harvell CD, Holt RD, Hudson P, Jolles A, Jones KE, Mitchell CE, Myers SS, Bogich T, Ostfeld RS (2010) Impacts of biodiversity on the emergence and transmission of infectious diseases. *Nature* 468(7324):647–652

Klinkenberg E, Konradsen F, Herrel N, Mukhtar M, van der Hoek W, Amerasinghe FP (2004) Malaria vectors in the changing environment of the southern Punjab, Pakistan. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 98(7):442–449

Kowalewski MM, Salzer JS, Deutsch JC, Rano M, Kuhlenschmidt MS, Gillespie TR (2011) Black and gold howler monkeys (*Alouatta caraya*) as sentinels of ecosystem health: patterns of zoonotic protozoa infection relative to degree of human-primate contact. *American Journal of Primatology* 73(1):75–83

Linard C, Lamarque P, Heyman P, Ducoffre G, Luyasu V, Tersago K, Vanwambeke SO, Lambin EF (2007) Determinants of the geographic distribution of Puumala virus and Lyme borreliosis infections in Belgium. *International Journal of Health Geographics* 6:15

Matson PA, Parton WJ, Power AG, Swift MJ (1997) Agricultural intensification and ecosystem properties. *Science* 277(5325): 504–509

Mayo CE, Gardner IA, Mullens BA, Barker CM, Gerry AC, Guthrie AJ, MacLachlan NJ (2012) Anthropogenic and meteorological factors influence vector abundance and prevalence of bluetongue virus infection of dairy cattle in California. *Veterinary Microbiology* 155(2–4):158–164

McCallum H, Dobson A (2002) Disease, habitat fragmentation and conservation. *Proceedings of the Royal Society B: Biological Sciences* 269(1504):2041–2049

Miller MA, Miller WA, Conrad PA, James ER, Melli AC, Leutenegger CM, Dabritz HA, Packham AE, Paradies D, Harris M, Ames J, Jessup DA, Worcester K, Grigg ME (2008) Type X *Toxoplasma gondii* in a wild mussel and terrestrial carnivores from coastal California: new linkages between terrestrial mammals, runoff and toxoplasmosis of sea otters. *International Journal for Parasitology* 38(11):1319–1328

Mutero CM, Kabutha C, Kimani V, Kabuage L, Gitau G, Ssennyonga J, Githure J, Muthami L, Kaida A, Musyoka L, Kiarie E, Oganda M (2004) A transdisciplinary perspective on the links between malaria and agroecosystems in Kenya. *Acta Tropica* 89(2):171–186

Ostfeld RS (2013) A Candide response to Panglossian accusations by Randolph and Dobson: biodiversity buffers disease. *Parasitology* 140(10):1196–1198

Patz JA, Graczyk TK, Geller N, Vittor AY (2000) Effects of environmental change on emerging parasitic diseases. *International Journal for Parasitology* 30(12–13):1395–1405

Plowright R, Sokolow S, Gorman M, Daszek P, Foley J (2008) Causal inference in disease ecology: investigating ecological drivers of disease emergence. *Frontiers in Ecology and the Environment* 6:420–429

Plowright RK, Foley P, Field HE, Dobson AP, Foley JE, Eby P, Daszak P (2011) Urban habituation, ecological connectivity and epidemic dampening: the emergence of Hendra virus from flying foxes (*Pteropus* spp.). *Proceedings of the Royal Society B: Biological Sciences* 278(1725):3703–3712

Pongsiri MJ, Roman J, Ezenwa VO, Goldberg TL, Koren HS, Newbold SC, Ostfeld RS, Pattanayak SK, Salkeld DJ (2009) Biodiversity loss affects global disease ecology. *BioScience* 59(11):945–954

Pulliam JR, Epstein JH, Dushoff J, Rahman SA, Bunning M, Jamaluddin AA, Hyatt AD, Field HE, Dobson AP, Daszak PThe Henipavirus Ecology Research (2012) Agricultural intensification, priming for persistence and the emergence of Nipah virus: a lethal bat-borne zoonosis. *Journal of the Royal Society Interface* 9(66):89–101

Randolph SE, Dobson ADM (2012) Pangloss revisited: a critique of the dilution effect and the biodiversity-buffers-disease paradigm. *Parasitology* 139(7):847–863

Raoult D, Roux V (1997) Rickettsioses as paradigms of new or emerging infectious diseases. *Clinical Microbiology Reviews* 10(4):694–719

Restif O, Hayman DT, Pulliam JR, Plowright RK, George DB, Luis AD, Cunningham AA, Bowen RA, Fooks AR, O'Shea TJ, Wood JL, Webb CT (2012) Model-guided fieldwork: practical guidelines for multidisciplinary research on wildlife ecological and epidemiological dynamics. *Ecology Letters* 15(10):1083–1094

Salkeld DJ, Padgett KA, Jones JH (2013) A meta-analysis suggesting that the relationship between biodiversity and risk of zoonotic pathogen transmission is idiosyncratic. *Ecology Letters* 16(5):679–686

Sorensen A, van Beest FM, Brook RK (2014) Impacts of wildlife baiting and supplemental feeding on infectious disease transmission risk: a synthesis of knowledge. *Preventive Veterinary Medicine* 113(4):356–363

Suzan G, Marce E, Giermakowski JT, Armien B, Pascale J, Mills J, Ceballos G, Gomez A, Aguirre AA, Salazar-Bravo J, Armien A, Parmenter R, Yates T (2008) The effect of habitat fragmentation and species diversity loss on hantavirus prevalence in *Panama*. *Annals of the New York Academy of Sciences* 1149:80–83

Telfer S, Lambin X, Birtles R, Beldomenico P, Burthe S, Paterson S, Begon M (2010) Species interactions in a parasite community drive infection risk in a wildlife population. *Science* 330(6001): 243–246

Tersago K, Schreurs A, Linard C, Verhagen R, Van Dongen S, Leirs H (2008) Population, environmental, and community effects on local bank vole (*Myodes glareolus*) Puumala virus infection in an area with low human incidence. *Vector-Borne and Zoonotic Diseases* 8(2):235–244

Tilman D (1999) Global environmental impacts of agricultural expansion: the need for sustainable and efficient practices. *Proceedings of the National Academy of Sciences of the United States of America* 96(11):5995–6000

Vaz VC, D'Andrea PS, Jansen AM (2007) Effects of habitat fragmentation on wild mammal infection by *Trypanosoma cruzi*. *Parasitology* 134(12):1785–1793

Vittor AY, Gilman RH, Tielsch J, Glass G, Shields T, Lozano WS, Pinedo-Cancino V, Patz JA (2006) The effect of deforestation on the human-biting rate of *Anopheles darlingi*, the primary vector of Falciparum malaria in the Peruvian Amazon. *American Journal of Tropical Medicine and Hygeine* 74(1):3–11

Woolhouse ME, Taylor LH, Haydon DT (2001) Population biology of multihost pathogens. *Science* 292(5519):1109–1112

Xia Y, Bjornstad ON, Grenfell BT (2004) Measles metapopulation dynamics: a gravity model for epidemiological coupling and dynamics. *The American Naturalist* 164(2):267–281

Yasuoka J, Levins R (2007) Impact of deforestation and agricultural development on anopheline ecology and malaria epidemiology. *American Journal of Tropical Medicine and Hygiene* 76(3):450–460