THESIS

LINKING HUMAN-DISTURBED LANDSCAPES WITH PATHOGEN PREVALENCE IN WILDLIFE: A META-ANALYSIS

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ABSTRACT

LINKING HUMAN MODIFIED LANDSCAPES WITH PATHOGEN PREVALENCE IN WILDLIFE: A META-ANYLISIS

The percentage of earth disturbed by humans is rapidly growing. In a review of the available literature in wildlife disease ecology we performed a meta-analysis to determine if human disturbed landscapes increased prevalence of pathogens and parasites, compared to undisturbed landscapes. We analyzed a total of 68 cases of host-pathogen and host-parasites reported in 34 publications. We carried out analyses at two levels: 1.) studies reporting prevalence values for both disturbed and undisturbed landscapes, of which 46 cases within 13 published studies were included in the final analysis and 2.) studies only reporting differences in disturbed and undisturbed landscapes (increase, decrease, varied, or no change) without published prevalence data (68 cases within 36 studies). Overall, we found that disturbed landscapes had higher pathogen prevalence. We reviewed potential indirect drivers (types of landscapes), direct drivers (features associated with landscapes), and mechanisms (changes in ecology caused by the indirect and direct drivers) that may account for the increase in pathogen prevalence between the landscapes. High pathogen prevalence in wildlife living in disturbed landscapes may serve as an indicator of the negative consequences of unsustainable human development. Having this understanding will enable wildlife managers to produce sustainable development solutions that will improve their predictions of infection and reduce prevalence of harmful pathogens in sensitive populations.

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Introduction

The consequences of landscape disturbance on wildlife are potentially tied to the emergence and prevalence of zoonotic diseases. High prevalence of pathogens in wildlife living in disturbed landscapes may serve as indicators of the negative consequences of human development. A synthesis of studies of disease ecology will increase understanding of the drivers and mechanisms of infection and pathogen prevalence. This study examines the impact of human disturbed landscapes on pathogen and parasite prevalence in wildlife, including direct drivers, indirect drivers and ecological mechanisms that may change transmission and rates of infection. Identifying whether landscape disturbance increases pathogen prevalence will enable health professionals, veterinarians and wildlife managers to focus their efforts on high risk locations, and close a potential gap that could divide human, domestic and wildlife health. It is increasingly important that we recognize direct drivers and mechanisms of pathogen prevalence across all landscapes, in order to successfully prevent, control and eradicate diseases of economic, agricultural and human health concern.

Zoonotic disease should be a high priority on the ecological conservation and human health agendas. Emerging infectious diseases (EIDs) are increasing around the world (Jones et al., 2008), as is the acreage of landscapes modified by humans. Of the 335 EIDs found between the years 1940-2004, 60.3% were zoonotic (Jones et al., 2008). Twelve percent of birds, 23% of mammals, 32% of amphibians, 31% of gymnosperms and 33% of corals are threatened with extinction (Keesing et al., 2010), disease is a tipping point for many of them. The modification of ecological systems creates changes that allow for pathogens to increase and emerge (Daszak, Cunningham, & Hyatt, 2001; Daszak et al., 2007; Field, 2009). Wildlife play a key role in the transmission of zoonotic disease, as they act as hosts and reservoirs (Daszak et al., 2001) that allow disease spillover to livestock, domestic pets and humans.

To understand the complexity of wildlife disease dynamics, ecosystems need to be examined at multiple levels. These include the indirect drivers, direct drivers, and mechanisms that cause pathogens to increase or emerge (Figure 1). Indirect drivers include landscape disturbance such as: agriculture, urbanization, deforestation, fragmentation and ecotourism and recreation. Direct drivers are features associated with indirect drivers, such as livestock. Direct drivers trigger mechanisms such as the amplification of pathogens through increased transmission and high host density. Pathways connecting landscape disturbance with pathogen prevalence are complex, and it is challenging to link any single factor to the increase or decrease of a particular disease.

Figure 1. Directionality of drivers and mechanisms.

Landscape disturbance as indirect drivers of pathogen prevalence

Eighty-three percent of the earth's land cover has been modified by humans (Sanderson et al., 2002). For the purposes of this study, a disturbed or modified landscape was defined as any area that has been influenced by humans leading to changes in the species composition of the landscape or ecosystem. The following anthropogenically disturbed landscapes may be considered indirect drivers of pathogen prevalence.

Agriculture

Human population is projected to reach 9 billion by 2030 (R. S. Miller, Farnsworth, & Malmberg, 2013), and the increased population will most likely require additional lands to be used for agriculture. Agriculture is the most common type of landscape disturbance, consuming 38% of the world's land cover (Foley et al., 2011). Change in soil composition, host and

pathogen diversity, use of harmful chemicals, and water runoff are consequences of agriculture (Ewel, Mazzarino, & Berish, 1991; Hurst et al., 2013; Koprivnikar & Redfern, 2012; Sanchez et al., 2014; Wasserberg et al., 2003). Koprivnikar & Redfern (2012) found that runoff of agricultural pollutants causes immunosuppression in some amphibian species leading to increased host susceptibility. Wasserberg et al (2003) concluded that the addition of water to soil provided ample breeding grounds for the insect vector *Phlebotomus papatasi*, leading to higher prevalence of *Leishmania major* (*Trypanosomatidae*) in rodents occupying agricultural landscapes. Agriculture also changes the host-pathogen relationship through the addition of hosts and generalist species, reduction in biodiversity, decreased resources, stress responses to chemicals and additional transmission routes (Koprivnikar & Redfern, 2012). Further, it appears that sustainable practices in agriculture, such as shade grown coffee, show no significant differences in pathogen prevalence rates between disturbed and undisturbed landscapes (Hernandez et al., 2013).

Urbanization

An increase in human population coupled with a higher standard of living in industrialized societies results in rapid urbanization. Ecological processes in urban areas are altered by: habitat degradation, change in host diversity, structural features that increase vector abundance and increased human interaction (Bradley, Gibbs, & Altizer, 2008; Hamer, Lehrer, & Magle, 2012). For example, the effects of changes in host diversity on prevalence in urban landscapes were demonstrated in Northern Cardinals (*Cardinalis cardinalis*) that had higher prevalence of West Nile Virus antibodies in urban areas (Bradley et al., 2008).

Urbanization is an indirect driver because it changes community composition by allowing urban adapters and generalist species to thrive (Lehrer, Fredebaugh, Schooley, & Mateus-Pinilla,

2010). Domestic animals act as maintenance hosts that allow new diseases to establish in existing communities though spillover and spillback effects. They can also act as amplifier hosts between wildlife and humans. The addition of maintenance hosts leads to novel transmission pathways. An example being the increase of *Toxoplasma gondii* in sea otters (*Enhydra lutris*), river otters (*Lontra canadensis*) , mink (*Neovison vison*), bobcats (*Lynx rufus*) and wood chucks (*Marmota monax*) near urbanized areas due to the spread of the pathogen's oocysts by domestic cats (*Felis catus*) (Lehrer et al., 2010; Riley, Foley, & Chomel, 2004; Sepúlveda et al., 2011).

Deforestation

In the humid tropics 2.3% of forests were deforested between 2000 and 2005 (Sehgal, 2010), following centuries of deforestation in other more temperate regions of the world. Predominantly, deforestation is a precursor for agriculture, urbanization, roads and harvesting of goods. Deforestation indirectly alters survival rates of pathogens and vectors by creating microclimates (Chasar et al., 2009). For instance, machinery can leave divots that fill with standing water creating an environment in which vectors can breed. Change in diversity, prevalence and distribution of parasites in the yellow-whiskered greenbill (*Andropadus latirosris*) and the olive sunbird (*Cyanomitra olivacea*) was seen in deforested habitats (Chasar et al., 2009). Deforestation also leads to fragmentation (Wolfe et al., 2005) which has its own set of ecological consequences.

Fragmentation

Fragmentation indirectly drives changes in the relationship between host and pathogen by means of altering the composition and density of hosts and vectors. Densely populated fragmented areas create crowding, which leads to high competition for limited resources, additional host encounters and pathogen contamination of shared space (Lane, Holley,

Hollocher, & Fuentes, 2011; Wobeser, 2006). It has been documented in red colobus (*Procolobus rufomitratus*) and mangabey (*Cercocebus galeritus galeritus*) populations that host density positively correlates with forest fragment size and pathogen prevalence increases with host density (Mbora & McPeek, 2009). Fragmentation changes parasite community composition by increasing vector abundance (Allan, Keesing, & Ostfeld, 2003; Gottdenker, Calzada, Saldana, & Carroll, 2011) and reducing host species diversity (Cottontail, Wellinghausen, & Kalko, 2009). This idea was reinforced in a study that attributed the higher levels of *trypanosome cruzi* in the common fruit bat (*Artibeus jamaicensis*) to lack of biodiversity and changes in vegetation that favored transmission in forest fragments (Cottontail et al., 2009). Edge effects are a consequence of fragmentation. Chapman (2006) found that a higher number of Red colobus living on the edge of forest fragments had multiple parasitic infections then those living in the forest interior. Edges create an environment where wildlife can have contact with humans. Direct contact with humans or their latrines in forest edges may be the reason for increased parasitic prevalence in Red as well as Black and White colobus occupying these areas (Chapman, Speirs, Gillespie, Holland, & Austad, 2006).

Ecotourism

Using economic incentives to provide a sustainable product has shown great promise in countries throughout the world (Xiang et al., 2011). Ecotourism provides incentive to local peoples to preserve land and species biodiversity by giving them income and decreasing the need for activities such as poaching and harvesting. Along with benefits, however, a variety of drawbacks arise that have indirect effects on pathogen prevalence. One of the most common problems is elevated stress in wildlife due to human presence (Hayward & Hayward, 2009; Mullner, Linsenmair, & Wikelski, 2004; Xiang et al., 2011). This was seen in a population of

hoatzins (*Opisthocomus hoazin*) chicks whose reproductive success was much lower in individuals used for ecotourism in the Cuyabeno Wildlife Reserve (Mullner et al., 2004). Hoatzins are an attraction for people looking to watch the big, colorful birds. Animals used in ecotourism face increased susceptibility to disease due to high levels of stress compromising their immune systems (Hayward & Hayward, 2009). High host mortality due to human transmitted respiratory disease was seen in chimpanzees (*Pan troglodytes*) participating in an ecotourism program designed to protect them in Côte d'Ivoire, West Africa (Kondgen et al., 2008). The increases in pathogen prevalence seen in these landscapes have been attributed to the presence of novel hosts (humans) and high host density (larger than normal populations) (Lafferty & Gerber, 2002).

In most cases, human food harms wildlife (Orams, 2002). The consumption of human food has shown changes in parasite prevalence particularly in long-tailed macaques (*Macaca fascicularis*) (Lane et al., 2011; Wenz-Mucke, Sithithaworn, Petney, & Taraschewski, 2013). In contradiction, a population of Balinese long-tailed macaques had lower levels of macro parasites because of feeding by tourists (Lane et al., 2011), illustrating that reaction to disturbance may differ within species.

Direct drivers of pathogen prevalence

Direct drivers of pathogen prevalence are features associated with indirect drivers. They include changes in resources, wildlife and pathogen biology and behavior, livestock and domestic species, host stress, loss of biodiversity, the introduction of invasive species, an increase in available alternate or reservoir hosts, and changing vector ecology. The following direct drivers alter mechanisms of disease ecology.

Change in resources

Wildlife in areas of limited resources are forced to consume prey that may not be optimal, but are available. Wildlife using sub optimal resources are susceptible to diseases because of a change in the pathways in which a host can become infected. Southern sea otters (*Enhydra lutris nereis*) who consumed marine snails, available in marine systems with poor otter resources, had higher rates of *Toxoplasma gondii* then their counterparts who consumed the favored prey of abalone. The change in otter resources led to a change in trophic transmission, in which the otters are now feeding on reservoir hosts and increasing their likelihood of contracting *Toxoplasma gondii* (Johnson et al., 2009). Other ways change in resources effect pathogens are through: change transmission pathways, increased nutrition through human feeding, lack of nutrition, changes in predation and food webs, and increased competition for limited resources.

Pollution

Human pollution is a consequence of urbanization, agriculture, ecotourism and roads (Bichet et al., 2013). Trace metals, common pollutants, have adverse consequences on hematological status, oxidative balance, immune function and reproduction of wildlife (Bichet et al., 2013). Parasite prevalence has been seen to be positively correlated with increased trace metals found in urban areas (Bichet et al., 2013). It is thought that pollution may decrease or stop lymphocyte proliferation leading to a decreased immune response, causing susceptibility to increased disease (Lewis, Cristol, Swaddle, Varian-Ramos, & Zwollo, 2013). Both phosphorus and nitrogen additions to the environment by fossil fuel combustion and fertilizer application increase infectivity of generalist pathogens with simple life cycles. Changes in host or vector density, distribution of hosts, degree of virulence resistance to infection are mechanisms thought to increase infectivity (Johnson et al., 2010).

Livestock and domestic animals

Livestock and domestic animals are frequently added to the original ecosystem and can act as definitive, intermediate or maintenance hosts. Increased contact with domestic pets and increase the potential for disease. Riley at. al. 2004 found that wild felids and canids that had potential contacts with domestic pets had higher seroprevalence of Canine parvovirus, Canine adenovirus and *T. gondii* than those who did not have contact with pets (Riley et al., 2004). Environmental contamination of pathogens can increase a wildlife host's chance of coming in contact with the pathogen when habitat between livestock and wildlife is shared. This was seen in White-tailed deer (*Odocoileus virginianus*) sharing habitat with bovine herd in in New York. White-tailed deer sharing habitat with bovine herds had higher prevalence of *Coxiella burnetii* antibodis (Kirchgessner, Dubovi, & Whipps, 2012). Red and Black and White Colobus living fragmented landscapes shared with humans and livestock had high levels of parasites that where maintained at high prevalence in human populations (Gillespie & Chapman, 2008). Gillespie and Chapman (2008) speculate that the increase of parasites in the colobus living near humans and livestock was most likely due to humans and livestock acting like reservoirs.

Spillover and spillback from livestock and domestic animals to wildlife will continue to be problematic as the habitat gap between the two closes. The predominant view is that wildlife transmits disease to livestock and domestics (Caron et al., 2013). However, this is not always the case (Delahay, Cheeseman, & Clifton-Hadley, 2001; Gillespie & Chapman, 2008; Lehrer et al., 2010; Prager et al., 2012). Changing wildlife population demographics, and human encroachment on habitat, led to additional contacts between wildlife and livestock (Miller et al., 2013), leading to potential transmission between the two.

Stress

Stress in wild populations has been found to increase disease by means of decreasing immunity in a variety of mammal populations (Goodrich & Buskirk, 1995; Hayward & Hayward, 2009; Owen, Nakamura, Coon, & Martin, 2012). Stress in wildlife diminishes glucose stores and suppresses immunity by stimulating the hypothalamic pituitary adrenal axis (Schell, Young, Lonsdorf, & Santymire, 2013). Disturbed landscapes elevate the number of stressors an animal is exposed to including: pesticides/herbicides, noise, pollution, invasive wildlife, predators, lack of resources and loss of adequate habitat (Lafferty & Gerber, 2002). The host's immunocompetence will greatly affect the overall pathogen prevalence within a population (Wobessor, 2006).

Cuban tree frog tadpoles (*Osteopilus septentrionalis*), whose systems were stressed with the herbicide atrazine had a higher mortality rate when infected with chytrid fungus (*Batrachochytrium dendrobatidi*) (Rohr et al., 2013). Elevated stress due to human presence has been recorded in lions (*Panthera leo*) who are watched by tourists (Hayward & Hayward, 2009). And finally, hair cortisol concentration in squirrel gliders (*Petaurus norfolcensis*) was found to be at higher levels at edges of fragmented landscapes then in the center (G. Brearley, McAlpine, Bell, & Bradley, 2012). These examples point to the physiological affects disturbed landscapes have on wildlife. Stress has been seen to increases the likeliness that an animal will be become infected, and thus contribute to a change on host/pathogen ecology.

Loss of biodiversity

Landscape disturbance drives biodiversity loss and thus alters transmission pathways (Keesing et al., 2010; Koprivnikar & Redfern, 2012). Transmission pathways change when deviations in behavior and condition of the pathogen, vector and host occur (Keesing et al.,

2010). A decrease in biodiversity diminishes wildlife populations and creates niches for nonnative species to invade. Loss of biodiversity also alters ecosystem functions such as food webs and seed dispersal by changing the number of predators and prey as well as the possible reduction in number of seed dispersers. Reduction in biodiversity commonly occurs through destruction of habitat, surge in generalist species and introduction of invasive species. When biodiversity is high (measured in species richness), the dilution effect will decrease overall prevalence in the population through an increase in species that are not competent hosts, hence lessoning encounter rates between infected and susceptible hosts (Bouchard et al., 2013; Huang et al., 2014). Experimental removal of mega fauna in the savanna of East Africa doubled the abundence and density of *Bartonella* spp. infected rodent hosts and their flea vectors, and displayed how reduction in biodiversity increases pathogen prevalence by allowing an increase in host abundence and density (Young et al., 2014).

Invasive species

Invasive species change the distribution of native wildlife by diminishing their numbers through competition and predation. This alteration of ecosystems leads to a cascade of negative effects. Invasive species can act as new susceptible hosts in the system. Invasive raccoons in Europe aid in the maintenance of canine distemper virus (Beltran-Beck, Garcia, & Gortazar, 2012). Coevolution between invasive species and pathogens has been extensively studied to gain insight into the use of pathogens as biological control agents (Di Giallonardo & Holmes, 2015; Elsworth et al., 2014). Myxoma virus was released as a biocontrol agent in the eradication of the invasive European rabbit (*Oryctolagus cuniculus*). The virus continues to evolve into more virulent strains (Kerr, 2012), as the rabbits evolve toward better immunity (Marchandeau et al., 2014), supporting the Red Queen hypothesis.

Vector ecology

Many pathogens, particularly viruses, are dependent on vectors for transmission (Begon, 2008). Pathogen ecology and rate of infection is dictated by the vectors' feeding ranges and functional differences in how vectors transmit the pathogen (Begon, 2008). Disturbed landscapes have potential to support vector resources and thus increase the pathogen's host range and abundance (Zylberberg et al., 2013). Vector density can indicate the probability of transmission. As vector density increases, probability of contact changes the likelihood a susceptible host can be infected. It has been shown that landscape disturbance is associated with increased abundance of vectors (Gottdenker et al., 2011). Abundance of the mosquito vector *Anopheles spp.* increases with sunlight, an outcome of deforested landscapes (Gottdenker et al., 2011). Likewise, the construction of irrigation ditches for agriculture supply many species of mosquitoes with ample breeding grounds.

Wildlife Biology and Behavior

The role of wildlife biology and behavior can influence how infectious a pathogen can be in an ecosystem. The behavior of the host plays a large role in transmission rates. The Tasmanian devil (*Sarcophilus harrisii*) is currently facing a population crisis because the spread of Devil Facial Tumor disease depends on how it is contracted. Devils bite each other's faces when fighting, causing the disease to spread via direct contact. Another key factor in the role of animal behavior in pathogen prevalence may be the dispersal and change in social structure of animal populations following population control measures. Spillover of *Mycobacterium bovis* from badgers (*Meles meles*) in the British Isles to cattle led to culling badger populations to eradicate the disease. The resulting social perturbation increased transmission of *Mycobacterium bovis* among badgers (Bielby, Donnelly, Pope, Burke, & Woodroffe, 2014).

Various wildlife behaviors have been documented that decrease exposure to pathogens (Wobeser, 2006). The avoidance tactic is used across many different species. An excellent example is domestic Soay sheep (*Ovis aries* L.) avoiding grass where others have defecated (thus contaminating the grass with parasitic eggs) (Hutchings, Kyriazakis, Gordon, & Jackson, 1999). Pathogens can also be controlled through competition, in which one hosts keeps the other below carrying capacity, potentially pushing both species under the joint abundance curve, diminishing pathogen prevalence (Begon, 2008). Starling species perform nest fumigation by making their nests with bactericidal materials (Clark & Mason, 1988). If, for instance, deforestation prevented them from finding these materials, they may show higher rates of pathogens when compared to Starlings who have these materials readily available.

Pathogen biology and behavior

Each pathogen has a unique function in the host and external environment, with substantial differences in the ecology of microparasites and macroparasites. Macroparasites tend to be endemic, with the tendency to re-infect a single host (Wobeser, 2006) and are sensitive to landscape change because they have longer periods of time when they must survive out of the host, in the environment. For this reason, small changes in landscape and climate will dictate macroparasite survival and abundance (Ostfeld, Keesing and Eviner 2008). Microparasites have the potential to become more virulent as the landscape changes due to increased transmission potential (Peter J. Hudson, 2002). Consequently, most epidemics are caused by microparasites, often due to a spillover effect consequential of environmental change (Peter J. Hudson, 2002).

Mechanisms leading to change in prevalence

Every ecosystem includes potential mechanisms that can alter pathogen prevalence within the system. Each mechanism plays a role in either pathogen transmission or host and

pathogen biological responses. The basic reproduction number (R_0) quantifies the potential for pathogens to spread within a susceptible population and may increase when any of the following mechanisms change: length of infection, number of susceptible hosts and the strength of transmission (Begon, 2009; Ostfeld, Glass, & Keesing, 2005).

Host density acts as a mechanism for pathogen prevalence when a change in abundance and density of hosts changes transmission rates and probability of contact (Wobesor, 2006). This is especially true in geographically isolated populations where animals are unable to disperse. Pathogens transmitted though vectors, environmental contamination (air/water borne, fomites), and close contacts (skin-to skin, secretions/excretions, carcasses) are expected to increase when host density increases. Vectors will have more opportunity for a blood meal and so will be able to infect susceptible hosts at a faster rate. Pathogens that can live outside the host and contaminate the environment, such as anthrax, do well in condensed populations because the probability of a competent hosts coming in contact with them is high. Transmission through close contact will also increase because hosts will come in contact with each other more frequently.

Amount and form of pathogen exposure will have an effect on the animal's chances of contracting the pathogen in an environment (Wobeser, 2006). This has been documented in urban systems where river otters are infected with *T. gondii* because of domestic cats defecating pathogen oocysts near water sources (Lehrer et al., 2010).

The Dilution Effect hypothesis predicts that high biodiversity will create an environment where mechanisms, such as the reduction of susceptible hosts and encounters between susceptible and infected hosts, will result in lower pathogen prevalence (Huang et al., 2013). This was seen when *Mycobacterium bovis*, responsible for Bovine Tuberculosis, decreased in

cattle populations near areas with high mammal species richness (Huang et al., 2013). When mammal species richness was high, higher densities of cattle were needed for Bovine Tuberculosis to persist and establish in the population (Huang et al., 2013).

When a seemingly diverse population contains multiple preferred hosts, especially for vector-borne diseases, the amplification effect will increase pathogen prevalence. In a population where the focal host species has poor host to host transmission, the addition of more competent hosts will increase prevalence in the focal species via spillover/spillback (Keesing, Holt, & Ostfeld, 2006). To demonstrate this concept, one can look at the example of *T. gondii* in river otters (*Lontra Canadensis*). Focal species transmission (otter to otter) is rare; however the addition of more competent hosts (domestic cats) can increase the prevalence in the population due to cats defecating oocysts, leading to environmental contamination of (M. A. Miller et al., 2002).

Herd immunity acts when the density and abundance of immune hosts is high enough that pathogens cannot encounter enough susceptible hosts to be successful. A sharp decrease in the prevalence of Usutu Virus was seen in collected birds in Australia and speculated to be the result of herd immunity caused by an increase in passive immunity (Chvala et al., 2007; Meister et al., 2008). The importance of passive immunity to the establishment of herd immunity has been documented in rabbits *(Oryctolagus cuniculus)* infected with Myxoma Virus; the more antibodies transferred from mother to young, the greater herd immunity found in the population (Marchandeau et al., 2014)

Frequency dependent transmission occurs most often in species with specific behavior that leads to transmission. This has been seen in Tasmanian Devils (*Sarcophilus harrisii*) battling the infectious cancer, Devil Facial Tumor Disease (McCallum et al., 2009). In this

study, reducing the density of Devils (up to 90% of the original population) had no effect on pathogen prevalence that continued to be maintained at more than 50% (McCallum et al., 2009).

The immune system plays a large role in ability of wildlife to fight off disease and cope with landscape disturbance. Change in landscape can activate an immune response for various reasons, including: depletion of resources, novel predators and competitors, human and domestic pet interaction and response to pollutants. Immune responses include both humoral and cell-mediated components (Acevedo-Whitehouse & Duffus, 2009). A host's immunocompetence is directly linked to their ability to fight disease. When faced with a stressor, an animal's immune system activates various interactions involving the hypothalamic–pituitary–gonadal axis, hypothalamic–pituitary–adrenocortical axis and the sympathetic adrenomedullary system (Acevedo-Whitehouse & Duffus, 2009; Lawrence & Kim, 2000). For a short period of time, this is the body acting as it should, however prolonged responses can compromise the animal's immunocompetence (Acevedo-Whitehouse & Duffus, 2009; Friedman & Lawrence, 2002).

The specificity and preference of the pathogen, vector and host can dictate pathogen prevalence in a system. Triatomine bugs (Family: *Reduviidae*) are vectors of *Trypanosoma cruzi* that show host preference dictated by habitat type and accessibility of hosts (Rabinovich et al., 2011). This can have implications for disease mitigation, as the preferred host is likely to change with habitat (Rabinovich et al., 2011).

Some of the discrepancies in prevalence among similar landscapes are due to the pathogens mode of transmission. Density dependent and frequency dependent pathogens require different patterns of contact between hosts for a pathogen to have optimal transmission (Begon, 2009). Where a pathogen sits on the continuum between frequency dependent transmission and

density dependent transmission can depend on spatial heterogeneity of resources and behavior (Begon, 2009; Habib, Merrill, Pybus, & Coltman, 2011).

Each of the mechanisms, direct and indirect drivers discussed here have distinct ecological processes that maintain host/pathogen relationships. Changes in ecological composition will be followed by a change in disease ecology. The mechanisms behind these changes are complex and do not fit a one size fits all cause and effect.

Methods

A meta-analysis was conducted to synthesize the current literature and examine in general, across numerous studies, whether pathogen prevalence differed between undisturbed and disturbed landscapes, with the expectation that prevalence would be higher in disturbed landscapes.

Search engines within the Web of Science™ and Academic Search Premier databases were used to search for peer-reviewed literature using key words such as: “landscape,” “anthropogenic,” “wildlife,” “disease”, and “human modified” (See appendix IV for additional keywords). The citation lists of these papers were used to find additional studies. Searches were not limited by year. For the analysis of prevalence values, sixteen papers with studies conducted between 2003 and 2013 were included. Papers included in the analysis of prevalence had to include a paired disturbed and undisturbed landscape. Studies included in the analysis provided field based data on the number of wildlife fecal samples or vectors sampled, the number of those wildlife or vectors infected, and pathogen prevalence. In this context pathogen was defined by Wobeser (1981) as a “disease causing agent” and disease was defined as "any impairment that interferes with or modifies the performance of normal functions, including responses to environmental factors such as nutrition, toxins, and climate, inherent or congenital defects, or combinations of these factors." Hosts had to show evidence of the pathogen, but not necessarily the disease. Marine wildlife and any pathogens that were not of zoonotic or economic concern were also omitted.

What may be considered disturbed/undisturbed is open to in interpretation by researchers, and so only studies that provided paired, in depth descriptions of what they considered disturbed/undisturbed were included in the analysis of prevalence. For the analysis of change in

occurrence, studies either had to be paired or show a gradient with clearly defined ends of undisturbed and disturbed. It has been strongly argued that most of the earth has been touched by human influence, and historic range of variation gives researchers leeway on what is considered human-modified. Common measurements of disturbance included an urban index (measure of the urban density of an area), fragment size, and aerial data. To be considered an undisturbed landscape, the land had to show no strong ecological changes that may have been caused by human intervention. In the best cases these were reserves where human traffic is minimal. When the author provided a gradient of disturbance (fragmentation) low quality sites (<200 ha) were classified as fragments and (>200 ha) as undisturbed, as outlined by Young, Griffin, Wood, & Nunn (2013).

The following information was recorded from each paper: types of disturbance, direct drivers, mechanisms, host species (common name, order and class), pathogen/parasite, vector, temporal variables, number of host species sampled (n), number infected, percent infected, composition of habitat matrix, landscape description, area sampled, and relation to sustainability.

Relationship between disturbed and undisturbed landscapes using pathogen prevalence rates

Sample size and prevalence for paired disturbed and undisturbed sites were totaled over study sites and averaged by sampling event. Only studies that included paired disturbed and undisturbed sites were included. Prevalence values were rounded to three significant figures. When prevalence values were reported as <1%, they were recorded as 0% (Gillespie & Chapman, 2008). In cases of multi-pathogen sampling with the same host population being used to estimate prevalence for different pathogens, each specific pathogen-host combination was considered separately. The statistical software R© was used to run all analysis. Studies were paired by paper, host and pathogen. Each effect size was weighted by the host sample size using

the escalc function in the Metafor package. A two-tailed, paired, weighted t-test (Welch) was run using the wtd.t.test function in in the "weights" package in R© on disturbed verse undisturbed mean prevalence. Prevalence was weighted by sample size. AIC values were calculated to measure the relative quality of the statistical tests based on weights of host sample size and sites. Effect size was calculated as the mean difference between undisturbed and disturbed landscapes for all analysis.

Publication bias

It is likely that animal taxa are not proportionally represented in the literature and that the dataset will be similarly biased. This may be due to ease of sampling, detection rate, a preference for mega fauna, or targeting species of conservation concern. The data set also included multiple papers by some authors, and some studies with multiple prevalence estimates (when multiple species or pathogens were evaluated in an individual paper). Variation of timescale, experimental protocol, and statistical analysis can lead to heterogeneity in effect sizes. The package Metafor© was used to run all analysis of publication bias using the pathogen prevalence data. A random effects model was used to account for the differences in true effect sizes across studies using the code res<-rma (yi=data$yi, vi=data$vi, measure="RD") (Kormos, Wilkinson, Davey, & Cunningham, 2014). A funnel plot was used to examine the symmetry of the mean effect size with the function funnel(taf). The effect size for each pairing of the particular host, pathogen and paper was calculated using the escalc function in the Metafor© package in which the output values yi and vi were used. Corresponding sampling variances were also calculated using the escalc function in the Metafor© package. A trim and fill function (taf <-trimfill(res)) was then preformed to see if missing studies would have had any effect on the results. We used an estimated variance of the prevalence estimate (Barendregt, Doi, Lee,

Norman, & Vos, 2013) because between-site variances were not provided for all studies. The funnel plot was supported with evidence from a quantile-quantile plot, tests for heterogeneity and Rosenthal's fail safe number.

Directionality of pathogen occurrence between undisturbed and disturbed landscapes

Many published studies did not include prevalence data, but reported directionality (increase, decrease, varied or no significant difference) of pathogen occurrence when comparing disturbed and undisturbed landscapes. In addition to paired studies, we also included studies that sampled on a disturbance gradient as long as they had undisturbed on one end and disturbed on the other. Studies in the dataset included those that sampled known zoonosis, pathogens of economic concern, and those that included both zoonotic and non-zoonotic disease within their study design. When prevalence data were given by pathogen and hosts, only zoonotic pathogens were included. When prevalence data were not given for papers containing both zoonotic and non-zoonotic pathogens, the overall occurrence in the studies was reported. To enlarge the data set we performed an Asymptotic Wilcoxon signed rank test to determine if the distribution between papers with disturbed verse undisturbed landscapes have identical distributions without assuming normality. The null hypothesis states that the median difference between pairs of observations is zero.

Papers chosen for the sign test had relaxed criteria compared to those in the full metaanalysis of prevalence. Instead of limiting the analysis to studies of known zoonoses, pathogens that also had significant potential economic impact were included. Studies that sampled non-zoonotic pathogens in addition to zoonotic pathogens in a single paper were included. This was done to broaden the study and still show that under a wider scope, wildlife disease may be altered by human-mediated disturbance. Data recorded for each paper included:

overall reaction to disturbance (directionality), landscape, pathogen/vector, host species, economic impact, what was sampled and pathogen.

Results

Characteristics of studies for analysis of pathogen prevalence

Studies included in the analysis of prevalence were carried out across the globe. Forty six cases within 13 published studies were included in the final analysis (Table 1). Mammals, birds and amphibians were all included.

The majority of sampling sites included a single disturbance type, and a few included multiple disturbance types. The types of disturbances included in the comparison of prevalence studies were deforestation (two papers), fragmentation (two papers), urbanization (four papers), agriculture (four papers), recreation/tourism (three papers), forest collection/hunting (two papers), livestock (one paper), roads (one paper) and combined disturbances including: deforestation, fragmentation, urbanization, agriculture, tourism, forest collection/hunting, forest collection, roads and livestock (four papers) (Figure 2).

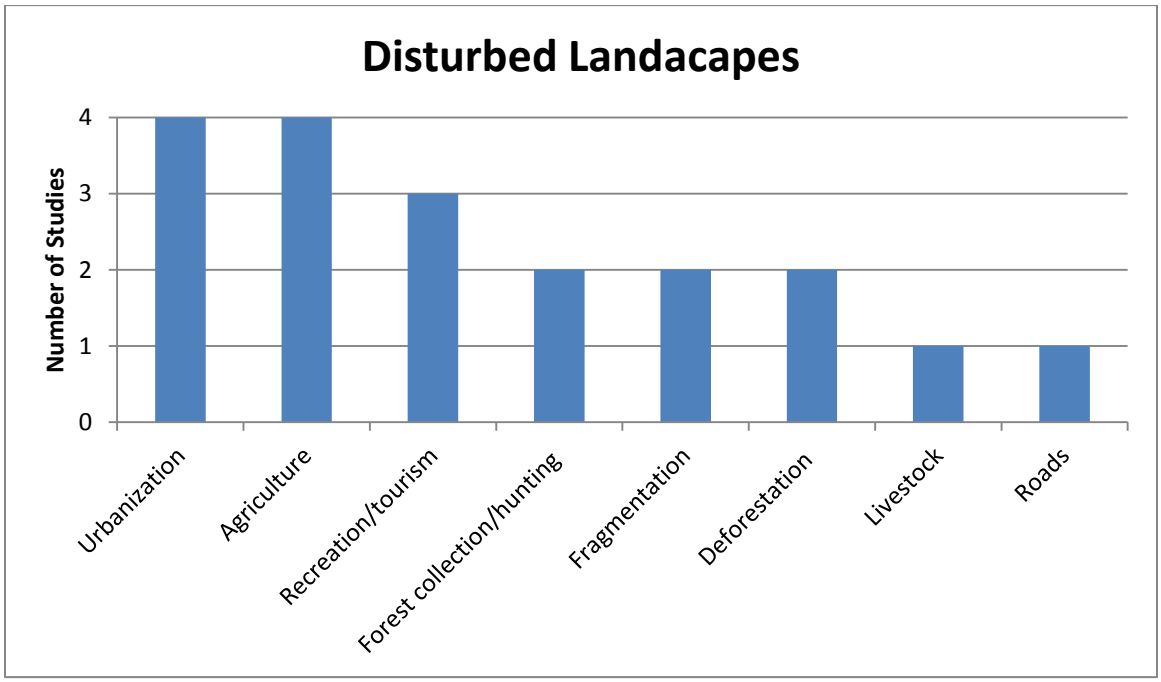

Figure 2. Common types of disturbed landscapes used in analysis of prevalence identified in the published literature. Many studies identified multiple landscapes.

Analysis of pathogen prevalence between disturbed and undisturbed landscapes

The results of the two tailed, weighted, paired t-test between the disturbed and undisturbed prevalence samples (Table 1.) showed a significant difference between the two (p-value< 0.000; df = 8792; Standard error: 0.004). Disturbed landscapes had an overall higher pathogen or parasite prevalence (mean=0.251), compared to undisturbed (mean= 0.128) (Figure 3).

Table 1. Summary of studies included in the analysis of prevalence.

Study	Landscape	Pathogen	Host	Sample Size Disturbed Landscape	Sample Size Undisturbed Landscape	Average Prevalence Disturbed Landscape (%)	Average Prevalence Undisturbed Landscape (%)
Cottontail et al 2009	Fragmentation, human-made islands	*Trypanosoma cruzi*	Common Fruit Bat	145	99.0	15.1	3.99
Gillespie and Chapman 2008	Fragmentation	*Ascaris* sp.	Black and White Colobus	94.0	106	6.00	0.00
Gillespie and Chapman 2008	Fragmentation	*Strongyloides fuelleborni*	Black and White Colobus	390	561	7.00	3.00
Gillespie and Chapman 2008	Fragmentation	*Trichuris* sp.	Black and White Colobus	94	106	90.0	84.0
Gillespie and Chapman 2008	Fragmentation	*Strongyloides fuelleborni*	Red Colobus	390	561	5.00	4.00
Gillespie and Chapman 2008	Fragmentation	*Giardia* sp.	Red Colobus	390	561	6.00	0.00
Gillespie and Chapman 2008	Fragmentation	*Strongyloides stercoralis*	Red Colobus	94.0	106	2.00	0.00
Gillespie and Chapman 2008	Fragmentation	*Trichuris* sp.	Red Colobus	390	361	50.0	36.0
Gómez, 2008	Urbanization, urban park	West Nile virus	Eastern Grey squirrel	141	1.00	52.0	1.00
Gómez, 2008	Urbanization, urban park	West Nile virus	Virginia opossum	23.0	8.00	52.0	37.5
Gómez, 2008	Urbanization, urban park	West Nile virus	White-footed mouse	9.00	17.00	33.3	0.00
Gómez, 2008	Urbanization, urban park	West Nile virus	Raccoon	7.00	2.00	85.7	0.00
Hamer, 2012	Urbanization, roads	West Nile virus	American Goldfinch	15.0	11.0	0.00	0.00
Hamer, 2012	Urbanization, roads	West Nile virus	Barn Swallow	5.00	3.00	0.00	0.00

Hamer, 2012	Urbanization, roads	West Nile virus	Black-capped Chickadee	6.00	1.00	0.00	0.00
Hamer, 2012	Urbanization, roads	West Nile virus	Brown-headed Cowbird	26.0	1.0.0	3.84	0.00
Hamer, 2012	Urbanization, roads	West Nile virus	Cedar Waxwing	1.00	2.00	0.00	0.0.0
Hamer, 2012	Urbanization, roads	West Nile virus	Downy Woodpecker	12.0	1.00	0.00	0.00
Hamer, 2012	Urbanization, roads	West Nile virus	Eastern Phoebe	1.00	1.00	0.00	0.00
Hamer, 2012	Urbanization, roads	West Nile virus	Gray Catbird	24.0	14.0	0.00	0.00
Hamer, 2012	Urbanization, roads	West Nile virus	Northern Cardinal	10.0	5.00	50.0	0.00
Hamer, 2012	Urbanization, roads	West Nile virus	Savannah Sparrow	3.00	1.00	0.00	0.00
Hamer, 2012	Urbanization, roads	West Nile virus	Song Sparrow	13.0	2.00	0.00	0.00
Hernandez 2013	Shade grown coffee	Paramyxovirus-1	Long-tailed manakin	4.00	3.00	0.00	0.00
Hernandez 2013	Shade grown coffee	Paramyxovirus-1	White-eared ground sparrow	56.0	45.0	0.00	2.22
Hernandez 2013	Shade grown coffee	Paramyxovirus-1	Blue-crowned motmot	17.0	10.0	11.8	0.00
Hernandez 2013	Shade grown coffee	Paramyxovirus-1	Rufous-and-white wren	24.0	25.0	4.17	0.00
Hernandez 2013	Shade grown coffee	Paramyxovirus-1	Orange-billed nightingale thrush	47.0	51.0	0.00	0.00
Johnston 2010	Deforestation, agriculture, forest collection	*Giardia duodenalis*	Red colobus, Black-and-white colobus, Red-tailed guenon	53.0	28.0	15.1	3.60
Junge 2011	Hunting, deforestation, tourism	*Bertiella* sp.	Indri	12.0	9.00	33.3	0.00
Koprivnikar 2012	Agriculture, roads	*Alaria* sp.	Grey Tree Frog larvae	79.0	78.0	10.3	51.2
Koprivnikar 2012	Agriculture, roads	Echinostome	Grey Tree Frog larvae	79.0	78.0	87.4	35.9
Lehmer 2008	Recreation, tourism	Sin Nombre virus	Deer Mice	202	203	11.4	15.6
Riley 2004	Urbanization	*Bartonella henselae*	Bobcat	12.0	13.0	73.0	75.0
Riley 2004	Urbanization	Leptospira interrogans	Gray Fox	27.0	14.0	7.00	7.00
Riley 2004	Urbanization	*Toxoplasma gondii*	Bobcat	12.0	13.0	100	77.0
Seplveda 2011	Urbanization	*Toxoplasma gondii*	American mink	16.0	14.0	100	35.7

Wasserberg 2003	Agriculture	*Leishmania major*	Sand Rat	252	161	16.9	6.67
Wenz-Mucke 2013	Livestock, roads, recreation/tourism	*Globocephalus* sp.	Long-tailed Macaques	101	34.0	10.8	11.8
Wenz-Mucke 2013	Livestock, roads, recreation/tourism	*Oesophagostomum* sp.	Long-tailed Macaques	101	34.0	5.93	14.0
Wenz-Mucke 2013	Livestock, roads, recreation/tourism,	*Strongyloides fuelleborni*	Long-tailed Macaques	101	34.0	50.5	2.96
Wenz-Mucke 2013	Livestock, roads, recreation/tourism,	*Trichuris* sp.	Long-tailed Macaques	101	34.0	58.4	32.3

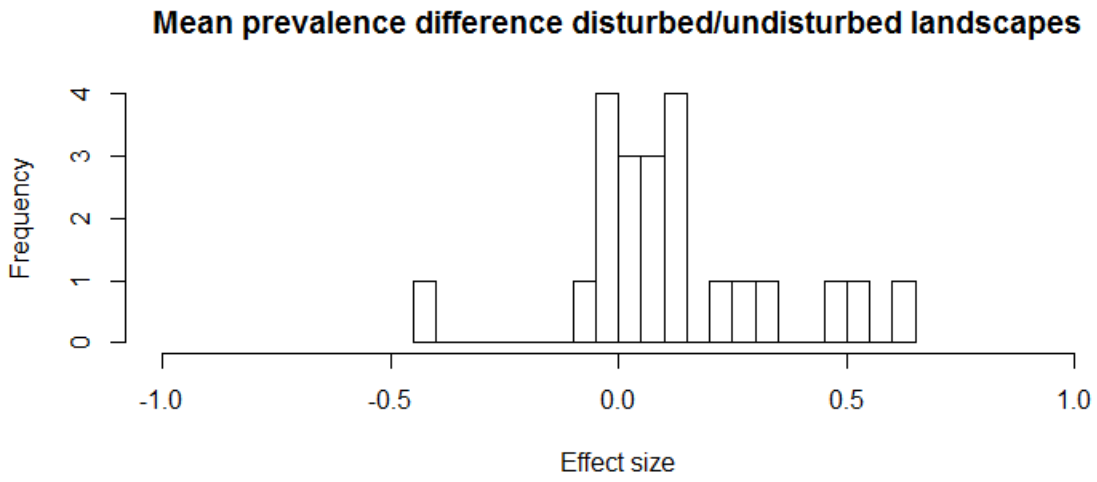

Figure 3. The distribution of effect sizes (difference in means of disturbed and undisturbed landscapes). Although some papers included data on multiple pathogen and host relationships, each case of a pathogen/host pair in the same study was considered independently.

Publication bias

All statistics for the publication bias and test for heterogeneity was determined using pathogen prevalence data (Table 1.) The I^2 test statistic (95.9) indicated the amount of variability due to heterogeneity instead of sampling error (Viechtbauer, 2010). The large amount of heterogeneity supports our choice of a random effects model for the funnel plot. The heterogeneity seen in the funnel plot (Figure 4) is likely caused by a correlated structure in the effect sizes and data set. Causes of these correlations include multiple data sets coming from one study, and phylogenetic effects where closely related species have similar effect sizes. The funnel plot (Figure 4) contains two studies (Geue & Partecke, 2008; Koprivnikar & Redfern, 2012) that have very low effect sizes (-0.274 and -0.409 respectively) and three studies (Koprivnikar & Redfern, 2012; Sepúlveda et al., 2011; Wenz-Mucke et al., 2013) that have high effect sizes (0.514, 0.643 and 0.475 respectively) and so it does not conform to the funnel shape. The symmetry of the funnel plot (Figure 4) and the lack of theoretical studies filled in with the trim and fill analysis indicate there is no publication bias. The quantile-quantile plot (Figure 5)

further supports the lack of publication bias with points that fall between the confidence limits and close to the regression line. The Rosenberg fail safe number (718) indicates the number of non-significant studies that would need to be published to make the results non-significant. Because this number is large, this test supports that there was no publication bias.

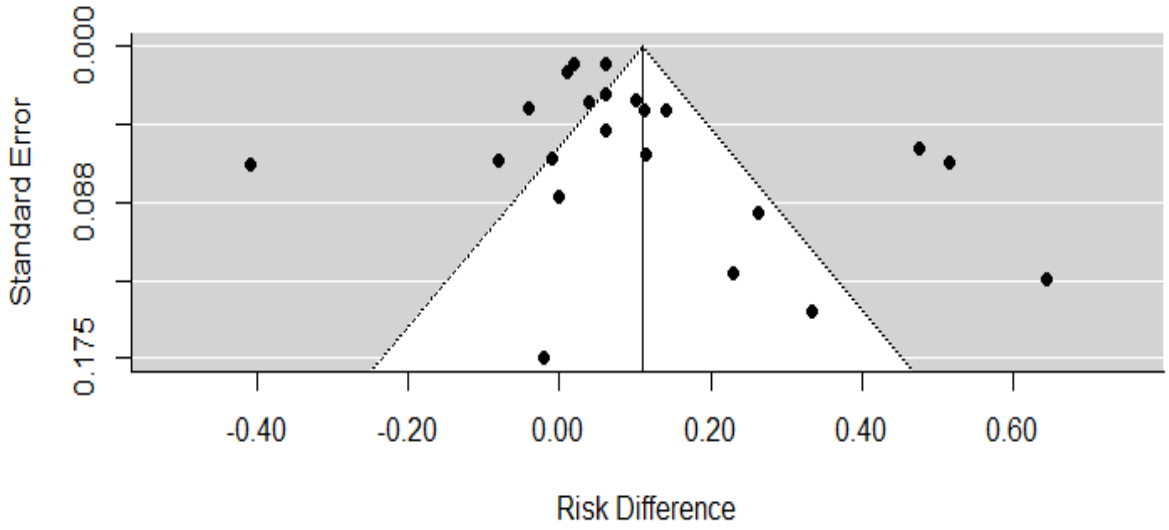

Figure 4. Funnel plot of publication bias. Sources of heterogeneity include taxonomic differences between studies and variation in study design. No publication bias is present.

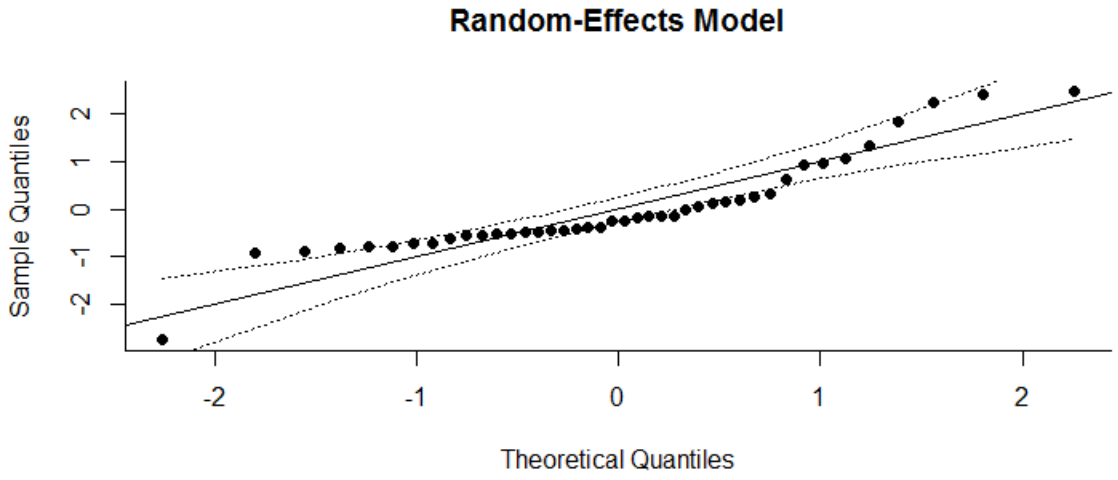

Figure 5. Quantile-quantile plot of random effects model shows little evidence of publication bias.

Change in pathogen occurrence between undisturbed and disturbed landscapes

The 36 papers collected for use in the sign test ranged from the years 2002-2013 (Table 2). Sixty eight cases were analyzed using ties to differentiate between differences seen between various pathogens and hosts. All the studies included in the analysis of prevalence were also included in the analysis of occurrence. Thirteen types of human disturbance were reported in the data set: urbanization (thirteen studies), agriculture (eight studies), fragmentation (seven studies), deforestation (five studies), roads (four studies), recreation and tourism (four studies), forest collection and hunting (two studies), livestock (two studies), freshwater runoff (one study), wildlife reintroduction (one study) and human population density (one study) (Figure 6). Overlap existed between landscape types, many studies sampled in areas with multiple disturbance types. The majority of studies showed pathogen prevalence was higher in disturbed landscapes (Figure 7). The results of the Asymptotic Wilcoxon signed rank test that included ties (no change in occurrence) showed that significantly more studies showed increases in pathogen and parasite occurrence in disturbed landscapes (p-value = 2.06e-05) with the alternative hypothesis: true median is not equal to zero

Table 2. Studies used to analyze occurrence of pathogens and parasites in undisturbed verse disturbed landscapes.

Paper	Change in pathogen occurrence from undisturbed to disturbed landscapes	Direct Driver(s) (Landscape)	Driver(s)	Mechanism(s)
Allan, 2003	Increase	Fragmentation	Loss of Biodiversity	Host density
Allan, 2008	Increase	Human population density	Loss of Biodiversity	Dilution effect
Beasley, 2013	Increase	Fragmentation	Wildlife biology and behavior	Host Density, amount and form of pathogen exposure
Becker, 2011	Decrease	Deforestation	Loss of Biodiversity, pathogen biology and behavior	Host abundence, amount and form of pathogen exposure
Bichet, 2013	Increase	Urbanization, pollution	Pollution	Immune function
Bradley et. a.l 2008	Increase	Urbanization, recreation/tourism	Loss of Biodiversity, vector ecology	Dilution effect
Chasar, 2009	Varied	Deforestation	Vector ecology, addition of other host species	Host/vector/pathogen specificity, dilution effect
Cottontail et al 2009	Increase	Fragmentation	Stress, loss of biodiversity, change in resources	Host density, dilution effect, vector abundence
Evans, 2009	Decrease	Urbanization	Vector ecology, change in resources, loss of biodiversity	Vector abundence
Geue and Partecke 2008	Decrease	Urbanization	Vector ecology	Vector abundence
Gillespie, 2009	No significant difference	Deforestation	None	None
Gillespie and Chapman, 2008	Varied	Urbanization	Livestock/human hosts, change in resources, stress	Amount and form of path exposure, Immune function
Gómez, 2008	Increase	Urbanization	Vector ecology	Vector abundence, host/vector/pathogen specificity
Hamer, 2012	Varied	Urbanization and Roads	Change in resources, stress	Host density, immune function
Hernandez, 2013	Varied	Agriculture	None	None
Hussain, 2013	Increase	Fragmentation, urban, agriculture	Livestock/human hosts	Host density
Johnston, 2010	Increase	Deforestation, agriculture, forest collection	Livestock/human hosts	Amount and form of path exposure
Junge, 2011	Increase	Hunting, deforestation, tourism	Change in recourses, human contact	Immune function, amount and form of pathogen exposure

Kellner, 2012	Increase	Urbanization	Alternate host	Host density
Kirchgessner, 2013	Increase	Agriculture	Livestock	Amount and form of pathogen exposure
Koprivnikar 2012	Varied	Agriculture, roads	None	None
Lane, 2011	Decrease	Urbanization	Change in resources	Immune function
Lehmer, 2008	Decrease	Recreation/tourism	Wildlife biology and behavior	Host abundence
Mbora, 2009	Increase	Fragmentation	Change in resources	Host density
Miller, 2002	Increase	Freshwater run off	Domestic reservoir	Amount and form of pathogen exposure
Page, 2008	Decrease	Urbanization	Wildlife biology and behavior, change in resources	Amount and form of pathogen exposure
Plowright, 2011	Increase	Urbanization	Wildlife biology and behavior	Host density
Riley, 2004	Varied	Urbanization	Livestock, domestic pets, humans	Amplification effect, host density
Schaumburg, 2012	Increase	Wildlife reintroduction	Human hosts	Amount and form of pathogen exposure
Sepúlveda, 2011	Increase	Urbanization	Domestic pet	Amount and form of pathogen exposure
Suz´an, 2008	Increase	Fragmentation	Loss of biodiversity	Host abundence, dilution effect
Urban, 2006	Increase	Roads	Addition of other host species	Amount and form of pathogen exposure
Vaz et al 2007	Increase	Agriculture, livestock, fragmentation	Loss of biodiversity	Dilution effect
Wasserberg, 2003	Increase	Agriculture	Vector ecology, change in resources	Vector abundence
Wenz-Mucke, 2013	Varied	Roads, Recreation/Tourism	Wildlife biology and behavior, change in resources, livestock	Amount and form of pathogen exposure
Zylberberg, 2013	Increase	Agriculture	Stress, change in resources	Immune function

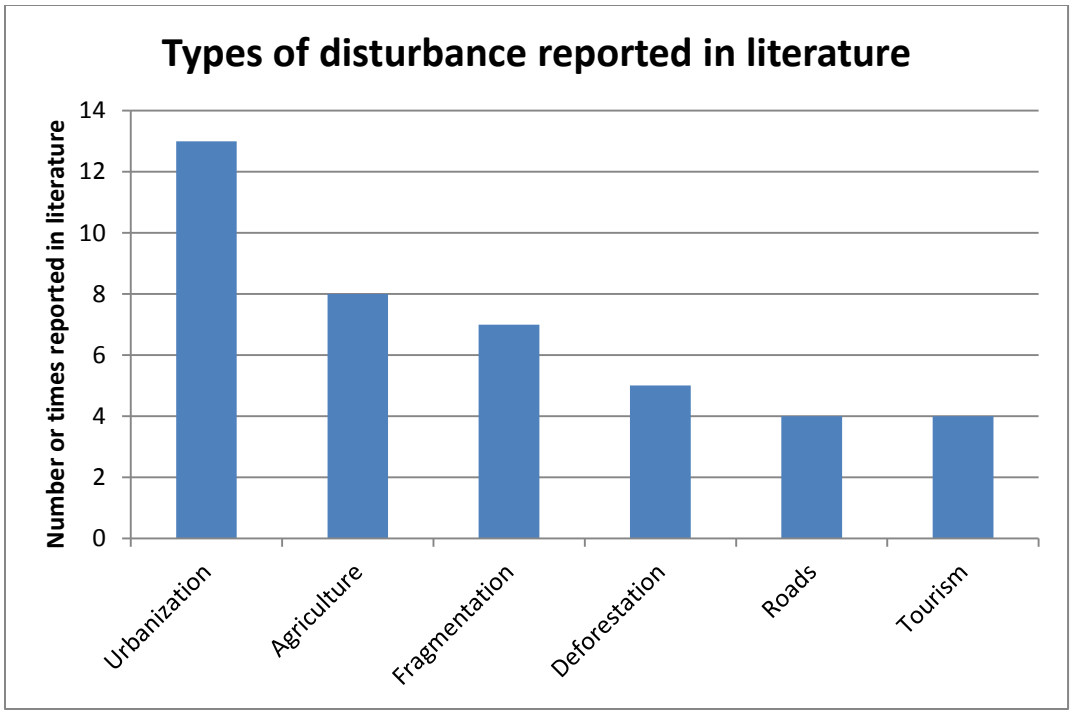

Figure 6. Landscapes commonly identified in the published literature used in analysis of occurrence. Many studies reported multiple disturbance types.

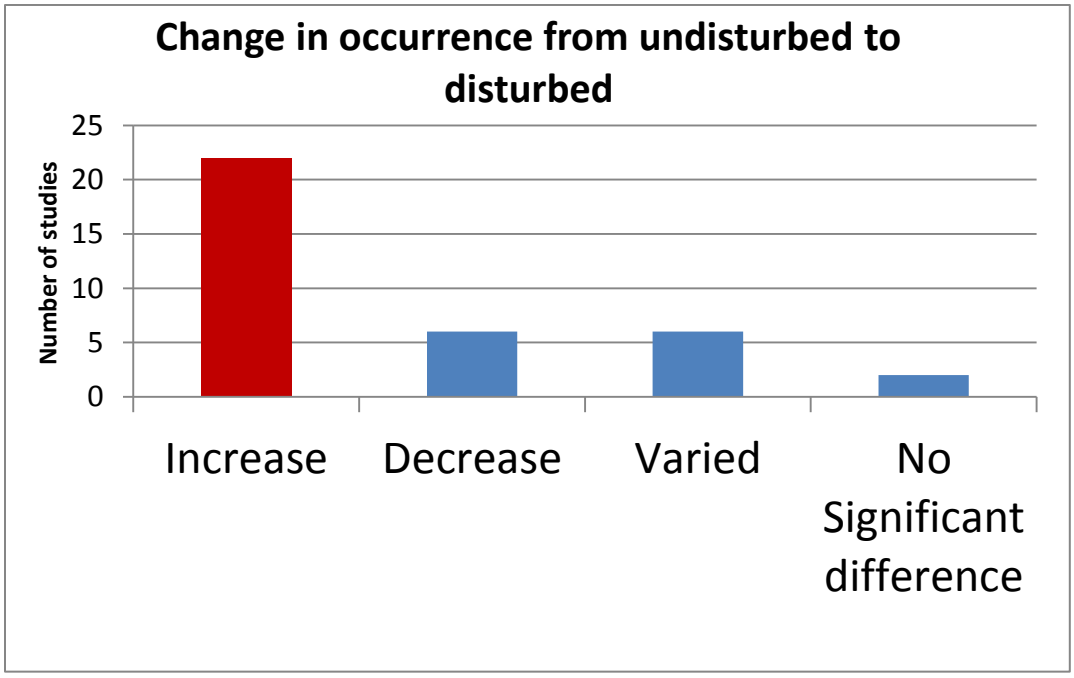

Figure 7. Number of papers that show an increase, decrease or no change in pathogen occurrence in the published literature.

Disease prevalence is a complex system and so few papers were able to provide certain causation of drivers and mechanisms. However, most studies were able to speculate within their study systems, deducing which drivers and mechanisms were the most likely contributing factors. The most common direct driver was change in available resources; the result of habitat destruction, growth of non-native vegetation or human feeding. The most common drivers found included: change in vegetation/resources (eleven studies), loss of biodiversity (eight studies), shared habitat or close proximity to humans, livestock or domestic pets (eight studies), change in vector ecology (six studies), change in wildlife biology or behavior (five studies), stress (three studies), addition of other host species (four studies), a change in pathogen biology or behavior (one study), pollution (one study) and no driver present (three studies) (Figure 8). Three studies did not specify a certain driver or mechanism. In each of these three studies, the prevalence between the landscapes either varied or resulted in no significant difference (Gillespie et al., 2009; Hernandez et al., 2013; Koprivnikar & Redfern, 2012).

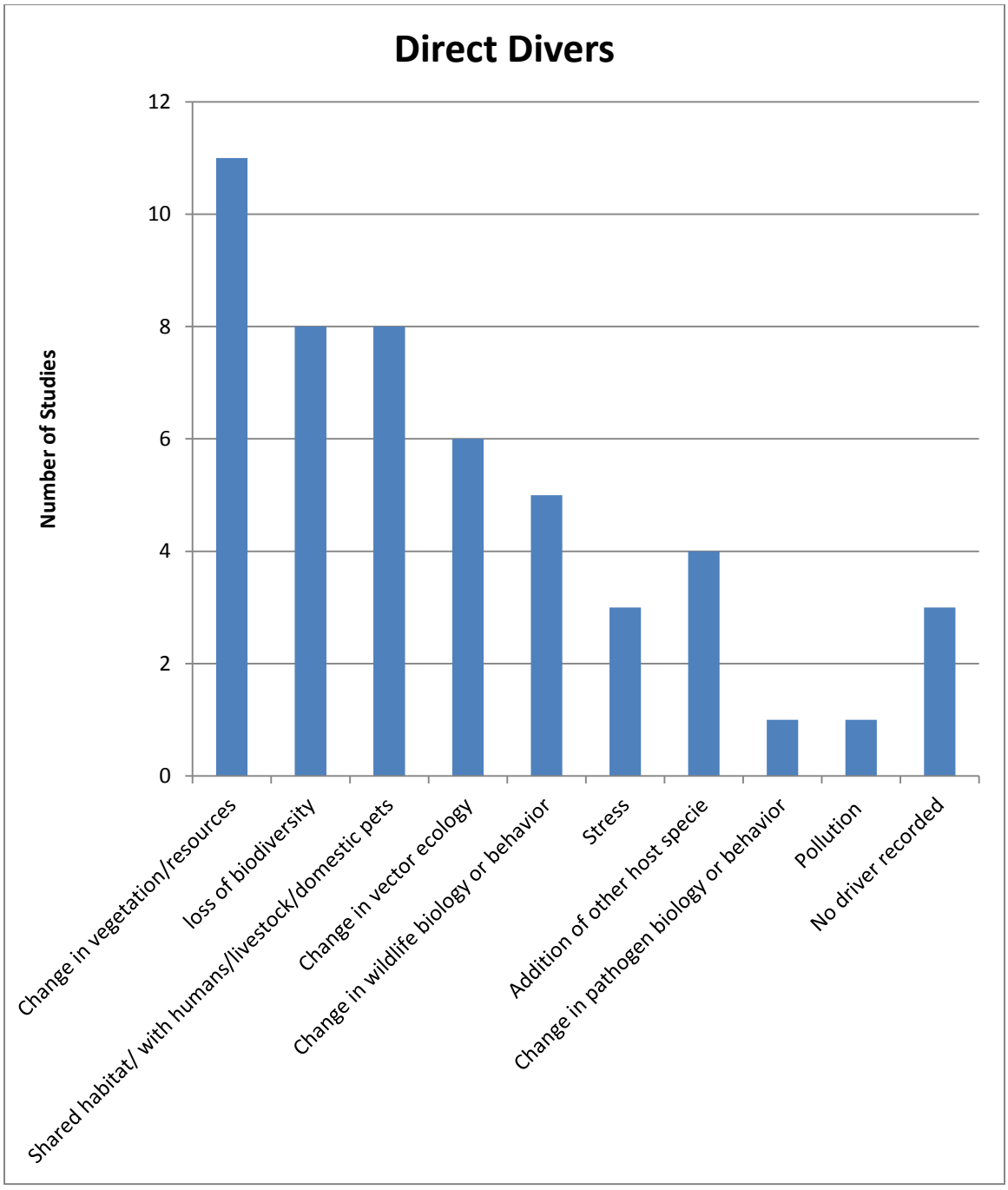

Figure 8. Number of times each driver was identified in the published literature as a possible cause or correlation.

Drivers and mechanisms do not function linearly, meaning that what drives a particular mechanism in one system may drive a different mechanism in another. A change in host density was the most commonly seen mechanism. In most cases, this change occurred as an increase in host density in the disturbed landscape, but that was not always the case (Lehmer, Clay, Pearce-

Duvet, St. Jeor, & Dearing, 2008). The mechanisms identified in the literature as contributing to a change in prevalence of pathogens include: a change in the amount and form of pathogen exposure (twelve studies), host density (eleven studies), the dilution effect (five studies), change in vector abundence (five studies), a change in immunity (six studies), host/vector/pathogen specificity (two studies), change in host abundence (two studies), the amplification effect (one study) and no identified mechanism (three studies) (Figure 9). Evidence of mechanisms such as herd immunity and frequency dependent transmission were not specifically stated in any of the studies, possibly a consequence of their measurability in wildlife.

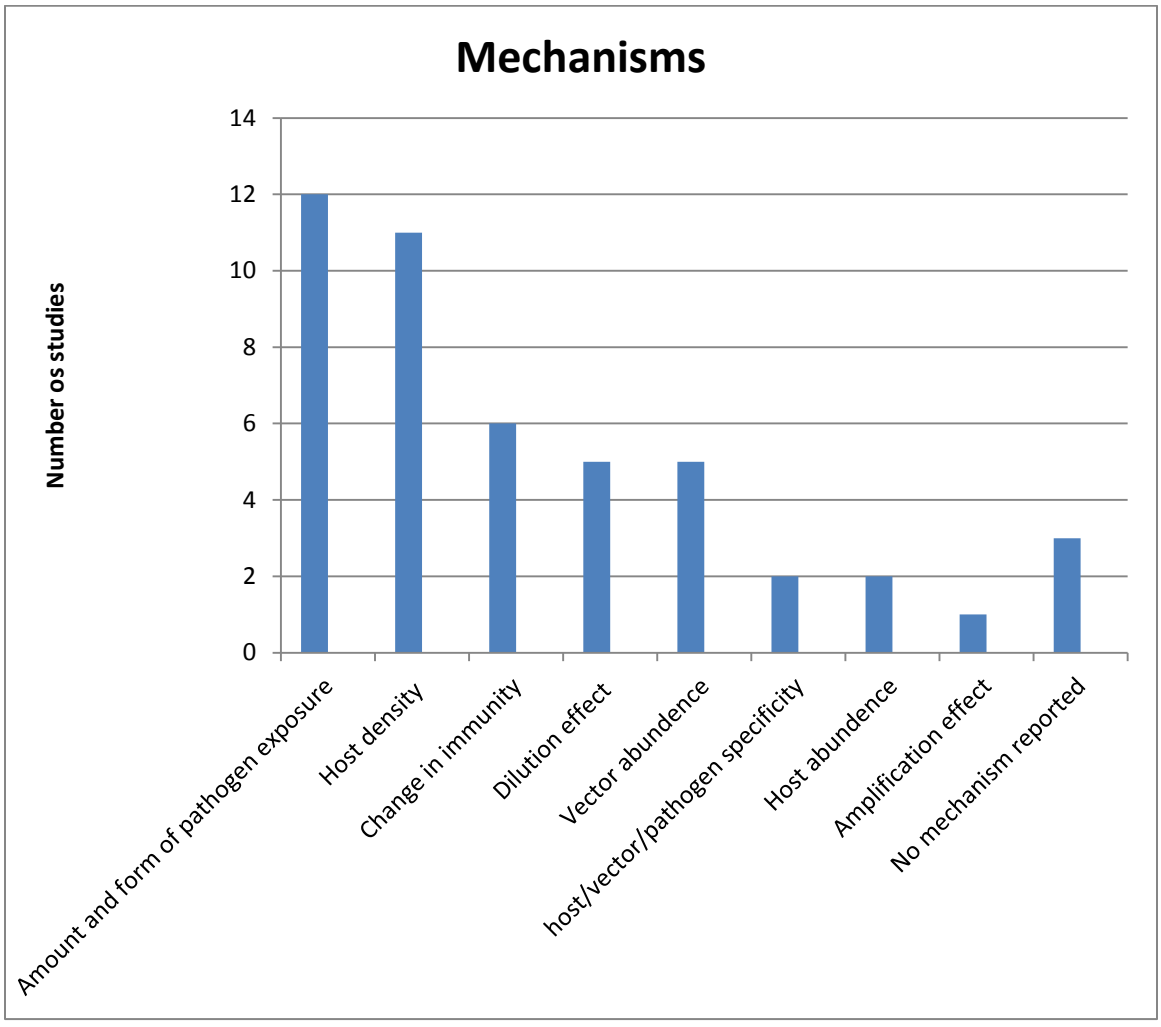

Figure 9. Number of times each mechanism was identified in the published literature as a possible cause or correlation. Some studies identified multiple drivers.

Discussion

The results of the metaanalysis confirm that wildlife in disturbed landscapes have significantly higher levels of pathogens and parasites than in undisturbed landscapes. The Asymptotic Wilcoxon signed rank test concluded that the majority of published studies showed an increase in pathogen and parasite occurrence from undisturbed to disturbed landscapes.

Ecological theory predicts that host density should be positively correlated with pathogen prevalence. Host density was the causal mechanism by which the Tana River red colobus (*Procolobus rufomitratus*) and mangabey (*Cercocebus galeritus galeritus*) became infected with 16 helminth and 5 protozoan parasites in fragmented landscapes along the Tana River, Kenya. Increase in density was driven by loss of suitable habitat, which was measured as loss of acreage and number of cut stems (Mbora & McPeek, 2009).

Changes in food resources is a driver that has been shown in cases such as Page (2008) to contribute to a decrease pathogen prevalence in definitive host species when they are no longer consuming an intermediate host as their primary food sources. Raccoons (*Procyon lotor*) in urban areas had fewer levels of *Baylisascaris procyonis* partially because human food was more readily available then small vertebrate intermediate hosts, which displayed the important role wildlife behavior plays in pathogen transmission. The density of latrine may have also played a role, decreasing juvenile exposure to infected eggs (Page, Gehrt, & Robinson, 2008).

One particular study in our data set (Lehmer et al., 2008) exemplifies how different wildlife biology and behavior can drive a mechanism such as host density to have the opposite effect and increase pathogen prevalence in the undisturbed landscapes. Here, mice living in landscapes used for recreation had fewer pathogens due to a higher emigration and mortality

rate, likely resulting from the need to acquire better resources. This resulted in the undisturbed landscapes having larger host density, which increased probability of transmission.

In the studies included in our meta-analysis, additional hosts such as livestock, domestic pets and humans were a driver of pathogen prevalence. *Giardia duodenalis* does well in the external environment and is common in ungulates and humans (Johnston et al., 2010). Primates that share habitat with humans and livestock that are infected with *Giardia duodenalis,* as shown in Johnston (2010), are at high risk of infection and have higher prevalence of the pathogen than primates that do not share habitat with humans and livestock. Pathogen exposure is high in these shared circumstances when compared to unshared spaces.

Strongyloides stercoralis, Ascaris sp. and *Giardia sp*. are common in the human population surrounding Kibale National Park, Uganda. These zoonotic parasites were found in red colobus living in forest fragments frequented by humans, and not found in those residing inside the park, where there is little human interaction. This suggests the possibility of humans being a reservoir host of these parasites, permitting Red colobus in close proximity to become infected (Gillespie & Chapman, 2008).

Host stress is a driver that is tied into encounters with humans and domestic pets. Stress leads to a reduction in immune response. Chapman (2006) showed how Red colobus living on the edge of forest fragments had negative encounters with humans and dogs, which may have been a mechanism leading to their high levels of gastrointestinal parasites. Chapman (2006) concluded that prevalence between landscapes was variable depending on the pathogen in question; showing that what drives an increase in one pathogen may have the opposite effect in another, and so pathogen biology and behavior needs to be considered further.

Host abundence nearing population thresholds can lead to nutritional stress. The Common fruit bat (*Artibeus jamaicensis*) has been seen to occupy fragments in Panama at abundances nearing the population threshold, leading to high competition for resources. The authors speculated that degraded immune function resulting from high competition was a mechanism by which haemoparasite prevalence increased. In the undisturbed landscape, high biodiversity of bat species was correlated with low trypanosome prevalence, potentially supporting a dilution effect (Cottontail et al., 2009).

Conserving biodiversity will aid in limiting the number of potential hosts in a population. Allan et. al. (2008) proposed this idea after concluding that West Nile Virus was negatively correlated with the number of bird species in an ecosystem. This conflicts with the findings of Becker et. al. (2011), who found low levels of chytrid fungus (*Batrachochytrium dendrobatidis*) in disturbed landscapes because the environment did not support a large enough population of host species. The main difference between these studies is that in Becker et. al. (2011), the reduction in host species brought the host density below the pathogen's critical threshold, whereas Allan et. al. (2008) saw that the disturbed landscape had fewer species (hosts and non-hosts), which inhibited the dilution effect.

It is unsurprising that a change in host resources was the most common driving factor regarding pathogen prevalence, as it is a generic driver that accompanies a large proportion of landscape types. Since population thresholds are largely dependent on available resources, it is not surprising that the most common mechanism is a change in host density.

Pathogen prevalence is linked with changes in landscape by a complex web of ecological functions. How the ecology of hosts, vectors and pathogens effect prevalence in one system may have the opposite effect in another. Because of this dichotomy we see undisturbed landscapes

with higher pathogen prevalence (see Table 1; Geue & Partecke, 2008; Gillespie et al., 2009). This is partially caused by major differences in pathology, life history, behavior and ecosystems in which the pathogens, hosts and vectors reside.

Some of the discrepancies in prevalence among similar landscapes are caused by the pathogens' mode of transmission. Density dependent and frequency dependent pathogens require different population structures and host behavior to have optimal transmission. Where a pathogen sits on the continuum between frequency dependent transmission and density dependent transmission depends on host abundance, behavior, density and biodiversity.

The tests for heterogeneity and publication bias indicated that there was a large amount of heterogeneity, but no publication bias in the meta-analysis. The heterogeneity is likely caused by the differences in sampling techniques and the varied species of hosts and pathogens. It is therefore not surprising that publication bias was not found, as many of the studies reported both their significant and non-significant findings.

The results synthesize what was previously found by other observational studies and generally agree with previous conclusions that pathogen and parasite prevalence is higher in disturbed landscapes (Aguirre & Tabor, 2008). However, our review provides a statistical meta-analysis that supports the current published hypotheses (Daszak et al., 2001; Dobson & Foufopoulos, 2001; Jones et al., 2008; Morens, Folkers, & Fauci, 2004). Results differ from those found in Brearley et al (2013), who concluded that disease prevalence is too variable to support any pattern. Although this was the case in some of the studies included here, it was by no means the majority. This difference may be accounted for because Brearley et al. (2013) considered all wildlife diseases, instead of only zoonotic, and included experimental studies.

The increase in zoonotic pathogens we observed is likely caused by increased transmission, a probable result of human disturbances altering ecosystem function.

Assumptions and Limitations

We make the assumption that sample size is a correct representation of the animal's abundance in the study area. This is necessary because most case studies publish do not include abundance data. The second assumption is that the landscapes have been correctly categorized by the authors.

The geographic range of the species in question will influence rates of disease transmission, as well as the probability that the diseased organism will be sampled. Larger geographic ranges enable the host to move out of the study area, and possibly become infected in an environment outside of the scope of the study. The study site needs to encompass a large percentage of the organisms' range to eliminate this bias. Because these data are not always published, it is assumed that the researchers who carried out the study have accounted for this potential bias in their study design.

The classification of *Giardia* spp. in Gillespie and Chapman (2008) was only to the genus level, and so the assumption was made that this sample is relevant to this study containing only zoonotic disease.

Significance

This work has shed light on the consistent links between landscape disturbance and pathogen and parasite prevalence. Humans will continue to modify the earth. Diseases will evolve and wildlife populations will continue to be dynamic. Understanding the mechanisms and drivers of zoonotic disease emergence will aid in planning sustainable solutions that will mitigate disease. Zoonotic disease is not only an issue of wildlife health and conservation, but also

human health and economics; and is a threat that warrants attention. It has been proposed that conserving undisturbed landscapes could prove an effective strategy for mitigating disease threats to humans (Young et al., 2014).

Unprecedented levels of disease can lead to extinctions of populations of conservation concern (Johnson et al., 2010). Conservation of these populations may be imperative to the people who depend on them for sustenance and livelihood. They also play a key role in economies by means of tourism and hunting. Wildlife heath needs to be part of the solution when conservation plans and objectives are put into action (Deem, Karesh, & Weisman, 2001). The role disease plays in extinction is not well documented (Heard et al., 2013), this needs to be examined further because extinction caused by pathogens and parasites will affect recovery plans.

Future research

Many of the studies included in the meta-analysis sampled single species of wildlife or a subset of potential hosts. If the studies included prevalence on all available hosts and or reservoirs, an even larger change in prevalence may have been observed at the ecosystem level.

Although the scientific literature is slowly uncovering mechanisms driving pathogen prevalence, additional research is needed to validate those studies across species and landscapes. This will give insight to which landscapes have the greatest amount of disease and link wildlife disease with a particular landscape. Land use tends to correlate with weather patterns, soil types and elevation. For this reason it is imperative that future research on this topic be absolute in differentiating the effects of land use and environmental effects on disease prevalence.

Conclusion

The results support the hypothesis that higher pathogen prevalence in disturbed landscapes is being driven by a multitude of factors that vary by land use. The mechanisms and drivers behind pathogen prevalence are complex and varied, but the connection between increased pathogen prevalence and landscape disturbance is clear. As the world's population continues to increase, humans will consequently modify more landscapes to fit their needs. To address future conservation and sustainable issues, it is imperative that we have an understating of where zoonotic pathogens are likely to arise, and what contributes to their increase and emergence. Having this information will lead to the ability to focus attention on potential hotspots, the most vulnerable areas where resources can be used wisely to control disease outbreaks. This analysis included studies from every continent but Antarctica, showing that is a global issue that transcends economic status. We know ecological disruption is leading to higher levels of pathogens, from here we can move forward towards solutions.

Literature Cited

Allan, B. F., Langerhans, R. B., Ryberg, W. A., Landesman, W. J., Griffin, N. W., Katz, R. S., . . . Chase, J. M. (2008). Ecological correlates of risk and incidence of West Nile virus in the United States. *Oecologia, 158*(4), 699-708. doi: 10.1007/s00442-008-1169-9

Acevedo-Whitehouse, K., & Duffus, A. L. J. (2009). Effects of environmental change on wildlife health. *Philosophical Transactions of the Royal Society B-Biological Sciences, 364*(1534), 3429-3438. doi: 10.1098/rstb.2009.0128

Aguirre, A. A., & Tabor, G. M. (2008). Global Factors Driving Emerging Infectious Diseases Impact on Wildlife Populations. In O. A. E. Sparagano, J. C. Maillard & J. V. Figueroa (Eds.), *Animal Biodiversity and Emerging Diseases: Prediction and Prevention* (Vol. 1149, pp. 1-3). Oxford: Blackwell Publishing.

Allan, B. F., Keesing, F., & Ostfeld, R. S. (2003). Effect of forest fragmentation on Lyme disease risk. *Conservation Biology, 17*(1), 267-272. doi: 10.1046/j.1523-1739.2003.01260.x

Barendregt, J. J., Doi, S. A., Lee, Y. Y., Norman, R. E., & Vos, T. (2013). Meta-analysis of prevalence. *Journal of Epidemiology and Community Health, 67*(11), 974-978. doi: 10.1136/jech-2013-203104

Becker, C. G., & Zamudio, K. R. (2011). Tropical amphibian populations experience higher disease risk in natural habitats. *Proceedings of the National Academy of Sciences of the United States of America, 108*(24), 9893-9898. doi: 10.1073/pnas.1014497108

Begon, M. (2008). Effects of host diversity on disease dynamics. In F. k. Richard Ostfeld, Valerie Eviner (Ed.), Infectious Disease Ecology: Effects of Ecosystems on Disease and Disease on ecosystems. New Jersey: Princeton University Press.

Begon, M. (2009). Ecological Epidemiology. In S. R. C. Simon A. Levin, H. Charles J. Godfray, Ann P. Kinzig, Michel Loreau, Jonathan B. Losos, Brian Walker, David S. Wilcove (Ed.), *The Princeton Guide to Ecology* (pp. 220-226). Princeton, New Jersey: Princeton University Press.

Beltran-Beck, B., Garcia, F. J., & Gortazar, C. (2012). Raccoons in Europe: disease hazards due to the establishment of an invasive species. *European Journal of Wildlife Research, 58*(1), 5-15. doi: 10.1007/s10344-011-0600-4

Bichet, C., Scheifler, R., Coeurdassier, M., Julliard, R., Sorci, G., & Loiseau, C. (2013). Urbanization, Trace Metal Pollution, and Malaria Prevalence in the House Sparrow. *Plos One, 8*(1). doi: 10.1371/journal.pone.0053866

Bielby, J., Donnelly, C. A., Pope, L. C., Burke, T., & Woodroffe, R. (2014). Badger responses to small-scale culling may compromise targeted control of bovine tuberculosis. *Proceedings of the National Academy of Sciences of the United States of America, 111*(25), 9193-9198. doi: 10.1073/pnas.1401503111

Bouchard, C., Beauchamp, G., Leighton, P. A., Lindsay, R., Belanger, D., & Ogden, N. H. (2013). Does high biodiversity reduce the risk of Lyme disease invasion? *Parasites & Vectors, 6*. doi: 10.1186/1756-3305-6-195

Bradley, C. A., Gibbs, S. E. J., & Altizer, S. (2008). Urban land use predicts West Nile Virus exposure in songbirds. *Ecological Applications, 18*(5), 1083-1092. doi: 10.1890/07-0822.1

Brearley, G., McAlpine, C., Bell, S., & Bradley, A. (2012). Influence of urban edges on stress in an arboreal mammal: a case study of squirrel gliders in southeast Queensland, Australia. *Landscape Ecology, 27*(10), 1407-1419. doi: 10.1007/s10980-012-9790-8

Brearley, G., Rhodes, J., Bradley, A., Baxter, G., Seabrook, L., Lunney, D., . . . McAlpine, C. (2013). Wildlife disease prevalence in human-modified landscapes. *Biological Reviews, 88*(2), 427-442. doi: 10.1111/brv.12009

Caron, A., Miguel, E., Gomo, C., Makaya, P., Pfukenyi, D. M., Foggin, C., . . . de Garine-Wichatitsky, M. (2013). Relationship between burden of infection in ungulate populations and

wildlife/livestock interfaces. *Epidemiology and Infection, 141*(7), 1522-1535. doi: 10.1017/s0950268813000204
Chapman, C. A., Speirs, M. L., Gillespie, T. R., Holland, T., & Austad, K. M. (2006). Life on the edge: Gastrointestinal parasites from the forest edge and interior primate groups. *American Journal of Primatology, 68*(4), 397-409. doi: 10.1002/ajp.20233
Chasar, A., Loiseau, C., Valkiunas, G., Iezhova, T., Smith, T. B., & Sehgal, R. N. M. (2009). Prevalence and diversity patterns of avian blood parasites in degraded African rainforest habitats. *Molecular Ecology, 18*(19), 4121-4133. doi: 10.1111/j.1365-294X.2009.04346.x
Chvala, S., Bakonyi, T., Bukovsky, C., Meister, T., Brugger, K., Rubel, F., . . . Weissenbock, H. (2007). Monitoring of Usutu virus activity and spread by using dead bird surveillance in Austria, 2003-2005. *Veterinary Microbiology, 122*(3-4), 237-245. doi: 10.1016/j.vetmic.2007.01.029
Clark, L., & Mason, J. R. (1988). Effect og biologically-active plants used as nest material and the derived benefit to starling nestlings. *Oecologia, 77*(2), 174-180. doi: 10.1007/bf00379183
Clay, C. A., Lehmer, E. M., Jeor, S. S., & Dearing, M. D. (2009). Sin Nombre Virus and Rodent Species Diversity: A Test of the Dilution and Amplification Hypotheses. *Plos One, 4*(7). doi: 10.1371/journal.pone.0006467
Cottontail, V. M., Wellinghausen, N., & Kalko, E. K. V. (2009). Habitat fragmentation and haemoparasites in the common fruit bat, Artibeus jamaicensis (Phyllostomidae) in a tropical lowland forest in Panama. *Parasitology, 136*(10), 1133-1145. doi: 10.1017/s0031182009990485
Daszak, P., Cunningham, A. A., & Hyatt, A. D. (2001). Anthropogenic environmental change and the emergence of infectious diseases in wildlife. *Acta Tropica, 78*(2), 103-116. doi: 10.1016/s0001-706x(00)00179-0
Daszak, P., Epstein, J. H., Kilpatrick, A. M., Aguirre, A. A., Karesh, W. B., & Cunningham, A. A. (2007). Collaborative research approaches to the role of wildlife in zoonotic disease emergence. *Wildlife and Emerging Zoonotic Diseases: The Biology, Circumstances and Consequences of Cross-Species Transmission, 315*, 463-475.
Deem, S. L., Karesh, W. B., & Weisman, W. (2001). Putting theory into practice: Wildlife health in conservation. *Conservation Biology, 15*(5), 1224-1233. doi: 10.1046/j.1523-1739.2001.00336.x
Delahay, R. J., Cheeseman, C. L., & Clifton-Hadley, R. S. (2001). Wildlife disease reservoirs: the epidemiology of Mycobacterium bovis infection in the European badger (Meles meles) and other British mammals. *Tuberculosis, 81*(1-2), 43-49. doi: 10.1054/tube.2000.0266
Di Giallonardo, F., & Holmes, E. C. (2015). Viral biocontrol: grand experiments in disease emergence and evolution. *Trends in Microbiology, 23*(2), 83-90. doi: 10.1016/j.tim.2014.10.004
Dobson, A., & Foufopoulos, J. (2001). Emerging infectious pathogens of wildlife. *Philosophical Transactions of the Royal Society of London Series B-Biological Sciences, 356*(1411), 1001-1012.
Elsworth, P., Cooke, B. D., Kovaliski, J., Sinclair, R., Holmes, E. C., & Strive, T. (2014). Increased virulence of rabbit haemorrhagic disease virus associated with genetic resistance in wild Australian rabbits (Oryctolagus cuniculus). *Virology, 464*, 415-423. doi: 10.1016/j.virol.2014.06.037
Ewel, J. J., Mazzarino, M. J., & Berish, C. W. (1991). Tropical soil fertility changes under monocultures and successional communities of different structure. *Ecological Applications, 1*(3), 289-302. doi: 10.2307/1941758
Field, H. E. (2009). Bats and Emerging Zoonoses: Henipaviruses and SARS. *Zoonoses and Public Health, 56*(6-7), 278-284. doi: 10.1111/j.1863-2378.2008.01218.x
Foley, J. A., Ramankutty, N., Brauman, K. A., Cassidy, E. S., Gerber, J. S., Johnston, M., . . . Zaks, D. P. M. (2011). Solutions for a cultivated planet. *Nature, 478*(7369), 337-342. doi: 10.1038/nature10452
Friedman, E. M., & Lawrence, D. A. (2002). Environmental stress mediates changes in neuroimmunological interactions. *Toxicological Sciences, 67*(1), 4-10.

Geue, D., & Partecke, J. (2008). Reduced parasite infestation in urban Eurasian blackbirds (Turdus merula): a factor favoring urbanization? *Canadian Journal of Zoology-Revue Canadienne De Zoologie, 86*(12), 1419-1425. doi: 10.1139/z08-129

Gillespie, T. R., & Chapman, C. A. (2008). Forest fragmentation, the decline of an endangered primate, and changes in host-parasite interactions relative to an unfragmented forest. *American Journal of Primatology, 70*(3), 222-230. doi: 10.1002/ajp.20475

Gillespie, T. R., Morgan, D., Deutsch, J. C., Kuhlenschmidt, M. S., Salzer, J. S., Cameron, K., . . . Sanz, C. (2009). A Legacy of Low-Impact Logging does not Elevate Prevalence of Potentially Pathogenic Protozoa in Free-Ranging Gorillas and Chimpanzees in the Republic of Congo: Logging and Parasitism in African Apes. *Ecohealth, 6*(4), 557-564. doi: 10.1007/s10393-010-0283-4

Goodrich, J. M., & Buskirk, S. W. (1995). Control of abundant native vertebrates for conservation of endangered species. *Conservation Biology, 9*(6), 1357-1364. doi: 10.1046/j.1523-1739.1995.09061357.x

Gottdenker, N. L., Calzada, J. E., Saldana, A., & Carroll, C. R. (2011). Association of Anthropogenic Land Use Change and Increased Abundance of the Chagas Disease Vector Rhodnius pallescens in a Rural Landscape of Panama. *American Journal of Tropical Medicine and Hygiene, 84*(1), 70-77. doi: 10.4269/ajtmh.2011.10-0041

Habib, T. J., Merrill, E. H., Pybus, M. J., & Coltman, D. W. (2011). Modelling landscape effects on density-contact rate relationships of deer in eastern Alberta: Implications for chronic wasting disease. *Ecological Modelling, 222*(15), 2722-2732. doi: 10.1016/j.ecolmodel.2011.05.007

Hamer, S. A., Lehrer, E., & Magle, S. B. (2012). Wild Birds as Sentinels for Multiple Zoonotic Pathogens Along an Urban to Rural Gradient in Greater Chicago, Illinois. *Zoonoses and Public Health, 59*(5), 355-364. doi: 10.1111/j.1863-2378.2012.01462.x

Hayward, M. W., & Hayward, G. J. (2009). The impact of tourists on lion Panthera leo behaviour, stress and energetics. *Acta Theriologica, 54*(3), 219-224. doi: 10.4098/j.at.0001-7051.074.2008

Heard, M. J., Smith, K. F., Ripp, K. J., Berger, M., Chen, J., Dittmeier, J., . . . Ryan, E. (2013). The Threat of Disease Increases as Species Move Toward Extinction. *Conservation Biology, 27*(6), 1378-1388. doi: 10.1111/cobi.12143

Hernandez, S. M., Peters, V. E., Weygandt, P. L., Jimenez, C., Villegas, P., O'Connor, B., . . . Carroll, C. R. (2013). Do Shade-Grown Coffee Plantations Pose a Disease Risk for Wild Birds? *Ecohealth, 10*(2), 145-158. doi: 10.1007/s10393-013-0837-3

Huang, Z. Y. X., de Boer, W. F., van Langevelde, F., Xu, C., Ben Jebara, K., Berlingieri, F., & Prins, H. H. T. (2013). Dilution effect in bovine tuberculosis: risk factors for regional disease occurrence in Africa. *Proceedings of the Royal Society B-Biological Sciences, 280*(1765). doi: 10.1098/rspb.2013.0624

Huang, Z. Y. X., Xu, C., van Langevelde, F., Prins, H. H. T., ben Jebara, K., & de Boer, W. F. (2014). Dilution effect and identity effect by wildlife in the persistence and recurrence of bovine tuberculosis. *Parasitology, 141*(7), 981-987. doi: 10.1017/s0031182013002357

Hurst, Z. M., McCleery, R. A., Collier, B. A., Fletcher, R. J., Silvy, N. J., Taylor, P. J., & Monadjem, A. (2013). Dynamic Edge Effects in Small Mammal Communities across a Conservation-Agricultural Interface in Swaziland. *Plos One, 8*(9). doi: 10.1371/journal.pone.0074520

Hutchings, M. R., Kyriazakis, I., Gordon, I. J., & Jackson, F. (1999). Trade-offs between nutrient intake and faecal avoidance in herbivore foraging decisions: the effect of animal parasitic status, level of feeding motivation and sward nitrogen content. *Journal of Animal Ecology, 68*(2), 310-323. doi: 10.1046/j.1365-2656.1999.00287.x

Johnson, C. K., Tinker, M. T., Estes, J. A., Conrad, P. A., Staedler, M., Miller, M. A., . . . Mazet, J. A. K. (2009). Prey choice and habitat use drive sea otter pathogen exposure in a resource-limited coastal system. *Proceedings of the National Academy of Sciences of the United States of America, 106*(7), 2242-2247. doi: 10.1073/pnas.0806449106

Johnson, P. T. J., Townsend, A. R., Cleveland, C. C., Glibert, P. M., Howarth, R. W., McKenzie, V. J., . . . Ward, M. H. (2010). Linking environmental nutrient enrichment and disease emergence in humans and wildlife. *Ecological Applications, 20*(1), 16-29. doi: 10.1890/08-0633.1

Johnston, A. R., Gillespie, T. R., Rwego, I. B., McLachlan, T. L. T., Kent, A. D., & Goldberg, T. L. (2010). Molecular Epidemiology of Cross-Species Giardia duodenalis Transmission in Western Uganda. *Plos Neglected Tropical Diseases, 4*(5). doi: 10.1371/journal.pntd.0000683

Jones, K. E., Patel, N. G., Levy, M. A., Storeygard, A., Balk, D., Gittleman, J. L., & Daszak, P. (2008). Global trends in emerging infectious diseases. *Nature, 451*(7181), 990-U994. doi: 10.1038/nature06536

Keesing, F., Belden, L. K., Daszak, P., Dobson, A., Harvell, C. D., Holt, R. D., . . . Ostfeld, R. S. (2010). Impacts of biodiversity on the emergence and transmission of infectious diseases. *Nature, 468*(7324), 647-652. doi: 10.1038/nature09575

Keesing, F., Holt, R. D., & Ostfeld, R. S. (2006). Effects of species diversity on disease risk. *Ecology Letters, 9*(4), 485-498. doi: 10.1111/j.1461-0248.2006.00885.x

Kerr, P. J. (2012). Myxomatosis in Australia and Europe: A model for emerging infectious diseases. *Antiviral Research, 93*(3), 387-415. doi: 10.1016/j.antiviral.2012.01.009

Kirchgessner, M. S., Dubovi, E. J., & Whipps, C. M. (2012). Seroepidemiology of Coxiella burnetii in Wild White-Tailed Deer (Odocoileus virginianus) in New York, United States. *Vector-Borne and Zoonotic Diseases, 12*(11), 942-947. doi: 10.1089/vbz.2011.0952

Kondgen, S., Kuhl, H., N'Goran, P. K., Walsh, P. D., Schenk, S., Ernst, N., . . . Leendertz, F. H. (2008). Pandemic human viruses cause decline of endangered great apes. *Current Biology, 18*(4), 260-264. doi: 10.1016/j.cub.2008.01.012

Koprivnikar, J., & Redfern, J. C. (2012). Agricultural effects on amphibian parasitism: Importance of general habitat perturbations and parasite life cycles. *Journal of Wildlife Diseases, 48*(4), 925-936. doi: 10.7589/2011-09-258

Kormos, C. E., Wilkinson, A. J., Davey, C. J., & Cunningham, A. J. (2014). Low birth weight and intelligence in adolescence and early adulthood: a meta-analysis. *Journal of Public Health, 36*(2), 213-224. doi: 10.1093/pubmed/fdt071

Lafferty, K. D., & Gerber, L. R. (2002). Good medicine for conservation biology: The intersection of epidemiology and conservation theory. *Conservation Biology, 16*(3), 593-604. doi: 10.1046/j.1523-1739.2002.00446.x

Lane, K. E., Holley, C., Hollocher, H., & Fuentes, A. (2011). The anthropogenic environment lessens the intensity and prevalence of gastrointestinal parasites in Balinese long-tailed macaques (Macaca fascicularis). *Primates, 52*(2), 117-128. doi: 10.1007/s10329-010-0230-6

Lawrence, D. A., & Kim, D. (2000). Central/peripheral nervous system and immune responses. *Toxicology, 142*(3), 189-201. doi: 10.1016/s0300-483x(99)00144-4

Lehmer, E. M., Clay, C. A., Pearce-Duvet, J., St. Jeor, S., & Dearing, M. D. (2008). Differential regulation of pathogens: the role of habitat disturbance in predicting prevalence of Sin Nombre virus. *Oecologia, 155*(3), 429-439. doi: 10.1007/s00442-007-0922-9

Lehrer, E. W., Fredebaugh, S. L., Schooley, R. L., & Mateus-Pinilla, N. E. (2010). Prevalence of Antibodies to Toxoplasma gondii in Woodchucks across an Urban-rural Gradient. *Journal of Wildlife Diseases, 46*(3), 977-980.

Lewis, C. A., Cristol, D. A., Swaddle, J. P., Varian-Ramos, C. W., & Zwollo, P. (2013). Decreased Immune Response in Zebra Finches Exposed to Sublethal Doses of Mercury. *Archives of Environmental Contamination and Toxicology, 64*(2), 327-336. doi: 10.1007/s00244-012-9830-z

Marchandeau, S., Pontier, D., Guitton, J. S., Letty, J., Fouchet, D., Aubineau, J., . . . Bertagnoli, S. (2014). Early infections by myxoma virus of young rabbits (Oryctolagus cuniculus) protected by maternal antibodies activate their immune system and enhance herd immunity in wild populations. *Veterinary Research, 45*. doi: 10.1186/1297-9716-45-26

Mbora, D. N. M., & McPeek, M. A. (2009). Host density and human activities mediate increased parasite prevalence and richness in primates threatened by habitat loss and fragmentation. *Journal of Animal Ecology, 78*(1), 210-218. doi: 10.1111/j.1365-2656.2008.01481.x

McCallum, H., Jones, M., Hawkins, C., Hamede, R., Lachish, S., Sinn, D. L., . . . Lazenby, B. (2009). Transmission dynamics of Tasmanian devil facial tumor disease may lead to disease-induced extinction. *Ecology, 90*(12), 3379-3392. doi: 10.1890/08-1763.1

Meister, T., Lussy, H., Bakonyi, T., Sikutova, S., Rudolf, I., Vogl, W., . . . Weissenboeck, H. (2008). Serological evidence of continuing high Usutu virus (Flaviviridae) activity and establishment of herd immunity in wild birds in Austria. *Veterinary Microbiology, 127*(3-4), 237-248. doi: 10.1016/j.vetmic.2007.08.023

Miller, M. A., Gardner, I. A., Kreuder, C., Paradies, D. M., Worcester, K. R., Jessup, D. A., . . . Conrad, P. A. (2002). Coastal freshwater runoff is a risk factor for Toxoplasma gondii infection of southern sea otters (Enhydra lutris nereis). *International Journal for Parasitology, 32*(8), 997-1006. doi: 10.1016/s0020-7519(02)00069-3

Miller, R. S., Farnsworth, M. L., & Malmberg, J. L. (2013). Diseases at the livestOck-wildlife interface: Status, challenges, and opportunities in the United States. *Preventive Veterinary Medicine, 110*(2), 119-132. doi: 10.1016/j.prevetmed.2012.11.021

Morens, D. M., Folkers, G. K., & Fauci, A. S. (2004). The challenge of emerging and re-emerging infectious diseases. *Nature, 430*(6996), 242-249. doi: 10.1038/nature02759

Mullner, A., Linsenmair, K. E., & Wikelski, M. (2004). Exposure to ecotourism reduces survival and affects stress response in hoatzin chicks (Opisthocomus hoazin). *Biological Conservation, 118*(4), 549-558. doi: 10.1016/j.biocon.2003.10.003

Orams, M. B. (2002). Feeding wildlife as a tourism attraction: a review of issues and impacts. *Tourism Management, 23*(3), 281-293. doi: 10.1016/s0261-5177(01)00080-2

Ostfeld, R. S., Glass, G. E., & Keesing, F. (2005). Spatial epidemiology: an emerging (or re-emerging) discipline. *Trends in Ecology & Evolution, 20*(6), 328-336. doi: 10.1016/j.tree.2005.03.009

Owen, J. C., Nakamura, A., Coon, C. A. C., & Martin, L. B. (2012). The effect of exogenous corticosterone on West Nile virus infection in Northern Cardinals (Cardinalis cardinalis). *Veterinary Research, 43*. doi: 10.1186/1297-9716-43-34

Page, L. K., Gehrt, S. D., & Robinson, N. P. (2008). Land-use effects on prevalence of raccoon roundworm (Baylisascaris procyonis). *Journal of Wildlife Diseases, 44*(3), 594-599.

Peter J. Hudson, A. R., Bryan T. Grenfell, Hans Heesterbeek, Andy P. Dobson (Ed.). (2002). *The Ecology of Wildlife Diseases*. Oxford, New York: Oxford University Press.

Prager, K. C., Mazet, J. A. K., Dubovi, E. J., Frank, L. G., Munson, L., Wagner, A. P., & Woodroffe, R. (2012). Rabies Virus and Canine Distemper Virus in Wild and Domestic Carnivores in Northern Kenya: Are Domestic Dogs the Reservoir? *Ecohealth, 9*(4), 483-498. doi: 10.1007/s10393-013-0815-9

Rabinovich, J. E., Kitron, U. D., Obed, Y., Yoshioka, M., Gottdenker, N., & Chaves, L. F. (2011). Ecological patterns of blood-feeding by kissing-bugs (Hemiptera: Reduviidae: Triatominae). *Memorias Do Instituto Oswaldo Cruz, 106*(4), 479-494.

Riley, S. P. D., Foley, J., & Chomel, B. (2004). Exposure to feline and canine pathogens in bobcats and gray foxes in urban and rural zones of a National Park in California. *Journal of Wildlife Diseases, 40*(1), 11-22.

Rohr, J. R., Raffel, T. R., Halstead, N. T., McMahon, T. A., Johnson, S. A., Boughton, R. K., & Martin, L. B. (2013). Early-life exposure to a herbicide has enduring effects on pathogen-induced mortality. *Proceedings of the Royal Society B-Biological Sciences, 280*(1772). doi: 10.1098/rspb.2013.1502

Sanchez, L. C., Lajmanovich, R. C., Peltzer, P. M., Manzano, A. S., Junges, C. M., & Attademo, A. M. (2014). First evidence of the effects of agricultural activities on gonadal form and function in Rhinella fernandezae and Dendropsophus sanborni (Amphibia: Anura) from Entre Rios Province, Argentina. *Acta Herpetologica, 9*(1), 75-88.

Sanderson, E. W., Jaiteh, M., Levy, M. A., Redford, K. H., Wannebo, A. V., & Woolmer, G. (2002). The human footprint and the last of the wild. *Bioscience, 52*(10), 891-904. doi: 10.1641/0006-3568(2002)052[0891:thfatl]2.0.co;2

Schell, C. J., Young, J. K., Lonsdorf, E. V., & Santymire, R. M. (2013). Anthropogenic and physiologically induced stress responses in captive coyotes. *Journal of Mammalogy, 94*(5), 1131-1140. doi: 10.1644/13-mamm-a-001.1

Sehgal, R. N. M. (2010). Deforestation and avian infectious diseases. *Journal of Experimental Biology, 213*(6), 955-960. doi: 10.1242/jeb.037663

Sepúlveda, M. A., Muñoz-Zanzi, C., Rosenfeld, C., Jara, R., Pelican, K. M., & Hill, D. (2011). Toxoplasma gondii in feral American minks at the Maullín river, Chile. *Veterinary Parasitology, 175*(1/2), 60-65. doi: 10.1016/j.vetpar.2010.09.020

Viechtbauer, W. (2010). Conducting Meta-Analyses in R with the metafor Package. *Journal of Statistical Software, 36*(3), 1-48.

Wasserberg, G., Abramsky, Z., Kotler, B. P., Ostfeld, R. S., Yarom, I., & Warburg, A. (2003). Anthropogenic disturbances enhance occurrence of cutaneous leishmaniasis in Israel deserts: patterns and mechanisms. *Ecological Applications, 13*(3), 868-881. doi: 10.1890/1051-0761(2003)013[0868:adeooc]2.0.co;2

Wenz-Mucke, A., Sithithaworn, P., Petney, T. N., & Taraschewski, H. (2013). Human contact influences the foraging behaviour and parasite community in long-tailed macaques. *Parasitology, 140*(6), 709-718. doi: 10.1017/s003118201200203x

Wobeser, G. (1981). *Diseases of WildWaterfowl*. New York, New York: Plenum Publishing Corporation.

Wobeser, G. A. (2006). *Essentials of Disease in Wild Animals*. Iowa, USA: Blackwell Publishing.

Wolfe, N. D., Daszak, P., Kilpatrick, A. M., & Burke, D. S. (2005). Bushmeat hunting deforestation, and prediction of zoonoses emergence. *Emerging Infectious Diseases, 11*(12), 1822-1827.

Xiang, Z. F., Yu, Y., Yang, M., Yang, J. Y., Niao, M. Y., & Li, M. (2011). Does flagship species tourism benefit conservation? A case study of the golden snub-nosed monkey in Shennongjia National Nature Reserve. *Chinese Science Bulletin, 56*(24), 2553-2558. doi: 10.1007/s11434-011-4613-x

Young, H. S., Dirzo, R., Helgen, K. M., McCauley, D. J., Billeter, S. A., Kosoy, M. Y., . . . Dittmar, K. (2014). Declines in large wildlife increase landscape-level prevalence of rodent-borne disease in Africa. *Proceedings of the National Academy of Sciences of the United States of America, 111*(19), 7036-7041. doi: 10.1073/pnas.1404958111

Zylberberg, M., Lee, K. A., Klasing, K. C., & Wikelski, M. (2013). Variation with Land Use of Immune Function and Prevalence of Avian Pox in Galapagos Finches. *Conservation Biology, 27*(1), 103-112. doi: 10.1111/j.1523-1739.2012.01944.x

Appendix I: References of data used in comparison of pathogen and parasite prevalence between disturbed and undisturbed landscapes

Cottontail, V. M., Wellinghausen, N., & Kalko, E. K. V. (2009). Habitat fragmentation and haemoparasites in the common fruit bat, Artibeus jamaicensis (Phyllostomidae) in a tropical lowland forest in Panama. *Parasitology, 136*(10), 1133-1145. doi: 10.1017/s0031182009990485

Gillespie, T. R., & Chapman, C. A. (2008). Forest fragmentation, the decline of an endangered primate, and changes in host-parasite interactions relative to an unfragmented forest. *American Journal of Primatology, 70*(3), 222-230. doi: 10.1002/ajp.20475

Gómez, A., Kilpatrick, A. M., Kramer, L. D., Dupuis Ii, A. P., Maffei, J. G., Goetz, S. J., . . . Aguirre, A. A. (2008). Land Use and West Nile Virus Seroprevalence in Wild Mammals. *Emerging Infectious Diseases, 14*(6), 962-965.

Hamer, S. A., Lehrer, E., & Magle, S. B. (2012). Wild Birds as Sentinels for Multiple Zoonotic Pathogens Along an Urban to Rural Gradient in Greater Chicago, Illinois. *Zoonoses and Public Health, 59*(5), 355-364. doi: 10.1111/j.1863-2378.2012.01462.x

Hernandez, S. M., Peters, V. E., Weygandt, P. L., Jimenez, C., Villegas, P., O'Connor, B., . . . Carroll, C. R. (2013). Do Shade-Grown Coffee Plantations Pose a Disease Risk for Wild Birds? *Ecohealth, 10*(2), 145-158. doi: 10.1007/s10393-013-0837-3

Johnston, A. R., Gillespie, T. R., Rwego, I. B., McLachlan, T. L. T., Kent, A. D., & Goldberg, T. L. (2010). Molecular Epidemiology of Cross-Species Giardia duodenalis Transmission in Western Uganda. *Plos Neglected Tropical Diseases, 4*(5). doi: 10.1371/journal.pntd.0000683

Junge, R. E., Barrett, M. A., & Yoder, A. D. (2011). Effects of Anthropogenic Disturbance on Indri (Indri indri) Health in Madagascar. *American Journal of Primatology, 73*(7), 632-642. doi: 10.1002/ajp.20938

Koprivnikar, J., & Redfern, J. C. (2012). Agricultural effects on amphibian parasitism: Importance of general habitat perturbations and parasite life cycles. *Journal of Wildlife Diseases, 48*(4), 925-936. doi: 10.7589/2011-09-258

Lehmer, E. M., Clay, C. A., Pearce-Duvet, J., St. Jeor, S., & Dearing, M. D. (2008). Differential regulation of pathogens: the role of habitat disturbance in predicting prevalence of Sin Nombre virus. *Oecologia, 155*(3), 429-439. doi: 10.1007/s00442-007-0922-9

Riley, S. P. D., Foley, J., & Chomel, B. (2004). Exposure to feline and canine pathogens in bobcats and gray foxes in urban and rural zones of a National Park in California. *Journal of Wildlife Diseases, 40*(1), 11-22.

Sepúlveda, M. A., Muñoz-Zanzi, C., Rosenfeld, C., Jara, R., Pelican, K. M., & Hill, D. (2011). Toxoplasma gondii in feral American minks at the Maullín river, Chile. *Veterinary Parasitology, 175*(1/2), 60-65. doi: 10.1016/j.vetpar.2010.09.020

Wasserberg, G., Abramsky, Z., Kotler, B. P., Ostfeld, R. S., Yarom, I., & Warburg, A. (2003). Anthropogenic disturbances enhance occurrence of cutaneous leishmaniasis in Israel deserts: patterns and mechanisms. *Ecological Applications, 13*(3), 868-881. doi: 10.1890/1051-0761(2003)013[0868:adeooc]2.0.co;2

Wenz-Mucke, A., Sithithaworn, P., Petney, T. N., & Taraschewski, H. (2013). Human contact influences the foraging behaviour and parasite community in long-tailed macaques. *Parasitology, 140*(6), 709-718. doi: 10.1017/s003118201200203x

Appendix II. References of data used to identify differences in pathogen occurrence between landscapes

Allan, B. F., Keesing, F., & Ostfeld, R. S. (2003). Effect of forest fragmentation on Lyme disease risk. *Conservation Biology, 17*(1), 267-272. doi: 10.1046/j.1523-1739.2003.01260.x

Allan, B. F., Langerhans, R. B., Ryberg, W. A., Landesman, W. J., Griffin, N. W., Katz, R. S., . . . Chase, J. M. (2008). Ecological correlates of risk and incidence of West Nile virus in the United States. *Oecologia, 158*(4), 699-708. doi: 10.1007/s00442-008-1169-9

Beasley, J. C., Eagan, T. S., Page, L. K., Hennessy, C. A., & Rhodes, O. E. (2013). Baylisascaris Procyonis infection in White-footed mice: Predicting patterns of infection from landscape habitat attributes. *Journal of Parasitology, 99*(5), 743-747. doi: 10.1645/ge-2887.1

Becker, C. G., & Zamudio, K. R. (2011). Tropical amphibian populations experience higher disease risk in natural habitats. *Proceedings of the National Academy of Sciences of the United States of America, 108*(24), 9893-9898. doi: 10.1073/pnas.1014497108

Bichet, C., Scheifler, R., Coeurdassier, M., Julliard, R., Sorci, G., & Loiseau, C. (2013). Urbanization, Trace Metal Pollution, and Malaria Prevalence in the House Sparrow. *Plos One, 8*(1). doi: 10.1371/journal.pone.0053866

Bradley, C. A., Gibbs, S. E. J., & Altizer, S. (2008). Urban land use predicts West Nile Virus exposure in songbirds. *Ecological Applications, 18*(5), 1083-1092. doi: 10.1890/07-0822.1

Chasar, A., Loiseau, C., Valkiunas, G., Iezhova, T., Smith, T. B., & Sehgal, R. N. M. (2009). Prevalence and diversity patterns of avian blood parasites in degraded African rainforest habitats. *Molecular Ecology, 18*(19), 4121-4133. doi: 10.1111/j.1365-294X.2009.04346.x

Cottontail, V. M., Wellinghausen, N., & Kalko, E. K. V. (2009). Habitat fragmentation and haemoparasites in the common fruit bat, Artibeus jamaicensis (Phyllostomidae) in a tropical lowland forest in Panama. *Parasitology, 136*(10), 1133-1145. doi: 10.1017/s0031182009990485

Evans, K. L., Gaston, K. J., Sharp, S. P., McGowan, A., Simeoni, M., & Hatchwell, B. J. (2009). Effects of urbanisation on disease prevalence and age structure in blackbird Turdus merula populations. *Oikos, 118*(5), 774-782. doi: 10.1111/j.1600-0706.2008.17226.x

Geue, D., & Partecke, J. (2008). Reduced parasite infestation in urban Eurasian blackbirds (Turdus merula): a factor favoring urbanization? *Canadian Journal of Zoology-Revue Canadienne De Zoologie, 86*(12), 1419-1425. doi: 10.1139/z08-129

Gillespie, T. R., & Chapman, C. A. (2008). Forest fragmentation, the decline of an endangered primate, and changes in host-parasite interactions relative to an unfragmented forest. *American Journal of Primatology, 70*(3), 222-230. doi: 10.1002/ajp.20475

Gillespie, T. R., Morgan, D., Deutsch, J. C., Kuhlenschmidt, M. S., Salzer, J. S., Cameron, K., . . . Sanz, C. (2009). A Legacy of Low-Impact Logging does not Elevate Prevalence of Potentially Pathogenic Protozoa in Free-Ranging Gorillas and Chimpanzees in the Republic of Congo: Logging and Parasitism in African Apes. *Ecohealth, 6*(4), 557-564. doi: 10.1007/s10393-010-0283-4

Gómez, A., Kilpatrick, A. M., Kramer, L. D., Dupuis Ii, A. P., Maffei, J. G., Goetz, S. J., . . . Aguirre, A. A. (2008). Land Use and West Nile Virus Seroprevalence in Wild Mammals. *Emerging Infectious Diseases, 14*(6), 962-965.

Hamer, S. A., Lehrer, E., & Magle, S. B. (2012). Wild Birds as Sentinels for Multiple Zoonotic Pathogens Along an Urban to Rural Gradient in Greater Chicago, Illinois. *Zoonoses and Public Health, 59*(5), 355-364. doi: 10.1111/j.1863-2378.2012.01462.x

Hernandez, S. M., Peters, V. E., Weygandt, P. L., Jimenez, C., Villegas, P., O'Connor, B., . . . Carroll, C. R. (2013). Do Shade-Grown Coffee Plantations Pose a Disease Risk for Wild Birds? *Ecohealth, 10*(2), 145-158. doi: 10.1007/s10393-013-0837-3

Hussain, S., Ram, M. S., Kumar, A., Shivaji, S., & Umapathy, G. (2013). Human Presence Increases Parasitic Load in Endangered Lion-Tailed Macaques (Macaca silenus) in Its Fragmented Rainforest Habitats in Southern India. *Plos One, 8*(5), 1-8. doi: 10.1371/journal.pone.0063685

Johnston, A. R., Gillespie, T. R., Rwego, I. B., McLachlan, T. L. T., Kent, A. D., & Goldberg, T. L. (2010). Molecular Epidemiology of Cross-Species Giardia duodenalis Transmission in Western Uganda. *Plos Neglected Tropical Diseases, 4*(5). doi: 10.1371/journal.pntd.0000683

Junge, R. E., Barrett, M. A., & Yoder, A. D. (2011). Effects of Anthropogenic Disturbance on Indri (Indri indri) Health in Madagascar. *American Journal of Primatology, 73*(7), 632-642. doi: 10.1002/ajp.20938

Kellner, K. F., Page, L. K., Downey, M., & McCord, S. E. (2012). Effects of Urbanization on Prevalence of Baylisascaris procyonis in Intermediate Host Populations. *Journal of Wildlife Diseases, 48*(4), 1083-1087. doi: 10.7589/2011-09-267

Kirchgessner, M. S., Dubovi, E. J., & Whipps, C. M. (2013). Disease Risk Surface for Coxiella burnetii Seroprevalence in White-Tailed Deer. *Zoonoses and Public Health, 60*(7), 457-460. doi: 10.1111/zph.12023

Koprivnikar, J., & Redfern, J. C. (2012). Agricultural effects on amphibian parasitism: Importance of general habitat perturbations and parasite life cycles. *Journal of Wildlife Diseases, 48*(4), 925-936. doi: 10.7589/2011-09-258

Lane, K. E., Holley, C., Hollocher, H., & Fuentes, A. (2011). The anthropogenic environment lessens the intensity and prevalence of gastrointestinal parasites in Balinese long-tailed macaques (Macaca fascicularis). *Primates, 52*(2), 117-128. doi: 10.1007/s10329-010-0230-6

Lehmer, E. M., Clay, C. A., Pearce-Duvet, J., St. Jeor, S., & Dearing, M. D. (2008). Differential regulation of pathogens: the role of habitat disturbance in predicting prevalence of Sin Nombre virus. *Oecologia, 155*(3), 429-439. doi: 10.1007/s00442-007-0922-9

Mbora, D. N. M., & McPeek, M. A. (2009). Host density and human activities mediate increased parasite prevalence and richness in primates threatened by habitat loss and fragmentation. *Journal of Animal Ecology, 78*(1), 210-218. doi: 10.1111/j.1365-2656.2008.01481.x

Miller, M. A., Gardner, I. A., Kreuder, C., Paradies, D. M., Worcester, K. R., Jessup, D. A., . . . Conrad, P. A. (2002). Coastal freshwater runoff is a risk factor for Toxoplasma gondii infection of southern sea otters (Enhydra lutris nereis). *International Journal for Parasitology, 32*(8), 997-1006. doi: 10.1016/s0020-7519(02)00069-3

Page, L. K., Gehrt, S. D., & Robinson, N. P. (2008). Land-use effects on prevalence of raccoon roundworm (Baylisascaris procyonis). *Journal of Wildlife Diseases, 44*(3), 594-599.

Plowright, R. K., Foley, P., Field, H. E., Dobson, A. P., Foley, J. E., 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. doi: 10.1098/rspb.2011.0522

Riley, S. P. D., Foley, J., & Chomel, B. (2004). Exposure to feline and canine pathogens in bobcats and gray foxes in urban and rural zones of a National Park in California. *Journal of Wildlife Diseases, 40*(1), 11-22.

Schaumburg, F., Mugisha, L., Peck, B., Becker, K., Gillespie, T. R., Peters, G., & Leendertz, F. H. (2012). Drug-Resistant Human Staphylococcus Aureus in Sanctuary Apes Pose a Threat to Endangered Wild Ape Populations. *American Journal of Primatology, 74*(12), 1071-1075. doi: 10.1002/ajp.22067

Sepúlveda, M. A., Muñoz-Zanzi, C., Rosenfeld, C., Jara, R., Pelican, K. M., & Hill, D. (2011). Toxoplasma gondii in feral American minks at the Maullín river, Chile. *Veterinary Parasitology, 175*(1/2), 60-65. doi: 10.1016/j.vetpar.2010.09.020

Suzán, G., Marc, E., Giermakowski, J. T., Armién, B., Pascale, J., Mills, J., . . . 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. doi: 10.1196/annals.1428.063

Urban, M. C. (2006). Road facilitation of trematode infections in snails of northern Alaska. *Conservation Biology, 20*(4), 1143-1149. doi: 10.1111/j.1523-1739.2006.00422.x

Vaz, V. C., D'Andrea, P. S., & Jansen, A. M. (2007). Effects of habitat fragmentation on wild mammal infection by Trypanosoma cruzi. *Parasitology, 134*, 1785-1793. doi: 10.1017/s003118200700323x

Wasserberg, G., Abramsky, Z., Kotler, B. P., Ostfeld, R. S., Yarom, I., & Warburg, A. (2003). Anthropogenic disturbances enhance occurrence of cutaneous leishmaniasis in Israel deserts: patterns and mechanisms. *Ecological Applications, 13*(3), 868-881. doi: 10.1890/1051-0761(2003)013[0868:adeooc]2.0.co;2

Wenz-Mucke, A., Sithithaworn, P., Petney, T. N., & Taraschewski, H. (2013). Human contact influences the foraging behaviour and parasite community in long-tailed macaques. *Parasitology, 140*(6), 709-718. doi: 10.1017/s003118201200203x

Zylberberg, M., Lee, K. A., Klasing, K. C., & Wikelski, M. (2013). Variation with Land Use of Immune Function and Prevalence of Avian Pox in Galapagos Finches. *Conservation Biology, 27*(1), 103-112. doi: 10.1111/j.1523-1739.2012.01944.x

Appendix III: R code

```
# Input Data
data<-read.csv("Diseasecalc.csv",header=T)
attach(data)
#Average
summary(data)
#Histogram
hist(data$yi, breaks=30,xlim=c(-1,1),main="Mean prevalence difference disturbed/undisturbed
landscapes", xlab="Effect size", ylab="Frequency")
#T-test
library("weights")
wtd.t.test(data$undist_prevalence_pro,data$dist_prevalence_pro, weight=data$undist_samples,
weighty=data$dist_samples, alternative="two.tailed")
#Asymptotic Wilcoxon signed rank test
library(coin)
library(exactRankTests)
#data
rm(list=ls())
data<-read.table("zoonotic_economic_sign_test_data_ with_ties_1.csv",sep=",",header=T)
attach(data)
names(data)
data
data$x_increase
data$y_decrease
# Wilcoxon exact test for data with ties, from libraries "coin" and "exactRankTests"
wilcox.exact(y_decrease,x_increase, paired=TRUE, alternative = "two.sided"))
#Calculate effect sizes and the corresponding sampling variances
library("metafor")
data("disease calc.csv")
library("metafor")
dat <- escalc(measure = "RD", ai = dist_num_infected, bi = dist_num_uninfected, ci =
undist_num_infected, di = undist_num_uninfected, data = data, append = TRUE)
print(dat[,-c(4:7)], row.names = FALSE)
k <- length(data$study)
dat.fm <- data.frame(study = factor(rep(1:k, each = 4)))
dat.fm$grp <- factor(rep(c("T", "T", "C", "C"), k), levels = c("T", "C"))
dat.fm$out <- factor(rep(c("+", "-", "+", "-"), k), levels = c("+", "-"))
dat.fm$freq <- with(data, c(data$dist_num_infected, data$dist_num_uninfected,
data$undist_num_infected, data$undist_num_uninfected))
dat.fm
```

```
escalc(out ~ grp | study, weights = freq, data = dat.fm, measure = "RD)
#Fit random-effects model
res<-rma(yi=data$yi,vi=data$vi,measure="RD")
#Carry out trim-and-fill analysis
taf <- trimfill(res)
# Draw funnel plot with missing studies filled in
funnel(taf)
taf
ranktest(res)
#Qqplot
res <- rma(yi, vi, data = dat)
qqnorm(res, main = "Random-Effects Model")
# I 2 statistic
confint(res)
# Rosenthal's Failsafe number
fsn(yi, vi, data=data, type="Rosenthal", alpha=.05, subset, digits=4)
```

Appendix IV: Search Keywords

Wildlife
Disease
Pathogen
Parasite
Wildlife
Animal
Health
Human
Anthropogenic
Disturbed
Undisturbed
Human modified
Prevalence
City
Urban
Agriculture
Ecotourism
Recreation
Monoculture
Deforestation
Fragmentation
Zoonotic
Livestock