Title: **Pathogen spillover during land conversion**

Running title: Spillover during land conversion

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*Statement of authorship***.** CLF, RKP, HIM, APD, NLG, LSPB, and TRG conceived and designed the study. CLF and NLG collated empirical data. CLF, RKP, HIM, and CJT analyzed and interpreted the results. CLF and RKP wrote the the manuscript and all authors contributed to editing and approved the final draft.

Data accessibility statement. Should the manuscript be accepted, all code will be made freely available on a public repository on github.com

ABSTRACT

Pathogen spillover from wildlife to domestic animals and humans, and the reverse, has caused significant epidemics and pandemics worldwide. Although pathogen emergence has been linked to anthropogenic land conversion, a general framework to disentangle underlying processes is lacking. We develop a multi-host model for pathogen transmission between species inhabiting intact and converted habitat. Interspecies contacts and host populations vary with the proportion of land converted; enabling us to quantify infection risk across a changing landscape. In a range of scenarios, the highest spillover risk occurs at intermediate levels of habitat loss. Whereas the largest, but rarest, epidemics occur at extremes of land conversion. This framework provides insights into the mechanisms driving disease emergence and spillover during land conversion. The finding that the risk of spillover is highest at intermediate levels of habitat loss provides important guidance for conservation and public health policy.

INTRODUCTION

Anthropogenic or human-driven land conversion has led to loss of natural habitat across the globe (Hansen *et al.* 2013). The processes of agricultural intensification and urbanization transform contiguous natural habitats into smaller, discrete remnant patches embedded in a *matrix* of human-modified land (Skole & Tucker 1993; Forman 1995). The proportion of the landscape that consists of *core* habitat is an essential structural feature of a landscape, as is the *edge* surrounding these habitats (Turner & Gardner 2015). The core may be intact natural habitat or similar, whereas edges form the boundary between the core and matrix habitats (Fagan *et al.* 1999). Initially, all forms of land conversion increase edge density, the total length of edge per unit area (Gardner & O'Neill 1991; McGarigal & McComb 1995; Ritters *et al.* 1995; Hargis *et al.* 1998; Fahrig 2003). However, at high levels of habitat conversion edge density declines – the point of habitat conversion when edge density is maximum depends on the shape of matrix patches and the processes by which reminant core habitat is converted (Zipperer 1993; Hargis *et al.* 1998). Land cover transformation and changes in edge densities relative to proportion of land converted have cascading ecological effects that influence resource availability, population carrying capacities, species persistence, and the community composition of plants and animals (Laurance 2000; Ries *et al.* 2004; Ewers & Didham 2007). In addition to these ecological implications, mounting evidence suggests that land conversion influences how infectious diseases are transmitted within and between animal species. Spillover across core-matrix boundaries has led to outbreaks (Gonzalez *et al.* 2005; Calvignac-Spencer *et al.* 2014), declines in populations (Thorne & Williams 1988; Berger *et al.* 1998), panzootics (Li *et al.* 2005; Keele *et al.* 2006), and even species extirpation (De Castro & Bolker 2004).

Human-driven land conversion has been associated with infectious disease emergence (Patz *et al.* 2004; Jones *et al.* 2008; Gottdenker *et al.* 2014), although clear mechanisms have been difficult to infer from empirical data. One hypothesis is that edges between core and matrix landscapes facilitate interspecies contact and pathogen transfer during land conversion (Chapman *et al.* 2005; Wolfe *et al.* 2005). Length of edge habitat is positively correlated with interspecies contact rates and

increases pathogen sharing between wildlife and humans in some systems (Goldberg *et al.* 2008; Walsh 2013; Paige *et al.* 2014). Yet there is minimal understanding about whether this increase is driven solely by changing contact patterns, or other consequences of land use change, such as changing habitat, altered resource availability, or changing species composition.

Models of emerging infectious diseases rarely focus on the pathogen spillover stage of emergence (Lloyd-Smith *et al.* 2009; Plowright *et al.* 2017). Explicit models of spillover often rely on fixed interspecies transmission rates from reservoir hosts to new hosts (Rogers 1988; Choi *et al.* 2002; Chaves & Hernandez 2004) or on an environmental reservoir that determines spillover risk (Rosenquist *et al.* 2003; Nauta *et al.* 2007). Time variation in interspecies transmission rates has been explored using a seasonally forced multi-host model (Ghosh & Tapaswi 1999), but this forcing was not linked to biological or environmental data. Moreover, these models do not consider landscape scale processes affecting transmission. Models that explore relationships between disease transmission and land conversion are primarily agent-based and parameterized for specific locations and diseases (Nunn *et al.* 2007; Li *et al.* 2012; Lane-deGraaf *et al.* 2013). Despite the common belief that land conversion leads to disease emergence, there is no theoretical framework integrating land conversion and critical transmission components of disease spillover.

We present a general mechanistic framework for understanding pathogen transmission among core and matrix species during land conversion. This framework can be adapted to a variety of systems with applications for public health, veterinary health, and conservation (Figure 2; Table S1). We develop a mathematical model of host populations and pathogen dynamics for two host species: one occupying core habitat and one occupying matrix habitat. We observe how variation in species' carrying capacities, contact rates between species, and efficiency of pathogen transmission between species are associated with pathogen spillover during land conversion. To explore the conditions under which the habitat of recipient hosts becomes permeable to pathogens, we use a deterministic multi-host model. We then use stochastic simulations to investigate how land conversion affects the

probability and size of outbreaks . We also adapt the deterministic simulations to examine how the magnitude and rate of land conversion affects transient and equilibrium pathogen prevalence.

Methods

Model assumptions

We model a single pathogen shared with two host species: one that primarily occupies core habitat and the other that primarily occupies converted matrix habitat. We assume that: (1) both species' carrying capacities are determined by the area of their respective key habitat, (2) species dwelling in the matrix landscape are humans or domestic animals, (3) wildlife live in core habitat, and (4) pathogens have a higher R_0 in endemic hosts. These assumptions can be adjusted to reflect many spillover scenarios (Figure 2). The equilibrium abundance of core species, $K_C[\phi]$, and matrix species, $K_M[\phi]$, are functions of the proportion of converted habitat (ϕ varies from an initial value of 0, when no core habitat has been converted, to 1.0 when all natural habitat is converted to matrix; Figure 1).

Species-specific parameters are denoted by a subscript for core (C) and matrix (M) hosts. For the deterministic simulations in the main text, all species specific parameters (including birth rates, death rates, disease recovery rates, disease induced mortality) were fixed and the same for all simulations (Table S2). Sensitivity analyses exploring how these parameters affect model predictions are detailed in the supporting information (Figure S4).

Deterministic model framework

In this two host system: S_c, I_c, R_c are susceptible, infected and recovered core hosts and we assume that the total host population ($N_c = S_c + I_c + R_c$) contributes to reproduction. S_M, I_M, R_M and N_M are the corresponding numbers for matrix hosts. We use coupled ODEs (Equations 1-6) to simulate the dynamics of both density-dependent ($\kappa = 1$) and frequency- dependent ($\kappa = 0$) pathogens. Adaptations of the SIR model - including SI, SIS, and SIRS structures - are detailed in the supplementary information (Figures S4-S7; Tables S5-S7).

$$\frac{dS_c}{dt} = b_c N_c \left(1 - \frac{N_c}{(1-\phi)K_c}\right) - \left(\frac{\beta_c S_c I_c}{N_c^{\kappa}} + \frac{\varepsilon[\phi]\psi\beta_M S_c I_m}{(N_c + \varepsilon[\phi]N_m)}\right) - d_c$$

$$\frac{dI_c}{dt} = \frac{\beta_c S_c I_c}{N_c^{\kappa}} + \frac{\varepsilon[\phi]\beta_M S_c I_m}{(N_c + \varepsilon[\phi]N_m)} - (d_c + \alpha_c + \gamma_c)I_c$$

$$\frac{dR_c}{dt} = \gamma_c I_c - d_c R_c$$

$$\frac{dS_m}{dt} = b_m N_m \left(1 - \frac{N_m}{\phi K_m}\right) - \left(\frac{\beta_m S_m I_m}{N_m^{\kappa}} + \frac{\varepsilon[\phi]\psi\beta_c S_m I_c}{(N_m + \varepsilon[\phi]N_c)}\right) - d_m$$

$$\frac{dI_c}{dt} = \frac{\beta_m S_m I_m}{N_m^{\kappa}} + \frac{\varepsilon[\phi]\psi\beta_c S_m I_c}{(N_m + \varepsilon[\phi]N_c)} - (d_m + \alpha_m + \gamma_m)I_m$$

$$\frac{dR_c}{dt} = \gamma_m I_m - d_m R_m$$

The rate of within species transmission (β_M, β_C) is independent of landscape conversion (but see Figure S1-S2 for extensions that do not assume this). Transmission rates are calculated from a fixed R_0 within a species ($R_{0.C}$ or $R_{0.M}$) in a landscape that is entirely its natural habitat ($\phi = 0, \phi = 1$; respectively). Unique transmission rates are calculated for density-dependent ($\kappa = 1$) and frequency-dependent ($\kappa = 0$) transmission (Table S2). Density-dependent transmission is appropriate for modelling pathogens with transmission rates that increase with host density, whereas frequency- dependent transmission is appropriate for modelling pathogens with transmission rates that do not change with host density (McCallum *et al.* 2001). These formulations represent two extremes on a continuum of potential transmission assumptions and are therefore useful for understanding the spectrum of possible transmission scenarios (McCallum *et al.* 2017).

Between species (core-matrix) transmission rates are a product of the source species transmission rate (β_M or β_C), the efficiency of between species transmission (a proportion, ψ), and the the boundary between the core and matrix habitats (edge effects; ε). We use a third order polynomial

function (Equation S5) to model edge effects, ε, as a function of landscape conversion ϕ (Figure 1). This function was parameterized using a representative dataset of land conversion (Wang *et al.* 2014). We assume that interspecies contact is most likely 200 m on either side of the edge and we use this to create a buffer area. Edge effects in this model can be thought of as the proportion of total habitat where both species are likely to interact; ε can exceed 1 when some regions are within more than one edge buffer. Variations of epsilon are explored in the supporting information and exemplify different patterns and processes during land conversion (Figure S10).

To explore a range of scenarios detailed in Figure 2, we calculate the community R_0 for three pathogen case studies. We explore how community R_0 changes for both density- and frequency-dependent transmission in these scenarios - 1) a pathogen that is endemic in core hosts ($\boldsymbol{R_{0.C}} > \boldsymbol{R_{0.M}}$, Figure 2A/B), 2) a pathogen that is endemic in matrix hosts ($\boldsymbol{R_{0.C}} < \boldsymbol{R_{0.M}}$, Figure 2C/D), and 3) a pathogen that is equally adapted to both species ($\boldsymbol{R_{0.C}} = \boldsymbol{R_{0.M}}$, Figure 2 E/F). The community R_0, or expected number of secondary cases when an infected individual is introduced to a completely naïve community, is calculated by linearizing the transmission terms using a next-generation matrix (Equations S1-S4) (Diekmann *et al.* 1990).

Stochastic simulations. We also model pathogen emergence as a closed stochastic SIR epidemic in matrix populations. Gillespie's direct method (Gillespie 1977) is used to simulate exponentially distributed variables and the event time between discrete events. The initial matrix population size is determined by the proportion of converted land and all individuals are assumed to be susceptible. Within-matrix transmission, recovery, and disease-induced mortality rates are parameterized based on a 2001 Ebola epidemic in Uganda (CDC (2001)); Ferrari *et al.* (2005); Table S4). Finally, the spillover rate is a product of the (1) size of core population (only for DD pathogens, $K_C[\phi]$), (2) transmission rate within core populations(β_C), (3) between species transmission efficiency (here

$\varphi = 0.5$), and (4) edge effects ($\varepsilon[\phi]$) – the spillover rate is therefore specific to the level of land conversion (ϕ, Figure S12). All of these processes are stochastic in our model.

We iterated the model over one year, keeping track daily of whether or not any individuals were infected in the matrix population, the total number of individuals infected during the epidemic (size of epidemic), and how many infections were caused by relative to the force of spillover (matrix:spillover cases). Simulations were run 10,000 times and the probability of spillover at a given level of land conversion was calculated as the proportion of simulations with at least one infected individual in the matrix population after 1 year.

Changes in the frequency and scale of land conversion. To examine the impact of spatial and temporal differences in the land conversion process on disease dynamics, we adapt the deterministic model framework to examine variation in the frequency and proportion of land converted. All simulations are run with the same demographic parameters (Table S2) and the pathogen is endemic in the core species (Table S3). Land conversion events begin after the system is at endemic equilibrium (t = 150 years) in a landscape that has a small population of matrix hosts ($\phi = 0.01$). We assume that each conversion event is instantaneous: changing the carrying capacities of each host and the potential contacts between them. There are delays between the conversion events and adjustment of populations to the new carrying capacities, as the birth rate increases or decreases according to the species. The simulations are run with a gradient of land conversion frequencies (conversion events biannually to every decade) and size of land converted (4%, 8%, or 12% every conversion event). There are nine conversion events and the number of hosts in each class (S ,I, R) is recorded in the core and matrix until the system returns to equilibrium (an additional 150 years).

RESULTS

Pathogen invasion in naïve communities is highest at intermediate levels of land conversion.

We determine R_0 for multi-host systems in the context of changing landscapes. We consider this community R_0 to be a proxy for invasion potential. We explore three scenarios in which a pathogen is endemic in core hosts ($R_{0.C} > R_{0.M}$, Figure 2A/B), a pathogen is endemic in matrix hosts ($R_{0.c} < R_{0.M}$, Figure 2C/D), and a pathogen is equally adapted to both species ($R_{0.c} = R_{0.M}$, Figure 2 E/F).

When transmission is density-dependent; invasion potential is affected by both endemic and non-endemic species' carrying capacity and edge effects (Figure 3A, C, E). If efficiency of between species transmission (ψ) is low, community R_0 tracks that of the species with the highest R_0 for the given amount of habitat conversion. Increasing efficiency of between species transmission magnifies the community R_0 beyond that of either species individually. This nonlinear relationship has the potential to lead to intermediate levels of habitat loss driving disease emergence, whereas community R_0 is lower at the extremes of habitat conversion (Figure 3). Depending on R_0 of endemic and spillover hosts, invasion of the pathogen is not possible (community $R_0 < 1$) over small (Figure 3E) or large (Figure 3A) proportions of habitat conversion. This relationship is driven by edge effects, replacement of one species with another host, and high between-species transmission efficiency. While these calculations assume a completely naïve population, as land conversion splinters the landscape, pathogens are likely to go extinct in isolated habitat patches. Subsequent introduction of pathogens into intermediate levels of converted landscape can be more likely (higher community R_0) relative to completely intact ecosystems (Figure 3C) or completely converted ecosytems (Figure 3A) depending on the habitat of the endemic host.

By contrast, when transmission is frequency-dependent, the community R_0 never goes below 1 because we assume the pathogen is endemic in at least one species and this maintains the same R_0 regardless of either host population size. Therefore, frequency-dependent pathogens (Figure 3B,D,F), are able to invade the community at any level of land conversion even if $R_0 < 1$ in one species, as long as $R_0 > 1$ in the other. For frequency-dependent pathogens, invasion potential is also highest at intermediate levels of land conversion, because the frequency of contacts increases with

length of the edge between habitats. The efficiency of between-species transmission affects the magnitude of the community R_0, but not the range of habitat loss over which a pathogen can invade a community.

Beyond community R_0, each species' peak prevalence and equilibrium prevalence is affected by a unique subset of demographic and disease parameters (Tables S5-S7). For example at intermediate conversion ($\phi = 0.5$), across an epidemic the number of infected non-endemic hosts is most affected by increasing interspecies transmission efficiency, but equilibrium prevalence increases most with birth rate (Figure S4). The magnitude and direction of influence of these parameters is also affected by the stage of habitat conversion and specifics of the disease process (SIR, SIRS, SI, SIS; Figures S4-S7; Tables S5-S7).

Probability of individual infection and occurrence of outbreaks is highest at intermediate levels of land conversion. We use stochastic models to understand the probability and average size of epidemics in matrix populations across a gradient of land conversion. We show that land conversion can drive a range of outcomes: from no transmission events, stuttering chains of transmissions, to epidemics (Figure 4). At low levels of converted habitat, the large infectious pool of core species creates a high force of infection and is combined with intermediate edge effects (see spillover rate; Figure S10). But as there are few susceptible individuals in the matrix habitat, these outbreaks tend to die out. As more habitat is converted, spillover risk from core habitats remains relatively high while matrix populations grow. These larger matrix populations sustain local chains of transmission (Figure 4). The key result is that the highest probability of an outbreak occurrs at intermediate levels of conversion, with high edge effects, and relatively large populations in the matrix.

At higher levels of land conversion ($\phi > 80\%$), spillover declines because the force of infection from dwindling core populations and edge effects are reduced. The highest levels of land conversion lead to the largest, but also rarest, epidemics (Figure 4C; median outbreak size = 0, mean outbreak size = 80). At these higher levels of habitat conversion, the distribution of outbreak sizes is bimodal. If

spillover occurs, the final outbreak size is large because of the large pool of susceptible hosts, but likelihood of spillover is low because core populations are small and edge is minimal. These patterns are similar in a model that excludes edge effects and simply changes the relative abundance of the two host populations.

Spatial scale and rate of land conversion affect transient and equilibrium disease dynamics. Regardless of the amount and frequency of land conversion, infection prevalence in the matrix population increases in the medium term (Figure 5) and similar patterns occur in the number of infected individuals (Figure S11). Initial decreases in prevalence are followed by a rise in the prevalence in infected core species and a delayed peak in matrix host prevalence. The magnitude of the change in prevalence is dependent upon both the amount and frequency of core habitat converted. When only a small amount of land (4% habitat) is transformed, increases in the frequency of land conversion events more quickly reach peak prevalence of infection in both the core and matrix hosts, but it is lower in magnitude compared to slower land transformation. By contrast, when a large amount of land (12% habitat) is transformed, increases in the frequency of land conversion events from decadal to biannual reduce peak and long-term prevalence in both core and matrix hosts below the initial levels. The combination of rapid rates of area and land conversion pushes the system past the risky intermediate land conversion phase (where edge effects are greatest) towards a system with lower edge effects. Thus, transient dynamics are dependent on both the rate and amount of land cleared and the interaction between the two.

DISCUSSION

The number of emerging infectious disease events are thought to be increasing and environmental change, such as land conversion, play a role in this increase (Jones *et al.* 2008; Jones *et al.* 2013; Gottdenker *et al.* 2014). Despite a correlation between pathogen transmission and land conversion,

specific mechanisms underlying increased infection risk in changing landscapes have been difficult to pinpoint (Gillespie & Chapman 2006; Plowright *et al.* 2008). Our mechanistic models of the dynamics of reservoir and recipient host populations highlight changing host population densities and edge effects as mechanisms driving disease emergence in converted landscapes. We show that a hump-shaped relationship of pathogen transmission occurs across a gradient of land conversion between two species, with highest disease risk at intermediate levels of habitat loss. The framework we developed provides a series of predictions about how pathogen transmission changes with land clearing and provides viable explanations for observed patterns of spillover events (Table 1).

The models emphasize two mechanisms driving spillover dynamics in converted landscapes: changes in host carrying capacities and changes in edge effects, using functions of edge density as a proxy for interspecies transmission. Land conversion modifies the carrying capacity for hosts (increasing carrying capacity for matrix species, decreasing carrying capacity for core species), which in turn affects transmission chains within each habitat type and across the patch-matrix interface. For density-dependent pathogens, dead-end spillover events are common during initial habitat conversion when there is a small matrix population size and infrequent interspecies contact events with small edge effects (Figure 4D). For example, outbreaks of monkeypox and Ebola in humans are linked to hotspots of deforestation (Rimoin *et al.* 2010; Olivero *et al.* 2017; Rulli *et al.* 2017). The recent Ebola outbreak in Guinea underscores the importance of high human population sizes in the matrix. Previous outbreaks of Ebola in Central Africa did not lead to major epidemics; however, in Guinea, when infected individuals sought medical treatment in large town centers, the ensuing chain of transmission sparked a major epidemic mirroring stochastic simulations presented here (Genton *et al.* 2014; Pigott *et al.* 2014).

Similar relationships between land conversion, host population size, and pathogen transmission can be expected in many systems. Fungal pathogen epidemics are driven by the most abundant plant hosts across a landscape (Fabiszewski *et al.* 2010). Agricultural intensification of pig farms (an

increased matrix population) adjacent to bat-attracting mango plantations in Malaysia provided the conditions for Nipah virus emergence in pig populations after spillover from bats (Pulliam *et al.* 2011). The carrying capacity of both core and matrix habitats will change the likelihood of onward transmission in the naïve species and is important to consider when predicting the extent of an outbreak.

Concomitant to risk mediated by changing population sizes in the matrix and core, land conversion alters edge density . We have assumed that the boundary between discrete habitat types (core and matrix) is a reasonable proxy for interspecies contact rates. This assumption is supported by empirical data showing that bushmeat consumption rates (Poulsen *et al.* 2009) and hunting contact rates (Friant *et al.* 2015) increase with habitat conversion. Transmision of enteric pathogens has also been documented between species at habitat interfaces (Johnston *et al.* 2010; Parsons *et al.* 2015). Additionally, distance to forest edge has been highlighted as a risk factor for cutaneous leishmania incidence in humans from wildlife reservoirs (Chaves *et al.* 2008; Quintana *et al.* 2010). Interspecies contact is key for studies of landscape spillover and can explain seasonal and interannual epidemics (Fabiszewski *et al.* 2010). How edge changes during conversion will affect the timing and magnitude of spillover (Figures S9,S10). While edge effects driving interspecies contact is an assumption built on the structural properties of how edge habitat changes during land conversion, there are other associated processes that can facilitate heightened interspecies transmission at intermediate levels of habitat conversion (Despommier *et al.* 2006). Species movement, especially when resources decline disproportionally to remaining core habitat during land conversion, can be facilitated by higher edge densities (Taylor *et al.* 1993

; Umetsu & Pardini 2007; Driscoll *et al.* 2013) . Edge density is also likely positively scale with contact rates driven by distribution of resources in converted landscapes (Rand *et al.* 2006). Habitat edges are a dominant feature globally – approximately 70% of forest habitat is within 1 km of the forest's edge (Haddad et al. 2008). Empirical investigation that explicitly quantifies how interspecies

transmision rates between core and matrix habitats differ as a function edge is an important future research focus for disease ecology and epidemiology studies.

Pathogens at each end of the density-dependent and frequency-dependent transition spectrum are expected to have different risk patterns associated with pathogen invasion during land conversion. Density-dependent pathogens may be less likely to persist in declining endemic core populations, and may require high rates of between species transmission to bolster infection risk at intermediate levels of habitat conversion. For frequency-dependent pathogens (such as vector-borne arboviruses), increased land conversion and contact between reservoir and recipient hosts will lead to increased disease incidence in the matrix and increased probability of spillover over a large range of parameter space. For example, in the Neotropics, leishmania spillover tends to occur in landscapes where forests dominate deforested matrices, suggesting high densities of core species are necessary to facilitate spillover (Chaves *et al.* 2008; Dantas-Torres *et al.* 2017). The impact of edge habitats on interspecies contact is the most important mechanism influencing transmission, as demonstrated by yellow fever that transmits from primate reservoirs into humans in both highly deforested landscapes and intact natural habitats (Bicca-Marques & de Freitas 2010; Almeida *et al.* 2012; Romano *et al.* 2014). Regardless, in both density-dependent and frequency-dependent cases, pathogens vulnerable to extinction in small isolated core populations may persist in a growing matrix population that maintains $R_0 > 1$.

Land conversion and disease emergence are dynamic processes. Our simulations show that time since initial habitat loss, in addition to the rate and scale of land conversion, may drive dynamic changes in infectious disease transmission. These results are supported by a number of empirical studies. For example, zoonotic malaria risk due to *Plasmodium knowlesi* is highest in areas that have 65% forest in a 5 km radius and have been deforested in the last 5 years (Fornace *et al.* 2016). The working hypothesis is that declining resources for reservoir hosts (*Macaca fascicularis*) drove them from their habitat, leaving infected vectors to obtain bloodmeals from the more readily available

human hosts (ref). This example supports the idea that host population sizes and contact patterns change following landscape modification. A survey of henipavirus antibody prevalence in humans in Cameroon revealed high exposure risk in recently deforested areas and low risk in intact rainforest, even though reservoir hosts were present in both locations (Pernet *et al.* 2014) ; the data are silent as to whether this is linked to changing host populations, contact rates or other processes. Our simulations point towards higher disease risk in non-endemic populations in these modified habitats.

The simulations also suggest that slow land conversion (e.g., selective logging) may increase spillover risk compared to rapid widespread land conversion (e.g., commercial agricultural development). Mismatches between the time-scales of conversion and the time-scales of species responses may drive interesting patterns of edge effects. For example, long-lived species may persist in rapidly changing landscapes beyond the point that their populations exceeded carrying capacity (Ewers *et al.* 2013). We did not account for such lags (known as extinction debts) in our simulations, but these lags may exacerbate disease risk.

Host demographic and disease transmission parameters have significant impacts on transient infection dynamics and equilibrium prevalence in a converted landscape. The impact of these parameters depends on the host abundance in the landscape and changes during the conversion process (Table S5-S7). It is important to consider how key reservoir species are affected by edges (Pfeifer *et al.* 2017) and these in turn influence key host demographics to either increase suspeptibility to spillover or change demographics to facilitiate additional spillover risk.

Pathogen spillover is a complex phenomenon that is influenced by many processes, including pathogen dynamics in reservoir hosts, environmental processes that determine pathogen survival and transport outside of these hosts, as well as the behavior and susceptibility of recipient hosts (Plowright *et al.* 2017). Each one of these factors may respond to changing landscapes and shape the relationship between land conversion and disease emergence. For instance, land conversion has been documented to affect individual nutrition, immunological responses, and population densities

(Chapman *et al.* 2006; Zylberberg *et al.* 2013; Becker *et al.* 2015; Chapman *et al.* 2015; Young *et al.* 2016; Seltmann *et al.* 2017). Specifically, nutritional stress after loss of winter nectar sources may drive Hendra virus shedding and spillover from fruit bats (Plowright *et al.* 2016). Land conversion can also affect behavior and therefore species interaction networks (Pellissier *et al.*). For example, increases in primate crop raiding frequency following land conversion increases *E. coli* transmission between humans and primates (Goldberg *et al.* 2008). Loss of important host predators has been highlighted as driving an increased risk of *Mycobacterium ulcerans*, the causative agent of Buruli ulcer, at intermediate levels of deforestion (Morris *et al.* 2016). These additional mechanisms were not incorporated into the models but could be extensions of the framework outlined here.

While our models represent common mechanisms of land conversion– forest clearing for agriculture or mixed human use—they can be applied to other systems with paired core and matrix habitats. For example, the equations can be applied to examine pathogen dynamics at the interface of primary and secondary forests, irrigated and non-irrigated agricultural lands, managed rangelands for separate species (elk and cattle). To assume changes in edges and carrying capacities, the habitats would have to be non overlapping.

Our core-matrix multi-host transmission model points to increased infection risk at intermediate levels of conversion given our assumptions about edges as a proxy for interspecies contacts. To synergize disease mitigation and conservation outcomes, conservation efforts should focus on minimizing the length of the core-matrix boundary (thus reducing edge densities) and preserving the integrity of core areas to reduce the likelihood that core species rely on resources in matrix populations. Large landscape conservation and minimizing edge effects are foundational principles of conservation biology (Wilcove *et al.* 1986) that should also reduce the risk of infectious disease spillover in changing landscapes. Managing disease emergence in concert with conservation objectives could also help focus resources on understanding species and contact patterns in areas undergoing dynamic landscape transformation. Integrated management could lead to a reduction in

the rate at which novel pathogens emerge (Woolhouse 2011), but more work will be needed to understand in what land conversion scenarios the model assumptions hold.

There is increasing speculation that anthropogenic landscape modification affects disease emergence (Daszak *et al.* 2001; Patz *et al.* 2004; Jones *et al.* 2013; Murray & Daszak 2013). Most primary literature on these topics are conceptual papers or reviews (Gottdenker *et al.* 2014). Model-guided research is needed to measure relationships between species pathogen transmission efficiency, matrix and host carrying capacities, and how edge density tracks between species contacts. Concrete empirical evidence linking land use change and disease requires long-term, cross-scale evaluation of core densities, edge densities, and matrix habitat structure, and surveillance of core and matrix hosts, vectors, and pathogens within these changing landscapes. Our model also suggests that research should focus on quantifying variations in host populations and interspecies contact rates as mechanisms leading to changes in disease incidence. Management of spillover and emerging pathogens will require an integrated understanding of how cascading impacts of land conversion affect disease outcomes.

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TABLE

Table 1. Empirical studies of land conversion and spillover.

PATHOGEN	CORE SPECIES	MATRIX SPECIES	INFECTION METRIC	LEVEL OF CONVERSION W/ HIGHEST RISK	PROPOSED MECHANISM	CITATION
Escherichia coli	guenons	humans and livestock	genetic relatedness between isolates	forest fragmentation increased	Increased contact between reservoirs and hosts	(Goldberg *et al.* 2008)
Rabies virus	vampire bats	cattle, humans	incidence of rabies in cattle	edge habitats	Increased edge which led to increased bat contact with cows	(Carrasco-Hernández *et al.* 2009)
Borrelia burdorferi s.l.	small rodents and birds	humans	PCR prevalence in tick vectors	woodland with higher fragmentation (larger edge)	Increased populations of more competent hosts (small mammals)	(Halos *et al.* 2010)
Hendra virus	Fruit bats	Horses and humans	virus spillover event	Peri-urban areas	Increased contact between reservoirs and hosts	(Plowright *et al.* 2011)
Trypanosoma cruzi	wild mammals	humans, domestic mammals	prevalence in vectors	highest in highly fragmented areas; lowest in completely deforested (pasture) areas	Change in host community structure led to a change in contact with infected of vectors	(Gottdenker *et al.* 2012)
Henipavirus	Fruit bats	humans	seroprevalence in humans	in villages with deforestation	increased contact due to consumption and butchering of bushmeat	Pernet *et al.* (2014)
Plasmodium knowlesi	*Macaca fascicularis* & other monkeys	humans	case incidence in humans	>60% forest cover, deforestation in last 5 year	Increase in human – vector contact driven by loss of reservoir species	Fornace *et al.* (2016)
Mycobacterium ulcerans	waterbugs & freshwater fish	humans	mean bacteria load per organism (qPCR)	intermediate deforestation	Loss of core species predators	Morris *et al.* (2016)
Ebola virus	fruit bats, apes, duikers	humans	outbreak location	forest fragmentation hotspots (rapid rates and extent of deforestation)	Edge effects change wildlife composition and lead to increased interspecies contact	Rulli *et al.* (2017)
Ebola virus	fruit bats, apes, duikers	humans	outbreak location	deforestation in last 2 years + >83% closed canopy	contact between humans and wildlife increases following recent deforestation	Olivero *et al.* (2017)

FIGURE LEGENDS

Figure 1. Land conversion and hypothesized effect on host carrying capacity and edge effects. Prior to land conversion, intact core habitat supports large populations of core species and few matrix hosts. We assume changes in carrying capacity are monotonic across land conversion and are simply a function of the proportion of habitat for the respective species. In addition to carrying capacity varying with land conversion, edge density peaks at intermediate levels (function fitted to data from

Wang *et al.* (2014), but different functional forms are in SI). In our models, edge effects is used as a proxy for interspecies contact. The proportion of land converted in which edge effects are maximum, and the magnitude of edge effects, will depend on the relative sizes and shapes of converted land and processes governing conversion (Hargis *et al.* 1998). The relationships shown here are a simplification of land transformation effects in real systems but offer a tractable series of assumptions for understanding impacts on infectious disease transmission within and between hosts.

Figure 2. Schematic diagram of pathogen spillover between core and matrix hosts. The diagram details the different routes of pathogen spillover among core (green) and matrix (tan) habitats and the species that dwell in these habitats. Blue arrows indicate the direction of movement of hosts and orange arrows indicate the direction of transmission between hosts (from endemic to spillover host). (A) Humans have contracted Ebola virus, HIV and monkeypox through bushmeat hunting in forested (core) areas in Africa (Leroy *et al.* 2004; Shchelkunov 2013). (B) When wildlife move into matrix habitats searching for resources or dispersing to other natural habitat areas, pathogens may move with these species and transmit into hosts living in the modified environments- such as Hendra virus spillover from flying foxes to horses in Australia (Plowright *et al.* 2015). While we often have an anthropocentric view of spillover, humans or livestock species can cause spillover of pathogens to core species; for example, (C) measles transmission from humans to apes during ecotourism activities (Rwego *et al.* 2008; Parsons *et al.* 2015), or (D) canine distemper from free ranging domestic dogs into carnivores within reserves (Viana *et al.* 2015). (E) Vectors can also facilitate transmission, as is the case with sylvatic dengue, zoonotic malaria, and yellow fever (Lounibos 2002; Brock *et al.* 2016). (F) Lastly, parasites like *E. coli* can be shared bidirectionally and transmission is facilitated by the movement of hosts (Thompson & Smith 2011).

Figure 3. Transmission potential as a function of land conversion. Within host R_0 for core (green) and matrix hosts (tan) species for density-dependent transmission (A-C) and frequency-dependent

transmission (D-F). The greyscale lines indicate the community R_0 at a given level of interspecies transmission efficiency (ψ). When the pathogen is endemic in core hosts (A,D), a density-dependent pathogen is unable to invade highly converted habitats, in contrast to density-dependent pathogens that are adapted matrix hosts (B). The final scenario (C, F), is an example of a pathogen that is equally adapted to core and matrix hosts.

Figure 4. Stochastic simulations of spillover into matrix populations. (A) At intermediate levels of land conversion, the probability of spillover is high (measured as the number of simulations that had at least one infected core individual. (B) The mean of epidemic size in the matrix is shown. (C) This violin plot show the density of stochastic simulations at a given outbreak size for five habitat conversion levels ($\phi = 0.1, 0.3, 0.5, 0.7, 0.9$). Solid points indicate the median outbreak size at the given level of conversion and open squares indicate the mean outbreak size. At intermediate ($\phi = 0.5$) conversion, the statistics are similar, however the median number of outbreaks is 0 at $\phi = 0.9$, where there are either very large outbreaks (that increase the average epidemic size) or, more frequently, none. (D) A heat map of 1000 simulations showing the number of simulations that resulted in a given epidemic size for each proportion of converted land.

Figure 5. Spatial and temporal variation of land conversion and its affect on disease dynamics. A density-dependent pathogen that is endemic in core species ($R_0 > 1$) increases in prevalence as habitat is converted (each conversion event is indicated in grey horizontal line). Decreasing the rate of conversion (left, biannual land conversion , to right, conversion every 10 years) increases the magnitude of change in prevalence in core and matrix hosts. The amount that is converted each time (4%, 8%, or 12%) is indicated by line thickness. After nine conversion events, there is between 76% (4% conversion rate) and 4% (12% conversion) of core habitat remaining.

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