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GOVERNANCE, LAND USE CHANGE, AND MITIGATING VIRAL ZOOONOTIC EMERGENCE AT THE HUMAN- ENVIRONMENT INTERFACE

A Review and Recommendations for Applied Research

OCTOBER 2021



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Front cover photo: Madagascar fruit bat (*Pteropus rufus*). Photograph by Cara Brook.

Back cover photo: Patches of deforestation branching out from a road outside La Esperanza, Honduras. Photo by [Esteban Benites](#) on [Unsplash](#).

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I. Executive Summary

The far-reaching impacts of the COVID-19 pandemic highlight the urgent need to understand and mitigate future zoonotic disease emergence. Zoonoses are diseases caused by pathogens that spread from animals to humans; ‘spillover’ is the process of cross-species pathogen transmission; and zoonotic spillover describes cross-species pathogen emergence from animal to human hosts. Over the past century, three out of every four emerging or reemerging infectious diseases in humans have been zoonotic in origin, and probably more. Zoonotic pathogens pose an ongoing and significant health and economic burden—as underscored by the COVID-19 pandemic. As of writing the SARS-CoV-2 virus has killed more than 3 million people and shut down the global economy, pushing millions of people into extreme poverty. SARS-CoV-2 is only one of several recent zoonotic viruses, which have resulted in large human outbreaks and caused significant impact on human livelihoods across the globe. As evidenced by the emergence and reemergence of SARS, MERS, Ebola, Chikungunya, and Zika viruses within the past half-century, pandemics are not once-in-a-century events, and the next pandemic-causing pathogen will likely originate in animal species.

Forest disturbance and land conversion can significantly increase risk for zoonoses in the months and years following change, but these risks may be possible to mitigate through integrated One Health programs and policies. Preventing emerging zoonoses in changing landscapes can provide simultaneous benefits to biodiversity conservation and public health. By addressing gaps in knowledge of the ecological and sociological drivers of zoonoses, we can inform effective interventions to prevent zoonoses and target disease surveillance. We build on previous research and draw on expertise from global health, land and resource governance, conservation, disease ecology, virology, forest economics, and other disciplines to synthesize gaps in understanding of viral zoonotic risk and quantify and evaluate the impacts of interventions aimed to mitigate viral zoonotic emergence at the human-environment interface.

Land use change is a key driver of zoonotic emergence. Conversion of natural habitat leads to biodiversity loss, changes in the distribution of zoonotic host species, and increased human-wildlife contact, all of which have cascading health consequences for humans and communities. Research has shown that intermediate levels of land conversion are likely to pose the highest risk to humans, but this risk is conditional on pathogen traits and the animal host communities that remain in these converted landscapes. Land use change is a dominant feature of landscapes globally and negative consequences of these changes will disproportionately affect already marginalized communities. There is an urgent need to: 1) identify landscapes, present and future, at greater risk of zoonotic disease emergence and 2) understand the mechanisms that drive this risk in changing landscapes in order to design more effective interventions.

This report derives from a March-May 2021 workshop series under the USAID Integrated Natural Resource Management (INRM) program, with participation by USAID and outside experts from across disciplines. Based on findings from the workshop, this report reviews the latest science across disciplines and proposes specific activities and applied research questions. The COVID-19 pandemic has underscored the importance of zoonoses prevention and mitigation. Global health and medical experts,

veterinarians, and environmentalists advocate for a ‘One Health approach’ to zoonoses—which integrates human, animal, and environmental health science to address mechanisms underlying pathogen transmission at the animal-environment-human interface. This report was prepared in the spirit of One Health.

A. Mapping and Modeling to Identify Areas at Higher Risk for Viral Zoonotic Emergence

PREDICT scientists and collaborators produced a global risk map for zoonotic emergence by identifying features of land use change, biodiversity, and human population growth that correlated with historical zoonotic outbreaks. Their statistical models are able to incorporate sampling bias and pinpoint key factors associated with spillover—including human population density, mammalian diversity, cropland area, active conversion to land cover, and recent loss of forest. Several regions are highlighted as high risk for zoonotic emergence: including, but not limited to, Central American tropical forests, coastal West Africa, the African Great Lakes Region, and India, and eastern China. This risk map provides useful signposts for prioritizing studies and potential interventions on a global scale, but it is unclear how this map can be refined at the national or subnational levels—where planning and surveillance policies are actually implemented.

Many factors that heighten risk for viral zoonotic emergence can be assessed on a much finer scale and could be leveraged for within-country planning. A recent survey of experts conducted by Grange et al. (2021) highlights key prerequisites for zoonotic emergence, including accessibility to mammalian biodiversity hot spots, frequency of interaction between wild animals and humans, and rates of forest conversion. These data could be used to develop more accurate zoonotic risk maps. It is possible that leveraging existing data collection efforts, such as the Demographic and Health survey and Earth Observation, could provide sufficient information to accurately identify areas of risk within a country or region. In addition, collection of additional information to identify specific cultural practices and behaviors, such as wild animal hunting and meat supply chains, particularly the trapping and transport of live animals, could greatly improve mapping efforts. Moreover, the enhanced data collection on viral zoonotic risk could be applied to various points in wild meat supply chains, including wildlife farming, and as part of efforts to combat wildlife trafficking.

Regional- or country-level risk maps would also enable targeted surveillance, educational activities and other interventions to prevent zoonoses. A key first step is identifying landscapes where interventions would have the most impact. Spatial statistical models have the potential to help identify high risk locations within a region. For example, these risk maps could incorporate future land use planning and be used to mitigate risks posed by new infrastructure development.

B. Understanding the Mechanisms of Viral Zoonotic Emergence

Wildlife conservation through the protection and restoration of ecosystems has the potential to reduce zoonotic spillover (Reaser et al., 2021a, Plowright et al., 2021), but this concept has not yet been

demonstrated in a real-world setting. A rigorous One Health research program in a focal region could help us understand key mechanisms affecting the emergence and establishment of zoonotic viruses in the human population (Plowright et al., 2021) and improve the design of key interventions to achieve positive outcomes for public health and ecosystems. Furthermore, identifying key mechanisms driving zoonotic risk will improve understanding of these dynamics beyond the focal region studied. A particular goal would be to identify mechanisms that help direct targeted interventions, and that highlight key variables and indicators for program monitoring and evaluation.

To quantify viral zoonotic risk in changing landscapes, it is essential to understand the associated spatiotemporal variation in ‘hazard’ measured by 1) human-wildlife contact, and 2) likelihood of infection given a contact. Identifying mechanisms leading to changes in any one of these drivers is essential for mitigating viral zoonotic emergence through development policies and programs. Mitigation efforts should be supplemented with targeted surveillance to evaluate their effectiveness. Implementation of any mitigation effort will require an integrated economic, sociological and ecological understanding of mechanisms facilitating zoonotic emergence. Key data to collect for each of these dynamic processes are: 1) reservoir host population distribution, dynamics and viral load; 2) reservoir-human contacts (directly or indirectly); and 3) probability of human infection given a contact.

Impact evaluations (IEs) offer one means by which to quantify and evaluate the effectiveness of programs or policies aimed to mitigate the above drivers of zoonotic spillover. Following on Gray et al. (2021), IEs are most likely to achieve statistical power if focused in systems where the following factors are high: “1) prevalence of the pathogen in the reservoir, (2) the reservoir-to-human contact rate, and (3) the probability of human infection with the animal pathogen.” Current data suggest that a subset of animal taxa (e.g., bats, rodents, primates, ungulates, and certain carnivores) are the source for the majority of zoonotic pathogens and offer a useful starting point for designing and evaluating a proof-of-concept program or policy for targeted, integrated conservation-based approaches for viral zoonotic risk mitigation. Yet, it is important to emphasize the significant biases in the host viral data; this introduces a lot of uncertainty as to taxa more likely to host viruses with zoonotic or pandemic potential and calls into doubt risk assessment efforts (Wille et al., 2021).

Programs that could be amenable to impact evaluations for viral zoonotic emergence are:

1. Forest restoration. Restoration of degraded forest ecosystems has benefits for biodiversity and ecosystem services, such as improvements in flood controls and water quality. Mounting evidence suggests that forest restoration could also benefit human health by increasing biodiversity (in particular species that do not amplify viral zoonotic risk), lowering disease prevalence in reservoir populations, and reducing reservoir host-human contacts. An impact evaluation that monitors reservoir populations, pathogen prevalence and human-reservoir contacts in communities with restoration and control sites without restoration would provide essential data for understanding the utility of this intervention for mitigating viral zoonotic risk.

2. Minimal fragmentation land use planning. In areas where forest clearance is ongoing, there is an opportunity to demonstrate how varying the location and rate of clearance impacts viral zoonotic risk. Empirical observations and modelling work suggests that forest clearance that minimizes edges (and therefore minimizes forest fragmentation) will reduce risk for viral zoonotic emergence compared to

highly fragmented and rapid deforestation. The three key inputs for spillover can be monitored in communities where this process is ongoing or can be part of land use planning prospective observations.

3. Reductions in wildmeat harvesting and transport or handling. Quantification of the impact of efforts to reduce farming, hunting, butchering, transport, and consumption of wild meat is needed to address a significant knowledge gap in our understanding of the viral zoonotic risk posed by wildmeat supply chains. The potential roles for contact through mucosal surfaces (e.g., nose, lungs), exposure to wounds, or other contacts with feces, urine, and contamination of food should be explored. What do these transmission routes imply for spillover risks for bushmeat hunters and traders? Longitudinal serology and PCR surveillance tests in a range of exposure contexts could show whether, for example, bushmeat traders who sell smoked or dried bushmeat exhibit lower risk levels at baseline compared to traders of live or freshly killed bushmeat or compared to poultry or fish traders, and whether such risk levels decline over time in response to specific interventions. Such an effort could complement and coordinate with next generation immunological surveillance and metagenomics (Wille et al., 2021).

We recommend a feasibility study to further explore the potential of IEs for measuring viral zoonotic risk and related outcomes.

2. Introduction

One of the concepts that underpins our understanding of disease emergence is that viruses may be common in wildlife reservoirs and these viruses may, under some circumstances, spillover to infect and spread as epidemics in humans. As exemplified by the recent pandemics of SARS CoV-2 and influenza H1N1, these emergent viruses may have high impacts on human health and wellbeing, and preventing or controlling future outbreaks would be an important goal. This report therefore proposes applied research questions and activities focused on the relationship between conservation, agriculture, land and resource governance, and mitigating viral zoonotic emergence at the human-environment interface. More specifically, this report is concerned with the forest disturbance and land conversion aspect of the development challenge posed by viral zoonotic emergence. By applied research we mean the generation of research and evidence to improve policy and program effectiveness for long term impact, while also advancing high quality science.

This report derives from a workshop series that ran from March to May 2021 under the USAID Integrated Natural Resource Management (INRM) program, with participation by the USAID and outside experts from across disciplines. Participants included: Caleb Stevens, Land and Resource Governance Advisor, USAID; Ioana Bouvier, Senior Geospatial Analyst, USAID; Mary Rowen, Biodiversity Division Chief, USAID; Andrew Tobiason, Biodiversity Conservation Advisor, USAID; Sara Carlson, Biodiversity and Natural Resources Advisor, USAID; Christina Faust, Disease Ecologist, Penn State University; Cara Brook, Disease Ecologist, University of Chicago; Colin Parrish, Virologist, Cornell University; Heather Huntington, Associate Director, DevLab at Duke University; David Wilkie, Executive Director, Wildlife Conservation Society; Yuliya Panfil, Director of Future of Land and Housing Program, New America; Tim Robustelli, Policy Analyst, New America; Andres Gomez, Deputy Chief of Party, INRM project.

Other USAID experts that participated in the series and provided comments on earlier drafts are: Patricia Bright, Senior One Health Technical Advisor; Rob Cohen, Senior Technical Advisor, Bureau for Global Health; Andrew Bisson, Senior Livestock Specialist; Tracey McCracken, Infectious Diseases and Food Systems; Elizabeth Daut, Natural Resources Specialist; Natalie Bailey, Biodiversity and Communications Officer; Megan Hill, Wildlife Demand Reduction; Timothy Meinke and David Stanton, Infectious Diseases, USAID/Indonesia; and Thang Nguyen, Countering Wildlife Trafficking, USAID/Vietnam. Special thanks to Eddie Holmes, virologist, University of Sydney, for comments on an earlier draft.

This report is organized as follows. Section III defines key terms and concepts from governance, conservation, virology, and disease ecology to facilitate an integrated, One Health approach to this development challenge. Section IV briefly reviews the evidence on the effectiveness of programs in achieving conservation outcomes. Section V proposes several activities and applied research questions, with particular emphasis on: 1) mapping and modeling to identify areas at higher risk for zoonotic viral emergence, and 2) understanding the mechanisms of viral zoonotic emergence—virological, ecological, social, and economic. Section VI briefly concludes.

3. Terms and Concepts

A. Land and Resource Governance

Land and resource governance (LRG or tenure) is concerned in large part with the study of people and their relationship to the natural environment. LRG experts seek to shape people’s incentives, norms, and behaviors through their responses to specific interventions in order to generate new, positive outcomes (see Figure 1). For instance, why do people cut down forests, not leave land fallow for forest restoration, and kill and consume wildlife to the point of extinction? And how do we reduce these pressures while still respecting people’s rights and achieving equitable outcomes? These are some of the central questions with which LRG wrestles. LRG has intellectual roots in legal pluralism, anthropology, ecology, forest and agricultural economics, conservation, and many others. Perhaps one of the first LRG experts was Nobel prize winning economist Elinor Ostrom, who transcended economics to work across disciplines. In doing so Ostrom helped us understand that people may sustainably manage common property systems without a descent into Hardin’s tragedy of the commons (Ostrom, 1990). Ostrom’s insights led to extensive research on which LRG interventions in what contexts are likely to generate positive environmental outcomes (Hajjar et al., 2020).

Yet, LRG also covers a variety of other rules people create to govern land and natural resources—common property is only one type (Robinson et al., 2014). When people hold land and natural resources, including wildlife, they invariably create rules governing those resources. Indeed, all land and natural resources are covered by some rules or ‘tenure types’ governing their management, use, access, withdrawal, and exclusion (Ostrom’s original ‘bundle of rights’). In general, these tenure types are: poorly designated public (de facto open access), public (e.g., protected areas), private, and community (which is distinct from but inclusive of common property) (Ibid.).

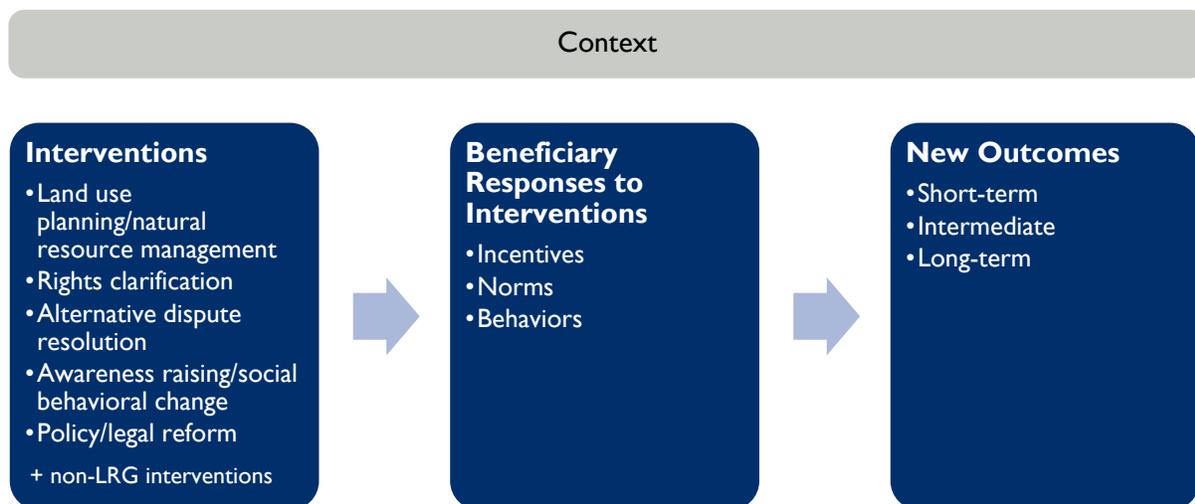


Figure 1: Conceptual model for land and resource governance. Source: McLain et al., 2018; Lisher 2019; Tseng et al., 2021; Stevens et al., 2020.

Figure 1 on the previous page lists the categories of LRG interventions. Depending on the context, each of these interventions may be relevant for mitigating viral zoonotic emergence at the human-environment interface. However, they are more likely to be effective if paired with non-LRG interventions, such as those from biodiversity conservation, agriculture, and public health.

B. Land Use Change, Viral Zoonotic Emergence, and the Human-Environment Interface

Although our title references ‘land use change,’ this is an imperfect term. As discussed below, land use change or land conversion has cascading effects on forest disturbance and access, exposure to wild animals, including effects on wild meat demand and wildlife supply. In this sense, we are concerned not only with land use change but changes in forest use, forest access, wild meat demand, wildlife populations, diversity, and contacts with humans.

For disease ecology the objective is to understand processes that affect transmission, population dynamics, and the evolution of infectious pathogens. Many applications of this field aim to protect populations from devastating disease outcomes by preventing exposure of vulnerable populations to pathogens, increasing the likelihood of pathogen extinction, and/or decreasing selection for deadly pathogens. For some diseases, the concept of critical community size (i.e., minimum susceptible population required to support the continued circulation of a specific pathogen) is an important quantity to measure and has correlates to conservation.

To protect animal populations from extinction, conservation biologists seek to reduce threats and drivers, particularly through protecting intact ecosystems through landscape- or seascape-scale planning, and by use of a suite of natural resource management and social interventions that address threats and drivers of species loss. Refracted through disease ecology, conservation’s landscape-based interventions may be described as ‘ecological countermeasures’ to reduce pathogen spillover in a given landscape by keeping landscapes intact or ‘immune.’ (Reaser et al., 2021a; Plowright et al., 2021).

The majority of pathogens that infect humans likely have zoonotic origins (Jones et al., 2008), meaning initially derived from an original animal host, and many recent epidemics and pandemics caused by emerging pathogens have started in this way, including SARS CoV-1, SARS CoV-2, influenza viruses, and Ebola viruses. Zoonotic spillover occurs when a virus crosses the host range barrier by transmission into an individual human or human population. Despite that initial infection, most zoonotic spillover events do not lead to sustained transmission in the new human host population (Lloyd-Smith et al., 2009; Wolfe et al., 2007). Most pathogens die out due to limited and dead-end transmission chains. Viral zoonotic emergence¹ is when a virus spills over into humans and the virus either has the intrinsic ability to transmit in humans or evolves variants or strains (virus ‘species’) adapted to the new human host

¹ Note that the term ‘emergence’ is somewhat contested. Other experts and sources consider any viral spillover into humans as synonymous with viral zoonotic emergence.

population such that sustained transmission is achieved ($R_0 > 1$).² These cases are more likely to be detected through targeted or routine health surveillance.

As mentioned above, viral zoonoses are thought to be relatively common but sustained zoonotic transmission in a human population is relatively rare. There is a significant bottleneck between the zoonotic potential of viruses (to cause single infections) and their emergence. Compared to the global diversity of viruses, very few viruses emerge into humans (Figure 2). However, the rate of viral spillover and emergence in humans may be increasing because of changes in various risk factors discussed in the next section (McCloskey et al., 2014; Marani et al., 2021).

R_0 = basic transmission rate

“Host Range Barrier”

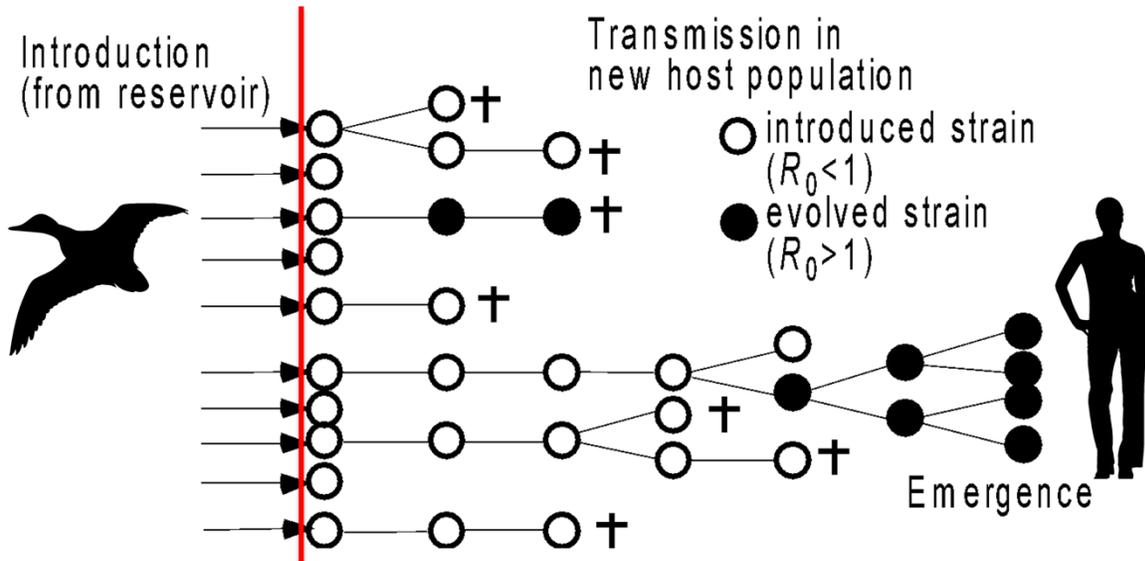


Figure 2: Viral Spillover, Zoonosis, and Emergence. Source: Presentation by Colin Parrish to INRM consortium on April 14, 2021.

Zoonosis (in our case we are focused on viral zoonosis as those appear to include the greatest risks) results from a layered series of improbable events related to reservoir hosts and recipient hosts, each of which must be surmounted for a potentially zoonotic virus to cross the species barrier and emerge in a human population (see Figure 3 on the next page). Figure 3 focuses on reservoir and recipient human host characteristics, but importantly for our purposes, forest disturbance and land conversion dynamics can increase many of these risk factors.

² Throughout this report when ‘spillover’, ‘emergence’ or ‘risk’ is used without a zoonotic modifier, the terms are inclusive of both human and non-human recipient hosts, unless otherwise noted.

For example, habitat conversion can lead to increases in cross-host exposure to viruses. Intensification of certain agricultural practices can increase resources for certain hosts and decrease resources for others, and land conversions can increase stress and reduce immune responses and increase pathogen load. Land use change also alters the interface between recipient human hosts and reservoir hosts. Even farm structure impacts viral spillover risk, as smallholder farmers increase their forest access because of more interface or contact points. And stress associated with transporting and warehousing live wildlife may result in higher levels of viral shedding. Understanding of zoonosis requires interdisciplinary integration of each of these layers and complexities, epitomized in the concept of ‘One Health’.

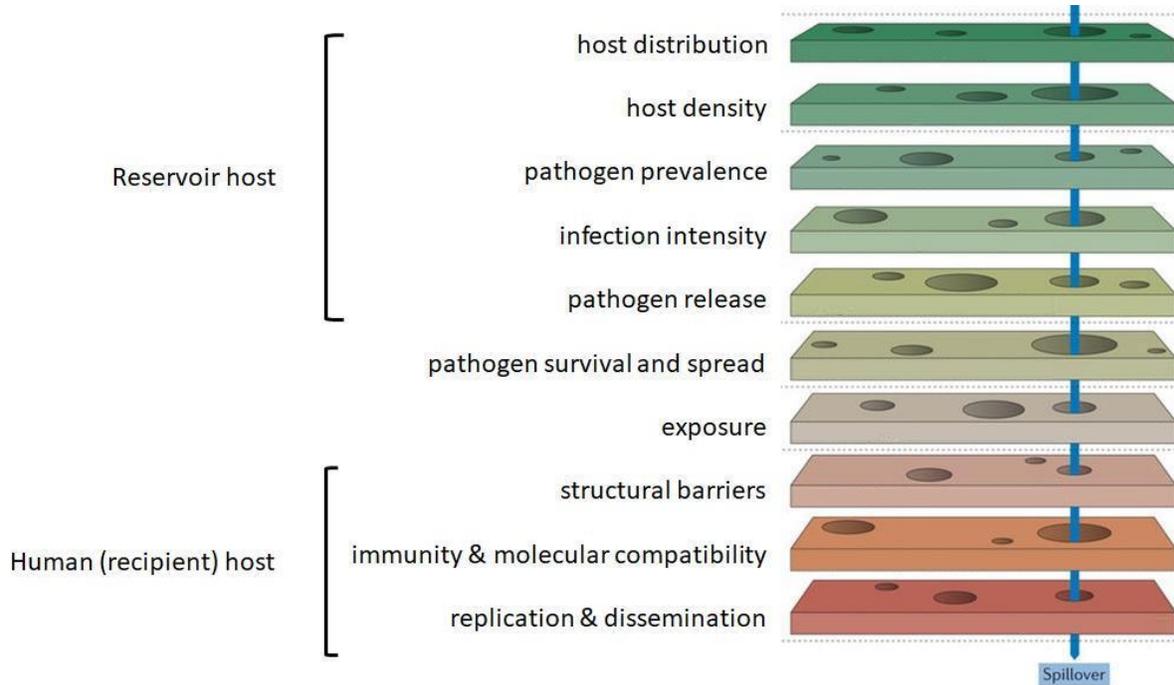


Figure 3: Barriers to Viral Zoonosis or Spillover into Humans. Source: Adapted from Plowright et al., 2017. Exposure between the reservoir host and human recipient host is a function of likelihood of contact and viral dose, among other factors, which we term ‘hazard.’

Viral zoonotic risk³ is a function of hazard or extent of human-animal contact and likelihood of infection upon contact (e.g., viral dose, how prevalent the virus is, and likelihood of transmitting to additional people). Across a landscape, ecosystem, wildmeat supply chain, or food system, including wildlife farming, there are risks of a virus in a reservoir host crossing the host range barrier into a new human host population (directly or indirectly). The level of risk depends on several factors, including human behavior, ecological conditions and virus characteristics. Viral zoonotic emergence risk, our primary concern, is the probability that a virus: spills over into humans (directly or indirectly), is able to infect

³ This term is not commonly used in the literature. A google scholar search revealed only 89 studies with the term. More recently the term was used by Mollentze and Streicker (2020) in their review of the host viral data to investigate zoonotic potential of viruses. The authors do not define the term.

that person, and then is able to spread among humans, or evolves variants/strains adapted to the new human host population such that sustained transmission is achieved.

Pandemic potential or risk⁴ is the probability that a zoonotic virus emerges with a certain combination of virulence and transmissibility in humans combined with a confluence of post-emergence factors, including public health responses and social trust levels (Driedger et al., 2018; Makridis and Wu, 2021). Even virulent zoonoses (causing severe infections of their index cases) do not often yield outbreaks or epidemics. Pandemic potential is therefore the most extreme example, and likely results from a number of virological traits impacting transmissibility in humans, in particular transmission routes (e.g., respiratory, invertebrate vector, or other routes of transmission). Thus, pandemic potential may not be associated with virulence or adaptation in the original reservoir host.

Our use of 'risk' and 'potential' denotes uncertainty given the stochastic nature of the development challenge. That is, viral zoonosis and emergence are probabilistic but with elements of randomness or uncertainty (Faust et al., 2018). Although analytically useful, the language of risk should not be employed with respect to social behavioral change messaging or otherwise in order to help prevent deeply misguided and counterproductive policies, such as eradication or mass killing of wildlife (Rocha et al., 2020; Olival et al., 2017; Guyton and Brook, 2015). To address this legitimate and real concern, we recommend communicating about viral zoonotic spillover or emergence risk "that deliver accurate information and practical recommendations, caution against persecution of [certain species] and promote public health" (Rocha et al., 2020).

Speaking in terms of 'risk' or 'potential' with respect to viral zoonosis is problematic because of weaknesses with host viral data. That is, "not only is our sampling of the virosphere extremely limited, but it is also strongly biased towards viruses of socioeconomic impact: those that impact human health, those in species we eat or keep as companions, and those that cause noticeable and major mortality events in domestic animals and wildlife" (Wille et al., 2021). The host viral data suffers from ascertainment bias. The last 10 years have revealed 10 times more viruses infecting fish than previously known, and a 3-fold increase for birds and shrews (Ibid.). As the number of viruses discovered increases the proportion of zoonotic viruses decreases significantly, consistent with the pinhole model whereby viruses in wildlife may be common but few are zoonotic (Ibid.).

For example, the host viral data suggests bats are much more likely to host virulent zoonoses than birds, despite the link between flight and bats' ability to host virulent zoonoses without exhibiting disease. If bats are special in part because they fly, why not birds? (Guth et al., 2021) One answer may be ascertainment bias. We find viruses where we look for them. Consequently, analyses of zoonotic risk or potential based on our flawed data may be of limited value (Wille et al., 2021).

Nonetheless, the current data clearly point to a number of questions worth pursuing. Does the host viral data and other evidence suggest that some taxa in certain contexts are more likely to host a zoonosis? Is there something 'special' about rodents, bats, primates, ungulates, and other taxa meriting

⁴ Neither the terms pandemic potential nor pandemic risk are defined in the literature to our knowledge although this is a rapidly evolving area of research.

further inquiry? How can we address these questions while working to refine our understanding of zoonotic disease risk and more effectively allocate resources?

Finally, we use the term 'human-environment interface' to mean both places and actions that bring humans into close contact with the natural world. The interface may be a forest edge or area consisting of intact or fragmented forest and human dominated land uses or matrix, as well as one of many points in wild meat supply chains, inclusive of hunting or harvest, local household consumption, bushmeat markets, and transnational movement of wildlife or wildlife products (Figure 4).



Figure 4: Source: Presentation by Christina Faust to INRM consortium on April 21, 2021.

4. Forest Disturbance, Land Conversion, and Viral Zoonotic Emergence: A Brief Review

This section briefly summarizes the forest disturbance and land conversion aspects of the development challenge, and the possible connections to viral zoonotic emergence, including the latest science and evidence on program effectiveness, with a particular emphasis on causal evidence. We will first discuss key studies within the virological and disease ecology literature, particularly analyses of host viral data and attempts at modeling viral spillover risk in a given landscape (sometimes referred to as 'edge effects' which is a broader conservation term but inclusive of spillover risk) (Fahrig, 2003). Then we will summarize the evidence base on the impact of LRG and conservation interventions with respect to forest and biodiversity conservation outcomes.

A. Viruses, Hosts, and Landscapes

In this section we discuss two critical lines of applied research. First: does the host viral data suggest certain mammalian orders are more likely to host viruses that pose significant zoonotic spillover risk or pandemic potential? Second: what is the current state of risk mapping and modeling to identify landscapes at greater viral zoonotic risk?

Does the host viral data suggest certain mammalian orders are more likely to host viruses that pose significant viral zoonotic risk?

The reservoir richness line of thought holds that certain orders (bats and rodents) have a lot of viruses because together they constitute about 60% of all terrestrial mammals. Thus, other orders should pro rata have as many viruses as bats and rodents, based on the number of species in that order (Mollentze and Streicker, 2020). Whereas the special reservoir hypothesis posits that certain taxa are more likely to host viruses with zoonotic or pandemic potential. The question of whether the host viral data suggest certain mammalian orders are more likely to host viruses that pose significant zoonotic risk is the subject of "link prediction," which aims to answer two questions:

- (1) What hosts are most likely to be the source of a zoonosis?
- (2) More specifically, what hosts are the most likely to be the source of a pandemic zoonosis?

To investigate these questions, researchers consider pathogen traits, in particular virulence (or the pathology induced by a virus on its host) and human-to-human transmissibility.

As noted above, there is a rather extreme bottleneck in that few viral zoonoses infect and spread among (emerge in) humans, suggesting a pinhole model (see Figure 5 on the next page). In large part, this bottleneck is a function of different species' "immunological protections against viral infections, along with different viral receptors on their cells." (Gray et al., 2021). A virus well adapted to one host

is unlikely to immediately infect a new human host, and viral adaptation to allow sustained transmission to be achieved within humans generally requires viral changes to occur through mutation, recombination, or reassortment. Mutation is the introduction of random genetic changes in an organism, in this case a virus' genome. Recombination is when two different viral strains infect the same host cell and results in a virus progeny with genes from both 'parent' viral strains. Reassortment is a modified form of recombination that is exclusive to some RNA viruses (such as influenza virus) and occurs when two variants infect the same host cell and shuffle their genes to create new variants with a proportion of gene segments from each parent. Natural selection acts on viral changes induced through all three mechanisms (mutation, recombination, reassortment) to increase or eliminate genomes containing those genetic changes in future virus generations.

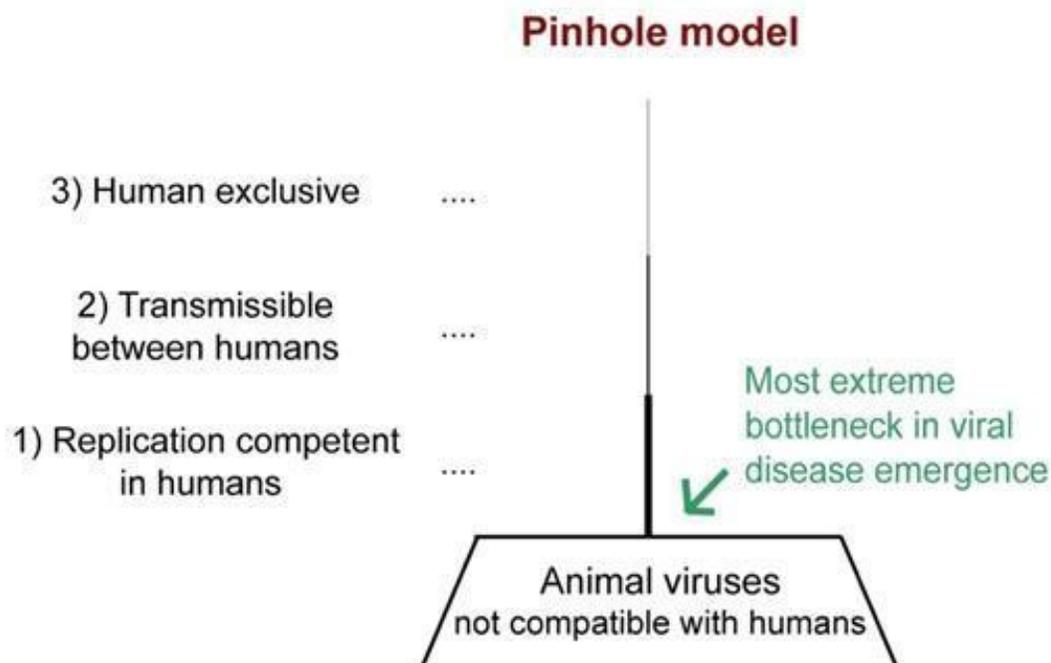


Figure 5: Pinhole Model for Viral Emergence. Source: Warren and Sawyer 2019.

Only a small number of papers have addressed the first question of which hosts are more likely to source a zoonosis. The first was Woolhouse and Gowtage-Sequeria (2005), which found that ungulates (e.g., deer, camels) are the major source of zoonoses, but this is due to bacterial/rickettsial infections, not viruses. The study did not conduct a comprehensive analysis of non-viral zoonoses, and there still is none. That study also lacks statistical rigor when compared to more recent work. Luis et al. (2013) looked at two different taxonomic groups, rodents versus bats, and asked what are the characteristics that drive the probability of being a zoonotic reservoir within each of these taxa. The study found that bats host more viruses per species than do rodents—although more recent virome discovery projects have clarified the likely number of viruses in different hosts. Bats represent 20% and rodents 40% of all mammalian diversity. Thus, by sheer number there are more rodent borne zoonoses. The study highlighted bats and rodents as peak interest for later link prediction studies.

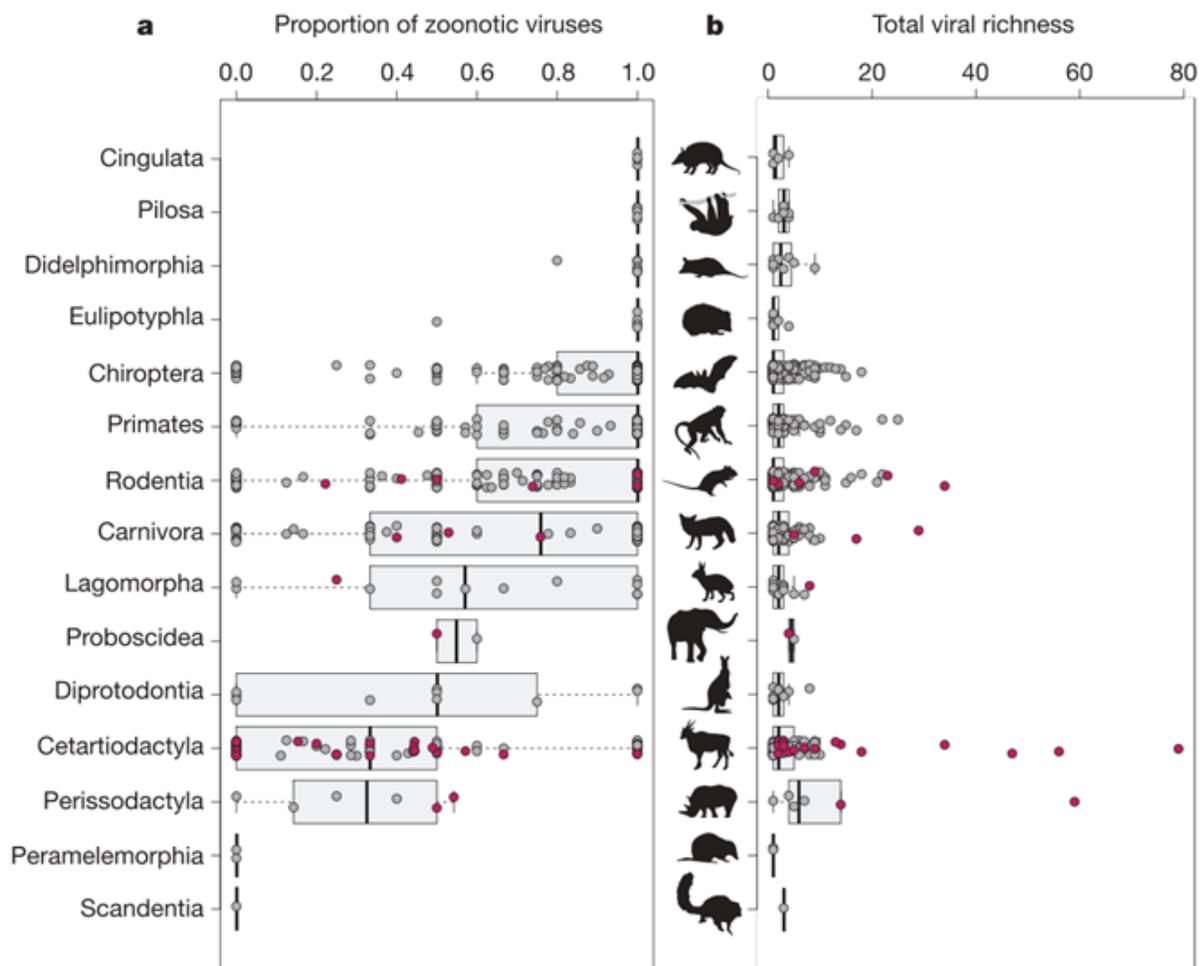


Figure 6: Mammalian Hosts and Viral Zoonosis. Points represent wild (light gray) and domestic (dark red) mammal species. “Observed viral richness in mammals. a, b, Box plots of proportion of zoonotic viruses (a) and total viral richness per species (b), aggregated by order. Data points represent wild (light grey, n=721) and domestic (dark red, n=32) mammal species; lines represent median, boxes, interquartile range.” Source: Olival et al., 2017.

Olival et al. (2017) found that the proportion zoonotic viruses in a host are predicted by: Host order; Host phylogenetic⁵ relatedness to humans; and Human population within a species range—which may reflect human–wildlife contact. Further, the study found that bats host a significantly higher proportion of zoonotic viruses than all other mammalian orders (Figure 6). Yet, bats are quite phylogenetically distant from humans (see Figure 7 on the next page). Typically, greater phylogenetic distance between two host species is correlated with reduced probability of inter-host pathogen sharing. In addition, viruses in hosts that are more phylogenetically distant to humans, such as bats, are more likely to cause

⁵ Phylogenesis is concerned with the evolutionary relationships among species and other taxa based on their physical or genetic differences or similarities.

virulence in humans (have higher case fatality rates) but are less transmissible in humans (Guth et al., 2019).

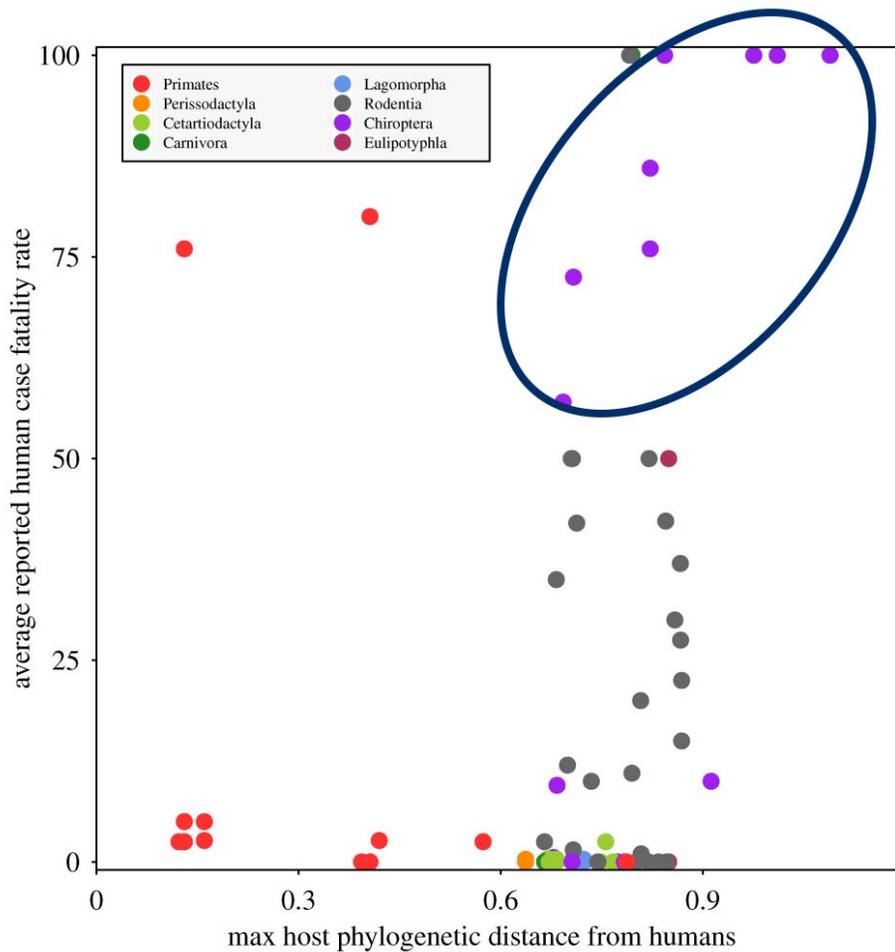


Figure 7: Case Fatality Rate of Host Viruses and Host Phylogenetic Distance. Source: Guth, Visher, Boots, and Brook. 2019.

Research on bat immunobiology and ecology, spurred by the SARS emergence in 2002, has advanced our understanding of why bats may be ‘special’ with respect to their ability to host so many zoonotic viruses without experiencing substantial disease.⁶ Bats are unique in a number of properties related to viral infection and disease. Bats are the longest-lived for their body size of any mammal group (see Figure 8 on the next page). Typically, body size and life span are correlated. Smaller animals have shorter

⁶ It is worth noting that the virological literature coverage of bats tends to ignore the vital role bats play in ecosystem services. Based on a systematic review of virological literature, bats were identified as a major public health concern in 51% of studies reviewed and their role in providing key ecosystem services were disregarded in 96% of studies identified (López-Baucells et al., 2017). This is further support for the research benefits of a One Health approach.

lives; larger animals live longer. This relationship is thought to be linked to metabolic rate. Larger bodied species tend to host slower mass-specific metabolic rates, which correspond to lower lifetime energy expenditures and reduced accumulation of damaging oxygen free radicals—a byproduct of metabolism. Bats, however, appear to defy this trend, exhibiting lifetime energy expenditures more than double that of a similarly sized non-flying mammal and yet experiencing a lifespan on average 3.5 times longer (Wilkinson and South, 2002).

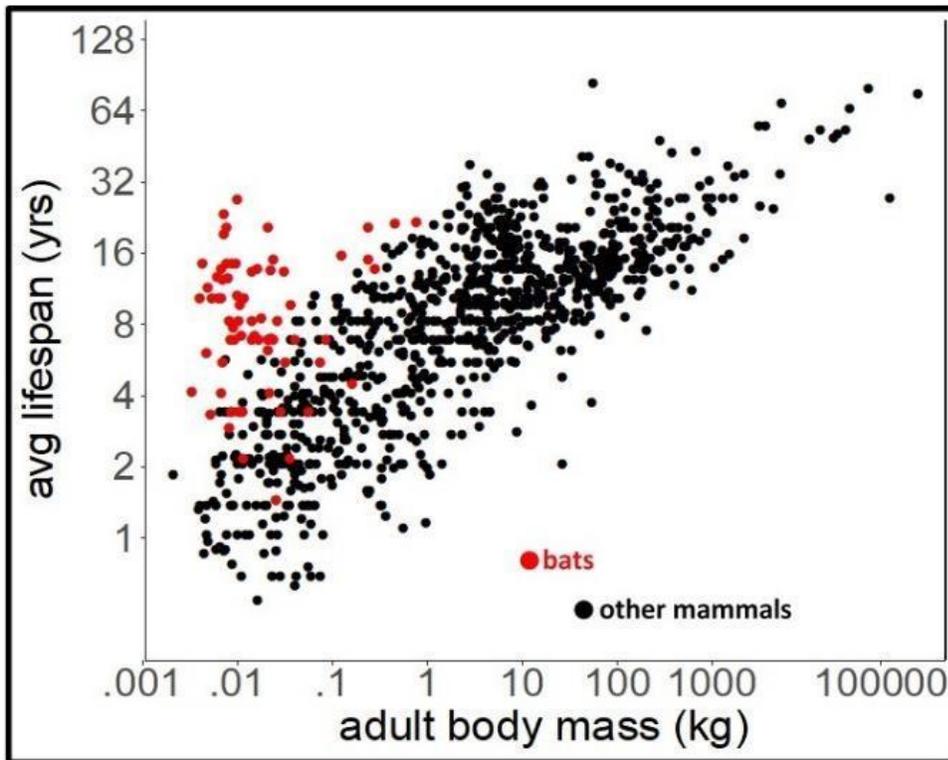


Figure 8: Bat Life Span and Adult Body Mass. Source: Jones et al., 2009.

Bats are the only flying mammal, and flight is the most physiologically intensive form of terrestrial locomotion. For instance, when flying, a bat's metabolic rate can be 34 times their resting levels and 8 times higher than an exercising rodent of comparable size (Thomas and Speakman, 2003; Thomas and Suthers, 1972). Bats' unique adaptations to flight may also lie at the heart of bats' unique resilience to both disease and aging processes. Flight is, indeed, so metabolically costly, that for it to evolve, bats needed to first evolve hyper-efficient DNA damage and repair, oxidative stress mitigation, and anti-inflammatory pathways at the cellular level. As a cascading consequence of these resilient cell level processes, bats appear to have also evolved extraordinary longevity and anti-viral tolerance (Ibid.). Their tolerance to viruses appears to be both through resilience to direct, oxidative damage incurred by viruses at the cellular level, as well as through mitigation of inflammation incurred by the recruitment of immune cells to the site of viral infection. By extension, evolutionary theory then predicts that bat viral tolerance should promote the evolution of virulent viruses (Brook et al., 2020).

More recently, Mollentze and Streicker (2020) concluded that zoonoses are proportional to total viruses and total viruses are proportional to host species diversity. The number of bat zoonoses is proportional to the number of bat species as compared with other mammalian orders. Zoonotic potential appears more driven by viral clade⁷ features rather than the host traits or host-viral interactions, “reservoir effects were isolated within individual virus families, such that no reservoir group altered the zoonotic risk of viruses across a broad range of viral families.” (Mollentze and Streicker, 2020). The authors found no effect of phylogeny on zoonosis (Ibid.). However, the authors took a constrained approach to phylogeny which holds many orders equivalent, and they were working with a narrow dataset because they excluded orders with five or fewer viruses described.

Yet, Mollentze and Streicker’s analysis revealed four mammalian orders that may be more likely to host viruses that pose significant zoonotic risk—rodents, primates, bats, and pigs (with the caveats previously noted) (Figure 9). Importantly, pigs are often potential intermediate hosts in and around the forest edge, which may amplify viral spillover risk for humans. It is important to further investigate the role of intermediate hosts with respect to viral zoonotic risk, particularly in relation to agriculture.

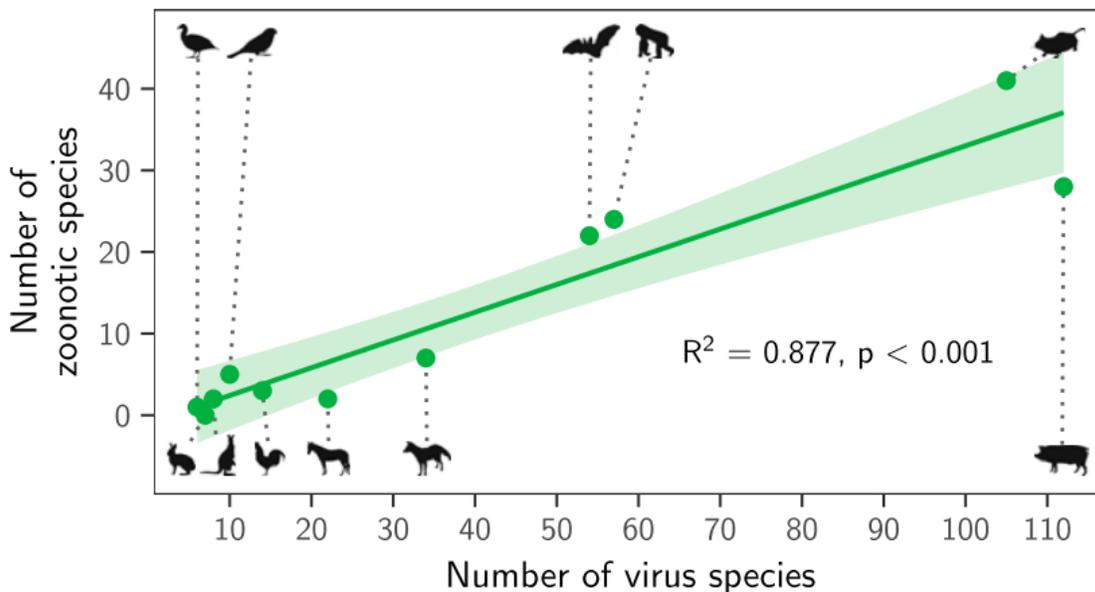


Figure 9: Hosts and Viral Zoonosis. Source: Mollentze and Streicker, 2020.

More recent research is answering the timely question of which hosts are the most likely to source a pandemic zoonosis. Unlike earlier prediction link research, this line of inquiry also considers two key pathogen traits: virulence and human-to-human transmissibility. A few papers explore drivers of virulence (Brierley et al., 2019) and transmissibility (Geoghegan et al., 2016) after zoonosis from the virus perspective. Only Guth et al., 2019 considers pathogen traits from the host perspective. More

⁷ A viral clade covers a virus species or variant and all of its descendants.

recently, Guth et al., 2019 reveal a positive correlation between phylogenetic distance from humans and case fatality rate, and a negative correlation between phylogenetic distance from humans and human transmissibility (Figure 10).

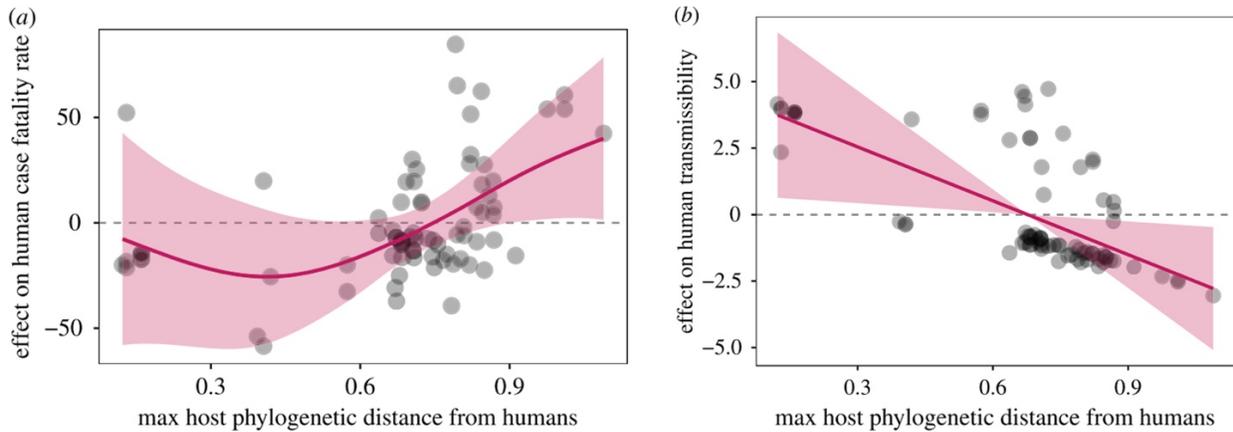


Figure 10: Viral Traits and Host Phylogenetic Distance to Humans. Source: Guth et al., 2019

Further, Guth et al., 2021 are attempting to disentangle host and virus effects on virulence, and are exploring ‘total death burden,’ which appears to be more the result of virological traits rather than host traits. Yet, bats do seem to be the source of significantly more virulent zoonoses than other host orders (Figure 11).

A. Effects of Host on Virulence (CFR)

B. Effects of Virus on Virulence (CFR)

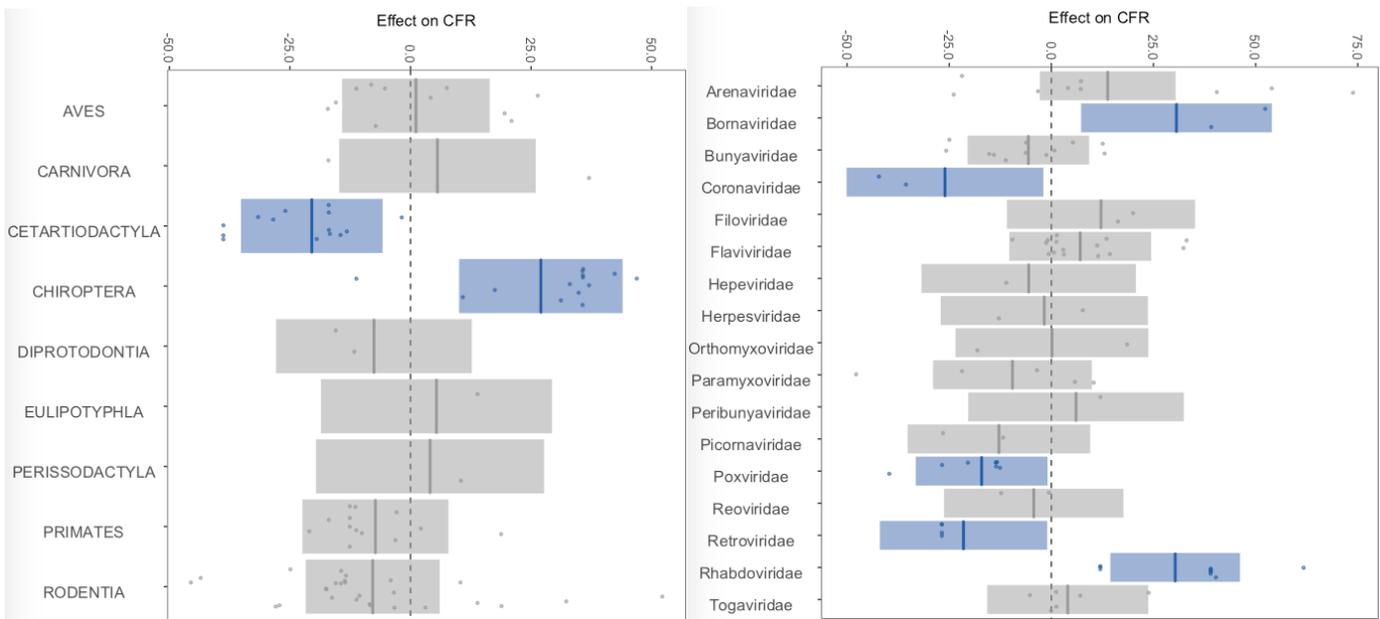


Figure 11: Host and Virus Effects on Virulence. Source: Guth et al., 2021

Nevertheless, the host viral data suffers from ascertainment bias, with Olival et al., finding that “research effort had the strongest effect on the total number of viruses per host, explaining 31.9% of the total deviance . . .” (Olival et al., 2017). There are likely more than 1 million viruses in mammals alone and possibly as many in avian species, with most taxa understudied. Indeed, about the same percentage of mammalian viruses (28.8% or 115/387) and avian viruses (30% or 9/30) are zoonotic (Mollentze and Streicker, 2020). To an extent, we find viruses where we look for them (Wille et al., 2021), but nonetheless the data suggests something ‘special’ about rodents, bats, primates, ungulates, pigs, and some carnivores meriting further inquiry. The next section will cover other spillover risk factors for humans within the context of a discussion on current risk mapping and modeling efforts to identify landscapes at greater risk for viral zoonotic emergence.

What is the current state of risk mapping and modeling to identify landscapes at greater viral zoonotic risk?

Spillover of viruses and other zoonotic pathogens⁸ from forest or natural habitats to human-dominated landscapes occurs in a variety of ways (see Figure 12 on the next page). Humans have contracted Ebola virus, HIV and monkeypox through wild animal and in particular bushmeat hunting in core forested areas in Africa (Leroy et al., 2004; Shchelkunov, 2013). When wildlife move into matrix habitats searching for resources or dispersing to other natural habitat areas, viruses and other pathogens may move with these species and transmit into hosts living in the modified environments—as has been seen for 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 also cause spillover (sometimes referred to as spillback) of pathogens to wild animal species that live in forested or natural habitats; for example, measles transmission from humans to apes during ecotourism activities (Rwego et al., 2008; Parsons et al., 2015), or canine distemper from free ranging domestic dogs into carnivores (Viana et al., 2015). Invertebrate vectors⁹ can also facilitate transmission, as is the case with sylvatic dengue, zoonotic malaria and yellow fever (Lounibos, 2002; Brock et al., 2016).

⁸ Zoonotic pathogens are agents hosted by animals, whether wildlife or (semi)domesticated species, that cause disease in humans. A zoonotic pathogen could be a virus, bacteria, prion, fungi, protozoa, helminth (parasitic worms), or arthropod (ticks, mosquitos, and fleas). Prions are misfolded proteins that can induce other normal prion proteins to become abnormally shaped, which in turn causes neurodegenerative diseases in humans and animals (e.g., mad cow disease). Prion zoonotic pathogens are relatively rare. Protozoa are single-celled animals. All mammals and other vertebrates are infected with protozoa, which are either asymptomatic or cause life threatening disease. Malaria is caused by a protozoan parasite (Bauerfeind et al., 2016).

⁹ For a discussion on the various definitions of ‘vector’ see Wilson et al., 2017.

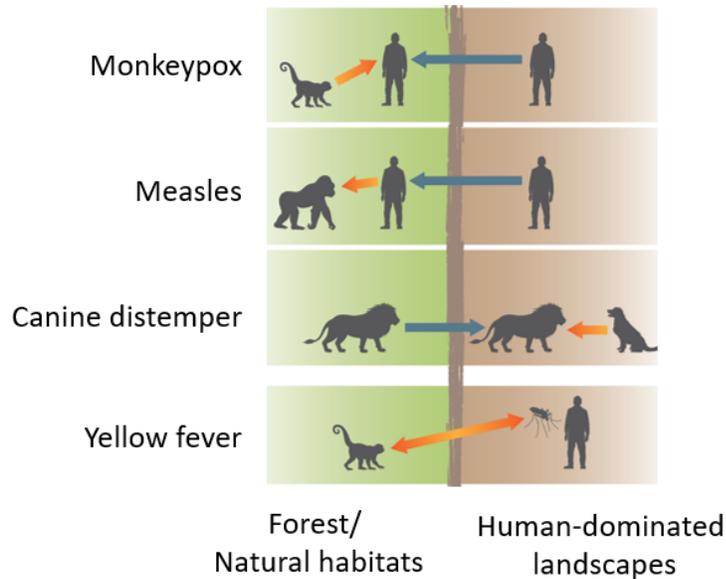


Figure 12: Examples of pathogen spillover. Source: Faust et al., 2018

A 2012 review of research on land use, land use change, and infectious disease found 302 papers published on the subject (Gottdenker et al., 2014). Ironically, 35% of these papers were themselves reviews—perhaps because those are more likely to get published and less difficult than obtaining new data in this area. Moreover, the underlying studies remain fairly data poor due to the challenges of obtaining the data at the true wildlife-human interfaces.

Most studies are cross-sectional surveys of land ‘use’ classes. Land cover—i.e., pasture, cropland—is used as a proxy for land use and studies sample from multiple grids within each land cover across a gradient of human density/ human intensification of land use. To characterize risk, studies often focus on quantifying host density or pathogen prevalence in the study area. More recently due to development of advanced statistical methodology and improvements in processing high resolution satellite imagery, researchers have taken a landscape approach with case control studies of one area where spillover occurred and another where it has not, but which appears otherwise ecologically suitable. Studies on Ebola and zoonotic malaria have found that many features of forest fragmentation significantly predict spillover risk (i.e., human outbreaks or cases) (Rulli et al., 2017, Brock et al., 2019).

Theoretical modelling of spillover risk during active landscape conversion makes a simplifying assumption of two land types—forest or natural habitats and human-dominated or matrix landscapes. In addition to changes in total area of each land type, these models also track the interface (or forest edge) between natural habitat and the matrix. Empirical data has shown that such an edge is a key indicator for accessibility and contact between humans and hosts (Bloomfield et al., 2020).

Figure 13 (on the next page) shows non-human host populations in their natural habitat in green. The yellow area represents the human populations in the matrix landscape. As humans convert forest to non-forest uses and alter the forest edge over time, the model estimates that these conversion processes will translate into increased contact between humans and hosts. The far right fully green square represents an intact or ‘immune’ forest landscape with limited conversion, human populations,

and low spillover risk. The model estimates higher spillover risk in areas of intermediate habitat loss, with reduced carrying capacity for host species, high accessibility and contact between species and elevated pathogen prevalence in reservoir populations. This prediction of high risk in highly fragmented landscapes is supported by empirical observations in at least ten disease systems, including Chagas disease (Gottdenker et al., 2012), Buruli ulcer (Morris et al., 2016), and henipaviruses (Pernet et al., 2014).

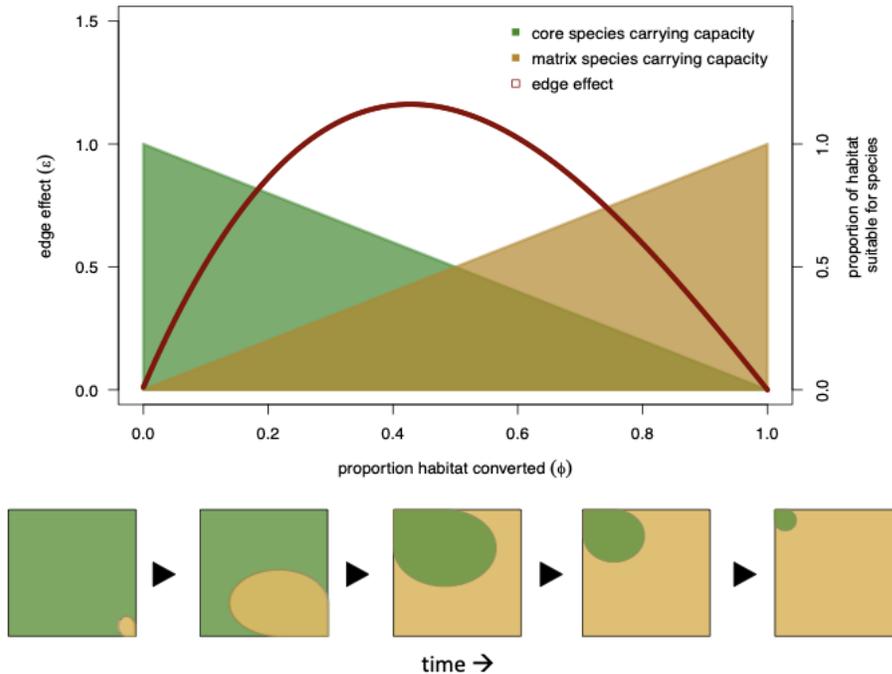


Figure 13: Population sizes and transmission changes during land conversion. Source: Faust et al., 2018.

At this intermediate conversion stage host species may also suffer increased stress and poor nutrition, perhaps contributing to viral load and shedding. They may also increasingly be drawn into human settlements. Given the discussion above, the risks may be compounded if such hosts are in a mammalian order potentially more likely to host zoonotic viruses or viruses with pandemic potential. Compounding this dynamic is the conversion of previous habitat to agriculture and livestock production (Plowright et al., 2015), which may attract weakened hosts into matrix landscapes with domestic species, such as pigs, that may serve as intermediate hosts before zoonosis occurs.

Compartmental models for viruses assign a population to different categories or compartments (e.g., susceptible, infectious, or recovered). These models are parameterized for certain viral taxa and can also refine our understanding of spillover risk factors. Given certain assumptions, known viruses are likely to result in a certain number of susceptible, infectious, and recovered individuals. For instance, Figure 14 (on the next page) estimates the probability of one human Ebolavirus infection over a one-year period (low transmissibility but high virulence and case fatality rate). The model finds that when over 20 percent of the habitat is converted there is a high probability of human infection, but the size of the epidemic can increase when over 60 percent of the habitat is converted because of the significant

increase in the human population. Thus, conservation efforts to prevent habitat conversion may be able to reduce these spillover risks and advance public health outcomes.

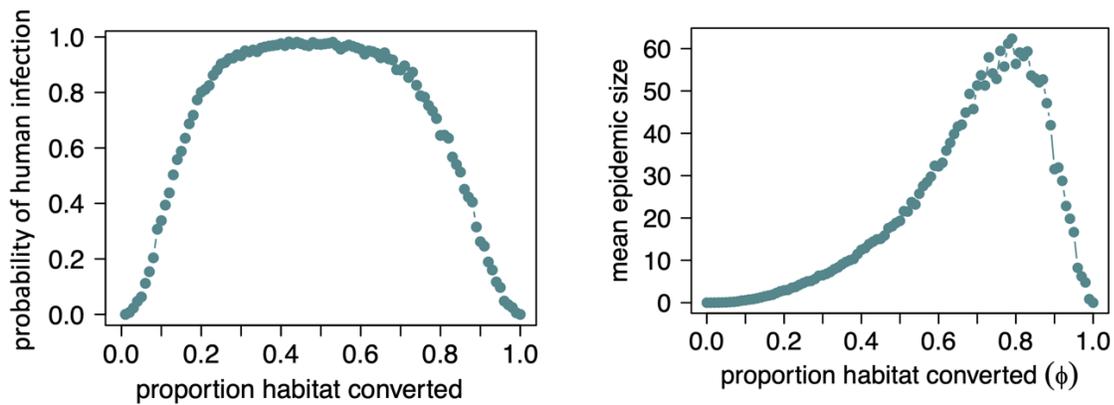


Figure 14: *Habitat Conversion, Human Infection, and Epidemic Size.* Source: Faust et al., 2018

Another key consideration is the amount and rate of habitat conversion. Figure 15 shows the results of simulations with the green line representing habitat prevalence and the yellow line representing the human population. Although dependent on other contextual factors, these simulations suggest that if conversion is occurring at a rapid rate there may be a period of relatively high but transient risk.

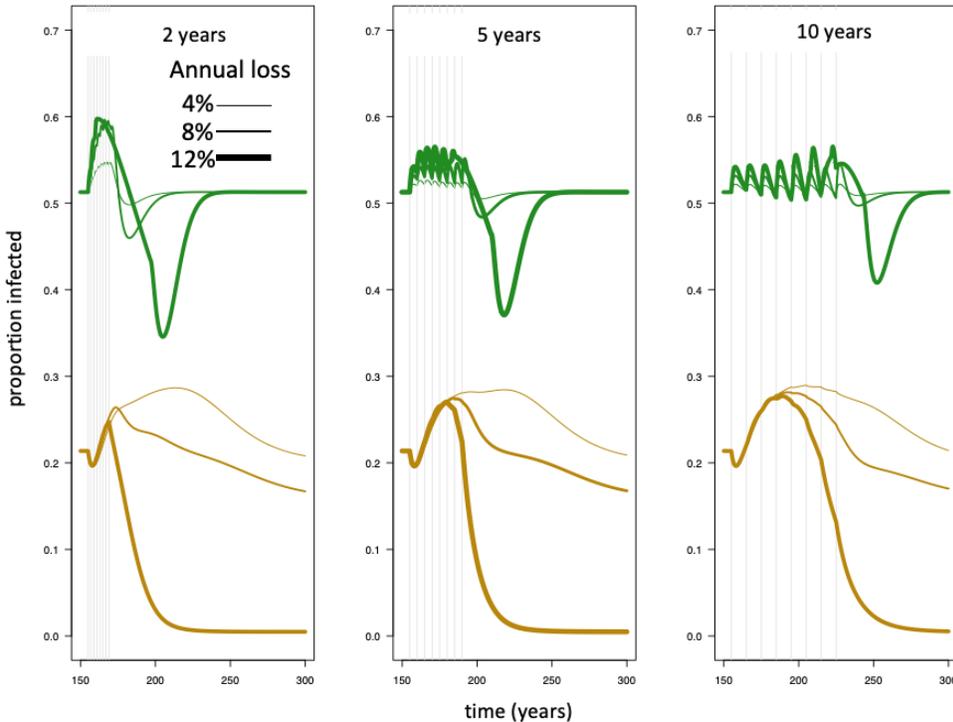


Figure 15: *Rate of Habitat Conversion and Human Infection.* Source: Faust et al., 2018

Consistent with the above, a recent survey by Grange et al. (2021) asked virologists, epidemiologists, and disease ecologists, among others, to rank risk factors derived from the literature. This list may suggest a way to improve risk models and our longitudinal understanding of the mechanism of viral zoonosis, provided sufficient data can be collected in one or more sites. Some of the top risk factors identified by the experts surveyed are:

1. **Transmission animal to human** or ability of virus to transmit between animals and humans (i.e., zoonotic potential).
2. **Transmission human to human** or ability of virus to transmit between humans. As noted above, this factor is likely driven by viral traits rather than host characteristics.
3. **Viral Infectivity to humans.** Capacity of viruses to enter a human cell and exploit its resources to replicate and produce viral progeny. This factor is similar to zoonotic potential except viral infectivity is concerned with the capacity of a virus to replicate and spread once zoonosis occurs.
4. Intimacy of interaction: wild animals to humans.
5. **Number of primary interfaces.** See discussion above on forest disturbance and land conversion.
6. Frequency of interaction: wild animals to humans.
7. **Virus transmission mode.** The types of transmission modes are: excretion, slaughter, or vector borne.
8. **Virus epidemicity.** Extent to which the virus has historically led to “small outbreaks (a noticeable but small number of cases), large outbreak (large number of cases over a small area), epidemics (an outbreak over a larger geographic area) or pandemic (an epidemic that has spread to multiple countries or regions of the world, with sustained transmission) in humans, animals or both.”
9. **Host plasticity: orders.** “Host plasticity is a measure of the diversity (number of species) and breadth (number of orders) of hosts the virus is known to infect.”
10. Frequency of interaction: animals – humans
11. Intimacy of interaction: domestic animals – humans (Grange et al., 2020)

Forest disturbance and land conversion impact many of these risk factors, such as the number of primary interfaces and frequency and intimacy of interactions. And each one of these factors, plus others, could be used to refine risk mapping and modelling at different spatial and temporal scales.

The above factors are also applicable to identifying risk at different points in the wild meat supply chain. For rodents in Vietnam coronavirus detection is significantly more likely as one moves across the wild meat supply chain from habitat to table. Coronavirus was detected in 20.7% of rodents sold by traders, 32% of rodents sold in large markets, and 55.6% of rodents sold and served in restaurants (Huong et al., 2020).

Adding to our understanding of risk factors is a study by Allan et al., which examined global, spatial risk of emerging zoonotic disease. They found that evergreen broadleaf forests are the most predictive of zoonosis (~9%), followed by more sparsely populated village settlements (matrix populations) (~8%), areas of high mammalian diversity (~7%), cropland and conversion to cropland (10%), and pasture and conversion to pasture (~10%) (Allen et al., 2017).

To what extent does current risk mapping and modeling to inform programs and policies take account of these factors and analyses? Disease risk mapping often occurs at the two extremes of spatial scales: local and global. These risk maps can provide overly detailed information on one pathogen at one point in time or provide general estimates on a much greater scale—neither of which are useful for informing policies and programs. Recent work on Lassa fever, caused by a sometimes-deadly zoonotic virus normally circulating in multimammate rats in West Africa, integrated ecological, landscape, climate and human health surveillance data to provide information on links between land conversion and spillover risk (Redding et al., 2016). Providing this detail on prediction required a large dataset across an entire region but can provide insights into mechanisms underlying changes in spillover risk for humans. Extending this framework into more viral zoonotic systems and places will greatly improve our understanding of how risk varies across time and different landscapes.

A potential opportunity for understanding these interconnections lies within the relationship between reforestation or forest restoration interventions and spillover risk. Although reforestation or restoration are core components of many countries' climate change mitigation commitments, the implications for zoonotic risk are unclear. Reforestation/restoration alters the biodiversity of an area, changes animal population densities and affects movement of individuals (Watts et al., 2020), which implies downstream consequences for pathogens they transmit. Outcomes will also likely depend on the type of reforestation and the resultant biodiversity richness (or lack thereof), and sustainable agroforestry raises other questions with respect to zoonotic disease risk.

But to what extent are our programs increasing or decreasing spillover risk and what combination of LRG, conservation, agriculture, and health interventions might mitigate this risk when combined with reforestation/restoration efforts? For instance, reforestation in the Northeastern United States may have increased the risk of Lyme disease due to changes in the white-footed mice and deer populations and their ticks (Kilpatrick et al., 2017), but an explicit test of this hypothesis is elusive. These gaps limit our ability to estimate risk levels and act upon sound data and evidence.

If our understanding of risk models and mapping could be refined and regularly updated, we could employ them as a tool to advance environmental, health, and human well-being outcomes through improved land use planning, ranging from large infrastructure projects that are anticipated to increase viral zoonotic risk to participatory land use planning for smallholder farming villages that experience increased interfaces or contact points with host habitat (Bloomfield et al., 2020; Allen et al., 2017). Such risk maps and modeling may also be beneficial to reforms and interventions in the wild meat supply chain and wildlife trafficking.

B. Interventions and Measuring Impact

In this section, we discuss several illustrative programmatic interventions that could serve to address this development challenge by reducing spillover risk (Reaser et al., 2021b). We describe how a rigorous research agenda of these interventions can be used to generate knowledge and improve the effectiveness of policy and programs.

Conservation employs a variety of interventions, usually implemented as a suite that span three levels à la the Conservation Measures Partnership taxonomy of conservation actions: (1) interventions to

improve the enabling environment for conservation, (2) interventions to change behavior/mitigate the threat, and (3) actions to relieve direct stress on species and ecosystems through land/water and species management. Common USAID interventions include protected area management, conservation enterprises, law enforcement, demand reduction/behavior change campaigns, and enabling environment (legal/policy reform, conservation planning, education/training, institution strengthening), as well as more innovative market-based and direct economic payment schemes. Depending on the context, any one of these may be appropriate for reducing viral zoonotic risk.

In addition to keeping forest landscapes intact or ‘immune’ by reducing deforestation, an intervention might also include native forest restoration outcomes, although the impact on spillover risk merits further study, as noted above (Ibid.). Models based on data from 104 sites across six landscapes in the Brazilian Atlantic Forest biome suggest that native forest restoration could significantly reduce viral zoonotic risk from rodents (Prist et al., 2021).¹⁰ Yet, this study suffers from the methodological weaknesses discussed above; it is not time series but cross sectional and without a rigorous comparison group. The study simply compares three native forest landscapes with three degraded forest landscapes.

Further, a presumptively effective intervention is halting or reducing the farming, killing, butchering, trade, transport and consumption of live and freshly killed birds and mammals in provincial towns and metropolitan cities, while not undermining the health and wellbeing of subsistence hunters. Finally, we might also increase access to alternative, sustainably and hygienically produced animal source foods. Yet, at present there is limited evidence on the impact of these interventions on viral zoonotic risk. Improved collection and analysis of longitudinal and counterfactual (or impact evaluation) data will help us better understand the mechanisms by which viral zoonotic emergence occurs, and the effectiveness of interventions to mitigate that risk.

Evidence on effectiveness of interventions to conserve biodiversity and improve forest outcomes?

Impact evaluations (IEs) are required to determine the causal effect of a program. IEs rely on a counterfactual or comparison/control group to rigorously distinguish causality from association. Impact evaluations can be prospective where the research design is embedded in the intervention. The most rigorous prospective method for constructing the counterfactual is through random assignment (the randomized control trial or RCT). IEs can also be retrospective, in which the control is constructed after the intervention has begun or concluded (i.e., the opportunity for pre-intervention baseline data collection has passed).

The treatment of interest for an IE can be designed for the community, household, or individual level. But different units of analysis are possible, such as focal species (e.g., rodents, bats, primates, ungulates, and pigs), a defined geographic area (e.g., forest or non-forest polygons), or farms. A minimum sample size is required for an IE to have the power to assess causality, and this depends on several factors, including the outcomes under investigation. It is important to note that conservation programs typically include a bundle of interventions not easily disentangled, such as bans on hunting focal species, habitat

¹⁰ Prist et al. used as their focal species *Oligoryzomys nigripes* (black-footed pygmy rice rat) and *Necromys lasiurus* (hairy-tailed bolo mouse).

maintenance, and alternative animal sourced foods. Impact evaluations can be designed to measure causal impact for a combination of interventions or seek to isolate the impact of one or more interventions.

IEs are rare in conservation science (Ribas et al., 2020). There is significant variation in the rigor of studies. Evidence of impact is vastly inadequate, with poor design, lack of scope and too few examples (Burivalova et al., 2019). RCTs are common in some development sectors, such as global health, but non-existent in conservation and limited in land and resource governance, although this is changing rapidly as more RCTs are employed in LRG (Persha et al., 2021). Many studies on the effectiveness of conservation strategies involve the simple monitoring of indicators or case studies (Ferraro and Pattanayak, 2006; Stem et al., 2005).

Also, too few studies cover the impact of LRG interventions with respect to environmental and biodiversity outcomes (Tseng et al., 2021). Tseng et al., found very few studies on the impact of LRG interventions on biodiversity conservation (2), forest condition (20), forest conservation (6) and none on wildlife trafficking, although the majority of LRG interventions had a positive effect on these outcomes (Ibid.).

There is a lack of robust impact evaluations for assessing efforts to reduce consumer demand for wildlife products. Rigorous M&E is also limited, although more recent advances to understand the impact on demand reduction are not captured in this review, such as before-after study designs using survey data (Verissimo and Wan, 2019). Verissimo and Wan examined 236 demand reduction campaigns for wildlife products. Twenty five percent of the campaigns presented evidence, which was anecdotal and often focused on knowledge and attitudes and self-reported behaviors. Studies on effectiveness of demand reduction lack rigor, with selection, data quality and design challenges. Thirty-seven percent of campaigns reported on outcomes and nine percent of studies reported on impact for indicators such as biological changes or threat reduction. Yet less than 9% of all studies reported data on biological impacts.

Burivalova et al. examined 161 studies assessing 570 environmental, social, and economic outcomes for forest certification and reduced impact logging, payments for ecosystem services (PES), protected areas, and community forest management. The authors found limited evidence on effectiveness of forest certification and reduced impact logging, but some rigorous studies show certification leads to reduced deforestation. PES is generally associated with a decline in deforestation or no significant change, but there is little data on biodiversity outcomes. Similarly, studies on the effectiveness of protected areas have little data on biodiversity, although in general protected areas are effective at reducing deforestation (Burivalova et al., 2019; Nelson and Chomitz, 2011).

Hajjar et al. (2020) reviewed 643 cases of community forest management across 51 countries to identify which factors are associated with social and environmental outcomes (forest cover, forest condition, and biodiversity) (Hajjar et al., 2020). Environmental condition improved in 56% of the 524 cases tracking environmental condition and decreased in 32% of cases. Environmental and income benefits often appear to be achieved together. About half of cases with environmental indicators saw increases in biodiversity (46 percent; n=317), forest cover (46 percent; n=247), and forest condition (51 percent; n=470). However, declining forest resource rights and distributional asymmetries (i.e., inequity) within

communities are common. Hajjar et al., 2020 concluded that the following contextual variables are associated with multiple win outcomes:

- Type of community forest management
- Time since policy change
- Type of forest
- Collective action levels
- Management and exclusion rights and ensure formalization does not reduce these rights de jure or de facto
- Population size of management community
- Migration (Ibid.).

Protected areas (PAs) are a standard conservation intervention to reduce biodiversity loss through avoided deforestation. Ribas et al. (2020) show that PAs have been effective in avoiding deforestation, but the estimates of PA effectiveness depend on the IE method (Ribas et al., 2020).

Counterfactual/causal studies are not prioritized in the conservation and land and governance space, relative to other development sectors for a variety of reasons. Measuring impact on biodiversity conservation is thought to be methodologically challenging and expensive (Ferraro, 2009; Rissman and Smail, 2015). The challenges include:

- large variability in ecological outcomes,
- long time lags between intervention and ecological response,
- programs with multiple interventions,
- complex spillover effects (e.g., due to species movement),
- large spatial scales of environmental processes, and
- data constraints, including an overreliance on self-reported behavioral indicators and lack of indicators for biodiversity outcomes.

Studies of the wildlife trade face similar challenges, including multifaceted drivers of demand that complicate the study of consumption, lack of data on actual behavioral change, and delayed responses for long-term behavior change (Verissimo and Wan, 2019). IEs that measure the effectiveness of conservation interventions or wildlife demand reduction campaigns are rare and vary in rigor. Many studies of the effect of conservation initiatives involve the simple monitoring of indicators (Ribas et al., 2020), and this is insufficient to establish cause-and-effect relationships (Ferraro and Pattanayak, 2006).

However, the above challenges are either misplaced or apply equally to governance and other sectors that have managed to adapt impact evaluation designs to the realities of those sectors. Conservation and the link between governance, conservation, and global health could follow suit. And the lack of robust impact evaluation makes it difficult to draw insights to inform future efforts. Thus, a number of studies over the past decade have emphasized the need for more rigorous experimental and quasi-experimental impact evaluations related to conservation outcomes (Curzon and Kontoleon, 2016; Ribas et al., 2020) and wildlife demand-reduction campaigns (Verissimo and Wan, 2019).

There is a common misconception that biodiversity conservation outcomes will take decades to observe, limiting their utility. In fact, depending on the species, adult annual mortality and host viral

dynamics (e.g., propensity to shed virus and viral load), could be observed within 10 years as a long-term outcome of interest, although modeling and analysis is needed to assess feasibility. Further, short-term outcomes within one to two years after interventions are completed are readily observable; namely, are people responding to the interventions the way one would expect suggesting long-term impact will be achieved? Impact evaluations also add value by strengthening a program's theory of change and connecting interventions to the evidence base during the feasibility stage. And baseline data can challenge assumptions and promote more effective, adaptive programming. Put another way, a long running, adapted program is not necessarily an impediment to an impact evaluation, but rather an opportunity for an impact evaluation to add value.

5. Recommendations for Applied Research

This section proposes activities motivated by clear and discrete research questions to improve our understanding of zoonotic emergence in changing landscapes and guide interventions that will simultaneously improve livelihoods, preserve biodiversity and ecosystem services, and mitigate risk of viral zoonotic emergence.

A. Mapping and Modeling to Identify Areas at Higher Risk for Viral Zoonotic Emergence

The probability or risk of animal-to-human pathogen emergence is concentrated in regions where key animal hosts, pathogens, human behavior and ecological conditions align to increase likelihood of spillover. PREDICT scientists and collaborators produced a global risk map for zoonotic emergence by identifying features of land use change, biodiversity, and human population growth that correlated with historical zoonotic outbreaks (see Figure 16 on the next page). Their statistical models are able to incorporate sampling bias and pinpoint key factors associated with spillover—including human population density, mammalian diversity, cropland area, active conversion to land cover, and recent loss of forest. Several regions are highlighted as high risk for zoonotic emergence: including, but not limited to, Central American tropical forests, coastal West Africa, the African Great Lakes Region, India, England, and eastern China. This risk map provides useful signposting for triaging studies on a global scale, but to what extent can this map be refined at the national or subnational levels—where planning and surveillance policies are actually implemented?

Factors that heighten risk for viral zoonotic emergence are available on a much finer scale and could be leveraged for within-country or for large or small regional planning. A recent survey of experts conducted by Grange and colleagues (2021) highlights key prerequisites for zoonotic emergence, including accessibility to mammalian biodiversity hot spots, frequency of interaction between wild

animals and humans, and rates of forest conversion. These data could be used to develop more actionable zoonotic risk maps at subnational scales. It is possible that leveraging existing data collection efforts, such as the Demographic and Health Surveys (DHS) and remotely sensed data, could provide additional information to identify potential areas of risk within a country. However, collection of additional information to identify specific cultural practices and behaviors, such as wild animal-derived meat supply chains, in particular the trapping and transport of live animals, could greatly improve mapping efforts; whether these efforts would be cost prohibitive needs to be investigated.

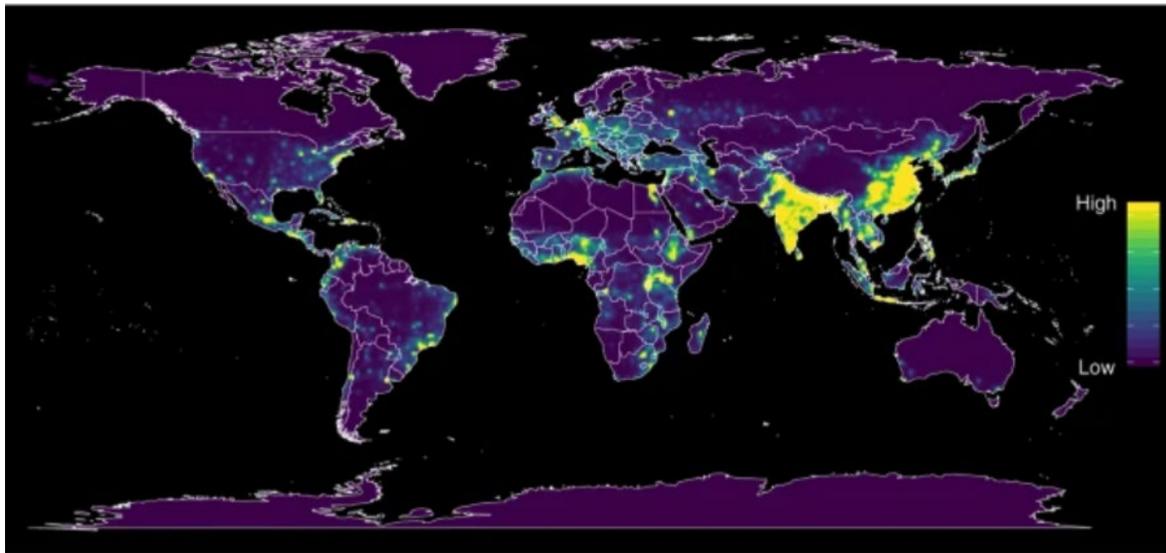


Figure 16: Emerging Zoonotic Disease Risk. Source: Allen et al., 2017

Regional- or country-level risk maps would enable targeted surveillance, educational activities and other interventions to prevent zoonoses. A key first step is identifying landscapes where interventions would have the most impact. Spatial statistical models have the potential to help identify high risk locations within a region. These risk maps could incorporate future land use planning and be used to mitigate risks posed by new infrastructure development, for example.

B. Understanding the Mechanisms of Viral Zoonotic Emergence

Wildlife conservation through the protection and restoration of ecosystems has the potential to reduce zoonotic spillover (Reaser et al., 2021a, Plowright et al., 2021), but this concept has not yet been demonstrated in a real-world setting. A rigorous One Health research program in focal regions could help us understand key mechanisms affecting the emergence and establishment of zoonotic viruses in the human population (Plowright et al., 2021) and improve the design of key interventions to achieve positive outcomes for public health and ecosystems. Furthermore, identifying key mechanisms driving zoonotic risk will improve understanding of these dynamics beyond the focal system. Identifying mechanisms will help direct targeted interventions and highlight key variables and indicators for program monitoring and evaluation.

To quantify zoonotic risk in changing landscapes, it is essential to understand the spatiotemporal variation in ‘hazard’ 1) human-wildlife contact, and 2) likelihood of infection given a contact. Identifying mechanisms leading to changes in any one of these drivers is essential for mitigating viral zoonotic emergence through development policies and programs. Mitigation efforts should be supplemented with targeted surveillance to evaluate their effectiveness. Implementation of any mitigation effort will require an integrated economic, sociological, and ecological understanding of mechanisms facilitating zoonotic emergence. Below we outline key data to collect for each of these dynamic processes and then give an overview of how impact evaluations can be used to identify and evaluate interventions to reduce viral zoonotic spillover.

Key data to collect to understand the mechanisms of viral zoonotic emergence are:

- 1) **Reservoir host population distribution, dynamics and viral load.** Decades of work has shown that zoonotic hazard (distribution of hosts and infection prevalence) is variable across spatial and temporal scales—making longitudinal surveys across multiple sites essential (albeit logistically challenging and rare in practice). Observational studies have shown that reservoir species are less likely to shed virus when they have sufficient resources, low stress levels and stable populations. Stressed and declining populations undergoing habitat loss are more likely to shed virus (thus increasing human risk), but the mechanism driving this relationship is not understood (Rocha et al., 2020). Fitting mechanistic models to empirical data allows testing different mechanisms (Gentles et al., 2020) and can improve forecasting of viral zoonotic risk in changing landscapes.
- 2) **Reservoir - human contacts.** Potential contacts can be measured through a variety of methodologies developed by different disciplines. Household surveys can be used to record sightings and contacts with animal hosts. Volunteers can be recruited to wear GPS tracking devices to record movements and or maintain activity diaries to identify duration and types of contacts, linked to recorded spatial locations. Contact between reservoirs identified in (1) and humans can be estimated based on survey responses and movement data relevant to pathogen-specific transmission mode.
- 3) **Probability of human infection given a contact.** Whole blood and serum samples from individuals can be obtained to understand variation in exposure to wildlife pathogens. Serology can be used to measure antibodies to past viral exposures (e.g., VirSCAN) and PCR and/or metagenomic sequencing can be used to measure active infections of focal pathogens. Semi-structured household questionnaires and rapid ethnographic appraisals can be used alongside these clinical techniques to identify protective measures that individuals employ to reduce contact with potentially infectious material (e.g., wearing waterproof boots, storing food apart from sleeping arrangements). Individual behaviors, including protective measures and movement, can be included in mechanistic models to understand factors affecting observed exposure signatures and active infections.

Impact evaluations (IEs) offer one means by which to quantify and evaluate the effectiveness of programs or policies aimed to mitigate the above drivers of zoonotic spillover. Following on Gray et al. (2021), IEs are most likely to achieve statistical power if focused in systems where the following factors are high: “1) prevalence of the pathogen in the reservoir, (2) the reservoir-to-human contact rate, and (3) the

probability of human infection with the animal pathogen.” Gray et al. point to surveilling livestock as more targeted and strategic than wildlife, though a long history of cohabitation between livestock and humans may have allowed humans to develop protective immunity against many livestock pathogens, thus reducing their potential for zoonotic emergence. Nonetheless, a subset of animal taxa, with caveats (e.g., bats, rodents, primates, ungulates, and certain carnivores), are believed to source the majority of zoonotic pathogens and offer a useful starting base for design and evaluating a proof-of-concept program or policy targeted towards the application of conservation-based approaches for viral zoonotic risk mitigation.

Programs that could be amenable to impact evaluations for viral zoonotic emergence are:

1. **Forest restoration.** Restoration of degraded forest ecosystems has benefits for biodiversity and ecosystem services, such as improvements in flood controls and water quality. Mounting evidence suggests that forest restoration could also benefit human health by increasing biodiversity (in particular species that do not amplify viral zoonotic risk), lowering disease prevalence in reservoir populations, and reducing reservoir host-human contacts. An impact evaluation that monitors reservoir populations, pathogen prevalence and human-reservoir contacts in communities with restoration and paired sites without restoration efforts would provide essential data for understanding the utility of this intervention for viral zoonotic risk mitigation. For instance, in Vietnam’s degraded forests USAID could test the relationship between viral zoonoses and restoration of degraded forest landscapes.
2. **Minimal fragmentation land use planning.** In areas where forest clearance is ongoing, there is an opportunity to demonstrate how varying the location and rate of clearance impacts viral zoonotic risk. Empirical observations and modelling work suggests that forest clearance that minimizes edges (and therefore minimizes forest fragmentation) will reduce risk for viral zoonotic emergence compared to highly fragmented and rapid deforestation. The three key inputs for spillover can be monitored in communities where this process is ongoing or can be part of land use planning prospective observations.
3. **Reductions in bushmeat harvesting.** Quantification of the impact of efforts to reduce consumption of wild meat (e.g., targeted social behavioral change, increase availability of affordable alternative animal source foods) on both wildlife populations and humans is needed to address a significant knowledge gap in our understanding of the viral zoonotic risk posed by bushmeat hunting. Bushmeat consumption can be challenging to reduce because of deeply entrenched cultural practices. Yet, the capturing, handling, and transporting of live animals would seem to pose the highest transmission route risk, and what do these and other transmission routes imply for spillover risks for bushmeat hunters and traders? Longitudinal serology and PCR surveillance tests in a range of exposure contexts could provide invaluable insights into whether, for example, bushmeat traders that sell smoked or dried bushmeat exhibit lower risk levels at baseline compared to bushmeat traders of live or freshly killed bushmeat or compared to poultry or fish traders, and whether such risk levels decline over time in response to specific interventions. Such an effort could complement and coordinate with next generation immunological surveillance and metagenomics. Though wild meat supply chains are often cited as major conduits of zoonotic risk, they may represent a more minor driver of spillover than

landscape-level changes, such as deforestation and ecosystem fragmentation. Impact evaluations may be essential to deciphering cause and effect.

Any of the above evaluations or research designs will need to be tailored to the realities of ongoing conservation programs. The efficacy of any number of interventions could be tested, but an impact evaluation design should be strategically planned to cost effectively quantify viral zoonotic risk. One option, which may reduce cost, is to limit serology and PCR data collection to specific subgroups within an intervention area. For example, this could include bushmeat hunters, particularly of mammalian orders which may be hosts to viruses with significant viral zoonotic risk or pandemic potential. For instance, a study in Cameroon found positive serology tests for Nipah virus antibodies in 3 to 4% of bat bushmeat hunters, and 48% of the sampled fruit bats (*Eidolon helvum*) (Pernet et al., 2014). We recommend a feasibility study to further explore the potential of IEs for measuring viral zoonotic risk and related outcomes.

Finally, it is important to note that an understanding of risk and the transdisciplinary mechanisms by which zoonosis occurs may reinforce one another. Field data and experiments to isolate causality can refine our understanding of which factors in what contexts drive zoonotic risk (Hassell et al., 2021), which can combine with surveillance and other data collection efforts as well as improved data quality and access (Wille et al., 2021).

6. Conclusion

Over the span of 14 months, the virus SARS-COV2, which causes the disease COVID-19, has killed more than 3 million people, and likely many more. Most Sub-Saharan Africans who died from COVID-19 were not diagnosed or treated (Mwananyanda et al., 2021). And SARS-COV2 brought the global economy to a halt. The disease and its associated global economic devastation have driven millions into extreme poverty (Gray et al., 2021; Dobson et al., 2020; Josephson et al., 2020). Given current trends, pandemics are not a once-in-a-century event, with the frequency of zoonosis increasing (McCloskey et al., 2014; Marani et al., 2021). Yet, pandemics and zoonoses are not mysterious or unstoppable; they are mechanistic and thus can be mitigated.

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