EPIDEMIOLOGY

The costs and benefits of primary prevention of zoonotic pandemics

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The lives lost and economic costs of viral zoonotic pandemics have steadily increased over the past century. Prominent policymakers have promoted plans that argue the best ways to address future pandemic catastrophes should entail, "detecting and containing emerging zoonotic threats." In other words, we should take actions only after humans get sick. We sharply disagree. Humans have extensive contact with wildlife known to harbor vast numbers of viruses, many of which have not yet spilled into humans. We compute the annualized damages from emerging viral zoonoses. We explore three practical actions to minimize the impact of future pandemics: better surveillance of pathogen spillover and development of global databases of virus genomics and serology, better management of wildlife trade, and substantial reduction of deforestation. We find that these primary pandemic prevention actions cost less than 1/20th the value of lives lost each year to emerging viral zoonoses and have substantial cobenefits.

INTRODUCTION: PREVENTION, NOT JUST CURE

Leaders in public health, medicine, multilateral organizations, global health nonprofits, and many prominent policymakers have promoted plans that argue that the best ways to address future pandemic catastrophes should entail "detecting and containing emerging zoonotic threats (*1*)." In other words, we should take actions only after humans get sick. We sharply disagree.

As prominent examples of these approaches that consider solutions only after humans get sick, consider The Global Preparedness Monitoring Board, a joint initiative of the World Bank and the World Health Organization (WHO). This board is tasked with ensuring "preparedness for global health crises." Its *World in Disorder* report (September 2020) makes a strong plea to improve global health security that focuses heavily on vaccines, pharmaceuticals, and diagnostic tests (*2*). Preventing spillover is not mentioned. As another example, the G-20 formed a high-level panel on "Financing the Global Commons for Pandemic Preparedness and Response" tasked with "assessing the current financing systems and suggesting viable solutions for the longer term." In their progress note of April 2021, the panel clarifies that it only considers financing of post-spillover activities (*3*).

Much research shows that the spillover of viruses from animals to humans is the major source of pandemic risk (*4*, *5*). The coronavirus disease 2019 (COVID-19) pandemic most likely had its origins in a zoonotic event (*6*). Hence, the failure to consider minimizing spillover in influential conversations dedicated to preventing the next pandemic perplexes us. These reports hammer on the need to invest more in technology to diagnose, treat, and quickly vaccinate after diseases emerge. If the current pandemic has taught us anything, then it is that no amount of technology can save us from poor governance once an epidemic takes hold in the human population.

Here, we address the need for spillover prevention by evaluating the rate of novel zoonotic virus emergence over the past century. By "novel" we mean previously unknown. We quantify the annualized mortality and economic costs of emerging viruses. We then contrast this with the costs of what we define as primary pandemic prevention actions. We explain the value of better knowledge of viral diversity to primary prevention and then address the three main drivers of pathogen emergence: (i) wildlife trade and hunting, (ii) agricultural intensification and expansion, and (iii) destruction of tropical forests. We examine China's recent wildlife trade restrictions to reduce spillover risk from wild animal capture and trade. We then illustrate that slowing tropical deforestation is essential to prevention. Last, we note that enhanced wildlife veterinary capabilities are needed to improve spillover surveillance. We conclude that primary prevention costs a fraction of the cost of cures.

ZOONOTIC PANDEMICS ARE FREQUENT AND RISING IN COST

Frequency

The COVID-19 pandemic was predictable but not prevented. Novel viral outbreaks appear at an irregular but increasing rate (Fig. 1 and

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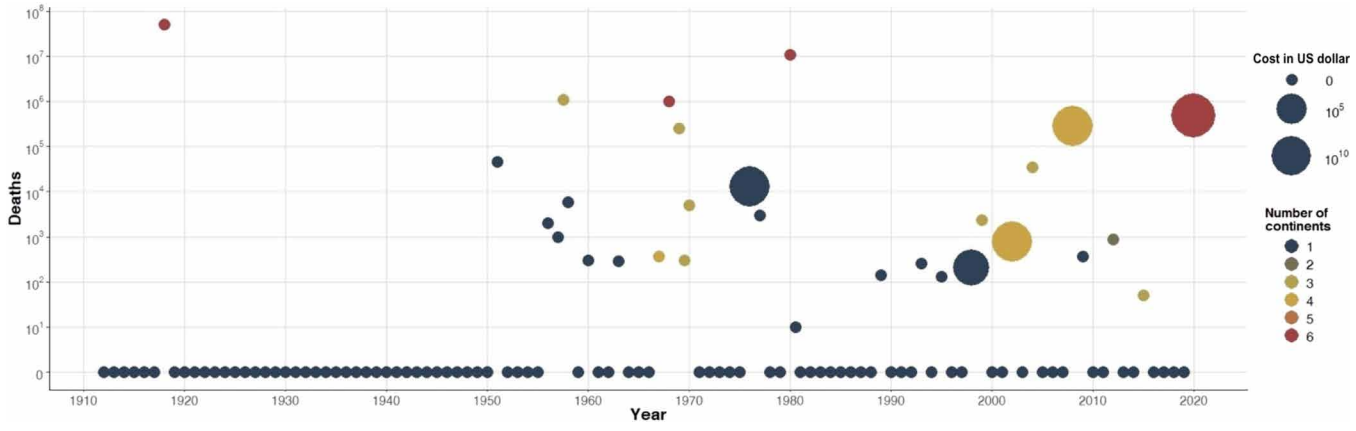

Fig. 1. Deaths per year from novel viral zoonotic outbreaks since 1912. Numbers are color-coded by the number of continents over which they spread. The size of the symbol shows economic costs, in addition to those based on loss of life, for just the five cases for which the World Bank provided estimates (*8*). Studies of economic costs from infectious outbreaks use different methods and their results may not be directly comparable. Our study concentrates on loss-of-life costs using the value of statistical life (VSL). VSL costs from other epidemics could be calculated retrospectively using the methods we have used for COVID-19. We have assigned HIV to 1980, although its mortality was spread over many years. Additional references are in the Supplementary Materials.

Table 1). More recent decades have fewer years between outbreaks, fewer years with no outbreaks, and outbreaks that spread to populations on more continents. Earlier work suggested that, over the past century, viruses are detected in humans at a roughly uniform rate of two novel species per year (*7*). The data illustrated in Fig. 1 show that a higher proportion of these spillover events now gives rise to larger outbreaks. If we express time between outbreaks as cumulative people-years or births, then the rate of pandemic emergence is curiously constant (fig. S1). This result points toward some form of criticality that requires further examination with richer datasets. Nonetheless, it implies that as the number of people alive increases, pandemics will occur more frequently and affect more people.

Costs of pandemics

Pandemics have become more frequent and more costly. We previously made preliminary cost estimates for reducing risks of future infectious outbreaks with pandemic potential and compared these to the cost of COVID-19 after its first 6 months (*9*). Here, we report on a more comprehensive economic approach that estimates the annualized value of lives lost and economic damages for emerging viral zoonoses over the past century. Calculating an annualized cost to viral zoonoses over a long time horizon provides a more robust estimate. It aims to inform policymakers about how much we should spend to prevent spillover each year, rather than an estimate based on a single and outsized pandemic.

To compute how much to spend on preventing spillover, we tabulated every novel viral zoonosis that has appeared since 1918 that killed at least 10 people (Fig. 1 and Table 1). Our core analysis includes Spanish influenza; this improves our ability to calibrate the tail of the distribution composed of severe events that only occur a few times in 100 years. We also present results obtained with that event excluded. Last, we used these data to calibrate a hyperbolic distribution of annual mortality relative to the current world population for novel emerging viral infections. The data provide the frequencies and mean severities of all outbreaks and of severe events. We then use this information to calibrate the remaining parameter of the hyperbolic distribution. See details in the Supplementary Materials.

The baseline expected annual mortality from viral disease epidemics with the current world population is 3.3 million lives. Estimated willingness to pay (WTP) to prevent mortality can range from $107,000 to $6.4 million per life or more, depending on the country's wealth (*10*, *11*). Applying the more conservative range of WTP, we find that avoiding this loss of life translates into a WTP of between $350 billion to $21 trillion annually. The broad range of values arises because we do not know in which countries future pandemics would occur.

Using the upper range of those WTP values and reducing the likelihood of extreme outbreaks by just 10% cut expected deaths by 300,000 and monetized mortality losses by up to $2 trillion each year (Table 2). Strategies that curtail the risk of any epidemic by half would save 1.6 million lives a year and reduce mortality costs by $10 trillion.

Policymakers and the public may neglect threats from low-probability, future catastrophic pandemics (*12*). We show the consequences of such neglect by calibrating a distribution of pandemic severity with data that exclude the Spanish influenza event. This oversight leads us to underestimate expected annual lives lost (and the associated costs) by almost an order of magnitude (Table 2, bottom row).

Beyond the WTP for preventing deaths described in Table 2, viral diseases exact direct economic losses that policymakers can use to justify public expenditures. The economic cost of emerging viral zoonoses comes from the lost fraction of world gross national income (GNI) from disease outbreaks of varying severity. Fan *et al.* (*13*) calculate the average lost GNI from a pandemic as 0.6% of world GNI. Applying that number to the world GNI of $87 trillion in 2019, the average lost GNI for an outbreak is $522 billion. We have observed 28 outbreaks since 1950, so the expected number of outbreaks of any severity per year is 0.40. Thus, the baseline annual expected loss in GNI from viral zoonotic disease outbreaks is $212 billion. If prevention actions cut those economic losses in half in addition to halving mortality costs, then the additional expected annual savings would be $106 billion. These GNI costs are additional to the WTP costs in Table 2.

In our cost estimates, we excluded major outbreaks of pathogens in domestic livestock or crops. The U.K. foot and mouth epidemic

Table 1. Mortality from zoonotic viral emergence since 1918. Mortality rounded to the nearest 10 of novel viral zoonotic outbreaks with greater than 10 deaths since 1918.

Virus	Year	Deaths	World population	Deaths per million
Spanish influenza	1918	50,000,000	1,830,000,000	27,322
Hantaan virus	1951	46,430	2,584,034,261	18
South American hantaviruses	1956	1990	2,822,443,282	0.71
Kyasanur forest disease	1957	1,000	2,873,306,090	0.35
H2N2 influenza	1957	1,100,000	2,873,306,090	383
Junin virus	1958	5,900	2,925,686,705	2.02
Lacrosse virus	1960	300	3,034,949,748	0.10
Machupo virus	1963	290	3,211,001,009	0.09
Marburg virus	1967	370	3,478,769,962	0.11
H3N2 influenza	1968	1,000,000	3,551,599,127	282
Lassa fever	1969	250,000	3,625,680,627	69
Venezuelan equine encephalitis	1969	300	3,625,680,627	0.08
Monkeypox	1970	5,000	3,700,437,046	1.35
Ebola	1976	12,930	4,154,666,864	3.11
Rift Valley fever	1977	3,000	4,229,506,060	0.71
HIV	1980	10,700,000	4,458,003,514	2,400*
Puumala virus	1980	10	4,458,003,514	0.00
Guanrito virus	1989	140	5,237,441,558	0.03
Sin Nombre virus	1993	260	5,581,597,546	0.05
Andes	1995	130	5,744,212,979	0.02
Nipah	1998	200	5,984,793,942	0.03
West Nile	1999	2,330	6,064,239,055	0.38
SARS	2002	770	6,301,773,188	0.12
Chikungunya	2004	35,000	6,461,159,389	5.42
H1N1 influenza	2008	284,000	6,789,088,686	42
Severe fever thrombocytopenia syndrome	2009	370	6,872,767,093	0.05
MERS	2012	860	7,125,828,059	0.12
Zika	2015	50	7,379,797,139	0.01
COVID-19†	2020	4,000,000†	7,794,798,739	496

*HIV mortality spread over the following decades. †COVID-19 deaths are those to July 2021.

of 2001 cost more than $8 billion, and the emergence of bovine spongiform encephalopathy in Europe in the 1990s had similar financial impact (*14*, *15*). The current outbreaks of swine disease in China and Southeast Asia and the continuing spread of chronic wasting disease in the United States are likewise costly. Each of these livestock pathogens may be only a handful of mutations away from triggering a human pandemic. So, too, are the frequent outbreaks of avian influenza in wild and domestic waterfowl. Emerging pathogens of livestock exploit the same routes to spillover as those that cause human pandemics. The mitigation measures that we describe below to prevent future human pandemics will also benefit livestock disease emergence risks. We can depict the costs graphically from the perspective of the cost during the year a major epidemic occurs and the average cost to prevent it.

The estimates in Table 1 also do not fully quantify the annual damage these viruses cause to human lives or the economy. There is no clear way, for example, to estimate the psychological impact of COVID-19 on people who have lost jobs, relatives, or have had to live in isolation. Nor can we easily ascertain additional costs that stem from medical care deferred because of the pandemic. Such costs may remain hidden for years after a pandemic arises. For example, billions of dollars are spent each year to care for individuals infected with HIV (*16*).

PRIMARY PREVENTION

The WHO identifies five phases of infectious disease emergence: pre-emergence, emergence, localized transmission, epidemic, and

Table 2. Expected annual WTP to avoid mortality losses under three scenarios.

	Total lives lost (millions)	Total WTP to avoid lives lost (trillion dollars)
Baseline from observed events	3.3	0.35–21
Extreme outbreaks 10% less likely	3.0	0.32–19
Prevention cuts all frequencies ½	1.7	0.18–11
Baseline without Spanish influenza	0.4	0.04–2.6

pandemic (*17*). We recognize spillover as a sixth and critical step in disease emergence (Fig. 2). Viruses spill over into people from wild animals, sometimes by way of domesticated ones (*18*, *19*). Among many causes, greater human and animal contact, livestock rearing, deforestation, and wildlife hunting and trade stand out as drivers of spillover (*20*).

What can we do to minimize the risk of future outbreaks and increase the speed of detecting novel pathogens before they spread locally and globally? The rest of this paper suggests three major courses of action. First, expand viral discovery and surveillance. Second, monitor wildlife hunting and trade as well as large, high-density animal husbandry for viral infections. Last, prevent deforestation and other land-use changes associated with agricultural expansion.

Viral discovery and surveillance: Foundations of primary prevention

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the agent responsible for COVID-19, is a single-stranded RNA virus. So too were all but one of the other pathogens that have caused novel and lethal pandemics over the past 70 years (Table 1). (The exception is monkeypox, a double-stranded DNA virus.) While other infectious pandemics such as cholera, tuberculosis, and a bevy of antimicrobial-resistant organisms remain major health threats, the ability of single-stranded RNA viruses to emerge and produce global upheaval within a year or two is unparalleled.

Even with many actions, including those presented below, taken to prevent viral spillover, some amount of spillover will inevitably occur. When it does, knowing the pathogens that may transfer from an animal to a person and detecting them quickly can foreshorten outbreak containment and inform primary prevention.

Humanity needs a global viral discovery project if we are to prevent future pandemics. An unbiased polymerase chain reaction–based approach targeting viral families [e.g., (*16*, *17*)] could identify the presence of potentially zoonotic pathogens, which may number in the hundreds of thousands (*23*). In relation to primary prevention, this library would help target where activities should be focused geographically. It would complement further downstream prevention through enabling rapid identification of pathogens when they emerge and accelerating diagnostic test and vaccine development. This pathogen catalog would also benefit livestock and wild animal populations that pathogens threaten.

As an example of the value of viral discovery, we consider Fig. 3 that shows viral accumulation curves for *Pteropid* bats and macaque monkeys. These curves illustrate the rate at which novel viral pathogens are identified with increasing numbers of animals sampled. They reveal the diversity of viruses to which people who encounter them may be exposed. For *Pteropid* bats, the data in Fig. 3 suggest that people may be exposed to ~50% of the potential viruses circulating in the wild population if they contact around 400 animals. As 50% represents approximately 30 viruses, this suggests that we have either been lucky not to have had more transmissions or that most viruses cannot replicate in humans. Roughly 50 to 60 viruses circulate in the bats for which we present data. People in the trade are likely exposed to many or all these viruses.

A caveat for Fig. 3 is that the viruses most frequently encountered—those that form the rising, left side of the accumulation curve—are predominantly those with the highest prevalence in wild host populations. The pathogens detected most frequently are likely to have more efficient transmission and limited virulence. In contrast, rarer viruses will have less efficient transmission, greater virulence, or potentially both. Identifying rare and potentially more virulent viruses will require more extensive sampling of host populations (*25*, *26*). The virulence and transmission efficiency expressed in one host may not correlate to those apparent when the pathogen infects a human or other hosts. Viruses that are relatively harmless in bats, for instance, may be severe in human and other nonvolant mammals (*27*). As a real-world example, we discuss China's efforts at pathogen surveillance in the Supplementary Materials.

The value of viral discovery has its limits. Viral genomes cannot be readily used to ascertain host preference or virulence, although there have been recent advances using metagenomic approaches (*28*). Coupling viral libraries with data from routine serological surveillance of wildlife and livestock farmers, market workers, traders, hunters, wildlife consumers, and other at-risk populations, as well as enhanced surveillance for unusual clusters of symptoms in these groups, would augment the library's value. A viral genomic library attached to serologic data can give insights into spillover rates and accelerate matching viral genotypes with probable hosts (*29*). As with the genomes of newly found viruses, the information obtained must be made nonproprietary and available to scientists from all nations to optimize viral identification.

Agriculture and disease emergence

Agricultural intensification and expansion play a major role in pathogen emergence (*20*, *30*). High-density livestock operations can serve as an opportune environment for spillover from wild animals into livestock or as incubators for pandemic influenza strains. Nipah virus emergence in Malaysia occurred on a large pig farm encircled by mango trees and set on the edge of native forests. This arrangement created favorable conditions for spillover of Nipah virus from bats to pigs and from pigs to people (*31*, *32*). Large pig and poultry farms are where the genetic reassortment needed to source pandemic influenza strains may most likely occur (*33*, *34*).

A distinct risk for spillover arises from the farming of wild animals. This practice has grown in the past two decades, and some advocate its use to reduce pressure on wild animal populations (*35*). With increasing headcounts and proximity to people, wild animal farms represent an emerging spillover risk (*36*).

Feeding 8 billion people today and many more in the coming decades puts pressure to convert forests and other lands into farms. Conversion of savannahs is also a source of pathogens that we discuss in the Supplementary Materials. Agriculture must be reformed

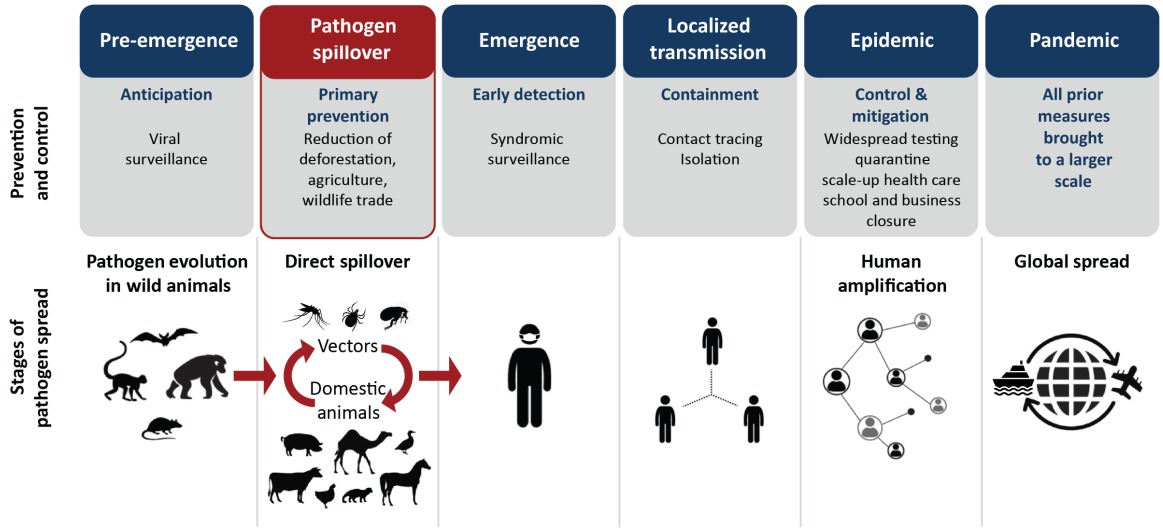

Fig. 2. Phases of pathogen emergence, from local to global. The World Health Organization identifies five phases to which we have added a sixth: pathogen spillover (in red).

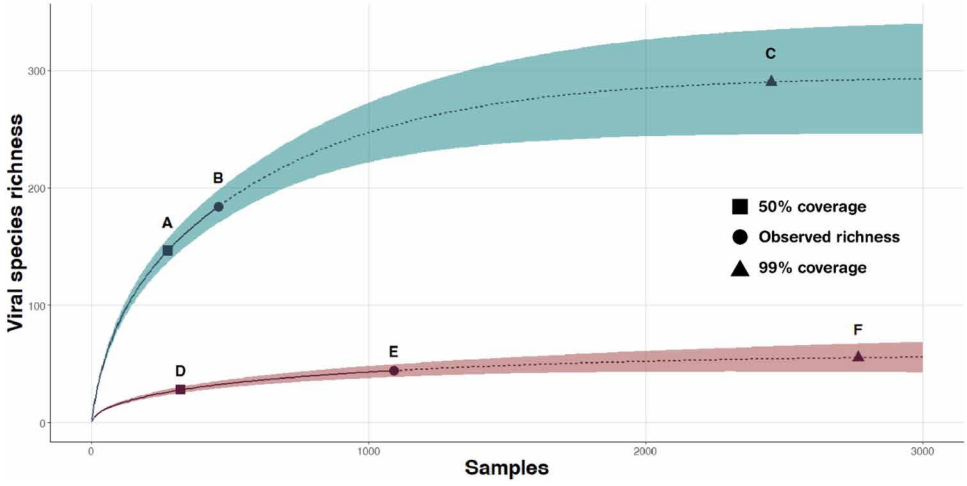

Fig. 3. Viral accumulation curves illustrating the rate at which novel viral pathogens are identified with increasing numbers of animals sampled. Viral species richness increases for macaque monkeys (blue) and *Pteropid* bats (red) with the number of animals sampled. Solid lines are from rarefaction; dotted lines are extrapolations (using double sample size). Dots A (samples 310 and richness 141) and D (samples 325 and richness 26) represent 50% sample of sample coverage, and dots C (samples 2325 and richness 284) and F (samples 2705 and richness 52) represent 99% of sample coverage. Dots B and E are the observed viral species richness. Shaded areas represent 95% confidence intervals. Data are from (*21*, *24*).

to minimize, or ideally reverse, land conversion (*37*), and demand for less sustainable food must also be curtailed (*38*–*40*).

An analysis of the hundred largest zoonotic outbreaks over the past 30 years points to agricultural intensification as a primary driver of the resurgence of older pathogens such as anthrax, brucellosis, and salmonellosis (*41*). All the measures that we propose to reduce novel pathogen emergence will also reduce the re-emergence of pathogens that have plagued humans and our domesticated animals for millennia.

The need for more veterinarians

Veterinarians have had a principal role as sentinels for disease emergence. They have been the principal proponents of the One Health concept that integrates human and animal welfare broadly and infectious diseases in particular (*42*). A country with few veterinarians, many reservoir species, and many people who consume or trade wildlife will be at greater risk for zoonoses. Figure 4 shows the ratio of veterinarians to nonveterinarians against the geographical size of a nation.

Only a small proportion of veterinary workers in any nation work on wildlife diseases and unusual viruses. Most are concerned with domestic livestock and pets. Figure 4 provides a rough view of how easily a virus may slip unnoticed into domestic livestock and then into the human population in places such as Africa, where few veterinarians practice. Southeast Asian countries tend to have more laboratory virologists to examine pathogens that have successfully

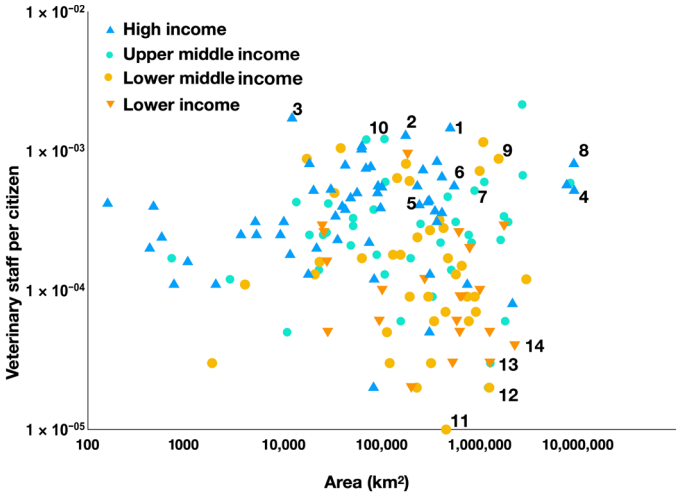

Fig. 4. The national density of veterinarians. The ratio of veterinarians to civilians plotted against the nation's area. Countries are color-coded based on World Bank income categories. The text mentions names in bold. Data were absent from the OIE database for several nations, including China and Russia.

established in previously uninfected hosts but relatively few people to monitor for pathogen emergence.

Figure 4 demonstrates the national density of veterinarians is independent of the geographical size of a nation. The plot has significant scatter ranging across two orders of magnitude from 2 veterinarians per 100,000 people in many parts of Africa to 2 per 1000 people in Spain (1), Uruguay (2), and the Falkland Islands (3). St. Maarten in the Caribbean has one veterinarian per thousand inhabitants. The United States (4), United Kingdom (5), and France (6) are roughly on a par with Venezuela (7) and not as well-endowed for veterinarians as Canada (8), Mongolia (9), or Cuba (10). Papua New Guinea (11), Angola (12), Peru (13), and South Africa (14) have relatively large land areas and few veterinarians to monitor disease in livestock, letting alone wild animals. More well-trained veterinarians, especially in spillover hotspots, are needed to prevent spillover from wildlife or livestock into people.

Wildlife hunting and trade

The human demand for wild animals also drives pathogen spillover (*43*). Spillover can occur when people hunt or consume wild animals (*44*, *45*). It can occur at any point in wildlife trade, from the individuals who hunt and capture wild animals to those who consume, wear, or keep wildlife as pets, and everyone in between. Pathogen prevalence in traded animals may grow along the chain of wildlife trade (*46*). Animals in trade, including wild animals raised in captivity, are often forced into close quarters and unnatural associations with other species (*47*). These animals may also have higher pathogen prevalence than their wild counterparts (*4*).

The global scope of wildlife hunting and trade is notable for its breadth and depth. The wildlife trade alone ensnares a quarter of all mammal species, including high percentages of rodents, bats, and primates, which host a high diversity of viral zoonoses (*22*, *48*, *49*). The wild animal biomass consumed is also large. In 2010, the annual take of wild animals from the Congo and Amazon basins was between 1.3 million and 4.5 million metric tons, respectively (*50*). (These are the equivalent weight of 1.8 and 6.2 million cows.) Such capture rates have eradicated entire populations of wildlife species from some countries. For example, in the past 40 years, 12 large vertebrate populations have been extirpated from Vietnam (*51*). Globally, wildlife hunting pressure threatens more than 300 terrestrial mammal species with extinction (*52*).

Need for better viral surveillance and data on trade

Data on the species, trade volumes and routes, and long-term trends in legal intranational and international wildlife trade (and certainly the illegal trade) are generally too sparse or unreliable to assess zoonotic disease risk quantitatively (*53*). Inadequate monitoring and surveillance of wildlife trade enable zoonotic disease emergence. Examples include the spread of the Ebola Reston virus from the Philippines to Maryland, USA via the laboratory animal primate trade (*54*) and the spread of monkeypox virus from Ghana to Texas through the pet trade in pouched rats (*47*).

We consider some of the better data available of international wildlife trade in the Supplementary Materials. There, we illustrate the limitations of the present data shortfalls and possible actions to improve surveillance.

Creating institutional capacity for primary prevention in wildlife trade

The world lacks the institutional capacity to monitor wildlife trade for zoonotic disease risk. The Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) is the principal international treaty governing trade in 36,000 plant and animal species listed by the Convention, and 183 countries are parties to it. The secretariat for CITES has stated explicitly that it is not within its mandate to monitor pathogens in the wildlife trade (*55*). The World Organization for Animal Health (OIE) is perhaps the most closely aligned to this purpose. It conducts rigorous assessments of infectious disease threats to livestock within trades of animals and their products. The OIE has more than 180 member states and authority to list diseases as notifiable, linked to World Trade Organization mandates. Member countries must report annually on the status of a notifiable disease in their country, which measures they are taking to test, control, or eradicate it, and whether they are designating areas as disease-free. Diseases are listed as notifiable primarily if they threaten profits from livestock trade. The OIE also has the authority and capacity to list diseases that threaten wildlife through environmental sources. It rarely uses it. OIE did list amphibian chytridiomycosis, as the disease threatens the trade in amphibians because of its spread in wild populations (*56*).

A sufficient budget for CITES, OIE, and national agencies charged with monitoring animal importation to conduct the research, monitoring, and enforcement necessary to reduce risky trade could greatly lower spillover risk. More funds alone will not suffice to provide the surveillance needed. Critical personnel to conduct surveillance, such as veterinarians, may be unavailable in many high-risk locations.

Wildlife trade management in China

Past zoonotic disease emergence events informed China's response to COVID-19. SARS, caused by a bat-borne coronavirus, emerged in China in 2002. Starting in 2003, highly pathogenic avian influenza has emerged and re-emerged in China among waterfowl and poultry, and occasionally among people (*34*). In 2017, another bat-borne coronavirus spilled into pigs, leading to the death of more than 24,000 piglets in southern China (*57*). Re-emerging zoonotic diseases including rabies, brucellosis, hemorrhagic fever with renal syndrome,

and severe fever with thrombocytopenia syndrome continue to afflict China.

With the advent of COVID-19, China has moved to place greater restrictions on wildlife trade. In January 2020, the Ministry of Agriculture, the State Administration for Market Regulation, and the National Forestry and Grassland Administration issued a temporary ban on all wildlife trade until the end of the epidemic. In February 2020, the Standing Committee of China's National People's Congress permanently banned wildlife food consumption to protect health. Food consumption of all terrestrial wildlife is prohibited except for a limited number of farmed species. Loopholes allow wildlife trade for fur, medicine, exhibition, pets, and research (*58*).

China's first Biosecurity Law entered into force in April 2021. The law aims to prevent and control infectious diseases and animal and plant epidemics, as well as to promote the development of biotechnology. A revision of the Animal Epidemic Prevention Law released in January 2021 specifies quarantine requirements for farmed wildlife and strengthens wildlife disease surveillance. We consider the wider implications of prevention measures in China and internationally in the Supplementary Materials. We also consider there the costs of reducing China's consumption of wildlife for food.

Deforestation

Deforestation is arguably the leading driver of pathogen emergence (*59*–*61*) and inarguably the greatest threat to terrestrial biodiversity (*62*, *63*). Between 2000 and 2012, 2.3 million km^2 of forest were lost globally and the loss in the tropics increased by 3% or 2,101 km^2/year (*64*). Deforestation, particularly in the tropics, brings people into contact with animals as they enter forests to clear them for agriculture or timber, build roads, or work in mines.

Past zoonotic viral disease emergence has been tied to deforestation (*65*). Models of global spillover risk based on the importance of land cover, especially forest cover, connect to novel virus emergence (*59*, *66*).

Figure S3 (A to E) shows maps of bat, primate, and rodent species richness; tropical and subtropical deforestation; and human population growth (per square kilometer from 2000 to 2020). We map wild bat, primate, and rodent orders as they have unusually high proportions of zoonotic viruses (*22*, *49*). Their diversity is greatest in tropical and subtropical forests, although their patterns differ between regions. These maps illustrate where spillover risk may be possible but not necessarily apparent from past emergence events.

Between 2000 and 2020, as in prior decades, deforestation was most extensive in the Amazon basin, West and Central Africa, and Southeast Asia (fig. S3D). Deforestation creates forest edges that facilitate contact between people and viral reservoir hosts [e.g., (*67*, *68*)]. For example, the detail in fig. S4A shows the deforestation in the Amazon. Linear patterns occur along roads, which also act as foci for further deforestation. Areas without deforestation are often Indigenous-led protected areas (*69*).

Rapid population growth has occurred in parts of South America, Asia, and Africa (fig. S3E) but does not usually correlate well with deforestation. The juxtaposition of rapid human population growth and deforestation in West Africa likely contributed to the unprecedented scale and location of the 2014 Ebola outbreaks (*67*).

To explore the interplay of deforestation, population, and host species diversity and to illustrate pathways to prevent spillover near forested regions, the Supplementary Materials discuss two contrasting examples, the Brazilian Amazon and Kibale National Park in Uganda.

Various evidence points to the need to mitigate Amazonian deforestation as a cornerstone of primary pandemic prevention. First, the Amazon is among the world's most biodiverse regions, particularly for bats and primates (fig. S3, A and B). While people may not eat bats in the Amazon, they commonly hunt primates and large rodents for food (*70*, *71*). Second, since 2012, deforestation in the Brazilian Amazon has risen due to persistent demand for livestock grazing land, with weakening of the country's forest protection policies and threats to Indigenous stewardship (*72*). We expect the rise in deforestation there to increase the risk from endemic infectious diseases (*73*). Third, Amazonian cities have limited capacity to contain infectious epidemics. Last, the Amazon's connectivity is growing. Flights connect its cities to major population centers in Brazil and abroad, such as Miami in the United States and Panama, which are the crossroads of trade across the Americas and two oceans.

Smaller forests are also important sources of emergent pathogens due to their proximity to densely populated settlements. Kibale National Park is a mere 795 km^2 but is one of the few remnant forest patches along the eastern limits of the African equatorial rainforest. Some of Africa's fastest-growing human populations surround it (fig. S6).

The Amazon example shows that policy improvement, coupled with improved monitoring and enforcement, can be effective at large scales. Countries may achieve robust forest conservation with policy measures similar to the Brazilian Amazon example (*74*). Recent experiments in Kibale have shown promise in tying conservation to investments in healthcare system strengthening, which the communities living in and around forests may desire (*75*).

THE COSTS OF PRIMARY PREVENTION

Previously, we provided preliminary estimates of how much primary prevention might cost (*9*). We presented six estimates of annual costs. We estimated $19 billion to close down China's wildlife farming industry, based on a Chinese report (*76*). A total of $476 million to $842 million were needed to reduce spillover from livestock based on (*77*) and the World Bank One World One Health farm biosecurity intervention program (*78*). The report provided the cost of implementing enhanced biosecurity for zoonoses around farming systems in low to middle income countries, and we extrapolated those data to the 31 countries with high risk of wildlife viral spillover risk from (*65*, *66*).

The other four were our estimates for viral discovery ($120 million to $340 million), early detection and control ($217 million to $279 million), wildlife trade surveillance ($250 million to $750 million), and programs to reduce spillover from livestock ($476 million to $852 million). The most complicated estimate was reducing deforestation by half ($1.53 billion to $9.59 billion). These broad-brush estimates provide essential insights into the relative magnitude of each task. Here, we provide more details of the underlying issues determining costs and the challenges of implementation.

The costs of viral discovery and spillover surveillance

To compute costs for viral discovery, we chose to use the proposed budget of the Global Virome Project, a decade-long project that seeks to identify 70% of the unknown potentially zoonotic viruses in wildlife globally. It has an estimated budget of $120 million to $340 million per year (*23*).

To determine the costs of early detection and control, we focused attention on the country surveillance targets of the decade-long United States Agency for International Development (USAID)

PREDICT project. The countries were identified due to their high risk of disease emergence from (*65*, *66*) and in Latin America, Africa, South, and Southeast Asia. PREDICT-1 worked in 20 countries for 5 years (Bangladesh, Bolivia, Brazil, Cambodia, Cameroon, China, Democratic Republic of Congo, Gabon, Indonesia, Lao PDR, Malaysia, Mexico, Nepal, Peru, Republic of Congo, Rwanda, Tanzania, Thailand, Uganda, and Vietnam) (*79*). PREDICT-2 worked in a further 11 countries (Cote d'Ivoire, Egypt, Ethiopia, Ghana, Guinea, Jordan, Kenya, Liberia, Myanmar, Senegal, and Sierra Leone), with minimal work in two others (India and Mongolia) (*80*). We assumed all programs in this section would need to run in all these 31 high-risk countries.

We identified pilot research projects that successfully identified spillover events for the Nipah virus in Bangladesh (*81*) and SARS-related coronaviruses in China (*82*). We analyzed budgets of the cited grant numbers in these papers by searching the U.S. National Institutes of Health database (*83*) and estimated the amount spent on surveillance in the field. To maximize the likelihood of early detection of small numbers of spillover cases, we estimated that these programs would need to be scaled up by an order of magnitude. We based this scaling on the three Nipah virus spillover events identified in Bangladesh by Nikolay *et al.* (*81*) and the geographical coverage of the "Nipah belt" that this project funded for syndromic hospital surveillance. We used the published budgets in the request for proposal document for National Institute of Allergy and Infectious Diseases Centers for Research in Emerging Infectious Diseases (NAIAD CREID) contracts (previously called "Emerging Infectious Disease Research Centers"). These are designed specifically to identify early spillover in emerging disease hotspot countries (*84*). We then estimated the cost of control programs for these early outbreaks to include testing, isolation, and quarantine of small numbers of cases to reduce stransmission based on costs from the budgets that funded (*81*), available in (*83*), and of partial budgets allocated for (*84*):

1) Pilot projects ($500 thousand to $700 thousand per year, 10 per country for 31 countries) = $155 million to $217 million.

2) NIAID CREID contracts ($1.5 million per year, for 31 countries) = $46.5 million per year.

3) Isolation and quarantine ($500 thousand per year, for 31 countries) = $15.5 million per year.

Summing these three programs, the total cost of early detection and control programs for the 31 high-risk countries would be between $217 million to $279 million per year.

The costs of monitoring and managing wildlife trade

Our estimate of monitoring wildlife trade had a relatively large range ($250 million to $750 million) because of the considerable complexities of expanding existing programs, which we now explore.

We suggest expanding the OIE's scope to achieve a more holistic approach to managing disease emergence from wildlife trade. This is consistent with recommendations put forward by the OIE itself in early 2021 (*85*). To do this will require more resources. The annual 2018 operating budget of the OIE was $35 million. Substantially increasing this budget should provide resources sufficient to drive a globally significant disruption of this pathway for disease emergence. The costs of surveillance could be covered by governments or passed to the wildlife trade businesses (e.g., fashion houses, pet, and aquarium sellers) and consumers, with traders requiring permits before import. Permits are already necessary for CITES-listed species. This must be the new cost of doing business in a world that must now live with COVID-19.

While CITES may not be well-positioned to address pathogen risk in wildlife trade, wildlife enforcement networks may. They are underfunded for this task. The ASEAN Wildlife Enforcement Network (WEN) is the longest standing. It launched on 1 December 2005, with 10 member countries, and has an annual budget of some $30,000 (*86*).

The current annual budgets of all WENs are low and insufficient to execute their missions. The U.S. State Department has been the primary supporter of WENs. Its funds channel through nongovernmental organizations (NGOs), such as TRAFFIC and WildAid. They have budgets of $17.4 million and $10.4 million (*87*, *88*), respectively. The U.S. State Department has been the sole supporter of the Central American and Dominican Republic Wildlife Enforcement Network (CAWEN or ROAVIS in Spanish). It provides additional support to related counter-trafficking of wild flora and fauna.

The Wildlife Trafficking, Response, Assessment and Priority Setting Project (TRAPS), financed by USAID and implemented by TRAFFIC and the International Union for Conservation of Nature (IUCN), identifies and advances interventions to break trafficking chains and disrupt organized criminal trade networks (*89*). Reducing Opportunities for Unlawful Transport of Endangered Species is a sister program to TRAPS and provides data analytics to support the transportation sector in battling illegal wildlife trade (*90*).

Other wildlife conservation networks supported by NGOs or countries offer similar opportunities to monitor zoonotic disease emergence from the wildlife trade. For example, "Red Jaguar" is supported by the Europe–Latin America Technical Assistance Programme against Transnational Organized Crime (El PAcCTO). It seeks to combat environmental crimes, including wildlife trafficking in Latin America. The U.S. Department of Interior's International Technical Assistance Program can extend its support for this effort, which closely aligns with WENs. It promotes more broadly based wildlife conservation and disease surveillance. Funding to support WENs and other transboundary law enforcement efforts is crucial to building the capacity to respond effectively to spillover risk from international wildlife trafficking.

As a major player in global wildlife trade, the United States has an incentive to lead the development of shared objectives and, ultimately, regional funding mechanisms for the self-sufficiency of WENs. They need between $0.5 million to $1 million per year to operate effectively. That sum is more than 20 times the amount ASEAN has had (*86*). The CITES Secretariat has the standing and international reach to advance WENs zoonotic spillover prevention measures as part of WENs' trade monitoring protocols. These measures should be buttressed through coordination with OIE, as would be consistent with the CITES-OIE memorandum of understanding.

The costs of managing landscapes and protecting forests

In the Supplementary Materials, we map out the species richness of bats, primates, and rodents—the three taxa most likely to cause viral spillover. More than two-thirds of all known species live between 30°N and 30°S. We also show the past two decades of deforestation and human population increase. Bats are most diverse in the Amazon, primates in the Congo, and rodents have major centers of diversity in South America, Africa, and Southeast Asia. Roads deep into the Amazon created extensive edge areas bringing people into contact with exceptionally diverse vertebrate communities. In West and Central

Africa, rapid human population growth into previously forested areas spurred wild animal meat consumption and the various HIV spillovers.

Previously, we used a broad range of evidence-based costs associated with preventing deforestation to estimate that cutting deforestation by half in emerging infection hotspots would cost between $1.53 billion and $9.59 billion per year (*9*). Using the low-end cost model estimates, 50% reduction of deforestation in the 10% of the tropics that are emerging infection hotspots and 34% reduction of deforestation in other tropical forests carry an annual cost of $3.23 billion (2020 USD) (*91*). The Supplementary Materials consider the costs of slowing deforestation for the Amazon, where population densities are low and for Kibale National Park, next to one of Africa's most rapidly expanding populations.

Several policies enabled better protection of the Amazon. These policies expanded protected areas, recognized Indigenous territories, put market restrictions on illegal landholdings, placed credit restrictions on municipalities with high deforestation rates, and created payment for ecosystem service programs benefiting small farmers (*92*, *93*). State-of-the-art science satellite monitoring and improved enforcement of existing laws buttressed these policies (*92*).

These actions to curtail deforestation cost the Brazilian government $1 billion per year (~0.1% of Brazil's total federal budget), primarily not only from federal funds but also with contributions from state and cities (*93*). An Amazon Fund, including a $1-billion commitment from Norway between 2009 and 2019, supported actions to reduce deforestation (*92*).

Reductions in deforestation for the sparsely populated and relatively intact Amazon were approximately $650 spent per hectare saved during 2005–2012 or roughly $93 per hectare per year on average. In contrast, thousands of dollars per hectare would pay the full opportunity cost to maintain privately held forest.

Conservation investments in more densely populated and fragmented forests differ. In one such place, Kibale National Park, Uganda, costs for community health system strengthening, education, law enforcement, and general park operations sum to $33 per hectare (estimated based on a compilation by authors of expenditures for programs in Kibale; data are available on request). When we apply this to the approximately 1,032,000 km^2 of forest in emerging infection hotspots worldwide (*66*, *91*), the sum is $3.3 billion per year.

DISCUSSION

Costs and benefits

Here, we estimate the annualized economic and health costs of viral zoonotic emergence and provide primary prevention activities and capacity building estimates substantially refined from prior work. We find that the sum of our median cost estimates of primary prevention (~$20 billion) are ~$^1/_{20}$ of the low-end annualized value of lives lost to emerging viral zoonoses and <$^1/_{10}$ of the annualized economic losses.

Our estimates of annualized WTP for the primary prevention of viral zoonoses depend heavily on severe events such as COVID-19, HIV, and Spanish influenza. Countervailing forces bear upon pandemic risk. Risks will fall with advances in technology that enable more rapid diagnostic tests, vaccines, and medications for newly emergent diseases. The efficacy of these advances depends on expanding viral surveillance in ways that increase our ability to develop tests and vaccines rapidly and deploy them widely. In addition, investments in strengthening health care systems may substantially reduce the disease burdens that exact heavy human and economic tolls in much of the world (*94*). They may also enhance the ability to detect and monitor disease outbreaks. At the same time, more people are living in densely populated cities, global travel has proliferated, and governance is unstable in many countries. All of these can increase the risk of disease spread and impact. More research dedicated to understanding how urbanization, global travel, and contact with more remote communities may alter the risk of pathogen spread would better inform potential damages from disease emergence.

We underestimate the economic and health costs of emerging viral zoonoses as we have omitted multiple causes of indirect damage. The estimates in Table 2 do not include costs from, as examples, (i) morbidity, including, e.g., the psychological harms that result from lost jobs, lost relatives, or social isolation; (ii) delayed medical treatments; or (iii) loss or delays of education. In short, the WTP for preventing death (in the value of a statistical life) from an emerging virus captures only a fraction of the value that may come from primary prevention activities.

The distinction between primary prevention and those actions taken after emergence has occurred is not semantic. The former creates a broad sweep of benefits, while the latter tends to affect a single disease. Most obviously, a vaccine can be effective at reducing the prevalence of a single, currently circulating, infectious disease, but it can never prevent the emergence of novel pathogens.

Consider preventing deforestation. It avoids carbon emissions, conserves water supplies, protects Indigenous Peoples' rights, conserves biodiversity, and suppresses the emergence of novel and well-known pathogens (*95*). Many of these values, especially emerging infectious disease risk abatement, are poorly understood and merit further scientific inquiry. Lacking a greater understanding of these values limits optimizing investments and decision-making to protect health and nature (*96*). Yet, considering the relatively better-known values—such as for carbon sequestration—the benefits of protecting forests are potentially massive, independent of any effect on pandemic risk reduction (*9*).

Furthermore, while growing urban populations and more frequent global travel amplify pandemic risks, the root cause of viral pandemics lies in a pathogen's movement from an animal to a person. No amount of travel restriction, nor surveillance, nor outmigration from cities is likely to prevent spillover.

In addition, the viral prospecting that forms a significant component of spillover prevention will concomitantly speed the development of tests and vaccines that will be essential components of control once spillover has occurred. Recent studies point to powerful new methods of identifying and prioritizing potential human infecting viruses from their genome sequences (*97*). Such advances would massively increase the cost efficiency of the Global Virome databases described here.

The case for prevention

We propose primary prevention actions and recommendations for their implementation as a blueprint for decision-makers to forestall the next viral pandemic. Our estimates of their cost-effectiveness would benefit from greater certainty as to how great a reduction of viral zoonotic disease emergence events would be achieved were

they implemented. Notwithstanding this, the orders of magnitude difference in costs between primary prevention actions and actions that work to control epidemics and pandemics make even small effects worthwhile. Even a 1% reduction in risk of viral zoonotic disease emergence would be cost-effective.

While each of the actions that we propose can reduce the potential threat of future pandemics, no single intervention will prevent a pandemic. One must view these interventions as complementary wedges akin to those proposed to slow and reverse climate change and biodiversity loss (*40*, *98*). Their implementation can create a significant number of jobs across a range of skills as the global economy reconfigures in the wake of the pandemic.

The health, societal, and economic shocks from the COVID-19 pandemic compel consideration of preventing similar future pandemic disasters. To date, most money has been spent after viruses reach epidemic or pandemic scale, and their economic and health damages have grown immensely. Monothetic "magic bullets," including diagnostic tests, treatments, and vaccines, failed to control COVID-19 as it spread around the globe and exacted the largest health and economic toll of any pathogen in recent history. This makes plain that we cannot solely rely upon post-spillover strategies to prevent a similar fate in the future.

We argue that substantial gaps in knowledge, institutional capacity, and financial resources limit the ability to avert pathogen emergence. We recommend scientific inquiry, policy actions, and financial and organizational resources needed to forestall the next pandemic and estimate that primary pandemic prevention actions are remarkably inexpensive compared to the many lives emerging viral zoonoses take or the direct economic damage they cause. The findings and recommendations of this paper bear upon recommendations that will emerge from the Convention on Biological Diversity's 15th Conference of the Parties as well as ongoing, high-level meetings to determine the most prudent paths forward to address pandemic risk and climate change.

SUPPLEMENTARY MATERIALS

Supplementary material for this article is available at https://science.org/doi/10.1126/sciadv.abl4183

REFERENCES AND NOTES

1. C. Elias, J. N. Nkengasong, F. Qadri, Emerging infectious diseases — Learning from the past and looking to the future. *N. Engl. J. Med.* **384**, 1181–1184 (2021).
2. A world in disorder: Global Preparedness Monitoring Board Annual report 2020 (World Health Organization and World Bank, Geneva, 2020).
3. Progress Note of the G20 High-Level Independent Panel on Financing the Global Commons for Pandemic Preparedness and Response (G20, 2021); https://pandemic-financing.org/wp-content/uploads/2021/05/Progress-Note-of-the-HLIP-Final.pdf.
4. S. S. Morse, J. A. K. Mazet, M. Woolhouse, C. R. Parrish, D. Carroll, W. B. Karesh, C. Zambrana-Torrelio, W. I. Lipkin, P. Daszak, Prediction and prevention of the next pandemic zoonosis. *Lancet* **380**, 1956–1965 (2012).
5. M. E. J. Woolhouse, S. Gowtage-Sequeria, Host range and emerging and reemerging pathogens. *Emerg. Infect. Dis.* **11**, 1842–1847 (2005).
6. E. C. Holmes, S. A. Goldstein, A. L. Rasmussen, D. L. Robertson, A. Crits-Christoph, J. O. Wertheim, S. J. Anthony, W. S. Barclay, M. F. Boni, P. C. Doherty, J. Farrar, J. L. Geoghegan, X. Jiang, J. L. Leibowitz, S. J. D. Neil, T. Skern, S. R. Weiss, M. Worobey, K. G. Andersen, R. F. Garry, A. Rambaut, The origins of SARS-CoV-2: A critical review. *Cell* **184**, 4848–4856 (2021).
7. M. E. Woolhouse, R. Howey, E. Gaunt, L. Reilly, M. Chase-Topping, N. Savill, Temporal trends in the discovery of human viruses. *Proc. Biol. Sci.* **275**, 2111–2115 (2008).
8. F. C. J. Berthe, T. Bouley, W. B. Karesh, I. C. Legall, C. C. Machalaba, C. A. Plante, R. M. Seifman, One health: Operational framework for strengthening human, animal, and environmental public health systems at their interface (World Bank Group, 2018); https://documents.worldbank.org/en/publication/documents-reports/documentdetail/961101524657708673/one-health-operational-framework-for-strengthening-human-animal-and-environmental-public-health-systems-at-their-interface.
9. A. P. Dobson, S. L. Pimm, L. Hannah, L. Kaufman, J. A. Ahumada, A. W. Ando, A. Bernstein, J. Busch, P. Daszak, J. Engelmann, M. F. Kinnaird, B. V. Li, T. Loch-Temzelides, T. Lovejoy, K. Nowak, P. R. Roehrdanz, M. M. Vale, Ecology and economics for pandemic prevention. *Science* **369**, 379–381 (2020).
10. W. K. Viscusi, C. J. Masterman, Income elasticities and global values of a statistical life. *J. Benefit Cost Anal.* **8**, 226–250 (2017).
11. J. K. Hammitt, Valuing mortality risk in the time of COVID-19. *J. Risk Uncertain.* **61**, 129–154 (2020).
12. N. Gennaioli, A. Shleifer, R. Vishny, Neglected risks: The psychology of financial crises. *Am. Econ. Rev.* **105**, 310–314 (2015).
13. V. Y. Fan, D. T. Jamison, L. H. Summers, Pandemic risk: How large are the expected losses? *Bull. World Health Organ.* **96**, 129–134 (2018).
14. M. J. Keeling, M. E. Woolhouse, D. J. Shaw, L. Matthews, M. Chase-Topping, D. T. Haydon, S. J. Cornell, J. Kappey, J. Wilesmith, B. T. Grenfell, Dynamics of the 2001 UK foot and mouth epidemic: Stochastic dispersal in a heterogeneous landscape. *Science* **294**, 813–817 (2001).
15. R. M. Anderson, C. A. Donnelly, N. M. Ferguson, M. E. J. Woolhouse, C. J. Watt, H. J. Udy, S. MaWhinney, S. P. Dunstan, T. R. E. Southwood, J. W. Wilesmith, J. B. M. Ryan, L. J. Hoinville, J. E. Hillerton, A. R. Austin, G. A. H. Wells, Transmission dynamics and epidemiology of BSE in British cattle. *Nature* **382**, 779–788 (1996).
16. Global Burden of Disease Health Financing Collaborator Network, Spending on health and HIV/AIDS: Domestic health spending and development assistance in 188 countries, 1995–2015. *Lancet* **391**, 1799–1829 (2018).
17. World Health Organization, *Managing epidemics* (World Health Organization, 2018); www.who.int/emergencies/diseases/managing-epidemics-interactive.pdf.
18. J. O. Lloyd-Smith, D. George, K. M. Pepin, V. E. Pitzer, J. R. C. Pulliam, A. P. Dobson, P. J. Hudson, B. T. Grenfell, Epidemic dynamics at the human-animal interface. *Science* **326**, 1362–1367 (2009).
19. C. Gortazar, L. A. Reperant, T. Kuiken, J. de la Fuente, M. Boadella, B. Martínez-Lopez, F. Ruiz-Fons, A. Estrada-Peña, C. Drosten, G. Medley, R. Ostfeld, T. Peterson, K. C. VerCauteren, C. Menge, M. Artois, C. Schultsz, R. Delahay, J. Serra-Cobo, R. Poulin, F. Keck, A. A. Aguirre, H. Henttonen, A. P. Dobson, S. Kutz, J. Lubroth, A. Mysterud, A. A. Aguirre, H. Henttonen, A. P. Dobson, S. Kutz, J. Lubroth, A. Mysterud, Crossing the interspecies barrier: Opening the door to zoonotic pathogens. *PLOS Pathog.* **10**, e1004129 (2014).
20. B. A. Jones, D. Grace, R. Kock, S. Alonso, J. Rushton, M. Y. Said, D. McKeever, F. Mutua, J. Young, J. McDermott, D. U. Pfeiffer, Zoonosis emergence linked to agricultural intensification and environmental change. *Proc. Natl. Acad. Sci. U.S.A.* **110**, 8399–8404 (2013).
21. S. J. Anthony, A. Islam, C. Johnson, I. Navarrete-Macias, E. Liang, K. Jain, P. L. Hitchens, X. Che, A. Soloyvov, A. L. Hicks, R. Ojeda-Flores, C. Zambrana-Torrelio, W. Ulrich, M. K. Rostal, A. Petrosov, J. Garcia, N. Haider, N. Wolfe, T. Goldstein, S. S. Morse, M. Rahman, J. H. Epstein, J. K. Mazet, P. Daszak, W. I. Lipkin, Non-random patterns in viral diversity. *Nat. Commun.* **6**, 8147 (2015).
22. K. J. Olival, P. R. Hosseini, C. Zambrana-Torrelio, N. Ross, T. L. Bogich, P. Daszak, Host and viral traits predict zoonotic spillover from mammals. *Nature* **546**, 646–650 (2017).
23. D. Carroll, P. Daszak, N. D. Wolfe, G. F. Gao, C. M. Morel, S. Morzaria, A. Pablos-Méndez, O. Tomori, J. A. K. Mazet, The global virome project. *Science* **359**, 872–874 (2018).
24. S. J. Anthony, J. H. Epstein, K. A. Murray, I. Navarrete-Macias, C. M. Zambrana-Torrelio, A. Solovyov, R. Ojeda-Flores, N. C. Arrigo, A. Islam, S. Ali Khan, P. Hosseini, T. L. Bogich, K. J. Olival, M. D. Sanchez-Leon, W. B. Karesh, T. Goldstein, S. P. Luby, S. S. Morse, J. A. K. Mazet, P. Daszak, W. I. Lipkin, A strategy to estimate unknown viral diversity in mammals. *MBio* **4**, e00598-13 (2013).
25. R. M. Anderson, R. M. May, Population biology of infectious diseases: Part I. *Nature* **280**, 361–367 (1979).
26. R. M. May, R. M. Anderson, Population biology of infectious diseases: Part II. *Nature* **280**, 455–461 (1979).
27. C. E. Brook, M. Boots, K. Chandran, A. P. Dobson, C. Drosten, A. L. Graham, B. T. Grenfell, M. A. Müller, M. Ng, L.-F. Wang, A. van Leeuwen, Accelerated viral dynamics in bat cell lines, with implications for zoonotic emergence. *eLife* **9**, e48401 (2020).
28. F. Young, S. Rogers, D. L. Robertson, Predicting host taxonomic information from viral genomes: A comparison of feature representations. *PLOS Comput. Biol.* **16**, e1007894 (2020).
29. M. J. Mina, C. J. E. Metcalf, A. B. McDermott, D. C. Douek, J. Farrar, B. T. Grenfell, A global Immunological observatory to meet a time of pandemics. *eLife* **9**, e58989 (2020).
30. J. R. Rohr, C. B. Barrett, D. J. Civitello, M. E. Craft, B. Delius, G. A. DeLeo, P. J. Hudson, N. Jouanard, K. H. Nguyen, R. S. Ostfeld, J. V. Remais, G. Riveau, S. H. Sokolow, D. Tilman, Emerging human infectious diseases and the links to global food production. *Nat. Sustain.* **2**, 445–456 (2019).

31. J. R. C. Pulliam, J. H. Epstein, J. Dushoff, S. A. Rahman, M. Bunning, A. A. Jamaluddin, A. D. Hyatt, H. E. Field, A. P. Dobson, P. Daszak; Henipavirus Ecology Research Group (HERG), Agricultural intensification, priming for persistence and the emergence of Nipah virus: A lethal bat-borne zoonosis. *J. R. Soc. Interface* **9**, 89–101 (2012).
32. J. H. Epstein, H. E. Field, S. Luby, J. R. C. Pulliam, P. Daszak, Nipah virus: Impact, origins, and causes of emergence. *Curr. Infect. Dis. Rep.* **8**, 59–65 (2006).
33. J. S. Malik Peiris, L. L. M. Poon, Y. Guan, Emergence of a novel swine-origin influenza A virus (S-OIV) H1N1 virus in humans. *J. Clin. Virol.* **45**, 169–173 (2009).
34. K. S. Li, Y. Guan, J. Wang, G. J. D. Smith, K. M. Xu, L. Duan, A. P. Rahardjo, P. Puthavathana, C. Buranathai, T. D. T. Nguyen, A. T. S. Estoepangestie, A. Chaisingh, P. Auewarakul, H. T. H. Long, N. T. H. Hanh, R. J. R. Webby, L. L. M. Poon, H. Chen, K. F. K. Shortridge, K. Y. Yuen, R. G. Webster, J. S. M. Peiris, Genesis of a highly pathogenic and potentially pandemic H5N1 influenza virus in eastern Asia. *Nature* **430**, 209–213 (2004).
35. L. Tensen, Under what circumstances can wildlife farming benefit species conservation? *Glob. Ecol. Conserv.* **6**, 286–298 (2016).
36. K. Magwedere, M. Y. Hemberger, L. C. Hoffman, F. Dziva, Zoonoses: A potential obstacle to the growing wildlife industry of Namibia. *Infect. Ecol. Epidemiol.* **2**, 18365 (2012).
37. D. Tilman, C. Balzer, J. Hill, B. L. Befort, Global food demand and the sustainable intensification of agriculture. *Proc. Natl. Acad. Sci. U.S.A.* **108**, 20260–20264 (2011).
38. K.-H. Erb, C. Lauk, T. Kastner, A. Mayer, M. C. Theurl, H. Haberl, Exploring the biophysical option space for feeding the world without deforestation. *Nat. Commun.* **7**, 11382 (2016).
39. U. Kreidenweis, F. Humpenöder, L. Kehoe, T. Kuemmerle, B. L. Bodirsky, H. Lotze-Campen, A. Popp, Pasture intensification is insufficient to relieve pressure on conservation priority areas in open agricultural markets. *Glob. Chang. Biol.* **24**, 3199–3213 (2018).
40. D. Leclère, M. Obersteiner, M. Barrett, S. H. M. Butchart, A. Chaudhary, A. De Palma, F. A. J. DeClerck, M. Di Marco, J. C. Doelman, M. Dürauer, R. Freeman, M. Harfoot, T. Hasegawa, S. Hellweg, J. P. Hilbers, S. L. L. Hill, F. Humpenöder, N. Jennings, T. Krisztin, G. M. Mace, H. Ohashi, A. Popp, A. Purvis, A. M. Schipper, A. Tabeau, H. Valin, H. van Meijl, W.-J. van Zeist, P. Visconti, R. Alkemade, R. Almond, G. Bunting, N. D. Burgess, S. E. Cornell, F. Di Fulvio, S. Ferrier, S. Fritz, S. Fujimori, M. Grooten, T. Harwood, P. Havlík, M. Herrero, A. J. Hoskins, M. Jung, T. Kram, H. Lotze-Campen, T. Matsui, C. Meyer, D. Nel, T. Newbold, G. Schmidt-Traub, E. Stehfest, B. B. N. Strassburg, D. P. van Vuuren, C. Ware, J. E. M. Watson, W. Wu, L. Young, Bending the curve of terrestrial biodiversity needs an integrated strategy. *Nature* **585**, 551–556 (2020).
41. P. R. Stephens, N. Gottdenker, A. M. Schatz, J. P. Schmidt, J. M. Drake, Characteristics of the 100 largest modern zoonotic disease outbreaks. *Philos. Trans. R. Soc. B* **376**, 20200535 (2021).
42. T. R. Kelly, W. B. Karesh, C. K. Johnson, K. V. K. Gilardi, S. J. Anthony, T. Goldstein, S. H. Olson, C. Machalaba, J. A. K. Mazet, One health proof of concept: Bringing a transdisciplinary approach to surveillance for zoonotic viruses at the human-wild animal interface. *Prev. Vet. Med.* **137**, 112–118 (2017).
43. W. B. Karesh, R. A. Cook, E. L. Bennett, J. Newcomb, Wildlife trade and global disease emergence. *Emerg. Infect. Dis.* **11**, 1000–1002 (2005).
44. J. Nsio, J. Kapetshi, S. Makiala, F. Raymond, G. Tshapenda, N. Boucher, J. Corbeil, A. Okitandjate, G. Mbuyi, M. Kiyele, V. Mondonge, M. J. Kikoo, M. Van Herp, P. Barboza, R. Petrucci, G. Benedetti, P. Formenty, B. Muyembe Muzinga, O. Ilunga Kalenga, S. Ahuka, H. Fausther-Bovendo, B. K. Ilunga, G. P. Kobinger, J.-J. T. Muyembe, 2017 outbreak of ebola virus disease in Northern Democratic Republic of Congo. *J Infect Dis* **221**, 701–706 (2019).
45. B. H. Hahn, G. M. Shaw, K. M. De Cock, P. M. Sharp, AIDS as a zoonosis: Scientific and public health implications. *Science* **287**, 607–614 (2000).
46. N. Q. Huong, N. T. T. Nga, N. Van Long, B. D. Luu, A. Latinne, M. Pruvot, N. T. Phuong, L. T. V. Quang, V. Van Hung, N. T. Lan, N. T. Hoa, P. Q. Minh, N. T. Diep, N. Tung, V. D. Ky, S. I. Roberton, H. B. Thuy, N. Van Long, M. Gilbert, L. Wicker, J. A. K. Mazet, C. K. Johnson, T. Goldstein, A. Tremeau-Bravard, V. Ontiveros, D. O. Joly, C. Walzer, A. E. Fine, S. H. Olson, Coronavirus testing indicates transmission risk increases along wildlife supply chains for human consumption in Viet Nam, 2013–2014. *PLOS ONE* **15**, e0237129 (2020).
47. Centers for Disease Control and Prevention (CDC), Update: Multistate outbreak of monkeypox—Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003. *MMWR Morb. Mortal. Wkly Rep.* **52**, 642–646 (2003).
48. B. R. Scheffers, B. F. Oliveira, I. Lamb, D. P. Edwards, Global wildlife trade across the tree of life. *Science* **366**, 71–76 (2019).
49. C. K. Johnson, P. L. Hitchens, P. S. Pandit, J. Rushmore, T. S. Evans, C. C. W. W. Young, M. M. Doyle, Global shifts in mammalian population trends reveal key predictors of virus spillover risk. *Proc. Biol. Sci.* **287**, 20192736 (2020).
50. R. Nasi, A. Taber, N. Van Vliet, Empty forests, empty stomachs? Bushmeat and livelihoods in the Congo and Amazon Basins. *Int. For. Rev.* **13**, 355–368 (2011).
51. E. L. Bennett, M. Rao, in *Links between Biodiversity, Conservation, Livelihoods and Food Security: The Sustainable Use of Wild Species for Meat*, S. Mainka, M. Trivedi, Eds. (IUCN, 2002), pp. 39–44.
52. W. J. Ripple, K. Abernethy, M. G. Betts, G. Chapron, R. Dirzo, M. Galetti, T. Levi, P. A. Lindsey, D. W. Macdonald, B. Machovina, T. M. Newsome, C. A. Peres, A. D. Wallach, C. Wolf, H. Young, Bushmeat hunting and extinction risk to the world's mammals. *R. Soc. Open Sci.* **3**, 160498 (2016).
53. H.-K. Chan, H. Zhang, F. Yang, G. Fischer, Improve customs systems to monitor global wildlife trade. *Science* **348**, 291–292 (2015).
54. P. B. Jahrling, T. W. Geisbert, E. D. Johnson, C. J. Peters, D. W. Dalgard, W. C. Hall, Preliminary report: Isolation of Ebola virus from monkeys imported to USA. *Lancet* **335**, 502–505 (1990).
55. Convention on International Trade in Endangered Species, CITES Secretariat's statement in relation to COVID-19 (CITES, 2021); https://cites.org/eng/CITES_Secretariat_statement_in_relation_to_COVID19.
56. L. Schloegel, P. Daszak, A. Cunningham, R. Speare, B. Hill, Two amphibian diseases, chytridiomycosis and ranaviral disease, are now globally notifiable to the World Organization for Animal Health (OIE): An assessment. *Dis. Aquat. Organ.* **92**, 101–108 (2010).
57. P. Zhou, H. Fan, T. Lan, X.-L. Yang, W.-F. Shi, W. Zhang, Y. Zhu, Y.-W. Zhang, Q.-M. Xie, S. Mani, X.-S. Zheng, B. Li, J.-M. Li, H. Guo, G.-Q. Pei, X.-P. An, J.-W. Chen, L. Zhou, K.-J. Mai, Z.-X. Wu, D. Li, D. E. Anderson, L.-B. Zhang, S.-Y. Li, Z.-Q. Mi, T.-T. He, F. Cong, P.-J. Guo, R. Huang, Y. Luo, X.-L. Liu, J. Chen, Y. Huang, Q. Sun, X.-L.-L. Zhang, Y.-Y. Wang, S.-Z. Xing, Y.-S. Chen, Y. Sun, J. Li, P. Daszak, L.-F. Wang, Z.-L. Shi, Y.-G. Tong, J.-Y. Ma, Fatal swine acute diarrhoea syndrome caused by an HKU2-related coronavirus of bat origin. *Nature* **556**, 255–258 (2018).
58. L. Xiao, Z. Lu, X. Li, X. Zhao, B. V. Li, Why do we need a wildlife consumption ban in China? *Curr. Biol.* **31**, R168–R172 (2021).
59. C. L. Faust, H. I. McCallum, L. S. P. Bloomfield, N. L. Gottdenker, T. R. Gillespie, C. J. Torney, A. P. Dobson, R. K. Plowright, Pathogen spillover during land conversion. *Ecol. Lett.* **21**, 471–483 (2018).
60. N. L. Gottdenker, D. G. Streicker, C. L. Faust, C. R. Carroll, Anthropogenic land use change and infectious diseases: A review of the evidence. *Ecohealth* **11**, 619–632 (2014).
61. T. R. Gillespie, K. E. Jones, A. P. Dobson, J. A. Clennon, M. Pascual, COVID-Clarity demands unification of health and environmental policy. *Glob. Chang. Biol.* **27**, 1319–1321 (2021).
62. G. Ceballos, Mammal population losses and the extinction crisis. *Science* **296**, 904–907 (2002).
63. S. L. Pimm, C. N. Jenkins, R. Abell, T. M. Brooks, J. L. Gittleman, L. N. Joppa, P. H. Raven, C. M. Roberts, J. O. Sexton, The biodiversity of species and their rates of extinction, distribution, and protection. *Science.* **344**, 1246752 (2014).
64. M. C. Hansen, P. V. Potapov, R. Moore, M. Hancher, S. A. Turubanova, A. Tyukavina, D. Thau, S. V. Stehman, S. J. Goetz, T. R. Loveland, A. Kommareddy, A. Egorov, L. Chini, C. O. Justice, J. R. G. Townshend, High-resolution global maps of 21st-century forest cover change. *Science* **342**, 850–853 (2013).
65. K. E. Jones, N. G. Patel, M. A. Levy, A. Storeygard, D. Balk, J. L. Gittleman, P. Daszak, Global trends in emerging infectious diseases. *Nature* **451**, 990–993 (2008).
66. T. Allen, K. A. Murray, C. Zambrana-Torrelio, S. S. Morse, C. Rondinini, M. Di Marco, N. Breit, K. J. Olival, P. Daszak, Global hotspots and correlates of emerging zoonotic diseases. *Nat. Commun.* **8**, 1124 (2017).
67. M. C. Rulli, M. Santini, D. T. S. Hayman, P. D'Odorico, The nexus between forest fragmentation in Africa and Ebola virus disease outbreaks. *Sci. Rep.* **7**, 41613 (2017).
68. L. S. P. Bloomfield, T. L. McIntosh, E. F. Lambin, Habitat fragmentation, livelihood behaviors, and contact between people and nonhuman primates in Africa. *Landsc. Ecol.* **35**, 985–1000 (2020).
69. J. M. Adeney, N. L. Christensen, S. L. Pimm, Reserves protect against deforestation fires in the amazon. *PLOS ONE* **4**, e5014 (2009).
70. C. A. Peres, Effects of subsistence hunting on vertebrate community structure in Amazonian forests. *Conserv. Biol.* **14**, 240–253 (2000).
71. H. R. El Bizri, T. Q. Morcatty, J. Valsecchi, P. Mayor, J. E. S. Ribeiro, C. F. A. Vasconcelos Neto, J. S. Oliveira, K. M. Furtado, U. C. Ferreira, C. F. S. Miranda, C. H. Silva, V. L. Lopes, G. P. Lopes, C. C. F. Florindo, R. C. Chagas, V. Nijman, J. E. Fa, Urban wild meat consumption and trade in central Amazonia. *Conserv. Biol.* **34**, 438–448 (2020).
72. M. M. Vale, E. Berenguer, M. Argollo, de Menezes, E. B. Viveiros de Castro, L. Pugliese de Siqueira, R. de Cássia Q Portela, The COVID-19 pandemic as an opportunity to weaken environmental protection in Brazil. *Biol. Conserv.* **255**, 108994 (2021).
73. M. C. Castro, A. Baeza, C. T. Codeço, Z. M. Cucunubá, A. P. Dal'Asta, G. A. De Leo, A. P. Dobson, G. Carrasco-Escobar, R. M. Lana, R. Lowe, A. M. V. Monteiro, M. Pascual, M. Santos-Vega, Development, environmental degradation, and disease spread in the Brazilian Amazon. *PLoS Biol.* **17**, e3000526 (2019).
74. R. DeFries, M. Herold, L. Verchot, M. N. Macedo, Y. Shimabukuro, Export-oriented deforestation in Mato Grosso: Harbinger or exception for other tropical forests? *Philos. Trans. R. Soc. B* **368**, 20120173 (2013).
75. I. J. Jones, A. J. MacDonald, S. R. Hopkins, A. J. Lund, Z. Y.-C. C. Liu, N. I. Fawzi, M. P. Purba, K. Fankhauser, A. J. Chamberlin, M. Nirmala, A. G. Blundell, A. Emerson, J. Jennings, L. Gaffikin, M. Barry, D. Lopez-Carr, K. Webb, G. A. De Leo, S. H. Sokolow, Improving rural health care reduces illegal logging and conserves carbon in a tropical forest. *Proc. Natl. Acad. Sci. U.S.A.* **117**, 28515–28524 (2020).

76. J. Ma, Report on sustainable development strategy of China's wildlife farming industry (Consulting Research Project of Chinese Academy of Engineering, 2017).
77. J. Pike, T. Bogich, S. Elwood, D. C. Finnoff, P. Daszak, Economic optimization of a global strategy to address the pandemic threat. *Proc. Natl. Acad. Sci. U.S.A.* **111**, 18519–18523 (2014).
78. The World Bank, People, Pathogens and Our Planet: The Economics of One Health (The World Bank, 2012).
79. Predict Consortium, Reducing Pandemic Risk, Promoting Global Health (One Health Institute, University of California, 2014); https://ohi.sf.ucdavis.edu/sites/g/files/dgvnsk5251/files/files/page/predict-final-report-lo.pdf.
80. Predict Consortium, PREDICT Annual Report Database (One Health Institute, University of California, 2020); https://ohi.vetmed.ucdavis.edu/programs-projects/predict-project/reports.
81. B. Nikolay, H. Salje, M. J. Hossain, A. K. M. D. Khan, H. M. S. Sazzad, M. Rahman, P. Daszak, U. Ströher, J. R. C. Pulliam, A. M. Kilpatrick, S. T. Nichol, J. D. Klena, S. Sultana, S. Afroj, S. P. Luby, S. Cauchemez, E. S. Gurley, Transmission of Nipah Virus — 14 years of investigations in Bangladesh. *N. Engl. J. Med.* **380**, 1804–1814 (2019).
82. N. Wang, S.-Y. Li, X.-L. Yang, H.-M. Huang, Y.-J. Zhang, H. Guo, C.-M. Luo, M. Miller, G. Zhu, A. A. Chmura, E. Hagan, J.-H. Zhou, Y.-Z. Zhang, L.-F. Wang, P. Daszak, Z.-L. Shi, Serological evidence of bat SARS-related coronavirus infection in humans, China. *Virol. Sin.* **33**, 104–107 (2018).
83. U.S. National Institutes of Health, NIH Research portfolio online reporting tools (RePORT) (2021); https://report.nih.gov.
84. U.S. National Institutes of Health, Funding Opportunities for Emerging Infectious Diseases Research Centers (2021), (available at https://www.niaid.nih.gov/grants-contracts/emerging-infectious-diseases-%0Aresearch-centers.
85. C. Stephen, J. Berezowki, L. P. Carmo, D. de las N. Montano, B. Friker, F. M. M. A. de Sousa, B. Vidondo, A rapid review of evidence on managing the risk of disease emergence in the wildlife trade (Geneva, 2021); https://www.oie.int/fileadmin/Home/eng/Internationa_Standard_Setting/docs/pdf/WGWildlife/OIE_review_wildlife_trade_March2021.pdf.
86. L. Elliott, W. H. Schaedla, in *Handbook of Transnational Environmental Crime*, L. Elliott, W. H. Schaedla, Eds. (Edward Elgar Publishing, 2016), pp. 269–387.
87. TRAFFIC, Our Accounts (TRAFFIC, 2020); www.traffic.org/about-us/our-organisation/our-accounts/.
88. WildAid, Wild Aid Annual Report 2019 (San Francisco, 2019); https://wildaid.org/wp-content/uploads/2020/06/WildAid_Annual-Report-2019.pdf.
89. Traffic, Wildlife TRAPS (2021); www.traffic.org/what-we-do/projects-and-approaches/education-and-outreach/wildlife-traps/.
90. USAID, ROUTES: Reducing Opportunities for Unlawful Transport of Endangered Species (2021); https://routespartnership.org/.
91. J. Busch, J. Engelmann, Cost-effectiveness of reducing emissions from tropical deforestation, 2016–2050. *Environ. Res. Lett.* **13**, 015001 (2017).
92. D. Nepstad, D. McGrath, C. Stickler, A. Alencar, A. Azevedo, B. Swette, T. Bezerra, M. DiGiano, J. Shimada, R. Seroa da Motta, E. Armijo, L. Castello, P. Brando, M. C. Hansen, M. McGrath-Horn, O. Carvalho, L. Hess, Slowing Amazon deforestation through public policy and interventions in beef and soy supply chains. *Science* **344**, 1118–1123 (2014).
93. F. A. F. de Souza Cunha, J. Börner, S. Wunder, C. A. N. Cosenza, A. F. P. Lucena, The implementation costs of forest conservation policies in Brazil. *Ecol. Econ.* **130**, 209–220 (2016).
94. M. H. Bonds, A. P. Dobson, D. C. Keenan, Disease ecology, biodiversity, and the latitudinal gradient in income. *PLOS Biol.* **10**, e1001456 (2012).
95. J. E. M. Watson, T. Evans, O. Venter, B. Williams, A. Tulloch, C. Stewart, I. Thompson, J. C. Ray, K. Murray, A. Salazar, C. McAlpine, P. Potapov, J. Walston, J. G. Robinson, M. Painter, D. Wilkie, C. Filardi, W. F. Laurance, R. A. Houghton, S. Maxwell, H. Grantham, C. Samper, S. Wang, L. Laestadius, R. K. Runting, G. A. Silva-Chávez, J. Ervin, D. Lindenmayer, The exceptional value of intact forest ecosystems. *Nat. Ecol. Evol.* **2**, 599–610 (2018).
96. R. P. Acharya, T. Maraseni, G. Cockfield, Global trend of forest ecosystem services valuation – An analysis of publications. *Ecosyst. Serv.* **39**, 100979 (2019).
97. N. Mollentze, S. A. Babayan, D. G. Streicker, Identifying and prioritizing potential human-infecting viruses from their genome sequences. *PLOS Biol.* **19**, e3001390 (2021).
98. S. Pacala, R. Socolow, Stabilization wedges: Solving the climate problem for the next 50 years with current technologies. *Science* **305**, 968 (2004).
99. F. L. Black, Measles endemicity in insular populations: Critical community size and its evolutionary implication. *J. Theor. Biol.* **11**, 207–211 (1966).
100. M. S. Bartlett, The critical community size for measles in the United States. *J. R. Stat. Soc. Ser. A.* **123**, 37 (1960).
101. C. J. Rhodes, R. M. Anderson, A scaling analysis of measles epidemics in a small population. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **351**, 1679–1688 (1996).
102. M. Roy, R. D. Zinck, M. J. Bouma, M. Pascual, Epidemic cholera spreads like wildfire. *Sci. Rep.* **4**, 3710 (2015).
103. The Joint United Nations Programme on HIV/AIDS, UNAIDS 2019 estimates (2019).
104. J. N. Abramovitz, *1980–1989: Vital Signs 2001: The Trends that are Shaping Our Future* (Worldwatch Institute, W.W. Norton and Company, 2001).
105. H. Leblebicioglu, R. Ozaras, M. Sunbul, Crimean-Congo hemorrhagic fever: A neglected infectious disease with potential nosocomial infection threat. *Am. J. Infect. Control* **45**, 815–816 (2017).
106. Y.-Z. Zhang, Y. Zou, Z. F. Fu, A. Plyusnin, Hantavirus infections in humans and animals, China. *Emerg. Infect. Dis.* **16**, 1195–1203 (2010).
107. L. X. Fonseca, S. V. de Oliveira, E. C. Duarte, Magnitude and distribution of deaths due to hantavirus in Brazil, 2007–2015. *Epidemiol. Serv. Saúde* **27**, e2017221 (2018).
108. L. T. M. Figueiredo, M. L. Moreli, G. M. Campos, R. L. M. Sousa, Hantaviruses in São Paulo State, Brazil. *Emerg. Infect. Dis.* **9**, 891–892 (2003).
109. U.S. Centers for Disease Control and Prevention, Kyasanur Forest Disease. CDC Fact Sheet (U.S. Centers for Disease Control and Prevention, 2020); www.cdc.gov/vhf/kyasanur/pdf/factsheet.pdf.
110. C. Viboud, L. Simonsen, R. Fuentes, J. Flores, M. A. Miller, G. Chowell, Global mortality impact of the 1957–1959 influenza pandemic. *J Infect Dis* **213**, 738–745 (2016).
111. D. A. Enria, A. M. Briggiler, Z. Sánchez, Treatment of Argentine hemorrhagic fever. *Antiviral Res.* **78**, 132–139 (2008).
112. U.S. Centers for Disease Control and Prevention, Epidemiology & Geographic Distribution | La Crosse encephalitis (U.S. Centers for Disease Control and Prevention, 2020); www.cdc.gov/lac/tech/epi.html.
113. M. Patterson, A. Grant, S. Paessler, Epidemiology and pathogenesis of Bolivian hemorrhagic fever. *Curr. Opin. Virol.* **5**, 82–90 (2014).
114. U.S. Centers for Disease Control and Prevention, Outbreaks Chronology: Marburg Hemorrhagic Fever (U.S. Centers for Disease Control and Prevention, 2020); www.cdc.gov/vhf/marburg/outbreaks/chronology.html.
115. U.S. Centers for Disease Control and Prevention, 1968 Pandemic (H3N2 virus) (U.S. Centers for Disease Control and Prevention, 2020); www.cdc.gov/flu/pandemic-resources/1968-pandemic.html.
116. U.S. Centers for Disease Control and Prevention, Lassa Fever (U.S. Centers for Disease Control and Prevention, 2020); www.cdc.gov/vhf/lassa/index.html.
117. K. Senior, Lassa fever: Current and future control options. *Lancet Infect. Dis.* **9**, 532 (2009).
118. P. V. Aguilar, J. G. Estrada-Franco, R. Navarro-Lopez, C. Ferro, A. D. Haddow, S. C. Weaver, Endemic Venezuelan equine encephalitis in the Americas: Hidden under the dengue umbrella. *Future Virol.* **6**, 721–740 (2011).
119. K. N. Durski, A. M. McCollum, Y. Nakazawa, B. W. Petersen, M. G. Reynolds, S. Briand, M. H. Djingarey, V. Olson, I. K. Damon, A. Khalakdina, Emergence of monkeypox — West and Central Africa, 1970–2017. *MMWR Morb. Mortal. Wkly Rep.* **67**, 306–310 (2018).
120. U.S. Centers for Disease Control and Prevention, Years of Ebola Virus Disease Outbreaks (U.S. Centers for Disease Control and Prevention); www.cdc.gov/vhf/ebola/history/chronology.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvhf%2Febola%2Foutbreaks%2Fhistory%2Fchronology.html.
121. M. O. Nanyingi, P. Munyua, S. G. Kiama, G. M. Muchemi, S. M. Thumbi, A. O. Bitek, B. Bett, R. M. Muriithi, M. K. Njenga, A systematic review of Rift Valley fever epidemiology 1931–2014. *Infect. Ecol. Epidemiol.* **5**, 28024 (2015).
122. Joint United Nations Programme on HIV/AIDS, AIDSinfo; http://aidsinfo.unaids.org/.
123. P. Makary, M. Kanerva, J. Ollgren, M. J. Virtanen, O. Vapalahti, O. Lyytikäinen, Disease burden of Puumala virus infections, 1995–2008. *Epidemiol. Infect.* **138**, 1484–1492 (2010).
124. C. J. Burrell, C. R. Howard, F. A. Murphy, in *Fenner and White's Medical Virology* (Elsevier, 2017), pp. 425–436; https://linkinghub.elsevier.com/retrieve/pii/B9780123751560000308.
125. U.S. Centers for Disease Control and Prevention, Hantavirus Disease, by State of Reporting (U.S. Centers for Disease Control and Prevention, 2017); www.cdc.gov/hantavirus/surveillance/reporting-state.html.
126. World Health Organization, *Hantavirus pulmonary syndrome – Argentine Republic* (World, Health Organization, 2019); www.who.int/csr/don/23-January-2019-hantavirus-argentina/en/.
127. Aditi, M. Shariff, Nipah virus infection: A review. *Epidemiol. Infect.* **147**, e95 (2019).
128. U.S. Centers for Disease Control and Prevention, West Nile virus disease cases reported to CDC by year and clinical presentation, 1999-2018 (U.S. Centers for Disease Control and Prevention, 2019); www.cdc.gov/westnile/resources/pdfs/data/WNV-Disease-Cases-by-Year_1999-2018-P.pdf.
129. U.S. Centers for Disease Control and Prevention, SARS | Frequently Asked Questions (U.S. Centers for Disease Control and Prevention, 2020); www.cdc.gov/sars/about/faq.html.
130. A. S. Lima Neto, G. S. Sousa, O. J. Nascimento, M. C. Castro, Chikungunya-attributable deaths: A neglected outcome of a neglected disease. *PLoS Negl. Trop. Dis.* **13**, e0007575 (2019).
131. F. S. Dawood, A. D. Iuliano, C. Reed, M. I. Meltzer, D. K. Shay, P.-Y. Cheng, D. Bandaranayake, R. F. Breiman, W. A. Brooks, P. Buchy, D. R. Feikin, K. B. Fowler, A. Gordon, N. T. Hien, P. Horby, Q. S. Huang, M. A. Katz, A. Krishnan, R. Lal, J. M. Montgomery, K. Mølbak, R. Pebody, A. M. Presanis, H. Razuri, A. Steens, Y. O. Tinoco,

J. Wallinga, H. Yu, S. Vong, J. Bresee, M.-A. Widdowson, Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: A modelling study. *Lancet Infect. Dis.* **12**, 687–695 (2012).
132. N. J. C. Robles, H. J. Han, S.-J. Park, Y. K. Choi, Epidemiology of severe fever and thrombocytopenia syndrome virus infection and the need for therapeutics for the prevention. *Clin. Exp. Vaccine Res.* **7**, 43–50 (2018).
133. World Health Organization, *Middle East respiratory syndrome coronavirus (MERS-CoV)* (World Health Organization, 2020); www.who.int/emergencies/mers-cov/en/.
134. J. A. Cardona-Ospina, V. Henao-SanMartin, W. F. Acevedo-Mendoza, K. M. Nasner-Posso, D. F. Martínez-Pulgarín, A. Restrepo-López, V. Valencia-Gallego, M. H. Collins, A. J. Rodriguez-Morales, Fatal Zika virus infection in the Americas: A systematic review. *Int. J. Infect. Dis.* **88**, 49–59 (2019).
135. Mortality Analyses - Johns Hopkins Coronavirus Resource Center (Johns Hopkins University, 2020); https://coronavirus.jhu.edu/data/mortality.
136. N. Wolfe, C. Dunavan, J. Diamond, Origins of major human infectious diseases. *Nature* **447**, 279–283 (2007).
137. A. Cliff, P. Haggett, M. Smallman-Raynor, Measles: An historical geography of a major human viral disease from global expansion to local retreat, 1840–1990 (Oxford Univ. Press, 1993).
138. J. A. Crump, K. M. Thomas, J. Benschop, M. A. Knox, D. A. Wilkinson, A. C. Midwinter, P. Munyua, J. B. Ochieng, G. M. Bigogo, J. R. Verani, M.-A. Widdowson, G. Prinsen, S. Cleaveland, E. D. Karimuribo, R. R. Kazwala, B. T. Mmbaga, E. S. Swai, N. P. French, R. N. Zadoks, Investigating the meat pathway as a source of human nontyphoidal Salmonella bloodstream infections and diarrhea in East Africa. *Clin. Infect. Dis.* **73**, e1570–e1578 (2021).
139. K. J. Allan, M. J. Maze, R. L. Galloway, M. P. Rubach, H. M. Biggs, J. E. B. Halliday, S. Cleaveland, W. Saganda, B. F. Lwezaula, R. R. Kazwala, B. T. Mmbaga, V. P. Maro, J. A. Crump, Molecular detection and typing of pathogenic leptospira in febrile patients and phylogenetic comparison with leptospira detected among animals in Tanzania. *Am. J. Trop. Med. Hyg.* **103**, 1427–1434 (2020).
140. J. E. B. Halliday, K. J. Allan, D. Ekwem, S. Cleaveland, R. R. Kazwala, J. A. Crump, Endemic zoonoses in the tropics: A public health problem hiding in plain sight. *Vet. Rec.* **176**, 220–225 (2015).
141. K. Hampson, J. Dushoff, S. Cleaveland, D. T. Haydon, M. Kaare, C. Packer, A. Dobson, Transmission dynamics and prospects for the elimination of canine rabies. *PLOS Biol.* **7**, e53 (2009).
142. R. K. Brook, S. J. Kutz, A. M. Veitch, R. A. Popko, B. T. Elkin, G. Guthrie, Fostering community-based wildlife health monitoring and research in the Canadian North. *Ecohealth* **6**, 266–278 (2009).
143. E. A. Eskew, A. M. White, N. Ross, K. M. Smith, K. F. Smith, J. P. Rodríguez, C. Zambrana-Torrelio, W. B. Karesh, P. Daszak, United States wildlife and wildlife product imports from 2000–2014. *Sci. Data* **7**, 22 (2020).
144. B. I. Pavlin, L. M. Schloegel, P. Daszak, Risk of importing zoonotic diseases through wildlife trade, United States. *Emerg. Infect. Dis.* **15**, 1721–1726 (2009).
145. Ö. E. Can, N. D'Cruze, D. W. Macdonald, Dealing in deadly pathogens: Taking stock of the legal trade in live wildlife and potential risks to human health. *Glob. Ecol. Conserv.* **17**, e00515 (2019).
146. P. Daszak, K. J. Olival, H. Li, A strategy to prevent future epidemics similar to the 2019-nCoV outbreak. *Biosaf. Health* **2**, 6–8 (2020).
147. Y. Guan, B. J. Zheng, Y. Q. He, X. L. Liu, Z. X. Zhuang, C. L. Cheung, S. W. Luo, P. H. Li, L. J. Zhang, Y. J. Guan, K. M. Butt, K. L. Wong, K. W. Chan, W. Lim, K. F. Shortridge, K. Y. Yuen, J. S. M. Peiris, L. L. M. Poon, Isolation and characterization of viruses related to the SARS coronavirus from animals in Southern China. *Science* **302**, 276–278 (2003).
148. C. M. Freuling, A. Breithaupt, T. Müller, J. Sehl, A. Balkema-Buschmann, M. Rissmann, A. Klein, C. Wylezich, D. Höper, K. Wernike, A. Aebischer, D. Hoffmann, V. Friedrichs, A. Dorhoi, M. H. Groschup, M. Beer, T. C. Mettenleiter, Susceptibility of raccoon dogs for experimental SARS-CoV-2 infection. *Emerg. Infect. Dis.* **26**, 2982–2985 (2020).
149. N. Oreshkova, R. J. Molenaar, S. Vreman, F. Harders, B. B. Oude Munnink, R. W. Hakze-van der Honing, N. Gerhards, P. Tolsma, R. Bouwstra, R. S. Sikkema, M. G. Tacken, M. M. de Rooij, E. Weesendorp, M. Y. Engelsma, C. J. Bruschke, L. A. Smit, M. Koopmans, W. H. van der Poel, A. Stegeman, SARS-CoV-2 infection in farmed minks, the Netherlands, April and May 2020. *Euro Surveill.* **25**, 2001005 (2020).
150. D. T. Cronin, S. Woloszynek, W. A. Morra, S. Honarvar, J. M. Linder, M. K. Gonder, M. P. O'Connor, G. W. Hearn, Long-term urban market dynamics reveal increased bushmeat carcass volume despite economic growth and proactive environmental legislation on Bioko Island, Equatorial Guinea. *PLOS ONE* **10**, e0134464 (2015).
151. Agencia Peruana de Noticias Andina, Coronavirus: Reordenan puestos de venta de mercado de Belén para evitar contagio | Noticias. *Andina* (2020); https://andina.pe/agencia/noticia-coronavirus-reordenan-puestor-venta-mercado-belen-para-evitar-contagio-796668.aspx.
152. P. F. C. Vasconcelos, A. P. A. Travassos da Rosa, S. G. Rodrigues, E. S. Travassos da Rosa, N. Dégallier, J. F. S. Travassos da Rosa, Inadequate management of natural ecosystem in the Brazilian Amazon region results in the emergence and reemergence of arboviruses. *Cad. Saude Publica* **17**, S155–S164 (2001).
153. E. A. Mordecai, J. M. Caldwell, M. K. Grossman, C. A. Lippi, L. R. Johnson, M. Neira, J. R. Rohr, S. J. Ryan, V. Savage, M. S. Shocket, R. Sippy, A. M. Stewart Ibarra, M. B. Thomas, O. Villena, Thermal biology of mosquito-borne disease. *Ecol. Lett.* **22**, 1690–1708 (2019).
154. N. M. Ferguson, Z. M. Cucunuba, I. Dorigatti, G. L. Nedjati-Gilani, C. A. Donnelly, M.-G. Basanez, P. Nouvellet, J. Lessler, Countering the Zika epidemic in Latin America. *Science* **353**, 353–354 (2016).
155. S. Cibulski, F. E. S. de Lima, P. M. Roehe, Coronaviruses in Brazilian bats: A matter of concern? *PLOS Negl. Trop. Dis.* **14**, e0008820 (2020).
156. M. C. Dos Santos, M. V. Guimarães De Lacerda, S. M. Benedetti, B. C. Albuquerque, A. A. B. V. De Aguiar Filho, M. D. R. Elkhoury, E. S. Travassos Da Rosa, P. F. Da Costa Vasconcelos, D. B. De Almeida Medeiros, M. P. Gomes Mourão, Human hantavirus infection, Brazilian Amazon. *Emerg. Infect. Dis.* **12**, 1165–1167 (2006).
157. T. H. Ricketts, B. Soares-Filho, G. A. B. da Fonseca, D. Nepstad, A. Pfaff, A. Petsonk, A. Anderson, D. Boucher, A. Cattaneo, M. Conte, K. Creighton, L. Linden, C. Maretti, P. Moutinho, R. Ullman, R. Victurine, Indigenous lands, protected areas, and slowing climate change. *PLOS Biol.* **8**, e1000331 (2010).
158. L. Nyakarahuka, S. Ayebare, G. Mosomtai, C. Kankya, J. Lutwama, F. N. Mwiine, E. Skjerve, Ecological niche modeling for filoviruses: A risk map for ebola and marburg virus disease outbreaks in Uganda. *PLOS Curr.* **9**, ecurrents.outbreaks.07992a87522e1f229c7cb023270a2af1 (2017).
159. S. J. Salyer, T. R. Gillespie, I. B. Rwego, C. A. Chapman, T. L. Goldberg, Epidemiology and molecular relationships of *Cryptosporidium* spp. in people, primates, and livestock from Western Uganda. *PLOS Negl. Trop. Dis.* **6**, e1597 (2012).
160. World Food Program, COVID-19 will double number of people facing food crises unless swift action is taken (World Food Programme, 2020); www.wfp.org/news/covid-19-will-double-number-people-facing-food-crises-unless-swift-action-taken.
161. C. A. MacKenzie, Trenches like fences make good neighbours: Revenue sharing around Kibale National Park, Uganda. *J. Nat. Conserv.* **20**, 92–100 (2012).
162. D. Kirumira, D. Baranga, J. Hartter, K. Valenta, C. Tumwesigye, W. Kagoro, C. Chapman, Evaluating a union between health care and conservation: A mobile clinic improves park-people relations, yet poaching increases. *Conserv. Soc.* **17**, 51–62 (2019).

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