10 Understanding How and Where Pathogens Emerge: Preparedness and Response for Zoonotic Diseases

Andrew Clements, Ian Mendenhall, and Daniel Schar

Contents

Learning Track Note: This chapter appears in Learning Tracks: Health Policy, Multilateral Cooperation, International Governance; One Health; Public Health and Epidemiology

Note: The views and opinions expressed in this paper are those of the authors and not necessarily the views and opinions of the United States Agency for International Development.

E. S. Higgs and R. A. Sorenson (eds.), *Principles and Practice of Emergency Research Response*, https://doi.org/10.1007/978-3-031-48408-7_12

Learning Objectives

This chapter will help readers understand and describe:

- Zoonotic diseases that have emerged or reemerged at the wildlife–livestock–human–environment interface and some indications of potential spillover
- Zoonotic pathogen circulation, pathways to emergence in humans, and potential for sustained human-to-human transmission
- Opportunities to deploy targeted preventive measures against spillover; how pre-outbreak information bolsters global health security
- Why many zoonotic pathogen spillovers cannot be predicted or anticipated
- New data streams needed to better characterize the wildlife–livestock–human–environment interface
- Recommendations for better preparedness for and response to infectious disease emergencies

1 Introduction

This chapter will examine what we know about how and where zoonotic disease threats[1] emerge and key gaps in the information needed for preparedness, both before an outbreak and in emergency response. The mechanisms of zoonotic pathogen spillover and adaptation to humans are in many cases poorly understood and require sustained and focused research to

1. Characterize spillover mechanisms.
2. Develop interventions to reduce spillover, amplification, and onward transmission of emerging zoonoses.
3. Design and assess interventions such as diagnostics, therapeutics, and vaccines.
4. Refine surveillance targets.
5. Prepare for accelerated response where risks are greatest, ideally through local capacity building.

In this chapter, "pre-outbreak information" refers to data on known or potential zoonotic pathogens circulating in animals, humans, or blood-feeding arthropods before the first cluster of infections among people is recognized and reported (Fig. 1). Spillover may also result in limited human-to-human transmission that does not sustain itself and is never detected.

1 In most usage "zoonotic" refers to pathogens like Ebola virus, some coronaviruses, and Nipah virus that are transmissible between vertebrate hosts and humans. This chapter will mostly focus on zoonotic viruses that can be transmitted from vertebrates to people by direct contact, but also includes vector-borne viruses.

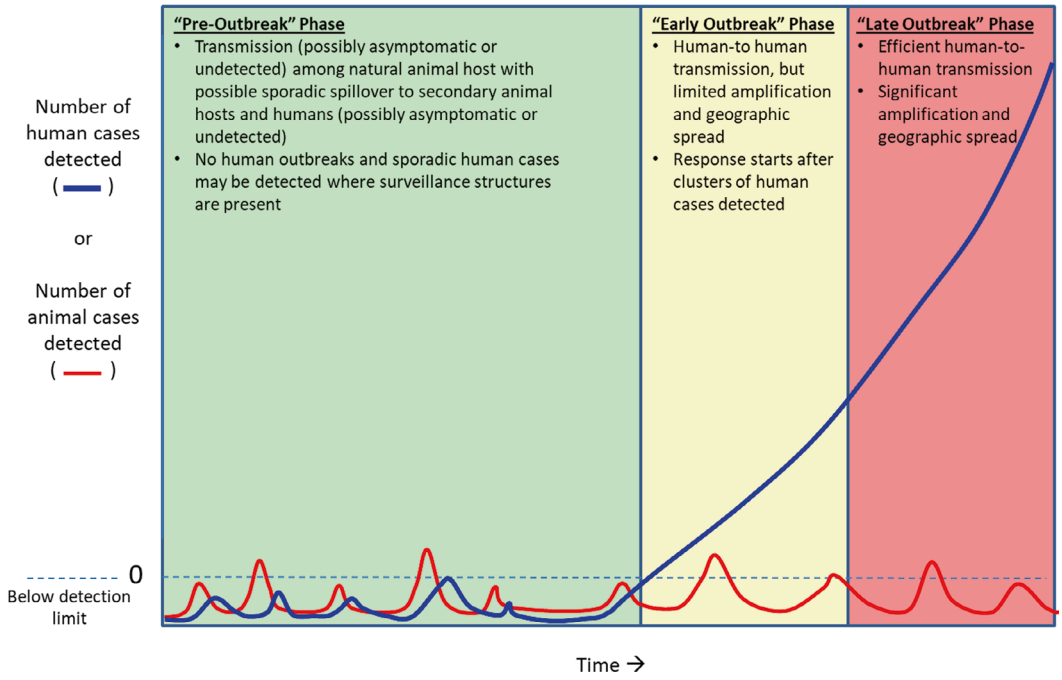

Fig. 1 Phases of human outbreaks with emerging zoonotic pathogens. (Authors)

2 Why Is Pre-outbreak Information Important?

Given the substantial impact of emerging zoonoses and the present scarcity of tools for prevention, detection, and response, along with the need to regularly update those that exist, investments in collecting and analyzing pre-outbreak information and using the results to reduce spillovers and limit their amplification and geographical spread would likely yield a high return on investment and strengthen global health security (Bernstein et al. 2022; Berry et al. 2022; World Bank 2012).

Collecting pre-outbreak information presents a unique opportunity to synthesize and distill pathogen, host, ecology, and other sources of data into actionable risk mitigation and to guide preparedness for future outbreaks in human populations. Reasons for investing in collecting pre-outbreak information are described below.

2.1 Impact of Uncontrolled Emerging Zoonoses

Novel pathogens have emerged in hominid populations over millions of years, sometimes followed by devastating epidemics or pandemics that have caused long-lasting social and economic damage, re-shaped society, and led to selection of protective genes in the human genome (Klunk et al. 2022). Since 1900, zoonotic pathogens have been responsible for at least six worldwide viral pandemics, caused by HIV, SARS-CoV-2, and influenza viruses, as well as numerous human outbreaks of highly pathogenic avian influenza, Ebola virus, Hendra virus, Marburg virus, MERS-CoV, mpox (previously known as monkeypox) virus (WHO 2022f), Nipah virus, and SARS-CoV-1 (Piret and Boivin 2021). The global health and economic impacts of some emerging threats have been enormous. For example, the 1918 influenza pandemic killed more than 50 million people

(CDC 2018a); HIV-AIDS has resulted in more than 36 million deaths (UNAIDS 2022); and the death toll of COVID-19 is more than 6.6 million people as of January 2023 (WHO 2023c). In many cases, the economic impacts of pandemics have driven people into poverty, especially in low- and middle-income countries (WBG 2022a).

By breaking down the expected costs of relatively infrequent pandemics on an annual basis, Fan et al. (2018) estimate the costs of influenza pandemics totaled approximately $500 billion annually, or about 0.6% of global income. For the COVID-19 pandemic, many economic sectors dropped by double-digit percentages in 2020 alone (Delardas et al. 2022), which is within the range of outcomes examined by Fan et al. With the rate of zoonotic pathogen emergence increasing, and climate-change related alterations at human–animal–environment interfaces, the future impact may be greater (Morand and Walther 2020). For example, one study estimated that while the probability of large epidemics varies over time, there is a 38% chance of experiencing a pandemic equivalent to COVID-19 in the next 100 years, and this may double in the coming decades (Marani et al. 2021).

2.2 Increasing Rates of Emergence and Potential Future Threats

Of the more than 1400 known human pathogens, over 60% are of zoonotic origin (Taylor et al. 2001). A retrospective study of new diseases emerging between 1940 and 2004 provides other key information:

- The rate of emergence (not merely the rate of detection) after adjusting for sampling bias has been increasing over time.
- Most new threats are viruses originating in wildlife.
- "Hot spots" for emergence are likely to be concentrated in tropical and sub-tropical regions.
- Resources for detection and response are not well distributed geographically or equally, and may be least available in low-latitude countries where the risks are greatest (Jones et al. 2008).

In addition, there are likely millions of uncharacterized viruses in mammals and birds, with roughly 700,000 of these estimated to be capable of crossing the species barrier to infect humans (Carroll et al. 2018). If new pathogens can cause asymptomatic infections, or if there is a long lag between infection and symptom onset, as with HIV, there may be "silent" (i.e., undetected) transmission in high-risk individuals.

Uncontained disease transmission among humans increases the risk of new pathogens becoming endemic in human populations and becoming established in previously uninfected animal species through spillback. Examples include SARS-CoV-2 spilling from people into multiple mammalian species and pandemic H1N1 influenza spilling from people into birds, pigs, and other mammals; spillback of mpox is also a concern (Blagrove et al. 2022; Frazzini et al. 2022; Keenliside 2013). The establishment of new animal reservoirs for zoonotic pathogens has important implications for their control and containment.

2.3 Availability of Targeted Interventions to Prevent, Detect, and Respond to Emerging Zoonoses

Many infectious diseases in humans, such as malaria, measles, and tuberculosis, have been known for centuries or millennia, and in many cases there are existing strategies and vaccines, therapeutics, and diagnostics (VTDs) to address them. However, for new and emerging zoonotic diseases, information, strategies, and tools to counter them may neither be available nor effective—particularly in acute outbreak

settings where pathogen characteristics, modes of transmission, and clinical presentation may yet to have been fully elucidated. Examples of delays in the initial recognition, reporting, and implementation of interventions include the responses to HIV/AIDS, the 2014–2016 West Africa Ebola epidemic, and the current mpox public health emergency; these have resulted in thousands or millions of human infections occurring (CDC 2022a; Gallo and Montagnier 2003; WHO 2022a, b, 2023d). Even the relatively swift identification and genome sequence publication of the SARS CoV-2 virus did not prevent the outbreak from spreading worldwide because many countries were operating without critical information to inform timely, evidence-based decision-making or chose to ignore expert advice, thereby delaying action. However, the genomic sequence information was rapidly used to develop diagnostics, therapeutics, and vaccines.

2.4 Time, Focus, and Resources Are Limited Once Outbreaks Start

Research and surveillance efforts to collect missing information on emerging zoonotic diseases require a number of necessary, but time-consuming steps: building trust and establishing partnerships with affected populations, securing approvals from regulatory bodies, national and local governments, and other stakeholders, developing strategies, and training and equipping staff and institutions to do the work. It is easier to implement these steps between outbreaks because there is more time available, although funding can be a challenge unless this work has been prioritized by countries and donors. Serial episodes of pandemic response and repeated cycles of panic and neglect undermine the ability to discern patterns of spillover risk and guide interventions aimed at prevention. A prime example is the Ebola virus, which was first reported in 1976. Despite more than 30 outbreaks affecting 19 countries (nine of which occurred between 2017 and 2022) (CDC 2022b), the natural and incidental animal hosts for this family of viruses in endemic countries have not been definitively identified, although some bat species are thought to play a significant role in viral maintenance and transmission (Schuh et al. 2017). Indeed, West Africa was not considered to be at risk for Ebola until the 2014–2016 outbreak.

In an ideal world, collection of pre-outbreak information through early warning surveillance would complement outbreak prevention, detection, and response efforts. These components would be adequately funded and coordinated to maximize the chances of reducing the incidence and impact of outbreaks, epidemics, and pandemics. Pre-outbreak information would support a global early warning system to detect and respond to outbreaks by providing early information on potential public health threats and allow for targeting of surveillance at specific locations, interfaces, and species associated with spillover. At the same time, pre-outbreak information would also contribute to pre-outbreak planning to include the development of spillover prevention strategies as well as the development of VTDs (Carroll et al. 2018).

3 Pre-outbreak Information: What We Already Know About How and Where Pathogens Emerge

Information gathered over the last few decades has provided valuable—though not complete—insights into the zoonotic disease emergence process. Key points are summarized below.

3.1 The Risk Landscape Is Not Uniform: Specific Conditions Create Spillover Hot Spots

Emergence of zoonotic threats is complex and requires that humans, infectious agents, their animal hosts, and arthropod vectors such as ticks, fleas, or mosquitoes (if needed for transmission) are all present in the same place and time (Plowright et al. 2017). These interactions are part of a dynamic and continually

evolving process (Hendry et al. 2017). Even when a pathogen infects humans, however, onward transmission is far from certain. Following spillover, if the infectious agent, host immune response, and population dynamics do not permit sustained human-to-human transmission, the event will likely die out. However, if the agent is capable of (or subsequently develops the capacity for) efficient human-to-human transmission in an immunologically naive population, as was the case for SARS-CoV-2, the spillover event may be followed by amplification and geographical spread, resulting in a country, regional, or global outbreak. Spillover of wildlife-hosted pathogens to people can happen directly (e.g., from wildlife to hunters or consumers) or indirectly via livestock.

If sufficient information is available on human, pathogen, animal host, and vector populations, predictive modeling can be a powerful tool to map potential spillover hot spots. As shown in Fig. 2, spillover risk for emerging zoonotic threats is predicted to be highest in forested regions in the tropics that are elevated and undergoing land-use changes, and also in areas with high wildlife biodiversity, primarily in sub-Saharan Africa, South and Southeast Asia, and East Asia (Allen et al. 2017; Jones et al. 2008). This hot spot mapping is mostly consistent with the location of spillovers of avian influenza viruses, Nipah virus, SARS-CoV-1, and SARS-CoV-2 in South and Southeastern Asia, as well as Ebola, HIV, Marburg, and Zika viruses in East and Central Africa. Regions with a high risk of spillover tend to have significant biodiverse and abundant wildlife populations (including species hosting emerging zoonotic threats), livestock production and trade with sub-optimal biosafety/biosecurity conditions, and land-use change. It is important to note that multiple spillover hot spots may be connected, existing as nodes in a transmission chain, and that the spillover potential may vary from location to location and at different times in the same location. For example, coronavirus detection rates increased as rodents in Vietnam were moved from their source along supply chains to markets (Huong et al. 2020).

While predictive model outputs are instructive and useful for framing risk profiles, it is important to recognize that they have inherent limitations, and that predictive accuracy is highly dependent upon data availability and use. Because of disparities in funding for research and surveillance, the United States and European countries often report individual human infections with Lassa virus, MERS-CoV, and mpox virus in travelers from endemic countries in Africa, Asia, and the Middle East (Allen et al. 2017). The fact that

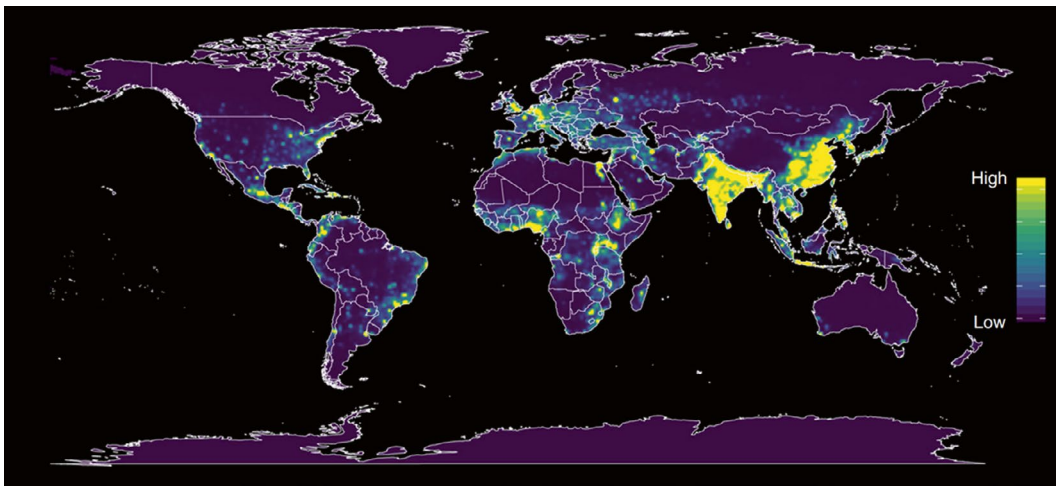

Fig. 2 Heat map of predicted relative risk distribution of zoonotic EID events, showing the estimated risk of event locations after factoring out reporting bias Hot-spots map 2.0. (Allen et al. 2017; open access)

biodiverse regions such as the Amazon that are experiencing increasing rates of land-use change do not show up as spillover hot spots suggests that zoonotic spillover risk is not captured equitably across the world (de Oliveira et al. 2022; Winck et al. 2022). This is supported by the emergence of MERS-CoV in the Arabian Peninsula, the 2009 H1N1 pandemic influenza virus in Mexico, and Lyme disease in the United States (Memish et al. 2014; Smith et al. 2009; Steere et al. 2004).

3.2 Specific Conditions and Human Behaviors at Hot Spots Affecting Spillover, Amplification, and Geographical Spread

Human behaviors and activities play an important role in the amplification, transmission, and dispersal of emerging zoonotic diseases (Lindahl and Grace 2015). The evolution and adaptation of humans have changed our exposure to the environment, while at the same time radically modifying our relationship with each other, the landscape, livestock and companion animals, wild animals, and vectors (Hendry et al. 2017; Nyhus 2016; Plowright et al. 2021). Anthropogenic environmental disruptions, including land-use change, agricultural intensification, and food production systems, drive the emergence of infectious diseases (Gibb et al. 2020; Keesing and Ostfeld 2021). The vast majority of tropical forest loss is caused by agricultural expansion; among the impacts is increasing zoonotic spillover (Pendrill et al. 2022). Within known geographical hot spot regions for spillover, specific animal–human interfaces may have increased frequency and duration of contact among humans, livestock, and wildlife (and vectors) because of agriculture and grain storage near homes (Lassa virus); raising livestock (avian influenza); mineral extraction and visiting caves (Marburg virus); collection of fruit tree sap (Nipah virus); and contact with wildlife during hunting, farming, or trade (Ebola, HIV, SARS-CoV-1, mpox) (CDC 2003; Glidden et al. 2021; Plowright et al. 2017). Other potential spillover interfaces include bats roosting in homes (Schuh et al. 2017), bat guano farming (Huong et al. 2020), and keeping primates and other wildlife as pets (Chomel et al. 2007). After spillover occurs, zoonotic pathogens can be amplified in human populations by crowded living or working conditions, congregation, inadequate infection prevention and control in healthcare facilities, and sexual behaviors, leading to geographical dispersion through travel and trade (Jones et al. 2013; Poletti et al. 2017). Shifting demographics—including a trend toward urbanization—and historically underserved and mobile populations without access to healthcare may further serve to amplify pathogen transmission among people and create routes for global dispersal. A summary of some pathogens, animal hosts, and spillover interfaces is shown in Fig. 3.

Human behavioral measures, the mainstay of early public health response to an infectious disease emergency, can also be protective in reducing spillover (Magouras et al. 2020; WHO et al. 2019). Examples include:

- Limiting contact with and consumption of animals, especially wildlife and sick animals
- Wearing protective gear when in contact with animals
- Vaccinating at-risk people (when available, e.g., rabies, yellow fever)
- Avoiding contaminated fruit
- Excluding wild animals from homes, whether as pests or pets
- Rearing livestock in biosafe and biosecure environments
- Implementing food safety measures, including boiling or pasteurizing beverages (e.g., water, milk), cooking food, and ensuring hygiene and sanitation in food preparation

Subsequent amplification and geographical spread of zoonotic pathogens in human populations can also be reduced by changing human behaviors, such as wearing masks; social distancing; infection prevention and control in healthcare facilities; vaccination (when available, e.g., influenza, COVID-19, yellow fever,

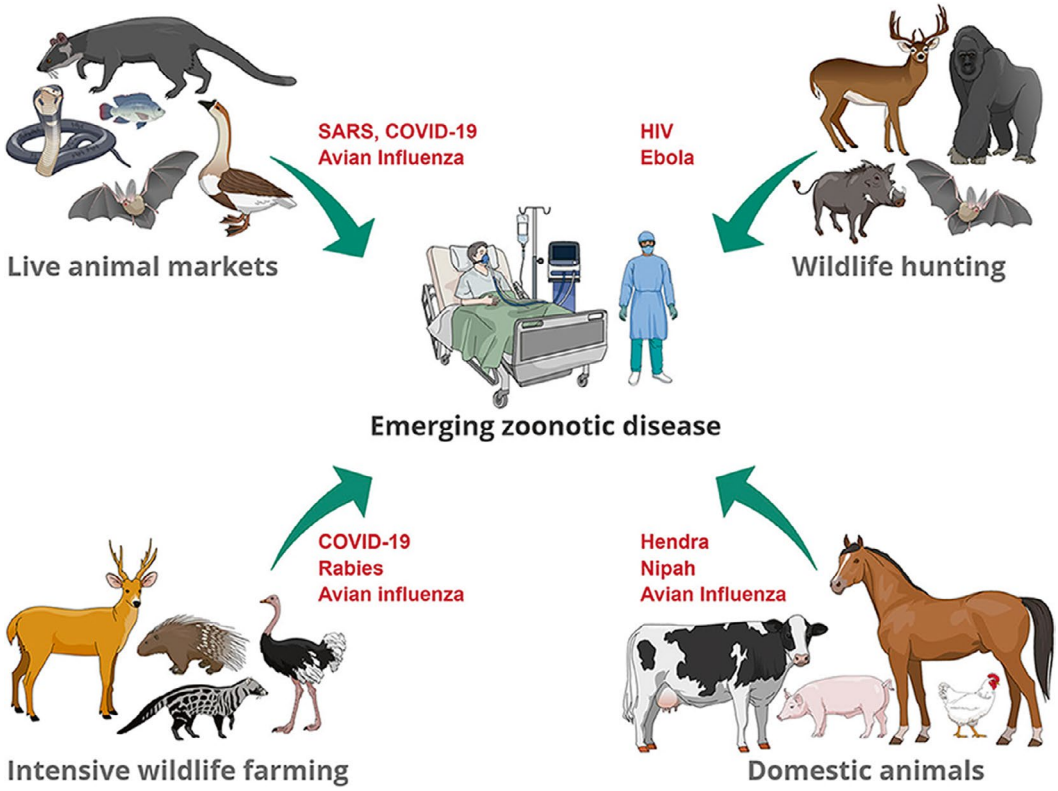

Fig. 3 Examples of zoonotic pathogens that have (re-)emerged at the animal–human–environment interface. Transmission pathways include direct contact through handling of living animals (wildlife trade, domestic animals) and preparation of slaughtered animals for consumption of meat or for traditional medicinal uses. (Magouras et al. 2020)

mpox); and pre- and post-exposure prophylaxis, partner reduction, and safe sex (Groves et al. 2021; Michie and West 2021).

3.3 Certain Animals Tend to Be Associated with Zoonotic Pathogens and Spillover Events

Numerous studies have shown that animals such as bats, rodents, nonhuman primates, and birds are more likely to be associated with zoonotic spillover than other animals (Luis et al. 2013; Olival et al. 2017). Pathogens may be widely distributed among these animal groups or limited to specific species (e.g., Marburg virus hosted by *Rousettus* bats). This is likely due to several factors, including the following:

- Their genetic relatedness to humans
- Relative abundance, density, and geographical distribution of species
- Biodiversity and loss of biodiversity in ecosystems
- The ability of some species to adapt to living in human-altered ecosystems
- Animals being farmed and traded because of their value for food and medicine or as pets

Furthermore, taxa predominating in human-altered landscapes are more likely hosts for zoonotic disease than those in undisturbed locations. The protective effects of biodiversity in mitigating disease emergence risk, possibly through a dilution effect, have also been observed (Keesing and Ostfeld 2021). Collectively, as Mollentze and Streicker (2020) note, four taxonomic groups (bats, rodents, nonhu-

man primates, and birds) are known to host many epidemic-prone pathogens, including pre-cursors of SARS-like coronaviruses and MERS-CoV; Ebola and Marburg viruses; avian influenza viruses; Hendra and Nipah viruses; and Hanta and Lassa viruses. In 2022, a study found that the overall rate of discovery of viruses in mammals, even those heavily sampled, is increasing or constant, illustrating that our understanding of virus diversity is still incomplete (Gibb et al. 2022).

In some animal hosts, biology and life history can result in seasonal shedding of zoonotic pathogens. For example, the reproductive pulses of bats appear to drive coronavirus shedding and filovirus and henipavirus seroprevalence patterns (Brook et al. 2019; Hayman 2015; Joffrin et al. 2022; Montecino-Latorre et al. 2020). Bird migration patterns and timing may play a role in the seasonality of avian influenza events, although not universally. In Bangladesh, little seasonality was observed in transmission within live bird markets (Berry et al. 2022; Tian et al. 2015; Wacharapluesadee et al. 2009). There is also evidence of seasonality of MERS-CoV in camels, Lassa virus in *Mastomys* rats, and Nipah virus in flying foxes in Thailand (Akhmetzhanov et al. 2019; Dudas et al. 2018; Wacharapluesadee et al. 2009). Vector-borne infectious diseases are also driven by seasonal patterns. In temperate climes, temperatures and rainfall drive the proliferation of mosquitoes and subsequent outbreaks, as seen with Rift Valley fever virus (Anyamba et al. 2009).

3.4 Some Zoonotic Pathogens Are More Capable of Spillover

Many properties are intrinsic to individual viruses or families of viruses and make them especially adept at spilling over from animals to people (Antonovics et al. 2017; Duffy et al. 2008; Finlay and McFadden 2006; Grassly and Fraser 2006; Kreuder Johnson et al. 2015). These include

- Adaptability through rapid mutation, especially for RNA viruses
- Stability in the environment
- Transmissibility via multiple routes (e.g., saliva, urine, feces, blood)
- The ability to infect multiple host species (i.e., host plasticity)
- Ability to evade or suppress host defenses

3.5 Spillover of Zoonotic Pathogens Can Change Over Time

Pathogen spillover is likely substantially more common than our current surveillance systems are able to detect (Sánchez et al. 2022) and can increase or decrease if the presence of humans, infectious agents, animal hosts, and arthropod vectors changes in response to anthropogenic, climatic, or environmental drivers (Smolinski et al. 2003). For example, spillover may decrease over time if the animal hosts for specific pathogens can no longer survive in that environment or humans change a behavior that was necessary for spillover. For example, research on Hendra virus in Australia demonstrated pathways to spillover risk where specific and actionable risk mitigation can be undertaken by changing land-use patterns (Eby et al. 2022).

On the other hand, spillover may increase if the frequency and duration of contact between people and the animal host(s) of a pathogen increases because of land-use change, climate change or other alterations in shared ecologies. These can change animal and human habitats by

- Forcing the sharing and cross-contamination of water due to limited supply
- Allowing for greater movement and mixing of species through
  - Building new roads and settlements
  - Increasing the number and species diversity of livestock and wildlife farmed and traded
- Displacing wildlife through deforestation followed by monoculture, such as palm oil plantations (Hassell et al. 2017; Morand and Lajaunie 2021; Plowright et al. 2021)

Changing habitats jeopardize wildlife health as global forest loss occurs at staggering rates, drastically reducing biodiversity (Betts et al. 2017). Loss of biodiversity tends to increase the transmission risk of zoonoses, such that zoonoses are positively correlated with the number of threatened bird and mammal species (Morand et al. 2019). Climate change can also drive the emergence of zoonoses (Betts et al. 2017). The expansion of suitable habitats for arthropod vectors can facilitate autochthonous (locally acquired) transmission of pathogens (Caminade et al. 2019), and warmer temperatures can also shorten developmental stages for arthropod vectors and decrease the intrinsic incubation period of the pathogen (Bartlow et al. 2019). Warmer temperatures can also stress animal hosts, resulting in decreasing immune function and increasing pathogen shedding that may lead to increased zoonotic disease spillover risk (Mora et al. 2022).

Within human-disrupted habitats, there are specific, synanthropic animals, such as some rat (*Rattus* spp.), mice (*Mus* spp.), and macaque (*Macaca* spp.) species that are able to take advantage of disruptions to the ecosystem, resulting in known wildlife hosts of human-shared pathogens and parasites overall comprising a greater proportion of local species richness (18–72% higher) and total abundance (21–144% higher) in sites under substantial human use (Mora et al. 2022). These species can also transport pathogens between human-modified habitats and natural habitats (McFarlane et al. 2012). They are often introduced and/or invasive, have flexible habitat and resource needs, and can rapidly adapt to changing environments including human domiciles, providing opportunities for zoonotic pathogen spillover (Hornok et al. 2015; Voigt et al. 2016).

The human population has grown from less than two billion to eight billion over the past century, with commensurate increases in livestock production, travel, trade, and land exploitation engendering more frequent contact among humans, animals, and microbes, as well as arthropod vectors (Smith et al. 2014). For example, the large-scale farming of waterfowl (e.g., ducks and geese) in Asia under sub-optimal biosecurity conditions facilitated the spread of avian influenza viruses from wild birds to high-density domestic flocks, where their amplification led to occasional spillover causing severe human infections and deaths (Liu et al. 2020; Webster and Hulse 2004).

3.6 Interventions to Reduce Spillover Risk

Even without knowing the exact mechanism by which some pathogens spill over from animals to humans, it is possible in some instances to reduce risk. For example, immunizing poultry with avian influenza (AI) vaccines specific for viral sub-types and variants can prevent or reduce infection in flocks and spillover to humans (Capua and Alexander 2006). A second approach is pathogen agnostic and involves employing good farm and market biosecurity to limit not only spillover, but also amplification and geographical spread of AI viruses and other pathogens. Good biosecurity limits pathogen spread from wildlife to poultry, from poultry to humans, and from poultry back to wild birds (Capua and Marangon 2006; Chowdhury et al. 2020; Liu et al. 2020). As mentioned above, excluding farm animals such as pigs and horses from areas with fruiting trees frequented by flying foxes can limit livestock exposure to Nipah virus and Hendra virus, respectively (Fig. 4) (Kummer and Kranz 2022).

Developing interventions to reduce spillover risk requires enough pre-outbreak information to identify the pathogen–host and transmission pathway(s). However, this information is not always collected or shared, which limits the ability of countries to prevent, prepare for, or respond to spillover events. In contrast to open-source outbreak tracking and reporting structures managed by international organizations such as the World Health Organization (WHO 2022c), the UN Food and Agriculture Organization, the World Organization for Animal Health, and the Program for Monitoring Emerging

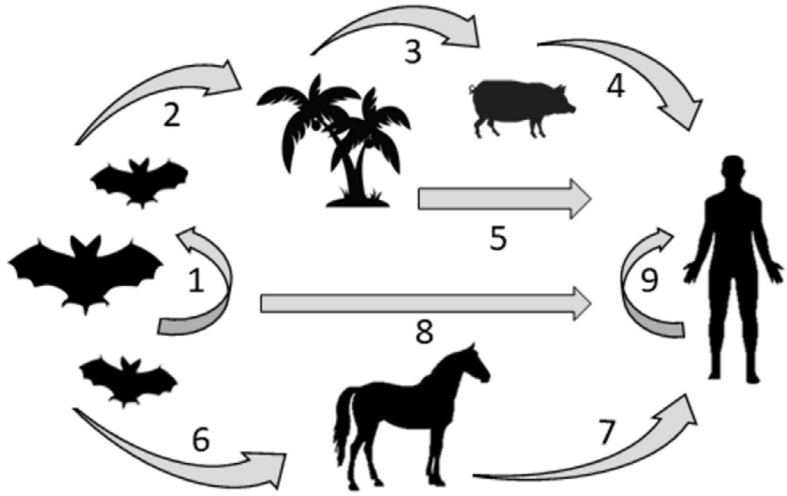

Fig. 4 Presumptive Henipavirus transmission routes: (1) from bats to bats via placental transmission, lactation, or mating; (2) fruit consumption; (3) excretion and partially eaten fruits; (4) from pig to farmer (Nipah virus Malaysia); (5) date palm consumption (Nipah Bangladesh); (6) excretion; (7) from horse to owner (Henipavirus, Nipah Philippines; Hendra virus, Australia); (8) bite, scratch, etc.; and (9) from human to human (Nipah Philippines, Nipah Bangladesh). (Kummer and Kranz 2022)

Diseases (PROMED 2022; WHO 2023a; WOAH 2022), findings from pre-outbreak research are disseminated more slowly.

4 What We Still Need to Know

While current data on zoonotic pathogen emergence have made it possible to better focus prevention, detection, and response capacities on specific locations and animal–human–environment interfaces, gaps remain in knowledge and in systems for analyzing and sharing information. Animal hosts and animal–human–environment interfaces where spillover occurs are known for some zoonotic pathogens, such as the Marburg and Nipah viruses, but considerable uncertainty remains for others, such as coronaviruses, Ebola, Lassa, and mpox viruses. In many cases, the primary animal host is uncertain. In others, the full range of animals that can serve as hosts, the specific behaviors and practices associated with spillover of each pathogen, and the frequency, duration, and dynamics of animal–human contact are unclear (Recht et al. 2020). However, research on infections in animals faces many challenges, not least the cost and scale of the programs required (Koopmans 2013).

Prioritizing resources to fill current knowledge gaps and improve data systems for reporting both ongoing research and new outbreaks should be a near-term goal for countries and the global community to enable targeted risk mitigation interventions and development of medical countermeasures (MCMs). Key gaps are summarized below.

4.1 Characterization of Risk at the Animal–Human–Environment Interface

For some zoonotic pathogens, enough information on hosts and interfaces is available to begin limiting risk. In the case of Marburg virus, demonstrated spillover routes include human contact with Egyptian fruit bats in caves or mines. Avoiding such locations or wearing protective gear may limit the risk (Adjemian et al. 2011; Timen et al. 2009). For many zoonotic pathogens, basic information is urgently needed to update risk maps and develop risk-reduction interventions, as well as diagnostics, therapeutics, and vaccines.

Missing information includes potential host species; the extent to which animals have been exposed to and carry pathogens of interest; specific practices facilitating or preventing spillover; seasonal patterns of host infections and pathogen shedding; and the capacity of specific host taxa to serve as reservoirs of additional, as-yet-unknown pathogens (Carlson et al. 2021; Roberts et al. 2021). Detection of animal host taxa and their range is still imperfect. Estimates of abundance, presence, and absence, especially for rare host taxa, may be highly variable and become more difficult as ecosystems change under pressure of human usage and climate change (Kellner and Swihart 2014). Leveraging large datasets facilitates testing of models to understand geographical hot spots for emergence, predicting the presence of host animals, the potential pathogens they may carry, which newly discovered microbes may be prone to infect humans, and how to prioritize viral research in zoonotic reservoirs (Allen et al. 2017; Becker et al. 2020; Carlson et al. 2021; Grange et al. 2021). Ideally, datasets would include the same metadata to make analyses more robust.

For Nipah virus, two spillover mechanisms have been described so far (◘ Fig. 4). In Malaysia, the virus moved from *Pteropus* bat species, through partially eaten fruit to farmed pigs, and then to people (Chua 2003). In Bangladesh, *Pteropus* bats shed virus into date palm sap collected for human consumption (Islam et al. 2013; Rahman et al. 2012). No further spillover has been documented in Malaysia since 1999, suggesting that the bat–pig–human interface was successfully disrupted. In Bangladesh, where sporadic human infections continue to occur, with short chains of human-to-human transmission (Nikolay et al. 2019), additional work is needed to determine why uptake of effective interventions to block Nipah virus transmission is low (Khan et al. 2012; Nahar et al. 2010, 2017). Additional knowledge gaps include why the Nipah virus can be detected seasonally from *Pteropus lylei* bats in Thailand, yet no human or domestic animal cases have been reported to date (Wacharapluesadee et al. 2009, 2021a). The interface and mechanism for repeated Nipah virus spillover to people in Kerala State, India, in recent years has not yet been identified (Yadav et al. 2022).

While some information is available on animal hosts for Lassa and mpox viruses (Monath et al. 1974; Parker and Buller 2013; Ter Meulen et al. 1996; Wozniak et al. 2021), the interface(s) and mechanism(s) for spillover in West Africa are unknown, hampering efforts to develop interventions. Although the first human infection with the H5N1 avian influenza was detected more than 25 years ago, and it is well known that direct and indirect contact with infected poultry is a major risk factor, the specific nature of the contact needed for transmission has not been definitively identified (Li et al. 2019). Possibilities include inhalation of air-borne virus or physical contact with contaminated birds during farming, slaughtering, defeathering, or processing (Wan et al. 2011), each of which would potentially require different types of risk-reduction interventions.

Many zoonotic diseases spill over directly from wildlife or livestock to people, but another key interface involves wildlife contact with livestock. This mechanism allows zoonotic pathogens to spill over from wildlife to livestock and then, following amplification in these domesticated species (with or without symptoms), into humans. Examples include avian influenza viruses moving from wild birds to poultry to people (Yoon et al. 2014); Nipah virus spilling from bats to pigs and then to people, and Hendra virus starting in bats and then infecting horses and finally humans (Kessler et al. 2018). With the increasing number of livestock produced each year to feed the growing human population, the wildlife–livestock interface could grow as a source of spillover events and should be regularly monitored.

Improving characterization of animal–human–environment interfaces requires improving the sharing of existing pre-outbreak information. For existing data, country, regional, and global partners routinely produce data from research studies and outbreaks, including information on pathogens, animal hosts, and sometimes human behavior, but their release is often via publica-

tion of peer-reviewed scientific papers, which may take years. In addition, data may be unavailable to many researchers if they are published in a journal with limited access, reported in a student thesis or doctoral dissertation, or the researcher does not have the ability to conduct specialized analyses. Thus, obstacles to researchers collectively sharing, analyzing, and using pre-outbreak information in near-real time constrains the ability of countries to improve prevention, detection, and response to emerging zoonotic diseases (Kucharski 2022). The urgency of understanding SARS-CoV-2 during the COVID-19 pandemic helped lead to more streamlined processes, with increased communications between researchers and public health officials, pre-prints of articles becoming available before full peer review, subscription-only journals making their COVID-19 articles open access, and genetic sequence data quickly posted on accessible platforms such as GISAID. Such interchanges must be improved and accelerated in routine practice for the global health ecosystem to prevent more outbreaks from becoming global emergencies and ensure that tools are available for prevention and response.

Another way to improve the characterization of animal–human–environment interfaces is to add new data streams, especially regularly updated data that reflect population-level changes. Satellites can now collect near-real-time data on habitat changes and forest loss or transformation of biodiverse forests into monocultures (e.g., oil palm)—phenomena that should be prioritized for spillover surveillance (Hansen et al. 2013). Useful data streams could also come from monitoring or screening:

- Human and animal population movements
- Wildlife migration
- Wildlife and pet trade, legal and illegal
- Extractive industry operations which can
  - Destroy habitat
  - Drive consumption of wildlife ("bush meat") by workers
- Livestock production near wildlife-rich locations
- Clean water availability for people and animals
- Pathogens in wastewater or sewage

Such data can add more detail on temporal and spatial variability in host distributions, shedding of potential pathogens, and reservoir host immunological status (Plowright et al. 2017).

The global capacity for genome sequencing and analysis has advanced at a remarkable pace for several decades and has facilitated a better understanding of microbial diversity and informed epidemiological studies of outbreaks (DeLong et al. 2022; Pappalardo et al. 2016). However, gaps remain in being able to use a pathogen's genetic instructions to predict key phenotypic features such as virulence, transmissibility, host range, host-cell binding, and host immune escape—analytical tools that could revolutionize risk assessments. Genome-predictive models of microbial zoonotic and epidemic potential remain nascent (Nwadiugwu and Monteiro 2022). Better understanding of pathogen diversity and use of next-generation sequencing to identify and then detect markers of virulence and host cell receptor binding targets could help prioritize surveillance efforts and interventions for those microbes with potential pathology in humans.

As the volume of data and the complexity of analyses increase, in-country bioinformatics and other analytic capacities must be strengthened to expedite the use of biological, behavioral, and environmental data for risk assessments, forecasting, identifying interventions, and developing risk-reduction measures and VTDs. Unhindered, expedited data sharing, including genetic sequences, among sectors and between scientists in different countries is essential for successful coordination and execution of research, surveillance, laboratory detection, spillover risk reduction, outbreak response, and development of VTDs before and during outbreaks. As seen with vaccines to counter SARS-CoV-2, global capabilities for accelerated vaccine development based on genome sequence opened new possibilities for rapid deployment of interventions, but emergency development of inter-

Selected Non-Pharmaceutical Interventions	Selected Medical Countermeasures (Pathogen specific or broad spectrum)
Social (physical) distancing	Vaccines
Masks and other personal protective equipment	Therapeutics: antivirals, monoclonal antibodies, antibiotics, immune-system modulators
Hand washing	Diagnostics
Heating potentially contaminated food and water	Patient care guidelines to optimize supportive care and disseminate information on MCMs
Practicing safer sex	
Minimizing contact with possible host animals	

Fig. 5 Examples of interventions against emerging zoonotic diseases

ventions VTDs still requires the timely sharing of genetic sequences and pathogen samples (▶ Chap. 7) (Pandemic Preparedness Partnership 2021).

4.2 Developing and Assessing Safety and Efficacy of Interventions to Reduce Spillover, Amplification, and Geographical Spread

Once sufficient data about a pathogen (e.g., hosts, pathogenesis, modes of transmission, and other factors) are available, interventions to reduce spillover risk can be developed and further assessed. Interventions broadly fall into the categories of nonpharmaceutical (a.k.a. public health) and MCMs, as shown in Fig. 5.

In order to develop broad-acting VTDs against families of pathogens that infect humans, genetic diversity across the virus family will need to be assessed and research done on key shared genetic sequences, antigen mapping, and pathogenic mechanisms.

As mentioned previously, interventions such as farm and market biosecurity along with animal vaccines have been shown to lower the number of human infections with influenza viruses (Youssef et al. 2021; Zhou et al. 2018). Emerging pathogens transmitted by arthropod vectors can potentially be addressed using vector-control measures, but these are difficult and expensive to implement at scale. At present, few interventions to prevent spillover are available for viruses such as Ebola, Lassa, mpox, and Nipah that are transmitted directly from wildlife to people. For Nipah, interventions have been proposed that would be expected to be effective, but they have not been widely adopted. For example, the boiling of date palm sap before consumption kills the virus, but also changes the composition of the product and its desirability (Khan et al. 2012). Bamboo "tree skirts" to block bats from accessing collected sap from date palm trees have been shown to prevent Nipah contamination of the sap, but collectors have not adopted the practice consistently because they lack the time and resources (Nahar et al. 2010).

In conclusion, filling in some of the gaps in pre-outbreak information will allow for more precise understanding of animal–human–environment interfaces, provide vital information to improve surveillance and early warning, and develop risk-reduction interventions to minimize the chances of future spillover.

5 Pre-outbreak Information: Best Practices and Recommendations

The dynamics between spillover of zoonotic pathogens and when an outbreak is detected and identified in humans are complex and

involve many sectors and disciplines. While previous efforts to establish pre-outbreak monitoring often have been a "learning-by-doing" exercise, there are some best practices that have emerged over the past few decades.

5.1 Strengthening Country Capacities Improves Detection and Response for Zoonotic Pathogens

Since spillover of emerging zoonotic pathogens can happen in any country, all nations should be able to prevent, detect, and respond to routine and emerging infectious disease threats. Regular surveillance to collect pre-outbreak information and detect unusual events should be established and linked to risk characterization and outbreak investigation (Institute of Medicine and National Research Council 2009). If regular surveillance is not in place, focused research studies can provide valuable insights, as demonstrated by community-level monitoring of SARS-CoV-2 and mpox virus in wastewater and sewage (Corpuz et al. 2020; Wolfe et al. 2022).

A strong, agile laboratory system is an important component for pre-outbreak monitoring (▶ Chap. 9). Virus detection, genetic sequencing, serology, and phylogenetic analyses provide valuable information on viral prevalence, composition, and diversity, helping to guide epidemiological investigations, target surveillance, and develop interventions. Ideally, there should be at least one highly capable laboratory facility in every country, though there are security concerns that a proliferation of biosafety level 4 facilities could present biosafety and biosecurity vulnerabilities. Laboratories must include facilities at the appropriate biosafety and security level for the work being carried out to minimize risks (Eaves 2020). Research data of this kind is also useful for generating serological tests to determine exposure and understand decay rates of antibody titers and immune escape (Andreano et al. 2021; Chia et al. 2021; Tan et al. 2020). Sensitive detection assays, such as quantitative polymerase chain reaction (qPCR), multiplex serological assays, and next-generation sequencing, can provide same-day turnaround for detection and preliminary characterization, even for use at the point of collection (Laing et al. 2021; Watsa et al. 2020). As some emerging microbes may be challenging to grow in a laboratory, models have been developed to predict the capacity for human infection (Mollentze et al. 2021). Other techniques include phylogenetic reconstruction of ancestral viruses to study adaptations that facilitate cross-species transmission, assessing immunological responses when exposing cell cultures to viral proteins, and understanding receptor binding sites to provide insight into which viruses are likely capable of infecting humans (Damas et al. 2020; Le Bert et al. 2020; Su et al. 2021; Zhao et al. 2005).

Because of the sheer volume and broad distribution of spillover interfaces, the limited staff and resources available for collecting pre-outbreak information must be deployed where spillover risk is greatest. Targeted surveillance can use currently available information on the mechanisms and relative risks of specific emerging zoonotic threats, based on factors like the size, density, and distribution of human, animal, and microbial populations; human behavior; and potentially high-risk chains of transmission that could lead to outbreaks, sustained human-to-human transmission, and geographical spread of emerging zoonotic pathogens (Alexander et al. 2018; Becker et al. 2019). An important aspect of detecting emerging threats early is understanding which human populations might be infected first and show clinical signs. Like SARS-CoV-2, some emerging zoonotic threats (e.g., H7N9 avian influenza, MERS-CoV) may be asymptomatic or mildly symptomatic in many healthy and younger individuals (Badawi and Ryoo 2016; Wang et al. 2017), highlighting the importance of monitoring comorbid or immunocompromised people. It is also critical to focus research on understanding the mechanisms of emergence of zoonotic pathogens in humans (including Ebola virus, MERS-CoV, Nipah virus, and SARS-CoV-1 and 2).

Better pre-outbreak information collection is necessary for improving prevention

and preparedness for a rapid response when needed. Pre-outbreak research programs during interpandemic periods can pivot to emergency response when necessary; in the case of zoonoses, research can focus on origins and spillover mechanisms to prevent recurrence and identify similar pathogens of concern. Funding and research sparked by the SARS-CoV-1 outbreak in 2002–2003, for example, informed surveillance and development of MCMs later used to address SARS-CoV-2 (Padron-Regalado 2020; Wang et al. 2006). After the publication of the SARS-CoV-2 genetic sequence, many countries quickly tested archived or new animal samples to learn more about the hosts of SARS-CoV-2-like viruses and their geographical distribution. Related viruses were detected in some horseshoe bat species and pangolins in Cambodia, Japan, Laos, Thailand, and Vietnam (Murakami et al. 2020; Wacharapluesadee et al. 2021b). Research on viruses related to SARS-CoV-2 in these countries improves risk assessment by expanding understanding of the host range of coronaviruses that can use human ACE-2 receptors (Delaune et al. 2021; Temmam et al. 2022).

The success of early warning surveillance systems in guiding effective response efforts depends on

- Contextual information collected during pre-outbreak monitoring and research.
- Ability to rapidly detect the first signal of an unusual infectious disease event and confirm the identity of the pathogen.
- Quality and completeness of pre-outbreak and post-outbreak data.
- Speed with which the information is collected, analyzed, and shared.

The detection of Marburg virus in bats sampled in Sierra Leone in 2017–2018 provided notice of the virus's presence in West Africa and allowed countries to prepare for future spillover events (Amman et al. 2020). Both Guinea in 2021 and Ghana in 2022 were then able to contain Marburg virus outbreaks with little or no onward spread in humans (WHO 2021, 2022d). In Thailand, diagnostic capacities developed for proactive monitoring of wildlife for zoonotic viruses were quickly repurposed in January 2020 to detect SARS-CoV-2 in visitors from Wuhan, China, allowing the government to immediately implement isolation and social-distancing measures before commercial testing kits were available (Wacharapluesadee et al. 2020).

Strengthening country capacities for collecting pre-outbreak information involves planning, staffing, training, equipment and supplies, coordination, communications, and funding to support efforts that span multiple sectors and levels of government. When research is supported by external funds or technical support, these partnerships must be equitable (▶ Chaps. 4 and 30). Numerous tools are available for countries to assess human and institutional capacities to identify gaps in pre-outbreak monitoring and outbreak detection and response. For example, the Joint External Evaluation, developed by WHO, brings together governments and other relevant stakeholders to develop a targeted National Action Plan for Health Security. The Electronic State Parties Self-Assessment Annual Reporting Tool (e-SPAR) provides a platform to develop accountability for meeting the requirements of the (WHO 2016). It should be noted that these rating systems for country capacity are more predictive of success in containing smaller outbreaks than for pandemics such as COVID-19 (Jain et al. 2022). After-action reviews and international negotiations to improve pandemic response are ongoing (WHO 2024). Simulation exercises can also be used to evaluate planned responses to infectious disease outbreaks in order to make program and policy improvements.

5.2 Systematic Collection of Pre-outbreak Information

The ability to collect, analyze, share, and use pre-outbreak information related to emerging zoonotic diseases in a targeted way is vital to prevention, preparedness, and response. Without such initial data, a vast number of samples may have to be collected in the dark, as it were, to understand the natural history of an emerging virus. For example, a 3-year

study in Guinea, Liberia, and Sierra Leone needed to test about 45,000 specimens from apparently healthy animals in order to detect Ebola Zaire in a bat from Liberia, Marburg virus in *Rousettus* bats from Sierra Leone, and a new species of Ebola (*Bombali ebolavirus*) in specific bat species in Guinea and Sierra Leone (PREDICT Consortium 2021). Along with identifying the bat species hosting these viruses, this work also indicated potential spillover interfaces (e.g., caves, homes).

Greater specificity of serosurveys to assess previous population exposure to viruses is critical for designing well-focused data collection tools and strategies (Epstein et al. 2020). Broad screening techniques have been valuable but are hampered by cross-reactivity issues (i.e., inability to distinguish between related viruses). Serological assays are becoming more refined, however, and it is now possible to distinguish exposure to SARS-CoV-2 from seasonal coronaviruses (Gilbert et al. 2013; Laing et al. 2021). One recent study from eastern Democratic Republic of the Congo used serology to detect previous exposure to Ebolaviruses (including Bombali virus) among people not otherwise known to have been infected (Goldstein et al. 2020). Other serological surveys have shown evidence for human exposure to several types of emerging zoonotic threats, including HIV, primate T-lymphotropic viruses, simian foamy viruses in primate hunters, and filoviruses in bat hunters (Dovih et al. 2019; Kurpiers et al. 2016; Wolfe et al. 2005).

But additional data on how and where pathogens emerge are of limited value if not analyzed, shared, and used to shape action by funders, policymakers, and at-risk populations. There are many obstacles to timely data sharing, as noted above, but there have been some recent advances in addressing some of the bottlenecks. For example, the researchers who detected Bombali virus in Sierra Leone rapidly presented their findings in ProMED (Archive Number: 20190408.6409703) and in a brief journal communication (Goldstein et al. 2018). In addition, the detection of Marburg virus in Sierra Leone was reported in ProMED and in brief communications in several other electronic venues more than a year in advance of peer-reviewed publication (Amman et al. 2020). Since the start of the COVID-19 pandemic, the use of data-sharing platforms such as GISAID, Our World in Data, and others, as well as preprint publication platforms, has accelerated the circulation of outbreak information and research data (Fraser et al. 2021; WHO 2022e).

5.3 Surveillance and Research Networks Improve Information Sharing, Preparedness, and Response

Cloud-based storage and sharing platforms such as GISAID[2] provide secure, rapid access for experts to analyze and assess influenza virus and SARS-CoV-2 sequence data in order to expeditiously identify and track viral variants and provide advice to policymakers and affected populations. The online availability of SARS-CoV-2 genetic sequence data in January 2020 was one of the factors that facilitated the development of diagnostic assays and safe, effective COVID-19 vaccines less than a year after the first human infections were noted (▶ Chap. 12).

Laboratories are more powerful if linked together to share data and workload. Laboratory networks may be based on a specific type of pathogen (e.g., influenza) (WHO 2023b); the surveillance data generated from both the animal and human health sectors are analyzed twice yearly to determine the composition of seasonal influenza vaccines for the human population (WHO 2023b). Other lab networks host data on multiple pathogens and may be regional or global, allowing for coordination, communications, standardization, and training before outbreaks occur (Africa CDC 2023; ECDC 2023; IAEA 2023). There have been recent discussions on further enhancing global and country surveillance by mobilizing a "coordinated network of multisector and multilateral stakeholders to collect

2 Originally the Global Initiative on Sharing Avian Influenza Data, now known simply as GISAID.

data, share insights, and respond to signals of early disease outbreaks" (Krofah et al. 2021). Though data provenance is a critical aspect of data collection, it is also critical that protocols are established and implemented that ensure data storage and sharing are safe and secure. This will minimize opportunities for the unintentional release or theft of such assets or the use of the data for harmful purposes. Safe data-sharing protocols should be developed, as they do not exist currently, so that both in-country and international partners are following similar standards.

Focused research projects such as the Centers for Research in Emerging Infectious Diseases (CREID) and the PREDICT emerging infection disease project have used a standardized surveillance and detection approach across many countries and regions to link scientists and laboratories together to generate pre-outbreak information on emerging pathogens (CREID 2022; PREDICT Consortium 2021).

5.4 Targeted Risk Reduction Interventions Work

There is evidence that when enough information on spillover dynamics is available for specific zoonotic pathogens (e.g., avian influenza viruses in Hong Kong live bird markets, Nipah virus in Malaysia), their spillover to people can be reduced (Leung et al. 2012; Nahar et al. 2017). Larger scale changes in policy (e.g., conditions on pig farms or live animal markets, vaccination of poultry) potentially yield much broader impact than efforts to change individual behaviors. Interventions to reduce spillover are generally not available for zoonotic diseases such as Ebola, Lassa fever, and mpox because information on the mechanisms of spillover is lacking. As a result, spillover events continue irregularly with the potential for any one of them escalating to a sustained outbreak, epidemic, or pandemic.

In order to support the application of spillover risk-reduction interventions, all countries should have the capacity to conduct pre-outbreak research and risk assessments across sectors to include cost–benefit analyses to aid decision-makers regarding policies and allocation of funds. Both the financial burden of inaction and the magnitude of previously hidden losses driven by "business-as-usual" must be captured and quantified to assess policy options (Schar et al. 2018). Disease emergence risks may be driven by practices that redound to the benefit of some and the detriment of others, and such economic factors must be considered in the planning and promotion of risk mitigation. Extractive industries, for example, may bring humans into new areas, destroy habitat, and pollute watercourses, all of which can drive disease emergence. The financial and quality of life burdens are distributed broadly across communities, livelihoods, and health systems, while the financial benefits may accrue to a handful of investors. Taking a whole-of-society approach to the analysis of costs and benefits helps identify equitable measures to minimize risks and promote sustainable interventions. Establishing benchmarks for low-risk industry practices paired with certification could (1) generate market-based pull incentives (e.g., premium pricing for quality-assured food products produced with minimal ecological disruption), and (2) establish a framework for corporate tax incentives (to the extent that the activities driving zoonotic risk are in the formal sector of the economy).

Given the substantial benefits to society of preventing disease outbreaks, this work should be supported financially by national and international stakeholders in both the public and private sectors. Illustrating the value of emerging disease prevention as a global public good, the promotion of avian influenza vaccination of commercial poultry through subsidized vaccines matched to currently circulating strains could be an important tool in reducing pandemic influenza risk (Wu et al. 2019). Finally, support should also go to longitudinal work to understand the dynamics of zoonoses in natural reservoirs subject to new pressures from climate and land-use change, as well as how interventions can influence current policies, business practices, and behaviors in order to reduce spillover risk.

5.5 Coordination with Other Infectious Disease Programs and Across Sectors to Improve Prevention, Detection, and Response

While infectious disease control programs and networks are often pathogen specific, it is important for existing programs to have some flexibility to adapt to a new pathogen. Every infectious disease program has experts with skills in surveillance, detection, prevention, risk communication, epidemiology, and research, among other areas. As occurred during the COVID-19 pandemic, such existing capacity can pivot to understanding and containing new threats in an emergency. For example, surveillance and laboratory systems for respiratory symptoms were able to test for SARS-CoV-2. In addition, many countries used their animal health labs to provide surge support for SARS-CoV-2 detection in human samples at the beginning of the COVID-19 pandemic or repurposed other surveillance and outbreak response structures (Drew et al. 2020; Wacharapluesadee et al. 2020). Risk communications and outreach expertise from HIV/AIDS programs were able to support interrupting person-to-person transmission of mpox virus, and, along with vaccination, appears to have helped bring the 2022 outbreak under control in Europe and North America (Kirby 2022). Successful redirection of resources to contain an outbreak of an emerging pathogen depends on the speed with which it can be accomplished as well as appropriate use of capabilities. This requires development (between outbreaks) of well-planned yet flexible preparedness and response strategies and standard operating procedures for how and when to launch an emergency research response, along with clear channels for emergency financing when necessary (▶ Chap. 28).

Given the complex interactions between emerging zoonotic pathogens, animal hosts, susceptible humans, vectors, and the environment, a multidisciplinary, collaborative, and coordinated research and response approach is required. Identifying and assessing potential hazards and having systems and procedures in place to detect, respond, and share information will prepare governments, businesses, communities, and others for future outbreaks. Some of the tools now available to facilitate multisectoral preparedness planning and response include.

- Table-top simulation exercises
- The *Tripartite Zoonoses Guide* compiled by the Food and Agriculture Organization of the United Nations (FAO), WHO, and the World Organization for Animal Health (WOAH) (WHO et al. 2019)
- One Health zoonotic disease prioritization workshops (CDC 2018b)
- Systematic incorporation of One Health perspectives, methodologies, and coordination into pandemic preparedness (NASEM 2022)
- Case studies from around the world conveying lessons from One Health programming (PREDICT Consortium 2021)

Together, these strategies, with support from global and regional partners, can assist countries in strengthening their capacities to promote preparedness and societal resilience. Preparedness planning must also try to avoid the common human error of applying the lessons of a past crisis without careful consideration of present needs.

5.6 Linking Action Plans to Resource Mapping

In most countries, strengthening surveillance, research capacity, and collection and dissemination of pre-outbreak data requires additional funding. Sustainable and innovative funding mechanisms are necessary to incentivize prevention, detection, and response. This includes access to grants or low-interest loans, especially to communities with lower resource bases and the highest spillover risk. WHO and other partners currently support countries in mapping internal and external funding sources available to support global health security National Action Plans (NAPs). These plans not only identify funding and capacity gaps but also allow prospective donors to see what their funds would support.

The World Bank has established a Pandemic Fund to finance pandemic prevention, preparedness, and response capabilities and address critical gaps in low- and middle-income countries (► Chap. 28) (WBG 2022b).

Several funding mechanisms have been created to improve early warning detection systems or research. The U.S. National Institutes of Health (NIH) established the Centers for Research in Emerging Infectious Diseases in 2020 to develop multidisciplinary studies into where and how zoonotic agents "emerge from wildlife and spillover to cause disease in people" (NIH 2021). These centers focus on natural reservoirs, high-risk interfaces, and urban areas, while developing diagnostics to improve detection and facilitate study of human immune responses to zoonotic pathogens. The U.S. National Science Foundation has created the Predictive Intelligence for Pandemic Prevention Development grant program to support research on infectious disease emergence through "state-of-the art forecasting, real-time monitoring, mitigation and prevention of the spread of pathogens" (NSF 2022). Other efforts include a French/European Commission program called PREZODE: PREventing ZOonotic Disease Emergence (Peyre et al. 2021) and current efforts by the U.S. Agency for International Development building upon more than a decade of support to advance viral zoonosis detection.

In the long term, all countries need sustainable funding mechanisms to maintain capacities to prevent, detect, and respond to infectious disease threats, including collection of pre-outbreak information. Given that the private sector has an interest in preventing the staffing, supply, and sales disruptions caused by epidemics and pandemics, companies should be included in discussions about financing pandemic prevention, preparedness, and response. Leveraging the resources of capital markets and environmental, social, and governance investing has facilitated the adoption of lower-risk food animal production practices (FAIRR 2022) and may have some potential to incentivize private sector-led innovation in shifting both endemic and emerging disease risk landscapes. Examples of private sector investments include the analysis of Google searches for influenza symptoms to help prioritize regional distribution of seasonal influenza vaccine in the United States (Ginsberg et al. 2009).

6 Recommendations

Despite the availability of the best practices discussed above, it is still not customary in many countries to collect and use pre-outbreak information to reduce the risk of zoonotic disease spillover and spread. To address this challenge, we recommend three broad mechanisms, each of them with suggested supporting activities. The overarching theme of these recommendations is to strengthen country's capacities to collect, analyze, and share pre-outbreak information while avoiding replacing existing capacity or building parallel systems. Equitable partnership with local and regional stakeholders from concept through design and implementation is critical. So is a risk-based approach that informs where resources and effort should be applied to provide the greatest impact. All of the suggestions below can and should be built on top of existing investments in global health security and the response to the COVID-19 pandemic.

6.1 Strengthen and Prioritize Collection of Pre-outbreak Information

Without the pre-outbreak information providing a sense of relative zoonotic disease risks, countries will be limited in their ability allocate their resources to prevent, detect, and respond to outbreaks.

6.1.1 Country Activities, Taking into Consideration the Best Practices and Gaps Previously Mentioned

- Identify and map stakeholders and potential partners, including sources of funding.
- Endorse and facilitate routine coordination and collaboration across infectious disease programs and across sectors.

- Conduct cross-sectoral risk assessments for priority zoonotic pathogens (and unknown pathogens) and identify what is needed to support risk reduction and data collection.
- Prioritize populations and animal-human-environment interfaces for routine monitoring based on cross-sectoral risk assessments.
- Strengthen surveillance and monitoring mechanisms to include routine collection of pre-outbreak information where it is most needed.
- Strengthen laboratory capacity for pathogen identification, sequencing, and further research, including emerging zoonotic diseases. Methods needed include serological studies, genetic sequencing, and rapid multiplexed assays.
- Introduce appropriate technological innovations to generate and utilize new data streams, especially genome sequencing and analysis methodologies, for example, wastewater monitoring.
- Ensure long-term funding and training for key technical support staff.

6.1.2 Regional and Global Activities, Taking into Consideration the Best Practices and Gaps Previously Mentioned

- Support regional reference lab structures that serve as common specialized resources where individual countries may not be able to support cutting-edge, expensive capacities.
- Provide technical guidance, strategies and tools, training, and financial support to improve the capacity for collection of pre-outbreak information.
- Provide back-up surge support for pathogen identification in case countries need assistance with preparedness, prevention, detection, and response.
- Provide financial support.

6.2 Strengthen In-County Data Systems and Their Linkages with International Databases

Given the wealth of data that can be generated by pre-outbreak monitoring and other biosurveillance, it is imperative that systems be in place for data collection, storage, and sharing with adequate controls to protect the rights of the data owners, including intellectual property, privacy, security, and sovereignty (▶ Chap. 7). Pre-outbreak information must be analyzed and shared expeditiously. Many countries have existing data systems that coordinate across different diseases and sectors, especially as a function of integrated national health systems, but they may not be optimally linked either domestically or internationally, may be slow in processing data, may not collect all information needed, and may not have adequate funding.

6.2.1 Country Activities, Taking into Consideration the Best Practices and Gaps Previously Mentioned

- Identify and map stakeholders and potential partners, including sources of funding and owners and end-users of pre-outbreak information.
- Identify and assess existing data systems that can compile and provide access to pre-outbreak information, including identifying gaps and bottlenecks.
- Update policies and regulations to facilitate linkages among existing data systems so they can routinely share essential pre-outbreak information across sectors and across borders.
- Prioritize and strengthen the capacities of existing data systems and staff to improve routine collection, analysis, and sharing of pre-outbreak information. Incorporate technological developments such as wastewater testing and more capable point-of-care diagnostics (veterinary as well as human) to increase the coverage and speed of detection.

6.2.2 Regional and Global Activities, Taking into Consideration the Best Practices and Gaps Previously Mentioned

- Develop or strengthen international standards, agreements, databases, and systems for sharing pre-outbreak information.
- Provide technical guidance, strategies and tools, training, and financial support to improve the equitable sharing of pre-outbreak information among sectors, countries, and international databases.

6.3 Distill Pre-outbreak Information into Actionable Disease Intelligence for Risk Mitigation

6.3.1 Country Activities, Taking into Consideration the Best Practices and Gaps Previously Mentioned

- Operationalize pre-outbreak information data systems to gather and synthesize diverse data across sectors for actionable disease intelligence.
- Identify and map stakeholders who can use pre-outbreak information to take action.
- Generate evidence-based risk profiles and policy recommendations tailored to local and national disease emergence risk dynamics.
- Leverage data availability and foresight analysis to identify trends informing disease early warning, pre-outbreak deployment of surveillance and response capacities, and targeted risk mitigation.
- Utilize advances in pathogen assessment and the prototype pathogen approach (Cassetti et al. 2022) to prepare for and rapidly implement MCM development, including prioritized VTDs.
- Apply findings from pre-outbreak information systems in the iterative refinement of priority surveillance targets and risk mitigation strategies.
- Use a shared lexicon to expedite scientific understanding and proactively avoid stigmatizing animals.

6.3.2 Regional and Global Activities, Taking into Consideration the Best Practices and Gaps Previously Mentioned

- Provide guidance, technical support, and funding for developing and validating risk mitigation measures.
- Assist with sharing and adapting validated risk-mitigation measures among countries.

7 Conclusion

Collection and use of pre-outbreak information is critical for much-needed improvements in country and global preparedness and response to emerging zoonotic diseases. Substantial progress has been made in collecting valuable information in advance of human-to-human transmission of zoonotic pathogens. However, there continue to be outbreaks caused by zoonotic pathogens such as Ebola virus, mpox virus, and SARS-CoV-2 that are not detected until there is sustained human-to-human transmission. These events highlight the significant risks involved in waiting for pathogens to emerge in the human population before developing and applying containment and mitigation measures. Strengthening capacity for collecting pre-outbreak information is crucial to the early warning that could be provided by effective surveillance. Investments to strengthen pre-outbreak information systems would also contribute to an interlinked global early warning system for emerging infectious disease threats.

Securing resources for in-country capacity improvements for global health security is frequently a major obstacle to pandemic prevention, preparedness, and response. Several internal and external options are potentially available for countries to support immediate needs. In the longer term, financing global

health security investments must transition to normal budgetary channels in both the public and private sectors. When viewed through an economic lens, expanding surveillance and prevention capacities have produced strong returns on investment by reducing the frequency, size, and impact of infectious disease outbreaks. It is vital that financial resources available to cover global health security include the collection, analysis, sharing, and use of pre-outbreak information.

Discussion Questions

1. What zoonotic diseases have emerged or reemerged recently? Discuss the potential for future zoonotic spillover and some targeted preventive measures against pathogen flow between wildlife or livestock and humans.
2. Investments in collecting pre-outbreak information on emerging zoonoses to prevent spillover, amplification, and geographical spread can yield a high return on investment and contribute significantly to strengthening global health security.
   (a) Why are pathogen spillovers frequently undetected, or detected only after harmful delays? Consider anthropogenic, climatic, and environmental factors when answering this question.
   (b) Why are certain vertebrate species (e.g., bats, rodents, nonhuman primates, and birds) more likely to be associated with zoonotic spillover and crossing into humans than other animals?
   (c) Discuss how to map potential spillover hot spots using information on where human, pathogen, animal host, vector populations, and other key factors converge.
   (d) Describe human behavioral interventions that can prevent or reduce spillover during an early public health response to infectious disease emergencies.
3. What is needed to improve the characterization of animal–human–environment interfaces by collecting new data streams reflecting population-level changes on a regular basis?
4. What are some measures that could enhance pre-outbreak monitoring of zoonotic spillovers of pathogens and detect outbreaks in humans more promptly?
5. Name some typical interventions against emerging infectious diseases that must be available to policymakers, scientists, health systems, businesses, and communities to reduce the frequency and impact of zoonotic disease spillover.
6. Provide several broad recommendations on how countries and the international community can improve detection, prevention, and response to future epidemic and pandemic threats.

References

Adjemian J, Farnon EC, Tschioko F, Wamala JF, Byaruhanga E, Bwire GS, et al. Outbreak of Marburg hemorrhagic fever among miners in Kamwenge and Ibanda Districts, Uganda, 2007. J Infect Dis. 2011;204(Suppl 3):S796–9. https://doi.org/10.1093/infdis/jir312.

Africa Centres for Disease Control and Prevention. Laboratory systems and networks. Addis Ababa: Africa Centres for Disease Control and Prevention; 2023. https://africacdc.org/programme/laboratory-systems-and-networks/. Accessed 19 Jan 2023.

Akhmetzhanov AR, Asai Y, Nishiura H. Quantifying the seasonal drivers of transmission for Lassa fever in Nigeria. Philos Trans R Soc Lond Ser B Biol Sci. 2019;374(1775):20180268. https://doi.org/10.1098/rstb.2018.0268.

Alexander KA, Carlson CJ, Lewis BL, Getz WM, Marathe MV, Eubank SG, et al. The ecology of pathogen spillover and disease emergence at the human-wildlife-environment interface. In: Hurst CJ, editor. The connections between ecology and infectious disease. Cham: Springer International Publishing; 2018. p. 267–98.

Allen T, Murray KA, Zambrana-Torrelio C, Morse SS, Rondinini C, Di Marco M, et al. Global hotspots and correlates of emerging zoonotic diseases. Nat Commun. 2017;8(1):1124. https://doi.org/10.1038/s41467-017-00923-8.

Amman BR, Bird BH, Bakarr IA, Bangura J, Schuh AJ, Johnny J, et al. Isolation of Angola-like Marburg virus from Egyptian rousette bats from West Africa. Nat Commun. 2020;11(1):510. https://doi.org/10.1038/s41467-020-14327-8.

Andreano E, Piccini G, Licastro D, Casalino L, Johnson NV, Paciello I, et al. SARS-CoV-2 escape from a

highly neutralizing COVID-19 convalescent plasma. Proc Natl Acad Sci USA. 2021;118(36):e2103154118. https://doi.org/10.1073/pnas.2103154118.

Antonovics J, Wilson AJ, Forbes MR, Hauffe HC, Kallio ER, Leggett HC, et al. The evolution of transmission mode. Philos Trans R Soc Lond Ser B Biol Sci. 2017;372(1719):20160083. https://doi.org/10.1098/rstb.2016.0083.

Anyamba A, Chretien J-P, Small J, Tucker CJ, Formenty PB, Richardson JH, et al. Prediction of a Rift Valley fever outbreak. Proc Natl Acad Sci USA. 2009;106(3):955–9. https://doi.org/10.1073/pnas.0806490106.

Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. Int J Infect Dis. 2016;49:129–33. https://doi.org/10.1016/j.ijid.2016.06.015.

Bartlow AW, Manore C, Xu C, Kaufeld KA, Del Valle S, Ziemann A, et al. Forecasting zoonotic infectious disease response to climate change: mosquito vectors and a changing environment. Vet Sci. 2019; https://doi.org/10.3390/vetsci6020040.

Becker DJ, Washburne AD, Faust CL, Pulliam JRC, Mordecai EA, Lloyd-Smith JO, et al. Dynamic and integrative approaches to understanding pathogen spillover. Philos Trans R Soc Lond Ser B Biol Sci. 2019;374(1782):20190014. https://doi.org/10.1098/rstb.2019.0014.

Becker DJ, Seifert SN, Carlson CJ. Beyond infection: integrating competence into reservoir host prediction. Trends Ecol Evol. 2020;35(12):1062–5. https://doi.org/10.1016/j.tree.2020.08.014.

Bernstein AS, Ando AW, Loch-Temzelides T, Vale MM, Li BV, Li H, et al. The costs and benefits of primary prevention of zoonotic pandemics. Sci Adv. 2022;8(5):eabl4183. https://doi.org/10.1126/sciadv.abl4183.

Berry I, Rahman M, Flora MS, Shirin T, Alamgir ASM, Khan MH, et al. Seasonality of influenza and coseasonality with avian influenza in Bangladesh, 2010–19: a retrospective, time-series analysis. Lancet Glob Health. 2022;10(8):e1150–e8. https://doi.org/10.1016/s2214-109x(22)00212-1.

Betts MG, Wolf C, Ripple WJ, Phalan B, Millers KA, Duarte A, et al. Global forest loss disproportionately erodes biodiversity in intact landscapes. Nature. 2017;547(7664):441–4. https://doi.org/10.1038/nature23285.

Blagrove MSC, Pilgrim J, Kotsiri A, Hui M, Baylis M, Wardeh M. Monkeypox virus shows potential to infect a diverse range of native animal species across Europe, indicating high risk of becoming endemic in the region. bioRxiv. 2022; https://doi.org/10.1101/2022.08.13.503846.

Brook CE, Ranaivoson HC, Broder CC, Cunningham AA, Héraud JM, Peel AJ, et al. Disentangling serology to elucidate henipa- and filovirus transmission in Madagascar fruit bats. J Anim Ecol. 2019;88(7):1001–16. https://doi.org/10.1111/1365-2656.12985.

Caminade C, McIntyre KM, Jones AE. Impact of recent and future climate change on vector-borne diseases. Ann N Y Acad Sci. 2019;1436(1):157–73. https://doi.org/10.1111/nyas.13950.

Capua I, Alexander DJ. The challenge of avian influenza to the veterinary community. Avian Pathol. 2006;35(3):189–205. https://doi.org/10.1080/03079450600717174.

Capua I, Marangon S. Control of avian influenza in poultry. Emerg Infect Dis. 2006;12(9):1319–24. https://doi.org/10.3201/eid1209.060430.

Carlson CJ, Farrell MJ, Grange Z, Han BA, Mollentze N, Phelan AL, et al. The future of zoonotic risk prediction. Philos Trans R Soc Lond Ser B Biol Sci. 2021;376(1837):20200358. https://doi.org/10.1098/rstb.2020.0358.

Carroll D, Daszak P, Wolfe N, Gao G, Morel C, Morzaria S, et al. The Global Virome Project. Science. 2018;359(6378):872–4. https://doi.org/10.1126/science.aap7463.

Cassetti MC, Pierson TC, Patterson LJ, et al. Prototype pathogen approach for vaccine and monoclonal antibody development: a critical component of the NIAID Plan for pandemic preparedness. J Infect Dis. 2022.

CDC. Update: multistate outbreak of monkeypox—Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003. MMWR Morb Mortal Wkly Rep. 2003;52(27):642–6.

CDC. History of 1918 flu pandemic. Atlanta: Centers for Disease Control and Prevention; 2018a. https://www.cdc.gov/flu/pandemic-resources/1918-commemoration/1918-pandemic-history.htm. Accessed 12 Oct 2022.

CDC. Prioritizing zoonotic diseases for multisectoral, One Health collaboration in the United States. Atlanta: Centers for Disease Control and Prevention; 2018b.

CDC. 2022 Monkeypox outbreak global map. Atlanta: Centers for Disease Control and Prevention; 2022a. https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html. Accessed 10 Oct 2022.

CDC. History of Ebola virus disease (EVD) outbreaks. Atlanta: Centers for Disease Control and Prevention; 2022b. https://www.cdc.gov/vhf/ebola/history/chronology.html#anchor_1526565058132. Accessed 10 Oct 2022.

Chia WN, Zhu F, Ong SWX, Young BE, Fong SW, Le Bert N, et al. Dynamics of SARS-CoV-2 neutralising antibody responses and duration of immunity: a longitudinal study. Lancet Microbe. 2021;2(6):e240–9. https://doi.org/10.1016/s2666--5247(21)00025-2.

Chomel BB, Belotto A, Meslin FX. Wildlife, exotic pets, and emerging zoonoses. Emerg Infect Dis. 2007;13(1):6–11. https://doi.org/10.3201/eid1301.060480.

Chowdhury S, Azziz-Baumgartner E, Kile JC, Hoque MA, Rahman MZ, Hossain ME, et al. Association of biosecurity and hygiene practices with environmental contamination with Influenza A viruses in live bird markets, Bangladesh. Emerg Infect Dis. 2020;26(9):2087–96. https://doi.org/10.3201/eid2609.191029.

Chua KB. Nipah virus outbreak in Malaysia. J Clin Virol. 2003;26(3):265–75. https://doi.org/10.1016/S1386-6532(02)00268-8.

Corpuz MVA, Buonerba A, Vigliotta G, Zarra T, Ballesteros F Jr, Campiglia P, et al. Viruses in wastewater: occurrence, abundance and detection methods. Sci Total Environ. 2020;745:140910. https://doi.org/10.1016/j.scitotenv.2020.140910.

CREID. Responding to emerging infectious diseases. RTI International; 2022. https://creid-network.org/. Accessed 11 Dec 2022.

Damas J, Hughes GM, Keough KC, Painter CA, Persky NS, Corbo M, et al. Broad host range of SARS-CoV-2 predicted by comparative and structural analysis of ACE2 in vertebrates. Proc Natl Acad Sci USA. 2020;117(36):22311–22. https://doi.org/10.1073/pnas.2010146117.

de Oliveira RC, Fernandes J, Gonçalves-Oliveira J, Guterres A, de Lemos ERS. Out of the shadows, into the spotlight: invisible zoonotic diseases in Brazil. Lancet Reg Health Am. 2022;8:100202. https://doi.org/10.1016/j.lana.2022.100202.

Delardas O, Kechagias KS, Pontikos PN, Giannos P. Socio-economic impacts and challenges of the coronavirus pandemic (COVID-19): an updated review. Sustainability. 2022; https://doi.org/10.3390/su14159699.

Delaune D, Hul V, Karlsson EA, Hassanin A, Ou TP, Baidaliuk A, et al. A novel SARS-CoV-2 related coronavirus in bats from Cambodia. Nat Commun. 2021;12(1):6563. https://doi.org/10.1038/s41467--021-26809-4.

DeLong JP, Al-Sammak MA, Al-Ameeli ZT, Dunigan DD, Edwards KF, Fuhrmann JJ, et al. Towards an integrative view of virus phenotypes. Nat Rev Microbiol. 2022;20(2):83–94. https://doi.org/10.1038/s41579-021-00612-w.

Dovih P, Laing ED, Chen Y, Low DHW, Ansil BR, Yang X, et al. Filovirus-reactive antibodies in humans and bats in Northeast India imply zoonotic spillover. PLoS Negl Trop Dis. 2019;13(10):e0007733. https://doi.org/10.1371/journal.pntd.0007733.

Drew DA, Nguyen LH, Steves CJ, Menni C, Freydin M, Varsavsky T, et al. Rapid implementation of mobile technology for real-time epidemiology of COVID-19. Science. 2020;368(6497):1362–7. https://doi.org/10.1126/science.abc0473.

Dudas G, Carvalho LM, Rambaut A, Bedford T. MERS-CoV spillover at the camel-human interface. Elife. 2018;7:e31257. https://doi.org/10.7554/eLife.31257.

Duffy S, Shackelton LA, Holmes EC. Rates of evolutionary change in viruses: patterns and determinants. Nat Rev Genet. 2008;9(4):267–76. https://doi.org/10.1038/nrg2323.

Eaves E. The risks of building too many bio labs. New Yorker. 2020.

Eby P, Peel AJ, Hoegh A, Madden W, Giles JR, Hudson PJ, et al. Pathogen spillover driven by rapid changes in bat ecology. Nature. 2022;613:340. https://doi.org/10.1038/s41586-022-05506-2.

ECDC. Emerging Viral Diseases-Expert Laboratory Network (EVD-LabNet). Solna, SE: European Centre for Disease Prevention and Control; 2023. https://www.ecdc.europa.eu/en/about-us/partnerships-and-networks/disease-and-laboratory-networks/evd-labnet. Accessed 19 Jan 2023.

Epstein JH, Anthony SJ, Islam A, Kilpatrick AM, Ali Khan S, Balkey MD, et al. Nipah virus dynamics in bats and implications for spillover to humans. Proc Natl Acad Sci USA. 2020;117(46):29190–201. https://doi.org/10.1073/pnas.2000429117.

FAIRR. FAIRR: the world's fastest-growing investor network focusing on ESG risks in the global food sector. London: The FAIRR Initiative; 2022. https://www.fairr.org/. Accessed 16 Oct 2022.

Fan VY, Jamison DT, Summers LH. Pandemic risk: how large are the expected losses? Bull World Health Organ. 2018;96(2):129–34. https://doi.org/10.2471/blt.17.199588.

Finlay BB, McFadden G. Anti-immunology: evasion of the host immune system by bacterial and viral pathogens. Cell. 2006;124(4):767–82. https://doi.org/10.1016/j.cell.2006.01.034.

Fraser N, Brierley L, Dey G, Polka JK, Pálfy M, Nanni F, et al. The evolving role of preprints in the dissemination of COVID-19 research and their impact on the science communication landscape. PLoS Biol. 2021;19(4):e3000959. https://doi.org/10.1371/journal.pbio.3000959.

Frazzini S, Amadori M, Turin L, Riva F. SARS CoV-2 infections in animals, two years into the pandemic. Arch Virol. 2022;167:2503. https://doi.org/10.1007/s00705-022-05609-1.

Gallo RC, Montagnier L. The discovery of HIV as the cause of AIDS. N Engl J Med. 2003;349(24):2283–5. https://doi.org/10.1056/NEJMp038194.

Gibb R, Redding DW, Chin KQ, Donnelly CA, Blackburn TM, Newbold T, et al. Zoonotic host diversity increases in human-dominated ecosystems. Nature. 2020;584(7821):398–402. https://doi.org/10.1038/s41586-020-2562-8.

Gibb R, Albery GF, Mollentze N, Eskew EA, Brierley L, Ryan SJ, et al. Mammal virus diversity estimates are unstable due to accelerating discovery effort. Biol Lett. 2022;18(1):20210427. https://doi.org/10.1098/rsbl.2021.0427.

Gilbert AT, Fooks AR, Hayman DTS, Horton DL, Müller T, Plowright R, et al. Deciphering serology to understand the ecology of infectious diseases in wildlife. EcoHealth. 2013;10(3):298–313. https://doi.org/10.1007/s10393-013-0856-0.

Ginsberg J, Mohebbi MH, Patel RS, Brammer L, Smolinski MS, Brilliant L. Detecting influenza epi-

demics using search engine query data. Nature. 2009;457(7232):1012–4. https://doi.org/10.1038/nature07634.

Glidden CK, Nova N, Kain MP, Lagerstrom KM, Skinner EB, Mandle L, et al. Human-mediated impacts on biodiversity and the consequences for zoonotic disease spillover. Curr Biol. 2021;31(19):R1342–r61. https://doi.org/10.1016/j.cub.2021.08.070.

Goldstein T, Anthony SJ, Gbakima A, Bird BH, Bangura J, Tremeau-Bravard A, et al. The discovery of Bombali virus adds further support for bats as hosts of ebolaviruses. Nat Microbiol. 2018;3(10):1084–9. https://doi.org/10.1038/s41564-018-0227-2.

Goldstein T, Belaganahalli MN, Syaluha EK, Lukusa JK, Greig DJ, Anthony SJ, et al. Spillover of ebolaviruses into people in eastern Democratic Republic of Congo prior to the 2018 Ebola virus disease outbreak. One Health Outlook. 2020;2(1):21. https://doi.org/10.1186/s42522-020-00028-1.

Grange ZL, Goldstein T, Johnson CK, Anthony S, Gilardi K, Daszak P, et al. Ranking the risk of animal-to-human spillover for newly discovered viruses. Proc Natl Acad Sci USA. 2021;118(15):e2002324118. https://doi.org/10.1073/pnas.2002324118.

Grassly NC, Fraser C. Seasonal infectious disease epidemiology. Proc Biol Sci. 2006;273(1600):2541–50. https://doi.org/10.1098/rspb.2006.3604.

Groves HE, Piché-Renaud PP, Peci A, Farrar DS, Buckrell S, Bancej C, et al. The impact of the COVID-19 pandemic on influenza, respiratory syncytial virus, and other seasonal respiratory virus circulation in Canada: a population-based study. Lancet Reg Health Am. 2021;1:100015. https://doi.org/10.1016/j.lana.2021.100015.

Hansen MC, Potapov PV, Moore R, Hancher M, Turubanova SA, Tyukavina A, et al. High-resolution global maps of 21st-century forest cover change. Science. 2013;342(6160):850–3. https://doi.org/10.1126/science.1244693.

Hassell JM, Begon M, Ward MJ, Fèvre EM. Urbanization and disease emergence: dynamics at the wildlife-livestock-human interface. Trends Ecol Evol. 2017;32(1):55–67. https://doi.org/10.1016/j.tree.2016.09.012.

Hayman DT. Biannual birth pulses allow filoviruses to persist in bat populations. Proc Biol Sci. 2015;282(1803):20142591. https://doi.org/10.1098/rspb.2014.2591.

Hendry AP, Gotanda KM, Svensson EI. Human influences on evolution, and the ecological and societal consequences. Philos Trans R Soc Lond Ser B Biol Sci. 2017;372(1712):20160028. https://doi.org/10.1098/rstb.2016.0028.

Hornok S, Földvári G, Rigó K, Meli ML, Gönczi E, Répási A, et al. Synanthropic rodents and their ectoparasites as carriers of a novel haemoplasma and vector-borne, zoonotic pathogens indoors. Parasites Vectors. 2015;8(1):27. https://doi.org/10.1186/s13071-014-0630-3.

Huong NQ, Nga NTT, Long NV, Luu BD, Latinne A, Pruvot M, et al. Coronavirus testing indicates transmission risk increases along wildlife supply chains for human consumption in Viet Nam, 2013–2014. PLoS One. 2020;15(8):e0237129. https://doi.org/10.1371/journal.pone.0237129.

IAEA. Zoonotic Disease Integrated Action (ZODIAC): current status and future direction. Vienna: International Atomic Energy Agency; 2023. https://www.iaea.org/newscenter/news/zoonotic-disease-integrated-action-zodiac-current-status-and-future-direction. Accessed 19 Jan 2023.

Institute of Medicine, National Research Council. Achieving an effective zoonotic disease surveillance system. In: Keusch GT, Pappaioanou M, González MC, Scott KA, Tsai P, editors. Sustaining global surveillance and response to emerging zoonotic diseases. Washington, DC: The National Academies Press; 2009. p. 338.

Islam M, Luby S, Gurley S. Developing culturally appropriate interventions to prevent person to person transmission of Nipah virus in Bangladesh: cultural epidemiology in action. In: Banwell C, Ulijaszek S, Dixon J, editors. When culture impacts health. London: Academic; 2013. p. 329–37.

Jain V, Sharp A, Neilson M, Bausch DG, Beaney T. Joint External Evaluation scores and communicable disease deaths: an ecological study on the difference between epidemics and pandemics. PLoS Glob Public Health. 2022;2(8):e0000246. https://doi.org/10.1371/journal.pgph.0000246.

Joffrin L, Hoarau AOG, Lagadec E, Torrontegi O, Köster M, Le Minter G, et al. Seasonality of coronavirus shedding in tropical bats. R Soc Open Sci. 2022;9(2):211600. https://doi.org/10.1098/rsos.211600.

Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, et al. Global trends in emerging infectious diseases. Nature. 2008;451(7181):990–3. https://doi.org/10.1038/nature06536.

Jones BA, Grace D, Kock R, Alonso S, Rushton J, Said MY, et al. Zoonosis emergence linked to agricultural intensification and environmental change. Proc Natl Acad Sci USA. 2013;110(21):8399–404. https://doi.org/10.1073/pnas.1208059110.

Keenliside J. Pandemic influenza A H1N1 in swine and other animals. In: Richt JA, Webby RJ, editors. Swine Influenza. Berlin, Heidelberg, Springer; 2013. p. 259–71.

Keesing F, Ostfeld RS. Impacts of biodiversity and biodiversity loss on zoonotic diseases. Proc Natl Acad Sci USA. 2021;118(17):e2023540118. https://doi.org/10.1073/pnas.2023540118.

Kellner KF, Swihart RK. Accounting for imperfect detection in ecology: a quantitative review. PLoS One. 2014;9(10):e111436. https://doi.org/10.1371/journal.pone.0111436.

Kessler MK, Becker DJ, Peel AJ, Justice NV, Lunn T, Crowley DE, et al. Changing resource landscapes

and spillover of henipaviruses. Ann N Y Acad Sci. 2018;1429(1):78–99. https://doi.org/10.1111/nyas.13910.

Khan SU, Gurley ES, Hossain MJ, Nahar N, Sharker MA, Luby SP. A randomized controlled trial of interventions to impede date palm sap contamination by bats to prevent Nipah virus transmission in Bangladesh. PLoS One. 2012;7(8):e42689. https://doi.org/10.1371/journal.pone.0042689.

Kirby T. From early alarm to gradual control of monkeypox. Lancet HIV. 2022;9:e824. https://doi.org/10.1016/S2352-3018(22)00299-5.

Klunk J, Vilgalys TP, Demeure CE, Cheng X, Shiratori M, Madej J, et al. Evolution of immune genes is associated with the Black Death. Nature. 2022;611:312. https://doi.org/10.1038/s41586-022-05349-x.

Koopmans M. Surveillance strategy for early detection of unusual infectious disease events. Curr Opin Virol. 2013;3(2):185–91. https://doi.org/10.1016/j.coviro.2013.02.003.

Kreuder Johnson C, Hitchens PL, Smiley Evans T, Goldstein T, Thomas K, Clements A, et al. Spillover and pandemic properties of zoonotic viruses with high host plasticity. Sci Rep. 2015;5:14830. https://doi.org/10.1038/srep14830.

Krofah E, Choe SH, Sud A, Degarmo A. A global early warning system for pandemics: a blueprint for coordination. Santa Monica, CA: Milken Institute; 2021.

Kucharski A. Fragmented outbreak data will lead to a repeat of COVID-19. Nature. 2022;608(7924):649. https://doi.org/10.1038/d41586-022-02268-9.

Kummer S, Kranz DC. Henipaviruses—a constant threat to livestock and humans. PLoS Negl Trop Dis. 2022;16(2):e0010157. https://doi.org/10.1371/journal.pntd.0010157.

Kurpiers LA, Schulte-Herbrüggen B, Ejotre I, Reeder DM. Bushmeat and emerging infectious diseases: lessons from Africa. In: Angelici FM, editor. Problematic wildlife: a cross-disciplinary approach. Cham: Springer International Publishing; 2016. p. 507–51.

Laing ED, Sterling SL, Richard SA, Epsi NJ, Coggins SA, Samuels EC, et al. Antigen-based multiplex strategies to discriminate SARS-CoV-2 natural and vaccine induced immunity from seasonal human coronavirus humoral responses. medRxiv. 2021; https://doi.org/10.1101/2021.02.10.21251518.

Le Bert N, Tan AT, Kunasegaran K, Tham CYL, Hafezi M, Chia A, et al. SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls. Nature. 2020;584(7821):457–62. https://doi.org/10.1038/s41586-020-2550-z.

Leung YH, Lau EH, Zhang LJ, Guan Y, Cowling BJ, Peiris JS. Avian influenza and ban on overnight poultry storage in live poultry markets, Hong Kong. Emerg Infect Dis. 2012;18(8):1339–41. https://doi.org/10.3201/eid1808.111879.

Li YT, Linster M, Mendenhall IH, Su YCF, Smith GJD. Avian influenza viruses in humans: lessons from past outbreaks. Br Med Bull. 2019;132(1):81–95. https://doi.org/10.1093/bmb/ldz036.

Lindahl JF, Grace D. The consequences of human actions on risks for infectious diseases: a review. Infect Ecol Epidemiol. 2015;5:30048. https://doi.org/10.3402/iee.v5.30048.

Liu S, Zhuang Q, Wang S, Jiang W, Jin J, Peng C, et al. Control of avian influenza in China: strategies and lessons. Transbound Emerg Dis. 2020;67(4):1463–71. https://doi.org/10.1111/tbed.13515.

Luis AD, Hayman DT, O'Shea TJ, Cryan PM, Gilbert AT, Pulliam JR, et al. A comparison of bats and rodents as reservoirs of zoonotic viruses: are bats special? Proc Biol Sci. 2013;280(1756):20122753. https://doi.org/10.1098/rspb.2012.2753.

Magouras I, Brookes VJ, Jori F, Martin A, Pfeiffer DU, Dürr S. Emerging zoonotic diseases: should we rethink the animal-human interface? Front Vet Sci. 2020;7:582743. https://doi.org/10.3389/fvets.2020.582743.

Marani M, Katul GG, Pan WK, Parolari AJ. Intensity and frequency of extreme novel epidemics. Proc Natl Acad Sci USA. 2021;118(35):e2105482118. https://doi.org/10.1073/pnas.2105482118.

McFarlane R, Sleigh A, McMichael T. Synanthropy of wild mammals as a determinant of emerging infectious diseases in the Asian-Australasian region. EcoHealth. 2012;9(1):24–35. https://doi.org/10.1007/s10393-012-0763-9.

Memish ZA, Cotten M, Meyer B, Watson SJ, Alsahafi AJ, Al Rabeeah AA, et al. Human infection with MERS coronavirus after exposure to infected camels, Saudi Arabia, 2013. Emerg Infect Dis. 2014;20(6):1012–5. https://doi.org/10.3201/eid2006.140402.

Michie S, West R. Sustained behavior change is key to preventing and tackling future pandemics. Nat Med. 2021;27(5):749–52. https://doi.org/10.1038/s41591-021-01345-2.

Mollentze N, Streicker DG. Viral zoonotic risk is homogenous among taxonomic orders of mammalian and avian reservoir hosts. Proc Natl Acad Sci USA. 2020;117(17):9423–30. https://doi.org/10.1073/pnas.1919176117.

Mollentze N, Babayan SA, Streicker DG. Identifying and prioritizing potential human-infecting viruses from their genome sequences. PLoS Biol. 2021;19(9):e3001390. https://doi.org/10.1371/journal.pbio.3001390.

Monath TP, Newhouse VF, Kemp GE, Setzer HW, Cacciapuoti A. Lassa virus isolation from *Mastomys natalensis* rodents during an epidemic in Sierra Leone. Science. 1974;185(4147):263–5. https://doi.org/10.1126/science.185.4147.263.

Montecino-Latorre D, Goldstein T, Gilardi K, Wolking D, Van Wormer E, Kazwala R, et al. Reproduction of East-African bats may guide risk mitigation for coronavirus spillover. One Health Outlook. 2020;2(1):2. https://doi.org/10.1186/s42522-019-0008-8.

Mora C, McKenzie T, Gaw IM, Dean JM, von Hammerstein H, Knudson TA, et al. Over half of known human pathogenic diseases can be aggravated by climate change. Nat Clim Chang. 2022;12(9):869–75. https://doi.org/10.1038/s41558-022-01426-1.

Morand S, Lajaunie C. Outbreaks of vector-borne and zoonotic diseases are associated with changes in forest cover and oil palm expansion at global scale. Front Vet Sci. 2021;8:661063. https://doi.org/10.3389/fvets.2021.661063.

Morand S, Walther BA. The accelerated infectious disease risk in the Anthropocene: more outbreaks and wider global spread. BioRxiv. 2020; https://doi.org/10.1101/2020.04.20.049866.

Morand S, Blasdell K, Bordes F, Buchy P, Carcy B, Chaisiri K, et al. Changing landscapes of Southeast Asia and rodent-borne diseases: decreased diversity but increased transmission risks. Ecol Appl. 2019;29(4):e01886. https://doi.org/10.1002/eap.1886.

Murakami S, Kitamura T, Suzuki J, Sato R, Aoi T, Fujii M, et al. Detection and characterization of bat Sarbecovirus phylogenetically related to SARS-CoV-2, Japan. Emerg Infect Dis. 2020;26(12):3025–9. https://doi.org/10.3201/eid2612.203386.

Nahar N, Sultana R, Gurley ES, Hossain MJ, Luby SP. Date palm sap collection: exploring opportunities to prevent Nipah transmission. EcoHealth. 2010;7(2):196–203. https://doi.org/10.1007/s10393-010-0320-3.

Nahar N, Asaduzzaman M, Sultana R, Garcia F, Paul RC, Abedin J, et al. A large-scale behavior change intervention to prevent Nipah transmission in Bangladesh: components and costs. BMC Res Notes. 2017;10(1):225. https://doi.org/10.1186/s13104-017-2549-1.

NASEM. Systematizing the One Health approach in preparedness and response efforts for infectious disease outbreaks: proceedings of a workshop. Washington, DC: National Academies Press (US); 2022.

NIH. Centers for Research in Emerging Infectious Diseases (CREID). Bethesda, MD: National Institutes of Health; 2021. https://www.niaid.nih.gov/research/centers-research-emerging-infectious-diseases. Accessed 16 Oct 2022.

Nikolay B, Salje H, Hossain MJ, Khan A, Sazzad HMS, Rahman M, et al. Transmission of Nipah virus—14 years of investigations in Bangladesh. N Engl J Med. 2019;380(19):1804–14. https://doi.org/10.1056/NEJMoa1805376.

NSF. NSF predictive intelligence for pandemic prevention: development grant (pipp phase I). Washington, DC: National Science Foundation; 2022. https://beta.nsf.gov/events/nsf-predictive-intelligence-pandemic-prevention#:~:text=Synopsis%20of%20Program%3A,pandemics%20through%20prediction%20and%20prevention. Accessed 16 Oct 2021.

Nwadiugwu MC, Monteiro N. Applied genomics for identification of virulent biothreats and for disease outbreak surveillance. Postgrad Med J. 2022;99:403. https://doi.org/10.1136/postgradmedj-2021-139916.

Nyhus PJ. Human–wildlife conflict and coexistence. Annu Rev Environ Resour. 2016;41(1):143–71. https://doi.org/10.1146/annurev-environ-110615-085634.

Olival KJ, Hosseini PR, Zambrana-Torrelio C, Ross N, Bogich TL, Daszak P. Host and viral traits predict zoonotic spillover from mammals. Nature. 2017;546(7660):646–50. https://doi.org/10.1038/nature22975.

Padron-Regalado E. Vaccines for SARS-CoV-2: lessons from other coronavirus strains. Infect Dis Ther. 2020;9(2):255–74. https://doi.org/10.1007/s40121-020-00300-x.

Pandemic Preparedness Partnership. 100 days mission to respond to future pandemic threats: reducing the impact of future pandemics by making diagnostics, therapeutics and vaccines available within 100 days: a report to the G7. London: G7 United Kingdom; 2021.

Pappalardo M, Juliá M, Howard MJ, Rossman JS, Michaelis M, Wass MN. Conserved differences in protein sequence determine the human pathogenicity of Ebolaviruses. Sci Rep. 2016;6(1):23743. https://doi.org/10.1038/srep23743.

Parker S, Buller RM. A review of experimental and natural infections of animals with monkeypox virus between 1958 and 2012. Future Virol. 2013;8(2):129–57. https://doi.org/10.2217/fvl.12.130.

Pendrill F, Gardner TA, Meyfroidt P, Persson UM, Adams J, Azevedo T, et al. Disentangling the numbers behind agriculture-driven tropical deforestation. Science. 2022;377(6611):eabm9267. https://doi.org/10.1126/science.abm9267.

Peyre M, Vourc'h G, Lefrançois T, Martin-Prevel Y, Soussana J-F, Roche B. PREZODE: preventing zoonotic disease emergence. Lancet. 2021;397(10276):792–3. https://doi.org/10.1016/S0140-6736(21)00265-8.

Piret J, Boivin G. Pandemics throughout history. Front Microbiol. 2021;11:631736. https://doi.org/10.3389/fmicb.2020.631736.

Plowright RK, Parrish CR, McCallum H, Hudson PJ, Ko AI, Graham AL, et al. Pathways to zoonotic spillover. Nat Rev Microbiol. 2017;15(8):502–10. https://doi.org/10.1038/nrmicro.2017.45.

Plowright RK, Reaser JK, Locke H, Woodley SJ, Patz JA, Becker DJ, et al. Land use-induced spillover: a call to action to safeguard environmental, animal, and human health. Lancet Planet Health. 2021;5(4):e237–45. https://doi.org/10.1016/s2542-5196(21)00031-0.

Poletti P, Visintainer R, Lepri B, Merler S. The interplay between individual social behavior and clinical symptoms in small clustered groups. BMC Infect

Dis. 2017;17(1):521. https://doi.org/10.1186/s12879-017-2623-2.
PREDICT Consortium. PREDICT: advancing global health security at the frontiers of disease emergence. Davis, CA: PREDICT Consortium; 2021.
PROMED. PROMED-mail. Brookline, MA: International Society for Infectious Diseases; 2022. https://promedmail.org/. Accessed 12 Oct 2022.
Rahman MA, Hossain MJ, Sultana S, Homaira N, Khan SU, Rahman M, et al. Date palm sap linked to Nipah virus outbreak in Bangladesh, 2008. Vector Borne Zoonotic Dis. 2012;12(1):65–72. https://doi.org/10.1089/vbz.2011.0656.
Recht J, Schuenemann VJ, Sánchez-Villagra MR. Host diversity and origin of zoonoses: The ancient and the new. Animals. 2020;10(9):1672.
Roberts M, Dobson A, Restif O, Wells K. Challenges in modelling the dynamics of infectious diseases at the wildlife-human interface. Epidemics. 2021;37:100523. https://doi.org/10.1016/j.epidem.2021.100523.
Sánchez CA, Li H, Phelps KL, Zambrana-Torrelio C, Wang LF, Zhou P, et al. A strategy to assess spillover risk of bat SARS-related coronaviruses in Southeast Asia. Nat Commun. 2022;13(1):4380. https://doi.org/10.1038/s41467-022-31860-w.
Schar DL, Yamey GM, Machalaba CC, Karesh WB. A framework for stimulating economic investments to prevent emerging diseases. Bull World Health Organ. 2018;96(2):138–40. https://doi.org/10.2471/blt.17.199547.
Schuh AJ, Amman BR, Towner JS. Filoviruses and bats. Microbiol Aust. 2017;38(1):12–6. https://doi.org/10.1071/ma17005.
Smith GJ, Vijaykrishna D, Bahl J, Lycett SJ, Worobey M, Pybus OG, et al. Origins and evolutionary genomics of the 2009 swine-origin H1N1 influenza A epidemic. Nature. 2009;459(7250):1122–5. https://doi.org/10.1038/nature08182.
Smith KF, Goldberg M, Rosenthal S, Carlson L, Chen J, Chen C, et al. Global rise in human infectious disease outbreaks. J R Soc Interface. 2014;11(101):20140950. https://doi.org/10.1098/rsif.2014.0950.
Smolinski MS, Hamburg MA, Lederberg J. Microbial threats to health: emergence, detection, and response. Washington, DC: Naional Academies Press; 2003.
Steere AC, Coburn J, Glickstein L. The emergence of Lyme disease. J Clin Invest. 2004;113(8):1093–101. https://doi.org/10.1172/jci21681.
Su W, Harfoot R, Su YCF, DeBeauchamp J, Joseph U, Jayakumar J, et al. Ancestral sequence reconstruction pinpoints adaptations that enable avian influenza virus transmission in pigs. Nat Microbiol. 2021;6(11):1455–65. https://doi.org/10.1038/s41564-021-00976-y.
Tan CW, Chia WN, Qin X, Liu P, Chen MI, Tiu C, et al. A SARS-CoV-2 surrogate virus neutralization test based on antibody-mediated blockage of ACE2-spike protein-protein interaction. Nat Biotechnol. 2020;38(9):1073–8. https://doi.org/10.1038/s41587--020-0631-z.
Taylor LH, Latham SM, Woolhouse ME. Risk factors for human disease emergence. Philos Trans R Soc Lond Ser B Biol Sci. 2001;356(1411):983–9. https://doi.org/10.1098/rstb.2001.0888.
Temmam S, Vongphayloth K, Baquero E, Munier S, Bonomi M, Regnault B, et al. Bat coronaviruses related to SARS-CoV-2 and infectious for human cells. Nature. 2022;604(7905):330–6. https://doi.org/10.1038/s41586-022-04532-4.
Ter Meulen J, Lukashevich I, Sidibe K, Inapogui A, Marx M, Dorlemann A, et al. Hunting of peridomestic rodents and consumption of their meat as possible risk factors for rodent-to-human transmission of Lassa virus in the Republic of Guinea. Am J Trop Med Hyg. 1996;55(6):661–6. https://doi.org/10.4269/ajtmh.1996.55.661.
Tian H, Zhou S, Dong L, Van Boeckel TP, Cui Y, Newman SH, et al. Avian influenza H5N1 viral and bird migration networks in Asia. Proc Natl Acad Sci U S A. 2015;112(1):172–7. https://doi.org/10.1073/pnas.1405216112.
Timen A, Koopmans MP, Vossen AC, van Doornum GJ, Günther S, van den Berkmortel F, et al. Response to imported case of Marburg hemorrhagic fever, the Netherlands. Emerg Infect Dis. 2009;15(8):1171–5. https://doi.org/10.3201/eid1508.090015.
UNAIDS. Fact sheet. Geneva: UNAIDS; 2022.
Voigt CC, Phelps KL, Aguirre LF, Corrie Schoeman M, Vanitharani J, Zubaid A. Bats and buildings: the conservation of synanthropic bats. In: Voigt CC, Kingston T, editors. Bats in the anthropocene: conservation of bats in a changing world. Cham: Springer International Publishing; 2016. p. 427–62.
Wacharapluesadee S, Boongird K, Wanghongsa S, Ratanasetyuth N, Supavonwong P, Saengsen D, et al. A longitudinal study of the prevalence of Nipah virus in *Pteropus lylei* bats in Thailand: evidence for seasonal preference in disease transmission. Vector Borne Zoonotic Dis. 2009;10(2):183–90. https://doi.org/10.1089/vbz.2008.0105.
Wacharapluesadee S, Buathong R, Iamsirithawon S, Chaifoo W, Ponpinit T, Ruchisrisarod C, et al. Identification of a novel pathogen using family-wide PCR: initial confirmation of COVID-19 in Thailand. Front Public Health. 2020;8:555013. https://doi.org/10.3389/fpubh.2020.555013.
Wacharapluesadee S, Ghai S, Duengkae P, Manee-Orn P, Thanapongtharm W, Saraya AW, et al. Two decades of one health surveillance of Nipah virus in Thailand. One Health Outlook. 2021a;3(1):12. https://doi.org/10.1186/s42522-021-00044-9.
Wacharapluesadee S, Tan CW, Maneeorn P, Duengkae P, Zhu F, Joyjinda Y, et al. Evidence for SARS-CoV-2 related coronaviruses circulating in bats and pangolins in Southeast Asia. Nat Commun. 2021b;12(1):972. https://doi.org/10.1038/s41467--021-21240-1.
Wan XF, Dong L, Lan Y, Long LP, Xu C, Zou S, et al. Indications that live poultry markets are a major

source of human H5N1 influenza virus infection in China. J Virol. 2011;85(24):13432–8. https://doi.org/10.1128/jvi.05266-11.

Wang LF, Shi Z, Zhang S, Field H, Daszak P, Eaton BT. Review of bats and SARS. Emerg Infect Dis. 2006;12(12):1834–40. https://doi.org/10.3201/eid1212.060401.

Wang X, Jiang H, Wu P, Uyeki TM, Feng L, Lai S, et al. Epidemiology of avian influenza A H7N9 virus in human beings across five epidemics in mainland China, 2013–17: an epidemiological study of laboratory-confirmed case series. Lancet Infect Dis. 2017;17(8):822–32. https://doi.org/10.1016/s1473--3099(17)30323-7.

Watsa M, Erkenswick GA, Pomerantz A, Prost S. Portable sequencing as a teaching tool in conservation and biodiversity research. PLoS Biol. 2020;18(4):e3000667. https://doi.org/10.1371/journal.pbio.3000667.

WBG. Finance for an equitable recovery. World Development Report. Washington, DC: World Bank Group; 2022a.

WBG. Pandemic fund. Washington, DC: World Bank Group; 2022b. https://www.worldbank.org/en/programs/financial-intermediary-fund-for-pandemic-prevention-preparedness-and-response-ppr-fif. Accessed 22 Nov 2022.

Webster RG, Hulse DJ. Microbial adaptation and change: avian influenza. Rev Sci Tech. 2004;23(2):453–65. https://doi.org/10.20506/rst.23.2.1493.

WHO. International Health Regulations (2005). 3rd ed. Geneva: World Health Organization; 2016. 74 p.

WHO. Marburg virus disease—Guinea. Disease Outbreak News; 2021.

WHO. Ebola: North Kivu/Ituri, Democratic Republic of the Congo, August 2018–June 2020. Geneva: World Health Organization; 2022a. https://www.who.int/emergencies/situations/Ebola-2019-drc-. Accessed 10 Oct 2022.

WHO. Ebola: West Africa, March 2014–2016. Geneva: World Health Organization; 2022b. https://www.who.int/emergencies/situations/ebola-outbreak-2014-2016-West-Africa. Accessed 10 Oct 2022.

WHO. Epidemic intelligence from open sources (EIOS): zero impact from health threats. Geneva: World Health Organization; 2022c. https://www.who.int/initiatives/eios. Accessed 11 Dec 2022.

WHO. Marburg virus—Ghana. Disease Outbreak News; 2022d.

WHO. Mitigating the COVID-19 outbreak through global data sharing. 2022e. https://www.who.int/teams/health-care-readiness/covid-19/data-platform/mitigating-the-covid-19-outbreak-through-global-data-sharing. Accessed 13 Oct 2022.

WHO. WHO recommends new name for monkeypox disease. Geneva: World Health Organization; 2022f.

WHO. International Negotiating Body Geneva: World Health Organization; 2024 [updated 1 Jun 2024]. Available from: https://inb.who.int.

WHO. Disease outbreak news. Geneva: World Health Organization; 2023a. https://www.who.int/emergencies/disease-outbreak-news. Accessed 17 Jan 2023.

WHO. Global Influenza Surveillance and Response System (GISRS). Geneva: World Health Organization; 2023b. https://www.who.int/initiatives/global-influenza-surveillance-and-response-system. Accessed 28 May 2023.

WHO. WHO coronavirus (COVID-19) dashboard. Geneva: World Health Organization; 2023c. https://covid19.who.int. Accessed 28 May 2023.

WHO. WHO coronavirus (COVID-19) dashboard. Geneva: World Health Organization; 2023d. https://covid19.who.int/. Accessed 10 Jan 2023.

WHO, FAO, WOAH. Taking a multisectoral, one health approach: a tripartite guide to addressing zoonotic diseases in countries. Geneva: World Health Organization, UN Food and Agriculture Organization, World Organization for Animal Health; 2019.

Winck GR, Raimundo RLG, Fernandes-Ferreira H, Bueno MG, D'Andrea PS, Rocha FL, et al. Socioecological vulnerability and the risk of zoonotic disease emergence in Brazil. Sci Adv. 2022;8(26):eabo5774. https://doi.org/10.1126/sciadv.abo5774.

WOAH. World Animal Health Information System: WAHIS Portal: animal health data. Paris: World Organisation for Animal Health; 2022. https://www.woah.org/en/what-we-do/animal-health-and--welfare/disease-data-collection/world-animal-health-information-system/. Accessed 12 Oct 2022.

Wolfe ND, Heneine W, Carr JK, Garcia AD, Shanmugam V, Tamoufe U, et al. Emergence of unique primate T-lymphotropic viruses among central African bushmeat hunters. Proc Natl Acad Sci USA. 2005;102(22):7994–9. https://doi.org/10.1073/pnas.0501734102.

Wolfe MK, Duong D, Hughes B, Chan-Herur V, White BJ, Boehm AB. Detection of monkeypox viral DNA in a routine wastewater monitoring program. medRxiv. 2022; https://doi.org/10.1101/2022.07.25.22278043.

World Bank. People, pathogens and our planet: the economics of One Health. Washington, DC: World Bank; 2012. Report No.: 69145-GLB.

Wozniak DM, Riesle-Sbarbaro SA, Kirchoff N, Hansen-Kant K, Wahlbrink A, Stern A, et al. Inoculation route-dependent Lassa virus dissemination and shedding dynamics in the natural reservoir—Mastomys natalensis. Emerg Microbes Infect. 2021;10(1):2313–25. https://doi.org/10.1080/22221751.2021.2008773.

Wu J, Ke C, Lau EHY, Song Y, Cheng KL, Zou L, et al. Influenza H5/H7 virus vaccination in poultry and reduction of zoonotic infections, Guangdong Province, China, 2017–18. Emerg Infect Dis. 2019;25(1):116–8. https://doi.org/10.3201/eid2501.181259.

Yadav PD, Sahay RR, Balakrishnan A, Mohandas S, Radhakrishnan C, Gokhale MD, et al. Nipah virus outbreak in Kerala State, India amidst of COVID-19 pandemic. Front Public Health. 2022;10:818545. https://doi.org/10.3389/fpubh.2022.818545.

Yoon SW, Webby RJ, Webster RG. Evolution and ecology of influenza A viruses. Curr Top Microbiol Immunol. 2014;385:359–75. https://doi.org/10.1007/82_2014_396.

Youssef DM, Wieland B, Knight GM, Lines J, Naylor NR. The effectiveness of biosecurity interventions in reducing the transmission of bacteria from livestock to humans at the farm level: a systematic literature review. Zoonoses Public Health. 2021;68(6):549–62. https://doi.org/10.1111/zph.12807.

Zhao P, Cao J, Zhao LJ, Qin ZL, Ke JS, Pan W, et al. Immune responses against SARS-coronavirus nucleocapsid protein induced by DNA vaccine. Virology. 2005;331(1):128–35. https://doi.org/10.1016/j.virol.2004.10.016.

Zhou X, Wang Y, Liu H, Guo F, Doi SA, Smith C, et al. Effectiveness of market-level biosecurity at reducing exposure of poultry and humans to avian influenza: a systematic review and meta-analysis. J Infect Dis. 2018;218(12):1861–75. https://doi.org/10.1093/infdis/jiy400.