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Evidence Note:
What we know about emerging zoonotic threats and how can we minimise future impact?

Key Points

- Zoonotic diseases are those that spread from animals to humans, such as HIV or avian influenza (bird flu). In many countries, they are endemic causing significant impacts on human and livestock health. DFID supported research estimates that they cause 2.5 billion cases of human illness and 2.7 million human deaths a year[1].
- COVID-19 is the latest new zoonotic disease to emerge and has spread to become a pandemic. Other zoonotic diseases have emerged in recent years (eg HIV, Ebola, Zika, bird flu) and around 75% of emerging human infections are zoonotic. The UK Government currently supports research on many epidemic and endemic diseases.
- There are multiple drivers that are increasing the threat posed by the emergence and spread of zoonotic disease, which can be grouped into three broad categories.
    - **Changes in food and agriculture systems** to meet increasing demand is increasing contact between animals (wild and domesticated) and humans through intensification of agriculture. There is also increased contact between animals as they move through the supply chain from producers to consumers and increased use of wildlife as food.
    - ***Emergence through ecosystem disruption*** as agriculture, extractive industries and people move into new ecosystems, increases the contact between wild animals, known reservoirs of potential disease, and livestock and humans.
    - ***Trade and travel*** increase interaction between people and the speed and scale at which new diseases can spread, as evidenced by COVID-19. Trade, both legal and illegal, in animals and animal products has also been linked to zoonotic disease outbreaks.
- These drivers are present against a back drop of the Sustainable Development Goals. With an increased focus on climate change adaptation and mitigation, conservation and sustainable use of biodiversity. Climate change is an indirect driver of zoonotic disease outbreaks through its impact on the movement of wild animals, and particularly for insect and tick-borne zoonotic diseases because it can result in the vectors of diseases expanding their range into new areas and countries where humans and livestock may be naïve to new diseases. It can also reduce vector range.
- Recent zoonotic disease outbreaks (SARS, Ebola, COVID-19) have demonstrated that interventions must be taken across sectors to address the growing threat. This includes human health, animal health, environment health, social sciences and wildlife conservation. Increasing numbers of outbreaks, increasing complexity of value chains, encroachment on natural environments, urbanisation and increased livestock production and consumption, highlight that no individual discipline or Ministry can manage the complexity of emerging pandemic zoonotic threats.

Definitions.

Pandemic: A pandemic is the worldwide spread of a new disease.

Epidemic: the appearance of a particular disease in a large number of people at the same time.

Endemic: the constant presence of a disease or infectious agent within a given geographic area or population.

Zoonosis: an infection or disease that is transmissible between animals and humans

One Health: is an approach to designing and implementing programmes, policies, legislation and research in which multiple sectors communicate and work together to achieve better public health outcomes

[1] ILRI 2012, Mapping of poverty and likely zoonoses hotspots.
https://cgspace.cgiar.org/bitstream/handle/10568/21161/ZooMap_July2012_final.pdf?sequence=4&isAllowed=y

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Comments or feedback should be sent to
duncan-barker@dfid.gov.uk

- Many of the tools needed for the early detection or, response to, and management of emerging disease threats already exist and are being utilised. This can reduce the cost of disease. However, the complex nature of the threat, and political economy[2] considerations, go some way to explaining why many countries have struggled to draft and implement national plans of action with specific activities, timelines, and budgets. There are asymmetries of power and influence between the different government departments that need to work together. However, evidence suggests that adopting these tools can be successful in improving surveillance, cross departmental working and responding to emerging threats. There is existing experience and momentum that can be built on in the aftermath of COVID-19.

Recommendations/Action for DFID

- DFID's Agriculture Research Team plans to develop thinking in this area, working with policy teams in DFID.

Introduction

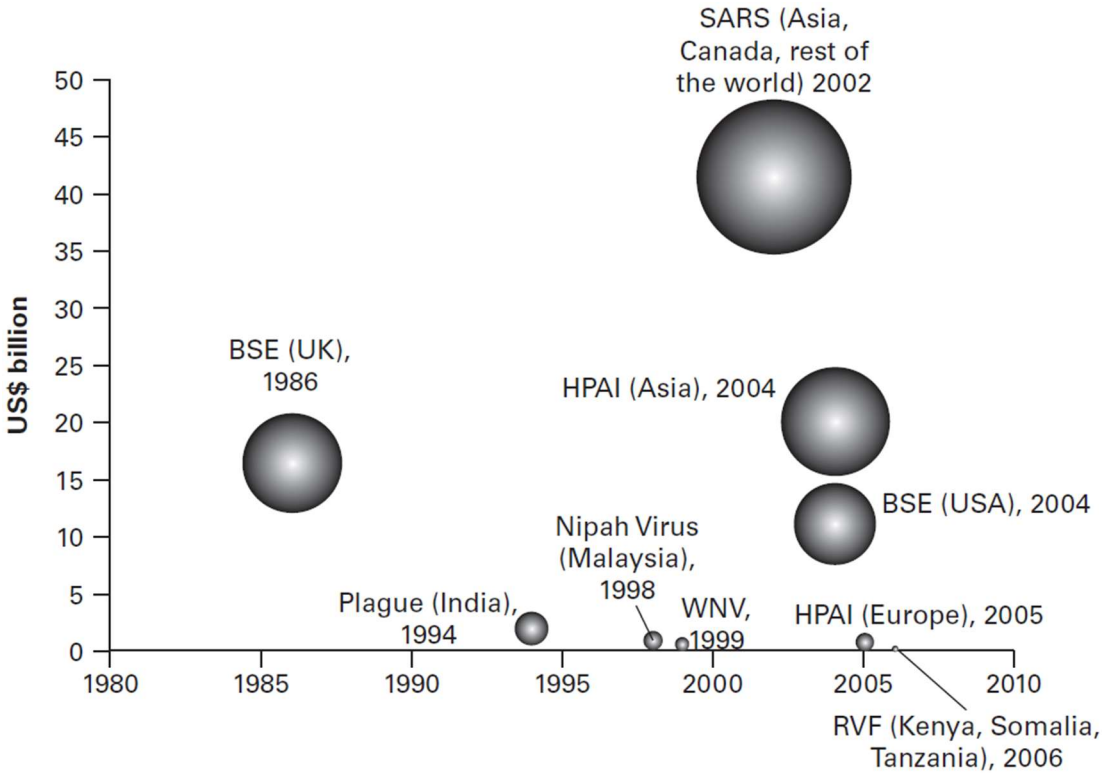
1. Zoonotic diseases are those that are transmitted between animals and humans. Emerging zoonotic diseases are not a new phenomenon and "emergence events" occur regularly. This paper will discuss some of the drivers causing them to happen with increasing regularity and increased severity.
2. COVID-19 is the latest zoonotic disease crisis facing the world. Caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the disease was first identified in December 2019 in Wuhan, the capital of China's Hubei province, and has since spread globally to eventually be declared a pandemic. It is currently causing massive disruption to economies and trade with significant loss of lives and livelihoods.
3. How can we mitigate the risks posed by zoonotic disease threats and why does the world appear to be so unprepared for the type of pandemic that has been identified as of high probability for well over 25 years[3]? This paper, drafted by DFID with inputs from external experts, will examine the drivers of these disease threats and what we have learnt from previous zoonoses outbreaks. The final sections provide information on the organisations and institutions working on tackling zoonotic disease threats and highlights resources that are already available to support a response.

Impact of zoonotic disease

4. Robust data on the economic, livelihood and human health impacts of zoonotic disease at a global level is incomplete. Figure 1 provides estimates from a World Bank report in 2012.

[2] Political economy is the interaction of political and economic processes in a society: the distribution of power and wealth between different groups and individuals, and the processes that create, sustain and transform these relationships over time.
[3] The Coming Plague : Newly Emerging Diseases in a World out of Balance was published in 1994

Figure 1: Estimated costs of emerging zoonotic diseases (1986 – 2006)[4]



5. Research in Kenya estimates the total social cost of brucellosis, bovine tuberculosis and of Non-typhoidal Salmonella to be around 6 billion USD PPP, which corresponds to 3.9 percent of national GDP[5]. And a systematic review in Kyrgyzstan estimated that in 2013, seven zoonotic diseases had a combined burden of over thirty-five thousand disability adjusted life years (DALYs)[6].

What drives current and potential zoonotic threats to human health?

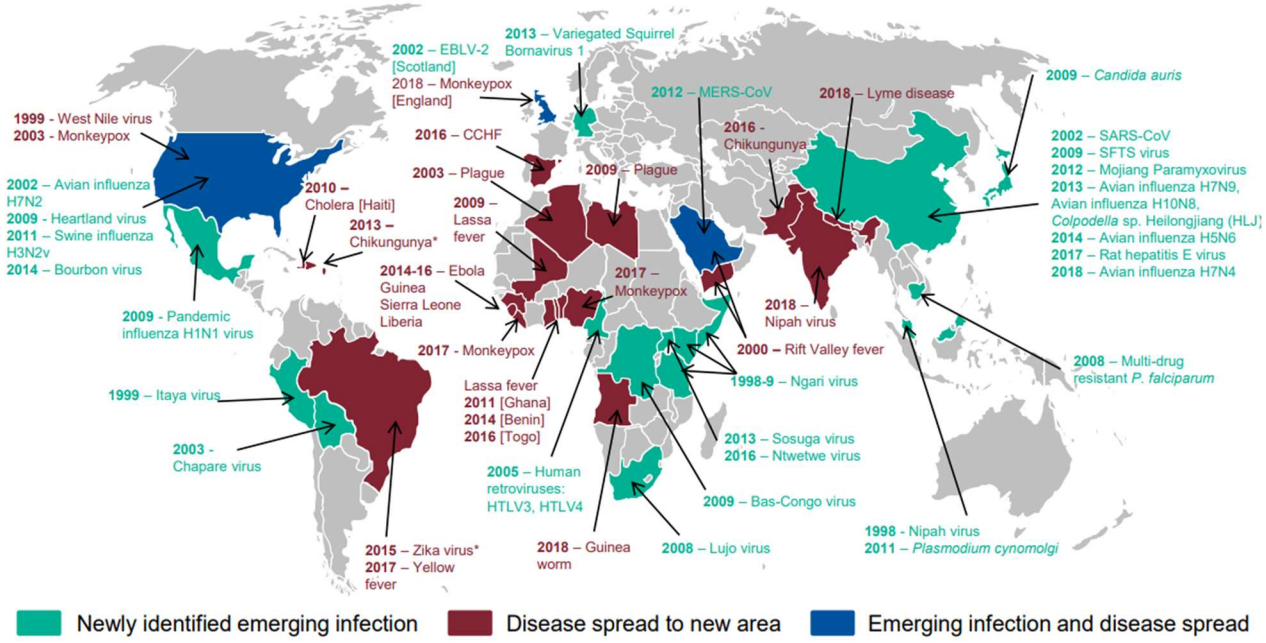
6. Analysis of global health datasets presents a mixed picture with respect to the total number of human disease outbreaks that are zoonotic in origin and the proportion of those outbreaks caused by new diseases. Although the number of diseases is increasing over time[7] it is not always the case that the number of people infected is increasing. Inconsistent surveillance and reporting and lack of tests for new threats contributes to this mixed picture.

7. On average one new emerging or re-emerging infectious disease is seen in humans and animals every eight months. Out of the 1,400 microbes that could cause human infections, more than 60% are shared with wild or domestic animals[8]. Many of these are vital in nature[9]. We know that around 75% of emerging human infections are zoonotic[7]. The transfer of a disease between species is known as a spillover event. For example, a disease that primarily occurs in wild animals but occasionally infects domestic animals and or humans. Most spillover events result in self-limited cases, with no further human to human transmission. There is emerging evidence that bat coronaviruses may be mutating to more easily infect humans[10].

[4] World Bank. 2012. People, Pathogens and Our Planet : The Economics of One Health. Washington, DC. © World Bank. https://openknowledge.worldbank.org/handle/10986/11892
[5] FAO 2018: The Monetary impact of zoonotic diseases on society in Kenya. Evidence from three zoonoses.
[6] Counotte MJ, Minbaeva G, Usubalieva J, Abdykerimov K, Torgerson PR. The Burden of Zoonoses in Kyrgyzstan: A Systematic Review. *PLoS Negl Trop Dis.* 2016;10(7):e0004831. Published 2016 Jul 7. https://dx.doi.org/10.1371%2Fjournal.pntd.0004831
[7] *Jones et al., 2008:* Global trends in emerging infectious diseases https://www.nature.com/articles/nature06536.pdf
[8] Taylor LH, Latham SM, Woolhouse ME. Risk factors for human disease emergence. *Philos Trans R Soc Lond B Biol Sci.* 2001;356(1411):983-989. https://doi:10.1098/rstb.2001.0888
[9] Cleaveland et al. (2001) Diseases of humans and their domestic mammals: pathogen characteristics, host range and the risk of emergence. https://royalsocietypublishing.org/doi/abs/10.1098/rstb.2001.0889
[10] Liangsheng et al 2020, Origin and Evolution of the 2019 Novel Coronavirus *Clinical Infectious Diseases* https://doi.org/10.1093/cid/ciaa112

8. Known events of new and emerging diseases in humans are occurring frequently and the majority of these are zoonotic in origin (Figure 2). If the newly emerged disease is then able to spread rapidly there is the potential for a major disease incident. The key factors affecting these two key parameters (spill over and dissemination/spread) are described below.

Figure 2: Global map of significant and new emerging and spreading infections in humans 1998 – 2018 (source Public Health England) (* incursion followed by regional spread)



Disease, food and agriculture systems

9. People have been moving from rural areas to cities for centuries for a range or reasons. People move as they get wealthier and because city jobs tend to pay more. It is now estimated that more than 4 billion people (50% of global population) live in cities and these cities are increasingly dense megacities of over 10 million people. It is projected that close to 7 billion people will live in urban areas by 2050.

10. People in urban and peri-urban areas still raise, and even share dwellings with livestock as well as their pets. Cities also create environments favourable to some pests or peri-domestic animals such as rats and pigeons. Combined with the fact that just under 1 in 3 people in urban areas live in informal settlements with constrained access to water/sanitation services, this increases the risk of zoonotic disease, and disease generally. Informal settlements are also expanding as cities grow.

11. A key source of food in these environments is outdoor or street markets. These food outlets frequently sell live animals both wild and domestic from near and far. This mixing of animals from different locations under conditions of poor hygiene has been described as a major contributor for new disease outbreaks[11]. This description followed close examination of the corona virus that caused the severe acute respiratory syndrome (SARS) outbreak of 2002/3. The SARS virus was likely transmitted by bats to masked palm civets and then spilled over from civets to humans in a peri-urban market in East Asia.

12. Despite their risks, it is important to recognise that street markets are an essential source of affordable food for billions of people[12][13]. A Farmer's Market could be considered as the UK

[11] Cheng, V.C., Lau, S.K., Woo, P.C and Kwok Yung Yuen. 2007. Severe Acute Respiratory Syndrome Coronavirus as an Agent of Emerging and Reemerging Infection. CLINICAL MICROBIOLOGY REVIEWS, Oct. 2007, p. 660–694 Vol. 20, No. 4. Accessed April 2020 https://cmr.asm.org/content/cmr/20/4/660.full.pdf

[12] Choosing between supermarkets and wet markets

[13] Zhong, S., Crang, M. & Zeng, G. Constructing freshness: the vitality of wet markets in urban China. Agric Hum Values 37, 175–185 (2020). https://doi.org/10.1007/s10460-019-09987-2

equivalent. Thus, better management of vital "informal food" outlets and street markets, rather than banning their existence, is key.

13. On average, living standards are higher in urban populations than in rural, though significant inequalities still exist. Income levels have been increasing globally for several decades and this has changed dietary patterns. Higher incomes allow people to consume more dairy, meat and egg products[14]. This has resulted in a rapid increase in demand in low and middle income (LMIC) countries. Concurrently, demand for wild animal products has increased[15]. Trade in wild animals and animal-based medicines frequently uses informal value chains that are both complex and vary by culture and geography. Consumption may be driven by poverty and need for protein in some settings and by increasing affluence, with eating exotic animals being seen as a status symbol, and cultural preferences[16] in other (e.g. urban) settings. In some countries small farmers unable to compete with large scale meat production have turned to niche 'wildlife farming', which is largely unregulated[17]. There is also evidence of wild meat being imported into developed countries[18].

14. Increased demand for meat, dairy and eggs has caused rapid and massive growth and change in livestock production and supply chains[19]. Intensive livestock production systems when poorly regulated, located in peri-urban areas and perhaps mixing with extensive livestock production systems can be serious public health threats through the amplification of a pathogen and have been associated with animal-to-human spill over, consequent pandemic risks, food safety hazards and high burdens of zoonotic diseases[20]. Evolutionary pressures within these "intensive animal monocultures" can increase the potential for disease emergence if not mitigated through appropriate use of veterinary medicines, good surveillance and biosecurity.

15. Whilst 'tolerance' of informal food supply chains in economies that lack a strong formal sector, is important to ensure food supply, the policies, institutions and animal health systems to support and improve these chains remain relatively weak in many LMICs. For example, avian influenza (AI) tends to persist in countries like Egypt and Indonesia where poorly regulated and managed intensive and extensive poultry production coexist[21]. The influenza virus is able to move from wild birds into outdoor farms and between indoor and outdoor farms and eventually up the supply chain to live bird markets to potentially infect consumers. A highly pathogenic avian influenza (HPAI) H5N1 emerged in domestic waterfowl in 1996, eventually paving the way for a pandemic of the H5N1 subclade 2.2 viruses in poultry. This virus moved via migratory birds across much of the globe in 2006[22]. A growing number of AI viruses, including the low pathogenic avian influenza H7N9 virus, first reported in 2013 in China and H9N2 in Egypt, carry a molecular signature associated with human adaptation and therefore remain a very significant public health risk[23].

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[16] Morsello, et al. 2015. Cultural attitudes are stronger predictors of bushmeat consumption and preference than economic factors among urban Amazonians from Brazil and Colombia. *Ecology and Society* 20(4):21. http://dx.doi.org/10.5751/ES-07771-200421

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[23] H9N2 = Naguib, Mahmoud & Arafa, Abd & Parvin, Rokshana & Beer, Martin & Vahlenkamp, Thomas & Harder, Timm. (2017). Insights into genetic diversity and biological propensities of potentially zoonotic avian influenza H9N2 viruses circulating in Egypt. Virology. 511. 165-174. 10.1016/j.virol.2017.08.028 .

16. Other externalities associated with poorly regulated intensive agriculture systems include the growing problems of antimicrobial resistance (AMR) and food borne disease, although evidence is less clear. Both are attracting significant policy attention and may be a means to enhance surveillance for a broader range of emerging pathogens.

17. Food borne pathogens, many of which are zoonotic, undermine food and nutritional security, human development and the broader food economy. More than 500,000 people are estimated to die every year as a result of foodborne disease, with certain groups, such as pregnant women, children and elderly persons most at risk.[24] According to the WHO, foodborne disease resulted in the loss of 33 million disability-adjusted life years (DALYs) in 2010 – a disease burden comparable to that of the 'big three' major infectious diseases, HIV/AIDS, malaria and tuberculosis. Sub-Saharan Africa suffers the highest per capita incidence of foodborne disease in the world, sustaining human capital losses of an estimated USD $16.7bn a year. As rising incomes increase the demand for fresh foods, and urbanisation increases the volume of food being transported between food producers and consumers, food safety and zoonotic disease threats in LMICs are expected to increase from new and largely unregulated markets[25].

18. Antimicrobial Resistance (AMR) is also a major global threat of increasing concern to human and animal health. It has implications for both food safety and food security and the economic wellbeing of millions of households. The health consequences and economic costs of AMR are respectively estimated at 10 million human fatalities a year and a 2 to 3.5 percent decrease in global Gross Domestic Product (GDP), amounting to US$100 trillion by 2050[26]. It is widely acknowledged that AMR also requires a multi-disciplinary and multi-sectoral approach encompassing the interface between humans, terrestrial and aquatic animals, crops and the environment.

Disease emergence through ecosystem disruption

19. Livestock farming requires large amounts of land and water resources to raise animals directly or to grow the grains and beans for animal feed. Agricultural encroachment into forest areas is of particular importance to public health because it increases the chance of wildlife-origin pathogens spilling over to humans and livestock[27]. Human interaction with animals and wildlife is not a new phenomenon. However, human-animal interactions are undergoing rapid change, providing new interfaces and opportunities for the emergence of zoonotic disease. Emerging infectious diseases in wildlife, domestic animals, plants or people can be exacerbated by human activities such as land clearing and habitat fragmentation[28]. Growing urbanisation also creates interfaces with peridomestic wildlife of many kinds e.g. rats and monkeys that further increase the risk of spill over[29]. Irrigation, especially in sub-arid landscapes brings new opportunities for vector borne disease emergence[30]

20. Around 75% percent of the infectious diseases that have emerged in humans since the 1940s can be traced back to wildlife. Wildlife sources comprise ungulates (eg antelope), carnivores, rodents, monkeys, bats, birds and other, mostly mammalian, species. Rodents, bats and

H7N9 = Schrauwen EJ, Fouchier RA. Host adaptation and transmission of influenza A viruses in mammals. Emerg Microbes Infect. 2014 Feb;3(2):e9. doi: 10.1038/emi.2014.9. Epub 2014 Feb 12. PMID: 26038511; PMCID: PMC3944123. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3944123/

[24] WHO (2015) Estimates of the Global Burden of Foodborne Diseases: http://www.who.int/iris/bitstream/10665/199350/1/9789241565165_eng.pdf

[25] While fresh foods such as fruits, vegetables and animal-source foods are among the most nutrient-rich, mounting evidence suggests that they are often the most contaminated foods.

[26] UK Govt review on antimicrobial resistance chaired by Jim O'Neill. Tackling drug-resistant infections globally: final report and recommendations. May 2016). https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf

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primates have been identified as the hosts for the majority of known zoonotic viruses[31]. Bats are reservoir hosts of several viruses that pose health risks to humans, including, among others, coronaviruses, Nipah and Hendra viruses, Ebola and rabies viruses. Examples of their spill over are numerous[32]. Hendra virus in horses and humans has been linked to deforestation, dwindling bat populations and the movement of fruit bats to urban areas[33].

21. Similarly, Nipah virus outbreaks have been associated with the dislocation of fruit bats and the contamination of pig food. Nipah virus reportedly first emerged in Malaysia in 1998 and spread within Malaysia and to Singapore via the transport of infected pigs. Massive numbers of pigs were culled to contain the epidemic. Most human cases were men working in pig farming or pork production[34]. More recent outbreaks in Bangladesh and India involved direct transmission to humans via fruits and date palm sap contaminated with the urine of fruit bats, and through human-to human transmission.

22. Perhaps the most significant example of spill over in recent decades has been HIV/AIDS. HIV1 virus is believed to have jumped from chimpanzee blood during bushmeat hunting and food preparation[35]. Mosquito-borne viruses that have used the relatedness of humans and monkeys to jump to humans encroaching into forests include dengue virus and Chikungunya virus. Zoonotic malaria, a plasmodium, has spread from macaques in south east Asia, linked to deforestation and climate change[36]. Dengue virus used to only circulate in monkeys (Macaca and Presbytis species), with sporadic cases in humans. It still circulates in monkeys[37], but the fast increase in human population, urbanization and travel has enabled sustained transmission in humans and now poses a major global problem. In 2003, there was an outbreak of monkeypox in the USA. Initially, there was concern that this was a mild form of smallpox and patients were hospitalized. Epidemiological studies determined that the virus had been introduced from West Africa in rodents legally imported for sale in the pet industry[38]. Previous outbreaks of human monkeypox, a disease known since 1970, had been largely restricted to rural areas in Central and West Africa.

23. Climate change is particularly relevant to insect and tick-borne zoonotic diseases because it can result in the vectors of diseases expanding their range into new areas and countries where humans and livestock may be naïve to new diseases[39]. Land use change associated with climate change can also alter disease dynamics[40]. There is limited evidence that climate change is impacting wildlife and livestock movements.

24. A combination of factors, including bird migration, the expansion of rice farming and the proximity of pig farms to urban centres is thought to have played a role in the progressive spread of Japanese encephalitis virus across much of the Pacific Rim, South East and South Asia. High rainfall is closely linked to outbreaks of Rift Valley fever (RVF)[41], and there are now

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[41] CDC. Rift Valley Fever. https://www.cdc.gov/vhf/rvf/transmission/virus-ecology.html

concerns about the emergence of RVF in peri-urban dairy value chains, whereby infected milk would have the potential to reach a large urban population with potentially devastating effects.

Disease spread through trade and international travel

25. Massively increased demand for meat, eggs and dairy and other food by large urban populations has driven the globalization of agriculture and by association spread pathogenic agents that threaten the health of humans and livestock. Legal and illegal shipments of wildlife[42] alongside transport of live domestic animals, animal feed and products have caused regular and significant outbreaks of animal and zoonotic disease[43].

26. For example, major outbreaks of Rift Valley Fever in people and livestock in Egypt and the Middle East have been associated with trade in livestock from sub-Saharan Africa[44].

27. Pigs have been indicated as "mixing vessels" for influenza because they support mixing of avian and human influenza viruses, resulting in novel variants. In 2009 a new H1N1 pandemic influenza A virus (pH1N1), presumably of pig origin, emerged in Mexico and the USA and rapidly spread throughout the world, causing the first influenza pandemic of the twenty-first century. The pH1N1 virus may have been circulating, primarily in pigs, for more than ten years. Genetic analysis revealed that this virus is derived from a triple mixture (human/avian/swine) and a Eurasian avian-like swine H1N1 virus. While the location of the pig-to-human virus jump remains unknown, the origin and emergence of this quadruple mixture suggest that the intercontinental movement of live pigs for intensive production had an effect on the swine influenza gene pool and was a causative factor in the resulting pandemic[45].

28. The last decade has seen huge growth in international travel by tourists and workers. 2019, reached a peak with 1.5 billion international tourist arrivals recorded. This was a 4% increase on the previous year. Until COVID 19, tourism was predicted to grow faster than the global economy for the next decade. Measures to contain the current pandemic have already slowed the speed and volume of travel.

29. Travel has the capacity to disseminate pathogens. Examples of rapid and massive spread of respiratory diseases, before local detection and response has been organised, have been seen with SARS in 2003, pH1N1 in 2009 and now COVID 19. The latter has proven particularly difficult to slow partially because of the large proportion of asymptomatic cases still capable of transmission to others. Migrant workers often have low paid jobs and may lack language skills and training to follow prevention measures. They have been associated with COVID-19 hotspots in slaughterhouses and nursing homes.

30. There are numerous examples of disease dissemination linked to international travel and trade in animals[46]. Ebola virus cases occurred in North America and Europe during the West Africa outbreak in 2013/16[47]. West Nile virus is another arbovirus that has global reach. In 1999 the virus was introduced to New York, USA most likely by an infected mosquito. The molecular characterization of the virus indicated it probably originated from Israel. Within a few years, the virus spread widely throughout the Americas causing disease in humans, horses and avian wildlife. It is now endemic[48].

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[47] https://en.wikipedia.org/wiki/Ebola_virus_cases_in_the_United_States#First_case:_Thomas_Eric_Duncan
[48] Gibbs, EPJ. (2005) Emerging zoonotic epidemics in the interconnected global community *Veterinary Record* **157,** 673-679. http://dx.doi.org/10.1136/vr.157.22.673

31. Animals and animal products are also traded for non-food uses, such as pets. Dogs recently imported from Asia were implicated as the source of infection for canine influenza[49]. Between 2004–2014, EU member states officially reported the import of 20,788,747 live reptiles[50]. Although no disease outbreak has been directly linked to these imports, the figures demonstrate the scale of animal movements.

What can we learn from previous zoonotic disease outbreaks?

32. Responses to earlier zoonoses and AMR have highlighted the need for a One Health approach, one that is able to work across sectors and between government and the private sector in a collaborative and joined up way to identify and mitigate zoonotic risks. One Health recognises that the drivers of zoonoses require a multisectoral and transdisciplinary approach, working at the local, regional, national, and global levels. Shifting towards a One Health approach requires a reorganisation of institutions and incentives, new policy and regulations, a common risk analysis and strategy, plus the capacity of human, animal and environmental health organisations to work closely together in real time as events unfold. This is challenge for developed countries, let alone weaker developing country governments[51]. However, there is emerging evidence of success in some countries[52].

33. Individual and organisational incentives may not easily align with One Heath objectives as the benefits and costs of One Health may be unequally distributed. For example the cost of doing business for farmers and traders may increase in order to protect public health (a public good) for which they receive little if any return. Often there is no clear incentive for investment if the benefits appear elsewhere. For example, a study in Uganda estimates that introducing biosecurity would reduce pig farmer profits by 6% but increase margins for other supply chain actors[53]. Compliance by the sectors bearing the brunt of the costs needs encouragement and investment from the highest level of governmental decision making particularly in countries where systems of regulatory control and enforcement are weak.

34. Leadership needs evidence and data to make good decisions. We know that the benefit to cost ratio of prevention is very high. Research on brucellosis shows good cost benefit ratios of control[54]. The Severe Acute Respiratory Syndrome (SARS), outbreak of 2002 caused 8,422 known cases and only 916 deaths across 30 countries[55] but caused economic damage estimated at $40 billion[56]. There is very strong evidence that the cost of control is much lower when emerging diseases are detected at an early stage and that these costs will rise exponentially with time as the disease spreads within either livestock or human populations. Early detection through active surveillance is therefore critical. However, funding is also needed to support the necessary research and monitoring needed.

35. Novel tools and techniques can be used effectively to prevent or detect emerging diseases early. For example, horizon scanning can help identify patterns of disease that indicate the emergence of a new disease and therefore where advance investments can be made in vaccine and drug technologies. Genomics can help predict which viruses are at a point of

[49] Weese J, Anderson M, Berhane Y, Doyle KF, Leutenegger C, Chan R, et al. Emergence and Containment of Canine Influenza Virus A(H3N2), Ontario, Canada, 2017–2018. Emerg Infect Dis. 2019;25(10):1810-1816. https://dx.doi.org/10.3201/eid2510.190196
[50] Auliya, M., et al, 2016. Trade in live reptiles, its impact on wild populations, and the role of the European market. Biol. Conserv. 204, 103e119. Part A. https://doi.org/10.1016/j.biocon.2016.05.017
[51] Tripartite 2019. Taking a Multisectoral, One Health Approach: A Tripartite Guide to Addressing Zoonotic Diseases in Countries. WHO, FAO, OIE. 2019. Contains an overview of One Health experience across the globe. http://www.fao.org/ag/againfo/resources/en/publications/TZG/TZG.htm
[52] Munyua, P.M., Njenga, M.K., Osoro, E.M. et al. Successes and challenges of the One Health approach in Kenya over the last decade. BMC Public Health 19, 465 (2019). https://doi.org/10.1186/s12889-019-6772-7
[53] E. Ouma, M. et al 2018. African swine fever control and market integration in Ugandan peri-urban smallholder pig value chains: an ex-ante impact assessment of interventions and their interaction. Prev. Vet. Med., 151 (2018), pp. 29-39, https://doi.org/10.1016/j.prevetmed.2017.12.010
[54] ILRI 2019, Why livestock matter – examples and evidence showing positive outcomes and impact of specific livestockrelated interventions and investments in Africa and Asia
[55] WHO 2003 Consensus document on the epidemiology of severe acute respiratory syndrome (SARS) https://www.who.int/csr/sars/en/WHOconsensus.pdf
[56] Lee JW, McKibbin WJ. Estimating the global economic costs of SARS. In: Institute of Medicine (US) Forum on Microbial Threats; Knobler S, Mahmoud A, Lemon S, et al., editors. Learning from SARS: Preparing for the Next Disease Outbreak: Workshop Summary. Washington (DC): National Academies Press (US); 2004. Available from: https://www.ncbi.nlm.nih.gov/books/NBK92473

mutating to become zoonotic and or transmissible between humans[57]. New biotechnologies like penside diagnostic tests coupled with the latest information and communications technology (ICT) reduce the time between detection and control. Innovative use of ICTs/digital tools also have potential in disease surveillance and response.

36. It is possible to understand complex value chains, assess risks, reduce the risks arising from agricultural intensification and target hotspots of zoonotic disease development and transmission, although more research is needed in this area. Hotspot targeting has to include the role of wildlife in the risks of zoonoses and an understanding of the interfaces between wildlife and livestock production. Biosecurity protocols[58] for emerging disease threats, whether this is with farmed and companion animals or linked to encroachment on natural environments are needed as are improved application of vaccines, movement controls and animal husbandry.

37. A variety of tools to assess capacity to prevent, detect and control emerging threats at various levels are now being used. These tools allow a normative approach to compare countries and identify where investment is needed, whether it be for a One Health platform, laboratories and surveillance systems or antimicrobial resistance. The tools can also be used to develop and advocate best practices. For example, local participation in surveillance and response to emerging disease threats can be improved by addressing locally-relevant diseases, including endemic zoonoses. Rabies remains a great exemplar of this for many reasons, but most recently, in East Africa, where contact-tracing teams working on rabies prevention have been asked to provide training for contact tracing of COVID-19 cases [pers comm].

38. Actions lie within the institutions and organisations that regulate and control the human health, livestock sectors, the wider food system, wildlife trade and the natural environment, which are often a complex mix of international, national government, formal and informal private sector.

Which organisations are involved in tackling zoonotic disease?

39. The global health architecture has undergone significant revision in the past two decades. The outbreak of SARS in 2003 was a wake-up call to the global public health community that it lacked an international vehicle for rapidly detecting and responding to a multi-country outbreak, particularly one caused by a respiratory-transmitted agent. Despite the World Health Organization's (WHO's) adoption of the International Health Regulations[59] in 2005 to address this concern, the 2009 pandemic of influenza A(H1N1) demonstrated that the world was still ill-prepared for global public health emergencies. Subsequent emerging microbial threats, including cholera in Haiti (2010), MERS coronavirus in the Middle East and Korea (2012), chikungunya (2013) and Zika (2015) in the Americas, yellow fever in Africa (2015–2016) and in South America (2016–2017), and cholera in Yemen (2017), highlight the challenges in accomplishing effective global public health preparedness. Most notably, the Ebola epidemic in West Africa in 2014–2016 provided a case study of global response deficiencies.

40. The Global Health Security Agenda (GHSA) was launched by 29 countries, the World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO), and the World Organisation for Animal Health (OIE) in 2014, just as the Ebola outbreak was unfolding. The GHSA has subsequently grown to include over 60 nations. GHSA pursues a multisectoral approach to strengthen global and national capacity to prevent, detect, and respond to human and animal infectious disease threats. It focuses resources on 19 action packages. The zoonotic disease package enables improvements in early warning and detection, timely data sharing, laboratory testing, and joint outbreak response capacities in the human, animal health and wildlife sectors to strengthen mechanisms necessary to effectively detect and respond to emerging zoonotic threats.

[57] SARS-like WIV1-CoV poised for human emergence: https://www.pnas.org/content/113/11/3048
[58] The biosecurity protocol supports the prevention or management of risks associated with harmful organisms, like pests and diseases.
[59] The International Health Regulations (IHR) are a binding international legal instrument for WHO Member States. Originally developed in 1969, in 2005, post SARS, the IHR were revised to take an all hazards approach to protecting public health, including chemical, radiation, and food safety, and zoonotic diseases.

41. WHO, OIE and FAO are key technical partners within the GHSA and they also work through a Tripartite agreement advocating for effective multisectoral, multidisciplinary, and transnational collaboration. The organisations have their own assessment tools and recently published best practice guidance to address zoonotic diseases in countries. The guide recognises that most countries and regional bodies have inadequate One Health mechanisms in place for administrative and technical collaboration. In zoonotic disease events and emergencies, lack of joint preparation and established mechanisms for collaboration can result in confusion and delayed responses. For endemic zoonotic disease threats, the lack of coordinated planning, information sharing, assessment, and control activities across all relevant sectors can obstruct and complicate the implementation of effective disease control programmes. The practical fact remains that operating surveillance systems at intersectoral interfaces is highly challenging.

42. For the world to minimise the impact of emerging zoonoses the capacity of all countries, particularly LMICs, needs to be significantly raised. Regional bodies have a key role to play in this process. They reflect local realities and concerns and can act to bring member states up to an agreed standard. Countries appear to recognise the relevance of a regional approach and One Health Ministerial Communiques have been published by most Regional Economic Communities (RECs).

43. For example, the Africa Centres for Disease Control and Prevention (CDC), was endorsed by the AU Assembly of Heads of State and launched in 2017 to improve surveillance, emergency response, and prevention of infectious diseases. Africa (CDC) has developed a five-year strategic plan that is providing the basis for several external funders to provide support. The Association of Southeast Asian Nations (ASEAN) established working regional groups on One Health and Livestock plus an ASEAN Coordinating Centre for Animal Health and Zoonoses' (ACCAHZ). On 20th Feb 2020 China and ASEAN held a special foreign ministers' meeting on the novel coronavirus (COVID-19) outbreak to discuss coordinating efforts in fighting the pandemic.

44. The Coalition for Epidemic Preparedness Innovations (CEPI), is an NGO that was founded in 2017 to coordinate and finance the development of new vaccines for diseases that might lead to a pandemic. CEPI works by identifying the most promising research, and then connecting it to industry and government resources, in order to bring multiple sets of "candidate" vaccines through initial clinical trials. The goal is to create a stockpile of potential treatments for known pandemic threats that could quickly go into production in a spill over.

45. A number of other organisations are also working to tackle issues related to the trade in wildlife, including the Convention on International Trade In Endangered Species of Wild Fauna and Flora (CITES), the Convention on Biological Diversity (CBD) and the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services (IPBES).

What are the political economy issues around tackling zoonotic disease threats systematically?

46. There has been significant global concern about the lack of preparedness at national and regional levels for emerging zoonotic disease threats. Until the emergence of Covid-19 the threat was seen as low risk and probably low impact. In 2016, the World Bank established an International Working Group on Financing Preparedness (IWG) to analyse why countries are so complacent when the cost to benefit of investing in preparedness is so high. The IWG's report found that countries frequently under invest because the requirements for preparedness are complicated to meet. At a minimum, countries need a solid legal and regulatory foundation, adequately trained and equipped public health workforce, strong surveillance and response framework, functional national public health laboratories, and robust multi-sectoral coordination. Many of these components lie in different parts of government and are often financed through a variety of different mechanisms, ranging from emergency allocations, routine sectoral provisions and ad-hoc apportionments.

47. A significant impediment is the asymmetry of economic power and political influence within governments between the agricultural and environment sector and associated ministries and the health sector and Minister of Health, and the protection of domains. Unless this is

acknowledged, one continually finds good tools and proposed national plans are not implemented or fall into disuse.

48. This complexity explains why many countries have struggled even to draft a national plan of action with specific activities, timelines, and budgets. Furthermore, without such plans, countries are less able to collaborate and crucial investments in basic training and infrastructure, surveillance and response services and even new technologies such as vaccines and treatments are neglected. The World Bank Global Preparedness Monitoring Board 2019 World at Risk Report also highlights the importance of strengthening animal health systems.

49. Despite the fact that the private sector has so much to lose when economies and trade shuts down due to zoonotic outbreaks, the levels of investment to identify and respond to zoonoses are limited for two reasons. Firstly, private sector companies lack adequate awareness of the risks of infectious zoonotic outbreaks and tend to underestimate the potential costs of those risks. Only those that have directly experienced disruption to customers, supply chain, and workforce from such causes attach much weight to such risks. Secondly, private sector companies find it difficult to justify investments in public goods, such as national disease surveillance systems, because these do not generate profits for their shareholders. In addition, many private sector firms in LMICs operate within the informal economy which tends to be less affected by government regulations designed to minimise the risks of zoonoses and with few incentives for regulatory compliance. It is therefore important that a case is made to show that preparedness is a good investment for business before formulating public private partnerships to ensure sustainable, efficient and effective coverage.

What political and practical options are there for countries to strengthen support surveillance and response capacity in developing countries?

50. OIE, FAO and WHO recently published the Tripartite Zoonoses Guide (TZG) to provide countries with operational guidance and tools for the implementation of a multisectoral, One Health approach to address zoonotic diseases and other shared health threats at the human, animal, environment interface. The TZG is to be followed with models and templates for standard operating procedures and processes, terms of reference, data collection and reporting templates, plus other practical resources that countries can adapt to their needs and contexts. Many of these tools already exist and are being utilised through numerous initiatives and can be used by institutions and countries to build strong systems in response to COVID19.

51. WHO's Joint External Evaluation (JEE) or the outcome of OIE's Performance of Veterinary Services (PVS) pathway analysis provide a systematic and objective assessment of country's capabilities across core domains and a prioritized list of gaps to be addressed. These assessments are proving to be increasingly important in raising surveillance and response capacity.

52. In order to persuade policy makers to commit to addressing zoonotic threats the IWG report describes detailed mechanisms for persuading governments to invest but also recognises that ensuring sustained commitment to financing preparedness will be difficult, since the mark of success is that nothing happens, and there will always be multiple competing priorities. In this context, the IWG has proposed to link the incentives that business and the financial markets can provide. to countries willingness to translate their JEE and PVS assessments into implemented action plans. Through developing indices that measure intrinsic risk, state of preparedness, and economic vulnerability, it could be possible to make the threat of infectious disease outbreaks much more visible and concrete to potential investors and incentivize governments and the private sector to mitigate these risks.

What are the key evidence/knowledge gaps that need to be addressed? (work in progress)

Systems, institutions and incentives

53. COVID 19 and previous zoonotic disease threats have demonstrated the need for prevention, early detection and rapid response systems. How to make systems functional, prepared and sufficiently invested is a major gap globally, regionally and nationally. It is generally agreed

that a One Health approach is needed but COVID 19 has recently demonstrated that the knowledge and tools for persuading senior policy makers, private companies and civil society to invest in the approach in terms of re-organisation, capacity development, budgets and strategy building remains weak.

54. Internationally recognised assessment tools are just starting to be used for gap analysis. Understanding how they might be used to develop indices that measure intrinsic risk, state of preparedness, and economic vulnerability to incentivise governments and the private sector to invest and mitigate these risks has still to be worked out.

55. Improved knowledge on the value for money of particular investments and how they can support work to address key challenges such as antimicrobial resistance and endemic disease control would be useful.

56. Further work on understanding the linkages between ecosystem degradation/habitat loss and pandemic risk

57. Within the food system there is a need for better understanding of how informal markets, and their supply chains, including processers and wholesalers, can be regulated to reduce threats including zoonoses, other food borne pathogens and AMR. We also need to understand more about the socioeconomic and cultural practices influencing reporting for notifiable diseases.

Surveillance and preparedness

58. Understanding how foresight and horizon scanning as tools can use new knowledge and big data to guide investments into new technologies and tools, including vaccines and treatments.

59. Improving involvement of communities and removing dis-incentives for reporting disease and installing incentives

60. Better use of new technologies such as drones, mobile phones, rapid test (corpse-side testing)

Behaviour change and food choices

61. How to improve food safety measures and SPS in rural and urban markets and their supply chains.

62. Behavioural economics, incentives and nudges

63. Changing social norms through role models, social media

Testing, diagnostics, vaccines and medicines.

64. Optimal use of technology, particularly genomics, penside diagnostics and information technologies for early detection and control can be significantly improved in most countries.

65. Development of panviral drugs and vaccines that would be effective against a wide range of potentially pandemic virus strains[60], for example, all types of influenza or a substantial group of coronaviruses rather than just one.

66. How to address co-infection in testing and diagnostics.? Coinfecting zoonoses complicate and confound diagnosis and epidemiology of emerging infections; the spread of food-borne pathogens; immune response to chronic parasitic infections of humans and animals, and the management of major global health challenges. Co-infecting zoonoses can also impact upon vaccine efficacy, AMR resistance and population level disease control strategies. Co-infection is considered the norm in host populations whether human, or animal.

[60] Amesh Adalja & Thomas Inglesby (2019) Broad-Spectrum Antiviral Agents: A Crucial Pandemic Tool, Expert Review of Anti-infective Therapy, 17:7, 467-470, DOI: 10.1080/14787210.2019.1635009