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Grappling with (re)-emerging infectious zoonoses: Risk assessment, mitigation framework, and future directions

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A B S T R A C T

Low-income countries (LICs) in Africa, southeast Asia, Latin America, and the Caribbeans constitute potential hotspots for future outbreaks of infectious zoonoses. A comprehensive framework on risk drivers, assessment, and mitigation in LICs is lacking. This paper presents the nature, history, risk factors, and drivers of zoonoses in LICs. A Quantitative Microbial Risk Assessment and Hazard Analysis of Critical Control Points are proposed for assessing human health risks. The mitigation framework entails: (i) learning from the COVID-19 pandemic, (ii) the precautionary principle, (iii) raising public and stakeholder awareness, and (iv) the One World, One Health concept. Future perspectives are discussed on: (i) curbing poaching and illicit wildlife trade, (ii) translating the 'One Health' concept to practice, (iii) the dilemma of dealing with wildlife hosts of zoonoses, including the morality and ethics of culling versus non-culling, (iv) the challenges of source tracking and apportionment of zoonoses, and (v) decision-making scenarios accounting for the high human health risks and the high uncertainty in current evidence. Future directions on zoonoses include: (i) the occurrence of antimicrobial resistance, (ii) environmental reservoirs and hosts, (iii) the development of tools for source tracking and apportionment, and (iv) host-receptor-pathogen interactions. Funding models and the application of novel tools, i.e., game theory, genomics, shell disorder analysis, and geographical information systems are also discussed. The proposed framework enables a better understanding of the key risk drivers, assessment, and mitigation in LICs. Further work is needed to test and validate the framework and develop generic lessons for risk assessment and mitigation in LICs.

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1. Introduction

The recurrent outbreaks of (re)-emerging infectious zoonotic diseases indicate the need to reflect on and develop more robust risk assessment and mitigation strategies. The recent COVID-19 pandemic caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), first detected in Wuhan (China) towards the end of 2019 [1], and its impacts on global health and economies give further credence to the need to rethink current mitigation measures. The implications of outbreaks of zoonoses on human health and society are global in nature and extent. The risk of epidemics is high in low-income countries/regions due to multiple risk factors, which will be discussed in subsequent sections. According to the World Bank (2021), for the 2021 fiscal year, countries are classified into four groups based on gross national income (GNI): (i) low-income countries, defined as those with a GNI per capita of $1035 or less, (ii) lower middle-income countries with a GNI per capita of between $1036 and $4,045, (iii) upper middle-income countries with a GNI per capita of between $4046 and $12,535, and (iv) high-income countries with a GNI per capita of $12,536 or more (Fig. 1). Broadly, low-income countries such as those in sub-Saharan Africa, south-east Asia, Latin America, and the Caribbeans share generic similarities, including multi-dimensional poverty, foodand nutrition insecurity, and lack of access to clean drinking water and improved sanitation [2–4,219]. Data on worldwide global indicators also indicate that LICs often have poor or weak governance systems [5]. Several international reports exist on these indicators differentiating low-income countries from high-income ones [2–5]; Zhou et al., 2018). One should note that, despite these generic similarities, some differences exist among and even within countries, while selected countries (e.g., South Africa [6], and even developed ones have a mixture of both high- and low-income characteristics. Here, we focus mainly on low-income countries, defined broadly by the World Bank (2021). Hence, a discussion of the problems and recommendations on a country-by-country basis and differences among and within low-income countries are beyond the scope of the current study. Consensus exists that low-income countries (LICs) in Africa, Asia, Latin America, and the Caribbean region constitute potential hotspots for future outbreaks of infectious zoonoses [7]. This is because of several risk factors, including close and frequent human-wildlife interactions caused by land-use changes and the increasing human population.

Thus, to mitigate future outbreaks of zoonoses, public and research attention should focus on developing and applying risk assessment and mitigation strategies, including preventive measures in these potential hotspots in LICs, rather than adopting a reactionary approach driven by actual outbreaks. The ongoing COVID-19 pandemic has provided many critical lessons for mitigating future zoonoses outbreaks [8,9]. For example, the following measures were offered by Halabowski and Rzymski [8]: (i) viral surveillance in animals, (ii) limiting wildlife trade, (iii) changes to mink production, (iv) changes to meat production, entailing the introduction of cultured meat, and (v) reducing hunting activities. However, a closer examination of these recommendations suggests that while they may be suitable for high-income countries, their implementation (e.g., viral surveillance) poses considerable challenges in low-income settings lacking comprehensive surveillance systems and diagnostic and analytical equipment. Moreover, mink farming

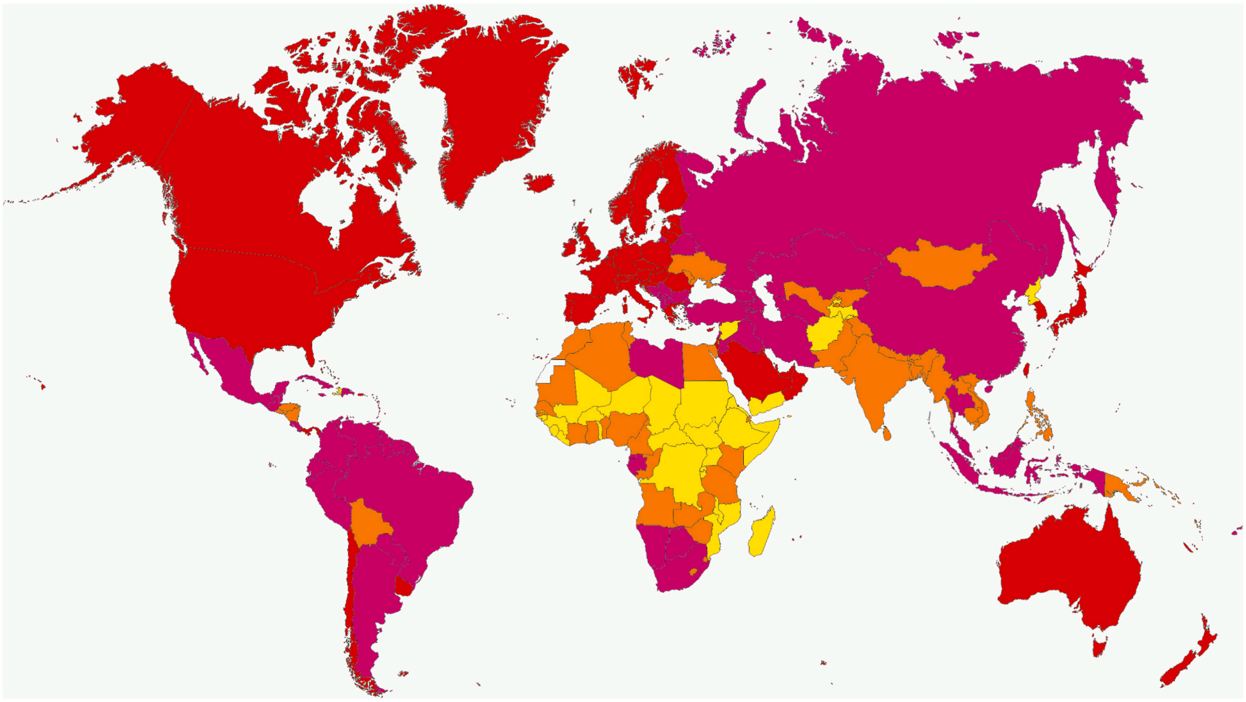

Fig. 1. Global distribution of low-income countries/regions based on gross national income (GNI) per capita. (i) Yellow: Low-income countries defined as those with a GNI per capita of $1035 or less in 2019, (ii) Orange: Lower-middle-income countries with a GNI per capita between $1036 and $4,045, (iii) Pink: upper-middle-income countries with a GNI per capita between $4046 and $12,535, and (iv) Red: High-income countries with a GNI per capita of $12,536 or more. Data source: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups(For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

is not prevalent in most LICs, while cultured meat is not the technology under development in these countries. Reducing hunting and trade in wildlife poses challenges in LICs due to weak governance and regulatory systems.

The present paper highlights the problems and the framework for (re)emerging zoonoses. The issues discussed are generic and cross-cutting, and hence also relevant to high-income countries. However, for brevity, and due to several risk factors, the current study pays particular attention to LICs that are at significant risk of future epidemic outbreaks. Moreover, the present paper expands on the discussion started by earlier work by Halabowski and Rzymski [8], which focused mainly on problems and recommendations targeting or relevant to high-income countries. In addition, it also makes the following further contributions: (i) discusses the risk factors, drivers, and challenges associated with zoonoses in the context of LICs, (ii) proposes frameworks for comprehensive risk assessment based on Quantitative Microbial Risk Assessment (QMRA) and Hazard Analysis of Critical Control Points (HACCP), and (iii) proposes mitigation measures, future perspectives, and research needs taking into account the socio-economic settings in LICs. Overall, the present paper presents a risk assessment and mitigation framework for zoonoses in the context of LICs. The framework discussed in the present article is generic and can be adapted to various infectious zoonotic diseases. However, for brevity, particular attention is given to viral zoonoses for two reasons: (i) they are amongst the most widely reported in LICs, and (ii) the ongoing COVID-19 pandemic and earlier human coronaviruses (e.g., SARS, MERS) give further impetus to viral zoonoses. The present study adopts a source-pathway-receptor-impact-mitigation continuum (SPRIM) as a guiding framework to assess and mitigate human health risks.

The present paper posits that: (i) several risk factors and drivers, coupled with weak governance and regulatory systems, predispose LICs to future outbreaks of infectious zoonoses, (ii) risk assessment based on Quantitative Microbial Risk Assessment (QMRA) and Hazard Analysis of Critical Control Points (HACCP) provide critical tools for a comprehensive understanding of human exposure and health risks in the source-pathway-receptor-impact-mitigation continuum, and (iii) a mitigation strategy integrating lessons from the COVID-19 pandemic, 'One World, One Health' and precautionary concepts, and raising awareness are all critical in safeguarding human health in low-income settings.

Finally, future perspectives are highlighted, including challenges, opportunities, research needs, and scope to apply emerging research tools to understand zoonoses better.

2. Infectious zoonoses in low-income countries

2.1. Nature and history of zoonotic infections

Zoonotic infections can be transferred between invertebrate and vertebrate animals, and humans. These infections can be caused by bacteria, viruses, fungi, and parasitic organisms. Some pathogens have more than one host reservoir species [10], which can significantly increase their transmission to people. The transmission of these infections between animals and humans can be: (i) direct (e.g., through contact with blood, urine, or saliva), (ii) indirect (by coming into contact with animal habitats, environments, or contaminated surfaces), and (iii) through vectors such as mosquitoes, tsetse flies and ticks with either the human or the animal as the recipient [11]. Selected zoonotic infections can be classified as enzootic, which are found in animal populations and can be transferred from animals to humans, but usually, there is little or no transmission from one person to the other. Rabies is an excellent example of such a zoonotic infection. This is the opposite of what is observed with some other zoonotic pathogens, where once transmitted from animals to humans, they can readily be passed from person to person [12]. Examples include pathogens such as HIV, Ebola virus, and SARS-CoV-2. Some major groups of animals responsible for transmitting pathogens to humans include carnivores, rodents, birds, ruminants, bats, and primates [13]. Both domesticated and wild animals can be sources of zoonotic infections, but wild animals have increasingly become the most significant source of such infections [14]. Therefore, people frequently in contact with wild animals or their habitats are more susceptible to contracting zoonotic infections than those who do not. This includes hikers, hunters, individuals camping in wildlife habitats, and even those who explore caves, among other activities. Clinically, more significant concern and emphasis are mostly placed on the transfer of infections from animals to humans than the opposite (from humans to animals) [15,16]. However, conservation-wise, the transfer from humans to animals becomes a big concern because some diseases originating from humans do infect wildlife [16,17], e.g., in the case of transfer of infections such as measles from humans to primates [18], which can affect the survival of the animal species.

The nature of each zoonotic pathogen plays a significant role in the emergence, re-emergence, rate of spread, pathogenicity, and virulence of such a pathogen. The emergence of a zoonotic pathogen involves the surfacing of a novel pathogen or one which has significantly evolved or the surfacing of a pathogen already recognized but in a region where it was not identified before [19]. On the other hand, there are cases where the incidence of a known pathogen in a given geographical area may increase significantly, or conditions are altered such that its potential pathogenicity in humans is increased. Such a case is referred to as re-emergence [19]. Typical zoonotic pathogens with a wildlife reservoir or source have little clinical impact on their primary wildlife host as compared to the effect they may have when transmitted to human hosts [20,21], although there are some exceptions.

Evidence has shown that some zoonotic pathogens can exhibit significant evolutionary changes even in a short period, e.g., during a single pandemic [22]. To date, numerous variants of SARS-CoV-2 have emerged within the course of the pandemic. Some of these variants have been classified as variants of concern (VOC), as they meet at least one of the following requirements at a degree of global public health significance: (i) transmissibility increase, elevated virulence, (ii) change in clinical disease presentation and/or (iii) decreased effectiveness of public health and social measures or available diagnostics, vaccines or therapeutics.

Over the past couple of decades, global changes, along with the increasing human population, have led to a spike in new zoonotic infections [12]. Zoonotic pathogens, especially those emerging from wild animals, have influenced some pandemics for over 100 years. This has tallied with the global increase in human population, particularly in areas where there is a combination of increased human activities and high wildlife biodiversity [23,225,226,24].

An assessment by Taylor et al. [25] showed that around 61% of the infectious species affecting humans in one way or the other are zoonotic in origin. Of the estimated 400 infectious diseases identified between the 1940s and around 2012, more than 60% of these were zoonotic [26]. This indicates that zoonotic pathogens play a significant role as the cause of infections in humans. Roche and Gue'gan [27] have argued that most pathogens and parasites responsible for affecting human populations are zoonotic. Some significant and relatively recent zoonotic pathogens include anthrax, Ebola, H1N1 influenza, HIV/AIDS, H5N1 bird influenza, SARS-CoV, MERS-CoV, andthe SARS-CoV-2 [8]. Some of these have resulted in pandemics, have led to high human mortality rates, caused substantial economic losses, and have led to significant changes in the global public health as a whole [26]. In 2012, it was estimated that, annually, roughly one billion illness cases and millions of deaths are due to zoonotic infections [28], and the figure might have even gone higher following the outbreak of the COVID-19 pandemic.

Although there is an increase in human infections attributed to zoonotic pathogens, including those causing pandemics, generally, there is not much research on zoonotic viruses compared to their bacterial and parasitic counterparts. Most of the studies in the field focus on the major viral zoonotic diseases (H1N1 influenza, HIV, H5N1 bird flu, SARS coronavirus) [23,225,29], which generally pose global human health and economic threats. The inferences from such research are not necessarily relevant to other zoonotic infections, especially those that are endemic and typically occur in LICs. Thus, very little research exist to present a clear picture of the current major global zoonotic diseases, which can cause infections in humans and their worldwide effects. This leaves the human population vulnerable to a wide range of zoonotic bacteria, viruses, fungi, and parasites, leading to detrimental consequences and burdens on the health sector, national economies, and even veterinary medicine and agricultural production worldwide [14]. The World Bank estimates that between 1997 and 2009, six significant epidemics attributed to zoonosis resulted in an economic loss of more than 80 billion dollars [30]. However, depending on the impact of these zoonotic diseases, some funding and research are being dedicated and conducted to address the problem, but most still remain neglected in decision- and policy-making[31]. Due to the above factors, it has always been the case that humans have been behind in predicting potential outbreaks of zoonotic diseases and in understanding variables that promote the spread of infections, making it difficult to prevent possible future outbreaks [20]. This may remain the case in the coming years if the situation does not improve.

2.2. Risk factors, risk behaviors, and drivers in LICs

It is crucial to understand the different factors that enable the transmission of zoonotic pathogens from wildlife to humans in LICs. Recognizing these will be the first step to better understanding the origins and spread of such diseases and finding ways to reduce or combat transmission and disease outbreaks. Usually, human influence or anthropogenic activities due to different socioeconomic factors, ecological changes, and behavioral changes pave the way for successfully transmitting zoonotic pathogens from animals to humans [20,220]. Large-scale land-use changes impact the dynamics and relationship between animal hosts, zoonotic pathogens and humans, which all play a significant role in disease ecology [12]. The mingling of people, animals and the environment promotes the successful transmission and emergence of these diseases. Examples of activities that increase the risk of transmission of zoonotic diseases include encroachment of wild animals' habitats due to land-use changes that often lead to habitat destruction and fragmentation, ecotourism, hunting, and land clearing for farming and grazing, which all commonly involve close and frequent wildlife-human interactions [20].

Sub-Saharan Africa has been declared a highly prevalent endemic zoonosis area due to the large rural populations that live close to wildlife and livestock (Kemuto et al., 2018; [32]. This creates new niches for the pathogens as well as new hosts (humans), which they adapt to [12], causing diseases in the process. Infections such as yellow fever, common in some tropical African countries, and Chagas disease, which mainly occurs in rural Latin American countries, have been attributed to land-use changes that cause deforestation mainly due to logging, mining, plantation development, and gas or oil extraction [33–35]. Such activities allow access to emerging zoonotic disease hotspots with abundant wildlife, which may be reservoirs of pathogens not encountered by humans before [23,225]. Ecotourism is an economic sector growing in some LICs, especially those with wildlife habitats that are still intact and unexploited. In ecotourism, humans subject themselves to such wildlife habitats for tourism purposes, where the probability of exposure to zoonotic pathogens is very high. Examples of such ecotourism activities include camping in these habitats, hiking, guided bush walks, and even exploring caves, which can be habitats of the bat species known as vectors of zoonotic pathogens. Some jobs or research activities also involve humans working in such habitats putting their life at high risk of contracting zoonotic infections as they work. For example, ecologists often conduct extensive fieldwork with frequent and direct animal interactions. At the same time, working in or visiting such environments increases the risk of being highly exposed to vectors such as mosquitoes and ticks, which can be carriers of vector-borne diseases and vectors of zoonoses between animals and humans.

Another common risk factor that leads to the emergence of zoonotic disease in LICs is the widespread consumption of animal food products from wild animals, especially in rural areas. Although fewer wildlife products are consumed than livestock products [36], these food sources are still widely used in LICs to supplement nutrition, especially the protein diet [37,38]; Harvey-Caroll et al., 2022 [39]. In addition, there is increased bushmeat hunting in some parts of Africa [37–40]. In Central African countries alone, the annual bushmeat consumption is estimated to be about one billion kilograms [41]. The process of acquiring such food products involves hunting and preparation, which leads to human-animal contact and, therefore, the risk of transmission of zoonotic diseases. For example, HIV-1 and HIV-2 are linked to the primary transmission and further mutation of simian immunodeficiency virus from chimpanzee and sooty mangabey monkeys, respectively, during the preparation and consumption of their meat [42,43], while the hunting of great apes led to the transmission of Ebola hemorrhagic fever [44].

Domestication of animals (both food and non-food animals) has also resulted in a zoonotic human infection leading to the transmission of diseases such as rabies and echinococcosis [12,45]. In most LICs, many domesticated and wild vertebrates and invertebrates are used as important food sources [46], which significantly increases the potential emergence of zoonotic infections harbored by these animals. This is especially the case in rural areas where most of the populations of these countries reside, thereby posing a need to have a wide range of food sources to supplement their diets. In sub-Saharan African countries such as Zimbabwe, even some of the wild vertebrates that are potential reservoirs of zoonotic infections are reared domestically for food purposes; examples include guinea fowls and quails reared together with domestic food animals such as chickens, pigs, and rabbits. As new animals (previously wild) are reared domestically, it presents new opportunities for the emergence of zoonotic pathogens. At the same time, the practice of animal rearing, whether domestic or wild, has now widely spread to urban areas rather than just the rural areas as was the norm before, which made the situation worse [47]. Due to cultural reasons, and the need to supplement the diet, there is also wide use of edible wild rodents (e.g., mice) and birds such as quelea birds, which can be potential reservoirs or intermediate hosts of zoonotic pathogens.

Most LICs are characterized by weak governance systems with high levels of corruption, which promote poaching and illicit wildlife trade. Although some of these countries are signatories of regulatory structures of trade in wild animals, such as the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES), there is still widespread illegal hunting and trade in wildlife mainly fuelled by high returns from such activities [48]. Such unregulated and illegal activities can fuel the transmission of disease pathogens from animals to humans [49,50] because the standard health protocols and regulations for handling animals are not followed when illegal activities are involved. The processing of wildlife and associated products from illegal and legal hunting potentially facilitates the spread and transmission of zoonotic infections. On the other hand, increased illegal hunting can significantly reduce the population of the animal species serving as preferred hosts and potentially make humans more vulnerable to infection. For example, arthropod vectors of zoonotic pathogens that feed on animal hosts can shift host to humans if their preferred animal host has reduced in numbers, leading to an outbreak of the disease in humans. The depletion of wildebeest and cattle population in East Africa due to rinderpest meant that tsetse flies had to shift their feeding to humans, which in turn led to a considerable outbreak of sleeping sickness [51].

Weak and poorly enforced public and animal health and food safety regulations contribute significantly to the spread, emergence, and re-emergence of zoonotic infections. Generally, within the rural areas in LICs, there is little or no awareness and education on health and safety regulations on zoonotic infections. This, together with poverty, has resulted in people utilizing or consuming contaminated food such as contaminated meat from their livestock, bush meat sold in informal markets, and unpasteurized milk [32]. As long as the level of education or awareness of zoonotic diseases is low, the risk of these diseases emerging and spreading will remain in LICs, like in regions of sub-Saharan Africa [52]. Practices such as consuming raw or undercooked animal and wildlife foods are a potentially under-estimated pathway for human exposure to zoonoses. In tropical Africa, outbreaks of trichinosis are mainly due to undercooked meat from pigs and wild boars [53]. Evidence also shows that consuming raw animal products such as blood, milk, and internal organs such as the liver is common in LICs [54–56]. The reasons for this practice vary. In the case of raw blood, this includes religious and cultural rituals. In the Maasai pastoralists of Tanzania, raw blood mixed with milk is given to women soon after childbirth in the belief that it replenishes lost blood and helps produce energy, while in young boys recently circumcised, it is believed that drinking raw blood will supplement its loss during the procedure [54]. The consumption of raw duck blood in south-east Asian countries such as Vietnam, when mixed with other dishes, has been suggested as a possible pathway for transmission of zoonotic avian influenza viruses to humans [57]. The consumption of raw fresh or sour milk is widespread in Africa [54], but if the milk contains pathogens from infected livestock, it becomes unsafe. Pastoralists regard raw milk as highly nutritious and culturally valuable as a staple food [58], and the campaigns to render raw milk safe may not be readily accepted. In most LICs, small and large livestock are highly valued, especially among low-income communities in urban and rural areas. Hence, eating carcasses or slaughtering ill animals for consumption is rampant in poor communities. For example, Dinka cattle keepers from South Sudan disregarded the possible transmission of diseases such as anthrax from livestock to humans and ate meat from dead cattle carcasses [59]. This is contrary to the global best practice in food hygiene and safety, where sick and dead animals should not enter the human food chain. In most LICs, food-borne zoonotic diseases such as brucellosis, salmonellosis, and bovine tuberculosis, among many others, are enzootic to livestock, leading to endemic infections in people, especially when sick or dead animals are consumed [12]. The methods used for slaughtering and processing the infected animals can also serve as pathways for disease outbreaks. All this highlights the limited understanding of the human health risks associated with such practices.

Generally, in most LICs, there is a weak, inadequate, or just complete lack of surveillance systems for zoonoses. Due to a lack of resources and limited monitoring from responsible authorities, unscrupulous business people take advantage of this and sell meat from dead animals while practicing poor food hygiene, which increases the risk of transmission of any associated zoonotic pathogens. This is compounded by a lack of microbial quality checks on various animal and wildlife meat and products. There is a lack of adequate infrastructure or enough resources to monitor zoonotic diseases, making it highly challenging to control them in most sub-Saharan countries, such as Zimbabwe [32,60]. The limited monitoring is confined chiefly to large animal production systems, particularly cattle, whereas small livestock establishments are often excluded. For example, in Zimbabwe, the focus is mainly on foot and mouth disease and anthrax, with minimal surveillance data on viral zoonoses. This is partly due to a lack of analytical equipment and funding. Therefore, the lack of adequate disease management and control in livestock production in LICs means that there is a high probability of the emergence of zoonotic pathogens linked with the livestock hosts [12], while on the other hand, the lack of proper veterinary infrastructure reduces the efforts to curb the spread of zoonotic diseases from the livestock.

Moreover, there is a lack of collaboration between the public and private sectors involved in livestock production [61]. Besides common cattle diseases such as foot and mouth disease, very few people are familiar with zoonoses and their transmission pathways and health risks. Even basic knowledge of the ecology of zoonotic food-borne pathogens is nearly non-existent in LICs, making identifying the animal reservoirs difficult [12], and almost impossible to monitor or detect the potential emergence of diseases before much harm is caused.

In most LICs, there is usually a lack of coping capacity for outbreaks due to inadequate healthcare systems and diagnostics [222]. Early detection and diagnosis of any zoonotic disease are crucial to help curb onward transmission to other individuals, thereby reducing the potential of massive outbreaks [62]. Countries with weaker healthcare systems face challenges in the early detection of these diseases leading to outbreaks and secondary infection due to rapid onward transmission. The lack of adequate diagnostic infrastructure in most LICs results in delayed identification of suspected cases, confirmation, and subsequent isolation [63]. This puts pressure on health systems that are already strained and barely coping. Limited resources to build enough hospitals to allow isolations of cases with highly transmissible zoonotic diseases translate into a high risk of their spread among humans [64]. Shortages of qualified and highly skilled health personnel also worsen the situation [65]. There is already a 'brain drain' problem where developed countries attract and hire health personnel from LICs, leaving a considerable gap to fill in these countries [66,67]. The outbreak of the COVID-19 pandemic has led to many developed countries hiring thousands of nurses and doctors from the African nations for their benefit, leaving many African health systems incapacitated and barely coping with thousands of COVID-19 cases.

It is noteworthy that the outbreak of COVID-19 and its global impacts and poor response systems at national and global scales occurred against a background of earlier efforts to address such challenges globally (Carson, 2020). For example, the USAID's Emerging Pandemics Threats program known as PREDICT, and led by the University of California, Davis's One Health Institute, initiated in 2009, sought to reduce pandemic risks and promote global health (https://p2.predict.global/). Yet ironically, in 2019, exactly at the end of the second phase of the project (PREDICT-2), nearly a decade later after the launch of PREDICT, COVID-19 broke out. Carlson (2020) presents a detailed commentary on the PREDICT program in light of COVID-19. The PREDICT program is a novel program aimed at profiling the health risks of pandemics and mobilizing resources on a global scale. Hence it can provide lessons to inform the design and implementation of future similar projects. In summary, this highlights that while programs such as PREDICT are a welcome development to address future pandemics, further work is still required with respect to resource mobilization, sustainable funding mechanisms, research, the establishment of global surveillance systems, capacity-building, and dissemination of research outputs. These aspects are discussed in detail in subsequent sections.

3. Human health risk assessment and mitigation framework

3.1. Human health risk assessment

Human health risk assessment is critical in safeguarding human health against zoonotic infections and their societal impacts. Broadly, health risk assessment protocols entail: (i) identification of hazards, in this case, the nature and sources of zoonotic pathogens, (ii) identification of people at high risk of exposure, (iii) understanding the human exposure routes and the likelihood of occurrence of such exposure, and (iv) estimation of the overall risk using qualitative or quantitative methods (Kitajima et al., 2020). Here, we highlight the tools available for human risk assessment and their current application status in LICs.

3.1.1. Tracking zoonoses in the environment-wildlife-human continuum

Regular systematic zoonoses surveillance in the environment-wildlife-livestock-human continuum is a critical component of human health risk assessment [68,69]. This includes pathogen and sero-surveillance in environmental compartments, humans, domestic animals, livestock, and wildlife. In this regard, particular attention should be paid to known and potential hosts and intermediates of zoonotic pathogens. Such surveillance systems act as early warning systems and can be used to identify zoonotic hotspots and used as a basis to trigger mitigation and control measures. However, pathogen surveillance systems, including zoonotic ones, are weak or even non-existent in most LICs, partly due to a lack of resources, expertise, and laboratory infrastructure [70,71]; 2022; [66,72].

3.1.2. Quantitative microbial risk assessment (QMRA)

Tools and models relying on quantitative microbial risk assessment (QMRA) are increasingly being proposed for comprehensive human health risk assessment, including for SARS-CoV-2 in various environmental media [70,71]; Kitajima et al., 2020). In the context of zoonoses, the application of QMRA requires data on: (i) the nature and pathogenicity of the pathogens, (ii) environmental behavior and the fate of the pathogens in the relevant environmental media, including intermediate hosts, (iii) multiple routes or pathways accounting for human exposure via contact with host animals, consumption of contaminated animal food products, and human-human transmission, and (iv) development of quantitative models relating human exposure to pathogens at a given dose or concentration to the likelihood of occurrence of a human health endpoint or outcome such as infection.

Yet, the development and applications of QMRA in LICs face several constraints, primarily because QMRA is data-intensive, and the bulk of such data is unavailable in LICs and even in developed countries. Firstly, dose-response models for most zoonotic pathogens, including SARS-CoV-2, are not yet developed. Secondly, most pathogens' behavior, transmission, and fate in the environment-wildlife-livestock-human continuum are still poorly understood. Last but not least, expertise in QMRA is often lacking in LICs, which often relies on external experts [66]. Thus, further research is required to develop and validate health risk assessment tools and models based on QMRA in LICs as part of a comprehensive research program to mitigate zoonoses in LICs.

3.1.3. Tracking food-borne zoonoses: HACCP as a decision-support tool

The Hazard Analysis of Critical Control Points (HACCP) framework can be adapted as a decision-support tool for risk assessment and control of food-borne zoonoses in the human food value chain [73]. HACCP entails identifying hazards, critical limits, critical control points, and subsequent monitoring and mitigation. In the context of zoonosis, the application of HACCP as a decision-support tool should entail the following:

(1) identification of the dominant sources and entry points for zoonoses into the human food chain,
(2) identifying the people most at risk, including wildlife and trophy hunters, workers in the meat industry including abattoirs, wildlife and safari operators, people consuming wildlife and game meat and food products, and communities living in proximity with wildlife hosts,
(3) the setting of acceptable and achievable critical limits or thresholds for zoonotic pathogens at various steps in the human food chain in order to identify occurrence or transmission hotspots,
(4) identification of critical control points characterized by unacceptable or high risks exceeding set critical limits or thresholds,
(5) development of monitoring and evaluation systems, including key indicators of food-borne zoonoses, and
(6) development and application of a mitigation strategy targeting critical control points.

Although HACCP has a long history in the food industry, its application for assessing and mitigating human health risks associated with zoonoses is still limited. This is particularly true in the context of LICs. Thus, adapting and validating the HACCP framework could be an integral part of human risk assessment and mitigation in LICs. Such efforts should include capacity-building in HACCP in the food industries at high risk of food-borne zoonoses and should be coupled with surveillance systems based on both conventional and emerging monitoring tools (*Section 5.6*).

3.2. *Mitigating the human health risks*

3.2.1. *Learning from the COVID-19 pandemic*

The COVID-19 pandemic has given both low-income and developed countries a rare learning opportunity to manage future pandemics and other infectious diseases. The scale at which COVID-19 spread into a pandemic, resulting in millions of deaths, has demonstrated ill-preparedness for a global pandemic and the need to draw crucial lessons to improve response for future pandemics [74]. Due to increased international travel and trade, a highly globalized and connected world contributed to the rapid spread of SARS-CoV-2 [74]. This clearly shows that the failure of one country to manage future emergent diseases may lead to a pandemic. Moreover, the successful mitigation of pandemics can only be achieved with global efforts - failure of one region to put the transmission of the pathogen under control may lead to the re-emergence of its mutated versions in other areas. It is, thus, essential to strengthen preparedness, coordination, and collaboration at national, regional, and international scales.

A delay in detecting the first known cases of COVID-19 in China and other countries contributed to a late response leading to a rapid spread to other countries [75]; Khana et al., 2021). A report by The Independent Panel for Pandemic Preparedness and Response [76] also made a similar observation on COVID-19. Intuitively, this is because a delayed detection at the point of the first outbreak promotes further spread and subsequently delays the implementation of prevention and control measures. Other factors that led to the rapid spread of SARS-CoV-2, besides its biological features, include: (i) poor national and international early detection and alert systems, (ii) deficiency or absence of real-time data and science, and (iii) weak global coordination. Robust detection systems, which entail research and surveillance of new viral agents, increase the chances of early detection of contagious diseases by instituting preventive or containment measures. Countries that acted swiftly and relied on real-time data and science, such as massive testing along with contact tracing, quarantining, and public awareness, fared well in managing the spread of COVID-19 [77]. This demonstrates that early detection and alert systems and reliance on real-time data are crucial for managing future communicable diseases, such as zoonoses.

While most countries immediately employed public awareness campaigns to mitigate the spread of the COVID-19 pandemic, the contemporary globalization of information, primarily through social media, led to a rapid spread of misinformation and conspiracy theories [78–80]. Lack of transparency, a void of reliable information, and communication of conflicting advice result in public mistrust and can lead to the spread of misinformation and conspiracy theories and unwillingness to follow guidelines [81–84]. These can negate the benefits of awareness campaigns. Thus, well-coordinated early alert and public awareness systems, transparency, and building public confidence in institutions are essential measures to counter skepticism, conspiracy theories, and misinformation while ensuring effective management of future zoonotic outbreaks.

3.2.2. *Overcoming high uncertainty and weak evidence: precautionary principle*

While data and science are a crucial part of evidence-based health strategies, the novelty of emerging pathogens means there is uncertainty and limited evidence regarding their etiology and transmission mechanisms. In such a situation, the precautionary principle - a proactive approach to risk mitigation, can help mitigate public health risks. A precautionary principle is an epistemological approach for decision-makers to adopt precautionary actions when extensive scientific knowledge regarding an environmental or health hazard lacks or is weak and when the human health risks or consequences are high [85,86]. The precautionary principle is increasingly becoming imperative due to the realization that the human-animal-environment interface poses severe risks of novel zoonotic pathogens spreading uncontrollably - producing extreme consequences. The COVID-19 pandemic demonstrated the importance of taking precaution as a guiding principle when blanket travel bans and strict lockdowns were implemented when scientific evidence was still weak, diagnostic methods were unreliable, and all transmission routes remained uncertain [86]. For such an approach to be effective in the long-term, there is a need for global cooperation, transparency in sharing relevant information, and quick response in the primary outbreak region.

3.2.3. *One World, One Health (OWOH): from concept to practice*

There is increasing recognition and consensus on the inextricable commonality and interactions among humans, animals, plants, and their shared environment. In this context, optimal human health outcomes can only be achieved through a One World, One Health (OWOH) concept - a collaborative and transdisciplinary approach that recognizes this link [87,88]. It is an expansion of the one medicine concept which recognizes the resemblance in the paradigm of human and veterinary medicine [89].

While the OWOH concept is not new, its application is now imperative because global anthropogenic changes, driven by human population growth, urbanization, agriculture, and their effects on the ecosystems, have changed the way humans, animals, plants, and the environment interact. These interactions and other disruptions in environmental functions caused by deforestation and pollution can provide new opportunities for the emergence of new pathogens and their transmission between humans and animals. Previous and current health challenges, such as antibiotic resistance and outbreaks of new viral diseases such as avian influenzas (H5N1 and HIN1) or MERS-CoV, demonstrate the interdependence of the health of humans, animals, and ecosystems. This calls for advancing our knowledge on the consequences of human activities, lifestyles, and how we interact with ecosystems on disease dynamics to guide public policy [90].

An integrated approach to addressing health necessitates elaborate collaboration and communication systems at the national, regional, and international levels. At the national level, the key challenge in transforming the OWOH from concept to practice remains the ability to set collaborative systems among various institutions and stakeholders. This is because while the OWOH concept provides an integrative approach to health, there is a challenge that human and animal health professionals still operate under disciplinary silos [88]. Therefore, it is necessary to break interdisciplinary barriers by incorporating integrative thinking in educational curricula, veterinary practice, clinical practice, and other sectors [90].

The International Health Regulations (IHR) (2005) set strategies that countries must follow to operationalize the OWOH concept (IHR, 2005). These include training and fostering collaboration among institutions (e.g., health, veterinary, trade, travel), and strengthening national capacity in areas of disease surveillance and response systems. Integrating data among various disciplines is thus important [87]. Implementation of these systems is crucial to improve preparedness among LICs.

3.2.4. Raising public and stakeholder awareness on zoonoses

The prevention and management of zoonotic outbreaks entail the participation and cooperation of the public and all stakeholders involved in human health (e.g., medical doctors, epidemiologists, public health scientists), animal welfare (veterinarians and farm staff), environmental scientists (e.g., wildlife scientists, ecologists), law enforcement, food suppliers and pet owners. Systematic educational and awareness programs tailored for each stakeholder, including the public, are necessary to implement zoonotic disease prevention and surveillance programs successfully. Education and awareness are critical in ensuring the public and stakeholders exercise proactive measures such as hygiene and reducing risk factors for zoonoses.

Several diseases are transmitted from animal hosts to humans through animal-derived products (e.g., meat, milk, blood). Thus, awareness and regulatory interventions on food safety play a crucial role in managing zoonotic outbreaks [91]. The weakness of most awareness campaigns is that they are reactive because they are initiated after an outbreak. However, proactive, systematic awareness campaigns on zoonoses are crucial as a behavioral change and preventive measure. Therefore, similar to other human pandemics, such as HIV/AIDS and malaria, there is a need to raise awareness of zoonoses in LICs.

3.2.5. Establishing and strengthening surveillance systems for zoonoses

Establishing robust zoonoses surveillance systems is critical for early detection to timeously initiate alert systems and mitigation measures [92]. However, zoonoses surveillance programs in LICs are hampered by a critical shortage of resources, a lack of a surveillance framework, and weak institutional collaboration. The source-pathway-receptor-impact (SPReI) framework in surveillance is an effective tool for understanding zoonoses in livestock, wild animals, humans, and the environment (IHR, 2005). The SPReI framework considers current and potential pathogens sources, their potential transmission pathways, and what will be impacted (receptors). Surveillance systems provide early warning data required to activate response and mitigation measures.

LICs must assess their national resource requirements for zoonoses surveillance and response and draw action plans to meet minimum standard requirements. Improving surveillance systems for zoonoses requires investment in equipped diagnostic and research facilities, building skills, and capacity, and establishing a coordinated and collaborative data-sharing system among various stakeholders [87].

4. The bumpy road ahead: opportunities and challenges

4.1. Curbing poaching, illicit wildlife trade, and loss of biodiversity

Firstly, it should be noted that the supply related to poaching and illegal trafficking is driven by the demand for wild animals and their parts. Therefore, poaching is justified in economic terms [93,94]. A decrease in biodiversity caused by the loss of habitats (including deforestation for agriculture and built-up areas) and their modification and introduction of pollutants into the environment promote zoonotic pathogens' transmission to humans. All this contributes to the increased possibility of physical contact between humans and wild animals [95,96]. There are well-documented examples of the emergence of zoonoses (e.g., hantavirus pulmonary syndrome, influenza, Nipah virus encephalitis, rabies) among people living in disturbed (border) natural habitats, including in LICs, e.g., Bangladesh and Uganda (e.g., Refs. [97–100]. Therefore, it has been shown that the reduction of biodiversity directly impacts the transmission of pathogens to farm animals and humans.

Consequently, high biodiversity is a barrier to protecting against zoonoses from wild animals [24,226, 101]. Platto et al. [96] indicate that this principle is not universal, although there is a relationship between species composition and the number of pathogens. Thus, an increased number of pathogen hosts will lead to higher densities of the pathogen in the environment and, subsequently, a greater risk of contact and transmission to humans. Moreover, LICs (such as Myanmar) are affected by the most severe loss of biodiversity, related not only to land deprivation but also to poaching, smuggling of animal parts, and illegal wildlife trade [94]. Poaching and illegal trade are particular threats that can contribute to the emergence or re-emergence of zoonotic diseases [8]. These activities, particularly in an organized form, have become more common and profitable in recent years (e.g., [94,102,103]. It is also known that LICs and other countries, such as Dagestan (in the Caucasus) or distant parts of the Golden Triangle in Southeast Asia, are known for illegal arms and/or drug trafficking and are also places of poaching and trafficking of wild animals [48,104–106]. The indicated problems are increased by the ubiquitous corruption in these countries and governments behaving opportunistically toward this type of activity [94]. To a large extent, they highly prevent the appropriate management and reduction of epidemiological threats as well as criminal activities.

The COVID-19 pandemic will undoubtedly reduce the profits from tourism in LICs, which, despite legal protection, may cause a crisis in the security of various endangered animal species. The Independent's "Stop the Illegal Wildlife Trade" campaign to undertake international efforts to stop illegal wildlife trafficking and poaching is a positive effect of the COVID-19 pandemic. It also monitors the impact of introducing restrictions on the trade-in of wild animals. An important event in the nature conservation of the LICs is their willingness for voluntary participation. Recently, the president of Rwanda supported the appeal and officially joined the initiative [107]. Rwanda has taken another step towards nature conservation, showing how wildlife can be used for economic purposes where income in wildlife can be earned legally and safely, at the same time satisfying the local community's needs. Therefore, Rwanda has outlined the direction of changes for other LICs that seem most feasible regarding reducing poaching, illegal wildlife trafficking, and loss of biodiversity, thus protecting the population and environmental health.

4.2. Translating the 'One World, One Health' (OWOH) concept to practice: easier said than done?

The OWOH is based on the assumption that cross-sectoral integration of public health infrastructure, specialist skills, and science is necessary to improve the ability to predict disease risk and intervene effectively in the case of an outbreak [108]. Given that the innovative OWOH paradigm has been widely accepted, it would be expected that the assumptions resulting from this concept would be adopted. However, this is not so obvious as the slaughter of animals is still used to respond to the risk of zoonoses. Traditional methods of combating and reducing animal-borne infectious diseases include: (i) restricting the movement of humans and potentially infected animals; (ii) reducing the interaction between humans and potentially infected pets and wild animals; (iii) vaccination or treatment without any exclusion, and finally, and (iv) culling of animals that are infected or at risk [109]. It is, however, challenging for LICs to implement expensive strategies such as extensive vaccinations and treatment without external help, e.g., from international organizations. However, selected activities, such as education and management of farm hygiene (biological safety), may be introduced. Therefore, in the context of globalization and the emerging zoonoses, it is essential to create strategies that should include: (i) a permanent source of financing for the prevention and treatment of animals, including humans, and (ii) in the light of the OWOH paradigm, taking a lesson from some LICs to protect biodiversity and the natural environment, and (iii) sustainable management of environmental resources.

Although strict protection of human interests and benefits is essential both in the OWOH approach and in the traditional approach to public health, the former approach aims to achieve optimal health not only for humans but also for animals and their environment. All these aspects are closely related and cannot be considered separately or only in the pure context of human health [110–113]. Hence, the OWOH concept, which can potentially promote the interests of animals and the environment beyond humans, may promote mutual benefits, such as avoiding another pandemic. However, it seems challenging to be universally accepted. Meanwhile, current science in the name of OWOH focuses primarily on pathogen evolution and host-pathogen relations [114]. It should be emphasized that the OWOH approach requires not only an understanding of these aspects, but also an acknowledgment that infectious agents are crucial components of ecosystems. Moreover, exposure to pathogens cannot be eliminated, especially in LICs. Therefore, the focus should not be exclusively limited to methods of killing microorganisms [114,115]. Additional research and formal assessments showing the social, health, and economic benefits of the OWOH concept are needed to gain more comprehensive support from the community and stakeholders [116]. Above all, complex environmental interactions need to be studied, considering the relations among pathogens, their hosts, and ecosystems.

4.3. The dilemma of dealing with wildlife hosts of zoonoses: to cull or not to cull?

As already mentioned, the primary strategy used in LICs to control emerging disease incidents in animal populations is the slaughter or elimination of sick and potentially diseased animals [109]. The intention of such action is evident as it concerns individuals of a given host species population, thus preventing the pathogen from infecting individuals in other populations. Slaughter is widely considered the most efficient and cost-effective way to reduce or eliminate pathogen reservoirs' population, thereby reducing or even stopping the frequency of transmission of pathogens to new hosts [114]. However, Lederman [117] indicates that the evidence of effectiveness in combating the epidemiological threat and profitability of such action in the context of a comprehensive (including sustainable) solution to many epidemiological threats is inconclusive. Besides, experts and the public have concerns about the rationality, ethics, and necessity of slaughter concerning animal protection and welfare. Also, viral pathogens can potentially spread in populations and worldwide in a way that is ahead of current vaccine production technologies [118]. Therefore, alternative methods of combating the epidemiological threat and zoonoses' occurrence should be used [114].

Bearing in mind the ethical aspects of the application of slaughter in LICs, it should also be considered whether the economic benefits of such a solution to prevent the spread of pathogens are superior to the costs of the applied prevention, biosecurity, treatment, and, finally, preservation of biodiversity [113,114]. It is worth calculating and comparing the actual costs resulting from various methods of combating pathogens and dealing with epidemiological threats. It seems that in the long term, prevention (e.g., vaccination) instead of a final response to an epidemiological threat (i.e., slaughter) could protect economic interests and livelihoods, e.g., livestock owners [114]. Under certain circumstances, the killing of livestock is justified, for example; (i) when the implementation of vaccination and other mitigation or preventive measures discussed earlier is not possible due to lack of effective vaccination, and/or

(ii) the disease is already spreading in part of the population. The killing of infected livestock is also essential in cases where the risk of transmission could be promoted via the free movement of such livestock and their interactions with wildlife. This is particular the case in communal grazing areas and livestock-animal-human interfaces such as game parks in sub-Saharan Africa [119,221]. This, however, may entirely not apply to wild animals – as shown by Olival [120]; it would not only be ineffective in reducing the risk of zoonotic emergence, but may even increase it. This is due to human contact with killed animals, their tissues and blood during the controlled hunting. Bats are the primary reservoirs and carriers of more than 100 viral diseases, which, if transmitted to other species, can cause enormous economic losses in agriculture and human mortality [121,122]. Attempts to address this through culling have been unsuccessful. Decreases in bat population density do not impact virus prevalence, and the increased stress levels and higher birth rates in populations subjected to culling increase viral shedding [123]. In light of this, a substantial effort has been put into bat preservation as it is evident that attempts to control their population can have catastrophic consequences on the ecosystem and crop production [121,124,125]. Moreover, such action is controversial regarding ethics and the OWOH paradigm. Besides, it is not economically justified, i.e., plant cultivations may suffer significantly (pollination and dispersal of seeds or maintaining a stable population of insects by bats), and local trophic chains may be affected. Moreover, the results of such action are challenging to predict, while the risks appear to outweigh the benefits.

4.4. Decision-making scenarios under high risks and high uncertainty caused by weak evidence

The current approach to outbreak detection involves clinical diagnostics and epidemiological modeling of outbreaks in the population (Cooper et al., 2016). However, this approach presupposes at least a partially developed public health system capable of successfully reporting any infection. Thus, it is impossible to fully implement this approach in LICs [126]; Cooper et al., 2016). Thus, LICs have a limited ability to cope with an outbreak with these tools. Hence, the greatest hope for LICs could lie in the OWOH approach, namely programs focused on early detection and response to potentially zoonotic virus threats at their source before the pathogen transmission. One such program is the USAID Emerging Pandemic Threats Program (the PREDICT project), which focuses on biodiversity hotspots (including the LICs areas) (see [116].

As previously mentioned, the OWOH approach builds on existing opportunities but represents a new solution by linking disciplines and sectors to deliver more comprehensive health benefits. Thus, increasing coordination in various aspects can help promote science-based decisions and reduce human, animal, and environmental health mismanagement. Besides, it helps address the disease burden's external factors more effectively [127,128]. There are many documented examples of the OWOH approach's effectiveness in detecting zoonoses. For instance, observations of the high mortality rate among great apes is a phenomenon that was often detected before human Ebola virus outbreaks. Another example is the use of weather conditions to predict episodes of zoonoses (e.g., Rift Valley fever) or, above all, the activities and results of the PREDICT project in the Democratic Republic of Congo [44,116,129]. Such activities allow time to react (e.g., implementing preventive measures in the surrounding area) to potential outbreaks of zoonoses in humans. Therefore, integrated multi-sectoral activities, consisting primarily of prevention, should use individual OWOH assumptions to detect the outbreak of an epidemic in animals before it occurs in humans. Unfortunately, some sectors of the LICs economy that rely on the commercial use of wild animals (e.g., poaching) and the destruction of wildlife habitats will be key sectors, and, at the same time, complicated problems difficult to solve may arise due to strong sectoral interests. Political instability and limited compliance with the law that can be observed in the case of some LICs can hinder possible actions. Therefore, comprehensive scenarios for dealing with these problems are needed, which must be supported by high external financing. These problems reinforce the need to continuously strengthen the capacity, integration, and communication of sectors at multiple levels adapted to the local context of risk and stakeholders in order to deal with crises [116]. In the face of global economic losses and the world health crisis caused by the COVID-19 pandemic, other countries should promote efforts to prevent new outbreaks of zoonoses as soon as possible. Indeed, analysis from the World Bank shows that introducing worldwide investments of $ 3.4 billion annually in the form of improved veterinary and public health services could avoid ten times that spending on responses to zoonoses worldwide annually [116,127]. This is just one example that could serve as a way of dealing with zoonotic outbreaks in LICs. However, due to climate change and other factors shifting the geographic range of species and their pathogens, activities and global funding that translate into projects such as the PREDICT project would have to be prioritized.

4.5. The challenges associated with source tracking and apportionment of zoonoses

According to WHO [130], any living organism and its population can be a reservoir of pathogens. Particular pathogens may use a limited or more broad number of species as a host and may also be transmitted to the novel host species and undergo adaptation. Importantly, it might happen that the pathogen reservoirs may not reveal any disease symptoms as seen, for example, in fruit bats infected with coronaviruses [131]. Pathogens and their reservoir hosts may co-exist (with or adapted over many millions of years) in mutual, commensal or parasitic relationships. Due to genetic and physiological adaptations evolved over long-term virus-host relationships, there may be no pathological symptoms visible in a reservoir host upon infection, i.e., fever, cytokine storms, innate immune signals, and other hallmarks observed in incidental hosts. In addition, antibody production may still be induced in reservoir hosts, but not necessarily [121,132,133]. Many viruses, bacteria, and parasites are not biochemically adapted to compromise their hosts' health and survival, and long-term co-evolution tends to lead to lower pathogenicity [134]. Many examples reveal the ecological balance between the pathogen and the reservoir host. A great example is the pathogenic *Leptospira* that causes Leptospirosis - a devastating zoonotic disease affecting animals and people worldwide. For example, there is much evidence that culture-positive cattle were found seronegative by microscopic agglutination test. While in rats, gene expression of immune-related genes of *L. interrogans* challenged animals was similar to that of uninfected controls [133,135,136]. However, when a pathogen jumps the species barrier, it can become deadly for its new host, which lacks genetic adaptations present in the reservoir host [121].

The emergence of zoonotic disease in humans is a significant public health problem worldwide, magnified by increasing contact with wild and farmed animals, and pets (Halabowski and Rzymski, 2020). As estimated, over 70% of the novel human pathogens reported in the past few decades, disproportionately represented by viruses, have originated in animals [23,25,137,138]. Following zoonotic transmission, certain pathogens can evolve in human-only strains (e.g., HIV). In contrast, others may have limited abilities to spread from human to human, but can induce recurrent outbreaks (e.g., MERS-CoV-2, Nipah virus) [130]. This shows the incredible diversity of the problem of zoonotic diseases. For example, about 1400 species of human pathogens are known, significantly less than 1% of the planet's total number of microbial species [139]. However, it is virtually impossible to determine the origin of all human pathogens. Indeed, there are over 200 known zoonoses to date [130], many of which have resulted in high mortality among humans [8]. Despite numerous studies, it is challenging to determine which will contribute to an outbreak in humans. However, the risk factors and the human groups at the highest risk of contracting the novel zoonotic pathogen are wellestablished. These include, in particular, individuals, who come in contact with domestic, farm, or wild animals, especially where public health and farming methods are least developed and where sustainable agriculture is not applied [130]. Besides, the ongoing urbanization and increased consumption and demand for environmental resources further promote the destruction of natural habitats. Many of these factors affect LICs. While the rapid detection of outbreaks in humans in developing and developed countries with the methods used to date (e.g. [140], is satisfactory, LICs with poorly developed healthcare systems are responding too late, with adverse consequences for human health [66]. This complicates the rapid remedial action in the form of formulating mitigation and control measures and subsequently creates an equifinality problem where multiple sources of new and known pathogens may lead to the subsequent outbreaks of the same zoonoses. Hence, new tools are required to understand zoonotic agents' source, transfer, and fate in various reservoirs and hosts, including possible amplifications and mutations.

5. A look ahead: future perspectives and research directions

5.1. Environmental reservoirs and hosts of zoonoses

Climate change and the loss of biodiversity caused by human activities are some of the major drivers of infectious disease spillover from animal reservoirs into human and livestock populations [141,142]. Wild animals are hosts to many pathogens, which regularly cause outbreaks of novel diseases [143], but in recent years we have started to see outbreaks of new zoonotic pathogens more often [141,144]. This is especially evident in the LICs, which interfere with natural habitats causing wild animals to move closer to human dwellings or farm animal shelters.

Spillover of a pathogen into a new host population is a relatively rare event. The pathogen must pass several barriers to establish active infection and even more to cause an epidemic [143]. These include limited exposure to the new hosts, structural barriers, innate immune responses, and molecular barriers [143]. The probability of that happening can be minimized with appropriate policies implementing OWOH approaches [36,144,145]. There is a need for further research into potential host ecology, population biology, and behavioral ecology. With the further growth of agriculture in LICs, we need to pay special attention to the landscape ecology, agricultural sciences, animal epidemiology and infectious disease dynamics in LICs. Loss of habitat and biodiversity pushes humans and wild animals to live closer together, while climate change pushes wild animals to migrate and find other environmental niches, sometimes rapidly changing the dynamics and the balance of existing ecosystems and introducing new pathogens with the potential of causing outbreaks of new diseases [146]. It is essential to understand that these drivers will make fatal zoonotic spillover possible and requires establishing surveillance systems that can monitor possible zoonotic reservoirs and hosts (e.g., bats, birds, or rodents).

LICs host a wide range of animal diversity, including primates, ungulates, and avian species. Yet to date, the occurrence of zoonoses has only been investigated in a few animal species from a few selected LICs. Identifying the major animal taxa that might be the sources of pandemics can help in surveillance and quick interventions in disease outbreaks. Indeed, birds spread most zoonotic pathogens [147,148]. Avian species have large populations worldwide, both as wild birds and domesticated poultry. They gather in flocks and can migrate over long distances, giving them the potential to spread infectious diseases rapidly, such as avian influenza, with outbreaks observed across the globe every year [147,148]. Potential zoonotic reservoirs need to be closely monitored globally. Appropriate ways of approaching potential zoonotic disease sources should be discussed and observed by the authorities to avoid interferences that might disturb delicate balances in the environment, and in turnt drive pathogen spillover [123,144]. Further work is needed to identify the environmental reservoirs and hosts for zoonoses, including a wide range of bat, primate, and avian species in Africa. Such studies should also include the transmission mechanisms and routes, including the role of vectors.

Nevertheless, domesticated and wild animal interactions are only one way of new infectious disease emergences into the population [142]. Direct human contact with wild animals, wild animal products, or bushmeat allows susceptible humans to be exposed to various pathogens previously encountered only very rarely. Understanding the cultural importance of practices using animal products in many LICs is a neglected part of how infectious diseases can spread and cause outbreaks in these susceptible communities [144].

To date, antimicrobial resistance in zoonotic pathogens, including bacterial infections, has received limited research attention. This is because of the notion that such pathogens have limited exposure to anthropogenic antimicrobials and other co-selecting agents. Hence, there is a need to determine the nature and severity of antimicrobial resistance and their resistance genes in zoonotic pathogens in various environmental compartments.

The introduction of antibiotics in human and veterinary medicine is seen as one of the most significant human achievements, which helped prevent millions of deaths caused by infectious diseases and led to the modernization of food production in agriculture [149]. A global increase in food demand has led several countries to look for more efficient ways to produce animal products on a bigger scale [150]. However, not long after introducing antimicrobials in large-scale farming and animal production, a rise in antimicrobial resistance began to be observed [151]. This growing antimicrobial resistance is a trend observed now for several years [223], limiting the effective lifespan of known antimicrobial agents while new ones cannot be developed at a pace high enough to replace those in use [152]. Antimicrobial resistance is recognized as one of the significant public health concerns, and it is estimated that it will cause 10 million deaths by 2050 and trillions of dollars if new policies are not introduced or new ways to tackle the problem are not developed [153,154,233].

A summary report published by the European Food Safety Authority (EFSA) and European Centre for Disease Prevention and Control (ECDPC) in 2017 (EFSA/ECDPC, 2019) shows worrying trends that in some Europena Union (EU) member states led to the rise of antibiotic-resistant strains of bacteria that were previously easily treated with standard types of antimicrobial drugs such as fluoroquinolones. This trend was observed in cases of large-scale farming in the EU, but it is not limited to these countries and is observed globally in Asia, Africa, North and Latin Americas [155,156,224]. Developed countries manage to limit antimicrobial resistance by the implementation of national policies. The crucial steps that have helped limit antibiotic resistance in zoonotic pathogens in extensive farming were running awareness campaigns to cut down on antibiotic use and prescription and improving hygiene by providing access to clean water and sanitation (IACG, 2019; EFSA/ECDPC, 2019). Unfortunately, in cases of LICs, surveillance of antimicrobial-resistant pathogens is limited, if performed at all, due to low laboratory capacity and inadequate resources allocated for public health [157]. This is particularly worrisome if one considers the higher probability of infectious disease outbreaks in LICs due to limited access to clean water and sanitation [157]. However, these issues can be tackled with global cooperation, data sharing, and policy changes [153, 157].

Antimicrobials in mass food production are used as therapeutics or prophylactics to manage an existing outbreak of infectious diseases, prevent an outbreak of a disease, or promote animal growth (Aarestrup, 2015; [155]. While in cases of a lack of other treatments, the need to use antibiotics to manage an existing outbreak to prevent growing epidemics and loss of resources is indisputable, the other two cases have debatable benefits, and in fact, some studies show that regular use of antibiotics in livestock might not be profitable in the long run [149,158]. A combination of other countermeasures like increased bio-surveillance and the use of vaccines might provide similar benefits without the risk of further driving up antimicrobial resistance. The use of antimicrobials in agriculture should be closely controlled and cut in places where antibiotics are not used to fight existing diseases, together with restrictions on the routine implementation of antibiotics that are used as the last-line drugs in human and veterinary medicine.

Another approach that might limit the rise of zoonotic pathogens' antimicrobial resistance is increased global surveillance of the outbreaks of infections, the level of resistance presented by the pathogens, and the usage and consumption of antimicrobial agents. While some countries already closely monitor these factors, one must ensure such surveillance is implemented globally. Many LICs lack the resources and infrastructure to monitor zoonotic pathogens, and data in these regions is greatly lacking [157]. Such 'blank spots' in existing data might prevent implementing appropriate steps to stop antimicrobial-resistant pathogens from spreading into regions that had not experienced such problems before. There is a need for global cooperation and data sharing between pharmaceutical companies that monitor bacterial susceptibility globally, private laboratories which can provide testing infrastructure not limited by the LICs government funding, and academia which has access to high-quality data regarding zoonotic pathogens and antimicrobial resistance [157].

Most of all, the prescription of antibiotics in large-scale farming and healthcare should be informed by diagnostics, with decisions being made based on test results rather than the usage of several compounds or broad-spectrum compounds without identifying the underlying cause of the disease. Additional resources should be put into developing rapid tests, which will help limit the unnecessary use of antibiotics in livestock to fight existing outbreaks of diseases. Finally, vaccines and non-antimicrobial therapeutics need to be promoted, and research into them should be encouraged. Vaccines prevent infections, and their broader use could limit the usage of antimicrobial compounds in livestock.

5.2. Source tracking and apportionment of zoonoses

Identifying reservoirs and hosts of zoonotic diseases in wild animals is challenging, even more so in LICs, which do not have well-developed surveillance or the backing of well-equipped diagnostic and research facilities [26,144]. Many countries with limited resources typically fight outbreaks of infectious diseases only when the threat is already present in the population. Not performing active observations of the possible sources of zoonoses lead to delays in source identification, often making it impossible or extremely challenging to identify further mitigation measures. The approach of dealing only with the emerging outbreak and not putting preventative measures in place first might seem attractive from the poorer countries' perspective, where the emergence of an epidemic is challenging to predict at any given time, and funds are limited [95]. However, this is also counterproductive and costs more compared to a more proactive rather than reactive approach and running active surveillance, which can prevent the human and economic losses caused by an uncontrolled infectious disease epidemic [159]. Targeting global surveillance at epidemic hotspots might be another way of tackling that problem [26].

Finding a host or reservoir becomes more challenging with time and might prove to become impossible in some cases if the search is not started soon enough. This was observed in the case of Ebola outbreaks in Africa [160] and recently in the case of the SARS-CoV-2 pandemic [161–163]. Identifying reservoir species is significant in fast-developing LICs that suffer from outbreaks caused by the same pathogens, such as paramyxoviruses in Asia.

The development of fast, cheap, and reliable methods of sequencing genomes and publicly available global databases of pathogen genome sequences and data gives hope to LICs and infectious disease hotspots with no established networks of diagnostic facilities [164,165]. Early detection and identification of emerging pathogens might help stop the spread of infection and prevent a potential epidemic from unraveling [26,166,167].

Zoonoses in the wildlife-human interface can be conceptualized as a network entailing complex behavior, including interactions and exchanges among the various components and even the emergence of novel variants via mutations. This complexity makes source tracking and apportionment difficult. However, tracing the origins of zoonoses is critical in developing risk assessment and mitigation measures. Hence, the development, validation, and application of tools for source tracking and apportionment, including those based on emerging tools (e.g., genomics and network analysis), require further attention (*Section 5.6*).

5.3. Behaviour and fate of zoonoses in the environment-wildlife-human continuum

A comprehensive understanding of the behavior and fate of zoonoses in the environmental-wildlife-human interface is still lacking. This includes: (i) the environmental occurrence, dissemination, and fate outside the host, (ii) the mutation and amplification in intermediate and human hosts, and (iii) factors controlling transmission, the duration of latent periods, and the onset of pathogenicity.

Zoonotic spillover can happen in one of the three ways: (i) introduction of the new pathogen into the susceptible host population, (ii) the pathogen gaining a new trait that allows it to infect a broader range of hosts, or (iii) the introduction of the pathogen into a new environment [12,168]. These three ways display different dynamics and might need to be dealt with differently. For example, an abundance of the reservoir host might cause the pathogen to start looking for a new host. Understanding the zoonotic spillover's trigger is crucial in epidemic control and future prevention [12].

In many LICs, epidemics occur regularly, and cyclical pattern in disease outbreaks can be observed over the years. Pathogens that co-evolve with their reservoir hosts can be subjected to their host's behavior and be more prone to cause an outbreak at certain times of the year [169]. A few recent studies show that animal reservoirs of zoonoses, such as African bats show distinct migratory, reproductive, and coronavirus shedding cycles (Plowright, 2015; [170]. Such behavior could provide cues for the mitigation of zoonoses. However, further work is required to validate the consistency of such cycles and the link with outbreaks of zoonoses. Real-world data, theoretical models, and approaches are needed to better understand zoonotic pathogens' cycles and triggers that might cause an outbreak [229].

An epidemic is an interaction between a pathogen and a host population. This virus spillover happens through intrusion into a reservoir species' ecological niche or infectious agent exposure from a reservoir host or the environment [143,171]. Zoonotic pathogens sometimes do not jump directly from their reservoir host to the new host but might also have an intermediate host in which they can circulate for a long time with no visible symptoms. Circulation in intermediate hosts can make pathogens better adapted to infect a human population [12].

Spillover events may be dead-end infections where the pathogen cannot spread efficiently or at all from the new host, but they can also lead to epidemics or pandemics [121]. The development of platform technologies for vaccines and new drugs, which can be quickly adjusted for an emerging pathogen, is crucial in tackling a quickly spreading outbreak of a new disease. For example, experience gained in fighting these diseases had helped in the rapid implementation of such platforms in developing the COVID-19 vaccine [172]. However, sometimes the development and rapid implementation can prove to be problematic - as has been seen with Ebola virus (EBOV), Hendra virus (HeV) and Nipah virus (NiV) outbreaks [173–177]. We also need a range of broad-spectrum new therapeutics which can be used in such an emergency. Research on new therapeutics and novel vaccine platforms should be a priority, together with allocating global funding schemes to deploy these and make them available in the LICs.

Pathogens also evolve at different rates, and in the case of viruses, they cannot evolve without the cells of their host. There is a high proportion of RNA viruses among zoonotic pathogens, e.g., coronaviruses, influenza viruses. These viruses have a fast mutation rate, with several of them (excluding coronaviruses) lacking proofreading mechanisms to correct mistakes during replication. That might make them more prone to host jumps with the genomic changes helping them to widen host and tissue tropism with time. But these mechanisms are not the only ones that can drive species jumps, and other factors are still poorly understood [143]. Mathematical modelling of the infectious disease's mutation rate and spillover risks can also help in epidemic prediction [178]. Mathematical models are relatively cheap and a fast way to learn about the evolution of zoonotic pathogens and potential pandemic progress. They can be one of the main components of epidemic control [178], and the collaboration between ecologists and public health scientists might help make them more accurate. Observations of the dynamics of a pathogen in the reservoir or intermediate host can help predict human infection risk and act as an early warning system reducing the risk of an outbreak and the number of fatalities and economic losses.

After introduction into a population, zoonoses can become endemic and established in the new host without subsequent reservoir host-to-human transmission if the pathogen transmits efficiently and efforts to contain it fail (e.g., HIV). Other zoonotic diseases cause local outbreaks regularly in certain regions but do not establish a constant presence in the new host population. This can be caused by control efforts or a low transmission ability in its new host. In such cases, novel outbreaks emerge when the pathogen has a chance to jump from its reservoir species into the human population (e.g., Nipah virus, Ebola virus). These sporadic outbreaks can be driven by host behavior, climate, or ecology (e.g., hantavirus).

The significant factor in spreading zoonoses is the increase in travel and trade at national, regional, and international levels. With more than 1.5 billion international travelers, infectious diseases can spread easily and widely in many geographical areas. The size of the COVID-19 pandemic was directly linked to international travel and could have been contained if more strict restrictions had been put into place by many of the most strongly hit countries [179]. The presence of known zoonotic diseases and the risk of the emergence of new zoonotic diseases in LICs that do not have proper diagnostic or reporting tools should be considered with the utmost caution, especially when considering the growing tourism and trade sectors in these places.

The food-borne zoonoses in livestock must also be taken into consideration. Many pathogens are endemic to cattle and other farm animals (e.g., bovine tuberculosis) and can easily spread in their population if there are no disease-control methods in place, which inherently will lead to subsequent outbreaks of the disease in humans who are involved in animal handling, food production, trade, or indeed the consumers of such products. Weak veterinary infrastructure might lead to regular outbreaks of such diseases, and some farming practices (e.g., mixing of species, feeding) can even further drive the outbreak's risk. The ways the animals are slaughtered and the methods by which animal products are handled and transported must be tightly controlled to avoid the spread of bacterial, viral, and parasitic pathogens. The spreading of such diseases can burden the healthcare of the LICs, e.g., the pig tapeworm causing cysticercosis, which affects millions of people every year [180].

The various aspects pertaining to host receptor-pathogen interactions driving the outbreaks and transmission of zoonoses are still poorly understood. Host receptor-pathogen interactions are critical in the transmission and pathogenicity of zoonotic pathogens. However, understanding the role of such host receptors in the transmission of zoonoses among intermediate and human hosts warrants further investigation.

One major change that drove the H5N1 avian influenza to infect mammalian hosts and started an epidemic was a change in receptor affinity [181,182]. With pathogens that can change tropism relatively quickly, e.g., coronaviruses [183], the host range can at least partially be predicted with the receptor specificity [184]. With further research concentrating on virus-receptor interactions and types of receptors bound by pathogens, we might be better able to understand further mechanisms relating to how spillovers happen and predict possible sources and hotspots for pathogens with pandemic potential. More work on animal models can help establish target pathogens that can infect humans or jump between hosts.

While highly specific virus receptor tropism is a barrier to infecting new hosts, we also need to learn about other intracellular barriers and host resistance factors to prevent an active infection. The differences in immune cells and receptors that can block infection at an early stage should be of particular interest [182], which might help answer some questions about infectious disease dynamics in the natural environment [26,182,185]. However, more analysis exists on host resistance factors against the bacterial than viral factors [186]. Thus, current experience with fast regular pandemic viruses shows that more work needs to be put into place to achieve a similar level of understanding in the case of other pathogens.

5.4. Development and validation of predictive tools for zoonoses

5.4.1. The case of shell disorder analysis

In a series of recent papers, Goh et al. [187]; b) pioneered the application of shell disorder analysis using machine learning and genomics. They applied shell disorder analysis to predict various zoonotic viruses' persistence, transmission mode, and virulence, including the Zika virus, Nipah, and SARS-CoV-2. The early findings of Goh et al. [187]; b)'s work based on the various zoonotic viruses provide essential insights on viral zoonoses summarized as follows: (i) high outer shell disorder of viruses as measured by a high protein intrinsic disorder (PID) is indicative of prolonged environmental persistence outside the human body, while the opposite is true for low PID, (ii) high, moderate and low PID values point to possible transmission via fecal-oral, a combination of fecal-oral and respiratory, and respiratory routes, respectively. Moreover, shell order or PID was also related to virulence. In this regard, shell disorder analysis constitutes a potential predictive tool for understanding zoonoses and developing mitigation measures. However, as highlighted earlier reviews focusing on SARS-CoV-2 in LICs, the predictive capacity of shell disorder analysis as a decision-support tool requires further development and validation using field data [70,71].

5.4.2. Understanding and predicting the cycles and triggers of zoonoses

An understanding of the ecological behaviour and cycles of the hosts could provide some cues for the mitigation of zoonoses. A few recent studies show that animal reservoirs of zoonoses such as African bats show distinct migratory, reproductive and coronavirus shedding cycles [170,188,189]. However, further work is required to understand and validate the following: (i) the consistency of such cycles in various host species, including intermediate ones, (ii) the link between the cycles and onset of outbreaks of various zoonoses, and (iii) the key environmental and anthropogenic triggers of zoonotic outbreaks.

5.5. Field validation and application of the risk assessment and mitigation framework

In the present paper, a comprehensive framework was presented entailing the following: (i) an understanding of the risk factors, behaviors, and drivers, (ii) risk assessment based on QMRA and HACCP, and (iii) a mitigation strategy based on a suite of measures, including, among others, the OWOH concept, precautionary principle, and lessons learnt from COVID-19 pandemic. Given the inherent differences among LICs, the testing and application of the framework need to account for such differences on a case-by-case basis. In this regard, specific framework components may need to be emphasized in some regions relative to others. However, to this point, the proposed framework remains a concept that is yet to be field-tested and validated. Therefore, further development, validation, and subsequent pilot testing and application of the framework in LICs are required to generate supporting empirical evidence. Such evidence is critical to the subsequent promotion, adoption, and scale-up of the framework in the fight against future outbreaks of zoonotic infections in LICs.

5.6. Unraveling the complexity of zoonoses: emerging tools to the rescue

Recent years have witnessed the development of various novel tools, including those based on genomics, game theory, big data analytics, and GIS and remote sensing. Yet their application in understanding zoonoses is vastly underutilized. These emerging tools highlight the need for experts in these disciplines to participate in collaborative research to better understand and mitigate zoonotic diseases. Here, an overview of the potential applications of these tools in research on zoonoses is presented.

5.6.1. Genomics as an indispensable tool for sero-surveillance of zoonoses

Genomic tools can be applied to better understand zoonoses' origins and circulation in various compartments, including intermediate and human hosts. They can also be used to elucidate the link to viral zoonoses across multiple host species and humans in different geographical regions. Moreover, genomics can be used as an indispensable tool for the sero-surveillance of zoonoses.

However, the lack of analytical equipment, and qualified and experienced technical and research expertise in genomics could constrain its application in LICs. Proposals to overcome this limitation are discussed under funding models.

5.6.2. Game theory as a decision-support tool to understand and combat the complexity of zoonoses

Game theory, a tool initially developed for decision-and-policy-making in economics, has potential application in understanding zoonoses. In simple terms, game theory conceptualizes and analyzes rational strategies to address competing demands or situations, where the outcome arising from an agent/participant's decision or choice of action is contingent or dependent on the decisions or choices of action of the other agents or participants [190,191]. In other words, in game theory, one player/agent's payoff critically depends on the strategy implemented by the other player/agent(s). In principle, game theory entails the following: (i) agents/players (e.g., people, institutions, countries) and their identities, (ii) agent/players' preferences, (iii) strategies or a complete plan of action available to the agents/players, and (iv) how the strategies influence the ultimate outcome [191]. A number of studies applied game theory to investigate various aspects of pandemics, including, among others: (i) human behavior, public health, and socio-economic outcomes [192], (ii) management of logistics and supply chains, including stocks [193], (iii) vaccination strategies [231], and (iv) use of incentives to promote cooperation or collaboration [194]; Yong et al., 2021).

One study used game theory to investigate the role of vaccination and depopulation in managing livestock diseases and zoonoses in small-scale farms [195]. Game theory has also been used to understand the effects of vaccination and integrated control methods on monkeypox, a zoonotic disease [196]. These limited studies point to the potential opportunity game theory offers as a research and management tool. Thus, scope exists for further research to apply game theory to understand the impacts of the following on the occurrence, spread, and control of zoonoses: (i) human behavior or institutional decision-making such as the choice of risk mitigation strategies, (ii) competing interests among individuals and/or institutions, (iii) collaboration and joint decision-making, (iv) use of penalties, incentives and disincentives, and (v) allocation and deployment of scarce resources such as vaccines. This calls for further research to develop and validate the tools based on game theory.

5.6.3. Revealing salient trends, patterns, and relationships in zoonoses through big data analytics

Big data refers to massive data sets with large, varied, and complex structures, which make it difficult to store, retrieve, analyze and visualize for further processing and results, including decision- and policy-making [197]. Thus, the various forms of data on the nature, occurrence of outbreaks, distribution, impacts, and control methods collected at different spatial and temporal scales (district, national, regional, global) for different zoonotic diseases may be regarded as big data. For example, research documenting zoonoses' nature, occurrence, transmission, and behavior in various compartments occurs in various disparate scientific papers, grey literature, institutional inventories, and databases focusing on specific zoonoses may be classified as big data. Thus, the integration of information from such disparate sources is often problematic. This is particularly so considering the complex nature of zoonoses, including pathogen-receptor-host interactions and the transmission dynamics in the environment-wildlife-human interface. In this regard, the determination of salient spatial and temporal trends, patterns, and relationships in such data using conventional analytical, and statistical tools is a daunting task.

Big data analytics refers to the process or techniques of researching or analysing massive amounts of data to reveal hidden spatial and temporal patterns, trends, and relationships [197]. A suite of big data analytical tools, including network analysis, artificial neural networks, and machine learning or artificial intelligence, provide ideal archiving, analysis, and visualization of large datasets from complex systems. To date, big data and big analytics have attracted attention in a few exploratory studies investigating the following potential applications: (i) enhancing the effectiveness of the OWOH approach for controlling zoonoses [198], and (ii) developing and strengthening evidence-based precision public health response [199]. A few scoping reviews also exist on using big data in zoonoses [200–202]. However, besides these exploratory studies and scoping reviews, literature on big data approaches in understanding the occurrence, spread, and control of zoonotic diseases remains limited.

5.6.4. Tracking zoonoses at the human-wildlife-livestock interface using GIS and remote sensing

The movement of humans, wildlife, and livestock at the interface among three contributes to zoonoses' spillover. Recent advances in geographical information systems (GIS) and remote sensing (RS) technology, including global positioning systems (GPS) present opportunities for real-time spatio-temporal tracking of human, wildlife and livestock movements. GIS/RS tools are ideal for monitoring human, wildlife, and livestock movements at potential zoonoses hotspots such as areas close to national parks or game reserves and even for curbing illicit extraction and trade in wildlife and wildlife products, including poaching. For example, GPS tagging of wildlife and livestock, and subsequent analysis of the data may provide information on the spatial and temporal dynamics of zoonoses in the human-wildlife-livestock interfaces such as areas close to game parks. However, few applications of such technology have been reported in LICs. One exception is a study conducted at the human-wildlife-livestock interface in Gonarezhou *Trans*-frontier National Part in Zimbabwe, where GPS-based GIS/RS has been used to understand wildlife and livestock movement and potential transmission of zoonoses through shared water points [203].

The use of remote sensing has also been aptly demonstrated in south-east Asia in the case of the London School of Hygiene and Tropical Medicine (LSHTM)'s Monkebar Project, focusing on *Plasmodium knowelsi*, a zoonotic malaria parasite [204,205]. The Monkeybar project used remote sensing to understand the spatial occurrence of *P. knowelsi* and its association with environmental factors. In this regard, remote sensing-based data could relate landscape factors to spatial patterns of *P. knowlesi* infections in Sabah, Malaysia [205]. In the same study, the results suggested that land use changes such as deforestation and their corresponding environmental changes were key drivers of the transmission of *P. knowlesi*. Still, in Malaysia, GPS devices were used to map patterns of human movement, land use, and their role in human exposure to zoonotic malaria [206,207]. The results showed higher mosquito biting rates in forests, and that intensified human interactions with pathogens and insect vectors through human movement and space use around habitat edges were essential control factors in human exposure to *P. knowlesi*. These limited studies suggest that scope exists to harness such tools better to understand the environmental and anthropogenic drivers of zoonotic diseases. However, the scientific evidence base using remote sensing and GIS to understand zoonoses is still limited.

Other remote sensing technologies for tracking human, wildlife, and livestock movement in zoonoses hotspots include the following: (i) unmanned air-vehicle systems or drones equipped with appropriate sensors or cameras, and (ii) laser-based camera traps. To date, laser-based camera traps equipped with appropriate sensors and software have been successfully used in wildlife ecology to estimate biometric parameters (e.g., body dimensions) of wild animals, including primates (e.g., monkeys), leopards, and small amphibians (e.g., lizards) [208–210]. GIS/RS-based data on wildlife and livestock movement can also be used to identify and prioritize animal species to focus on during preliminary sampling and surveillance for zoonoses and the design of field experiments. Thus, the application of these RS technologies and subsequent GIS analysis constitutes a new research frontier in the study of zoonoses in LICs.

5.7. Beyond knowledge gaps: a handful of research funding models

The lack of resources as a constraint to research in human health and other fields in LICs is well-recognized. However, in the case of Africa, the constraints to research extend beyond funding, to include generally weak research systems caused by human factors (e.g., perceptions), lack of expertise, weak education system, and poor working conditions. A detailed discussion of these factors is presented in the previous review [66]. Here, three pathways are proposed for mobilizing resources to support research on zoonoses: (i) establishment and strengthening global collaboration, (ii) global fund targeting zoonoses in LICs, and (iii) mobilizing local funding resources through financial instruments.

5.7.1. Establishment and strengthening of global collaboration

Strong collaboration between LICs and international agencies (e.g., WHO, FAO, UNEP) and global partners in developing countries to develop and conduct joint research is needed. In such collaborations, international agencies and developing countries could provide the following: (i) critical expertise currently lacking in LICs, (ii) support capacity-building in various aspects of zoonoses at various levels, including analytical laboratories, technicians, researchers, and decision-and policy-makers, (iii) mobilizing of research funding, and (iv) development of regulatory and policy frameworks, including the development of surveillance systems for zoonoses. In return, LICs could provide the following: (i) local technical staff and researchers with a comprehensive understanding of the local biophysical and economic settings in LICs, (ii) co-funding of research projects to enable joint-ownership of the research process and outputs, and (iii) political will to implement research recommendations, appropriate regulations and policies, and sound governance systems, including a commitment to curb corruption. Moreover, LICs provide ideal sites to investigate various aspects of zoonoses, given the high-risk factors, and close and frequent human-wildlife interactions. However, targeting LICs as pilot research sites for specific thematic topics on public health could be met with suspicion and resistance, including fears that such research seeks to use people in LICs for testing of new pharmaceuticals (e.g., vaccines). Mechanisms to overcome these concerns and ensure transparency are discussed in an earlier paper [70,71]. In summary, this includes strong collaboration with local governments and researchers at all levels of the research process, from conceptualization to sharing of outputs, including intellectual property rights arising from such research.

5.7.2. A call for a global fund targeting zoonoses in LICs

A global fund targeting LICs needs to be established to strengthen the fight against zoonoses. Global funds targeting LICs are not a new concept, and have been used to fight against HIV-AIDS and tuberculosis in regions such as sub-Saharan Africa (https://www.theglobalfund.org/en/; [211,212,232]. Such global funds are used to support research, surveillance, and mitigation measures in LICs [211,212, White et al., 2022]. Zoonoses are a global human health problem extending beyond their region of origin, while their impacts on society, as evidenced by the COVID-19 pandemic, are more far-reaching than initially perceived. Hence, a strong motivation exists for the global community to fund and support a global fund targeting LICs as part of the worldwide fight against zoonoses [213]; e.g., PREDICT, https://p2.predict.global/). Global agencies such as FAO, WHO, and UNEP could provide leadership and a facilitatory role in establishing such a global fund. Initially, such an international fund may focus on a few developing regions or LICs to draw lessons for a broader application in other LICs. This funding model should be directly linked to co-funding mechanisms supported by local resources such as levies to ensure sustainability and co-ownership.

5.7.3. Mobilizing local funding resources through financial instruments

Local funding support for research in LICs is often low due to low levels of economic development, especially in Africa [70,71]; 2022, [66]. The low research funding and productivity in low-income countries, especially in Africa, are discussed in detail in earlier papers [70,71], [66]. However, innovative funding mechanisms based on financial instruments such as taxes and levies could be vital in mobilizing local financial resources. An African example of this is the widely acclaimed HIV/AIDS levy that successfully mobilizes local resources to fight HIV/AIDS in Zimbabwe [214–216]. The AIDS levy is a compulsory income tax directly deducted from every employee in the public and private sectors. The levy has been used to support the procurement of HIV-AIDS drugs and offer free treatment to HIV-AIDS patients [214]. Thus, a similar levy targeting zoonoses can be modeled in a similar framework and introduced to support research and mitigation of zoonoses. Similar industry-specific levies may also be applied to the livestock value-chain and wildlife tourism industries. Although the individual amounts collected from such levies are often too limited to maintain the competitiveness of local livestock and tourism industries, the cumulative aggregate could be quite considerable. Thus, it can sustain local research in the long term without external funding. However, given the high levels of corruption in most LICs, there is a need to strengthen the governance systems of such funds to ensure transparency and avoid abuse of such funds. To date, this funding model has been limited to HIV-AIDS in just one country (Zimbabwe) [214], but its validity and applicability in other LICs remain unknown. Hence, further work, including pilot testing of this funding model in a few countries, is required before large-scale adoption and scaling up to other LICs.

6. Conclusions and outlook

Low-income countries constitute a potential hotspot for future outbreaks of global zoonotic infections due to close and frequent human-wildlife interactions driven by land-use changes and increasing human population and the corresponding increase in food demand. The recurrent outbreaks of viral zoonoses in LICs and the recent COVID-19 pandemic highlight the vulnerabilities of humans to (re)-emerging infectious zoonoses. In the present paper, we propose that public and research attention should focus on understanding the risk drivers, risk assessment, and mitigating future outbreaks of zoonoses in hotspots in LICs, rather than reacting to outbreaks when they occur. The nature, history, and the risk factors, drivers, and challenges associated with zoonoses were presented. Specifically, evidence shows that LICs have a long account of outbreaks of various zoonotic infections, including Nipah, Zika, Ebola, West Nile virus, avian flu, and coronaviruses (SARS, MERS), among others. These outbreaks are driven by several risks factors, including: (i) close and significant human-wildlife interactions, (ii) poor governance and regulatory systems promoting corruption, poaching, and illicit trade in wildlife and wildlife products, (iii) lack of surveillance systems for zoonoses, and (iv) lack of public and stakeholder awareness. The source-pathway-receptor-impact continuum was used to understand human exposure and health risks better. The Quantitative Microbial Risk Assessment (QMRA) and Hazard Analysis of Critical Control Points (HACCP) were discussed as risk assessment tools. However, their application is still limited and constrained by the lack of data. A mitigation framework was presented integrating the following components: (i) lessons learned from the ongoing COVID-19 pandemic, (ii) precautionary principle, (iii) raising public and stakeholder awareness on zoonoses, and (iv) the OWOH concept. Several decision-making scenarios and their merits and limitations were discussed. These decision-making scenarios accounted for the putatively high human health risks of viral zoonoses and the high uncertainty in current evidence caused by weak evidence base on zoonoses' various aspects.

Future perspectives were discussed, addressing the following: (i) curbing poaching and illicit wildlife trade, (ii) translating the notion of OWOH from concept to practice, (iii) the dilemma of dealing with wildlife hosts of zoonoses, including the morality and ethics of culling versus non-culling, and (iv) the challenges of source tracking and apportionment of zoonoses, including the equifinality problem. Finally, the following future research directions on zoonoses were highlighted: (i) the occurrence and behavior of antimicrobial resistance, (ii) environmental reservoirs and hosts, (iii) source tracking and apportionment, and (iv) host-receptor-pathogen interactions, including the behavior and fate and potential amplification and mutations. Research funding models and the application of novel tools such as game theory, genomics, shell disorder analysis, GIS/remote sensing techniques, and advanced analytical tools such as big data analytics were discussed. Overall, the present paper outlines a framework for a better understanding of the critical risk factors and drivers of zoonoses and risk assessment and mitigation. Hence, further work is needed to pilot test, validate and refine the proposed framework in LICs, which are potential zoonoses hotspots. Such further research will generate local and generic lessons on assessing and mitigating zoonoses in low-income settings. Given that the outbreaks of infectious zoonotic diseases are a global human health risk that transcends national and continental boundaries, the international research community and funders should prioritize research on zoonoses. The framework outlined in the present paper should form the basis of such global north-south collaborative research.

CRediT author statement

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Data availability

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References

[1] Who, Pneumonia of Unknown Cause – China, WHO, 2020. https://www.who.int/csr/don/05-january-2020-pneumonia-of-unkown-cause-china/en/.
[2] S. Alkire, U. Kanagaratnam, N. Suppa, The Global Multidimensional Poverty Index (MPI): 2018 Revision, vol. 46, OPHI MPI methodological notes, 2018.
[3] S. Alkire, U. Kanagaratnam, N. Suppa, The Global Multidimensional Poverty Index (MPI) 2021, 2021.
[4] A. Allee, L.R. Lynd, V. Vaze, Cross-national analysis of food security drivers: comparing results based on the food insecurity experience scale and global food security index, Food Secur. 13 (5) (2021) 1245–1261.
[5] The World Bank, The Worldwide Global Governance Indicator, Available at:, 2022. Accessed: 26 September 2022, http://info.worldbank.org/governance/wgi/#home.
[6] I. Bassier, I. Woolard, Exclusive growth? Rapidly increasing top incomes amid low national growth in South Africa, S. Afr. J. Econ. 89 (2) (2021) 246–273.
[7] E. Barclay, Predicting the next pandemic, Lancet 372 (9643) (2008) 1025–1026.
[8] D. Halabowski, P. Rzymski, Taking a lesson from the COVID-19 pandemic: preventing the future outbreaks of viral zoonoses through a multi-faceted approach, Sci. Total Environ. 757 (2021), 143723, https://doi.org/10.1016/j.scitotenv.2020.143723.
[9] P. Rzymski, M. Kulus, M. Jankowski, C. Dompe, R. Bryl, J.N. Petitte, B. Kempisty, P. Mozdziak, COVID-19 pandemic is a call to search for alternative protein sources as food and feed: a review of possibilities, Nutrients 13 (2021) 150.
[10] M.E.J. Woolhouse, S. Gowtage-Sequeria, Host range and emerging and reemerging pathogens, Emerg. Infect. Dis. 11 (2005) 1842–1847.
[11] Z. Hubalek, Emerging human infectious diseases: anthroponoses, zoonoses, and sapronoses, Emerg. Infect. Dis. 9 (2003) 403–404.
[12] W. Karesh, A. Dobson, J.O. Lloyd-Smith, J. Lubroth, M.A. Dixon, M. Bennett, S. Aldrich, T. Harrington, P. Formenty, E.H. Loh, C.C. Machalaba, M.J. Thomas, D. L. Heymann, Ecology of zoonoses: natural and unnatural histories, Lancet 380 (2012) 1936–1945.
[13] M.E.J. Woolhouse, D.T. Haydon, R. Antia, Emerging pathogens: the epidemiology and evolution of species jumps, TREE 20 (2005) 238–244.
[14] L. Cristou, The global burden of bacterial and viral zoonotic infections, Clin. Microbiol. Infect. 17 (2011) 326–330.
[15] J.L.N. Wood, M. Leach, L. Waldman, H. MacGregor, A.R. Fooks, K.E. Jones, O. Restif, D. Dechmann, D.T.S. Hayman, K.S. Baker, A.J. Peel, A.O. Kamins, J. Fahr, Y. Ntiamoa-Baidu, R. Suu-Ire, R.F. Breiman, J.H. Epstein, H.E. Field, A.A. Cunningham, A framework for the study of zoonotic disease emergence and its drivers: spillover of bat pathogens as a case study, Phil. Trans. Roy. Soc. Lond. B 367 (2012) 2881–2892.
[16] T. Kooriyama, M. Okamoto, T. Yoshida, T. Nishida, T. Tsubota, A. Saito, M. Tomonaga, T. Matsuzawa, H. Akari, H. Nishimura, T. Miyabe-Nishiwaki, Epidemiological study of zoonoses derived from humans in captive chimpanzees, Primates 54 (2013) 89–98.
[17] S. Salyer, T.R. Gillespie, I.B. Rwego, C.A. Chapman, T.L. Goldberg, Epidemiology and molecular relationships of Cryptosporidium spp. in people, primates, and livestock from Western Uganda, PLoS Neglected Trop. Dis. 6 (2012), e1597.
[18] J. Wallis, D.R. Lee, Primate conservation: the prevention of disease transmission, Int. J. Primatol. 20 (1999) 803–826.
[19] S.J. Cutler, A.R. Fooks, W.H. van der Poel, Public health threat of new, reemerging, and neglected zoonoses in the industrialized world, Emerg. Infect. Dis. 16 (2010) 1–7.
[20] A.R.C. Thompson, Parasite zoonoses and wildlife: one health, spillover and human activity, Int. J. Parasitol. 43 (2013) 1079–1088.
[21] A. Wartecki, P. Rzymski, On the coronaviruses and their associations with the aquatic environment and wastewater, Water 12 (2020) 1598, https://doi.org/10.3390/w12061598.
[22] D.M. Hawley, K.V. Dhondt, A.P. Dobson, J.L. Grodio, W.M. Hochachka, D.H. Ley, E.E. Osnas, K.A. Schat, A.A. Dhondt, Common garden experiment reveals pathogen isolate but no host genetic diversity effect on the dynamics of an emerging wildlife disease, J. Evol. Biol. 23 (2010) 1680–1688.
[23] K.E. Jones, N. Patel, M. Levy, A. Storeygard, D. Balk, J.L. Gittleman, P. Daszak, Global trends in emerging infectious diseases, Nature 451 (2008) 990–994, https://doi.org/10.1038/nature06536.
[24] F.F. Keesing, L.K. Belden, P. Daszak, A. Dobson, C.D. Harvell, R.D. Holt, P. Hudson, A. Jolles, K.E. Jones, C.E. Mitchell, S.S. Myers, T. Bogich, R.S. Ostfeld, Impacts of biodiversity on the emergence and transmission of infectious diseases, Nature 468 (2010) 647–652, https://doi.org/10.1038/nature09575.
[25] L.H. Taylor, S.M. Latham, M.E. Woolhouse, Risk factors for human disease emergence, Philos. Trans. R. Soc. Lond. B Biol. Sci. 356 (2001) 983–989, https://doi.org/10.1098/rstb.2001.0888.
[26] S.S. Morse, J.A. Mazet, M. Woolhouse, C.R. Parrish, D. Carroll, W.B. Karesh, C. Zambrana-Torrelio, W.I. Lipkin, P. Daszak, Prediction and prevention of the next pandemic zoonosis, Lancet 380 (2012) 1956–1965.
[27] B. Roche, F. Guégan, Ecosystem dynamics, biological diversity and emerging infectious Diseases, C. R. Biologies 334 (2011) 385–392.
[28] International Livestock Research Institute, Mapping of Poverty and Likely Zoonoses Hotspots. Zoonoses Project 4. Report to Department for International Development, International Livestock Research Institute, UK. Nairobi, Kenya, 2012.
[29] D. Quammen, Spillover. Animal Infections and the Next Human Pandemic, vol. 7, The Bodley Head, London, 2012, e7630, https://doi.org/10.7717/peerj.7630, 157–160.
[30] E.D. Belay, J.C. Kile, A.J. Hall, C. Barton-Behravesh, M.B. Parsons, J. Stephanie, S.J. Salyer, H. Walke, Zoonotic disease programs for enhancing global health security, Emerg. Infect. Dis. 23 (2017) 65–70.
[31] P.J. Hotez, Nuclear weapons and neglected diseases: the 'ten-thousand- to-one gap, PLoS Neglected Trop. Dis. 4 (2010), e680.
[32] B.M. Gadaga, E.M.C. Etter, B. Mukamuri, K.J. Makwangudze, D.M. Pfukenyi, G. Matope, Living at the edge of an interface area in Zimbabwe: cattle owners, commodity chain and health workers' awareness, perceptions and practices on zoonoses, BMC Publ. Health 16 (2015).
[33] J.F. Walsh, D.H. Molyneux, M.H. Birley, Deforestation: effects on vector-borne disease, Parasitology 106 (1993) 55–75.
[34] B.A. Wilcox, B. Ellis, Forests and emerging infectious diseases of humans, Unasylva 57 (2006) 11–18.
[35] E. Henao, J.R. Cantera, P. Rzymski, Conserving the amazon river basin: the case study of the yahuarcaca lakes system in Colombia, Sci. Total Environ. 724 (2020), 138186.
[36] W.B. Karesh, R.A. Cook, The Human-Animal Link, One world—one health, Foreign Aff. 84 (2005) 38–50.
[37] W.J. Ripple, K. Abernethy, M.G. Betts, G. Chapron, R. Dirzo, M. Galetti, T. Levi, P.A. Lindsey, D.W. Macdonald, B. Machovina, T.M. Newsome, Bushmeat hunting and extinction risk to the world's mammals, R. Soc. Open Sci. 3 (10) (2016), 160498. https://royalsocietypublishing.org/doi/10.1098/rsos.160498.
[38] S. Ziegler, J.E. Fa, C. Wohlfart, B. Streit, S. Jacob, M. Wegmann, Mapping bushmeat hunting pressure in Central Africa, Biotropica 48 (3) (2016) 405–412, https://doi.org/10.1111/btp.12286.
[39] H.N. Sackey, J. McNamara, E.J. Milner-Gulland, Y. Ntiamoa-Baidu, The Bushmeat Trade in Northern Ghana: Market Dynamics, Drivers of Trade and Implications for Conservation, Oryx, 2022, pp. 1–12.
[40] J. Harvey-Carroll, F.T. Simo, T. Sonn-Juul, J.P. Tsafack, S.J. Aka'a, F.N. Tarla, A. Fowler, D.J. Ingram, Continued availability and sale of pangolins in a major urban bushmeat market in Cameroon despite national bans and the COVID-19 outbreak, Afr. J. Ecol. 20 (2022) 146–152, https://doi.org/10.1111/aje.12969.
[41] W.B. Karesh, R.A. Cook, E.L. Bennett, J. Newcomb, Wildlife trade and global disease emergence, Emerg. Infect. Dis. 11 (2005) 1000–1002.
[42] Z. Chen, A. Luckay, D.L. Sodora, P. Telfer, P. Reed, A. Gettie, J.M. Kanu, R.F. Sadek, J. Yee, D.D. Ho, et al., Human immunodeficiency virus type 2 (HIV-2) seroprevalence and characterization of a distinct HIV-2 genetic subtype from the natural range of simian immunodeficiency virus-infected sooty mangabeys, J. Virol. 71 (1997) 3953–3960.
[43] P.M. Sharp, B.H. Hahn, Origins of HIV and the AIDS pandemic, Cold Spring Harb. Perspect. Med. 1 (2011), a006841.
[44] P. Rouquet, J.M. Froment, M. Bermejo, A. Kilbourne, W.B. Karesh, P. Reed, B. Kumulungui, P. Yaba, A. Délicatet, P.E. Rollin, E.M. Leroy, Wild animal mortality monitoring and human ebola outbreaks, Gabon and Republic of Congo, 2001-2003, 2005, Emerg. Infect. Dis. 11 (2005) 283–290, https://doi.org/10.3201/eid1102.040533.
[45] N.D. Wolfe, C.P. Dunavan, J. Diamond, Origins of major human infectious diseases, Nature 447 (2007) 279–283.
[46] C. Delgado, M. Rosegrant, H. Steinfeld, S. Ehui, C. Courbois, Livestock to 2020 the Next Food Revolution. Food, Agriculture, and the Environment Discussion Paper, International Food Policy Research Institute, Washington, DC, 1999.

[47] J. Lindahl, U. Magnusson, Zoonotic pathogens in urban animals: enough research to protect the health of the urban population? Anim. Health Res. Rev. 21 (1) (2020) 50–60.
[48] D.P. van Uhm, R.W.Y. Wong, Establishing trust in the illegal wildlife trade in China, Asian J. Crim. 14 (2019) 23–40, https://doi.org/10.1007/s11417-018-9277-x.
[49] D. Cucinotta, M. Vanelli, WHO declares COVID-19 a pandemic, Acta Biomed. 91 (2020).
[50] K.D. Reed, Viral Zoonoses, Reference Module in Biomedical Sciences, 2018. B978-0-12-801238-3.95729-5.
[51] J. Ford, The Role of Trypanosomiasis in African Ecology, Clarendon Press, Oxford, UK, 1971.
[52] R. Sandip, F.M. Terry, W. Yan, A network control theory approach to modeling and optimal control of zoonoses: case study of brucellosis transmission in sub-Saharan Africa, PLoS Neglected Trop. Dis. 10 (2011) e1259.
[53] D.G. Newell, M. Koopmans, L. Verhoef, E. Duizer, A. Aidara-Kane, H. Sprong, M. Opsteegh, M. Langelaar, J. Threfall, F. Scheutz, J. van der Giessen, H. Kruse, Food-borne diseases—the challenges of 20 years ago still persist while new ones continue to emerge, Int. J. Food Microbiol. 139 (2010). S3–15.
[54] P.E. Mangesho, M.O. Neselle, E.D. Karimuribo, J.E. Mlangwa, K. Queenan, L.E.G. Mboera, J. Rushton, R. Kock, B. Häsler, A. Kiwara, M. Rweyemamu, Exploring local knowledge and perceptions on zoonoses among pastoralists in northern and eastern Tanzania, PLoS Neglected Trop. Dis. 11 (2017), e0005345.
[55] M. Moritz, D. Ewing, R. Garabed, On not knowing zoonotic diseases: pastoralists' ethnoveterinary knowledge in the far north region of Cameroon, Hum. Organ. 72 (2013) 1–11.
[56] K.M. Homewood, Development and the ecology of Maasai pastoralist food and nutrition, Ecol. Food Nutr. 29 (1992) 61–80.
[57] T.C. Harder, S. Buda, H. Hengel, M. Beer, T.C. Mettenleiter, Poultry food products - a source of avian influenza virus transmission to humans? Clin. Microbiol. Infect. 22 (2016) 141–146.
[58] J.T. McCabe, Risk and uncertainty among the Maasai of the Ngorongoro conservation area in Tanzania: a case study in economic change, Nomadic Peoples 1 (1997) 54–65.
[59] C.W. Schwabe, I.M. Kuojok, Practices and beliefs of the traditional Dinka healer in relation to provision of modern medical and veterinary services for the Southern Sudan, Hum. Organ. 40 (1981) 231–238.
[60] A. Mhlanga, Assessing the impact of optimal health education programs on the control of zoonotic diseases, Comput. Math. Methods Med. (2020), 6584323.
[61] D.H. Molyneux, Control of human parasitic disease: context and overview, Adv. Parasitol. 61 (2006) 1–43.
[62] P. Sands, C. Mundaca-Shah, V.J. Dzau, The neglected dimension of global security—a framework for countering infectious-disease crises, N. Engl. J. Med. 374 (2016) 1281–1287.
[63] M. Gilbert, G. Pullano, F. Pinotti, E. Valdano, C. Poletto, P. Boëlle, E. D'Ortenzio, Y. Yazdanpanah, S.P. Eholie, M. Altmann, B. Gutierrez, M.U.G. Kraemer, V. Colizza, Preparedness and vulnerability of African countries against importations of COVID-19: a modelling study, Lancet 395 (2020) 871–877.
[64] J.L.L. Waya, D. Ameh, J.L.K. Mogga, J.F. Wamala, O.O. Olu, COVID-19 case management strategies: what are the options for Africa? Infectious Diseases of Poverty 10 (2) (2021) 38–43.
[65] J. Hopman, B. Allegranzi, S. Mehtar, Managing COVID-19 in low-and middle-income countries, JAMA 323 (16) (2020) 1549–1550.
[66] W. Gwenzi, P. Rzymski, When silence goes viral, Africa sneezes! A perspective on Africa's subdued research response to COVID-19 and a call for local scientific evidence, Environ. Res. 194 (2021), 110637, https://doi.org/10.1016/j.envres.2020.110637.
[67] J.U. Onu, S.O. Oriji, D.O. Aluh, T.C. Onyeka, Aftermath of COVID-19: forestalling irreparable medical brain drain in sub-saharan Africa, J. Health Care Poor Underserved 32 (4) (2021) 1742–1751.
[68] R. de Macedo Couto, G.O. Santana, O.T. Ranzani, E.A. Waldman, One Health and surveillance of zoonotic tuberculosis in selected low-income, middle-income and high-income countries: a systematic review, PLoS Neglected Trop. Dis. 16 (6) (2022) e0010428.
[69] S.D. Nana, J.H. Caffin, R. Duboz, N. Antoine-Moussiaux, A. Binot, P.S. Diagbouga, P. Hendrikx, M. Bordier, Towards an integrated surveillance of zoonotic diseases in Burkina Faso: the case of anthrax, BMC Publ. Health 22 (1) (2022) 1–17.
[70] W. Gwenzi, Dangerous liaisons?: as the COVID-19 wave hits Africa with potential for novel transmission dynamics, J. Public Health (2020), https://doi.org/10.1007/s10389-020-01467-.
[71] W. Gwenzi, Leaving no stone unturned in light of the COVID-19 faecal-oral hypothesis? A water, sanitation and hygiene (WASH) perspective targeting low income countries, Sci. Total Environ. 753 (2020), 141751, https://doi.org/10.1016/j.scitotenv.2020.141751.
[72] G.R. Winck, R.L. Raimundo, H. Fernandes-Ferreira, M.G. Bueno, P.S. D'Andrea, F.L. Rocha, G.L. Cruz, E.M. Vilar, M. Brandão, J.L.P. Cordeiro, C.S. Andreazzi, Socioecological vulnerability and the risk of zoonotic disease emergence in Brazil, Sci. Adv. 8 (26) (2022) eabo5774.
[73] K.L. Edmunds, P.R. Hunter, R. Few, D.J. Bell, Hazard analysis of critical control points assessment as a tool to respond to emerging infectious disease outbreaks, PLoS One 8 (8) (2013), e72279.
[74] R.C. Khanna, M.V. Cicinelli, S.S. Gilbert, S.G. Honavar, G.V.S. Murthy, COVID-19 pandemic: lessons learned and future directions, Indian J. Ophthalmol. 68 (5) (2020) 703–710, https://doi.org/10.4103/ijo.IJO_843_20.
[75] H. Clark, E.J. Sirleaf, Report of the independent Panel for pandemic preparedness and response: making COVID-19 the last pandemic, Lancet 398 (10295) (2021) 101–103.
[76] The Independent Panel for Pandemic Preparedness and Response, COVID-19: Make it the Last Pandemic, 2021. Available at: https://theindependentpanel.org/wp-content/uploads/2021/05/COVID-19-Make-it-the-Last-Pandemic_final.pdf. (Accessed 25 September 2022). Accessed: 30 September 2022.
[77] A. Iwasaki, N.D. Grubaugh, Why does Japan have so few cases of COVID-19? EMBO Mol. Med. 12 (5) (2020), e12481 https://doi.org/10.15252/emmm.202012481.
[78] Z. Barua, S. Barua, S. Aktar, N. Kabir, M. Li, Effects of misinformation on COVID-19 individual responses and recommendations for resilience of disastrous consequences of misinformation, Progress in Disaster Science 8 (2020), 100119.
[79] D. Freeman, F. Waite, L. Rosebrock, A. Petit, C. Causier, A. East, L. Jenner, A.-L. Teale, L. Carr, S. Mulhall, E. Bold, S. Lambe, Coronavirus conspiracy beliefs, mistrust, and compliance with government guidelines in England, Psychol. Med. 1–13 (2020), https://doi.org/10.1017/S0033291720001890.
[80] M.S. Islam, A.-H.M. Kamal, A. Kabir, D.L. Southern, S.H. Khan, S.M.M. Hasan, T. Sarkar, S. Sharmin, S. Das, T. Roy, M.G.D. Harun, A.A. Chughtai, N. Homaira, H. Seale, COVID-19 vaccine rumors and conspiracy theories: the need for cognitive inoculation against misinformation to improve vaccine adherence, PLoS One 16 (5) (2021), e0251605, https://doi.org/10.1371/journal.pone.0251605.
[81] D.H.P. Balog-Way, K.A. McComas, COVID-19: reflections on trust, tradeoffs, and preparedness, J. Risk Res. 23 (7–8) (2020) 838–848, https://doi.org/10.1080/13669877.2020.1758192.
[82] S. Van der Linden, J. Roozenbeek, J. Compton, Inoculating against fake news about COVID-19, Front. Psychol. 11 (2020), 566790.
[83] B.M. Nowak, C. Miedziarek, S. Pełczyński, P. Rzymski, Misinformation, fears and adherence to preventive measures during the early phase of COVID-19 pandemic: a cross-sectional study in Poland, Int. J. Environ. Res. Publ. Health 18 (22) (2021), 12266.
[84] P. Rzymski, L. Borkowski, M. Drąg, R. Flisiak, J. Jemielity, J. Krajewski, A. Mastalerz-Migas, A. Matyja, K. Pyrć, K. Simon, M. Sutkowski, J. Wysocki, J. Zajkowska, A. Fal, The strategies to support the COVID-19 vaccination with evidence-based communication and tackling misinformation, Vaccines 9 (2021) 109.
[85] M. Basili, M. Franzini, Understanding the risk of an avian flu pandemic: rational waiting or precautionary failure? Risk Anal. 26 (3) (2006) 617–630, https://doi.org/10.1111/j.1539-6924.2006.00761.x.
[86] L. Crosby, E. Crosby, Applying the precautionary principle to personal protective equipment (PPE) guidance during the COVID-19 pandemic: did we learn the lessons of SARS? Canadian Journal of Anaesthesia = Journal Canadien d'anesthesie 67 (10) (2020) 1327–1332, https://doi.org/10.1007/s12630-020-01760-y.
[87] J.S. Mackenzie, M. McKinnon, M. Jeggo, One health: from concept to practice. Confronting emerging zoonoses, The One Health Paradigm (2014) 163–189, https://doi.org/10.1007/978-4-431-55120-1_8.
[88] J. Zinsstag, E. Schelling, D. Waltner-Toews, M. Tanner, From "one medicine" to "one health" and systemic approaches to health and well-being, Prev. Vet. Med. 101 (3) (2011) 148–156, https://doi.org/10.1016/j.prevetmed.2010.07.003.

[89] C. Schwabe, Veterinary Medicine and Human Health, vol. 19, Williams & Wilkins, 1984. Issue 1.
[90] D. Destoumieux-Garzón, P. Mavingui, G. Boetsch, J. Boissier, F. Darriet, P. Duboz, C. Fritsch, P. Giraudoux, F. Le Roux, S. Morand, C. Paillard, D. Pontier, C. Sueur, Y. Voituron, The one health concept: 10 Years old and a long road ahead, Front. Vet. Sci. 5 (2018) 14. https://www.frontiersin.org/article/10.3389/fvets.2018.00014.
[91] A. Aiyar, P. Pingali, Pandemics and food systems - towards a proactive food safety approach to disease prevention & management, Food Secur. 12 (4) (2020) 749–756, https://doi.org/10.1007/s12571-020-01074-3.
[92] L. Vrbova, C. Stephen, N. Kasman, R. Boehnke, M. Doyle-Waters, A. Chablitt-Clark, B. Gibson, M. FitzGerald, D.M. Patrick, Systematic review of surveillance systems for emerging zoonoses, Transboundary and Emerging Diseases 57 (3) (2010) 154–161, https://doi.org/10.1111/j.1865-1682.2010.01100.x.
[93] A. Nurse, T. Wyatt, Wildlife Criminology, Bristol University Press, Bristol, 2020.
[94] T. Wyatt, D. van Uhm, A. Nurse, Differentiating criminal networks in the illegal wildlife trade: organized, corporate and disorganized crime, Trends Organ. Crime 23 (2020) 350–366, https://doi.org/10.1007/s12117-020-09385-9.
[95] N.D. Wolfe, P. Daszak, A.M. Kilpatrick, D.S. Burke, Bushmeat hunting, deforestation, and prediction of zoonoses emergence, Emerg. Infect. Dis. 11 (2005) 1822–1827, https://doi.org/10.3201/eid1112.040789.
[96] S. Platto, J. Zhou, Y. Wang, H. Wang, E. Carafoli, Biodiversity loss and COVID-19 pandemic: the role of bats in the origin and the spreading of the disease, Biochem. Biophys. Res. Commun. 538 (2021) 2–13, https://doi.org/10.1016/j.bbrc.2020.10.028.
[97] D. Despommier, B.R. Ellis, B.A. Wilcox, The role of ecotones in emerging infectious diseases, EcoHealth 3 (2006) 281–289, https://doi.org/10.1007/s10393-006-0063-3.
[98] R.J. Eisen, G.E. Glass, L. Eisen, J. Cheek, R.E. Enscore, P. Ettestad, K.L. Gage, A spatial model of shared risk for plague and hantavirus pulmonary syndrome in the southwestern United States, Am. J. Trop. Med. Hyg. 77 (2007) 999–1004.
[99] T. Goldberg, T.R. Gillespie, I.B. Rwego, E.L. Estoff, C.A. Chapman, Forest fragmentation as cause of bacterial transmission among nonhuman primates, humans, and livestock, Uganda, Emerg. Infect. Dis. 14 (2008) 1375–1382, https://doi.org/10.3201/eid1409.071196.
[100] M.B. Hahn, E.S. Gurley, J.H. Epstein, M.S. Islam, J.A. Patz, P. Saszak, S.P. Luby, The role of landscape composition and configuration on Pteropus giganteus roosting ecology and Nipah virus spillover risk in Bangladesh, Am. J. Trop. Med. Hyg. 90 (2014) 247–255, https://doi.org/10.4269/ajtmh.13-0256.
[101] F. Keesing, R.D. Holt, R.S. Ostfeld, Effects of species diversity on disease risk, Ecol. Lett. 9 (2006) 485–498, https://doi.org/10.1111/j.1461-0248.2006.00885.x.
[102] S. Søyland, Criminal Organisations and Crimes against the Environment – A Desktop Study, United Nations Interregional Crime and Justice Research Institute, Turin, 2000.
[103] M.E. Zimmerman, The black market for wildlife: combatting transnational organized crime in the illegal wildlife trade, Vanderbilt J. Transnatl. Law 36 (2003) 1657–1689.
[104] D. Cook, M. Roberts, J. Lowther, The International Wildlife Trade and Organised Crime: a Review of the Evidence and Role of the United Kingdom, 2002 (accessed: 25 March 2021), http://www.wwf.org.uk/filelibrary/pdf/organisedCrime.pdf.
[105] D. van Uhm, The Illegal Wildlife Trade: inside the World of Poachers, Smugglers and Traders (Studies of Organized Crime), Springer, New York, 2016, https://doi.org/10.1007/978-3-319-42129-2.
[106] D. van Uhm, R. Nijman, The convergence of environmental crime with other serious crimes: subtypes within the environmental crime continuum, Eur. J. Criminol. (2020) 1–20, https://doi.org/10.1177/1477370820904585.
[107] A.N. Alim, Rwandan President Paul Kagame Backs the Independent's Stop the Illegal Wildlife Trade Campaign, 2021. The Independent, https://www.independent.co.uk/stop-the-illegal-wildlife-trade/giants-club-rwanda-paul-kagame-b1810160.html. (Accessed 21 March 2021). Accessed.
[108] J. Zinsstag, J. Mackenzie, M. Jeggo, D. Heymann, J. Patz, P. Daszak, Mainstreaming one health, EcoHealth 9 (2012) 107–110, https://doi.org/10.1007/s10393-012-0772-8.
[109] M. Johansen, M. Penrith, Has culling been properly assessed as a valid and justified control intervention measure for zoonotic diseases? PLoS Neglected Trop. Dis. 3 (2008) e541, https://doi.org/10.1371/journal.pntd.0000541.
[110] J. Rushton, The Economics of Animal Health and Production, CABI, Wallingford, Oxfordshire, 2009.
[111] J. Coggon, What Makes Health Public? A Critical Evaluation of Moral, Legal, and Political Claims in Public Health, Cambridge University Press, New York, 2012.
[112] B. Capps, Z. Lederman, One Health and paradigms of public biobanking, J. Med. Ethics 41 (2014) 258–262, https://doi.org/10.1136/medethics-2013-101828.
[113] M.J. Rock, C. Degeling, Public health ethics and more-than-human solidarity, Soc. Sci. Med. 129 (2015) 61–67, https://doi.org/10.1016/j.socscimed.2014.05.050.
[114] C. Degeling, Z. Lederman, M. Rock, Culling and the common good: Re-evaluating harms and benefits under the One Health pradigm, Publ. Health Ethics 9 (2016) 244–254, https://doi.org/10.1093/phe/phw019.
[115] S. Hinchliffe, More than one world, more than one health: Re-configuring interspecies health, Soc. Sci. Med. 129 (2015) 28–35, https://doi.org/10.1016/j.socscimed.2014.07.007.
[116] T.R. Kelly, C. Machalaba, W.B. Karesh, P.Z. Crook, K. Gilardi, J. Nziza, M.M. Uhart, E.A. Robles, K. Saylors, D.O. Joly, C. Monagin, P.M. Mangombo, P. M. Kingebeni, R. Kazwala, D. Wolking, W. Smith, J.A.K. Mazet, Implementing One Health approaches to confront emerging and re-emerging zoonotic disease threats: lessons from PREDICT, One Health Outlook 2 (2020) 1, https://doi.org/10.1186/s42522-019-0007-9.
[117] Z. Lederman, One Health and culling as a public health measure, Publ. Health Ethics 9 (2016) 5–23, https://doi.org/10.1093/phe/phw002.
[118] M. Peiris, H. Yen, Animal and human influenzas, Rev. - Off. Int. Epizoot. 33 (2014) 539–553, https://doi.org/10.20506/rst.33.2.2289.
[119] M. De Garine-Wichatitsky, A. Caron, R. Kock, R. Tschopp, M. Munyeme, M. Hofmeyr, A. Michel, A review of bovine tuberculosis at the wildlife–livestock–human interface in sub-Saharan Africa, Epidemiol. Infect. 141 (7) (2013) 1342–1356.
[120] K.J. Olival, To cull, or not to cull, bat is the question, EcoHealth 13 (2016) 6–8, https://doi.org/10.1007/s10393-015-1075-7.
[121] C.H. Calisher, J.E. Childs, H.E. Field, K.V. Holmes, T. Schountz, Bats: important reservoir hosts of emerging viruses, Clin. Microbiol. Rev. 19 (3) (2006) 531–545.
[122] T. Omatsu, S. Watanabe, H. Akashi, Y. Yoshikawa, Biological characters of bats in relation to natural reservoir of emerging viruses, Comp. Immunol. Microbiol. Infect. Dis. 30 (5–6) (2007) 357–374.
[123] R.K. Plowright, P. Eby, P.J. Hudson, I.L. Smith, D. Westcott, W.L. Bryden, D. Middleton, P.A. Reid, R.A. McFarlane, G. Martin, G.M. Tabor, Ecological dynamics of emerging bat virus spillover, Proc. Biol. Sci. 282 (1798) (2015), 20142124.
[124] F. Mayen, Haematophagous bats in Brazil, their role in rabies transmission, impact on public health, livestock industry and alternatives to an indiscriminate reduction of bat population, J. Vet. Med. Ser. B 50 (10) (2003) 469–472.
[125] G. Wibbelt, M.S. Moore, T. Schountz, C.C. Voigt, Emerging Diseases in Chiroptera: Why Bats?, 2010.
[126] M. Wagner, F. Tsui, G. Cooper, J.U. Espino, H. Harkema, J. Levander, R. Villamarin, R. Voorhees, N. Millett, C. Keane, A. Dey, M. Razdan, Y. Hu, M. Tsai, S. Brown, B.Y. Lee, A. Gallagher, M. Potter, Probabilistic, decision-theoretic disease surveillance and control, Online J. Public Health Inform. 3 (2011), https://doi.org/10.5210/ojphi.v3i3.3798.
[127] The World Bank, People, pathogens, and our planet, The Economics of One Health 2 (2012). Report #69145-GLB.
[128] The World Bank, Operational Framework for Strengthening Human, Animal and Environmental Public Health Systems at Their Interface, 2018 (accessed: 25 March 2021), https://documents.worldbank.org/en/publication/documents-reports/documentdetail/703711517234402168/operational-framework-for-strengthening-human-animal-and-environmental-public-health-systems-at-their-interface.
[129] A. Anyamba, J.P. Chretien, J. Small, C.J. Tucker, P.B. Formenty, J.H. Richardson, S.C. Britch, D.C. Schnabel, R.L. Erickson, K.J. Linthicum, Prediction of a Rift Valley fever outbreak, Proc. Natl. Acad. Sci. U.S.A. 106 (2009) 955–959, https://doi.org/10.1073/pnas.0806490106.
[130] Who, Zoonoses, 2020 (accessed: 25 March 2021), https://www.who.int/news-room/fact-sheets/detail/zoonoses.

[131] S. Watanabe, J.S. Masangkay, N. Nagata, S. Morikawa, T. Mizutani, S. Fukushi, P. Alviola, T. Omatsu, N. Ueda, K. Iha, S. Taniguchi, H. Fujii, S. Tsuda, M. Endoh, K. Kato, Y. Tohya, S. Kyuwa, Y. Yoshikawa, H. Akashi, Bat coronaviruses and experimental infection of bats, the Philippines, Emerg. Infect. Dis. 16 (2010) 1217–1223, https://doi.org/10.3201/eid1608.100208.
[132] L.F. Wang, P.J. Walker, L.L. Poon, Mass extinctions, biodiversity and mitochondrial function: are bats 'special' as reservoirs for emerging viruses? Curr. Opin. Virol. 1 (6) (2011) 649–657.
[133] E.J. Putz, J.E. Nally, Investigating the immunological and biological equilibrium of reservoir hosts and pathogenic Leptospira: balancing the solution to an acute problem? Front. Microbiol. 11 (2020) 2005.
[134] D.J. Taylor, R.W. Leach, J. Bruenn, Filoviruses are ancient and integrated into mammalian genomes, BMC Evol. Biol. 10 (2010) 193.
[135] J.E. Nally, R.L. Hornsby, D.P. Alt, D. Bayles, J.H. Wilson-Welder, D.E. Palmquist, N.E. Bauer, Isolation and characterization of pathogenic leptospires associated with cattle, Vet. Microbiol. 218 (2018) 25–30.
[136] J.E. Nally, J.H. Wilson-Welder, R.L. Hornsby, M.V. Palmer, D.P. Alt, Inbred rats as a model to study persistent renal leptospirosis and associated cellular immune responsiveness, Front. Cell. Infect. Microbiol. 8 (2018) 66.
[137] F.M. Tomley, M.W. Shirley, Livestock infectious diseases and zoonoses, Philos. Trans. R. Soc. Lond. B Biol. Sci. 364 (2009) 2637–2642, https://doi.org/10.1098/rstb.2009.0133.
[138] M. Woolhouse, E. Gaunt, Ecological origins of novel human pathogens, Crit. Rev. Microbiol. 33 (2007) 231–242, https://doi.org/10.1080/10408410701647560.
[139] Nature, Microbiology by numbers, Nat. Rev. Microbiol. 9 (2011) 628, https://doi.org/10.1038/nrmicro2644.
[140] G.F. Cooper, R. Villamarin, F.C. Rich Tsui, N. Millett, J.U. Espino, M.M. Wagner, A method for detecting and characterizing outbreaks of infectious disease from clinical reports, J. Biomed. Inf. 53 (2015) 15–26, https://doi.org/10.1016/j.jbi.2014.08.011.
[141] R. Gibb, L.H. Franklinos, D.W. Redding, K.E. Jones, Ecosystem perspectives are needed to manage zoonotic risks in a changing climate, Br. Med. J. (2020) 371.
[142] A. Engering, L. Hogerwerf, J. Slingenbergh, Pathogen–host–environment interplay and disease emergence, Emerg. Microb. Infect. 2 (1) (2013) 1–7.
[143] R.K. Plowright, C.R. Parrish, H. McCallum, P.J. Hudson, A.I. Ko, A.L. Graham, J.O. Lloyd-Smith, Pathways to zoonotic spillover, Nat. Rev. Microbiol. 15 (8) (2017) 502–510.
[144] B.H. Bird, J.A. Mazet, Detection of emerging zoonotic pathogens: an integrated one health approach. body dimensions of leopards (Panthera pardus) from camera trap photographs, PeerJ (2018).
[145] R. Coker, J. Rushton, S. Mounier-Jack, E. Karimuribo, P. Lutumba, D. Kambarage, D.U. Pfeiffer, K. Stärk, M. Rweyemamu, Towards a conceptual framework to support one-health research for policy on emerging zoonoses, Lancet Infect. Dis. 11 (4) (2011) 326–331.
[146] G. Martin, C. Yanez-Arenas, C. Chen, R.K. Plowright, R.J. Webb, L.F. Skerratt, Climate change could increase the geographic extent of Hendra virus spillover risk, EcoHealth 15 (3) (2018) 509–525.
[147] K.D. Reed, J.K. Meece, J.S. Henkel, S.K. Shukla, Birds, migration and emerging zoonoses: West Nile virus, Lyme disease, influenza A and enteropathogens, Clin. Med. Res. 1 (1) (2003) 5–12.
[148] M. Friend, R.G. McLean, F. Joshua Dein, Disease emergence in birds: challenges for the twenty-first century, Auk 118 (2) (2001) 290–303.
[149] F.M. Aarestrup, The livestock reservoir for antimicrobial resistance: a personal view on changing patterns of risks, effects of interventions and the way forward, Phil. Trans. Biol. Sci. 370 (1670) (2015), 20140085.
[150] A. Koluman, A. Dikici, Antimicrobial resistance of emerging foodborne pathogens: status quo and global trends, Crit. Rev. Microbiol. 39 (1) (2013) 57–69.
[151] S. Levy, Microbial resistance to antibiotics. An evolving and persistent problem, Lancet 2 (1982) 83–88.
[152] S.R. Norrby, C.E. Nord, R. Finch, Lack of development of new antimicrobial drugs: a potential serious threat to public health, Lancet Infect. Dis. 5 (2) (2005) 115–119.
[153] J. O'Neill, Tackling Drug-Resistant Infections Globally: Final Report and Recommendations, 2016.
[154] S.A. Strathdee, S.C. Davies, J.R. Marcelin, Confronting antimicrobial resistance beyond the COVID-19 pandemic and the 2020 US election, Lancet 396 (10257) (2020) 1050–1053.
[155] A.I. Moreno Switt, D. Rivera, M.L. Caipo, D.C. Nowell, A.D. Adell, Antimicrobial resistance in water in Latin America and the caribbean: available research and gaps, Front. Vet. Sci. 7 (2020) 546.
[156] D. Ortega-Paredes, S. De Janon, F. Villavicencio, K.J. Ruales, K. De La Torre, J.E. Villacís, J.A. Wagenaar, J. Matheu, C. Bravo-Vallejo, E. Fernández-Moreira, C. Vinueza-Burgos, Broiler farms and carcasses are an important reservoir of multi-drug resistant escherichia coli in Ecuador, Front. Vet. Sci. 7 (2020) 979.
[157] K. Iskandar, L. Molinier, S. Hallit, M. Sartelli, T.C. Hardcastle, M. Haque, H. Lugova, S. Dhingra, P. Sharma, S. Islam, I. Mohammed, Surveillance of antimicrobial resistance in low-and middle-income countries: a scattered picture, Antimicrob. Resist. Infect. Control 10 (1) (2021) 1–19.
[158] A.C.B. Berge, D.A. Moore, T.E. Besser, W.M. Sischo, Targeting therapy to minimize antimicrobial use in preweaned calves: effects on health, growth, and treatment costs, J. Dairy Sci. 92 (9) (2009) 4707–4714.
[159] P.R. Torgerson, C.N. Macpherson, The socioeconomic burden of parasitic zoonoses: global trends, Vet. Parasitol. 182 (1) (2011) 79–95.
[160] H. Feldmann, V. Wahl-Jensen, S.M. Jones, U. Ströher, Ebola virus ecology: a continuing mystery, Trends Microbiol. 12 (10) (2004) 433–437.
[161] M.A. Mahdy, W. Younis, Z. Ewaida, An overview of SARS-CoV-2 and animal infection, Front. Vet. Sci. 7 (2020).
[162] J. Zhao, W. Cui, B.P. Tian, The potential intermediate hosts for SARS-CoV-2, Front. Microbiol. 11 (2020).
[163] A. Banerjee, A.C. Doxey, K. Mossman, A.T. Irving, Unravelling the Zoonotic Origin and Transmission of SARS-CoV-2, Trends in ecology & evolution, 2020.
[164] C.A. Gilchrist, S.D. Turner, M.F. Riley, W.A. Petri, E.L. Hewlett, Whole-genome sequencing in outbreak analysis, Clin. Microbiol. Rev. 28 (3) (2015) 541–563.
[165] A.E. Mongan, J.S.B. Tuda, L.R. Runtuwene, Portable sequencer in the fight against infectious disease, J. Hum. Genet. 65 (1) (2020) 35–40.
[166] W.I. Lipkin, Microbe hunting, Microbiol. Mol. Biol. Rev. 74 (3) (2010) 363–377.
[167] D.A. Relman, Microbial genomics and infectious diseases, N. Engl. J. Med. 365 (4) (2011) 347–357.
[168] J.M. Hughes, M.E. Wilson, B.L. Pike, K.E. Saylors, J.N. Fair, M. LeBreton, U. Tamoufe, C.F. Djoko, A.W. Rimoin, N.D. Wolfe, The origin and prevention of pandemics, Clin. Infect. Dis. 50 (12) (2010) 1636–1640.
[169] B.A. Han, A.M. Kramer, J.M. Drake, Global patterns of zoonotic disease in mammals, Trends Parasitol. 32 (7) (2016) 565–577.
[170] D. Montecino-Latorre, T. Goldstein, K. Gilardi, D. Wolking, E. Van Wormer, R. Kazwala, B. Ssebide, J. Nziza, Z. Sijali, M. Cranfield, J.A. Mazet, Reproduction of East- African bats may guide risk mitigation for coronavirus spillover, One Health Outlook 2 (1) (2020) 1–13.
[171] R.E. Shope, Pathogenesis and virulence of zoonotic infections in humans, in: The Emergence of Zoonotic Diseases: Understanding the Impact on Animal and Human Health: Workshop Summary, 2002, pp. 10–14.
[172] Y. Liu, K. Wang, T.F. Massoud, R. Paulmurugan, SARS-CoV-2 vaccine development: an overview and perspectives, ACS Pharmacology & Translational Science 3 (5) (2020) 844–858.
[173] J.N. Hanna, et al., Australian bat lyssavirus infection: a second human case, with a long incubation period, Med. J. Aust. 172 (12) (2000) 597–599.
[174] J.S. Mackenzie, H.E. Field, K.J. Guyatt, Managing emerging diseases borne by fruit bats (flying foxes), with particular reference to henipaviruses and Australian bat lyssavirus, J. Appl. Microbiol. 94 (Suppl) (2003) 59S–69S.
[175] E.M. Leroy, B. Kumulungui, X. Pourrut, P. Rouquet, A. Hassanin, et al., Fruit bats as reservoirs of Ebola virus, Nature 438 (2005) 575–576.
[176] S. Wong, et al., Bats as a continuing source of emerging infections in humans, Rev. Med. Virol. 17 (2) (2007) 67–91.
[177] Y. Guan, B.J. Zheng, Y.Q. He, X.L. Liu, Z.X. Zhuang, C.L. Cheung, S.W. Luo, P.H. Li, L.J. Zhang, Y.J. Guan, K.M. Butt, Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China, Science 302 (5643) (2003) 276–278.
[178] K. Royce, F. Fu, Mathematically modeling spillovers of an emerging infectious zoonosis with an intermediate host, PLoS One 15 (8) (2020) e0237780.
[179] M. Chinazzi, J.T. Davis, M. Ajelli, C. Gioannini, M. Litvinova, S. Merler, A.P. y Piontti, K. Mu, L. Rossi, K. Sun, C. Viboud, The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak, Science 368 (6489) (2020) 395–400.
[180] J. Maurice, Of pigs and people—WHO prepares to battle cysticercosis, Lancet 384 (9943) (2014) 571–572.
[181] J.C. Paulson, R.P. de Vries, H5N1 receptor specificity as a factor in pandemic risk, Virus Res. 178 (1) (2013) 99–113.

[182] R. Webby, E. Hoffmann, R. Webster, Molecular constraints to interspecies transmission of viral pathogens, Nat. Med. 10 (12) (2004) S77–S81.
[183] R.J.G. Hulswit, C.A.M. De Haan, B.J. Bosch, Coronavirus spike protein and tropism changes, Adv. Virus Res. 96 (2016) 29–57.
[184] M. Woolhouse, F. Scott, Z. Hudson, R. Howey, M. Chase-Topping, Human viruses: discovery and emergence, Phil. Trans. Biol. Sci. 367 (1604) (2012) 2864–2871.
[185] K.M. Pepin, S. Lass, J.R. Pulliam, A.F. Read, J.O. Lloyd-Smith, Identifying genetic markers of adaptation for surveillance of viral host jumps, Nat. Rev. Microbiol. 8 (11) (2010) 802–813.
[186] C.R. Parrish, E.C. Holmes, D.M. Morens, E.C. Park, D.S. Burke, C.H. Calisher, C.A. Laughlin, L.J. Saif, P. Daszak, Cross-species virus transmission and the emergence of new epidemic diseases, Microbiol. Mol. Biol. Rev. 72 (3) (2008) 457–470.
[187] G.K.M. Goh, A.K. Dunker, J.A. Foster, V.N. Uversky, Shell Disorder Analysis Predicts Greater Resilience of the SARS-CoV-2 (COVID-19) outside the Body and in Body Fluids, Microbial Pathogenesis, 2020, 104177.
[188] L. Joffrin, A.O. Hoarau, E. Lagadec, O. Torrontegi, M. Köster, G. Le Minter, M. Dietrich, P. Mavingui, C. Lebarbenchon, Seasonality of coronavirus shedding in tropical bats, R. Soc. Open Sci. 9 (2) (2022), 211600, https://doi.org/10.1098/rsos.211600.
[189] J.K. Lane, Y. Negash, N. Randhawa, N. Kebede, H. Wells, G. Ayalew, S.J. Anthony, B. Smith, T. Goldstein, T. Kassa, J.A. Mazet, Coronavirus and paramyxovirus shedding by bats in a cave and buildings in Ethiopia, EcoHealth 19 (2) (2022) 216–232, https://doi.org/10.1007/s10393-022-01590-y.
[190] R. Fischer, A. Toffolo, Is total system cost minimization fair to all the actors of an energy system? Not according to game theory. Energy, 239, p.122253. for remotely measuring body dimensions on mantled howling monkeys (Alouatta palliata), Am. J. Primatol. 77 (8) (2022) 823–832, https://doi.org/10.1002/ajp.22416.
[191] H. Zhang, Game theory, in: H. Zhang (Ed.), Models and Methods for Management Science. Management for Professionals, Springer, Singapore, 2022, https://doi.org/10.1007/978-981-19-1614-4_7.
[192] M. Dufwenberg, K.L. Reed, Pandemics and Psychological Game Theory, 2022.
[193] P.C. DeLaurentis, E. Adida, M. Lawley, A game theoretical approach for hospital stockpile in preparation for pandemics, Hospital 101 (2008) 1.
[194] A. Caparros, M. Finus, The corona-pandemic: a game-theoretic perspective on regional and global Governance, Environ. Resour. Econ. 76 (4) (2020) 913–927.
[195] A. Delabouglise, M.F. Boni, Game theory of vaccination and depopulation for managing livestock diseases and zoonoses on small-scale farms, Epidemics 30 (2020), 100370.
[196] S.V. Bankuru, S. Kossol, W. Hou, P. Mahmoudi, J. Rychtář, D. Taylor, A game-theoretic model of Monkeypox to assess vaccination strategies, PeerJ 8 (2020) e9272.
[197] S. Sagiroglu, D. Sinanc, Big data: a review, in: 2013 International Conference on Collaboration Technologies and Systems (CTS), IEEE, 2013, May, pp. 42–47.
[198] G.V. Asokan, V. Asokan, Leveraging "big data" to enhance the effectiveness of "one health" in an era of health informatics, Journal of epidemiology and global health 5 (4) (2015) 311–314.
[199] G.V. Asokan, M.Y. Mohammed, Harnessing big data to strengthen evidence-informed precise public health response, in: Big Data in Psychiatry# X0026; Neurology, Academic Press, 2021, pp. 325–337.
[200] Z. Ouyang, J. Sargeant, A. Thomas, K. Wycherley, R. Ma, R. Esmaeilbeigi, A. Versluis, D. Stacey, E. Stone, Z. Poljak, T.M. Bernardo, A scoping review of 'big data','informatics', and 'bioinformatics' in the animal health and veterinary medical literature, Anim. Health Res. Rev. 20 (1) (2019) 1–18.
[201] J.F. Doherty, X. Chai, L.E. Cope, D. de Angeli Dutra, M. Milotic, S. Ni, E. Park, A. Filion, The rise of big data in disease ecology, Trends Parasitol. 37 (12) (2021) 1034–1037.
[202] M.E. McCue, A.M. McCoy, The scope of big data in one medicine: unprecedented opportunities and challenges, Front. Vet. Sci. 4 (2017) 194.
[203] M. Ndengu, G. Matope, M. de Garine-Wichatitsky, M. Tivapasi, M. Scacchia, B. Bonfini, D.M. Pfukenyi, Seroprevalence of brucellosis in cattle and selected wildlife species at selected livestock/wildlife interface areas of the Gonarezhou National Park, Zimbabwe, Prev. Vet. Med. 146 (2017) 158–165.
[204] K. Fornace, Spatial Epidemiology of Plasmodium Knowlesi in Sabah, Malaysia, Doctoral dissertation, London School of Hygiene & Tropical Medicine, 2019.
[205] K.M. Fornace, T.R. Abidin, N. Alexander, P. Brock, M.J. Grigg, A. Murphy, T. William, J. Menon, C.J. Drakeley, J. Cox, Association between landscape factors and spatial patterns of Plasmodium knowlesi infections in Sabah, Malaysia, Emerg. Infect. Dis. 22 (2) (2016) 201.
[206] K.M. Fornace, N. Alexander, T.R. Abidin, P.M. Brock, T.H. Chua, I. Vythilingam, H.M. Ferguson, B.O. Manin, M.L. Wong, S.H. Ng, J. Cox, Local human movement patterns and land use impact exposure to zoonotic malaria in Malaysian Borneo, Elife 8 (2019).
[207] K.M. Fornace, P.M. Brock, T.R. Abidin, L. Grignard, L.S. Herman, T.H. Chua, S. Daim, T. William, C.L. Patterson, T. Hall, M.J. Grigg, Environmental risk factors and exposure to the zoonotic malaria parasite Plasmodium knowlesi across northern Sabah, Malaysia: a population-based cross-sectional survey, Lancet Planet. Health 3 (4) (2019) e179–e186.
[208] N.L. Barrickman, A.L. Schreier, K.E. Glander, Testing parallel laser image scaling for remotely measuring body dimensions on mantled howling monkeys (Alouatta palliata), Am. J. Primatol. 77 (8) (2015) 823–832.
[209] M.R. Lambert, C.M. Yasuda, B.D. Todd, Evaluation of a photographic technique for estimating body size in lizards from a distance, Herpetol. Conserv. Biol. 7 (2012) 83–88.
[210] A. Tarugara, B.W. Clegg, E. Gandiwa, V.K. Muposhi, C.M. Wenham, Measuring, 2019.
[211] K. Kalu, Assessing the impacts of donor support on Nigeria's health system: the global fund in perspective, Int. Soc. Sci. J. 72 (243) (2022) 243–253.
[212] M. Reid, E. Goosby, Securing Global Fund Replenishment to Avoid Another Cassandra Moment, The Lancet Global Health, 2022.
[213] WHO (World Health Organization), World Health Organization, 2017, Available at:, Roadmap for zoonotic tuberculosis, 2017. Accessed: 27 September 2022, https://apps.who.int/iris/bitstream/handle/10665/259229/9789241513043-eng.pdf.
[214] A. Mpofu, P. Nyahoda, National Health Financing in Zimbabwe 2005: Contribution of the National AIDS Levy to National Health Care Support, Regional Network for Equity in Health in Southern Africa, Harare, 2008.
[215] D.T. Halperin, O. Mugurungi, T.B. Hallett, B. Muchini, B. Campbell, T. Magure, C. Benedikt, S. Gregson, A surprising prevention success: why did the HIV epidemic decline in Zimbabwe? PLoS Med. 8 (2) (2011) e1000414.
[216] S. O'Brien, A. Broom, The rise and fall of HIV prevalence in Zimbabwe: the social, political and economic context, Afr. J. AIDS Res. 10 (3) (2011) 281–290.
[219] X. Zhou, Z. Li, T. Zheng, Y. Yan, P. Li, E.A. Odey, H.P. Mang, S.M.N. Uddin, Review of global sanitation development, Environ. Int. 120 (2018) 246–261.
[220] L. Brierley, M.J. Vonhof, K.J. Olival, P. Daszak, K.E. Jones, Quantifying global drivers of zoonotic bat viruses: a process-based perspective, Am. Nat. 187 (2) (2016) E53–E64.
[221] A. Caron, E. Miguel, C. Gomo, P. Makaya, D.M. Pfukenyi, C. Foggin, T. Hove, M. de Garine-Wichatitsky, Relationship between burden of infection in ungulate populations and wildlife/livestock interfaces, Epidemiol. Infect. 141 (7) (2013) 1522–1535.
[222] A.C. Chua, J. Cunningham, F. Moussy, M.D. Perkins, P. Formenty, The case for improved diagnostic tools to control Ebola virus disease in West Africa and how to get there, PLoS Neglected Trop. Dis. 9 (6) (2015) e0003734.
[223] EFSA/ECDPC (European Food Safety Authority and European Centre for Disease Prevention and Control), The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2017, EFSA J. 17 (2) (2019), e05598.
[224] N. Galarce, F. Sánchez, V. Fuenzalida, R. Ramos, B. Escobar, L. Lapierre, E. Paredes-Osses, G. Arriagada, R. Alegría-Morán, N. Lincopán, D. Fuentes-Castillo, Phenotypic and genotypic antimicrobial resistance in non-O157 Shiga toxin-producing Escherichia coli isolated from cattle and swine in Chile, Front. Vet. Sci. 7 (2020) 367.
[225] K.E. Jones, C.E. Mitchell, S.S. Myers, T. Bogich, R.S. Ostfeld, Impacts of biodiversity on the emergence and transmission of infectious diseases, Nature 468 (2010) 647–652.
[226] F. Keesing, L.K. Belden, P. Daszak, A. Dobson, D.C. Harvell, R.D. Holt, P. Hudson, A. Jolles, N. Kemuto, E. Mogoa, E. Osoro, A. Bitek, M.K. Njenga, S. M. Thumbi, Zoonotic disease research in East Africa, BMC Infect. Dis. 18 (2018) 545.
[229] K.F. Smith, A.P. Dobson, F.E. McKenzie, L.A. Real, D.L. Smith, M.L. Wilson, Ecological theory to enhance infectious disease control and public health policy, Front. Ecol. Environ. 3 (1) (2005) 29–37.

[231] X. Wang, D. Jia, S. Gao, C. Xia, X. Li, Z. Wang, Vaccination behavior by coupling the epidemic spreading with the human decision under the game theory, Appl. Math. Comput. 380 (2020), 125232.
[232] A.C. White, M. Péchevis, A.J. Cuen, Lessons learnt from UNAIDS virtual technical support to countries applying for funding from the Global Fund COVID-19 Response Mechanism, Afr. J. AIDS Res. 21 (2) (2022) 100–109.
[233] IACG (Interagency Coordination Group on Antimicrobial Resistance), 2019. No time to wait–securing the future from drug-resistant infections. Report to the Secretary General of the United Nations. Available at: https://www.who.int/publications/i/item/no-time-to-wait-securing-the-future-from-drug-resistant-infections Accessed: 26 July 2022.