Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Preparing for Emerging Zoonotic Viruses

Reina S Sikkema and Marion PG Koopmans, Erasmus Medical Center, Rotterdam, The Netherlands

Emerging infectious diseases (EID) have been defined as diseases whose incidence increased over the past decades or are predicted to increase in the foreseeable future ("see Relevant Websites section"). This definition includes known infections with new properties, or known infections in new geographic regions, infections that were not previously recognized, and new infections resulting from spillover of pathogens from an animal reservoir to humans. Although difficult to state with certainty, current consensus is that EID outbreaks have increased significantly in the past decades, both in terms of size and number of causative pathogens (Smith *et al.*, 2014; Allen *et al.*, 2017). The majority of EIDs are thought to originate from animals, of which wildlife is the most important source of human outbreaks (Allen *et al.*, 2017; Jones *et al.*, 2008). Such spillovers can occur directly, or through vectors such as mosquitos, ticks and sandflies. Examples of past outbreaks are SARS (Peiris *et al.*, 2004), MERS (Zaki *et al.*, 2012), Avian Influenza (Lai *et al.*, 2016), Ebola (Dudas *et al.*, 2017) and Zika virus (Gubler *et al.*, 2017). Compared to common endemic diseases, the burden of disease may be relatively limited, but the unexpected nature, high case fatality rate, the uncertainty of sources and modes of transmission, and the paucity of medical and non-medical countermeasures make EIDs a threat to global human and animal health. Fear of spread, travel restrictions, and unpredictable self-imposed avoidance of a region can cause serious socio-economic disruptions on local and global level (McCloskey *et al.*, 2014).

Drivers of (Emerging) Zoonotic Diseases

Infectious disease emergence has proven extremely challenging to predict, and human cases of a wide range of emerging or re-emerging pathogens have been reported all over the world and throughout the year. However, when outbreak data of emerging disease outbreaks in the last decades are combined, some specific conditions or risk factors seem to drive disease emergence (Woolhouse, 2011). The main general drivers that have been described can be summarized as changes in (1) human demographics with the consequential growing demand for food production (Jones *et al.*, 2008), (2) land use, including agricultural changes (Jones *et al.*, 2013; Gortazar *et al.*, 2014) (3) international travel and trade (Gortazar *et al.*, 2014; Randolph and Rogers, 2010), (4) climate change and weather (Allen *et al.*, 2017; Gortazar *et al.*, 2014) (**Fig. 1**).

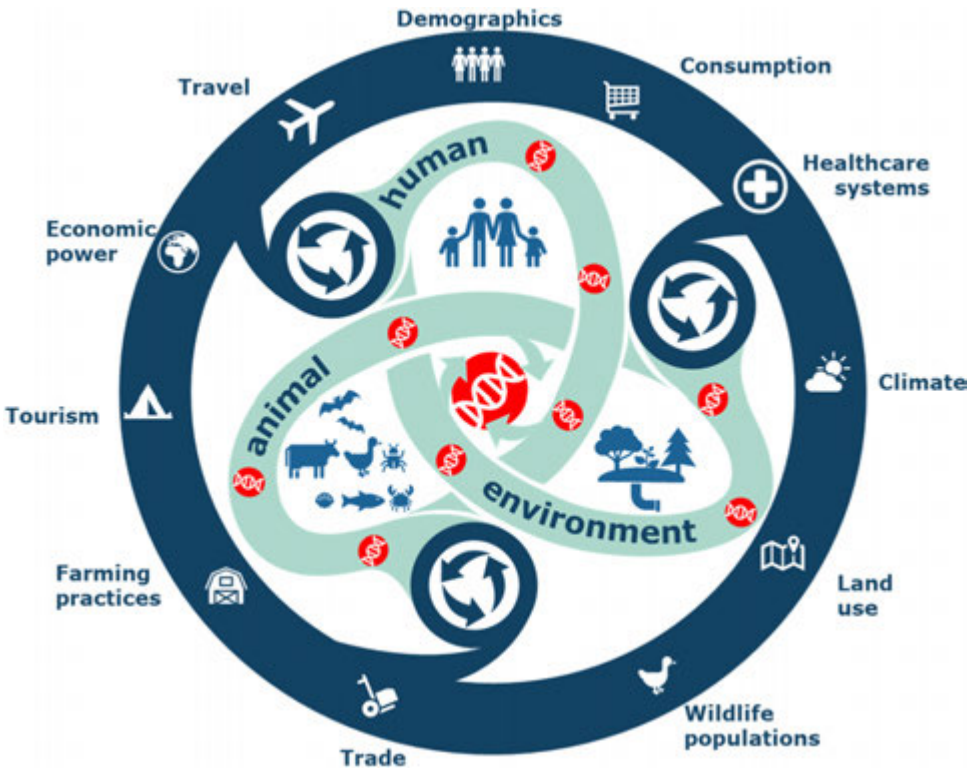

Fig. 1 Global changes acting as drivers of infectious disease emergence and spread in the One Health domains.

 doi:10.1016/B978-0-12-814515-9.00150-8

In the case of zoonotic EIDs, the first step towards an outbreak of human disease or mortality is the occurrence of spill-over of a pathogen from an animal reservoir host to humans. (Plowright *et al.*, 2017; Karesh *et al.*, 2012; Petersen *et al.*, 2018). The majority of human EIDs originate from wildlife (Jones *et al.*, 2008; Allen *et al.*, 2017). However, humans are usually not in close contact with wildlife. Therefore, occasionally there is an additional intermediate host species involved where a pathogen is amplified and that is in closer contact with humans (Karesh *et al.*, 2012; Plowright *et al.*, 2015). Well known examples are Nipah virus, Hendra virus or SARS-CoV, that originate from bats and amplify in pigs, horses and civet cats used as food source, respectively (Plowright *et al.*, 2015). The risk of animal to human spill-over depends on a plethora of factors. The aforementioned drivers of disease emergence create circumstances that facilitate such spill-over. Additionally, the risk of spillover is influenced by the pathogen itself. In general, RNA viruses are zoonotic more often than DNA viruses (Olival *et al.*, 2017). A possible explanation for this is their genetic plasticity, caused by the replication mechanism: most RNA viruses replicate with the use of virus-encoded RNA polymerases which – in contrast to the host cell DNA polymerase- do not have so-called proof-reading capacity. Proofreading is a mechanism to reduce the amount of errors in the nascent strands of newly produced copies of (pathogen) genomes, and the lack of proofreading leads to copies that contain a higher number of mutations when comparing the progeny genomes with those of the parent sequences. As a consequence, hosts infected with such RNA viruses shed a mutant swarm of viruses. When they then encounter a bottleneck, for instance an exposure of a new host, chances are that within the swarm variants exist that are better adapted (by chance) to infect a new host (Domingo and Perales, 2019).

One possible consequence of this flexibility is described as "phylogenetic host breadth" and "host plasticity", which reflect the diversity of known hosts, and therefore are significant predicting factors for zoonotic potential of viruses (Olival *et al.*, 2017; Kreuder Johnson *et al.*, 2015). Additionally, the dynamics of a pathogen in a reservoir host population is a very important factor for human health risk, and is governed by population structure, host density, host behavior and contact patterns, shedding patterns, stability of pathogens outside a host, levels of immunity, events that stress the population, and more. As a consequence, the resulting risk of infection for humans may vary depending on season, location, weather and host distribution for example (Plowright *et al.*, 2017; Karesh *et al.*, 2012).

The second step towards outbreaks of emerging diseases is the ability of a pathogen to transmit between humans. In general, it is thought to be less likely that enveloped viruses and segmented viruses are associated with human-to-human transmission, similar to viruses with acute durations of infection but the evidence for that is largely observational and certainly not black and white (Geoghegan *et al.*, 2016; Walker *et al.*, 2018). For instance, the majority of top ranking epidemic and pandemic threats listed by the world health organization (WHO) are enveloped viruses ("see Relevant Websites section"). Viral host plasticity is not only associated with spill-over but also increases the risk of human-to-human transmission and international spread (Kreuder Johnson *et al.*, 2015). Moreover, the increased interconnectivity and the overall increase of the human population facilitate rapid spread of novel pathogens.

Disease X

A recent report by the Global Preparedness Monitoring Board warned that a global Influenza pandemic, similar to the 1918 Spanish flu, could spread around the world within 36–50 h, and would take the lives of 50–80 million people. Such an epidemic could destroy nearly 5% of the global economy ("see Relevant Websites section"). The examples of Ebola, SARS, and avian influenza have shown that zoonotic disease outbreaks can be very disruptive because of fear for spread and uncertainty of how to contain them even when there is limited onward transmission (Bartsch *et al.*, 2015; Qiu *et al.*, 2018). ("see Relevant Websites section"). The devastating Ebola outbreak in West Africa in 2014–1015 led to a specific call for action by the members of the World Health Assembly, charging the WHO to come up with a new vision to be better prepared for the future, given the increasing likelihood of such outbreaks. A list of priority diseases was developed, for which an urgent need for accelerated research and development of countermeasures was identified, due to their potential to cause a public health emergency. ("see Relevant Websites section"). In an update in 2018, the term disease X was used to describe a serious international epidemic caused by a pathogen currently unknown to cause human disease. The rationale behind the inclusion of disease X is that a completely unknown disease etiology limits the ability for development of fast track diagnostics, vaccines and therapeutics. Therefore, preparedness and response in case of disease X requires a significantly different approach compared to the other diseases on the list.

According to the International Health Regulations, WHO Member States are obliged to maintain effective disease surveillance and laboratory systems and to report newly emerging diseases that could spread internationally ("see Relevant Websites section"). However, setting up surveillance for diseases that are still unknown is complicated, and extensive surveillance can be costly, especially in the case of diseases that emerge at the human-animal interface. The disease X track therefore is thought to stimulate thinking in terms of generic solutions that increase EID preparedness.

Emerging Disease Detection and the One Health Concept

A key component of early control of emerging diseases is their early detection (Bonacic Marinovic *et al.*, 2014; Chan *et al.*, 2010). As part of the WHO Blueprint initiative, the need for diagnostics for the priority diseases has been stressed. The West African Ebola virus outbreak in 2014 had already disseminated widely into three countries by the time it was confirmed by an international

laboratory, almost 4 months after the index case succumbed to the disease (Baize *et al.*, 2014; Coltart *et al.*, 2017). Similarly, phylogenetic reconstruction of Zika in the Americas predated the time of introduction to almost two years before it was recognized as a health emergency (Thézé *et al.*, 2018). Although easily criticized, the delays in disease detection are not surprising as symptoms of most EID are not specific, and overlap with major "common" diseases that clinicians are familiar with (Sigfrid *et al.*, 2018). Similarly, clinical diagnostic laboratories focus on these common conditions, and may not have the expertize to detect rare and novel causes of disease (Sigfrid *et al.*, 2018). Efforts to increase preparedness for EID are increasingly moving towards risk-based early detection. As most EID come from animal reservoirs, the need for this has reinvigorated the One Health approach.

The concept of One Health is described by the US Center of Disease Control (CDC) as follows: "*One Health recognizes that the health of people is connected to the health of animals and the environment. It is a collaborative, multisectoral, and transdisciplinary approach—working at the local, regional, national, and global levels—with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment.*" Although the concept has already been known since Hippocrates launched his theories on human health around 400 BCE ("On Airs, Waters, and Places"; Aristotle "Historia Animalium") The specific term "One Health" however only came up in the 21st century (Evans and Leighton, 2014; Sikkema and Koopmans, 2016). Since then, the One Health concept is increasingly being endorsed and implemented in national and international policy and research. An important milestone was the publication of the FAO-OIE-WHO tripartite concept note, on "Collaboration, sharing responsibilities and coordinating global activities to address health risks at the animal-human-ecosystems interfaces" ("see Relevant Websites section") Also, the number of scientific publications that mention the term "One Health" showed a major increase in the recent decade (Sikkema and Koopmans, 2016). Although in practice true integration of information and collaboration between different sectors still proves to be challenging (Sikkema and Koopmans, 2016; Farag *et al.*, 2019; Dos *et al.*, 2019; Manlove *et al.*, 2016), the implementation of the One Health concept has great potential for EID preparedness and response.

Moreover, there has been a vast increase of (digital) data in the past decade that has great potential to be used for zoonotic disease prediction, early detection and control (Becker *et al.*, 2019; Masri *et al.*, 2019). This is not only caused by the shift of traditional diagnostics to multi-analyte technologies such as next generation sequencing, but also by the large increase of for example environmental, financial and social media information collection (Simonsen *et al.*, 2016; Shi and Wang, 2019). However, the use of this "Big Data" with different data types of multiple origins also makes the analysis much more challenging (Khoury and Ioannidis, 2014). The use of big data has been advocated and explored in some aspects of public health and infectious disease prediction, but this is also mostly restricted to only one of the required domains (clinical, public health, academia) or sectors (human health, animal health, environmental health, informatics, artificial intelligence) instead of a true crosscutting One Health analysis. Moreover, this, again, calls for multidisciplinary collaborations, since the traditional expertize involved in One Health or Public Health, such as veterinary or medical specialists or epidemiologists, generally do not have sufficient experience in working with such large and diverse data sets.

Developing Targeted, Risk Based Sampling

To identify risk areas, or so-called hotspots of disease emergence or spread, both knowledge of possible drivers or risk factors for emergence can be used, as well as detailed spatial and quantitative information on these drivers, for example locations where ecosystem disruptions took place or where farming systems or livestock population sizes have gone through significant changes. Other information, that could be mapped to identify risk areas for known and unknown diseases are vectors, animal reservoirs, human population, habitat and climate. ("see Relevant Websites section"). There are currently many open-access databases available online, that contain information that has great potential to be used for zoonotic disease prediction, early detection and control. Examples of currently available information are: animal tracking data (Tian *et al.*, 2015) ("see Relevant Websites section"; "see Relevant Websites section" United States Geological Survey), animal and human outbreak information (Cauchemez *et al.*, 2014) (WAHID; ADNS; WHO), animal populations and trade (Simons *et al.*, 2016) (FAOSTAT), weather and climate (Ryan *et al.*, 2015) (NASA; ECA&D; USGS FEWS NET), country economic data (Farag *et al.*, 2018) (World Bank) and many others.

After defining geographical hotspot areas, risk of EID outbreaks also requires a detailed understanding of human and animal populations at risk. For example, past research indicates that humans in contact with animals, especially in the case of wildlife or animal populations that experienced changes in husbandry, population size or other characteristics are at a higher risk of infection with an (emerging) zoonotic pathogen (Jones *et al.*, 2008; Jones *et al.*, 2013; Allen *et al.*, 2017). However, the intensity and nature of the human-animal interface differs greatly, depending on animal species, animal husbandry systems, eating habits, traditions, etc. Additionally, with human demography, migration and travel, current populations and communities are no longer homogeneous or isolated. Selecting a human population at-risk therefore is complex and people-at-risk move in an increasingly large geographical area. ("see Relevant Websites section").

Therefore, there is an increasing need and necessity to tailor surveillance and risk predictions to local circumstances. This calls for the inclusion of social sciences in disease surveillance and infectious disease preparedness (Bedford *et al.*, 2019). ("see Relevant Websites section").

Animal trading patterns and common practices surrounding animal trading have been shown to be particularly important factors in the spread of zoonotic infectious diseases. Livestock farming has undergone massive changes and expansion in the past decades, with increasing international trade ("see Relevant Websites section"). Increasing size and connectivity of the trading networks, including human contacts such as farmers, traders and consumers, result in increased risks of disease transmission and

spread ("see Relevant Websites section"). Within the poultry production sector, for example, there are large differences between large scale, intensive industrialized production systems and traditional small-scale rural poultry production systems, and associated animal and public health risks. The main type of production system, as well as the organization of the trade chain, and the degree and frequency of human and wildlife contact differs greatly between regions. In South East Asia, the majority of poultry is reared in backyard farms, with complicated subsequent trade chains, involving many traders and live poultry markets (Moyen *et al.*, 2018; Sealy *et al.*, 2019). This influences infectious disease risk and possible spread. Farms that keep their poultry outdoors generally have a higher chance of AI outbreaks, because of their contact with wild birds (Bouwstra *et al.*, 2017; Wibawa *et al.*, 2018). Moreover, trading involving middlemen is associated with higher likelihood of AI spread, as well as density of live-poultry markets (Sealy *et al.*, 2019; Gilbert *et al.*, 2014) Also, it has been shown that the prevalence and risk of infectious diseases, such as AI, differs per stage of the poultry supply chain (Wu *et al.*, 2019). In other regions of the world, such as Europe and the US, backyard farms and live animal markets are very uncommon, and poultry is often transported directly from farm to slaughterhouse. Therefore, risk profiles and set-up of surveillance differ greatly between farming and trading systems in different geographical areas, and detailed information on the local situation is crucial (Martin *et al.*, 2011; Delabouglise *et al.*, 2017). This is not only important for livestock and poultry, but wildlife and wildlife product trading can also pose a significant risk of infectious disease introduction and spread ("see Relevant Websites section") (Smith *et al.*, 2012).

Also, habits and behaviors of humans around animals matter. Live bird markets are not only a risk for AI transmission because of mixing of birds of different origins and species but also because of particular preferences in some regions for fresh poultry meat and on-site slaughtering (Zhou *et al.*, 2015). In-depth knowledge of (cultural) habits and their history, has proven to be extremely valuable in outbreak investigations of emerging diseases. Case investigations of a Nipah outbreak in humans in Bangladesh in 2004–2005 involved anthropological expertize that was used for in-depth interviews and questionnaires in local language to gain knowledge on possible exposures and risk behaviors. It became clear that drinking raw date palm sap was significantly associated with disease. Several interviews pointed towards fruit bats (Pteropus giganteus) as probable source of infection as they drink from the sap collection pots during the night, contaminating the sap with their infectious saliva. (Luby *et al.*, 2006; Halpin *et al.*, 2011). Infrared cameras captured fruit bats feeding on palm sap collection devices, and urinating when flying away, thus potentially contaminating the sap with viruses (Halpin *et al.*, 2011). Protecting the collection devices by a simple bamboo barrier rather than a ban on drinking palm sap was accepted by the local population as intervention (Nahar *et al.*, 2017).

MERS-CoV is another example of a disease where an inventory of the local situation revealed very specific traditions and behaviors around dromedary camels, the reservoir host of the virus. Camel racing and associated movement and mixing of camels is thought to be an important risk factor for spread (Farag *et al.*, 2018). Moreover, local customs involve kissing camels, and drinking raw camel milk and urine, all of which should be considered in the investigations of MERS-CoV (Farag *et al.*, 2018; Gossner *et al.*, 2016) Only with extensive knowledge about the history and background of specific risk behaviors, a strategy to discourage or reduce such behavior can be developed. Another clear example of high risk behavior that has proven to be very difficult to change, are burial rituals in Western Africa, that greatly increase the number of people infected with Ebola in times of an outbreak (Masumbuko Claude *et al.*, 2019). The family and community members of the deceased person touch and wash the bodies before the funeral, which has caused a large number of secondary infections because of their contact with Ebola infected bodily fluids (Nielsen *et al.*, 2015).

Sample Collection

Appropriate sample collection is essential for reliable surveillance and outbreak investigations. If human, animal or environmental samples are not collected and stored in a technically appropriate manner, subsequent laboratory analyses will not be reliable or will not generate the anticipated results. A deep understanding of kinetics of shedding of a pathogen and of the antibody response is important to decide on the optimal sampling protocol, the use of detection methods and the interpretation of results. Moreover, subject selection (especially in an outbreak situation), appropriate sample type and sufficient and timely metadata collections are all crucial for subsequent analyses. In addition, to be able to compare data between studies or between countries, laboratory analyses, information collection and study designs should be standardized. For example, comparing human serological data to assess zoonotic influenza exposure has proven to be very difficult because there are significant differences between studies when assessing the collection of epidemiological data, laboratory methods used and the study population, amongst other things (Sikkema *et al.*, 2016). Therefore, international organizations and laboratory networks are increasing their efforts to publish guidelines and training materials to stimulate a uniform approach to investigate infectious diseases and increase the comparability of surveillance and research.

Not only diagnostic testing methods and quality are carefully assessed and compared (Reusken *et al.*, 2015; Charrel *et al.*, 2017; Pas *et al.*, 2015) ("see Relevant Websites section") but also the standardized collection of metadata is increasingly important in the era of big data and NGS, for correct interpretation and analysis of the large amount of data that is generated. Therefore, standardized epidemiological questionnaires are being developed and published alongside of the guidelines for infectious disease diagnosis. In practice, complete and timely collection of metadata proves to be challenging. When routine diagnostic data in the Netherlands was assessed for its use for surveillance of arboviral infection in travelers, researchers found that essential information such as vaccination history was only reported in 0.4%, and travel destination was completed in only 42% of patient dossiers

(Cleton *et al.*, 2014). Especially during outbreaks, medical records and associated epidemiological information is often incomplete or absent. This has been illustrated for example in Sierra Leone during the Ebola outbreak (Owada *et al.*, 2016).

Examples of efforts to standardize infectious disease surveillance and clinical research are the global Consortium for the Standardization of Influenza Seroepidemiology (CONSISE) that is aiming to standardize influenza sero-epidemiology and develop investigation protocols ("see Relevant Websites section") and the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC), a federation of clinical research networks, providing tools and protocols for research response to outbreak-prone infectious disease ("see Relevant Websites section"). Moreover, the WHO, FAO and OIE publish extensive laboratory diagnosis guidelines and are involved in training and capacity building activities.

The Value of Non-Invasive and Bulk Samples

Although smart, risk-based strategies can be developed to optimize sampling efficiency, reliable disease monitoring, especially in the case of emerging diseases, requires a huge sample size to reach sufficient population and/or geographical representation. Traditional surveillance of humans and animals make use of invasive sampling, to screen blood samples or swabs for pathogens. However, the use of such samples needs medical-ethical approval that is increasingly difficult to obtain, as well as approval for animal population studies and experiments. Additionally, invasive sampling can cause significant discomfort, can pose an additional risk for infection of healthcare workers or animal care-takers and can only be executed by specialists in the human or veterinary field. Therefore, setting up and validating surveillance using non-invasive sampling can potentially be easier to execute and to scale up as well as better for human and animal welfare.

Feces or urine collection and testing can be a practical and animal friendly surveillance method. Especially in the case of wildlife, where catching and sampling animals can be particularly stressful for an animal, fecal or urine surveillance is very suitable. Feces, or even urine, can be collected without handling the animal or even be in the vicinity at the time of sample collection. This has been described for multiple pathogens, such as Lyssaviruses and Paramyxovirus in bats (Begeman *et al.*, 2020; Peel *et al.*, 2019) and tapeworms in foxes (Umhang *et al.*, 2016). In humans, there may also be a large number of pathogens that can be detected via saliva, urine or feces, although it is generally not included in standard diagnostic algorithms (Niedrig *et al.*, 2018).

Although alternative, non-invasive sample types increase the ease of sample collection and welfare of the sampled subject, the number of samples will not decrease. Therefore, validation of pooled samples or novel sample types that can be used to monitor groups or populations of humans, animals or a certain geographical area. In Asia, environmental surveillance of live animal markets is routinely implemented as main means of monitoring of Avian Influenza viruses (Bai *et al.*, 2019; Henning *et al.*, 2019; Khan *et al.*, 2018). Various surfaces, such as poultry cages, chopping boards and defeathering machines, are sampled and tested on a regular basis as an indirect measure of poultry infections and public health risk. Similarly, environmental sampling are also being used for the detection of pathogens in healthcare settings (Kim *et al.*, 2016; Kapetshi *et al.*, 2018). Additionally, air sampling may be promising, both in hospital settings, farms and even markets and airports (Scoizec *et al.*, 2018; Zhou *et al.*, 2016; Bailey *et al.*, 2018).

Sewage or wastewater monitoring is another example of such a sample type, that can be used to monitor infectious diseases of large numbers of humans. Sewage monitoring has already been used for many years to monitor polio (Asghar *et al.*, 2014) as well as the monitoring and detection of emerging Norovirus and Enterovirus strains (Mabasa *et al.*, 2018; Majumdar and Martin, 2018). However, sewage could have great potential to be used for virus discovery and emerging disease detection (Fernandez-Cassi *et al.*, 2018; Nordahl Petersen *et al.*, 2015). Other sample types, representing large numbers of animals, that can be can be used to monitor circulating of pathogens are: manure composting plants, bulk milk and ponds (Himsworth *et al.*, 2019; Garcia *et al.*, 2014; Balmer *et al.*, 2014).

However, the use of non-invasive sampling or pooled sample types may impact the sensitivity of pathogen detection. In the case of non-invasive sampling, each pathogen may have different shedding characteristics, making it impossible to know the optimal sample type to detect emerging diseases. This also impacts the use of sewage for emerging disease surveillance, for example, because not all pathogens are excreted via feces or urine, making it difficult to detect via sewage sampling.

Catch-All Detection Methods

A challenge for risk-based surveillance is the huge potential diversity of pathogens that could cause human disease when spilling over from an animal reservoir. Therefore, even if targeting detection efforts through the approaches described above would succeed, the choice of diagnostic method is a critical one. Depending on how the risk-based surveillance was organized, the choice of potential pathogens to target may be limited or more extensive. An interesting development is the use of unbiased third-generation metagenomic sequencing to characterize all genomic material (DNA and RNA) in a sample, without prior knowledge of possible etiologies. Clinical and environmental samples can be processed with procedures that either enrich for bacteria, parasites or viruses, and subsequently be subjected to sequencing (Wilson *et al.*, 2019; Takhampunya *et al.*, 2019; Zolfo *et al.*, 2018; Nieuwenhuijse and Koopmans, 2017; Hendriksen *et al.*, 2019).

Analysis generally takes place by assembly of sequence reads and annotating the resulting reads using reference databases of (publicly) known sequences. The metagenomics research field, studying and profiling genetic material abundance in diverse matrices and environments is rapidly growing, as well as the number of novel viruses that are being discovered and described (Simmonds and Aiewsakun, 2018). Often the aim of metagenomics studies of the environment is to map all micro-organisms in

potential reservoirs in order to identify potential human health threats (Carroll *et al.*, 2018). However, all viruses that have been characterized to date likely only make up a minor fraction (estimated to be around 0.005%) of the estimated total number of viruses on earth (Geoghegan and Holmes, 2017). This means that the number of new viruses and virus families will increase immensely in the coming years. Moreover, the lack of closely related reference virus genomes makes public health risk assessment of novel viruses very complicated (Geoghegan and Holmes, 2017). Moreover, even if viruses belong to a known virus family with known human viruses, this does not necessarily mean that there is a risk of spill-over.

From Genotype to Phenotype: Deriving Meaningful Information From Genomic Data

The pathogen genomic sequence alone will often give insufficient information on possible human health risks. Therefore, ideally, metagenomics or NGS approaches are supplemented with phenotypic data such as antigenic characteristics, pathogenicity, virulence, host-specificity and transmission characteristics. For novel variants of known viruses, some indications of phenotype or zoonotic risks can be derived from the sequence, based on experimental study outcomes. The impact of inferring phenotype traits from genotype data can be exemplified by the "H5N1 inventory" compiled by the United States Centers for Disease Control ("see Relevant Websites section"). This inventory summarizes all mutations that have been shown to affect virus replication, virulence, tissue or cellular tropism, host-range, transmission, antigenic properties, immune escape, and antiviral drug resistance.

However, in the case of an emerging virus that was previously unknown, novel phenotypic data needs to be generated. This data is important for risk assessment, but information on potentially relevant sequences or epitopes can also be used for development of diagnostics and preventive antiviral strategies. For example, one of the key components influencing ability to spread for an emerging pathogen from a spill-over event is the level of measured or predicted immunity in the population, as this impacts on the likelihood of infection of individuals (humans, livestock, wildlife) and their ability to shed and spread the infection.

In silico epitope prediction can predict B-cell epitopes based on sequence data (Potocnakova *et al.*, 2016). The predicted immunogenic virus proteins can then be used to set up serological assays to determine the prevalence and host range of the virus. For this, multiplex antigen arrays can be used to not only measure antibodies to the newly identified antigen, but also to (distantly) related variants of the same virus family, thus providing information on potential cross-protection or disease enhancing antibodies (Mina *et al.*, 2019; Cleton *et al.*, 2017; Freidl *et al.*, 2015). Possible resistance markers can be predicted when analyzing the sequences, for instance for drugs targeting the polymerase or protease genes. Host binding motifs can be predicted from their location on predicted protein structures. However, all such inferences need to be validated as the choice of in vitro systems and animal models can have a significant impact on their validity (Rothenburg and Brennan, 2020; Setoh *et al.*, 2019; Reyes-Ruiz *et al.*, 2019).

Conclusion

The risk of emergence of novel human pathogens has increased in the past decades. Early detection is becoming even more important due to the potential rapid spread and impact considering the ever increasing size of human and animal populations and their movements all over the globe. The unpredictable nature of emergence of diseases makes surveillance and preparedness a huge challenge. However, recent history has shown that outbreaks of emerging diseases will happen again, and all sectors involved in infectious disease surveillance and response need to be ready to detect and handle the next disease X. It has been argued that the design of infectious disease surveillance and response should therefore move from crisis response to true integration and evaluation of a strategy to detect and control emerging diseases (Bedford *et al.*, 2019). This involves a One Health approach, integrating not only the humans, animal and environmental health sectors, but also social sciences, bioinformatics and more. Technical developments in recent years, such as the use of Big Data and metagenomic sequencing will aid the rapid detection of novel pathogens on the human-animal interface.

Note Added in Proof: December 2020

SARS-CoV-2

In December 2019 several cases of pneumonia of unexplained etiology in patients in Wuhan city (China) linked to a seafood wholesale market were reported to the WHO ("see Relevant Websites section"). In the beginning of 2020 it became clear that this Disease X that had emerged was also a betacoronavirus, most closely related to SARS, that was already on the WHO Blueprint priority list in public health emergency contexts ("see Relevant Websites section"). In the following months the outbreak developed into a pandemic, with over 68 million human cases and 1,55 million deaths, as of 8 December 2020 (Dong *et al.*, 2020).

One Health and Animal Reservoirs

Bats are known to harbor a range of different coronaviruses (Cui *et al.*, 2019). Indeed, closely related SARS-like viruses have previously been detected in horse shoe bats, in China (Zhou *et al.*, 2020; Hu *et al.*, 2018). However, although the SARS-CoV-2 genome is 96% identical to the closest bat sequence, the genetic distance between the closest horseshoe bat SARS-like coronavirus

and SARS-COV-2 likely reflects several years and even decades of virus evolution (Boni *et al.*, 2020). SARS-related coronaviruses are also found in pangolins, where specifically the RBD domain is closely related to SARS-CoV-2 (Boni *et al.*, 2020). Therefore, the role of bats as SARS-CoV-2 reservoir remains to be proven and other mammalian species are considered as possible intermediate hosts, as was previously the case for SARS, MERS and Nipah (Epstein *et al.*, 2006; Wang *et al.*, 2005; Reusken *et al.*, 2013). To date, an animal intermediate host of SARS-CoV-2 has not been found yet ("see Relevant Websites section").

However, multiple animal species are found to be susceptible for SARS-CoV-2. Ferrets, raccoon dogs, cats and hamsters show infection and virus replication after experimental infection as well as the ability to transmit the virus (Shi *et al.*, 2020; Richard *et al.*, 2020; Sia *et al.*, 2020; Freuling *et al.*, 2020). Other animals that showed infection after experimental inoculation include rabbits, dogs and tree shrews (Shi *et al.*, 2020; Mykytyn *et al.*, 2020; Bosco-Lauth *et al.*, 2020). Additionally, animal infections have been detected in the field, mainly in dogs, cats and mink (Sit *et al.*, 2020; Barrs *et al.*, 2020). Although there is evidence for efficient transmission between cats, infection in these animals is not considered a major concern given the small numbers of animals in households. This is different for the recent outbreaks in mink farms in Europe and the US (Cahan, 2020), with the first described SARS-CoV-2 animal-to-human transmissions (Oude Munnink *et al.*, 2020b). These outbreaks were the first large scale outbreaks in animal populations, and large scale mink passages have specifically sparked concern on the risk of specific mutations, affecting virus properties and possibly resulting in immune escape (Koopmans, 2020).

The multiple susceptible animal species and the search for the original animal reservoir, that was at the origin of the SARS-CoV-2 pandemic, clearly shows the need for a One Health approach. Introductions of SARS-CoV-2 into susceptible animal populations can continue to occur, possible resulting in (additional) animal reservoirs and virus evolution and the risk of continuing evolution and spill backs into the human population (Koopmans, 2020; Olival *et al.*, 2020). Therefore, collaboration between different disciplines remains crucial in monitoring, understanding and containing the SARS-CoV-2 pandemic as well as many other (emerging) pathogens.

Emerging Disease Detection, Full Genome Sequencing and Rapid Data Sharing

The Chinese authorities officially announced the isolation of a novel coronavirus (2019-nCoV) as the causative agent on 7 January 2020 ("see Relevant Websites section") and the full sequence was released in a publicly accessible discussion forum ("see Relevant Websites section") 5 days later ("see Relevant Websites section"). Four other sequences were shared on 12 January in the Global Initiative on Sharing All Influenza Data (GISAID) database. A validated real-time RT-PCR assay was developed, validated and published online only 5 days later, on 17 January 2020, and published for PCR validation in a peer-reviewed journal on the 23rd of January ("see Relevant Websites section") (Corman *et al.*, 2020). Validation panels were available on the European Virus Archive ("see Relevant Websites section") shortly after. The first validated serological assay followed early April (Okba *et al.*, 2020). This clearly illustrates the technical progress that has been made in the last 17 years, as well as the value of virus sequencing and rapid data and sample sharing.

Samples of the first patients in Wuhan city were sequenced using an unbiased deep meta-transcriptomic sequencing method (Wu *et al.*, 2020). When the sequence was known, amplicon-based methods were developed to sequence the new virus in a timely and sensitive manner ((Oude Munnink *et al.*, 2020a) "see Relevant Websites section") Whole genome sequencing was performed at unprecedented scale, with almost 250.000 SARS-CoV-2 whole genome sequences that had been shared on the GISAID platform as of 8 December 2020. The timely release of unpublished genomic information through GISAID was essential for fast track development of diagnostics, vaccines and therapeutics as well as the application of WGS in outbreak investigation and public health control measures (Oude Munnink *et al.*, 2020a; Voeten *et al.*, 2020).

With the ever-increasing numbers of sequences that are being generated, the need for rapid characterization of viruses with specific mutations remains high. A high number of papers are published describing the evolution and mutations in the SARS-CoV-2 genome, but assessing the relevance and effect on virus properties, and, consequently, public health, is still challenging (Grubaugh *et al.*, 2020).

Population Surveys and Sero-epidemiological Studies

Serologic studies can provide important information for understanding the extent of past transmission, the current state of the epidemic, and future transmission in an affected population. Moreover, serology is a very useful tool on the human-animal interface (Wernike *et al.*, 2020). It can be used to screen potential animal reservoirs, as has been used to determine the likely reservoir species for MERS-CoV, (Reusken *et al.*, 2013; Deng *et al.*, 2020). Serological surveys in several animal species did not point towards the SARS-CoV-2 animal reservoir species, but did show significant exposure of dogs and cats in Wuhan and Italy, which were severely affected by SARS-CoV-2 (Zhang *et al.*, 2020; Patterson *et al.*, 2020). Also, serological assays can be an additional tool to gain insight in the potential and scale of animal-to-human transmission, when combined with epidemiological information on exposure, as was done for mink farm employees on SARS-CoV-2 on infected mink farms (Oude Munnink *et al.*, 2020b; Sikkema *et al.*, 2016). However, it is important to realize that coronaviruses including betacoronaviruses are common in many animal species, and can result in cross reactivity and false positives (Franzo *et al.*, 2020; Nemoto *et al.*, 2019; Erles and Brownlie, 2008).

In addition to patient diagnostics and surveillance efforts in symptomatic and asymptomatic individuals, wastewater sampling can be used to monitor the circulation of SARS-CoV-2 in the population (Medema *et al.*, 2020; Hart and Halden, 2020). This approach is currently integrated in the national COVID-19 surveillance in multiple counties ("see Relevant Websites section").

Concluding Remarks

With the emergence and worldwide spread of a novel coronavirus, the disease X scenario that many scientists had warned about came true. The SARS-CoV-2 pandemic lead to drastic government measures worldwide, with massive economic and social consequences. The spread of the virus has proven to be difficult to contain, despite extensive lockdowns, information campaigns, travel bans and compulsory mouth masks. However, previous investments in surveillance, diagnostics, novel laboratory techniques, open data sharing and vaccine platforms did pay off. A cluster of pneumonia of unknown origin was detected in December 2019 in Wuhan, and at the end of January 2020, a set of whole genomes are publicly shared and a validated PCR assay has been set up which was implemented in 24 of 30 EU/EEA countries and many more worldwide (Reusken *et al.*, 2020). Moreover, in December 2020, the first COVID-19 vaccine was licensed ("see Relevant Websites section"). The speed of these key developments in the surveillance and control of the new virus is unprecedented. How the SARS-CoV-2 pandemic will evolve remains to be seen, but recent developments reinforce the call for preparedness research and a One Health approach, as highlighted in the current article.

References

Allen, T., *et al.*, 2017. Global hotspots and correlates of emerging zoonotic diseases. Nature Communications 8 (1), 1124.
Asghar, H., *et al.*, 2014. Environmental surveillance for polioviruses in the Global Polio Eradication Initiative. The Journal of Infectious Diseases 210 (Suppl 1), S294–S303.
Bai, R., *et al.*, 2019. Antigenic variation of avian influenza A(H5N6) viruses, Guangdong Province, China, 2014-2018. Emerging Infectious Diseases 25 (10), 1932–1945.
Bailey, E.S., *et al.*, 2018. Molecular surveillance of respiratory viruses with bioaerosol sampling in an airport. Tropical Diseases, Travel Medicine and Vaccines 4, 11.
Baize, S., *et al.*, 2014. Emergence of Zaire Ebola virus disease in Guinea. The New England Journal of Medicine 371 (15), 1418–1425.
Balmer, S., *et al.*, 2014. Serosurveillance of Schmallenberg virus in Switzerland using bulk tank milk samples. Preventive Veterinary Medicine 116 (4), 370–379.
Barrs, V.R., Peiris, M., Tam, K.W.S., *et al.*, 2020. SARS-CoV-2 in Quarantined Domestic Cats from COVID-19 Households or Close Contacts, Hong Kong, China. Emerging Infectious Diseases 26 (12), 3071–3074.
Bartsch, S.M., Gorham, K., Lee, B.Y., 2015. The cost of an Ebola case. Pathogens and Global Health 109 (1), 4–9.
Becker, D.J., *et al.*, 2019. Dynamic and integrative approaches to understanding pathogen spillover. Philosophical Transactions of the Royal Society B: Biological Sciences 374 (1782), 20190014.
Bedford, J., *et al.*, 2019. A new twenty-first century science for effective epidemic response. Nature 575 (7781), 130–136.
Begeman, L., *et al.*, 2020. Faeces as a novel material to estimate lyssavirus prevalence in bat populations. Zoonoses and Public Health 67, 198–202.
Bonacic Marinovic, A.A.,., *et al.*, 2014. Speed versus coverage trade off in targeted interventions during an outbreak. Epidemics 8, 28–40.
Boni, M.F., Lemey, P., Jiang, X., *et al.*, 2020. Evolutionary origins of the SARS-CoV-2 sarbecovirus lineage responsible for the COVID-19 pandemic. Nature Microbiology 5 (11), 1408–1417.
Bosco-Lauth, A.M., Hartwig, A.E., Porter, S.M., *et al.*, 2020. Experimental infection of domestic dogs and cats with SARS-CoV-2: Pathogenesis, transmission, and response to reexposure in cats. Proceedings of the National Academy of Sciences of the United States of America 117 (42), 26382–26388.
Bouwstra, R., *et al.*, 2017. Risk for low pathogenicity avian influenza virus on poultry farms, the Netherlands, 2007-2013. Emerging Infectious Diseases 23 (9), 1510–1516.
Cahan, E., 2020. COVID-19 hits US mink farms after ripping through Europe. Science. 10.
Carroll, D., *et al.*, 2018. The Global Virome Project. Science 359 (6378), 872–874.
Cauchemez, S., *et al.*, 2014. Middle East respiratory syndrome coronavirus: Quantification of the extent of the epidemic, surveillance biases, and transmissibility. Lancet Infectious Diseases 14 (1), 50–56.
Chan, E.H., *et al.*, 2010. Global capacity for emerging infectious disease detection. Proceedings of the National Academy of Sciences of the United States of America 107 (50), 21701–21706.
Charrel, R., *et al.*, 2017. Variable sensitivity in molecular detection of Zika virus in European expert laboratories: External quality assessment, November 2016. Journal of Clinical Microbiology 55 (11), 3219–3226.
Cleton, N., *et al.*, 2014. Using routine diagnostic data as a method of surveillance of arboviral infection in travellers: A comparative analysis with a focus on dengue. Travel Medicine and Infectious Disease 12 (2), 159–166.
Cleton, N.B., *et al.*, 2017. A serological protein microarray for detection of multiple cross-reactive flavivirus infections in horses for veterinary and public health surveillance. Transboundary and Emerging Diseases 64 (6), 1801–1812.
Coltart, C.E.M., *et al.*, 2017. The Ebola outbreak, 2013-2016: Old lessons for new epidemics. Philosophical Transactions of the Royal Society of London Series B, Biological Sciences 372 (1721), 20160297.
Corman, V.M., Landt, O., Kaiser, M., *et al.*, 2020. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Eurosurveillance 25 (3).
Cui, J., Li, F., Shi, Z.L., 2019. Origin and evolution of pathogenic coronaviruses. Nature Reviews Microbiology 17 (3), 181–192.
Delabouglise, A., *et al.*, 2017. Cultural practices shaping zoonotic diseases surveillance: The case of highly pathogenic avian influenza and Thailand native chicken farmers. Transboundary and Emerging Diseases 64 (4), 1294–1305.
Deng, J., Jin, Y., Liu, Y., *et al.*, 2020. Serological survey of SARS-CoV-2 for experimental, domestic, companion and wild animals excludes intermediate hosts of 35 different species of animals. Transboundary and Emerging Diseases 67 (4), 1745–1749.
Domingo, E., Perales, C., 2019. Viral quasispecies. PLoS Genetics 15 (10), e1008271.
Dong, E., Du, H., Gardner, L., 2020. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infectious Diseases 20 (5), 533–534.
Dos, S.R.C., van de Burgwal, L.H.M., Regeer, B.J., 2019. Overcoming challenges for designing and implementing the One Health approach: A systematic review of the literature. One Health 7, 100085.
Dudas, G., *et al.*, 2017. Virus genomes reveal factors that spread and sustained the Ebola epidemic. Nature 544 (7650), 309–315.
Epstein, J.H., Field, H.E., Luby, S., Pulliam, J.R., Daszak, P., 2006. Nipah virus: Impact, origins, and causes of emergence. Current Infectious Disease Reports 8 (1), 59–65.
Erles, K., Brownlie, J., 2008. Canine respiratory coronavirus: An emerging pathogen in the canine infectious respiratory disease complex. Veterinary Clinics of North America: Small Animal Practice 38 (4), 815–825. viii.
Evans, B.R., Leighton, F.A., 2014. A history of One Health. Revue scientifique et technique 33 (2), 413–420.
Farag, E.A.B., *et al.*, 2019. Survey on implementation of One Health approach for MERS-CoV preparedness and control in Gulf Cooperation Council and Middle East countries. Emerging Infectious Diseases 25 (3), e171702.
Farag, E., *et al.*, 2018. Drivers of MERS-CoV Emergence in Qatar. Viruses 11 (1), 22.
Fernandez-Cassi, X., *et al.*, 2018. Metagenomics for the study of viruses in urban sewage as a tool for public health surveillance. Science of the Total Environment 618, 870–880.
Franzo, G., Drigo, M., Legnardi, M., *et al.*, 2020. Bovine Coronavirus: Variability, Evolution, and Dispersal Patterns of a No Longer Neglected Betacoronavirus. Viruses 12 (11),

Freidl, G.S., *et al.*, 2015. Serological evidence of influenza A viruses in frugivorous bats from Africa. PLoS One 10 (5), e0127035.
Freuling, C.M., Breithaupt, A., Müller, T., *et al.*, 2020. Susceptibility of Raccoon Dogs for Experimental SARS-CoV-2 Infection. Emerging Infectious Diseas 26 (12), 2982–2985.
Garcia, M., Fernandez-Barredo, S., Perez-Gracia, M.T., 2014. Detection of hepatitis E virus (HEV) through the different stages of pig manure composting plants. Microbial Biotechnology 7 (1), 26–31.
Geoghegan, J.L., *et al.*, 2016. Virological factors that increase the transmissibility of emerging human viruses. Proceedings of the National Academy of Sciences of the United States of America 113 (15), 4170–4175.
Geoghegan, J.L., Holmes, E.C., 2017. Predicting virus emergence amid evolutionary noise. Open Biology 7, 10.
Gilbert, M., *et al.*, 2014. Predicting the risk of avian influenza A H7N9 infection in live-poultry markets across Asia. Nature Communications 5, 4116.
Gortazar, C., *et al.*, 2014. Crossing the Interspecies Barrier: opening the Door to Zoonotic Pathogens. PLOS Pathogens 10 (6), e1004129.
Gossner, C., *et al.*, 2016. Human-dromedary camel interactions and the risk of acquiring zoonotic Middle East respiratory syndrome coronavirus infection. Zoonoses Public Health 63 (1), 1–9.
Grubaugh, N.D., Hanage, W.P., Rasmussen, A.L., 2020. Making Sense of Mutation: What D614G Means for the COVID-19 Pandemic Remains Unclear. Cell 182 (4), 794–795.
Gubler, D.J., Vasilakis, N., Musso, D., 2017. History and emergence of Zika virus. The Journal of Infectious Diseases 216 (suppl_10), S860–S867.
Halpin, K., *et al.*, 2011. Pteropid bats are confirmed as the reservoir hosts of henipaviruses: A comprehensive experimental study of virus transmission. The American Journal of Tropical Medicine and Hygiene 85 (5), 946–951.
Hart, O.E., Halden, R.U., 2020. Computational analysis of SARS-CoV-2/COVID-19 surveillance by wastewater-based epidemiology locally and globally: Feasibility, economy, opportunities and challenges. Science of the Total Environment 730, 138875.
Hendriksen, R.S., *et al.*, 2019. Global monitoring of antimicrobial resistance based on metagenomics analyses of urban sewage. Nature Communications 10 (1), 1124.
Henning, J., *et al.*, 2019. Risk factors for H5 avian influenza virus prevalence on urban live bird markets in Jakarta, Indonesia - Evaluation of long-term environmental surveillance data. PLoS One 14 (5), e0216984.
Himsworth, C.G., *et al.*, 2019. Targeted resequencing of wetland sediment as a tool for avian influenza virus surveillance. Journal of Wildlife Diseases 56, 397–408.
Hu, D., Zhu, C., Ai, L., *et al.*, 2018. Genomic characterization and infectivity of a novel SARS-like coronavirus in Chinese bats. Emerging Microbes & Infections 7 (1), 154.
Jones, K.E., *et al.*, 2008. Global trends in emerging infectious diseases. Nature 451 (7181), 990–993.
Jones, B.A., *et al.*, 2013. Zoonosis emergence linked to agricultural intensification and environmental change. Proceedings of the National Academy of Sciences of the United States of America 110 (21), 8399–8404.
Kapetshi, J., *et al.*, 2018. Contribution of environment sample-based detection to Ebola outbreak management. The Journal of Infectious Diseases 218 (suppl_5), S292–S296.
Karesh, W.B., *et al.*, 2012. Ecology of zoonoses: Natural and unnatural histories. The Lancet 380 (9857), 1936–1945.
Koopmans, M., 2020. SARS-CoV-2 and the human-animal interface: Outbreaks on mink farms. Lancet Infectious Diseases.
Khan, S.U., *et al.*, 2018. Avian influenza surveillance in domestic waterfowl and environment of live bird markets in Bangladesh, 2007-2012. Scientific Reports 8 (1), 9396.
Khoury, M.J., Ioannidis, J.P.A., 2014. Medicine. Big data meets public health. Science 346 (6213), 1054–1055.
Kim, S.H., *et al.*, 2016. Extensive viable Middle East Respiratory Syndrome (MERS) coronavirus contamination in air and surrounding environment in MERS isolation wards. Clinical Infectious Diseases 63 (3), 363–369.
Kreuder Johnson, C.,., *et al.*, 2015. Spillover and pandemic properties of zoonotic viruses with high host plasticity. Scientific Reports 5, 14830.
Lai, S., *et al.*, 2016. Global epidemiology of avian influenza A H5N1 virus infection in humans, 1997-2015: A systematic review of individual case data. Lancet Infectious Diseases 16 (7), e108–e118.
Luby, S.P., *et al.*, 2006. Foodborne transmission of Nipah virus, Bangladesh. Emerging Infectious Diseases 12 (12), 1888–1894.
Mabasa, V.V., *et al.*, 2018. Environmental surveillance for noroviruses in selected South African wastewaters 2015-2016: Emergence of the Novel GII.17. Food and Environmental Virology 10 (1), 16–28.
Majumdar, M., Martin, J., 2018. Detection by direct next generation sequencing analysis of emerging enterovirus D68 and C109 strains in an environmental sample from Scotland. Frontiers in Microbiology 9, 1956.
Manlove, K.R., *et al.*, 2016. "One Health" or Three? Publication silos among the One Health disciplines. PLoS Biology 14 (4), e1002448.
Martin, V., *et al.*, 2011. Risk-based surveillance for avian influenza control along poultry market chains in South China: The value of social network analysis. Preventive Veterinary Medicine 102 (3), 196–205.
Masri, S., *et al.*, 2019. Use of Twitter data to improve Zika virus surveillance in the United States during the 2016 epidemic. BMC Public Health 19 (1), 761.
Masumbuko Claude, K., Underschultz, J., Hawkes, M.T., 2019. Social resistance drives persistent transmission of Ebola virus disease in Eastern Democratic Republic of Congo: A mixed-methods study. PLoS One 14 (9), e0223104.
McCloskey, B., *et al.*, 2014. Emerging infectious diseases and pandemic potential: Status quo and reducing risk of global spread. The Lancet Infectious Diseases 14 (10), 1001–1010.
Medema, G., Heijnen, L., Elsinga, G., Italiaander, R., Brouwer, A., 2020. Presence of SARS-Coronavirus-2 RNA in Sewage and Correlation with Reported COVID-19 Prevalence in the Early Stage of the Epidemic in The Netherlands. Environmental Science & Technology Letters. doi:10.1101/acs.estlett.0c00357.
Mina, M.J., *et al.*, 2019. Measles virus infection diminishes preexisting antibodies that offer protection from other pathogens. Science 366 (6465), 599–606.
Moyen, N., *et al.*, 2018. A large-scale study of a poultry trading network in Bangladesh: Implications for control and surveillance of avian influenza viruses. BMC Veterinary Research 14 (1), 12.
Mykytyn, A.Z., Lamers, M.M., Okba, N.M.A., *et al.*, 2020. Susceptibility of rabbits to SARS-CoV-2. bioRxiv. doi:10.1101/2020.08.27.263988.
Nahar, N., *et al.*, 2017. A controlled trial to reduce the risk of human Nipah virus exposure in Bangladesh. Ecohealth 14 (3), 501–517.
Nemoto, M., Schofield, W., Cullinane, A., 2019. The First Detection of Equine Coronavirus in Adult Horses and Foals in Ireland. Viruses 11 (10).
Niedrig, M., *et al.*, 2018. Find the right sample: A study on the versatility of saliva and urine samples for the diagnosis of emerging viruses. BMC Infectious Diseases 18 (1), 707.
Nielsen, C.F., *et al.*, 2015. Improving burial practices and cemetery management during an Ebola virus disease epidemic - Sierra Leone, 2014. MMWR Morbidity and Mortality Weekly Report 64 (1), 20–27.
Nieuwenhuijse, D.F., Koopmans, M.P., 2017. Metagenomic sequencing for surveillance of food- and waterborne viral diseases. Frontiers in Microbiology 8, 230.
Nordahl Petersen, T., *et al.*, 2015. Meta-genomic analysis of toilet waste from long distance flights; a step towards global surveillance of infectious diseases and antimicrobial resistance. Scientific Reports 5, 11444.
Okba, N.M.A., Müller, M.A., Li, W., *et al.*, 2020. Severe Acute Respiratory Syndrome Coronavirus 2-Specific Antibody Responses in Coronavirus Disease Patients. Emerging Infectious Diseases 26 (7), 1478–1488.
Olival, K.J., *et al.*, 2017. Host and viral traits predict zoonotic spillover from mammals. Nature 546 (7660), 646–650.
Olival, K.J., Cryan, P.M., Amman, B.R., *et al.*, 2020. Possibility for reverse zoonotic transmission of SARS-CoV-2 to free-ranging wildlife: A case study of bats. PLOS Pathogens 16 (9), e1008758.
Oude Munnink, B.B., Nieuwenhuijse, D.F., Stein, M., *et al.*, 2020a. Rapid SARS-CoV-2 whole-genome sequencing and analysis for informed public health decision-making in the Netherlands. Nature Medicine 26 (9), 1405–1410.
Oude Munnink, B.B., Sikkema, R.S., Nieuwenhuijse, D.F., *et al.*, 2020b. Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans. Science.
Owada, K., *et al.*, 2016. Epidemiological data management during an outbreak of Ebola virus disease: Key issues and observations from Sierra Leone. Frontiers in Public Health 4, 163.
Pas, S.D., *et al.*, 2015. First international external quality assessment of molecular diagnostics for MERS-CoV. Journal of Clinical Virology 69, 81–85.

Patterson, E.I., Elia, G., Grassi, A., *et al.*, 2020. Evidence of exposure to SARS-CoV-2 in cats and dogs from households in Italy. Nature Communications 11 (1), 6231.
Peel, A.J., *et al.*, 2019. Synchronous shedding of multiple bat paramyxoviruses coincides with peak periods of Hendra virus spillover. Emerging Microbes & Infections 8 (1), 1314–1323.
Peiris, J.S., Guan, Y., Yuen, K.Y., 2004. Severe acute respiratory syndrome. Nature Medicine 10 (12 Suppl), S88–S97.
Petersen, E., *et al.*, 2018. Emerging infections – An increasingly important topic: Review by the Emerging Infections Task Force. Clinical Microbiology and Infection 24 (4), 369–375.
Plowright, R.K., *et al.*, 2017. Pathways to zoonotic spillover. Nature Reviews Microbiology 15, 502–510.
Plowright, R.K., *et al.*, 2015. Ecological dynamics of emerging bat virus spillover. Proceedings of the Royal Society B: Biological Sciences 282 (1798), 20142124.
Potocnakova, L., Bhide, M., Pulzova, L.B., 2016. An introduction to B-cell epitope mapping and in silico epitope prediction. Journal of Immunology Research 2016, 6760830.
Qiu, W., *et al.*, 2018. The impacts on health, society, and economy of SARS and H7N9 outbreaks in China: A case comparison study. Journal of Environmental and Public Health 2018, 2710185.
Randolph, S.E., Rogers, D.J., 2010. The arrival, establishment and spread of exotic diseases: Patterns and predictions. Nature Reviews Microbiology 8 (5), 361–371.
Reusken, C.B., Haagmans, B.L., Müller, M.A., *et al.*, 2013. Middle East respiratory syndrome coronavirus neutralising serum antibodies in dromedary camels: A comparative serological study. Lancet Infectious Diseases 13 (10), 859–866.
Reusken, C., *et al.*, 2015. Identification of essential outstanding questions for an adequate European laboratory response to Ebolavirus Zaire West Africa 2014. Journal of Clinical Virology 62, 124–134.
Reusken, C., Broberg, E.K., Haagmans, B., *et al.*, 2020. Laboratory readiness and response for novel coronavirus (2019-nCoV) in expert laboratories in 30 EU/EEA countries, January 2020. Eurosurveillance 25 (6).
Reyes-Ruiz, J.M., *et al.*, 2019. Mosquito cells persistently infected with dengue virus produce viral particles with host-dependent replication. Virology 531, 1–18.
Rothenburg, S., Brennan, G., 2020. Species-specific host-virus interactions: Implications for viral host range and virulence. Trends in Microbiology 28 (1), 46–56.
Richard, M., Kok, A., de Meulder, D., *et al.*, 2020. SARS-CoV-2 is transmitted via contact and via the air between ferrets. Nature Communications 11 (1), 3496.
Ryan, S.J., *et al.*, 2015. Mapping physiological suitability limits for malaria in Africa under climate change. Vector-Borne and Zoonotic Diseases 15 (12), 718–725.
Scoizec, A., *et al.*, 2018. Airborne detection of H5N8 highly pathogenic avian influenza virus genome in poultry farms, France. Frontiers in Veterinary Science 5, 15.
Sealy, J.E., *et al.*, 2019. Poultry trading behaviours in Vietnamese live bird markets as risk factors for avian influenza infection in chickens. Transboundary and Emerging Diseases 66 (6), 2507–2516.
Setoh, Y.X., *et al.*, 2019. Determinants of Zika virus host tropism uncovered by deep mutational scanning. Nature Microbiology 4 (5), 876–887.
Sia, S.F., Yan, L.-M., Chin, A.W.H., *et al.*, 2020. Pathogenesis and transmission of SARS-CoV-2 in golden hamsters. Nature 583 (7818), 834–838.
Shi, J., Wen, Z., Zhong, G., *et al.*, 2020. Susceptibility of ferrets, cats, dogs, and other domesticated animals to SARS–coronavirus 2. Science 368 (6494), 1016–1020.
Shi, L., Wang, Z., 2019. Computational strategies for scalable genomics analysis. Genes 10 (12), 1017.
Sigfrid, L., *et al.*, 2018. Strengthening preparedness for (re-) emerging arboviruses in Europe. Clinical Microbiology and Infection 24 (3), 219–220.
Sikkema, R.S., Freidl, G.S., de Bruin, E., Koopmans, M., 2016. Weighing serological evidence of human exposure to animal influenza viruses – A literature review. Euro surveillance 21 (44).
Sikkema, R.S., *et al.*, 2016. Weighing serological evidence of human exposure to animal influenza viruses – A literature review. Eurosurveillance 21 (44), 30388.
Sikkema, R., Koopmans, M., 2016. One Health training and research activities in Western Europe. Infection Ecology & Epidemiology 6, 33703.
Simmonds, P., Aiewsakun, P., 2018. Virus classification – Where do you draw the line? Archives of Virology 163 (8), 2037–2046.
Simonsen, L., *et al.*, 2016. Infectious disease surveillance in the big data era: Towards faster and locally relevant systems. The Journal of Infectious Diseases 214 (suppl_4), S380–S385.
Simons, R.R.L., *et al.*, 2016. A generic quantitative risk assessment framework for the entry of bat-borne zoonotic viruses into the European Union. PLOS ONE 11 (10), e0165383.
Sit, T.H.C., Brackman, C.J., Ip, S.M., Tam, K.W.S., *et al.*, 2020. Infection of dogs with SARS-CoV-2. Nature 586 (7831), 776–778.
Smith, K.F., *et al.*, 2014. Global rise in human infectious disease outbreaks. Journal of the Royal Society Interface 11 (101), 20140950.
Smith, K.M., *et al.*, 2012. Zoonotic viruses associated with illegally imported wildlife products. PLoS One 7 (1), e29505.
Takhampunya, R., *et al.*, 2019. Metagenomic approach to characterizing disease epidemiology in a disease-endemic environment in Northern Thailand. Frontiers in Microbiology 10, 319.
Thézé, J., *et al.*, 2018. Genomic epidemiology reconstructs the introduction and spread of Zika virus in Central America and Mexico. Cell Host & Microbe 23 (6), 855–864.
Tian, H., *et al.*, 2015. Avian influenza H5N1 viral and bird migration networks in Asia. Proceedings of the National Academy of Sciences of the United States of America 112 (1), 172–177.
Umhang, G., *et al.*, 2016. Surveillance and management of Echinococcus multilocularis in a wildlife park. Parasitology International 65 (3), 245–250.
Voeten, H., Sikkema, R.S., Damen, M., *et al.*, 2020. Unravelling the modes of transmission of SARS-CoV-2 during a nursing home outbreak: Looking beyond the church super-spread event. Clinical Infectious Diseases.
Walker, J.W., *et al.*, 2018. Transmissibility of emerging viral zoonoses. PLoS One 13 (11), e0206926.
Wang, M., Yan, M., Xu, H., *et al.*, 2005. SARS-CoV infection in a restaurant from palm civet. Emerging Infectious Diseases 11 (12), 1860–1865.
Wernike, K., Aebischer, A., Michelitsch, A., *et al.*, 2020. Multi-species ELISA for the detection of antibodies against SARS-CoV-2 in animals. Transboundary and Emerging Diseases.
Wibawa, H., *et al.*, 2018. Exploring contacts facilitating transmission of influenza A(H5N1) virus between poultry farms in West Java, Indonesia: A major role for backyard farms? Preventive Veterinary Medicine 156, 8–15.
Wilson, M.R., *et al.*, 2019. Clinical metagenomic sequencing for diagnosis of meningitis and encephalitis. The New England Journal of Medicine 380 (24), 2327–2340.
Woolhouse, M., 2011. How to make predictions about future infectious disease risks. Philosophical Transactions of the Royal Society B: Biological Sciences 366 (1573), 2045–2054.
Wu, J.Y., *et al.*, 2019. Transmission risk of avian influenza virus along poultry supply chains in Guangdong, China. Journal of Infection 79 (1), 43–48.
Wu, F., Zhao, S., Yu, B., *et al.*, 2020. A new coronavirus associated with human respiratory disease in China. Nature 579 (7798), 265–269.
Zaki, A.M., *et al.*, 2012. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. The New England Journal of Medicine 367 (19), 1814–1820.
Zhang, Q., Zhang, H., Gao, J., *et al.*, 2020. A serological survey of SARS-CoV-2 in cat in Wuhan. Emerging Microbes & Infections 9 (1), 2013–2019.
Zhou, P., *et al.*, 2015. Avian influenza A(H7N9) virus and mixed live poultry–animal markets in Guangdong province: A perfect storm in the making? Emerging Microbes & Infections 4 (1), 1–3.
Zhou, J., *et al.*, 2016. Isolation of H5N6, H7N9 and H9N2 avian influenza A viruses from air sampled at live poultry markets in China, 2014 and 2015. Eurosurveillance 21 (35), 30331.
Zhou, P., Yang, X.L., Wang, X.G., *et al.*, 2020. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 579 (7798), 270–273.
Zolfo, M., *et al.*, 2018. Profiling microbial strains in urban environments using metagenomic sequencing data. Biology Direct 13 (1), 9.

Relevant Websites

https://reliefweb.int/report/world/world-risk-annual-report-global-preparedness-health-emergencies-global-preparedness
A World at Risk: Annual report on global preparedness for health emergencies.
Global Preparedness Monitoring Board [EN/AR/RU/ZH].
https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2014.3884
An update on the risk of transmission of Ebola virus (EBOV) via the food chain.
https://apps.who.int/iris/bitstream/handle/10665/252646/WHO-OHE-PED-2016.2-eng.pdf
Anticipating Emerging Infectious Disease Epidemic.
World Health Organization.
https://wwwnc.cdc.gov/eid/page/background-goals
Background and Goals.
CDC.
https://isaric.tghn.org/protocols
CCP UK & Annual Activation.
ISARIC.
https://www.who.int/blueprint/priority-diseases/en/
Coronavirus disease (COVID-19) pandemic.
http://www.fao.org/3/a-i2198e.pdf
Developing sustainable value chains for small-scale livestock producers.
https://www.who.int/docs/default-source/coronaviruse/protocol-v2-1.pdf?sfvrsn=a9ef618c_2
Diagnostic detection of 2019-nCoV by real-time RT-PCR.
https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/
COVID-19 vaccine tracker.
http://www.fao.org/avianflu/documents/Economic-and-social-impacts-of-avian-influenza-Geneva.pdf
Economic and social impacts of avian influenza.
https://www.ecdc.europa.eu/en/about-us/partnerships-and-networks/disease-and-laboratory-networks/evd-labnet
Emerging Viral Diseases-Expert Laboratory Network (EVD-LabNet).
https://life.eurobirdportal.org
EuroBirdPortal.
LIFE EuroBirdPortal overview.
https://EVAg:eur-opean-virus-archive.com
European Virus Archive - GLOBAL.
https://reliefweb.int/report/world/exploring-machine-learning-map-yellow-fever-risk
Exploring Machine Learning to Map Yellow Fever Risk.
https://consise.tghn.org
Home.
CONSISE.
https://www.who.int/news-room/feature-stories/detail/how-who-is-working-to-track-down-the-animal-reservoir-of-the-sars-cov-2-virus
How WHO is working to track down the animal reservoir of the SARS-CoV-2 virus.
http://www.cdc.gov/flu/pdf/avianflu/h5n1-inventory.pdf
H5N1 Genetic Changes Inventory.
FluTrackers.
https://www.who.int/ihr
International health regulations.
World Health Organization.
www.movebank.org
Movebank.org.
https://doi.org/10.17504/protocols.io.bdp7i5rn
nCoV-2019 sequencing protocol v2 (GunIt) V.2.
https://www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/
Novel Coronavirus
China.
https://virological.org/t/novel-2019-coronavirus-genome/319
Novel 2019 coronavirus genome.
https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-context
Prioritizing diseases for research and development in emergency contexts.
https://www.who.int/csr/don/05-january-2020-pneumonia-of-unkown-cause-china/en/
Pneumonia of unknown cause
China.
https://www.glopid-r.org/our-work/social-science-research/
Social Science Research.
GloPID-R.
https://www.who.int/news-room/commentaries/detail/status-of-environmental-surveillance-for-sars-cov-2-virus
Status of environmental surveillance for SARS-CoV-2 virus.
https://www.who.int/foodsafety/zoonoses/final_concept_note_Hanoi.pdf?ua=1
The FAO-OIE-WHO.
http://www.fao.org/3/i0680e/i0680e02.pdf
2. Change in the livestock sector.