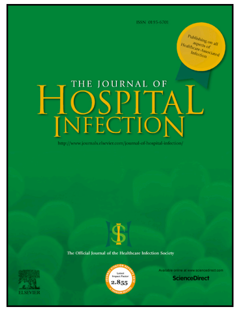
Journal Pre-proof



Understanding the emerging coronavirus: what it means for health security and infection prevention

Alexandra Peters, Pauline Vetter, Chloé Guitart, Nasim Lotfinejad, Didier Pittet

PII: S0195-6701(20)30099-2

DOI: https://doi.org/10.1016/j.jhin.2020.02.023

Reference: YJHIN 5928

To appear in: *Journal of Hospital Infection*

Received Date: 25 February 2020

Accepted Date: 28 February 2020

Please cite this article as: Peters A, Vetter P, Guitart C, Lotfinejad N, Pittet D, Understanding the emerging coronavirus: what it means for health security and infection prevention, *Journal of Hospital Infection*, https://doi.org/10.1016/j.jhin.2020.02.023.

Understanding the emerging coronavirus: what it means for health security and infection prevention

Authors: Alexandra Peters[1], Pauline Vetter[2], Chloé Guitart[1], Nasim Lotfinejad[3], Didier Pittet[1]

Affiliations: [1] Infection Control Programme, [2] Division of Infectious Diseases, University of Geneva Hospitals and Faculty of Medicine, Geneva, Switzerland, [3] Department of Research, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Correspondance: Professor Didier Pittet, Infection Control Programme, University of Geneva Hospitals and Faculty of Medicine, 4 Rue Gabrielle-Perret-Gentil, 1211 Geneva 14, Switzerland.
Tel: +41 22 372 9828 /+41 22 372 9833 (direct); e-mail: didier.pittet.@hcuge.ch

Word count: 4579 (text only); 2 Figures

Keywords: infection prevention and control; infection control; hand hygiene; World Health Organization; healthcare-associated infection; global health; survey

Conflict of interest: None declared

Acknowledgements

This work is supported by the Infection Control Programme (SPCI), University of Geneva Hospitals and Faculty of Medicine, Geneva, Switzerland; hand hygiene research activities at the SPCI are also supported by the Swiss National Science Foundation (grant no. 32003B_163262).

Didier Pittet works with WHO in the context of the WHO initiative 'Private Organizations for Patient Safety – Hand Hygiene'. The aim of this WHO initiative is to harness industry strengths to align and improve implementation of WHO recommendations for hand hygiene in health care indifferent parts of the world, including in least developed countries. In this instance, companies/industry with a focus on hand hygiene and infection control related advancement have the specific aim of improving access to affordable hand hygiene products as well as through education and research. All listed authors declare no financial support, grants, financial interests or consultancy that could lead to conflicts of interest.

The authors alone are responsible for the views expressed in this article and they do not necessarily represent the views, decisions or policies of the institutions with which they are affiliated. WHO takes no responsibility for the information provided or the views expressed in this paper.

Introduction

The current outbreak (COVID-19) of the new coronavirus (SARS-CoV-2) in China and the beginning of its subsequent global spread is already impacting global health systems and the global economy.[1] How countries and international organizations respond to the challenges it presents may have profound lasting impacts for global health. The decisions taken, both on national and international levels, will help inform how we react to future pandemics and health security challenges.

Global disease outbreaks and pandemics have been increasing exponentially over the last 40 years, and experts have long been warning of the potentially devastating effects of a severe pandemic, though it is important to note that the improvement in diagnostic capabilities undoubtedly plays a role (Figures 1 and 2).[2,3] By analyzing the causes of this and similar pandemics, as well as the physiopathological, human, and political influences on its spread, we hope to shed some light on the current health risks, decision-making dynamics, and future implications of the current coronavirus pandemic.

Coronaviruses (CoV) are single-stranded, positive-sense enveloped RNA virus of the subfamiliy *Orthocoronavirinae*, family *Coronaviridae*, order *Nidovirales*. Among those, four are widely distributed human coronaviruses (HCoV-229E, HCoV-OC43, HCoV-NL63, HCoV-HKU1) and cause the common cold. Severe Acute Respiratory Syndrome (SARS-CoV) and Middle East Respiratory Syndrome Coronaviruses (MERS-CoV) are zoonotic. In 2002-2003, SARS-CoV caused an outbreak of pneumonia in 8,000 affected cases, distributed over 30 countries and 5 continents, and is now considered eradicated. MERS-CoV was discovered in 2012.[4] It originates from bats, with dromedary camel as the intermediate host, causes pneumonia in humans and has a mortality rate of over 30%. Nosocomial spread has also been described. No specific antiviral treatment is available and treatment is mainly supportive and symptomatic.[5]

A novel 2019 coronavirus (SARS-CoV-2) belongs to the *Betacoronavirus* genus of the *Coronaviridae* family. It shares more than 79% homology with SARS-CoV,[6] and causes mild to severe disease, with fatal bilateral viral pneumonia described in humans.[7,8] It is referred to as a novel coronavirus because it has not previously been observed in the human population. Its likely reservoir is bats, with pangolins identified as the likely intermediate host.[9] It is worth mentioning that pangolins are endangered and the most trafficked animal in the world.[10] Because the pangolin trade is illegal, this would explain why they were not listed in the official registers of the Wuhan market, making it difficult for researchers to identify the source of the virus. Some researchers are suggesting that the virus may have been circulating previously, and the market may have been an amplification setting and not the source of the spillover.[11]

Why the rate of pandemics is increasing

There are numerous reasons for the exponential growth of global pandemics, but the most frequently cited include the expansion of the human population, destabilization of ecosystems and globalization. Humans are coming into contact with environments that were previously untouched, meaning that they will also come into contact with the viruses and bacteria that are inherent to those environments. Many of these will have no impact on human health but some do.[2,12]

Human actions that impact animals, such as changes in land use and climate change have a profound effect on how these diseases spread. As our climate changes, certain populations of animals (especially mosquitos or other animals that function as disease vectors) increase and spread into geographic zones that were previously uninhabitable to them, they are more likely to spread the diseases that they carry to new regions. Changes in land use and changes in human/animal contact, also affect the emergence/reemergence and spread of disease, as does the unmanageable explosion of the global wildlife trade. Legal and illegal wildlife trade is estimated to affect 1 in 4 mammal and bird species globally, and to generate between $7.8 and $10 billion annually. [13,14] In response to COVID-19, China has placed a temporary ban on wildlife trade on the 26th of January.[15] Although this will likely only affect the legal wildlife trade (temporarily), it is a step in the right direction.

How we raise our food is just as important, and zoonotic diseases such as avian influenza (including the 2006 H5N1 epidemic) and the swine influenza (including the 2009 H1N1 pandemic) are often associated with industrial farming. The "monoculture effect" is well known in agriculture, but there is mounting evidence that it is important in animal farming as well.[16,17] Although the aforementioned studies look at wild animal populations, there is a high indication that it holds true for animals raised for food. Often large populations of specific species of animal raised for food are kept in suboptimal conditions. Without even mentioning the inherent issues of waste management and animal welfare, industrial farming also creates health risks for humans in multiple ways if these populations are not isolated from wild animals of similar species. In the case of avian influenza, the virus, which circulates naturally in wild bird populations, came into contact with large homogeneous populations of birds in poultry farms.[18]

Because of the disease potential associated with intensive animal farming, animals are often treated with vaccines and antibiotics. Both the avian and swine influenza continue to be managed through the regular vaccination of livestock.[19] Though the main reason for antibiotic use in farming is to preserve human and animal health and prevent zoonoses, widespread use of antibiotics in terrestrial animal production (including first line antibiotics such as colistin) promotes antibiotic resistance.[20,21] In farming, antibiotics are used as prophylactics to make up for crowded unhealthy conditions, and growth promoters as well as therapeutic treatments for specific disease outbreaks. So although they are relevant tools for decreasing zoonoses, antibiotic use in animals can also become the catalyst for the development of zoonoses that are resistant to antibiotics.[22]

These issues are compounded by globalization in two main ways: interconnectedness and mobility. Our interconnectedness means that there are huge global markets for specific products from specific environments, which can speed up environmental degradation. Deforestation has already been linked to the emergence (and reemergence) of Nipah virus, Lassa fever, Lyme disease, and possibly Zika.[3,23]

A current example of this would be how the international drive for palm oil (a cheap and stable oil) in Malaysia has led to the upsurge of malaria in the region. Currently the world’s highest rate of deforestation is of Malaysian forests for the creation of palm oil plantations.[24–26] The zoonotic malaria species *Plasmodium knowlesi* has recently become the principal cause of human malaria in Borneo, and this has been directly linked to the deforestation on the island.[27,28] Considering the dynamics at the human- animal- ecosystem interface, it is not surprising that the worst epidemics and pandemics (including HIV, SARS-CoV, avian influenza, swine influenza, Ebola virus, and Zika virus) of the past 40 years were all of zoonotic or vector origin.

Human populations are also more mobile than they have ever been, and air travel enables a pathogen to be transported across the globe in a matter of hours. Currently, over four billion trips are taken by air every year, and this frequency of travel in an infected and moving global population gives a disease unprecedented opportunity to spread and spread quickly.[29] In that sense, the timing of the COVID-19 was very bad luck. Chinese New Year is the biggest mass migration in the world and 385 million people making around 3 billion trips during the holiday period.[30,31] The fact that the outbreak happened during this time makes it that much harder to trace and control, and certainly influences the speed at which it is spreading. In a globalized world, countries' security is interdependent, and in the case of a severe global pandemic, the world is (arguably) only as prepared as its weakest country.[32]

Potential Impact

The issue that needs to be assessed is the level of risk that more frequent outbreaks of emerging and reemerging diseases pose for the human population. Impact can be assessed in different ways, including global morbidity, mortality, and economic burden, and geopolitical implications.

The stakes are high: WHO estimates that a moderate to severe pandemic would cost about $500 billion, or 0.6% of global income.[33] As has been shown repeatedly, an epidemic doesn't need to reach severe levels or have many (or technically speaking even any) casualties in order to destabilize national health systems or put a strain on the networks responsible for international and global response and the economy.

In order to quantify risk and forecast possible scenarios of transmission, it is necessary to look at the traits of a specific pathogen. There are numerous characteristics that can predict how well a pathogen could spread through and damage a population. These traits include virulence, clinical severity, ease of human-to-human transmission, if the pathogen is transmissible during the disease incubation period (and if yes, then how long that incubation period is).

There are health system and human factors as well that will impact the spread of a virus. Health system capacity factors include the availability of treatment or vaccine, and the level of resources (both human, material, and financial) available for allocation. Human factors include whether the population is immunologically naïve or not, how well the human immune system can respond to the virus, age structure of a population, population density, as well as mobility, and cultural behaviors.

Individuals' behavior that is informed by cultural beliefs and mores, and these can impact movement within a community, contact with others, and likelihood to comply with official recommendations. Level of education and previous knowledge of general infection prevention measures also play a role.[34]

Systemic factors that will determine the severity of an outbreak or pandemic include the resilience of health systems, co-existing external factors that would hinder an appropriate response, and the ability of a governing body to respond to the outbreak, implement infection control measures in the population, and continue to function despite a health emergency. Health systems are varied, a small outbreak of the flu in a high resource country with a robust health system will likely only have a small impact on the continual habitual or average delivery of health services that have nothing to do with the outbreak. A health system that is fragile, or already overloaded by either routine care or another emergency needs only a little disruption to damage it or even causes it to collapse. Traditionally, supranational organizations, international institutions and non-governmental organizations will fill that response vacuum as well as is possible. An example of this and how difficult it is to implement effectively would be the international response to the 2014 Ebola epidemic.[35,36]

An outbreak in one country can deeply affect not only that country's economy, the world economy, but also its political relationships with other countries such as trade agreements, opening or closing national borders, etc. Economists are expecting China's economic growth to slow down to 4.5% because of the outbreak.[37]

Close-up of the SARS-CoV-2

The SARS-CoV-2 fulfills a lot of the qualities that a pathogen needs to cause a worldwide pandemic. It seems to be quite virulent. As SARS-CoV-2 has not been seen before in humans, the population is completely naïve. The virus has also shown to have high inter-human transmission. There is not yet enough data available for exact figures concerning the spread, but there have been initial estimates that each infected person would infect, on average, 2.6

other people (uncertainty range: 1.5-3.5).[38] The WHO estimates are a bit less daunting, reporting a preliminary R_0 estimate of 1.4-2.5.[39] Importantly, the Imperial College London calculations estimate that infection control measures need to block well over 60% of transmission to be effective in controlling the outbreak.[38] That number is most likely inaccurate, but this will be easier to assess as time goes on. In the case that the virus can be transmitted by an asymptomatic individual,[40] then having a 60% effective infection and control (IPC) strategy will be even more difficult to implement, especially because most of the people infected are in the community and not in healthcare settings. However, the initial report of asymptomatic transmission in Germany was inaccurate, which is encouraging.[41] A further challenge is posed by the decision of foreign governments to evacuate and repatriate their citizens from China. The inevitable quarantines and infection control measures that need to be taken as people arrive back to their home countries will be crucial for preventing the spread of the virus.[42] The Diamond Princess cruise ship outbreak of the SARS-CoV-2 in Japan, with more than 691 infected people and four deaths (as of Feb 25th), is an example of the inadequate IPC in the community that led to a disaster.[43–45]

The SARS-CoV-2 genome has already been sequenced and countries are working hard to find develop a vaccine.[46–48] It is difficult to tell what the actual mortality of the virus is, as the current death toll includes all-cause mortality of infected people and is likely overestimated by the testing of mostly sicker patients, though this information will emerge over time. SARS-CoV-2 seems to mostly be spread by droplets, and not through air. Nosocomial transmission have been described,[49] and superspreading events in hospital settings may occur. SARS-CoV-2 is possibly spreading indirectly through contaminated surfaces and hand contamination as well, but the lack of aerosol transmission will make the spread less efficient. According to the WHO, 25% of current cases are considered severe,[39] but this proportion would presumably decrease while more patients and contacts would have been searched for and screened.

Contact tracing of the SARS-CoV-2 suggests that there is a low R_0 and limited person to person transmission.[50] The exponential spread of the number of cases, however may suggest that super spreaders of the virus may be playing a major role, either from individuals or a zoonotic source.[50] Super spreading individuals were found to have a major impact in the previous MERS, SARS, and Ebola pandemics.[34]

The current death toll is rising much more slowly than the current number of cases. (80,234 confirmed cases and 2,701 deaths (as of Feb 25th) for an overall fatality rate of 3.36%).[51] It is highly likely that the death rate- due to underreporting, a shortage of test kits, reporting of all-cause mortality, and a prevalence of patients with mild symptoms- is much lower than initially expected.[52,53] There are some estimates that currently only approximately 5% of the current cases of the virus have been identified.[53] If this is true, then COVID-19 is far less lethal than it seems.

What this means for infection prevention and control

It might be easy for IPC experts to get caught up in the frenzy of getting prepared for a new pandemic. Granted, we don't know what, if any, the long-term effects of this virus might be on the human body. But what is most important is to keep a healthy perspective, and avoid getting distracted by all of the hype and forecasting. Although there is not yet enough information available, the SARS-CoV-2 may be less deadly than the influenza virus that hospitals deal with on a yearly basis, and transmission seems to mostly occur through droplets. Even a high estimate of the R_0 rate is many times lower than for airborne diseases such as measles, for instance.[54] It's important to remember that the R_0 rate refers to the average transmissibility of the disease, and does not give information on how fast it will spread. Seasonal influenza has an R_0 of around 1.3, but circulates through the whole human population every year.[55] HIV, on the other hand, spread far more slowly through a population, yet has a highly variable reproductive rate[56]. Still, SARS-CoV-2 causes pneumonia in healthy people,[57] even if most of the deaths are described in elderly, comorbid patients. More epidemiological data are needed in order to precise the whole spectrum of the disease.

In order to better understand this dynamic, it might make sense to look at SARS-CoV, also a coronavirus. It has a similar reproductive rate to estimates of the R_0 of SARS-CoV-2, but only infected around 8,000 people. In the early phase of the 2003 SARS-CoV outbreak, the lack or inappropriateness of IPC measures used proved to be associated with an increased risk for cross-transmission and within-hospitals spread of the disease among both visitors and healthcare staff.[58–60] In contrast, when appropriately applied, IPC measures were extremely effective during the SARS epidemic.[61] Similarly, IPC measures will certainly prove to be extremely effective in respect to SARS-CoV-2, but we need more detailed transmission models.[62] In a 2003 analysis of SARS in Hong Kong that excluded super-spreading events, the reproductive rate dropped from 2.9 during the initial phase of the epidemic, to 0.4 after the implementation of IPC measures.[63] Usually, once the reproductive rate falls below 1, the outbreak will die out on its own. Therefore, having a strong and adapted IPC response to this outbreak will be crucial to stopping it. An additional factor is that people infected by SARS-CoV felt unwell and were likely to seek care in hospitals. SARS-CoV-2 seems to cause a wider range of symptoms, and if people only show mild infections, the infection may stay unnoticed (with people thinking that they have a common cold). This can cause the disease to be underdiagnosed, which means that people will be more likely to continue to spread the virus.

It is essential that we prepare ourselves for what seems like will be the inevitability of having the virus at our doorstep, but we must think ahead to enact common sense policies that will not cripple the normal functioning of our healthcare institutions. That may mean sending people home while waiting for a test result to come back or even providing home care to mild cases,[64] or figuring ahead of time how to handle an extra influx of patients.

Healthcare institutions can organize beds and isolation rooms, and IPC teams can set up hotlines in anticipation of the virus. Though more easily said than done, having a clear definition of what constitutes a suspect case is crucial. The case definition will evolve rapidly in a context where the epidemiological risk changes with geographic spread of the disease, and possible new information about its epidemiology. In order to contain the outbreak, the case definition should be broad at an early stage. It is also important for IPC teams to work with hospitals in expanding their triage capacity and deciding how to organize the activities during a period with a potentially unusually high influx of patients suspected to have the virus. Liaising with the virology laboratory to define additional hours and workforce if needed, can be an additional step to help ready an institution. Healthcare staff must be reminded on the importance of hand hygiene and of standard precautions, contact precautions, as well as any complementary measures in preventing the spread of the disease.

Developing countries face with more critical challenges during outbreaks compared with higher income countries, preventing effective management worldwide (Major Issues and Challenges of Influenza Pandemic Preparedness in Developing Countries: oshitani). The lack of IPC in developing countries with limited resources is a major dilemma that leads to high rates of healthcare-associated infections.[65] Hand hygiene is arguably, the most important infection control procedure, and is often neglected by health-care workers in these countries.[66] While developing countries still lack the equipment, expertise, and health infrastructure to detect and manage patients,[65] SARS-CoV-2 is spreading rapidly in these unprepared countries .[67] It has been recommended to promptly prioritize resources, precise surveillance, and capacity development in countries with low preparedness for diagnosing the virus and limiting transmission.[68]

What is most essential is that regular care activities do not suffer because of a pandemic condition, and that control of the far more common (and far more deadly) pathogens hospitals deal with on a daily basis remains of utmost importance.

Response and the Politics of Pandemics

The scale of China's response to the pandemic is unprecedented. Extreme *cordon sanitaire*-type quarantine measures have questionable efficacy and can jeopardize trust between healthcare providers and the population. This was seen in the 2014 Ebola epidemic, when Sierra Leone's government imposed a three day quarantine and sent police and military house to house both to educate the population and to find people harboring Ebola patients in their homes.[69,70] That said it, the COVID-19 outbreak is a delicate situation, and a difficult decision for China's government to take- any decision will have major risks. Still, quarantining a major region will most certainly result in practices that could be considered human rights violations.[71]

It is worth noting, that such a large scale dedicated disaster response by the government would be much more difficult to implement in a democratic country. China worked day and night to construct two hospitals within a matter of days. They were made of prefabricated buildings, and serve to help handle the overwhelming number of patients.[72] On the 28th of January, after just 48 hours of construction, they opened another 1,000 bed hospital that had been retrofitted into an empty building.[73] China has an impressive track record for being able to implement huge engineering projects at a record pace: during the 2003 SARS epidemic, they were able to construct a 1,000 bed hospital in under a week, using prefabricated buildings. At the height of the epidemic, the Xiaotangshan Hospital treated one seventh of the SARS patients in the country.[74]

Countries are often motivated to be cautious in declaring an emergency rather than alarmist, as this has severe economic repercussions. The speculations that China knew about the outbreak before they declared it seems to be well-founded: on January 27th, the mayor of Wuhan, Zhou Xianwang, admitted that “we haven’t disclosed information in a timely manner and also did not use effective information to improve our work.” [75] Locally, officials might have little motivation to declare an emergency to their superiors.[53] Quarantines were announced hours before they were put in place which could have encouraged people to flee- around 5 million residents reportedly left Wuhan before the quarantine was in place.[75] Deciding when to declare a national or international emergency is always difficult risk-benefit analysis. The risks of doing so can disrupt trade and severely hurt a region’s economy, but policy makers often don’t have a lot of options, especially when faced with public scrutiny.

Europe is not faced with the same dilemma after the recent spike of cases in Italy, (but on a far smaller scale). The Italian government has put a number of towns on lock down and canceled Carnival celebrations to attempt to stem the spread of COVID-19. The first example of major spread of the virus in Europe also highlights issues concerning the open borders between European countries.[76]

Epidemics impact people’s health and livelihoods far beyond the direct effects of the outbreak in the sectors of the countries where the disease occurs.[77] During the 2003 SARS epidemic, the global economy lost an estimated $40 billion.[78] The direct economic burden of the 2014 Ebola outbreak is estimated between $2.8 billion [79] and $32.6 billion of lost gross domestic product. With the comprehensive economic and social costs factored in, the cost to the global economy was estimated at over $51 billion, with $18 billion in deaths from non-Ebola causes.[80] The impact of the outbreak of the SARS-CoV-2 has spread from Asia to other parts of the world including Europe. With the emergence of many SARS-CoV-2 cases in Italy and South Korea as two of the world’s major economies, concerns have been raised regarding a global economic damage.[81]

After some debate, the WHO declared SARS-CoV-2 a Public Health Emergency of International Concern (PHEIC) on the 30th of January. The process leading up to this decision is complex and impacts many people; on the one hand such a declaration is an international call for alarm, but on the other, it does not guarantee that the outbreak will be ended or the exact nature of the international response. [82] The WHO initially declined to label the coronavirus outbreak as a PHEIC, as doing so would be extremely disruptive. The member views concerning this decision were quite divided during the first meeting, but the WHO agreed to reassess this decision in a few days' time,[39] and changed its global risk assessment for SARS-CoV-2 from "moderate" to "high".[83] It maintains that there is no evidence that donors withheld disaster relief funds if a PHEIC was not declared.[84] It is worth noting that the WHO repeatedly declined labeling the 2018 Ebola outbreak as such as well, showing that there is a tendency to err to the side of caution.[85] When it did in 2019, there was prevailing opinion that the PHEIC designation would be game changing in terms of resources allocated and international response.[86] We predict that the PHEIC designation for coronavirus will help mobilize response on a global scale.

What Now?

Although China has been praised for its rapid sequencing of the virus genome, and the impressive construction of health facilities and mobilization of the response, it has been struggling with managing the human element.[53] Effects of outbreak situations such as SARS-CoV-2 are always difficult to predict because there are so many variables to consider. First, we do not know much about this virus, and secondly, so much of its spread will be dictated by human behavior, decisions, and ultimately, luck.

There is much that can be done in terms of reducing the chances that novel viruses jump from animals to humans, but these measures often include the kind of environmental regulation that is difficult to implement in an international system inherently focused on growth and short-term profit. There are also cultural and practical issues associated with changing how we farm and stopping the wildlife trade, which are equally hard to implement.

The magnitude of effort needed to address this issue is daunting. Warning systems, response networks and real time tracking are important tools for containing outbreaks, but they do not actually prevent them from occurring in the first place. Projects that catalogue and study novel viruses do not equal preparedness. The same scientific work that is used to study a disease can in and of itself create biological risk.[87,88] Both national governments and supranational organizations state that this issue is of utmost importance, and have pledged their commitment.[89–91] Nonetheless, expert consensus is that there is a high chance of the world dealing with a devastating pandemic in the near future, and that we are quite unprepared. [87,92–94]

So far, there have been relatively few cases abroad, but a great many in China. Still, the number of cases in countries other than China continues to grow. Outside of China, there is a growing number of cases and casualties, with 12 deaths in Iran, 10 in South Korea, 7 in Italy, 4 on the Diamond Priness cruise ship, 2 in Hong Kong, and 1 each in France, Japan, Taiwan, and the Phillippines.[45] Coupled with the exponential growth of the pandemic, the very short pre or pauci-symptomatic and infectious incubation period of the virus, as well as the possible prolonged high-level carriage, makes it quite difficult to contain. [40] One probable scenario is that SARS-CoV-2 will just become another human virus that the world deals with on a regular basis. WHO director- general Dr. Tedros warned of a potential global pandemic: “The window of opportunity is still there, but our window of opportunity is narrowing,” he said on Friday. “We need to act quickly before it closes completely.”[95] It seems to not be as dangerous as initially thought, so perhaps, once again, humanity will be lucky. Hopefully we can learn from our mistakes before our luck runs out.

Work Cited

1. Rapid Risk Assessment: Outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): increased transmission beyond China – fourth update. (2020).

2. Smith KF, Goldberg M, Rosenthal S, Carlson L, Chen J, Chen C *et al.* Global rise in human infectious disease outbreaks. J R Soc Interface 2014;11(101):20140950.

3. Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, *et al.* Global trends in emerging infectious diseases. Nature 2008;451:990–3.

4. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus ADME, Fouchier RAM. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N Engl J Med 2012;367:1814–20.

5. World Health Organization. WHO | Middle East respiratory syndrome coronavirus (MERS-CoV). *WHO* (2019). Available at: http://www.who.int/emergencies/mers-cov/en/. (Accessed: 4th February 2020)

6. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, *et al.* Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020; 395:565-74.

7. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395:497-506.

8. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, *et al.* A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020; 382:727-33.

9. Cyranoski, D. Did pangolins spread the China coronavirus to people? Nature 2020. doi:10.1038/d41586-020-00364-2

10. Pangolins: Rare insight into world's most trafficked mammal - BBC News. Available at: https://www.bbc.com/news/science-environment-47200816. (Accessed: 24th February 2020)

11. Pangolins Are Suspected as a Potential Coronavirus Host - The New York Times. Available at: https://www.nytimes.com/2020/02/10/science/pangolin-coronavirus.html. (Accessed: 24th February 2020)

12. Carroll D, Daszak P, Wolfe ND, Gao GF, Morel CM, Morzaria S, *et al.* The Global Virome Project. Science 2018; 359:872-874.

13. Fine Maron, D. 1 in 4 mammal and bird species are part of global trade. Here's what may be next. *National Geographic* (2019). Available at: https://www.nationalgeographic.com/animals/2019/10/wildlife-trade-species/. (Accessed: 27th January 2020)

14. Global Wildlife Program. Global Wildlife Program: reducing poaching, reducing trafficking, reducing demand. (2017).

15. Leng C, Shen S, Lee SY. China bans wildlife trade nationwide due to coronavirus outbreak. *Reuters* (2020).

16. King KC, Lively CM. Does genetic diversity limit disease spread in natural host populations? Heredity 2012;109:199–203.

17. Ekroth AKE, Rafaluk-Mohr C, King KC. Diversity and disease: evidence for the monoculture effect beyond agricultural systems. Proc Biol Sci 2019;286:20191811

18. Centers for Disease Control and Prevention. Avian Influenza in Birds | Avian Influenza (Flu). (2018). Available at: https://www.cdc.gov/flu/avianflu/avian-in-birds.htm. (Accessed: 27th January 2020)

19. Spickler, A. R. Influenza: Flu, Grippe, Avian Influenza, Grippe Aviaire, Fowl Plague, Swine Influenza, Hog Flu, Pig Flu, Equine Influenza, Canine Influenza. (2016).

20. Food and Agriculture Organization of the United Nations. Animal production | Antimicrobial Resistance | Food and Agriculture Organization of the United Nations. Available at: http://www.fao.org/antimicrobial-resistance/key-sectors/animal-production/en/. (Accessed: 27th January 2020)

21. WHO | Antibiotic use in poultry: a survey of eight farms in Thailand. *WHO* doi:10.2471/BLT.17.195834

22. Zoonoses: antimicrobial resistance shows no signs of slowing down. *European Centre for Disease Prevention and Control* (2019). Available at: https://www.ecdc.europa.eu/en/news-events/zoonoses-antimicrobial-resistance-shows-no-signs-slowing-down. (Accessed: 27th January 2020)

23. Deforestation is leading to more infectious diseases in humans. *Science* (2019). Available at: https://www.nationalgeographic.com/science/2019/11/deforestation-leading-to-more-infectious-diseases-in-humans/. (Accessed: 28th January 2020)

24. Vijay V, Pimm SL, Jenkins CN, Smith SJ. The impacts of oil palm on recent deforestation and biodiversity loss. PLoS One 2016;11:e0159668.

25. Malaysia has the world's highest deforestation rate, reveals Google forest map. *Mongabay Environmental News* (2013). Available at: https://news.mongabay.com/2013/11/malaysia-has-the-worlds-highest-deforestation-rate-reveals-google-forest-map/. (Accessed: 27th January 2020)

26. Morrison J. Did Deforestation Contribute to Zika's Spread? | Science | Smithsonian Magazine. (2016). Available at: https://www.smithsonianmag.com/science-nature/did-deforestation-contribute-zikas-spread-180959305/. (Accessed: 28th January 2020)

27. Fornace KM, Abidin TR, Alexander N, Brock P, Grigg MJ, Murphy A, *et al.* Association between landscape factors and spatial patterns of *Plasmodium knowlesi* infections in Sabah, Malaysia. Emerg Infect Dis 2016;22:201-8.

28. Robbins J. How Forest Loss Is Leading To a Rise in Human Disease. *Yale E360* (2016). Available at: https://e360.yale.edu/features/how_forest_loss_is_leading_to_a_rise_in_human_disease_malaria_zika_climate_change. (Accessed: 28th January 2020)

29. IATA. Traveler Numbers Reach New Heights. (2018). Available at: https://www.iata.org/en/pressroom/pr/2018-09-06-01/. (Accessed: 27th January 2020)

30. Bloomberg Analysis. China Will Rack Up Three Billion Trips During World's Biggest Human Migration. *Washington Post* Available at: https://www.washingtonpost.com/business/china-will-rack-up-three-billion-trips-during-worlds-biggest-human-migration/2020/01/20/8bbc0f3e-3b52-11ea-afe2-090eb37b60b1_story.html. (Accessed: 28th January 2020)

31. Chinese New Year: The World's Largest Human Migration Is About To Begin [Infographic]. Available at: https://www.forbes.com/sites/niallmccarthy/2018/02/14/chinese-new-year-the-worlds-largest-human-migration-is-about-to-begin-infographic/. (Accessed: 28th January 2020)

32. Global pandemics: 7 reasons they're inevitable. CNN Available at: https://www.cnn.com/2017/04/03/health/pandemic-risk-virus-bacteria/index.html. (Accessed: 28th January 2020)

33. Fan VY, Jamison DT, Summers LH. Pandemic risk: how large are the expected losses? Bull World Health Organ 2018;96:129-34.

34. Wong G, Liu W, Liu Y, Zhou B, Bi Y, Gao GF. MERS, SARS, and Ebola: The role of super-spreaders in infectious disease. Cell Host Microbe 2015;18:398-401.

35. Gostin LO, Friedman EA. Ebola: a crisis in global health leadership. Lancet 2014;384:1323–5.

36. Largent EA. EBOLA and FDA: reviewing the response to the 2014 outbreak, to find lessons for the future. J Law Biosci 2016;3:489–537.

37. The economic effects of the coronavirus around the world. *World Economic Forum* Available at: https://www.weforum.org/agenda/2020/02/coronavirus-economic-effects-global-economy-trade-travel/. (Accessed: 24th February 2020)

38. Natsuko Imai *et al.* Report 3: Transmissibility of 2019-nCoV. (2020).

39. Statement on the meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus 2019 (n-CoV) on 23 January 2020. Available at: https://www.who.int/news-room/detail/23-01-2020-statement-on-the-meeting-of-the-

international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov). (Accessed: 29th January 2020)

40. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, *et al.* Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. N Engl J Med 2020; Jan 30 doi: 10.1056/NEJMc2001468.

41. Kupferschmidt K. Study claiming new coronavirus can be transmitted by people without symptoms was flawed. *Science | AAAS* (2020). Available at: https://www.sciencemag.org/news/2020/02/paper-non-symptomatic-patient-transmitting-coronavirus-wrong. (Accessed: 4th February 2020)

42. Welle D. Countries evacuate citizens from China as coronavirus infections rise. *DW.COM* (2020). Available at: https://www.dw.com/en/countries-evacuate-citizens-from-china-as-coronavirus-infections-rise/a-52181706. (Accessed: 29th January 2020)

43. Japanese expert who sneaked onto Diamond Princess cruise ship describes ‘zero infection control’ for coronavirus. *ABC News* Available at: https://abcnews.go.com/Health/japanese-expert-sneaked-diamond-princess-describes-infection-control/story?id=69071246. (Accessed: 25th February 2020)

44. Fourth passenger from cruise ship dies in Japan: Reports. Available at: https://www.channelnewsasia.com/news/asia/covid-19-coronavirus-japan-diamond-princess-cruise-death-12467980. (Accessed: 25th February 2020)

45. Coronavirus COVID-19 (2019-nCoV). Available at: https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6. (Accessed: 25th February 2020)

46. Novel Coronavirus 2019 Situation Summary, Wuhan, China | CDC. (2020). Available at: https://www.cdc.gov/coronavirus/2019-ncov/summary.html. (Accessed: 28th January 2020)

47. Scott S, Timms SRTP, Florance L. ‘We got it’: The game-changing moment when this Australian lab copied coronavirus. *ABC News* (2020). Available at: https://www.abc.net.au/news/2020-01-29/wuhan-coronavirus-created-in-australian-lab-outside-of-china/11906390. (Accessed: 29th January 2020)

48. Covid-19: Partnerships for coronavirus vaccines development. *Clinical Trials Arena* (2020).

49. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, *et al.* Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. N. Engl J Med 2020. doi:10.1056/NEJMoa2001316

50. Gralinski LE, Menachery VD. Return of the coronavirus: 2019-nCoV. Viruses 2020;12:135.

51. 2019-nCoV Global Cases. *Johns Hopkins CSSE* (2020). Available at: https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6. (Accessed: 4th February 2020)

52. Symptoms of Novel Coronavirus (2019-nCoV) | CDC. (2020). Available at: https://www.cdc.gov/coronavirus/2019-ncov/about/symptoms.html. (Accessed: 29th January 2020)

53. Confusion and lost time: how testing woes slowed China’s coronavirus response. *Reuters* (2020).

54. Guerra FM, Bolotin S, Lim G, Heffernan J, Deeks SL, Li Y, *et al.* The basic reproduction number (R0) of measles: a systematic review. Lancet Infect Dis 2017:17:e420–e428.

55. Coburn B J, Wagner BG, Blower S. Modeling influenza epidemics and pandemics: insights into the future of swine flu (H1N1). BMC Med 2009;7:30.

56. Garnett G. P. The basic reproductive rate of infection and the course of HIV epidemics. AIDS Patient Care STDS 1998;12:435-49.

57. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, *et al.* First case of 2019 novel coronavirus in the United States. N Engl J Med 2020 Jan 31. doi: 10.1056/NEJMoa2001191.

58. Lee N, Sung JJY. Nosocomial transmission of SARS. Curr Infect Dis Rep 2003;5:473–6.

59. McDonald LC, Simor AE, Su IJ, Maloney S, Ofner M, Chen KT, *et al.* SARS in healthcare facilities, Toronto and Taiwan. Emerg Infect Dis 2004;10:777–81.

60. Gomersall CD, Joynt GM, Ho OM, Ip M, Yap F, Derrick JL, *et al.* Transmission of SARS to healthcare workers. The experience of a Hong Kong ICU. Intensive Care Med 2006;32:564–9.

61. Seto WH, Tsang D, Yung RW, Ching TY, Ng TK, Ho M, *et al.* Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). Lancet 2003;361:1519-20.

62. Global Health Security Epidemic Alert and Response : Consensus document on the epidemiology of severe acute respiratory syndrome (SARS). (2003).

63. Donnelly CA, Ghani AC, Leung GM, Hedley AJ, Fraser C, Riley S, *et al.* Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. Lancet 2003;361:1761–6.

64. Home care for patients with suspected novel coronavirus (nCoV) infection presenting with mild symptoms and management of contacts: Interim guidance 20 January 2020. (2020).

65. Pittet D, Allegranzi B, Storr J, Bagheri Nejad S, Dziekan G, Leotsakos A, *et al.* Infection control as a major World Health Organization priority for developing countries. J Hosp Infect 2008;68:285–92.

66. Allegranzi B, Bagheri Nejad S, Combescure C, Graafmans W, Attar H, Donaldson L, *et al.* Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. Lancet 2011;377:228–41.

67. China coronavirus outbreak: All the latest updates | News | Al Jazeera. Available at: https://www.aljazeera.com/news/2020/02/cloneofchina-coronavirus-outbreak-latest-updates-200223232154013.html. (Accessed: 25th February 2020)

68. Preparedness and vulnerability of African countries against importations of COVID-19: a modelling study - The Lancet. Available at: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30411-6/fulltext. (Accessed: 25th February 2020)

69. Nossiter A. Sierra Leone to Impose 3-Day Ebola Quarantine. *The New York Times* (2014).

70. Mark M. Ebola lockdown in Sierra Leone: nationwide three-day curfew. *The Guardian* (2014).

71. Levenson M. Scale of China's Wuhan Shutdown Is Believed to Be Without Precedent. *The New York Times* (2020).

72. Esfandiari S. Videos show the shockingly rapid progress China is making with 2 hospitals it's panic-building to fight the coronavirus. *Business Insider* Available at: https://www.businessinsider.com/china-rapid-progress-panic-building-a-hospital-in-6-days-2020-1. (Accessed: 29th January 2020)

73. Hartley-Parkinson R. China completes 1,000-bed coronavirus hospital in just 48 hours. *Metro* (2020). Available at: https://metro.co.uk/2020/01/29/china-opens-1000-bed-coronavirus-hospital-just-48-hours-construction-12142899/. (Accessed: 29th January 2020)

74. Williams S. How can China build a hospital so quickly? *BBC News* (2020).

75. Ratcliffe R, Standaert M. China coronavirus: mayor of Wuhan admits mistakes. *The Guardian* (2020).

76. Horowitz J, Povoledo E. Europe Confronts Coronavirus as Italy Battles an Eruption of Cases. *The New York Times*

77. WHO | Pandemic risk: how large are the expected losses? *WHO* doi:10.2471/BLT.17.199588

78. Lee J-W, McKibbin WJ. Estimating the global economic costs of SARS. (National Academies Press (US), 2004).

79. 2014-2015 West Africa Ebola Crisis: Impact Update. Available at: https://www.worldbank.org/en/topic/macroeconomics/publication/2014-2015-west-africa-ebola-crisis-impact-update. (Accessed: 29th January 2020)

80. Huber C, Finelli L, Stevens W. The Economic and Social Burden of the 2014 Ebola Outbreak in West Africa. J Infect Dis 2018;218;S698–S704.

81. Coronavirus is fast becoming an 'economic pandemic'. *CNN* Available at: https://www.cnn.com/2020/02/24/business/coronavirus-global-economy/index.html. (Accessed: 25th February 2020)

82. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). Available at: https://www.who.int/news-room/detail/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov). (Accessed: 1st February 2020)

83. Guzman, J. WHO admits error in assessment of deadly coronavirus risk. *TheHill* (2020). Available at: https://thehill.com/changing-america/well-being/prevention-cures/480291-who-admits-error-in-assessment-of-deadly. (Accessed: 29th January 2020)

84. DR Congo Ebola outbreak now an international Public Health Emergency, UN health agency declares. *UN News* (2019). Available at: https://news.un.org/en/story/2019/07/1042681. (Accessed: 29th January 2020)

85. Maxme, A, Reardon S. World Health Organization resists declaring Ebola emergency — for third time. Nature 2019;570:283–4.

86. Lewis, T. Why the WHO's Emergency Declaration for Ebola Is a Big Deal. *Scientific American* (2019). Available at: https://www.scientificamerican.com/article/why-the-whos-emergency-declaration-for-ebola-is-a-big-deal/. (Accessed: 29th January 2020)

87. The Characteristics of Pandemic Pathogens. (2018).

88. Peters A. The global proliferation of high-containment biological laboratories: understanding the phenomenon and its implications. Rev Sci Tech 2018;37:857-8*3.*

89. FACT SHEET: The Global Health Security Agenda. *whitehouse.gov* (2015). Available at: https://obamawhitehouse.archives.gov/the-press-office/2015/07/28/fact-sheet-global-health-security-agenda. (Accessed: 29th January 2020)

90. WHO | Health security. *WHO* Available at: http://www.who.int/health-security/en/. (Accessed: 29th January 2020)

91. Anonymous. Health Security Committee activities. *Public Health - European Commission* (2016). Available at: https://ec.europa.eu/health/preparedness_response/risk_management/hsc_en. (Accessed: 29th January 2020)

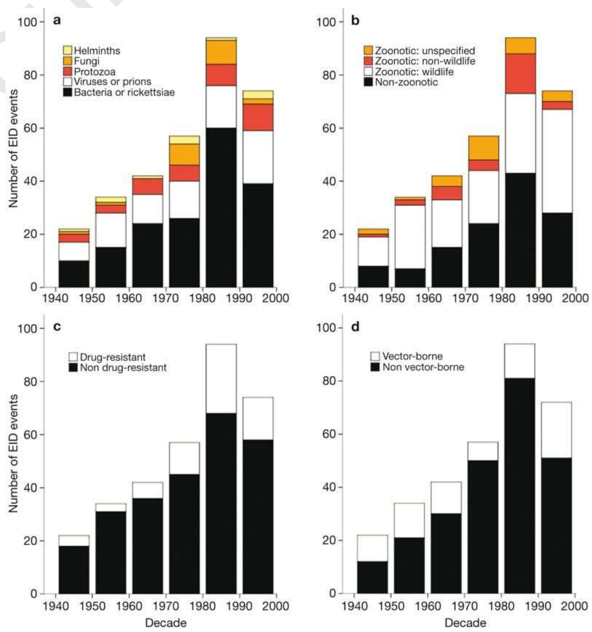
92. The Coming Plague: Newly Emerging Diseases in a World Out of Balance: Laurie Garrett: 9780140250916: Amazon.com: Books. Available at: https://www.amazon.com/Coming-Plague-Emerging-Diseases-Balance/dp/0140250913. (Accessed: 29th January 2020)

93. Global Preparedness Monitoring Board. A World at Risk: Annual report on global preparedness for health emergencies. (2019).

94. Global Monitoring of Disease Outbreak Preparedness Preventing the Next Pandemic: A Shared Framework. (2018).

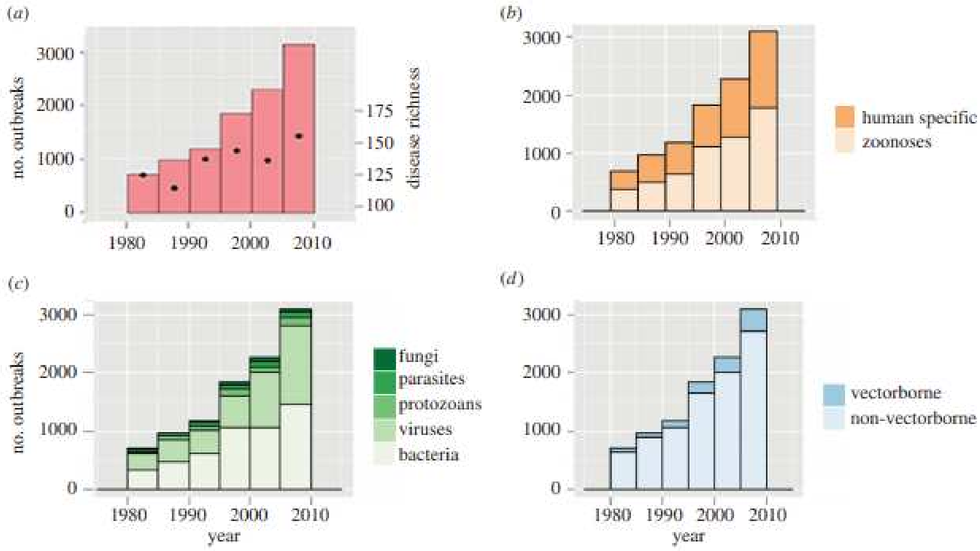
95. Feuer W. Watch: World Health Organization holds press conference on the coronavirus outbreak. *CNBC* (2020). Available at: https://www.cnbc.com/2020/02/24/watch-world-health-organization-holds-press-conference-on-the-coronavirus-outbreak.html. (Accessed: 25th February 2020)

Figure 1. Emerging Infectious Disease Events[2]



EID events (defined as the temporal origin of an EID, represented by the original case or cluster of cases that represents a disease emerging in the human population—see Methods) are plotted with respect to **a**, pathogen type, **b**, transmission type, **c**, drug resistance and **d**, transmission mode (see keys for details).

Figure 2. Global number of human infectious disease outbreaks and richness of causal diseases 1980 – 2010[1]



Outbreak records are plotted with respect to (a) total global outbreaks (left axis, bars) and total number of diseases causing outbreaks in each year (right axis, dots), (b) host type, (c) pathogen taxonomy and (d) transmission mode.