Journal of Hospital Infection 104 (2020) 440–448

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin

Opinion

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

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ARTICLE INFO

Article history:
Received 25 February 2020
Accepted 28 February 2020
Available online 5 March 2020

Keywords:
Infection prevention and control
Infection control
Hand hygiene
World Health Organization
Healthcare-associated infection
Global health
Survey

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 at national and international levels, will help to 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, although it is important to note that the improvement in diagnostic capabilities undoubtedly plays a role (Figures 1 and 2) [2,3]. By analysing 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 are single-stranded, positive-sense enveloped RNA viruses of the subfamily Orthocoronavirinae, family Coronaviridae, order Nidovirales. Among those, four are widely distributed human coronaviruses (HCoV-229E, HCoV-OC43, HCoV-NL63 and HCoV-HKU1) and cause the common cold. Severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are zoonotic. In 2002–2003, SARS-CoV caused an outbreak of pneumonia in 8000 affected cases, distributed over 30 countries and five continents, and is now considered to be eradicated. MERS-CoV was discovered in 2012 [4]. It originates from bats, with dromedary camels 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].

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 been observed previously in humans. Its likely reservoir is bats, with pangolins identified as the likely intermediate host [9].

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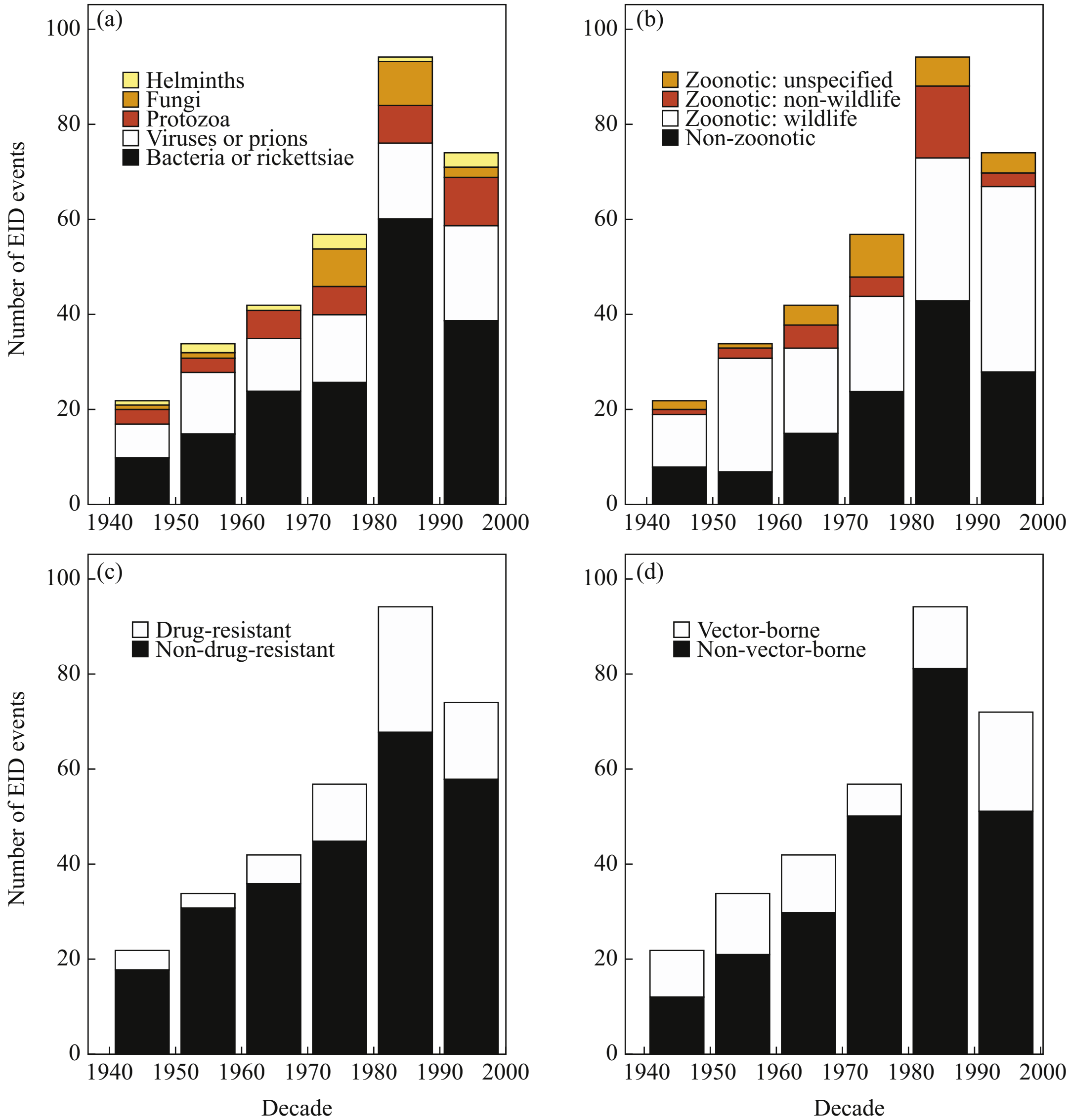

Figure 1. Emerging infectious disease (EID) events (defined as the temporal origin of an EID, represented by the original case or cluster of cases that represents a disease emerging in the human population — see Methods) are plotted with respect to: (a) pathogen type, (b) transmission type, (c) drug resistance and (d) transmission mode.

It is worth mentioning that pangolins are endangered and the most trafficked animal in the world [10]. As 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 rather than the source of the spill-over [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 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, and 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/re-emergence and spread of disease, as does the unmanageable explosion of the global wildlife trade. Legal and illegal wildlife trade is estimated to affect one in four mammal and bird species globally, and to generate between US$7.8 and US$10 billion annually [13,14]. In response to

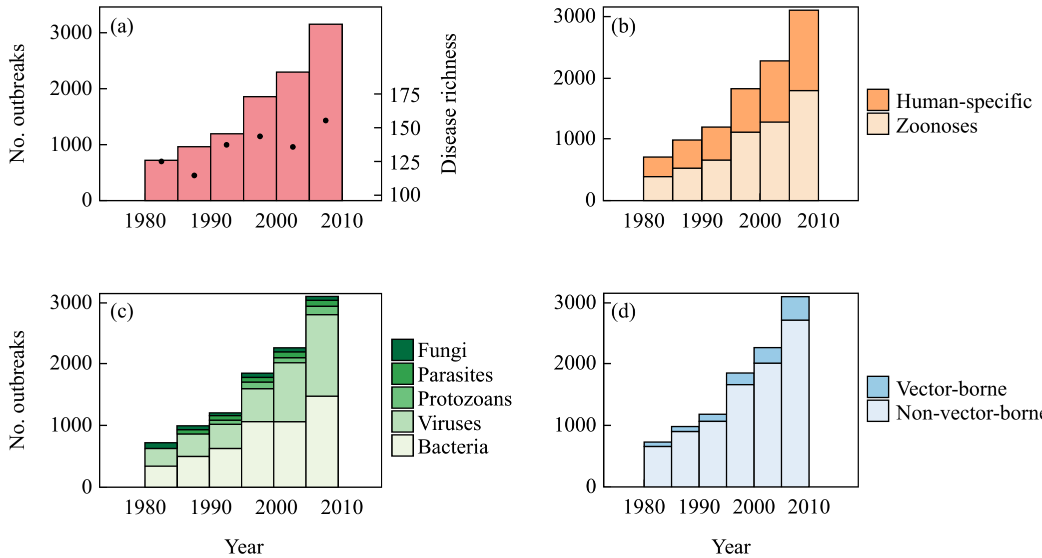

Figure 2. Global number of human infectious disease outbreaks and richness of causal diseases 1980—2010. Outbreak records are plotted with respect to: (a) total global outbreaks (left axis, bars) and total number of diseases causing outbreaks in each year (right axis, dots), (b) host type, (c) pathogen taxonomy and (d) transmission mode.

COVID-19, China placed a temporary ban on wildlife trade on 26th January 2020 [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 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 also important in animal farming [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 animals 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].

Due to the disease potential associated with intensive animal farming, animals are often treated with vaccines and antibiotics. Both avian and swine influenza continue to be managed through regular vaccination of livestock [19]. Although 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. Therefore, 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 re-emergence) of Nipah virus, Lassa fever, Lyme disease and, possibly, Zika virus [3,23].

A current example of this is 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 linked directly to 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 human immunodeficiency virus, 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 4 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 COVID-19 was very bad luck. Chinese New Year is the biggest mass migration in the world, with 385 million people making approximately 3 billion trips during the holiday period [30,31]. The fact that the outbreak happened during this time makes it that much more difficult to trace and control, and certainly influences the speed at which it is spreading. In a globalized world, the security of countries 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 re-emerging diseases pose for the human population. Impact can be assessed in different ways, including global morbidity, mortality, economic burden and geopolitical implications.

The stakes are high: the World Health Organization (WHO) estimates that a moderate to severe pandemic would cost approximately US$500 billion or 0.6% of global income [33]. As has been shown repeatedly, an epidemic does not need to reach severe levels or have many (or, technically speaking, 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, and if the pathogen is transmissible during the disease incubation period (if it is, the length of the incubation period is of importance).

Health system and human factors will also impact the spread of a virus. Health system capacity factors include the availability of treatment or vaccine, and the level of resources (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, mobility and cultural behaviours.

Individuals' behaviour 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 influenza 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 cause 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, but also the world economy and the country's political relationships with other countries (e.g. trade agreements, opening or closing national borders, etc.). Economists are expecting China's economic growth to slow to 4.5% because of the outbreak [37].

Close-up of SARS-CoV-2

SARS-CoV-2 fulfils many 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 been shown to have high interhuman transmission. Sufficient data are not yet 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]. WHO estimates are a little less daunting, reporting a preliminary reproductive number (R_0) estimate of 1.4–2.5 [39]. Importantly, calculations from Imperial College London estimate that infection control measures need to block well over 60% of transmissions 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], it will be even more difficult to implement a 60% effective infection and control (IPC) strategy, especially because most of the people infected will be 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 in their home countries will be crucial for preventing the spread of the virus [42]. The *Diamond Princess* cruise ship outbreak of SARS-CoV-2 in Japan, with more than 691 infected people and four deaths (as of 25th February 2020), is an example of 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 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, although this information will emerge over time. SARS-CoV-2 seems to be spread mainly by droplets and not through air. Nosocomial transmission has 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 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. The reason for this is that most of the cases screened are for relatively severe infections, especially in areas where tests are limited. Once more people are screened (including milder cases), the percentage of severe cases (and the death rate) will inevitable drop and get closer to its true value.

Contact tracing of 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 superspreaders of the virus may be playing a major role, either from individuals or a zoonotic source [50]. Superspreading 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 2701 deaths (as of 25th February 2020), overall fatality rate of 3.36%] [51]. Due to under-reporting, a shortage of test kits, reporting of all-cause mortality and a prevalence of patients with mild symptoms, it is highly likely that the death rate will be much lower than initially expected [52,53]. There are some estimates that currently only approximately 5% of 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 do not know what, if any, long-term effects this virus might have 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 sufficient information is not yet available, SARS-CoV-2 may be less deadly than the influenza virus that hospitals deal with on an annual basis, and transmission seems to occur mainly 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 is 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 approximately 1.3, but circulates through the whole human population every year [55]. Human immunodeficiency virus, on the other hand, spreads far more slowly through the 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 determine the full spectrum of the disease.

In order to better understand this dynamic, it might make sense to look at SARS-CoV. This has a similar reproductive rate to estimates of the R_0 of SARS-CoV-2, but only infected approximately 8000 people. In the early phase of the 2003 SARS-CoV outbreak, the lack or inappropriateness of IPC measures used proved to be associated with increased risk for cross-transmission and within-hospital spread of the disease among both visitors and healthcare staff [58–60]. In contrast, when applied appropriately, 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 more detailed transmission models are needed [62]. In a 2003 analysis of SARS in Hong Kong that excluded superspreading 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 go 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 the inevitability of having the virus at our doorstep, but we must think ahead to enact commonsense 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, 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. Although 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 prepare an institution. Healthcare staff must be reminded of the importance of hand hygiene, standard precautions, contact precautions and any complementary measures in preventing the spread of the disease.

Developing countries face 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) [96]. 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 healthcare 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]. Prompt prioritization of resources, precise surveillance and capacity development have been recommended 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 that hospitals deal with on a daily basis remains of utmost importance.

Response and 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 the Government of Sierra Leone imposed a 3-day quarantine, and sent police and military house to house to educate the population and to find people harbouring patients with Ebola patients in their homes [69,70].

That said, the COVID-19 outbreak is a delicate situation and a difficult decision for the Chinese Government to make – 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 it would be much more difficult for a government to implement such a large-scale dedicated disaster response in a democratic country. China worked day and night to construct two hospitals within a matter of days. They are made of prefabricated buildings, and serve to help handle the overwhelming number of patients [72]. On 28th January 2020, after just 48 h of construction, China opened another 1000-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 record pace; during the 2003 SARS epidemic, they were able to construct a 1000-bed hospital in under 1 week using prefabricated buildings. At the height of the epidemic, the Xiaotangshan Hospital treated one-seventh of patients with SARS in China [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 seem to be well founded: on 27th January 2020, 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; approximately 5 million residents reportedly left Wuhan before the quarantine was in place [75]. Deciding when to declare a national or international emergency is always a difficult risk–benefit analysis. The risks of doing so can disrupt trade and severely hurt a region's economy, but policy makers often do not have many options, especially when faced with public scrutiny.

Europe is now 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 cancelled 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 US$40 billion [78]. The direct economic burden of the 2014 Ebola outbreak is estimated to be between US$2.8 billion [79] and US$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 US$51 billion, with US$18 billion in deaths from non-Ebola causes [80]. The impact of the outbreak of 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 global economic damage [81].

After some debate, WHO declared SARS-CoV-2 a public health emergency of international concern (PHEIC) on 30th January 2020. 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 hand, it does not guarantee that the outbreak will be ended or the exact nature of the international response [82]. 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 WHO agreed to re-assess 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 withhold disaster relief funds if a PHEIC is not declared [84]. It is worth noting that WHO repeatedly declined to label the 2018 Ebola outbreak as a PHEIC, showing that there is a tendency to err on the side of caution [85]. When it did so 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 SARS-CoV-2 will help to mobilize the 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. Firstly, we do not know much about this virus, and secondly, so much of its spread will be dictated by human behaviour, decisions and, ultimately, luck.

There is much that can be done in terms of reducing the likelihood that novel viruses will jump from animals to humans, but these measures often include the type 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 difficult 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].

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, seven in Italy, four on the *Diamond Princess* cruise ship, two in Hong Kong, and one 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 21st February 2020. 'We need to act quickly before it closes completely' [95]. It seems to be less dangerous than initially thought, so perhaps, once again, humanity will be lucky. Hopefully, we can learn from our mistakes before our luck runs out.

Conflict of interest statement
None declared.

Funding sources
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 SPCI are also supported by the Swiss National Science Foundation (Grant No. 32003B_163262).

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