Movement and Nutrition in Health and Disease

The prevention of COVID-19 and the need for reliable data | Viewpoint

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Abstract: The previously unknown coronavirus (SARS-CoV-2) is the cause of the novel infectious coronavirus disease 2019 (COVID-19), which has been declared a global pandemic by the World Health Organisation. How much of a threat this pandemic poses in terms of infectiousness, virulence, need for medical care and case fatalities is unknown. Reliable data on the prevalence and incidence of SARS-CoV-2 and the number of deaths of (and not just with) COVID-19 confirmed at autopsy in representative random samples of the general population is currently unavailable. Exact figures are crucially important when introducing public health measures as far-reaching as prolonged social distancing and economic lockdowns. The imperiling of livelihoods resulting from drastic economic interventions is likely to put at risk the mental and physical health of those affected. Reliable epidemiological data describing the real course of the pandemic is urgently needed. In the uncertain scientific and political environment of the present coronavirus crisis, it may seem advisable to prepare for the worst. Measures capable of preventing the spread of the virus should be employed, thereby flattening the curve of infections and avoiding overwhelmed health systems unable to provide essential treatment for common diseases, resulting in avoidable deaths. Historical analyses may provide clues to the feasibility and effectiveness of public health measures in halting the spread of infections. During the influenza pandemic of 1918–1919, non-pharmaceutical interventions introduced across cities in the United States, such as personal hygiene, quarantine and limitations of public gatherings, were implemented unevenly. The key to flattening the curve of infection in 1918 appeared to be social distancing. However, this worked only when introduced decisively and quickly. In relation to social (physical) distancing, a similar pattern may be found during the current pandemic when comparing the effects of the uneven application of this measure in various countries in Asia, Europe and America. Multiple interventions, such as mandatory wearing of face masks and physical distancing, can be expected to delay the progression and decrease the peak of the COVID-19 pandemic. These measures may reduce the potential strain on health care systems and allow more time for collecting representative epidemiological data and for developing therapies. Once the number of new infections has been reduced significantly, widespread viral testing, contact tracing and isolation of people with the virus may be the best way to tackle the pandemic. Following this approach, restrictive measures may be confined to a limited number of people instead of the entire population.

The evidence base underlying the assumption of a worst-case scenario and the need for drastic measures such as lockdowns is, at present, insufficient. A major goal should therefore be the collection of representative and reliable data allowing a more profound and accurate risk analysis of the infectiousness and virulence of the virus, the role of predisposing factors (age, other medical conditions, environment), the full clinical presentation of COVID-19 (organs affected other than the lungs), medical care required and the case fatality ratio. The search for effective and safe medications and vaccines should be encouraged. Societies may need to adapt to a modus vivendi that controls the spread of coronavirus while affecting economic, social, cultural and political life as little as possible. Striking a balance between protection of public health and economic considerations will be a challenge facing governments worldwide.

Keywords: Coronavirus; COVID-19; pandemic; public health; prevention; social distancing; influenza.

1. Introduction

In December 2019, a previously unknown coronavirus (severe acute respiratory syndrome coronavirus 2, SARS-CoV-2) emerged in the Chinese city of Wuhan [1–3]. This virus is the cause of the novel infectious coronavirus disease 2019 (COVID-19), typical symptoms of which are fever, cough, respiratory problems and diarrhoea and, in severe cases, atypical pneumonia. Since the infection may be associated with mild symptoms or proceed asymptomatically, the number of undetected and unreported cases is likely to be high.

As of March 30, 2020, COVID-19 has spread to over 200 countries and has been officially declared a global pandemic by the World Health Organisation (WHO) [4]. In the second half of March 2020, the COVID-19 pandemic moved quickly westward, with the WHO declaring Europe the current centre of the outbreak. The past reluctance to prepare for a pandemic and the sluggish response to the present crisis in Europe and the United States is surprising and reprehensible in view of a widespread acceptance among scientists that a pandemic would one day occur ("not if, but when"). This is in stark contrast to the decisive action taken in mainland China and the swift responses in South Korea and Taiwan at the beginning of this year. While they have taken their recent experience with outbreaks of the severe acute respiratory syndrome (SARS) epidemic (2002–2003) and the Middle East respiratory syndrome (MERS) in 2015 seriously, the United States and Europe may have declined to take decisive action at the beginning of the current pandemic in the hope that it could be contained in its place of origin. The 2019 Global Health Security Index, assessing the capacity of 195 countries to manage outbreaks of infectious diseases, ranked the United States and the United Kingdom first and second, respectively [5]. However, the governments of these countries—and those of others—have responded extremely poorly to the present coronavirus pandemic, showing vacillation, obfuscation, dishonesty and incompetence.

2. Lessons from previous pandemics

Even though two pandemics are never identical, certain parallels can be found between COVID-19 and pandemics in the past. We have recently commemorated the centenary of the influenza pandemic that spread worldwide during 1918–1919. Around 500 million people or one-third of the world's population is estimated to have been infected with the influenza virus. According to approximate estimates, 50 million people or more lost their lives worldwide [6]. The influenza outbreak of 1918, also known as the Spanish Flu, is considered the most severe and deadly pandemic in modern history. Historical analysis is considered an important source of information on the effectiveness and feasibility of public health measures during a pandemic [7]. Hence, the Spanish Flu outbreak has been studied for clues to the most effective means to halt a global pandemic. Since neither a vaccine to protect against influenza infection nor antibiotics to treat secondary bacterial infections were available at the time of the outbreak, available control measures were limited. Although the cause of the influenza outbreak was unclear, there was a general understanding that it was spread through close contact. To prevent the spread of influenza across America, U.S. cities implemented various non-pharmaceutical public health interventions, including hygiene measures, use of disinfectants, obligatory wearing of masks, case isolation, closure of schools and churches and banning of mass gatherings. The outcomes of these measures may offer lessons for battling the present coronavirus crisis.

For example, following the detection of the first cases of a fast-spreading, deadly strain of influenza, the city of Philadelphia attempted to halt the spread of the virus by launching a campaign against coughing, sneezing and spitting in public. However, the city hosted a parade that was attended by 200,000 people [8]. An outbreak of the virus followed within days of the parade. The decision to close schools, theatres, dance halls and churches and to shut down public gatherings came only eight days after the beginning of an increase in the rate of deaths in Philadelphia. Ultimately, the city endured the highest peak death rate of the U.S. cities studied. In contrast, when the first influenza cases were reported in St. Louis, the city banned most public gatherings, including a planned parade, and quarantined victims in their homes. As a result, deaths due to the influenza virus were estimated at 385 people per 100,000 in St Louis, compared to a fatality rate more than twice as high (807 per 100,000) in Philadelphia during the first six months of the pandemic [8]. Time-limited interventions decreased total mortality only moderately (perhaps 10–30%). The impact of these measures was frequently very limited since they were introduced too late and lifted too early [9]. Cities, such as St. Louis, San Francisco, Milwaukee and

Kansas City, which, in imposing strict closures of public gatherings, responded quickest and most effectively, experienced transmission rates approximately 30 to 50 percent lower than in other places [9]. Those U.S. cities implementing multiple interventions at an early phase of the epidemic had peak death rates around 50% lower than those that did not, and their epidemic curves were less steep; early introduction of multiple interventions was also associated with a trend toward reduced cumulative excess mortality [10]. It is important to note that it was the simultaneous implementation of interventions, i.e. closure of schools, churches and theatres as well as banning of public gatherings, that was associated with decreased peak death rates, while no single intervention showed an association with improved aggregate outcomes for the 1918 phase of the pandemic [10]. These findings suggest that rapid implementation of multiple non-pharmaceutical interventions can significantly reduce influenza transmission, but spreading of the virus will be renewed following relaxation of such measures. St. Louis, for example, due to its relatively low death rate early on, lifted restrictions on public gatherings less than two months after the influenza outbreak began. A wave of new cases soon followed, while a second wave was less prevalent in cities keeping interventions in place.

In summary, social distancing appears to have been the key to flattening the curve of infection in 1918. However, historical analysis has its limitations and needs to take into account possibly differing biological, medical, social and political factors. Therefore, extrapolation from pandemics in the past to the present COVID-19 crisis requires great caution. There may, for example, be differences in respect to infectiousness or the bodily organs affected by the viruses involved. Furthermore, a wide range of sociodemographic conditions in the United States at the time of the 1918 influenza epidemic differed greatly from those today. In 1918, the average number of household members was much larger, interaction with extended families was commonplace, crowded boarding house accommodation was common among workers, malnutrition was more prevalent and the general mortality related to infectious diseases was significantly higher. All of these factors may have made both influenza transmission and fatalities far more likely.

With only 215 confirmed cases and two deaths as of March 24 [11], the present situation in Taiwan is in stark contrast to the SARS experience of 2003. Taiwan's present approach has been shaped by the devastating effect of the SARS epidemic, following which Taiwan overhauled its entire public health system, increasing the numbers of infectious diseases testing laboratories, of emergency rooms in hospitals and of doctors employed at the Centres for Disease Control. In addition, basic items such as surgical masks were stockpiled [12]. Furthermore, a unique management structure, the Central Epidemic Command Centre, was introduced. This is an expert panel whose chair has equal rank with government ministers and can therefore override policy decisions and ensure a rapid response. Early travel restrictions, widespread testing and contact screening as well as strict quarantine rules appear to have been pivotal in constraining the virus. Pro-active and transparent communication helped foster the willingness of the population to co-operate with these measures. Early mobilization of specific plans and strategies has succeeded in containing SARS-CoV-2 in Taiwan.

3. Social (physical) distancing measures

Physical distancing involves avoiding situations that may encourage virus transmission and include refraining from hand shaking, compulsory wearing of facial masks and maintaining a physical distance of at least 2 metres between individuals not living together. A more radical variant of social distancing is a lockdown of public life, including exit restrictions and the closure of shops, restaurants, schools and non-essential community services.

Social distancing and lockdowns aim to reduce the basic reproductive ratio, R_0. In epidemiology, R_0 is an important parameter of an infection's potential transmissibility and describes the speed of transmission. R_0 estimates how contagious an infection is and indicates the average number of individuals who may contract the disease from a single infected person in a homogeneous population not previously exposed to the disease. When R_0 is greater than one, the infection is likely to keep spreading exponentially and presents a serious threat to public health. If, for example, one infected person passes the infection to three others, R_0 is 3. The greater the value of R_0, the more rapidly an epidemic will progress. By contrast, when each existing infection causes less than one new infection, the outbreak will probably decline and eventually peter out. R_0 is difficult to calculate, especially at early stages of an epidemic when the number of cases is unclear, with infected individuals either asymptomatic or not reporting their symptoms to authorities. Even when R_0 equals or is lower than one, high numbers of infected people transmitting the virus to almost the same number of healthy individuals can easily cause serious problems for health systems. This means that the reproduction number should always be interpreted in the context of the number of infected cases.

3.1. Physical distancing in China in 2020

Local and national governments in mainland China have taken unprecedented measures in response to the SARS-CoV-2 outbreak in Wuhan. Exit screening and travel restrictions were introduced in Wuhan and the province of Hubei around the Lunar New Year holidays (January 25, 2020), thereby halting all unauthorised travel both into and out of the city and province [13]. Non-pharmaceutical public health interventions, such as school closures and workplace social distancing, had been shown to markedly change age-specific mixing patterns within the population during previous outbreaks of other respiratory infectious diseases [14,15]. Therefore, in addition to measures limiting traffic within and between cities, interventions in Wuhan included physical distancing (school closures and workplace distancing), home confinement, centralised quarantine and improvements of medical resources [16]. These measures appear to have been associated, at least temporally, with improved control of the COVID-19 outbreak. It has been estimated that the travel ban introduced in Wuhan delayed the progression of the epidemic by 3 to 5 days in mainland China [17,18] and decreased the export of cases to other regions by approximately 80% in February 2020 [17]. Using real-time mobility data from Wuhan and detailed case data including travel history, the findings of another study suggest that the drastic control measures substantially mitigated the spread of COVID-19 [19]. The estimates of a modelling study suggest that physical distancing may, to some extent, have delayed and reduced the peak of the epidemic in Wuhan [20]. Reducing and flattening the peak is particularly important, since this affords the health-care system more time to expand and respond. The sustaining of restrictive measures in Wuhan until April may also produce benefits in terms of median epidemic size at the end of 2020 [20]. Premature and sudden lifting of public health measures could result in an earlier secondary peak, which would necessitate the reintroduction of restrictions and could be flattened by the gradual relaxation of these interventions [20].

In summary, the interventions deployed in mainland China appear to be effectively containing the COVID-19 outbreak. Sustained physical distancing has a strong potential to decrease the magnitude of the epidemic peak of COVID-19 and the overall number of cases. Since a range of interventions were introduced simultaneously by the Chinese government, identification of the respective roles of single measures is difficult. Early case detection and contact reduction may be the most effective interventions [21].

3.2. Side effects of social distancing

While epidemiological models are effective at predicting prevalence and mortality, they are less suited to assessing the subjective experience of distancing measures and the human cost of imposing radical changes to behavior. An economic lockdown may present a choice between different health outcomes: vulnerable groups are likely to benefit from isolation from the virus, while the costs of isolation and loneliness may predominate in others. The burden on physical wellbeing and mental health associated with social distancing needs to be considered, since confinement to indoor spaces may have detrimental effects. Seniors may be less comfortable with virtual means of communication [22], and the feeling of social isolation among all age groups may be associated with an increase in the prevalence of substance use, depression, and suicidality and even a decrease in anti-viral immune responses [23–25]. School closures may lead to an increase in child abuse.

The measures taken to prevent the spread of SARS-CoV-2 should not cause more serious effects than the virus itself. A cornerstone in this conflict of objectives is robust and reliable data. Daily counts of new infections and fatality ratios will not suffice. Instead, contextual information is required, for example, regarding effective reproduction number and geographical distribution. The acceptable real-time effective reproductive number depends on circumstances and may vary between different communities. It is therefore important to ascertain the number of new infections that a particular health system can cope with.

3.3. Easing physical distancing measures

While various forms of physical distancing and lockdowns appear to successfully curb the spread of COVID-19 and decrease case fatality rates as long as they remain in effect, their severely compromising effects on economy, social life and individuals' emotional and mental wellbeing preclude their indefinite implementation. The experiences of the influenza pandemic 100 years ago showed that once closures were lifted, large bounces and a second and third wave of infection followed [26]. While the first wave usually starts in a limited number of places, a second wave may spread from many locations, thus having a greater impact and being more difficult to control. The easing of restrictions therefore presents us with the problem of how to prevent further surges. As soon as social and economic activities restart, local and imported cases of coronavirus could lead to new outbreaks of COVID-19.

When taking into consideration the effective reproduction number, i.e. the actual transmission rate at a given time, several scenarios involving the easing of restrictions are conceivable. If easing leads to a ratio greater than 1, the health system may be overwhelmed by a possibly exponential rise in transmissions, and cycles of repeated lockdowns and loosening of restrictions will follow. If interventions are continued with a ratio of around 1, gradual easing of restrictions may be considered as long as the number of infected people is not too high, with lockdowns being relaxed earlier in lower intensity regions and later in hotspot areas. However, it may be necessary to keep restrictions in place for several years to come. Pushing the ratio significantly below 1 by strict tightening of restriction measures for some weeks may gain the time needed to install alternative protective measures and to optimise viral testing and (digital) contact tracing. From a scientific point of view, the last scenario may be the most promising.

The aim of the latter scenario could be to reduce the number of new infections to such an extent that it is possible to track contacts completely. At the same time, extensive testing would need to be performed in order to discover each new infection focus as quickly as possible. The implementation of these two strategies could achieve a stable and sustainable situation aiming to consistently control all infection chains. The fewer the number of new infections, the easier it will be to further reduce their number, since the fewer uncontrolled infection chains that exist, the more effectively contact tracing will work. Mobile software applications (contact-tracing apps) aiding in the identification of people who may have been in contact with an infected person are being developed [27]. Widely deployed digital contact tracing will probably be more effective than traditional methods. With complete contact tracing, the number of new infections could, theoretically, be brought to zero. In practice, however, an absolute and permanent value of zero is not possible as long as the virus exists.

Scientific evidence needs to inform decisions of when, how and under what circumstances restrictions should be eased. A trade-off between the objectives of fighting COVID-19, keeping society intact and protecting the economy will be inevitable. The more rapidly restrictions are withdrawn, the lower the economic cost and the higher the human cost will be. However, severe economic losses may also eventually lead to societal costs. Public acceptance is necessary to avoid widespread social unrest, as willingness to accept drastic measures for extended periods of time may decline. The SARS-CoV-2 crisis is a most uncertain threat to the world's economy. The COVID-19 outbreak carries the potential to cause a global recession, with a major disruption of global supply chains [28]. Repeated lockdowns could cause mass unemployment, bankruptcies and rising national debt, affecting the prosperity, employment, health and wellbeing of people all around the world.

4. Uncertainties about SARS-CoV-2

Numerous uncertainties surround the transmission, contagiousness, virulence and infection fatality rate of SARS-CoV-2, and research has as yet yielded neither a potential treatment for nor a vaccination against COVID-19.

4.1. Transmission of SARS-CoV-2

Data from China suggests that up to 85% of SARS-CoV-2 transmission has occurred in family clusters [29], suggesting that close and unprotected exposure is required for transmission by direct contact. This hypothesis is supported by reports of transmission among people attending the same social events or those in confined areas such as offices or cruise ships [30,31].

The number of virus particles (viral load) to which an individual is exposed can affect the likelihood of infection. The minimum infectious dose of SARS-CoV-2, i.e. the amount of virus necessary to infect an individual, is unknown. Higher viral loads may lead to more severe clinical symptoms of COVID-19.

Possible routes of SARS-CoV-2 transmission include respiratory droplets, e.g. from the coughing, sneezing or talking of an infected individual, and direct or indirect contact (smear infections) [32]. The virus is believed to spread mainly by larger respiratory droplets remaining in the air for a short time, sinking to the ground very quickly and thus travelling short distances only. This means of transmission underlies the common recommendation of maintaining a physical distance of 1.5–2 metres. However, it is also possible that clouds of tiny viral particles (aerosolised droplets) persist in the air or travel longer distances. Aerosol clouds could be able to infect a person walking through them. It may therefore be necessary to maintain greater distances from infected individuals exhaling clouds of large numbers of microdroplets while exercising (walking, running, cycling). Similar problems could occur during the playing of sports such as football.

In regard to social proximity, aerosols will pose a greater risk of infection in enclosed spaces than in well-ventilated areas.

Whether asymptomatic carriers of coronavirus play a role in transmitting infection is unclear [29]. This issue is important in the containment of the outbreak, as is the question of presymptomatic infectiousness. While the vast majority of infected children appear to show no or only mild symptoms of COVID-19, they may nevertheless be able to transmit the virus.

4.2. Prevalence and incidence of SARS-CoV-2 infections

Reliable data on the prevalence of SARS-CoV-2 in representative random samples of the general population are currently unavailable. Given the limited testing for the new coronavirus so far, the vast majority of infections are likely to have gone unreported. By what factor infections (and deaths due to COVID-19) go undetected is, at present, completely unknown. If more tests are carried out when the estimated, but unconfirmed, number of people infected with SARS-CoV-2 is high, it is probable that the more widespread testing will detect more cases of infection, even though the spread of the virus and the true incidence of infection, i.e. the rate of new cases occurring within a period of time, have not changed. In fact, one could imagine the paradoxical situation in which the number of people found to be infected over a certain time period increases as a result of more extensive testing, while the actual prevalence and incidence of SARS-CoV-2 infections have decreased. In order to reliably estimate the current prevalence of SARS-CoV-2, tests in a sufficiently large random sample of a population would need to be performed. Repeated testing in the same sample at regular time intervals would allow an estimation of the incidence of new infections.

4.3. Mutation of SARS-CoV-2 and climatic effects

The question of whether SARS-CoV-2 is affected by seasonal changes remains, as yet, unanswered. Longitudinal studies will be able to reveal a link between climatic factors (temperature, humidity) and COVID-19 [33]. Furthermore, viruses tend to mutate, and mutations may lead to variances in infection rates in different parts of the world. Whether SARS-CoV-2 will change into a more dangerous virus remains to be seen.

4.4. Clinical effects of COVID-19

Most people infected with the coronavirus appear to present with few, mild or even no symptoms at all [34]. However, others may be severely affected by pneumonia and may need medical care and, in some cases, hospitalisation. In severe cases, intensive care, including ventilation, may be required, and the disease may be fatal. The reasons why the severity of symptoms and survival vary among people infected with COVID-19 is, at present, unknown. Factors that seem to influence an individual's likelihood of suffering severe symptoms include age, other medical conditions, sex, genetic susceptibility and previous immunisations. The role of environmental factors, such as air pollution and fine-particle pollution, and modifiable lifestyle factors, e.g. smoking and diet, in the susceptibility to infection with SARS-CoV-2 requires further investigation. Obesity and metabolic syndrome, for example, are known to decrease immune function and could be a factor in virus-related deaths [35]. Furthermore, the effects of SARS-CoV-2 on organs other than the respiratory tract should be explored.

4.5. Case fatality ratio for COVID-19

The case fatality ratio indicates the proportion of deaths from a certain disease in relation to the total number of people diagnosed with this disease within a certain period of time. Most known infections with SARS-CoV-2 may cause only a mild form of the disease; the case fatality ratio has been reported to range from 2.9% in Hubei province to 0.4% in other Chinese provinces [36]. Elderly people, especially those over 80 years, and individuals with comorbidities, such as cardiac disease, respiratory disease and diabetes, are at the greatest risk of serious symptoms and death [36]. Furthermore, older people in nursing homes seem to be at particular risk of severe illness [37].

Reliable information with respect to deaths of (and not just with) COVID-19 confirmed at autopsy does not exist. In some individuals, SARS-CoV-2 infection may co-occur with serious medical conditions: these may cause death or may hasten a death that was in any case imminent. As long as the actual numbers regarding infections and fatalities are unknown, both numerator and denominator for calculating case fatality ratios are unreliable. The reported ratios are therefore meaningless and probably too high, since SARS-CoV-2 testing is mainly performed in patients with severe symptoms and poor outcomes. Since the true case fatality risk remains unknown, we are forced to accept at best rough approximations which may not even approach the true values. However, the availability of exact figures is of utmost importance when far-reaching decisions regarding drastic measures of social distancing and economic lockdowns are made. For example, if the true case fatality risk of COVID-19 were in the same range as that of seasonal influenza, it would be utterly unreasonable to lock down entire societies, with all the social and economic consequences involved.

4.6. Herd immunity

An alternative strategy in the attempt to control the COVID-19 pandemic is to allow SARS-CoV-2 to spread among the population in order to increase the numbers of people with immunity to the virus. The pandemic may come under control when around 60–80% of the population have been infected [38]. Given the uncertain case fatality rate of COVID-19, the estimated number of people who could potentially die from COVID-19 could be unacceptable. However, the immune status of people who have been infected with SARS-CoV-2 is still unclear. It is not known whether re-infection, even when antibodies are present, is possible and how long immunity will last.

4.7. Medications and vaccines against COVID-19

At present, there are no anti-viral agents known to shorten the duration, mitigate the severity or reduce the death rate of COVID-19. Some preliminary data from non-randomised observational studies suggest that several drugs that have shown promise in treating other coronaviruses, including SARS and MERS, could have an impact on the coronavirus [39]. However, more research is needed to determine whether these medications can effectively treat COVID-19. To date, treatments with proven efficacy are not available.

Producing, manufacturing and distributing an effective and safe COVID-19 vaccine will be of great importance. There is a compelling case for global investment in developing a vaccine which would be available worldwide, including in the poorest countries. The contribution of wealthier countries to such an endeavour can be advocated on grounds of both self-interest and humanitarian considerations. However, there is no guarantee that a vaccine can eventually be found. We should remind ourselves that so far, despite substantial efforts, no vaccine has been developed against other coronavirus strains causing the common cold. Even were vaccine tests to prove successful, more time would be needed for the mass production of the vaccine. Furthermore, the efficacy and safety of a vaccine would need to be demonstrated in all age groups and people with compromised immune systems. In consideration of the many years needed for the development of vaccines in the past [40], an expectation that the clinical trials and safety approvals required to bring a COVID-19 vaccine to the market could be completed by 2021 may be far too optimistic. The feasibility and efficacy of passive immunotherapy using human antibodies obtained from blood of donors recovered from COVID-19 infection remain to be investigated.

5. Conclusions

The extent of the danger posed by the present COVID-19 pandemic, in terms of infectiousness, virulence, need for medical care and case fatalities is unknown. Factors that appear to be associated with a greater risk of severe symptoms include age, other medical conditions, sex, genetic susceptibility, previous immunisations and lifestyle. Reliable data on the prevalence of SARS-CoV-2 and the number of deaths of (and not just with) COVID-19 confirmed at autopsy in representative random samples of the general population are currently unavailable. However, the availability of exact figures is crucial when introducing public health measures as far-reaching and drastic as prolonged social distancing and economic lockdowns, which affect physical wellbeing, mental health and civil liberties. Data obtained from sufficiently large and representative samples are therefore urgently needed.

In view of the lack of clarity in the present coronavirus crisis, preparation for the worst may be prudent. It would seem advisable to seek measures capable of preventing the spread of the virus, thereby flattening the curve of infections, in order to avoid overwhelming of health systems and loss of life due to common diseases left inadequately treated. While historical analyses have limitations, they may nevertheless provide clues to the feasibility and effectiveness of public health measures in halting the spread of infections. During the influenza epidemic in 1918–1919, non-pharmaceutical interventions introduced across cities in the United States, such as personal hygiene, quarantine and limitations of public gatherings, were applied unevenly. The key to flattening the curve of infection in 1918 appeared to be social distancing. This is likely to remain true in the fight against coronavirus today. However, in 1918, social distancing was effective only when introduced decisively and quickly. A pattern similar to the experience of American cities in 1918 in relation to social (physical) distancing appears to be found when comparing the effects of the uneven application of this measure in various countries in Asia, Europe and America during the current coronavirus pandemic.

Table 1. Overview of the need for reliable data related to COVID-19

Prevalence and incidence	Prevalence and incidence of SARS-CoV-2 infection and COVID-19 in representative random samples of the general population are unknown.
Transmission of SARS-CoV-2	The minimum infectious dose of SARS-CoV-2 and the relationship between infectious dose and severity of COVID-19 are unknown. The proportion of people infected with SARS-CoV-2 and actually developing COVID-19 is unknown. The role of transmission by presymptomatic and asymptomic individuals with SARS-CoV-2 is unclear. The role of duration and place of contact (open versus enclosed spaces, household, public transport) with an infected person is unclear. The role of respiratory droplets, clouds of aerosolised droplets and smear infections is unclear. The effects of seasonal and climatic factors (temperature, humidity) are unclear.
Clinical aspects	The exact effects of SARS-CoV-2 on the respiratory tract and possibly other organ systems (cardiovascular, urinary, nervous) are unclear. The proportion of people infected with SARS-CoV-2 and in need of medical care is unknown.
Risk factors	The role of factors influencing the risk of severe symptoms and death of COVID-19, such as age, sex, previous immunisations, other medical conditions (obesity, metabolic syndrome, cardiac and kidney diseases), environment (air pollution), socioeconomic status and lifestyle (nutrition, physical exercise) is unclear.
Case fatality ratio	The number of deaths of (and not just with) COVID-19 confirmed at autopsy in representative random samples of the general population is unknown.
Preventive interventions	Prevention of the spread of SARS-CoV-2 may be advisable to protect public health and health care systems and to avoid a worst-case scenario. Multiple non-pharmaceutical interventions (face masks, social/physical distancing, e.g. exit restrictions, closure of schools, shops, restaurants and theatres, banning of mass gatherings) may delay the progression and reduce the peak of the COVID-19 pandemic ("flattening" the curve of infection). Identifying (widespread SARS-CoV-2 testing), contact tracing (widely deployed mobile apps) and isolating people with the virus may be able to "crush" the curve of infection. The effects of single measures (e.g. school closures) are unclear. Early case detection and contact reduction may be the most effective interventions.
Side effects of preventive measures	Social distancing may cause loneliness, domestic violence and impaired physical wellbeing and mental health (e.g. anxiety, depression, substance use and suicidality). School closures may lead to an increase in child abuse.
Immunity	The immune status of people who have been infected with SARS-CoV-2 is unclear. Re-infection, even in the presence of antibodies, might be possible. The COVID-19 pandemic might be under control when approximately 60–80% of the population have been infected (herd immunity).
Treatment and vaccination	Medications and vaccines against COVID-19 are unavailable; the development of effective and safe options in the foreseeable future is uncertain. The potential of passive immunotherapy using human antibodies from donors recovered from COVID-19 infection is unknown.
Summary	The threat posed by the COVID-18 pandemic in terms of infectiousness, virulence, need for medical care and case fatalities is unknown. Unbiased prevalence and incidence data describing the real course of the pandemic is urgently needed. Reliable data is crucial when introducing far-reaching public health measures. The evidence for the assumption of a worst-case scenario and the need for drastic interventions, such as economic lockdowns, is insufficient. Balancing public health, social life and economy is the major challenge.

The unprecedented and drastic measures taken in response to the SARS-CoV-2 outbreak in mainland China highlight the effectiveness of physical distancing. China's experience will also be essential to understanding how careful calibration of lifting of restrictions can avoid subsequent COVID-19 waves. Without resorting to extreme measures, other areas in East Asia have been able to avert a major COVID-19 outbreak and to delay the peak of the pandemic. Analysis of the associations of various measures implemented to control the spreading of SARS-CoV-2 in China and elsewhere may inform public health policy globally in combating the COVID-19 pandemic.

6. Future perspectives

SARS-CoV-2 appears to spread globally and may become a fifth endemic coronavirus in addition to the currently circulating four strains within the human population. We can only conjecture at present as to whether a return to the pre-pandemic way of life is possible or whether life will be transformed in ways that cannot yet be imagined. Normality may not return until an effective treatment for the great majority of cases or a safe vaccine are available. This, however, may take several years, and repeated outbreaks of COVID-19 are likely to occur. Therefore, measures needed to prevent the spread of coronavirus may continue well into the future. The effectiveness and social acceptability of preventive interventions as well as the economic, societal and political implications of such measures will challenge societies globally. Scientific evidence needs to inform decisions regarding restrictive measures, since economic loss as a result of lockdowns may also have harmful effects on physical and mental health and may eventually take an unacceptable toll on society.

The pressing task of scientists will be to collect, provide and interpret empirical or experimental data related to transmission, epidemiology, prevention and treatment of COVID-19. On the basis of the available evidence, it is the responsibility of politicians to weigh arguments, make decisions, take action, introduce public health measures and adapt health systems. Clear and transparent communication is vital to ensure credibility, compliance and social acceptability. The media also plays an important role in presenting and explaining facts to the public without dramatising and sensationalising.

7. The bottom line

Much remains to be discovered about the transmission of and immune responses to the new coronavirus as well as to the clinical significance and treatment of COVID-19 (see Table 1). Reliable scientific data is therefore urgently needed. In order to avoid a potential worst-case scenario (the evidence base of which is insufficient to date), it may be prudent to prevent the spread of SARS-CoV-2 and to maintain restriction measures until science can provide the answers to the most pressing questions. In the meantime, societies need to find a modus vivendi that keeps the spread of coronavirus at bay, while interfering as little as possible with economic, social, cultural and political life. Striking a balance between a functioning economy and protecting public health will be the challenge facing governments worldwide.

Conflict of interest

The author declares no conflict of interest.

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