The end of the COVID-19 pandemic

John P. A. Ioannidis

Abstract

There are no widely accepted, quantitative definitions for the end of a pandemic such as COVID-19. The end of the pandemic due to a new virus and the transition to endemicity may be defined based on a high proportion of the global population having some immunity from natural infection or vaccination. Other considerations include diminished death toll, diminished pressure on health systems, reduced actual and perceived personal risk, removal of restrictive measures and diminished public attention. A threshold of 70% of the global population having being vaccinated or infected was probably already reached in the second half of 2021. Endemicity may still show major spikes of infections and seasonality, but typically less clinical burden, although some locations are still hit more than others. Death toll and ICU occupancy figures are also consistent with a transition to endemicity by end 2021/early 2022. Personal risk of the vast majority of the global population was already very small by end 2021, but perceived risk may still be grossly overestimated. Restrictive measures of high stringency have persisted in many countries by early 2022. The gargantuan attention in news media, social media and even scientific circles should be tempered. Public health officials need to declare the end of the pandemic. Mid- and long-term consequences of epidemic waves and of adopted measures on health, society, economy, civilization and democracy may perpetuate a pandemic legacy long after the pandemic itself has ended.

KEYWORDS

COVID-19, endemicity, excess deaths, pandemic, population immunity

1 | INTRODUCTION

Claiming a time-stamped end-date for the COVID-19 pandemic is precarious. There is no rigorously quantitative definition of pandemics, let alone their end. In dictionary terms, a pandemic is ‘an epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people’. To avoid naming ‘pandemics’ all seasonal viral waves, unusual severity (death toll, healthcare burden) may be sought. However, not all new viruses that become widely spread have high clinical burden. Thus, one may call the wide spread of a new virus (against which populations have little prior immunity) a pandemic, regardless of severity. One has to define carefully how the term ‘pandemic’ is used to avoid misunderstandings. Once a high population immunity threshold (from infection or vaccination) is attained, the pandemic transitions to an endemic phase.

Selecting any quantitative immunity threshold is arbitrary. Thresholds defined on basic reproduction number
considerations \((1-(1/R_0))\) make a lot of assumptions, do not allow properly for population heterogeneity, depend on \(R_0\) estimates that may not be accurate and are expected to change when variants with different \(R_0\) emerge and become dominant. Realistically, the threshold should be high, but not 100%. Probably, considerable population segments will remain unvaccinated despite all vaccination campaign efforts, and some unvaccinated people may still escape infection for many years. For noneradiated infectious agents, community transmission continues with recurrent seasonal waves and spikes of various heights in the endemic phase and with large differences across countries and locations. Despite high vaccination and prior infection rates, immunity may be insufficient to protect from mild infection and transmission (even less so, when new variants emerge), but may still markedly decrease serious outcomes.\(^4\)

If transition to SARS-CoV-2 endemicity requires a prior vaccination/infection threshold of 70%, this threshold was probably already reached globally during 2021, as discussed below. However, several other considerations should be evaluated before safely relegateing the pandemic to the past. These include the persisting death toll, clinical burden, actual and perceived personal risk, continuing measures taken against COVID-19, public attention and the legacy of both epidemic waves and adopted measures.

## 2 | POPULATION IMMUNITY

By end 2021, 58% of the global population had received some vaccine and 49% had been fully vaccinated\(^5\) (although ‘fully’ may be a misnomer in the long-run). The proportion of people infected has uncertainty, because only a minority of infections are documented by testing.\(^6\) Based on almost 3000 seroprevalence estimates generated in various surveys to-date,\(^7\) probably 35–55% of the global population had been infected at least once by end 2021. By end 2021, probably 73–81% of the global population had been vaccinated, infected or both (Table 1). This may be even an underestimate. Therefore, a 70% threshold for the end of pandemic was already crossed during 2021 and SARS-CoV-2 entered its endemic phase. Massive Omicron variant surges since late 2021 added far more infections but were accompanied with lower mortality/clinical impact.\(^8\)–\(^10\) While Omicron may also be intrinsically less lethal, the picture could be largely explained also as an endemic escape variant surging against widespread background population immunity.

Seroprevalence surveys performed in late 2021 agree with these population immunity estimates (Table 1).\(^7\) Arguably, surveys can be biased and only few countries have recent data. However, almost all Table 1 data show seroprevalence estimates >70% in the second half of 2021. With continued vaccinations and infections, estimates probably increased further since then. By end February 2022, 63% of the global population had received some vaccine (55% ‘fully’ vaccinated), almost as many people had probably been infected at least once and probably close to 90% of the global population was vaccinated or infected at least once.

Even if 70–90% of the global population has some immunity, heterogeneity may exist across regions. By end 2021, population immunity was probably still <70% in Oceania, and there is uncertainty about Africa. Some poor countries with low vaccination rates may have also been relatively spared from infectious waves. Conversely, countries in Europe spared from strong epidemic waves (e.g. most Scandinavian countries) achieved very high vaccination rates. Substantial heterogeneity may still exist across and within countries and smaller communities. Pockets with low immunity may persist for years, allowing local and regional outbreaks of at least moderate intensity. Importantly, vaccination or infection do not always guarantee effective immune responses; and durability and adequacy to prevent from newer variants and prevent serious clinical outcomes carries substantial uncertainty.\(^10\)–\(^11\)

Population immunity may continue being renewed with new infections and vaccinations. The need for any repeated vaccinations requires dispassionate study. This is all an expected part of the endemic phase, no longer a pandemic. Waning immunity, waning vaccine effectiveness, emergence of novel (more or less pathogenic) variants because of evolution and the role of the well documented animal reservoirs may shape the emergence and magnitude of SARS-CoV-2 epidemic waves in the future and several of these factors are unpredictable. For a review of natural, vaccine, hybrid immunity and their waning rates see ref.\(^12\)

## 3 | DEATH TOLL

### 3.1 | ‘Normal’ death toll, COVID-19 and past pandemics

It is important to understand how far from ‘normal’ this pandemic has taken us, to navigate what ‘return to normal’ would mean. ‘Normal’ is already an elusive concept, because substantial fluctuation exists from 1 year to next and large (largely unexplained) variability exists across different countries and locations every year. One may compare typical recent seasons of influenza, against respective death burdens of past pandemics of the 20\(^{th}\) and 21\(^{st}\) centuries (Table 2). For fair comparison, one should adjust for global population size. Moreover, one should consider the age distribution of infection-caused deaths and life expectancy at
<table>
<thead>
<tr>
<th>Region (population in millions)</th>
<th>Vaccinated Any (fully) (%)</th>
<th>Infected at least once (%)</th>
<th>Either (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Indicative seroprevalence [location, month, n]&lt;sup&gt;c&lt;/sup&gt; (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe (748)</td>
<td>65 (61)</td>
<td>30–60</td>
<td>76–86</td>
<td>76 [Sweden, September, 2959]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>97 [Sweden, September, 402]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>77 [Estonia, September, 2302]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>82 [Estonia, December, 2290]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>83 [Finland, August, 110]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>84 [Slovakia-Bratislav, July, 1928]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100 [Scotland, September, 2494]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>86 [Scotland, October, 2882]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100 [Scotland, October, 2496]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>87 [Scotland, December, 2815]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100 [Scotland, December, 2493]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>86 [Portugal, October, 4545]</td>
</tr>
<tr>
<td>China (1439)</td>
<td>87 (84)</td>
<td>&lt;1</td>
<td>87</td>
<td>83 [India-Kerala, July, 13000]</td>
</tr>
<tr>
<td>Asia - other (3261)</td>
<td>58 (44)</td>
<td>50–80</td>
<td>79–92</td>
<td>83 [India-Kerala, September, 4429]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>78 [India-Kerala, September, 1521]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>88 [India-Kerala, September, 1476]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>97 [India-Delhi, October, 27811]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>75 [India-Jharkhand, July, 4575]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>80 [India-Punjab, July, 1200]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>72 [India-Vellore, July, 1205]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>69 [Nepal, July, 13161]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>39 [Japan, July, 1000]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>73 [S. Africa, November, 7010]</td>
</tr>
<tr>
<td>N. America&lt;sup&gt;a&lt;/sup&gt; (579)</td>
<td>68 (58)</td>
<td>40–70</td>
<td>81–90</td>
<td>96 [Canada, August, 8457]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>97 [Canada-BC, September, 9363]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>98 [Canada, October, 9627]</td>
</tr>
<tr>
<td>S. America (436)</td>
<td>76 (64)</td>
<td>50–80</td>
<td>88–95</td>
<td></td>
</tr>
<tr>
<td>Oceania (43)</td>
<td>61 (58)</td>
<td>1–5</td>
<td>61–63</td>
<td></td>
</tr>
<tr>
<td>WORLD (7,894)</td>
<td>58 (49)</td>
<td>35–55</td>
<td>73–81</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Includes Central America.

<sup>b</sup>In this calculation, it is assumed that vaccination and natural infection are independent and thus the proportion of unvaccinated people who have been infected at least once is the same as the proportion of vaccinated people who have been infected at least once. However, in reality unvaccinated people are more likely to have been infected, because the vaccine does offer some protection against infection, and because vaccinated people may be more health conscious than unvaccinated ones and thus may have been less likely to have been infected. Therefore, the proportion vaccinated or infected may be larger than shown here. Conversely, it may be lower if vaccinated people engage in far more unprotected activities that more than fully compensate for the protection offered by vaccination.

<sup>c</sup>Studies of household and community samples, residual samples, or blood donors from serotracker.com (search February 7, 2022) including adults (with or without children) with mid-date of sampling after July 15, 2021, assessment of spike antibodies, >100 samples assessed, no high risk of bias (as assessed by serotracker.com). The month given is the month of the mid-date of sampling for the seroprevalence survey, but the sampling may have extended in more than 1 month.

<sup>Note added in the proof stage:</sup> Since the last search additional studies have been released that show equally high or even higher levels of seroprevalence, e.g. according to the US Centers for Disease Control and Prevention, blood donor samples in the USA in December 2021 were 95% positive for antibodies.
that time to estimate person-years lost among the deceased. Finally, one can express the magnitude of the pandemic as a proportion of the total expected person-years of life for the population at that time that were lost from infection-caused deaths. For example, if a population has cumulative life expectancy of 100,000 person-years and infection-caused deaths generate 1000 lost person-years, proportion lost is 1%. Furthermore, quality-of-life adjustment for lost person-years is useful, but requires meticulous data.

There is large ambiguity about the number of deaths caused by influenza in each past pandemic (Table 2). Estimated deaths for the Spanish flu range from 17 to over 100 million,13–17 typical figures for the 1957–1959 pandemic are 0.7–1.5 million,18 the Hong Kong flu may have caused 1–4 million deaths,19 and death counts for the 2009 pandemic range from ~0.2 to ~0.6 million but these estimates do not capture some extra deaths that happened later in 2010–2011.20,21 Even seasonal influenza deaths estimates vary: 0.3–0.65 million respiratory deaths per year are estimated, but all-cause influenza mortality (including cardiovascular deaths) may be double these figures.22,23 As for COVID-19, despite almost half a million scientific papers written in 2020–2021,24,25 its exact death burden remains debated. There is probably both over- and under-counting of deaths in different settings and based on different definitions26; and the pandemic death

<table>
<thead>
<tr>
<th>Pandemic (global population, billions)</th>
<th>Proportion of global population dying (%)</th>
<th>Age distribution of deaths</th>
<th>Life expectancy at birth (years)</th>
<th>Relative magnitude*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1918–20 (1.8)</td>
<td>1–6 or more</td>
<td>30 40 25 5 38</td>
<td>100–1000</td>
<td></td>
</tr>
<tr>
<td>1957–9 (2.9)</td>
<td>0.02–0.05</td>
<td>50 10 5 20 65 56</td>
<td>1.5–4</td>
<td></td>
</tr>
<tr>
<td>1968–70 (3.5)</td>
<td>0.03–0.12</td>
<td>10 5 20 65 56 1.5–4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2009–11 (6.8)</td>
<td>0.003–0.01</td>
<td>30 30 20 20 66 1–3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COVID-19 (7.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Due to infection</td>
<td>0.06–0.12</td>
<td>&lt;1 5 20 75 73 1.5–4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excess deaths</td>
<td>0.1–0.28</td>
<td>? ? ? ? ? 73 2–10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seasonal flu (7.5)b</td>
<td>0.015–0.03</td>
<td>10 10 20 60 73 1</td>
<td>(reference)</td>
<td></td>
</tr>
</tbody>
</table>

Note: Estimates for deaths and their age distribution have very large uncertainty for all pandemics as well as for seasonal influenza and extreme caution is warranted. For seasonal flu, prior calculations have focused on data of excess respiratory mortality but it is estimated that all-cause mortality from influenza may be double these figures.2,23 For the 2009 pandemic, the prior calculations have focused mostly on 2009 and on respiratory mortality, but additional deaths occurred later in 2010 and 2011 and in hard-hit countries it seems that all-cause mortality (including cardiovascular mortality) due to influenza was double the respiratory mortality.21 For the 1957–1959 and 1968–1970 pandemics, the estimates are based on data of respiratory excess mortality, but this may also lead to underestimates.15–18 Uncertainty is highest for the Spanish flu, where very different estimates have been proposed based on very fragmentary data.13–16 For COVID-19, two separate sets are provided here, one for deaths from SARS-CoV-2 infection and another for excess all-cause deaths. While this distinction may not be as relevant for seasonal flu and prior pandemics in the last 100 years, it may be extremely relevant for COVID-19, as far more aggressive measures were taken and there were many indirect effects of both the pandemic and the measures taken on diverse aspects of health care and health (probably mostly harmful). For example, while only <1% of the deaths due to SARS-CoV-2 infection occurred in children and adolescents, the excess all-cause deaths may reflect a larger share of deaths in such young populations in non-high-income countries due to induced starvation and other hardships while wealthy children in high-income countries probably had no excess mortality in the short-term and may have had even fewer deaths due to some causes (e.g. accidents). The proportions of deaths in each of the four presented age-bins (<20, 20–40, 40–65, >65 years) is only approximate and needs extreme caution. It is based on refs. 13–23 and typically age-stratified information is only available from certain countries (and has to be extrapolated globally) and/or for some types of deaths (e.g. respiratory mortality). Discrepancies between different sources and calculations can be substantial and age distribution of deaths differs in different countries (e.g. for 1957 and 1968, mean age of death in Europe and USA is estimated as 65 and 62 years, respectively). Even for the seasonal flu, the age distribution may vary from one season to another, e.g. Iuliano et al.14 estimates 9243–105,690 deaths for children <5 years old per year based on data from 92 countries and a total of 290–645 thousand respiratory deaths from seasonal influenza. Furthermore, the relative magnitude estimates pertain to the global picture and the entire period of interest. Peaks of excess deaths may be far more extreme in specific locations and specific time periods when there is strong epidemic activity and this is true even for seasonal influenza. Differences across hard-hit versus spared locations in each year are typically more than 10-fold. Finally, there is substantial uncertainty about COVID-19 deaths especially in low-income countries, and some uncertainty exists even in high-income countries. Autopsies series in high-income countries27–31 suggest that 55–95% of claimed COVID-19 deaths are indeed due to COVID-19, but the number of autopsies is limited and they are very selected. COVID-19 deaths must have been missed, conversely, especially in early waves due to limited testing. Audits of death certificates and medical records would need to be performed more systematically. Some US counties have revised downward their COVID-19 deaths counts22,23 and preliminary data from Gangelt in Germany34 suggest also some non-COVID-19 deaths coded as COVID-19. In non-high-income countries, speculated estimates of COVID-19 deaths vary widely. Estimates typically use excess death calculations35–37 which make many assumptions and which cannot differentiate between deaths from COVID-19, deaths indirectly induced by the pandemic, and deaths induced by the measures taken. A final source of uncertainty is where to put an end to the pandemic period and/or whether to use asynchronous ends in different countries.

*Based on proportion of person-years lost.
*bCounting a total of 3 seasons, for a fair comparison against pandemic circles.
count also depends on when exactly the pandemic phase ends, transitioning to the endemic phase. Autopsies27–31 and death certificate or medical record audit efforts to-date32–34 are still very fragmentary and preliminary, and excess death assessments are difficult and show large variability.35–37 Comparisons of pandemics are also precarious because past pandemics used limited viral testing, while COVID-19 ushered in massive testing.

Acknowledging these caveats, for COVID-19, 1957–9, 1968–70, and 2009–11 their relative magnitude (in proportion of person-years lost from infection) was probably 1.5–4-fold the ‘normal’ magnitude of three consecutive, typical seasonal influenza years. Overall, pandemic excess mortality and deaths due to infection were probably very close for 1957–9, 1968–70 and 2009–11. Conversely, for COVID-19 pandemic, excess deaths may be substantially more than the deaths caused directly from SARS-CoV-2, and include deaths caused by the disruption induced by both the pandemic and the aggressive measures taken. Spanish flu has the highest uncertainty about its mortality impact, but probably, it was at an entirely different league. However, another difficulty in making any comparisons between different pandemics spanning more than a century is that the availability of different treatment management options (e.g. intensive care) and the access of people to them has changed a lot overtime. Similarly, availability and roll out of effective vaccines has differed a lot. Moreover, the different restrictive measures taken in different pandemics may have caused different direct and indirect benefits and harms. It is beyond of the scope of this paper to discuss the relative merits and harms of different non-pharmacological measures. It is possible that the relative fatality impact of the Spanish flu would have been less, if the same virus had struck in 2019 for the first time rather than a century ago.

### 3.2 | Heterogeneity

Comparisons within specific countries and specific locations may show different relative magnitude for these pandemics. COVID-19 distinguished itself by disproportionately affecting high-income countries (at least as far as documented cases and deaths are concerned), because these countries have far more elderly individuals and more frequent comorbidities such as obesity. A heightened sense of threat emerged because COVID-19 affected epicentres of global information and power. Conversely, while 800 million people worldwide live in hunger, another 2 billion live in hidden hunger, and deaths from hunger (mostly of young people) are far more than COVID-19 deaths and rapidly increase with the pandemic response, conflicts, and climate change38,39 this devastation has received embarrassingly negligible attention compared with COVID-19.

Moreover, the relative magnitude of pandemics varies markedly according to age groups. COVID-19 probably caused substantially fewer deaths in children and adolescents <20 years old (~20,000)40 versus 3 seasons of typical influenza.23 Conversely, the vast majority of COVID-19 fatalities worldwide occurred in people >65 years old, including probably ~1 million deaths in institutionalized residents of long-term care facilities.41,42 A large share of further excess deaths in these facilities was probably due to abandonment, thirst, and hunger.42

### 3.3 | Return to normal

A ‘return to normal’ is not abrupt and pacing varies across countries and populations. A decrease in COVID-19 deaths (overall and per age group) back to typical seasonal influenza levels may not necessarily happen in 2022 or even beyond. With increasingly ageing global population and massive testing, ‘normal’ may still correspond to higher death counts than pre-COVID-19 influenza-related illnesses. This should not be mistaken as a continued pandemic phase. Moreover, seasonal peaks of fatalities may continue, higher in some locations than others. While some locations are hit more each year for poorly understood reasons, spikes often track with low local immunity from waning immune responses and/or escape variants.

At end 2021, only 5 countries with population exceeding 1 million had 7-day COVID-19 deaths exceeding 70 per million population. All these countries were in Eastern Europe and had low vaccination coverage (Georgia 25%, Hungary 62%, Poland 53%, Croatia 47%, Bulgaria 30% as of November 1, 2021).5 Importantly, vaccine coverage was low in these countries especially for the elderly (who contribute most deaths). Unsurprisingly, at end February 2022, highest rates of COVID-19 deaths per population were still seen in Eastern European countries and in some other countries/locations with many frail elderly and/or disadvantaged people, low elderly vaccination rates and ailing health systems from austerity (e.g. Greece) or large inequality (e.g. USA), but even there, death trends were improving. (Note added in the proof stage: In end March 2022, no country worldwide had 7-day COVID-19 deaths exceeding 45 per million population, except for Hong Kong that had long pursued a zero COVID policy and had suboptimal vaccination coverage among the elderly.)

### 4 | CLINICAL BURDEN

Pandemics stress the entire health system. The discussion here will focus, illustratively, on ICU beds, as the strain is perceived to be more critical than for regular hospital beds (that follow fairly similar peaks and troughs of utilization
anyhow). However, primary care disruption is also major and can lead to major consequences (e.g. disrupted preventive services).43

In 23 countries with data (Table 3),44–46 COVID-19 occupied more than 25% of the pre-pandemic ICU bed capacity for an average of 2 months in November 2020 to February 2021. The average period of such high COVID-19 occupancy was less than half in the respective period November 2021 to February 2022 even though all these countries witnessed high peaking (and subsequently receding) Omicron waves in this time frame: 4–39% of their populations had documented infection during these 4 months (the total infections may be double or more). Most countries (13 of 23) had no period during November 2021 to February 2022 where COVID-19 bed occupancy accounted for more than 25% of their pre-pandemic ICU capacity. Given that many countries also increased their ICU capacity during the pandemic, the period during which there was high stress was probably even substantially shorter. In all 10 countries where COVID-19 bed occupancy exceeded 25% of their pre-pandemic capacity, peaks were lower in the 2021–2022 season than in 2020–2021.

For 12 of 23 countries, COVID-19 ICU bed occupancy also exceeded 25% of their pre-pandemic capacity during some time in spring 2021. As spring 2022 was starting, only 2 of these countries (Slovakia and Slovenia) had COVID-19 occupancy that exceeded 25% of their pre-pandemic ICU bed capacity.

5 | ACTUAL AND PERCEIVED PERSONAL RISK

Pandemics instil justifiable fear to many people for their lives. The infection fatality rate (IFR, risk of dying if infected) is critical for risk perception. COVID-19 shows a tremendous age-related risk gradient and risk is also modified by the presence of several disease comorbidities.47 Early estimates of IFR were exaggerated. Globally, IFR until early 2021 was probably 0.15–0.23%,48,49 although lower (0.11%)50 and higher51 estimates have been proposed. The differences pertain mostly to the exact risk for elderly people, while analyses agree on the very low risk of young age strata.52 IFR was substantially different across countries and locations, not only because of the different age structure, but also because of very different rates of background comorbidities, different success in protecting vulnerable populations (e.g. institutionalized or immunocompromised people), different use of effective or ineffective/harmful interventions, and different health systems. Indicative IFR estimates are52 0.001%, 0.01%, 0.023%, 0.05%, 0.15%, and 0.49%, at 0–19, 20–29, 30–39, 40–49, 50–59, and 60–69 years, respectively. IFR in 2020 was 2.2% in community-dwelling elderly >70-year-olds in high-income countries, probably much lower in the elderly in other countries, and substantially higher in frail, long-term care residents.52

With advent of vaccination, IFR probably decreased substantially. If vaccination maintains 80% efficacy for averting death among those infected (probably a conservative estimate)53–55 the IFR estimates above should be decreased 5-fold for vaccinated individuals; for example, for vaccinated community-dwelling elderly people >70-year-olds, IFR may have decreased to 0.45%; for those 50–59-year-olds, it would be 0.03%. For previously infected people, IFR is also probably much lower than in uninfected, although exact numbers are difficult to obtain currently. Maintenance of very low IFR figures will depend on persistence of protection through vaccination or infections, including repeat events. Improved treatment options should also translate to even further IFR lowering.56–58

Similar considerations apply for other serious outcomes besides death. They do not apply to infection risk, where prior infection or vaccination seem to confer much less protection than for hard outcomes.59 Risk compensation (increased exposures of vaccinated people) further erodes protection.60 Therefore, if perception of risk focuses on number of documented cases, the spurious perception of emergency situations may be difficult to quell.

Importantly, actual risk may matter less than perceived risk. Many people have very distorted perceptions about their risk of poor outcome after SARS-CoV-2 infection. For example, in the USA, a third of the population has believed that more than half of infected people require hospitalization.61 Conversely, the risk of hospitalization among documented cases was about 7% and 3% during the Delta and Omicron waves, respectively.62 Given that infections may have been 2–4 times more than the documented infections, the risk of hospitalization after infection was probably only 1–2%. On average, the US population also believed in early 2021 that 8% of deaths had occurred in people younger than 24 years,61 while the true percentage was ~0.1% at that time (0.3% by early 2022). In another survey in Austria,63 children and adolescents believed that they had a 1.2–3.3% risk of hospitalization from COVID-19 in a year, that is more than 1000-fold higher than reality, and they also had massively inflated perceptions of risk for their parents. Another difficulty in appreciating risk is that the likelihood of long COVID and of long-term sequelae of the infection is still estimated with great uncertainty. There is large heterogeneity across population groups on the extent of inflated
risk perception, and some people may underestimate risks compared with reality. Risk perception may be important for shaping the response to COVID-19, behaviours, depression and mental health. Proper risk perception recalibration is essential for a genuine transition to the endemic phase.

### 6 | RESTRICTIVE MEASURES

Broadly defined, a pandemic may persist regardless of epidemic and clinical indicators, if aggressive restrictive measures continue to be in place and/or attention and preoccupation with it remain heightened. The Oxford stringency index for governmental measures was lower in the end of 2021 compared with 1 year earlier in most countries, but much of the global population continued to suffer aggressive restrictive measures and the same was true at end February 2022 (Figure 1). Moreover, during 2021 and early 2022, many new types of measures were adopted, as governments and public health authorities chartered perilous territories and scrambled with new measures. Mandates and measures that discriminate people based on their pandemic-related status (e.g. vaccination record) may be particularly problematic. One should avoid fostering divisiveness, discord and backsliding of democracy standards.
COVID-19 monopolized the top ranks of public attention from early 2020 onwards. COVID-19 coverage captured 25% of 26 million news articles from the front pages of 172 major online news sources in 11 countries between January and October 2020. Social media presence has also been vehemently strong. A database of COVID-19-related tweets included as of December 27, 2021 a total of 2.17 billion relevant tweets. Social media and media are responsible for a massive info-demic (an epidemic of information that includes a lot of mis- and dis-information). A strong sign that the pandemic has ended would be the drastic reduction in public attention. However, media and social media

---

**FIGURE 1** Oxford stringency index for governmental response to COVID-19. (A) December 31, 2020, (B) December 31, 2021, (C) February 23, 2022
are incentivized to maintain heightened attention long after epidemiological and clinical indicators have entered the territory of endemicity. Polarization and the sad entanglement of politics in COVID-19 make the prospects worse.

7.2 Science

Science has also been radically affected by the COVID-19 pandemic in unprecedented ways. More than 400,000 COVID-19-related papers were published in 2020–2021. In Scopus (with data as of August 2021), 98 of the top 100 most-cited scientific papers in 2020 were COVID-19-related; this metric declined to 75/100 most-cited papers in 2021, but it remains extraordinarily high. The fact that many scientists have entangled themselves in news, social media wars, and even outright political and financial agendas related to COVID-19 does not portend good omens. Overblown scientific interest may prolong the pandemic perceptions.

7.3 Public health

Public health fought valiantly against COVID-19. Regardless of whether outcomes were fair or poor in different locations, rumination with failures and a blame culture should not prevail. We can carefully dissect what we have learned from this unique experience without perpetuating it. Public health authorities should call the end of the pandemic. This does not mean that the problem is inappropriately minimized or forgotten, but that our communities move on with life. It is unknown when the next pandemic may happen—in less than a year or in more than a century. SARS-CoV-2 has proven to be very unpredictable and unpredictability exists also for influenza. Pandemic preparedness should be carefully thought and pre-organized, but should not disrupt life.

8 Pandemic Legacy

The pandemic legacy includes effects on other dimensions of health (besides directly due to COVID-19), society, economy, civilization, democracy, value systems and more. The pandemic and the response to it have affected mental and physical health with excess deaths. Total excess deaths may far surpass those due to SARS-CoV-2 infection. However, excess death estimates are very preliminary, they depend on weak data and fragile modelling assumptions and they are highly uncertain. Importantly, excess deaths include indirect effects of the pandemic and direct and indirect effects of the measures taken.

The dramatic increase in number of people suffering hunger is only one aspect of the harms of the disruption due to the pandemic and the measures taken. There is still large uncertainty about the relative impact of economic contraction and inflation on health. Past experience from economic crises shows a major negative impact on health, but there is no full consensus in the literature and COVID-19 is a very special situation. The number of indirectly induced deaths may even exceed those from COVID-19, but much will depend on how quickly the economic shock can be reversed and whether additional complications (e.g. wars) may arise. As of this writing, in many countries, inflation rates already reached values higher than those seen in decades, for example 7.5% in the USA (January 2022 data), 5.6% in the European Union (January 2022) and 5.9% in New Zealand (December 2021). The increased inequality induced by the pandemic and measures taken makes things worse. The World Bank expects that by 2023, ‘all advanced economies will have achieved a full output recovery; yet output in emerging and developing economies will remain 4 per cent below its pre-pandemic trend. For many vulnerable economies, the setback is even larger: output of fragile and conflict-affected economies will be 7.5 per cent below its pre-pandemic trend, and output of small island states will be 8.5 per cent below.'

Projections need to be seen with extreme caution, but disadvantaged, poor people are likely to suffer the most both in poor countries and within high-income countries.

Additional health consequences may appear in the mid- or long-term. Their exact impact depends on whether one can shift attention to these problems at least now and diminish their impact. Continued rumination on COVID-19 cases and other superfluous SARS-CoV-2 indicators may not help. The short-, mid- and long-term impact on society, economy, civilization, democracy and value system is heavily debated and its detailed discussion is beyond the scope of this paper. Nevertheless, the pandemic legacy may continue to haunt us for decades, if it results in irreversible damage for humanity on these frontiers.

CONFLICT OF INTEREST

None.

ORCID

John P. A. Ioannidis © https://orcid.org/0000-0003-3118-6859
REFERENCES


