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

Counting the global COVID-19 dead

WHO has estimated that 14·9 million excess deaths (uncertainty range 13·3 million–16·6 million) from COVID-19 occurred globally in 2020–21.[1] WHO's global estimates are lower than the 18·2 million deaths (17·1 million–19·6 million) reported by the Institute for Health Metrics and Evaluation (IHME)[2] and the 17·7 million deaths (13·9 million–21·1 million) estimated by *The Economist* for the same time period. By contrast, government counts of global deaths from COVID-19 in 2020–21, captured on Coronavirus App, suggest the figure is below 6 million.

Excess deaths are a proxy for the mortality effects of SARS-CoV-2 infection. The key assumption is that increases in all-cause mortality during peak weeks of COVID-19 compared to pre-pandemic periods are nearly all due to the infection, even if SARS-CoV-2 infection was not confirmed. The validity of this method is supported in part by documenting modest reductions (negative excess) in overall mortality in selected east Asian countries that effectively prevented the original wave from March to June, 2020.[1]

The difference of 3 million deaths across the three models is far from trivial. However, given that WHO imprimatur carries substantial influence on countries, a more relevant question is whether WHO estimates are credible. About half of WHO's estimate is derived from observed data, the other half from modelled data. IHME combines six different approaches and applies complex methods to create estimates for various countries. Yet IHME's method yields implausibly narrow uncertainty intervals. *The Economist* applies machine learning, using many covariates, and has appropriately wider uncertainty intervals; like WHO, it makes its model fully open source.

In high-income countries, much of the discrepancy between excess and reported COVID-19 deaths occurred during the first viral wave, from March to June, 2020, when SARS-CoV-2 infections and COVID-19 deaths swept through nursing homes. Italy, for example, has robust and rapid reporting of COVID-19 deaths, and WHO estimated 161 000 excess deaths, as did Italian researchers.[3] By contrast, IHME[2] and *The Economist* estimated 259 000 deaths and 192 000 deaths, respectively. That at least 9 million COVID-19 deaths were missed by official reports raises a few key issues.

First, gaps in actual mortality data persist in the 21st century. In WHO's analyses of 194 countries, mortality data were not available for 85 countries, 41 of which are in Africa.[1] Solutions to advance death registration and certification of causes exist,[4] particularly for the growing proportion of deaths occurring in facilities. Yet funding for such solutions is negligible. Paradoxically, the availability of short-term model-derived estimates might discourage governments from investments in statistical systems, which require several years to reach fruition.

Second, India contributes the most missed COVID-19 deaths (2·5 million–4·5 million). 3 million of India's annual 10 million deaths are not registered, with the largest gaps in poorer states and among women. 8 million deaths lack medical certification of the cause.[5] The Indian Government[2] has thus far refused to budge from its official total of 0·5 million COVID-19 deaths. Their low estimate is implausible.[5]

Third, the severe lockdown of Wuhan, China, in early 2020 led to very few deaths in the rest of the country.[6] However, China now faces a large omicron wave, with large numbers of unvaccinated or under-vaccinated older people, which in the case of Hong Kong led to sharp but brief spikes in death rates. China might prove to be the major contributor to global COVID-19 deaths in 2022, perhaps exceeding 1 million. Optimistically, the Chinese Government will not withhold release of timely death data. WHO's publication of global estimates despite the Indian Government's objections is an important signal to encourage transparency by all governments.

Fourth, the major surprise in COVID-19 mortality might yet arise from Africa. Preliminary data[7] suggest that populations across many urban settings in Africa, with various viral waves, have SARS-CoV-2 seropositivity exceeding 60% but relatively few deaths. Caution is needed as India also faced widespread infection in 2020 with low deaths, but a large killer delta wave in the spring of 2021 followed.[5] Urgent investigation of possible unique biological factors or existing immunity in Africa is required. Interestingly, these findings might point to a similar effect as achieved from vaccines—far stronger protection against serious disease than against infection.[8]

Finally, of the 55 million people in the world who died in 2019, nearly 50 million were older than 15 years. Yet, most demographic surveys focus on child and maternal deaths, with little attention to adult mortality. It would be advisable for every country conducting a census to at least 2025 to add two simple questions: Was there a death in the household during 2020, 2021, or 2022? If yes, what was the sex, age in completed years, and date? This information would not only provide direct evidence of excess deaths from COVID-19 but would also help fill the large gaps in knowledge on adult death rates.

Estimates for deaths from the 1918–19 influenza pandemic range widely, from 40 million to 100 million. A century later, a modern effort to count the global COVID-19 dead should be a priority. Mortality data not only meet our moral duty

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For ***The Economist's* excess death estimates** see https://www.economist.com/graphic-detail/coronavirus-excess-deaths-estimates

For the **Coronavirus App** see https://coronavirus.app/map

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to those who died and their families but are also of enormous practical use to explain the widespread variation in COVID-19 infection that preliminary data have revealed, and its consequences.[9] Mortality data would help evaluate vaccination and other public health efforts. Counting the global COVID-19 dead will help the living.

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Where is the next SARS-CoV-2 variant of concern?

The COVID-19 pandemic has been characterised by successive waves of new variants of concern sweeping the population. The ultimate source of these variants is not known with certainty, but preliminary evidence suggests at least some have emerged from long-term SARS-CoV-2 infections, such as those observed in immunocompromised patients.[1] As a result, it is of the utmost urgency that those with long-term infections should be able to access quality health care and be prioritised for curative therapy because a failure to properly manage these infections poses a risk to the individual and to public health.

Immunocompromised patients, such as those infected with HIV or recipients of organ transplants, can have difficulty eliminating SARS-CoV-2 infections.[2] Preliminary data suggest that infections often persist for many months with viruses acquiring new mutations over time[3] as they presumably evade immune-mediated neutralisation[4] and hone their ability to infect human cells. Because the virus population size within persistent infections is not limited by bottlenecks at transmission, the rate of mutation is accelerated in comparison with the population at large, so these infections typically generate considerable genetic novelty. Although the evolutionary pressures on a virus within an individual host might be different from the adaptation to transmit between hosts, it is reasonable to assume that the next variant of concern could arise from a virus population with a high degree of genetic diversity and containing mutations allowing infection of resistant individuals.

The alpha (B.1.1.7) variant arose during a period of intense surveillance in the UK and was readily seen to be highly divergent from its nearest common ancestor, having accumulated a constellation of mutations with worrisome properties more rapidly than the rest of the virus population.[1] The omicron (B.1.1.529) variant arose under similar circumstances and had about 45 mutations that separated it from its ancestor at a time when the distantly related delta (B.1.617.2) variant was dominant.[1] The beta (B.1.351) and gamma (P.1) variants are similarly divergent from their closest relatives, consistent with comparable origins.[1] The possibility of SARS-CoV-2 evolving resistance to existing therapies during such infections is real.[5] Hence, curing COVID-19 infections in immunocompromised individuals is of crucial importance as it is possible that an existing patient might harbour the next variant, a highly transmissible new variant of concern that challenges immunity and existing therapeutics.

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