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.

Real estimates of mortality following COVID-19 infection

As of March 1, 2020, 79 968 patients in China and 7169 outside of China had tested positive for coronavirus disease 2019 (COVID-19).[1] Among Chinese patients, 2873 deaths had occurred, equivalent to a mortality rate of 3·6% (95% CI 3·5–3·7), while 104 deaths from COVID-19 had been reported outside of China (1·5% [1·2–1·7]). However, these mortality rate estimates are based on the number of deaths relative to the number of confirmed cases of infection, which is not representative of the actual death rate; patients who die on any given day were infected much earlier, and thus the denominator of the mortality rate should be the total number of patients infected at the same time as those who died. Notably, the full denominator remains unknown because asymptomatic cases or patients with very mild symptoms might not be tested and will not be identified. Such cases therefore cannot be included in the estimation of actual mortality rates, since actual estimates pertain to clinically apparent COVID-19 cases.

The maximum incubation period is assumed to be up to 14 days,[2] whereas the median time from onset of symptoms to intensive care unit (ICU) admission is around 10 days.[3,4] Recently, WHO reported that the time between symptom onset and death ranged from about 2 weeks to 8 weeks.[5]

We re-estimated mortality rates by dividing the number of deaths on a given day by the number of patients with confirmed COVID-19 infection 14 days before. On this basis, using WHO data on the cumulative number of deaths to March 1, 2020, mortality rates would be 5·6% (95% CI 5·4–5·8) for China and 15·2% (12·5–17·9) outside of China. Global mortality rates over time using a 14-day delay estimate are shown in the figure, with a curve that levels off to a rate of 5·7% (5·5–5·9), converging with the current WHO estimates. Estimates will increase if a longer delay between onset of illness and death is considered. A recent time-delay adjusted estimation indicates that mortality rate of COVID-19 could be as high as 20% in Wuhan, the epicentre of the outbreak.[6] These findings show that the current figures might underestimate the potential threat of COVID-19 in symptomatic patients.

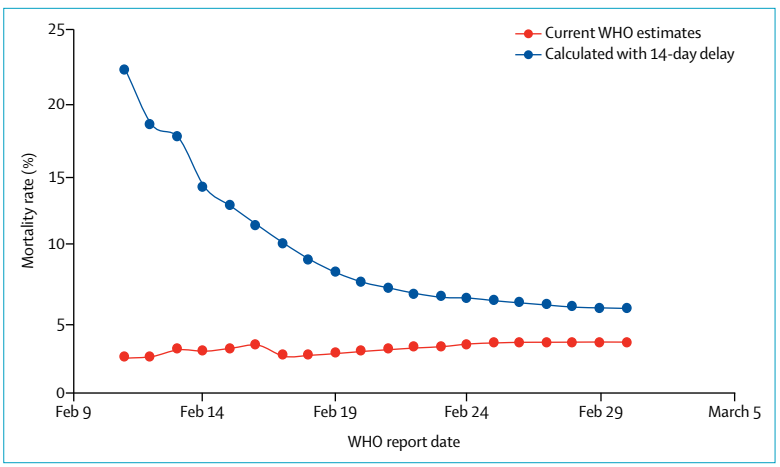

Figure: **Global COVID-19 mortality rates (Feb 11 to March 1, 2020)**
Current WHO mortality estimates (total deaths divided by total confirmed cases), and mortality rates calculated by dividing the total number of deaths by the total number of confirmed cases 14 days previously.

We declare no competing interests.

David Baud, Xiaolong Qi, Karin Nielsen-Saines, Didier Musso, Léo Pomar, Guillaume Favre
david.baud@chuv.ch

Materno-fetal and Obstetrics Research Unit, Department Woman-Mother-Child, Lausanne University Hospital, 1011 Lausanne, Switzerland (DB, LP, GF); CHESS Center, The First Hospital of Lanzhou University, Lanzhou, Gansu, China (XQ); Division of Pediatric Infectious Diseases, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA (KN-S); Aix Marseille Université, Institut de Recherche pour le Développement, Assistance Publique–Hôpitaux de Marseille, Service de Santé des Armées, Vecteurs—Infections Tropicales et Méditerranéennes (VITROME), Institut Hospitalo-Universitaire–Méditerranée Infection, Marseille, France (DM); and Laboratoire Eurofins—Labazur Guyane, French Guiana, France (DM)

1 WHO. Coronavirus disease 2019 (COVID-19). Situation Report—41. March 1, 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200301-sitrep-41-covid-19.pdf?sfvrsn=6768306d_2 (accessed March 5, 2020).
2 Backer JA, Klinkenberg D, Wallinga J. Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20–28 January 2020. *Euro Surveill* 2020; **25:** 2000062.
3 Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; **395:** 497–506.
4 Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020; published online Feb 7. DOI:10.1001/jama.2020.1585.
5 WHO. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Feb, 2020. https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf (accessed March 5, 2020).
6 Mizumoto K, Chowell G. Estimating the risk of 2019 novel coronavirus death during the course of the outbreak in China, 2020. *medRxiv* 2020; published online Feb 23. DOI:10.1101/2020.02.19.20025163 (preprint).

Published **Online**
March 12, 2020
https://doi.org/10.1016/S1473-3099(20)30195-X

Estimating case fatality rates of COVID-19

In their model, David Baud and colleagues[1] exclude individuals who die within 14 days of testing positive for severe acute respiratory syndrome coronavirus 2. If an individual contracts symptoms on March 1, tests positive on March 10, and dies on March 11, they would not be included in the denominator for case fatality rate (CFR) on March 11. In addition, patients might test positive up to 13 days after recovery.[2] As testing is

Published **Online**
March 31, 2020
https://doi.org/10.1016/S1473-3099(20)30234-6

expanded, an asymptomatic patient infected 1 week before testing positive on March 3 should, but will not, be included in calculations for March 16.

For the stated purpose of the authors, it might be useful to also include everyone who was symptomatic for 14 days before the calculated date. Consider a CFR calculation for March 15. If an individual was symptomatic on March 1 and tested positive on March 10, they would not be included in the denominator, even though the patient probably contracted the disease before the 14-day lag time.

Moreover, patients with mild symptoms might not undergo testing and so might not be included in the overall denominator. A further consideration is the delay between testing and receipt of results. Consequently, individuals might not test positive until after the suggested 14-day incubation period. With disease spread, indications for COVID-19 testing will expand, thereby increasing the denominator size. These factors might act as time-varying confounding variables in the authors' calculation of CFR.

One other published lag-time calculation has included half the additional cumulative deaths in the numerator and time from illness to death as the lag-time (13 days).[3] For example, if calculating the CFR for March 15, the denominator would be cumulative cases until March 2, and the numerator would be cumulative deaths until March 2, in addition to half of the deaths recorded from March 2–15. This method assumes a normal distribution of time from illness to death.

Although underestimation of CFRs risks the population not taking the threat seriously, overestimation might lead to unnecessary additional panic and concern. During a rapidly evolving pandemic, accurate measures of disease characterisation are important. Future estimates will probably involve patient-specific data for refined calculation. However, the provided CFR estimate of 15·2% for countries outside China might be a premature statistic owing to the limitations of their methods.

We declare no competing interests.

*David Dongkyung Kim, Akash Goel
david.kim@medportal.ca

The authors contributed equally.

Department of Clinical Neurological Sciences, Western University, London, Ontario, Canada (DDK); Department of Anesthesia, University of Toronto, Toronto, Ontario, Canada (AK)

1 Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, Favre G. Real estimates of mortality following COVID-19 infection. *Lancet Infect Dis* 2020; published online March 12. https://doi.org/10.1016/S1473-3099(20)30195-X.

2 Lan L, Xu D, Ye G, et al. Positive RT-PCR test results in patients recovered from COVID-19. *JAMA* 2020; published online Feb 27, 2020 DOI:10.1001/jama.2020.2783.

3 Wilson N, Kvalsvig A, Barnard LT, Baker MG. Case-fatality risk estimates for COVID-19 calculated by using a lag time for fatality. *Emerg Infect Dis* 2020; published March 13, 2020. DOI:10.3201/eid2606.200320.

Published Online March 31, 2020 https://doi.org/10.1016/S1473-3099(20)30246-2

We congratulate David Baud and colleagues[1] for their apt observations regarding the burden of the coronavirus disease 2019 (COVID-19) epidemic and the possibly higher than expected proportion of cases that are fatal. Precision, however, is as necessary in calculations as in semantics.

According to the *Dictionary of Epidemiology*, the mortality rate is an "estimate of the portion of a population that dies during a specified period".[2] In the case of this outbreak, the mortality rate over a period of 1 year per 100 000 Chinese citizens would be around 0·23 (as of March 16, 2020). Therefore, precisely speaking, neither older estimates nor Baud and colleagues' new calculation can be referred to as the mortality rate.

In both trade press and newspapers, the case fatality rate (CFR) is often used to describe the situation pertaining to COVID-19, as well as to any other epidemic. The definition of the CFR in the *Dictionary of Epidemiology* states that it is "the proportion of cases of a specified condition that are fatal within a specified time".[2] On the one hand, as accurately pointed out by Baud and colleagues, the CFR might be underestimated because of a type of time-lag bias associated with diagnosing and reporting cases. Furthermore, calculations are based on the questionable assumption that all cases are being tested. On the other hand, as Pueyo suggests,[3] the CFR might be overestimated due to the definition of a case. During an epidemic, cases might be defined either as total cases (ie, every confirmed case) or as closed cases (ie, only those who have recovered or died). Hence, the denominator for the CFR might be either of these numbers. In the initial phase of the epidemic, the number of closed cases is relatively small, and so the CFR calculated per closed cases is an overestimate. By contrast, when the CFR is calculated per total cases, the numerator is underestimated, and thus the whole calculation becomes an underestimate.

Baud and colleagues' calculation, although interesting, is biased as well. As shown in the figure, it vastly overestimates the fatality of COVID-19 if one uses data from the initial phase of the outbreak. This overestimation is obviously due to undertesting and a time-lag bias, which is more pronounced in the beginning of an outbreak. As demonstrated in the figure, irrespective of the method used, all calculations are biased, especially in the initial part of an outbreak, and converge once all cases are closed. Nevertheless, it seems that the CFR calculated per total cases is the least affected by reporting biases.

As of March 16, the CFR per total cases in China is 4·00%, per closed cases is 4·44%, and as calculated with Baud and colleagues' method is 4·03%. However, despite the downturn of the outbreak in China,