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8043 cases are still open, of which 2622 are serious or critical. According to Wu and McGoogan's estimates based on 72 314 cases from Wuhan,⁴ 81% of patients are classified as mild, 14% as severe, and 5% as critical. CFRs in these subgroups are 0%, 0%, and 49%, respectively. Based on these estimates, of 8043 open cases in China, about 377 are in a critical condition and of those 184 will die. Therefore, once all active cases are closed, we might expect the CFR in China to be around 3.85%.

On a technical note, Baud and colleagues' calculation seems to be an attempt at reporting the cumulative death rate, which is defined as "the proportion of a group that dies over a specified time", rather than the mortality rate.²

In summary, the CFR calculated per total cases seems to remain the best tool to express the fatality of the disease, even though it might underestimate this figure in the initial phase of an outbreak.

All calculations were based on data acquired from worldometer.info/coronavirus and are available in the appendix. We declare no competing interests.

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- 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](https://doi.org/10.1016/S1473-3099(20)30195-X).
- 2 Porta M. A dictionary of epidemiology. 5th edn. Oxford: Oxford University Press, 2008.
- 3 Pueyo T. Coronavirus: why you must act now. Available from: <https://medium.com/@tomaspuoyo/coronavirus-act-today-or-people-will-die-f4d3d9cd99ca> (accessed March 18, 2020).
- 4 Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; published online February 24. DOI:10.1001/jama.2020.2648. FUE.

In their Correspondence, David Baud and colleagues¹ suggest that case fatality rates (CFRs) for coronavirus disease 2019 have been underestimated and propose to divide deaths at time *t* by cases at time *t* minus 14 days to correct this underestimation and provide so-called real estimates. Many biases in both directions afflict CFR estimates during outbreaks,² and experts have spent 2 decades (since the outbreak of severe acute respiratory syndrome coronavirus) finding ways to overcome these.³ The delay problem highlighted by Baud and colleagues produces falsely low estimates, whereas the underascertainment of mild cases produces falsely high estimates.⁴ These issues are well appreciated in the field and have been discussed in the popular press in recent weeks.^{5,6}

No expert thinks the 3.6% raw ratio of deaths to cases on March 1 is an accurate estimate of the CFR because it suffers from all of these biases. The authors make the situation worse: correcting for delay (with an invalid method) without correcting for ascertainment of mild cases inflates the estimates, bringing them further from what most experts believe are the true numbers, around the 1–2% range for symptomatic cases.^{7,8}

Baud and colleagues' estimates are not real; they are in fact less real than the biased calculations they claim to correct. Especially in a time of great urgency, authors have a responsibility to read and understand relevant background literature and look for obvious flaws in their own analysis. This work does not appear to have met that standard. The fact that peer review did not pick up these flaws should be a caution against hastening the peer review process at the expense of due care.

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- 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](https://doi.org/10.1016/S1473-3099(20)30195-X).

- 2 Lipsitch M, Donnelly CA, Fraser C, et al. Potential biases in estimating absolute and relative case-fatality risks during outbreaks. *PLoS Negl Trop Dis* 2015; **9**: e0003846.
- 3 Donnelly CA, Ghani AC, Leung GM, et al. Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. *Lancet* 2003; **361**: 1761–66.
- 4 Wilson N, Baker MG. The emerging influenza pandemic: estimating the case fatality ratio. *Euro Surveill* 2009; **14**: 19255.
- 5 Baumgaertner E. How deadly is the new coronavirus? Scientists race to find the answer. Feb 12, 2020. <https://www.latimes.com/science/story/2020-02-11/how-deadly-is-coronavirus-fatality-rate> (accessed March 19, 2020).
- 6 Lipsitch M. Why it's so hard to pin down the risk of dying from coronavirus. March 6, 2020. <https://www.washingtonpost.com/opinions/2020/03/06/why-its-so-hard-pin-down-risk-dying-coronavirus> (accessed March 19, 2020).
- 7 Wu JT, Leung K, Bushman M, et al. Estimating clinical severity of COVID-19 from the transmission dynamics in Wuhan, China. *Nat Med* 2020; published online March 19. DOI:10.1038/s41591-020-0822-7.
- 8 Wighton K, van Elsland S L. Coronavirus fatality rate estimated by Imperial scientists. Feb 11, 2020. <https://www.imperial.ac.uk/news/195217/coronavirus-fatality-rate-estimated-imperial-scientists> (accessed March 19, 2020).

Authors' reply

We thank David Dongkyung Kim and Akash Goel,¹ Piotr Spychalski and colleagues,² and Marc Lipsitch³ for their critical reading of our Correspondence.⁴ In response to the points raised regarding our statistical methods, we agree that our model might not be appropriate for the early epidemic period because of the rapid increase in the number of cases in the 14 days preceding reported deaths. During this period, many patients were certainly diagnosed with coronavirus disease 2019 (COVID-19) at the time they developed critical illness or even at the time of death. By contrast, asymptomatic patients and those with mild disease remained untested. These two factors probably explain the overestimates of mortality at the beginning of the curve (Feb 12–24 in our model,⁴ as exemplified in the appendix).

As mentioned by Spychalski and colleagues, "irrespective of the method used, all calculations are



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biased, especially in the initial part of an outbreak, and converge once all cases are closed". During and after the epidemic peak, patient denominators correspond to the best estimates of people presenting with clinical COVID-19 because of access to diagnostic testing and stabilisation of the number of new daily cases. At that time, we consider that patients were screened close to symptom onset. According to reports from WHO,⁵ the time from symptom onset to death ranges from 2 to 8 weeks. In our estimates, we chose to use the minimum time between symptom onset and death so not to overestimate mortality rates. Another factor that is still unknown and could bias the model is the number of asymptomatic cases, as acknowledged in our Correspondence. Most asymptomatic patients are not captured by screening, leading to underestimates in the denominator. We presented our model as a mortality rate estimate among people presenting with clinical COVID-19—that is, symptomatic cases. In our experience, patients are mostly interested in knowing mortality rates when symptomatic, and less so of asymptomatic carriers.

There are other limitations that would apply to any statistical method, such as the possible change in testing frequency due to a shortage of tests. In some places, patients might even die before being tested. In the extreme, the mortality rate would reach 100% if only patients who had died were tested, whereas mortality rates would significantly drop if the entire population was to be tested. Thus, ideally, estimates should be adjusted according to test availability. Another consideration is that mortality in this epidemic is highly age-dependent, and so will vary according to the number of older individuals in the population. In high-income countries, the demographic pyramid is such that there are higher proportions of

older individuals in the population. With larger numbers of vulnerable individuals exposed, one will observe higher overall mortality rates. In addition, mortality will vary across communities depending on access to tertiary medical centres and well equipped critical care units.

For the time being, in Europe, we are still in the early epidemic period, with a rapid increase in the number of cases; additional data are needed for the assessment of cumulative mortality rates due to confirmed COVID-19 cases over time.⁶ Thus, the goal of our publication was to share our vision of the potential impact of COVID-19 using a model that integrated the viral incubation period and the time to death following diagnosis. As with every model, estimates will improve as the number of cases increase.

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- 1 Kim DD, Goel A. Estimating case fatality rates of COVID-19. *Lancet Infect Dis* 2020; published online March 31. [https://doi.org/10.1016/S1473-3099\(20\)30234-6](https://doi.org/10.1016/S1473-3099(20)30234-6).
- 2 Spychalski P, Błażyńska-Spychalska A, Kobiela J. Estimating case fatality rates of COVID-19. *Lancet Infect Dis* 2020; published online March 31. [https://doi.org/10.1016/S1473-3099\(20\)30246-2](https://doi.org/10.1016/S1473-3099(20)30246-2).
- 3 Lipsitch M. Estimating case fatality rates of COVID-19. *Lancet Infect Dis* 2020; published online March 31. [https://doi.org/10.1016/S1473-3099\(20\)30245-0](https://doi.org/10.1016/S1473-3099(20)30245-0).
- 4 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](https://doi.org/10.1016/S1473-3099(20)30195-X).

- 5 WHO. Report of the WHO–China Joint Mission on Coronavirus Disease 2019 (COVID-19). Feb 16–24, 2020. [https://www.who.int/publications-detail/report-of-the-who-china-joint-mission-on-coronavirus-disease-2019-\(covid-19\)](https://www.who.int/publications-detail/report-of-the-who-china-joint-mission-on-coronavirus-disease-2019-(covid-19)) (accessed March 22, 2020).
- 6 WHO. Coronavirus disease 2019 (COVID-19). Situation Report—57. March 17, 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200317-sitrep-57-covid-19.pdf?sfvrsn=a26922f2_2 (accessed March 22, 2020).

The many estimates of the COVID-19 case fatality rate

Since the outbreak of coronavirus disease 2019 (COVID-19) began in December, a question at the forefront of many people's minds has been its mortality rate. Is the mortality rate of COVID-19 higher than that of influenza, but lower than that of severe acute respiratory syndrome (SARS)?

The trend in mortality reporting for COVID-19 has been typical for emerging infectious diseases. The case fatality rate (CFR) was reported to be 15% (six of 41 patients) in the initial period,¹ but this estimate was calculated from a small cohort of hospitalised patients. Subsequently, with more data emerging, the CFR decreased to between 4.3% and 11.0%,^{2,3} and later to 3.4%.⁴ The rate reported outside China in February was even lower (0.4%; two of 464).⁵

This pattern of decreasing CFRs is not surprising during the initial phase of an outbreak. Hard outcomes such as the CFR have a crucial part in forming strategies at national and international levels from a public health perspective. It is imperative that health-care leaders and policy makers are guided by estimates of mortality and case fatality.

However, several factors can restrict obtaining an accurate estimate of the CFR. The virus and its clinical course are new, and we still have little information about them. Health care capacity and capability factors,