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.

the impact of Qom pilgrimage[4] on SARS-CoV-2 transmission in eastern Saudi Arabia until then. The country's attempt to identify and quarantine returning Saudi pilgrims proved inefficient initially owing to non-direct routes of travel to Saudi Arabia through Gulf Cooperation Council countries. Saudi Arabia then encouraged returning citizens to voluntarily declare travel to Iran and repatriated stranded citizens using special flights.

Saudi Arabia mitigated international and domestic superspreader transmission of SARS-CoV-2 in its international pilgrim sites with early restrictions of access to its holy sites. Saudi Arabia was unsuccessful in limiting transmission among returning Saudi nationals who participated in an unmitigated superspreader event. The ongoing domestic transmission in the country is largely fueled by returning Saudi-national pilgrims.

We declare no competing interests.

*Ziad A Memish, Nawfal Aljerian, Shahul H Ebrahim
zmemish@yahoo.com

Research & Innovation Center, King Saud Medical City (ZAM), and Medical Referral Center, National Health Command Center (NA), Ministry of Health, Riyadh, Saudi Arabia; College of Medicine, Alfaisal University, Riyadh, Saudi Arabia (ZAM); King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia (NA); Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA (ZAM); and University of Sciences, Technique and Technology, Bamako, Mali (SHE)

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COVID-19 and the difficulty of inferring epidemiological parameters from clinical data

Knowing the infection fatality ratio (IFR) is crucial for epidemic management: for immediate planning, for balancing the life-years saved against those lost to the consequences of management, and for considering the ethics of paying substantially more to save a life-year from the epidemic than from other diseases. Impressively, Robert Verity and colleagues[1] rapidly assembled case data and used statistical modelling to infer the IFR for COVID-19. We have attempted an in-depth statistical review of their paper, eschewing statistical nit-picking, but attempting to identify the extent to which the (necessarily compromised) data are more informative about the IFR than are the modelling assumptions. First, the data.

Individual-level data for outside China appear problematic because different countries have differing levels of ascertainment and different disease-severity thresholds, even for classification as a case. The data's use in IFR estimation would require model-ascertainment parameters that are country specific, about which we have no information. Consequently, these data provide no useful information on the IFR.

Repatriation flight data provide the sole information on the prevalence in Wuhan, China (excepting the lower bound of confirmed cases). 689 foreign nationals who were eligible for repatriation are doubtfully representative of the susceptible population of Wuhan. Hence, seeing how to usefully incorporate the six positive cases from this sample is difficult.

Case mortality data from China provide an upper bound for the IFR, and with extra assumptions these data also supply information on how the IFR varies with age. Because prevalence is unknown, the data contain no information for estimating the absolute IFR magnitude.

Because of extensive testing, the outbreak on the *Diamond Princess*, the quarantined cruise liner (used only for validation by Verity and colleagues) supplies data on infections and symptomatic cases, with fewer ascertainment problems. These data appear directly informative about the IFR, although the comorbidity load on the *Diamond Princess* is unlikely to fully represent any population of serious interest (perhaps having fewer individuals with very severe but more with mild comorbidities).

Second, the modelling assumptions, in which we see two primary problems. The first problem is that Verity and colleagues correct the Chinese case data by assuming that ascertainment differences across age groups determine case rate differences. Outside of Wuhan, the authors replace observed case data by the cases that would have occurred if each age group had the same per-capita observed case rate as the 50–59 years age group. The authors assume complete ascertainment for this age group. These are very strong modelling assumptions that will greatly affect the results, but the published uncertainty bounds reflect no uncertainty about these assumptions. In Wuhan, the complete ascertainment assumption is relaxed by introducing a parameter, but one for which the data appear uninformative, so the results will be driven by the assumed uncertainty.

The second problem is that, generically, Bayesian models describe uncertainty both in the data and in prior beliefs about the studied system. Only when data are informative about the targets of modelling can we be sure that prior beliefs play a small role in what the model tells us about the world. In this case, the data are especially uninformative: we suspect

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results are mostly the consequence of what our prior beliefs were.

Taken together these problems indicate that Verity and colleagues' IFRs should be treated very cautiously when planning epidemic management. While awaiting actual measurements, we would base IFRs on the *Diamond Princess* outbreak data, with the Chinese case-fatality data informing the dependence of IFR on age. We have included a crude Bayesian model with its IFR estimates by age in the appendix. IFR estimates for corresponding populations are China 0·43% (95% credible interval 0·23–0·65), UK 0·55% (0·30–0·82), and India 0·20% (0·11–0·30). The strong assumptions required, by this approach too, emphasise the need for improved data. We should replace complex models of inadequate clinical data with simpler models of epidemiological prevalence data from appropriately designed random sampling using antibody or PCR tests.

See Online for appendix

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*Simon N Wood, Ernst C Wit, Matteo Fasiolo, Peter J Green
simon.wood@bath.edu

Università della Svizzera Italiana, Switzerland (ECW); and School of Mathematics, University of Bristol, Bristol BS8 1UG, UK

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Authors' reply

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We are grateful for Simon Wood and colleagues' comments on our study,[1] which explore some important sensitivities in the data that were available early in the COVID-19 pandemic. Wood and colleagues' re-analysis puts more weight on the *Diamond Princess* outbreak data, arriving at an infection fatality ratio (IFR) in the range 0·23–0·65%, whereas our analysis used data from repatriation flights out of Wuhan, leading to an IFR in the range 0·39–1·33%. Both datasets are opportunistic, and neither is perfectly representative of the underlying population of interest. For example, although the *Diamond Princess* outbreak has a uniquely well characterised population, the transmission setting is unusual and therefore not necessarily representative of the broader populations that such estimates would be applied to. Furthermore, the health status of cruise ship passengers is not necessarily the same as the general population of a similar age, and the standard of care received by these passengers is likely to be different to that received in settings where the health system is under more strain. Given these limitations and the fact that the *Diamond Princess* outbreak data were incomplete at the time of our analysis (late February, 2020), we opted to focus on repatriation flight data.

Epidemics of novel diseases are inherently rapidly changing environments, which bring unique challenges from a data analysis point of view. Our position was neatly summarised by Michael Ryan, executive director of the WHO Health Emergencies Programme, who said that "perfection is the enemy of the good when it comes to emergency management. Speed trumps perfection."[2] Having early estimates, although imperfect, of the order of magnitude of the IFR (ie, knowing whether the IFR is nearer to 1% or 0·01%) is essential for strategic planning, and in this sense, the re-analysis by Wood and colleagues places the IFR on the same scale as our initial estimate. We also strongly support the call for appropriately designed prevalence studies, which are now urgently needed to provide direct estimates of the IFR with fewer limitations.

We declare no competing interests.

*Robert Verity, Lucy Okell, Ilaria Dorigatti, Peter Winskill, Charlie Whittaker, Patrick Walker, Christl Donnelly, Neil Ferguson, *Azra Ghani
a.ghani@imperial.ac.uk

MRC Centre for Global Infectious Disease Analysis, Imperial College London, London, UK

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Re-examining the notion of irrational antimicrobial prescribing in LMICs

The increasing consumption of Reserve antibiotics in low-income and middle-income countries (LMICs), as reported by Eili Klein and colleagues,[1] represents an intractable public health challenge. Given the high burden of antimicrobial resistance despite low per-person consumption, optimising antimicrobial prescribing in LMICs requires achieving a balance between reducing excess prescribing without stifling access to antibiotics when needed. Considering inappropriate or irrational prescribing to be a major cause for the high antimicrobial-resistance burden in LMICs, WHO has emphasised the need to improve antimicrobial resistance awareness among physicians in LMICs by promoting rational use of antibiotics.[2] However, research has shown that physicians in LMICs have adequate awareness of antimicrobial resistance.[3] This evidence prompts a closer examination of the notion of irrationality in antimicrobial prescribing in these countries.

Research investigating antimicrobial prescribing in LMICs highlights the conditions of uncertainty within which these physicians operate: at the level of the diagnosis, the patient, and the health-care system.[4] These uncertainties arise out of various scarcities. For example, diagnostic uncertainties (eg, whether the complaints are due to an infection, and if so, the pathogen responsible, its antimicrobial sensitivity pattern,