3 Kandel N, Chungong S, Mahjour J. Improvement in annual report of self-assessments to the International Health Regulations (2005). *Wkly Epidemiol Rec* 2019; **94** (special issue): iii–vi.

4 Global Preparedness Monitoring Board. A world at risk: annual report on global preparedness for health emergencies. Geneva: World Health Organization, 2019.

5 Center for Health Security. Preparedness for a high-impact respiratory pathogen pandemic. Baltimore: Johns Hopkins Bloomberg School of Public Health, 2019.

6 WHO. Road map for access to medicines, vaccines and other health products 2019–2023. Geneva: World Health Organization, 2019.

7 Aitsi-Selmi A, Murray V. Protecting the health and well-being of populations from disasters: health and health care in the Sendai Framework for Disaster Risk Reduction 2015–2030. *Prehosp Disaster Med* 2016; **31:** 74–78.

8 Lee VJ, Aguilera X, Heymann D, Wilder-Smith A. Preparedness for emerging epidemic threats: a *Lancet Infectious Diseases* Commission. *Lancet Infect Dis* 2020; **20:** 17–19.

9 Zumla A, Dar O, Kock R, et al. Taking forward a 'One Health' approach for turning the tide against the Middle East respiratory syndrome coronavirus and other zoonotic pathogens with epidemic potential. *Int J Infect Dis* 2016; **47:** 5–9.

10 Jacobsen KH, Aguirre AA, Bailey CL, et al. Lessons from the Ebola outbreak: action items for emerging infectious disease preparedness and response. *EcoHealth* 2016; **13:** 200–12.

11 Kelly TR, Karesh WB, Johnson CK, et al. One Health proof of concept: bringing a transdisciplinary approach to surveillance for zoonotic viruses at the human-wild animal interface. *Prev Vet Med* 2017; **137:** 112–18.

Clinical course and mortality risk of severe COVID-19

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Several published reports of early clinical descriptions of coronavirus disease 2019 (COVID-19) have emerged from Hubei province in China, and many more will come. These early reports, typically simple descriptive case series of patients hospitalised with COVID-19 (mostly with pneumonia), provide valuable information on the more severe end of the disease spectrum. We tend to hear more about the most severe cases in the early stages of a new disease, as these are the ones first brought to the public's attention and are associated with deaths. However, it is important to bear in mind that the current best estimate is that about 81% of people with COVID-19 have mild disease[1] and never require hospitalisation. These cases have not yet featured much in published clinical descriptions.

In *The Lancet*, Fei Zhou and colleagues[2] provide further insight into the clinical course and mortality risk for adults with COVID-19 severe enough to require hospitalisation. They report findings from 191 patients with COVID-19 from Wuhan during the first month of the outbreak, and follow them through to discharge (n=137) or death (n=54). The follow-up until discharge or death is a point of difference from other case series to date. Their cohort had many characteristics in common with other reports[3–5]—a median age of 56·0 years (IQR 46·0–67·0), a high percentage (62%) of men, and nearly half (48%) of patients with comorbidities. In-hospital death was associated with, on admission, older age (odds ratio 1·10, 95% CI 1·03–1·17; p=0·0043), a higher Sequential Organ Failure Assessment score (5·65, 2·61–12·23; p<0·0001), and blood d-dimer greater than 1 µg/mL (18·42, 2·64–128·55; p=0·0033), findings known to be associated with severe pneumonia.[6,7] The study also presents early data on changes in clinical and laboratory findings over time, which could help clinicians to identify patients who progress to more severe disease. In-hospital mortality was high (28%), much higher than in other reports that had incomplete follow-up data,[3,5,8] and was very high among the 32 patients requiring invasive mechanical ventilation, of whom 31 (97%) died. This might reflect a higher proportion of patients admitted with severe disease in the early stages of the outbreak. In another report from Wuhan, mortality was 62% among critically ill patients with COVID-19 and 81% among those requiring mechanical ventilation.[9] While the world awaits further information from other locations, including from outside China, the current message is that mortality is high among the minority of people with COVID-19 who get severe disease.

The cohort design of this study provides excellent front-line information about mortality risk. It is essential for readers to understand that this truly is a retrospective cohort design, even if it might appear otherwise at first. Careful consideration of the design is essential to understanding the findings. The authors were able to collect a wealth of information from admission to discharge on many of the earliest known cases of coronavirus in the world. By identifying this large group of patients united by their disease and tracking them to these endpoints, the authors have provided us with insight into risk factors for in-hospital death. Even though their cohort does not include the censored observations of patients admitted during the study timeframe but not discharged by the end timepoint, these results can still be considerably useful for epidemiological description of the disease in terms of person-level risk. By excluding incomplete observations, it is possible that the reported mortality rate is biased to appear larger than it is, as

data from those patients who were not discharged by the end timepoint were not included. However, as a true population at risk of mortality, these patients are representative of the earliest onset of COVID-19. Excluding patients who began treatment well into the epidemic brings homogeneity to the exposure level and treatment. These preliminary data provide an important framework to build on as the world moves forward in the fight against this pandemic. The timeliness and value of this information far outweigh the slight bias stemming from the exclusion of patients with incomplete data at the end of the study period.

The report by Zhou and colleagues also provides data on viral shedding.[2] Throat swabs were obtained every other day and were PCR positive for a median of 20·0 days (IQR 16·0–23·0) after onset of symptoms. In survivors, median duration of viral shedding was 20·0 days (17·0–24·0), ranging from 8 to 37 days, but the virus was detectable until death in non-survivors. These early findings are similar to those reported for the severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome coronaviruses,[10–12] and we await more detailed information on viral load kinetics and shedding of SARS coronavirus 2 in various disease states. Importantly, PCR positivity does not necessarily indicate viable virus, and additional data are needed to better understand the infectious period of COVID-19 and implications for treatment and infection control.

Although there is always the limitation of generalisability in epidemic investigations, this study adds to a rapidly growing knowledge base on the clinical course and mortality risk of COVID-19. We now have a better understanding of the severity of hospitalised COVID-19, but more data are needed on treatment options that improve survival.

We declare no competing interests.

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1 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 Feb 24. DOI:10.1001/jama.2020.2648.
2 Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020. published online March 9. https://doi.org/10.1016/S0140-6736(20)30566-3.
3 Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; **395:** 507–13.
4 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.
5 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.
6 Ahnert P, Creutz P, Horn K, et al. Sequential organ failure assessment score is an excellent operationalization of disease severity of adult patients with hospitalized community acquired pneumonia—results from the prospective observational PROGRESS study. *Crit Care* 2019; **23:** 110.
7 Snijders D, Schoorl M, Schoorl M, Bartels PC, van der Werf TS, Boersma WG. D-dimer levels in assessing severity and clinical outcome in patients with community-acquired pneumonia. A secondary analysis of a randomised clinical trial. *Eur J Intern Med* 2012; **23:** 436–41.
8 Guan W-J, Ni Z-Y, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; published online Feb 28. DOI:10.1056/NEJMoa2002032.
9 Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* 2020; published online Feb 24. https://doi.org/10.1016/S2213-600(20)30079-5.
10 Cheng PKC, Wong DA, Tong LKL, et al. Viral shedding patterns of coronavirus in patients with probable severe acute respiratory syndrome. *Lancet* 2004; **363:** 1699–700.
11 Corman VM, Albarrak AM, Omrani AS, et al. Viral shedding and antibody response in 37 patients with Middle East Respiratory Syndrome coronavirus infection. *Clin Infect Dis* 2016; **62:** 477–83.
12 Oh M-D, Park WB, Choe PG, et al. Viral load kinetics of MERS coronavirus infection. *N Engl J Med* 2016; **375:** 1303–05.

COVID-19: towards controlling of a pandemic

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During the past 3 weeks, new major epidemic foci of coronavirus disease 2019 (COVID-19), some without traceable origin, have been identified and are rapidly expanding in Europe, North America, Asia, and the Middle East, with the first confirmed cases being identified in African and Latin American countries. By March 16, 2020, the number of cases of COVID-19 outside China had increased drastically and the number of affected countries, states, or territories reporting infections to WHO was 143.[1] On the basis of "alarming levels of spread and severity, and by the alarming levels of inaction", on March 11, 2020, the Director-General of WHO characterised the COVID-19 situation as a pandemic.[2]

The WHO Strategic and Technical Advisory Group for Infectious Hazards (STAG-IH) regularly reviews and updates its risk assessment of COVID-19 to make recommendations to the WHO health emergencies programme. STAG-IH's most recent formal meeting on March 12, 2020, included an update of the global COVID-19 situation and an overview of the research priorities established by the