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Study of critically ill patients with COVID-19 in New York City

Cummings and colleagues¹ reported the epidemiology, clinical course, and outcomes of 257 critically ill adults with laboratory-confirmed COVID-19 admitted to two hospitals in New York City. The primary outcome was the rate of in-hospital death, and each patient had at least 28 days of observation. The authors report that, as of April 28, 2020, 101 (39%) of 257 patients had died, 94 (37%) remained hospitalised, four (2%) were transferred to another hospital, and 58 (23%) were discharged alive. Surprisingly, the authors show in figure 1 of their Article¹ a cumulative incidence of in-hospital death of approximately 45% at 28 days. Given the numbers of patients at risk reported below the figure, we have identified that this result is not correct. Apparently, the authors censored the patients discharged alive (n=58) at the day of discharge. This methodological error has led to overestimation of the cumulative incidence of death, and distorted the results of the Cox proportional hazards regression. A fundamental assumption in survival analysis is that censoring should be non-informative—ie, that patients censored have the same survival prospects as those who continue to be followed up.² Patients discharged alive should not have been censored; their status should be considered as event-free (ie, alive) throughout the study observation period. This methodological error in the COVID-19 literature is common yet serious.³ We kindly ask the authors to reanalyse the data, and correctly report the cumulative incidence, and the risk factors of in-hospital mortality, considering the above aspects.

We declare no competing interests.

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- 1 Cummings MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *Lancet* 2020; **395**: 1763–70.
- 2 Bland JM, Altman DG. Survival probabilities (the Kaplan–Meier method). *BMJ* 1998; **317**: 1572.
- 3 Bonovas S, Piovani D. Compassionate use of remdesivir in Covid-19. *N Engl J Med* 2020; **382**: e101.

Authors' reply

We agree with Daniele Piovani and Stephanos Bonovas that informative censoring, if present, could represent a potential source of bias in the survival analyses in our Article.¹ However, sensitivity analysis suggests that any such bias is likely to be minimal.

To evaluate the effect of assigning different observation times on our regression estimates, we reconstructed our primary Cox model with patients discharged from hospital alive considered event-free throughout the study period, as suggested by Piovani and Bonovas. The generated hazard ratios were consistent with those we previously reported, with older age (adjusted hazard ratio 1.31 [95% CI 1.10–1.56] per 10-year increase), chronic cardiac disease (1.71 [1.05–2.78]), chronic pulmonary disease (3.12 [1.58–6.19]), and higher concentrations of interleukin-6 (1.13 [1.04–1.23] per decile increase), and D-dimer (1.10 [1.01–1.20] per decile increase) associated with mortality in the multivariable model. Regarding the cumulative incidence of hospital mortality at 28 days, reconstruction of this function yielded an estimate of approximately 40%.

In addition, more definitive in-hospital outcomes for the patients included in our cohort are now available. As of July 2, 2020, by which time all patients had at least 90 days of observation, a final in-hospital outcome was known for 250 (97%) of 257 patients. 113 (44%) patients had died (including 96 [47%] of 203 patients who received invasive

mechanical ventilation), 133 (52%) patients were discharged alive, four (2%) were transferred to another hospital, and seven (3%) remained hospitalised.

MJC and MRO'D participated as investigators for completed and ongoing clinical trials evaluating the efficacy and safety of remdesivir (sponsored by Gilead Sciences) and convalescent plasma (sponsored by Amazon), respectively, in hospitalised patients with COVID-19. Support for this work is paid to Columbia University.

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- 1 Cummings MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *Lancet* 2020; **395**: 1763–70.

Undermining breastfeeding will not alleviate the COVID-19 pandemic

Breastfeeding offers numerous immunological, developmental, and psychological advantages to the infant–mother dyad. The risks posed to infant and maternal health through any loss of support for breastfeeding mean that public health messaging during the COVID-19 pandemic should be careful. As academic leads of human milk banks, we are acutely aware of the importance of understanding the risks posed by novel infectious pathogens in human milk and the mitigation of risk to susceptible infants.

It is therefore essential that published data related to COVID-19 are valid beyond question. In their Correspondence, Rüdiger Groß and colleagues¹ describe the detection of viral particles in human breastmilk, but no cell culture to measure viral viability was done. Furthermore, the likelihood of severe acute respiratory syndrome