

Now, more than ever, is the time for evidence-based medicine

R Hofmeyr, BM Biccard

Department of Anaesthesia and Perioperative Medicine, Grootte Schuur Hospital and University of Cape Town, South Africa

Humankind is currently facing an unprecedented pandemic; a global onslaught of proportions which may have been predictable, but for which we were clearly highly unprepared. Although partly due to limited knowledge of how to manage patients with SARS-CoV-2 infection, this limitation has been made more palpable by the ability of the pandemic to overwhelm health systems with severely ill patients, many of whom have poor outcomes.¹ Rapid and effective management of critical illness will undoubtedly increase our overall capability to respond, prevent loss of life, and ultimately strengthen our health systems for the future.

Regrettably, it appears that many worldwide – but particularly those in the medical profession – are falling prey to a second pandemic: a deluge of viral information from which we struggle to sift the verbose, extract the vital, assess for veracity, and select the valuable. At a time of exceptional quantities of data, we have never needed the light of evidence-based medicine more. In responding to a new clinical problem – whether it be a new virus, disease, or emerging complication – the value of rapid publication of peer-reviewed clinical data and interpretation cannot be underestimated. In an era when information can be disseminated around the world *literally* at the speed of light, when enormous datasets can be instantaneously interrogated by both human and artificial intelligence, and where technological advancements are breaking down the barriers erected by language, culture, wealth and class, we stand poised to unite in creating rapid collaborative solutions to new clinical problems. There is a critical interplay however, between speed and quality. To paraphrase the reported words of physicist Wolfgang Pauli, “*I don't mind you publishing rapidly, just not more rapidly than you can think.*”²

The rate and volume at which publications on coronavirus disease are appearing in the literature is astounding. PubMed lists nearly 8 000 publications on coronavirus for 2020 (15 May 2020). In this edition of the journal, the systematic review and meta-analysis of intensive care unit (ICU) mortality for patients with COVID-19 illustrates the problems which occur when data is ‘*published more rapidly than you can think.*’³ A search of studies published between January and early April 2020 yielded nearly 500 abstracts, of which 59 were considered relevant to the enquiry. However, very few studies yielded data suitable for meta-analysis: in most cases, only gross mortality data was available, or the studies had been so rapidly published that large proportions of the patients included were still undergoing treatment in ICU at

the time of submission.⁴ In other studies, granular mortality data for risk factors of interest were not reported, and attempts to obtain original data from researchers was stymied by limitations on data sharing, citing governmental restrictions. Thus, at the very moment where we stand to learn most from the early experiences of treating COVID-19, and we have the capacity for the rapid assimilation of these data, we are thwarted by a lack of usable data of sufficient detail to allow effective meta-analysis. We cannot see the wood for the trees. Considering the number of patients that have required ICU management across China, Europe and North America, it is astounding how little useful data was extractable to inform practice in this systematic review, with most comparisons yielding less than a hundred patients.³ This is an embarrassment to our profession, and a disservice to society. As scientists, we have a responsibility to push back the darkness at the boundaries of knowledge, but as busy clinicians in a pandemic, it is irresponsible to publish obfuscatory data which burns precious time without providing illumination.

What can be done to rectify the situation? It is our social responsibility to provide timely and useful research outputs in a pandemic. However, in order to contribute meaningful research data, it is important to follow some simple rules. Firstly, we must select and report appropriate and clear hard endpoints (such as patient mortality), or accepted standardised outcomes, to allow for sensible and appropriate amalgamation of data in meta-analyses.⁵ Secondly, we need to minimise bias between groups, or provide enough data that the bias can be controlled for statistically. This means that we need to report known or suspected prognostic factors, we need an accepted and objective method for detecting the outcome, and we must ensure complete follow-up of all patients.⁶ Thirdly, we must strive to ensure the rapid availability of raw de-identified data to allow early data interrogation, when dealing with developing public health emergencies of international concern. Ideally, these datasets should include pre-specified patient characteristics, and standardised interventional, outcome and variable definitions, to allow rapid integration of datasets across different centres in multiple countries. Data sharing agreements are common practice and afford the opportunity for important individual patient data meta-analyses, which are powerful tools to quickly generate evidence. Journal editors and reviewers have a responsibility to call out inadequate research papers, reject them, or demand sufficient supplementary data to ensure that they are useful to clinicians.

African resources are limited,⁷ and early appropriate risk stratification and management decisions could positively impact the healthcare system. As we are behind the pandemic curve of China, Europe and North America, we thought that a rapid systematic review would provide useful data to inform clinical practice on the continent. The publications in this systematic review had the potential to mitigate morbidity and potentially save lives, but instead they fell far short of this mark. This irresponsible haste by researchers and editors should not be tolerated, lest the rush to print leaves papers published, but patients perishing.

References

1. 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;395(10229):1054-62. [published Online First: 2020/03/15].[https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3).
2. Clapham P. Publish or perish. *Bioscience* 2005;55(5):390-91. [https://doi.org/10.1641/0006-3568\(2005\)055\[0390:POP\]2.0.CO;2](https://doi.org/10.1641/0006-3568(2005)055[0390:POP]2.0.CO;2).
3. Taylor EH, Hofmeyr R, Torborg A, et al. Risk factors and interventions associated with mortality or survival in adult COVID-19 patients admitted to critical care: A systematic review and meta-analysis. *South Afr J Anaesth Analg* 2020;26(3):116-127. <https://doi.org/10.36303/SAJAA.2020.26.3.2428>.
4. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. *JAMA*. 2020;323(16):1574-1581. [published Online First: 2020/04/07]. <https://doi.org/10.1001/jama.2020.5394>.
5. Myles PS, Grocott MP, Boney O, et al. Standardizing end points in perioperative trials: towards a core and extended outcome set. *Br J Anaesth* 2016;116(5):586-9. <https://doi.org/10.1093/bja/aew066>.
6. Guyatt GH, Rennie D, Meade MO, et al. *Users' guides to the medical literature: A manual for evidence-based clinical practice*. Third ed. New York: McGraw-Hill Education 2015.
7. Houred K, Lewis D, McNeill R, et al. Virus exposes gaping holes in Africa's health systems: Reuters; 2020 [cited 2020 10 May]. Available from: <https://graphics.reuters.com/HEALTH-CORONAVIRUS/AFRICA/yzdpxoqbdvx/>.