

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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. Yet, other histories reveal midwives improving midwifery education, and thus outcomes for mothers and babies, before obstetrics and gynaecology became a medical specialty. Although conflict between male doctors and female midwives has received much attention, there is a need to embrace a wider and more complex historical narrative, a useable past that is authentic and empowering for midwives in the face of a crisis in maternal and neonatal mortality.

We declare no competing interests.

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## Decoupling of omicron variant infections and severe COVID-19

SARS-CoV-2 omicron (B.1.1.529) was designated a variant of concern by WHO because of specific mutations that might increase transmissibility, risk of reinfection, or vaccine breakthrough infection. Many of these mutations affect the receptor-binding domain and N-terminal domain of the spike

protein, which might, paradoxically, increase binding to ACE-2 while evading antibody recognition.<sup>1</sup>

Emergence of omicron appears to have parallels with the beta variant (B.1.351) in South Africa. It was demonstrated that there are decreased neutralising antibody titres with beta in infection-naive individuals who received two doses of AZD1222 (ChAdOx1 nCoV-19) or BNT162b.<sup>2,3</sup> Nevertheless, realworld data showed more than 80% effectiveness against severe disease and hospitalisations.<sup>4,5</sup>

Although preliminary evidence suggests booster doses might enhance protection against omicron,<sup>6</sup> studies are underway to fully determine vaccine effectiveness. Given the natural lag between infection and severe outcomes, we await further data on omicron for effectiveness of vaccinations in preventing severe disease-the key intended outcome of vaccination.7 In the meantime, the South Africa National Institute for Communicable Diseases has shared preliminary data indicating a decoupling of infection rates from hospitalisations and deaths with omicron. These data suggest underlying immune responses following infection and that primary and booster vaccination might attenuate the course of illness.

Complementary humoral (antibody) and cellular (T cell) immune responses are activated following natural SARS-CoV-2 infection or vaccination. T-cell responses encompass a broad range of spikeprotein-specific T-cell receptors that recognise multiple epitopes both within and outside of mutated regions in variants of concern.<sup>8</sup> Thus, even if spike protein mutations enable neutralising antibody escape, non-neutralising antibodies or T-cellmediated responses can provide protection. The beta variant has only a few mutations in the spike gene that affect T-cell epitopes, meaning T-cell response is maintained; this is expected to be the case with omicron.  $^{\scriptscriptstyle 1,8}$ 

At this stage of the pandemic, omicron is spreading in populations where many individuals have been previously infected with SARS-CoV-2 and are now being vaccinated, or where many have received two or three COVID-19 vaccine doses. These populations might be expected to have greater depth of antibody response and a broader and deeper poly-epitopic T-cell response,<sup>9,10</sup> which should overcome some of the anticipated antibody evasion of omicron. In these scenarios, protection against severe disease is anticipated. Most cases of severe disease and hospitalisation with omicron are among the unvaccinated; we recommend an accelerated and equitable roll-out of COVID-19 vaccines, which have a continued role in enhancing protection against omicron.

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# Disparity in the selection of patients in clinical trials

Evidence-based medicine is the universally accepted cutting-edge standard of care. The framework heavily relies on protocols typically derived from the systematic reviews of randomised clinical trials (RCTs), the gold standard of research in biomedical sciences. However, the results obtained from RCTs might not be applicable to real-world populations if the study sample was not representative of real populations of patients.

A systematic review of the trials conducted in the fields of cardiology, mental health, and oncology revealed that in more than 70% of 52 studied trials, there were significant disparities between the study sample and the typical population of patients, which hampers the external validity (and generalisability) of the results obtained.1 Compared with real-world patients with cancer, the patients in oncology RCT studies were often younger, more likely to be male, and had a better prognosis. Rates of participation in RCTs are typically low for some minority racial and ethnic groups. For example, a study of more than 1000 oncology trials revealed that the likelihood of a non-Hispanic White patient being enrolled in a trial is three times that for a Hispanic patient, and nearly twice the likelihood of that for an African American patient.<sup>2</sup>

The existing disparity and mismatch between the study sample and realworld patient population has resulted in a shortage of information for many people in the world with racial and ethnic backgrounds not equitably included in trials. One study conducted on 230 US-based vaccine clinical trials revealed that many ethnic minority groups were under-represented in the trial study samples.<sup>4</sup> Although it seems that this issue has been alleviated in the USA, there is still a problem in Europe and other parts of the world.<sup>3</sup> The existing mismatch between the trial study sample and the real-world target population observed in many trials would cause selection bias that ultimately results in a waste of resources and a distortion of the body of evidence.

Every single member of the institutional review board or ethics committee evaluating proposed RCTs has a moral duty to ensure that the existing systematic mismatch between the trial sample and the real-world population vanishes so that the trial findings can be used in daily practice for the treatment of all real-world patients. This step will pave the way for abolishing disparities in outcomes and uphold equity in health care throughout the globe.

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### **Department of Error**

Osman M, Alassam MN. Military attacks on health workers in Sudan. Lancet 2022; **399:** 1045—In this Correspondence, references have been corrected. This correction has been made to the online version as of March 10, 2022 and the print version is correct.

Shoib S, Essar MY, Mohd Saleem S, Legris Z, Chandradasa M. The children of Afghanistan need urgent mental health support. Lancet 2022; **399**: 1045–46—In this Correspondence, a reference to the 2018 cross-sectional survey of children in Afghanistan was missing. This correction has been made to the online version as of March 10, 2022, and the print version is correct.