



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.



Prioritisation of COVID-19 boosters in the omicron era



Giannis Alexopoulos/NurPhoto via Getty Images

See [Articles](#) page 1305

Vaccines are a primary component of the COVID-19 pandemic response. Up until August, 2022, all available COVID-19 vaccines targeted only the ancestral strain of SARS-CoV-2. Emergence of the highly transmissible omicron (B.1.1.529) variant in November, 2021, has been associated with reduced effectiveness of first-generation COVID-19 vaccines against infection.¹ Omicron and other variants of concern pose substantial challenges to optimising COVID-19 vaccination strategies. Thankfully, a growing body of literature shows that a COVID-19 vaccine booster dose protects against symptomatic omicron infection^{1,2} and against hospitalisation with omicron infection, although protection is lower with more recently emerging omicron sublineages (ie, BA.4 and BA.5) compared with earlier variants.^{3,4} With the rapid spread of new SARS-CoV-2 variants and sublineages, and demonstrated reduced effectiveness of current COVID-19 vaccines, development of next-generation vaccines is crucial. Bivalent vaccines optimised for BA.4 and BA.5 omicron sublineages have been developed for use as a booster dose, but roll-out of these new vaccines will be slow. To prioritise the limited supply of bivalent boosters, it is imperative to enhance our understanding of the populations at highest risk of severe COVID-19 breakthrough infections.

Before the development of COVID-19 vaccines, researchers in the UK developed QCOVID, a population-based prediction model that estimates the risk of hospitalisation with COVID-19.⁵ After the mass roll-out of COVID-19 vaccines, additional research determined that older age, immunosuppression, and specific underlying chronic conditions were associated with severe outcomes (ie, hospitalisation and death) resulting from COVID-19 breakthrough infections among those with the primary vaccine series.^{6,7} Investigations of risk factors for severe outcomes in boosted populations, however, are sparse. In *The Lancet*, Utkarsh Agrawal and colleagues⁸ identify risk factors for COVID-19-related hospitalisation and death among nearly 14 million adults aged 18 years and older in the UK who had received a COVID-19 booster dose in addition to a primary vaccine series. The boosted study population was 53% female and 80% White, with 41% in the 18–49-year age group.

Between Dec 20, 2021, and Feb 28, 2022, Agrawal and colleagues identified severe COVID-19 outcomes

in boosted individuals at a rate of 7.6 events per 1000 person-years. Although the authors did not design the study to investigate differences by booster dose product, they found a difference in the rate of severe events among individuals who received mRNA-1273 (elasomeran; Moderna; 3.0 events per 1000 person-years) versus BNT162b2 (tozinameran; Pfizer–BioNTech; 9.0 events per 1000 person-years), although individuals who received BNT162b2 had more comorbidities.⁸ The authors also examined the associations between 36 individual covariates and severe COVID-19 outcomes in this boosted population. Characteristics identified as the greatest risk factors for severe COVID-19 outcomes included the presence of five or more comorbidities (≥ 5 comorbidities vs none; adjusted rate ratio 9.51 [95% CI 9.07–9.97]), immunosuppressed status (yes vs no; 5.80 [5.53–6.09]), history of neurological disorders (yes vs no; 5.30 [4.90–5.74]), presence of chronic kidney disease (chronic kidney disease stage 5 vs no; 3.71 [2.90–4.74]), and older age (aged ≥ 80 years vs 18–49 years; 3.60 [3.45–3.75]).

The work by Agrawal and colleagues is the largest and most comprehensive work to date, examining severe COVID-19 outcomes in a UK population with a COVID-19 vaccine booster dose. The study's limitations are a result of the rapidly evolving pandemic. New omicron sublineages have emerged and become dominant in the months after the study period, leaving questions about how the findings might compare in the current BA.4 and BA.5 era. Additionally, interplay between the timing of primary and booster vaccination delivery and the initial emergence of omicron in the study population could have led to residual confounding. However, the highly significant estimates identified using these large, population-based, government-mandated datasets give us confidence in the validity of the findings.

We are pleased to see the reduction in the rate of severe COVID-19 outcomes after the booster dose identified by Agrawal and colleagues, but the absolute numbers are still disheartening, translating to life-altering events for more than 26 000 families over the 2-month study period.⁸ Protection of the individuals at highest risk must be a priority as we continue to develop and refine response strategies for the COVID-19 pandemic. In addition to the authors confirming that previously identified risk

factors for severe COVID-19 outcomes continue to apply in the boosted population, Agrawal and colleagues identified novel risk factors, specifically underweight BMI (<18.5 kg/m²) and urban residence, which might warrant further examination. These findings are crucial for targeted policy recommendations and interventions.

The growing evidence indicating continued risk for severe COVID-19 outcomes among some individuals who receive one booster dose^{3,4,8} leaves us contemplating future directions for enhancing protection in these populations at high risk. The authorisation from the US Food and Drug Administration in August, 2022, and subsequent recommendation from the US Centers for Disease Control and Prevention for the use of bivalent COVID-19 vaccines is a laudable first step,⁹ as early research shows that these new COVID-19 vaccines induce relatively higher and broad-spectrum cross-neutralising activities compared with the original COVID-19 vaccines.¹⁰ Where supply of bivalent vaccine is limited, roll-out should be targeted to groups identified as at high risk of severe COVID-19 outcomes, especially older age groups and those with multimorbidity. Additionally, individuals with a hindered immune response due to immune senescence or immunosuppression should also be prioritised for SARS-CoV-2 pre-exposure prophylaxis and COVID-19 therapeutics.

Consistent with recent findings of high COVID-19 booster vaccine effectiveness against hospitalisation,^{3,4} Agrawal and colleagues reported lower rates of severe COVID-19 outcomes in a boosted population compared with the population with only primary series vaccination in the UK. Their findings also identify groups who remain

at unacceptably high risk of COVID-19 hospitalisation and death even after receiving a booster, providing key insights for further improving the global COVID-19 response.

MES has received research support from GlaxoSmithKline for respiratory syncytial virus research. SAI reports no competing interests.

*Stephanie A Irving, Maria E Sundaram
stephanie.a.irving@kpchr.org

Kaiser Permanente Center for Health Research, Portland, OR 97227, USA (SAI);
Center for Clinical Epidemiology and Population Health, Marshfield Clinic,
Marshfield WI, USA (MES)

- 1 Andrews N, Stowe J, Kirsebom F, et al. COVID-19 vaccine effectiveness against the omicron (B.1.1.529) variant. *N Engl J Med* 2022; **386**: 1532–46.
- 2 Sheikh A, Kerr S, Woolhouse M, et al. Severity of omicron variant of concern and effectiveness of vaccine boosters against symptomatic disease in Scotland (EAVE II): a national cohort study with nested test-negative design. *Lancet Infect Dis* 2022; **22**: 959–66.
- 3 Link-Gelles R, Levy ME, Gaglani M, et al. Effectiveness of 2, 3, and 4 COVID-19 mRNA vaccine doses among immunocompetent adults during periods when SARS-CoV-2 omicron BA.1 and BA.2/BA.2.12-1 sublineages predominated—VISION Network, 10 states, December 2021–June 2022. *MMWR Morb Mortal Wkly Rep* 2022; **71**: 931–39.
- 4 Kirsebom FCM, Andrews N, Stowe J, et al. COVID-19 vaccine effectiveness against the omicron (BA.2) variant in England. *Lancet Infect Dis* 2022; **22**: 931–33.
- 5 Clift AK, Coupland CAC, Keogh RH, et al. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. *BMJ* 2020; **371**: m3731.
- 6 Yek C, Warner S, Wiltz JL, et al. Risk factors for severe COVID-19 outcomes among persons aged ≥18 years who completed a primary COVID-19 vaccination series—465 health care facilities, United States, December 2020–October 2021. *MMWR Morb Mortal Wkly Rep* 2022; **71**: 19–25.
- 7 Agrawal U, Katikireddi SV, McCowan C, et al. COVID-19 hospital admissions and deaths after BNT162b2 and ChAdOx1 nCoV-19 vaccinations in 2.57 million people in Scotland (EAVE II): a prospective cohort study. *Lancet Respir Med* 2021; **9**: 1439–49.
- 8 Agrawal U, Bedston S, McCowan C, et al. Severe COVID-19 outcomes after full vaccination of primary schedule and initial boosters: pooled analysis of national prospective cohort studies of 30 million individuals in England, Northern Ireland, Scotland, and Wales. *Lancet* 2022; **400**: 1305–20.
- 9 Centers for Disease Control and Prevention. CDC recommends the first updated COVID-19 booster. 2022. <https://www.cdc.gov/media/releases/2022/s0901-covid-19-booster.html> (accessed Sept 29, 2022).
- 10 Burki T. COVID vaccine booster doses for omicron variants. *Lancet Respir Med* 2022; **10**: 936.

Dedicated and designated approaches to task-shared psychological interventions

Leveraging community health workers (CHWs) to deliver interventions is an evidenced-based approach to reducing the mental treatment gap in health systems in low-income and middle-income countries.¹ However, how best to sustainably integrate CHWs into mainstream public health services remains an issue.^{2,3} In *The Lancet*, Bronwyn Myers and colleagues⁴ try to address whether CHWs should have designated or dedicated roles in the provision of psychological interventions within public health systems in

low-income and middle-income countries. Their work with CHWs based at primary health clinics in South Africa shows that both approaches were equally effective in reducing symptoms of depression but that only the dedicated approach led to a reduction in alcohol use disorder symptom severity.

This cluster randomised trial compared the effectiveness of dedicated and designated approaches to CHW-delivered psychological interventions compared with treatment



See [Articles](#) page 1321