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post-randomisation (0.6%, 95% CI 0.4–1.0 vs 1.6%, 1.2–2.3; absolute risk difference –1.0%, 95% CI –1.7 to –0.4), albeit this difference was not present at 5 years.

Although the researchers who were involved in this work deserve appreciation for their efforts to conduct the trials and this individual patient data meta-analysis, the data show that the totality of patients randomly assigned across all the trials to date is insufficient to clearly establish superiority or non-inferiority of PCI over the current gold standard of CABG. A trial larger than the aggregate of SYNTAX, PRECOMBAT, NOBLE, and EXCEL should be a priority in the field.

A limitation of this meta-analysis is that it focused only on superiority, which was not established for PCI. The authors did not attempt to directly inform the non-inferiority of PCI relative to CABG by setting a non-inferiority boundary; however, physicians and patients can draw their own conclusions given the 85.7% probability that PCI compared to CABG had a higher risk of death at 5 years and a 49.1% probability the excess absolute risk was 1% or greater.

Although we agree with Sabatine and colleagues³ that cardiac surgeons and interventional cardiologists need to be involved in the process of choosing the revascularisation approach, patient preference needs to be central to the process. Until definitive trial data become available, patients deserve to be presented with the advantages, disadvantages, and uncertainties of both approaches.

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COV-BOOST: evidence to support rapid booster deployment



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With accruing evidence that the effectiveness of COVID-19 vaccines wanes over time,^{1,4} and the recent emergence of the omicron (B.1.1.529) variant,⁵ some countries are rapidly deploying vaccine boosters.⁶ In the UK, the COVID-19 vaccination campaign launched in

December, 2020, and began with prioritised population groups, including people most likely to be at higher risk for severe outcomes or those providing health services or care for these individuals. With emerging evidence from Israel and the UK of vaccine waning, the Joint



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Committee on Vaccination and Immunisation (JCVI) in September, 2021, recommended boosting individuals in a phased way 6 months after completion of their primary course of COVID-19 immunisation.⁷ Additionally, with concerns around the mutational profile of omicron, with WHO designating it a variant of concern on Nov 26, 2021,⁵ acceleration of a third dose in the UK was proposed as a key response strategy for COVID-19, resulting in widening eligibility to all people aged 18 years and older and reducing the minimum time interval between doses two and three.^{8,9}

In *The Lancet*, Alasdair Munro and colleagues¹⁰ report the outcomes of the COV-BOOST trial, which is timely and provides valuable evidence on the immunogenicity and safety of seven COVID-19 vaccines administered as boosters. This multicentre UK trial recruited 2878 healthy participants older than 30 years across 18 sites who had received either two doses of BNT162b2 or ChAdOx1 nCov-19, with no history of previous SARS-CoV-2 infection, and randomly assigned them to receive one of seven COVID-19 vaccines; namely, NVX-CoV2373 (Novavax, NVX), ChAdOx1 nCov-19 (Oxford–AstraZeneca, ChAd), BNT162b2 (Pfizer–BioNtech, BNT), VLA2001 (Valneva, VLA), Ad26.COVS.5 (Janssen), mRNA1273 (Moderna, m1273), CVnCov (CureVac), three of which were also used as half doses (BNT, VLA, and NVX) or a quadrivalent meningococcal conjugate vaccine (MenACWY) as a control. The coprimary outcomes were safety and immunogenicity of anti-spike IgG measured by ELISA at day 28. In the ChAd/ChAd-primed participants, the median age was 53 years (IQR 44–61) in the younger group and 76 years (73–78) in the older group. In the BNT/BNT-primed participants, the median age was 51 years (41–59) in the younger group and 78 years (75–82) in the older group. In the ChAd/ChAd-primed group, 676 (46.7%) participants were female and 1380 (95.4%) were white, and in the BNT/BNT-primed group 770 (53.6%) participants were female and 1321 (91.9%) were white.

Munro and colleagues¹⁰ report that vaccines were effective in boosting neutralising antibody and cellular responses within 28 days of administration. They also identify no safety concerns and the profiles of side-effects were similar to those seen with the primary course across all vaccines, which should inform public health messaging on boosters, or third doses, and provide reassurance. The more detailed data on variability in immunogenicity and

side-effect profiles by vaccine type are valuable to inform decisions on booster regimens, alongside considerations of vaccine availability and population primary vaccine course regimens. ChAd, BNT, and m1273 demonstrated significantly increased cellular responses geometric mean ratio to the beta (B.1.351) strain within 14 days, for either primary course, which one would hope would be similar to the responses seen with omicron.

COV-BOOST was a robustly conducted study and therefore provides strong evidence that these vaccine boosters are immunogenic and safe, in a trial context, among healthy adult participants older than 30 years. The inclusion of seven different COVID-19 vaccines provides options for adapting regimens according to supply and ensure the findings are relevant to varied global communities. The finding of rapid boosting supports the recent UK decision to expand access to third doses as a precaution to increase population protection against the omicron variant, although more time and evidence are required to gain a fuller understanding of the performance of COVID-19 vaccines against this new variant. While recognising that longer intervals between dose two and three are likely to be more immunogenic,¹¹ the dosing interval in this study was shortened by necessity (minimum 70 days for ChAd, 84 days for BNT), and therefore provides evidence of effect at shorter intervals, which has informed the UK decision following the emergence of omicron to shorten the minimum interval between second and third doses from 6 months to 3 months.

Understandably, as a clinical trial, there are limitations, chiefly in the generalisability of findings beyond the trial setting, particularly to younger populations, those with previous SARS-CoV-2 infection, and to recipients of different primary course regimens, and in assessing impacts, of both safety and effectiveness, at scale and longer follow-up. The latter point highlights the complementarity between clinical trials, observational studies, and surveillance, with large cohort studies well placed to determine whether the immunogenicity generated after boosters translates to real-world protection from SARS-CoV-2 infection, and ongoing surveillance essential to detect potential rare adverse events.

Finally, we consider it necessary to highlight that although the focus in highly vaccinated high-income countries like the UK is currently on boosters, only 6% of

people in low-income countries have received at least one dose.⁶ In addition to efforts to increase vaccine affordability and access globally, it is important to ensure that COVID-19 vaccination and research are inclusive. For many low-income countries with high seroprevalence after infection, the focus must be maintained on rapidly giving the first and second doses of COVID-19 vaccine to boost immunity gained from primary infection, endorsing the WHO targets to vaccinate 40% of the global population by the end of 2021 and 70% by mid-2022.¹²

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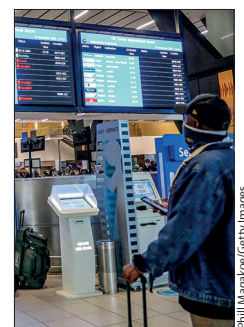
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The political theatre of the UK's travel ban on South Africa

On Dec 24, 2020, the UK's Prime Minister Boris Johnson announced an immediate travel ban on all flights to South Africa after the detection of SARS-CoV-2 beta variant by South African scientists.¹ The resulting travel restriction was lifted 291 days later. On Nov 25, 2021, South African scientists reported a new SARS-CoV-2 variant, B.1.1.529, that was subsequently designated omicron. Although the omicron variant has mutations that could make it less susceptible to neutralising antibody activity and possibly as transmissible as or more transmissible than the delta variant,² such concerns have yet to be determined by in-vitro and in-vivo evidence. Furthermore, it is also relevant to consider that although antibody activity induced by the ChAdOx1 nCoV-19 vaccine (AZD1222) had nominal neutralising activity against the beta variant and failed to protect against mild to moderate COVID-19 due to the beta variant, the vaccine still reduced risk of severe COVID-19 due to beta or gamma variants by 80%.^{3,4}

2 days after the identification of omicron, the UK Government promptly reapplied a travel ban on travel from South Africa and some other African countries.⁵ Several other countries, such as Israel and the USA, swiftly followed suit with travel bans from countries in sub-Saharan Africa, citing this action as a precautionary measure.⁶ This unwarranted action has generated intense anger and frustration. Travel restrictions are unlikely to be able to stop the spread of coronaviruses unless countries are able to completely seal their borders to travellers from all nations. Predictably, soon after the UK travel ban announcement, cases of the omicron variant were reported in Europe,⁷ the UK, North America, and, as of Dec 2, 2021, 25 countries in total.^{8–10} Paradoxically, the most concerning SARS-CoV-2 variants for a highly vaccinated population would likely arise in a high transmission environment where there are high levels of vaccine coverage, such as the UK, France, or Italy, to name but a few.^{11,12}

New Zealand has comprehensively restricted COVID-19 numbers but only through its geographical



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