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.

7 Frampton D, Rampling T, Cross A, et al. Genomic characteristics and clinical effect of the emergent SARS-CoV-2 B.1.1.7 lineage in London, UK: a whole-genome sequencing and hospital-based cohort study. *Lancet Infect Dis* 2021; published online April 12. https://doi.org/10.1016/S1473-3099(21)00170-5.

8 Grint DJ, Wing K, Williamson E, et al. Case fatality risk of the SARS-CoV-2 variant of concern B.1.1.7 in England, 16 November to 5 February. *Euro Surveill* 2021; **26:** 2100256.

9 Challen R, Brooks-Pollock E, Read JM, Dyson L, Tsaneva-Atanasova K, Danon L. Risk of mortality in patients infected with SARS-CoV-2 variant of concern 202012/1: matched cohort study. *BMJ* 2021; **372:** n579.

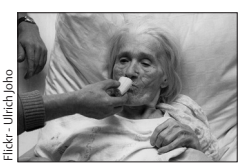
10 Sundaram ME, Calzavara A, Mishra S, et al. The individual and social determinants of COVID-19 diagnosis in Ontario, Canada: a population-wide study. *medRxiv* 2021; published online March 19. https://doi.org/10.1101/2020.11.09.20223792 (preprint).

11 Griffith GJ, Morris TT, Tudball MJ, et al. Collider bias undermines our understanding of COVID-19 disease risk and severity. *Nat Commun* 2020; **11:** 5749.

12 Davies NG, Jarvis CI, Edmunds WJ, et al. Increased mortality in community-tested cases of SARS-CoV-2 lineage B.1.1.7. *Nature* 2021; **593:** 270–74.

13 Rossman H, Meir T, Somer J, et al. Hospital load and increased COVID-19 related mortality in Israel. *Nat Commun* 2021; **12:** 1904.

Single-dose SARS-CoV-2 vaccination efficacy in the elderly



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The development of multiple successful vaccines against SARS-CoV-2 provided much-needed good news at the end of 2020. The first vaccines approved in the UK were the Pfizer–BioNTech BNT162b2 mRNA-based vaccine and the Oxford–AstraZeneca non-replicating adenoviral-vectored vaccine ChAdOx1 nCoV-19.[1,2] Responses to single-dose vaccine were not reported in published clinical trials; however, in December, 2020, the UK Joint Committee on Vaccination and Immunisation adopted the strategy of delaying second vaccination to 12 weeks to maximise the public health impact of first-dose vaccination.[3]

Older adults, and those with substantial comorbidity, were under-represented in vaccine trials, despite those who are frail or living in long-term care facilities having disproportionate morbidity and mortality from COVID-19. In *The Lancet Infectious Diseases*, two studies provide estimates of first-dose vaccine efficacy in older individuals and those living in long-term care facilities.[4,5]

Catherine Hyams and colleagues report a test-negative, case-control study of people aged at least 80 years who were admitted to two hospitals in Bristol, UK with acute respiratory symptoms between Dec 18, 2020, and Feb 26, 2021. All patients were tested for SARS-CoV-2 by PCR, and those with symptoms that started more than 10 days before hospital admission were excluded to avoid the inclusion of false-negative PCR results. This detailed study included individual patient information on comorbidities, frailty, and index of deprivation, and logistic regression analyses were done to address these potential confounders. The authors also did a week-by-week analysis to control for differing background rates of COVID-19. Estimated vaccine efficacy for symptomatic disease 14 days after one dose of vaccine was 71·4 % (95% CI 46·5–90·6) for BNT162b2 and 80·4% (36·4–94·5) for ChAdOx1 nCoV-19.

Madhumita Shrotri and colleagues report a large prospective cohort study of vaccine efficacy in 10 412 residents of long-term care facilities in England, all aged 65 years and older, using national testing data linked within the COVID-19 Datastore, including monthly asymptomatic screening, between Dec 8, 2020, and March 15, 2021. The cohort acted as their own controls, transitioning from the unvaccinated to vaccinated group until censoring at time of second vaccination dose, or last available PCR result. Analysis controlling for age, sex, local SARS-CoV-2 infection rates, and long-term care facility bed capacity, and previous SARS-CoV-2 infection estimated efficacy to be 56% (95% CI 19–76) at 28–34 days, and 62% (23–81) at 35–48 days post-vaccination. Sensitivity analysis, excluding participants never vaccinated despite its availability in their long-term care facility, increased the estimate of efficacy to 76% (95% CI 37–91%) at 35–48 days post-vaccination. This group had lower infection rates than the overall cohort, which the authors suggest might be due to a proportion receiving end-of-life care, leading to reduced interaction with other residents and staff, and thus decreased risk of exposure.

Benefit of vaccination with ChAdOx1 nCoV-19 was also seen at 0–6 days post-vaccination (efficacy 49% [95% CI 1–73]), albeit with a wide confidence interval. This effect is not a biologically plausible effect of vaccination, and a positive PCR test in this time period might indicate exposure before vaccination. Notably, the same effect was seen in a large Scottish data-linkage study of COVID-19 hospital admissions after vaccination, and in the SIREN study of UK health-care workers.[6,7] Shrotri and colleagues suggest that this

phenomenon might be due to deferral effects, whereby long-term care facilities with an active outbreak of COVID-19 delayed vaccination. A similar deferral effect might explain why an early effect of vaccination was seen in all three of these large population-based studies.

Another insight from the study by Shrotri and colleagues is that single-dose vaccination might affect the transmissibility of SARS-CoV-2. Comparison of mean PCR cycle threshold values showed a significantly higher value for positive PCR tests at least 28 days after vaccination (31·3 [SD 8·7]) than for those before vaccination (26·6 [6·6]; p<0·0001), indicating lower rates of viral shedding.

Although the authors of both studies[4,5] take care not to draw conclusions comparing the two vaccines, it might be tempting for the reader to do so. The results highlight some of the difficulties in trying to make such a comparison in real-world studies.

For example, the period of time covered by each vaccine differs because ChAdOx1 nCoV-19 was approved for use in the UK after BNT162b2, and both studies, therefore, control for background rates of infection. However, when Hyams and colleagues restricted their analysis to the same time period for both vaccines, the estimate of efficacy for BNTb162b increased to match that of ChAdOx1 nCoV-19. This finding suggests that other factors not controlled for in the overall analysis might affect COVID-19 risk. Both studies attempted to control for differences in the patient group receiving each vaccine. In the study by Shrotri and colleagues, each long-term care facility predominantly used one vaccine type and, in the Hyams study, patients receiving ChAdOx1 nCoV-19 were more likely to be frail or to be resident in a long-term care facility. However, it is probable that there are both patient and community characteristics not accounted for that modify COVID-19 risk.

These two studies report that the risk of symptomatic and asymptomatic disease substantially reduces after single-dose vaccination in groups at the highest risk of severe or fatal outcomes from COVID-19. The effect on symptomatic disease was seen from 14 days post-vaccination, and on asymptomatic disease from 28 days after vaccination. In both studies, the confidence intervals for estimates of vaccine efficacy are wide. However, these results provide reassurance that—in older adults (some of whom were frail and had many comorbidities)—both ChAdOx1 nCoV-19 and BNT162b2 provide protection from COVID-19 and, in cases of breakthrough infection, probably decrease the likelihood of viral transmission. Results from at least 42 days after vaccination will be interesting, given the UK strategy of delaying the second dose; however, these findings will be of less direct relevance for older adults in the UK given that more than 90% of people older than 65 years have now received two doses.[8] These two studies give cause for optimism; despite older individuals developing decreased humoural responses to vaccines, including SARS-CoV-2,[9,10] vaccine efficacy is high, and second doses will probably increase efficacy further. We await data on clinical vaccine efficacy in other vulnerable groups, including those at risk of vaccine hyporesponsiveness, such as those with organ transplants or receiving immunosuppression.

We declare no competing interests.

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1 Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet* 2021; **397:** 99–111.

2 Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020; **383:** 2603–15.

3 Department of Health and Social Care. Optimising the COVID-19 vaccination programme for maximum short-term impact. Jan 26, 2021. https://www.gov.uk/government/publications/prioritising-the-first-covid-19-vaccine-dose-jcvi-statement/optimising-the-covid-19-vaccination-programme-for-maximum-short-term-impact (accessed June 8, 2021).

4 Hyams C, Marlow R, Maseko Z, et al. Effectiveness of BNT162b2 and 1 ChAdOx1n CoV-19 COVID19 vaccination at preventing hospitalisations in people aged at least 80 years: a test-negative, case-control study. *Lancet Infect Dis* 2021; published online June 23. https://doi.org/10.1016/S1473-3099(21)00330-3.

5 Shrotri M, Krutikov M, Palmer T, et al. Vaccine effectiveness of the first dose of ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of long-term care facilities in England (VIVALDI): a prospective cohort study. *Lancet Infect Dis* 2021; published online June 23. https://doi.org/10.1016/S1473-3099(21)00289-9.

6 Hall VJ, Foulkes S, Saei A, et al. COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study. *Lancet* 2021; **397:** 1725–35.

7 Vasileiou E, Simpson CR, Shi T, et al. Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study. *Lancet* 2021; **397:** 1646–57.

8 NHS England. COVID-19 weekly announced vaccinations 03 June 2021. June, 2021. https://www.england.nhs.uk/statistics/wp-content/uploads/sites/2/2021/06/COVID-19-weekly-announced-vaccinations-03-June-2021.xlsx (accessed June 8, 2021).

9 Djennad A, Ramsay ME, Pebody R, et al. Effectiveness of 23-valent polysaccharide pneumococcal vaccine and changes in invasive pneumococcal disease incidence from 2000 to 2017 in those aged 65 and over in England and Wales. *EClinicalMedicine* 2018; **6:** 42–50.

10 Abu Jabal K, Ben-Amram H, Beiruti K, et al. Impact of age, ethnicity, sex and prior infection status on immunogenicity following a single dose of the BNT162b2 mRNA COVID-19 vaccine: real-world evidence from healthcare workers, Israel, December 2020 to January 2021. *Euro Surveill* 2021; **26:** 2100096.