CORRESPONDENCE

BNT162b2 and ChAdOx1 nCoV-19 Vaccine Effectiveness against Death from the Delta Variant

TO THE EDITOR: We recently reported vaccine effectiveness for the BNT162b2 vaccine (Pfizer–BioNTech) and the ChAdOx1 nCoV-19 vaccine (AstraZeneca) against infection and hospitalization caused by the B.1.617.2 (delta) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Scotland.[1] At that time, the number of deaths was too small to allow estimation of vaccine effectiveness against death from infection with the delta variant.

We used a Scotland-wide surveillance platform (Early Pandemic Evaluation and Enhanced Surveillance of COVID-19 [EAVE II]) that includes individual-level linked data on vaccination, testing, viral sequencing, primary care, hospital admissions, and mortality among 5.4 million people (approximately 99% of the Scottish population).[2,3] We conducted a cohort study and used Cox regression to estimate vaccine effectiveness against death from delta variant infection from April 1 to August 16, 2021, among adults 18 years of age or older, who were followed up to September 27, 2021.[3] Our methods and findings are summarized below, with additional details provided in the Supplementary Appendix, available with the full text of this letter at NEJM.org. The EAVE II protocol is also available at NEJM.org.

At the date of swab testing, persons were defined as being unvaccinated or vaccinated with either one or two vaccine doses.[4] Cases of SARS-CoV-2 infection were defined by a positive result on reverse-transcriptase–polymerase-chain-reaction (RT-PCR) testing. Testing was performed with the TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific). True *S* gene "dropout" (indicating the presence of an *S* gene mutation not found in the delta variant) was defined as a negative result for the *S* gene and cycle threshold (Ct) values of less than 30 for the *OR* and *N* genes. Positivity for the *S* gene was defined as Ct values of less than 30 for the *S* gene and valid Ct values for the *OR* and *N* genes.[1] Death from coronavirus disease 2019 (Covid-19) was defined as a death for which Covid-19 was recorded on the death certificate or death that occurred within 28 days after a positive RT-PCR test.[1,4]

Hazard ratios were adjusted for age, sex, socioeconomic status, and number of relevant coexisting conditions.[5] Vaccine effectiveness was estimated as 1 minus the hazard ratio.

A total of 1,563,818 adults underwent testing in the community. Our mortality analysis was based on 114,706 adults who tested positive for SARS-CoV-2. Sequencing data showed that 99.5% of *S*-positive infections were caused by the delta variant and that 98.8% of delta variant infections were *S*-positive (Fig. S1 and Table S1 in the Supplementary Appendix). Among adults who tested positive, those who were unvaccinated tended to be much younger, to have fewer coexisting conditions, and to have a lower socioeconomic status and were more likely to be men than those who were vaccinated; these differences tended to be especially pronounced in comparison with those who received the ChAdOx1 nCoV-19 vaccine (Table S2).

Overall, 201 deaths from Covid-19 were caused by SARS-CoV-2 that had been tested and found to be *S*-positive or *S*-negative (Table 1). Among persons 18 to 39 years of age who had infections for which data on *S* gene status were available, no deaths occurred among those who were fully vaccinated, as compared with 17 deaths among those who were unvaccinated. Among those who were 40 to 59 years of age, vaccine effectiveness against death from Covid-19 was 88% (95% confidence interval [CI], 76 to 93) for ChAdOx1 nCoV-19 and 95% (95% CI, 79 to 99) for BNT162b2; vaccine effectiveness was 90% (95% CI, 84 to 94) and 87% (95% CI, 77 to 93), respectively, among those 60 years of age or older. Overall, vaccine effectiveness against death from the delta variant 14 or more days after the second vaccine dose was 90% (95% CI, 83 to 94) for BNT162b2 and 91% (95% CI, 86 to 94) for ChAdOx1 nCoV-19 (Table S3).

Table 1. Vaccine Effectiveness in Preventing Death from Covid-19, Stratified According to Age Group, Vaccination Status, and Vaccine (All Community Cases from April 1 to August 16, 2021, with Follow-up Conducted until September 27, 2021).*

Age Group, Vaccination Status, and Vaccine	Person-Years of Follow-up	No. of Persons	No. of Deaths	Rate per 100 Person-Years	Adjusted Hazard Ratio (95% CI)†
18 to 39 Years of Age					
Unvaccinated	8669.5	35,449	17	0.20	—
One vaccine dose 0–27 days before test					
ChAdOx1 nCoV-19	56.6	150	0	0.00	—
BNT162b2	2338.4	10,535	1	0.04	—
One vaccine dose ≥28 days before test or two doses with second dose 0–13 days before test					
ChAdOx1 nCoV-19	463.0	1,793	0	0.00	—
BNT162b2	1706.3	10,167	1	0.06	—
Two vaccine doses with second dose ≥14 days before test					
ChAdOx1 nCoV-19	767.7	4,140	0	0.00	—
BNT162b2	567.3	3,040	0	0.00	—
40 to 59 Years of Age					
Unvaccinated	1230.3	4,803	33	2.68	Reference
One vaccine dose 0–27 days before test					
ChAdOx1 nCoV-19	453.8	1,497	2	0.44	0.24 (0.06–1.01)
BNT162b2	86.9	286	0	0.00	0.00 (0.00–∞)
One vaccine dose ≥28 days before test or two doses with second dose 0–13 days before test					
ChAdOx1 nCoV-19	1865.2	7,945	2	0.11	0.04 (0.01–0.15)
BNT162b2	477.9	2,022	0	0.00	0.00 (0.00–∞)
Two vaccine doses with second dose ≥14 days before test					
ChAdOx1 nCoV-19	1707.4	9,587	16	0.94	0.12 (0.07–0.24)
BNT162b2	629.8	3,318	2	0.32	0.05 (0.01–0.21)
≥60 Years of Age					
Unvaccinated	81.4	380	24	29.49	Reference
One vaccine dose 0–27 days before test					
ChAdOx1 nCoV-19	19.1	46	0	0.00	0.00 (0.00–∞)
BNT162b2	0.2	1	0	0.00	0.00 (0.00–∞)
One vaccine dose ≥28 days before test or two doses with second dose 0–13 days before test					
ChAdOx1 nCoV-19	213.9	692	2	0.93	0.03 (0.01–0.14)
BNT162b2	69.8	190	4	5.73	0.25 (0.09–0.74)
Two vaccine doses with second dose ≥14 days before test					
ChAdOx1 nCoV-19	973.8	5,262	73	7.50	0.10 (0.06–0.16)
BNT162b2	351.0	1,952	24	6.84	0.13 (0.07–0.23)

* Vaccine effectiveness was estimated as 1 minus the hazard ratio. Some adults had received the mRNA-1273 vaccine (Moderna) at the time of their positive test (4135 persons, contributing 379 person-years of follow-up). No deaths from coronavirus disease 2019 (Covid-19) occurred among the persons who received the mRNA-1273 vaccine, and estimates and numbers are not provided in the table.

† Hazard ratios are not provided for the 16-to-39-year age group because only two deaths occurred among vaccinated persons in this group and no deaths occurred among those who were fully vaccinated (i.e., those who had received two doses with the second dose received ≥14 days before testing).

A limitation of this study is the fact that it was based on an analysis of community samples. In addition, 1.8% of samples did not yield *S* gene categorization because of missing data in the Ct fields.

In summary, we found that the BNT162b2 and ChAdOx1 nCoV-19 vaccines offered substantial protection against death from Covid-19 caused by the delta variant.

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The data used to undertake this analysis are not publicly available because they are based on deidentified national clinical records. These data are available, subject to approval by the NHS Scotland Public Benefit and Privacy Panel, by application through the Scotland National Safe Haven. The R code used to perform this analysis is available from https://github.com/EAVE-II.

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