Supplementary appendix

Effectiveness of COVID-19 vaccines against hospital admission with the Delta (B.1.617.2) variant.

Methods

Data sources

COVID-19 testing and variant identification

COVID-19 PCR testing in the UK is undertaken through hospital and public health laboratories, as well as community testing through drive through or home testing which is available to anyone with symptoms consistent with COVID-19 (high temperature, new continuous cough, loss or change in sense of smell or taste). Individuals reporting symptoms and testing positive on PCR between 12th April and 4th June 2021 were included in the analysis. Variants were identified as Delta (B.1.617.2) through sequencing or if they were S-gene target positive on the TaqPath PCR assay. Cases were identified as Alpha (B.1.1.7)on sequencing or if they were S-gene target negative on the TaqPath PCR assay. Children aged under 16 years as of March 21st 2021 were excluded as were any subsequent positive tests in the same individual within any 90 day period. Samples were dropped from the analysis if they were repeats of the same variant within the same individual, if different variants were detected in the same individual within a 14 day period. Data were restricted to individuals reporting symptoms and only individuals tested within 10 days of symptom onset were included to account for reduced sensitivity of PCR testing beyond this period. National Health Service (NHS) number, date of birth, surname, first name, postcode and specimen identifiers and sample dates were used to link this testing data to the vaccine data.

Vaccination status

COVID-19 vaccine information such as date of each dose of vaccine and the vaccine type are captured and recorded on the National Immunisation Management System (NIMS) in England. Data were extracted on the 6th June 2021 with vaccinations up to the 5th June 2021 and were linked to the testing data. If the individual had received a mixed vaccination schedule (with two different vaccines) or had received two doses less than 19 days apart they were excluded from the analysis. Vaccination status was according to vaccination at date of test and assigned as unvaccinated, 0-20 days after dose one, 21 days after dose one to 13 days after dose two (if given), and from 14 days after dose 2.

Hospital admission records

Emergency Care attendances which were not injury related and resulted in an inpatient admission were identified from the Emergency Care Data Set (ECDS) on the 9th June 2021 and linked to the positive symptomatic testing data using NHS number and date of birth if the ECDS attendance was within 14 days of the positive test date. ECDS data includes hospital admissions through NHS emergency departments in England but not elective admissions. Only first attendances in the period were selected if a person had more than one admission from Emergency Care. To allow for delays in the ECDS data flow, data were censored at 3rd June 2021.

Statistical analysis

In order to estimate the effect of vaccination on hospitalisation within the following 14 days from the date of sample cox proportional hazards survival modelling was done. This was done separately

on the Alpha and Delta variant cases. When fitting the survival model confounding variables considered were age (10 year intervals), whether the person is clinically extremely vulnerable (CEV), ethnicity, test week, sex, region, care home resident, health and social care worker, index of multiple deprivation and recent travel. Only those factors that changed the estimate for the hazard ratio in the 21 days period after the first dose by more than 3% for either Delta or Alpha were included in the final model. Proportions hospitalised were described split by age below and above 50.

The analysis was done both irrespective of vaccine manufacturer and by manufacturer. Note that individuals who received the Moderna vaccine were dropped from all analyses as this was a very small number.

Odds ratios (OR) for symptomatic disease from a test negative case control analysis (1) were then combined with the hazard ratios (HR) for hospitalisation among symptomatic cases to estimate vaccine effectiveness against hospitalisation as $VE = 1 - (OR_{\text{symptomatic disease}} \times HR_{\text{hospitalisation}})$.

Results

A total of 27,211 positive tests among individuals reporting symptoms were identified in the study period 12th April to the 4th June 2021. There were 160 (55.56%) admission in males and 128 in females. The highest proportion of the admissions were in the in the 70 to 79 age group for the Alpha variant (5/146) and 80 years and over for the Delta variant, (6.25% (3/48)) (Supplementary table 1).

Supplementary table 2 shows numbers and proportions hospitalised by age and vaccination status. These crude numbers should be interpreted with caution because they include cases with sample dates in recent weeks where follow-up is not complete and because there is strong residual confounding by age. They generally show lower hospitalisation rates in the vaccinated groups, but some groups have small numbers.

In the adjusted Cox model the largest confounding factor was age, with additional minor potential confounding from CEV status, ethnicity and test week which were also included in the model.

In those vaccinated 21 days after dose 1 the HR was 0.37 (95% CI 0.22-0.63) with the Delta variant and 0.44 (95% CI 0.28-0.70) with the Alpha variant, demonstrating additional protection against hospitalisation within symptomatic cases of 63% and 56% respectively. In the period 14 days after dose 2 the HR was 0.29 (95% CI 0.11-0.72) with the Delta variant and 0.64 (95% CI 0.24-1.72), demonstrating additional protection by vaccination of 71% and 36% respectively (Supplementary table 3).

In the Cox model by vaccine type in those vaccinated with Pfizer 21 days after dose 1 the HR was 0.10 (95% CI 0.01-0.76) with the Delta variant and 0.32 (95% CI 0.14-0.73) (Supplementary table 5). In the period 14 days after dose 2 the HR was 0.34 (95% CI 0.10-1.18) with the Delta variant and 0.88 (95% CI 0.21-3.77) (Supplementary table 3). For the AZ 21 days after dose 1 the HR was 0.41 (95% CI 0.24-0.70) with the Delta variant and 0.48 (95% CI 0.30-0.77). In the period 14 days after dose 2 the HR was 0.25 (95% CI 0.08-0.78) with the Delta variant and 0.53 (95% CI 0.15-1.80) (Supplementary table 4).

Supplementary table 1: Distribution by age group of the cases which were included in the analysis

	Delta			Alpha		
	Admitted (n)	Denom (N)	%	Admitted (n)	Denom (N)	%
16-29	16	5,913	0.27%	25	4,776	0.52%
30-39	33	3,636	0.91%	42	3,675	1.14%
40-49	28	2,342	1.20%	47	2,650	1.77%
50-59	22	1,509	1.46%	30	1,363	2.20%
60-69	16	459	3.49%	17	554	3.07%
70-79	4	112	3.57%	5	146	3.42%
80+	3	48	6.25%	0	28	0.00%
Total	122	14,019	0.87%	166	13,192	1.26%

Supplementary table 2: Counts and percentage of hospital admissions in people testing positive aged 16 to 49 and 50 years and over by variant and vaccination status

Delta								
	16 to 49				**50 and over**			
	Not admitted	Admitted	Total	%	Not admitted	Admitted	Total	%
Unvaccinated	7,892	57	7949	0.72%	202	12	214	5.61%
Dose 1: 0-20 days	1,416	9	1425	0.63%	30	0	30	0.00%
Dose 1: 21 days plus	2,070	8	2078	0.38%	1,383	25	1408	1.78%
Dose 2: 14 days Plus	436	3	439	0.68%	468	8	476	1.68%
Overall Dose1: 21+	2,506	11	2,517	0.44%	1,851	33	1884	1.75%
Alpha								
	16 to 49				**50 and over**			
	Not admitted	Admitted	Total	%	Not admitted	Admitted	Total	%
Unvaccinated	8,679	82	8761	0.94%	338	20	358	5.59%
Dose 1: 0-20 days	649	15	664	2.26%	102	2	104	1.92%
Dose 1: 21 days plus	1,542	15	1557	0.96%	1,502	26	1528	1.70%
Dose 2: 14 days Plus	117	2	119	1.68%	97	4	101	3.96%
Overall Dose1: 21+	1,659	17	1676	1.01%	1,599	30	1629	1.84%

Supplementary table 3: Hazard Ratios for the risk of being admitted to hospital in unvaccinated compared to vaccinated with any vaccine by variant.

	Delta		Alpha	
	HR*	**95% CI**	**HR***	**95% CI**
Unvaccinated	baseline		baseline	
Dose 1: 0-20 days	0.61	0.30-1.26	1.07	0.59-1.91
Dose 1: 21 days plus	0.37	0.22-0.63	0.44	0.28-0.70
Dose 2: 14 days Plus	0.29	0.11-0.72	0.64	0.24-1.72
Overall Dose1: 21+	0.36	0.22-0.60	0.46	0.29-0.71

* adjusted for age, CEV, ethnicity and test week

Supplementary table 4: Hazard Ratios for admission to hospital in vaccinated compared to unvaccinated by variant and manufacturer.

Delta				Alpha		
		HR*	**95% CI**		**HR***	**95% CI**
Unvaccinated		baseline		Unvaccinated		baseline
Pfizer	Dose 1: 0-20 days	0.54	0.19-1.49	Dose 1: 0-20 days	0.63	0.09-4.67
	Dose 1: 21 days plus	0.10	0.01-0.76	Dose 1: 21 days plus	0.32	0.14-0.73
	Dose 2: 14 days Plus	0.34	0.10-1.18	Dose 2: 14 days Plus	0.88	0.21-3.77
AZ	Dose 1: 0-20 days	0.71	0.27-1.85	Dose 1: 0-20 days	1.14	0.62-2.09
	Dose 1: 21 days plus	0.41	0.24-0.70	Dose 1: 21 days plus	0.48	0.30-0.77
	Dose 2: 14 days Plus	0.25	0.08-0.78	Dose 2: 14 days Plus	0.53	0.15-1.80

* adjusted for age, CEV, ethnicity and test week