Effectiveness of COVID-19 vaccines against the Omicron (B.1.1.529) variant of concern

Nick Andrews PhD[1,2], Julia Stowe PhD[1], Freja Kirsebom PhD[1], Samuel Toffa PhD[1], Tim Rickeard[1], Eileen Gallagher PhD[1], Charlotte Gower DPhil[1], Meaghan Kall[1], Natalie Groves MSc[1], Anne-Marie O'Connell[1], David Simons[1], Paula B. Blomquist[1], Gavin Dabrera MBBS, FFPH[1], Richard Myers[1], Shamez N Ladhani PhD, MRCPCH[1,3], Gayatri Amirthalingam MFPH[1,2], Saheer Gharbia[1], Jeffrey C. Barrett D Phil[4], Richard Elson[1], Neil Ferguson[5,6], Maria Zambon PhD, FRCPath[1,6], Colin NJ Campbell MPH, FFPH[1,2], Kevin Brown MRCP FRCPath[1,2], Susan Hopkins FRCP, FFPH[1,7], Meera Chand MRCP, FRCPath[1,8], Mary Ramsay MBBS, FFPH[1,2], Jamie Lopez Bernal PhD ,MBBS [1,2,6]

1. UK Health Security Agency (UKHSA), London, United Kingdom
2. NIHR Health Protection Research Unit in Vaccines and Immunisation, London School of Hygiene and Tropical Medicine, London, United Kingdom
3. Paediatric Infectious Diseases Research Group (PIDRG), St George's University of London, London, United Kingdom
4. Wellcome Sanger Institute, Hinxton, UK
5. MRC Centre for Global Infectious Disease Analysis, Imperial College London, London, UK.
6. NIHR Health Protection Research Unit in Respiratory Infections, Imperial College London, United Kingdom
7. Healthcare Associated Infections and Antimicrobial Resistance, University of Oxford, Oxford, UK
8. Guys and St Thomas's Hospital NHS Trust, London, UK

Introduction

On 26 November 2021 the World Health Organization (WHO) Technical Advisory Group on SARS-CoV-2 Virus Evolution named the B.1.1.529 COVID-19 variant, first detected in Botswana and South Africa, as the Omicron variant of concern (1). This classification was based on a rapid increase in cases in South Africa, coinciding with an increase in detections of Omicron, a number of concerning mutations and early evidence suggesting an increased risk of reinfections.

A large number of mutations have been identified in the Omicron variant, including multiple mutations to the receptor binding domain of the spike protein which have been associated with reduced antibody response (2). Emerging laboratory data indicate a reduced neutralising antibody response to Omicron compared to the original COVID-19 virus or the Delta variant in vaccinated individuals, though booster doses increased the antibody titres (3, 4). Neutralising antibody has been found to correlate with protection against reinfection and vaccine effectiveness against infection, therefore reduced vaccine effectiveness against Omicron is anticipated based on the early laboratory findings (5, 6, 7).

COVID-19 vaccines have been found to be highly effective against symptomatic disease and, more so, against severe disease outcomes with the original COVID-19 virus as well as the Alpha variant that predominated in early 2021 (8-14). Modest reductions in vaccine effectiveness against infection and mild disease have been seen with the Beta variant and the Delta variant, though effectiveness against severe disease has remained high (15-18). Waning of protection several months after a primary course has been observed with the Delta variant, however, booster doses lead to a significant increase in protection against both mild and severe disease outcomes (18-23).

Omicron cases identified through whole genome sequencing first began to be detected in the UK in specimens from mid-November 2021. Initially cases occurred primarily in travellers and their close contacts but there was evidence of community transmission from late November (24). The UK COVID-19 vaccination programme has been in place since December 2020 with primary courses of 2 doses of either BNT162b2 (Pfizer-BioNTech, Comirnaty®), ChAdOx1-S (Vaxzevria, AstraZeneca) or mRNA-1273 (Spikevax, Moderna). Coverage with 2 doses is over 60% in all cohorts over 20 years and over 80% in all cohorts over 50 years and vaccinations are now also being offered to children over the age of 12 years (25). Booster vaccination with either BNT162b2 or a half dose (50µg) of mRNA-1273 was introduced in September 2021 to adults over 50 years and those in risk groups, and later expanded to all adults. Initially boosters were offered 6 months after completion of the primary course. With the emergence of the Omicron variant, this interval was reduced to 3 months.

In this study we estimate vaccine effectiveness against symptomatic disease with 2 dose courses of BNT1622 and ChAdOx1-S as well as booster doses of BNT162b2 following a primary course of either BNT1622 or ChAdOx1-S.

Methods

Study design

A test negative case control design was used to estimate vaccine effectiveness against symptomatic COVID-19 with the Omicron variant compared to the Delta variant. The odds of vaccination in PCR positive cases is compared to the odds of vaccination in those who test negative.

Data sources

COVID-19 testing data

SARS-CoV-2 Testing Polymerase-chain-reaction (PCR) testing for SARS CoV-2 in the United Kingdom is undertaken by hospital and public health laboratories, as well as by community testing with the use of drive through or at-home testing, which is available to anyone with symptoms consistent with COVID-19 (high temperature, new continuous cough, or loss or change in sense of smell or taste), is a contact of a confirmed case, for care home staff and residents or who have self-tested as positive using a lateral flow device. Regular COVID-19 lateral flow testing (LFT) is available to all members of the population. Data on all positive PCR and LFT tests, and on negative Pillar 2 PCR tests from symptomatic individuals with an onset date after 16 October 2020 were extracted up to 6 December 2021. Individuals who reported symptoms and were tested in Pillar 2 (community testing) between 27 November and 3 December 2021 were included in the analysis. Any negative tests taken within 7 days of a previous negative test, or where symptoms were recorded, with symptoms within 10 days of symptoms for a previous negative test were dropped as these likely represent the same episode. Negative tests taken within 21 days before a positive test were also excluded as there is a high chance of these being false negatives. Positive and negative tests within 90 days of a previous positive test were also excluded, however where participants had later positive tests within 7 days of a positive then preference was given to PCR tests, symptomatic tests and tests with sequencing or S-gene testing done. Data were restricted to persons who had reported symptoms and gave an onset date within the 10 days prior to testing to account for reduced PCR sensitivity beyond this period in an infection event. Data from cases who had reported recent travel were excluded due to differences in exposure risk and possible misclassification of vaccination status. Only samples tested in one of the community testing laboratories using the TaqPath assay were included in the final analysis, and only positive cases with S-gene test or sequencing results available were included. A small number of positive tests were excluded where sequencing found them to be neither the Delta nor Omicron variant. Finally, only samples taken from 27 November were retained

for analysis as this corresponded to the period when S-gene negative status was predictive of being the Omicron variant.

Vaccination data

The National Immunisation Management System (NIMS) (26) contains demographic information on the whole population of England who are registered with a GP in England and is used to record all COVID-19 vaccinations. These data were accessed on 9 December 2021. The information used from NIMS was dates of vaccination and manufacturer (27). Demographic data such as sex, date of birth, ethnicity, and residential address were extracted. Addresses were used to determine index of multiple deprivation quintile and were also linked to Care Quality Commission registered care homes using the unique property reference number. Data on geography (NHS region), risk group status, clinically extremely vulnerable status, and health/social care worker were also extracted from the NIMS. Booster doses were identified as being a third dose 140 days or more after a second dose and given after 13 September 2021. Individuals with 4 or more doses of vaccine, a mix of vaccines in their primary schedule or less than 19 days between their first and second dose were excluded.

Identification of Delta and Omicron variants and assignment to cases

Sequencing is undertaken at a network of laboratories, including the Wellcome Sanger Institute, and whole-genome sequences are assigned to UKHSA definitions of variants based on mutations. Spike gene (S-gene) target status on PCR is a second approach for identifying each variant as the Omicron variant has been associated with a negative S-gene target (S-gene target failure, SGTF) result on PCR testing with the Taqpath assay whereas with the Delta variant the S-gene target is almost always positive (24).

Approximately 40% of Pillar 2 Community testing in the UK is carried out by laboratories using the TaqPath assay (Thermo Fisher Scientific). Cases were defined as the Delta or Omicron variant based on whole genome sequencing or S-gene target status, with sequencing taking priority.

Testing data were linked to NIMS on 9 December 2021 using combinations of National Health Service number (a unique identifier for each person receiving medical care in the United Kingdom), date of birth, surname, first name, and postcode using deterministic linkage with 92.2% uniqueness.

Statistical analysis

Analysis was by logistic regression with the PCR test result as the dependent variable where cases are those testing positive (stratified in separate analyses as either Omicron or Delta) and controls are those testing negative. Vaccination status was included as an independent variable and effectiveness defined as 1- odds of vaccination in cases/odds of vaccination in controls.

Vaccine effectiveness was adjusted in logistic regression models for age (5 year bands up to age 60, then everyone age 60+), sex, index of multiple deprivation (quintile), ethnic group, geographic region (NHS region), period (day of test), health and social care worker status, clinical risk group status, clinically extremely vulnerable, and previously testing positive. These factors were all considered potential confounders so were included in all models.

Analyses were stratified by which primary doses had been received (ChAdOx1-S or BNT162b2). Any mixed primary courses were excluded. Vaccine effectiveness was assessed for each primary course in intervals of 2-9, 10-14, 15-19, 20-24 and 25+ weeks post dose 2. Vaccine effectiveness was also assessed for both primary courses followed by a BNT162b2 booster for the period 1 week and at least 2 weeks post vaccination. Comparison was to unvaccinated individuals to estimate the absolute effectiveness of vaccination against Omicron and Delta variants.

Numbers were too small to estimate vaccine effectiveness with mRNA-1273 as either a primary course or a booster.

Results

A priori, we considered that S-gene target failure (SGTF) would be used to define the Omicron variant when Omicron accounts for at least 80% of S-gene target failure cases. Within sequenced cases from Pillar 2 testing where S-gene testing was done the proportion of S-gene negative tests that were sequenced as Omicron was 6/12 (50%) on 25 November, 13/20 (65%) on 26 November, 18/20 (90%) on 27 November, 10/11 (91%) on 28 November and 17/19 (89%) on 29 November. We therefore used cases tested from 27 November where the positive predictive value was above 80%. Sequencing or S-gene target status were both used to identify Omicron and Delta cases, with the sequencing result taking priority.

There were 581 symptomatic Omicron cases which were identified during the study period by sequencing or SGTF and linked to NIMS for vaccination status. Over the same period there were 56,439 eligible Delta cases and 130,867 test negative controls. A description of the eligible tests is given in Table 1.

Vaccine effectiveness against symptomatic disease by period after dose 2 and the booster dose is shown in Figure 1 and Table 2 for those who received a primary course of the ChAdOx1 or BNT162b2 vaccines. For both primary courses, the booster dose given was BNT162b2. Apart from 2-9 weeks post dose 2 for BNT162b2, effectiveness was lower for Omicron compared to Delta post vaccination at all time interval investigated. Among those who had received 2 doses of ChAdOx1, there was no protective effect of vaccination against symptomatic disease with Omicron from 15 weeks after the second dose. Among those who had received 2 doses of BNT162b2, vaccine effectiveness was 88.0% (95%CI:

65.9 to 95.8%) 2-9 weeks after dose 2, dropping to 48.5% (95%CI: 24.3 to 65.0%) at 10-14 weeks post dose 2 and dropping further to between 34 and 37% from 15 weeks post dose 2. Among those who received ChAdOx1 as the primary course, from 2 weeks after a BNT162b2 booster dose, vaccine effectiveness increased to 71.4% (95%CI: 41.8 to 86.0%). Vaccine effectiveness increased to 75.5% (95%CI: 56.1 to 86.3%) after the booster among those who had received BNT162b2 as the primary course.

With the Delta variant, effectiveness drops from 76.2% (95%CI: 63.7 to 84.4%) 2-9 weeks after dose 2 down to 41.8% (95%CI: 39.4-44.1%) at 25+ weeks after dose 2 with a ChAdOx1 primary course. Effectiveness increases to 93.8% (95%CI: 93.2-94.3%) 2 weeks after a BNT162b2 booster. With a BNT162b2 primary course, effectiveness drops from 88.2% (95%CI: 86.7 to 89.5%) 2-9 weeks after dose 2 down to 63.5% (95%CI: 61.4 to 65.5%) 25+ weeks after dose 2, increasing to 92.6% (95%CI: 92.0-93.1%) 2 weeks after the booster.

All of the Omicron estimates are subject to significant uncertainty with wide confidence intervals.

Discussion

Our findings show that vaccine effectiveness against symptomatic disease with the Omicron variant is significantly lower than with the Delta variant. We are unable to determine protection against severe forms of disease due to the small number of Omicron cases so far and the natural lag between infection and more severe outcomes. Previous UK experience with the Delta variant suggested that protection against hospitalisation after 2 doses of vaccine was relatively well maintained (18). Despite the low effectiveness in the longer intervals after primary vaccination shown here, moderate to high vaccine effectiveness against mild infection of 70-75% was seen in the early period after a booster dose of BNT162b2 following either ChAdOx1-S or BNT162b2 as a primary course.

These findings are consistent with preliminary neutralisation data for the Omicron variant. The South African and German studies, as well as unpublished data from the UK indicate a 20 to 40 fold reduction in neutralising activity in sera from 2 dose BNT162b2 vaccine recipients compared to early pandemic viruses and at least a 10 fold reduction compared to the Delta variant (3, 4, 28). In sera from recipients of 2 doses of ChAdOx1, a greater reduction was seen with a high proportion of sera with neutralising activity below the limit of quantification in the assay (28). Higher neutralising activity was seen after a booster dose (3, 4, 28).

The correlation between neutralising antibody and protection against severe disease is much less certain. With previous variants, vaccine effectiveness against severe disease, including hospitalisation and death, has been higher than effectiveness against mild disease (15, 18). It will be some time before effectiveness against severe disease with

Omicron can be estimated but, based on experience with other variants, this is likely to be substantially higher than the estimates against symptomatic disease.

It is important to note that there are differences in the populations that have received different vaccines as a primary course. For example, ChAdOx1 was the main vaccine used early in the programme in care homes and among those in clinical risk groups. Furthermore, mRNA vaccines were the main vaccines used in under 40 year olds following the association between ChAdOx1 and vaccine induced thrombotic thrombocytopenia (29). While adjustments were made for age and clinical risk factors, this may explain some of the differences in the findings for the primary course – for example the high vaccine effectiveness against Omicron 2-9 weeks after the second dose of BNT162b2 is likely to be primarily among recently vaccinated young adults and teenagers. The early observations for two doses of AstraZeneca are particularly likely to be unreliable as they are based on relatively small numbers and are likely to reflect an older population and a population with more co-morbidities than those given the Pfizer vaccine - this may explain the negative point estimates. There will also be differences in populations that have received a booster dose compared to those who have only received 2 doses, with the former skewed towards older populations with more comorbidities. Those that have not yet received a booster could have done for reasons that may be associated with exposure risk, for example, booster vaccination may have been delayed due to an outbreak in a closed setting.

The large scale of testing and sequencing in the UK, as well as the use of a national vaccination register has enabled rapid evaluation of vaccine effectiveness against symptomatic infection with the Omicron variant. Nevertheless, there are a number of limitations to this study and findings should be interpreted with caution. During this early period of circulation of the new variant, a large proportion of cases have occurred among travellers. Individuals who reported travel in the preceding 2 weeks were excluded from this analysis, however, this may not exclude all travellers and will not exclude contacts of travellers. This group is likely to have different exposure to the wider population and may also have different levels of vaccine coverage, therefore residual confounding may be present. Due to the relatively small number of cases of Omicron in the UK to date, there is significant uncertainty to our estimates and we are unable to break down estimates by population characteristics by which vaccine effectiveness has been shown to vary previously (such as age and clinical risk group) (18). In this analysis, our comparator group is unvaccinated individuals, who comprise a very small proportion of individuals in several age cohorts. These people are likely to differ from the general population according to characteristics that could confound our vaccine effectiveness estimates. In this analysis that covers all ages, this may be less of an issue than in analyses restricted to elderly populations. Furthermore, recent analyses using different control groups have found good concordance when using an unvaccinated control compared to relative vaccine effectiveness between those who have received a booster dose and those who have received 2 doses. Booster doses have only recently been rolled out in England, therefore

we are only able to estimate vaccine effectiveness for a short period after booster vaccination and we do not have information on the duration of protection following a booster dose. There may also be misclassification in our study due to both imperfect sensitivity and specificity of PCR testing, as well as the use of SGTF to identify Omicron cases.

Our findings indicate that 2 doses of vaccination with BNT162b2 or ChAdOx1 are insufficient to give adequate levels of protection against infection and mild disease with the Omicron variant, although we cannot comment on protection against severe disease. Booster doses of BNT162b2 provide a significant increase in protection against mild disease and are likely to offer even greater levels of protection against severe disease. As such our findings support maximising coverage with third doses of vaccine in highly vaccinated populations such as the UK. Further follow-up will be needed to assess the duration of protection of booster vaccination.

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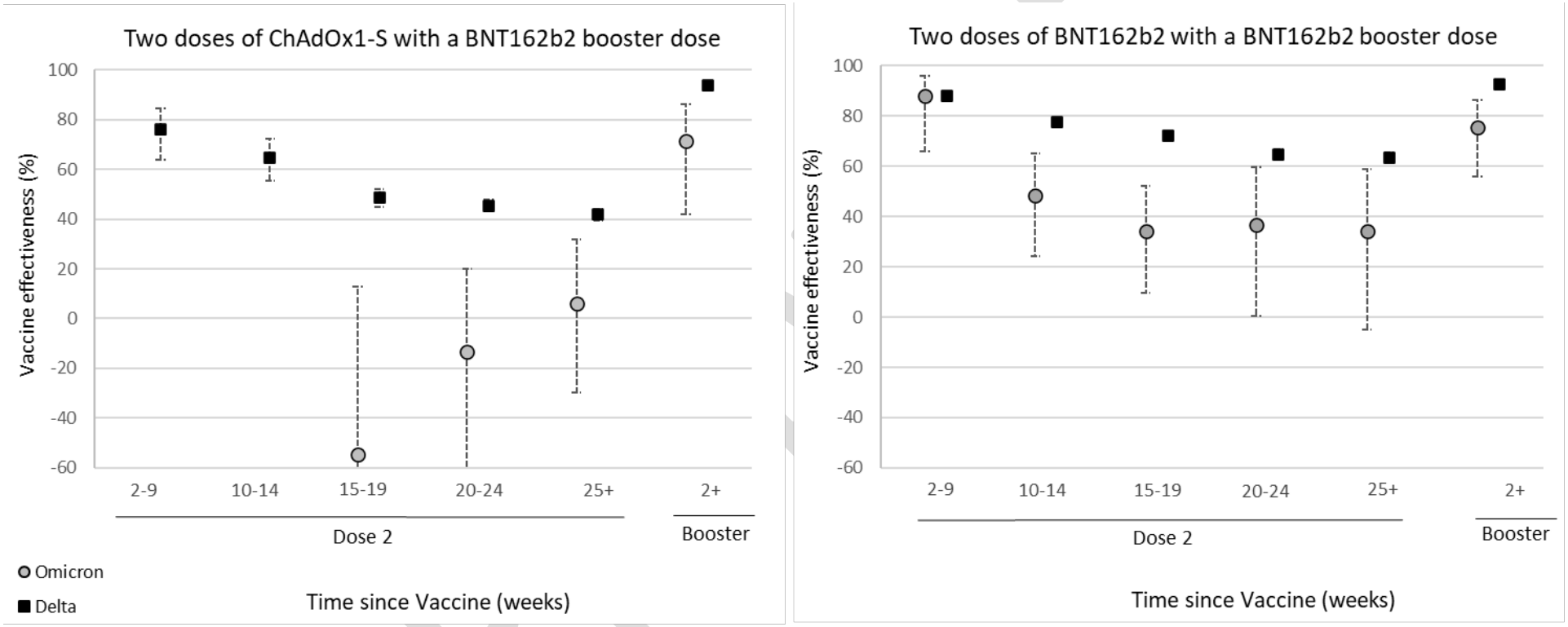
Figure 1: Vaccine effectiveness against symptomatic diseases by period after dose 1 and dose 2 for Delta (black squares) and Omicron (grey circles) for (A) recipients of 2 doses of Astrazeneca vaccine as the primary course and a Pfizer as a booster and (B) recipients of 2 doses of Pfizer vaccine as the primary course and a Pfizer as a booster*



- The early observations for two doses of AstraZeneca are particularly likely to be unreliable as they are based on relatively small numbers and are likely to reflect an older population and a population with more co-morbidities than those given the Pfizer vaccine - this may explain the negative point estimates.

Table 1: Descriptive characteristics of positive and negative test results in individuals tested for SARS-CoV-2 in England for the study population

				Overall		Delta		Omicron		Negative	
				n	%	n	%	n	%	n	%
				187,887	**100**	**56,439**	**30.0**	**581**	**0.3**	**130,867**	**69.7**
Vaccination Status and intervals after vaccine	**Manufacturer**	**Dose**	**Weeks**								
	Unvaccinated			19,940	10.6	9,823	5.2	115	0.1	10002	5.3
	ChAdOx1-S	Dose 1	0-4	6	0.0	2	0.0	0	0.0	4	0.0
			4+	1,472	0.8	553	0.3	6	0.0	913	0.5
		Dose 2	0-2	27	0.0	8	0.0	0	0.0	19	0.0
			2-9	138	0.1	29	0.0	1	0.0	108	0.1
			10-14	327	0.2	97	0.1	0	0.0	230	0.1
			15-19	4,501	2.4	1,751	0.9	17	0.0	2,733	1.5
			20-24	26,247	14.0	10,728	5.7	76	0.0	15,443	8.2
			25+	32,524	17.3	13,376	7.1	96	0.1	19,052	10.1
		Booster (BNT162b2)	0-1 days	1,437	0.8	603	0.3	1	0.0	833	0.4
			2-6 days	3,029	1.6	1,153	0.6	6	0.0	1,870	1.0
			1-2 weeks	3,045	1.6	430	0.2	3	0.0	2,612	1.4
			2+weeks	9,559	5.1	669	0.4	10	0.0	8,880	4.7
	BNT162b2	Dose 1	0-4	758	0.4	277	0.1	4	0.0	477	0.3
			4+	7,149	3.8	2,715	1.4	28	0.0	4,406	2.3
		Dose 2	0-2	831	0.4	238	0.1	5	0.0	588	0.3
			2-9	3394	1.8	336	0.2	4	0.0	3054	1.6
			10-14	10731	5.7	1818	1.0	39	0.0	8874	4.7
			15-19	22,047	11.7	4,746	2.5	83	0.0	17,218	9.2
			20-24	6,865	3.7	1,877	1.0	27	0.0	4,961	2.6
			25+	9,366	5.0	2,528	1.3	25	0.0	6,813	3.6
		Booster (BNT162b2)	0-1 days	431	0.2	139	0.1	0	0.0	292	0.2
			2-6 days	1,035	0.6	281	0.1	0	0.0	754	0.4
			1-2 weeks	1,710	0.9	142	0.1	2	0.0	1,566	0.8

			2+weeks	15,633	8.3	1,135	0.6	16	0.0	14,482	7.7
	mRNA-12732	Dose 1	0-4	53	0.0	20	0.0	1	0.0	32	0.0
			4+	358	0.2	100	0.1	2	0.0	256	0.1
		Dose 2	0-2	38	0.0	3	0.0	0	0.0	35	0.0
			2-9	384	0.2	31	0.0	1	0.0	352	0.2
			10-14	1,495	0.8	197	0.1	6	0.0	1292	0.7
			15-19	2,340	1.2	372	0.2	4	0.0	1964	1.0
			20-24	1,015	0.5	262	0.1	3	0.0	750	0.4
		Booster (BNT162b2)	2-6 days	2	0.0	0	0.0	0	0.0	2	0.0
Gender	Female			112,541	59.9	30,715	16.3	346	0.2	81,480	43.4
	Male			75,088	40.0	25,658	13.7	234	0.1	49,196	26.2
	Missing			258	0.1	66	0.0	1	0.0	191	0.1
Age	16-19			10,857	5.8	3,714	2.0	45	0.0	7,098	3.8
	20-24			13,373	7.1	3,358	1.8	104	0.1	9,911	5.3
	25-29			19,626	10.4	4,960	2.6	102	0.1	14,564	7.8
	30-34			25,759	13.7	6,583	3.5	89	0.0	19,087	10.2
	35-39			27,518	14.6	7,593	4.0	68	0.0	19,857	10.6
	40-44			24,973	13.3	8,623	4.6	51	0.0	16,299	8.7
	45-49			20,217	10.8	7,626	4.1	53	0.0	12,538	6.7
	50-54			16,014	8.5	5,883	3.1	32	0.0	10,099	5.4
	55-59			12,334	6.6	4,264	2.3	27	0.0	8,043	4.3
	60+			17,216	9.2	3,835	2.0	10	0.0	13,371	7.1
Ethnicity	African			2,037	1.1	458	0.2	116	0.1	1,463	0.8
	Caribbean			1,150	0.6	397	0.2	32	0.0	721	0.4
	White			159,622	85.0	49,069	26.1	337	0.2	110,216	58.7
	Other			19,064	10.1	4,844	2.6	66	0.0	14,154	7.5
	Prefer not to say			6,014	3.2	1,671	0.9	30	0.0	4,313	2.3
NHS Region	East of England			27,460	14.6	7,538	4.0	82	0.0	19,840	10.6
	London			21,293	11.3	5,873	3.1	223	0.1	15,197	8.1
	Midlands			37,703	20.1	11,845	6.3	66	0.0	25,792	13.7
	North East			22,821	12.1	7,591	4.0	16	0.0	15,214	8.1

	North West	37,239	19.8	12,425	6.6	102	0.1	24,712	13.2
	South East	26,611	14.2	7,478	4.0	66	0.0	19,067	10.1
	South West	14,759	7.9	3,689	2.0	26	0.0	11,044	5.9
	Missing	1	0.0	0	0.0	0	0.0	1	0.0
IMD Quintiles	1	31,885	17.0	10,322	5.5	110	0.1	21,453	11.4
	2	34,425	18.3	10,442	5.6	143	0.1	23,840	12.7
	3	37,989	20.2	11,211	6.0	83	0.0	26,695	14.2
	4	40,938	21.8	12,052	6.4	118	0.1	28,768	15.3
	5	42,195	22.5	12,301	6.5	124	0.1	29,770	15.8
	Missing	455	0.2	111	0.1	3	0.0	341	0.2
Previously positive	No	182,959	97.4	55,463	29.5	521	0.3	126,975	67.6
	Yes	4,928	2.6	976	0.5	60	0.0	3,892	2.1
Vaccine priority groups	Healthcare worker	10,581	5.6	1,367	0.7	35	0.0	9,179	4.9
	CEV	8,922	4.7	1,852	1.0	14	0.0	7,056	3.8
	At risk	33,035	17.6	8924	4.7	55	0.0	24,056	12.8
Date of test	27/11/2021	12,763	6.8	4,518	2.4	8	0.0	8,237	4.4
	28/11/2021	14,704	7.8	4,744	2.5	6	0.0	9,954	5.3
	29/11/2021	30,253	16.1	8,202	4.4	12	0.0	22,039	11.7
	30/11/2021	30,419	16.2	7,976	4.2	34	0.0	22,409	11.9
	01/12/2021	28,926	15.4	8,491	4.5	56	0.0	20,379	10.8
	02/12/2021	23,751	12.6	6,934	3.7	65	0.0	16,752	8.9
	03/12/2021	19,849	10.6	6,301	3.4	81	0.0	13,467	7.2
	04/12/2021	12,011	6.4	4,288	2.3	109	0.1	7,614	4.1
	05/12/2021	12,700	6.8	4,116	2.2	162	0.1	8,422	4.5
	06/12/2021	2,511	1.3	869	0.5	48	0.0	1,594	0.8

Table 2: Vaccine effectiveness (%) against symptomatic diseases by period after dose 1 and dose 2 for Delta and Omicron*

					Omicron		Delta
Primary dose Manufacturer	Doses	Interval (weeks)	Controls	Cases	Vaccine Effectiveness *	Cases	Vaccine Effectiveness*+
Unvaccinated			10,002	115	Baseline	9,823	baseline
ChAdOx1-S	Dose 1	4+	913	6		553	45.4 (38.9 to 51.1)
	Dose 2	2-9	108	1		29	76.2 (63.7 to 84.4)
		10-14	230	0		97	64.9 (55.2 to 72.4)
		15-19	2,733	17	-54.7 (-174 to 12.6)	1751	48.5 (44.7 to 52)
		20-24	15,443	76	-13.2 (-60.2 to 20.1)	10728	45.4 (43 to 47.6)
		25+	19,052	96	5.9 (-29.7 to 31.7)	13376	41.8 (39.4 to 44.1)
	Booster (BNT162b2)	1-2 weeks	2612	3	71.9 (9.1 to 91.3)	430	87 (85.5 to 88.4)
		2+weeks	8880	10	71.4 (41.8 to 86)	669	93.8 (93.2 to 94.3)
BNT162b2	Dose 1	4+	4406	28	34.2 (-3.5 to 58.1)	2715	36.1 (32.3 to 39.8)
	Dose 2	2-9	3,054	4	88 (65.9 to 95.8)	336	88.2 (86.7 to 89.5)
		10-14	8,874	39	48.5 (24.3 to 65)	1818	77.7 (76.3 to 79)
		15-19	17,218	83	34.1 (9.7 to 52)	4746	72.2 (71 to 73.4)
		20-24	4,961	27	36.6 (0.4 to 59.6)	1877	64.8 (62.6 to 66.9)
		25+	6,813	25	34.2 (-5 to 58.7)	2528	63.5 (61.4 to 65.5)
	Booster (BNT162b2)	1-2 weeks	1566	2		142	92.2 (90.7 to 93.4)
		2+weeks	14482	16	75.5 (56.1 to 86.3)	1135	92.6 (92 to 93.1)

* The early observations for two doses of AstraZeneca are particularly likely to be unreliable as they are based on relatively small numbers and are likely to reflect an older population and a population with more co-morbidities than those given the Pfizer vaccine - this may explain the negative point estimates. + To ensure reasonable precision estimates are given if there are at least 10 cases or 2000 controls.