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

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Abstract

Background

A rapid increase in cases due to the SARS-CoV-2 Omicron (B.1.1.529) variant in highly vaccinated populations has raised concerns about the effectiveness of current vaccines.

Methods

We used a test-negative case-control design to estimate vaccine effectiveness (VE) against symptomatic disease caused by the Omicron and Delta variants in England. VE was calculated after primary immunisation with two BNT162b2 or ChAdOx1 doses, and at 2+ weeks following a BNT162b2 booster.

Results

Between 27 November and 06 December 2021, 581 and 56,439 eligible Omicron and Delta cases respectively were identified. There were 130,867 eligible test-negative controls. There was no effect against Omicron from 15 weeks after two ChAdOx1 doses, while VE after two BNT162b2 doses was 88.0% (95%CI: 65.9 to 95.8%) 2-9 weeks after dose 2, dropping to between 34 and 37% from 15 weeks post dose 2.From two weeks after a BNT162b2 booster, VE increased to 71.4% (95%CI: 41.8 to 86.0%) for ChAdOx1 primary course recipients and 75.5% (95%CI: 56.1 to 86.3%) for BNT162b2 primary course recipients.

For cases with Delta, VE was 41.8% (95%CI: 39.4-44.1%) at 25+ weeks after two ChAdOx1 doses, increasing to 93.8% (95%CI: 93.2-94.3%) after a BNT162b2 booster. With a BNT162b2 primary course, VE was 63.5% (95%CI: 61.4 to 65.5%) 25+ weeks after dose 2, increasing to 92.6% (95%CI: 92.0-93.1%) two weeks after the booster.

Conclusions

Primary immunisation with two BNT162b2 or ChAdOx1 doses provided no or limited protection against symptomatic disease with the Omicron variant. Boosting with BNT162b2 following either primary course significantly increased protection.

Word Count

3023

Key Words

COVID-19, Omicron, Delta, Vaccine Effectiveness, Test Negative Case Control, Immunisation

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Introduction

On 26 November 2021 the World Health Organization 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 confirmed SARS-CoV-2 infection in South Africa, coinciding with an increase in detections of the Omicron variant, identification of a number of concerning mutations and early evidence of an increased risk of reinfection in recently-infected individuals.

A large number of mutations have been identified in the Omicron variant, including multiple mutations in the receptor binding domain of the spike protein which have been associated with increased transmissibility and immune evasion after natural infection and vaccination.(2) Emerging laboratory data indicate significantly reduced neutralising antibody response to Omicron compared to the original COVID-19 virus or the Delta variant in vaccinated individuals, although booster doses improved neutralising activity.(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 these early laboratory findings.(5-7)

COVID-19 vaccines are highly effective against symptomatic disease and, more so, against severe disease and fatal outcomes with the original strain 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 observed with Beta and Delta variants, although effectiveness against severe disease has remained high for at least 6 months after primary immunisation with two COVID-19 vaccine doses.(15-18) Waning of protection has been observed with time since vaccination, and especially with the Delta variant which is able to at least partially evade natural and vaccine-induced immunity.(19) However, third (booster) doses provide a rapid and significant increase in protection against both mild and severe disease outcomes.(18, 20-24)

In the UK, Omicron cases were first identified in mid-November 2021 through whole genome sequencing of polymerase chain reaction (PCR) positive swabs. Initially cases occurred primarily in travellers and their close contacts but there was already evidence of community transmission from late November.(25) The UK COVID-19 vaccination programme has been in place since December 2020 with primary courses of two doses of either BNT162b2 (Pfizer-BioNTech, Comirnaty®), ChAdOx1-S (Vaxzevria, AstraZeneca) or mRNA-1273 (Spikevax, Moderna). Two dose vaccine uptake is more than 60% in all cohorts over 20 years and over 80% in all cohorts over 50 years of age, with vaccinations now being offered to children over the age of 12 years.(26) 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.(27)

In this study we estimate vaccine effectiveness against symptomatic disease after 2 doses of BNT162b2 and ChAdOx1-S, and after booster doses of BNT162b2 following a primary immunisation with either BNT162b2 or ChAdOx1-S.

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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.(16) The odds of vaccination in
symptomatic PCR positive cases was compared to the odds of vaccination in symptomatic individuals
who tested negative for SARS-CoV-2 in England.

Data Sources

COVID-19 Testing Data

SARS-CoV-2 Testing PCR testing for SARS CoV-2 in England is undertaken by hospital and public
health laboratories (Pillar 1), as well as by community testing (Pillar 2) including drive through and
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. SARS-CoV-2 lateral flow tests (LFT) are freely available to all members of the population
for regular home testing. Data on all positive PCR and LFT tests, and on negative Pillar 2 PCR tests
from symptomatic individuals with an onset date after 16th October 2020 were extracted up to 6th
December 2021. Individuals who reported symptoms and were tested in Pillar 2 between November
27th and December 3rd 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 seven
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 November 27th 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) 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.(28) NIMS was accessed on 09 December 2021 for dates of vaccination and
manufacturer, sex, date of birth, ethnicity, and residential address.(29) 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 a third dose given at least 140 days after a second dose and administered after 13 September 2021. Individuals with four or more doses of vaccine, heterologous primary schedule or fewer than 19 days between their first and second dose were excluded.

Identification of Delta and Omicron Variants and assignment to cases

Sequencing of PCR positive samples is undertaken through a network of laboratories, including the Wellcome Sanger Institute. Whole-genome sequences are assigned to UKHSA definitions of variants based on mutations. Spike gene (S-gene) target status on PCR-testing is a second approach for identifying each variant because the Omicron variant has been associated with a negative S-gene target (S-gene target failure, SGTF) on PCR testing with the Taqpath assay whereas the Delta variant almost always has a positive S-gene target.(25) Approximately 40% of Pillar 2 Community testing in England 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. *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.

Testing data were linked to NIMS on 09 December 2021 using combinations of the unique individual National Health Service (NHS) number, date of birth, surname, first name, and postcode using deterministic linkage - 92.2% of eligible tests could be linked to the NIMS.

Statistical Analysis

Logistic regression was used, with the PCR test result as the dependent variable and cases being those testing positive (stratified in separate analyses as either Omicron or Delta) and controls being 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 primary immunisation course (ChAdOx1-S or BNT162b2). Any heterologous primary schedules 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 at least two weeks after a BNT162b2 booster for primary immunisation with ChAdOx1-S or BNT162b2. 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

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 25th November, 13/20 (65%) on 26th November, 18/20 (90%) on 27th November, 10/11 (91%) on 28th November and 17/19 (89%) on 29th November. We therefore used cases tested from 27th 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. Omicron cases 14+ days after a booster occurred a median of 41 days after the booster (range 14-72 days).

Vaccine effectiveness against symptomatic disease in individuals who received a primary course of the ChAdOx1 or BNT162b2 is shown by period after primary immunisation with 2 doses and after a third dose with BNT162b2 is shown in Figure 1 and Table 2. 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 two ChAdOx1 doses, there was no protective effect of vaccination against symptomatic disease with Omicron from 15 weeks after the second dose. Among those who had received two BNT162b2 doses, 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 dropped 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%) two 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%) two weeks after the booster.

All vaccine effectiveness estimates for the Omicron variant have with wide confidence intervals because of small case numbers.

Discussion

Our findings indicate 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 two 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 UK data indicate a 20 to 40 fold reduction in neutralising activity in sera from two dose BNT162b2 vaccine recipients compared to early pandemic viruses and at least a 10 fold reduction compared to the Delta variant.(3, 4, 30) In sera from recipients of two doses of ChAdOx1, a greater reduction in neutralising activity was observed with a high proportion of post-vaccination sera exhibiting neutralising activity below the limit of quantification in the assay.(30) Reassuringly though, higher neutralising activity was observed after a booster dose.(3, 4, 30)

Whilst a correlation between neutralising antibody levels and vaccine effectiveness against symptomatic SARS-CoV-2 infection has been observed at a population level,(5) a similar correlation with effectiveness against severe disease is much less certain. With previous variants, vaccine effectiveness against severe disease, including hospitalisation and death, has been higher and retained for a longer period than effectiveness against mild disease.(15, 18) Cellular immune responses are likely to play a relatively more important role in protection as antibodies wane with time since infection or vaccination; antibody waning may increase the risk of SARS-CoV-2 infection while cellular immunity likely limits progression to severe disease.(31) Cellular immunity is also likely to play a more important role in protection against SARS-CoV-2 variants than antibodies.(31) REF It will be some time before effectiveness against severe disease with Omicron can be estimated but, based on experience with other variants,(18) 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.(32) 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 two 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 some limitations and findings should be interpreted with caution. During this early period of circulation of the new variant, a large proportion of cases occurred among travellers. Individuals who reported travel in the preceding two 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, there is significant uncertainty to our estimates and we are unable to break down estimates by population characteristics by that may affect vaccine effectiveness (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 two 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 some misclassification 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 two 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. Boosting with BNT162b2, however, provides a significant increase in protection against mild disease and will likely offer even greater levels of protection against severe and fatal disease. 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 protection against severe disease and the duration of protection after booster vaccination.

Acknowledgements

Ethics

Surveillance of coronavirus disease 2019 (Covid-19) testing and vaccination is undertaken under Regulation 3 of the Health Service (Control of Patient Information) Regulations 2002 to collect confidential patient information (www.legislation.gov.uk/uksi/2002/1438/regulation/3/made. opens in new tab) under Sections 3(i) (a) to (c), 3(i)(d) (i) and (ii), and 3. The study protocol was subject to an internal review by the Public Health England Research Ethics and Governance Group and was found to be fully compliant with all regulatory requirements. Given that no regulatory issues were identified and that ethics review is not a requirement for this type of work, it was decided that a full ethics review would not be necessary.

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Figure 1: Vaccine effectiveness against symptomatic diseases by period after dose 2 and a booster dose for Delta (black squares) and Omicron (grey circles) for recipients of two doses of ChAdOx1-S as the primary course and BNT162b2 as a booster and for recipients of two doses of BNT162b2 as the primary course and BNT162b2 as a booster
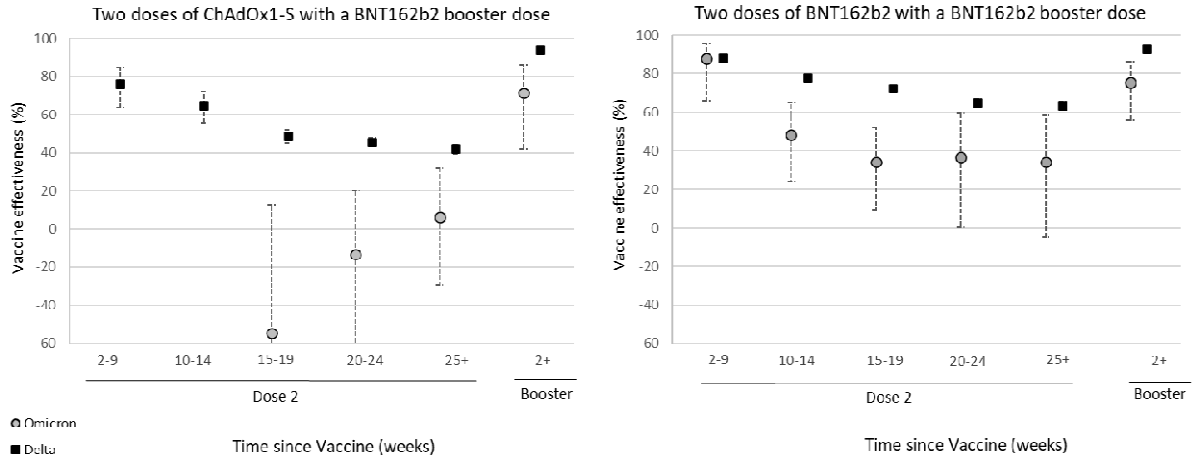
Table 1: Descriptive characteristics of positive and negative test results in individuals tested for SARS-CoV-2 in England for the study population

Category			Overall n	Overall %	Delta n	Delta %	Omicron n	Omicron %	Negative n	Negative %
			187,887	100	56,439	30.0	581	0.3	130,867	69.7
Manufacturer	**Dose**	**Weeks**								
Unvaccinated			19,940	10.6	9,823	17.4	115	19.8	10002	7.6
ChAdOx1-S	Dose 1	0-4	6	0.0	2	0.0	0	0.0	4	0.0
		4+	1,472	0.8	553	1.0	6	1.0	913	0.7
	Dose 2	0-2	27	0.0	8	0.0	0	0.0	19	0.0
		2-9	138	0.1	29	0.1	1	0.2	108	0.1
		10-14	327	0.2	97	0.2	0	0.0	230	0.2
		15-19	4,501	2.4	1,751	3.1	17	2.9	2,733	2.1
		20-24	26,247	14.0	10,728	19.0	76	13.1	15,443	11.8
		25+	32,524	17.3	13,376	23.7	96	16.5	19,052	14.6
	Booster (BNT162b2)	0-1 days	1,437	0.8	603	1.1	1	0.2	833	0.6
		2-6 days	3,029	1.6	1,153	2.0	6	1.0	1,870	1.4
		1-2 weeks	3,045	1.6	430	0.8	3	0.5	2,612	2.0
		2+weeks	9,559	5.1	669	1.2	10	1.7	8,880	6.8
BNT162b2	Dose 1	0-4	758	0.4	277	0.5	4	0.7	477	0.4
		4+	7,149	3.8	2,715	4.8	28	4.8	4,406	3.4
	Dose 2	0-2	831	0.4	238	0.4	5	0.9	588	0.4
		2-9	3394	1.8	336	0.6	4	0.7	3054	2.3
		10-14	10731	5.7	1818	3.2	39	6.7	8874	6.8
		15-19	22,047	11.7	4,746	8.4	83	14.3	17,218	13.2
		20-24	6,865	3.7	1,877	3.3	27	4.6	4,961	3.8
		25+	9,366	5.0	2,528	4.5	25	4.3	6,813	5.2
	Booster (BNT162b2)	0-1 days	431	0.2	139	0.2	0	0.0	292	0.2
		2-6 days	1,035	0.6	281	0.5	0	0.0	754	0.6
		1-2 weeks	1,710	0.9	142	0.3	2	0.3	1,566	1.2
		2+weeks	15,633	8.3	1,135	2.0	16	2.8	14,482	11.1
mRNA-12732	Dose 1	0-4	53	0.0	20	0.0	1	0.2	32	0.0
		4+	358	0.2	100	0.2	2	0.3	256	0.2
	Dose 2	0-2	38	0.0	3	0.0	0	0.0	35	0.0
		2-9	384	0.2	31	0.1	1	0.2	352	0.3
		10-14	1,495	0.8	197	0.3	6	1.0	1292	1.0
		15-19	2,340	1.2	372	0.7	4	0.7	1964	1.5
		20-24	1,015	0.5	262	0.5	3	0.5	750	0.6
	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	54.4	346	59.6	81,480	62.3
	Male		75,088	40.0	25,658	45.5	234	40.3	49,196	37.6
	Missing		258	0.1	66	0.1	1	0.2	191	0.1
Age	16-19		10,857	5.8	3,714	6.6	45	7.7	7,098	5.4
	20-24		13,373	7.1	3,358	5.9	104	17.9	9,911	7.6
	25-29		19,626	10.4	4,960	8.8	102	17.6	14,564	11.1
	30-34		25,759	13.7	6,583	11.7	89	15.3	19,087	14.6
	35-39		27,518	14.6	7,593	13.5	68	11.7	19,857	15.2

Vaccination Status and intervals after vaccine

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	40-44	24,973	13.3	8,623	15.3	51	8.8	16,299	12.5
	45-49	20,217	10.8	7,626	13.5	53	9.1	12,538	9.6
	50-54	16,014	8.5	5,883	10.4	32	5.5	10,099	7.7
	55-59	12,334	6.6	4,264	7.6	27	4.6	8,043	6.1
	60+	17,216	9.2	3,835	6.8	10	1.7	13,371	10.2
Ethnicity	African	2,037	1.1	458	0.8	116	20.0	1,463	1.1
	Caribbean	1,150	0.6	397	0.7	32	5.5	721	0.6
	White	159,622	85.0	49,069	86.9	337	58.0	110,216	84.2
	Other	19,064	10.1	4,844	8.6	66	11.4	14,154	10.8
	Prefer not to say	6,014	3.2	1,671	3.0	30	5.2	4,313	3.3
NHS Region	East of England	27,460	14.6	7,538	13.4	82	14.1	19,840	15.2
	London	21,293	11.3	5,873	10.4	223	38.4	15,197	11.6
	Midlands	37,703	20.1	11,845	21.0	66	11.4	25,792	19.7
	North East	22,821	12.1	7,591	13.4	16	2.8	15,214	11.6
	North West	37,239	19.8	12,425	22.0	102	17.6	24,712	18.9
	South East	26,611	14.2	7,478	13.2	66	11.4	19,067	14.6
	South West	14,759	7.9	3,689	6.5	26	4.5	11,044	8.4
	Missing	1	0.0	0	0.0	0	0.0	1	0.0
IMD Quintiles	1	31,885	17.0	10,322	18.3	110	18.9	21,453	16.4
	2	34,425	18.3	10,442	18.5	143	24.6	23,840	18.2
	3	37,989	20.2	11,211	19.9	83	14.3	26,695	20.4
	4	40,938	21.8	12,052	21.4	118	20.3	28,768	22.0
	5	42,195	22.5	12,301	21.8	124	21.3	29,770	22.7
	Missing	455	0.2	111	0.2	3	0.5	341	0.3
Previously positive	No	182,959	97.4	55,463	98.3	521	89.7	126,975	97.0
	Yes	4,928	2.6	976	1.7	60	10.3	3,892	3.0
Vaccine priority groups	Healthcare worker	10,581	5.6	1,367	2.4	35	6.0	9,179	7.0
	CEV	8,922	4.7	1,852	3.3	14	2.4	7,056	5.4
	At risk	33,035	17.6	8924	15.8	55	9.5	24,056	18.4
Date of test	27/11/2021	12,763	6.8	4,518	8.0	8	1.4	8,237	6.3
	28/11/2021	14,704	7.8	4,744	8.4	6	1.0	9,954	7.6
	29/11/2021	30,253	16.1	8,202	14.5	12	2.1	22,039	16.8
	30/11/2021	30,419	16.2	7,976	14.1	34	5.9	22,409	17.1
	01/12/2021	28,926	15.4	8,491	15.0	56	9.6	20,379	15.6
	02/12/2021	23,751	12.6	6,934	12.3	65	11.2	16,752	12.8
	03/12/2021	19,849	10.6	6,301	11.2	81	13.9	13,467	10.3
	04/12/2021	12,011	6.4	4,288	7.6	109	18.8	7,614	5.8
	05/12/2021	12,700	6.8	4,116	7.3	162	27.9	8,422	6.4
	06/12/2021	2,511	1.3	869	1.5	48	8.3	1,594	1.2

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

Primary dose Manufacturer	Doses	Interval (weeks)	Controls	Cases	Omicron Vaccine Effectiveness *	Cases	Delta 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)

*to ensure reasonable precision estimates are given if there are at least 10 cases or 2000 controls.