Effectiveness of BNT162b2 (Comirnaty, Pfizer-BioNTech) COVID-19 booster vaccine against COVID-19 related symptoms and hospitalisation in England: test negative case-control study

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Abstract

Booster vaccination with mRNA vaccines have been offered to adults over 50 years and those in clinical risk groups since September 2021.

We used a test-negative case-control design to estimate the relative effectiveness of a booster dose of BNT162b2 (Comirnaty, Pfizer-BioNTech) compared to only a 2 dose primary course (at least 140 days after the second dose) as well as compared to unvaccinated individuals. Outcomes were symptomatic coronavirus (COVID-19) and hospitalisation.

The relative effectiveness against symptomatic disease in the 14 days after the booster, was 89.1 (95%CI 88.3-89.9) and 84.5 (95%CI 83.7-85.3) in those who received of ChAdOx1-S and BNT162b2 as a primary course respectively. Absolute VE 93.8 (95%CI 93.3-94.3) and 94.3 (93.9-94.6) respectively. Against hospitalisation relative effectiveness was 88.8 (95%CI 74.9-95.0) and 82.7 (95%CI 73.0-88.9) for ChAdOx1-S versus BNT162b2 as primary course. Absolute VE 98.8% (95%CI 97.4-99.5) and 98.8% (95%CI 98.1-99.2). There was a small benefit in VE with a longer interval between 2nd and 3rd dose.

This study provides real world evidence of significant increased protection from the booster vaccine dose against symptomatic disease and hospitalisation irrespective of the primary course.

Background

Real world effectiveness data demonstrated high levels of short-term protection by COVID-19 vaccines against clinical disease and, more so, against severe outcomes including hospitalization and death (1 to 7). Nevertheless, there is evidence that protection against symptomatic disease wanes over time (8, 9). Booster doses have now been implemented in the UK in order to combat the rise in COVID-19 cases and the additional threat of the winter 2021 influenza season.

We recently reported that vaccine effectiveness against symptomatic disease peaked in the early weeks after the second dose and then fell to 47.3 (95% CI 45 to 49.6) and 69.7 (95% CI 68.7 to 70.5) by 20+ weeks against the Delta variant for ChAdOx1-S (Vaxzevria, AstraZeneca) and Pfizer-BioNTech (BNT162b2/ Comirnaty®), respectively. Vaccine effectiveness against severe disease outcomes remained high to 20+ weeks after vaccination in most groups, nevertheless, greater waning was seen in older adults and those with underlying medical conditions compared to young, healthy adults (8).

In the UK, COVID-19 booster vaccines were introduced on 14 September 2021. Using evidence from the COV-BOOST trial, which demonstrated that the mRNA vaccines provide a strong booster effect with low reactogenicity , regardless of the vaccine given in the primary course, the UK Joint Committee on Vaccination and Immunisation (JCVI) recommended either a BNT162b2 or a half dose (50µg) of mRNA-1273 (Spikevax, Moderna) vaccine to be given as a booster dose no earlier than 6 months after completion of the primary vaccine course (10)(11). In this initial phase of the UK booster programme the following groups were eligible: all adults over 50 and those 16 to 49 years with underlying health conditions that put them at higher risk of severe COVID-19, adult carers and adult household contacts (aged 16 or over) of immunosuppressed individuals, and healthcare workers.

In this study, we aimed to estimate the effectiveness of booster vaccination against symptomatic disease and hospitalisation in adults aged 50 years and older.

Methods

Study design

We used a test-negative case-control design to estimate vaccine effectiveness of a booster dose of BNT162b2 vaccine against PCR-confirmed symptomatic disease and hospitalisation. We compared vaccination status in symptomatic adults over 50 years of age with PCR-confirmed SARS-COV-2 infection with the vaccination status in individuals which reported symptoms but had a negative SARS-COV-2 PCR test. As mRNA-1273 vaccine, as a primary course, was not made available until later in the vaccine programme insufficient time had elapsed for a booster dose to be indicated in this group. In addition, there were very few individuals that had received the half dose (50µg) of mRNA-1273 vaccine as a booster dose so we were unable to assess the VE of this vaccine in our study.

Data sources

Vaccination data

The National Immunisation Management System (NIMS) (12) 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 01 November 2021. The information used from NIMS was all dates of COVID-19 vaccination, vaccine manufacturer for each dose. Demographic data such as sex, date of birth, ethnicity, and residential address was 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. NIMS also contained data on geography (NHS region), risk groups status, clinically extremely vulnerable, and health or social care worker.

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.

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, is a contact of a confirmed case, for care home staff and residents or who has self-tested as positive using a lateral flow device. Initially data on all positive and negative tests for the period 08 December 2020 to 19 November 2021 were extracted for individuals aged ≥ 50 years on 23 November 2021. 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 these are likely to be false negatives. Positive and negative tests within 90 days of a previous positive test were also excluded. Participants contributed a maximum of 4 randomly chosen negative test results in the follow-up period. Data were restricted to persons who had reported symptoms and gave an onset date. Only persons who had undergone testing within 10 days after symptom onset were included in order to account for reduced sensitivity of PCR testing beyond this period. A small number of positive samples where sequencing was done and they were found not to be the Delta variant were excluded. Finally, only samples taken from 13 September 2021 (week 37, 2021) were retained for analysis.

Testing data were linked to NIMS on 23 November 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 >95.5% uniqueness. The NIMS denominator file included information on potential confounding variables related to targeted populations.

Hospitalisations

Testing data were linked to the Emergency Care Dataset (ECDS) to assess vaccine effectiveness against hospitalisation. We included emergency care attendances among symptomatic cases within 14 days of the positive test, which were not injury related, and resulted in an inpatient admission. ECDS data include hospital admissions through NHS emergency departments in England but not elective admissions. Only first attendances in the 14-day period were selected if a person had more than one admission from Emergency Care. Data were extracted on 24 November 2021 with cases included if tested by 04 November 2021 to allow for lags in hospitalisation.

Statistical analysis

Analysis was by logistic regression with the PCR test result as the dependent variable where those testing positive are cases and those testing negative controls. 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), sex, index of multiple deprivation (quintile), ethnic group, care home residence status, geographic region (NHS region), period (calendar week of onset), health and social care worker status, clinical risk group status, clinically extremely vulnerable, severely immunosuppressed, 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 and any mixed primary courses were excluded. Vaccine effectiveness was assessed for each primary course of vaccine with a BNT162b2 booster in 0 to 1, 2 to 6, 7 to 13, 14+ day post booster vaccine intervals. In the primary analysis, those that had received the booster were compared to individuals who had received 2 primary doses with at least 140 days prior to the onset but with no booster dose recorded. In secondary analyses, we also compare to completely unvaccinated individuals and to the 2 to 6 day period after the booster was received. The 2 to 6 day period was selected after plotting the data on case and control numbers after the booster dose and to avoid days 0 and 1 post booster when vaccine reactogenicity may affect the case-control ratio (figure 1). The analyses comparing to 2 doses or the 2 to 6 day post booster period measures relative effectiveness to 2 doses, whilst the comparison to unvaccinated is absolute effectiveness of 2 doses and a booster. In the analysis comparing to unvaccinated we also assessed the remaining effectiveness of 2 doses at least 140 days (20 weeks) post second dose.

Among individuals who received BNT162b2 as their primary course, an additional analysis was undertaken estimating the odds of testing positive in shorter intervals between dose 2 and booster (25 to 29 and 30 to 34 weeks) relative to the longest interval (35 or more weeks). A test for the interaction effect of age was also performed. Vaccine effectiveness compared to unvaccinated was also stratified by the interval between dose 2 and the booster.

Results

Descriptive statistics and characteristics

From week 37 onwards there were a total of 462,591 eligible tests in those aged 50 years and over, with a test date within 10 days of their symptom onset date and had linked to the National Immunisation Management system, with a 94.4% match rate. Of these 20,098 (4.3%) were unvaccinated, 266,505 received ChAdOx1-S 140 days post a second dose, 108,290 received BNT162b2 140 days post a second dose. Of those that had received a BNT162b2 booster dose 21,716 had received an ChAdOx1-S primary course and 42,013 received a BNT162b2 primary course. Of the positive cases included in the analysis, 2,829 (1.5%) were hospitalised within 14 days of the test. A description of the eligible tests is given in Table 1.

Vaccine effectiveness estimates

An overall effect on the proportion of cases and controls can be seen from around day 7 after the booster dose and stabilises at day 11 (figure 1). Vaccine effectiveness of a BNT162b2 booster dose relative to those that had received only 2 doses was 89.1% (95% confidence interval 88.3-89.9) where the primary course was ChAdOx1-S and 84.5% (95% confidence interval 83.7-85.3) where BNT162b2 was used as the primary course (table 2 and figure 2).

In the secondary analysis, which used the 2 to 6 day period post the booster dose as the baseline results were similar to the primary analysis with a relative VE from 14 days after the booster dose of 87.5% (95% confidence interval 86.4-88.5) with a ChAdOx1-S primary course and 82.5% (95% confidence interval 81.3-83.6) with BNT162b2 as the primary course (table 2 and figure 3). In the analysis using the unvaccinated individuals as the baseline, the booster dose was associated with an absolute VE from 14 days after vaccination to 93.8% (95% confidence interval 93.3-94.3) after a ChAdOx1-S primary course and 94.3 (95% confidence interval 93.9-94.6) after a BNT162b2 primary course (table 2 and figure 4). In the analysis using the unvaccinated baseline the effectiveness of 2 doses of ChAdOx1-S and BNT162b2 ≥20 weeks after being given were 43.7% (95% confidence interval 41.9-45.4) and 63.4% (95% confidence interval 62.1 – 64.6), respectively (table 2 and figure 4).

High levels of protection were also seen against hospitalisation, with the vaccine effectiveness of a BNT162b2 booster dose relative to those that had received only 2 doses of 88.8% (95% confidence interval 74.9-95.0) where the primary course was ChAdOx1-S and 82.7% (95% confidence interval 73.0-88.9) where BNT162b2 was used as the primary course. In the secondary analysis using the unvaccinated individuals as the baseline, the booster dose was associated with an absolute VE from 14 days after vaccination of 98.8% (95% confidence interval 97.4-99.5) after an ChAdOx1-S primary course and 98.8% (95% confidence interval 98.1-99.2) after a BNT162b2 primary course (table 3 and figures 5 and 6)

After assessing the distribution of intervals between dose 2 and the booster dose for cases and controls by age group and manufacturer the interval between dose 2 and booster was split into 3 periods; 25 to 29, 30 to 34 and 35 or more weeks (figure 7). Due to the roll out of the vaccine programme, there were more individuals who had received a second dose of BNT162b2 at an earlier timepoint, therefore, the majority of the individuals who had the longest interval between dose 2 and the booster had a BNT162b2 primary course. Analyses by interval between dose 2 and dose 3 were thus restricted to those who received BNT162b2 as the primary course. A shorter interval between dose 2 and the booster of 25 to 29 weeks compared to the baseline interval of 35 weeks or more was associated with an increased adjusted odds ratio of 1.63 (95% confidence interval 1.37-1.95) for becoming a symptomatic case. This was also seen in the 30 to 34 week interval, adjusted odds ratio 1.54 (1.23-1.94). Although remaining high the adjusted VE estimates also reduced from 95.8% (95% confidence interval 95.0-96.5) in the 35 weeks or more interval to 93.3% (95% confidence interval 92.8-93.8) in the shortest interval between dose 2 and the booster (table 4). A test for the interaction effect of age was not significant (p=0.15).

Discussion

Key findings
This study provides evidence of a significant increase in protection against symptomatic COVID-19 disease and hospitalisation with a booster dose of BNT162b2 following a primary course of 2 doses of either BNT162b2 or ChAdOx1-S in adults aged 50 years and older. Vaccine effectiveness was very similar for either priming vaccine. A longer interval between dose 2 and the booster doses was associated with small improvements in vaccine effectiveness.

Interpretation
These findings suggest that the booster offers very high levels of protection against symptomatic disease and hospitalisation, at least in the short-term. Given the recent deployment of the booster programme in the UK, further follow-up is needed to understand how protection changes over time against both mild and severe disease. The slightly lower relative VE estimates of the booster in individuals with BNT162b2 as a primary course compared to the ChAdOx1-S in the primary

analysis is due to the different baseline with higher VE after 2 doses of BNT162b2 as compared to ChAdOx1-S (8). When using unvaccinated controls, there was little difference in observed vaccine effectiveness of the booster dose with either primary course. We also observed a peak in testing at day 1 after the booster dose which is likely to be reactogenicity effects so shortly after the vaccine, as has been reported previously (13). The improved vaccine effectiveness with a longer interval between dose 2 and the booster suggests that there will be some benefit in delaying booster doses. Though this has to be balanced with the reduced protection among those that have received just 2 doses (where protection may have waned), compared to protection from the booster even with a relatively short interval. This finding was also similar to the reduced effectiveness among those that had a shorter interval between dose 1 and 2 (8, 14).

Comparison with existing literature

In Israel a booster programme began in July 2021. Bar-On and others reported an adjusted rate ratios of 11.3 (10.4-12.3) against confirmed infection in booster dose recipients compared to those who received only 2 doses (equivalent to relative vaccine effectiveness of 91.2%) (15). This is slightly higher than the relative vaccine effectiveness that we report, which could reflect lower 2 dose vaccine effectiveness in the comparison group in Israel where a greater degree of waning has previously been reported. (9, 16, 17) Even greater protection has been reported in Israel against severe disease.(15, 18)

Limitations

This is an observational study with a number of possible biases and should be interpreted with caution. The imperfect sensitivity PCR testing could cause misclassification of both cases and controls, which could attenuate vaccine effectiveness estimates. Many individuals will also have been previously infected so the VE measured is in the context of a population where many have already had natural exposure. We adjust for measured confounders, however, there may be residual confounding that we could not account for. Nevertheless, the similarity of the VE estimates using those with 2 doses and no booster as the baseline and using the 2 to 6 day period post booster as the baseline suggests that residual confounding is small. Use of the unvaccinated as a comparator to obtain absolute effectiveness is most susceptible to residual confounding as the totally unvaccinated population may differ in many ways to those who have had vaccine doses, many of which may lead to underestimation of VE (8). Despite this potential underestimation, using the unvaccinated comparator the absolute VE estimates were over 93%. Due to small numbers at this early stage of the booster roll out this study only assesses symptomatic disease and hospitalisation, there is currently insufficient follow-up to estimate the effects on severe disease which leads to death. For the same reason, we are only able to report the early effects of the booster programme and it is not yet clear how long protection against COVID-19 following booster vaccination will last.

For the analysis by interval between dose 2 and dose 3, it should be noted that those that had a longer interval between dose 2 and dose 3 are likely to have had a shorter interval between dose 1 and dose 2. As these will be colinear it is not possible to adjust for interval between dose 1 and 2 in this analysis.

In these analyses, we were unable to report on the half dose (50µg) of mRNA-1273 vaccine due to low numbers as the majority of booster doses given in this period were BNT162b2. We were unable to assess the VE in all those targeted for a booster dose such as individuals with underlying health conditions, adult carers and adult household contacts of immunosuppressed individuals due to small numbers and difficultly identifying these individuals with the dataset.

Conclusions

Our study provides real world evidence of significant increased protection from the booster dose against symptomatic disease and hospitalisation in those aged over 50 year of age irrespective of which primary course was received. This indicates that a high level of protection is achieved among older adults who are more vulnerable to severe COVID-19. This will be important in the 2021 to 2022 winter period when COVID-19 is likely to co-circulate alongside other respiratory viruses, including seasonal influenza virus.

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

		Overall		Positive		Negative	
		n	%	n	%	n	%
	Test Result	**462,591**	**100.0%**	**189,993**	**41.1%**	**272,598**	**58.9%**
Vaccination Status and intervals after vaccine**	Unvaccinated	20,098	**4.3%**	11,476	**6.0%**	8,622	**3.2%**
	AZ dose 2: 140+	266,505	**57.6%**	126,786	**66.7%**	139,719	**51.3%**
	PF dose 2:140+	108,290	**23.4%**	36,446	**19.2%**	71,844	**26.4%**
	MD dose 2:140+	12	**0.0%**	5	**0.0%**	7	**0.0%**
	AZ primary /PF booster: 0-13 days	17,158	**3.7%**	6720	**3.5%**	10,438	**3.8%**
	AZ primary /PF booster: 14+ days	8,514	**1.8%**	897	**0.5%**	7,617	**2.8%**
	PF primary /PF booster: 0-13 days	20,120	**4.3%**	5,539	**2.9%**	14,581	**5.3%**
	PF primary /PF booster: 14+ days	21,893	**4.7%**	2,124	**1.1%**	19,769	**7.3%**
	MD primary/PF booster: 0-13 days	1	**0.0%**	0	0	1	**0.0%**
Age Group	50-64	313,238	**67.7%**	129,199	**68.0%**	184,039	**67.5%**
	65-79	129,954	**28.1%**	54,175	**28.5%**	75,779	**27.8%**
	80+	19,399	**4.2%**	6,619	**3.5%**	12,780	**4.7%**
Gender	female	270,467	**58.5%**	97,886	**51.5%**	172,581	**63.3%**
	male	191,598	**41.4%**	91,906	**48.4%**	99,692	**36.6%**
	missing	526	**0.1%**	201	**0.1%**	325	**0.1%**
Ethnicity	African	2,188	**0.5%**	721	**0.4%**	1,467	**0.5%**
	Another Asian background	3,312	**0.7%**	1,122	**0.6%**	2,190	**0.8%**
	Another Black background	427	**0.1%**	162	**0.1%**	265	**0.1%**
	Another ethnic background	1,938	**0.4%**	626	**0.3%**	1,312	**0.5%**
	Arab	787	**0.2%**	274	**0.1%**	513	**0.2%**
	Bangladeshi	1,294	**0.3%**	510	**0.3%**	784	**0.3%**
	Caribbean	2,817	**0.6%**	1,257	**0.7%**	1,560	**0.6%**
	Chinese	1,099	**0.2%**	393	**0.2%**	706	**0.3%**
	Indian	12,416	**2.7%**	4,054	**2.1%**	8,362	**3.1%**
	Mixed or multiple ethnic groups	3,112	**0.7%**	1,126	**0.6%**	1,986	**0.7%**
	Pakistani	4,149	**0.9%**	1,522	**0.8%**	2,627	**1.0%**
	Prefer not to say	13,211	**2.9%**	4,895	**2.6%**	8,316	**3.1%**
	White	415,841	**89.9%**	173,331	**91.2%**	242,510	**89.0%**
NHS Region	East of England	52,687	**11.4%**	21,376	**11.3%**	31,311	**11.5%**
	London	40,474	**8.7%**	14,658	**7.7%**	25,816	**9.5%**
	Midlands	92,254	**19.9%**	38,879	**20.5%**	53,375	**19.6%**

	North East	82,120	**17.8%**	36,003	**18.9%**	46,117	**16.9%**
	North West	65,610	**14.2%**	25,882	**13.6%**	39,728	**14.6%**
	South East	72,074	**15.6%**	29,463	**15.5%**	42,611	**15.6%**
	South West	57,372	**12.4%**	23,732	**12.5%**	33,640	**12.3%**
IMD Quintiles	1	64,441	**13.9%**	26,567	**14.0%**	37,874	**13.9%**
	2	79,704	**17.2%**	32,700	**17.2%**	47,004	**17.2%**
	3	96,144	**20.8%**	39,682	**20.9%**	56,462	**20.7%**
	4	108,035	**23.4%**	44,598	**23.5%**	63,437	**23.3%**
	5	113,827	**24.6%**	46,260	**24.3%**	67,567	**24.8%**
	Missing	440	**0.1%**	186	**0.1%**	254	**0.1%**
Vaccine priority groups	Heathcare worker	23,492	**5.1%**	4,660	**2.5%**	18,832	**6.9%**
	CEV	51,720	**11.2%**	17,344	**9.1%**	34,376	**12.6%**
	Care home resident	1,611	**26.3%**	418	**23.9%**	76,377	**28.0%**
	Immunosuppressed	9,285	**1.9%**	3,224	**0.9%**	6,061	**2.2%**
	At risk	121,792	**0.0%**	45,415	**0.0%**	76,377	**28.0%**
	Tested Positive >90 days previously	8,649	**0.4%**	1,740	**0.9%**	6,909	**2.5%**

* test or onset date from week 37 onwards in those aged 50 years and over with a sample date within 10 days of symptom onset.

AZ: ChAdOx1-S (Vaxzevria, AstraZeneca), PF: BNT162b2 (Comirnaty, Pfizer-BioNTech)

Table 2: Vaccine effectiveness against symptomatic disease for the BNT162b2 (Comirnaty, Pfizer-BioNTech) booster vaccine in England. Table values are VE (95% CI).

Primary Course (with second dose 140+ days before)	Interval since PF Booster	Controls	Cases	rVE (140+ days post dose 2 baseline)	rVE (dose 3: 2-6 days post booster baseline)	VE (unvaccinated base)
Unvaccinated	No booster	8622	11476			baseline
2AZ	No booster	139719	126786	baseline		43.7 (41.9 to 45.4)
2AZ	0-1 days	2068	1888	10.1 (4.1 to 15.7)		49.1 (45.3 to 52.6)
2AZ	2-6 days	3773	3456	12.7 (8.4 to 16.8)	base	50.4 (47.5 to 53.2)
2AZ	7-13 days	4597	1376	71.9 (70.1 to 73.6)	67.8 (65.3 to 70.2)	84 (82.9 to 85.1)
2AZ	14+ days	7617	897	**89.1 (88.3 to 89.9)**	87.5 (86.4 to 88.5)	**93.8 (93.3 to 94.3)**
2PF	No booster	71844	36446	baseline		63.4 (62.1 to 64.6)
2PF	0-1 days	2236	1359	-6.2 (-14.0 to 1.1)		61.1 (58.0 to 63.9)
2PF	2-6 days	5163	2780	11.5 (6.9 to 15.8)	baseline	67.4 (65.5 to 69.2)
2PF	7-13 days	7182	1400	69.4 (67.5 to 71.2)	65.4 (62.8 to 67.9)	88.7 (87.9 to 89.4)
2PF	14+ days	19769	2124	**84.5 (83.7 to 85.3)**	82.5 (81.3 to 83.6)	**94.3 (93.9 to 94.6)**

AZ: ChAdOx1-S (Vaxzevria, AstraZeneca), PF: BNT162b2 (Comirnaty, Pfizer-BioNTech), VE: vaccine effectiveness compared to zero doses, rVE: relative vaccine effectiveness compared to dose 2 (either 140+ days post dose 2 with no booster or 140+ days post dose 2 and 2 to 6 days after he booster).

Table 3: Vaccine effectiveness against hospitalisation for the BNT162b2 (Comirnaty, Pfizer-BioNTech) booster vaccine in England. Table values are VE (95% CI).

Primary Course (with second dose 140+ days before)	Interval since PF Booster	Controls	Cases	rVE (140+ days post dose 2 baseline)	VE (unvaccinated base)
Unvaccinated	No booster	6919	487		baseline
2AZ	No booster	100198	1181	baseline	89.5 (88.1 to 90.7)
2AZ	0-1 days	1034	23	-9 (-66.9 to 28.8)	88.6 (82.3 to 92.6)
2AZ	2-6 days	1900	25	45.7 (18.4 to 63.8)	94.3 (91.3 to 96.3)
2AZ	7-13 days	2128	16	68.8 (48.5 to 81.1)	96.7 (94.5 to 98.0)
2AZ	14+ days	2289	6	88.8 (74.9 to 95.0)	98.8 (97.4 to 99.5)
2PF	No booster	62787	558	baseline	93.1 (92.0 to 94.0)
2PF	0-1 days	1701	17	19.4 (-34.2 to 51.5)	94.4 (90.6 to 96.7)
2PF	2-6 days	3854	34	30.4 (0.5 to 51.3)	95.2 (93.0 to 96.7)
2PF	7-13 days	5117	17	75.9 (60.6 to 85.3)	98.3 (97.2 to 99.0)
2PF	14+ days	8870	22	82.7 (73.0 to 88.9)	98.8 (98.1 to 99.2)

AZ: ChAdOx1-S (Vaxzevria, AstraZeneca), PF: BNT162b2 (Comirnaty, Pfizer-BioNTech), VE: vaccine effectiveness compared to zero doses, rVE: relative vaccine effectiveness compared to dose 2 (either 140+ days post dose 2 with no booster or 140+ days post dose 2 and 2 to 6 days after he booster).

Table 4: Odds ratio of testing positive compared to the longest interval between dose 2 and booster and vaccine effectiveness 14 days after booster by interval between second dose and booster

vaccination status	interval between dose 2 and 3	Negative Test	Positive Test	aOR vs 35+ weeks* (95 %CI)	aVE** (95% CI)
unvaccinated	n/a	8622	11476		base
PF-PF / PF boost 14+ days ago	25-29 wks	15184	1705	1.63 (1.37-1.95)	93.3 (92.8-93.8)
PF-PF / PF boost 14+ days ago	30-34 wks	2068	192	1.54 (1.23-1.94)	93.9 (92.9-94.8)
PF-PF / PF boost 14+ days ago ***	35+ wks	2087	153	baseline	95.8 (95.0-96.5)

* model without unvaccinated included ** model with unvaccinated included as baseline

Figure 1: Distribution (%) and counts of cases and controls by interval from booster to onset
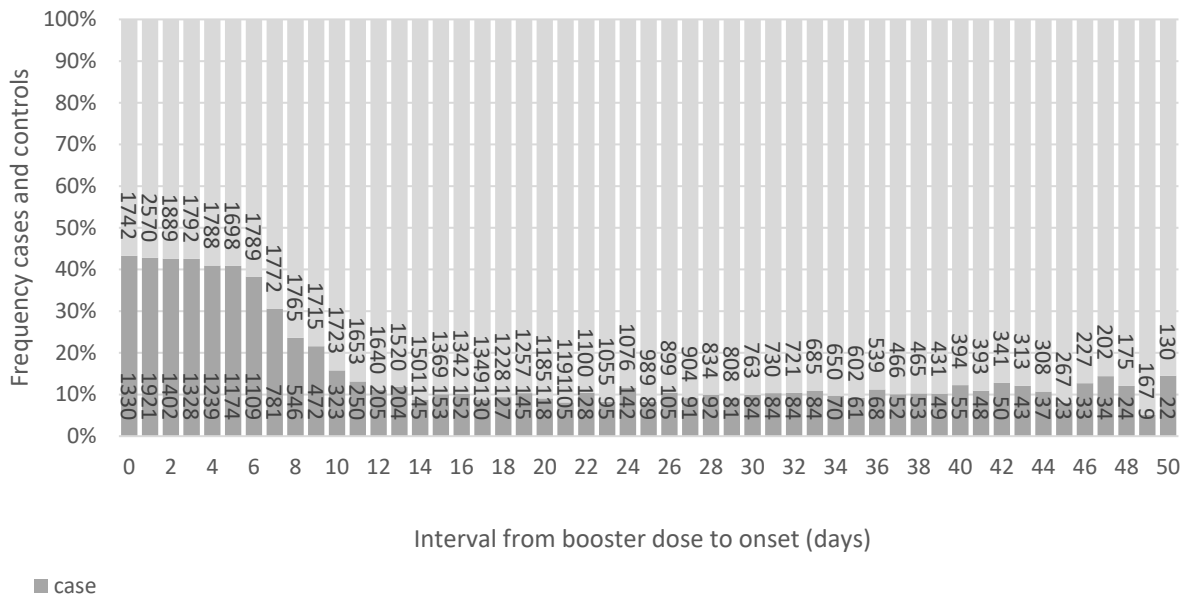
Figure 2: Relative vaccine effectiveness estimates in time intervals post booster according to primary course: 140+ days post dose 2 as baseline (set at 0% VE)
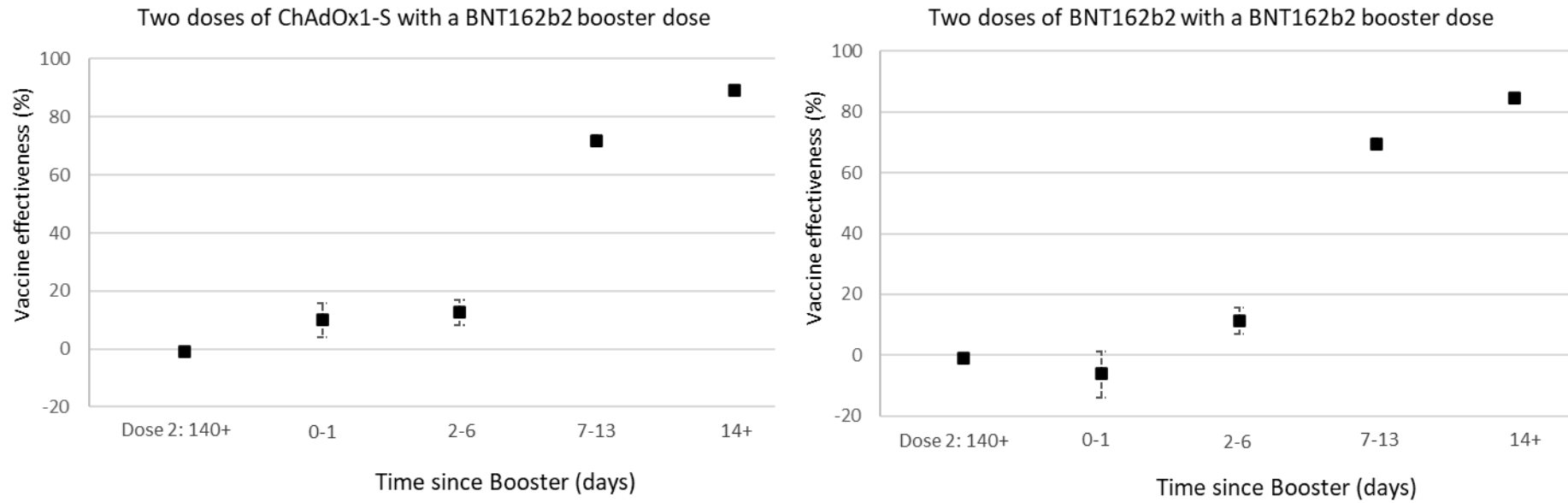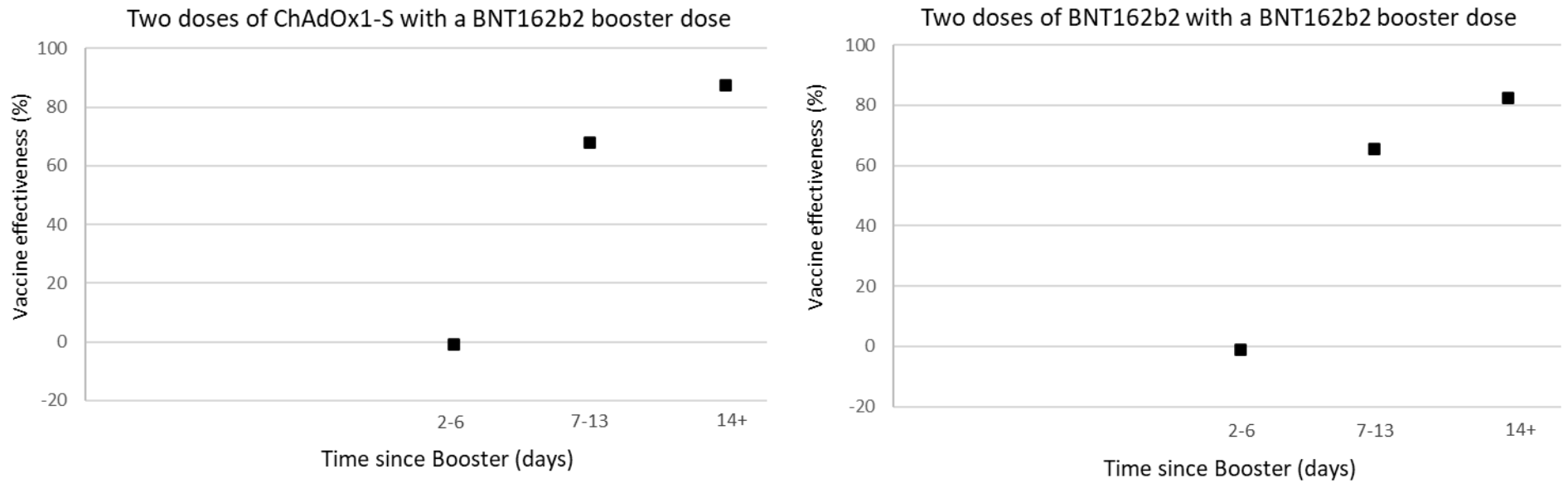

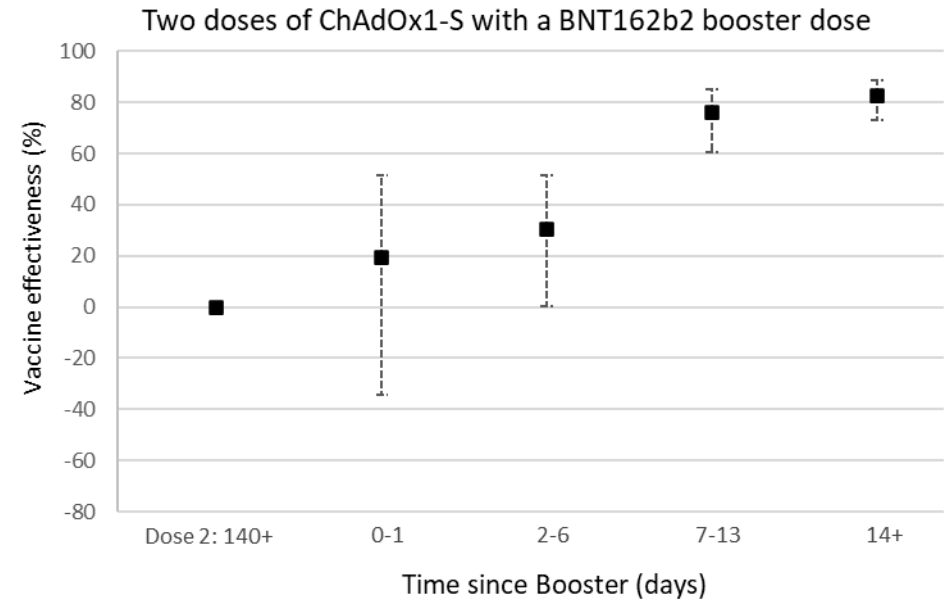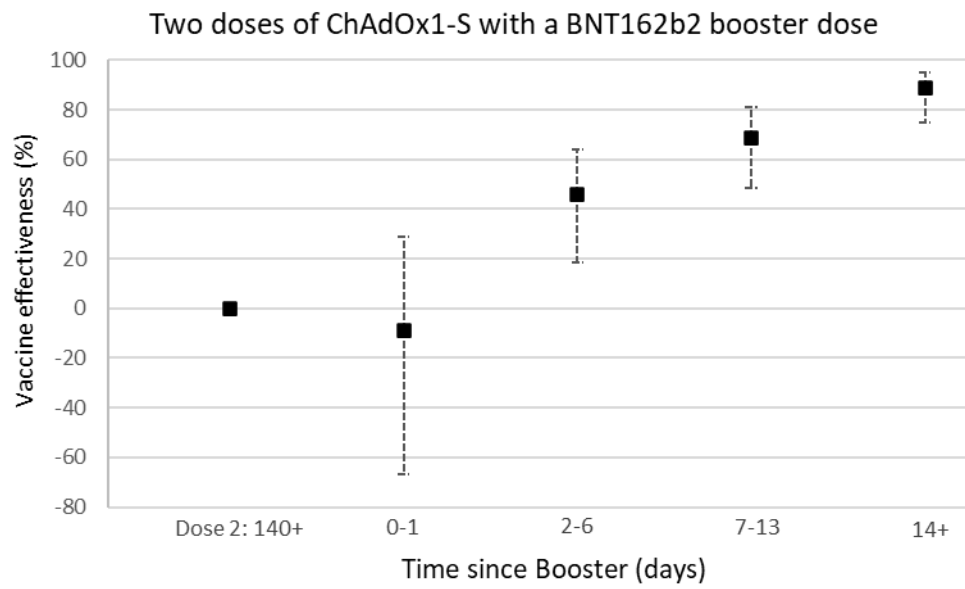Two doses of ChAdOx1-S with a BNT162b2 booster dose

Two doses of BNT162b2 with a BNT162b2 booster dose

Figure 3: Relative vaccine effectiveness estimates in time intervals post booster according to primary course: 2 to 6 days post booster as baseline (set at 0% VE)

Figure 4: Vaccine Effectiveness estimates for at least 140 days post dose 2 (given with no booster) or for time intervals post dose 3 (booster) according to primary course: Unvaccinated as baseline
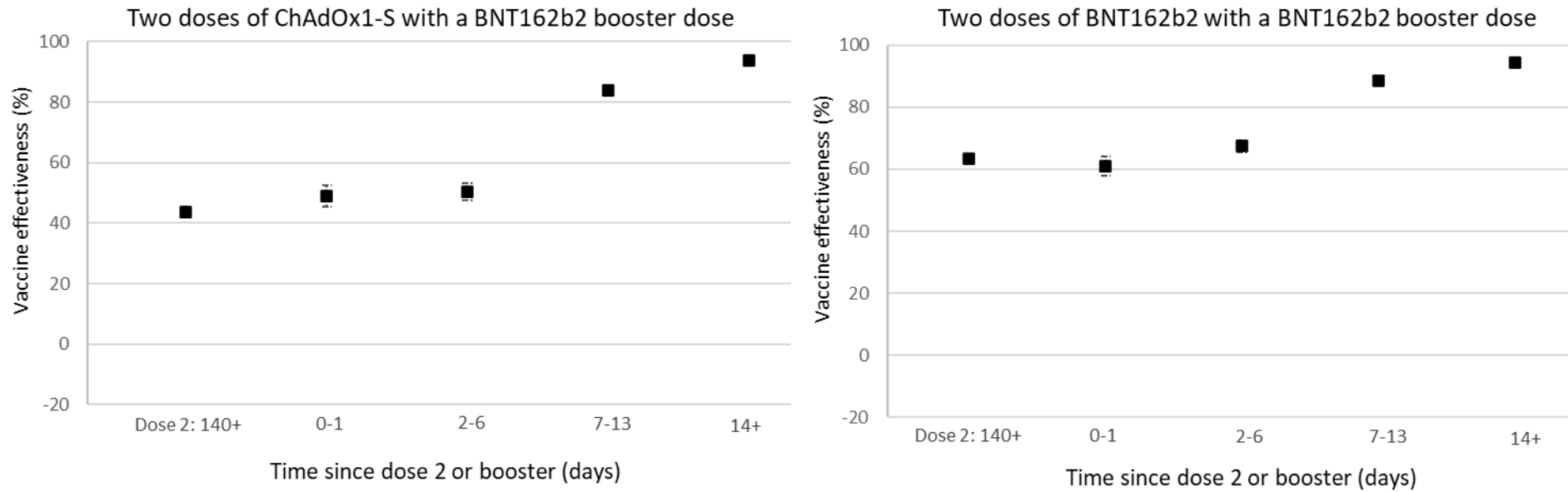
Figure 5: Vaccine Effectiveness estimates against hospitalisation in time intervals post booster according to primary course: 140+ days post dose 2 as baseline (set at 0% VE)

Two doses of ChAdOx1-S with a BNT162b2 booster dose

Two doses of ChAdOx1-S with a BNT162b2 booster dose

Figure 6: Vaccine Effectiveness estimates against hospitalisation in time intervals post booster according to primary course: Unvaccinated as baseline
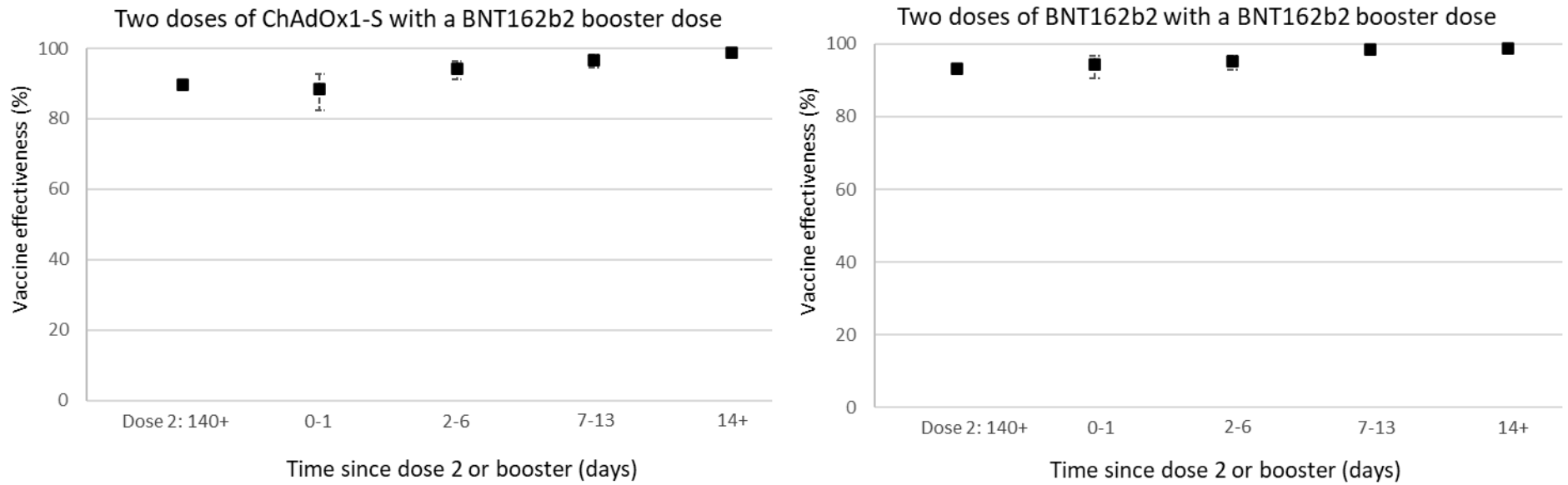
Figure 7: The distribution of intervals between dose 2 and the booster dose for cases and controls by age group and manufacturer
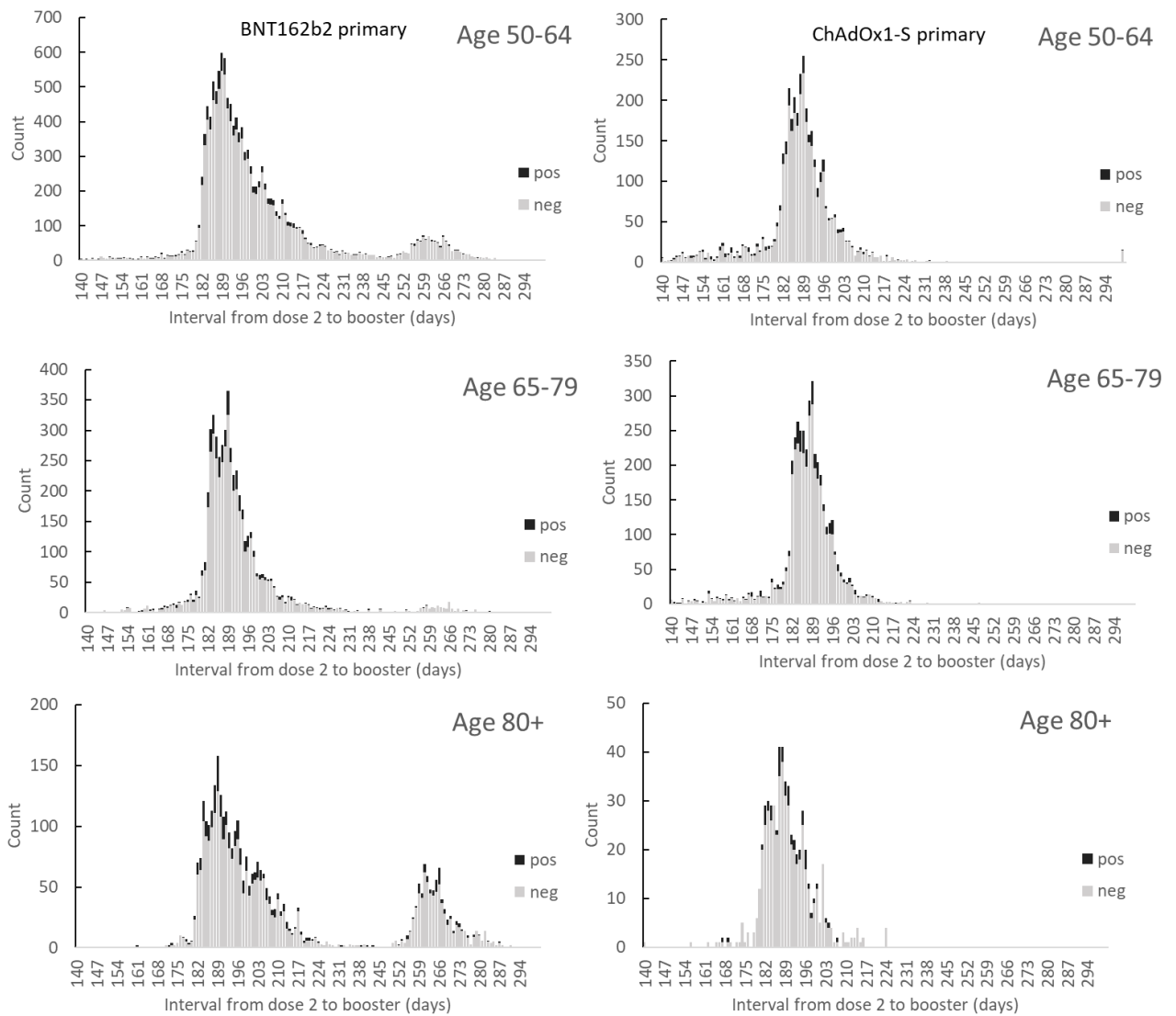
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Ethical approval: Surveillance of COVID-19 testing and vaccination is undertaken under Regulation 3 of the [Health Service (Control of Patient Information) Regulations 2002](#) to collect confidential patient information under Sections 3(i) (a) to (c), 3(i)(d) (i) and (ii) and 3(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. As no regulatory issues were identified, and ethical review is not a requirement for this type of work, it was decided that a full ethical review would not be necessary.

Code availability Statement: Model fitting code can be made available

Data sharing: No additional data available.