THE LANCET

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Emary KRW, Golubchik T, Aley PK, et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): an exploratory analysis of a randomised controlled trial. *Lancet* 2021; published online March 30. http://dx.doi.org/10.1016/S0140-6736(21)00628-0.

Supplementary Material

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Table S1A Demographics in the SD/SD and LD/SD primary efficacy cohort (ChAdOx1 nCoV-19 and control recipients pooled)

Demographics	Primary efficacy cohort (n=8534)	NAAT+ cases (n=520)	B.1.1.7 (n=75)	Non-B.1.1.7 (n=144)	No result (n=101)	Not sequenced (n=200)	p-value B.1.1.7 vs non-B.1.1.7*
Age							
18-55 years	6636 (77.8%)	459 (88.3%)	65 (86.7%)	122 (84.7%)	87 (86.1%)	185 (92.5%)	
56-69 years	955 (11.2%)	33 (6.3%)	6 (8.0%)	16 (11.1%)	5 (5.0%)	6 (3.0%)	0.912
≥70 years	943 (11.0%)	28 (5.4%)	4 (5.3%)	6 (4.2%)	9 (8.9%)	9 (4.5%)	
missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Sex (female) n%	5065 (59.4%)	326 (62.7%)	44 (58.7%)	89 (61.8%)	67 (66.3%)	126 (63.0%)	0.652
BMI (median, IQR) kg/m^2	25.4 [22.9, 28.9]	25.6 [23.2, 29.7]	25.2 [22.6, 28.0]	26.1 [23.2, 30.1]	25.3 [22.9, 27.9]	25.6 [23.4, 30.3]	0.097
Ethnicity							
White	7863 (92.1%)	484 (93.1%)	70 (93.3%)	136 (94.4%)	96 (95.0%)	182 (91.0%)	
Black	40 (0.5%)	2 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.0%)	
Asian	424 (5.0%)	29 (5.6%)	4 (5.3%)	6 (4.2%)	4 (4.0%)	15 (7.5%)	0.849
Mixed	139 (1.6%)	3 (0.6%)	1 (1.3%)	1 (0.7%)	1 (1.0%)	0 (0.0%)	
Other	68 (0.8%)	2 (0.4%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.5%)	
missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Health and social care setting workers n%	5623 (65.9%)	378 (72.7%)	48 (64.0%)	109 (75.7%)	68 (67.3%)	153 (76.5%)	0.068
Co-morbidities							
Cardiovascular disease	1029 (12.1%)	54 (10.4%)	5 (6.7%)	18 (12.5%)	8 (7.9%)	23 (11.5%)	0.181
Respiratory disease	1042 (12.2%)	61 (11.7%)	10 (13.3%)	23 (16.0%)	10 (9.9%)	18 (9.0%)	0.604
Diabetes	185 (2.2%)	10 (1.9%)	1 (1.3%)	4 (2.8%)	0 (0.0%)	5 (2.5%)	0.663
Prime-boost interval							
<6 weeks	1742 (20.4%)	63 (12.1%)	10 (13.3%)	20 (13.9%)	16 (15.8%)	17 (8.5%)	
6-8 weeks	1045 (12.2%)	69 (13.3%)	5 (6.7%)	16 (11.1%)	19 (18.8%)	29 (14.5%)	0.540
9-11 weeks	2517 (29.5%)	170 (32.7%)	34 (45.3%)	37 (25.7%)	25 (24.8%)	74 (37.0%)	
≥12 weeks	3230 (37.8%)	218 (41.9%)	26 (34.7%)	71 (49.3%)	41 (40.6%)	80 (40.0%)	

*p-values from Chi-squared and Fisher Exact tests, Wilcoxon Rank Sum tests (BMI) and Cochran-Armitage tests (ordinal age groups and prime-boost intervals), testing for associations between the corresponding variable and B.1.1.7 vs Non-B.1.1.7 variants.

Table S1B Demographics in the SD/SD and LD/SD primary efficacy cohort, recipients of ChAdOx1 nCoV-19 only

Demographics	Primary efficacy cohort (n=4244)	NAAT+ cases (n=173)	B.1.1.7 (n=21)	Non-B.1.1.7 (n=27)	No result (n=44)	Not sequenced (n=81)
Age						
18-55 years	3300 (77.8%)	150 (86.7%)	18 (85.7%)	23 (85.2%)	38 (86.4%)	71 (87.7%)
56-69 years	476 (11.2%)	10 (5.8%)	0 (0.0%)	4 (14.8%)	3 (6.8%)	3 (3.7%)
≥70 years	468 (11.0%)	13 (7.5%)	3 (14.3%)	0 (0.0%)	3 (6.8%)	7 (8.6%)
missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sex (female) n%	2485 (58.6%)	110 (63.6%)	10 (47.6%)	15 (55.6%)	31 (70.5%)	54 (66.7%)
BMI (median, IQR) kg/m^2	25.4 [23.0, 28.8]	25.6 [23.2, 30.0]	25.4 [23.0, 27.0]	26.7 [23.1, 30.9]	25.6 [22.9, 28.0]	26.1 [23.5, 30.9]
Ethnicity						
White	3894 (91.8%)	163 (94.2%)	20 (95.2%)	27 (100.0%)	41 (93.2%)	75 (92.6%)
Black	23 (0.5%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)
Asian	222 (5.2%)	8 (4.6%)	0 (0.0%)	0 (0.0%)	3 (6.8%)	5 (6.2%)
Mixed	72 (1.7%)	1 (0.6%)	1 (4.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other	33 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Health and social care setting workers n%	2774 (65.4%)	120 (69.4%)	11 (52.4%)	19 (70.4%)	30 (68.2%)	60 (74.1%)
Co-morbidities						
Cardiovascular disease	514 (12.1%)	27 (15.6%)	2 (9.5%)	8 (29.6%)	5 (11.4%)	12 (14.8%)
Respiratory disease	504 (11.9%)	19 (11.0%)	2 (9.5%)	4 (14.8%)	6 (13.6%)	7 (8.6%)
Diabetes	97 (2.3%)	4 (2.3%)	0 (0.0%)	2 (7.4%)	0 (0.0%)	2 (2.5%)
Prime-boost interval						
<6 weeks	870 (20.5%)	21 (12.1%)	3 (14.3%)	4 (14.8%)	5 (11.4%)	9 (11.1%)
6-8 weeks	548 (12.9%)	41 (23.7%)	3 (14.3%)	5 (18.5%)	14 (31.8%)	19 (23.5%)
9-11 weeks	1222 (28.8%)	47 (27.2%)	9 (42.9%)	6 (22.2%)	9 (20.5%)	23 (28.4%)
≥12 weeks	1604 (37.8%)	64 (37.0%)	6 (28.6%)	12 (44.4%)	16 (36.4%)	30 (37.0%)

Table S1C Demographics in the SD/SD and LD/SD primary efficacy cohort, recipients of control (MenACWY) only

Demographics	Primary efficacy cohort (n=4290)	NAAT+ cases (n=347)	B.1.1.7 (n=54)	Non-B.1.1.7 (n=117)	No result (n=57)	Not sequenced (n=119)
Age						
18-55 years	3336 (77.8%)	309 (89.0%)	47 (87.0%)	99 (84.6%)	49 (86.0%)	114 (95.8%)
56-69 years	479 (11.2%)	23 (6.6%)	6 (11.1%)	12 (10.3%)	2 (3.5%)	3 (2.5%)
≥70 years	475 (11.1%)	15 (4.3%)	1 (1.9%)	6 (5.1%)	6 (10.5%)	2 (1.7%)
missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Sex (female) n%	2580 (60.1%)	216 (62.2%)	34 (63.0%)	74 (63.2%)	36 (63.2%)	72 (60.5%)
BMI (median, IQR) kg/m^2	25.4 [22.9, 28.9]	25.5 [23.1, 29.5]	24.5 [22.4, 28.2]	26.0 [23.4, 29.8]	25.1 [22.9, 27.9]	25.6 [23.4, 29.1]
Ethnicity						
White	3969 (92.5%)	321 (92.5%)	50 (92.6%)	109 (93.2%)	55 (96.5%)	107 (89.9%)
Black	17 (0.4%)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)
Asian	202 (4.7%)	21 (6.1%)	4 (7.4%)	6 (5.1%)	1 (1.8%)	10 (8.4%)
Mixed	67 (1.6%)	2 (0.6%)	0 (0.0%)	1 (0.9%)	1 (1.8%)	0 (0.0%)
Other	35 (0.8%)	2 (0.6%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (0.8%)
missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Health and social care setting workers n%	2849 (66.4%)	258 (74.4%)	37 (68.5%)	90 (76.9%)	38 (66.7%)	93 (78.2%)
Co-morbidities						
Cardiovascular disease	515 (12.0%)	27 (7.8%)	3 (5.6%)	10 (8.5%)	3 (5.3%)	11 (9.2%)
Respiratory disease	538 (12.5%)	42 (12.1%)	8 (14.8%)	19 (16.2%)	4 (7.0%)	11 (9.2%)
Diabetes	88 (2.1%)	6 (1.7%)	1 (1.9%)	2 (1.7%)	0 (0.0%)	3 (2.5%)
Prime-boost interval						
<6 weeks	872 (20.3%)	42 (12.1%)	7 (13.0%)	16 (13.7%)	11 (19.3%)	8 (6.7%)
6-8 weeks	497 (11.6%)	28 (8.1%)	2 (3.7%)	11 (9.4%)	5 (8.8%)	10 (8.4%)
9-11 weeks	1295 (30.2%)	123 (35.4%)	25 (46.3%)	31 (26.5%)	16 (28.1%)	51 (42.9%)
≥12 weeks	1626 (37.9%)	154 (44.4%)	20 (37.0%)	59 (50.4%)	25 (43.9%)	50 (42.0%)

Table S2 Vaccine efficacy against B.1.1.7 and non- B.1.1.7 lineages for SD/SD and LD/SD seronegative participants

Variant		N (%)	ChAdOx1 nCoV-19	Control	VE 95% CI
Primary Symptomatic COVID-19					
B.1.1.7	SD/SD	36 (69%)	9/2857	27/2904	66.7% (29.2%, 84.3%)
	LD/SD	16 (31%)	3/1387	13/1386	77.9% (22.5%, 93.7%)
Other variants	SD/SD	61 (64%)	11/2857	50/2904	78.0% (57.7%, 88.5%)
	LD/SD	34 (36%)	4/1387	30/1386	87.2% (63.7%, 95.5%)
No sequence result*	SD/SD	22 (73%)	5/2857	17/2904	70.6% (20.3%, 89.1%)
	LD/SD	8 (27%)	0/1387	8/1386	N/a
Not sequenced**	SD/SD	57 (62%)	18/2857	39/2904	53.8% (19.3%, 73.6%)
	LD/SD	35 (38%)	9/1387	26/1386	66.8% (29.2%, 84.5%)
Asymptomatic/Unknown infections					
B.1.1.7	SD/SD	9 (47%)	5/2857	4/2904	-25.0% (-365.2%, 66.4%)
	LD/SD	10 (53%)	3/1387	7/1386	58.9% (-58.6%, 89.4%)
Other variants	SD/SD	23 (68%)	5/2857	18/2904	72.2% (25.2%, 89.7%)
	LD/SD	11 (32%)	3/1387	8/1386	64.1% (-35.4%, 90.5%)
No sequence result*	SD/SD	45 (70%)	27/2857	18/2904	-50.0% (-172.1%, 17.3%)
	LD/SD	19 (30%)	9/1387	10/1386	13.7% (-112.1%, 64.9%)
Not sequenced**	SD/SD	62 (67%)	35/2857	27/2904	-29.6% (-114.3%, 21.6%)
	LD/SD	30 (33%)	10/1387	20/1386	52.1% (-2.4%, 77.6%)
Any PCR+					
B.1.1.7	SD/SD	47 (63%)	15/2857	32/2904	53.1% (13.6%, 74.6%)
	LD/SD	28 (37%)	6/1387	22/1386	73.9% (35.7%, 89.4%)
Other variants	SD/SD	94 (65%)	19/2857	75/2904	74.7% (58.1%, 84.7%)
	LD/SD	50 (35%)	8/1387	42/1386	81.7% (61.1%, 91.4%)
No sequence result*	SD/SD	73 (72%)	35/2857	38/2904	7.9% (-45.7%, 41.7%)
	LD/SD	28 (28%)	9/1387	19/1386	54.6% (-0.2%, 79.4%)
Not sequenced**	SD/SD	130 (65%)	60/2857	70/2904	14.3% (-21.1%, 39.3%)
	LD/SD	70 (35%)	21/1387	49/1386	58.9% (31.5%, 75.4%)

Table S3 Summary statistics for Ct values from Lighthouse laboratory NAAT assays

		ChAdOx1 nCoV-19					Control					P value*
Outcome	**Variant**	**N**	**Mean**	**Median**	**Q1**	**Q3**	**N**	**Mean**	**Median**	**Q1**	**Q3**	
Primary	**B.1.1.7**	10	18.0	17.4	15.3	20.2	38	17.9	15.8	14.1	19.5	
	Non-B.1.1.7	15	21.7	22.5	16.1	24.3	71	19.1	17.6	14.9	23.4	
	No result	5	28.2	30.7	24.0	33.5	25	22.0	19.6	16.2	29.5	
	Not sequenced	19	22.3	20.6	15.0	30.3	35	21.9	20.8	16.1	26.7	
	All	**49**	**21.9**	**20.6**	**15.4**	**24.5**	**169**	**19.8**	**17.9**	**15.0**	**25.1**	**0.0726**
Asymptomatic/ Unknown	**B.1.1.7**	8	22.6	20.5	17.8	27.5	11	17.3	13.7	11.7	16.7	
	Non-B.1.1.7	8	28.5	29.5	23.7	34.2	25	22.5	20.7	18.3	27.9	
	No result	36	30.9	32.6	29.9	34.5	28	29.8	32.3	27.2	34.3	
	Not sequenced	41	28.7	29.5	24.9	33.2	41	27.5	30.1	22.1	31.6	
	All	**93**	**29.0**	**30.3**	**24.9**	**34.1**	**105**	**25.9**	**28.3**	**19.5**	**32.6**	**0.0045**
B.1.1.7	**All†**	**18**	**20.1**	**19.3**	**15.4**	**22.0**	**49**	**17.8**	**15.2**	**13.0**	**19.3**	**0.0256**
Non-B.1.1.7	**All†**	**23**	**24.2**	**24.1**	**17.6**	**29.6**	**96**	**20.0**	**18.4**	**15.0**	**25.1**	**0.0167**
All	**All†**	**142**	**26.6**	**28.8**	**20.5**	**33.5**	**274**	**22.1**	**20.2**	**15.5**	**29.6**	**<0.0001**

*P values from Wilcoxon Rank Sum test comparing ChAdOx1 nCoV-19 with Control. Wilcoxon Rank Sum test: primary symptomatic cases vs asymptomatic cases: p<0.0001, B.1.1.7 cases vs non-B.1.1.7 p=0.0087. † includes only primary symptomatic cases, asymptomatic cases and cases where symptoms were unknown. Non-primary symptomatic cases (those with other symptoms such as nausea or diarrhoea) are excluded.

Table S4 Summary statistics of the number of weeks of the NAAT-positive period per participant

	Arm	No. of positive participants	N(%) returning only one positive swab	Median	Q1	Q2	P value*
Asymptomatic/Unknown	ChAdOx1 nCoV-19	97	87 (90)	1.0	1.0	1.0	
	Control	112	82 (73)	1.0	1.0	1.0	
	Overall	**209**	**169 (81)**	**1.0**	**1.0**	**1.0**	**0.0484**
Primary symptomatic	ChAdOx1 nCoV-19	59	20 (34)	1.0	1.0	2.0	
	Control	210	36 (17)	2.0	1.0	3.0	
	Overall	**269**	**56 (21)**	**2.0**	**1.0**	**3.0**	**0.0010**
Asymptomatic/Unknown/Primary symptomatic†							
B.1.1.7	ChAdOx1 nCoV-19	20	9 (45)	1.0	1.0	3.0	
	Control	51	8 (16)	2.0	1.0	4.0	
	Overall	**71**	**17 (24)**	**2.0**	**1.0**	**4.0**	**0.0493**
Non-B.1.1.7	ChAdOx1 nCoV-19	23	8 (35)	1.0	1.0	1.5	
	Control	106	19 (18)	2.0	1.0	4.0	
	Overall	**129**	**27 (21)**	**2.0**	**1.0**	**3.0**	**0.0006**
Not sequenced	ChAdOx1 nCoV-19	72	56 (78)	1.0	1.0	1.0	
	Control	112	64 (57)	1.0	1.0	1.0	
	Overall	**184**	**120 (65)**	**1.0**	**1.0**	**1.0**	**0.4506**

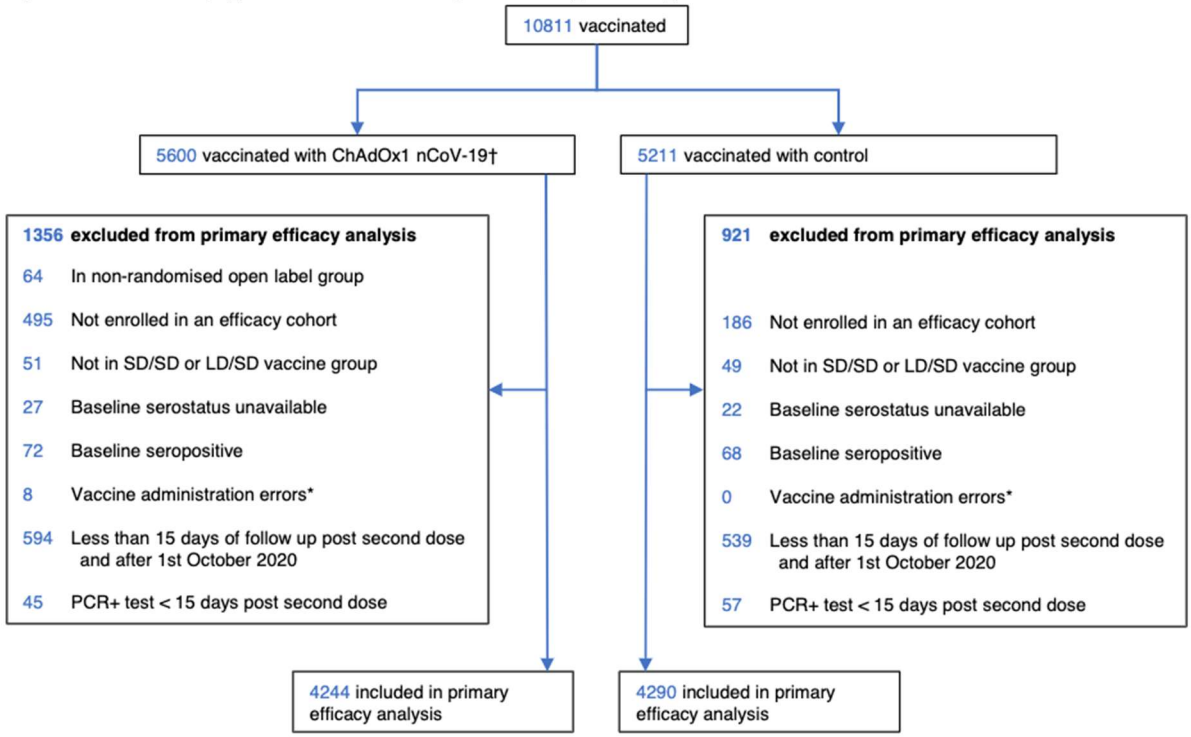
*P values from Wilcoxon Rank Sum test comparing ChAdOx1 nCoV-19 with Control. Wilcoxon Rank Sum test: primary symptomatic cases vs asymptomatic cases: $p<0.0001$, B.1.1.7 cases vs non-B.1.1.7 $p=0.8516$, ChAdOx1 nCoV-19 vs Control (all Asymptomatic/Unknown/Primary symptomatic) $p<0.0001$. † includes only primary symptomatic cases, asymptomatic cases and cases where symptoms were unknown. Unknown swabs are included as asymptomatic. Non-primary symptomatic cases (those with other symptoms such as nausea or diarrhoea) are excluded.

Table S5 Prior ChAdox1 recipients

Vaccine Administered	Interval between 1st dose of prior ChadOx1 and ChadOx1-nCov19 (months)	Interval between 2nd dose of prior ChadOx1 and ChadOx1-nCov19 (months)
ChAdOx1 MERS	28	N/A
ChAdOx1 MERS	28	N/A
ChAdOx1 MERS	29	N/A
ChAdOx1 MenB.1	25	13
ChAdOx1 MenB.1	26	N/A
ChAdOx1 MenB.1	13	19
ChAdOx1 MenB.1	26	N/A
ChAdOx1 MenB.1	29	N/A
ChAdOx1 MenB.1	26	N/A
ChAdOx1 MenB.1	26	N/A

ChAdOx1 MERS vaccine contained either $5x10^9$ or $5x10^{10}$ virus particles (vp) of a ChAdox1 vector with a sequence encoding Middle East respiratory syndrome (MERS) coronavirus spike protein. ChAdOx1-MenB.1 vaccine contained $5x10^{10}$ vp of a ChAdOx1 vector with a sequence encoding a meningococcal capsular group B surface antigen.

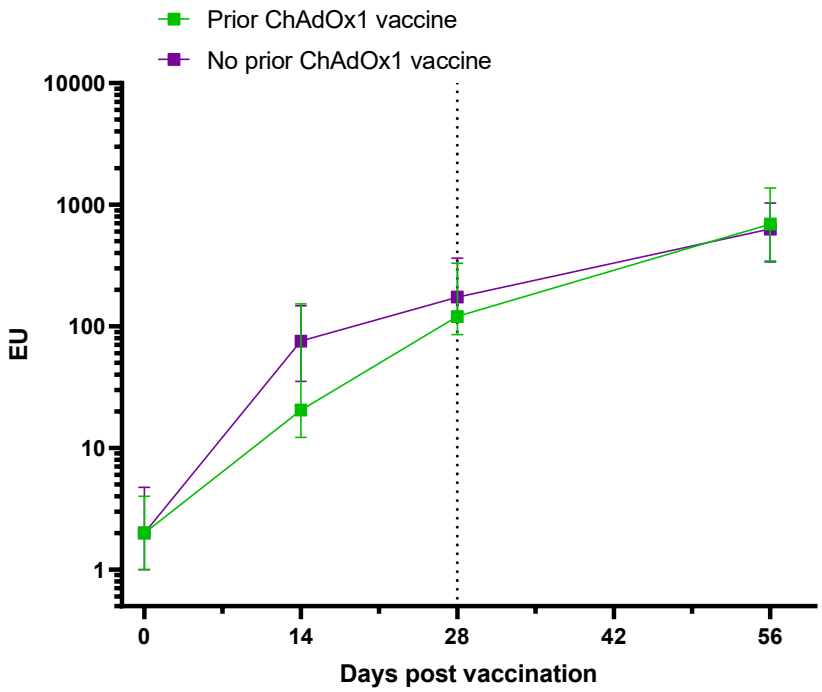
Figure S1. Study profile indicating flow of participants in the COV002 trial



† Includes all participants who received at least a single dose of ChAdOx1 nCoV-19

*Participants who received a different vaccine for their first and second dose. Five participants received a ChAdOx1 nCoV-19 vaccine for their first dose and MenACWY for their second dose, and three received MenACWY for their first dose and ChAdOx1 nCoV-19 for their second dose.

Figure S2. Effect of receipt of a different prior ChAdOx1 vaccine on anti-spike IgG titres by standardised ELISA



SARS-CoV-2 IgG responses to trimeric spike protein in individuals who had (n=10) and had not (n=48) previously received a ChAdOx1-vectored vaccine. Datapoints are medians with whiskers showing the IQR. All participants received 2 standard doses of ChAdOx1 nCoV-19 at D0 and D28 as indicated by the vertical black line. EU = ELISA units. Data for ChAdOx1 naïve recipients published previously. [34]

Table S6 Summary statistics for anti-spike IgG by standardised ELISA in participants with and without prior ChAdOx1 vaccination

Day	Prior ChAdOx1 Vaccine			No Prior ChAdOx1 Vaccine			
	N	Median [IQR]	GMT (95% CI)	N	Median [IQR]	GMT (95% CI)	p value*
D0	10	2 [1, 4]	1.966 (1.16, 3.333)	48	2 [1, 4.75]	2.532 (1.717, 3.735)	
D14	10	20.5 [12.25, 153]	32.81 (11.36, 94.8)	48	75.5 [35.25, 147.8]	70.51 (47.25, 105.2)	0.133
D28 (B)	10	120.5 [85.5, 331.5]	132.1 (54.55, 319.9)	48	174 [129.5, 364.3]	214.1 (156.3, 293.4)	0.099
D56	10	692.5 [344, 1375]	679.5 (399.4, 1156)	47	631 [338, 1037]	616.5 (478.2, 794.9)	0.684

*Wilcoxon Rank Sum Test. (B) day of boost.

Statistical Models

SAS code for robust Poisson model

```
* model;
proc genmod data=dataset;
      class vaccine_group (param=ref ref='Control') agegroup ldsd subject_id;
      model outcome = group agegroup ldsd / dist=poisson link=log alpha=0.05 offset=log_futime;
      repeated subject= subject_id / type=unstr;
      ods output GEEEmpPEst=temp1;
run;

* calculate rr and confidence interval;
data temp2;
      set temp1;
      rr=exp(Estimate);
      rr_lci=exp(LowerCL);
      rr_uci=exp(UpperCL);
      ve=(1-rr)*100;
      ve_uci=(1-rr_lci)*100;
      ve_lci=(1-rr_uci)*100;
run;
```

Sequencing Methods

Unique dual indexed (UDI) libraries were constructed using the SMARTer Stranded Total RNA-Seq Kit v2—Pico Input Mammalian (Takara Bio USA, California, USA) with no RNA fragmentation. An equal volume of library from each sample was pooled for capture, and size-selected to exclude fragments shorter than 400nt. Target enrichment of SARS-CoV-2 was carried out with a custom xGen Lockdown Probes panel (IDT, Coralville, USA), using the SeqCap EZ Accessory Kits v2 and SeqCap Hybridization and Wash Kit (Roche, Madison, USA) for hybridization of the probes and removal of unbound DNA. Following 12 cycles of PCR for post-capture amplification, the final product was purified using Agencourt AMPure XP (Beckman Coulter, California, USA). Sequencing was performed on the Illumina NovaSeq (Illumina, California, USA) at the Oxford Genomics Centre (OGC), generating 250bp paired-end reads. Each sequencing batch of up to 96 samples included a non-SARS-CoV-2 in-run control (purified *in vitro* transcribed HIV RNA from clone p92BR025.8, obtained from the National Institute for Biological Standards and Control (NIBSC)), as well as positive and negative quantification controls consisting of in vitro transcribed SARS-CoV-2 RNA (Twist Synthetic SARS-CoV-2 RNA Control 1 (MT007544.1), Twist Bioscience) diluted into Universal Human Reference RNA (UHRR) to a final concentration of SARS-CoV-2 RNA of 500,000, 50,000, and 0 copies/reaction. Controls were checked to ensure no evidence of amplification in the negatives and expected RNA quantification consistent with Ct values provided by the testing laboratories.

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Laura Thomson

Acknowledgements

Advent, South Africa
Michael Breese
Aneurin Bevan University Health Board
Catherine Bailey
Jessica Harris
BioIndustry Association
Annette England
Ian McCubbin
Cell & Gene Therapy Catapult
Stephen Ward
CobraBio
Clinical Trials Research Governance Office, University of Oxford
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The Cambridge NIHR CRF COVID Vaccine Group
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The Imperial CRF COVID Vaccine Group
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Philip Taylor
Oto Velicka
Oxford Biomedica
Oxford Research Services (Contracts)
Carly Banner
Sally Pelling-Deeves
Gary Priest
Oxford University Hospitals NHS Trust
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