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Supplemental information

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do adenovirus-vector vaccines have beneficial non-specific effects?

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Table S1. Background information about included RCTs, Related to tables 1 and 2.

	Pfizer [1]	**Moderna** [2]	**CVnCoV** [3]	**AZ US/Chile/Peru** [4]	**AZ South Africa** [5,6]	**AZ UK/Brazil** [7]	**Johnson&Johnson** [8]	**Gam-COVID-Vac** [9]	**Ad5-nCoV** [10]
Trial registration number	NCT04368728	NCT04470427	NCT04652102	NCT04516746	NCT04444674	ISRCTN89951424 NCT04324606 NCT04400838	NCT04505722	NCT04530396	NCT04526990
N	44,165	30,415	39,680	32,451	2021	22119	39,321	21,977	36,717
Vaccine	mRNA	mRNA	mRNA	Chimpanzee Adenovirus Y25	Chimpanzee Adenovirus Y25	Chimpanzee Adenovirus Y25	Human Adenovirus 26	Human Adenovirus 26 and 5	Human Adenovirus 5
No of doses	2	2	2	2	2	2	1	2	1
Phase	2/3	3	2b/3	3	1/2	1/2/3	3	3	3
Randomization ratio	1:1	1:1	1:1	2:1	1:1	1:1	1:1	3:1	1:1
Intervention	BNT162b2	mRNA-1273	CVnCoV	AZD1222	AZD1222	AZD1222	Ad26.COV2.S	Gam-COVID-Vac	Ad5-nCoV
Control group	Saline	Placebo[b]	Saline	Saline	Saline	Control vaccine (MenACWY)	Saline	Vaccine buffer	Vaccine buffer
Vaccine efficacy[a]	91% (89-93%)	93% (91-95%)	48% (31-61%)	74% (65-81%)	22% (-50-60%)	67% (57-74%)	67% (59-73%)	92% (86-95%)	58% (40-70%)
Age enrolled (years)	16+	18+	18+	18+	18-65	18+	18+	18+	18+
Male %	51	53	55	56	57	42	55	61	71
Age (mean or median (range))	51 (16-91)	51 (18-95)	43 (IQR 31-54)	50 (18-100)	30 (18-64)	83%<55years	52 (18-100)	45 (SD 12)	38 (18-94)
Geographical location	US, Argentina, Brazil, South Africa, Germany, Turkey	US	Belgium, Germany, Netherlands, Spain, Argentina, Colombia, Dominican	US, Chile, Peru	South Africa	UK, Brazil	US, Argentina, Brazil, Chile, Colombia, Mexico, Peru, South Africa	Russia	Argentina, Chile, Mexico, Pakistan, Russia

			Republic, Mexico, Panama, Peru						
Proportion recruited in the US	76%	100%	0%	89%	0%	0%	44%	0%	0%
Enrolment period and data cut-off	July 27, to Oct 29, 2020 Data cut-off March 13, 2021	July 27 to Oct 23, 2020 Data cut-off March 26, 2021	Dec 11, 2020 to April 12, 2021 Data cut-off June 18, 2021	Aug 28, 2020, to Jan 15, 2021 Data cut-off March 5,2021	June 24 and Nov 9, 2020	April 23 and Dec 6, 2020 Data cut-off Dec 6, 2020	Sept 21, 2020, to Jan 22, 2021 Data cut-off Jan 22, 2021	Sept 7 to Nov 24, 2020 Data cut-off Nov 24, 2020	Sept 22, 2020 to Jan 15, 2021 Data cut-off Jan 15, 2021
Duration of follow-up	Mean follow-up from 7 days after 2nd dose: 108 days	Median follow-up from 1st dose: 5.3 months	Mean follow-up from 15 days after 2nd dose: 48 days	Median follow-up from 2nd dose: 61 days	Median follow-up from 1st dose: 156 days	Mean follow-up from 1st dose: 4.2 months	Median follow-up: 58 days	Median follow-up from 1st dose: 48 days	Median follow-up from 28 days post-vaccination: 45 days
Follow-up days in control group	2,937,414	2,441,082	N/A	960,488	157,560	1,384,427	1,269,504	260,880	N/A
COVID-19 infection in control group	4.1% (850/20713)	5.3% (744/14164)	1.2% (145/12211)	1.5% (130/8550)	3.2% (23/717)	2.9% (248/8581)	1.8% (348/19544)	1.3% (62/4902)	1.5% (211/14586)
Cardiovascular deaths: % of all deaths	52% (15/29)	38% (12/32)	No information	14% (2/14)	0%	0%	11% (2/19)	25% (1/4)	No information
COVID-19 death: % of all deaths	10% (3/29)	13% (4/32)	No information	14% (2/14)	0%	20% (1/5)	26% (5/19)	50% (2/4)	No information

a.The calculations of vaccine efficacy differ with respect to the number of days after vaccination that observation is started

b.no information on preparation

Table S2. The rate of causes of death per 10,000 person-years (pyrs) in the control groups by type of vaccine, Related to Tables 1 and 2

Cause of death	Rate deaths per 10,000 pyrs (number of deaths/pyrs) in the control group		Relative risk (95% CI) mRNA vs Adenovirus-vector vaccine in the control group
	mRNA RCTs: 14,725.5 pyrs	Adenovirus-vector RCTs: 11,041 pyrs	
COVID-19 deaths	3.4 (5/14726)	7.2 (8/11041)	0.47 (0.15-1.43)
Accidents	1.4 (2/14726)	5.4 (6/11041)	0.25 (0.05-1.24)
Non-accident, non-COVID-19 deaths	15.6 (23/14726)	14.5 (16/11041)	1.08 (0.57-2.04)
Overall mortality	20.4 (30/14726)	27.2 (30/11041)	0.75 (0.45-1.24)

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