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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: Krause PR, Fleming TR, Peto R, et al. Considerations in boosting COVID-19 vaccine immune responses. *Lancet* 2021; published online Sept 13. http://dx.doi.org/10.1016/S0140-6736(21)02046-8.

Supplementary Material

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Supplement to **Considerations in boosting COVID vaccine immune responses**
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Search strategy and selection criteria

We searched studies reported in English that described an effort to account for confounding variables and reported efficacy or effectiveness of a complete vaccination series against viral variants, or in a time-dependent manner.

We specifically considered all studies indexed by the COVID-NMA initiative[1], all studies identified by experts and co-authors tasked with summarizing these data at a WHO meeting on August 13, 2021[2], and all studies referenced by the US Centers for Disease Control in presentations to the Advisory Committee on Immunization Practices on August 13, 2021 and August 30, 2021[3]. In addition, we searched Pubmed, medRxiv and SSRN preprint databases for the terms “COVID vaccine variant efficacy” and “COVID vaccine variant effectiveness”.

Of the identified studies, we excluded preprints published before June 1, 2021 (allowing >3 months for these studies to be peer reviewed and published), and articles that made no clear mention of prevalent variants at the time of the study.

Statistical methods

For a given set of vaccine efficacy values, each with its variance estimated from its cited 95% confidence interval, the inverse-variance-weighted average the vaccine efficacy values was calculated either by the fixed-effect method (ignoring any between-study variation) or by the DerSimonian-Laird random effect method (which gives similar point estimates but ascribes wider confidence interval to the weighted average).

Both inverse-variance-weighted averages are provided in the supplementary tables, but only the former is plotted in the Figure.

[1] Boutron I, Chaimani A, Meerpohl JJ, et al. The COVID-NMA Project: Building an Evidence Ecosystem for the COVID-19 Pandemic. *Ann Intern Med* 2020; **173**(12): 1015-7.
[2] World Health Organization. Considerations in boosting COVID vaccine immune responses: WHO consultation on COVID-19 vaccines research- 13 August 2021. 2010. https://www.who.int/news-room/events/detail/2021/08/13/default-calendar/who-consultation-on-covid-19-vaccines-research-13-august-2021.
[3] Centers for Disease Control and Prevention. ACIP Meeting Information: August 13, 2021. 2021. https://www.cdc.gov/vaccines/acip/meetings/index.html.

Table S1. Studies reporting vaccine efficacy against any infection (50% to <80%, 80% to <90%, ≥ 90%)

Group	Vaccine	Study Location (reference)	Variant	Effectiveness vs. severe disease or hospitalization	Lower limit of 95% CI	Upper limit of 95% CI	Effectiveness vs. symptomatic disease or infection	Lower limit of 95% CI	Upper limit of 95% CI
1	BBV152	India [1] [2]	All	93.4	57.1	99.8	77.8	65.2	86.4
1	BNT162b2	Qatar [3]	Beta	100	73.7	100	75	70.5	78.9
1	BNT162b2	Qatar [4]	Delta	89.7	61	98.1	53.5	43.9	61.4
1	BNT162b2	Israel [5]	Mostly Delta	91.4	82.5	95.7	40.5	8.7	61.2
1	BNT162b2	France [6]	Beta	86	67	94	49	14	69
1	ChadOx1nCoV-19	UK [7], [8]	Delta	92	75	97	67	61	72
1	BNT162b2 or mRNA-1273	USA [9]	Epsilon	90	89	92	73	72	74
1	BNT162b2 or mRNA-1273	USA [9]	Delta	93	84	96	75	71	78
1	BNT162b2 or mRNA-1273	Finland [10]	Beta	93	70	98	75	65	82
1	BNT162b2 or mRNA-1273	USA [11]	B.1.427/ 429 & Alpha	100	NA	NA	68.3	27.9	85.7
1	mRNA-1273	Canada [12]	Gamma	79	48	91	66	34	82
1	Ad26.COV2.S	Worldwide [13]	All	83.5	54.2	96.9	66.5	55.5	75.1
1	Ad26.COV2.S	Worldwide [13]	Beta	81.7	46.2	95.4	64	41.2	78.7
1	ChadOx1nCoV-19	Canada [14]	Alpha	85	81	88	64	60	68
1	ChadOx1nCoV-19	Canada [14]	Beta/ Gamma	83	66	92	48	28	63
1	ChadOx1nCoV-19	Canada [14]	Delta	88	60	96	67	44	80
1	ChadOx1nCoV-19	India [15]	Mostly Delta	95	44	100	64	38	78
1	ChadOx1nCoV-19	India [16]	Mostly Delta	81.5	10	99	63.1	52	72
1	ChadOx1nCoV-19	UK [8]	Alpha	86	53	96	74	68	79
1	ChadOx1nCoV-19	UK [8]	Delta	92	75	97	67	61	72
1	ChadOx1nCoV-19	Brazil [17]	Gamma	87.6	78.2	92.9	77.9	69.2	84.2
1	Coronavac	China [18]	Delta	100	NA	NA	59	16	81.6
1	Coronavac	Brazil [19]	Gamma	56	47	63	47	39	54
1	Coronavac	Brazil [20]	Gamma	59	44	70	42	27	53
1	Coronavac	Chile [21]	Alpha/Gamma	86.3	84.5	87.9	66	65	67
1	Inactivated vaccines*	Singapore [22]	Delta	100	NA	NA	69.5	42.8	96.3
	Weighted mean (fixed)			**87.74**	**86.75**	**88.73**	**69.35**	**68.71**	**69.99**
	Weighted mean (random)			**86.24**	**82.94**	**89.53**	**66.42**	**63.47**	**69.37**
2	BNT162b2	Qatar [3]	Alpha	100	81.7	100	89.5	85.9	92.3
2	BNT162b2	Canada [23]	Alpha	95	92	97	89	86	91
2	BNT162b2	Canada [14]	Beta/Gamma	95	81	99	84	69	92
2	BNT162b2	UK [8]	Delta	96	86	99	88	85	90
2	BNT162b2	Denmark [24]	Original and Alpha	94	90	96	82	79	84
2	BNT162b2 or mRNA-1273	Canada [25]	Beta/Gamma	100	NA	NA	88	61	96
2	BNT162b2	UK [8]	Delta	96	86	99	88	85	99
2	ChadOx1nCoV-19	UK [8]	Alpha	86	53	96	88	85	99
2	ChadOx1nCoV-19	Denmark [26]	Alpha	100	NA	NA	88	83	92
2	mRNA-1273	USA [27]	Mostly Delta	96	91	98	88.3	86	90
2	mRNA-1273	Qatar [28]	Delta	100	41.2	100	84.8	75.9	90.8
2	ChadOx1nCoV-19	UK [29]	Alpha	94	81	98	82	78	85
2	Covishield & Covaxin	India [30]	Delta	88	55	97	83	73	89
	Weighted mean (fixed)			**95.60**	**94.18**	**97.02**	**86.82**	**85.84**	**87.80**
	Weighted mean (random)			**95.60**	**94.18**	**97.02**	**86.56**	**84.69**	**88.42**
3	BNT162b2	Israel [31]	Mostly Alpha	97.5	97.1	97.8	95.3	94.9	95.7
3	BNT162b2	Israel [32]	Alpha	92	75	100	94	87	98
3	BNT162b2	UK [8]	Alpha	95	78	99	94	92	95
3	BNT162b2	Israel [33]	Alpha	94	94	95	93	92.5	93.4
3	BNT162b2	Israel [34]	Alpha	88	80	95	90	84	94
3	BNT162b2	UK [29]	Alpha	98	96	99	94	92	95
3	BNT162b2	Italy [35]	Original and Alpha	98	87	100	98	97	99
3	BNT162b2 or mRNA-1273	Canada [25]	Alpha	94	59	99	90	85	94
3	BNT162b2	UK [8]	Alpha	95	78	99	94	92	95
3	BNT162b2 or mRNA-1273	USA [36]	Alpha	100	97	100	97	97	98
3	BNT162b2	Israel [37]	Alpha	93	92	95	93	93	93
3	BNT162b2 or mRNA-1273	USA [38]	Alpha	89	81	93	91	87	93
3	mRNA-1273	Canada [14]	Alpha	94	89	97	92	86	96
3	mRNA-1273	USA [39]	All	98.2	92.8	99.6	93.2	90	94.8
3	NVX-CoV2373	UK [40]	Mostly Alpha	100	87	100	90.4	82.9	94.6
	Weighted mean (fixed)			**96.39**	**96.12**	**96.66**	**95.01**	**94.77**	**95.24**
	Weighted mean (random)			**95.83**	**94.14**	**97.53**	**93.97**	**92.77**	**95.17**

Table S2. Studies reporting vaccine efficacy against four main variants

Vaccine	Study Location (reference)	Variant	Effectiveness vs. severe disease or hospitalization	Lower limit of 95% CI	Upper limit of 95% CI	Effectiveness vs. symptomatic disease or infection	Lower limit of 95% CI	Upper limit of 95% CI
BNT162b2	Qatar [3]	Alpha	100	81.7	100	89.5	85.9	92.3
BNT162b2	Canada [14]	Alpha	95	92	97	89	86	91
BNT162b2	Israel [31]	Mostly Alpha	97.5	97.1	97.8	95.3	94.9	95.7
BNT162b2	Israel [32]	Alpha	92	75	100	94	87	98
BNT162b2	UK [8]	Alpha	95	78	99	94	92	95
BNT162b2	Israel [33]	Alpha	94	94	95	93	92.5	93.4
BNT162b2	Israel [34]	Alpha	88	80	95	90	84	94
BNT162b2	UK [29]	Alpha	98	96	99	94	92	95
BNT162b2	Italy [35]	Original and Alpha	98	87	100	98	97	99
BNT162b2	Denmark [24]	Original and Alpha	94	90	96	82	79	84
BNT162b2 or mRNA-1273	Canada [25]	Alpha	94	59	99	90	85	94
BNT162b2 or mRNA-1273	USA [11]	B.1.427/ 429 & Alpha	100	NA	NA	68.3	27.9	85.7
BNT162b2	UK [8]	Alpha	95	78	99	94	92	95
ChadOx1nCoV-19	UK [8]	Alpha	86	53	96	88	85	99
BNT162b2 or mRNA-1273	USA [9]	Epsilon/Alpha	90	89	92	73	72	74
BNT162b2 or mRNA-1273	USA [36]	Alpha	100	97	100	97	97	98
BNT162b2	Israel [37]	Alpha	93	92	95	93	93	93
BNT162b2 or mRNA-1273	USA [38]	Alpha	89	81	93	91	87	93
ChadOx1nCoV-19	Denmark [26]	Alpha	100	NA	NA	88	83	92
mRNA-1273	Canada [14]	Alpha	94	89	97	92	86	96
ChadOx1nCoV-19	Canada [14]	Alpha	85	81	88	64	60	68
ChadOx1nCoV-19	UK [8]	Alpha	86	53	96	74	68	79
ChadOx1nCoV-19	UK[29]	Alpha	94	81	98	82	78	85
NVX-CoV2373	UK [40]	Mostly Alpha	100	87	100	90.4	82.9	94.6
Coronavac	Chile [21]	Alpha/Gamma	86.3	84.5	87.9	66	65	67
Weighted mean (fixed)			**95.87**	**95.61**	**96.13**	**92.15**	**91.93**	**92.38**
Weighted mean (random)			**93.99**	**92.25**	**95.72**	**87.30**	**83.63**	**90.97**
BNT162b2	Qatar [3]	Beta	100	73.7	100	75	70.5	78.9
BNT162b2	France [6]	Beta	86	67	94	49	14	69
BNT162b2 or mRNA-1273	Finland [10]	Beta	93	70	98	75	65	82
Ad26.COV2.S	Worldwide [13]	Beta	81.7	46.2	95.4	64	41.2	78.7
Weighted mean (fixed)			**92.08**	**84.63**	**99.53**	**74.12**	**70.46**	**77.78**
Weighted mean (random)			**92.08**	**84.63**	**99.53**	**72.71**	**66.49**	**78.92**
BNT162b2	Israel [5]	Mostly Delta	91.4	82.5	95.7	40.5	8.7	61.2
mRNA-1273	USA [27]	Mostly Delta	96	91	98	88.3	86	90
ChadOx1nCoV-19	India [15]	Mostly Delta	95	44	100	64	38	78
ChadOx1nCoV-19	India [16]	Mostly Delta	81.5	10	99	63.1	52	72
BNT162b2	Qatar [28]	Delta	89.7	61	98.1	53.5	43.9	61.4
BNT162b2	UK [8]	Delta	96	86	99	88	85	90
BNT162b2 or mRNA-1273	USA [9]	Delta	93	84	96	75	71	78
mRNA-1273	Qatar [28]	Delta	100	41.2	100	84.8	75.9	90.8
ChadOx1nCoV-19	UK [8]	Delta	92	75	97	67	61	72
ChadOx1nCoV-19	Canada [14]*	Delta	88	60	96	67	44	80
ChadOx1nCoV-19	UK [8]	Delta	92	75	97	67	61	72
Coronavac and China NationalBiotec	China [18]	Delta	100	NA	NA	59	16	81.6
Inactivated vaccines*	Singapore [22]	Delta	100	NA	NA	69.5	42.8	96.3
Covishield & Covaxin	India [30]	Delta	88	55	97	83	73	89
Weighted mean (fixed)			**94.52**	**92.33**	**96.70**	**82.63**	**81.39**	**83.88**
Weighted mean (random)			**94.52**	**92.33**	**96.70**	**73.38**	**67.42**	**79.34**
BNT162b2	Canada [14]	Beta/Gamma	95	81	99	84	69	92
BNT162b2 or mRNA-1273	Canada [25]	Beta/Gamma	100	NA	NA	88	61	96
mRNA-1273	Canada [12]	Gamma	79	48	91	66	34	82
ChadOx1nCoV-19	Canada [14]*	Beta/Gamma	83	66	92	48	28	63
ChadOx1nCoV-19	Brazil [17]	Gamma	87.6	78.2	92.9	77.9	69.2	84.2
Coronavac	Brazil [19]	Gamma	56	47	63	47	39	54
Coronavac	Brazil [19]	Gamma	59	44	70	42	27	53
Weighted mean (fixed)			**78.55**	**74.59**	**82.51**	**63.92**	**59.74**	**68.10**
Weighted mean (random)			**79.66**	**65.94**	**93.37**	**64.60**	**49.63**	**79.57**

Table S3. Studies reporting vaccine efficacy by type of vaccine (viral vector, inactivated SARS-CoV-2, adjuvanted protein subunit, or mRNA).

Vaccine	Study Location (reference)	Variant	Effectiveness vs. severe disease or hospitalization	Lower limit of 95% CI	Upper limit of 95% CI	Effectiveness vs. symptomatic disease or infection	Lower limit of 95% CI	Upper limit of 95% CI
BNT162b2	Qatar [3]	Alpha	100	81.7	100	89.5	85.9	92.3
BNT162b2	Qatar [3]	Beta	100	73.7	100	75	70.5	78.9
BNT162b2	Qatar [28]	Delta	89.7	61	98.1	53.5	43.9	61.4
BNT162b2	Canada [14]	Alpha	95	92	97	89	86	91
BNT162b2	Canada [14]	Beta/Gamma	95	81	99	84	69	92
BNT162b2	Israel [31]	Mostly Alpha	97.5	97.1	97.8	95.3	94.9	95.7
BNT162b2	Israel [5]	Mostly Delta	91.4	82.5	95.7	40.5	8.7	61.2
BNT162b2	Israel [32]	Alpha	92	75	100	94	87	98
BNT162b2	UK [8]	Alpha	95	78	99	94	92	95
BNT162b2	UK [8]	Delta	96	86	99	88	85	90
BNT162b2	Israel [33]	Alpha	94	94	95	93	92.5	93.4
BNT162b2	Israel [34]	Alpha	88	80	95	90	84	94
BNT162b2	UK [29]	Alpha	98	96	99	94	92	95
BNT162b2	France [6]	Beta	86	67	94	49	14	69
BNT162b2	Italy [35]	Original and Alpha	98	87	100	98	97	99
BNT162b2	Denmark [24]	Original and Alpha	94	90	96	82	79	84
BNT162b2 or mRNA-1273	Canada [25]	Alpha	94	59	99	90	85	94
BNT162b2 or mRNA-1273	Canada [25]	Beta/Gamma	100	NA	NA	88	61	96
BNT162b2 or mRNA-1273	USA [11]	B.1.427/ 429 and Alpha	100	NA	NA	68.3	27.9	85.7
BNT162b2	UK [8]	Alpha	95	78	99	94	92	95
BNT162b2	UK [8]	Delta	96	86	99	88	85	99
BNT162b2 or mRNA-1273	USA [9]	Epsilon	90	89	92	73	72	74
BNT162b2 or mRNA-1273	USA [9]	Delta	93	84	96	75	71	78
BNT162b2 or mRNA-1273	USA [36]	Alpha	100	97	100	97	97	98
Pfizer BNT162b2	Israel [37]	Alpha	93	92	95	93	93	93
BNT162b2 or mRNA-1273	USA [38]	Alpha	89	81	93	91	87	93
BNT162b2 or mRNA-1273	Finland [10]	Beta	93	70	98	75	65	82
mRNA-1273	USA [27]	Mostly Delta	96	91	98	88.3	86	90
mRNA-1273	Canada [14]	Alpha	94	89	97	92	86	96
mRNA-1273	Qatar [28]	Delta	100	41.2	100	84.8	75.9	90.8
mRNA-1273	USA [39]	All	98.2	92.8	99.6	93.2	90	94.8
mRNA-1273	Canada [12]	Gamma	79	48	91	66	34	82
Weighted mean (fixed)			**96.14**	**95.88**	**96.40**	**93.39**	**93.16**	**93.61**
Weighted mean (random)			**94.88**	**93.49**	**96.27**	**86.84**	**84.38**	**89.31**
Bharat BBV152	India [1 2]	All	93.4	57.1	99.8	77.8	65.2	86.4
Coronavac	China [18]	Delta	100	NA	NA	59	16	81.6
Coronavac	Brazil [19]	Gamma	56	47	63	47	39	54
Coronavac	Brazil [17]	Gamma	59	44	70	42	27	53
Coronavac	Chile [21]	Alpha/Gamma	86.3	84.5	87.9	66	65	67
Inactivated vaccines*	Singapore [22]	Delta	100	NA	NA	69.5	42.8	96.3
Covishield & Covaxin	India [30]	Delta	88	55	97	83	73	89
Weighted mean (fixed)			**84.74**	**83.11**	**86.38**	**65.89**	**64.92**	**66.87**
Weighted mean (random)			**80.69**	**65.81**	**95.57**	**63.79**	**53.47**	**74.12**
ChadOx1nCoV-19	UK [8]	Alpha	86	53	96	88	85	99
ChadOx1nCoV-19	UK [8]	Delta	92	75	97	67	61	72
ChadOx1nCoV-19	Denmark [26]	Alpha	100	NA	NA	88	83	92
Ad26.COV2.S	Worldwide [13]	All	83.5	54.2	96.9	66.5	55.5	75.1
Ad26.COV2.S	Worldwide [13]	Beta	81.7	46.2	95.4	64	41.2	78.7
ChadOx1nCoV-19	Canada [14]*	Alpha	85	81	88	64	60	68
ChadOx1nCoV-19	Canada [14]*	Beta/Gamma	83	66	92	48	28	63
ChadOx1nCoV-19	Canada [14]*	Delta	88	60	96	67	44	80
ChadOx1nCoV-19	India [15]	Mostly Delta	95	44	100	64	38	78
ChadOx1nCoV-19	India [16]	Mostly Delta	81.5	10	99	63.1	52	72
ChadOx1nCoV-19	UK [8]	Alpha	86	53	96	74	68	79
ChadOx1nCoV-19	UK [8]	Delta	92	75	97	67	61	72
ChadOx1nCoV-19	UK [29]	Alpha	94	81	98	82	78	85
ChadOx1nCoV-19	Brazil [17]	Gamma	87.6	78.2	92.9	77.9	69.2	84.2
Weighted mean (fixed)			**90.20**	**87.95**	**92.44**	**74.73**	**73.07**	**76.39**
Weighted mean (random)			**89.87**	**85.30**	**94.43**	**71.47**	**65.73**	**77.20**
NVX-CoV2373	UK [40]	Mostly Alpha	100	87	100	90.4	82.9	94.6

*Only one dose of two dose series given

Table S4. Studies reporting vaccine efficacy early (more recently relative to vaccination) or later (less recently relative to vaccination) during the follow-up of the same observational study.

Period	Vaccine	Study Location (reference)	Time period of vaccination	Time period of assessment	Effectiveness vs. severe disease or hospitalization	Lower limit of 95% CI	Upper limit of 95% CI	Effectiveness vs. symptomatic disease or infection	Lower limit of 95% CI	Upper limit of 95% CI
Early	BNT162b2	USA Minnesota [41]	before July	Jan-July	85	73	93	76	69	81
Early	BNT162b2	Israel [5]	March	6/20-7/17/21	94	80	98	69	50	80
Early	BNT162b2	Israel [5]	April	6/20-7/17/21	84	24	96	79	61	88
Early	mRNA-1273	USA Minnesota [41]	before July	Jan-July	91.6	81	97	86	81	91
Early	BNT162b2; mRNA-1273; Ad26.COV2.S	USA New York [42]	before May	May	95.3	94.4	96	91.7	91	92.3
Early	BNT162b2	Israel [43]	Mar (40-59 y)	7/11-7/31/21	98	94	99	74	70	77
Early	BNT162b2	Israel [43]	Mar (60+ y)	7/11-7/31/21	91	85	95	72	70	77
Early	BNT162b2; mRNA-1273; Ad26.COV2.S	USA [42, 44]	Before June	April 4–June 19	92.5	91.2	93.6	91.0	87.2	93.7
	Weighted mean (fixed)				**94.55**	**93.92**	**95.18**	**90.24**	**89.63**	**90.85**
	Weighted mean (random)				**93.92**	**91.78**	**96.07**	**80.46**	**73.14**	**87.77**
Later	BNT162b2	USA Minnesota [41]	before July	July (>70% delta)	75	24	94	42	13	62
Later	BNT162b2	Israel [5]	Jan	6/20-7/17/21	86	70	93	16	-12	45
Later	BNT162b2	Israel [5]	Feb	6/20-7/17/21	91	78	96	44	13	63
Later	mRNA-1273	USA Minnesota [41]	Before July	July (>70% delta)	81	33	96	76	58	97
Later	BNT162b2; mRNA-1273; Ad26.COV2.S	USA New York [42]	Before June	June	93.3	91.6	94.6	89.7	88.4	90.8
Later	BNT162b2; mRNA-1273; Ad26.COV2.S	USA New York [42]	Before July	July (>70% delta)	94.4	92.7	95.7	82.4	81	83.7
Later	BNT162b2	Israel [43]	Jan (40-59 y)	7/11-7/31/21	94	87	97	58	54	62
Later	BNT162b2	Israel [43]	Jan (60+ y)	7/11-7/31/21	86	82	90	57	52	62
Later	BNT162b2	Israel [43]	Feb (40-59 y)	7/11-7/31/21	98	95	99	63	59	66
Later	BNT162b2	Israel [43]	Feb (60+ y)	7/11-7/31/21	88	84	91	65	57	71
Later	BNT162b2; mRNA-1273; Ad26.COV2.S	USA [42, 44]	Before July	June 20–July 17	90.4	87.7	92.5	78.3	60.0	88.2
	Weighted mean (fixed)				**93.42**	**92.61**	**94.24**	**82.63**	**81.81**	**83.46**
	Weighted mean (random)				**91.84**	**89.42**	**94.26**	**64.93**	**56.53**	**73.33**
	BNT162b2 and mRNA-1273	USA California [45]	March					93.9	78	98
	BNT162b2 and mRNA-1273	USA California [45]	April					96.2	89	98
	BNT162b2 and mRNA-1273	USA California [45]	May					95.9	85	99
	BNT162b2 and mRNA-1273	USA California [45]	June					94.3	84	98
	BNT162b2 and mRNA-1273	USA California [45]	July					65.5	49	77

Excludes Israel [46] (BNT162b2), as it did not give the vaccine efficacies in the two time periods it studied.

Table S5. Additional studies reporting vaccine efficacy only on severe disease

Vaccine	Study design	Study location (reference)	Variants addressed	Effectiveness vs. severe disease or hospitalization (95% CIs)
BNT162b2	Observational	Qatar [3]	All	97% (92-100)
BNT162b2	Observational	USA [47]	Original	85% (74-91)
BNT162b2	Observational	USA [48]	Alpha	89% (79-94)
BNT162b2	Observational	USA [49]	All including Delta	94%
BNT162b2 or mRNA-1273	Observational	Singapore [22]	Delta	93% (66-98)
BNT162b2	Observational	USA [50]	Delta	87% (85-90)
mRNA-1273	Observational	Qatar [51]	All	96% (73-100)
mRNA-1273	Observational	USA [48]	Alpha	92% (82-97)
mRNA-1273	Observational	Qatar [51]	All	96% (73-100)
mRNA-1273	Observational	USA [48]	Alpha	92% (82-97)
Gam-COVID-Vac	Observational	Russia [52]	Delta mostly	81% (68-88)
Inactivated COVID-19 vaccines	Observational	China [53]	Delta	89% (55-98)
mRNA-1273	Observational	USA [50]	Delta	91% (89-93)
Ad26.COV2.S	Observational	US [50]	Delta	68% (50-79)
BNT162b2 or mRNA-1273	Observational	Portugal [54]	Alpha (Feb-Mar), Delta (May onward)	94% (88-97) Hospitalization, 65-79 years
BNT162b2 or mRNA-1273	Observational	Portugal [54]	Alpha (Feb-Mar), Delta (May onward)	96% (92-98) Death, 65-79 years
BNT162b2 or mRNA-1273	Observational	Portugal [54]	Alpha (Feb-Mar), Delta (May onward)	82% (72-89) Hospitalization, 80+ years
BNT162b2 or mRNA-1273	Observational	Portugal [54]	Alpha (Feb-Mar), Delta (May onward)	81% (74-87) Death, 80+ years
BNT162b2 or mRNA-1273	Observational	USA [48]	Original and Alpha	86.6% (79-91.4), hospitalization, adults
BNT162b2	Observational	USA [48]	Original and Alpha	84.7% /74.1-91) hospitalization, adults
mRNA-1273	Observational	USA [48]	Original and Alpha	88.9% (78.7-94) hospitalization, adults
BNT162b2 or mRNA-1273	Observational	USA [48]	Alpha	92.1% (82.3-96.5), hospitalization, adults
BNT162b2	Observational	USA [55]	Mostly Delta	80% (73-85)
mRNA-1273	Observational	USA [55]	Mostly Delta	95% (92-97)
Ad26.COV2.S	Observational	USA [55]	Mostly Delta	60% (31-77)
BNT162b2	Observational	USA [56]		83.4% (74-89)
mRNA-1273	Observational	USA [56]		91.6% (84-96)
mRNA-1273	Observational	USA [56]	Feb 1-June 30 (pre-Delta)	84.1% (74-90)
mRNA-1273	Observational	USA [56]	July 1-Aug 6 (Delta)	89% (80-94)
mRNA-1273	Observational	USA [56]	<90 days since vaccination	86.1% (77-92)
mRNA-1273	Observational	USA [56]	>90 days since vaccination	87.2% (78-93)
BNT162b2 or mRNA-1273	Observational	USA [57]	2-12 wks since vaccination	86% (82-88)
BNT162b2 or mRNA-1273	Observational	USA [57]	13-24 wks since vaccination	84% (77-90)

Table S6. Additional studies reporting vaccine efficacy only on symptomatic disease or infection

Vaccine	Study design	Study location (reference)	Variants addressed	Effectiveness vs. symptomatic disease or infection (i) (95% CIs)
Ad26.COV2.S	Observational	USA [58]	Delta	51% (-2-76)
Ad26.COV2.S	Observational	Italy [59]	Delta	96.0% (82.2–99)
BBV152	Observational	India [1], [2]*	Delta	65% (33-83)
BNT162b2 and mRNA-1273	Observational	Qatar [3]	Original, Alpha, and Beta	78 (72-83)
BNT162b2 and mRNA-1273	Observational	Qatar [3]	Original, Alpha, and Beta	78 (72-83)
BNT162b2 or mRNA-1273	Observational	USA [60]	Non-VOC and Alpha	91 (83-95)
BNT162b2	Observational	USA [36]	Alpha and Original	96 (96-97)
BNT162b2	Observational	Israel [61]	Alpha and Original**	81% (60-93)(I)
BNT162b2	Observational	Kuwait [62]	Alpha mostly	94.5% (89.4-97.2) (I)
BNT162b2	Observational	UK [63]	Alpha mostly	78% (68-84) (i)
BNT162b2 and mRNA-1273	Observational	Canada [64]	Alpha and Gamma	79% (65-88), 2 dose
BNT162b2, ChadOx1, mRNA-1273	Observational	Norway [65]	Alpha	84% (82–87), fully vaccinated, infection
BNT162b2	Observational	Israel [66]	Alpha	96% (50-100), 2 dose, symptomatic
BNT162b2	Observational	Israel [67]	Alpha	98% (94-100)
BNT162b2	Observational	Israel [43]	Alpha	89% (82-94)
BNT162b2	Observational	Israel [68], [69]	Alpha	89% (82-94)
BNT162b2	Observational	UK [7]	Alpha	85% (74–96), 2 dose, infection
BNT162b2	Observational	UK [70], [71]	Alpha	95% (91-98)
BNT162b2	Observational	Scotland [72]	Alpha	92% (90-93)
BNT162b2	Observational	UK [73–75]	Alpha	94% (92-95)
BNT162b2 and mRNA-1273	Observational	Canada [76], [77]	Alpha	67% (57-75)#
BNT162b2 and mRNA-1273	Observational	Canada [78]	Alpha	93% (87-96)
BNT162b2 or ChadOx1	Observational	UK [79]	Alpha	90% (62-98)
BNT162b2	Observational	Qatar [3]	Alpha	90% (86-92) (i)
BNT162b2 mRNA	Observational	Western Europe [80]	Alpha	87% (74– 93)
BNT162b2	Observational	France [81]	Beta	50% (34-73)*
BNT162b2	Observational	Qatar [3]	Beta	75% (71-79) (i)
BNT162b2 and mRNA-1273	Observational	Canada [64,82]	Alpha and Gamma	79.2% (64.6-87.8) (I)
BNT162b2	Observational	Canada [12]	Gamma	26% (-158-79)
BNT162b2 and mRNA-1273	Observational	Canada [76]	Gamma	61% (45-72)#
BNT162b2	Observational	UK [63]	Delta mostly	82% (79-85) (i)
BNT162b2	Observational	Scotland [72]	Delta	79% (75-82)
BNT162b2, ChadOx1, mRNA-1273	Observational	Norway [65]	Delta	65% (61–68), fully vaccinated, infection
BNT162b2	Observational	UK [74]	Delta	88% (85-90)
mRNA vaccines	Observational	France [6]	Alpha	88% (82-91), 2D, symptomatic , age 18-54 years
mRNA vaccines	Observational	France [6]	Alpha	88% (80-92), 2D, symptomatic, age 55+ years
mRNA vaccines	Observational	France [6]	Beta and Gamma	83% (68-91), 2D, symptomatic , age 18-54 years
mRNA vaccines	Observational	France [6]	Beta and Gamma	76 (47-89), 2D symp, age 55+ years
mRNA-1273	Observational	Qatar [51]	Alpha	100% (92-100) (i)
mRNA-1273	Observational	USA [36]	Alpha and Original	98 (98-99)
mRNA-1273	Observational	Qatar [51]	Beta	96% (92-99) (i)
mRNA vaccines	Observational	France [6]	Alpha	88% (82-91), 2D, symptomatic, age 18-54 years
mRNA vaccines	Observational	France [6]	Alpha	88% (80-92), 2D, symptomatic, age 55+ years
mRNA vaccines	Observational	France [6]	Beta and Gamma	83% (68-91), 2D, symptomatic, age 18-54 years
mRNA vaccines	Observational	France [6]	Beta and Gamma	76 (47-89), 2D symp, age 55+ years
mRNA-1273	Observational	Qatar [51]	Alpha	100% (92-100) (i)
mRNA-1273	Observational	USA [36]	Alpha and Original	98 (98-99)
mRNA-1273	Observational	Qatar [51]	Beta	96% (92-99) (i)
ChAdOx1	Observational	Scotland [72]	Alpha	73% (66-78)
ChAdOx1	RCT	UK [83,84]	Alpha	70% (44-85)
ChAdOx1	Observational	UK [74]	Alpha	75% (68-79)
ChAdOx1	Observational	UK [63]	Alpha mostly	79% (56-90) (i)
ChAdOx1	Observational	South Africa [85]	Beta	10% (-76- 55)
ChAdOx1	Observational	India [86]	Delta	0.83 (0.72-0.97) OR, 2 dose, infection
ChAdOx1	Observational	Scotland [72]	Delta	60% (53-66)
ChAdOx1	Observational	UK [74]	Delta	67% (61-72)
ChAdOx1	Observational	UK [63]	Delta mostly	67% (62-71) (i)
ChAdOx1-S; BNT162b2; mRNA-1273; Ad26.COV2.S	Observational	Netherlands [87]	Mostly Alpha	75% (72-78) (i)
Coronavac	Observational	Brazil [19]	Gamma	37% (-55-74), 2 dose, symptomatic
NVX-CoV2373	RCT	UK [40]	Alpha	86% (71, 94)
NVX-CoV2373	RCT	South Africa [88]	Beta	51% (-1 – 76)
BNT162b2	Observational	USA [89]	Non-VOC and Alpha (before Delta circulation)	74.2% (69–78.7), documented infection
mRNA-1273	Observational	USA [89]	Non-VOC and Alpha (before Delta circulation)	74.7%(66.2-81.1), documented infection
BNT162b2	Observational	USA [89]	Alpha (Delta circulating but not dominant)	66.5% (58.3-73.1), documented infection
mRNA-1273	Observational	USA [89]	Alpha (Delta circulating but not dominant)	70.4% (60.1-78.0), documented infection
BNT162b2	Observational	USA [89]	Delta	52.4% (48–56.4), documented infection
mRNA-1273	Observational	USA [89]	Delta	50.6% (45–55.7), documented infection
BNT162b2	Observational	UK [90]	Alpha	77% (56-88), 80+ years, documented infection, interval 19-29 days
BNT162b2	Observational	UK [90]	Alpha	90% (83-94), 80+ years, documented infection, interval 65-84 days
BNT162b2	Observational	UK [90]	Alpha	77% (66-85), 65-79 years, documented infection, interval 19-29 days
BNT162b2	Observational	UK [90]	Alpha	89% (86-92), 65-79 years, documented infection, interval 65-84 days
BNT162b2 and mRNA-1273	Observational	USA [60]	Non-VOC and Alpha	91 % (83-95), symptomatic
BNT162b2	Observational	UK [91]	Original and Alpha	93.3% (85.8-96.8), symptomatic
ChAdOx1	Observational	UK [91]	Original and Alpha	78% (69.7-84)
BNT162b2 and mRNA-1273	Observational	Qatar [92]	Original, Alpha and Beta	78% (72-83) documented infection
BNT162b2	Observational	France [93]	Alpha	86% (81-90) symptomatic
Sputnik V	Observational	Russian Federation [52]	Delta	100% against ICU admission, 99.5% (98.5-99.9) against death
BNT162b2	Observational	USA [11]	B.1.427/.429 and Alpha	87% (68.6-94.6) infection
mRNA-1273	Observational	USA [11]	B.1.427/.429 and Alpha	86.2% (68.4-93.9) infection

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