Supplemental Material for

Predicting Vaccine Effectiveness for Hospitalization and Symptomatic Disease for Novel SARS-CoV-2 Variants Using Neutralizing Antibody Titers

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Table S1. Fold reductions or inverse of neutralizing antibody titers relative to wild-type virus ($1/NATR_{var}$). Comparisons that were not made in the Reference are denoted with a "-".

Ref.	Alpha	Gamma	Delta	Beta	BA.1	BA.2	BA.4/5	BA.1 (Dec. 2021)
[1]	1.1	1.2	-	4.2	-	-	-	-
[2]	-	-	-	-	19.3	14	23.3	-
[3]	-	-	-	7	32.3	-	-	-
[4]	1.5	4	-	2.5	-	-	-	-
[5]	-	-	-	-	-	-	-	41.4
[6]	-	-	7.7	-	-	-	-	-
[7]	-	-	-	11.4	66.3	-	-	-
[8]	2.5	1.1	-	4.6	-	-	-	-
[9]	2.1	6.3	-	39.4	-	-	-	-
[10]	1.6	-	3.2	13.7	68.3	-	-	-
[11]	-	-	-	-	6.2	6.2	6.2	-
[12]	-	-	-	-	9.6	8.9	-	-
[13]	2.1	2.3	-	12.2	-	-	-	-
[14]	-.8	1.2	-	2.7	-	-	-	-
[15]	-	-	2	6.2	12.9	-	-	-
[16]	1.5	2	2.2	8.8	-	-	-	-
[17]	-	-	-	-	7.2	5.6	9.3	-
[18]	1.5	2.2	-	3.4	-	-	-	-
[19]	-	-	-	-	4.9	-	13.6	-
[20]	1.4	1.8	-	9.1	-	-	-	-
[21]	3.5	4.8	-	12.1	-	-	-	-
[22]	1.9	2.3	4.4	5.3	-	-	-	-
[23]	-	-	-	-	-	-	-	37

[24]	2	3.2	2.2	7.5	-	-	-	-
[25]	-	-	-	-	27	23	-	-
[26]	2.2	1.9	-	4.6	-	-	-	-

Table S2. The fitted model for the fold-reduction ln(1/NATRvar) in neutralizing antibody titers for virus variants relative to WT with variant as a fixed effect and study as a random effect. Alpha was the reference level; the standard deviation of the random effect, study, was 0.51.

Predictor	**Estimate**	**SE**	**t-value**	**P-value**
Alpha (Intercept)	0.45	0.16	2.75	0.0087
Gamma	0.32	0.16	2.05	0.048
Delta	0.37	0.23	1.63	0.11
Beta	1.37	0.15	9.26	<0.001
BA.1	2.47	0.22	11.06	<0.001
BA.2	2.17	0.29	7.49	<0.001
BA.4/5	2.54	0.31	8.25	<0.001
BA.1 Dec. 2021	3.22	0.49	6.63	<0.001

Table S3. Estimates of fold-reduction ($1/NATR_{var}$) in neutralizing antibody titers for virus variants relative to WT with 95% CIs.

Variant	**Fold Reduction (95% CI)**
Alpha	1.57 (1.14-2.16)
Gamma	2.15 (1.55-2.99)
Delta	2.27 (1.45-3.55)
Beta	6.17 (4.58-8.30)
BA.1	18.5 (12.8-26.7)
BA.2	13.6 (8.3-22.4)
BA.4/5	19.9 (11.6-34.1)
BA.1 (Dec. 2021)	39.1 (16.0-96.0)

Table S4. Vaccine effectiveness against symptomatic disease estimates used to fit the VE-NATR$_{tot}$ model and shown in Figure 2A.

Variant	Ref.	Vaccine	VE	95% CI	Effective cases vaccine group	Effective cases control group
Alpha	[31]	BNT162b2	0.97	0.97-0.97	30	1000[a]
Alpha	[32]	BNT162b2	0.82	0.73-0.88	27.9	155.2
Alpha	[33]	BNT162b2	0.89	0.87-0.9	110	1000[b]
Alpha	[33]	mRNA-1273	0.92	0.88-0.95	24.7	308.2
Alpha	[33]	ChAdOx1 nCoV-19	0.91	0.62-0.98	2	22.4
Alpha	[38]	BNT162b2	0.937	0.92-0.95	49.7	788.2
Alpha	[29]	BNT162b2	0.95	0.94-0.96	50	1000[c]
Alpha	[38]	ChAdOx1 nCoV-19	0.745	0.68-0.79	104.5	409.7
Alpha	[39]	NVX-CoV2373	0.83	0.71-0.94	14.1	82.7
Alpha	[40]	ChAdOx1 nCoV-19	0.7	0.44-0.85	12.6	42.1
Beta	[33]	BNT162b2	0.87	0.08-0.98	1.1	8.7
Beta	[33]	BNT162b2	1	0.54-1	0	17.8
Beta	[41]	Ad26.COV2.S	0.64	0.41-0.79	21	58.2
Beta	[42]	NVX-CoV2373	0.51	0-0.76	11.2	22.9
Beta	[43]	ChAdOx1 nCoV-19	0.1	-0.77-0.55	15.7	17.5
D614G	[41]	Ad26.COV2.S	0.66	0.55-0.75	62.2	182.9
D614G	[44]	ChAdOx1 nCoV-19	0.67	0.57-0.74	81.9	248.1
D614G	[45]	CoronaVac	0.84	0.65-0.92	7.5	47
D614G	[46]	CoronaVac	0.65	0.20-0.85	7.4	21.2
D614G	[47]	mRNA-1273	0.94	0.89-0.97	10.7	177.9
D614G	[48]	NVX-CoV2373	0.9	0.83-0.95	14.5	145.4
D614G	[49]	BNT162b2	0.95	0.90-0.98	8.2	164.2
D614G	[50]	Sputnik V	0.92	0.86-0.95	13.9	173.5
Delta	[33]	BNT162b2	0.92	0.90-0.94	69.6	869.9
Delta	[33]	mRNA-1273	0.95	0.91-0.97	11.6	233
Delta	[33]	ChAdOx1 nCoV-19	0.87	0.69-0.95	5.8	44.5
Delta	[38]	BNT162b2	0.88	0.85-0.90	108.3	902.5
Delta	[51]	BNT162b2	0.444	0.37-0.51	381	685

Delta	[29]	BNT162b2	0.835	0.83-0.84	165	1000[d]
Delta	[52]	BNT162b2	0.78	0.78-0.79	220	1000[e]
Delta	[51]	mRNA-1273	0.739	0.66-0.80	67.0	257
Delta	[38]	ChAdOx1 nCoV-19	0.67	0.61-0.72	201.2	609.8
Gamma	[33]	BNT162b2	0.88	0.73-0.94	6.4	53.3

[a-e]Estimated sample sizes in the control group (I_c) and vaccine group (I_v) to match the original study VE 95% CI; these were rescaled to limit I_c to 1000 but maintain the correct VE: [a]I_c = 19,183, I_v = 575; [b] I_c = 1973, I_v = 217; [c] I_c = 1855, I_v = 93; [d] I_c = 270,217, I_v = 44,586; [e] I_c = 40,917, I_v = 9002

Table S5. Vaccine effectiveness against hospitalization estimates used to fit the VE-$NATR_{tot}$ model and shown in Figure 2B.

Variant	Ref.	Vaccine	VE	95% CI	Est. cases vaccine group	Est. cases control group
Alpha	[27]	Ad26.COV2.S	0.81	0.79-0.84	190	1000[a]
Alpha	[28]	BNT162b2	0.96	0.83-0.99	1.9	46.9
Alpha	[29]	BNT162b2	0.979	0.91-1	2	94
Alpha	[29]	ChAdOx1 nCoV-19	0.939	0.85-0.98	5	81.6
Alpha	[30]	BNT162b2	0.95	0.78-0.99	1.8	36.6
Alpha	[30]	ChAdOx1 nCoV-19	0.86	0.53-0.96	3	21.3
Alpha	[31]	BNT162b2	0.972	0.97-0.98	28	1000[b]
Alpha	[32]	BNT162b2	0.94	0.6-0.99	1.1	18.6
Alpha	[33]	BNT162b2	0.96	0.94-0.97	27.3	681.3
Alpha	[33]	mRNA-1273	0.95	0.92-0.97	17.8	356.3
Alpha	[33]	ChAdOx1 nCoV-19	0.92	0.41-0.99	1	12.9
Beta	[33]	BNT162b2	0.92	0.39-0.99	1	12.4
Delta	[27]	Ad26.COV2.S	0.85	0.73-0.91	12.9	85.8
Delta	[34]	Ad26.COV2.S	0.6	0.31-0.77	17.8	44.5
Delta	[34]	BNT162b2	0.8	0.73-0.85	52.2	261
Delta	[34]	mRNA-1273	0.95	0.92-0.97	17.4	347.5
Delta	[28]	BNT162b2	0.98	0.97-0.98	20	1000[c]
Delta	[28]	mRNA-1273	0.97	0.96-0.98	30	1000[d]
Delta	[28]	ChAdOx1 nCoV-19	0.92	0.86-0.95	13.5	169.2

Delta	[29]	BNT162b2	0.967	0.96-0.97	33	1000[e]
Delta	[29]	ChAdOx1 nCoV-19	0.93	0.92-0.94	70	1000[f]
Delta	[35]	BNT162b2	0.93	0.84-0.96	6	85.8
Delta	[36]	BNT162b2	0.976	0.93-0.99	3.3	135.6
Delta	[30]	BNT162b2	0.96	0.86-0.99	2.6	65
Delta	[30]	ChAdOx1 nCoV-19	0.92	0.75-0.97	3	37.7
Delta	[33]	BNT162b2	0.98	0.96-0.99	8.2	410.4
Delta	[33]	mRNA-1273	0.98	0.93-1	2.5	123.6
Delta	[33]	ChAdOx1 nCoV-19	0.9	0.67-0.97	2.9	28.7
Gamma	[28]	BNT162b2	0.95	0.83-0.99	2.7	53.6
Gamma	[37]	Ad26.COV2.S	0.729	0.35-0.91	6.2	23
Gamma	[33]	BNT162b2	0.94	0.59-0.99	1.1	18.3

[a-f]Estimated sample sizes in the control group (I_c) and vaccine group (I_v) to match the original study VE 95% CI; these were rescaled to limit I_c to 1000 but maintain the correct VE: [a]I_c = 1469, I_v = 279; [b] I_c = 8784, I_v = 245; [c] I_c = 1794, I_v = 36; [d] I_c = 1289, I_v = 39; [e] I_c = 10577, I_v = 349; [f] I_c = 9085, I_v = 636

Table S6. Statistics for the fitted model between neutralizing antibody titers and VE given by the equation $\mathrm{VE} = 1 - \frac{1}{1+e^{-c_0-c_1\log_2(\mathrm{NATR_{tot}})}}$.

Endpoint	Coefficient	Estimate	SE	Z value	p-value
Symptomatic Disease	c_0	-1.60	0.028	-56.4	< 2.2x10^{-16}
	c_1	0.53	0.031	-17.2	< 2.2x10^{-16}
Hospitalization	c_0	-2.91	0.052	-56.1	< 2.2x10^{-16}
	c_1	-0.51	0.038	-13.6	< 2.2x10^{-16}

Table S7. Predicted VE, 95% CIs and 95% PIs for two vaccines, two variants, two endpoints, and two immune statuses using the model shown in Figure 2.

Variant	Prediction	Vaccine	Endpoint	Status	VE	95% PI	95% CI
Omicron	Updated	mRNA-1273	Hospitalization	Three-dose boosted	0.9	0.82-0.95	0.89-0.91
Omicron	Updated	BNT162b2	Hospitalization	Three-dose boosted	0.91	0.84-0.96	0.9-0.92
Omicron	Updated	mRNA-1273	Hospitalization	Two-dose waned	0.56	0.37-0.71	0.48-0.64

Omicron	Updated	BNT162b2	Hospitalization	Two-dose waned	0.46	0.25-0.63	0.37-0.56
Omicron	Updated	mRNA-1273	Symptomatic disease	Three-dose boosted	0.69	0.56-0.8	0.67-0.72
Omicron	Updated	BNT162b2	Symptomatic disease	Three-dose boosted	0.72	0.6-0.82	0.7-0.74
Omicron	Updated	mRNA-1273	Symptomatic disease	Two-dose waned	0.24	-0.01-0.43	0.18-0.3
Omicron	Updated	BNT162b2	Symptomatic disease	Two-dose waned	0.18	-0.09-0.38	0.13-0.24
Omicron	Updated	mRNA-1273	All infections	Three-dose boosted	0.69	0.56-0.8	0.66-0.72
Omicron	Updated	BNT162b2	All infections	Three-dose boosted	0.71	0.57-0.81	0.68-0.73
Omicron	Updated	mRNA-1273	All infections	Two-dose waned	0.44	0.21-0.62	0.33-0.55
Omicron	Updated	BNT162b2	All infections	Two-dose waned	0.38	0.14-0.59	0.27-0.52
Omicron	Dec. 11 2021	mRNA-1273	Hospitalization	Three-dose boosted	0.83	0.73-0.91	0.81-0.85
Omicron	Dec. 11 2021	BNT162b2	Hospitalization	Three-dose boosted	0.85	0.76-0.92	0.83-0.87
Omicron	Dec. 11 2021	mRNA-1273	Hospitalization	Two-dose waned	0.42	0.19-0.6	0.33-0.52
Omicron	Dec. 11 2021	BNT162b2	Hospitalization	Two-dose waned	0.33	0.08-0.53	0.24-0.44
Omicron	Dec. 11 2021	mRNA-1273	Symptomatic disease	Three-dose boosted	0.56	0.39-0.7	0.52-0.6
Omicron	Dec. 11 2021	BNT162b2	Symptomatic disease	Three-dose boosted	0.59	0.43-0.72	0.56-0.63
Omicron	Dec. 11 2021	mRNA-1273	Symptomatic disease	Two-dose waned	0.15	-0.11-0.36	0.11-0.21
Omicron	Dec. 11 2021	BNT162b2	Symptomatic disease	Two-dose waned	0.11	-0.17-0.32	0.07-0.16
Omicron	Dec. 11 2021	mRNA-1273	All infections	Three-dose boosted	0.62	0.46-0.75	0.57-0.67
Omicron	Dec. 11 2021	BNT162b2	All infections	Three-dose boosted	0.64	0.49-0.76	0.6-0.68
Omicron	Dec. 11 2021	mRNA-1273	All infections	Two-dose waned	0.36	0.12-0.57	0.24-0.51

Omicron	Dec. 11 2021	BNT162b2	All infections	Two-dose waned	0.31	0.06-0.54	0.2-0.47
Delta	Delta	mRNA-1273	Hospitalization	Three-dose boosted	0.98	0.94-1	0.97-0.98
Delta	Delta	BNT162b2	Hospitalization	Three-dose boosted	0.98	0.95-1	0.97-0.98
Delta	Delta	mRNA-1273	Hospitalization	Two-dose waned	0.86	0.77-0.93	0.84-0.87
Delta	Delta	BNT162b2	Hospitalization	Two-dose waned	0.81	0.7-0.89	0.78-0.83
Delta	Delta	mRNA-1273	Symptomatic disease	Three-dose boosted	0.92	0.86-0.97	0.91-0.93
Delta	Delta	BNT162b2	Symptomatic disease	Three-dose boosted	0.93	0.87-0.97	0.92-0.94
Delta	Delta	mRNA-1273	Symptomatic disease	Two-dose waned	0.61	0.45-0.74	0.58-0.65
Delta	Delta	BNT162b2	Symptomatic disease	Two-dose waned	0.52	0.33-0.66	0.47-0.56
Delta	Delta	mRNA-1273	All infections	Three-dose boosted	0.84	0.74-0.92	0.8-0.88
Delta	Delta	BNT162b2	All infections	Three-dose boosted	0.85	0.75-0.93	0.81-0.89
Delta	Delta	mRNA-1273	All infections	Two-dose waned	0.65	0.5-0.77	0.61-0.69
Delta	Delta	BNT162b2	All infections	Two-dose waned	0.6	0.43-0.73	0.54-0.66

Table S8. VE validation data for the Omicron variant shown in Figure 3 for two vaccines, two endpoints, and two immune statuses (two-dose waned and boosted with a third dose).

Ref.	Vaccine	Dose	Endpoint	VE	CI	Est. cases vaccine group	Est. cases control group
[53]	mRNA-1273	Three-dose boosted	Hospitalization	97.5	96.3 - 98.3	25.9	1037
[54]	BNT162b2	Two-dose waned	Hospitalization	51.6	47.2 - 55.6	776.8	1604.9
[54]	BNT162b2	Three-dose boosted	Hospitalization	88.8	87.3 - 90.1	273.1	2438.4
[54]	mRNA-1273	Three-dose boosted	Hospitalization	90.2	87.3 - 92.5	60.7	618.9

[55]	BNT162b2	Two-dose waned	Hospitalization	34.9	17.7 - 48.4	116.2	178.5
[56]	BNT162b2	Two-dose waned	Symptomatic disease	8.8	7 - 10.5	20033.7	21966.8
[56]	BNT162b2	Three-dose boosted	Symptomatic disease	67.2	66.5 - 67.8	12151	37045.9
[56]	mRNA-1273	Two-dose waned	Symptomatic disease	14.9	2.9 - 24.7	426.3	500.9
[56]	mRNA-1273	Three-dose boosted	Symptomatic disease	66.3	63.7 - 68.8	902.5	2678

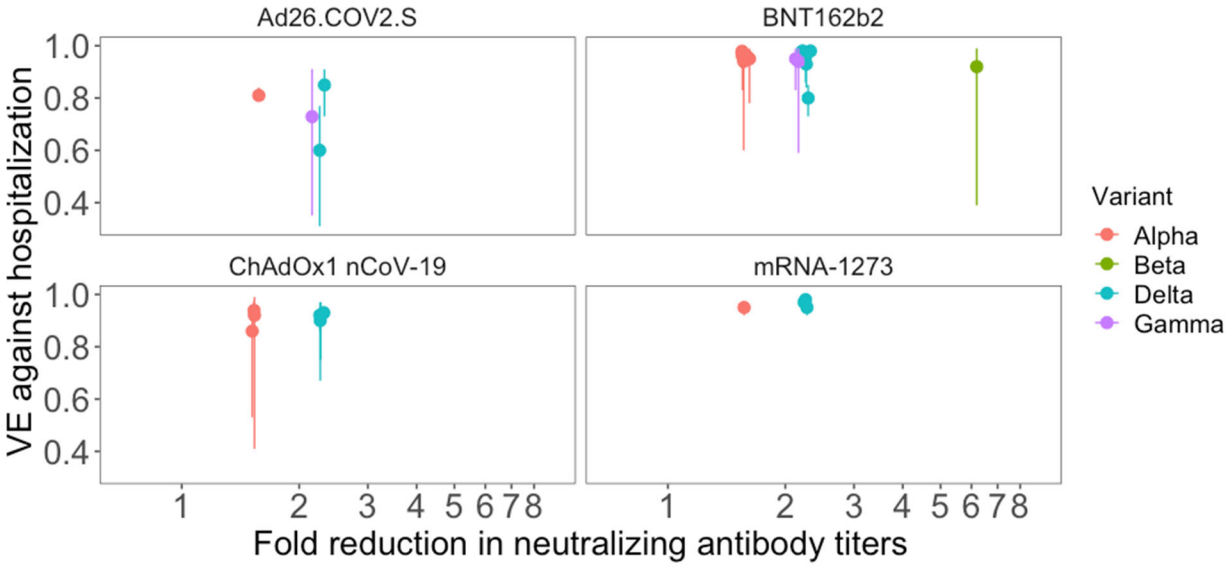

Figure S1. VE against hospitalization by vaccine plotted against variant-specific reductions in neutralizing antibody titers relative to WT virus. Each point (and 95% CI) represents a single estimate of VE for a single vaccine & virus variant from an observational study. Points have been slightly jittered along the x-axis to facilitate presentation.

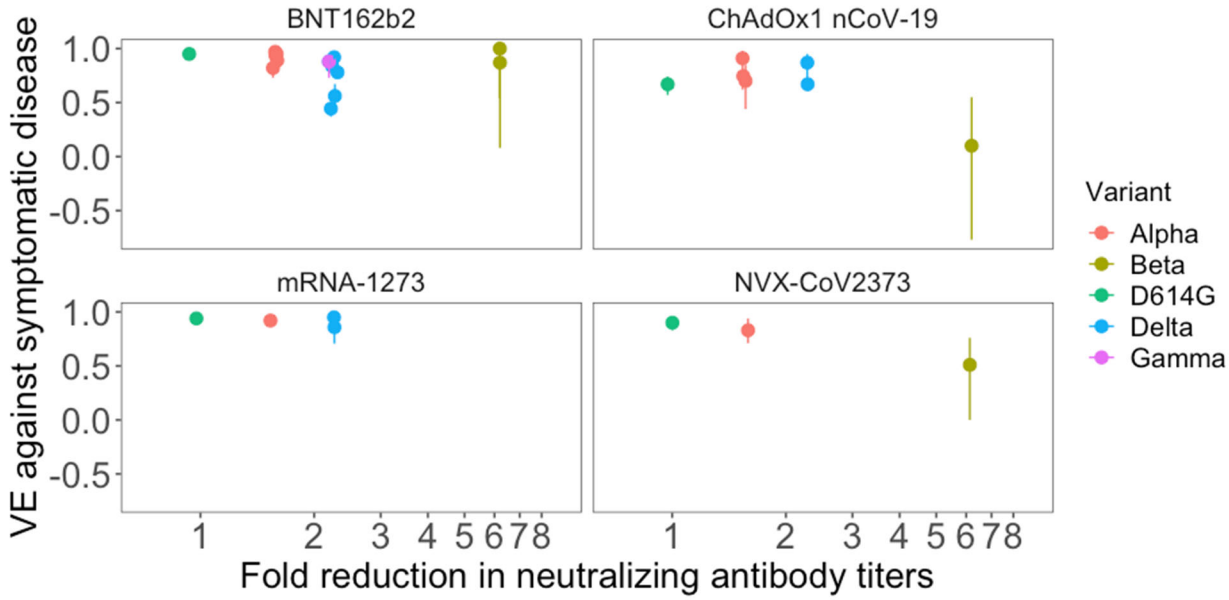

Figure S2. VE against symptomatic disease by vaccine plotted against variant-specific reductions in neutralizing antibody titers relative to WT virus. Each point (and 95% CI) represents a single estimate of VE for a single vaccine & virus variant from an observational study. Points have been slightly jittered along the x-axis to facilitate presentation.

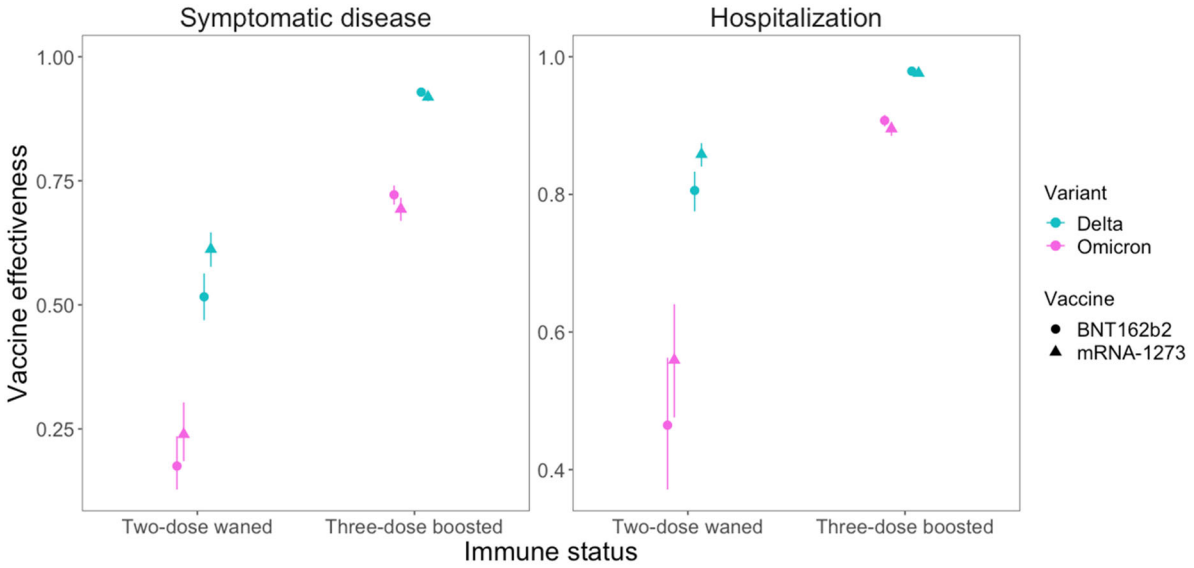

Figure S3. Comparison of estimated VE for the Omicron variant and Delta variants for two endpoints, two vaccines, and two immune statuses (6+ months after two doses (Waned) and shortly after a 3rd dose (Boosted)).

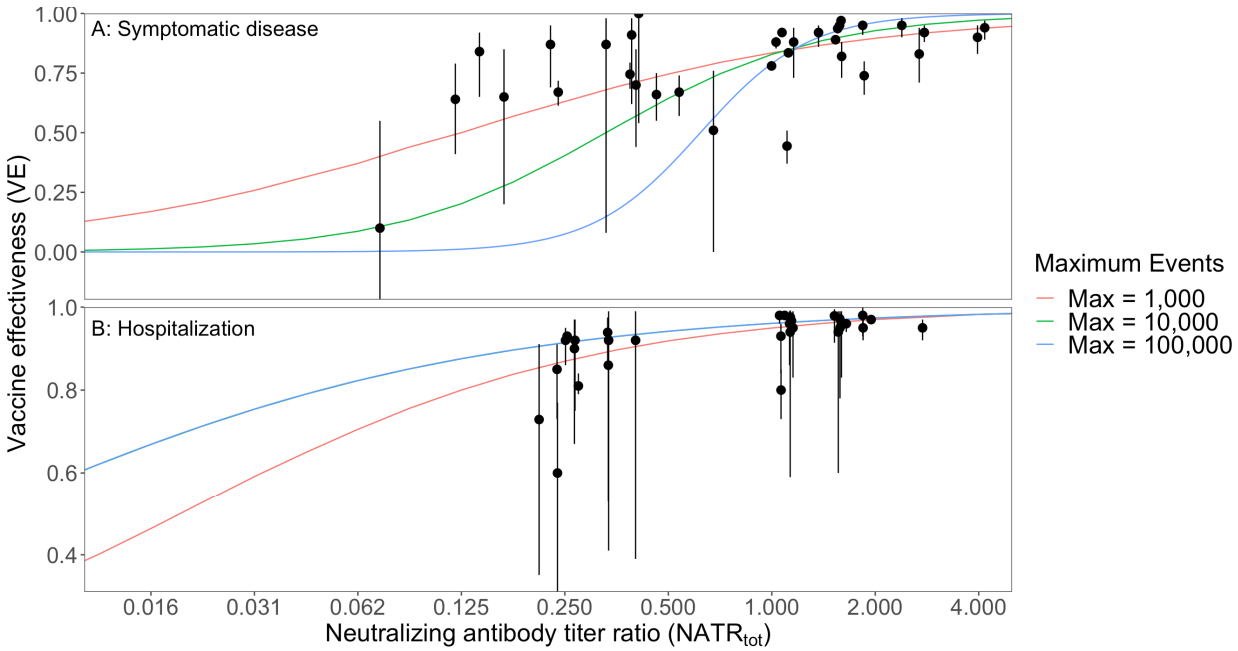

Figure S4. Illustration of the effect of large studies on the fitted relationship between VE and NATR$_{tot}$. Vaccine Effectiveness (VE) is plotted against variant- and vaccine-specific neutralizing antibody titer ratios (NATR$_{tot}$) for (A) symptomatic disease and (B) hospitalization. Each point (and 95% CI represents a single empirical estimate of VE for a single vaccine & virus variant. Points are jittered slightly along the x-axis to facilitate presentation. Each line shows the fitted model using a different maximum value for events (symptomatic cases or hospitalizations) in the control group, corresponding to a different maximum weight given to any one data point. When the maximum value is 10,000 or 100,000, a few points at high NATR$_{tot}$ with very large sample sizes distort the relationship leading to a poor fit at low NATR$_{tot}$.

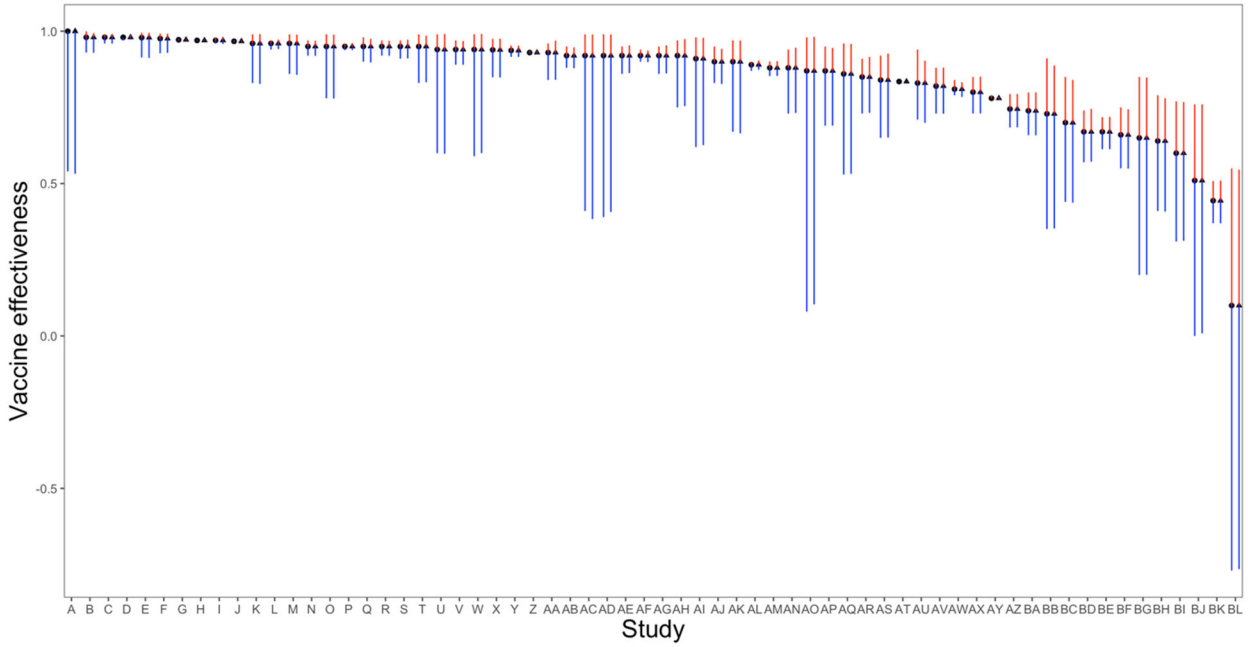

Figure S5. Vaccine effectiveness and 95% CIs for each study (circles) and generated using estimated infections in each arm of each study (triangles), which were not reported in most studies. Upper CIs are shown in red and lower CIs are shown in blue.

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