Coronavirus Variants Rapid Response Network | Réseau de réponse rapide aux variants du coronavirus

COVID-END COVID-19 Evidence Network to support Decision-making ... in Canada

COVID-19 Living Evidence Synthesis #6

(Version 29:02 February 2022)

Question

What is the efficacy and effectiveness of available COVID-19 vaccines for variants of concern?

Findings

For vaccine effectiveness in variants of concern (VOC), we present a visual summary of evidence in Table 1 and Table 2 and details in Table 3.

Methods are presented in Box 1 and in the following appendices:

1) reference list
2) glossary
3) data-extraction template
4) process for assigning variant of concern to studies
5) research question and critical appraisal process
6) detailed description of the narrative summary statement.

Overall, 379 studies were appraised and 132 used to complete this summary. The reasons for excluding the remaining 247 studies are reported in the second section of Appendix 2.

8 new studies have been added since the previous edition of this living evidence synthesis, all of which are signaled by a last-updated date of 02 February 2022 (highlighted in yellow). The new studies included results for VOC Omicron (1), VOC Delta (3), VOC Gamma to VOC Delta (3), and VOC Alpha to VOC Delta (2).

Box 1: Our approach

We retrieved candidate studies and updates to living evidence syntheses on vaccine effectiveness using the following mechanisms: 1) PubMed via COVID-19+ Evidence Alerts; 2) systematic scanning of pre-print servers; 3) updates to the COVID-END inventory of best evidence syntheses; and 4) cross-check with updates from the VESPa team. We included studies and updates to living evidence syntheses identified up to two days before the version release date. We did not include press releases unless a preprint was available. A full list of included and excluded studies is provided in **Appendix 1**. A glossary is provided in **Appendix 2**.

Prioritized outcome measures: Infection, severe disease (as defined by the study investigators), death, and transmission.

Data extraction: We prioritized variant-confirmed and vaccine-specific data over total study population data (variant assumed and/or vaccine unspecified). We extracted data from each study in duplicate using the template provided in **Appendix 3**. Relevance to VOC is determined directly, when reported by study authors, or indirectly where reasonable assumptions can be made about the variant prevalent in the jurisdiction at the time of the study as described in **Appendix 4**.

Critical appraisal: We assessed risk of bias, direction of effect, and certainty of evidence. **Risk of bias:** assessed in duplicate for individual studies using an adapted version of ROBINS-I. **Direction of vaccine effect:** "prevented" or "protects" was applied to mean estimates or range of mean estimates of effect that are greater than or equal to 50% (the lowest acceptable limit for vaccine effectiveness as determined by WHO). **Certainty of evidence:** assessed for the collection of studies for each vaccine according to variant of concern using a modified version of GRADE. Details of the research question for this synopsis and the critical appraisal process are provided in **Appendix 5**.

Summaries: We summarized the evidence by presenting narrative evidence profiles across studies, with or without pooling, as appropriate. A template for the summary statements used on page 1 under "Findings" and in Table 1 under each VOC is provided in **Appendix 6**.

We update this document every Wednesday and post it on the COVID-END website.

Highlights of changes this week

- The only new VOC Omicron study (that wasn't critical risk of bias) compared 2 doses versus 3 doses therefore it only appears in Appendix (ref 151)
- New data on Sinovac [CoronaVac] against VOC Delta has been added to Table 1 and Table 2 including one moderate risk of bias study (ref 154)

VOC Omicron

We have low certainty evidence that 2 doses of **BNT162b2 [Pfizer]** prevented infection from VOC **Omicron** (6 to 55% - 2 Obs) up to 44 days after 2nd dose and provided no protection (-76.5% [95% CI, -95.3 to -59.5] – 1 Obs) up to 164 days after 2nd dose.

We have low certainty evidence that 2 doses of **BNT162b2 [Pfizer]** prevented symptomatic infection from VOC **Omicron** (88% [95% CI, 65.9 to 95.8] – 1 Obs) at 14 to 63 days after 2nd dose and limited protection (34.3% [95% CI, -5 to 58.7] – 1 Obs) up to 175 days after 2nd dose.

We have low certainty evidence that 2 doses of **mRNA-1273 [Moderna]** prevented infection from VOC **Omicron** (30 to 37% – 2 Obs) 14 to 90 days after 2nd dose and provided no protection (-39.3% [95% CI, -61.6 to -20] – 1 Obs) up to 164 days after 2nd dose.

We have low certainty evidence that 2 doses of **ChAdOx1 [AstraZeneca]** provided no protection from symptomatic infection by VOC **Omicron** (5.9% [95% CI, -29.7 to 31.7] – 1 Obs) at 175 days after 2nd dose.

We have low certainty evidence that **3 doses** of **BNT162b2 [Pfizer]** prevented infection from VOC **Omicron** (34 to 55% – 2 Obs) 7 to 30 days after 3rd dose. We have low certainty evidence that **3 doses** of **BNT162b2 [Pfizer]** prevented symptomatic infection from VOC **Omicron** (75.5% [95% CI, 56.1 to 86.3] – 1 Obs) up to 14 days after 3rd dose

We have moderate certainty evidence that 2 doses of **ChAdOx1 [AstraZeneca] followed by BNT162b2 [Pfizer]** provided protection from symptomatic infection by VOC Omicron (93 to 94% - 2 Obs) at 14 days after last dose.

We have low certainty evidence that **2 doses of ChAdOx1 [Astra Zeneca] followed by an mRNA vaccine [Pfizer or Moderna]** provided protection from symptomatic infection by VOC **Omicron** (71.4% [95% CI, 41.8 to 86] – 1 Obs) at 175 days after last dose.

Table 1: Visual summary of evidence for COVID-19 vaccines for variants of concern (up to 30 days after 2 doses)

Percentages indicate level of effectiveness from 0% (no effect) to 100% (full protection): ranges of estimated means are provided when ≥ 1 study is available; estimated mean value is provided for single studies

Colour indicates **Level of Certainty** based on the evidence

High certainty evidence	Moderate certainty evidence	Low certainty evidence
pooling of low to moderate risk of bias RCTs or pooling of observational studies with low risk of bias and consistent findings	single RCT with low to moderate risk of bias or >one observational study with low to moderate risk of bias and at least partially consistent findings	single RCT or observational study with serious risk of bias or multiple low to serious risk of bias observational studies with inconsistent findings

Outcome (and vaccine)	Vaccine Effectiveness (2 doses unless otherwise stated) up to 30 days after last dose each combination of vaccine, variant, and outcome				
	Alpha	Beta	Gamma	Delta	Omicron
Any Infection					
Pfizer	78 to 95%		93%	42 to 91%	
Moderna	86 to 100%	96%	95%	52 to 91%	
AstraZeneca (AZ)	62 to 79%		90%	45 to 73%	
Johnson & Johnson				3 to 71%*	
Novavax					
Sinovac			66%	74%	
AZ followed by Pfizer or Moderna	82 to 91%		96%	88%	
Symptomatic Infection (reported when data on "any infection" is limited)					
Pfizer		84 to 88%	84 to 88%	63 to 94%	
Moderna			88%	87%	
AstraZeneca		10%**	65%	61 to 92%	
Johnson & Johnson				51%*	
Novavax	86%	43%**			
Sinovac				59%	

Outcome (and vaccine)	Vaccine Effectiveness (2 doses unless otherwise stated) for each combination of vaccine, variant, and outcome				
	Alpha	**Beta**	**Gamma**	**Delta**	**Omicron**
Covaxin				50%	
AZ followed by Pfizer or Moderna				67 to 79%	
Transmission					
Pfizer	70 to 82%			31 to 63% (unvacc contact) 10 to 40% (vacc contact)	
Moderna	88%			62 to 77%	
AstraZeneca	58 to 63%			36%	
Johnson & Johnson	77%*				
Novavax					
Sinovac					
AZ followed by Pfizer or Moderna				86%	
Severe Disease (may include death for some studies)					
Pfizer	92 to 100%			82 to 98%	
Moderna	96%	96%		93 to 100%	
AstraZeneca			76%		
Johnson & Johnson		82%*			
Novavax					
Sinovac				46 to 89%	
Sinopharm					
Sputnik V					
Death					
Pfizer	91 to 97%			90%	
Moderna					
AstraZeneca				91%*	
Johnson & Johnson					
Novavax					
Sinovac			86%	77%	
Sinopharm					
Sputnik V					

*single dose

**mean estimate of effect less than the lowest acceptable limit for vaccine effectiveness as determined by WHO

AZ, AstraZeneca; unvacc, unvaccinated; vacc, vaccinated

Table 2: Visual summary of evidence for COVID-19 vaccines for variants of concern – Delta and Omicron [2 doses>30 days since last dose; 3 doses (anytime frame)]

Percentages indicate level of effectiveness from 0% (no effect) to 100% (full protection): ranges of estimated means are provided when ≥ 1 study is available; estimated mean value is provided for single studies

Colour indicates **Level of Certainty** based on the evidence

High certainty evidence	Moderate certainty evidence	Low certainty evidence
pooling of low to moderate risk of bias RCTs or pooling of observational studies with low risk of bias and consistent findings	single RCT with low to moderate risk of bias or >one observational study with low to moderate risk of bias and at least partially consistent findings	single RCT or observational study with serious risk of bias or multiple low to serious risk of bias observational studies with inconsistent findings

Outcome (vaccine)	Variant	Number of Doses	Time since Last Dose (days)	Vaccine Effectiveness
Infection – Omicron (2 doses)				
Pfizer	Omicron	2	7 to 59	6 to 55%
			164	-76.5% (-95.3 to -59.5)
Moderna			14 to 90	30 to 37%
			164	-39.3% (-61.6 to -20)
Infection – Delta (2 doses)				
Pfizer	Delta	2	120	53 to 85%
Moderna				81 to 88%
AstraZeneca				72% (66 to 77)
AZ followed by mRNA vaccine		1/1	120	86% (81 to 89)
Pfizer		2	150 to 180	57 to 84%
Moderna			150 to 180	65 to 88%
Johnson & Johnson		1	150	74% (70 to 76)
Sinovac		2	150	30% (18.4 to 39.9)
Infection – Omicron (3 doses)				
Pfizer	Omicron	3	7 to 30	34 to 55%
Moderna				59 to 64%
Infection – Delta (3 doses)				
Pfizer	Delta	3	7 to 30	81 to 93%
Moderna				83 to 96%
AZ followed by Pfizer		2/1	7	82% (68 to 90)
Symptomatic Infection – Omicron (2 doses)				
Pfizer	Omicron	2	14 to 63	88% (65.9 to 95.8)
Pfizer			175	34% (-5 to 58.7)
AstraZeneca				6% (-29.7 to 31.7)
Symptomatic Infection – Delta (2 doses)				
Pfizer		2	60 to 89	72% (61 to 80)
AstraZeneca				65% (48 to 76)

Johnson & Johnson	Delta	1		52% (33 to 66)
Moderna		2	70 to 98	90%
AstraZeneca		2	119	41 to 49%
AZ followed by mRNA vaccine		1/1	120	66% (41 to 80)
Moderna		2	121 to 180	71% (56 to 81)
Pfizer				47% (39 to 55)
Johnson & Johnson		1	150	64.3% (62.3 to 66.1)
Pfizer		2	210	70.1% (69 to 71)
Moderna				81.9% (81 to 82.7)
Symptomatic Infection – Omicron (3 doses)				
Pfizer	Omicron	3	14	75.5% (56.1 to 86.3)
AZ followed by mRNA vaccine		2/1		71.4% (41.8 to 86)
Symptomatic Infection – Delta (3 doses)				
Sinovac	Delta	3 doses	14	78.8% (76.8 to 80.6)
AZ followed by Pfizer		2/1	14	93 to 94%
Sinovac followed by Pfizer		2/1	14	96.5% (96.2 to 96.7)
Sinovac followed by AZ		2/1	14	93.2% (92.9 to 93.6)
Severe Disease – Delta (2 doses)				
AstraZeneca	Delta	2	112 to 119	70.5% (67 to 73.7)
Moderna			120	91.5% (60.8 to 98.1)
Pfizer			150	57 to 86%
Moderna			150	85.2% (82.7 to 87.7)
Sinovac			150	30.2% (7.6 to 47.3)
Sinovac followed by Pfizer		2/1	14	96.2% (94.6 to 97.3)
Sinovac followed by AZ		2/1	14	98.9% (98.5 to 99.2)
Death – Delta (2 doses)				
Johnson & Johnson	Delta	1	120	89.4% (52.3 to 97.6)
Pfizer		2	150	81 to 89%
Sinovac		2	150	75.7% (67 to 82.1)
Moderna		2	210	93.7% (90.2 to 95.9)
Sinovac followed by Pfizer		2/1	14	96.8% (93.9 to 98.3)
Sinovac followed by AZ		2/1	14	98.1% (97.3 to 98.6)

Table 3: Key findings about vaccine effectiveness (revised format 13 Dec 2021)

VOC	Vaccine	Findings
Omicron	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 (2 doses) provided protection against VOC Omicron for the following outcomes: • 55.2% (95% CI, 23.5 to 73.7) from infection up to 44 days after 2nd dose • 6% (95% CI, -25 to 30) from infection 7 to 59 days after 2nd dose • -76.5% (95% CI, -95.3 to -59.5) from infection up to 164 days after 2nd dose (2 Obs) [137][147]; *last update 2022-01-18* BNT162b2 or mRNA-1273 (2 doses) provided protection against infection by VOC Omicron: • 6% (95% CI, -25 to 30) 7 to 59 days after 2nd dose • 13% (95% CI, -38 to 8) 60 to 119 days after 2nd dose • -38% (95% CI, -61 to -18) 120 to 179 days after 2nd dose • -16% (95% CI, -62 to 17) ≥240 days after 2nd dose (1 Obs) [147]; *last update 2022-01-18* BNT162b2 (2 doses) provided protection against VOC Omicron for the following outcomes: • 88% (95% CI, 65.9 to 95.8) from symptomatic infection at 14 to 63 days after 2nd dose • 34.3% (95% CI, -5 to 58.7) from symptomatic infection at 175 days after 2nd dose (1 Obs) [136]; *last update 2022-01-05* BNT162b2 (3 doses) provided protection against VOC Omicron for the following outcomes: • 34 to 54.6% from infection at 7 to 30 days after 3rd dose (RME) (2 Obs) [137][147]; *last update 2022-01-18* BNT162b2 (3 doses) provided protection against VOC Omicron for the following outcomes: • 75.5% (95% CI, 56.1 to 86.3) from symptomatic infection at 14 days after 3rd dose (1 Obs) [136]; *last update 2022-01-05*
Omicron	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 (2 doses) provided protection against VOC Omicron for the following outcomes: • 30.4% (95% CI, 5 to 49) from infection at 14 to 90 days after 2nd dose • 36.7% (95% CI, -69.9 to 76.4) from infection up to 44 days after 2nd dose • -39.3% (95% CI, -61.6 to -20) from infection up to 164 days after 2nd dose • 15.2% (95% CI, 0 to 30.7) from infection at 91 to 180 days after 2nd dose • 0% (95% CI, 0 to 1.2) from infection at 181 to 270 days after 2nd dose (2 Obs) [137][148]; *last update 2022-01-18* mRNA-1273 (3 doses) provided protection against VOC Omicron for the following outcomes: • 59 to 64% (95% CI, 16 to 80) from infection at 7 to 30 days after 3rd dose • (2 Obs) [147][148]; *last update 2022-01-18*

VOC	Vaccine	Findings
		(2 Obs) [147][148]; *last update 2022-01-18*
Omicron	**AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]**	ChAdOx1 (2 doses) provided limited protection against VOC Omicron for the following outcomes: • 5.9% (95% CI, -29.7 to 31.7) from symptomatic infection at 175 days after 2nd dose (1 Obs) [136]; *last update 2022-01-05*
Omicron **2 doses followed by mRNA vaccine**	**AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]**	ChAdOx1 (2 doses) followed by BNT162b2 provided protection against VOC Omicron for the following outcomes: • 71.4% (95% CI, 41.8 to 86) from symptomatic infection at 14 days after 3rd dose (1 Obs) [136]; *last update 2022-01-05*
Delta	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 provided protection against VOC Delta for the following outcome at least 14 to 21 days after 1st dose: • 30 to 65% from infection (RME) • 33 to 47.5% from symptomatic infection (RME) • 87 to 94% from hospitalization (RME) • 100% (95% CI, not reported) against severe, critical, or fatal disease BNT162b2 provided protection against VOC Delta for the following outcome at least 7 days after 2nd dose: • 42 to 91% from infection (RME) • 63 to 94% from symptomatic infection (RME) • 82 to 98% from severe, critical, or fatal disease (RME) • 90% from death (RME) (25 Obs) [29][38][42][47][57][63][64][71][74][76][84][88][92][97][102][109][110][111][118][119][121][123][133][138][156]; *last update 2022-02-02*
Delta	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 provided protection against VOC Delta for the following outcomes at least 14 days after 1st dose: • 75 to 86.7% from infection (RME) • 72% (95% CI, 57 to 82) from symptomatic infection • 96% (95% CI, 72 to 99) from hospitalization • 93 to 100% from severe, critical, or fatal disease (RME) mRNA-1273 provided protection against VOC Delta for the following outcomes 14 days after 2nd dose: • 52 to 91% from infection (RME) • 87% (95% CI, 84 to 88) from symptomatic infection • 93 to 100% from severe, critical, or fatal disease(RME) (18 Obs) [47][57][63][64][71][74][97][101][102][109][110][111][118][121][123][133][138][140]; *last update 2022-01-05*
Delta	**AstraZeneca [ChAd0x1] Vaxzevria**	ChAdOx1 provided protection against VOC Delta for the following outcome at least 21 days after 1st dose: • 18 to 46% from infection (RME) • 33 to 58% from symptomatic infection (RME)

VOC	Vaccine	Findings
	Serum Institute of India [Covishield]	• 71% (95% CI, 51 to 83) from hospitalization ChAdOx1 provided protection against VOC Delta for the following outcome at least 7 days after 2nd dose: • 44.8 to 73% from infection (RME) • 61 to 92% from symptomatic infection (RME) • 92% (95% CI, 75 to 97) from hospitalization • 91% (95% CI, 83 to 94) from death (10 Obs) [29][38][42][47][71][92][118][119][123][131][141]; *last update 2021-12-15*
Delta	**Johnson & Johnson [AD26.COV 2.S]**	Ad26.COV2.S provided protection against VOC Delta for the following outcomes ≥ 14 days after dose: • 3% to 71% against infection (RME) • 50.9% (95% CI, 35.5 to 63.0) from symptomatic infection • 92.5% (95% CI, 54.9 to 99.6) from ICU admission • 90.5% (95% CI, 31.5 to 99.6) from death (6 Obs) [97][109][110][111][117][133]; *last update 2021-12-15*
Delta	**Sinovac [CoronaVac]**	CoronaVac provided protection against VOC Delta for the following outcome ≥ 14 days after 2nd dose: • 74.4% (95% CI, 70.4 to 77.8) from infection • 59% (95% CI, 16 to 81.6) from symptomatic infection • 46 to 89% from severe disease (RME) • 76.5% (95% CI, 72.9 to 79.6) from death (2 Obs) [91][156]; *last update 2022-02-02*
Delta **1 dose followed by an mRNA vaccine**	**AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]**	ChAdOx1 followed by BNT162b2 at least 14 days after 2nd dose provided protection against VOC Delta for the following outcomes: • 67% (95% CI, 59 to 73) against symptomatic infection (1 Obs) [121]; *last update 2021-12-01* ChAdOx1 followed by mRNA-1273 at least 14 days after 2nd dose provided protection against VOC Delta for the following outcomes: • 79% (95% CI, 62 to 88) against symptomatic infection (1 Obs) [121]; *last update 2021-12-01* ChAdOx1 followed by either BNT162b2 or mRNA-1273 at least 14 days after 2nd dose provided protection against VOC Delta for the following outcomes: • 88% (95% CI, 85 to 89) against infection (1 Obs) [123]; *last update 2021-12-01* ChAdOx1 followed by BNT162b2 provided protection against infection by VOC Delta compared to ChAdOx1 (homologous): • HR 0.61 (95% CI, 0.52 to 0.71) unreported number of days after 2nd dose (1 Obs) [128]; *last update 2021-12-01*
Delta **>14 days after 2nd dose**	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 showed a higher risk of infection by VOC Delta in participants fully vaccinated (≥14 days after 2nd dose) longer than or equal to 146 days ago vs fully vaccinated less than 146 days ago [OR 2.06 (95% CI, 1.69 to 2.51)] (1 Obs) [69]; *last update 2021-08-25*

VOC	Vaccine	Findings
Varying intervals for 2nd dose		BNT162b2 provided protection against infection by VOC Delta for the following number of days after 2nd dose: • 93% (95% CI, 85 to 87) from infection at 7 to 30 days • 86.7% (95% CI, 84.6 to 88.6) from infection up to 44 days • 53 to 85% from infection up to ≥120 days (RME) • 57 to 84% from infection up to 150 days (RME) (6 Obs) [76][84][123][137][152][156]; *last update 2022-02-02* BNT162b2 provided protection against symptomatic infection by VOC Delta for the following number of days after 2nd dose: • 62.7% (95% CI, 61.7 to 63.8) – at 7 days • 76% (95% CI, 72 to 81) – at 30 to 59 days (age 30-59) • 72% (95% CI, 61 to 80) – at 60 to 89 days (age 30-59) • 47% (95% CI, 39 to 55) – at 121 to 180 days • 70.1% (95% CI, 68.9 to 71.2) – at 7 months (210 days) (4 Obs) [92][114][124][141]; *last update 2022-01-05* BNT162b2 provided protection against severe, critical, or fatal disease by VOC Delta for the following number of days after 2nd dose: • 92 to 94% - age 40 to 59 up to 150 days (RME) • 57 to 86% - age 60+ up to 150 days (RME) (3 Obs) [76][125][156]; *last update 2022-02-02* BNT162b2 provided protection against death by VOC Delta for the following number of days after 2nd dose: • 81 to 89% up to 150 days (RME) (3 Obs) [124][125][156]; *last update 2022-02-02* BNT162b2 provided protection against infection by VOC Delta at the following intervals between doses: • 92% (95% CI, 91 to 93) at 14 to 27 days after 2nd dose (interval 7+ weeks) • 90% (95% CI, 88 to 91) at 4 months after 2nd dose (interval 7+ weeks) (1 Obs) [123]; *last update 2021-11-17*
Delta **>14 days after 2nd dose** **Varying intervals for 2nd dose**	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 provided protection against infection by VOC Delta the following number of days after 2nd dose: • 88 to 94% (RME) at 14 to 60 days • 82.8% (95% CI, 69.6 to 90.3) at 14 to 90 days • 63.6% (95% CI, 51.8 to 72.5) at 91 to 180 days • 81 to 88% (RME) at 120 days • 65 to 88% (RME) at 151 to 180 days • 61.4% (95% CI, 56.8 to 65.5) at 181 to 270 days • 52.9% (95% CI, 43.7 to 60.5) at >270 days (6 Obs) [101][123][137][143][152][157]; *last update 2022-02-02* mRNA-1273 provided protection against symptomatic infection by VOC Delta the following number of days after 2nd dose: • 95.2% (95% CI, 94.4 to 95.9) – at 7 days • 91% (95% CI, 85 to 95) – at 30 to 59 days (age 30-59)

VOC	Vaccine	Findings
		• 90% – at 70 to 98 days (RME) • 71% (95% CI, 56 to 81) – at 121 to 180 days • 81.9% (95% CI, 81 to 82.7) – at 7 months (210 days) (4 Obs) [92][114][124][141]; *last update 2022-01-05* mRNA-1273 provided protection against severe disease by VOC Delta the following number of days after 2nd dose: • 97.8% (95% CI, 83.7 to 99.7) at 60 days • 91.5% (95% CI, 60.8 to 98.1) at 120 days • 85.2% (95% CI, 82.7 to 87.7) at 150 days (2 Obs)[143][157]; *last update 2022-02-02* mRNA-1273 provided protection against death by VOC Delta the following number of days after 2nd dose: • 96% (95% CI, 91.9 to98) at 60 days • 93.7% (95% CI, 90.2 to 95.9) at 210 days (1 Obs) [124]; *last update 2022-02-02* mRNA-1273 provided protection against infection by VOC Delta at the following intervals between doses: • 92% (95% CI, 90 to 94) at 14 to 27 days after 2nd dose (interval 7+ weeks) • 91% (95% CI, 87 to 94) at 4 months after 2nd dose (interval 7+ weeks) (1 Obs) [123]; *last update 2021-11-17*
Delta **>14 days after 2nd dose** **Varying intervals for 2nd dose**	**AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]**	ChAdOx1 provided protection against infection by VOC Delta the following number of days after 2nd dose: • 72% (95% CI, 66 to 77) at 120 days (1 Obs) [123]; *last update 2022-01-05* ChAdOx1 provided protection against symptomatic infection by VOC Delta the following number of days after 2nd dose: • 92.4% (95% CI, 92.1 to 92.7) – at 7 days • 63 to 67% – at 30 to 59 days (RME) • 65% (95% CI, 48 to 76) – at 60 to 89 days • 41 to 49% – at 120 days (17 weeks) (RME) • 69.7% (95% CI, 68.7 to 70.5) – at 140 days (4 Obs) [92][114][141][142]; *last update 2022-01-05* ChAdOx1 provided protection against severe disease by VOC Delta the following number of days after 2nd dose: • 79.0% (95% CI, 75.9 to 81.7) at 56 to 63 days • 70.5% (95% CI, 67 to 73.7) at 112 to 119 (1 Obs)[142]; *last update 2022-01-05* ChAdOx1 provided protection against infection by VOC Delta at the following intervals between doses: • 85% (95% CI, 60 to 94) at 14 to 27 days after 2nd dose (interval 7+ weeks) • 72% (95% CI, 66 to 77) at 84+ days after 2nd dose (interval 7+ weeks) (1 Obs) [123]; *last update 2021-11-17*

VOC	Vaccine	Findings
Delta **>14 days after dose**	**Johnson & Johnson [AD26.COV 2.S]**	Ad26.COV2.S provided protection against the following outcomes by VOC Delta the following number of days after 2nd dose: • 74% (95% CI, 70 to 76) from infection at ≥150 days • 89.4% (95% CI, 52.3 to 97.6) from death at 120 days (2 Obs) [124][152]; *last update 2022-02-02* Ad26.COV2.S provided protection against symptomatic infection by VOC Delta the following number of days after dose: • 50% (95% CI, 36 to 62) – at 30 to 59 days • 52% (95% CI, 33 to 66) – at 60 to 89 days • 64.3% (95% CI, 62.3 to 66.1) – at 150 days (2 Obs) [124][141]; *last update 2022-01-05*
Delta **>14 days after 2nd dose**	**Sinovac [CoronaVac]**	CoronaVac provided protection against the following outcomes by VOC Delta: • 30% (95% CI, 18.4 to 39.9) from infection up to 150 days • 30.2% (95% CI, 7.6 to 47.3) from ICU admission up to 150 days • 75.7% (95% CI, 67.0 to 82.1) from death up to 150 days (1 Obs) [156]; *last update 2022-02-02*
Delta **>14 days after 2nd dose**	**ChAdOx1 (1 dose) followed by mRNA vaccine**	ChAdOx1 followed by an mRNA provided protection against infection by VOC Delta the following number of days after 2nd dose: • 86% (95% CI, 81 to 89) at 120 days (1 Obs) [123]; *last update 2021-11-17* ChAdOx1 followed by an mRNA provided protection against symptomatic infection by VOC Delta the following number of days after 2nd dose: • 67% (95% CI, 59 to 73) at least 14 days (BNT162b2) • 79% (95% CI, 62 to 88) at least 14 days (mRNA-1273) • 66% (95% CI, 41 to 80) – > 120 days (17 weeks) (2 Obs) [114][121]; *last update 2022-01-05*
Delta **3 doses**	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 (3 doses) provided protection against the following outcomes compared to unvaccinated: • 81 to 93% from infection up to 30 days after 3rd dose (RME) (3 Obs) [137][139][147]; *last update 2022-01-18* BNT162b2 (3 doses) provided protection against symptomatic infection compared to unvaccinated: • 94% (95% CI, 93.4 to 94.6) – at least 14 days after 3rd dose (age 50+) (1 Obs) [126]; *last update 2021-12-15* BNT162b2 (3 doses) provided protection against infection by VOC Delta compared to 2 doses: • 84.0% (95% CI, 79 to 88) at 14 to 20 days after 3rd dose • 45.7% (95% CI, 37.9 to 53.5) median of 30 days after 3rd dose (2 Obs) [93][132]; *last update 2021-12-15* BNT162b2 (3 doses) provided protection against the following outcomes by VOC Delta compared to 2 doses: • Rate ratio 11.3 to 12.3 from infection at least 12 days after 3rd dose • Rate ratio 17.9 to 19.5 from severe illness at least 12 days after 3rd dose

VOC	Vaccine	Findings
		• Rate ratio 14.7 (95% CI, 10 to 21.4) from death at least 12 days after 3rd dose • 90% (95% CI, 86 to 93) from death unclear number of days after 3rd dose (3 Obs)[100][134][135]; *last update 2022-01-05*
Delta **3 doses**	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 (3 doses) provided protection against infection by VOC Delta compared to unvaccinated: • 83 to 95.7% up to 30 days after 3rd dose (RME) (4 Obs) [137][139][147][148]; *last update 2022-01-18* mRNA-1273 (3 doses) provided protection against infection by VOC Delta compared to 2 doses: • 46.6% (95% CI, 36.4 to 55.3) median of 16 days after 3rd dose (1 Obs) [132]; *last update 2021-12-15*
Delta **2 doses followed by 1 dose of another vaccine**	**ChAdOx1**	ChAdOx1 (2 doses) followed by BNT162b2 provided protection against VOC Delta for the following outcomes: • 82% (95% CI, 68 to 90) from infection at least 7 days after 3rd dose • 93.1 to 93.8% from symptomatic infection at least 14 days after 3rd dose (RME) (3 Obs) [126][136][139]; *last update 2022-01-18* ChAdOx1 (2 doses) followed by mRNA-1273 provided protection against VOC Delta for the following outcomes: • 91% (95% CI, 63 to 98) from infection at least 7 days after 3rd dose (1 Obs) [139]; *last update 2022-01-05*
Delta **3 doses**	**Sinovac [CoronaVac]**	CoronaVac (3 doses) provided protection against VOC Delta for the following outcome ≥ 14 days after 3rd dose: • 78.8% (95% CI, 76.8 to 80.6) from symptomatic infection (1 Obs) [154]; *last update 2022-02-02*
Delta **2 doses followed by 1 dose of another vaccine**	**Sinovac [CoronaVac]**	CoronaVac (2 doses) followed by BNT162b2 provided protection against VOC Delta for the following outcomes ≥14 days after 3rd dose: • 96.5% (95% CI, 96.2 to 96.7) from symptomatic infection • 96.2% (95% CI, 94.6 to 97.3) from ICU admission • 96.8% (95% CI, 93.9 to 98.3) from death (1 Obs) [155]; *last update 2022-02-02* CoronaVac (2 doses) followed by ChAdOx1 provided protection against VOC Delta for the following outcomes ≥14 days after 3rd dose: • 93.2% (95% CI, 92.9 to 93.6) from symptomatic infection • 98.9% (95% CI, 98.5 to 99.2) from ICU admission • 98.1% (95% CI, 97.3 to 98.6) from death (1 Obs) [155]; *last update 2022-02-02*
Delta **Transmission Household or close contacts of index case**	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	Fully vaccinated index cases by BNT162b showed VET to unvaccinated (hh contact): • 31 to 63% (RME) Fully vaccinated index cases by BNT162b showed VET to fully vaccinated household contacts: • 10 to 40% (RME)

VOC	Vaccine	Findings
		Fully vaccinated index cases by BNT162b showed VET for hh contacts (unclear status): • 65% (95% CI, 52 to 74) Fully vaccinated hh contacts by BNT162b showed VES: • 46% (95% CI, 40 to 52) (vaccinated index case) • 61% (95% CI, 59 to 63) (unvaccinated index case) • 62 to 90% from infection (unclear status of index case) (RME) • 100% (95% CI, not reported) from severe disease (5 Obs) [105][107][108][129][149]; *last update 2021-01-18*
Delta **Transmission Household or close contacts of index case**	**Moderna Spikevax [mRNA-1723]**	Fully vaccinated household contacts by mRNA-1273 showed VES (unclear status of index): • 62 to 77% from infection (RME) (2 Obs) [108][129]; *last update 2021-12-01*
Delta **Transmission Household or close contacts of index case**	**AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]**	Fully vaccinated index cases by ChAdOx1 showed VET for household contacts (unclear status): • 36% (95% CI, 28 to 43) from infection Fully vaccinated household contacts by ChAdOx1 showed VES (unclear status of index): • 55 to 72% from infection (RME) (2 Obs)[107][108]; *last update 2021-11-03*
Delta **Transmission Household or close contacts of index case**	**ChAdOx1 followed by mRNA vaccine**	Fully vaccinated household contacts by ChAdOx1 followed by mRNA showed VES (unclear status of index): • 86% (95% CI, 45 to 97) from infection (1 Obs)[108]; *last update 2021-11-03*
Gamma	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 provided protection against VOC Gamma for the following outcomes 14 days after 1st dose: • 85% (95% CI, 71 to 92) from infection • 77% (95% CI, 63 to 86) from symptomatic infection • 89% (95% CI, 73 to 95) from hospitalization mRNA-1273 provided protection against VOC Gamma (or Beta) for the following outcomes 35-41 days after 1st dose: • 43% (95% CI, 22 to 59) from symptomatic infection mRNA-1273 provided protection against VOC Gamma for the following outcome ate least 7 days after 2nd dose: • 95% from infection (RME) • 88% (95% CI, 61 to 96) from symptomatic infection (4 Obs – 5 refs) [23][47][101][122][123]; *last update 2021-12-01*
Gamma	**AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]**	ChAdOx1 provided protection against VOC Gamma for the following outcomes at least 14 days after 1st dose: • 60% (95% CI, 48 to 69) from infection • 42 to 48% from symptomatic infection (RME) • 83% (95% CI, 66 to 92) from hospitalization

VOC	Vaccine	Findings
		ChAdOx1 provided protection against VOC Gamma for the following outcomes at least 14 days after 2nd dose: • 90% (95% CI, 61 to 98) from infection • 65.4% (95% CI, 64.6 to 66.2) from symptomatic infection at 56 to 63 days after 2nd dose • 58.7% (95% CI, 56.7 to 60.5) from symptomatic infection at 112 to 119 days after 2nd dose • 75.6% (95% CI, 73.4 to 77.6) from severe disease at 56 to 63 days after 2nd dose • 50.5% (95% CI, 43.4 to 56.6) from severe disease at 112 to 119 days after 2nd dose (5 Obs)[47][116][122][123][142]; *last update 2022-01-05*
Gamma	**Johnson & Johnson [AD26.COV 2.S]**	Ad26.COV2-S provided protection against VOC Gamma for the following outcomes 28 days after dose: • 50.9% (95% CI, 35.5 to 63.0) from symptomatic infection • 92.5% (95% CI, 54.9 to 99.6) from ICU admission • 90.5% (95% CI, 31.5 to 99.6) from death (1 Obs) [117], *last update 2021-11-17*
Gamma	**Sinovac [CoronaVac]**	CoronaVac provided protection against VOC Gamma for the following outcome ≥ 14 days after 2nd dose: • 65.9% (95% CI, 65.2 to 66.6) from infection CoronaVac provided protection against VOC Gamma for the following outcome ≥ 14 days after 2nd dose for people over age 70: • 41.6% (95% CI, 26.9 to 63.3) from symptomatic infection (2 Obs) [30][49]; *last update 2021-07-14*
Gamma	**ChAdOx1 followed by mRNA vaccine**	ChAdOx1 followed by either BNT162b2 or mRNA-1273 at least 14 days after 2nd dose provided protection against VOC Gamma for the following outcomes: • 96% (95% CI, 70 to 99) against infection (1 Obs) [123]; *last update 2021-11-17*
Beta	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 provided protection against VOC Beta for the following outcomes 14 days after 1st dose: • 61.3% (95% CI, 56.5 to 65.5) from infection • 77% (95% CI, 63 to 86) from symptomatic infection • 89% (95% CI, 73 to 95) from hospitalization • 81.6% (95% CI, 71.0 to 88.8) from severe, critical, or fatal disease (combined with Alpha) mRNA-1273 provided protection against VOC Beta for the following outcomes 35-41 days after 1st dose: • 43% (95 CI, 22 to 59) from symptomatic infection mRNA-1273 provided protection against VOC Beta for the following outcome 7 days after 2nd dose: • 96.4% (95% CI, 91.9 to 98.7) from infection • 88% (95% CI, 61 to 96) from symptomatic infection • 95.7% (95% CI, 73.4 to 99.9) from severe, critical, or fatal disease (combined with Alpha) (2 Obs – 3 refs) [23][47][50]; *last update 2021-07-14*

VOC	Vaccine	Findings
Beta	**AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]**	ChAdOx1 provided protection against VOC Beta for the following outcome 14 days after 1st dose: • 48% (95% CI, 28 to 63) from symptomatic infection • 83% (95% CI, 66 to 92) from hospitalization ChAdOx1 provided protection against VOC Beta for the following outcome after 2 doses: • 10.4% (95% CI, -76.8 to 54.8) from mild to moderate disease (1 RCT, moderate quality; 1 Obs) [4][47]; *last update 2021-07-07*
Beta	**Novavax [NVX-CoV2373**	NVX-CoV2373 provided protection against VOC Beta for the following outcome after 7 days after 2nd dose: • Post-hoc: 43% (95% CI, -9.8 to 70.4) from symptomatic infection (1 RCT, moderate quality), [17]; *last update 2021-07-14*
Alpha	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 provided protection against VOC Alpha for the following outcomes 14-41 days after 1st dose: • 58.9 to 88.1% from infection (RME) • 60 to 61% from symptomatic infection (RME) • 81.6% (95% CI, 71.0 to 88.8) from severe, critical, or fatal disease (combined with Beta) mRNA-1273 provided protection against VOC Alpha for the following outcomes at least 7 days after 2nd dose: • 86 to 100% from infection (RME) • 90 to 95.7% from symptomatic infection (RME) • 95.7% (95% CI, 73.4 to 99.9) from severe, critical, or fatal disease (combined with Beta) (10 Obs – 11 refs) [8][23][31][34][37][47][50][60][74][101][102]; *last update 2021-10-20*
Alpha	**AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]**	ChAdOx1 provided protection against VOC Alpha for the following outcome 14 days after 1st dose: • 64% (95% CI, 60 to 68) from symptomatic infection • 85% (95% CI, 81 to 88) from hospitalization ChAdOx1 provided protection against VOC Alpha for the following outcome 21 to 28 days after 1st dose: • 44 to 74% from infection (RME) ChAdOx1 provided protection against confirmed VOC Alpha for the following outcome at least 14 days after 2 doses: • 62 to 79% from infection (RME) (1 RCT, moderate quality; 5 Obs)[9][10][5][47][70][71][]; *last update 2021-08-25*
Alpha	**Novavax [NVX-CoV2373**	NVX-CoV2373 provided protection against VOC Alpha for the following outcome after 2 doses: • 89.7% (95% CI, 80.2 to 94.6) from symptomatic infection. • No hospitalizations or deaths in vaccinated group • Post hoc: 86.3% (95% CI, 71.3 to 93.5) from confirmed Alpha symptomatic infection (1 RCT, moderate quality), [19]; *last update 2021-06-16*
Alpha	**ChAdOx1 followed by mRNA vaccine**	ChAdOx1 followed by BNT162b2 or mRNA-1273 at least 14 days after 2nd dose provided protection against VOC Alpha for the following outcomes: • 88% (95% CI, 83 to 92) against infection (1 Obs) [70]; *last search date* 2021-08-25

VOC	Vaccine	Findings
Alpha **Transmission Household or close contacts of index case**	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 reduced transmission of VOC Alpha (VET) from a vaccinated index case (14 to 21 days after 1st dose) to household contacts compared to households of unvaccinated index cases: • 30 to 49% from infection (RME) BNT162b2 reduced transmission of VOC Alpha (VET) from a vaccinated HCW (10 weeks after 1st dose) to household spouse: • 42.9% (95% CI, 22.3 to 58.1) from infection Fully vaccinated index cases showed VET for household contacts (unclear status): • 70 to 82% from infection (RME) Fully vaccinated household contacts showed VES (unclear status of index): • 65 to 94% from infection (RME) (8 Obs) [6][14][33][40][48][104][107][108]; *last update 2021-11-03*
Alpha **Transmission Household or close contacts of index case**	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 reduced transmission of VOC Alpha (VET) from a vaccinated HCW (10 weeks after 1st dose) to household spouse: • 42.9% (95% CI, 22.3 to 58.1) from infection Fully vaccinated index cases by mRNA-1273 showed VET for household contacts (unclear status): • 88% (95% CI, 50 to 97) from infection Fully vaccinated household contacts by mRNA-1273 showed VES (unclear status of index): • 86 to 91% from infection (RME) (3 Obs)[33][104][108]; *last update 2021-11-03*
Alpha **Transmission Household or close contacts of index case**	**AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]**	ChAdOx1 reduced transmission of VOC Alpha (VET) from a vaccinated index case (14 to 21 days after 1st dose) to household contacts compared to households of unvaccinated index cases: • 30 to 47% from infection (RME) Fully vaccinated index cases by ChAdOx1 showed VET to household contacts (unclear status): • 58 to 63% from infection (RME) Fully vaccinated household contacts by ChAdOx1 showed VES (unclear status of index case): • 38 to 87% from infection (RME) (6 Obs) [6][14][40][104][107][108]; *last update 2021-12-01*
Alpha **Transmission Household or close contacts of index case**	**Johnson & Johnson [AD26.COV 2.S]**	Fully vaccinated index cases by Ad26.COV2.S showed VET for household contacts (unclear status): • 77% (95% CI, 6 to 94) from infection Fully vaccinated household contacts by Ad26.COV2.S showed VES (unclear status of index): • 12% (95% CI, -71 to 54) from infection (1 Obs) [104]; *last update 2021-11-03*

Studies Covering Time Frame for More than One VOC (insufficient data to divide them into separate VOC)		
Alpha to Delta	**Pfizer/ BioNTech** **Comirnaty [BNT162b2]**	BNT162b2 provided protection against infection by VOC Alpha to Delta at least 7 days after 2nd dose: • 69.7% (95% CI, 68.6 to 70.8)

Studies Covering Time Frame for More than One VOC (insufficient data to divide them into separate VOC)		
		BNT162b2 or mRNA-1273 provided protection against VOC Alpha to Delta for the following outcomes ≥ 14 days after 2nd dose: • 57% (95% CI, 53 to 60) from infection at 144 days after 2nd dose • 68% (95% CI, 64 to 71) from symptomatic infection at 42 to 69 days after 2nd dose • 39% (95% CI, 29 to 48) from symptomatic infection at 98 to 148 days after 2nd dose • 92% (95% CI, 85 to 96) from severe disease in people with no risk conditions • 72% (95% CI, 51 to 84) from severe disease with very high risk conditions • 95% (95% CI, 88 to 98) from death at 14 to 41 days after 2nd dose • 86 to 93% from death at 70 to 148 days after 2nd dose(RME) BNT162b2 showed OR 1.61 (95% CI, 1.45 to 1.79) for infection comparing fully vaccinated Jan to Feb (VOC_Alpha) vs fully vaccinated Mar to May (VOC Delta). (5 Obs) [95][96][127][144][145]; *last update* 2022-12-01
Alpha to Delta	**Pfizer/ BioNTech (3 doses)** **Comirnaty [BNT162b2]**	BNT162b2 (3 doses) provided protection against VOC Alpha to Delta for the following outcomes compared to unvaccinated: • 88% (95% CI, 86 to 89) from infection at least 14 days after 3rd dose (age>18) BNT162b2 (3 doses) provided protection against VOC Alpha to Delta for the following outcomes: • 75% (95% CI, 71 to 78) from infection at least 14 days after 3rd dose compared to 2 doses (given at least 6 months previously) (age>18) (1 Obs) [146]; *last update 2022-01-05*
Alpha to Delta	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 provided protection against infection by VOC Alpha to Delta at least 7 days after 2nd dose: • 78.2% (95% CI, 76.7 to 79.6) mRNA-1273 or BNT162b2 provided protection against VOC Alpha to Delta for the following outcomes ≥ 14 days after 2nd dose: • 73% (95% CI, 70 to 76) from infection at 144 days after 2nd dose • 92% (95% CI, 85 to 96) from severe disease in people with no risk conditions • 72% (95% CI, 51 to 84) from severe disease with very high risk conditions • 93% (95% CI, 81 to 97) from death at 144 days after 2nd dose (3 Obs) [95][127][145]; *last update 2022-01-05*
Alpha to Delta	**AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]**	ChAdOx1 provided protection against infection by VOC Alpha to Delta at least 7 days after 2nd dose: • 43.4% (95% CI, 4.4 to 66.5) ChAdOx1 provided protection against VOC Alpha to Delta for the following outcomes ≥ 14 days after 2nd dose:

Studies Covering Time Frame for More than One VOC (insufficient data to divide them into separate VOC)		
		• 94% (95% CI, 90 to 96) from severe disease in people with no risk conditions • 63% (95% CI, 46 to 75) from severe disease with very high risk conditions • 33% (95% CI, 23 to 42) from symptomatic infection at 42 to 69 days after 2nd dose • 34% (95% CI, 10 to 52) from symptomatic infection at 70 to 140 days after 2nd dose • 95% (95% CI, 90 to 97) from death at least 14 days after 2nd dose (2 Obs) [95][127][144]; *last update 2022-01-05*
Alpha to Delta	**Johnson & Johnson [AD26.COV2.S]**	Ad26.COV2.S provided protection against VOC Alpha to Delta for the following outcomes ≥ 14 days after 2nd dose: • 36% (95% CI, 30 to 42) from infection at 144 days after 2nd dose • 72% (95% CI, 49 to 85) from death at 144 days after 2nd dose (1 Obs) [145]; *last update 2022-01-05*
Alpha to Delta	**Heterologous mRNA vaccines ChAdOx1 followed by mRNA vaccine**	Heterologous mRNA vaccines provided protection against infection by VOC Alpha to Delta at least 7 days after the 2nd dose: • 84.7% (83.1 to 86.1) ChAdOx1 followed by either BNT162b2 or mRNA-1273 provided protection against infection by VOC Alpha to Delta at least 7 days after 2nd dose: • 60.7% (95% CI, 57.5 to 63.6) (1 Obs) [127]; *last update 2021-12-01*
Alpha to Delta **Maintenance hemodialysis** (not updated after Nov 5, 2021)	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 or BNT162b showed OR of 8.89 (95% CI, 5.92 to 13.34) for unvaccinated vs fully vaccinated against infection (VOC Alpha) mRNA-1273 or BNT162b showed OR of 2.27 (95% CI, 1.72 to 3.00) for unvaccinated vs fully vaccinated against infection (VOC Delta) (1 Obs) [106]; *last update 2021-11-03*
Alpha or Beta **Immunosuppressed, renal transplant** (not updated after Nov 5, 2021)	**Pfizer/ BioNTech** **Comirnaty [BNT162b2]**	BNT162b2 or mRNA-1273 provided protection against infection by VOC Alpha or Beta at the following number of days after 2nd dose: • 46.6% (95% CI, 0.0 to 73.7) ≥14 days • 66.0% (95% CI, 21.3 to 85.3) ≥42 days • 73.9% (95% CI, 33 to 98.9) ≥56 days BNT162b2 or mRNA-1273 provided protection against severe, critical, or fatal disease by VOC Alpha or Beta at the following number of days after 2nd dose: • 72.3% (95% CI, 0.0 to 90.9) ≥14 days • 85% (95% CI, 35.7 to 96.5) ≥42 days • 83.8% (95% CI, 31.3 to 96.2) ≥56 days (1 Obs) [90]; *last update 2021-09-22*
Alpha or Beta **Immunosuppressed, renal transplant**	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 or BNT162b2 provided protection against infection by VOC Alpha or Beta at the following number of days after 2nd dose: • 46.6% (95% CI, 0.0 to 73.7) ≥14 days • 66.0% (95% CI, 21.3 to 85.3) ≥42 days • 73.9% (95% CI, 33 to 98.9) ≥56 days

Studies Covering Time Frame for More than One VOC (insufficient data to divide them into separate VOC)		
(not updated after Nov 5, 2021)		mRNA-1273 or BNT162b2 provided protection against severe, critical, or fatal disease by VOC Alpha or Beta at the following number of days after 2nd dose: • 72.3% (95% CI, 0.0 to 90.9) ≥14 days • 85% (95% CI, 35.7 to 96.5) ≥42 days • 83.8% (95% CI, 31.3 to 96.2) ≥56 days (1 Obs) [90]; *last update 2021-09-22*
Alpha or Beta **Previously infected** (not updated after Nov 5, 2021)	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 (2 doses) after prior infection provided protection against VOC Alpha (or Beta) for the following outcomes: • 85% (95% CI, 80 to 89) against re-infection compared to BNT162b2 without prior infection (1 Obs) [72]; *last update 2021-08-25*
Alpha or Beta **Previously infected** (not updated after Nov 5, 2021)	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 (2 doses) after prior infection did not offer additional protection against VOC Alpha (or Beta) for the following outcomes: • 15% (95% CI, -105 to 66) against re-infection compared to mRNA-1273 without prior infection (1 Obs) [72]; *last update 2021-08-25*
Beta to Delta	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 provided protection against infection by VOC Beta to VOC Delta for the following number of days after the 2nd dose: • 65.8% (95% CI, 63.8 to 67.7) at 5 to 9 weeks • 29.7% (95% CI, 21.7 to 36.9) at 15 to 19 weeks • 0% (95% CI, 0 to 0) 20 to 24 weeks BNT162b2 provided protection against hospitalization or death by VOC Beta to VOC Delta for the following number of days after the 2nd dose: • 94.2% (95% CI, 91.0 to 96.5) at 5 to 9 weeks • 86.4% (95% CI, 69.9 to 94.8) at 15 to 19 weeks • 95.3% (95% CI, 70.5 to 99.9) at 20 to 24 weeks (1 Obs) [98]; *last update* 2021-10-06
Beta or Gamma **HCW** (not updated after Nov 5, 2021)	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 provided protection against VOC Beta or Gamma for the following outcomes 14 to 42 days after 1st dose: • 37.2% (95% CI, 16.6 to 52.7) from infection BNT162b2 provided protection against VOC Beta or Gamma for the following outcome 7 days after 2nd dose: • 79.2% (95% CI, 64.6 to 87.8) from infection (1 Obs)[27]; *last update 2021-06-01*
Beta or Gamma **Transmission Vaccinated HCW vs unvaccinated community**	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 reduced transmission of VOC Beta or Gamma from vaccinated HCW (VET) compared to unvaccinated community ≥14 days after 1st dose: • 54.7% (95% CI, 44.8 to 62.9) from infection BNT162b2 reduced transmission of VOC Beta or Gamma from vaccinated HCW (VETompared to unvaccinated community ≥7 days after 2nd dose: • 84.8% (95% CI, 75.2 to 90.7) from infection (1 Obs) [27]; *last update 2021-06-08*

Special Populations (will not be updated after November 5, 2021)		
Delta **Adolescents** (moved to Pediatric/Adolescent LES)	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 provided protection against VOC Delta for the following outcomes at least 14 days after 1st dose: • 59% (95% CI, 52 to 65) from infection BNT162b2 provided protection against VOC Delta for the following outcomes at least 7 days after 2nd dose: • 90 to 92% against infection (RME) (2 Obs) [112][120]; *last update 2021-11-17*
Delta **HCW**	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 provided protection against VOC Delta for the following outcomes ≥ 14 days after 2nd dose: • 66% (95% CI, 26 to 84) (1 Obs) [81]; *last update 2021-09-22*
Delta **HCW**	**AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]**	ChAdOx1 provided protection against VOC Delta for the following outcomes at least 14 days after 2nd dose: • 54 to 85% from infection (RME) • 64% (95% CI, 38 to 78) from symptomatic infection (2 Obs) [59][66]; *last update* 2021-10-06
Delta **Previously infected, (65+)**	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 (2 doses) provided protection against VOC Delta for the following outcomes compared to natural immunity after prior infection: • 66% (95% CI, 22 to 86) from infection (1 Obs) [103]; *last update 2021-10-20*
Delta **Previously infected (65+)**	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 (2 doses) provided protection against VOC Delta for the following outcomes compared to natural immunity after prior infection: • 68% (95% CI, 30 to 86) from infection • 30% (-11 to 1) from death (1 Obs) [103]; *last update 2021-10-20*
Delta **Prison**	**Moderna Spikevax** **[mRNA-1723]**	mRNA-1273 provided protection against VOC Delta for the following outcomes at least 14 days after 2nd dose: 57% (95% CI, 42 to 67.5) (1 Obs) [113]; *last update 2021-11-03*
Gamma **HCW**	**Sinovac [CoronaVac]**	CoronaVac provided protection against VOC Gamma for the following outcomes ≥14 days after 1st dose: • 35.1% (95% CI, -6.6 to 60.5) from infection • 49.6% (95% CI, 11.3 to 71.4) from symptomatic infection (1 Obs)[18]; last update 2021-05-07
Gamma **LTC residents**	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 (or mRNA-1273) provided protection against VOC Gamma 14 days after 2nd dose: • 52.5% (95% CI, 26.9 to 69.1) against infection • 78.6% (95% CI, 47.9 to 91.2) against severe disease (1 Obs) [61]; *last update 2021-08-11*
Gamma **LTC residents**	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 (or BNT162b2) provided protection against VOC Gamma for the following outcomes 14 days after 2nd dose: • 52.5% (95% CI, 26.9 to 69.1) against infection • 78.6% (95% CI, 47.9 to 91.2) against severe disease (1 Obs) [61]; *last update 2021-08-11*
Gamma	**Pfizer/ BioNTech**	BNT162b2 provided protection against VOC Gamma for the following outcomes ≥ 21 days after 1st dose:

Special Populations (will not be updated after November 5, 2021)		
Over 70 years	**Comirnaty [BNT162b2]**	• 61% (95% CI, 45 to 72) from infection (1 Obs)[35]; *last update 2021-07-07*
Gamma **Over 70 years**	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 provided protection against VOC Gamma for the following outcome ≥21 days after 1st dose: • 61% (95% CI, 45 to 72) from infection (1 Obs) [35]; *last update 2021-06-23*
Alpha **HCW**	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 provided protection against VOC Alpha for the following outcomes 14 to 21 days after 1st dose: • 64 to 84% from infection (RME) BNT162b2 provided protection against VOC Alpha for the following outcomes at least 7 days after 2nd dose: • 90 to 97% from infection (RME) BNT162b2 provided protection against VOC Alpha for the following outcome 7 days after 2nd dose: • 86% (95% CI, 69 to 93) from asymptomatic infection [25] BNT162b2 provided protection against infection by VOC Alpha for the following number of days after 2nd dose: • 85% (95% CI, 68 to 93) at 14 to 119 days • 73% (95% CI, 49 to 86) ≥150 days (6 Obs)[11][34][45][46][56][81]; *last update 2021-11-17*
Alpha **HCW**	**AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]**	ChAdOx1 provided protection against VOC Alpha for the following outcomes at least 14 days after 1st dose: • 64% (95% CI, 50 to 74) from infection ChAdOx1provided protection against VOC Alpha for the following outcomes at least 14 days after 2nd dose: • 90% (95% CI, 62 to 98) from infection (1 Obs) [46]; *last update 2021-07-07*
Alpha **LTC residents**	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 provided protection against VOC Alpha for the following outcomes 7 days after 2nd dose: • 53% (95% CI, 29 to 69) from infection • 89% (95% CI, 81 to 93) from death (1 Obs)[32]; *last update 2021-10-06*
Alpha **Over 65 years, requiring home support**	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 provided protection against VOC Alpha for the following outcomes 7 days after 2nd dose: • 86% (95% CI, 78 to 91) from infection • 97% (95% CI, 88 to 99) from death (1 Obs)[32]; *last update 2021-07-07*
Alpha **Over 70 years**	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 provided protection against VOC Alpha for the following outcomes at least 21 days after 1st dose: • 41 to 67% from infection (RME) BNT162b2 provided protection against VOC Alpha for the following outcomes at least 7 days after 2nd dose: • 75 to 90% from infection (RME) (3 Obs)[28][35][51]; *last update 2021-10-06*
Alpha **Over 70 years**	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 provided protection against VOC Alpha for the following outcome ≥21 days after 1st dose: • 67% (95% CI, 57 to 75) from infection (1 Obs) [35]; *last update 2021-06-23*

Special Populations (will not be updated after November 5, 2021)		
Alpha **Over 80 years**	**AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]**	ChAdOx1 provided protection against VOC Alpha for the following outcomes at least 14 days after 2nd dose: • 88% (95% CI, 48 to 97) from symptomatic infection (1 Obs) [79]; *last update 2021-10-20*
Alpha **Pregnant**	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 provided protection against VOC Alpha for the following outcomes at least 28 days after 1st dose: • 78% (95% CI, 57 to 89) from infection BNT162b2 provided protection against VOC Alpha for the following outcomes 7 to 56 days after 2nd dose: • 86.1% (95% CI, 82.4 to 89.1) from infection • 89% (95% CI, 43 to 100) from hospitalization (2 Obs) [52][54]; *last update 2021-07-28*
Epsilon	**Pfizer/ BioNTech Comirnaty [BNT162b2]**	BNT162b2 provided protection against VOC Epsilon for the following outcome 15 days after 1st dose: • 58.9% (95% CI, −9.7 to 84.5) from infection BNT162b2 provided protection against VOC Epsilon for the following outcome 15 days after 2nddose: • 85.7% (67.2 to 93.9) from infection (2 Obs) [8][31]; *last update 2021-06-08*
Epsilon	**Moderna Spikevax [mRNA-1723]**	mRNA-1273 provided protection against VOC Epsilon for the following outcome 15 days after 1st dose: • 58.9% (95% CI, −9.7 to 84.5) from infection mRNA-1273 provided protection against VOC Epsilon for the following outcome 15 days after 2nddose: • 85.7% (67.2 to 93.9) from infection (2 Obs) [8][31]; *last update 2021-06-08*

Links to references are provided in Appendix 1

Pan American Health Organization/World Health Organization. Pharmacovigilance for COVID-19 Vaccines. https://covid-19pharmacovigilance.paho.org

The COVID-19 Evidence Network to support Decision-making (COVID-END) is supported by an investment from the Government of Canada through the Canadian Institutes of Health Research (CIHR). To help Canadian decision-makers as they respond to unprecedented challenges related to the COVID-19 pandemic, COVID-END in Canada is preparing rapid evidence responses like this one. The opinions, results, and conclusions are those of the evidence-synthesis team that prepared the rapid response, and are independent of the Government of Canada and CIHR. No endorsement by the Government of Canada or CIHR is intended or should be inferred.

Appendix 1: Summary of Study Findings and Appraisals

Section 1: included studies				
Ref	**Author**	**Bottom line**	**ROBINS-I***	**Design, Notes**
*Note: ROBINS-I score risk of bias: Low risk of bias indicates high quality				
1	Dagan	BNT162b2 showed VE 46% (95% CI, 40 to 51) against infection 14 to 20 days after 1st dose and VE 92% (95% CI, 88 to 95) 7 days after 2nd dose. BNT162b2 showed VE 92% (95% CI, 75 to 100) for severe disease at 7 days after 2nd dose.	Moderate	Data-linkage study in Israel; .5 M matched participants (2 M excluded – also (possible overlap with Haas); time and setting for VOC Alpha (estimated 80%).
2	Haas	BNT162b2 showed VE 95.3% (95% CI, 94.9 to 95.7) against infection; VE 97.5% (95% CI, 97.1 to 97.8) against severe or critical COVID-19-related hospitalization; VE 96.7% (95% CI, 96.0 to 97.3) against death 7 days after 2nd dose.	Serious	Data-linkage study in Israel; >6.5 M matched participants (possible overlap with Dagan) Updated May 14 due to final publication; sample confirmed VOC Alpha (estimated 94%).
3	Kustin *Delayed exclusion-only included infected	BNT162b2 showed lower relative VE (2.4:1) against Alpha. after 1st dose; and lower VE (8:1) against Beta after 2nd dose in a population with >90% of Alpha and <1% Beta	Moderate	Case-control study in Israel; small sample for Beta (no overlap CHS cohort); confirmed VOC Alpha and Beta.
4	Madhi	ChAdOx1 nCoV-19 showed VE 10.4% (95% CI, -76.8 to 54.8) against mild to moderate disease 14 days after 2nd dose.	Moderate quality (RCT)	RCT in South Africa; Underpowered for 20% efficacy (42 cases); VOC Beta.
5	Emary	ChAdOx1nCoV-19 showed VE 61.7% (95% CI, 36.7 to 76.9) against infection by VOC Alpha ≥ 15 days after 2nd dose.	Moderate quality (RCT)	RCT in UK; neutralization of Alpha 9 times lower; no sequencing for 45% of cases; 52 cases (19%) had VOC Alpha.
6	Shah	ChAdOx1nCoV-19 or BNT162b2 reduced infection in unvaccinated household contacts of vaccinated HCW by about 30% (HR, 0.70, 95% CI, 0.63 to 0.78) ≥ 14 days after 1st dose; ChAdOx1nCoV-19 or BNT162b2 reduced infection in HCW by about 55% (HR 0.45, 95% CI, 0.42 to 0.49) and hospitalization by 84% (HR 0.16, 95% CI, 0.09 to 0.27) ≥ 14 days after 1st dose.	Moderate	Data-linkage study in Scotland - (25% of cases had received 2 doses); time and setting for VOC Alpha.
7	Sadoff	Single dose Ad26.COV2.S showed VE 52.0% (95% CI, 30.3 to 67.4) at 14 days and VE 64.0% (95% CI, 41.2 to 78.7) at 28 days against moderate to severe disease and VE 81.7% (95% CI, 46.2 to 95.4) at 28 days	Moderate quality (RCT)	RCT; over 40,000 participants; Argentina, Brazil, Chile, Colombia, Mexico, Peru, South Africa, and the United

		against severe disease (VOC Beta in South Africa).		States; 86 of 91 cases sequenced for VOC Beta.
8	Andrejko	BNT162b2 or mRNA-1273 showed VE 58.9% (95% CI, −9.7 to 84.5) at 15 days after 1st dose, and VE 85.7% (95% CI, 67.2 to 93.9) 15 days after 2nd dose against infection.	Serious	Test-negative study in California; 645 participants; 69% of population at time had VOC Alpha or Epsilon.
9	Glampson	ChAdOx1nCoV-19 showed VE 74% (95% CI, 65 to 81) against infection 28 days after 1st dose. BNT162b2 showed VE 78% (95% CI, 73 to 82) against infection 28 days after 1st dose.	Serious	Retrospective cohort in UK; 2M participants; time and setting for VOC Alpha.
10	Pritchard	ChAdOx1nCoV-19 or BNT162b2 showed VE 66% (95% CI, 59 to 72%) 21 days after 1st dose and 78% (95% CI, 68 to 85%) after 2nd dose against infection.	Serious	Survey of randomly selected private households with longitudinal follow-up in UK; 370,000 participants; sample confirmed VOC Alpha.
11	Hall (SIREN)	BNT162b2 vaccine showed VE of 70% (95% CI, 55 to 85) 21 days after 1st dose and 85% (95% CI, 74 to 96) 7 days after 2nd dose against infection in HCW.	Moderate	Prospective cohort with standardized testing for HCW over all of England; 23,000 participants; time and setting for VOC Alpha
12	Shrotri *Delayed exclusion – critical ROB	Similar effect sizes were seen for ChAdOx1 (aHR 0.32, 95% CI, 0.15 to 0.66) and BNT162b2 (aHR 0.35, 95% CI, 0.17 to 0.71) at 35-48 days after 1st dose.	Critical	Prospective cohort in England: 9160 of 10412 frail LTC residents; routine screening; time and setting for VOC Alpha
13	Hyams *Delayed exclusion – did not report clinical outcomes of interest for this LES	BNT162b2 showed VE 71.4% (95% CI, 43.1 to 86.2) against hospitalization 14 days after 1st dose; ChAdOx1nCoV-19 showed VE 80.4% (95% CI, 36.4 to 94.5) against hospitalization 14 days after 1st dose for 80+. When effectiveness analysis for BNT162b2 was restricted to the period covered by ChAdOx1nCoV-19, the estimate was 79.3% (95% CI, 47.0 to 92.5).		Test negative case-control study in Scotland. Single center; 466 participants, 80+; time and setting for VOC Alpha
14	Harris	BNT162b2 or ChAdOx1 reduced likelihood of VET by vaccinated HCW to household contacts by 40-50% 21 days after 1st dose.	Serious	Data-linkage and case-control study in England; 338,887 participants; time and setting for VOC Alpha
15	Goldberg	Prior infection (in unvaccinated) has similar VE against infection [94.8%], and severe illness [96.4%] as two doses of BNT162b2.	Serious	Data-linkage study in Israel; 6,351,903 participants; likely overlaps with Dagan and Haas; time and setting for VOC Alpha

16	Cavanaugh *Delayed exclusion – VOI instead of VOC	VE 66.2% (95% CI, 40.5% to 80.8%) against infection among LTC residents and 75.9% (95% CI, 32.5% to 91.4%) among HCW. VE 94.4% (95% CI, 73.9% to 98.8%) against hospitalization among residents; no HCW were hospitalized. Three residents died, two of whom were unvaccinated (VE 94.4%; 95% CI, 44.6% to 99.4%).	Critical	Outbreak analysis in LTC in Kentucky; small number of events; VOI R.1
17	Shinde	NVX-CoV2372 VE showed VE 50.4% (95% CI, 16.6 to 70.5) against symptomatic infection 7 days after 2nd dose.	Moderate quality (RCT)	RCT in South Africa; 4387 participants; 38/41 cases VOC Beta
18	Hitchings	CoronaVac showed VE of 35.1% (95% CI, -6.6 to 60.5) against infection in HCW after 1st dose.	Serious	Case-control study in HCWs in Manaus; 53,176 participants; 75% prevalence of Gamma; 776 (28%) of 2797 PCR were used for the case-controls; rate of previous infection high in the population
19	Heath	NVX-CoV2373 showed VE 89.7% (95% CI, 80.2 to 94.6) against symptomatic infection after 2nd dose. No hospitalizations or deaths in vaccinated group.	Moderate quality (RCT)	RCT; 15,187 participants in UK Post hoc: VE 86.3% (95% CI, 71.3 to 93.5) against Alpha variant; 10 cases in vaccinated participants; 66 infections confirmed Alpha; 11 infections no sequencing available
20	Ismail *Delayed exclusion – did not report clinical outcomes of interest for this LES	BNT162b2 showed VE 81% (95% CI, 76 to 85) against hospitalization 28 days after 1st dose and 93% (95% CI, 89 to 95) 14 days after the 2nd dose for people 80+. ChAdOx1 showed VE 73% (95% CI, 60 to 81) against hospitalization 28 days after 1st dose; sample size too small to report VE after 2nd dose for people 80+.		Screening study in UK; 13,907 hospitalized patients; results for age 80+; time and setting for VOC Alpha
21	Bernal (2) *Delayed exclusion – critical ROB	BNT162b2 showed VE 44% (95% CI, 32 to 53) after 1st dose and 69% (95% CI, 31 to 86) after 2nd dose against symptomatic infection in 70+. Single dose ChAdOx1 showed VE 55% (95% CI, 41 to 66) against death.	Critical	Data-linkage study in England; 48,096 cases above age 70+; 12.7% BNT162b2 and 8.2% ChAdOx1; VE also reported for 80+ and LTC; time and setting for VOC Alpha
22	Chodick	BNT162b2 showed VE 90% (95% CI, 79 to 95) against infection and VE 94% (95% CI, 88 to 97) against death 7-27 days after 2nd dose; 71% (95% CI, 37 to 87) in immunosuppressed.	Serious	Data-linkage study in Israel (Maccabi Health Care Organization); 1,178,597 participants; time and setting for VOC Alpha

23	Chung	BNT162b2 or mRNA-1273 showed VE 61% (95% CI, 56 to 66) against symptomatic infection by VOC Alpha 14 days after 1st dose and 90% (95% CI, 85 to 94) 7 days after 2nd dose; 43% (95% CI, 22 to 59) against symptomatic infection by VOC Beta or Gamma 14 days after 1st dose and 88% (95% CI, 61 to 96) 7 days after 2nd dose.	Moderate	Test-negative study in Ontario 324,033 participants; screening for variants started 2 months into study period; results also reported for age>70 and according to vaccine (but not according to confirmed variant)
24	Bailly *Delayed exclusion – critical ROB	BNT162b2 showed VE 50% (95% CI, 34 to 73) against infection with VOC Beta >28 days after 2 doses.	Critical	Outbreak in a single LTC in France; 90 participants; all samples genome sequenced for VOC Beta; 2 deaths in vaccinated group
25	Angel	BNT162b2 showed VE 97% (95% CI, 94 to 99) against symptomatic infection and 86% (95% CI, 69 to 93) against asymptomatic infection ≥ 7 days after 2 doses in HCW.	Serious	Retrospective cohort at a single centre tertiary medical centre in Israel, 6,710 participants; testing strategy was different between vaccinated and unvaccinated; time and setting for VOC Alpha
26	Bianchi *Delayed exclusion – critical ROB	BNT162b2 showed VE 61.9% (95% CI, 19.2 to 82) against infection 14 to 20 days after 1st dose; 96% (95% CI, 82.2 to 99.1) ≥ 7 days after 2nd dose in HCW.	Critical	Data-linkage, single centre medical centre in Italy, 2,034 participants; time and setting for VOC Alpha
27	Yassi	BNT162b2 (93%) or mRNA-1273 showed VE 37.2% (95% CI, 16.6 to 52.70) against infection by VOC Beta or Gamma 14 to 42 days after 1st dose and 79.2% (95% CI, 64.6 to 87.8) 7 days after 2nd dose in HCW.	Serious	Data-linkage, 25,558 Canadian HCW; evenly split between VOC Gamma and VOC Beta by end of study period
28	Bernal (1)	BNT162b2 showed VE 60% (95% CI, 40 to 73) against confirmed symptomatic infection by VOC Alpha at least 28 days after 1st dose and 90% (95% CI, 84 to 94) at least 14 days after 2nd dose for people 70+.	Serious	Test-negative in England, 156,930 participants; spike gene target failure as proxy for confirmed VOC Alpha
29	Bernal (3)	BNT162b2 showed VE 47.5% (95% CI, 41.6 to 52.8) at least 21 days after 1st dose and VE 93.7% (95% CI, 91.6 to 95.3) at least 14 days after 2nd dose against symptomatic infection by confirmed VOC Alpha. ChadOx1showed VE 48.7% (95% CI, 45.2 to 51.9) at least 21 days after 1st dose and VE 74.5% (95% CI, 68.4 to 79.4) at least 14 days after 2nd dose against symptomatic infection by confirmed VOC Alpha.	Serious	Test-negative in England; 19,109 sequenced cases: 14,837 VOC Alpha and 4,272 VOC Delta.

		BNT162b2 showed VE 35.6% (95% CI, 22.7 to 46.4) at least 21 days after 1st dose and VE 88% (95% CI, 85.3 to 90.1) at least 14 days after 2nd dose against symptomatic infection by confirmed VOC Delta. ChAdOx1 showed VE 30% (95% CI, 24.3 to 35.3) at least 21 days after 1st dose and VE 67% (95% CI, 61.3 to 71.8) at least 14 days after 2nd dose against symptomatic infection by confirmed VOC Delta.		
30	Ranzani	CoronaVac reduced risk of symptomatic infection by VOC Gamma VE 41.6% (95% CI, 26.9 to 63.3) ≥ 14 days after 2nd dose for people 70+.	Serious	Test-negative in Brazil; 44,055 participants; sequencing not performed; effectiveness declined with age; time and setting for VOC Gamma
31	Andrejko (2)	BNT162b2 and mRNA-1273 showed VE 86.8% (95% CI, 68.6 to 94.7) and VE 86.10% (95% CI, 69.1 to 93.9), respectively, against infection 15 days after 2nd dose.	Serious	Test-negative in California; 1,023 participants; expansion of sample size and timeline since previous study by same authors; VOC Alpha, Epsilon
32	Emborg	BNT162b2 showed VE 53-86% against infection across high-risk groups, VE 75-87% against hospitalization across high-risk groups, VE 89% (95% CI, 81 to 93) against death in LTCF residents and VE 97% (95% CI, 88 to 99) against death in 65+ requiring personal care 7 days after 2nd dose.	Serious	Data-linkage population study of high-risk groups in Denmark; 864,096 participants; sample confirmed VOC Alpha
33	Salo	BNT162b2 showed VE 42.9% (95% CI, 22.3 to 58.1) against infection in unvaccinated household members of vaccinated HCW 10 weeks after 1st dose.	Moderate	Data-linkage for household contacts of HCW in Finland; 52,766 spouses of vaccinated HCW; time and setting for VOC Alpha
34	Shrestha	BNT162b2 or mRNA-1273 showed VE 97.1% (95% CI, 94.3 to 98.5) against infection ≥14 days after 2nd dose (based on multivariable model).	Moderate	Retrospective cohort of employees of a health care system in Ohio; 46,866 participants (60%) vaccinated by end of study; time and setting for VOC Alpha
35	Skowronski	BNT162b2 (85%) or mRNA-1273 showed VE 67% (95% CI, 57 to 75) against infection by confirmed VOC Alpha ≥21 days after 1st dose for 70+. BNT162b2 (85%) or mRNA-1273 showed VE 61% (95% CI, 45 to 72) against infection by confirmed VOC Gamma ≥21 days after 1st dose for 70+.	Serious	Test-negative in Canada; 16,993 specimens; out of 1,131 genetically sequenced: 45% VOC Alpha and 28% Gamma; results reported by vaccine but not according to confirmed variant
36	Abu-Raddad	BNT162b2 showed VE 89.5% (95% CI, 85.9 to 92.3) against infection, VE 100%	Serious	Test-negative in Qatar; 17,293 cases; sequencing showed 50%

		(95% CI, 81.7 to 100) against any severe, critical, or fatal disease by VOC Alpha ≥ 14 days after 2nd dose. BNT162b2 showed VE 75% (95% CI, 70.5 to 78.9) against infection, VE 100% (95% CI, 73.7 to 100) against severe, critical, or fatal disease by VOC Beta ≥ 14 days after 1st dose.		VOC Beta and 45% VOC Alpha between February-March 2021
37	Akhrass *Delayed exclusion - failure to report outcomes of interest for this LES	BNT162b2 or mRNA-1273 showed overall VE 60.4% (95% CI, 30 to 77.6) against symptomatic infection ≥ 14 days after 1st dose; BNT162b2 or mRNA-1273 showed overall VE 95.7% (95% CI, 90 to 98.2) against symptomatic infection ≥ 14 days after 2nd dose.	Critical	Retrospective cohort of HCW at a single centre in Kentucky, USA; 2,134 participants; time and setting for VOC Alpha
38	Sheikh	BNT162b2 showed VE 30% (95% CI, 17 to 41) against confirmed VOC Delta infection and VE 33% (95% CI, 15 to 47) against symptomatic infection at least 28 days after 1st dose; VE 79% (95% CI, 75 to 82) against infection and VE 83% (95% CI, 78 to 87) against symptomatic infection at least 14 days after 2nd dose. ChAdOx1 showed VE 18% (95% CI, 9 to 25) against confirmed VOC Delta infection and VE 33% (95% CI, 23 to 41) against symptomatic infection at least 28 days after 1st dose; VE 60% (95% CI, 53 to 66) against infection and VE 61% (95% CI, 51 to 70%) against symptomatic infection at least 14 days after 2nd dose.	Serious	Test-negative in Scotland; 626,900 specimens; also compared hospitalization rates between S gene positive (VOC Delta) and S gene negative specimens within 14 days of positive test result (not summarized here)
39	Furer *Delayed exclusion – critical risk of bias	BNT162b2 reported no symptomatic infections in the vaccinated group (0/686) compared to 0.83% infections in the vaccinated general population control group.	Critical	Prospective cohort of adults with autoimmune inflammatory rheumatic diseases in Israel; 686 participants; time and setting for VOC Alpha
40	Martinez-Baz	BNT162b2 showed VE 65% (95% CI, 56 to 73) against infection and VE 94% (95% CI, 60 to 99) against hospitalization at least 14 days after 2nd dose in close contacts of COVID+ index cases. ChAdOx1 showed VE 44% (95% CI, 31 to 54) against infection and VE 92% (95% CI, 46 to 99) against hospitalization at least 14 days after 1st dose in close contacts of index cases. Second dose results not reported.	Serious	Prospective cohort of close contacts of COVID+ people in Spain; 20,961 participants; VOC Alpha confirmed for small sample; sample size for Moderna too small to report results separately

41	Chodick (2)	BNT162b2 showed VE 51.4% (95% CI, 16.3 to 71.8) against infection 13 to 24 days after 1st dose.	Serious	Data-linkage study in Israel (Maccabi Health Care Services); 351,897 participants; time and setting for VOC Alpha
42	Stowe	BNT162b2 showed VE 94% (95% CI, 46 to 99) at least 21 days after 1st dose and VE 96% (95% CI, 86 to 99) at least 14 days after 2nd dose against hospitalization by confirmed VOC Delta. ChAdOx1 showed VE 71% (95% CI, 51 to 83) at least 21 days after 1st dose and VE 92% (95% CI, 75 to 97) 14 days after 2nd dose against hospitalization by confirmed VOC Delta.	Serious	Same cohort as Bernal (3) with extended time frame for symptomatic infection and adding in data-linkage to hospitalization; 14,019 participants; sample confirmed VOC Delta
43	Saciuk	BNT162b2 showed VE 93% (95% CI, 92.6 to 93.4) against infection, VE 93.4% (95% CI, 91.9 to 94.7) against hospitalization and VE 91.1% (95% CI, 86.5 to 94.1) against death at least 7 days after 2nd dose	Serious	Retrospective cohort of members of a health management organization in Israel; 1,650,885 participants; time and setting for VOC Alpha
44	Zacay *Delayed exclusion – critical risk of bias	BNT162b2 showed VE 61% (95% CI, 49 to 71) at least 14 days after 1st dose and VE 89% (95% CI, 82 to 94) at least 7 days after 2nd dose against infection	Serious	Retrospective cohort of a subpopulation of members of a health management organization in Israel who had undergone repeated PCR testing; 6,286 participants; time and setting for VOC Alpha
45	Azamgarhi	BNT162b2 showed VE 70% (95% CI, 6 to 91) against infection at least 14 days after 1st dose	Serious	Single centre cohort study of HCW in UK; 2,260 participants; time and setting for VOC Alpha
46	Lumley	BNT162b2 (63%) or ChAdOx1showed VE 64% (95% CI, 50 to 74) 14 days after 1st dose and VE 90% (95% CI, 62 to 98) 14 days after 2nd dose against infection	Serious	Prospective cohort of HCWs in Oxfordshire, UK; 13,109 participants; confirmed VOC Alpha
47	Nasreen	BNT162b2 showed VE 89% (95% CI, 86 to 91) against symptomatic infection and VE 95% (95% CI, 92 to 97) against hospitalization at least 7 days after 2nd dose (VOC Alpha); VE 84% (95% CI, 69 to 92) against symptomatic infection and VE 95% (95% CI, 81 to 99) against hospitalization at least 7 days after 2nd dose (VOC Beta/Gamma); VE 87% (95% CI, 64 to 95) against symptomatic infection at least 7 days after 2nd dose (VOC Delta).	Moderate	Test-negative study in Ontario 421,073 participants (same population as for Chung but extended to May 2021 and more detailed with respect to reporting of VOC); screening for VOC Alpha, Beta/Gamma and Delta varied during study period

		BNT162b2 showed VE 78% (95% CI, 65 to 86) against hospitalization at least 7 days after 2nd dose (VOC Delta). mRNA-1273 showed VE 92% (95% CI, 86 to 96) against symptomatic infection and VE 94% (95% CI, 89 to 97) against hospitalization at least 7 days after 2nd dose (VOC Alpha). mRNA-1273 showed VE 77% (95% CI, 63 to 86) against symptomatic infection and VE 89% (95% CI, 73 to 95) against hospitalization at least 14 days after 1st dose (VOC Beta/Gamma); VE 72% (95% CI, 57 to 82) against symptomatic infection and VE 96% (95% CI, 72 to 99) against hospitalization at least 14 days after 1st dose (VOC Delta). ChAdOx1 showed VE 64% (95% CI, 60 to 68) against symptomatic infection and VE 85% (95% CI, 81 to 88) against hospitalization at least 14 days after 1st dose (VOC Alpha); VE 48% (95% CI, 28 to 63) against symptomatic infection and VE 83% (95% CI, 66 to 92) against hospitalization at least 14 days after 1st dose (VOC Beta/Gamma); VE 67% (95% CI, 44 to 80) against symptomatic infection and VE 88% (95% CI, 60 to 96) against hospitalization at least 14 days after 1st dose (VOC Delta).		
48	Gazit	BNT162b2 showed VE 80% (95% CI, 73 to 85) at least 7 days after 2nd dose against infection in vaccinated household members of a confirmed COVID+ case.	Serious	Retrospective cohort of household members (household = 2 adults with no children) of a health management organization in Israel; 173,569 households; time and setting for VOC Alpha
49	Jara	CoronaVac showed VE 65.9% (95% CI, 65.2 to 66.6) against infection and VE 86.3% (95% CI, 84.5 to 87.9) against death at least 14 days after 2nd dose.	Moderate	Prospective cohort in Chile; 10.2 million participants; time and setting for VOC Gamma
50	Chemaitelly	mRNA-1273 showed VE 88.1% (95% CI, 83.7 to 91.5) and VE 100% (95% CI, 91.8 to 100) against infection by confirmed VOC Alpha at least 14 days after 1st and 2nd dose, respectively.	Serious	Test-negative in Qatar; >75,000 participants; sample sequenced for VOC Alpha and VOC Beta

		mRNA-1273 showed VE 61.3% (95% CI, 56.5 to 65.5) and VE 96.4% (95% CI, 91.9 to 98.7) against infection by confirmed VOC Beta at least 14 days after 1st and 2nd dose, respectively. mRNA-1273 showed VE 81.6% (95% CI, 71.0 to 88.8) and VE 95.7% (95% CI, 73.4 to 99.9) against severe, critical, or fatal disease at least 14 days after 1st and 2nd dose, respectively (combined VOC Alpha and Beta).		
51	Baum	BNT162b2 or mRNA-1273 showed VE 41% (95% CI, 25 to 54) against infection ≥ 21 days after 1st dose; BNT162b2 or mRNA-1273 showed VE 75% (95% CI, 65 to 82) against infection ≥ 7 days after 2nd dose in age 70+. BNT162b2 or mRNA-1273 showed VE 41% (95% CI, 17 to 58) against infection ≥ 21 days after 1st dose; BNT162b2 or mRNA-1273 showed VE 77% (95% CI, 65 to 85) against infection ≥ 7 days after 2nd dose in chronically ill (age 16-69). ChAdOx1 showed VE 24% (95% CI, -1 to 43) against infection ≥ 21 days after 1st dose in chronically ill (age 16-69).	Serious	Data-linkage study in Finland; 901,092 participants age 70+ and 774,526 participants age 16 to 69 years with chronic illness; time and setting for VOC Alpha; results for mRNA vaccines not reported separately
52	Balicer	BNT162b2 showed VE 86.1% (95% CI, 82.4 to 89.1) against infection; VE 89% (95% CI, 43 to 100) against hospitalization 7 to 56 days after 2nd dose. Too few events to report VE for severe disease or death.	Serious	Data-linkage study of pregnant women over age 16 in Israel (same database as Dagan); 21,722 participants; time and setting for VOC Alpha.
53	Mateo-Urdiales	BNT162b2 (61%) or ChAdOx1 (31%) or mRNA-1273 (7%) or Ad26.COV$_2$-S (0.6%) showed VE 78% (95% CI, 76 to 79) against infection 42 to 49 days after at least 1st dose; VE 93% (95% CI, 89 to 96) against death 35 to 42 days after at least 1st dose.	Serious	Data-linkage study in Italy; 13,721,506 participants; time and setting for VOC Alpha. Results not reported by vaccine and some participants (42%) who also received 2nd dose were included in estimates.
54	Goldshtein	BNT162b2 showed VE 78% (95% CI, 57 to 89) against infection at least 28 days after 1st dose.	Serious	Data-linkage study of pregnant women in Israel (same database as Gazit); 15,060 participants; time and setting for VOC Alpha.
55	Mason	BNT162b2 showed VE 55.2% (95% CI, 40.8 to 66.8) and VE 70.1% (95% CI, 55.1	Moderate	Case-control study of age 80-83 vs 76-79 community-

		to 80.1) against infection 21 to 27 days and 35 to 41 days after 1st dose, respectively.		dwelling unvaccinated residents in England; time and setting for VOC Alpha
56	Fabiani	BNT162b2 showed VE 84.1% (95% CI, 39.7 to 95.8) and VE 85.4% (95% CI, -35.3 to 98.4) against infection 14 to 21 days and ≥21 days after 1st dose, respectively in HCW. BNT162b2 showed VE 95.1% (95% CI, 62.4 to 99.4) against infection ≥7 days after 2nd dose in HCW.	Serious	Retrospective cohort of HCW in Italy; 6,423 participants; time and setting for VOC Alpha
57	Chia	BNT162b2 or mRNA-1273 showed VE 92.7% (95% CI, 65.7 to 98.4) against severe disease (defined as requiring supplemental oxygen) > 14 days after 2nd dose.	Serious	Retrospective cohort of confirmed VOC Delta admitted to hospital (including asymptomatic) in Singapore; 218 participants; not reported by vaccine
58	Kaur *Delayed exclusion – critical ROB	Two doses of Covishield showed VE 87% (95% CI, 33 to 97) against severe disease when compared with one dose (timing of doses not reported).	Critical	Preliminary report of prospective cohort in India; 1500 participants; time and setting for VOC Delta
59	Pramod *Delayed exclusion – critical ROB	Covishield showed VE 49% (95% CI, 17 to 68) against infection 21 days after 1st dose and VE 54% (95% CI, 27 to 71) against infection 14 days after 2nd dose. Covishield showed VE 58% (95% CI, 28 to 75) against symptomatic infection 21 days after 1st dose and VE 64% (95% CI, 38 to 78) against symptomatic infection 14 days after 2nd dose.	Critical	Test-negative study in a single hospital site in India; 360 matched pairs (203 symptomatic pairs); time and setting for VOC Delta
60	Carazo	BNT162b2 or mRNA-1273 showed VE 60% (95% CI, 53.6 to 65.5) against infection by confirmed VOC Alpha 14 days after 1st dose. BNT162b2 or mRNA-1273 showed VE 92.6% (95% CI, 87.1 to 95.8) against infection by confirmed VOC Alpha 7 days after 2nd dose.	Serious	Test-negative study in Quebec, Canada; 58,476 participants; sample confirmed VOC Alpha; reported according to vaccine but not concurrently for VOC Alpha
61	Williams	BNT162b2 or mRNA-1273 showed VE 52.5% (95% CI, 26.9 to 69.1) against infection and VE 78.6% (95% CI, 47.9 to 91.2) against severe disease 14 days after 2nd dose in residents at LTCF. Two deaths in vaccinated residents but were palliative prior to infection. BNT162b2 or mRNA-1273 showed VE 66.2% (95% CI, 2.3 to 88.3) against	Serious	Outbreak in a single LTCF in Ontario; 60 residents and 83 staff; sample confirmed VOC Gamma

		infection 14 days after 2nd dose in staff at LTCF. None of the staff developed severe disease.		
62	Hitchings(2) *Delayed exclusion – critical ROB	ChAdOx1 showed VE 33.4% (95% CI, 26.4 to 39.7) against symptomatic infection and VE 50.9% (95% CI, 33.6 to 63.8) against ICU admission and VE 61.8% (95% CI, 48.9 to 71.4) against death at least 28 days after 1st dose for 60+. ChAdOx1 showed VE 77.9% (95% CI, 69.2 to 84.2) against symptomatic infection and VE 89.9% (95% CI, 70.9 to 96.5) against ICU admission and VE 93.6% (95% CI, 81.9 to 97.7) against death at least 14 days after 2nd dose.	Critical	Test-negative study in Sao Paulo, Brazil; 61,164 participants over age 60; time and setting for VOC Gamma
63	Tang	BNT162b2 showed VE 65.5% (95% CI, 40.9 to 79.9) against infection ≥ 14 days after 1st dose; BNT162b2 showed VE 59.6% (95% CI, 50.7 to 66.9) against infection ≥ 14 days after 2nd dose. BNT162b2 showed VE 100% (95% CI, not reported) against severe, critical or fatal disease ≥ 14 days after 1st dose; BNT162b2 showed VE 97.3% (95% CI, 84.4 to 99.5) against severe, critical or fatal disease ≥ 14 days after 2nd dose. mRNA-1273 showed VE 79.7% (95% CI, 60.8 to 89.5) against infection ≥ 14 days after 1st dose; mRNA-1273 showed VE 86.1% (95% CI, 78.0 to 91.3) against infection ≥ 14 days after 2nd dose. mRNA-1273 showed VE 100% (95% CI, not reported) against severe, critical or fatal disease ≥ 14 days after 1st dose; mRNA-1273 showed VE 100% (95% CI, not reported) against severe, critical or fatal disease ≥ 14 days after 2nd dose.	Serious	Test-negative study in Qatar; 1,140,337 participants; weekly random sequencing of positive samples for VOC Delta
64	Puranik	BNT162b2 showed VE 42% (95% CI, 13 to 62) against infection 14 days after 2nd dose. mRNA-1273 showed VE 76% (95% CI, 58 to 87) against infection 14 days after 2nd dose.	Serious	Data-linkage study involving Mayo Clinic Health in USA; 25,859 matched triples from Minnesota only; time and setting for Delta at end of study time frame so only last month of data (July 2021) reported here
65	Elliot	BNT162b2 or ChAdOx1 showed VE 64% (95% CI, 11 to 85) against infection	Critical	Surveillance study in England; 121,872 participants; time and

	*Delayed exclusion – critical ROB	unreported number of days after 2nd dose (Round 12: 2021-05-20 to 2021-06-07). BNT162b2 or ChAdOx1 showed VE 49% (95% CI, 22 to 67) against infection unreported number of days after 2nd dose (Round 13: 2021-06-24 to 2021-07-12).		setting for VOC Delta; only included data from aged 18 to 64 years due to lowest risk for misclassification bias due to self-reported vaccination status
66	Issac	ChAdOx1 showed VE 85% (95% CI, 71 to 92) against infection 14 days after 2nd dose.	Serious	Prospective cohort of HCW at a single hospital in India; 342 participants; time and setting for VOC Delta.
67	Marco *Delayed exclusion – critical ROB	ChAdOx1 showed VE 23% (95% CI, not reported) against infection at least 21 days after 1st dose.	Critical	Outbreak study of prison inmates in Barcelona; 217 participants (184 inmates); sequenced for VOC Alpha
68	Kale *Delayed exclusion – critical ROB	ChAdOx1 showed VE 60% (95% CI, 45 to 70) against infection at least 14 days after 2nd dose.	Critical	Prospective cohort of HCW at a single hospital in India; 1858 participants; sample sequenced for VOC Delta
69	Israel	BNT162b2 showed OR 2.06 (95% CI, 1.69 to 2.51) for infection comparing fully vaccinated ≥146 days vs fully vaccinated less than 146 days.	Moderate	Retrospective cohort of fully vaccinated members of a health management organization in Israel who underwent testing; 33,993 participants; time and setting for VOC Delta
70	Gram	ChAdOx1 showed VE 44% (95% CI, 29 to 56) against infection 21 to 27 days after 1st dose. No deaths in vaccinated participants. First dose ChAdOx1 followed by second dose BNT162b2 or mRNA-1273 showed VE 88% (95% CI, 83 to 92) against infection ≥ 14 days after 2nd dose.	Serious	Data-linkage study in Denmark; 5,542,079 participants; sequenced for VOC Alpha (includes heterologous vaccines)
71	Pouwels	BNT162b2 showed VE 59% (95% CI, 52 to 65%) against infection ≥21 days after 1st dose and VE 78% (95% CI, 68 to 84) against infection ≥ 14 days after 2nd dose (VOC Alpha age 18+). BNT162b2 showed VE 57% (95% CI, 50 to 63) against infection ≥21 days after 1st dose and VE 80% (95% CI, 77 to 83) against infection ≥ 14 days after 2nd dose (VOC Delta age 18+). ChAdOx1 showed VE 63% (95% CI, 55 to 69) against infection ≥21 days after 1st dose and VE 79% (95% CI, 56 to 90) against infection ≥ 14 days after 2nd dose (VOC Alpha age 18+).	Serious	Survey of randomly selected private households with longitudinal follow-up in UK; 743,526 participants; also reported for 18-64 years; sample sequenced for VOC Alpha and VOC Delta

		ChAdOx1 showed VE 46% (95% CI, 35 to 55) against infection ≥21 days after 1st dose and VE 67% (95% CI, 62 to 71) against infection ≥ 14 days after 2nd dose (VOC Delta age 18+). mRNA-1273 showed VE 75% (95% CI: 64 to 83) against infection ≥21 days after 1st dose (VOC Delta age 18 to 64).		
72	Abu-Raddad (2)	BNT162b2 after prior infection showed VE 85% (95% CI, 80 to 89) against re-infection compared to BNT162b2 without prior infection. mRNA-1273 after prior infection showed VE 15% (95% CI, -105 to 66) against re-infection compared to mRNA-1273 without prior infection.	Serious	Retrospective matched cohorts (2) of fully vaccinated in Qatar; 151,076 participants; sample sequenced for VOC Alpha and VOC Beta
73	Gazit (2)	BNT162b2 showed OR 13.06 (95% CI, 8.08 to 21.11) against infection and OR 27.02 (95% CI, 12.7 to 57.5) against symptomatic disease compared to prior infection.	Moderate	Retrospective matched cohorts of fully vaccinated in Israel; 778,658 participants; time and setting for VOC Delta
74	Rosenberg	BNT162b2 (51%), mRNA-1273 (40%) or Ad26.COV2.S (9%) showed VE 91.7% against infection ≥14 days after 2nd dose (Week of May 3, 2021: VOC Alpha). BNT162b2 (51%), mRNA-1273 (40%) or Ad26.COV2.S (9%) showed VE 79.8% against infection ≥14 days after 2nd dose (Week of July 19, 2021: VOC Delta).	Serious	Surveillance report in New York, USA; >13 million participants; time and setting for VOC Delta (from 2% to 80% during study period)
75	Al-Qahtani *Delayed exclusion due to critical ROB	BNT162b2 ≥14 days after 2nd dose, showed VE 99.9% (95% CI, 99.2 to 100) against ICU admission, and VE 99.5% (95% CI, 98.4 to 99.8) against death (VOC Alpha and Delta). ChAdOx1 ≥14 days after 2nd dose, showed VE 99.2% (95% CI, 97.6 to 99.7) against ICU admission, and VE 99.6% (95% CI, 97.2 to 100) against death (VOC Alpha and Delta). BBIBP-CorV ≥14 days after 2nd dose, showed VE 95.4% (95% CI, 94.6 to 96.2) against ICU admission, and VE 94.3% (95% CI, 93.1 to 95.4) against death (VOC Alpha and Delta).	Critical	Retrospective cohort of fully vaccinated (>14 days after 2nd dose) in Bahrain; 1,242,279 participants; time and setting for VOC Alpha (dominant before May 2021) and Delta (dominant after May 2021).

		Sputnik V ≥14 days after 2nd dose, showed VE 100% (95% CI, 99.2 to 100) against ICU admission, and VE 99.5% (95% CI, 98.5 to 99.9) against death (VOC Alpha and Delta).		
76	Goldberg (2)	BNT162b2 showed VE 50% (95% CI, 45 to 55) for those vaccinated in January 2021, and VE 73% (95% CI, 67 to 78) for those vaccinated in May 2021 against infection after the 2nd dose (VOC Delta age 16 to 39). BNT162b2 showed VE 58% (95% CI, 54 to 62) for those vaccinated in January 2021, and VE 80% (95% CI, 71 to 86) for those vaccinated in May 2021 against infection after the 2nd dose (VOC Delta age 40 to 59). BNT162b2 showed VE 57% (95% CI, 52 to 62) for those vaccinated in January 2021, and VE 75% (95% CI, 58 to 85) for those vaccinated in May 2021 against infection after the 2nd dose (VOC Delta age 60+). BNT162b2 showed VE 94% (95% CI, 87 to 97) for those vaccinated in January 2021, and VE 98% (95% CI, 94 to 99) for those vaccinated in March 2021 against severe, critical, or fatal disease after the 2nd dose (VOC Delta age 40 to 59). BNT162b2 showed VE 86% (95% CI, 82 to 90) for those vaccinated in January 2021, and VE 91% (95% CI, 85 to 95) for those vaccinated in March 2021 against severe, critical, or fatal disease after the 2nd dose (VOC Delta age 60+).	Serious	Data-linkage study of fully vaccinated in Israel; 4,785,245 participants; sequenced for VOC Delta (dominant after May 2021) (results over varying time periods since vaccination reported)
77	Herlihy *Delayed exclusion – critical risk of bias	BNT162b2, mRNA-1273, or Ad26.COV2.S showed VE 78% (95% CI, 71 to 84) in Mesa County and VE 89% (95% CI, 88 to 91) in other Colorado counties against symptomatic infection an unreported number of days after 2nd dose (VOC Delta).	Critical	Surveillance report in Mesa County-Colorado, USA; 37,439 cases participants; sample sequenced for VOC Delta (43% to 88% during study period)
78	Ghosh *Delayed exclusion – critical risk of bias	ChAdOx1 showed unadjusted VE 75.2% (95% CI, 73.8 to 76.8) against infection ≥14 days after 1st dose, and unadjusted VE 54.6% (95% CI, 52.6 to 56.6) ≥14 days after 2nd dose against infection in HCW (VOC Alpha to Delta).	Critical	Retrospective cohort of Armed Forces HCW and frontline workers in India; 1,595,630 participants; time and setting for VOC Delta at end of study only.
79	Amirthalingam	BNT162b2 showed VE 77% (95% CI, 56 to 88) against symptomatic infection when 2nd	Moderate	Test-negative study in England; 750 participants;

		dose given 19-29 days after 1st dose, and VE 94% (95% CI, 73 to 99) against symptomatic infection when 2nd dose given 85+ days after 1st dose (VOC Alpha age 80+). BNT162b2 showed VE 77% (95% CI, 66 to 85) against symptomatic infection when 2nd dose given 19-29 days after 1st dose, and VE 86% (95% CI, 70 to 94) against symptomatic infection when 2nd dose given 85+ days after 1st dose (VOC Alpha age 65 to 79). ChAdOx1 showed VE 96% (95% CI, 72 to 100) against symptomatic infection when 2nd dose given 19-29 days after 1st dose, and VE 88% (95% CI, 48 to 97) against symptomatic infection when 2nd dose given 85+ days after 1st dose after 2nd dose (VOC Alpha age 80+). ChAdOx1 showed VE 66% (95% CI, 47 to 77) against symptomatic infection when 2nd dose given 19-29 days after 1st dose, and VE 73% (95% CI, 56 to 83) against symptomatic infection when 2nd dose given 85+ days after 1st dose after 2nd dose (VOC Alpha age 65 to 79).		time and setting for VOC Alpha (dominant before May 2021) and Delta (dominant after May 2021). (results over varying time periods since vaccination reported)
80	Butt (2) *Delayed exclusion – critical ROB	Unvaccinated participants had HR 2.84 (95% CI, 1.80 to 4.47) of severe disease compared to BNT162b2 ≥14 days after 2nd dose.	Critical	Case-control study in Qatar; 456 matched cases; time and setting for VOC Alpha
81	Fowlkes	BNT162b2 (65%), mRNA-1273 (33%), or Ad26.COV2.S (2%) showed VE 91% (95% CI, 81 to 96) against infection ≥ 14 days after 2nd dose (during time of VOC Alpha). BNT162b2 (65%), mRNA-1273 (33%), or Ad26.COV2.S (2%) showed VE 66% (95% CI, 26 to 84) against infection ≥ 14 days after 2nd dose (during time of VOC Delta). BNT162b2 (65%), mRNA-1273 (33%), or Ad26.COV2.S (2%) showed VE 85% (95% CI, 68 to 93) against infection 14-119 days after full vaccination) and VE 73% (95% CI, 49 to 86) against infection ≥150 days after full vaccination (during time of VOC Alpha to Delta).	Moderate	Prospective cohort of HCW and other essential frontline workers in 6 states in the USA; 7,112 participants; updated report to cover VOC Delta period

82	Bhattacharya *Delayed exclusion due to critical ROB	Covaxin (94%) and Covishield showed VE 83% (95% CI, 73 to 89) against symptomatic infection ≥ 14 days after 2nd dose. Covaxin (94%) and Covishield showed VE 93% (95% CI, 64 to 99) against ICU admission or death ≥ 14 days after 2nd dose.	Critical	Cross-sectional cohort of HCW and their families at a single site in India; 638 participants (55 inpatients); time and setting of VOC Delta
83	Nunes	BNT162b2 (45%) or mRNA-1273 (8%) showed VE 96% (95% CI, 92 to 98) against COVID-related death ≥14 days after 2nd dose (age 65 to 79). BNT162b2 (80%) or mRNA-1273 (2%) showed VE 81% (95% CI, 74 to 87) against COVID-related death ≥14 days after 2nd dose (age ≥80). BNT162b2 (80%) or mRNA-1273 (2%) showed VE 86% (95% CI, 68 to 93) against COVID-related death 14 to 41 days after 2nd dose and VE 74% (95% CI, 60 to 83) against COVID-related death ≥ 98 days after 2nd dose for HR 1.80 (0.77 to 4.25) (age ≥80).	Moderate	Data-linkage study of community-dwelling adults≥65 in Portugal; 2,050,950 participants; time and setting for VOC Alpha to VOC Delta
84	Tartof	BNT162b2 showed VE 75% (95% CI, 71 to 78) against infection 7 days after 2nd dose (confirmed VOC Delta). BNT162b2 showed VE 91% (95% CI, 88 to 92) against infection 7 days after 2nd dose (confirmed non-VOC Delta). BNT162b2 showed VE 93% (95% CI, 85 to 87) against infection 7 to 30 days after 2nd dose and VE 53% (95% CI, 39 to 65) against infection ≥ 127+ days after 2nd dose (confirmed VOC Delta). BNT162b2 showed VE 97% (95% CI, 95 to 99) against infection 7 to 30 days after 2nd dose and VE 67% (95% CI, 45 to 80) against infection ≥ 127+ days after 2nd dose (confirmed non-VOC Delta).	Moderate	Retrospective cohort of members of a health management organization in California; 3,436,957 participants; VOC Alpha to VOC Delta (only 28% confirmed Delta) (results over varying time periods since vaccination reported)
85	Li (3) *Delayed exclusion – critical ROB	CoronaVac (combined with other inactivated vaccines) showed VE 59% (95% CI, 16 to 81.6) against symptomatic infection and VE 100% against severe infection ≥14 days after 2nd dose.	Critical	Test-negative study in Guangzhou, China; 366 participants; sample sequenced for VOC Delta
86	Scobie	BNT162b2 or mRNA-1273 (92%), or Ad26.COV2.S showed VE 90% (95% CI	Critical	Surveillance study in 13 states in the USA; 615,454; time and

	*Delayed exclusion – critical ROB	not reported) against infection and VE 93% (95% CI not reported) against death ≥ 14 days after 2nd dose (April to June: VOC Alpha). BNT162b2, mRNA-1273, or Ad26.COV2.S showed VE 76% (95% CI not reported) against infection and VE 90% (95% CI not reported) against death ≥ 14 days after 2nd dose (June to July: VOC Delta>50%).		setting for VOC Alpha to VOC Delta
87	Satwik *Delayed exclusion due to critical ROB	ChAdOx1 showed VE 18% (95% CI, -10 to 38) against symptomatic infection; VE 37% (-24 to 68) against moderate to severe disease and VE 69% (95% CI, -160 to 97) against death ≥21 days after 1st dose. ChAdOx1 showed VE 28% (95% CI, 10 to 41) against symptomatic infection; VE 67% (44 to 81) against moderate to severe disease and VE 97% (95% CI, 43 to 99.8) against death ≥14 days after 2nd dose.	Critical	Retrospective cohort study of HCW at a single hospital in New Delhi, India; 4276 participants; sample sequenced for VOC Delta
88	Seppala	BNT162b2 (74%) or ChAdOx1 (22%) or mRNA-1273 (10%) showed VE 84.4% (95% CI, 81.8 to 86.5) against infection ≥7 days after 2nd dose (VOC Alpha). BNT162b2 (74%) or ChAdOx1 (22%) or mRNA-1273 (10%) showed VE 64.6% (95% CI, 60.6 to 68.2) against infection ≥7 days after 2nd dose (VOC Delta).	Serious	Population cohort in Norway; 4,204,859 participants; sequenced for VOC Alpha and VOC Delta
89	Polinski	Ad26.COV2.S showed VE* 67% (95% 60 to 73) against infection unknown number of days after dose (June to July: VOC Delta in high prevalence states). *unadjusted for substantial under-reporting of vaccination status	Serious	Data-linkage of members of a medical insurance group in USA; 1,914,670 participants; time and setting for VOC Alpha to Delta (only data for VOC Delta reported here)
90	Chemaitelly (2)	BNT162b2 or mRNA-1273 showed VE 46.6% (95% CI, 0.0 to 73.7) against infection ≥14 days after 2nd dose, VE 66.0% (95% CI, 21.3 to 85.3) ≥42 days after 2nd dose, and VE 73.9% (95% CI, 33 to 98.9) ≥56 days after 2nd dose (VOC Alpha and Beta). BNT162b2 or mRNA-1273 showed VE 72.3% (95% CI, 0.0 to 90.9) against severe, critical, or fatal disease ≥14 days after 2nd dose, VE 85% (95% CI, 35.7 to 96.5) ≥42 days after 2nd dose, and VE 83.8% (95% CI, 31.3 to 96.2) ≥56 days after 2nd dose (VOC Alpha and Beta).	Serious	Retrospective cohort of immunosuppressed kidney transplant recipients in Qatar; 782 participants; time and setting for VOC Alpha and VOC Beta.

91	Hu	Inactivated vaccines (CoronaVac) showed VE 89% (95% CI, 55 to 98) against severe, critical, or fatal disease ≥14 days after 2nd dose (VOC Delta).	Serious	Outbreak report of hospitalized cases in China; 476 participants; PCR population for VOC Delta.
92	Andrews	BNT162b2 showed VE 62.7% (61.7 to 63.8) against symptomatic infection 1 week after 2nd dose and VE 47.3% (45.0 to 49.6) 20+ weeks after 2nd dose (VOC Delta). ChAdOx1showed VE 92.4% (92.1 to 92.7) against symptomatic infection 1 week after 2nd dose and VE 69.7% (68.7 to 70.5) 20+ weeks after 2nd dose (VOC Delta). mRNA-1273 showed VE 95.2% (94.4 to 95.9) against symptomatic infection 1 week after 2nd dose and VE 90.3% (67.2 to 97.1) 10 to 14 weeks after 2nd dose (VOC Delta).	Moderate	Test-negative study in England; 1,475,391 participants; VOC Alpha to VOC Delta (only data for VOC Delta reported here)
93	Patalon	BNT162b2 (3 doses) showed relative VE 3% (95% CI, -5 to 10) against infection 0 to 6 days after 3rd dose; relative VE 84.0% (95% CI, 79 to 88) 14 to 20 days after 3rd dose compared to 2 doses.	Moderate	Test-negative study of fully vaccinated in Israel comparing (2 doses versus 3 doses); 182,076 participants; time and setting for VOC Delta
94	Kissling	BNT162b2 showed VE 87% (95% CI, 74 to 93) against symptomatic infection 14 days after 2nd dose.	Serious	Test-negative study of adults >65 years in primary care setting in I-MOVE group (England, France, Ireland, the Netherlands, Portugal, Scotland, Spain and Sweden); 4,964 participants; sample sequenced for VOC Alpha.
95	McKeigue	BNT162b2 or mRNA-1273 showed VE 92% (95% CI, 85 to 96) against severe disease in people with no risk conditions and VE 72% (95% CI, 51 to 84) against severe disease in people eligible for shielding at least 14 days after 2nd dose. ChAdOx1 showed VE 94% (95% CI, 90 to 96) against severe disease in people with no risk conditions and VE 63% (95% CI, 46 to 75) against severe disease in people eligible for shielding ≥ 14 days after 2nd dose.	Serious	Case-control study of people with clinical risk conditions in Scotland; 50,935 participants; time and setting for VOC Alpha to VOC Delta
96	Kertes	BNT162b2 showed OR 1.61 (95% CI, 1.45 to 1.79) for infection comparing fully vaccinated Jan to Feb vs fully vaccinated Mar to May.	Serious	Data-linkage study of people fully vaccinated 6 months previously in Israel; 1,423,098 participants; time and setting for VOC Alpha to VOC Delta
97	Barlow	BNT162b2 or mRNA-1273 showed VE 74% (95% CI, 65 to 82) against infection ≥ 14 days after 2nd dose.	Serious	Test-negative study in Oregon; 1000 participants; time and setting for VOC Delta

		Ad26.COV2.S showed VE 51% (95% CI, -2 to 76) against infection ≥ 14 days after 2nd dose.		
98	Chemaitelly (3)	BNT162b2 showed VE 65.8% (95% CI, 63.8 to 67.7) against infection 5 to 9 weeks after 2nd dose; VE 29.7% (95% CI, 21.7 to 36.9) against infection 15 to 19 weeks after 2nd dose and VE 0% (95% CI, 0 to 0) against infection 20 to 24 weeks after 2nd dose. BNT162b2 showed VE 94.2% (95% CI, 91.0 to 96.5) against hospitalization or death 5 to 9 weeks after 2nd dose; VE 86.4% (95% CI, 69.9 to 94.8) against hospitalization or death 15 to 19 weeks after 2nd dose and VE 95.3% (95% CI, 70.5 to 99.9) against hospitalization or death 20 to 24 weeks after 2nd dose.	Serious	Test-negative study in Qatar; 1,472,761 participants; time and setting for VOC Beta to VOC Delta (results over varying time periods since vaccination reported)
99	Thompson (3)	BNT162b2 or mRNA-1273 showed VE 90% (95% CI, 86 to 93) against ICU admission ≥14 days after 2nd dose. BNT162b2 showed VE 92% (95% CI, 88 to 94) against hospitalization at 28 to 41 days after 2nd dose and VE 86% (95% CI, 74 to 93) ≥112 days after 2nd dose.	Serious	Test-negative study of adults ≥50 years in the USA; 76,463 participants; time and setting for VOC Alpha (results over varying time periods since vaccination reported)
100	Bar-On	BNT162b2 (3 doses) showed adjusted rate ratio of 11.3 (95% CI, 10.4 to 12.3) against any infection and adjusted rate ratio of 19.5 (95% CI, 12.9 to 29.5) against severe illness ≥12 days after 3rd dose compared to 2 doses.	Serious	Data-linkage study of fully vaccinated (age>60) (2 doses versus 3 doses) in Israel; 1,137,804 participants; time and setting for VOC Delta
101	Bruxvoort (2)	mRNA-1273 showed VE 98.4% (95% CI, 96.9 to 99.1) against infection ≥14 days after 2nd dose (VOC Alpha). mRNA-1273 showed VE 95.5% (95% CI, 90.9 to 97.8) against infection ≥14 days after 2nd dose (VOC Gamma). mRNA-1273 showed VE 86.7% (95% CI, 84.3 to 88.7) against infection ≥14 days after 2nd dose (VOC Delta). mRNA-1273 showed VE 94.1% (95% CI, 90.5 to 96.3) against infection 14 to 60 days after 2nd dose (VOC Delta).	Serious	Test-negative study in Kaiser Permanente group in California; 48,918 participants; sequenced for VOC Alpha, VOC Delta, VOC Gamma and VOI Mu (results not included in this LES) (results over varying time periods since vaccination reported)

		mRNA-1273 showed VE 80.0% (95% CI, 70.2 to 86.6) against infection 151 to 180 days after 2nd dose (VOC Delta).		
102	Tande (2)	BNT162b2 or mRNA-1273 showed VE 91% (95% CI, 72 to 98) against infection ≥14 days after 2nd dose (January to March – VOC Alpha). BNT162b2 or mRNA-1273 showed VE 63% (95% CI, 44 to 76) against infection ≥14 days after 2nd dose (June to August – VOC Delta).	Serious	Point prevalence screening study in Mayo Clinic, USA; 46,008 participants; time and setting for VOC Alpha to VOC Delta
103	Young-Xu (2)	Two doses of BNT162b2 reduced risk of infection by HR 66% (95% CI, 22 to 86) compared to previously infected adults age 65+ (June to August VOC Delta). Two doses of mRNA-1273 reduced risk of infection by HR 68% (95% CI, 30 to 86) and death by HR 30% (95% CI, -11 to 1) compared to previously infected adults age 65+ (June to August VOC Delta).	Moderate	Retrospective cohort study of previously infected adults followed by Veterans Affairs in USA; 47,102 participants; time and setting for VOC Delta
104	de Gier (1)	Fully vaccinated index to unvaccinated (hh contact) showed VET 73% (95% CI: 65 to 79). BNT162b (case) showed VET 70% (95% CI, 61 to 77) when fully vaccinated. mRNA-1273 (case) showed VET 88% (95% CI, 50 to 97) when fully vaccinated. ChAdOx1 (case) showed VET 58% (95% CI, -12 to 84) when fully vaccinated. Ad26.COV2.S (case) showed VET 58% (95% CI, -12 to 84) when fully vaccinated. BNT162b showed VE 65% (95% CI, 60 to 70) when hh contact was fully vaccinated. mRNA-1273 showed VE 91% (95% CI, 79 to 97) when hh contact was fully vaccinated. ChAdOx1 showed VE 87% (95% CI, 77 to 93) when hh contact was fully vaccinated. Ad26.COV2.S showed VE 12% (95% CI, -71 to 54) when hh contact was fully vaccinated.	Serious	Retrospective cohort of household and close contacts in the Netherlands; 113,582 cases and 253,168 contacts; time and setting for VOC Alpha (hh = household)

105	de Gier (2)	Fully vaccinated index to unvaccinated (hh contact) showed VET 63% (95% CI: 46 to 75). BNT162b (>50%) or mRNA-1273 or ChAdOx1 or Ad26.COV2.S (case) showed VET 40% (95% CI, 20 to 54) when both case and contacts are fully vaccinated.	Serious	Retrospective cohort of household and close contacts in the Netherlands; 4,921 cases and 7,771 contacts; time and setting for VOC Delta
106	Manley	mRNA-1273 (50%) or BNT162b (48%) or Ad26.COV2.S (2%) showed OR of 8.89 (95% CI, 5.92 to 13.34) for unvaccinated vs fully vaccinated against infection (VOC Alpha) mRNA-1273 (50%) or BNT162b (48%) or Ad26.COV2.S (2%) showed OR of 2.27 (95% CI, 1.72 to 3.00) for unvaccinated vs fully vaccinated against infection (VOC Delta)	Serious	Retrospective cohort of maintenance dialysis patients in USA; 15,251 participants; time and setting for VOC Alpha to VOC Delta
107	Eyre	BNT162b2 (cases) showed VET 82% (95% CI, 71 to 88) against transmission after 2nd dose. (VOC Alpha) ChAdOx1 (cases) showed VET 63% (95% CI, 37 to 78) against transmission after 2nd dose. (VOC Alpha) BNT162b2 (contacts) showed VE 94% (95% CI, 90 to 96) against infection after 2nd dose. (VOC Alpha) ChAdOx1 (contacts) showed VE 71% (95% CI, 51 to 83) against infection after 2nd dose. (VOC Alpha) BNT162b2 (cases) showed VET 65% (95% CI, 52 to 74) against transmission after 2nd dose. (VOC Delta) ChAdOx1 (cases) showed VET 36% (95% CI, 28 to 43) against transmission after 2nd dose. (VOC Delta) BNT162b2 (contacts) showed VE 90% (95% CI, 87 to 92) against infection after 2nd dose. (VOC Delta) ChAdOx1 (contacts) showed VE 72% (95% CI, 68 to 75) against infection after 2nd dose. (VOC Delta).	Serious	Retrospective cohort of contacts in England; 99,597cases and 151,821 contacts; S-gene proxy for VOC Alpha and VOC Delta

108	Martinez-Baz (2)	BNT162b2 (contacts) showed VE 71% (95% CI, 61 to 78) against infection after 2nd dose (VOC Alpha) mRNA-1273 (contacts) showed VE 86% (95% CI, 56 to 95) against infection after 2nd dose (VOC Alpha) ChAdOx1 (contacts) showed VE 38% (95% CI, -42 to 73) against infection after 2nd dose (VOC Alpha) BNT162b2 (contacts) showed VE 67% (95% CI, 59 to 74) against infection after 2nd dose (VOC Delta) mRNA-1273 (contacts) showed VE 77% (95% CI, 64 to 85) against infection after 2nd dose (VOC Delta) ChAdOx1 (contacts) showed VE 55% (95% CI, 39 to 67) against infection after 2nd dose (VOC Delta) ChAdOx1 followed by BNT162b2 (contacts) showed VE 86% (95% CI, 45 to 97) against infection (VOC Delta)	Serious	Prospective cohort of close contacts in Spain; 12,263 cases and 30,240 contacts; sequenced for VOC Alpha to VOC Delta (includes heterologous vaccines)
109	Cohn	BNT162b2 showed VE 49% (95% CI, 47 to 52) against infection at least 15 days after last dose (August: VOC Delta) mRNA-1273 showed VE 64% (95% CI, 62 to 66) against infection at least 15 days after last dose (August: VOC Delta) Ad26.COV2.S showed VE 3% (95% CI, -0.1 to 12) against infection at least 15 days after last dose (August: VOC Delta)	Serious	Data-linkage study of veterans in USA; 619,755 participants; time and setting for VOC Alpha to VOC Delta (only Delta reported here)
110	Rosenberg (2)	BNT162b2 showed VE 69% (95% CI, 67.4 to 70.6) against infection at least 15 days after last dose (August: VOC Delta; age 18-49) mRNA-1273 showed VE 78.4% (95% CI, 75.9 to 79.6) against infection at least 15 days after last dose (August: VOC Delta; age 18-49) Ad26.COV2.S showed VE 70.2% (95% CI, 67.4 to 73.0) against infection at least 15	Serious	Prospective study in New York; 8,834,604 participants; time and setting for VOC Alpha to VOC Delta (only Delta reported here). Also compared VE over time since vaccination (results not reported here)

		days after last dose (August: VOC Delta; age 18-49) BNT162b2 showed VE 77.8% (95% CI, 67.4 to 70.6) against infection at least 15 days after last dose (August: VOC Delta; age 65+) mRNA-1273 showed VE 84.3% (95% CI, 82.8 to 85.7) against infection at least 15 days after last dose (August: VOC Delta; age 65+) Ad26.COV2.S showed VE 70.8% (95% CI, 65.7 to 76.0) against infection at least 15 days after last dose (August: VOC Delta; age 65+)		
111	Robles-Fontan	BNT162b2 showed VE 56% (95% CI, 53 to 59) against infection at least 15 days after 2nd dose (October: VOC Delta) mRNA-1273 showed VE 71% (95% CI, 68 to 74) against infection at least 15 days after 2nd dose (October: VOC Delta) Ad26.COV2.S showed VE 27% (95% CI, 17 to 37) against infection at least 15 days after last dose (October: VOC Delta)	Serious	Data-linkage study in Puerto Rico; 1,913,454 person-years; time and setting for VOC Alpha to VOC Delta (only results for Delta reported here)
112	Glatman-Freedman (2)	BNT162b2 showed VE 91.5% (95% CI, 88.2 to 93.9) against infection at least 8 days after 2nd dose in adolescents age 12 to 15 years. There were no deaths in either group.	Serious	Population cohort in Israel of adolescents age 12 to 15 years; 2,034,591 vaccinated person-days and 13,623,714 unvaccinated person-days; time and setting for VOC Delta
113	Chin	mRNA-1273 showed VE 56.6% (95% CI, 42 to 67.5) against infection at least 14 days after 2nd dose.	Serious	Outbreak report from a prison in California; 827 participants; sample sequenced for VOC Delta
114	Nordstrum	BNT162b2 showed VE 47% (95% CI, -39 to 55) against symptomatic infection 121 to 180 days after second dose. mRNA-1273 showed VE 71% (95% CI, 56 to 81) against symptomatic infection 121 to 180 days after second dose. ChAdOx1 showed VE 41% (95% CI, 29 to 51) against symptomatic infection to 120 days after second dose.	Serious	Case-control study in Sweden; 1,684,958 participants; time and setting for VOC Alpha to VOC Delta (only Delta results reported here) (includes heterologous vaccines) (results over varying time periods since vaccination reported)

		ChAdOx1 followed by mRNA vaccine showed VE 66% (95% CI, 41 to 80) against symptomatic infection >120 days after second dose. BNT162b2 or mRNA-1273 or ChAdOx1 showed VE 42% (95% CI, -35 to 75) against severe disease (hospitalization or death) >180 days after second dose		
116	Ranzani (2)	ChAdOx1 showed VE 42.4% (95% CI, 24.6 to 56.0) against symptomatic infection 21 days after 1st dose.	Low	Test-negative study in Brazil; 9,197 tests; time and setting for VOC Gamma to Delta
117	Ranzani(3)	Ad26.COV2.S showed VE 50.9% (95% CI, 35.5 to 63.0) against symptomatic infection, VE 92.5% (95% CI, 54.9 to 99.6) against ICU admission, and VE 90.5% (95% CI, 31.5 to 99.6) against death 28 days after dose.	Serious	Test-negative study in Brazil; 11,817 tests; time and setting for VOC Gamma to Delta
118	Chadeau-Hyam	BNT162b2 showed VE 71.3% (95% CI, 56.6 to 81.0) against infection unreported number of days after 2nd dose (Round 13 and Round 14) mRNA-1273 showed VE 75.1% (95% CI, 22.7 to 92.0) against infection unreported number of days after 2nd dose (Round 13 and Round 14) ChAdOx1showed VE 44.8% (95% CI, 22.5 to 60.7) against infection unreported number of days after 2nd dose (Round 13 and Round 14)	Serious	Surveillance study in England; 87,966 participants who consented to data-linkage for vaccine status; sequenced for VOC Delta
119	Sheikh (2)	BNT162b2 showed VE 90% (95% CI, 86 to 94) against death at least 14 days after 2nd dose (confirmed VOC Delta) ChAdOx1 showed VE 91% (95% CI, 83 to 94) against death at least 14 days after 2nd dose (confirmed VOC Delta)	Serious	Retrospective cohort in Scotland; 114,706 participants; sequenced for VOC Delta
120	Reis	BNT162b2 showed VE 59% (95% CI, 52 to 65) against infection 14 to 20 days after 1st dose (age 12 to 18) BNT162b2 showed VE 90% (95% CI, 88 to 92) against infection 7 to 21 days after 2nd dose (age 12 to 18)	Moderate	Case-control study in Israel; 94,354 vaccinated matched to 94,354 unvaccinated adolescents age 12 to 18; time and setting for VOC Delta
121	Nordstrom (2)	BNT162b2 showed VE 78% (95% CI, 78 to 79) against symptomatic infection at least 14 days after 2nd dose.	Serious	Retrospective cohort study in Sweden; 721,787 participants; time and setting for VOC Delta

		mRNA-1273 showed VE 87% (95% CI, 84 to 88) against symptomatic infection at least 14 days after 2nd dose. ChAdOx1 showed VE 50% (95% CI, 41 to 58) against symptomatic infection at least 14 days after 2nd dose. ChAdOx1 followed by BNT162b2 showed VE 67% (95% CI, 59 to 73) against symptomatic infection at least 14 days after 2nd dose. ChAdOx1 followed by mRNA-1273 showed VE 79% (95% CI, 62 to 88) against symptomatic infection at least 14 days after 2nd dose.		(includes heterologous vaccines)
122	Skowronski (2)	BNT162b2 showed VE 79% (95% CI, 73 to 84) against infection at least 21 days after 1st dose (VOC Gamma) mRNA-1273 showed VE 85% (95% CI, 71 to 92) against infection at least 21 days after 1st dose (VOC Gamma) ChAdOx1 showed VE 60% (95% CI, 48 to 69) against infection at least 21 days after 1st dose (VOC Gamma)	Serious	Test-negative study in Canada; 68,074 participants; sample sequenced for VOC Alpha, Gamma and Delta (only VOC Gamma reported here)
123	Skowronski (3)	Delta BNT162b2 showed VE 89% (95% CI, 88 to 89) against infection at least 14 days after 2nd dose (Quebec- VOC Delta) mRNA-1273 showed VE 91% (95% CI, 90 to 92) against infection at least 14 days after 2nd dose (Quebec- VOC Delta) ChAdOx1 showed VE 73% (95% CI, 69 to 78) against infection at least 14 days after 2nd dose (Quebec- VOC Delta) ChAdOx1 followed by mRNA vaccine showed VE 88% (95% CI, 85 to 89) against infection at least 14 days after 2nd dose (Quebec- VOC Delta) Gamma BNT162b2 showed VE 93% (95% CI, 89 to 95) against infection at least 14 days after 2nd dose (BC- VOC Gamma)	Serious	Test-negative study in Canada; 380,532 British Columbia and 854,915 Quebec participants; sequenced for VOC Alpha, Gamma and Delta (selected data only reported here due to space constraints) (includes heterologous vaccines) (results over varying time periods since vaccination reported)

		mRNA-1273 showed VE 95% (95% CI, 85 to 99) against infection at least 14 days after 2nd dose (BC- VOC Gamma) ChAdOx1 showed VE 90% (95% CI, 61 to 98) against infection at least 14 days after 2nd dose (BC- VOC Gamma) ChAdOx1 followed by mRNA vaccine showed VE 96% (95% CI, 70 to 99) against infection at least 14 days after 2nd dose (BC- VOC Gamma) Time since vaccination (Delta) BNT162b2 showed VE 85% (95% CI, 84 to 86) against infection at 4 months after 2nd dose (Quebec – VOC Delta) mRNA-1273 showed VE 88% (95% CI, 86 to 90) against infection at 4 months after 2nd dose (Quebec – VOC Delta) ChAdOx1 showed VE 72% (95% CI, 66 to 77) against infection at 4 months after 2nd dose (Quebec – VOC Delta) ChAdOx1 followed by mRNA vaccine showed VE 86% (95% CI, 81 to 89) against infection at 4 months after 2nd dose (Quebec – VOC Delta) Time since vaccination and interval between doses (VOC Alpha to Delta) BNT162b2 showed VE 92% (95% CI, 91 to 93) at 14 to 27 days after 2nd dose (interval 7+ weeks) and VE 90% (95% CI, 88 to 91) at 4 months after 2nd dose (interval 7+ weeks) (Quebec) mRNA-1273 showed VE 92% (95% CI, 90 to 94) at 14 to 27 days after 2nd dose (interval 7+ weeks) and VE 91% (95% CI, 87 to 94) at 112+ days after 2nd dose (interval 7+ weeks) (Quebec) ChAdOx1 showed VE 85% (95% CI, 60 to 94) at 14 to 27 days after 2nd dose (interval 7+ weeks) and VE 72% (95% CI, 66 to 77) at 84 days after 2nd dose (interval 7+ weeks) (Quebec)		

124	Lin	BNT162b2 showed VE 94.9% (94.5 to 95.2) against symptomatic infection and VE 95.9% (95% CI, 92.9 to 97.6) against death at 60 days months after 2nd dose. BNT162b showed VE 70.1% (95% CI, 68.9 to 71.2) against symptomatic infection and VE 88.4% (95% CI, 83 to 92.1) against death at 210 days after 2nd dose) mRNA-1273 showed VE 96% (95.6 to 96.4) against symptomatic infection at 60 days; VE 96% (95% CI, 91.9 to 98) against death at 90 days after 2nd dose. mRNA-1273 showed VE 81.9% (95% CI, 81 to 82.7) against symptomatic infection and VE 93.7% (95% CI, 90.2 to 95.9) against death at 210 days after 2nd dose) Ad26.COV2.S showed VE 79% (77.1 to 80.7) against symptomatic infection at 30 days and VE 64.3% (95% CI, 62.3 to 66.1) at 150 days months after 2nd dose. Ad26.COV2.S showed VE 89.4% (95% CI, 52.3 to 97.6) against death at 120 days after 2nd dose)	Serious	Data-linkage study in North Carolina; 10,600,823 participants; time and setting for VOC Alpha to Delta (results over varying time periods since vaccination reported)
125	Barda	BNT162b2 (3 doses) showed VE 92% (82 to 97) against severe disease and VE 81% (95% CI, 59 to 97) against death at least 7 days after 3rd dose compared to 2 doses (given 5 months previously).	Serious	Data-linkage study of fully vaccinated (2 doses vs 3 doses) participants in Israel; 728,321 participants in each group; time and setting for VOC Delta
126	Andrews (2)	BNT162b2 (3 doses) showed VE 94% (95% CI, 93.4 to 94.6) against symptomatic infection at least 14 days after 3rd dose in age>50 (compared to unvaccinated) ChAdOx1 (2 doses followed by BNT162b2) showed VE 93.1% (95% CI, 91.7 to 94.3) against symptomatic infection at least 14 days after 3rd dose in age>50 (compared to unvaccinated)	Moderate	Test-negative study of fully vaccinated participants (>140 days since 2nd dose) over age 50 in England; 271,747 participants; sequencing for VOC Delta
127	Starrfelt (2)	BNT162b2 showed VE 69.7% (95% CI, 68.6 to 70.8) against infection at least 7 days after 2nd dose (VOC Alpha to Delta) mRNA-1273 showed VE 78.2% (95% CI, 76.7 to 79.6) against infection at least 7 days after 2nd dose (VOC Alpha to Delta)	Moderate	Population cohort study in Norway; 4,293,544 participants; time and setting for VOC Alpha to VOC Delta (includes heterologous vaccines)

		ChAdOx1 showed VE 43.4% (95% CI, 4.4 to 66.5) against infection at least 7 days after 2nd dose (VOC Alpha to Delta) Heterologous mRNA showed VE 84.7% (95% CI, 83.1 to 86.1) against infection at least 7 days after 2nd dose (VOC Alpha to Delta) ChAdOx1 followed by mRNA showed VE 60.7% (95% CI, 57.5 to 63.6) against infection at least 7 days after 2nd dose (VOC Alpha to Delta)		
128	Preio-Alhambra	ChAdOx1 followed by BNT162b2 showed HR 0.61 (95% CI, 0.52 to 0.71) against infection vs ChAdOx1 (homologous) – unreported number of days after 2nd dose	Serious	Retrospective cohort study in Spain; 28,650 participants aged 19 to 59 years; time and setting for VOC Delta (compared heterologous vaccines with homologous vaccines)
129	Ng	BNT162b2 or mRNA-1273 showed VE 61.6% (95% CI, 37.5 to 80.4) against transmission to fully vaccinated hh contacts and VE 100% (95% CI, not reported) against severe disease in fully vaccinated hh contacts	Serious	Retrospective cohort study of household contacts in Singapore; 753 contacts; index sequenced for VOC Delta
130	Desai	BBV152 showed VE 50% (95% CI, 33 to 62) against symptomatic infection at least 14 days after 2nd dose	Serious	Test-negative study of HCW in India; 1,068 matched pairs; time and setting for VOC Delta
131	Thiruvengadam(pub)	ChAdOx1showed VE 46.2% (95% CI, 31.6 to 57.7) against infection at least 21 days after 1st dose. ChAdOx1showed VE 63.1% (95% CI, 51.5 to 72.1) against infection at least 14 days after 2nd dose.	Serious	Test-negative study in India; 5,143 participants; sequencing for VOC Delta
132	Sharma	BNT162b2 showed VE 45.7% (95% CI, 37.9 to 52.5) against infection median of 30 days after 3rd dose compared to 2 doses (given at least 180 days previously) mRNA-1273 showed VE 46.6% (95% CI, 36.4 to 55.3) against infection median of 16 days after 3rd dose compared to 2 doses (given at least 180 days previously)	Serious	Case-control study of fully vaccinated (2 doses versus 3 doses) in veterans in USA; 129,130 pairs; time and setting for VOC Delta

133	Cohn (2)	BNT162b2 showed VE 43% (95% CI, 42 to 45) against infection after unclear number of days after 2nd dose (September 2021) mRNA-1273 showed VE 58% (95% CI, 57 to 59) after unclear number of days against infection after 2nd dose (September 2021) Ad26.COV2.S showed VE 13% (95% CI, 9 to 17) against infection after unclear number of days after dose (September 2021)	Serious	Retrospective cohort study of Veterans in the US; 780,225 Veterans; time and setting for VOC Delta (same population as Cohn but extended study time frame)
134	Arbel	BNT162b2 (3 doses) showed VE 90% (95% CI, 86 to 93) against death at 7 to 54 days after 3rd dose compared to 2 doses (given at least 5 months previously)	Moderate	Data-linkage study of fully vaccinated (>50 years) (2 doses versus 3 doses) in Israel; 843,208 participants; time and setting for VOC Delta
135	Bar-On (2)	BNT162b2 (3 doses) showed adjusted rate ratio of 12.3 (95% CI, 11.8 to 12.8) against infection and adjusted rate ratio of 17.9 (95% CI, 15.1 to 21.2) against severe disease and adjusted rate ratio of 14.7 (95% CI, 10 to 21.4) against death at least 12 days after 3rd dose compared to 2 doses (given at least 5 months previously) (age>60). BNT162b2 (3 doses) showed adjusted rate ratio of 9.0 (95% CI, 8.4 to 9.7) against infection at least 12 days after 3rd dose compared to 2 doses (given at least 5 months previously) (age 30-39).	Serious	Data-linkage study of fully vaccinated (>16 years) (2 doses versus 3 doses) in Israel; 4,696,865 participants; time and setting for VOC Delta (same population as Bar-On but extended end of study and additional ages and outcomes)
136	Andrews (3)	BNT162b2 (2 doses) showed VE 88% (65.9 to 95.8) against symptomatic infection at 2-9 weeks after 2nd dose (VOC Omicron) BNT162b2 (2 doses) showed VE 34.3% (-5 to 58.7) against symptomatic infection at 25+ weeks after 2nd dose (VOC Omicron) BNT162b2 (3 doses) showed VE 75.5% (56.1 to 86.3) against symptomatic infection at least 2+ weeks after 3rd dose (VOC Omicron) ChAdOx1 (2 doses) showed VE 5.9% (-29.7 to 31.7) against symptomatic infection at 25+ weeks after 2nd dose (VOC Omicron) ChAdOx1 (2 doses followed by 1 dose of BNT162b2) showed VE 71.4% (41.8 to 86) against symptomatic infection at least 2 weeks after 3rd (VOC Omicron)	Moderate	Test-negative study of fully vaccinated participants in England; 187,887 (581 Omicron) participants; sequencing for VOC Delta and Omicron

		BNT162b2 (2 doses) showed VE 88.2% (86.7 to 89.5) against symptomatic infection at least 2-9 weeks after 2nd dose (VOC Delta) BNT162b2 (2 doses) showed VE 63.5% (61.4 to 65.5) against symptomatic infection at 25+ weeks after 2nd dose (VOC Delta) BNT162b2 (3 doses) showed VE 92.6% (92 to 93.1) against symptomatic infection at least 2 weeks after 3rd dose (VOC Delta) ChAdOx1 (2 doses) showed VE 76.2% (63.7 to 84.4) against symptomatic infection at 2-9 weeks after 2nd dose (VOC Delta) ChAdOx1 (2 doses) showed VE 41.8% (39.4 to 44.1) against symptomatic infection at least 25+ weeks after 2nd dose (VOC Delta) ChAdOx1 (2 doses followed by 1 dose of BNT162b2) showed VE 93.8% (93.2 to 94.3) against symptomatic infection at least 2 weeks after 3rd (VOC Delta)		
137	Hansen	BNT162b2 showed VE 55.2% (95% CI, 23.5 to 73.7) against infection up to 44 days after 2nd dose (VOC Omicron) BNT162b2 showed VE -76.5% (95% CI, -95.3 to -59.5) against infection up to 164 days after 2nd dose (VOC Omicron) BNT162b2 (3 doses) showed VE 54.6% (95% CI, 30.4 to 70.4) against infection up to 30 days after 3rd dose (VOC Omicron) mRNA-1273 showed VE 36.7% (95% CI, -69.9 to 76.4) against infection up to 44 days after 2nd dose (VOC Omicron) mRNA-1273 showed VE -39.3% (95% CI, -61.6 to -20) against infection up to 164 days after 2nd dose (VOC Omicron) BNT162b2 showed VE 86.7% (95% CI, 84.6 to 88.6) against infection up to 44 days after 2nd dose (VOC Delta)	Serious	Retrospective cohort study in Denmark; 5,767 identified Omicron cases; sequenced for VOC Delta and Omicron (results over varying time periods since vaccination reported)

		BNT162b2 showed VE 53.8% (95% CI, 52.9 to 54.6) against infection up to 164 days after 2nd dose (VOC Delta) BNT162b2 (3 doses) showed VE 81.2% (95% CI, 79.2 to 82.9) against infection up to 30 days after 3rd dose (VOC Delta) mRNA-1273 showed VE 88.2% (95% CI, 83.1 to 91.8) against infection up to 44 days after 2nd dose (VOC Delta) mRNA-1273 showed VE 65.0% (95% CI, 63.6 to 66.3) against infection up to 164 days after 2nd dose (VOC Delta) mRNA-1273 (3 doses) showed VE 82.8% (95% CI, 58.8 to 92.9) against infection up to 30 days after 3rd dose (VOC Delta)		
138	McLean	BNT162b2 showed VE 59% (95% CI, 24 to 78) against infection at least 14 days after 2nd dose (VOC Delta - June to Dec 2021) mRNA-1273 showed VE 52% (95% CI, 20 to 71) against infection at least 14 days after 2nd dose (VOC Delta - June to Dec 2021)	Serious	Prospective cohort in Wisconsin, USA; 1,518 participants; time and setting for VOC Delta
139	Berec	BNT162b2 (3 doses) showed VE 92% (95% CI, 91 to 92) against infection at least 7 days after 3rd dose. mRNA-1273 (3 doses) showed VE 94% (95% CI, 91 to 95) against infection at least 7 days after 3rd dose. ChAdOx1 (2 doses) followed by BNT162b2 showed VE 82% (95% CI, 68 to 90) against infection at least 7 days after 3rd dose ChAdOx1 (2 doses) followed by mRNA1273 showed VE 91% (95% CI, 63 to 98) against infection at least 7 days after 3rd dose	Serious	Population cohort in Czech Republic; 693,579 fully vaccinated participants; time and setting for VOC Delta (includes heterologous vaccines)
140	Florea	mRNA-1273 showed VE 86.5% (95% CI, 84.8 to 88.0) against infection at least 14 days after 2nd dose	Serious	Prospective matched cohort study in California, USA; 1,854,008 participants; sequencing for VOC Delta
141	Kissling (2)	BNT162b2 showed VE 76% (95% CI, 72 to 81) against symptomatic infection at 30 -59 days after 2nd dose; VE 72% (95% CI, 61 to 80) at 60-89 days after 2nd dose and VE 65%	Serious	Test-negative study in 10 out of 14 I-MOVE countries; 14,282 participants; sample sequenced for VOC Delta

		(95% CI, 56 to 71) >90 days after 2nd dose (age 30-59) mRNA-1273 showed VE 91% (95% CI, 85 to 95) against symptomatic infection at 30 - 59 days after 2nd dose; VE 90% (95% CI, 76 to 96) at 60-89 days after 2nd dose (age 30-59) ChAdOx1 showed VE 67% (95% CI, 57 to 75) against symptomatic infection at 30 -59 days after 2nd dose; VE 65% (95% CI, 48 to 76) at 60-89 days after 2nd dose (age 30-59) Ad26.COV2.S showed VE 50% (95% CI, 36 to 62) against symptomatic infection at 30 -59 days after dose; VE 52% (95% CI, 33 to 66) at 60-89 days after dose (age 30-59)		(results over varying time periods since vaccination reported)
142	Katikireddi	ChAdOx1 showed VE 63.3% (95% CI, 61.3 to 65.3) against symptomatic infection at 8 to 9 weeks after 2nd dose; VE 48.7% (95% CI, 45.9 to 51.4) against symptomatic infection at 16 to 17 weeks after 2nd dose (VOC Delta) ChAdOx1 showed VE 79.0% (95% CI, 75.9 to 81.7) against severe disease (hospitalization or death) at 8 to 9 weeks after 2nd dose; VE 70.5% (95% CI, 67.0 to 73.7) against severe disease 16 to 17 weeks after 2nd dose (VOC Delta) ChAdOx1 showed VE 65.4% (95% CI, 64.6 to 66.2) against symptomatic infection at 8 to 9 weeks after 2nd dose; VE 58.7% (95% CI, 56.7 to 60.5) against symptomatic infection at 16 to 17 weeks after 2nd dose (VOC Gamma) ChAdOx1 showed VE 75.6% (95% CI, 73.4 to 77.6) against severe disease (hospitalization or death) at 8 to 9 weeks after 2nd dose; VE 50.5% (95% CI, 43.4 to 56.6) against severe disease 16 to 17 weeks after 2nd dose (VOC Gamma)	Serious	Retrospective cohort in Scotland and Brazil; 1,972,454 fully vaccinated participants in Scotland (Delta); 42,558,839 fully vaccinated participants in Brazil (Gamma); time and setting for VOC Delta and VOC Gamma (results over varying time periods since vaccination reported)

143	Abu-Raddad (4)	mRNA-1273 showed VE 90.6% (95% CI, 88.7 to 92.1) against infection at 60 days after 2nd dose; VE 80.7% (95% CI, 77 to 83.8) against infection at 120 days after 2nd dose mRNA-1273 showed VE 97.8% (95% CI, 83.7 to 99.7) against severe disease (hospitalization or death) at 60 days after 2nd dose; VE 91.5% (95% CI, 60.8 to 98.1) against infection at 120 days after 2nd dose	Serious	Test-negative study in Qatar; 1,781,505 participants; time and setting for VOC Beta to VOC Delta (same setting and methodology as Chemaitelly 3) (results over varying time periods since vaccination reported)
144	Machado	BNT162b2 (majority) or mRNA-1273 showed VE 68% (95% CI, 64 to 71) against symptomatic infection at 42-69 days after 2nd dose; VE 39% (95% CI, 29 to 48) against symptomatic infection at 98-148 days after 2nd dose ChAdOx1 showed VE 33% (95% CI, 23 to 42) against symptomatic infection at 42-69 days after 2nd dose; VE 34% (95% CI, 10 to 52) against symptomatic infection at 70-140 days after 2nd dose BNT162b2 (majority) or mRNA-1273 showed VE 95% (95% CI, 88 to 98) against death at 14-41 days after 2nd dose; VE 93% (95% CI, 87 to 96) against death at 70-148 days after 2nd dose ChAdOx1 showed VE 95% (95% CI, 90 to 97) against death at least 14 days after 2nd dose	Moderate	Retrospective cohort study of community-dwelling adults≥65 in Portugal; 2,117,002 participants; time and setting for VOC Alpha to VOC Delta (same population as Nunes) (results over varying time periods since vaccination reported)
145	Irizarry	BNT162b2 showed VE 57% (95% CI, 53 to 60) against infection at 144 days after 2nd dose; VE 86% (95% CI, 75 to 92) against death at 144 days after 2nd dose mRNA-1273 showed VE 73% (95% CI, 70 to 76) against infection at 144 days after 2nd dose; VE 93% (95% CI, 81 to 97) against death at 144 days after 2nd dose Ad26.COV2.S showed VE 36% (95% CI, 30 to 42) against infection at 144 days after 2nd dose; VE 72% (95% CI, 49 to 85) against death at 144 days after 2nd dose	Serious	Retrospective cohort study in Puerto Rico; 2,276,966 participants; time and setting for VOC Alpha to VOC Delta (same population as Robles-Fontan?) (results over varying time periods since vaccination reported)

146	Tartof (2)	BNT162b2 (3 doses) showed VE 88% (95% CI, 86 to 89) against infection at least 14 days after 3rd dose compared to unvaccinated (age>18) BNT162b2 (3 doses) showed VE 75% (95% CI, 71 to 78) against infection at least 14 days after 3rd dose compared to 2 doses (given at least 6 months previously) (age>18)	Moderate	Retrospective cohort study in California, USA; 3,133,075 participants; time and setting for VOC Alpha to VOC Delta
147	Buchan	BNT1652b2 or mRNA-1273 (2 doses) showed VE 6% (95% CI, -25 to 30) against infection at 7 to 59 days after 2nd dose; VE -13% (95% CI, -38 to 8) against infection at 60 to 119 days after 2nd dose; VE -38% (95% CI, -61 to -18) against infection at 120 to 179 days after 2nd dose; VE -16% (95% CI, -62 to 17) against infection at >240 days after 2nd dose (VOC Omicron) BNT162b2 (3 doses) showed VE 34% (95% CI, 16 to 49) against infection at 7 days after 3rd dose (VOC Omicron) mRNA-1273 (3 doses) showed VE 59% (95% CI, 16 to 80) against infection at 7 days after 3rd dose (VOC Omicron) BNT1652b2 or mRNA-1273 (2 doses) showed VE 84% (95% CI, 81 to 86) against infection at 7 to 59 days after 2nd dose; VE 81% (95% CI, 79 to 82) against infection at 60 to 119 days after 2nd dose; VE 80% (95% CI, 79 to 81) against infection at 120 to 179 days after 2nd dose; VE 71% (95% CI, 66 to 75) against infection at >240 days after 2nd dose (VOC Delta) BNT162b2 (3 doses) showed VE 93% (95% CI, 91 to 94) against infection at 7 days after 3rd dose (VOC Delta) mRNA-1273 (3 doses) showed VE 93% (95% CI, 90 to 96) against infection at 7 days after 3rd dose (VOC Delta)	Moderate	Test-negative study in Ontario, Canada; 484,188 fully vaccinated participants; sample sequenced for VOC Delta and VOC Omicron (results over varying time periods since vaccination reported)

148	Tseng	mRNA-1273 (2 doses) showed VE 30.4% (95% CI, 5.0 to 49.0) against infection at 14 to 90 days after 2nd dose; VE 15.2% (0 to 30.7) against infection at 91 to 180 days after 2nd dose; VE 0% (95% CI, 0 to 1.2) against infection at 181 to 270 days after 2nd dose (VOC Omicron) mRNA-1273 (3 doses) showed VE 63.6% 95% CI, 57.4 to 68.9) against infection at median of 35 days after 3rd dose (VOC Omicron) mRNA-1273 (2 doses) showed VE 82.8% (95% CI, 69.6 to 90.3) against infection at 14 to 90 days after 2nd dose; VE 63.6% (51.8 to 72.5) against infection at 91 to 180 days since 2nd dose; VE 61.4% (95% CI, 56.8 to 65.5) against infection at 181 to 270 days after 2nd dose; VE 52.9% (95% CI, 43.7 to 60.5) against infection at >270 days after 2nd dose (VOC Delta) mRNA-1273 (3 doses) showed VE 95.7% 95% CI, 94.2 to 96.8) against infection at median of 35 days after 3rd dose (VOC Delta)	Serious	Test-negative study in California, USA; 60,420 participants; sample sequenced for VOC Delta and VOC Omicron (results over varying time periods since vaccination reported)
149	Lyngse	BNT162b2* (cases) showed VET 10% (95% CI, 0 to 18) against transmission to vaccinated household contacts at least 7 days after 2nd dose BNT162b2* (cases) showed VET 31% (95% CI, 26 to 36) against transmission to unvaccinated household contacts at least 7 days after 2nd dose BNT162b2* (contacts) showed VES 46% (95% CI, 40 to 52) against susceptibility to infection from vaccinated case at least 7 days after 2nd dose BNT162b2* (contacts) showed VES 61% (95% CI, 59 to 63) against susceptibility to infection from unvaccinated household contacts at least 7 days after 2nd dose *vast majority	Serious	Household transmission study in Denmark; 24,693 index cases; sequencing for VOC Delta

150	Hitchings (3)	CoronaVac (2 doses) showed OR 1.59 (95% CI, 0.60 to 4.24) for infection comparing fully vaccinated ≥182 days vs fully vaccinated 14 to 41 days (age 40-64) CoronaVac (2 doses) showed OR 3.32 (95% CI, 1.85 to 5.94) for infection comparing fully vaccinated ≥182 days vs fully vaccinated 14 to 41 days (age 80+)	Serious	Test-negative study in Brazil; 37,929 matched fully vaccinated participants; time and setting for VOC Gamma and VOC Delta
151	Abu-Raddad (5)	BNT162b2 (3 doses) showed VE 50.1% (95% CI, 47.3 to 52.8) against symptomatic infection; VE 100% (71.4 to 100) against hospitalization and death compared to 2 doses mRNA-1273 (3 doses) showed VE 50.8% (95% CI, 43.4 to 57.3) against symptomatic infection compared to 2 doses	Serious	Retrospective cohort studies in Qatar; 2,232,224 fully vaccinated participants; sample sequenced for VOC Omicron
152	Zheutlin	BNT162b2 showed VE 84% (95% CI, 82 to 85) against infection ≥5 months after 2nd dose mRNA-1273 showed VE 88% (95% CI, 87 to 89) against infection ≥5 months after 2nd dose Ad26.COV2.S showed VE 74% (95% CI, 70 to 76) against infection ≥5 months after dose	Serious	Matched case-control in USA; 17,017,435 fully vaccinated participants; time and setting for VOC Alpha to VOC Delta (only Delta data shown here) (results over varying time periods since vaccination reported)
153	Cerqueira-Silva	BNT162b2 showed VE 64.8% (95% CI, 54.9 to 72.4) against symptomatic infection ≥14 days after 2nd dose ChAdOx1 showed VE 56% (95% CI, 51.4 to 60.2) ≥14 days after 2nd dose CoronaVac showed VE 39.4% (95% CI, 36.1 to 42.6) against symptomatic infection ≥14 days after 2nd dose Ad26.COV2.S showed VE 44% (95% CI, 31.5 to 54.2) against symptomatic infection ≥14 days after dose	Serious	Test-negative study in Brazil; 231,212 previously infected participants; time and setting for VOC Gamma to VOC Delta
154	Jara (2)	CoronaVac (3 doses) showed VE 78.8% (95% CI, 76.8 to 80.6) against symptomatic infection; VE 92.2% (95% CI, 88.7 to 94.6) against ICU admission; VE 86.7% (95% CI, 80.5 to 91.0) against death ≥14 days after 3rd dose	Moderate	Prospective cohort in Chile; 11,174,257 fully vaccinated participants; time and setting for VOC Delta (includes heterologous vaccines)

		BNT162b2 booster after CoronaVac (2 doses) showed VE 96.5% (95% CI, 96.2 to 96.7) against symptomatic infection; VE 96.2% (95% CI, 94.6 to 97.3) against ICU admission; VE 96.8% (95% CI, 93.9 to 98.3) against death ≥14 days after 3rd dose ChAdOx1 booster after CoronaVac (2 doses) showed VE 93.2% (95% CI, 92.9 to 93.6) against symptomatic infection; VE 98.9% (95% CI, 98.5 to 99.2) against ICU admission; VE 98.1% (95% CI, 97.3 to 98.6) against death ≥14 days after 3rd dose		
155	Tan	BNT162b2 (3 doses) showed VE 73% (95% CI, 71 to 74) against infection; VE 95% (95% CI, 92 to 97) against severe disease ≥12 days after 3rd dose compared to 2 doses mRNA-1273 (3 doses) showed VE 86% (95% CI, 81 to 90) against infection ≥12 days after 3rd dose compared to 2 doses of BNT162b2 BNT162b2 (2 doses) followed by mRNA-1273 showed VE 82% (95% CI, 77 to 86) against infection; VE 92% (95% CI, 44 to 99) against severe disease ≥12 days after 3rd dose compared to 2 doses of BNT162b2 mRNA-1273 (2 doses) followed by BNT162b2 showed VE 90% (95% CI, 73 to 96) against infection ≥12 days after 3rd dose compared to 2 doses of BNT162b2	Serious	Retrospective cohort study in Singapore; 73,209 fully vaccinated participants (age>60); time and setting for VOC Delta (includes heterologous vaccines)
156	Suah	BNT162b2 (2 dose vaccinated July to August) showed VE 90.8% (95% CI, 89.4 to 92.0) against infection; VE 83.8% (95% CI, 78.5 to 87.8) against ICU admission; VE 90.3% (95% CI, 88.1 to 92.2) against death in September (at least 14 days after 2nd dose) (Age>60) BNT162b2 (2 dose vaccinated April to June) showed VE 79.1% (95% CI, 75.8 to 81.9) against infection; VE 57.2% (95% CI, 43.4 to 67.6) against ICU admission ; VE 89.3% (95% CI, 85.9 to 91.9) against death in September (at least 14 days after 2nd dose) (Age>60) CoronaVac (2 dose vaccinated July to August) showed VE 74.4% (95% CI, 70.4 to	Serious	Retrospective cohort study in Malaysia; 9,927,350 fully vaccinated participants; time and setting for VOC Delta (results over varying time periods since vaccination reported)

		77.8) against infection; VE 46.1% (95% CI, 37.2 to 53.7) against ICU admission; VE 76.5% (95% CI, 72.9 to 79.6) against death in September (at least 14 days after 2nd dose) (Age>60) CoronaVac (2 dose vaccinated April to June) showed VE 30% (95% CI, 18.4 to 39.9) against infection; VE 30.2% (95% CI, 7.6 to 47.3) against ICU admission; VE 75.7% (95% CI, 67.0 to 82.1) against death in September (at least 14 days after 2nd dose) (Age>60)		
157	Amodio	mRNA-1273 showed VE 69.2% (95% CI, 67.6 to 70.8) against infection; VE 85.2% (95% CI, 82.7 to 87.7) against severe disease at 6 months after 2nd dose mRNA-1273 showed VE 69.2% (95% CI, 67.6 to 70.8) against infection; VE 90.3% (95% CI, 86.2 to 94.4) against severe disease at 8 months after 2nd dose	Serious	Retrospective cohort study in Italy; 3,966,976 participants; time and setting for VOC Alpha to VOC Delta (only Delta data shown here) (results over varying time periods since vaccination reported)

Section 2: excluded studies	
Author	**Reason for exclusion**
Abu-Raddad (3)	Vaccine effectiveness not reported
Akhrass	Delayed exclusion – Clinical outcomes of interest for this LES not reported
Albahrani	Prevalence of variants unknown and suspected to be <50%
Alencar	Critical risk of bias
Alhamlan	Vaccine effectiveness not reported
Alharbi	Prevalence of variants unknown and suspected to be <50%
Ali	Prevalence of variants unknown and suspected to be <50%
Alkhafaji	Prevalence of variants unknown and suspected to be <50%
Allen	Serious risk of bias
Almufty	Prevalence of variants unknown and suspected to be <50%
Al-Qahtani	Delayed exclusion – critical risk of bias
Andeweg	Vaccine effectiveness not reported
Apisarnthanarak	Vaccine effectiveness not reported
Arashiro	Vaccine effectiveness not reported
Araujo	Clinical outcomes of interest for this LES not reported
Ayass	Clinical outcomes of interest for this LES not reported
Baden	Critical risk of bias
Bailly	Delayed exclusion – critical risk of bias
Bajema	Clinical outcomes of interest for this LES not reported
Bajema (2)	Clinical outcomes of interest for this LES not reported
Bal	Vaccine effectiveness not reported
Barchuk	Clinical outcomes of interest for this LES not reported
Bergwerk	Vaccine effectiveness not reported
Bernal (2)	Delayed exclusion – critical risk of bias
Bhatnagar	Critical risk of bias
Bhattacharya	Delayed exclusion – critical risk of bias
Bianchi	Delayed exclusion – critical risk of bias
Bjork	Prevalence of variants unknown and suspected to be <50%
Blaiszik	Clinical outcomes of interest for this LES not reported
Blaiszik	Clinical outcomes of interest for this LES not reported
Borobia	Clinical outcomes of interest for this LES not reported
Bosch	Clinical outcomes of interest for this LES not reported
Britton	Prevalence of variants unknown and suspected to be <50%
Brown	Vaccine effectiveness not reported
Brunelli	Prevalence of variants unknown and suspected to be <50%
Bruxvoort	Prevalence of variants unknown and suspected to be <50%
Butt	Prevalence of variants unknown and suspected to be <50%
Butt	Critical risk of bias
Butt (2)	Delayed exclusion – critical risk of bias

Cabezas	Prevalence of variants unknown and suspected to be <50%
Caillard	Clinical outcomes of interest for this LES not reported
Cardona	Vaccine effectiveness not reported
Cavanaugh	Delayed exclusion – VOI not VOC
Chadeau-Hyams(2)	Results not reported according to vaccine type/brand
Charles Pon Ruban	Vaccine effectiveness not reported
Charmet	Serious risk of bias
Chau	Vaccine effectiveness not reported
Christensen	Vaccine effectiveness not reported
Chung (2)	Results not reported according to vaccine type/brand
Clemens	Prevalence of variants unknown and suspected to be <50%
Cohen	Vaccine effectiveness not reported
Cohen(2)	Vaccine effectiveness not reported
Collie	Clinical outcomes of interest for this LES not reported
Corchado-Garcia	Prevalence of variants unknown and suspected to be <50%
Dash	Critical risk of bias
Davies	Results not reported according to vaccine type/brand
de Gier Brechje	Prevalence of variants unknown and suspected to be <50%
Dickerman	Clinical outcomes of interest for this LES not reported
Dolzhikova	Critical risk of bias
Domi	Prevalence of variants unknown and suspected to be <50%
Drawz	Critical risk of bias
El Sahly	Prevalence of variants unknown and suspected to be <50%
Ella	Prevalence of variants unknown and suspected to be <50%
Elliot	Delayed exclusion – critical risk of bias
El-Sahly	Prevalence of variants unknown and suspected to be <50%
Falsey	Prevalence of variants unknown and suspected to be <50%
Fang	Modelling study
Farah	Clinical outcomes of interest for this LES not reported
Farinholt	Vaccine effectiveness not reported
Fisher	Prevalence of variants unknown and suspected to be <50%
Fisman (2)	Results not reported according to vaccine type/brand
Frenck	Prevalence of variants unknown and suspected to be <50%
Furer	Delayed exclusion – critical risk of bias
Gardner	Modelling study
Geisen	Clinical outcomes of interest for this LES not reported
Gharpure	Vaccine effectiveness not reported
Ghosh	Delayed exclusion – critical risk of bias
Gils	Clinical outcomes of interest for this LES not reported
Goga	Vaccine effectiveness not reported
Gorgels	Prevalence of variants unknown and suspected to be <50%
Grannis	Clinical outcomes of interest for this LES not reported
Gray	Prevalence of variants unknown and suspected to be <50%

Gray (2)	Clinical outcomes of interest for this LES not reported
Griffin	Vaccine effectiveness not reported
Guijarro	Prevalence of variants unknown and suspected to be <50%
Gupta	Prevalence of variants unknown and suspected to be <50%
Gupta	Vaccine effectiveness not reported
Haas (2)	Modelling study
Hacisuleyman	Critical risk of bias
Harris	Modelling study
Herlihy	Delayed exclusion – critical risk of bias
Hetemaki	Vaccine effectiveness not reported
Hitchings (3)	Vaccine effectiveness not reported
Hitchings(2)	Delayed exclusion – critical risk of bias
Hollinghurst	Serious risk of bias
Hyams	Delayed exclusion - Clinical outcomes of interest for this LES not reported
Iliaki	Prevalence of variants unknown and suspected to be <50%
Iliaki	Prevalence of variants unknown and suspected to be <50%
Ismail	Delayed exclusion - Clinical outcomes of interest for this LES not reported
Jacobson	Critical risk of bias
John	Prevalence of variants unknown and suspected to be <50%
Jones	Critical risk of bias
Kaabi	Prevalence of variants unknown and suspected to be <50%
Kale	Delayed exclusion – critical risk of bias
Kaur	Delayed exclusion – critical risk of bias
Keegan	Critical risk of bias
Kemp	Modelling study
Khan	Prevalence of variants unknown and suspected to be <50%
Khawaja	Critical risk of bias
Kislaya	Vaccine effectiveness not reported
Kojima	Prevalence of variants unknown and suspected to be <50%
Kshirsagar	Vaccine effectiveness not reported
Kustin	Delayed exclusion - only included infected population
Lamprini	Clinical outcomes of interest for this LES not reported
Lan	Results not reported according to vaccine type/brand
Lefèvre	Critical risk of bias
Levin-Rector	Only included previously infected
Lewis	Clinical outcomes of interest for this LES not reported
Li	Phase 1 trial
Li (2)	Clinical outcomes of interest for this LES not reported
Li (3)	Delayed exclusion – critical risk of bias
Ling	Prevalence of variants unknown and suspected to be <50%
Linsenmeyer	Vaccine effectiveness not reported
Lippi	Results not reported according to vaccine type/brand
Lippi (2)	Critical risk of bias

Liu	Vaccine effectiveness not reported
Loconsole	Vaccine effectiveness not reported
Luo	Vaccine effectiveness not reported
Maeda	Critical risk of bias
Marco	Delayed exclusion – critical risk of bias
Marquis	Vaccine effectiveness not reported
Mattar	Prevalence of variants unknown and suspected to be <50%
Mattiuzzi	Results not reported according to vaccine type/brand
Maurya	Prevalence of variants unknown and suspected to be <50%
Mazgatos	Critical risk of bias
McEvoy	Prevalence of variants unknown and suspected to be <50%
McKeigue(2)	Results not reported according to vaccine type/brand
Menni	Serious risk of bias
Mielke	Clinical outcomes of interest for this LES not reported
Mirahmadizadeh	Prevalence of variants unknown and suspected to be <50%
Mizrahi	Modelling study
Monge	Prevalence of variants unknown and suspected to be <50%
Mor	Prevalence of variants unknown and suspected to be <50%
Moustsen-Helms	Prevalence of variants unknown and suspected to be <50%
Munitz	Clinical outcomes of interest for this LES not reported
Munro	Clinical outcomes of interest for this LES not reported
Musser	Vaccine effectiveness not reported
Mutnal	Vaccine effectiveness not reported
Nanduri	Critical risk of bias
Niessen	Clinical outcomes of interest for this LES not reported
Oduwole	Clinical outcomes of interest for this LES not reported
Olmedo	Clinical outcomes of interest for this LES not reported
Olson	Clinical outcomes of interest for this LES not reported
Open-SAFELY	Vaccine effectiveness not reported
Ostropolets	Not reported separately according to variant
Palacios	Prevalence of variants unknown and suspected to be <50%
Paredes	Clinical outcomes of interest for this LES not reported
Paris	Prevalence of variants unknown and suspected to be <50%
Pattni	Modelling study
Pawlowski	Critical risk of bias
Perry	Clinical outcomes of interest for this LES not reported
Peter	Vaccine effectiveness not reported
Peter	Vaccine effectiveness not reported
Pilishvili	Prevalence of variants unknown and suspected to be <50%
Piltch-Loeb	Prevalence of variants unknown and suspected to be <50%
Polinski	Delayed exclusion – critical risk of bias
Poukka	Critical risk of bias
Pulliam	Modelling study

Raches Ella	Phase 1 trial
Rana	Critical risk of bias
Regev-Yochay	Prevalence of variants unknown and suspected to be <50%
Reynolds	Results not reported according to vaccine type/brand
Riemersma	Clinical outcomes of interest for this LES not reported
Riley	Critical risk of bias
Rivelli	Clinical outcomes of interest for this LES not reported
Rosero-Bixby	Clinical outcomes of interest for this LES not reported
Rovida	Critical risk of bias
Rudolph	Prevalence of variants unknown and suspected to be <50%
Salmeron Rios	Prevalence of variants unknown and suspected to be <50%
Sansone	Critical risk of bias
Satwik	Delayed exclusion – critical risk of bias
Scobie	Delayed exclusion – critical risk of bias
Self	Clinical outcomes of interest for this LES not reported
Sharma	Prevalence of variants unknown and suspected to be <50%
Sheikh (3)	Results not reported according to vaccine type/brand
Shimabukuro	Clinical outcomes of interest for this LES not reported
Shrotri	Delayed exclusion – critical risk of bias
Simon	Prevalence of variants unknown and suspected to be <50%
Şimşek-Yavuz	Clinical outcomes of interest for this LES not reported
Starrfelt	Serious risk of bias
Suri	Vaccine effectiveness not reported
Swift	Prevalence of variants unknown and suspected to be <50%
Tande	Prevalence of variants unknown and suspected to be <50%
Tanriover	Prevalence of variants unknown and suspected to be <50%
Taquet	Modelling study
Tartof (3)	Clinical outcomes of interest for this LES not reported
Tenforde	Clinical outcomes of interest for this LES not reported
Tenforde (2)	Clinical outcomes of interest for this LES not reported
Thangaraj	Critical risk of bias
Thiruvengadam	Critical risk of bias
Thompson (1)	Prevalence of variants unknown and suspected to be <50%
Thompson (2)	Prevalence of variants unknown and suspected to be <50%
thompson (4)	Clinical outcomes of interest for this LES not reported
Tobolowsky	Clinical outcomes of interest for this LES not reported
Ulloa	Vaccine effectiveness not reported
Uschner	Critical risk of bias
Vahidy	Prevalence of variants unknown and suspected to be <50%
Vasileiou	Clinical outcomes of interest for this LES not reported
Veneti	Clinical outcomes of interest for this LES not reported
Victor	Critical risk of bias
Volkov	Modelling study

Voysey	Prevalence of variants unknown and suspected to be <50%
Waldhorn	Serious risk of bias
Wang	Clinical outcomes of interest for this LES not reported
Waxman	Clinical outcomes of interest for this LES not reported
Wickert	Critical risk of bias
Wijtvliet	Clinical outcomes of interest for this LES not reported
Williams (2)	Critical risk of bias
Xiang	Clinical outcomes of interest for this LES not reported
Young-Xu	Prevalence of variants unknown and suspected to be <50%
Young-Xu (4)	Critical risk of bias
Zacay	Delayed exclusion – critical risk of bias
Zhong	Clinical outcomes of interest for this LES not reported

Appendix 2: Glossary

AZ: AstraZeneca

Alpha: variant of concern B.1.1.7

Beta: variant of concern B.1.351

Delta: variant of concern B.1.617.2

Gamma: variant of concern P.1

Epsilon: variant of concern B.1.427/B.1.429

HCW: Healthcare workers

LTC: Long-term care

LTCF: Long-term care facility

MOD: Moderna

Obs: observational study

Omicron: variant of concern B.1.1.529

OR: odds ratio

PF: Pfizer

RME: range of mean estimates across 2 or more studies

VE (Vaccine effectiveness): measure of how well a vaccine protects people from getting the outcome of interest in real-world practice (For example: VE of 92% against infection means that 92% of people will be protected from becoming infected with COVID and 8% of people will still be at risk of becoming infected with COVID)

VES: vaccine effectiveness against susceptibility (vaccinated contact)

VET: vaccine effectiveness against transmission (vaccinated index case)

VOC: variant of concern

VOI: variant of interest

Appendix 3: Data-extraction template

Vaccine product	
Source	First author of study
Link	DOI or Pubmed ID
Date published	in format YYYY/MM/DD or preprint
Country	
Funding	public or industry
Study details	
Study type	RCT/cohort/data-linkage/test-negative/case-control/other
Surveillance	routine screening Y or N
Population(s)	general public/LTC/Households/HCW/Other
Control group	not vaccinated, <7day vaccinated internal control, none, other
Total (N)	number of all study participants
Female	number or %
LTC	number or %
HCW	number or %
Households	number or %
>80	number or %
>70	number or %
>60	number or %
Outcomes	outcomes separated by VOC type
Outcomes	confirmed infection/asymptomatic/mild symptomatic/severe symptoms/hospitalized/ICU/death
1st Dose VE	VE with 95% CI
Days post 1st dose	days post 1st dose when VE provided
2nd Dose VE	VE with 95% CI
Days post 2nd dose	days post 2nd dose when VE provided
Rates per X person-days/years	vaccinated vs control
HR	vaccinated vs control
RR	vaccinated vs control
Adjusted	Regression, stratification, matching and associated variables
Transmission	infection rates in unvaccinated contacts of vaccinated individuals
Critical appraisal	See Appendix 5

Appendix 4: Process for assigning Variant of Concern to studies

A Variant of Concern is considered to be the dominant (≥50%) strain in a study if any of the following conditions apply:
i) the authors make a statement about prevalence of VOC during the study time frame
ii) time and setting of the study is consistent with a VOC being dominant according to the following open tracking sources:

Nextstrain. Real-time tracking of pathogen evolution. https://nextstrain.org/
Outbreak Info. https://outbreak.info/location-reports

Appendix 5: Research question and critical appraisal process (revised 06 Oct 2021)

Review question:

Participants	People at risk of COVID-19 (usually without but sometimes with previous COVID-19 infection)
Intervention	COVID-19 Vaccine
Comparator	Unvaccinated people (*)
Outcomes	PCR-diagnosis of COVID-19 infection (**); symptomatic disease; hospital/ICU admission; death; transmission

(*) before-after studies, where the infection rate in the first 2 weeks after the vaccination are used as control are (**)
(**) commonly performed and may be appraised confirmation of specific variant, or reasonable evidence the variant was the dominant circulating strain

Critical Appraisal Process

We appraise the quality of the individual studies using an adapted version of ROBINS-I. This tool classifies the Risk of Bias of a study as **Low, Moderate, Serious, Critical, or No Information**. Low Risk of Bias indicates High Quality, and Critical Risk of Bias indicates Very Low (insufficient) Quality. ROBINS-I appraises 7 bias domains and judges each study against an ideal reference randomized controlled trial. To improve the utility of ROBINS-I for assessing studies reporting vaccine effectiveness, we have focused on study characteristics that introduce bias as reported in the vaccine literature. (WHO. Evaluation of COVID-19 vaccine effectiveness. Interim Guidance. 17 March 2021). Studies rated as "critical" risk of bias will not be included in the Summary statements on Page 1-2 (exception: if limited data available for an outcome for a VOC). An overall judgement of "serious" or "critical" is given when the study is judged to be at critical risk of bias in at least one domain. Three of more serious risk of bias domains is given an overall risk of bias of critical.

VE Study Characteristics that may introduce bias	Description
Study design ROBINS-I: Bias in selection of participants into study	In cohort studies, people who get vaccinated may differ in health-seeking behaviour from people who do not get vaccinated; using a test-negative study design minimizes this type of bias Examples and typical judgement: • test-negative design with a clearly defined symptomatic study population (low) • test-negative design (mixed or unclear study population) or case-control or cohort design or data-linkage with no concerns (moderate) • cross-sectional design or case-control (concerns about whether controls had same access to vaccines/risk of exposure to COVID or unclear) or cohort design (concerns that exposed and non-exposed were not drawn from the same population) (serious)
Method for confirming vaccination ROBINS-I: Bias in classification of interventions	Questionnaires are prone to recollection bias; Population databases developed for purpose of tracking COVID vaccines minimize this type of bias Examples and typical judgement: • database linkage study (low)

	• Questionnaire with confirmation by an additional method (e.g. registry) of at least a subset of study population (moderate) • Questionnaire without confirmation by an additional method (serious) • Estimating vaccination status based on surveillance data alone (critical)
Databases used for retrieval of COVID test results, participant prognostic factors, and clinical outcomes ROBINS-I: Bias in classification of interventions	Databases developed for collecting data on COVID are less prone to bias due to missing information and misclassification Examples and typical judgement: • database for non-COVID purpose but with individual level data (moderate) • database for non-COVID purpose without individual level data (serious) • no or unclear description of database type (critical)
Assignment of infection start date ROBINS-I: Bias in classification of interventions	Using date of symptom onset (if within 10 days of testing) as infection start date reduces risk of misclassification bias (e.g., vaccinated participant who is reported as COVID+ may have been infected prior to receiving the vaccine or during non-immune period) and sensitivity of assays decreases over time Examples and typical judgement: • using a PCR positive test that was part of an ongoing standardized monitoring system (e.g., within a health network) (low) • using sample date without interview or documented confirmation of symptoms ≤ 10 days (relevant for symptomatic disease only) (serious)
Verification of symptoms ROBINS-I: Bias in classification of interventions	Prospective, standardized collection of symptoms from patients reduces risk of missing information bias; testing within 10 days after symptom onset reduces risk of false-negative COVID test Examples and typical judgement: • using sample date without patient report/ documented confirmation of symptoms ≤ 10 days (relevant for symptomatic disease only) (serious) • if symptomatic COVID is not an outcome (no information)
Accounting for non-immune period (first 14 days after first vaccine dose) ROBINS-I: Bias due to confounding	Reported absence of vaccine effect during non-immune period reduces risk of residual confounding bias Example/common case: • presence of an effect during non-immune period or result not reported (moderate) • unclear that non-immune period was considered (serious)
Inclusion of participants with prior COVID infection ROBINS-I: Bias due to confounding	Exclusion (or separate analysis) of participants with prior COVID infection reduces concern about differences in infectivity as well as risk-taking and health-seeking behaviour Examples and typical judgement: • inclusion of prior infection status as a covariate in the models (moderate) • previously infected not excluded or analyzed separately (serious)

Accounting for calendar time ROBINS-I: Bias due to confounding (time-varying confounding)	Accounting for calendar time reduces bias due to differences in vaccine accessibility and risk of exposure over time Examples and typical judgement: • use of time-varying statistics without explicit mention of adjustment for calendar time (moderate) • not taken into account but short-time frame (e.g. ≤2 months) (serious) • not taken into account and time frame >2 months (critical)
Adjustment for prognostic factors ROBINS-I: Bias due to confounding	Adjustment for prognostic factors for COVID infection, severity of disease, and vaccination, such as age, gender, race, ethnicity, socioeconomic factors, occupation (HCW, LTC), and chronic medical conditions Examples and typical judgement: • no or insufficient adjustment for occupation (or number of tests as a surrogate for exposure risk) -exception age>65 or LTCF resident (moderate) • no or insufficient adjustment for socioeconomic factors (or neighborhood or income as a surrogate), race, ethnicity (serious) • no or insufficient adjustment for age (any study population) or chronic medical conditions (LTC)(critical)
Testing frequency ROBINS-I: Bias in measurement of outcomes	Similar frequency of testing between groups reduces risk of bias introduced by detecting asymptomatic infection in one group but not in another (e.g. when only one group undergoes surveillance screening) Examples and typical judgement: • no systematic screening but consistent methods for detection in one group vs. the other, e.g., within health networks (moderate) • screening performed for a subset of both study groups (serious) • screening performed routinely in one study group but not in the other (critical)

Appendix 6: Detailed description of the narrative summary statement

We include studies with the following clinical outcomes: prevention of infection, severe disease (as defined by the study investigators), death, and prevention of transmission. These outcomes were selected because they are less susceptible to bias. If data are not available for these specific outcomes, but are available for symptomatic infection and/or hospitalization, data for these additional outcomes are provided temporarily. Studies reporting only antibody responses are excluded.

We aim at providing a lay language, standardized summary statement for each combination of vaccine and VOC for which we found evidence.

Where more than one study was found, we will provide a summary statement with a **range of the estimates across the studies**.

Where a single study provided data, we will provide the **estimate plus 95% confidence interval** for that study. As additional studies are added, the estimate plus confidence interval will be replaced by a range as described above.

In the summaries, "prevented" or "protects" will be applied to mean estimates or range of mean estimates that are greater than or equal to 50%.

Section 3: Special Groups (after 5 November 2021)	
Author	**Special Group**
Bedston	Elderly >75 years
Bekker	Healthcare workers
Bukatko	Homeless shelter residents
Dujmovic	Nursing Home residents
Embi	Immunocompromised
Gaio	Healthcare workers
Goldhaber-Fiebert	Prison residents and staff
Hall (2)	Healthcare workers
Helmsdal	Healthcare workers
Iskander	Coast guard personnel
Krutikov	LTCF
Lustig	Healthcare workers
Malhotra	Healthcare workers
Muhsen	Healthcare workers
Paixao	Pregnant women
Petráš	Healthcare workers
Quach	Healthcare workers
Salvatore	Prison staff and prisoners
Spensley	End-stage Kidney disease patients
Spitzer	Healthcare workers
Subbarao	LTCF
Sultan	Healthcare workers
Yassi (2)	Healthcare workers
Young-Xu (3)	Male Veterans