



## COVID-19 Living Evidence Synthesis #6 (Version 26: 15 December 2021)

### **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 [detailed statements in Table 2](#).

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, 293 studies were appraised and 110 used to complete this summary. The [reasons for excluding](#) the remaining 183 studies are reported in the second section of Appendix 2.

Five 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 15 December 2021 (highlighted in yellow). The new studies included results for VOC Delta [B.1.617.2] (5).

### **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.

<sup>1</sup> As of August 9, inclusion of Alpha studies may be temporarily delayed to permit resource allocation to Delta.

## VOC Delta

We have low certainty evidence that 2 doses of **BNT162b2** prevented infection from VOC **Delta** (range of mean estimates: 42 to 89%); moderate certainty evidence it prevented symptomatic infection from VOC **Delta** (range of mean estimates: 63 to 88%). We have low certainty evidence it prevented severe, critical, or fatal disease (range of mean estimates: 93 to 98%) and low certainty evidence it prevented death (90% [95% CI, 86 to 94] – 1 Obs) from VOC **Delta** . We have low certainty evidence that it prevented transmission of VOC **Delta** to close contacts (65% [95% CI, 52 to 74] - 1 Obs).

We have low certainty evidence that 2 doses of **mRNA-1273** prevented infection (range of mean estimates: 58 to 91%) and prevented symptomatic infection from VOC **Delta** (87% [95% CI, 84 to 88] – 1 Obs). We have low certainty evidence that it prevented severe, critical, or fatal disease (range of mean estimate: 93 to 100%) and prevented transmission of VOC **Delta** to close contacts (range of mean estimates: 62 to 77%).

We have low certainty evidence that 2 doses of **ChAdOx1** prevented infection (range of mean estimates: 45 to 73%) and prevented symptomatic infection from VOC **Delta** (range of mean estimates: 61 to 92%). We have low certainty evidence that 2 doses of **ChAdOx1** prevented death 91% [95% CI, 83 to 94] – 1 Obs) and provided limited protection from transmission of VOC **Delta** (36% [95% CI, 28 to 43] – 1 Obs).

We have low certainty evidence that **AD26.COV2.S** prevented infection (range of mean estimates: 3 to 71%), prevented symptomatic infection (51% [95% CI, 35.5 to 63] – 1 Obs) and prevented death due to VOC **Delta** (90.5% [95% CI, 31.5 to 99.6] – 1 Obs).

We have low certainty evidence that 2 doses of **Covaxin [BBV152]** prevented symptomatic infection due to VOC **Delta** (50% [95% CI, 33 to 62] – 1 Obs).

We low certainty evidence that 2 doses of **Sinovac [CoronaVac]** prevented symptomatic infection (59% [95% CI, 16 to 81.6] – 1 Obs) and prevented severe infection (89% [95% CI, 55 to 98%]- 1 Obs) due to VOC **Delta**.

We have low certainty evidence that **ChAdOx1 followed by BNT162b2** prevented symptomatic infection by VOC **Delta** (67% [95% CI, 59 to 73]- 1 Obs). We have low certainty evidence that **ChAdOx1 followed by mRNA-1273** prevented symptomatic infection by VOC **Delta** (79% [95% CI, 62 to 88] – 1 Obs).

We have low certainty evidence that **ChAdOx1 followed by BNT162b2 or mRNA-1273** prevented infection (88% [95% CI, 85 to 89]- 1 Obs) and prevented transmission of VOC **Delta** (86% [95% CI, 45 to 97} – 1 Obs).

## VOC Gamma

We have low certainty evidence that **BNT162b2** prevented infection (93% [95% CI, 81 to 99]- 1 Obs) and moderate certainty of evidence it prevented symptomatic disease from VOC **Gamma** (range of mean estimates: 84 to 88% - 2 reports from the same study population).

We have low certainty evidence that 2 doses of **mRNA-1273** prevented infection (range of mean estimates: 95%) and low certainty evidence that it prevented symptomatic infection from VOC **Gamma** (88% [95% CI, 61 to 96] – 1 Obs).

We have low certainty evidence that 2 doses of **CoronaVac** prevented infection (65.9% [95% CI, 65.2 to 66.6] – 1 Obs) and death (86.3% [95% CI, 84.5 to 87.9] – 1 Obs) from VOC **Gamma**.

We have low certainty evidence that **ChAdOx1 followed by BNT162b2 or mRNA-1273** prevented infection by VOC **Gamma** (96% [95% CI, 70 to 99] – 1 Obs).

### VOC Beta

We have low certainty evidence that 2 doses of **BNT162b2** prevented infection (93% [95% CI, 89 to 95%] – 1 Obs) and moderate certainty evidence that it prevented symptomatic infection from VOC **Beta** (range of mean estimates: 84 to 88%).

We have low certainty evidence that 2 doses of **mRNA-1273** prevented infection from VOC **Beta** (96.4% [95% CI, 92 to 99] – 1 Obs).

We have moderate certainty evidence that 2 doses of **ChAdOx1** provided limited protection from infection by VOC **Beta** (10.4% [95% CI, -76.8 to 54.8]- 1 RCT).

We have moderate evidence that **AD26.COVS.S** prevented severe disease from VOC **Beta** (81.7% [95% CI, 46.2 to 95.4] - 1 RCT).

We have moderate certainty evidence that 2 doses of **Novavax [NVX-Co2373]** provided limited protection against symptomatic infection from VOC **Beta** (43% [95% CI, -9.8 to 70.4] - 1 RCT).

### VOC Alpha

We have low certainty evidence that 2 doses of **BNT162b2** prevented infection (range of mean estimates: 78 to 95%), prevented severe disease (range of mean estimates: 92 to 100%), prevented death (range of mean estimates: 91 to 97%), and prevented transmission of VOC **Alpha** to close contacts (range of mean estimates: 70 to 82%).

We have low certainty evidence that 2 doses of **mRNA-1273** prevented infection from VOC **Alpha** (range of mean estimates: 86 to 100%). We have low certainty evidence that it prevented severe, critical, or fatal disease from VOC **Alpha** (combined with Beta) (95.7% [95% CI, 73.4 to 99.9] – 1 Obs) and prevented transmission of VOC **Alpha** to close contacts (88% [95% CI, 50 to 97] – 1 Obs).

We have moderate certainty evidence that 2 doses of **ChAdOx1** prevented infection (range of mean estimates: 62 to 79%) and low certainty evidence it prevented transmission of VOC **Alpha** (range of mean estimates: 58 to 63%).

We have low certainty evidence that **Johnson & Johnson [AD26.COVS.S]** prevented transmission of VOC **Alpha** (77% [95% CI, 6 to 94] – 1 Obs).

We have low certainty evidence that **ChAdOx1 followed by BNT162b2 or mRNA-1273** prevented infection by VOC **Alpha** (88% [95% CI, 83 to 92] – 1 Obs).

**Table 1a: Visual summary of evidence for COVID-19 vaccines for variants of concern**

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

**Colour** indicates level of certainty based on the evidence

**High certainty evidence** = pooling of low to moderate risk of bias RCTs or pooling of observational studies with low risk of bias and consistent findings

**Moderate certainty evidence** = 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 (modified Dec 1, 2021)

**Low certainty evidence** = single RCT or observational study with serious risk of bias or multiple low to serious risk of bias observational studies with inconsistent findings (modified Dec 1, 2021)

Outcome (and vaccine)	Vaccine Effectiveness (2 doses unless otherwise stated) for each combination of vaccine, variant, and outcome			
	Alpha	Beta	Gamma	Delta
<b>Any Infection</b>				
Pfizer	78 to 95%		93%	42 to 89%
Moderna	86 to 100%	96%	95%	58 to 91%
AstraZeneca (AZ)	62 to 79%			45 to 73%
Johnson & Johnson				3 to 71%*
Novavax				
CoronaVac			66%	
AZ followed by Pfizer or Moderna	88%		96%	88%
<b>Symptomatic Infection</b> (reported when data on “any infection” is limited)				
Pfizer		84 to 88%	84 to 88%	63 to 88%
Moderna			88%	87%
AstraZeneca		10%**		61 to 92%
Johnson & Johnson				51%*
Novavax	86%	43%**		
CoronaVac				59%
Covaxin				50%
AZ followed by Pfizer or Moderna				67 to 79%
<b>Transmission</b>				
Pfizer	70 to 82%			65%
Moderna	88%			62 to 77%
AstraZeneca	58 to 63%			36%
Johnson & Johnson	77%*			
Novavax				
CoronaVac				
AZ followed by Pfizer or Moderna				86%

	Alpha	Beta	Gamma	Delta
<b>Severe Disease (may include death for some studies)</b>				
Pfizer	92 to 100%			93 to 98%
Moderna	96%	96%		93 to 100%
AstraZeneca				
Johnson & Johnson		82%*		
Novavax				
CoronaVac				89%
Sinopharm				
Sputnik V				
<b>Death</b>				
Pfizer	91 to 97%			90%
Moderna				
AstraZeneca				91%*
Johnson & Johnson				
Novavax				
CoronaVac			86%	
Sinopharm				
Sputnik V				

\*single dose

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

AZ, AstraZeneca

**Table 1b: Visual summary of evidence for COVID-19 vaccines for variants of concern  
(Moderate to Low Risk of Bias Studies compared to All studies)**

Top orange row = moderate or low risk of bias studies only

Bottom yellow row = serious risk of bias studies only

Outcome (and vaccine)	Vaccine Effectiveness (2 doses unless otherwise stated) for each combination of vaccine, variant, and outcome			
	Alpha	Beta	Gamma	Delta
<b>Any Infection</b>				
Pfizer	92% (1 Obs – ref 1)			75% (1 Obs – ref 84)
	78 to 95% (11 Obs)			42 to 89% (13 Obs)
Moderna				
AstraZeneca	62% (1 RCT – ref 5)			
	78 to 79% (2 Obs)			
Johnson & Johnson				
Novavax				
CoronaVac				
AZ/PF or MOD				
<b>Symptomatic Infection</b> (reported when data on “any infection” is limited)				
Pfizer		84 to 88% (2 Obs – refs 23,47)	84 to 88% (2 Obs – refs 23,47)	63 to 87% (2 Obs – refs 47,92)
		same 2 studies	same 2 studies	78 to 88% (3 Obs)
Moderna				
AstraZeneca		10% <sup>**</sup> (1 RCT – ref 4)		92% (1 Obs – ref 92)
		same single study		61 to 67% (2 Obs)
Johnson & Johnson				
Novavax	86% (1 RCT – ref 19)	43% <sup>**</sup> (1 RCT – ref 7)		
	same single study	same single study		
CoronaVac				
<b>Transmission</b>				
Pfizer				
Moderna				
AstraZeneca				
Johnson & Johnson				
Novavax				
CoronaVac				

Severe Disease (may include death for some studies)				
Pfizer				
Moderna				
AstraZeneca				
Johnson & Johnson		82% (1 RCT – ref 7)		
		same single study		
Novavax				
CoronaVac				
Sinopharm				
Sputnik V				
Death				
Pfizer				
Moderna				
AstraZeneca				
Johnson & Johnson				
Novavax				
CoronaVac				
Sinopharm				
Sputnik V				

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

AZ, AstraZeneca; MOD, Moderna; PF, Pfizer

Notes:

Comparing Table 1a with Table 1b allows you to see whether it is an RCT or multiple Obs studies that determined the “moderate certainty of evidence” rating on Table 1

**Pfizer/Alpha/Any Infection:**

Table 1 = yellow because only a single Obs study of moderate ROB (need more than 1 moderate ROB study to turn square orange on Table 1)

**AZ/Alpha/Any Infection:**

Table 1 = orange because only a single RCT of moderate ROB is needed to turn square orange

Table 2: Key findings about vaccine effectiveness (revised format Dec 13, 2021)

VOC	Vaccine	Findings
Delta	Pfizer/ BioNTech Comirnaty [BNT162b2]	<p>BNT162b2 provided protection against VOC Delta for the following outcome at least 14 to 21 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>• 30 to 65% from infection (RME)</li> <li>• 33 to 47.5% from symptomatic infection (RME)</li> <li>• 87 to 94% from hospitalization (RME)</li> <li>• 100% (95% CI, not reported) against severe, critical, or fatal disease</li> </ul> <p>BNT162b2 provided protection against VOC Delta for the following outcome at least 7 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>• 42 to 89% from infection (RME)</li> <li>• 62 to 93.7% from symptomatic infection (RME)</li> <li>• 96% (95% CI, 86 to 99) from hospitalization</li> <li>• 93 to 98% from severe, critical, or fatal disease (RME)</li> <li>• 90% (95% CI, 86 to 94) from death</li> </ul> <p>(23 Obs)  <a href="#">[29]</a><a href="#">[38]</a><a href="#">[42]</a><a href="#">[47]</a><a href="#">[57]</a><a href="#">[63]</a><a href="#">[64]</a><a href="#">[71]</a><a href="#">[74]</a><a href="#">[76]</a><a href="#">[84]</a><a href="#">[88]</a><a href="#">[92]</a><a href="#">[97]</a><a href="#">[102]</a><a href="#">[109]</a><a href="#">[110]</a><a href="#">[111]</a><a href="#">[118]</a><a href="#">[119]</a><a href="#">[121]</a><a href="#">[123]</a><a href="#">[133]</a>; last update 2021-12-15</p>
Delta	Moderna Spikevax [mRNA-1723]	<p>mRNA-1273 provided protection against VOC Delta for the following outcomes at least 14 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>• 75 to 86.7% from infection (RME)</li> <li>• 72% (95% CI, 57 to 82) from symptomatic infection</li> <li>• 96% (95% CI, 72 to 99) from hospitalization</li> <li>• 93 to 100% from severe, critical, or fatal disease (RME)</li> </ul> <p>mRNA-1273 provided protection against VOC Delta for the following outcomes 14 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>• 58 to 91% from infection (RME)</li> <li>• 87% (95% CI, 84 to 88) from symptomatic infection</li> <li>• 93 to 100% from severe, critical, or fatal disease(RME)</li> </ul> <p>(16 Obs)  <a href="#">[47]</a><a href="#">[57]</a><a href="#">[63]</a><a href="#">[64]</a><a href="#">[71]</a><a href="#">[74]</a><a href="#">[97]</a><a href="#">[101]</a><a href="#">[102]</a><a href="#">[109]</a><a href="#">[110]</a><a href="#">[111]</a><a href="#">[118]</a><a href="#">[121]</a><a href="#">[123]</a><a href="#">[133]</a>; last update 2021-12-15</p>
Delta	AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]	<p>ChAdOx1 provided protection against VOC Delta for the following outcome at least 21 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>• 18 to 46% from infection (RME)</li> <li>• 33 to 58% from symptomatic infection (RME)</li> <li>• 71% (95% CI, 51 to 83) from hospitalization</li> </ul> <p>ChAdOx1 provided protection against VOC Delta for the following outcome at least 7 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>• 44.8 to 73% from infection (RME)</li> <li>• 61 to 92% from symptomatic infection (RME)</li> <li>• 92% (95% CI, 75 to 97) from hospitalization</li> <li>• 91% (95% CI, 83 to 94) from death</li> </ul> <p>(10 Obs) <a href="#">[29]</a><a href="#">[38]</a><a href="#">[42]</a><a href="#">[47]</a><a href="#">[71]</a><a href="#">[92]</a><a href="#">[118]</a><a href="#">[119]</a><a href="#">[123]</a><a href="#">[131]</a>; last update 2021-12-15</p>
Delta	Johnson & Johnson [AD26.COVS.S]	<p>Ad26.COVS.S provided protection against VOC Delta for the following outcomes ≥ 14 days after dose:</p> <ul style="list-style-type: none"> <li>• 3% to 71% against infection (RME)</li> </ul>



VOC	Vaccine	Findings
		<ul style="list-style-type: none"> <li>50.9% (95% CI, 35.5 to 63.0) from symptomatic infection</li> <li>92.5% (95% CI, 54.9 to 99.6) from ICU admission</li> <li>90.5% (95% CI, 31.5 to 99.6) from death</li> </ul> (6 Obs) <a href="#">[97]</a> <a href="#">[109]</a> <a href="#">[110]</a> <a href="#">[111]</a> <a href="#">[117]</a> <a href="#">[133]</a> ; <i>last update 2021-12-15</i>
Delta	Sinovac [CoronaVac]	CoronaVac provided protection against VOC Delta for the following outcome $\geq 14$ days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>59% (95% CI, 16 to 81.6) from symptomatic infection</li> <li>89% (95% CI, 55 to 98) from severe infection</li> </ul> (1 Obs) <a href="#">[91]</a> ; <i>last update 2021-11-03</i>
Delta	ChAdOx1 followed by mRNA vaccine	ChAdOx1 followed by BNT162b2 at least 14 days after 2 <sup>nd</sup> dose provided protection against VOC Delta for the following outcomes: <ul style="list-style-type: none"> <li>67% (95% CI, 59 to 73) against symptomatic infection</li> </ul> ChAdOx1 followed by mRNA-1273 at least 14 days after 2 <sup>nd</sup> dose provided protection against VOC Delta for the following outcomes: <ul style="list-style-type: none"> <li>79% (95% CI, 62 to 88) against symptomatic infection</li> </ul> ChAdOx1 followed by either BNT162b2 or mRNA-1273 at least 14 days after 2 <sup>nd</sup> dose provided protection against VOC Delta for the following outcomes: <ul style="list-style-type: none"> <li>88% (95% CI, 85 to 89) against infection</li> </ul> ChAdOx1 followed by BNT162b2 provided protection against infection by VOC Delta compared to ChAdOx1 (homologous): <ul style="list-style-type: none"> <li>HR 0.61 (95% CI, 0.52 to 0.71) unreported number of days after 2<sup>nd</sup> dose</li> </ul> (3 Obs) <a href="#">[121]</a> <a href="#">[123]</a> <a href="#">[128]</a> ; <i>last update 2021-12-01</i>
Delta  >14 days after 2 <sup>nd</sup> dose  Varying intervals for 2 <sup>nd</sup> dose	Moderna Spikevax [mRNA-1723]	mRNA-1273 provided protection against infection by VOC Delta the following number of days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>94.1% (95% CI, 90.5 to 96.3) – at 14 to 60 days</li> <li>88% (95% CI, 86 to 90) - at 120 days</li> <li>80.0% (95% CI, 70.2 to 86.6) – at 151 to 180 days</li> </ul> (2 Obs) <a href="#">[101]</a> <a href="#">[123]</a> ; <i>last update 2021-11-17</i>  mRNA-1273 provided protection against infection by VOC Delta at the following intervals between doses: <ul style="list-style-type: none"> <li>92% (95% CI, 90 to 94) at 14 to 27 days after 2<sup>nd</sup> dose (interval 7+ weeks)</li> <li>91% (95% CI, 87 to 94) at 4 months after 2<sup>nd</sup> dose (interval 7+ weeks)</li> </ul> mRNA-1273 provided protection against symptomatic infection by VOC Delta the following number of days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>95.2% (95% CI, 94.4 to 95.9) – at 1 week</li> <li>90.3% (95% CI, 67.2 to 97.1) – at 10 to 14 weeks</li> <li>71% (95% CI, 56 to 81) – at 121 to 180 days</li> <li>81.9% (95% CI, 81 to 82.7) – at 7 months (210 days)</li> </ul>

VOC	Vaccine	Findings
		mRNA-1273 provided protection against death by VOC Delta at 7 months after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>96% (95% CI, 91.9 to 98)</li> </ul> (4 Obs) <a href="#">[92]</a> <a href="#">[114]</a> <a href="#">[123]</a> <a href="#">[124]</a> ; <i>last update 2021-11-17</i>
Delta  >14 days after 2 <sup>nd</sup> dose  Varying intervals for 2 <sup>nd</sup> dose	AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]	ChAdOx1 provided protection against infection by VOC Delta the following number of days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>72% (95% CI, 66 to 77) – at 120 days</li> </ul> ChAdOx1 provided protection against infection by VOC Delta at the following intervals between doses: <ul style="list-style-type: none"> <li>85% (95% CI, 60 to 94) at 14 to 27 days after 2<sup>nd</sup> dose (interval 7+ weeks)</li> <li>72% (95% CI, 66 to 77) at 84+ days after 2<sup>nd</sup> dose (interval 7+ weeks)</li> </ul> ChAdOx1 provided protection against symptomatic infection by VOC Delta the following number of days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>92.4% (95% CI, 92.1 to 92.7) – at 1 week</li> <li>-19% (95% CI, -97 to 28) – &gt; 120 days (17 weeks)</li> <li>69.7% (95% CI, 68.7 to 70.5) – at 20 weeks</li> </ul> (3 Obs) <a href="#">[92]</a> <a href="#">[114]</a> <a href="#">[123]</a> ; <i>last update 2021-11-17</i>
Delta  >30 days after dose	Johnson & Johnson [AD26.COV2.S]	Ad26.COV2.S provided protection against symptomatic infection by VOC Delta the following number of days after dose: <ul style="list-style-type: none"> <li>64.3% (95% CI, 62.3 to 66.1) – at 5 months</li> </ul> Ad26.COV2.S provided protection against death by VOC Delta at 3 months after dose: <ul style="list-style-type: none"> <li>89.4% (95% CI, 52.3 to 97.6)</li> </ul> (1 Obs) <a href="#">[124]</a> ; <i>last update 2021-11-17</i>
Delta  >120 days after 2 <sup>nd</sup> dose	ChAdOx1 followed by mRNA vaccine	ChAdOx1 followed by an mRNA provided protection against infection by VOC Delta the following number of days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>86% (95% CI, 81 to 89) at 120 days</li> </ul> ChAdOx1 followed by an mRNA provided protection against symptomatic infection by VOC Delta the following number of days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>66% (95% CI, 41 to 80) – &gt; 120 days (17 weeks)</li> </ul> (2 Obs) <a href="#">[114]</a> <a href="#">[123]</a> ; <i>last update 2021-11-17</i>
Delta  3 doses vs 2 doses	Pfizer/ BioNTech Comirnaty [BNT162b2]	BNT162b2 (3 doses) provided protection against <b>symptomatic</b> infection <b>compared to unvaccinated</b> : <ul style="list-style-type: none"> <li>94% (95% CI, 93.4 to 94.6) – at least 14 days after 3<sup>rd</sup> dose (age 50+)</li> </ul> BNT162b2 (3 doses) provided protection against <b>infection</b> by VOC Delta <b>compared to 2 doses</b> : <ul style="list-style-type: none"> <li>84.0% (95% CI, 79 to 88) at 14 to 20 days after 3<sup>rd</sup> dose</li> <li>45.7% (95% CI, 37.9 to 53.5) median of 30 days after 3<sup>rd</sup> dose</li> </ul> BNT162b2 (3 doses) provided protection against the following outcomes by VOC Delta <b>compared to 2 doses</b> : <ul style="list-style-type: none"> <li>Rate ratio <b>12.3</b> (95% CI, 11.8 to 12.8) from infection at least 12 days after 3<sup>rd</sup> dose</li> <li>Rate ratio <b>17.9</b> (95% CI, 15.1 to 21.2) from severe illness at least 12 days after 3<sup>rd</sup> dose</li> <li>Rate ratio <b>14.7</b> (95% CI, 10 to 21.4) from death at least 12 days after 3<sup>rd</sup> dose</li> </ul>

VOC	Vaccine	Findings
		<ul style="list-style-type: none"> <li>90% (95% CI, 86 to 93) from death unclear number of days after 3<sup>rd</sup> dose (6 Obs) [93][100][126][132][134][135]; last update 2021-12-15</li> </ul>
Delta 3 doses vs 2 doses	Moderna Spikevax [mRNA-1723]	<p>mRNA-1273 (3 doses) provided protection against infection by VOC Delta compared to 2 doses:</p> <ul style="list-style-type: none"> <li>46.6% (95% CI, 36.4 to 55.3) median of 16 days after 3<sup>rd</sup> dose (1 Obs) [132]; last update 2021-12-15</li> </ul>
Delta 3 doses vs 2 doses	AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]	<p>ChAdOx1 (3 doses) provided protection against symptomatic infection compared to unvaccinated:</p> <ul style="list-style-type: none"> <li>93.1% (95% CI, 91.7 to 94.3) – at least 14 days after 3<sup>rd</sup> dose (age 50+) (1 Obs) [126]; last update 2021-12-01</li> </ul>
Delta Transmission Household or close contacts of index case	Pfizer/ BioNTech Comirnaty [BNT162b2]	<p>Fully vaccinated index cases by BNT162b showed VET for unvaccinated (hh contact):</p> <ul style="list-style-type: none"> <li>63% (95% CI: 46 to 75) from infection</li> </ul> <p>Fully vaccinated index cases by BNT162b showed VET for fully vaccinated household contacts:</p> <ul style="list-style-type: none"> <li>40% (95% CI, 20 to 54) from infection</li> </ul> <p>Fully vaccinated index cases by BNT162b showed VET for hh contacts (unclear status):</p> <ul style="list-style-type: none"> <li>65% (95% CI, 52 to 74) from infection</li> </ul> <p>Fully vaccinated hh contacts by BNT162b showed VE (unclear status of index case):</p> <ul style="list-style-type: none"> <li>62 to 90% from infection (RME)</li> <li>100% (95% CI, not reported) from severe disease (4 Obs) [105][107][108][129]; last update 2021-12-01</li> </ul>
Delta Transmission Household or close contacts of index case	Moderna Spikevax [mRNA-1723]	<p>Fully vaccinated household contacts by mRNA-1273 showed VE (unclear status of index):</p> <ul style="list-style-type: none"> <li>62 to 77% from infection (RME) (2 Obs) [108][129]; last update 2021-12-01</li> </ul>
Delta Transmission Household or close contacts of index case	AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]	<p>Fully vaccinated index cases by ChAdOx1 showed VET for household contacts (unclear status):</p> <ul style="list-style-type: none"> <li>36% (95% CI, 28 to 43) from infection</li> </ul> <p>Fully vaccinated household contacts by ChAdOx1 showed VE (unclear status of index):</p> <ul style="list-style-type: none"> <li>55 to 72% from infection (RME) (2 Obs)[107][108]; last update 2021-11-03</li> </ul>
Delta Transmission Household or close contacts of index case	ChAdOx1 followed by mRNA vaccine	<p>Fully vaccinated household contacts by ChAdOx1 followed by mRNA showed VE (unclear status of index):</p> <ul style="list-style-type: none"> <li>86% (95% CI, 45 to 97) from infection (1 Obs)[108]; last update 2021-11-03</li> </ul>

<b>Gamma</b>	<b>Moderna Spikevax [mRNA-1723]</b>	<p>mRNA-1273 provided protection against VOC Gamma for the following outcomes 14 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>• 85% (95% CI, 71 to 92) from infection</li> <li>• 77% (95% CI, 63 to 86) from symptomatic infection</li> <li>• 89% (95% CI, 73 to 95) from hospitalization</li> </ul> <p>mRNA-1273 provided protection against VOC Gamma (or Beta) for the following outcomes 35-41 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>• 43% (95% CI, 22 to 59) from symptomatic infection</li> </ul> <p>mRNA-1273 provided protection against VOC Gamma for the following outcome at least 7 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>• 95% from infection (RME)</li> <li>• 88% (95% CI, 61 to 96) from symptomatic infection</li> </ul> <p>(4 Obs – 5 refs) <a href="#">[23]</a><a href="#">[47]</a><a href="#">[101]</a><a href="#">[122]</a><a href="#">[123]</a>; <i>last update 2021-12-01</i></p>
<b>Gamma</b>	<b>AstraZeneca [ChAdOx1] Vaxzevria Serum Institute of India [Covishield]</b>	<p>ChAdOx1 provided protection against VOC Gamma for the following outcomes at least 14 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>• 60% (95% CI, 48 to 69) from infection</li> <li>• 42 to 48% from symptomatic infection (RME)</li> <li>• 83% (95% CI, 66 to 92) from hospitalization</li> </ul> <p>ChAdOx1 provided protection against VOC Gamma for the following outcomes at least 14 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>• 90% (95% CI, 61 to 98) from infection</li> </ul> <p>(4 Obs)<a href="#">[47]</a><a href="#">[116]</a><a href="#">[122]</a><a href="#">[123]</a>; <i>last update 2021-11-17</i></p>
<b>Gamma</b>	<b>Johnson &amp; Johnson [AD26.COVS.S]</b>	<p>Ad26.COVS-S provided protection against VOC Gamma for the following outcomes 28 days after dose:</p> <ul style="list-style-type: none"> <li>• 50.9% (95% CI, 35.5 to 63.0) from symptomatic infection</li> <li>• 92.5% (95% CI, 54.9 to 99.6) from ICU admission</li> <li>• 90.5% (95% CI, 31.5 to 99.6) from death</li> </ul> <p>(1 Obs) <a href="#">[117]</a>, <i>last update 2021-11-17</i></p>
<b>Gamma</b>	<b>Sinovac [CoronaVac]</b>	<p>CoronaVac provided protection against VOC Gamma for the following outcome ≥ 14 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>• 65.9% (95% CI, 65.2 to 66.6) from infection</li> </ul> <p>CoronaVac provided protection against VOC Gamma for the following outcome ≥ 14 days after 2<sup>nd</sup> dose for people over age 70:</p> <ul style="list-style-type: none"> <li>• 41.6% (95% CI, 26.9 to 63.3) from symptomatic infection</li> </ul> <p>(2 Obs) <a href="#">[30]</a><a href="#">[49]</a>; <i>last update 2021-07-14</i></p>
<b>Gamma</b>	<b>ChAdOx1 followed by mRNA vaccine</b>	<p>ChAdOx1 followed by either BNT162b2 or mRNA-1273 at least 14 days after 2<sup>nd</sup> dose provided protection against VOC Gamma for the following outcomes:</p> <ul style="list-style-type: none"> <li>• 96% (95% CI, 70 to 99) against infection</li> </ul> <p>(1 Obs) <a href="#">[123]</a>; <i>last update 2021-11-17</i></p>
<b>Beta</b>	<b>Moderna Spikevax [mRNA-1723]</b>	<p>mRNA-1273 provided protection against VOC Beta for the following outcomes 14 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>• 61.3% (95% CI, 56.5 to 65.5) from infection</li> <li>• 77% (95% CI, 63 to 86) from symptomatic infection</li> <li>• 89% (95% CI, 73 to 95) from hospitalization</li> <li>• 81.6% (95% CI, 71.0 to 88.8) from severe, critical, or fatal disease (combined with Alpha)</li> </ul>

		<p>mRNA-1273 provided protection against VOC Beta for the following outcomes 35-41 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>• 43% (95% CI, 22 to 59) from symptomatic infection</li> </ul> <p>mRNA-1273 provided protection against VOC Beta for the following outcome 7 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>• 96.4% (95% CI, 91.9 to 98.7) from infection</li> <li>• 88% (95% CI, 61 to 96) from symptomatic infection</li> <li>• 95.7% (95% CI, 73.4 to 99.9) from severe, critical, or fatal disease (combined with Alpha)</li> </ul> <p>(2 Obs – 3 refs) <a href="#">[23]</a><a href="#">[47]</a><a href="#">[50]</a>; <i>last update 2021-07-14</i></p>
<b>Beta</b>	<p><b>AstraZeneca</b> [ChAd0x1] <b>Vaxzevria</b> <b>Serum Institute of India</b> [Covishield]</p>	<p>ChAdOx1 provided protection against VOC Beta for the following outcome 14 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>• 48% (95% CI, 28 to 63) from symptomatic infection</li> <li>• 83% (95% CI, 66 to 92) from hospitalization</li> </ul> <p>ChAdOx1 provided protection against VOC Beta for the following outcome after 2 doses:</p> <ul style="list-style-type: none"> <li>• 10.4% (95% CI, -76.8 to 54.8) from mild to moderate disease (1 RCT, moderate quality; 1 Obs) <a href="#">[4]</a><a href="#">[47]</a>; <i>last update 2021-07-07</i></li> </ul>
<b>Beta</b>	<p><b>Novavax</b> [NVX-CoV2373]</p>	<p>NVX-CoV2373 provided protection against VOC Beta for the following outcome after 7 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>• Post-hoc: 43% (95% CI, -9.8 to 70.4) from symptomatic infection</li> </ul> <p>(1 RCT, moderate quality), <a href="#">[17]</a>; <i>last update 2021-07-14</i></p>

<b>Alpha</b>	<p><b>Moderna</b> <b>Spikevax</b> [mRNA-1723]</p>	<p>mRNA-1273 provided protection against VOC Alpha for the following outcomes 14-41 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>• 58.9 to 88.1% from infection (RME)</li> <li>• 60 to 61% from symptomatic infection (RME)</li> <li>• 81.6% (95% CI, 71.0 to 88.8) from severe, critical, or fatal disease (combined with Beta)</li> </ul> <p>mRNA-1273 provided protection against VOC Alpha for the following outcomes at least 7 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>• 86 to 100% from infection (RME)</li> <li>• 90 to 95.7% from symptomatic infection (RME)</li> <li>• 95.7% (95% CI, 73.4 to 99.9) from severe, critical, or fatal disease (combined with Beta)</li> </ul> <p>(10 Obs – 11 refs) <a href="#">[8]</a><a href="#">[23]</a><a href="#">[31]</a><a href="#">[34]</a><a href="#">[37]</a><a href="#">[47]</a><a href="#">[50]</a><a href="#">[60]</a><a href="#">[74]</a><a href="#">[101]</a><a href="#">[102]</a>; <i>last update 2021-10-20</i></p>
<b>Alpha</b>	<p><b>AstraZeneca</b> [ChAd0x1] <b>Vaxzevria</b> <b>Serum Institute of India</b> [Covishield]</p>	<p>ChAdOx1 provided protection against VOC Alpha for the following outcome 14 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>• 64% (95% CI, 60 to 68) from symptomatic infection</li> <li>• 85% (95% CI, 81 to 88) from hospitalization</li> </ul> <p>ChAdOx1nCoV-19 provided protection against VOC Alpha for the following outcome 21 to 28 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>• 44 to 74% from infection (RME)</li> </ul> <p>ChAdOx1 provided protection against confirmed VOC Alpha for the following outcome at least 14 days after 2 doses:</p> <ul style="list-style-type: none"> <li>• 62 to 79% from infection (RME)</li> </ul>

		(1 RCT, moderate quality; 5 Obs)[9][10][5][47][70][71]; <i>last update 2021-08-25</i>
Alpha	Novavax [NVX-CoV2373]	NVX-CoV2373 provided protection against VOC Alpha for the following outcome after 2 doses: <ul style="list-style-type: none"> <li>• 89.7% (95% CI, 80.2 to 94.6) from symptomatic infection.</li> <li>• No hospitalizations or deaths in vaccinated group</li> <li>• Post hoc: 86.3% (95% CI, 71.3 to 93.5) from confirmed Alpha symptomatic infection</li> </ul> (1 RCT, moderate quality), [19]; <i>last update 2021-06-16</i>
Alpha	ChAdOx1 followed by mRNA vaccine	ChAdOx1 followed by BNT162b2 or mRNA-1273 at least 14 days after 2 <sup>nd</sup> dose provided protection against VOC Alpha for the following outcomes: <ul style="list-style-type: none"> <li>• 88% (95% CI, 83 to 92) against infection</li> </ul> (1 Obs) [70]; <i>last search date 2021-08-25</i>
Alpha  Transmission Household or close contacts of index case	Pfizer/ BioNTech Comirnaty [BNT162b2]	BNT162b2 reduced transmission of VOC Alpha from a vaccinated index case (14 to 21 days after 1 <sup>st</sup> dose) to household contacts compared to households of unvaccinated index cases: <ul style="list-style-type: none"> <li>• 30 to 49% from infection (RME)</li> </ul> BNT162b2 reduced transmission of VOC Alpha from a vaccinated HCW (10 weeks after 1 <sup>st</sup> dose) to household spouse: <ul style="list-style-type: none"> <li>• 42.9% (95% CI, 22.3 to 58.1) from infection</li> </ul> <u>Fully vaccinated index cases</u> showed VET for household contacts (unclear status): <ul style="list-style-type: none"> <li>• 70 to 82% from infection (RME)</li> </ul> <u>Fully vaccinated household contacts</u> showed VE (unclear status of index): <ul style="list-style-type: none"> <li>• 65 to 94% from infection (RME)</li> </ul> (8 Obs) [6][14][33][40][48][104][107][108]; <i>last update 2021-11-03</i>
Alpha  Transmission Household or close contacts of index case	Moderna Spikevax [mRNA-1723]	mRNA-1273 reduced transmission of VOC Alpha from a vaccinated HCW (10 weeks after 1 <sup>st</sup> dose) to household spouse: <ul style="list-style-type: none"> <li>• 42.9% (95% CI, 22.3 to 58.1) from infection</li> </ul> <u>Fully vaccinated index cases by mRNA-1273</u> showed VET for household contacts (unclear status): <ul style="list-style-type: none"> <li>• 88% (95% CI, 50 to 97) from infection</li> </ul> <u>Fully vaccinated household contacts by mRNA-1273</u> showed VE (unclear status of index): <ul style="list-style-type: none"> <li>• 86 to 91% from infection (RME)</li> </ul> (3 Obs)[33][104][108]; <i>last update 2021-11-03</i>
Alpha  Transmission Household or close contacts of index case	AstraZeneca [ChAdOx1] Vaxzevria Serum Institute of India [Covishield]	ChAdOx1 reduced transmission of VOC Alpha from a vaccinated index case (14 to 21 days after 1 <sup>st</sup> dose) to household contacts compared to households of unvaccinated index cases: <ul style="list-style-type: none"> <li>• 30 to 47% from infection (RME)</li> </ul> <u>Fully vaccinated index cases by ChAdOx1</u> showed VET to household contacts (unclear status): <ul style="list-style-type: none"> <li>• 58 to 63% from infection (RME)</li> </ul> <u>Fully vaccinated household contacts by ChAdOx1</u> showed VE (unclear status of index case): <ul style="list-style-type: none"> <li>• 38 to 87% from infection (RME)</li> </ul>

		(6 Obs) <a href="#">[6]</a> <a href="#">[14]</a> <a href="#">[40]</a> <a href="#">[104]</a> <a href="#">[107]</a> <a href="#">[108]</a> ; <i>last update 2021-12-01</i>
<b>Alpha</b> <b>Transmission</b> <b>Household or close</b> <b>contacts of index</b> <b>case</b>	<b>Johnson &amp; Johnson</b> <b>[AD26.COVS2.S]</b>	<u>Fully vaccinated index cases by Ad26.COVS2.S</u> showed VET for household contacts (unclear status): <ul style="list-style-type: none"> <li>• 77% (95% CI, 6 to 94) from infection</li> </ul> <u>Fully vaccinated household contacts by Ad26.COVS2.S</u> showed VE (unclear status of index): <ul style="list-style-type: none"> <li>• 12% (95% CI, -71 to 54) from infection</li> </ul> (1 Obs) <a href="#">[104]</a> ; <i>last update 2021-11-03</i>

<b>Studies Covering Time Frame for More than One VOC (insufficient data to divide them into separate VOC)</b>		
<b>Alpha to Delta</b>	<b>Pfizer/ BioNTech</b>  <b>Comirnaty</b> <b>[BNT162b2]</b>	BNT162b2 provided protection against infection by VOC Alpha to Delta at least 7 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 69.7% (95% CI, 68.6 to 70.8)</li> </ul> BNT162b2 or mRNA-1273 provided protection against VOC Alpha to Delta for the following outcomes $\geq$ 14 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 92% (95% CI, 85 to 96) from severe disease in people with no risk conditions</li> <li>• 72% (95% CI, 51 to 84) from severe disease with very high risk conditions</li> </ul> BNT162b2 showed OR 1.61 (95% CI, 1.45 to 1.79) for infection comparing <u>fully vaccinated Jan to Feb</u> (VOC_Alpha) vs <u>fully vaccinated Mar to May</u> (VOC Delta). (3 Obs) <a href="#">[95]</a> <a href="#">[96]</a> <a href="#">[127]</a> ; <i>last update 2021-12-01</i>
<b>Alpha to Delta</b>	<b>Moderna</b> <b>Spikevax</b> <b>[mRNA-1723]</b>	mRNA-1273 provided protection against infection by VOC Alpha to Delta at least 7 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 78.2% (95% CI, 76.7 to 79.6)</li> </ul> mRNA-1273 or BNT162b2 provided protection against VOC Alpha to Delta for the following outcomes $\geq$ 14 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 92% (95% CI, 85 to 96) from severe disease in people with no risk conditions</li> <li>• 72% (95% CI, 51 to 84) from severe disease with very high risk conditions</li> </ul> (2 Obs) <a href="#">[95]</a> <a href="#">[127]</a> ; <i>last update 2021-12-01</i>
<b>Alpha to Delta</b>	<b>AstraZeneca</b> <b>[ChAdOx1]</b> <b>Vaxzevria</b> <b>Serum Institute of</b> <b>India</b> <b>[Covishield]</b>	ChAdOx1 provided protection against infection by VOC Alpha to Delta at least 7 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 43.4% (95% CI, 4.4 to 66.5)</li> </ul> ChAdOx1 provided protection against VOC Alpha to Delta for the following outcomes $\geq$ 14 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 94% (95% CI, 90 to 96) from severe disease in people with no risk conditions</li> <li>• 63% (95% CI, 46 to 75) from severe disease with very high risk conditions</li> </ul> (2 Obs) <a href="#">[95]</a> <a href="#">[127]</a> ; <i>last update 2021-12-01</i>
<b>Alpha to Delta</b>	<b>Heterologous</b> <b>mRNA vaccines</b> <b>ChAdOx1 followed</b> <b>by mRNA vaccine</b>	Heterologous mRNA vaccines provided protection against infection by VOC Alpha to Delta at least 7 days after the 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 84.7% (83.1 to 86.1)</li> </ul> ChAdOx1 followed by either BNT162b2 or mRNA-1273 provided protection against infection by VOC Alpha to Delta at least 7 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 60.7% (95% CI, 57.5 to 63.6)</li> </ul>

		(1 Obs) [127]; <i>last update 2021-12-01</i>
<b>Alpha to Delta</b> <b>Maintenance hemodialysis</b>  (not updated after Nov 5, 2021)	<b>Moderna Spikevax [mRNA-1723]</b>	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]; <i>last update 2021-11-03</i>
<b>Alpha or Beta</b> <b>Immunosuppressed, renal transplant</b>  (not updated after Nov 5, 2021)	<b>Pfizer/ BioNTech Comirnaty [BNT162b2]</b>	BNT162b2 or mRNA-1273 provided protection against infection by VOC Alpha or Beta at the following number of days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 46.6% (95% CI, 0.0 to 73.7) ≥14 days</li> <li>• 66.0% (95% CI, 21.3 to 85.3) ≥42 days</li> <li>• 73.9% (95% CI, 33 to 98.9) ≥56 days</li> </ul> BNT162b2 or mRNA-1273 provided protection against severe, critical, or fatal disease by VOC Alpha or Beta at the following number of days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 72.3% (95% CI, 0.0 to 90.9) ≥14 days</li> <li>• 85% (95% CI, 35.7 to 96.5) ≥42 days</li> <li>• 83.8% (95% CI, 31.3 to 96.2) ≥56 days</li> </ul> (1 Obs) [90]; <i>last update 2021-09-22</i>
<b>Alpha or Beta</b> <b>Immunosuppressed, renal transplant</b>  (not updated after Nov 5, 2021)	<b>Moderna Spikevax [mRNA-1723]</b>	mRNA-1273 or BNT162b2 provided protection against infection by VOC Alpha or Beta at the following number of days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 46.6% (95% CI, 0.0 to 73.7) ≥14 days</li> <li>• 66.0% (95% CI, 21.3 to 85.3) ≥42 days</li> <li>• 73.9% (95% CI, 33 to 98.9) ≥56 days</li> </ul> mRNA-1273 or BNT162b2 provided protection against severe, critical, or fatal disease by VOC Alpha or Beta at the following number of days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 72.3% (95% CI, 0.0 to 90.9) ≥14 days</li> <li>• 85% (95% CI, 35.7 to 96.5) ≥42 days</li> <li>• 83.8% (95% CI, 31.3 to 96.2) ≥56 days</li> </ul> (1 Obs) [90]; <i>last update 2021-09-22</i>
<b>Alpha or Beta</b> <b>Previously infected</b>  (not updated after Nov 5, 2021)	<b>Pfizer/ BioNTech Comirnaty [BNT162b2]</b>	BNT162b2 (2 doses) <u>after prior infection</u> provided protection against VOC Alpha (or Beta) for the following outcomes: <ul style="list-style-type: none"> <li>• 85% (95% CI, 80 to 89) against re-infection compared to BNT162b2 without prior infection</li> </ul> (1 Obs) [72]; <i>last update 2021-08-25</i>
<b>Alpha or Beta</b> <b>Previously infected</b>  (not updated after Nov 5, 2021)	<b>Moderna Spikevax [mRNA-1723]</b>	mRNA-1273 (2 doses) <u>after prior infection</u> did not offer additional protection against VOC Alpha (or Beta) for the following outcomes: <ul style="list-style-type: none"> <li>• 15% (95% CI, -105 to 66) against re-infection compared to mRNA-1273 without prior infection</li> </ul> (1 Obs) [72]; <i>last update 2021-08-25</i>
<b>Beta to Delta</b>	<b>Pfizer/ BioNTech Comirnaty [BNT162b2]</b>	BNT162b2 provided protection against infection by VOC Beta to VOC Delta for the following number of days after the 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 65.8% (95% CI, 63.8 to 67.7) at 5 to 9 weeks</li> <li>• 29.7% (95% CI, 21.7 to 36.9) at 15 to 19 weeks</li> <li>• 0% (95% CI, 0 to 0) 20 to 24 weeks</li> </ul>



		BNT162b2 provided protection against hospitalization or death by VOC Beta to VOC Delta for the following number of days after the 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 94.2% (95% CI, 91.0 to 96.5) at 5 to 9 weeks</li> <li>• 86.4% (95% CI, 69.9 to 94.8) at 15 to 19 weeks</li> <li>• 95.3% (95% CI, 70.5 to 99.9) at 20 to 24 weeks</li> </ul> (1 Obs) [98]; <i>last update</i> 2021-10-06
<b>Beta or Gamma</b> <b>HCW</b>  (not updated after Nov 5, 2021)	<b>Pfizer/ BioNTech Comirnaty [BNT162b2]</b>	BNT162b2 provided protection against VOC Beta or Gamma for the following outcomes 14 to 42 days after 1 <sup>st</sup> dose: <ul style="list-style-type: none"> <li>• 37.2% (95% CI, 16.6 to 52.7) from infection</li> </ul> BNT162b2 provided protection against VOC Beta or Gamma for the following outcome 7 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 79.2% (95% CI, 64.6 to 87.8) from infection</li> </ul> (1 Obs)[27]; <i>last update</i> 2021-06-01
<b>Beta or Gamma</b> <b>Transmission</b> <b>Vaccinated HCW vs</b> <b>unvaccinated</b> <b>community</b>	<b>Pfizer/ BioNTech Comirnaty [BNT162b2]</b>	BNT162b2 reduced transmission of VOC Beta or Gamma from vaccinated HCW compared to unvaccinated community $\geq$ 14 days after 1 <sup>st</sup> dose: <ul style="list-style-type: none"> <li>• 54.7% (95% CI, 44.8 to 62.9) from infection</li> </ul> BNT162b2 reduced transmission of VOC Beta or Gamma from vaccinated HCW compared to unvaccinated community $\geq$ 7 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 84.8% (95% CI, 75.2 to 90.7) from infection</li> </ul> (1 Obs) [27]; <i>last update</i> 2021-06-08

**Special Populations (will not be updated after November 5, 2021)**

<b>Delta</b> <b>Adolescents</b>  (moved to Pediatric/ Adolescent LES)	<b>Pfizer/ BioNTech Comirnaty [BNT162b2]</b>	BNT162b2 provided protection against VOC Delta for the following outcomes at least 14 days after 1 <sup>st</sup> dose: <ul style="list-style-type: none"> <li>• 59% (95% CI, 52 to 65) from infection</li> </ul> BNT162b2 provided protection against VOC Delta for the following outcomes at least 7 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 90 to 92% against infection (RME)</li> </ul> (2 Obs) [112][120]; <i>last update</i> 2021-11-17
<b>Delta</b> <b>HCW</b>	<b>Pfizer/ BioNTech Comirnaty [BNT162b2]</b>	BNT162b2 provided protection against VOC Delta for the following outcomes $\geq$ 14 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 66% (95% CI, 26 to 84)</li> </ul> (1 Obs) [81]; <i>last update</i> 2021-09-22
<b>Delta</b> <b>HCW</b>	<b>AstraZeneca [ChAd0x1] Vaxzevria Serum Institute of India [Covishield]</b>	ChAdOx1 provided protection against VOC Delta for the following outcomes at least 14 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 54 to 85% from infection (RME)</li> <li>• 64% (95% CI, 38 to 78) from symptomatic infection</li> </ul> (2 Obs) [59][66]; <i>last update</i> 2021-10-06
<b>Delta</b> <b>Previously infected, (65+)</b>	<b>Pfizer/ BioNTech Comirnaty [BNT162b2]</b>	BNT162b2 (2 doses) provided protection against VOC Delta for the following outcomes compared to <u>natural immunity after prior infection</u> : <ul style="list-style-type: none"> <li>• 66% (95% CI, 22 to 86) from infection</li> </ul> (1 Obs) [103]; <i>last update</i> 2021-10-20

<b>Delta</b> <b>Previously infected</b> <b>(65+)</b>	<b>Moderna</b> <b>Spikevax</b> <b>[mRNA-1723]</b>	mRNA-1273 (2 doses) provided protection against VOC Delta for the following outcomes compared to <u>natural immunity after prior infection</u> : <ul style="list-style-type: none"> <li>• 68% (95% CI, 30 to 86) from infection</li> <li>• 30% (-11 to 1) from death</li> </ul> (1 Obs) <a href="#">[103]</a> ; <i>last update 2021-10-20</i>
<b>Delta</b> <b>Prison</b>	<b>Moderna</b> <b>Spikevax</b> <b>[mRNA-1723]</b>	mRNA-1273 provided protection against VOC Delta for the following outcomes at least 14 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 57% (95% CI, 42 to 67.5)</li> </ul> (1 Obs) <a href="#">[113]</a> ; <i>last update 2021-11-03</i>
<b>Gamma</b> <b>HCW</b>	<b>Sinovac [CoronaVac]</b>	CoronaVac provided protection against VOC Gamma for the following outcomes ≥14 days after 1 <sup>st</sup> dose: <ul style="list-style-type: none"> <li>• 35.1% (95% CI, -6.6 to 60.5) from infection</li> <li>• 49.6% (95% CI, 11.3 to 71.4) from symptomatic infection</li> </ul> (1 Obs) <a href="#">[18]</a> ; <i>last update 2021-05-07</i>
<b>Gamma</b> <b>LTC residents</b>	<b>Pfizer/</b> <b>BioNTech</b> <b>Comirnaty</b> <b>[BNT162b2]</b>	BNT162b2 (or mRNA-1273) provided protection against VOC Gamma 14 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 52.5% (95% CI, 26.9 to 69.1) against infection</li> <li>• 78.6% (95% CI, 47.9 to 91.2) against severe disease</li> </ul> (1 Obs) <a href="#">[61]</a> ; <i>last update 2021-08-11</i>
<b>Gamma</b> <b>LTC residents</b>	<b>Moderna</b> <b>Spikevax</b> <b>[mRNA-1723]</b>	mRNA-1273 (or BNT162b2) provided protection against VOC Gamma for the following outcomes 14 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 52.5% (95% CI, 26.9 to 69.1) against infection</li> <li>• 78.6% (95% CI, 47.9 to 91.2) against severe disease</li> </ul> (1 Obs) <a href="#">[61]</a> ; <i>last update 2021-08-11</i>
<b>Gamma</b> <b>Over 70 years</b>	<b>Pfizer/</b> <b>BioNTech</b> <b>Comirnaty</b> <b>[BNT162b2]</b>	BNT162b2 provided protection against VOC Gamma for the following outcomes ≥ 21 days after 1 <sup>st</sup> dose: <ul style="list-style-type: none"> <li>• 61% (95% CI, 45 to 72) from infection</li> </ul> (1 Obs) <a href="#">[35]</a> ; <i>last update 2021-07-07</i>
<b>Gamma</b> <b>Over 70 years</b>	<b>Moderna</b> <b>Spikevax</b> <b>[mRNA-1723]</b>	mRNA-1273 provided protection against VOC Gamma for the following outcome ≥21 days after 1 <sup>st</sup> dose: <ul style="list-style-type: none"> <li>• 61% (95% CI, 45 to 72) from infection</li> </ul> (1 Obs) <a href="#">[35]</a> ; <i>last update 2021-06-23</i>
<b>Alpha</b> <b>HCW</b>	<b>Pfizer/</b> <b>BioNTech</b> <b>Comirnaty</b> <b>[BNT162b2]</b>	BNT162b2 provided protection against VOC Alpha for the following outcomes 14 to 21 days after 1 <sup>st</sup> dose: <ul style="list-style-type: none"> <li>• 64 to 84% from infection (RME)</li> </ul> BNT162b2 provided protection against VOC Alpha for the following outcomes at least 7 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 90 to 97% from infection (RME)</li> </ul> BNT162b2 provided protection against VOC Alpha for the following outcome 7 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 86% (95% CI, 69 to 93) from asymptomatic infection <a href="#">[25]</a></li> </ul> BNT162b2 provided protection against infection by VOC Alpha for the following number of days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 85% (95% CI, 68 to 93) at 14 to 119 days</li> <li>• 73% (95% CI, 49 to 86) ≥150 days</li> </ul> (6 Obs) <a href="#">[11]</a> <a href="#">[34]</a> <a href="#">[45]</a> <a href="#">[46]</a> <a href="#">[56]</a> <a href="#">[81]</a> ; <i>last update 2021-11-17</i>
<b>Alpha</b>	<b>AstraZeneca</b> <b>[ChAd0x1]</b>	ChAdOx1 provided protection against VOC Alpha for the following outcomes at least 14 days after 1 <sup>st</sup> dose:

<b>HCW</b>	<b>Vaxzevria Serum Institute of India [Covishield]</b>	<ul style="list-style-type: none"> <li>64% (95% CI, 50 to 74) from infection</li> </ul> <p>ChAdOx1 provided protection against VOC Alpha for the following outcomes at least 14 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>90% (95% CI, 62 to 98) from infection</li> </ul> <p>(1 Obs) <a href="#">[46]</a>; <i>last update 2021-07-07</i></p>
<b>Alpha LTC residents</b>	<b>Pfizer/ BioNTech Comirnaty [BNT162b2]</b>	<p>BNT162b2 provided protection against VOC Alpha for the following outcomes 7 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>53% (95% CI, 29 to 69) from infection</li> <li>89% (95% CI, 81 to 93) from death</li> </ul> <p>(1 Obs) <a href="#">[32]</a>; <i>last update 2021-10-06</i></p>
<b>Alpha Over 65 years, requiring home support</b>	<b>Pfizer/ BioNTech Comirnaty [BNT162b2]</b>	<p>BNT162b2 provided protection against VOC Alpha for the following outcomes 7 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>86% (95% CI, 78 to 91) from infection</li> <li>97% (95% CI, 88 to 99) from death</li> </ul> <p>(1 Obs) <a href="#">[32]</a>; <i>last update 2021-07-07</i></p>
<b>Alpha Over 70 years</b>	<b>Pfizer/ BioNTech Comirnaty [BNT162b2]</b>	<p>BNT162b2 provided protection against VOC Alpha for the following outcomes at least 21 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>41 to 67% from infection (RME)</li> </ul> <p>BNT162b2 provided protection against VOC Alpha for the following outcomes at least 7 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>75 to 90% from infection (RME)</li> </ul> <p>(3 Obs) <a href="#">[28]</a> <a href="#">[35]</a> <a href="#">[51]</a>; <i>last update 2021-10-06</i></p>
<b>Alpha Over 70 years</b>	<b>Moderna Spikevax [mRNA-1723]</b>	<p>mRNA-1273 provided protection against VOC Alpha for the following outcome <math>\geq 21</math> days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>67% (95% CI, 57 to 75) from infection</li> </ul> <p>(1 Obs) <a href="#">[35]</a>; <i>last update 2021-06-23</i></p>
<b>Alpha Over 80 years</b>	<b>AstraZeneca [ChAdOx1] Vaxzevria Serum Institute of India [Covishield]</b>	<p>ChAdOx1 provided protection against VOC Alpha for the following outcomes at least 14 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>88% (95% CI, 48 to 97) from symptomatic infection</li> </ul> <p>(1 Obs) <a href="#">[79]</a>; <i>last update 2021-10-20</i></p>
<b>Alpha Pregnant</b>	<b>Pfizer/ BioNTech Comirnaty [BNT162b2]</b>	<p>BNT162b2 provided protection against VOC Alpha for the following outcomes at least 28 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>78% (95% CI, 57 to 89) from infection</li> </ul> <p>BNT162b2 provided protection against VOC Alpha for the following outcomes 7 to 56 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>86.1% (95% CI, 82.4 to 89.1) from infection</li> <li>89% (95% CI, 43 to 100) from hospitalization</li> </ul> <p>(2 Obs) <a href="#">[52]</a> <a href="#">[54]</a>; <i>last update 2021-07-28</i></p>
<b>Epsilon</b>	<b>Pfizer/ BioNTech Comirnaty [BNT162b2]</b>	<p>BNT162b2 provided protection against VOC Epsilon for the following outcome 15 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>58.9% (95% CI, -9.7 to 84.5) from infection</li> </ul> <p>BNT162b2 provided protection against VOC Epsilon for the following outcome 15 days after 2<sup>nd</sup> dose:</p> <ul style="list-style-type: none"> <li>85.7% (67.2 to 93.9) from infection</li> </ul> <p>(2 Obs) <a href="#">[8]</a> <a href="#">[31]</a>; <i>last update 2021-06-08</i></p>
<b>Epsilon</b>	<b>Moderna Spikevax [mRNA-1723]</b>	<p>mRNA-1273 provided protection against VOC Epsilon for the following outcome 15 days after 1<sup>st</sup> dose:</p> <ul style="list-style-type: none"> <li>58.9% (95% CI, -9.7 to 84.5) from infection</li> </ul>

		mRNA-1273 provided protection against VOC Epsilon for the following outcome 15 days after 2 <sup>nd</sup> dose: <ul style="list-style-type: none"> <li>• 85.7% (67.2 to 93.9) from infection (2 Obs) [8][31]; <i>last update 2021-06-08</i></li> </ul>
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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>

Iorio A, Little J, Linkins L, Abdelkader W, Bennett D, Lavis JN. COVID-19 living evidence synthesis #6 (version 6.26): What is the efficacy and effectiveness of available COVID-19 vaccines in general and specifically for variants of concern? Health Information Research Unit (HIRU); McMaster and Ottawa Knowledge Synthesis and Application Unit, 15 December 2021.

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	<a href="#">Dagan</a>	BNT162b2 showed VE 46% (95% CI, 40 to 51) against infection 14 to 20 days after 1 <sup>st</sup> dose and VE 92% (95% CI, 88 to 95) 7 days after 2 <sup>nd</sup> dose.  BNT162b2 showed VE 92% (95% CI, 75 to 100) for severe disease at 7 days after 2 <sup>nd</sup> 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	<a href="#">Haas</a>	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 2 <sup>nd</sup> 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	<a href="#">Kustin</a>  *Delayed exclusion-only included infected	BNT162b2 showed lower relative VE (2.4:1) against Alpha. after 1 <sup>st</sup> dose; and lower VE (8:1) against Beta after 2 <sup>nd</sup> 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	<a href="#">Madhi</a>	ChAdOx1 nCoV-19 showed VE 10.4% (95% CI, -76.8 to 54.8) against mild to moderate disease 14 days after 2 <sup>nd</sup> dose.	Moderate quality (RCT)	RCT in South Africa; Underpowered for 20% efficacy (42 cases); VOC Beta.
5	<a href="#">Emery</a>	ChAdOx1nCoV-19 showed VE 61.7% (95% CI, 36.7 to 76.9) against infection by VOC Alpha ≥ 15 days after 2 <sup>nd</sup> 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	<a href="#">Shah</a>	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 1 <sup>st</sup> 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 1 <sup>st</sup> dose.	Moderate	Data-linkage study in Scotland - (25% of cases had received 2 doses); time and setting for VOC Alpha.
7	<a href="#">Sadoff</a>	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	Moderate quality (RCT)	RCT; over 40,000 participants; Argentina, Brazil, Chile, Colombia, Mexico, Peru, South Africa, and the United

		81.7% (95% CI, 46.2 to 95.4) at 28 days against severe disease (VOC Beta in South Africa).		States; 86 of 91 cases sequenced for VOC Beta.
8	<a href="#">Andrejko</a>	BNT162b2 or mRNA-1273 showed VE 58.9% (95% CI, -9.7 to 84.5) at 15 days after 1 <sup>st</sup> dose, and VE 85.7% (95% CI, 67.2 to 93.9) 15 days after 2 <sup>nd</sup> dose against infection.	Serious	Test-negative study in California; 645 participants; 69% of population at time had VOC Alpha or Epsilon.
9	<a href="#">Glampson</a>	ChAdOx1nCoV-19 showed VE 74% (95% CI, 65 to 81) against infection 28 days after 1 <sup>st</sup> dose.  BNT162b2 showed VE 78% (95% CI, 73 to 82) against infection 28 days after 1 <sup>st</sup> dose.	Serious	Retrospective cohort in UK; 2M participants; time and setting for VOC Alpha.
10	<a href="#">Pritchard</a>	ChAdOx1nCoV-19 or BNT162b2 showed VE 66% (95% CI, 59 to 72%) 21 days after 1 <sup>st</sup> dose and 78% (95% CI, 68 to 85%) after 2 <sup>nd</sup> dose against infection.	Serious	Survey of randomly selected private households with longitudinal follow-up in UK; 370,000 participants; sample confirmed VOC Alpha.
11	<a href="#">Hall (SIREN)</a>	BNT162b2 vaccine showed VE of 70% (95% CI, 55 to 85) 21 days after 1 <sup>st</sup> dose and 85% (95% CI, 74 to 96) 7 days after 2 <sup>nd</sup> 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	<a href="#">Shrotri</a>  *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 1 <sup>st</sup> dose.	Critical	Prospective cohort in England: 9160 of 10412 frail LTC residents; routine screening; time and setting for VOC Alpha
13	<a href="#">Hyams</a>  *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 1 <sup>st</sup> dose; ChAdOx1nCoV-19 showed VE 80.4% (95% CI, 36.4 to 94.5) against hospitalization 14 days after 1 <sup>st</sup> 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	<a href="#">Harris</a>	BNT162b2 or ChAdOx1 reduced likelihood of transmission by 40-50% for household contacts of HCW 21 days after 1 <sup>st</sup> dose.	Serious	Data-linkage and case-control study in England; 338,887 participants; time and setting for VOC Alpha
15	<a href="#">Goldberg</a>	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	<a href="#">Cavanaugh</a>  *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	<a href="#">Shinde</a>	NVX-CoV2372 VE showed VE 50.4% (95% CI, 16.6 to 70.5) against symptomatic infection 7 days after 2 <sup>nd</sup> dose.	Moderate quality (RCT)	RCT in South Africa; 4387 participants; 38/41 cases VOC Beta
18	<a href="#">Hitchings</a>	CoronaVac showed VE of 35.1% (95% CI, -6.6 to 60.5) against infection in HCW after 1 <sup>st</sup> 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	<a href="#">Heath</a>	NVX-CoV2373 showed VE 89.7% (95% CI, 80.2 to 94.6) against symptomatic infection after 2 <sup>nd</sup> 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	<a href="#">Ismail</a>  *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 1 <sup>st</sup> dose and 93% (95% CI, 89 to 95) 14 days after the 2 <sup>nd</sup> dose for people 80+.  ChAdOx1 showed VE 73% (95% CI, 60 to 81) against hospitalization 28 days after 1 <sup>st</sup> dose; sample size too small to report VE after 2 <sup>nd</sup> dose for people 80+.		Screening study in UK; 13,907 hospitalized patients; results for age 80+; time and setting for VOC Alpha
21	<a href="#">Bernal (2)</a>  *Delayed exclusion – critical ROB	BNT162b2 showed VE 44% (95% CI, 32 to 53) after 1 <sup>st</sup> dose and 69% (95% CI, 31 to 86) after 2 <sup>nd</sup> 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	<a href="#">Chodick</a>	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 2 <sup>nd</sup> 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	<a href="#">Chung</a>	BNT162b2 or mRNA-1273 showed VE 61% (95% CI, 56 to 66) against symptomatic infection by VOC Alpha 14 days after 1 <sup>st</sup> dose and 90% (95% CI, 85 to 94) 7 days after 2 <sup>nd</sup> dose; 43% (95% CI, 22 to 59) against symptomatic infection by VOC Beta or Gamma 14 days after 1 <sup>st</sup> dose and 88% (95% CI, 61 to 96) 7 days after 2 <sup>nd</sup> 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	<a href="#">Bailly</a> *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	<a href="#">Angel</a>	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	<a href="#">Bianchi</a> *Delayed exclusion – critical ROB	BNT162b2 showed VE 61.9% (95% CI, 19.2 to 82) against infection 14 to 20 days after 1 <sup>st</sup> dose; 96% (95% CI, 82.2 to 99.1) ≥ 7 days after 2 <sup>nd</sup> dose in HCW.	Critical	Data-linkage, single centre medical centre in Italy, 2,034 participants; time and setting for VOC Alpha
27	<a href="#">Yassi</a>	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 1 <sup>st</sup> dose and 79.2% (95% CI, 64.6 to 87.8) 7 days after 2 <sup>nd</sup> dose in HCW.	Serious	Data-linkage, 25,558 Canadian HCW; evenly split between VOC Gamma and VOC Beta by end of study period
28	<a href="#">Bernal (1)</a>	BNT162b2 showed VE 60% (95% CI, 40 to 73) against confirmed symptomatic infection by VOC Alpha at least 28 days after 1 <sup>st</sup> dose and 90% (95% CI, 84 to 94) at least 14 days after 2 <sup>nd</sup> dose for people 70+.	Serious	Test-negative in England, 156,930 participants; spike gene target failure as proxy for confirmed VOC Alpha
29	<a href="#">Bernal (3)</a>	BNT162b2 showed VE 47.5% (95% CI, 41.6 to 52.8) at least 21 days after 1 <sup>st</sup> dose and VE 93.7% (95% CI, 91.6 to 95.3) at least 14 days after 2 <sup>nd</sup> dose against symptomatic infection by confirmed VOC Alpha.  ChadOx1 showed VE 48.7% (95% CI, 45.2 to 51.9) at least 21 days after 1 <sup>st</sup> dose and VE 74.5% (95% CI, 68.4 to 79.4) at least 14 days after 2 <sup>nd</sup> 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.

		<p>BNT162b2 showed VE 35.6% (95% CI, 22.7 to 46.4) at least 21 days after 1<sup>st</sup> dose and VE 88% (95% CI, 85.3 to 90.1) at least 14 days after 2<sup>nd</sup> dose against symptomatic infection by confirmed VOC Delta.</p> <p>ChAdOx1 showed VE 30% (95% CI, 24.3 to 35.3) at least 21 days after 1<sup>st</sup> dose and VE 67% (95% CI, 61.3 to 71.8) at least 14 days after 2<sup>nd</sup> dose against symptomatic infection by confirmed VOC Delta.</p>		
30	<a href="#">Ranzani</a>	CoronaVac reduced risk of symptomatic infection by VOC Gamma VE 41.6% (95% CI, 26.9 to 63.3) ≥ 14 days after 2 <sup>nd</sup> 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	<a href="#">Andrejko (2)</a>	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 2 <sup>nd</sup> 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	<a href="#">Emborg</a>	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 2 <sup>nd</sup> dose.	Serious	Data-linkage population study of high-risk groups in Denmark; 864,096 participants; sample confirmed VOC Alpha
33	<a href="#">Salo</a>	BNT162b2 showed VE 42.9% (95% CI, 22.3 to 58.1) against infection in unvaccinated household members of vaccinated HCW 10 weeks after 1 <sup>st</sup> dose.	Moderate	Data-linkage for household contacts of HCW in Finland; 52,766 spouses of vaccinated HCW; time and setting for VOC Alpha
34	<a href="#">Shrestha</a>	BNT162b2 or mRNA-1273 showed VE 97.1% (95% CI, 94.3 to 98.5) against infection ≥14 days after 2 <sup>nd</sup> 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	<a href="#">Skowronski</a>	<p>BNT162b2 (85%) or mRNA-1273 showed VE 67% (95% CI, 57 to 75) against infection by confirmed VOC Alpha ≥21 days after 1<sup>st</sup> dose for 70+.</p> <p>BNT162b2 (85%) or mRNA-1273 showed VE 61% (95% CI, 45 to 72) against infection by confirmed VOC Gamma ≥21 days after 1<sup>st</sup> dose for 70+.</p>	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	<a href="#">Abu-Raddad</a>	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 $\geq$ 14 days after 2 <sup>nd</sup> 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 $\geq$ 14 days after 1 <sup>st</sup> dose.		VOC Beta and 45% VOC Alpha between February-March 2021
37	<a href="#">Akhrass</a> *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 $\geq$ 14 days after 1 <sup>st</sup> dose; BNT162b2 or mRNA-1273 showed overall VE 95.7% (95% CI, 90 to 98.2) against symptomatic infection $\geq$ 14 days after 2 <sup>nd</sup> dose.	Critical	Retrospective cohort of HCW at a single centre in Kentucky, USA; 2,134 participants; time and setting for VOC Alpha
38	<a href="#">Sheikh</a>	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 1 <sup>st</sup> 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 2 <sup>nd</sup> 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 1 <sup>st</sup> 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 2 <sup>nd</sup> 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	<a href="#">Furer</a> *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	<a href="#">Martinez-Baz</a>	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 2 <sup>nd</sup> 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 1 <sup>st</sup> 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	<a href="#">Chodick (2)</a>	BNT162b2 showed VE 51.4% (95% CI, 16.3 to 71.8) against infection 13 to 24 days after 1 <sup>st</sup> dose.	Serious	Data-linkage study in Israel (Maccabi Health Care Services); 351,897 participants; time and setting for VOC Alpha
42	<a href="#">Stowe</a>	BNT162b2 showed VE 94% (95% CI, 46 to 99) at least 21 days after 1 <sup>st</sup> dose and VE 96% (95% CI, 86 to 99) at least 14 days after 2 <sup>nd</sup> dose against hospitalization by confirmed VOC Delta.  ChAdOx1 showed VE 71% (95% CI, 51 to 83) at least 21 days after 1 <sup>st</sup> dose and VE 92% (95% CI, 75 to 97) 14 days after 2 <sup>nd</sup> 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	<a href="#">Saciuk</a>	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 2 <sup>nd</sup> dose	Serious	Retrospective cohort of members of a health management organization in Israel; 1,650,885 participants; time and setting for VOC Alpha
44	<a href="#">Zacay</a>  *Delayed exclusion – critical risk of bias	BNT162b2 showed VE 61% (95% CI, 49 to 71) at least 14 days after 1 <sup>st</sup> dose and VE 89% (95% CI, 82 to 94) at least 7 days after 2 <sup>nd</sup> 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	<a href="#">Azamgarhi</a>	BNT162b2 showed VE 70% (95% CI, 6 to 91) against infection at least 14 days after 1 <sup>st</sup> dose	Serious	Single centre cohort study of HCW in UK; 2,260 participants; time and setting for VOC Alpha
46	<a href="#">Lumley</a>	BNT162b2 (63%) or ChAdOx1 showed VE 64% (95% CI, 50 to 74) 14 days after 1 <sup>st</sup> dose and VE 90% (95% CI, 62 to 98) 14 days after 2 <sup>nd</sup> dose against infection	Serious	Prospective cohort of HCWs in Oxfordshire, UK; 13,109 participants; confirmed VOC Alpha
47	<a href="#">Nasreen</a>	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 2 <sup>nd</sup> 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 2 <sup>nd</sup> dose (VOC Beta/Gamma); VE 87% (95% CI, 64 to 95) against symptomatic infection at least 7 days after 2 <sup>nd</sup> 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

		<p>BNT162b2 showed VE 78% (95% CI, 65 to 86) against hospitalization at least 7 days after 2<sup>nd</sup> dose (VOC Delta).</p> <p>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 2<sup>nd</sup> dose (VOC Alpha).</p> <p>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 1<sup>st</sup> 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 1<sup>st</sup> dose (VOC Delta).</p> <p>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 1<sup>st</sup> 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 1<sup>st</sup> 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 1<sup>st</sup> dose (VOC Delta).</p>		
48	<a href="#">Gazit</a>	BNT162b2 showed VE 80% (95% CI, 73 to 85) at least 7 days after 2 <sup>nd</sup> 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	<a href="#">Jara</a>	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 2 <sup>nd</sup> dose.	Moderate	Prospective cohort in Chile; 10.2 million participants; time and setting for VOC Gamma
50	<a href="#">Chemaitelly</a>	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 1 <sup>st</sup> and 2 <sup>nd</sup> dose, respectively.	Serious	Test-negative in Qatar; >75,000 participants; sample sequenced for VOC Alpha and VOC Beta

		<p>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 1<sup>st</sup> and 2<sup>nd</sup> dose, respectively.</p> <p>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 1<sup>st</sup> and 2<sup>nd</sup> dose, respectively (combined VOC Alpha and Beta).</p>		
51	<a href="#">Baum</a>	<p>BNT162b2 or mRNA-1273 showed VE 41% (95% CI, 25 to 54) against infection <math>\geq</math> 21 days after 1<sup>st</sup> dose; BNT162b2 or mRNA-1273 showed VE 75% (95% CI, 65 to 82) against infection <math>\geq</math> 7 days after 2<sup>nd</sup> dose in age 70+.</p> <p>BNT162b2 or mRNA-1273 showed VE 41% (95% CI, 17 to 58) against infection <math>\geq</math> 21 days after 1<sup>st</sup> dose; BNT162b2 or mRNA-1273 showed VE 77% (95% CI, 65 to 85) against infection <math>\geq</math> 7 days after 2<sup>nd</sup> dose in chronically ill (age 16-69).</p> <p>ChAdOx1 showed VE 24% (95% CI, -1 to 43) against infection <math>\geq</math> 21 days after 1<sup>st</sup> dose in chronically ill (age 16-69).</p>	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	<a href="#">Balicer</a>	<p>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 2<sup>nd</sup> dose.</p> <p>Too few events to report VE for severe disease or death.</p>	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	<a href="#">Mateo-Urdiales</a>	<p>BNT162b2 (61%) or ChAdOx1 (31%) or mRNA-1273 (7%) or Ad26.COV<sub>2</sub>-S (0.6%) showed VE 78% (95% CI, 76 to 79) against infection 42 to 49 days after at least 1<sup>st</sup> dose; VE 93% (95% CI, 89 to 96) against death 35 to 42 days after at least 1<sup>st</sup> dose.</p>	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 2 <sup>nd</sup> dose were included in estimates.
54	<a href="#">Goldshtein</a>	<p>BNT162b2 showed VE 78% (95% CI, 57 to 89) against infection at least 28 days after 1<sup>st</sup> dose.</p>	Serious	Data-linkage study of pregnant women in Israel (same database as Gazit); 15,060 participants; time and setting for VOC Alpha.
55	<a href="#">Mason</a>	<p>BNT162b2 showed VE 55.2% (95% CI, 40.8 to 66.8) and VE 70.1% (95% CI, 55.1</p>	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 1 <sup>st</sup> dose, respectively.		dwelling unvaccinated residents in England; time and setting for VOC Alpha
56	<a href="#">Fabiani</a>	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 1 <sup>st</sup> dose, respectively in HCW.  BNT162b2 showed VE 95.1% (95% CI, 62.4 to 99.4) against infection ≥7 days after 2 <sup>nd</sup> dose in HCW.	Serious	Retrospective cohort of HCW in Italy; 6,423 participants; time and setting for VOC Alpha
57	<a href="#">Chia</a>	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 2 <sup>nd</sup> dose.	Serious	Retrospective cohort of confirmed VOC Delta admitted to hospital (including asymptomatic) in Singapore; 218 participants; not reported by vaccine
58	<a href="#">Kaur</a> *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	<a href="#">Pramod</a> *Delayed exclusion – critical ROB	Covishield showed VE 49% (95% CI, 17 to 68) against infection 21 days after 1 <sup>st</sup> dose and VE 54% (95% CI, 27 to 71) against infection 14 days after 2 <sup>nd</sup> dose.  Covishield showed VE 58% (95% CI, 28 to 75) against symptomatic infection 21 days after 1 <sup>st</sup> dose and VE 64% (95% CI, 38 to 78) against symptomatic infection 14 days after 2 <sup>nd</sup> 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	<a href="#">Carazo</a>	BNT162b2 or mRNA-1273 showed VE 60% (95% CI, 53.6 to 65.5) against infection by confirmed VOC Alpha 14 days after 1 <sup>st</sup> 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 2 <sup>nd</sup> 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	<a href="#">Williams</a>	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 2 <sup>nd</sup> dose in residents at LTCF. Two deaths in vaccinated residents but were palliative prior to infection.	Serious	Outbreak in a single LTCF in Ontario; 60 residents and 83 staff; sample confirmed VOC Gamma

		BNT162b2 or mRNA-1273 showed VE 66.2% (95% CI, 2.3 to 88.3) against infection 14 days after 2 <sup>nd</sup> dose in staff at LTCF. None of the staff developed severe disease.		
62	<a href="#">Hitchings(2)</a>  *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 1 <sup>st</sup> 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 2 <sup>nd</sup> dose.	Critical	Test-negative study in Sao Paulo, Brazil; 61,164 participants over age 60; time and setting for VOC Gamma
63	<a href="#">Tang</a>	BNT162b2 showed VE 65.5% (95% CI, 40.9 to 79.9) against infection ≥ 14 days after 1 <sup>st</sup> dose; BNT162b2 showed VE 59.6% (95% CI, 50.7 to 66.9) against infection ≥ 14 days after 2 <sup>nd</sup> dose.  BNT162b2 showed VE 100% (95% CI, not reported) against severe, critical or fatal disease ≥ 14 days after 1 <sup>st</sup> dose; BNT162b2 showed VE 97.3% (95% CI, 84.4 to 99.5) against severe, critical or fatal disease ≥ 14 days after 2 <sup>nd</sup> dose.  mRNA-1273 showed VE 79.7% (95% CI, 60.8 to 89.5) against infection ≥ 14 days after 1 <sup>st</sup> dose; mRNA-1273 showed VE 86.1% (95% CI, 78.0 to 91.3) against infection ≥ 14 days after 2 <sup>nd</sup> dose.  mRNA-1273 showed VE 100% (95% CI, not reported) against severe, critical or fatal disease ≥ 14 days after 1 <sup>st</sup> dose; mRNA-1273 showed VE 100% (95% CI, not reported) against severe, critical or fatal disease ≥ 14 days after 2 <sup>nd</sup> dose.	Serious	Test-negative study in Qatar; 1,140,337 participants; weekly random sequencing of positive samples for VOC Delta
64	<a href="#">Puranik</a>	BNT162b2 showed VE 42% (95% CI, 13 to 62) against infection 14 days after 2 <sup>nd</sup> dose.  mRNA-1273 showed VE 76% (95% CI, 58 to 87) against infection 14 days after 2 <sup>nd</sup> 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	<a href="#">Elliot</a> *Delayed exclusion – critical ROB	BNT162b2 or ChAdOx1 showed VE 64% (95% CI, 11 to 85) against infection unreported number of days after 2 <sup>nd</sup> 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 2 <sup>nd</sup> dose (Round 13: 2021-06-24 to 2021-07-12).	Critical	Surveillance study in England; 121,872 participants; time and 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	<a href="#">Issac</a>	ChAdOx1 showed VE 85% (95% CI, 71 to 92) against infection 14 days after 2 <sup>nd</sup> dose.	Serious	Prospective cohort of HCW at a single hospital in India; 342 participants; time and setting for VOC Delta.
67	<a href="#">Marco</a> *Delayed exclusion – critical ROB	ChAdOx1 showed VE 23% (95% CI, not reported) against infection at least 21 days after 1 <sup>st</sup> dose.	Critical	Outbreak study of prison inmates in Barcelona; 217 participants (184 inmates); sequenced for VOC Alpha
68	<a href="#">Kale</a> *Delayed exclusion – critical ROB	ChAdOx1 showed VE 60% (95% CI, 45 to 70) against infection at least 14 days after 2 <sup>nd</sup> dose.	Critical	Prospective cohort of HCW at a single hospital in India; 1858 participants; sample sequenced for VOC Delta
69	<a href="#">Israel</a>	BNT162b2 showed OR 2.06 (95% CI, 1.69 to 2.51) for infection comparing <u>fully vaccinated longer than or equal to 146 days</u> vs <u>fully vaccinated less than 146 days</u> .	Moderate	Retrospective cohort of <b>fully vaccinated</b> members of a health management organization in Israel who underwent testing; 33,993 participants; time and setting for VOC Delta
70	<a href="#">Gram</a>	ChAdOx1 showed VE 44% (95% CI, 29 to 56) against infection 21 to 27 days after 1 <sup>st</sup> 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 $\geq$ 14 days after 2 <sup>nd</sup> dose.	Serious	Data-linkage study in Denmark; 5,542,079 participants; <b>sequenced for VOC Alpha (includes heterologous vaccines)</b>
71	<a href="#">Pouwels</a>	BNT162b2 showed VE 59% (95% CI, 52 to 65%) against infection $\geq$ 21 days after 1 <sup>st</sup> dose and VE 78% (95% CI, 68 to 84) against infection $\geq$ 14 days after 2 <sup>nd</sup> dose (VOC Alpha age 18+).  BNT162b2 showed VE 57% (95% CI, 50 to 63) against infection $\geq$ 21 days after 1 <sup>st</sup> dose and VE 80% (95% CI, 77 to 83) against infection $\geq$ 14 days after 2 <sup>nd</sup> dose (VOC Delta age 18+).  ChAdOx1 showed VE 63% (95% CI, 55 to 69) against infection $\geq$ 21 days after 1 <sup>st</sup> dose	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

		<p>and VE 79% (95% CI, 56 to 90) against infection <math>\geq 14</math> days after 2<sup>nd</sup> dose (VOC Alpha age 18+).</p> <p>ChAdOx1 showed VE 46% (95% CI, 35 to 55) against infection <math>\geq 21</math> days after 1<sup>st</sup> dose and VE 67% (95% CI, 62 to 71) against infection <math>\geq 14</math> days after 2<sup>nd</sup> dose (VOC Delta age 18+).</p> <p>mRNA-1273 showed VE 75% (95% CI: 64 to 83) against infection <math>\geq 21</math> days after 1<sup>st</sup> dose (VOC Delta age 18 to 64).</p>		
72	<a href="#">Abu-Raddad (2)</a>	<p>BNT162b2 <u>after prior infection</u> showed VE 85% (95% CI, 80 to 89) against re-infection compared to BNT162b2 <u>without prior infection</u>.</p> <p>mRNA-1273 <u>after prior infection</u> showed VE 15% (95% CI, -105 to 66) against re-infection compared to mRNA-1273 <u>without prior infection</u>.</p>	Serious	Retrospective matched cohorts (2) of <b>fully vaccinated</b> in Qatar; 151,076 participants; sample sequenced for VOC Alpha and VOC Beta
73	<a href="#">Gazit (2)</a>	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 <b>prior infection</b> .	Moderate	Retrospective matched cohorts of <b>fully vaccinated</b> in Israel; 778,658 participants; time and setting for VOC Delta
74	<a href="#">Rosenberg</a>	<p>BNT162b2 (51%), mRNA-1273 (40%) or Ad26.COVS (9%) showed VE 91.7% against infection <math>\geq 14</math> days after 2<sup>nd</sup> dose (Week of May 3, 2021: VOC Alpha).</p> <p>BNT162b2 (51%), mRNA-1273 (40%) or Ad26.COVS (9%) showed VE 79.8% against infection <math>\geq 14</math> days after 2<sup>nd</sup> dose (Week of July 19, 2021: VOC Delta).</p>	Serious	Surveillance report in New York, USA; >13 million participants; time and setting for VOC Delta (from 2% to 80% during study period)
75	<a href="#">Al-Qahtani</a>  *Delayed exclusion due to critical ROB	<p>BNT162b2 <math>\geq 14</math> days after 2<sup>nd</sup> 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).</p> <p>ChAdOx1 <math>\geq 14</math> days after 2<sup>nd</sup> 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).</p> <p>BBIBP-CorV <math>\geq 14</math> days after 2<sup>nd</sup> dose, showed VE 95.4% (95% CI, 94.6 to 96.2) against ICU admission, and VE 94.3% (95%</p>	Critical	Retrospective cohort of <b>fully vaccinated</b> (>14 days after 2 <sup>nd</sup> dose) in Bahrain; 1,242,279 participants; time and setting for VOC Alpha (dominant before May 2021) and Delta (dominant after May 2021).

		<p>CI, 93.1 to 95.4) against death (VOC Alpha and Delta).</p> <p>Sputnik V <math>\geq 14</math> days after 2<sup>nd</sup> 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).</p>		
76	<a href="#">Goldberg (2)</a>	<p>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 2<sup>nd</sup> dose (VOC Delta age 16 to 39).</p> <p>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 2<sup>nd</sup> dose (VOC Delta age 40 to 59).</p> <p>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 2<sup>nd</sup> dose (VOC Delta age 60+).</p> <p>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 2<sup>nd</sup> dose (VOC Delta age 40 to 59).</p> <p>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 2<sup>nd</sup> dose (VOC Delta age 60+).</p>	Serious	Data-linkage study of <b>fully vaccinated</b> in Israel; 4,785,245 participants; <b>sequenced</b> for VOC Delta (dominant after May 2021) ( <b>results over varying time since vaccination reported</b> )
77	<a href="#">Herlihy</a> *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 2 <sup>nd</sup> 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	<a href="#">Ghosh</a> *Delayed exclusion –	ChAdOx1 showed unadjusted VE 75.2% (95% CI, 73.8 to 76.8) against infection $\geq 14$ days after 1st dose, and unadjusted VE 54.6% (95% CI, 52.6 to 56.6) $\geq 14$ 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.

	critical risk of bias			
79	<a href="#">Amirthalingam</a>	<p>BNT162b2 showed VE 77% (95% CI, 56 to 88) against symptomatic infection when 2<sup>nd</sup> dose given 19-29 days after 1<sup>st</sup> dose, and VE 94% (95% CI, 73 to 99) against symptomatic infection when 2<sup>nd</sup> dose given 85+ days after 1<sup>st</sup> dose (VOC Alpha age 80+ ).</p> <p>BNT162b2 showed VE 77% (95% CI, 66 to 85) against symptomatic infection when 2<sup>nd</sup> dose given 19-29 days after 1<sup>st</sup> dose, and VE 86% (95% CI, 70 to 94) against symptomatic infection when 2<sup>nd</sup> dose given 85+ days after 1<sup>st</sup> dose (VOC Alpha age 65 to 79).</p> <p>ChAdOx1 showed VE 96% (95% CI, 72 to 100) against symptomatic infection when 2<sup>nd</sup> dose given 19-29 days after 1<sup>st</sup> dose, and VE 88% (95% CI, 48 to 97) against symptomatic infection when 2<sup>nd</sup> dose given 85+ days after 1<sup>st</sup> dose after 2<sup>nd</sup> dose (VOC Alpha age 80+).</p> <p>ChAdOx1 showed VE 66% (95% CI, 47 to 77) against symptomatic infection when 2<sup>nd</sup> dose given 19-29 days after 1<sup>st</sup> dose, and VE 73% (95% CI, 56 to 83) against symptomatic infection when 2<sup>nd</sup> dose given 85+ days after 1<sup>st</sup> dose after 2<sup>nd</sup> dose (VOC Alpha age 65 to 79).</p>	Moderate	Test-negative study in England; 750 participants; time and setting for VOC Alpha (dominant before May 2021) and Delta (dominant after May 2021). (results over varying time since vaccination reported)
80	<a href="#">Butt (2)</a>  *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 2 <sup>nd</sup> dose.	Critical	Case-control study in Qatar; 456 matched cases; time and setting for VOC Alpha
81	<a href="#">Fowlkes</a>	<p>BNT162b2 (65%), mRNA-1273 (33%), or Ad26.COV2.S (2%) showed VE 91% (95% CI, 81 to 96) against infection ≥ 14 days after 2<sup>nd</sup> dose (during time of VOC Alpha).</p> <p>BNT162b2 (65%), mRNA-1273 (33%), or Ad26.COV2.S (2%) showed VE 66% (95% CI, 26 to 84) against infection ≥ 14 days after 2<sup>nd</sup> dose (during time of VOC Delta).</p> <p>BNT162b2 (65%), mRNA-1273 (33%), or Ad26.COV2.S (2%) showed VE 85% (95% CI, 68 to 93) against infection 14-119 days</p>	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

		after full vaccination) and VE 73% (95% CI, 49 to 86) against infection $\geq$ 150 days after full vaccination (during time of VOC Alpha to Delta).		
82	<a href="#">Bhattacharya a</a>  *Delayed exclusion due to critical ROB	Covaxin (94%) and Covishield showed VE 83% (95% CI, 73 to 89) against symptomatic infection $\geq$ 14 days after 2 <sup>nd</sup> dose.  Covaxin (94%) and Covishield showed VE 93% (95% CI, 64 to 99) against ICU admission or death $\geq$ 14 days after 2 <sup>nd</sup> 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	<a href="#">Nunes</a>	BNT162b2 (45%) or mRNA-1273 (8%) showed VE 96% (95% CI, 92 to 98) against COVID-related death $\geq$ 14 days after 2 <sup>nd</sup> dose (age 65 to 79).  BNT162b2 (80%) or mRNA-1273 (2%) showed VE 81% (95% CI, 74 to 87) against COVID-related death $\geq$ 14 days after 2 <sup>nd</sup> dose (age $\geq$ 80).  BNT162b2 (80%) or mRNA-1273 (2%) showed VE 86% (95% CI, 68 to 93) against COVID-related death 14 to 41 days after 2 <sup>nd</sup> dose and VE 74% (95% CI, 60 to 83) against COVID-related death $\geq$ 98 days after 2 <sup>nd</sup> dose for HR 1.80 (0.77 to 4.25) (age $\geq$ 80).	Moderate	Data-linkage study of community-dwelling adults $\geq$ 65 in Portugal; 2,050,950 participants; time and setting for VOC Alpha to VOC Delta
84	<a href="#">Tartof</a>	BNT162b2 showed VE 75% (95% CI, 71 to 78) against infection 7 days after 2 <sup>nd</sup> dose (confirmed VOC Delta).  BNT162b2 showed VE 91% (95% CI, 88 to 92) against infection 7 days after 2 <sup>nd</sup> dose (confirmed non-VOC Delta).  BNT162b2 showed VE 93% (95% CI, 85 to 87) against infection 7 to 30 days after 2 <sup>nd</sup> dose and VE 53% (95% CI, 39 to 65) against infection $\geq$ 127+ days after 2 <sup>nd</sup> dose (confirmed VOC Delta).  BNT162b2 showed VE 97% (95% CI, 95 to 99) against infection 7 to 30 days after 2 <sup>nd</sup> dose and VE 67% (95% CI, 45 to 80) against infection $\geq$ 127+ days after 2 <sup>nd</sup> 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 since vaccination reported)
85	<a href="#">Li (3)</a>	CoronaVac (combined with other inactivated vaccines) showed VE 59% (95% CI, 16 to 81.6) against symptomatic	Critical	Test-negative study in Guangzhou, China; 366

	*Delayed exclusion – critical ROB	infection and VE 100% against severe infection $\geq 14$ days after 2 <sup>nd</sup> dose.		participants; sample sequenced for VOC Delta
86	<a href="#">Scobie</a> *Delayed exclusion – critical ROB	BNT162b2 or mRNA-1273 (92%), or Ad26.COVS2 showed VE 90% (95% CI not reported) against infection and VE 93% (95% CI not reported) against death $\geq 14$ days after 2 <sup>nd</sup> dose (April to June: VOC Alpha).  BNT162b2, mRNA-1273, or Ad26.COVS2 showed VE 76% (95% CI not reported) against infection and VE 90% (95% CI not reported) against death $\geq 14$ days after 2 <sup>nd</sup> dose (June to July: VOC Delta >50%).	Critical	Surveillance study in 13 states in the USA; 615,454; time and setting for VOC Alpha to VOC Delta
87	<a href="#">Satwik</a>  *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 $\geq 21$ days after 1 <sup>st</sup> 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 $\geq 14$ days after 2 <sup>nd</sup> dose.	Critical	Retrospective cohort study of HCW at a single hospital in New Delhi, India; 4276 participants; sample sequenced for VOC Delta
88	<a href="#">Seppala</a>	BNT162b2 (74%) or ChAdOx1 (22%) or mRNA-1273 (10%) showed VE 84.4% (95% CI, 81.8 to 86.5) against infection $\geq 7$ days after 2 <sup>nd</sup> 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 $\geq 7$ days after 2 <sup>nd</sup> dose (VOC Delta).	Serious	Population cohort in Norway; 4,204,859 participants; sequenced for VOC Alpha and VOC Delta
89	<a href="#">Polinski</a>	Ad26.COVS2 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	<a href="#">Chemaitelly (2)</a>	BNT162b2 or mRNA-1273 showed VE 46.6% (95% CI, 0.0 to 73.7) against infection $\geq 14$ days after 2 <sup>nd</sup> dose, VE 66.0% (95% CI, 21.3 to 85.3) $\geq 42$ days after 2 <sup>nd</sup> dose, and VE 73.9% (95% CI, 33 to 98.9) $\geq 56$ days after 2 <sup>nd</sup> dose (VOC Alpha and Beta).  BNT162b2 or mRNA-1273 showed VE 72.3% (95% CI, 0.0 to 90.9) against severe,	Serious	Retrospective cohort of immunosuppressed kidney transplant recipients in Qatar; 782 participants; time and setting for VOC Alpha and VOC Beta.

		critical, or fatal disease $\geq 14$ days after 2 <sup>nd</sup> dose, VE 85% (95% CI, 35.7 to 96.5) $\geq 42$ days after 2 <sup>nd</sup> dose, and VE 83.8% (95% CI, 31.3 to 96.2) $\geq 56$ days after 2 <sup>nd</sup> dose (VOC Alpha and Beta).		
91	<a href="#">Hu</a>	Inactivated vaccines (CoronaVac) showed VE 89% (95% CI, 55 to 98) against severe, critical, or fatal disease $\geq 14$ days after 2 <sup>nd</sup> dose (VOC Delta).	Serious	Outbreak report of hospitalized cases in China; 476 participants; PCR population for VOC Delta.
92	<a href="#">Andrews</a>	BNT162b2 showed VE 62.7% (61.7 to 63.8) against symptomatic infection 1 week after 2 <sup>nd</sup> dose and VE 47.3% (45.0 to 49.6) 20+ weeks after 2 <sup>nd</sup> dose (VOC Delta).  ChAdOx1 showed VE 92.4% (92.1 to 92.7) against symptomatic infection 1 week after 2 <sup>nd</sup> dose and VE 69.7% (68.7 to 70.5) 20+ weeks after 2 <sup>nd</sup> dose (VOC Delta).  mRNA-1273 showed VE 95.2% (94.4 to 95.9) against symptomatic infection 1 week after 2 <sup>nd</sup> dose and VE 90.3% (67.2 to 97.1) 10 to 14 weeks after 2 <sup>nd</sup> 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	<a href="#">Patalon</a>	BNT162b2 showed marginal VE 3% (95% CI, -5 to 10) against infection 0 to 6 days after 3 <sup>rd</sup> dose and marginal VE 84.0% (95% CI, 79 to 88) 14 to 20 days after 3 <sup>rd</sup> dose compared to 2 doses.	Moderate	Test-negative study of <b>fully vaccinated</b> in Israel comparing 2 doses of vaccine versus 3 doses of vaccine; 182,076 participants; time and setting for VOC Delta
94	<a href="#">Kissling</a>	BNT162b2 showed VE 87% (95% CI, 74 to 93) against symptomatic infection 14 days after 2 <sup>nd</sup> 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	<a href="#">McKeigue</a>	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 2 <sup>nd</sup> 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 $\geq 14$ days after 2 <sup>nd</sup> 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	<a href="#">Kertes</a>	BNT162b2 showed OR 1.61 (95% CI, 1.45 to 1.79) for infection comparing <u>fully vaccinated Jan to Feb</u> vs <u>fully vaccinated Mar to May</u> .	Serious	Data-linkage study of people <b>fully vaccinated</b> 6 months previously in Israel; 1,423,098 participants; time and setting for VOC Alpha to VOC Delta
97	<a href="#">Barlow</a>	BNT162b2 or mRNA-1273 showed VE 74% (95% CI, 65 to 82) against infection $\geq$ 14 days after 2 <sup>nd</sup> dose.  Ad26.COVS showed VE 51% (95% CI, -2 to 76) against infection $\geq$ 14 days after 2 <sup>nd</sup> dose.	Serious	Test-negative study in Oregon; 1000 participants; time and setting for VOC Delta
98	<a href="#">Chemaitelly</a> (3)	BNT162b2 showed VE 65.8% (95% CI, 63.8 to 67.7) against infection 5 to 9 weeks after 2 <sup>nd</sup> dose; VE 29.7% (95% CI, 21.7 to 36.9) against infection 15 to 19 weeks after 2 <sup>nd</sup> dose and VE 0% (95% CI, 0 to 0) against infection 20 to 24 weeks after 2 <sup>nd</sup> dose.  BNT162b2 showed VE 94.2% (95% CI, 91.0 to 96.5) against hospitalization or death 5 to 9 weeks after 2 <sup>nd</sup> dose; VE 86.4% (95% CI, 69.9 to 94.8) against hospitalization or death 15 to 19 weeks after 2 <sup>nd</sup> dose and VE 95.3% (95% CI, 70.5 to 99.9) against hospitalization or death 20 to 24 weeks after 2 <sup>nd</sup> dose.	Serious	Test-negative study in Qatar; 1,472,761 participants; time and setting for VOC Beta to VOC Delta
99	<a href="#">Thompson</a> (3)	BNT162b2 <b>or mRNA-1273</b> showed VE 90% (95% CI, 86 to 93) against ICU admission $\geq$ 14 days after 2 <sup>nd</sup> dose.  BNT162b2 showed VE 92% (95% CI, 88 to 94) against hospitalization at 28 to 41 days after 2 <sup>nd</sup> dose and VE 86% (95% CI, 74 to 93) $\geq$ 112 days after 2 <sup>nd</sup> dose.	Serious	Test-negative study of adults $\geq$ 50 years in the USA; 76,463 participants; time and setting for VOC Alpha ( <b>results over varying time since vaccination reported</b> )
100	<a href="#">Bar-On</a>	BNT162b2 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 $\geq$ 12 days after 3 <sup>rd</sup> dose compared to 2 doses.	Serious	Data-linkage study of <b>fully vaccinated (age&gt;60) comparing 2 doses of vaccine versus 3 doses</b> in Israel; 1,137,804 participants; time and setting for VOC Delta
101	<a href="#">Bruxvoort</a> (2)	mRNA-1273 showed VE 98.4% (95% CI, 96.9 to 99.1) against infection $\geq$ 14 days after 2 <sup>nd</sup> dose (VOC Alpha).  mRNA-1273 showed VE 95.5% (95% CI, 90.9 to 97.8) against infection $\geq$ 14 days after 2 <sup>nd</sup> dose (VOC Gamma).	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) ( <b>results</b> )



		<p>mRNA-1273 showed VE 86.7% (95% CI, 84.3 to 88.7) against infection <math>\geq 14</math> days after 2<sup>nd</sup> dose (VOC Delta).</p> <p>mRNA-1273 showed VE 94.1% (95% CI, 90.5 to 96.3) against infection 14 to 60 days after 2<sup>nd</sup> dose (VOC Delta).</p> <p>mRNA-1273 showed VE 80.0% (95% CI, 70.2 to 86.6) against infection 151 to 180 days after 2<sup>nd</sup> dose (VOC Delta).</p>		over varying time since vaccination reported)
102	<a href="#">Tande (2)</a>	<p>BNT162b2 or mRNA-1273 showed VE 91% (95% CI, 72 to 98) against infection <math>\geq 14</math> days after 2<sup>nd</sup> dose (January to March – VOC Alpha).</p> <p>BNT162b2 or mRNA-1273 showed VE 63% (95% CI, 44 to 76) against infection <math>\geq 14</math> days after 2<sup>nd</sup> dose (June to August – VOC Delta).</p>	Serious	Point prevalence screening study in Mayo Clinic, USA; 46,008 participants; time and setting for VOC Alpha to VOC Delta
103	<a href="#">Young-Xu (2)</a>	<p>Two doses of BNT162b2 reduced risk of infection by HR 66% (95% CI, 22 to 86) compared to <b>previously infected</b> adults age 65+ (June to August VOC Delta).</p> <p>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 <b>previously infected</b> adults age 65+ (June to August VOC Delta).</p>	Moderate	Retrospective cohort study of <b>previously infected adults</b> followed by Veterans Affairs in USA; 47,102 participants; time and setting for VOC Delta
104	<a href="#">de Gier (1)</a>	<p>Fully vaccinated index to unvaccinated (hh contact) showed <b>VET</b> 73% (95% CI: 65 to 79).</p> <p>BNT162b (case) showed <b>VET</b> 70% (95% CI, 61 to 77) when fully vaccinated.</p> <p>mRNA-1273 (case) showed <b>VET</b> 88% (95% CI, 50 to 97) when fully vaccinated.</p> <p>ChAdOx1 (case) showed <b>VET</b> 58% (95% CI, -12 to 84) when fully vaccinated.</p> <p>Ad26.COV2.S (case) showed <b>VET</b> 58% (95% CI, -12 to 84) when fully vaccinated.</p> <p>BNT162b showed VE 65% (95% CI, 60 to 70) when hh contact was fully vaccinated.</p> <p>mRNA-1273 showed VE 91% (95% CI, 79 to 97) when hh contact was fully vaccinated.</p>	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)

		<p>ChAdOx1 showed VE 87% (95% CI, 77 to 93) when hh contact was fully vaccinated.</p> <p>Ad26.COVS2.S showed VE 12% (95% CI, -71 to 54) when hh contact was fully vaccinated.</p>		
105	<a href="#">de Gier (2)</a>	<p>Fully vaccinated index to unvaccinated (hh contact) showed <b>VET</b> 63% (95% CI: 46 to 75).</p> <p>BNT162b (&gt;50%) or mRNA-1273 or ChAdOx1 or Ad26.COVS2.S (case) showed <b>VET</b> 40% (95% CI, 20 to 54) when both case and contacts are fully vaccinated.</p>	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	<a href="#">Manley</a>	<p>mRNA-1273 (50%) or BNT162b (48%) or Ad26.COVS2.S (2%) showed OR of 8.89 (95% CI, 5.92 to 13.34) for unvaccinated vs fully vaccinated against infection (VOC Alpha)</p> <p>mRNA-1273 (50%) or BNT162b (48%) or Ad26.COVS2.S (2%) showed OR of 2.27 (95% CI, 1.72 to 3.00) for unvaccinated vs fully vaccinated against infection (VOC Delta)</p>	Serious	Retrospective cohort of maintenance dialysis patients in USA; 15,251 participants; time and setting for VOC Alpha to VOC Delta
107	<a href="#">Eyre</a>	<p>BNT162b2 (cases) showed <b>VET</b> 82% (95% CI, 71 to 88) against transmission after 2<sup>nd</sup> dose. (VOC Alpha)</p> <p>ChAdOx1 (cases) showed <b>VET</b> 63% (95% CI, 37 to 78) against transmission after 2<sup>nd</sup> dose. (VOC Alpha)</p> <p>BNT162b2 (contacts) showed VE 94% (95% CI, 90 to 96) against infection after 2<sup>nd</sup> dose. (VOC Alpha)</p> <p>ChAdOx1 (contacts) showed VE 71% (95% CI, 51 to 83) against infection after 2<sup>nd</sup> dose. (VOC Alpha)</p> <p>BNT162b2 (cases) showed <b>VET</b> 65% (95% CI, 52 to 74) against transmission after 2<sup>nd</sup> dose. (VOC Delta)</p> <p>ChAdOx1 (cases) showed <b>VET</b> 36% (95% CI, 28 to 43) against transmission after 2<sup>nd</sup> dose. (VOC Delta)</p>	Serious	Retrospective cohort of contacts in England; 99,597 cases and 151,821 contacts; S-gene proxy for VOC Alpha and VOC Delta

		<p>BNT162b2 (contacts) showed VE 90% (95% CI, 87 to 92) against infection after 2<sup>nd</sup> dose. (VOC Delta)</p> <p>ChAdOx1 (contacts) showed VE 72% (95% CI, 68 to 75) against infection after 2<sup>nd</sup> dose. (VOC Delta).</p>		
108	<a href="#">Martinez-Baz (2)</a>	<p>BNT162b2 (contacts) showed VE 71% (95% CI, 61 to 78) against infection after 2<sup>nd</sup> dose (VOC Alpha)</p> <p>mRNA-1273 (contacts) showed VE 86% (95% CI, 56 to 95) against infection after 2<sup>nd</sup> dose (VOC Alpha)</p> <p>ChAdOx1 (contacts) showed VE 38% (95% CI, -42 to 73) against infection after 2<sup>nd</sup> dose (VOC Alpha)</p> <p>BNT162b2 (contacts) showed VE 67% (95% CI, 59 to 74) against infection after 2<sup>nd</sup> dose (VOC Delta)</p> <p>mRNA-1273 (contacts) showed VE 77% (95% CI, 64 to 85) against infection after 2<sup>nd</sup> dose (VOC Delta)</p> <p>ChAdOx1 (contacts) showed VE 55% (95% CI, 39 to 67) against infection after 2<sup>nd</sup> dose (VOC Delta)</p> <p>ChAdOx1 <b>followed by</b> BNT162b2 (contacts) showed VE 86% (95% CI, 45 to 97) against infection (VOC Delta)</p>	Serious	Prospective cohort of close contacts in Spain; 12,263 cases and 30,240 contacts; sequenced for VOC Alpha to VOC Delta ( <b>includes heterologous vaccines</b> )
109	<a href="#">Cohn</a>	<p>BNT162b2 showed VE 49% (95% CI, 47 to 52) against infection at least 15 days after last dose (August: VOC Delta)</p> <p>mRNA-1273 showed VE 64% (95% CI, 62 to 66) against infection at least 15 days after last dose (August: VOC Delta)</p> <p>Ad26.COVS showed VE 3% (95% CI, -0.1 to 12) against infection at least 15 days after last dose (August: VOC Delta)</p>	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	<a href="#">Rosenberg (2)</a>	<p>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)</p>	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

		<p>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)</p> <p>Ad26.COVS2.S showed VE 70.2% (95% CI, 67.4 to 73.0) against infection at least 15 days after last dose (August: VOC Delta; age 18-49)</p> <p>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+)</p> <p>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+)</p> <p>Ad26.COVS2.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+)</p>		vaccination (results not reported here)
111	<a href="#">Robles-Fontan</a>	<p>BNT162b2 showed VE 56% (95% CI, 53 to 59) against infection at least 15 days after last dose (October: VOC Delta)</p> <p>mRNA-1273 showed VE 71% (95% CI, 68 to 74) against infection at least 15 days after last dose (October: VOC Delta)</p> <p>Ad26.COVS2.S showed VE 27% (95% CI, 17 to 37) against infection at least 15 days after last dose (October: VOC Delta)</p>	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	<a href="#">Glatman-Freedman (2)</a>	BNT162b2 showed VE 91.5% (95% CI, 88.2 to 93.9) against infection at least 8 days after 2 <sup>nd</sup> 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	<a href="#">Chin</a>	mRNA-1273 showed VE 56.6% (95% CI, 42 to 67.5) against infection at least 14 days after 2 <sup>nd</sup> dose.	Serious	Outbreak report from a prison in California; 827 participants; sample sequenced for VOC Delta
114	<a href="#">Nordstrum</a>	BNT162b2 showed VE 47% (95% CI, -39 to 55) against symptomatic infection 121 to 180 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

		<p>mRNA-1273 showed VE 71% (95% CI, 56 to 81) against symptomatic infection 121 to 180 days after second dose.</p> <p>ChAdOx1 showed VE -19% (95% CI, --97 to 28) against symptomatic infection &gt;120 days after second dose.</p> <p>ChAdOx1 followed by mRNA vaccine showed VE 66% (95% CI, 41 to 80) against symptomatic infection &gt;120 days after second dose.</p> <p>BNT162b2 or mRNA-1273 or ChAdOx1 showed VE 42% (95% CI, -35 to 75) against severe disease (hospitalization or death) &gt;180 days after second dose</p>		heterologous vaccines) (results over varying time since vaccination reported)
116	<a href="#">Ranzani (2)</a>	ChAdOx1 showed VE 42.4% (95% CI, 24.6 to 56.0) against symptomatic infection 21 days after 1 <sup>st</sup> dose.	Low	Test-negative study in Brazil; 9,197 tests; time and setting for VOC Gamma to Delta
117	<a href="#">Ranzani(3)</a>	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	<a href="#">Chadeau-Hyam</a>	<p>BNT162b2 showed VE 71.3% (95% CI, 56.6 to 81.0) against infection unreported number of days after 2<sup>nd</sup> dose (Round 13 and Round 14)</p> <p>mRNA-1273 showed VE 75.1% (95% CI, 22.7 to 92.0) against infection unreported number of days after 2<sup>nd</sup> dose (Round 13 and Round 14)</p> <p>ChAdOx1 showed VE 44.8% (95% CI, 22.5 to 60.7) against infection unreported number of days after 2<sup>nd</sup> dose (Round 13 and Round 14)</p>	Serious	Surveillance study in England; 87,966 participants who consented to data-linkage for vaccine status; sequenced for VOC Delta
119	<a href="#">Sheikh (2)</a>	<p>BNT162b2 showed VE 90% (95% CI, 86 to 94) against death at least 14 days after 2<sup>nd</sup> dose (confirmed VOC Delta)</p> <p>ChAdOx1 showed VE 91% (95% CI, 83 to 94) against death at least 14 days after 2<sup>nd</sup> dose (confirmed VOC Delta)</p>	Serious	Retrospective cohort in Scotland; 114,706 participants; sequenced for VOC Delta
120	<a href="#">Reis</a>	BNT162b2 showed VE 59% (95% CI, 52 to 65) against infection 14 to 20 days after 1 <sup>st</sup> dose (age 12 to 18)	Moderate	Case-control study in Israel; 94,354 vaccinated matched to 94,354 unvaccinated

		BNT162b2 showed VE 90% (95% CI, 88 to 92) against infection 7 to 21 days after 2 <sup>nd</sup> dose (age 12 to 18)		adolescents age 12 to 18; time and setting for VOC Delta
121	<a href="#">Nordstrom (2)</a>	<p>BNT162b2 showed VE 78% (95% CI, 78 to 79) against symptomatic infection at least 14 days after 2<sup>nd</sup> dose.</p> <p>mRNA-1273 showed VE 87% (95% CI, 84 to 88) against symptomatic infection at least 14 days after 2<sup>nd</sup> dose.</p> <p>ChAdOx1 showed VE 50% (95% CI, 41 to 58) against symptomatic infection at least 14 days after 2<sup>nd</sup> dose.</p> <p>ChAdOx1 followed by BNT162b2 showed VE 67% (95% CI, 59 to 73) against symptomatic infection at least 14 days after 2<sup>nd</sup> dose.</p> <p>ChAdOx1 followed by mRNA-1273 showed VE 79% (95% CI, 62 to 88) against symptomatic infection at least 14 days after 2<sup>nd</sup> dose.</p>	Serious	Retrospective cohort study in Sweden; 721,787 participants; time and setting for VOC Delta <b>(includes heterologous vaccines)</b>
122	<a href="#">Skowronski (2)</a>	<p>BNT162b2 showed VE 79% (95% CI, 73 to 84) against infection at least 21 days after 1<sup>st</sup> dose (VOC Gamma)</p> <p>mRNA-1273 showed VE 85% (95% CI, 71 to 92) against infection at least 21 days after 1<sup>st</sup> dose (VOC Gamma)</p> <p>ChAdOx1 showed VE 60% (95% CI, 48 to 69) against infection at least 21 days after 1<sup>st</sup> dose (VOC Gamma)</p>	Serious	Test-negative study in Canada; 68,074 participants; sample sequenced for VOC Alpha, Gamma and Delta (only VOC Gamma reported here)
123	<a href="#">Skowronski (3)</a>	<p><b>Delta</b></p> <p>BNT162b2 showed VE 89% (95% CI, 88 to 89) against infection at least 14 days after 2<sup>nd</sup> dose (Quebec- VOC Delta)</p> <p>mRNA-1273 showed VE 91% (95% CI, 90 to 92) against infection at least 14 days after 2<sup>nd</sup> dose (Quebec- VOC Delta)</p> <p>ChAdOx1 showed VE 73% (95% CI, 69 to 78) against infection at least 14 days after 2<sup>nd</sup> dose (Quebec- VOC Delta)</p> <p>ChAdOx1 <b>followed by</b> mRNA vaccine showed VE 88% (95% CI, 85 to 89) against</p>	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) <b>(includes heterologous vaccines) (results over varying time since vaccination reported)</b>

	<p>infection at least 14 days after 2<sup>nd</sup> dose (Quebec- VOC Delta)</p> <p><u>Gamma</u></p> <p>BNT162b2 showed VE 93% (95% CI, 89 to 95) against infection at least 14 days after 2<sup>nd</sup> dose (BC- VOC Gamma)</p> <p>mRNA-1273 showed VE 95% (95% CI, 85 to 99) against infection at least 14 days after 2<sup>nd</sup> dose (BC- VOC Gamma)</p> <p>ChAdOx1 showed VE 90% (95% CI, 61 to 98) against infection at least 14 days after 2<sup>nd</sup> dose (BC- VOC Gamma)</p> <p>ChAdOx1 followed by mRNA vaccine showed VE 96% (95% CI, 70 to 99) against infection at least 14 days after 2<sup>nd</sup> dose (BC- VOC Gamma)</p> <p><u>Time since vaccination (Delta)</u></p> <p>BNT162b2 showed VE 85% (95% CI, 84 to 86) against infection at 4 months after 2<sup>nd</sup> dose (Quebec – VOC Delta)</p> <p>mRNA-1273 showed VE 88% (95% CI, 86 to 90) against infection at 4 months after 2<sup>nd</sup> dose (Quebec – VOC Delta)</p> <p>ChAdOx1 showed VE 72% (95% CI, 66 to 77) against infection at 4 months after 2<sup>nd</sup> dose (Quebec – VOC Delta)</p> <p>ChAdOx1 followed by mRNA vaccine showed VE 86% (95% CI, 81 to 89) against infection at least 14 days after 2<sup>nd</sup> dose (Quebec – VOC Delta)</p> <p><u>Time since vaccination and interval between doses (VOC Alpha to Delta)</u></p> <p>BNT162b2 showed VE 92% (95% CI, 91 to 93) at 14 to 27 days after 2<sup>nd</sup> dose (interval 7+ weeks) and VE 90% (95% CI, 88 to 91) at 4 months after 2<sup>nd</sup> dose (interval 7+ weeks) (Quebec)</p> <p>mRNA-1273 showed VE 92% (95% CI, 90 to 94) at 14 to 27 days after 2<sup>nd</sup> dose (interval 7+ weeks) and VE 91% (95% CI,</p>		
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		<p>87 to 94) at 112+ days after 2<sup>nd</sup> dose (interval 7+ weeks) (Quebec)</p> <p>ChAdOx1 showed VE 85% (95% CI, 60 to 94) at 14 to 27 days after 2<sup>nd</sup> dose (interval 7+ weeks) and VE 72% (95% CI, 66 to 77) at 84 days after 2<sup>nd</sup> dose (interval 7+ weeks) (Quebec)</p>		
124	<a href="#">Lin</a>	<p>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 2 months after 2<sup>nd</sup> dose.</p> <p>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 7 months after 2<sup>nd</sup> dose)</p> <p>mRNA-1273 showed VE 96% (95.6 to 96.4) against symptomatic infection and VE 96% (95% CI, 91.9 to 98) against death at 2 months after 2<sup>nd</sup> dose.</p> <p>mRNA-1273 showed VE 81.9% (95% CI, 81 to 82.7) against symptomatic infection and VE 96% (95% CI, 91.9 to 98) against death at 7 months after 2<sup>nd</sup> dose)</p> <p>Ad26.COVS2.S showed VE 79% (77.1 to 80.7) against symptomatic infection at 1 month and VE 64.3% (95% CI, 62.3 to 66.1) at 5 months after 2<sup>nd</sup> dose.</p> <p>Ad26.COVS2.S showed VE 89.4% (95% CI, 52.3 to 97.6) against death at 3 months after 2<sup>nd</sup> dose)</p>	Serious	Data-linkage study in North Carolina; 10,600,823 participants; time and setting for VOC Alpha to Delta (results over varying time since vaccination reported)
125	<a href="#">Barda</a>	BNT162b2 showed VE 92% (82 to 97) against severe disease and VE 81% (95% CI, 59 to 97) against death at least 5 months after 2 <sup>nd</sup> dose.	Serious	Data-linkage study of fully vaccinated participants in Israel; 728,321 participants in each group; time and setting for VOC Delta
126	<a href="#">Andrews(2)</a>	<p>BNT162b2 showed VE 94% (95% CI, 93.4 to 94.6) against symptomatic infection at least 14 days after 3<sup>rd</sup> dose in age&gt;50 (compared to unvaccinated)</p> <p>ChAdOx1 showed VE 93.1% (95% CI, 91.7 to 94.3) against symptomatic infection at least 14 days after 3<sup>rd</sup> dose in age&gt;50 (compared to unvaccinated)</p>	Moderate	Test-negative study of fully vaccinated participants (>140 days since 2 <sup>nd</sup> dose) over age 50 in England; 271,747 participants; sequencing for VOC Delta



127	<a href="#">Starrfelt (2)</a>	<p>BNT162b2 showed VE 69.7% (95% CI, 68.6 to 70.8) against infection at least 7 days after 2<sup>nd</sup> dose (VOC Alpha to Delta)</p> <p>mRNA-1273 showed VE 78.2% (95% CI, 76.7 to 79.6) against infection at least 7 days after 2<sup>nd</sup> dose (VOC Alpha to Delta)</p> <p>ChAdOx1 showed VE 43.4% (95% CI, 4.4 to 66.5) against infection at least 7 days after 2<sup>nd</sup> dose (VOC Alpha to Delta)</p> <p><b>Heterologous mRNA</b> showed VE 84.7% (95% CI, 83.1 to 86.1) against infection at least 7 days after 2<sup>nd</sup> dose (VOC Alpha to Delta)</p> <p>ChAdOx1 <b>followed by</b> mRNA showed VE 60.7% (95% CI, 57.5 to 63.6) against infection at least 7 days after 2<sup>nd</sup> dose (VOC Alpha to Delta)</p>	Moderate	Population cohort study in Norway; 4,293,544 participants; time and setting for VOC Alpha to VOC Delta <b>(includes heterologous vaccines)</b>
128	<a href="#">Preio-Alhambra</a>	ChAdOx1 <b>followed by</b> BNT162b2 showed HR 0.61 (95% CI, 0.52 to 0.71) against infection vs ChAdOx1 (homologous) – unreported number of days after 2 <sup>nd</sup> dose	Serious	Retrospective cohort study in Spain; 28,650 participants aged 19 to 59 years; time and setting for VOC Delta <b>(compared heterologous vaccines with homologous vaccines)</b>
129	<a href="#">Ng</a>	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	<a href="#">Desai</a>	BBV152 showed VE 50% (95% CI, 33 to 62) against symptomatic infection at least 14 days after 2 <sup>nd</sup> dose	Serious	Test-negative study of HCW in India; 1,068 matched pairs; time and setting for VOC Delta
131	<a href="#">Thiruvengadam(pub)</a>	<p>ChAdOx1 showed VE 46.2% (95% CI, 31.6 to 57.7) against infection at least 21 days after 1<sup>st</sup> dose.</p> <p>ChAdOx1 showed VE 63.1% (95% CI, 51.5 to 72.1) against infection at least 14 days after 2<sup>nd</sup> dose.</p>	Serious	Test-negative study in India; 5,143 participants; sequencing for VOC Delta

132	<a href="#">Sharma</a>	<p>BNT162b2 showed VE 45.7% (95% CI, 37.9 to 52.5) against infection median of 30 days after 3<sup>rd</sup> dose <b>compared to 2 doses</b> (given at least 180 days previously)</p> <p>mRNA-1273 showed VE 46.6% (95% CI, 36.4 to 55.3) against infection median of 16 days after 3<sup>rd</sup> dose <b>compared to 2 doses</b> (given at least 180 days previously).</p>	Serious	Case-control study of <b>fully vaccinated comparing 2 doses of vaccine versus 3 doses</b> in veterans in USA; 129,130 pairs; time and setting for VOC Delta
133	<a href="#">Cohn (2)</a>	<p>BNT162b2 showed VE 43% (95% CI, 42 to 45) against infection after unclear number of days after 2<sup>nd</sup> dose (September 2021)</p> <p>mRNA-1273 showed VE 58% (95% CI, 57 to 59) after unclear number of days against infection after 2<sup>nd</sup> dose (September 2021)</p> <p>Ad26.COV2.S showed VE 13% (95% CI, 9 to 17) against infection after unclear number of days after dose (September 2021)</p>	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	<a href="#">Arbel</a>	BNT162b2 showed VE 90% (95% CI, 86 to 93) against death after 3 <sup>rd</sup> dose <b>compared to 2 doses</b> (given at least 5 months previously)	Moderate	Data-linkage study of <b>fully vaccinated (&gt;50 years) comparing 2 doses of vaccine versus 3 doses</b> in Israel; 843,208 participants; time and setting for VOC Delta
135	<a href="#">Bar-On (2)</a>	<p>BNT162b2 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 3<sup>rd</sup> dose compared to 2 doses (given at least 5 months previously) (age&gt;60).</p> <p>BNT162b2 showed adjusted rate ratio of 9.0 (95% CI, 8.4 to 9.7) against infection at least 12 days after 3<sup>rd</sup> dose compared to 2 doses (given at least 5 months previously) (age 30-39).</p>	Serious	Data-linkage study of <b>fully vaccinated (&gt;16 years) comparing 2 doses of vaccine versus 3 doses</b> 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)

## Section 2: excluded studies

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

<a href="#">Cavanaugh</a>	Delayed exclusion – VOI not VOC
<a href="#">Charles Pon Ruban</a>	Vaccine effectiveness not reported
<a href="#">Charmet</a>	Serious risk of bias
<a href="#">Chau</a>	Vaccine effectiveness not reported
<a href="#">Clemens</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Clifford</a>	Modelling study
<a href="#">Cohen</a>	Vaccine effectiveness not reported
<a href="#">Cohen(2)</a>	Vaccine effectiveness not reported
<a href="#">Corchado-Garcia</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Dash</a>	Critical risk of bias
<a href="#">de Gier Brechje</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Dolzhikova</a>	Critical risk of bias
<a href="#">Domi</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">El Sahly</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Ella</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Elliot</a>	Delayed exclusion – critical risk of bias
<a href="#">El-Sahly</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Falsey</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Fang</a>	Modelling study
<a href="#">Farinholt</a>	Vaccine effectiveness not reported
<a href="#">Fisher</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Frenck</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Furer</a>	Delayed exclusion – critical risk of bias
<a href="#">Gardner</a>	Modelling study
<a href="#">Geisen</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Ghosh</a>	Delayed exclusion – critical risk of bias
<a href="#">Gils</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Gorgels</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Grannis</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Gray</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Griffin</a>	Vaccine effectiveness not reported
<a href="#">Guijarro</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Gupta</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Gupta</a>	Vaccine effectiveness not reported
<a href="#">Haas (2)</a>	Modelling study
<a href="#">Hacisuleyman</a>	Critical risk of bias
<a href="#">Harris</a>	Modelling study
<a href="#">Herlihy</a>	Delayed exclusion – critical risk of bias
<a href="#">Hetemaki</a>	Vaccine effectiveness not reported
<a href="#">Hitchings(2)</a>	Delayed exclusion – critical risk of bias
<a href="#">Hollinghurst</a>	Serious risk of bias
<a href="#">Hyams</a>	Delayed exclusion - Clinical outcomes of interest for this LES not reported

<a href="#">Iliaki</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Iliaki</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Ismail</a>	Delayed exclusion - Clinical outcomes of interest for this LES not reported
<a href="#">Jacobson</a>	Critical risk of bias
<a href="#">John</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Jones</a>	Critical risk of bias
<a href="#">Kaabi</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Kale</a>	Delayed exclusion – critical risk of bias
<a href="#">Kaur</a>	Delayed exclusion – critical risk of bias
<a href="#">Keegan</a>	Critical risk of bias
<a href="#">Kemp</a>	Modelling study
<a href="#">Khan</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Khawaja</a>	Critical risk of bias
<a href="#">Kislaya</a>	Vaccine effectiveness not reported
<a href="#">Kojima</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Kustin</a>	Delayed exclusion - only included infected population
<a href="#">Lamprini</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Lan</a>	Did not report results according to vaccine type
<a href="#">Lefèvre</a>	Critical risk of bias
<a href="#">Li</a>	Phase 1 trial
<a href="#">Li (2)</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Li (3)</a>	Delayed exclusion – critical risk of bias
<a href="#">Ling</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Linsenmeyer</a>	Vaccine effectiveness not reported
<a href="#">Liu</a>	Vaccine effectiveness not reported
<a href="#">Loconsole</a>	Vaccine effectiveness not reported
<a href="#">Luo</a>	Vaccine effectiveness not reported
<a href="#">Marco</a>	Delayed exclusion – critical risk of bias
<a href="#">Mattar</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Maurya</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Mazgatos</a>	Critical risk of bias
<a href="#">McEvoy</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">McKeigue(2)</a>	Vaccine brand not reported
<a href="#">Menni</a>	Serious risk of bias
<a href="#">Mizrahi</a>	Modelling study
<a href="#">Monge</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Mor</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Moustsen-Helms</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Munitz</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Munro</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Musser</a>	Vaccine effectiveness not reported
<a href="#">Mutnal</a>	Vaccine effectiveness not reported
<a href="#">Nanduri</a>	Critical risk of bias

<a href="#">Oduwole</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Olmedo</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Olson</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Open-SAFELY</a>	Vaccine effectiveness not reported
<a href="#">Palacios</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Paredes</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Paris</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Pattni</a>	Modelling study
<a href="#">Pawlowski</a>	Critical risk of bias
<a href="#">Perry</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Pilishvili</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Piltch-Loeb</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Polinski</a>	Delayed exclusion – critical risk of bias
<a href="#">Poukka</a>	Critical risk of bias
<a href="#">Pulliam</a>	Modelling study
<a href="#">Raches Ella</a>	Phase 1 trial
<a href="#">Rana</a>	Critical risk of bias
<a href="#">Regev-Yochay</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Riemersma</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Riley</a>	Critical risk of bias
<a href="#">Rivelli</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Rosero-Bixby</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Rovida</a>	Critical risk of bias
<a href="#">Rudolph</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Salmeron Rios</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Sansone</a>	Critical risk of bias
<a href="#">Satwik</a>	Delayed exclusion – critical risk of bias
<a href="#">Scobie</a>	Delayed exclusion – critical risk of bias
<a href="#">Self</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Sharma</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Shimabukuro</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Shrotri</a>	Delayed exclusion – critical risk of bias
<a href="#">Simon</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Starrfelt</a>	Serious risk of bias
<a href="#">Suri</a>	Vaccine effectiveness not reported
<a href="#">Swift</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Tande</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Tanriover</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Taquet</a>	Modelling study
<a href="#">Tenforde</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Tenforde (2)</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Thangaraj</a>	Critical risk of bias

<a href="#">Thiruvengadam</a>	Critical risk of bias
<a href="#">Thompson (1)</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Thompson (2)</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Uschner</a>	Critical risk of bias
<a href="#">Vahidy</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Vasileiou</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Veneti</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Victor</a>	Critical risk of bias
<a href="#">Volkov</a>	Modelling study
<a href="#">Voysey</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Waldhorn</a>	Serious risk of bias
<a href="#">Wickert</a>	Critical risk of bias
<a href="#">Wijtvliet</a>	Clinical outcomes of interest for this LES not reported
<a href="#">Williams (2)</a>	Critical risk of bias
<a href="#">Young-Xu</a>	Prevalence of variants unknown and suspected to be <50%
<a href="#">Zacay</a>	Delayed exclusion – critical risk of bias
<a href="#">Zhong</a>	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

**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)

**VET:** vaccine effectiveness against transmission

**VOC:** variant of concern

**VOI:** variant of interest



### Appendix 3: Data-extraction template

<b>Vaccine product</b>	
Source	First author of study
Link	DOI or Pubmed ID
Date published	in format YYYY/MM/DD or preprint
Country	
Funding	public or industry
<b>Study details</b>	
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 %
<b>Outcomes</b>	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
<b>Transmission</b>	infection rates in unvaccinated contacts of vaccinated individuals
<b>Critical appraisal</b>	See Appendix 5

#### **Appendix 4: Process for assigning Variant of Concern to studies**

A Variant of Concern is considered to be the dominant ( $\geq 50\%$ ) 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
<b>Study design</b>  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  <u>Examples and typical judgement:</u> <ul style="list-style-type: none"> <li>• test-negative design with a clearly defined symptomatic study population (low)</li> <li>• test-negative design (mixed or unclear study population) or case-control or cohort design or data-linkage with no concerns (moderate)</li> <li>• 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)</li> </ul>
<b>Method for confirming vaccination</b>  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  <u>Examples and typical judgement:</u>

	<ul style="list-style-type: none"> <li>• database linkage study (low)</li> <li>• Questionnaire with confirmation by an additional method (e.g. registry) of at least a subset of study population (moderate)</li> <li>• Questionnaire without confirmation by an additional method (serious)</li> <li>• Estimating vaccination status based on surveillance data alone (critical)</li> </ul>
<b>Databases used for retrieval of COVID test results, participant prognostic factors, and clinical outcomes</b>  <b>ROBINS-I: Bias in classification of interventions</b>	<p>Databases developed for collecting data on COVID are less prone to bias due to missing information and misclassification</p> <p><u>Examples and typical judgement:</u></p> <ul style="list-style-type: none"> <li>• database for non-COVID purpose but with individual level data (moderate)</li> <li>• database for non-COVID purpose without individual level data (serious)</li> <li>• no or unclear description of database type (critical)</li> </ul>
<b>Assignment of infection start date</b>  <b>ROBINS-I: Bias in classification of interventions</b>	<p>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</p> <p><u>Examples and typical judgement:</u></p> <ul style="list-style-type: none"> <li>• using a PCR positive test that was part of an ongoing standardized monitoring system (e.g., within a health network) (low)</li> <li>• using sample date without interview or documented confirmation of symptoms <math>\leq 10</math> days (relevant for symptomatic disease only) (serious)</li> </ul>
<b>Verification of symptoms</b>  <b>ROBINS-I: Bias in classification of interventions</b>	<p>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</p> <p><u>Examples and typical judgement:</u></p> <ul style="list-style-type: none"> <li>• using sample date without patient report/ documented confirmation of symptoms <math>\leq 10</math> days (relevant for symptomatic disease only) (serious)</li> <li>• if symptomatic COVID is not an outcome (no information)</li> </ul>

<p><b>Accounting for non-immune period (first 14 days after first vaccine dose)</b></p> <p>ROBINS-I: Bias due to confounding</p>	<p>Reported absence of vaccine effect during non-immune period reduces risk of residual confounding bias</p> <p><u>Example/common case:</u></p> <ul style="list-style-type: none"> <li>• presence of an effect during non-immune period or result not reported (moderate)</li> <li>• unclear that non-immune period was considered (serious)</li> </ul>
<p><b>Inclusion of participants with prior COVID infection</b></p> <p>ROBINS-I: Bias due to confounding</p>	<p>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</p> <p><u>Examples and typical judgement:</u></p> <ul style="list-style-type: none"> <li>• inclusion of prior infection status as a covariate in the models (moderate)</li> <li>• previously infected not excluded or analyzed separately (serious)</li> </ul>
<p><b>Accounting for calendar time</b></p> <p>ROBINS-I: Bias due to confounding (time-varying confounding)</p>	<p>Accounting for calendar time reduces bias due to differences in vaccine accessibility and risk of exposure over time</p> <p><u>Examples and typical judgement:</u></p> <ul style="list-style-type: none"> <li>• use of time-varying statistics without explicit mention of adjustment for calendar time (moderate)</li> <li>• not taken into account but short-time frame (e.g. <math>\leq 2</math> months) (serious)</li> <li>• not taken into account and time frame <math>&gt; 2</math> months (critical)</li> </ul>
<p><b>Adjustment for prognostic factors</b></p> <p>ROBINS-I: Bias due to confounding</p>	<p>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</p> <p><u>Examples and typical judgement:</u></p> <ul style="list-style-type: none"> <li>• no or insufficient adjustment for occupation (or number of tests as a surrogate for exposure risk) - exception age <math>&gt; 65</math> or LTCH resident (moderate)</li> <li>• no or insufficient adjustment for socioeconomic factors (or neighborhood or income as a surrogate), race, ethnicity (serious)</li> <li>• no or insufficient adjustment for age (any study population) or chronic medical conditions (LTC)(critical)</li> </ul>
<p><b>Testing frequency</b></p> <p>ROBINS-I: Bias in measurement of outcomes</p>	<p>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)</p>

	<p><u>Examples and typical judgement:</u></p> <ul style="list-style-type: none"><li>• no systematic screening but consistent methods for detection in one group vs. the other, e.g., within health networks (moderate)</li><li>• screening performed for a subset of both study groups (serious)</li><li>• screening performed routinely in one study group but not in the other (critical)</li></ul>
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## 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%.

