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

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

# COVID-19 Living Evidence Synthesis #6

(Version 23: 03 November 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, 245 studies were appraised and 89 used to complete this summary. The reasons for excluding the remaining 156 studies are reported in the second section of Appendix 2.

Eleven 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 03 November 2021 (highlighted in yellow). The new studies included results for VOC Alpha[1] [B.1.1.7] (4), and VOC Delta [B.1.617.2] (10).

**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.

[1] As of August 9, inclusion of Alpha studies may be temporarily delayed to permit resource allocation to Delta.

**Pfizer/Comirnaty [BNT162b2]**

We have moderate certainty evidence that 2 doses of BNT162b2 prevented infection (range of mean estimates: 70 to 97%), prevented severe disease (range of mean estimates: 92 to 98%), prevented death (range of mean estimates: 91 to 98%), and prevented transmission of VOC **Alpha** to close contacts (range of mean estimates: 70 to 82%).

We have moderate certainty evidence that 2 doses of BNT162b2 prevented symptomatic infection from VOC **Beta** (range of mean estimates: 84 to 88%).

We have low certainty evidence that 2 doses of BNT162b2 prevented infection from VOC **Delta** (range of mean estimates: 42 to 80%); moderate certainty evidence it prevented symptomatic infection from VOC Delta (range of mean estimates: 62 to 94%); and low certainty evidence it prevented severe, critical, or fatal disease from VOC Delta (range of mean estimates: 93 to 98%). We have low certainty evidence that 2 doses of BNT162b prevented transmission of VOC **Delta** to close contacts (65% [95% CI, 52 to 74] 1 Obs).

We have low certainty evidence that BNT162b2 prevented symptomatic disease from VOC **Gamma** (range of mean estimates: 84 to 88% - 2 reports from the same study population).

**Moderna/Spikevax [mRNA-1273]**

We have moderate certainty evidence that 2 doses of mRNA-1273 prevented infection from VOC **Alpha** (range of mean estimates: 86 to 100%) and low certainty evidence it prevented infection from VOC **Beta** (96.4% [95% CI, 92 to 99] – 1 Obs). 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). We have low certainty evidence that 2 doses of mRNA-1273 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 mRNA-1273 prevented infection from VOC **Delta** (range of mean estimates: 63 to 87%) and low certainty evidence that it prevented severe, critical, or fatal disease (range of mean estimate: 93 to 100%).

We have low certainty evidence that 2 doses of mRNA-1273 prevented symptomatic infection from VOC **Delta** (90.3% [95% CI, 67.2 to 97.1] – 1 Obs).

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

**AstraZeneca/Vaxzevria [ChAdOx1]**

We have moderate certainty evidence that 2 doses of ChAdOx1 prevented infection from VOC **Alpha** (range of mean estimates: 62 to 79%) and low certainty evidence it prevented transmission of VOC **Alpha** (range of mean estimates: 63 to 65%).

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

We have low certainty evidence that 2 doses of ChAdOx1 prevented infection from VOC **Delta** (range of mean estimates: 60 to 67%) and moderate certainty evidence it prevented symptomatic

infection from VOC Delta (range of mean estimates: 61 to 67%). We have low certainty evidence that 2 doses of ChAdOx1 provided limited protection from transmission of VOC **Delta** (36% [95% CI, 28 to 43] – 1 Obs).

We have low certainty evidence one dose of ChAdOx1 provided limited protection against symptomatic infection against VOC **Gamma** (48% [95% CI, 28 to 63] – 1 Obs). ***** combined with Alpha

**Other vaccines**

We have low certainty evidence that **Johnson & Johnson** [**AD26.COV2.S]** prevented transmission of VOC **Alpha** (77% [95% CI, 6 to 94] – 1 Obs).

We have moderate evidence that AD26.COV2.S prevented severe disease from VOC **Beta** (81.7% [95% CI, 46.2 to 95.4] - 1 RCT). We have low certainty evidence that AD26.COV2.S prevented infection from VOC **Delta** (range of mean estimates: 3 to 71%).

We have moderate certainty evidence that 2 doses of **Novavax [NVX-Co2373]** prevented symptomatic infection from VOC **Alpha** (86.3% [95% CI, 71.3 to 93.5] - 1 RCT) and moderate certainty evidence that it prevented symptomatic infection from VOC **Beta** (43% [95% CI, -9.8 to 70.4] - 1 RCT).

We low certainty evidence that 2 doses of **Sinovac** [**CoronaVac]** prevented symptomatic infection due to VOC **Delta** (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 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.**

**Combinations of vaccines**

We have low certainty evidence that 1 dose of **AstraZeneca [ChAdOx1]** followed by 1 dose of **Pfizer [BNT162b2]** or **Moderna [mRNA-1273]** prevented infection by VOC **Alpha** (88% [95% CI, 83 to 92] – 1 Obs) and low certainty evidence that it prevented transmission of VOC **Delta** (86% [95% CI, 45 to 97} – 1 Obs).

**Table 1: 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 ≥ 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 moderate to high quality RCTs or pooling of observational studies with low risk of bias and with consistent findings

**Moderate certainty evidence** = single RCT of moderate to high quality or ≥ one observational study with low to moderate risk of bias and with at least partially consistent findings

**Low certainty evidence** = single RCT of low quality or single observational study of any quality or multiple low or moderate observational studies with inconsistent findings

| Outcome (and vaccine) | Vaccine Effectiveness (2 doses unless otherwise stated) for each combination of vaccine, variant, and outcome | | | |
|---|---|---|---|---|
| | **Alpha** | **Beta** | **Gamma** | **Delta** |
| **Any Infection** | | | | |
| Pfizer | 70 to 97% | | | 42 to 80% |
| Moderna | 86 to 100% | 96% | | 63 to 87% |
| AstraZeneca | 62 to 79% | | | 60 to 67% |
| Johnson & Johnson | | | | 3 to 71% |
| Novavax | | | | |
| CoronaVac | | | 66% | |
| AZ/PF or MOD | 88% | | | |
| **Symptomatic Infection** (reported when data on "any infection" is limited) | | | | |
| Pfizer | | 84 to 88% | 84 to 88% | 62 to 94% |
| Moderna | | | 88% | 90% |
| AstraZeneca | | 10%** | 48%* | 61 to 67% |
| Johnson & Johnson | | | | |
| Novavax | 86% | 43%** | | |
| CoronaVac | | | | 59% |
| **Transmission** | | | | |
| Pfizer | 70 to 82% | | | 65% |
| Moderna | 88% | | | |
| AstraZeneca | 63 to 65% | | | 36% |
| Johnson & Johnson | 77% | | | |
| Novavax | | | | |
| CoronaVac | | | | |
| AZ/PF or MOD | | | | 86% |
| **Severe Disease (may include death for some studies)** | | | | |
| Pfizer | 92 to 98% | | | 93 to 98% |
| Moderna | 96% | 96% | | 93 to 100% |
| AstraZeneca | | | | |
| Johnson & Johnson | | 82%* | | |
| Novavax | | | | |
| CoronaVac | | | | 89% |

| | | | | |
|---|---|---|---|---|
| Sinopharm | | | | |
| Sputnik V | | | | |
| **Outcome (and vaccine)** | **Vaccine Effectiveness (2 doses unless otherwise stated) for each combination of vaccine, variant, and outcome** | | | |
| | **Alpha** | **Beta** | **Gamma** | **Delta** |
| **Death** | | | | |
| Pfizer | 91 to 98% | | | |
| Moderna | | | | |
| AstraZeneca | | | | |
| 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; MOD, Moderna; PF, Pfizer

**Table 2: Key findings about vaccine effectiveness**

| Vaccine | Effectiveness | Findings |
|---|---|---|
| **Pfizer/ BioNTech**<br><br>**Comirnaty**<br><br>**[BNT162b2]** | From COVID-NMA | Compared to placebo, vaccination with BNT162b2 reduces the incidence of symptomatic cases of COVID-19 and probably reduces severe and critical disease substantially, although there remains uncertainty about the effect on mortality; it may increase the incidence of severe adverse events. Review of RCTs (AMSTAR 10/11); *last search date 2021-09-03;* GRADE evidence profile updated on *2021-09-17.*<br>[BNT162b2 to complete vaccination scheme started with Astra Zeneca vaccine] Synthesis pending. Review of RCTs (AMSTAR 8/9); *last search date 2021-09-17.*<br><br>[BNT162b2 to complete vaccination scheme started with Astra Zeneca at 28 days vs two doses Astra Zeneca separated by 28 days] Compared to vaccination with Astra Zeneca vaccine, having a second dose of BNT16b2 after a first dose of Astra Zeneca may not increase the risk of any adverse event, while the incidence of serious adverse events is uncertain. Review of RCTs (AMSTAR 10/11); *last search date 2021-09-17;* GRADE evidence profile updated on 2021-07-19 |
| | By variant of concern | |
| | • Alpha | BNT162b2 provided protection against VOC Alpha for the following outcomes 14 days after 1st dose:<br>• 46 to 78% from infection (RME)<br>BNT162b2 provided protection against VOC Alpha for the following outcomes 42 to 49 days after at least one dose:<br>• 93% (95% CI, 89 to 96) from death<br>BNT162b2 provided protection against VOC Alpha for the following outcomes at least 7 days after 2nd dose:<br>• 70 to 97% from infection (RME)<br>• 87% (95% CI, 74 to 93) from symptomatic infection<br>• 92 to 98% from severe disease (RME)<br>• 90% (86 to 93) from ICU admission<br>• 91 to 98% from death (RME)<br>(23 Obs) [1][2][8][9][10][15][21][22][23][28][31][34][36][41][43][53][60][74][79][88][94][99][102]; *last update 2021-11-03* |
| | • Alpha, VE over time | BNT162b2 provided protection against symptomatic infection by VOC Alpha when the 2nd dose was given the following number of days after 1st dose:<br>• 77% (95% CI, 66 to 85) at 19-29 days (age 65 to 79)<br>• 86% (95% CI, 70 to 94) at 85+ days (age 65 to 79)<br>BNT162b2 provided protection against hospitalization by VOC Alpha for the following number of days after the 2nd dose:<br>• 92% (95% CI, 88 to 94) at 28 to 41 days<br>• 86% (95% CI, 74 to 93) at ≥112 days<br>(2 Obs) [79][99]; *last update 2021-10-06* |
| | • Beta | BNT162b2 provided protection against VOC Beta for the following outcomes at least 14 days after 1st dose: |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | | • 75% (95% CI, 70 to 79) from infection<br>• 100% (95% CI, 74 to 100) from severe, critical or fatal disease<br>BNT162b2 provided protection against VOC Beta (or Gamma) for the following outcomes 35-41 days after 1st dose:<br>• 43% (95% CI, 22 to 59) from symptomatic infection<br>BNT162b2 provided protection against VOC Beta (or Gamma) for the following outcome 7 days after 2nd dose:<br>• 84 to 88% from symptomatic infection (RME)<br>• 95% (95% CI, 81 to 99) from hospitalization<br>(2 Obs – 3 refs)[23][36][47]; *last update 2021-07-14* |
| | • Beta to Delta | BNT162b2 provided protection against infection by VOC Beta to VOC Delta for the following number of days after the 2nd dose:<br>• 65.8% (95% CI, 63.8 to 67.7) at 5 to 9 weeks<br>• 29.7% (95% CI, 21.7 to 36.9) at 15 to 19 weeks<br>• 0% (95% CI, 0 to 0) 20 to 24 weeks<br>BNT162b2 provided protection against hospitalization or death by VOC Beta to VOC Delta for the following number of days after the 2nd dose:<br>• 94.2% (95% CI, 91.0 to 96.5) at 5 to 9 weeks<br>• 86.4% (95% CI, 69.9 to 94.8) at 15 to 19 weeks<br>• 95.3% (95% CI, 70.5 to 99.9) at 20 to 24 weeks<br>(1 Obs) [98]; *last update* 2021-10-06 |
| | • Alpha to Delta | BNT162b2 or mRNA-1273 provided protection against VOC Alpha to Delta for the following outcomes ≥ 14 days after 2nd dose:<br>• 92% (95% CI, 85 to 96) from severe disease in people with no risk conditions<br>• 72% (95% CI, 51 to 84) from severe disease with very high risk conditions<br>BNT162b2 showed OR 1.61 (95% CI, 1.45 to 1.79) for infection comparing fully vaccinated Jan to Feb (VOC_Alpha) vs fully vaccinated Mar to May (VOC Delta).<br>(2 Obs) [95][96]; *last update* 2021-10-06 |
| | • Delta | BNT162b2 provided protection against VOC Delta for the following outcome at least 14 to 21 days after 1st dose:<br>• 30 to 65% from infection (RME)<br>• 33 to 47.5% from symptomatic infection (RME)<br>• 87 to 94% from hospitalization (RME)<br>• 100% (95% CI, not reported) against severe, critical or fatal disease<br>BNT162b2 provided protection against VOC Delta for the following outcome at least 7 days after 2nd dose:<br>• 42 to 80% from infection (RME)<br>• 62 to 93.7% from symptomatic infection (RME)<br>• 96% (95% CI, 86 to 99) from hospitalization<br>• 93 to 98% from severe, critical, or fatal disease (RME)<br>(18 Obs)<br>[29][38][42][47][57][63][64][71][74][76][84][88][92][97][102][109][110][111]; *last update 2021-11-03* |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | • Delta, VE over time | BNT162b2 showed a higher risk of infection by VOC Delta in participants fully vaccinated (≥14 days after 2nd dose) longer than or equal to 146 days ago vs fully vaccinated less than 146 days ago [OR 2.06 (95% CI, 1.69 to 2.51)]<br>(1 Obs) [69]; *last update 2021-08-25*<br>BNT162b2 provided protection against infection by VOC Delta for the following number of days after 2nd dose:<br>• 93% (95% CI, 85 to 87) at 7 to 30 days<br>• 53% (95% CI, 39 to 65) at ≥127 days<br>BNT162b2 provided protection against infection by VOC Delta 5 months after 2nd dose:<br>• 50% (95% CI, 45 to 55) - age 16 to 39<br>• 58% (95% CI, 54 to 62) - age 40 to 59<br>• 57% (95% CI, 52 to 62) - age 60+<br><br>BNT162b2 provided protection against symptomatic infection by VOC Delta for the following number of days after 2nd dose:<br>• 62.7% (95% CI, 61.7 to 63.8) – at 1 week<br>• 47.3% (95% CI, 45 to 49.6) – at 20+ weeks<br>• 47% (95% CI, 39 to 55) 121 to 180 days (up to 25 weeks)<br><br>BNT162b2 provided protection against severe, critical, or fatal disease by VOC Delta 5 months after 2nd dose:<br>• 94% (95% CI, 87 to 97) - age 40 to 59<br>• 86% (95% CI, 82 to 90) - age 60+<br>(4 Obs) [76][84][92][114]; *last update 2021-11-03* |
| | • Delta, prior infection | BNT162b2 (2 doses) provided protection against VOC Delta for the following outcomes:<br>• OR 13.06 (95% CI, 8.08 to 21.11) against infection compared to previously infected (unvaccinated)<br>• OR 27.02 (95% CI, 12.7 to 57.5) against symptomatic infection compared to previously infected (unvaccinated)<br>(1 Obs) [73]; *last update 2021-09-02* |
| | • Delta, 3 doses | BNT162b2 (3 doses) provided protection against infection by VOC Delta compared to 2 doses:<br>• 3% (95% CI, -5 to 10) – at 0 to 6 days after 3rd dose<br>• 84.0% (95% CI, 79 to 88) – at 14 to 20 days after 3rd dose<br>(1 Obs) [93]; *last update 2021-09-22*<br>BNT162b2 (3 doses) provided protection against the following outcomes by VOC Delta compared to 2 doses:<br>• Rate ratio 11.3 (95% CI, 10.4 to 12.3) from infection at least 12 days after 3rd dose<br>• Rate ratio 19.5 (95% CI, 12.9 to 29.5) from severe illness at least 12 days after 3rd dose<br>(1 Obs) [100]; *last update 2021-10-20* |
| | • Gamma | BNT162b2 provided protection against VOC Gamma (or Beta) for the following outcomes 35-41 days after 1st dose:<br>• 43% (95% CI, 22 to 59) from symptomatic infection |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | | BNT162b2 provided protection against VOC Gamma (or Beta) for the following outcome 7 days after 2nd dose:<br>• 84 to 88% from symptomatic infection (RME)<br>• 95% (95% CI, 81 to 99) from hospitalization<br>(1 Obs – 2 refs)[23][47]; *last update 2021-07-14* |
| | • Epsilon | BNT162b2 provided protection against VOC Epsilon for the following outcome 15 days after 1st dose:<br>• 58.9% (95% CI, −9.7 to 84.5) from infection<br>BNT162b2 provided protection against VOC Epsilon for the following outcome 15 days after 2nddose:<br>• 85.7% (67.2 to 93.9) from infection<br>(2 Obs) [8][31]; *last update 2021-06-08* |
| | By special population | |
| | • HCW, Alpha | BNT162b2 provided protection against VOC Alpha for the following outcomes 14 to 21 days after 1st dose:<br>• 64 to 84% from infection (RME)<br>BNT162b2 provided protection against VOC Alpha for the following outcomes at least 7 days after 2nd dose:<br>• 90 to 96% from infection (RME)<br>BNT162b2 provided protection against VOC Alpha for the following outcome 7 days after 2nd dose:<br>• 86% (95% CI, 69 to 93) from asymptomatic infection [25]<br>BNT162b2 provided protection against infection by VOC Alpha for the following number of days after 2nd dose:<br>• 85% (95% CI, 68 to 93) at 14 to 119 days<br>• 73% (95% CI, 49 to 86) ≥150 days<br>(5 Obs)[11][45][46][56][81]; *last update 2021-10-20* |
| | • Over 65 years, requiring support at home, Alpha | BNT162b2 provided protection against VOC Alpha for the following outcomes 7 days after 2nd dose:<br>• 86% (95% CI, 78 to 91) from infection<br>• 97% (95% CI, 88 to 99) from death<br>(1 Obs)[32]; *last update 2021-07-07* |
| | • Over 70 years, Alpha | BNT162b2 provided protection against VOC Alpha for the following outcomes at least 21 days after 1st dose:<br>• 41 to 67% from infection (RME)<br>BNT162b2 provided protection against VOC Alpha for the following outcomes at least 7 days after 2nd dose:<br>• 75 to 90% from infection (RME)<br>(3 Obs)[28][35][51]; *last update 2021-10-06* |
| | • Over 80 years, Alpha | BNT162b2 provided protection against VOC Alpha for the following outcomes at least 14 days after 1st dose:<br>• 42 to 55.2% from infection (RME)<br>BNT162b2 provided protection against VOC Alpha for the following outcomes >14 days after 2nd dose:<br>• 94% (95% CI, 73 to 99) from symptomatic infection<br>• 81% (95% CI, 74 to 87) from death<br>BNT162b2 provided protection against death by VOC Alpha for the following number of days after 2nd dose: |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | | • 86% (95% CI, 68 to 93) at 14 to 41 days<br>• 74% (95% CI, 60 to 83) ≥98 days<br>(3 Obs)[55][79][83]; *last update 2021-10-20* |
| | • LTC, Alpha | BNT162b2 provided protection against VOC Alpha for the following outcomes 7 days after 2nd dose:<br>• 53% (95% CI, 29 to 69) from infection<br>• 89% (95% CI, 81 to 93) from death<br>(1 Obs)[32]; *last update 2021-10-06* |
| | • Pregnant, Alpha | BNT162b2 provided protection against VOC Alpha for the following outcomes at least 28 days after 1st dose:<br>• 78% (95% CI, 57 to 89) from infection<br>BNT162b2 provided protection against VOC Alpha for the following outcomes 7 to 56 days after 2nd dose:<br>• 86.1% (95% CI, 82.4 to 89.1) from infection<br>• 89% (95% CI, 43 to 100) from hospitalization<br>(2 Obs) [52][54]; *last update 2021-07-28* |
| | • Previously infected, Alpha or Beta | BNT162b2 (2 doses) after prior infection provided protection against VOC Alpha (or Beta) for the following outcomes:<br>• 85% (95% CI, 80 to 89) against re-infection compared to BNT162b2 without prior infection<br>(1 Obs) [72]; *last update 2021-08-25* |
| | • Immunosuppressed, renal transplant, Alpha or Beta | BNT162b2 or mRNA-1273 provided protection against infection by VOC Alpha or Beta at the following number of days after 2nd dose:<br>• 46.6% (95% CI, 0.0 to 73.7) ≥14 days<br>• 66.0% (95% CI, 21.3 to 85.3) ≥42 days<br>• 73.9% (95% CI, 33 to 98.9) ≥56 days<br>BNT162b2 or mRNA-1273 provided protection against severe, critical, or fatal disease by VOC Alpha or Beta at the following number of days after 2nd dose:<br>• 72.3% (95% CI, 0.0 to 90.9) ≥14 days<br>• 85% (95% CI, 35.7 to 96.5) ≥42 days<br>• 83.8% (95% CI, 31.3 to 96.2) ≥56 days<br>(1 Obs) [90]; *last update 2021-09-22* |
| | • HCW, Beta or Gamma | BNT162b2 provided protection against VOC Beta or Gamma for the following outcomes 14 to 42 days after 1st dose:<br>• 37.2% (95% CI, 16.6 to 52.7) from infection<br>BNT162b2 provided protection against VOC Beta or Gamma for the following outcome 7 days after 2nd dose:<br>• 79.2% (95% CI, 64.6 to 87.8) from infection<br>(1 Obs)[27]; *last update 2021-06-01* |
| | • HCW, Delta | BNT162b2 provided protection against VOC Delta for the following outcomes ≥ 14 days after 2nd dose:<br>• 66% (95% CI, 26 to 84)<br>(1 Obs) [81]; *last update 2021-09-22* |
| | • Previously infected, Delta (65+) | BNT162b2 (2 doses) provided protection against VOC Delta for the following outcomes compared to natural immunity after prior infection:<br>• 66% (95% CI, 22 to 86) from infection |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | | (1 Obs) [103]; *last update 2021-10-20* |
| | • Maintenance hemodialysis, Alpha and Delta | BNT162b or mRNA-1273 showed OR of 8.89 (95% CI, 5.92 to 13.34) for unvaccinated vs fully vaccinated against infection (VOC Alpha)<br><br>BNT162b or mRNA-1273 showed OR of 2.27 (95% CI, 1.72 to 3.00) for unvaccinated vs fully vaccinated against infection (VOC Delta)<br>(1 Obs) [106]; *last update 2021-11-03* |
| | • Adolescents, Delta | BNT162b2 provided protection against VOC Delta for the following outcomes at least 8 days after 2nd dose:<br>• 91.5% (95% CI, 88.2 to 93.9) against infection<br>(1 Obs) [112]; *last update 2021-11-03* |
| | • Over 70 years, Gamma | BNT162b2 provided protection against VOC Gamma for the following outcomes ≥ 21 days after 1st dose:<br>• 61% (95% CI, 45 to 72) from infection<br>(1 Obs)[35]; *last update 2021-07-07* |
| | • LTC, Gamma (residents) | BNT162b2 (or mRNA-1273) provided protection against VOC Gamma 14 days after 2nd dose:<br>• 52.5% (95% CI, 26.9 to 69.1) against infection<br>• 78.6% (95% CI, 47.9 to 91.2) against severe disease<br>(1 Obs) [61]; *last update 2021-08-11* |
| | Transmission | |
| | • Household or close contacts of index case, Alpha | BNT162b2 reduced transmission of VOC Alpha from a vaccinated index case (14 to 21 days after 1st dose) to household contacts compared to households of unvaccinated index cases:<br>• 30 to 49% from infection (RME)<br>BNT162b2 reduced transmission of VOC Alpha from a vaccinated HCW (10 weeks after 1st dose) to household spouse:<br>• 42.9% (95% CI, 22.3 to 58.1) from infection<br><br>Fully vaccinated index cases showed VET for household contacts (unclear status):<br>• 70 to 82% from infection (RME)<br>Fully vaccinated hh contacts showed VE (unclear status of index):<br>• 65 to 94% from infection (RME)<br><br>(8 Obs) [6][14][33][40][48][104][107][108]; *last update 2021-11-03* |
| | • Vaccinated HCW vs unvaccinated community, Beta and Gamma | BNT162b2 reduced transmission of VOC Beta or Gamma from vaccinated HCW compared to unvaccinated community ≥14 days after 1st dose:<br>• 54.7% (95% CI, 44.8 to 62.9) from infection<br>BNT162b2 reduced transmission of VOC Beta or Gamma from vaccinated HCW compared to unvaccinated community ≥7 days after 2nd dose:<br>• 84.8% (95% CI, 75.2 to 90.7) from infection<br>(1 Obs) [27]; *last update 2021-06-08* |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | • Household or close contacts of index case, Delta | Fully vaccinated index cases by BNT162b showed VET for unvaccinated (hh contact):<br>• 63% (95% CI: 46 to 75) from infection<br><br>Fully vaccinated index cases by BNT162b showed VET for fully vaccinated household contacts:<br>• 40% (95% CI, 20 to 54) from infection<br><br>Fully vaccinated index cases by BNT162b showed VET for hh contacts (unclear status):<br>• 65% (95% CI, 52 to 74) from infection<br>Fully vaccinated hh contacts by BNT162b showed VE (unclear status of index case):<br>• 67 to 90% from infection (RME)<br>(3 Obs) [105][107][108]; *last update 2021-11-03* |
| **Moderna**<br><br>**Spikevax**<br><br>**[mRNA-1723]** | From COVID-NMA | Compared to placebo, vaccination with mRNA-1723 probably reduces the incidence of symptomatic cases of COVID-19 substantially and it may reduce severe disease, while the incidence of serious adverse events is probably not increased. Review of RCTs (AMSTAR 10/11); *last search date 2021-09-17;* GRADE evidence profile updated on 2021-01-25 |
| | By variant of concern | |
| | • Alpha | mRNA-1273 provided protection against VOC Alpha for the following outcomes 14-41 days after 1st dose:<br>• 58.9 to 88.1% from infection (RME)<br>• 60 to 61% from symptomatic infection (RME)<br>• 81.6% (95% CI, 71.0 to 88.8) from severe, critical, or fatal disease (combined with Beta)<br>mRNA-1273 provided protection against VOC Alpha for the following outcomes at least 7 days after 2nd dose:<br>• 86 to 100% from infection (RME)<br>• 90 to 95.7% from symptomatic infection (RME)<br>• 95.7% (95% CI, 73.4 to 99.9) from severe, critical, or fatal disease (combined with Beta)<br>(10 Obs – 11 refs) [8][23][31][34][37][47][50][60][74][101][102]; *last update 2021-10-20* |
| | • Beta | mRNA-1273 provided protection against VOC Beta for the following outcomes 14 days after 1st dose:<br>• 61.3% (95% CI, 56.5 to 65.5) from infection<br>• 77% (95% CI, 63 to 86) from symptomatic infection<br>• 89% (95% CI, 73 to 95) from hospitalization<br>• 81.6% (95% CI, 71.0 to 88.8) from severe, critical, or fatal disease (combined with Alpha)<br>mRNA-1273 provided protection against VOC Beta for the following outcomes 35-41 days after 1st dose:<br>• 43% (95 CI, 22 to 59) from symptomatic infection<br>mRNA-1273 provided protection against VOC Beta for the following outcome 7 days after 2nd dose: |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | | • 96.4% (95% CI, 91.9 to 98.7) from infection<br>• 88% (95% CI, 61 to 96) from symptomatic infection<br>• 95.7% (95% CI, 73.4 to 99.9) from severe, critical, or fatal disease (combined with Alpha)<br>(2 Obs – 3 refs) [23][47][50]; *last update 2021-07-14* |
| | • Alpha to Delta | mRNA-1273 or BNT162b2 provided protection against VOC Alpha to Delta for the following outcomes ≥ 14 days after 2nd dose:<br>• 92% (95% CI, 85 to 96) from severe disease in people with no risk conditions<br>• 72% (95% CI, 51 to 84) from severe disease with very high risk conditions<br>(1 Obs) [95]; *last update* 2021-10-06 |
| | • Delta | mRNA-1273 provided protection against VOC Delta for the following outcomes at least 14 days after 1st dose:<br>• 75 to 86.7% from infection (RME)<br>• 72% (95% CI, 57 to 82) from symptomatic infection<br>• 96% (95% CI, 72 to 99) from hospitalization<br>• 93 to 100% from severe, critical, or fatal disease (RME)<br>mRNA-1273 provided protection against VOC Delta for the following outcomes 14 days after 2nd dose:<br>• 63 to 86.7% from infection (RME)<br>• 93 to 100% from severe, critical, or fatal disease(RME)<br>(12 Obs) [47][57][63][64][71][74][97][101][102][109][110][111]; *last update 2021-11-03* |
| | • Delta, VE over time | mRNA-1273 provided protection against infection by VOC Delta the following number of days after 2nd dose:<br>• 94.1% (95% CI, 90.5 to 96.3) – at 14 to 60 days<br>• 80.0% (95% CI, 70.2 to 86.6) – at 151 to 180 days<br>(1 Obs) [101]; *last update 2021-10-20*<br><br>mRNA-1273 provided protection against symptomatic infection by VOC Delta the following number of days after 2nd dose:<br>• 95.2% (95% CI, 94.4 to 95.9) – at 1 week<br>• 90.3% (95% CI, 67.2 to 97.1) – at 10 to 14 weeks<br>• 71% (95% CI, 56 to 81) – at 121 to 180 days (up to 25 weeks)<br>(2 Obs) [92][114]; *last update 2021-11-03* |
| | • Gamma | mRNA-1273 provided protection against VOC Gamma for the following outcomes 14 days after 1st dose:<br>• 77% (95% CI, 63 to 86) from symptomatic infection<br>• 89% (95% CI, 73 to 95) from hospitalization<br>mRNA-1273 provided protection against VOC Gamma (or Beta) for the following outcomes 35-41 days after 1st dose:<br>• 43% (95% CI, 22 to 59) from symptomatic infection<br>mRNA-1273 provided protection against VOC Gamma (or Beta) for the following outcome 7 days after 2nd dose:<br>• 88% (95% CI, 61 to 96) from symptomatic infection<br>(1 Obs – 2 refs) [23][47]; *last update 2021-07-07* |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | • Epsilon | mRNA-1273 provided protection against VOC Epsilon for the following outcome 15 days after 1st dose:<br>• 58.9% (95% CI, −9.7 to 84.5) from infection<br>mRNA-1273 provided protection against VOC Epsilon for the following outcome 15 days after 2nddose:<br>• 85.7% (67.2 to 93.9) from infection<br>(2 Obs) [8][31]; *last update 2021-06-08* |
| | Special population | |
| | • Over 70 years, Alpha | mRNA-1273 provided protection against VOC Alpha for the following outcome ≥21 days after 1st dose:<br>• 67% (95% CI, 57 to 75) from infection<br>(1 Obs) [35]; *last update 2021-06-23* |
| | • Previously infected, Alpha or Beta | mRNA-1273 (2 doses) after prior infection did not offer additional protection against VOC Alpha (or Beta) for the following outcomes:<br>• 15% (95% CI, -105 to 66) against re-infection compared to mRNA-1273 without prior infection<br>(1 Obs) [72]; *last update 2021-08-25* |
| | • Previously infected, Delta (65+) | mRNA-1273 (2 doses) provided protection against VOC Delta for the following outcomes compared to natural immunity after prior infection:<br>• 68% (95% CI, 30 to 86) from infection<br>• 30% (-11 to 1) from death<br>(1 Obs) [103]; *last update 2021-10-20* |
| | • Immunosuppressed, renal transplant, Alpha or Beta | mRNA-1273 or BNT162b2 provided protection against infection by VOC Alpha or Beta at the following number of days after 2nd dose:<br>• 46.6% (95% CI, 0.0 to 73.7) ≥14 days<br>• 66.0% (95% CI, 21.3 to 85.3) ≥42 days<br>• 73.9% (95% CI, 33 to 98.9) ≥56 days<br>mRNA-1273 or BNT162b2 provided protection against severe, critical, or fatal disease by VOC Alpha or Beta at the following number of days after 2nd dose:<br>• 72.3% (95% CI, 0.0 to 90.9) ≥14 days<br>• 85% (95% CI, 35.7 to 96.5) ≥42 days<br>• 83.8% (95% CI, 31.3 to 96.2) ≥56 days<br>(1 Obs) [90]; *last update 2021-09-22* |
| | • Maintenance hemodialysis, Alpha and Delta | 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)<br><br>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)<br>(1 Obs) [106]; *last update 2021-11-03* |
| | • Over 70 years, Gamma | mRNA-1273 provided protection against VOC Gamma for the following outcome ≥21 days after 1st dose:<br>• 61% (95% CI, 45 to 72) from infection<br>(1 Obs) [35]; *last update 2021-06-23* |
| | • LTC, Gamma (residents) | mRNA-1273 (or BNT162b2) provided protection against VOC Gamma for the following outcomes 14 days after 2nd dose: |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | | • 52.5% (95% CI, 26.9 to 69.1) against infection<br>• 78.6% (95% CI, 47.9 to 91.2) against severe disease<br>(1 Obs) [61]; *last update 2021-08-11* |
| | • Prison, Delta | mRNA-1273 provided protection against VOC Delta for the following outcomes at least 14 days after 2nd dose:<br>57% (95% CI, 42 to 67.5)<br>(1 Obs) [113]; *last update 2021-11-03* |
| | Transmission | |
| | • Household or close contacts of index case, Alpha | mRNA-1273 reduced transmission of VOC Alpha from a vaccinated HCW (10 weeks after 1st dose) to household spouse:<br>• 42.9% (95% CI, 22.3 to 58.1) from infection<br><br>Fully vaccinated index cases by mRNA-1273 showed VET for household contacts (unclear status):<br>• 88% (95% CI, 50 to 97) from infection<br>Fully vaccinated hh contacts by mRNA-1273 showed VE (unclear status of index):<br>• 86 to 91% from infection (RME)<br>(3 Obs)[33][104][108]; *last update 2021-11-03* |
| | • Household or close contacts of index case, Delta | Fully vaccinated hh contacts by mRNA-1273 showed VE (unclear status of index):<br>• 77% (95% CI, 64 to 85) from infection<br>(1 Obs) [108]; *last update 2021-11-03* |
| **AstraZeneca [ChAd0x1]**<br><br>**Vaxzevria**<br><br>**Serum Institute of India [Covishield]** | From COVID-NMA | Compared to vaccinating with MedACWY (meningitis vaccine), vaccination with ChAd0x1 probably reduces the cases of symptomatic COVID-19 infection. The effects on severe or critical disease and mortality are uncertain. (*)Review of RCTs (AMSTAR 10/11); *last search date 2021-09-17;* GRADE evidence profile updated on 2021-01-25 . (*) Rare cases of serious blood clots associated with a low platelet count known as vaccine-induced thrombotic thrombocytopenia (VITT or VIPIT) have been reported. The frequency of VITT varies by age and country.<br><br>[AstraZeneca to complete vaccination scheme started with BNT16b2 at 28 days vs two doses of BNT16b2 separated by 28 days] Compared to vaccination with BNT16b2 vaccine, having a second dose of AstraZeneca after a first dose of BNT 16b2 may increase the risk of any adverse event, while the incidence of serious adverse events is uncertain. Review of RCTs (AMSTAR 10/11); *last search date 2021-09-17;* GRADE evidence profile updated on 2021-07-19 |
| | By variant of concern | |
| | • Alpha | ChAdOx1 provided protection against VOC Alpha for the following outcome 14 days after 1st dose:<br>• 64% (95% CI, 60 to 68) from symptomatic infection<br>• 85% (95% CI, 81 to 88) from hospitalization<br>ChAdOx1nCoV-19 provided protection against VOC Alpha for the following outcome 21 to 28 days after 1st dose:<br>• 44 to 74% from infection (RME) |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | | ChAdOx1provided protection against confirmed VOC Alpha for the following outcome at least 14 days after 2 doses:<br>• 62 to 79% from infection (RME)<br>(1 RCT, moderate quality; 5 Obs)[9][10][5][47][70][71][]; *last update 2021-08-25* |
| | • Alpha, VE over time | ChAdOx1 provided protection against symptomatic infection by VOC Alpha when the 2nd dose was given the following number of days after 1st dose:<br>• 66% (95% CI, 47 to 77) at 19-29 days (age 65 to 79)<br>• 73% (95% CI, 56 to 83) at 85+ days (age 65 to 79)<br>(1 Obs) [79]; *last update 2021-09-22* |
| | • Beta | ChAdOx1 provided protection against VOC Beta for the following outcome 14 days after 1st dose:<br>• 48% (95% CI, 28 to 63) from symptomatic infection<br>• 83% (95% CI, 66 to 92) from hospitalization<br>ChAdOx1 provided protection against VOC Beta for the following outcome after 2 doses:<br>• 10.4% (95% CI, -76.8 to 54.8) from mild to moderate disease<br>(1 RCT, moderate quality; 1 Obs) [4][47]; *last update 2021-07-07* |
| | • Alpha to Delta | ChAdOx1 provided protection against VOC Alpha to Delta for the following outcomes ≥ 14 days after 2nd dose:<br>• 94% (95% CI, 90 to 96) from severe disease in people with no risk conditions<br>• 63% (95% CI, 46 to 75) from severe disease with very high risk conditions<br>(1 Obs) [95]; *last update* 2021-10-06 |
| | • Delta | ChAdOx1 provided protection against VOC Delta for the following outcome at least 21 days after 1st dose:<br>• 18 to 46% from infection (RME)<br>• 33 to 58% from symptomatic infection (RME)<br>• 71% (95% CI, 51 to 83) from hospitalization<br>ChAdOx1 provided protection against VOC Delta for the following outcome 14 to 21 days after 2nd dose:<br>• 60 to 67% from infection (RME)<br>• 61 to 67% from symptomatic infection (RME)<br>• 92% (95% CI, 75 to 97) from hospitalization<br>(5 Obs) [29][38][42][47][71]; *last update 2021-11-03* |
| | • Delta, VE over time | ChAdOx1 provided protection against symptomatic infection by VOC Delta the following number of days after 2nd dose:<br>• 92.4% (95% CI, 92.1 to 92.7) – at 1 week<br>• -19% (95% CI, -97 to 28) – > 120 days (17 weeks)<br>• 69.7% (95% CI, 68.7 to 70.5) – at 20 weeks<br>(2 Obs) [92][114]; *last update 2021-11-03* |
| | • Gamma | ChAdOx1nCoV-19 provided protection against VOC Gamma for the following outcome 14 days after 1st dose:<br>• 48% (95% CI, 28 to 63) from symptomatic infection<br>• 83% (95% CI, 66 to 92) from hospitalization<br>(1 Obs)[47]; *last update 2021-07-07* |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | • Epsilon | no data |
| | Special populations | |
| | • HCW, Alpha | ChAdOx1provided protection against VOC Alpha for the following outcomes at least 14 days after 1st dose:<br>• 64% (95% CI, 50 to 74) from infection<br>ChAdOx1provided protection against VOC Alpha for the following outcomes at least 14 days after 2nd dose:<br>• 90% (95% CI, 62 to 98) from infection<br>(1 Obs) [46]; *last update 2021-07-07* |
| | • Over 80 years, Alpha | ChAdOx1provided protection against VOC Alpha for the following outcomes at least 14 days after 2nd dose:<br>• 88% (95% CI, 48 to 97) from symptomatic infection<br>(1 Obs) [79]; *last update 2021-10-20* |
| | • HCW, Delta | ChAdOx1 provided protection against VOC Delta for the following outcomes at least 14 days after 2nd dose:<br>• 54 to 85% from infection (RME)<br>• 64% (95% CI, 38 to 78) from symptomatic infection<br>(2 Obs) [59][66]; *last update* 2021-10-06 |
| | Transmission | |
| | • Household or close contacts of index case, Alpha | ChAdOx1nCoV-19 reduced transmission of VOC Alpha from a vaccinated index case (14 to 21 days after 1st dose) to household contacts compared to households of unvaccinated index cases:<br>• 30 to 47% from infection (RME)<br>Fully vaccinated index cases by ChAdOx1 showed VET to hh contacts (unclear status):<br>• 63 to 65% from infection (RME)<br>Fully vaccinated hh contacts by ChAdOx1 showed VE (unclear status of index case):<br>• 38 to 87% from infection (RME)<br>(5 Obs) [6][14][104][107][108]; *last update 2021-11-03* |
| | • Household or close contacts of index case, Delta | Fully vaccinated index cases by ChAdOx1 showed VET for household contacts (unclear status):<br>• 36% (95% CI, 28 to 43) from infection<br>Fully vaccinated hh contacts by ChAdOx1 showed VE (unclear status of index):<br>• 55 to 72% from infection (RME)<br>(2 Obs)[107][108]; *last update 2021-11-03* |
| | • Vaccinated close contacts of COVID+, Alpha | ChAdOx1nCoV-19 reduced transmission to close contacts COVID+ index cases at least 14 days after 2nd dose:<br>• 44% (95% CI, 31 to 54) from infection<br>• 92% (95% CI, 46 to 99) from hospitalization<br>(1 Obs)[40]; *last update 2021-06-23* |
| **Johnson & Johnson [AD26.COV2.S]** | From COVID-NMA | [Johnson & Johnson's Janssen vaccine] Vaccination with AD26.COV2.S probably reduces the incidence of symptomatic cases of COVID-19 by around 67%, and it probably reduces severe disease and mortality, while the incidence of serious adverse events may not increase. Review of RCTs (AMSTAR 10/11); *last search update 2021-09-17*. GRADE evidence profile updated on 2021-05-28 |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | | Interim summary, provided by VOC-study group: Ad26.COV2.S VE in ~40,000 randomized subjects was 66.9%; adjusted (95% CI, 59.0 to 73.4) at 14 days and 66.1% (95% CI, 55.0 to 74.8) at 28 days. For severe cases VE was 76.7% (95% CI, 54.6 to 89.1) at ≥14 days and 85.4% (95% CI, 54.2 to 96.9) at ≥28 days). (1 RCT, moderate quality of evidence) [7]<br>Rare cases of serious blood clots associated with a low platelet count known as vaccine-induced thrombotic thrombocytopenia (VITT, VIPIT) have been reported. The frequency of VITT varies by age and country. (data not systematically reviewed); *last update 2021-05-17* |
| | By variant of concern | |
| | • Alpha | no data |
| | • Beta | VE against VOC 20H/501Y.V2 variant (Beta) was 52.0% and 64.0% at 14 days and 28 days for moderate, and 73.1% and 81.7% for severe cases. (1 RCT) [7]; *last update 2021-04-22* |
| | • Delta | Ad26.COV2.S provided protection against VOC Delta for the following outcomes ≥ 14 days after 2nd dose:<br>• 3% to 71% against infection (RME)<br>(3 Obs) [97][109][110][111]; *last update 2021-11-03* |
| | • Gamma | no data |
| | • Epsilon | no data |
| | Transmission | |
| | • Household of index case, Alpha | Fully vaccinated index cases by Ad26.COV2.S showed VET for household contacts (unclear status):<br>• 77% (95% CI, 6 to 94) from infection<br>Fully vaccinated hh contacts by Ad26.COV2.S showed VE (unclear status of index):<br>• 12% (95% CI, -71 to 54) from infection<br>(1 Obs) [104]; *last update 2021-11-03* |
| **Sinovac [CoronaVac]** | • Overall | [Coronavac vaccine] Compared to placebo, vaccination with CoronaVac may reduce the incidence of symptomatic cases of COVID-19 by 50%, close to the lowest level deemed effective by the WHO and it may substantially reduce the incidence of severe disease due to COVID-19; the evidence for any difference in serious adverse events is uncertain, although the vaccination probably increases the incidence of any adverse event. Review of RCTs (AMSTAR 10/11); *last search date 2021-09-17*; GRADE evidence profile updated 2021-06-25 |
| | By variant of concern | |
| | • Delta | CoronaVac provided protection against VOC Delta for the following outcome ≥ 14 days after 2nd dose:<br>• 59% (95% CI, 16 to 81.6) from symptomatic infection<br>• 89% (95% CI, 55 to 98) from severe infection<br>(1 Obs) [91]; *last update 2021-11-03* |
| | • Gamma | CoronaVac provided protection against VOC Gamma for the following outcome ≥ 14 days after 2nd dose:<br>• 65.9% (95% CI, 65.2 to 66.6) from infection |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | | CoronaVac provided protection against VOC Gamma for the following outcome ≥ 14 days after 2nd dose for people over age 70:<br>• 41.6% (95% CI, 26.9 to 63.3) from symptomatic infection<br>(2 Obs) [30][49]; *last update 2021-07-14* |
| | • Epsilon | no data |
| | By special population | |
| | • HCW, Gamma | CoronaVac provided protection against VOC Gamma for the following outcomes ≥14 days after 1st dose:<br>• 35.1% (95% CI, -6.6 to 60.5) from infection<br>• 49.6% (95% CI, 11.3 to 71.4) from symptomatic infection<br>(1 Obs)[18]; last update 2021-05-07 |
| **Sinopharm (Wuhan) [WIV04]**<br><br>**Sinopharm (Beijing) [HBO2] [BBIBP-CorV]** | • From COVID-NMA | [Sinopharm - strain HBO2] Vaccination with Sinopharm HBO2 probably reduces the incidence of symptomatic cases of COVID-19, and it may reduce severe disease, while the incidence of adverse events is probably not increased. Review of RCTs (AMSTAR 10/11); *last search date 2021-09-17*. GRADE evidence profile updated on 2021-06-11<br><br>[Sinopharm - strain WIV04] Vaccination with Sinopharm WIV04 probably reduces the incidence of symptomatic cases of COVID-19, and it may reduce severe disease, while the incidence of adverse events is probably not increased. Review of RCTs (AMSTAR 10/11); *last search date 2021-09-17*. GRADE evidence profile updated on 2021-06-11 |
| | • Delta | |
| **Novavax [NVX-CoV2373]** | • From COVID-NMA | [Novavax vaccine] The effects of vaccination against COVID-19 with the Novavax vaccine are currently uncertain; it probably slightly increase the risk of any adverse events Review of RCTs (AMSTAR 10/11); last search date *2021-09-17*; GRADE evidence profile updated on 2021-07-01 |
| | By variant of concern | |
| | • Alpha | NVX-CoV2373 provided protection against VOC Alpha for the following outcome after 2 doses:<br>• 89.7% (95% CI, 80.2 to 94.6) from infection.<br>• No hospitalizations or deaths in vaccinated group<br>• Post hoc: 86.3% (95% CI, 71.3 to 93.5) from confirmed Alpha symptomatic infection<br>(1 RCT, moderate quality), [19]; *last update 2021-06-16* |
| | • Beta | NVX-CoV2373 provided protection against VOC Beta for the following outcome after 7 days after 2nd dose:<br>• Post-hoc: 43% (95% CI, -9.8 to 70.4) from symptomatic infection<br>(1 RCT, moderate quality), [17]; *last update 2021-07-14* |
| **FBRI [EpiVacCorona]** | • From COVID-NMA | [EpiVacCorona] The effects of using vaccination with EpiVacCorona are uncertain. Review of RCTs (AMSTAR 10/11); *last search date 2021-09-17*; GRADE evidence profile updated on 2021-06-11 |
| **Bharat Biotech [Covaxin]** | • From COVID-NMA | [COVAXIN] Vaccination with BBV152 probably reduces the incidence of symptomatic cases of COVID-19, and it may reduce severe disease, while the incidence of serious adverse events is |

| Vaccine | Effectiveness | Findings |
|---|---|---|
| | | probably not increased. Review of RCTs (AMSTAR 10/11); *last search date 2021-09-17*. GRADE evidence profile updated on 2021-07-29. |
| | By special population | |
| | • HCW, Delta | |
| **Gamaleya [Sputnik V] [Gam-COVID-Vac]** | | |
| | • Delta | |
| **Combinations of Vaccines** | | |
| **AstraZeneca followed by Pfizer or Moderna** | • Alpha | First dose ChAdOx1 followed by second dose BNT162b2 or mRNA-1273 (≥ 14 days) provided protection against VOC Alpha for the following outcomes:<br>• 88% (95% CI, 83 to 92) against infection<br>(1 Obs) [70]; *last search date* 2021-08-25 |
| | • Delta, VE over time | ChAdOx1 followed by an mRNA provided protection against symptomatic infection by VOC Delta the following number of days after 2nd dose:<br>• 66% (95% CI, 41 to 80) – > 120 days (17 weeks)<br>(1 Obs) [114]; *last update 2021-11-03* |
| | • Household contacts of index case, Delta | Fully vaccinated hh contacts by ChAdOx1 followed by mRNA showed VE (unclear status of index):<br>• 86% (95% CI, 45 to 97) from infection<br>(1 Obs)[108]; *last update 2021-11-03* |

*delayed exclusion (see Section 2: excluded studies for reason)

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 6.23): What is the efficacy and effectiveness of available COVID-19 vaccines in general and specifically for variants of concern? Hamilton: Health Information Research Unit, 3 November 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: Reference list**

| Section 1: included studies | | | | |
|---|---|---|---|---|
| **Ref** | **Author** | **Bottom line** | **ROBINS-I*** | **Design, Notes** |
| *Note: ROBINS-I score risk of bias: Low risk of bias indicates high quality | | | | |
| 1 | Dagan | BNT162b2 showed VE 46% (95% CI, 40 to 51) against infection 14 to 20 days after 1st dose and VE 92% (95% CI, 88 to 95) 7 days after 2nd dose. | Moderate | Data-linkage study in Israel; .5 M matched participants (2 M excluded – also (possible overlap with Haas); time and setting for VOC Alpha (estimated 80%). |
| 2 | Haas | BNT162b2 showed VE 95.3% (95% CI, 94.9 to 95.7) against infection; VE 97.5% (95% CI, 97.1 to 97.8) against severe or critical COVID-19-related hospitalization; VE 96.7% (95% CI, 96.0 to 97.3) against death 7 days after 2nd dose. | Serious | Data-linkage study in Israel; >6.5 M matched participants (possible overlap with Dagan) Updated May 14 due to final publication; sample confirmed VOC Alpha (estimated 94%). |
| 3 | Kustin<br><br>*Delayed exclusion-only included infected | BNT162b2 showed lower relative VE (2.4:1) against Alpha. after 1st dose; and lower VE (8:1) against Beta after 2nd dose in a population with >90% of Alpha and <1% Beta | Moderate | Case-control study in Israel; small sample for Beta (no overlap CHS cohort); confirmed VOC Alpha and Beta. |
| 4 | Madhi | ChAdOx1 nCoV-19 showed VE 10.4% (95% CI, -76.8 to 54.8) against mild to moderate disease 14 days after 2nd dose. | Moderate quality (RCT) | RCT in South Africa; Underpowered for 20% efficacy (42 cases); VOC Beta. |
| 5 | Emary | ChAdOx1nCoV-19 showed VE 61.7% (95% CI, 36.7 to 76.9) against infection by VOC Alpha ≥ 15 days after 2nd dose. | Moderate quality (RCT) | RCT in UK; neutralization of Alpha 9 times lower; no sequencing for 45% of cases; 52 cases (19%) had VOC Alpha. |
| 6 | Shah | ChAdOx1nCoV-19 or BNT162b2 reduced infection in unvaccinated household contacts of vaccinated HCW by about 30% (HR, 0.70, 95% CI, 0.63 to 0.78) ≥ 14 days after 1st dose; ChAdOx1nCoV-19 or BNT162b2 reduced infection in HCW by about 55% (HR 0.45, 95% CI, 0.42 to 0.49) and hospitalization by 84% (HR 0.16, 95% CI, 0.09 to 0.27) ≥ 14 days after 1st dose. | Moderate | Data-linkage study in Scotland - (25% of cases had received 2 doses); time and setting for VOC Alpha. |
| 7 | Sadoff | Single dose Ad26.COV2.S showed VE 52.0% (95% CI, 30.3 to 67.4) at 14 days and VE 64.0% (95% CI, 41.2 to 78.7) at 28 days against moderate to severe disease and VE 81.7% (95% CI, 46.2 to | Moderate quality (RCT) | RCT; over 40,000 participants; Argentina, Brazil, Chile, Colombia, Mexico, Peru, South Africa, and the United States; 86 |

| | | | | |
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| | | 95.4) at 28 days against severe disease (VOC Beta in South Africa). | | of 91 cases sequenced for VOC Beta. |
| 8 | Andrejko | BNT162b2 or mRNA-1273 showed VE 58.9% (95% CI, −9.7 to 84.5) at 15 days after 1st dose, and VE 85.7% (95% CI, 67.2 to 93.9) 15 days after 2nd dose against infection. | Serious | Test-negative study in California; 645 participants; 69% of population at time had VOC Alpha or Epsilon. |
| 9 | Glampson | ChAdOx1nCoV-19 showed VE 74% (95% CI, 65 to 81) against infection 28 days after 1st dose.<br><br>BNT162b2 showed VE 78% (95% CI, 73 to 82) against infection 28 days after 1st dose. | Serious | Retrospective cohort in UK; 2M participants; time and setting for VOC Alpha. |
| 10 | Pritchard | ChAdOx1nCoV-19 or BNT162b2 showed VE 66% (95% CI, 59 to 72%) 21 days after 1st dose and 78% (95% CI, 68 to 85%) after 2nd dose against infection. | Serious | Survey of randomly selected private households with longitudinal follow-up in UK; 370,000 participants; sample confirmed VOC Alpha. |
| 11 | Hall (SIREN) | BNT162b2 vaccine showed VE of 70% (95% CI, 55 to 85) 21 days after 1st dose and 85% (95% CI, 74 to 96) 7 days after 2nd dose against infection in HCW. | Moderate | Prospective cohort with standardized testing for HCW over all of England; 23,000 participants; time and setting for VOC Alpha |
| 12 | Shrotri<br><br>*Delayed exclusion – critical ROB | Similar effect sizes were seen for ChAdOx1 (aHR 0.32, 95% CI, 0.15 to 0.66) and BNT162b2 (aHR 0.35, 95% CI, 0.17 to 0.71) at 35-48 days after 1st dose. | Critical | Prospective cohort in England: 9160 of 10412 frail LTC residents; routine screening; time and setting for VOC Alpha |
| 13 | Hyams<br><br>*Delayed exclusion – did not report clinical outcomes of interest for this LES | BNT162b2 showed VE 71.4% (95% CI, 43.1 to 86.2) against hospitalization 14 days after 1st dose; ChAdOx1nCoV-19 showed VE 80.4% (95% CI, 36.4 to 94.5) against hospitalization 14 days after 1st dose for 80+.<br><br>When effectiveness analysis for BNT162b2 was restricted to the period covered by ChAdOx1nCoV-19, the estimate was 79.3% (95% CI, 47.0 to 92.5). | | Test negative case-control study in Scotland. Single center; 466 participants, 80+; time and setting for VOC Alpha |
| 14 | Harris | BNT162b2 or ChAdOx1 reduced likelihood of transmission by 40-50% for household contacts of HCW 21 days after 1st dose. | Serious | Data-linkage and case-control study in England; 338,887 participants; time and setting for VOC Alpha |
| 15 | Goldberg | Prior infection (in unvaccinated) has similar VE against infection [94.8%], and severe illness [96.4%] as two doses of BNT162b2. | Serious | Data-linkage study in Israel; 6,351,903 participants; likely overlaps with Dagan and Haas; time and setting for VOC Alpha |

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

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

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

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| | | against infection by confirmed VOC Gamma ≥21 days after 1st dose for 70+. | | |
| 36 | Abu-Raddad | BNT162b2 showed VE 89.5% (95% CI, 85.9 to 92.3) against infection, VE 100% (95% CI, 81.7 to 100) against any severe, critical, or fatal disease by VOC Alpha ≥ 14 days after 2nd dose.<br><br>BNT162b2 showed VE 75% (95% CI, 70.5 to 78.9) against infection, VE 100% (95% CI, 73.7 to 100) against severe, critical, or fatal disease by VOC Beta ≥ 14 days after 1st dose. | Serious | Test-negative in Qatar; 17,293 cases; sequencing showed 50% VOC Beta and 45% VOC Alpha between February-March 2021 |
| 37 | Akhrass<br>*Delayed exclusion - failure to report outcomes of interest for this LES | BNT162b2 or mRNA-1273 showed overall VE 60.4% (95% CI, 30 to 77.6) against symptomatic infection ≥ 14 days after 1st dose; BNT162b2 or mRNA-1273 showed overall VE 95.7% (95% CI, 90 to 98.2) against symptomatic infection ≥ 14 days after 2nd dose. | Critical | Retrospective cohort of HCW at a single centre in Kentucky, USA; 2,134 participants; time and setting for VOC Alpha |
| 38 | Sheikh | BNT162b2 showed VE 30% (95% CI, 17 to 41) against confirmed VOC Delta infection and VE 33% (95% CI, 15 to 47) against symptomatic infection at least 28 days after 1st dose; VE 79% (95% CI, 75 to 82) against infection and VE 83% (95% CI, 78 to 87) against symptomatic infection at least 14 days after 2nd dose.<br><br>ChAdOx1 showed VE 18% (95% CI, 9 to 25) against confirmed VOC Delta infection and VE 33% (95% CI, 23 to 41) against symptomatic infection at least 28 days after 1st dose; VE 60% (95% CI, 53 to 66) against infection and VE 61% (95% CI, 51 to 70%) against symptomatic infection at least 14 days after 2nd dose. | Moderate | Test-negative in Scotland; 626,900 specimens; also compared hospitalization rates between S gene positive (VOC Delta) and S gene negative specimens within 14 days of positive test result (not summarized here) |
| 39 | Furer<br>*Delayed exclusion – critical risk of bias | BNT162b2 reported no symptomatic infections in the vaccinated group (0/686) compared to 0.83% infections in the vaccinated general population control group. | Critical | Prospective cohort of adults with autoimmune inflammatory rheumatic diseases in Israel; 686 participants; time and setting for VOC Alpha |
| 40 | Martinez-Baz | BNT162b2 showed VE 65% (95% CI, 56 to 73) against infection and VE 94% (95% CI, 60 to 99) against hospitalization at least 14 days after 2nd | Serious | Prospective cohort of close contacts of COVID+ people in Spain; 20,961 participants; VOC Alpha confirmed for small sample; sample size for |

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| | | dose in close contacts of COVID+ index cases.<br><br>ChAdOx1 showed VE 44% (95% CI, 31 to 54) against infection and VE 92% (95% CI, 46 to 99) against hospitalization at least 14 days after 1st dose in close contacts of index cases. Second dose results not reported. | | Moderna too small to report results separately |
| 41 | Chodick (2) | BNT162b2 showed VE 51.4% (95% CI, 16.3 to 71.8) against infection 13 to 24 days after 1st dose. | Serious | Data-linkage study in Israel (Maccabi Health Care Services); 351,897 participants; time and setting for VOC Alpha |
| 42 | Stowe | BNT162b2 showed VE 94% (95% CI, 46 to 99) at least 21 days after 1st dose and VE 96% (95% CI, 86 to 99) at least 14 days after 2nd dose against hospitalization by confirmed VOC Delta.<br><br>ChAdOx1 showed VE 71% (95% CI, 51 to 83) at least 21 days after 1st dose and VE 92% (95% CI, 75 to 97) 14 days after 2nd dose against hospitalization by confirmed VOC Delta. | Serious | Same cohort as Bernal (3) with extended time frame for symptomatic infection and adding in data-linkage to hospitalization; 14,019 participants; sample confirmed VOC Delta |
| 43 | Saciuk | BNT162b2 showed VE 93% (95% CI, 92.6 to 93.4) against infection, VE 93.4% (95% CI, 91.9 to 94.7) against hospitalization and VE 91.1% (95% CI, 86.5 to 94.1) against death at least 7 days after 2nd dose | Serious | Retrospective cohort of members of a health management organization in Israel; 1,650,885 participants; time and setting for VOC Alpha |
| 44 | Zacay<br><br>*Delayed exclusion – critical risk of bias | BNT162b2 showed VE 61% (95% CI, 49 to 71) at least 14 days after 1st dose and VE 89% (95% CI, 82 to 94) at least 7 days after 2nd dose against infection | Serious | Retrospective cohort of a subpopulation of members of a health management organization in Israel who had undergone repeated PCR testing; 6,286 participants; time and setting for VOC Alpha |
| 45 | Azamgarhi | BNT162b2 showed VE 70% (95% CI, 6 to 91) against infection at least 14 days after 1st dose | Serious | Single centre cohort study of HCW in UK; 2,260 participants; time and setting for VOC Alpha |
| 46 | Lumley | BNT162b2 (63%) or ChAdOx1showed VE 64% (95% CI, 50 to 74) 14 days after 1st dose and VE 90% (95% CI, 62 to 98) 14 days after 2nd dose against infection | Serious | Prospective cohort of HCWs in Oxfordshire, UK; 13,109 participants; confirmed VOC Alpha |
| 47 | Nasreen | BNT162b2 showed VE 89% (95% CI, 86 to 91) against symptomatic infection and VE 95% (95% CI, 92 to 97) against hospitalization at least 7 days after 2nd | Moderate | Test-negative study in Ontario 421,073 participants (same population as for Chung but extended to May 2021 and more |

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| | | dose (VOC Alpha); VE 84% (95% CI, 69 to 92) against symptomatic infection and VE 95% (95% CI, 81 to 99) against hospitalization at least 7 days after 2nd dose (VOC Beta/Gamma); VE 87% (95% CI, 64 to 95) against symptomatic infection at least 7 days after 2nd dose (VOC Delta).<br><br>BNT162b2 showed VE 78% (95% CI, 65 to 86) against hospitalization at least 7 days after 2nd dose (VOC Delta).<br><br>mRNA-1273 showed VE 92% (95% CI, 86 to 96) against symptomatic infection and VE 94% (95% CI, 89 to 97) against hospitalization at least 7 days after 2nd dose (VOC Alpha).<br><br>mRNA-1273 showed VE 77% (95% CI, 63 to 86) against symptomatic infection and VE 89% (95% CI, 73 to 95) against hospitalization at least 14 days after 1st dose (VOC Beta/Gamma); VE 72% (95% CI, 57 to 82) against symptomatic infection and VE 96% (95% CI, 72 to 99) against hospitalization at least 14 days after 1st dose (VOC Delta).<br><br>ChAdOx1 showed VE 64% (95% CI, 60 to 68) against symptomatic infection and VE 85% (95% CI, 81 to 88) against hospitalization at least 14 days after 1st dose (VOC Alpha); VE 48% (95% CI, 28 to 63) against symptomatic infection and VE 83% (95% CI, 66 to 92) against hospitalization at least 14 days after 1st dose (VOC Beta/Gamma); VE 67% (95% CI, 44 to 80) against symptomatic infection and VE 88% (95% CI, 60 to 96) against hospitalization at least 14 days after 1st dose (VOC Delta). | | detailed with respect to reporting of VOC); screening for VOC Alpha, Beta/Gamma and Delta varied during study period |
| 48 | Gazit | BNT162b2 showed VE 80% (95% CI, 73 to 85) at least 7 days after 2nd dose against infection in vaccinated household members of a confirmed COVID+ case. | Serious | Retrospective cohort of household members (household = 2 adults with no children) of a health management organization in Israel; 173,569 households; time and setting for VOC Alpha |

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| 49 | Jara | CoronaVac showed VE 65.9% (95% CI, 65.2 to 66.6) against infection and VE 86.3% (95% CI, 84.5 to 87.9) against death at least 14 days after 2nd dose. | Moderate | Prospective cohort in Chile; 10.2 million participants; time and setting for VOC Gamma |
| 50 | Chemaitelly | mRNA-1273 showed VE 88.1% (95% CI, 83.7 to 91.5) and VE 100% (95% CI, 91.8 to 100) against infection by confirmed VOC Alpha at least 14 days after 1st and 2nd dose, respectively.<br><br>mRNA-1273 showed VE 61.3% (95% CI, 56.5 to 65.5) and VE 96.4% (95% CI, 91.9 to 98.7) against infection by confirmed VOC Beta at least 14 days after 1st and 2nd dose, respectively.<br><br>mRNA-1273 showed VE 81.6% (95% CI, 71.0 to 88.8) and VE 95.7% (95% CI, 73.4 to 99.9) against severe, critical, or fatal disease at least 14 days after 1st and 2nd dose, respectively (combined VOC Alpha and Beta). | Serious | Test-negative in Qatar; >75,000 participants; sample sequenced for VOC Alpha and VOC Beta |
| 51 | Baum | BNT162b2 or mRNA-1273 showed VE 41% (95% CI, 25 to 54) against infection ≥ 21 days after 1st dose; BNT162b2 or mRNA-1273 showed VE 75% (95% CI, 65 to 82) against infection ≥ 7 days after 2nd dose in age 70+.<br><br>BNT162b2 or mRNA-1273 showed VE 41% (95% CI, 17 to 58) against infection ≥ 21 days after 1st dose; BNT162b2 or mRNA-1273 showed VE 77% (95% CI, 65 to 85) against infection ≥ 7 days after 2nd dose in chronically ill (age 16-69).<br><br>ChAdOx1 showed VE 24% (95% CI, -1 to 43) against infection ≥ 21 days after 1st dose in chronically ill (age 16-69). | Serious | Data-linkage study in Finland; 901,092 participants age 70+ and 774,526 participants age 16 to 69 years with chronic illness; time and setting for VOC Alpha; results for mRNA vaccines not reported separately |
| 52 | Balicer | BNT162b2 showed VE 86.1% (95% CI, 82.4 to 89.1) against infection; VE 89% (95% CI, 43 to 100) against hospitalization 7 to 56 days after 2nd dose.<br><br>Too few events to report VE for severe disease or death. | Serious | Data-linkage study of pregnant women over age 16 in Israel (same database as Dagan); 21,722 participants; time and setting for VOC Alpha. |

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| 53 | Mateo-Urdiales | BNT162b2 (61%) or ChAdOx1 (31%) or mRNA-1273 (7%) or Ad26.$COV_2$-S (0.6%) showed VE 78% (95% CI, 76 to 79) against infection 42 to 49 days after at least 1st dose; VE 93% (95% CI, 89 to 96) against death 35 to 42 days after at least 1st dose. | Serious | Data-linkage study in Italy; 13,721,506 participants; time and setting for VOC Alpha. Results not reported by vaccine and some participants (42%) who also received 2nd dose were included in estimates. |
| 54 | Goldshtein | BNT162b2 showed VE 78% (95% CI, 57 to 89) against infection at least 28 days after 1st dose. | Serious | Data-linkage study of pregnant women in Israel (same database as Gazit); 15,060 participants; time and setting for VOC Alpha. |
| 55 | Mason | BNT162b2 showed VE 55.2% (95% CI, 40.8 to 66.8) and VE 70.1% (95% CI, 55.1 to 80.1) against infection 21 to 27 days and 35 to 41 days after 1st dose, respectively. | Moderate | Case-control study of age 80-83 vs 76-79 community-dwelling unvaccinated residents in England; time and setting for VOC Alpha |
| 56 | Fabiani | BNT162b2 showed VE 84.1% (95% CI, 39.7 to 95.8) and VE 85.4% (95% CI, -35.3 to 98.4) against infection 14 to 21 days and ≥21 days after 1st dose, respectively in HCW.<br><br>BNT162b2 showed VE 95.1% (95% CI, 62.4 to 99.4) against infection ≥7 days after 2nd dose in HCW. | Serious | Retrospective cohort of HCW in Italy; 6,423 participants; time and setting for VOC Alpha |
| 57 | Chia | BNT162b2 or mRNA-1273 showed VE 92.7% (95% CI, 65.7 to 98.4) against severe disease (defined as requiring supplemental oxygen) > 14 days after 2nd dose. | Serious | Retrospective cohort of confirmed VOC Delta admitted to hospital (including asymptomatic) in Singapore; 218 participants; not reported by vaccine |
| 58 | Kaur<br>*Delayed exclusion – critical ROB | Two doses of Covishield showed VE 87% (95% CI, 33 to 97) against severe disease when compared with one dose (timing of doses not reported). | Critical | Preliminary report of prospective cohort in India; 1500 participants; time and setting for VOC Delta |
| 59 | Pramod<br><br>*Delayed exclusion – critical ROB | Covishield showed VE 49% (95% CI, 17 to 68) against infection 21 days after 1st dose and VE 54% (95% CI, 27 to 71) against infection 14 days after 2nd dose.<br><br>Covishield showed VE 58% (95% CI, 28 to 75) against symptomatic infection 21 days after 1st dose and VE 64% (95% CI, 38 to 78) against symptomatic infection 14 days after 2nd dose. | Critical | Test-negative study in a single hospital site in India; 360 matched pairs (203 symptomatic pairs); time and setting for VOC Delta |
| 60 | Carazo | BNT162b2 or mRNA-1273 showed VE 60% (95% CI, 53.6 to 65.5) against infection by confirmed VOC Alpha 14 days after 1st dose. | Serious | Test-negative study in Quebec, Canada; 58,476 participants; sample confirmed VOC Alpha; reported according to vaccine |

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| | | BNT162b2 or mRNA-1273 showed VE 92.6% (95% CI, 87.1 to 95.8) against infection by confirmed VOC Alpha 7 days after 2nd dose. | | but not concurrently for VOC Alpha |
| 61 | Williams | BNT162b2 or mRNA-1273 showed VE 52.5% (95% CI, 26.9 to 69.1) against infection and VE 78.6% (95% CI, 47.9 to 91.2) against severe disease 14 days after 2nd dose in residents at LTCF. Two deaths in vaccinated residents but were palliative prior to infection.<br><br>BNT162b2 or mRNA-1273 showed VE 66.2% (95% CI, 2.3 to 88.3) against infection 14 days after 2nd dose in staff at LTCF. None of the staff developed severe disease. | Serious | Outbreak in a single LTCF in Ontario; 60 residents and 83 staff; sample confirmed VOC Gamma |
| 62 | Hitchings(2)<br><br>*Delayed exclusion – critical ROB | ChAdOx1 showed VE 33.4% (95% CI, 26.4 to 39.7) against symptomatic infection and VE 50.9% (95% CI, 33.6 to 63.8) against ICU admission and VE 61.8% (95% CI, 48.9 to 71.4) against death at least 28 days after 1st dose for 60+.<br><br>ChAdOx1 showed VE 77.9% (95% CI, 69.2 to 84.2) against symptomatic infection and VE 89.9% (95% CI, 70.9 to 96.5) against ICU admission and VE 93.6% (95% CI, 81.9 to 97.7) against death at least 14 days after 2nd dose. | Critical | Test-negative study in Sao Paulo, Brazil; 61,164 participants over age 60; time and setting for VOC Gamma |
| 63 | Tang | BNT162b2 showed VE 65.5% (95% CI, 40.9 to 79.9) against infection ≥ 14 days after 1st dose; BNT162b2 showed VE 59.6% (95% CI, 50.7 to 66.9) against infection ≥ 14 days after 2nd dose.<br><br>BNT162b2 showed VE 100% (95% CI, not reported) against severe, critical or fatal disease ≥ 14 days after 1st dose; BNT162b2 showed VE 97.3% (95% CI, 84.4 to 99.5) against severe, critical or fatal disease ≥ 14 days after 2nd dose.<br><br>mRNA-1273 showed VE 79.7% (95% CI, 60.8 to 89.5) against infection ≥ 14 days after 1st dose; mRNA-1273 showed VE 86.1% (95% CI, 78.0 to 91.3) | Serious | Test-negative study in Qatar; 1,140,337 participants; weekly random sequencing of positive samples for VOC Delta |

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| | | against infection ≥ 14 days after 2nd dose.<br><br>mRNA-1273 showed VE 100% (95% CI, not reported) against severe, critical or fatal disease ≥ 14 days after 1st dose; mRNA-1273 showed VE 100% (95% CI, not reported) against severe, critical or fatal disease ≥ 14 days after 2nd dose. | | |
| 64 | Puranik | BNT162b2 showed VE 42% (95% CI, 13 to 62) against infection 14 days after 2nd dose.<br><br>mRNA-1273 showed VE 76% (95% CI, 58 to 87) against infection 14 days after 2nd dose. | Serious | Data-linkage study involving Mayo Clinic Health in USA; 25,859 matched triples from Minnesota only; time and setting for Delta at end of study time frame so only last month of data (July 2021) reported here |
| 65 | Elliot<br><br>*Delayed exclusion – critical ROB | BNT162b2 or ChAdOx1 showed VE 64% (95% CI, 11 to 85) against infection unreported number of days after 2nd dose (Round 12: 2021-05-20 to 2021-06-07).<br><br>BNT162b2 or ChAdOx1 showed VE 49% (95% CI, 22 to 67) against infection unreported number of days after 2nd dose (Round 13: 2021-06-24 to 2021-07-12). | 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 | Issac | ChAdOx1 showed VE 85% (95% CI, 71 to 92) against infection 14 days after 2nd dose. | Serious | Prospective cohort of HCW at a single hospital in India; 342 participants; time and setting for VOC Delta. |
| 67 | Marco<br>*Delayed exclusion – critical ROB | ChAdOx1 showed VE 23% (95% CI, not reported) against infection at least 21 days after 1st dose. | Critical | Outbreak study of prison inmates in Barcelona; 217 participants (184 inmates); sequenced for VOC Alpha |
| 68 | Kale<br>*Delayed exclusion – critical ROB | ChAdOx1 showed VE 60% (95% CI, 45 to 70) against infection at least 14 days after 2nd dose. | Critical | Prospective cohort of HCW at a single hospital in India; 1858 participants; sample sequenced for VOC Delta |
| 69 | Israel | BNT162b2 showed OR 2.06 (95% CI, 1.69 to 2.51) for infection comparing fully vaccinated longer than or equal to 146 days vs fully vaccinated less than 146 days. | Moderate | Retrospective cohort of fully vaccinated members of a health management organization in Israel who underwent testing; 33,993 participants; time and setting for VOC Delta |
| 70 | Gram | ChAdOx1 showed VE 44% (95% CI, 29 to 56) against infection 21 to 27 days after 1st dose. No deaths in vaccinated participants. | Serious | Data-linkage study in Denmark; 5,542,079 participants; time and setting for VOC Alpha |

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| | | First dose ChAdOx1 followed by second dose BNT162b2 or mRNA-1273 showed VE 88% (95% CI, 83 to 92) against infection ≥ 14 days after 2nd dose. | | |
| 71 | Pouwels | BNT162b2 showed VE 59% (95% CI, 52 to 65%) against infection ≥21 days after 1st dose and VE 78% (95% CI, 68 to 84) against infection ≥ 14 days after 2nd dose (VOC Alpha age 18+).<br><br>BNT162b2 showed VE 57% (95% CI, 50 to 63) against infection ≥21 days after 1st dose and VE 80% (95% CI, 77 to 83) against infection ≥ 14 days after 2nd dose (VOC Delta age 18+).<br><br>ChAdOx1 showed VE 63% (95% CI, 55 to 69) against infection ≥21 days after 1st dose and VE 79% (95% CI, 56 to 90) against infection ≥ 14 days after 2nd dose (VOC Alpha age 18+).<br><br>ChAdOx1 showed VE 46% (95% CI, 35 to 55) against infection ≥21 days after 1st dose and VE 67% (95% CI, 62 to 71) against infection ≥ 14 days after 2nd dose (VOC Delta age 18+).<br><br>mRNA-1273 showed VE 75% (95% CI: 64 to 83) against infection ≥21 days after 1st dose (VOC Delta age 18 to 64). | 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 |
| 72 | Abu-Raddad (2) | BNT162b2 after prior infection showed VE 85% (95% CI, 80 to 89) against re-infection compared to BNT162b2 without prior infection.<br><br>mRNA-1273 after prior infection showed VE 15% (95% CI, -105 to 66) against re-infection compared to mRNA-1273 without prior infection. | Serious | Retrospective matched cohorts (2) of fully vaccinated in Qatar; 151,076 participants; sample sequenced for VOC Alpha and VOC Beta |
| 73 | Gazit (2) | BNT162b2 showed OR 13.06 (95% CI, 8.08 to 21.11) against infection and OR 27.02 (95% CI, 12.7 to 57.5) against symptomatic disease compared to prior infection. | Moderate | Retrospective matched cohorts of fully vaccinated in Israel; 778,658 participants; time and setting for VOC Delta |
| 74 | Rosenberg | BNT162b2 (51%), mRNA-1273 (40%) or Ad26.COV2.S (9%) showed VE 91.7% against infection ≥14 days after | Serious | Surveillance report in New York, USA; >13 million participants; time and setting for |

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| | | 2nd dose (Week of May 3, 2021: VOC Alpha).<br><br>BNT162b2 (51%), mRNA-1273 (40%) or Ad26.COV2.S (9%) showed VE 79.8% against infection ≥14 days after 2nd dose (Week of July 19, 2021: VOC Delta). | | VOC Delta (from 2% to 80% during study period) |
| 75 | Al-Qahtani<br><br>*Delayed exclusion due to critical ROB | BNT162b2 ≥14 days after 2nd dose, showed VE 99.9% (95% CI, 99.2 to 100) against ICU admission, and VE 99.5% (95% CI, 98.4 to 99.8) against death (VOC Alpha and Delta).<br><br>ChAdOx1 ≥14 days after 2nd dose, showed VE 99.2% (95% CI, 97.6 to 99.7) against ICU admission, and VE 99.6% (95% CI, 97.2 to 100) against death (VOC Alpha and Delta).<br><br>BBIBP-CorV ≥14 days after 2nd dose, showed VE 95.4% (95% CI, 94.6 to 96.2) against ICU admission, and VE 94.3% (95% CI, 93.1 to 95.4) against death (VOC Alpha and Delta).<br><br>Sputnik V ≥14 days after 2nd dose, showed VE 100% (95% CI, 99.2 to 100) against ICU admission, and VE 99.5% (95% CI, 98.5 to 99.9) against death (VOC Alpha and Delta). | Critical | Retrospective cohort of fully vaccinated (>14 days after 2nd dose) in Bahrain; 1,242,279 participants; time and setting for VOC Alpha (dominant before May 2021) and Delta (dominant after May 2021). |
| 76 | Goldberg (2) | BNT162b2 showed VE 50% (95% CI, 45 to 55) for those vaccinated in January 2021, and VE 73% (95% CI, 67 to 78) for those vaccinated in May 2021 against infection after the 2nd dose (VOC Delta age 16 to 39).<br><br>BNT162b2 showed VE 58% (95% CI, 54 to 62) for those vaccinated in January 2021, and VE 80% (95% CI, 71 to 86) for those vaccinated in May 2021 against infection after the 2nd dose (VOC Delta age 40 to 59).<br><br>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 | Serious | Data-linkage study of fully vaccinated in Israel; 4,785,245 participants; time and setting for VOC Delta (dominant after May 2021). |

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| | | against infection after the 2nd dose (VOC Delta age 60+).<br><br>BNT162b2 showed VE 94% (95% CI, 87 to 97) for those vaccinated in January 2021, and VE 98% (95% CI, 94 to 99) for those vaccinated in March 2021 against severe, critical, or fatal disease after the 2nd dose (VOC Delta age 40 to 59).<br><br>BNT162b2 showed VE 86% (95% CI, 82 to 90) for those vaccinated in January 2021, and VE 91% (95% CI, 85 to 95) for those vaccinated in March 2021 against severe, critical, or fatal disease after the 2nd dose (VOC Delta age 60+). | | |
| 77 | Herlihy<br><br>*Delayed exclusion – critical risk of bias | BNT162b2, mRNA-1273, or Ad26.COV2.S showed VE 78% (95% CI, 71 to 84) in Mesa County and VE 89% (95% CI, 88 to 91) in other Colorado counties against symptomatic infection an unreported number of days after 2nd dose (VOC Delta). | Critical | Surveillance report in Mesa County-Colorado, USA; 37,439 cases participants; sample sequenced for VOC Delta (43% to 88% during study period) |
| 78 | Ghosh<br><br>*Delayed exclusion – critical risk of bias | ChAdOx1 showed unadjusted VE 75.2% (95% CI, 73.8 to 76.8) against infection ≥14 days after 1st dose, and unadjusted VE 54.6% (95% CI, 52.6 to 56.6) ≥14 days after 2nd dose against infection in HCW (VOC Alpha to Delta). | Critical | Retrospective cohort of Armed Forces HCW and frontline workers in India; 1,595,630 participants; time and setting for VOC Delta at end of study only. |
| 79 | Amirthalingam | BNT162b2 showed VE 77% (95% CI, 56 to 88) against symptomatic infection when 2nd dose given 19-29 days after 1st dose, and VE 94% (95% CI, 73 to 99) against symptomatic infection when 2nd dose given 85+ days after 1st dose (VOC Alpha age 80+ ).<br><br>BNT162b2 showed VE 77% (95% CI, 66 to 85) against symptomatic infection when 2nd dose given 19-29 days after 1st dose, and VE 86% (95% CI, 70 to 94) against symptomatic infection when 2nd dose given 85+ days after 1st dose (VOC Alpha age 65 to 79).<br><br>ChAdOx1 showed VE 96% (95% CI, 72 to 100) against symptomatic | Moderate | Test-negative study in England; 750 participants; time and setting for VOC Alpha (dominant before May 2021) and Delta (dominant after May 2021). |

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| | | infection when 2nd dose given 19-29 days after 1st dose, and VE 88% (95% CI, 48 to 97) against symptomatic infection when 2nd dose given 85+ days after 1st dose after 2nd dose (VOC Alpha age 80+).<br><br>ChAdOx1 showed VE 66% (95% CI, 47 to 77) against symptomatic infection when 2nd dose given 19-29 days after 1st dose, and VE 73% (95% CI, 56 to 83) against symptomatic infection when 2nd dose given 85+ days after 1st dose after 2nd dose (VOC Alpha age 65 to 79). | | |
| 80 | Butt (2)<br><br>*Delayed exclusion – critical ROB | Unvaccinated participants had HR 2.84 (95% CI, 1.80 to 4.47) of severe disease compared to BNT162b2 ≥14 days after 2nd dose. | Critical | Case-control study in Qatar; 456 matched cases; time and setting for VOC Alpha |
| 81 | Fowlkes | BNT162b2 (65%), mRNA-1273 (33%), or Ad26.COV2.S (2%) showed VE 91% (95% CI, 81 to 96) against infection ≥ 14 days after 2nd dose (during time of VOC Alpha).<br><br>BNT162b2 (65%), mRNA-1273 (33%), or Ad26.COV2.S (2%) showed VE 66% (95% CI, 26 to 84) against infection ≥ 14 days after 2nd dose (during time of VOC Delta).<br><br>BNT162b2 (65%), mRNA-1273 (33%), or Ad26.COV2.S (2%) showed VE 85% (95% CI, 68 to 93) against infection 14-119 days after full vaccination) and VE 73% (95% CI, 49 to 86) against infection ≥150 days after full vaccination (during time of VOC Alpha to Delta). | Moderate | Prospective cohort of HCW and other essential frontline workers in 6 states in the USA; 7,112 participants; updated report to cover VOC Delta period |
| 82 | Bhattacharya<br><br>*Delayed exclusion due to critical ROB | Covaxin (94%) and Covishield showed VE 83% (95% CI, 73 to 89) against symptomatic infection ≥ 14 days after 2nd dose.<br><br>Covaxin (94%) and Covishield showed VE 93% (95% CI, 64 to 99) against ICU admission or death ≥ 14 days after 2nd dose. | Critical | Cross-sectional cohort of HCW and their families at a single site in India; 638 participants (55 inpatients); time and setting of VOC Delta |
| 83 | Nunes | BNT162b2 (45%) or mRNA-1273 (8%) showed VE 96% (95% CI, 92 to 98) | Moderate | Data-linkage study of community-dwelling adults≥65 |

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| | | against COVID-related death ≥14 days after 2nd dose (age 65 to 79).<br><br>BNT162b2 (80%) or mRNA-1273 (2%) showed VE 81% (95% CI, 74 to 87) against COVID-related death ≥14 days after 2nd dose (age ≥80).<br><br>BNT162b2 (80%) or mRNA-1273 (2%) showed VE 86% (95% CI, 68 to 93) against COVID-related death 14 to 41 days after 2nd dose and VE 74% (95% CI, 60 to 83) against COVID-related death ≥ 98 days after 2nd dose for HR 1.80 (0.77 to 4.25) (age ≥80). | | in Portugal; 2,050,950 participants; time and setting for VOC Alpha to VOC Delta |
| 84 | Tartof | BNT162b2 showed VE 75% (95% CI, 71 to 78) against infection 7 days after 2nd dose (confirmed VOC Delta).<br><br>BNT162b2 showed VE 91% (95% CI, 88 to 92) against infection 7 days after 2nd dose (confirmed non-VOC Delta).<br><br>BNT162b2 showed VE 93% (95% CI, 85 to 87) against infection 7 to 30 days after 2nd dose and VE 53% (95% CI, 39 to 65) against infection ≥ 127+ days after 2nd dose (confirmed VOC Delta).<br><br>BNT162b2 showed VE 97% (95% CI, 95 to 99) against infection 7 to 30 days after 2nd dose and VE 67% (95% CI, 45 to 80) against infection ≥ 127+ days after 2nd dose (confirmed non-VOC Delta). | Moderate | Retrospective cohort of members of a health management organization in California; 3,436,957 participants; VOC Alpha to VOC Delta (only 28% confirmed Delta) |
| 85 | Li (3)<br><br>*Delayed exclusion – critical ROB | CoronaVac (combined with other inactivated vaccines) showed VE 59% (95% CI, 16 to 81.6) against symptomatic infection and VE 100% against severe infection ≥14 days after 2nd dose. | Critical | Test-negative study in Guangzhou, China; 366 participants; sample sequenced for VOC Delta |
| 86 | Scobie<br>*Delayed exclusion – critical ROB | BNT162b2 or mRNA-1273 (92%), or Ad26.COV2.S showed VE 90% (95% CI not reported) against infection and VE 93% (95% CI not reported) against death ≥ 14 days after 2nd dose (April to June: VOC Alpha).<br><br>BNT162b2, mRNA-1273, or Ad26.COV2.S showed VE 76% (95% | Critical | Surveillance study in 13 states in the USA; 615,454; time and setting for VOC Alpha to VOC Delta |

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

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

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| | | fully vaccinated Jan to Feb vs fully vaccinated Mar to May. | | previously in Israel; 1,423,098 participants; time and setting for VOC Alpha to VOC Delta |
| 97 | Barlow | BNT162b2 or mRNA-1273 showed VE 74% (95% CI, 65 to 82) against infection ≥ 14 days after 2nd dose.<br><br>Ad26.COV2.S showed VE 51% (95% CI, -2 to 76) against infection ≥ 14 days after 2nd dose. | Serious | Test-negative study in Oregon; 1000 participants; time and setting for VOC Delta |
| 98 | Chemaitelly (3) | BNT162b2 showed VE 65.8% (95% CI, 63.8 to 67.7) against infection 5 to 9 weeks after 2nd dose; VE 29.7% (95% CI, 21.7 to 36.9) against infection 15 to 19 weeks after 2nd dose and VE 0% (95% CI, 0 to 0) against infection 20 to 24 weeks after 2nd dose.<br><br>BNT162b2 showed VE 94.2% (95% CI, 91.0 to 96.5) against hospitalization or death 5 to 9 weeks after 2nd dose; VE 86.4% (95% CI, 69.9 to 94.8) against hospitalization or death 15 to 19 weeks after 2nd dose and VE 95.3% (95% CI, 70.5 to 99.9) against hospitalization or death 20 to 24 weeks after 2nd dose. | Serious | Test-negative study in Qatar; 1,472,761 participants; time and setting for VOC Beta to VOC Delta |
| 99 | Thompson (3) | BNT162b2 showed VE 90% (95% CI, 86 to 93) against ICU admission ≥14 days after 2nd dose.<br><br>BNT162b2 showed VE 92% (95% CI, 88 to 94) against hospitalization at 28 to 41 days after 2nd dose and VE 86% (95% CI, 74 to 93) ≥112 days after 2nd dose. | Serious | Test-negative study of adults ≥50 years in the USA; 76,463 participants; time and setting for VOC Alpha |
| 100 | Bar-On | 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 ≥12 days after 3rd dose compared to after 2nd dose. | Serious | Data-linkage study of fully vaccinated adults ≥60 in Israel comparing 2 doses of vaccine versus 3 doses of vaccine; 1,137,804 participants; time and setting for VOC Delta |
| 101 | Bruxvoort (2) | mRNA-1273 showed VE 98.4% (95% CI, 96.9 to 99.1) against infection ≥14 days after 2nd dose (VOC Alpha).<br><br>mRNA-1273 showed VE 86.7% (95% CI, 84.3 to 88.7) against infection ≥14 days after 2nd dose (VOC Delta). | Serious | Test-negative study in Kaiser Permanente group in California; 48,918 participants; sequenced for VOC Alpha, VOC Delta and VOI Mu (results not included in this LES) |

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| | | mRNA-1273 showed VE 94.1% (95% CI, 90.5 to 96.3) against infection 14 to 60 days after 2nd dose (VOC Delta).<br><br>mRNA-1273 showed VE 80.0% (95% CI, 70.2 to 86.6) against infection 151 to 180 days after 2nd dose (VOC Delta). | | |
| 102 | Tande (2) | BNT162b2 or mRNA-1273 showed VE 91% (95% CI, 72 to 98) against infection ≥14 days after 2nd dose (January to March – VOC Alpha).<br><br>BNT162b2 or mRNA-1273 showed VE 63% (95% CI, 44 to 76) against infection ≥14 days after 2nd dose (June to August – VOC Delta). | Serious | Point prevalence screening study in Mayo Clinic, USA; 46,008 participants; time and setting for VOC Alpha to VOC Delta |
| 103 | Young-Xu (2) | Two doses of BNT162b2 reduced risk of infection by HR 66% (95% CI, 22 to 86) compared to previously infected adults age 65+ (June to August VOC Delta).<br><br>Two doses of mRNA-1273 reduced risk of infection by HR 68% (95% CI, 30 to 86) and death by HR 30% (95% CI, -11 to 1) compared to previously infected adults age 65+ (June to August VOC Delta). | Moderate | Retrospective cohort study of previously infected adults followed by Veterans Affairs in USA; 47,102 participants; time and setting for VOC Delta |
| 104 | de Gier (1) | Fully vaccinated index to unvaccinated (hh contact) showed VET 73% (95% CI: 65 to 79).<br><br>BNT162b (case) showed VET 70% (95% CI, 61 to 77) when fully vaccinated.<br><br>mRNA-1273 (case) showed VET 88% (95% CI, 50 to 97) when fully vaccinated.<br><br>ChAdOx1 (case) showed VET 58% (95% CI, -12 to 84) when fully vaccinated.<br><br>Ad26.COV2.S (case) showed VET 58% (95% CI, -12 to 84) when fully vaccinated. | Serious | Retrospective cohort of household and close contacts in the Netherlands; 113,582 cases and 253,168 contacts; time and setting for VOC Alpha<br><br>(hh = household) |

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| | | BNT162b showed VE 65% (95% CI, 60 to 70) when hh contact was fully vaccinated.<br><br>mRNA-1273 showed VE 91% (95% CI, 79 to 97) when hh contact was fully vaccinated.<br><br>ChAdOx1 showed VE 87% (95% CI, 77 to 93) when hh contact was fully vaccinated.<br><br>Ad26.COV2.S showed VE 12% (95% CI, -71 to 54) when hh contact was fully vaccinated. | | |
| 105 | de Gier (2) | Fully vaccinated index to unvaccinated (hh contact) showed VET 63% (95% CI: 46 to 75).<br><br>BNT162b (>50%) or mRNA-1273 or ChAdOx1 or Ad26.COV2.S (case) showed VET 40% (95% CI, 20 to 54) when both case and contacts are fully vaccinated. | Serious | Retrospective cohort of household and close contacts in the Netherlands; 4,921 cases and 7,771 contacts; time and setting for VOC Delta |
| 106 | Manley | mRNA-1273 (50%) or BNT162b (48%) or Ad26.COV2.S (2%) showed OR of 8.89 (95% CI, 5.92 to 13.34) for unvaccinated vs fully vaccinated against infection (VOC Alpha)<br><br>mRNA-1273 (50%) or BNT162b (48%) or Ad26.COV2.S (2%) showed OR of 2.27 (95% CI, 1.72 to 3.00) for unvaccinated vs fully vaccinated against infection (VOC Delta) | Serious | Retrospective cohort of maintenance dialysis patients in USA; 15,251 participants; time and setting for VOC Alpha to VOC Delta |
| 107 | Eyre | BNT162b2 (cases) showed VET 82% (95% CI, 71 to 88) against transmission after 2nd dose. (VOC Alpha)<br><br>ChAdOx1 (cases) showed VET 63% (95% CI, 37 to 78) against transmission after 2nd dose. (VOC Alpha)<br><br>BNT162b2 (contacts) showed VE 94% (95% CI, 90 to 96) against infection after 2nd dose. (VOC Alpha)<br><br>ChAdOx1 (contacts) showed VE 71% (95% CI, 51 to 83) against infection after 2nd dose. (VOC Alpha) | Serious | Retrospective cohort of contacts in England; 99,597cases and 151,821 contacts; S-gene proxy for VOC Alpha and VOC Delta |

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| | | BNT162b2 (cases) showed VET 65% (95% CI, 52 to 74) against transmission after 2nd dose. (VOC Delta)<br><br>ChAdOx1 (cases) showed VET 36% (95% CI, 28 to 43) against transmission after 2nd dose. (VOC Delta)<br><br>BNT162b2 (contacts) showed VE 90% (95% CI, 87 to 92) against infection after 2nd dose. (VOC Delta)<br><br>ChAdOx1 (contacts) showed VE 72% (95% CI, 68 to 75) against infection after 2nd dose. (VOC Delta). | | |
| 108 | Martinez-Baz (2) | BNT162b2 (contacts) showed VE 71% (95% CI, 61 to 78) against infection after 2nd dose (VOC Alpha)<br><br>mRNA-1273 (contacts) showed VE 86% (95% CI, 56 to 95) against infection after 2nd dose (VOC Alpha)<br><br>ChAdOx1 (contacts) showed VE 38% (95% CI, -42 to 73) against infection after 2nd dose (VOC Alpha)<br><br>BNT162b2 (contacts) showed VE 67% (95% CI, 59 to 74) against infection after 2nd dose (VOC Delta)<br><br>mRNA-1273 (contacts) showed VE 77% (95% CI, 64 to 85) against infection after 2nd dose (VOC Delta)<br><br>ChAdOx1 (contacts) showed VE 55% (95% CI, 39 to 67) against infection after 2nd dose (VOC Delta)<br><br>ChAdOx1 plus BNT162b2 (contacts) showed VE 86% (95% CI, 45 to 97) against infection (VOC Delta) | Serious | Prospective cohort of close contacts in Spain; 12,263 cases and 30,240 contacts; sequenced for VOC Alpha to VOC Delta |
| 109 | Cohn | BNT162b2 showed VE 49% (95% CI, 47 to 52) against infection at least 15 days after last dose (August: VOC Delta)<br><br>mRNA-1273 showed VE 64% (95% CI, 62 to 66) against infection at least 15 | Serious | Data-linkage study of veterans in USA; 619,755 participants; time and setting for VOC Alpha to VOC Delta (only Delta reported here) |

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| | | days after last dose (August: VOC Delta)<br><br>Ad26.COV2.S showed VE 3% (95% CI, -0.1 to 12) against infection at least 15 days after last dose (August: VOC Delta) | | |
| 110 | Rosenberg (2) | BNT162b2 showed VE 69% (95% CI, 67.4 to 70.6) against infection at least 15 days after last dose (August: VOC Delta; age 18-49)<br><br>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)<br><br>Ad26.COV2.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)<br><br>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+)<br><br>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+)<br><br>Ad26.COV2.S showed VE 70.8% (95% CI, 65.7 to 76.0) against infection at least 15 days after last dose (August: VOC Delta; age 65+) | Serious | Prospective study in New York; 8,834,604 participants; time and setting for VOC Alpha to VOC Delta (only Delta reported here). Also compared VE over time since vaccination (results not reported here) |
| 111 | Robles-Fontan | BNT162b2 showed VE 56% (95% CI, 53 to 59) against infection at least 15 days after last dose (October: VOC Delta)<br><br>mRNA-1273 showed VE 71% (95% CI, 68 to 74) against infection at least 15 days after last dose (October: VOC Delta)<br><br>Ad26.COV2.S showed VE 27% (95% CI, 17 to 37) against infection at least 15 days after last dose (October: VOC Delta) | Serious | Data-linkage study in Puerto Rico; 1,913,454 person-years; time and setting for VOC Alpha to VOC Delta (only results for Delta reported here) |

| | | | | |
|---|---|---|---|---|
| 112 | Glatman-Freedman (2) | BNT162b2 showed VE 91.5% (95% CI, 88.2 to 93.9) against infection at least 8 days after 2nd dose in adolescents age 12 to 15 years. There were no deaths in either group. | Serious | Population cohort in Israel of adolescents age 12 to 15 years; 2,034,591 vaccinated person-days and 13,623,714 unvaccinated person-days; time and setting for VOC Delta |
| 113 | Chin | mRNA-1273 showed VE 56.6% (95% CI, 42 to 67.5) against infection at least 14 days after 2nd dose. | Serious | Outbreak report from a prison in California; 827 participants; sample sequenced for VOC Delta |
| 114 | Nordstrum | BNT162b2 showed VE 47% (95% CI, -39 to 55) against symptomatic infection 121 to 180 days after second dose.<br><br>mRNA-1273 showed VE 71% (95% CI, 56 to 81) against symptomatic infection 121 to 180 days after second dose.<br><br>ChAdOx1 showed VE -19% (95% CI, --97 to 28) against symptomatic infection >120 days after second dose.<br><br>ChAdOx1/mRNA showed VE 66% (95% CI, 41 to 80) against symptomatic infection >120 days after second dose.<br><br>BNT162b2 or mRNA-1273 or ChAdOx1 showed VE 42% (95% CI, -35 to 75) against severe disease (hospitalization or death) >180 days after second dose | Serious | Case-control study in Sweden; 1,684,958 participants; time and setting for VOC Alpha to VOC Delta (only Delta results reported here) |

| Section 2: excluded studies | |
|---|---|
| **Author** | **Reason for exclusion** |
| Akhrass | Delayed exclusion – Clinical outcomes of interest for this LES not reported |
| Albahrani | Prevalence of variants unknown and suspected to be <50% |
| Alencar | Critical risk of bias |
| Alhamlan | Vaccine effectiveness not reported |
| Alharbi | Prevalence of variants unknown and suspected to be <50% |
| Ali | Prevalence of variants unknown and suspected to be <50% |
| Alkhafaji | Prevalence of variants unknown and suspected to be <50% |
| Allen | Serious risk of bias |
| Almufty | Prevalence of variants unknown and suspected to be <50% |
| Al-Qahtani | Delayed exclusion – critical risk of bias |
| Apisarnthanarak | Vaccine effectiveness not reported |
| Arashiro | Vaccine effectiveness not reported |
| Ayass | Clinical outcomes of interest for this LES not reported |
| Baden | Critical risk of bias |
| Bailly | Delayed exclusion – critical risk of bias |
| Bajema | Clinical outcomes of interest for this LES not reported |
| Barchuk | Clinical outcomes of interest for this LES not reported |
| Bergwerk | Vaccine effectiveness not reported |
| Bernal (2) | Delayed exclusion – critical risk of bias |
| Bhattacharya | Delayed exclusion – critical risk of bias |
| Bianchi | Delayed exclusion – critical risk of bias |
| Bjork | Prevalence of variants unknown and suspected to be <50% |
| Blaiszik | Clinical outcomes of interest for this LES not reported |
| Blaiszik | Clinical outcomes of interest for this LES not reported |
| Borobia | Clinical outcomes of interest for this LES not reported |
| Britton | Prevalence of variants unknown and suspected to be <50% |
| Brown | Vaccine effectiveness not reported |
| Bruxvoort | Prevalence of variants unknown and suspected to be <50% |
| Butt | Prevalence of variants unknown and suspected to be <50% |
| Butt | Critical risk of bias |
| Butt (2) | Delayed exclusion – critical risk of bias |
| Cabezas | Prevalence of variants unknown and suspected to be <50% |
| Caillard | Clinical outcomes of interest for this LES not reported |
| Cavanaugh | Delayed exclusion – VOI not VOC |
| Charles Pon Ruban | Vaccine effectiveness not reported |
| Charmet | Serious risk of bias |
| Chau | Vaccine effectiveness not reported |
| Clemens | Prevalence of variants unknown and suspected to be <50% |

| | |
|---|---|
| Corchado-Garcia | Prevalence of variants unknown and suspected to be <50% |
| Dash | Critical risk of bias |
| de Gier Brechje | Prevalence of variants unknown and suspected to be <50% |
| Dolzhikova | Critical risk of bias |
| Domi | Prevalence of variants unknown and suspected to be <50% |
| El Sahly | Prevalence of variants unknown and suspected to be <50% |
| Ella | Prevalence of variants unknown and suspected to be <50% |
| Elliot | Delayed exclusion – critical risk of bias |
| El-Sahly | Prevalence of variants unknown and suspected to be <50% |
| Falsey | Prevalence of variants unknown and suspected to be <50% |
| Farinholt | Vaccine effectiveness not reported |
| Fisher | Prevalence of variants unknown and suspected to be <50% |
| Frenck | Prevalence of variants unknown and suspected to be <50% |
| Furer | Delayed exclusion – critical risk of bias |
| Geisen | Clinical outcomes of interest for this LES not reported |
| Ghosh | Delayed exclusion – critical risk of bias |
| Gils | Clinical outcomes of interest for this LES not reported |
| Gorgels | Prevalence of variants unknown and suspected to be <50% |
| Grannis | Clinical outcomes of interest for this LES not reported |
| Gray | Prevalence of variants unknown and suspected to be <50% |
| Griffin | Vaccine effectiveness not reported |
| Guijarro | Prevalence of variants unknown and suspected to be <50% |
| Gupta | Prevalence of variants unknown and suspected to be <50% |
| Gupta | Vaccine effectiveness not reported |
| Haas (2) | Modelling study |
| Hacisuleyman | Critical risk of bias |
| Herlihy | Delayed exclusion – critical risk of bias |
| Hetemaki | Vaccine effectiveness not reported |
| Hitchings(2) | Delayed exclusion – critical risk of bias |
| Hollinghurst | Serious risk of bias |
| Hyams | Delayed exclusion - Clinical outcomes of interest for this LES not reported |
| Iliaki | Prevalence of variants unknown and suspected to be <50% |
| Iliaki | Prevalence of variants unknown and suspected to be <50% |
| Ismail | Delayed exclusion - Clinical outcomes of interest for this LES not reported |
| Jacobson | Critical risk of bias |
| John | Prevalence of variants unknown and suspected to be <50% |
| Jones | Critical risk of bias |
| Kaabi | Prevalence of variants unknown and suspected to be <50% |
| Kale | Delayed exclusion – critical risk of bias |
| Kaur | Delayed exclusion – critical risk of bias |
| Keegan | Critical risk of bias |
| Khan | Prevalence of variants unknown and suspected to be <50% |

| | |
|---|---|
| Khawaja | Critical risk of bias |
| Kojima | Prevalence of variants unknown and suspected to be <50% |
| Kustin | Delayed exclusion - only included infected population |
| Lamprini | Clinical outcomes of interest for this LES not reported |
| Lefèvre | Critical risk of bias |
| Li | Phase 1 trial |
| Li (2) | Clinical outcomes of interest for this LES not reported |
| Li (3) | Delayed exclusion – critical risk of bias |
| Ling | Prevalence of variants unknown and suspected to be <50% |
| Linsenmeyer | Vaccine effectiveness not reported |
| Liu | Vaccine effectiveness not reported |
| Loconsole | Vaccine effectiveness not reported |
| Luo | Vaccine effectiveness not reported |
| Marco | Delayed exclusion – critical risk of bias |
| Mattar | Prevalence of variants unknown and suspected to be <50% |
| Mazgatos | Critical risk of bias |
| McEvoy | Prevalence of variants unknown and suspected to be <50% |
| Menni | Serious risk of bias |
| Mizrahi | Modelling study |
| Monge | Prevalence of variants unknown and suspected to be <50% |
| Mor | Prevalence of variants unknown and suspected to be <50% |
| Moustsen-Helms | Prevalence of variants unknown and suspected to be <50% |
| Munitz | Clinical outcomes of interest for this LES not reported |
| Musser | Vaccine effectiveness not reported |
| Mutnal | Vaccine effectiveness not reported |
| Nanduri | Critical risk of bias |
| Oduwole | Clinical outcomes of interest for this LES not reported |
| Olmedo | Clinical outcomes of interest for this LES not reported |
| Olson | Clinical outcomes of interest for this LES not reported |
| Palacios | Prevalence of variants unknown and suspected to be <50% |
| Paris | Prevalence of variants unknown and suspected to be <50% |
| Pattni | Modelling study |
| Pawlowski | Critical risk of bias |
| Perry | Clinical outcomes of interest for this LES not reported |
| Pilishvili | Prevalence of variants unknown and suspected to be <50% |
| Piltch-Loeb | Prevalence of variants unknown and suspected to be <50% |
| Polinski | Delayed exclusion – critical risk of bias |
| Raches Ella | Phase 1 trial |
| Rana | Critical risk of bias |
| Regev-Yochay | Prevalence of variants unknown and suspected to be <50% |
| Riemersma | Clinical outcomes of interest for this LES not reported |
| Riley | Critical risk of bias |

| | |
|---|---|
| Rivelli | Clinical outcomes of interest for this LES not reported |
| Rovida | Critical risk of bias |
| Rudolph | Prevalence of variants unknown and suspected to be <50% |
| Salmeron Rios | Prevalence of variants unknown and suspected to be <50% |
| Sansone | Critical risk of bias |
| Satwik | Delayed exclusion – critical risk of bias |
| Scobie | Delayed exclusion – critical risk of bias |
| Self | Clinical outcomes of interest for this LES not reported |
| Sharma | Prevalence of variants unknown and suspected to be <50% |
| Shimabukuro | Clinical outcomes of interest for this LES not reported |
| Shrotri | Delayed exclusion – critical risk of bias |
| Starrfelt | Serious risk of bias |
| Swift | Prevalence of variants unknown and suspected to be <50% |
| Tande | Prevalence of variants unknown and suspected to be <50% |
| Tanriover | Prevalence of variants unknown and suspected to be <50% |
| Tenforde | Clinical outcomes of interest for this LES not reported |
| Tenforde (2) | Clinical outcomes of interest for this LES not reported |
| Thangaraj | Critical risk of bias |
| Thiruvengadam | Critical risk of bias |
| Thompson (1) | Prevalence of variants unknown and suspected to be <50% |
| Thompson (2) | Prevalence of variants unknown and suspected to be <50% |
| Vahidy | Prevalence of variants unknown and suspected to be <50% |
| Vasileiou | Clinical outcomes of interest for this LES not reported |
| Veneti | Clinical outcomes of interest for this LES not reported |
| Victor | Critical risk of bias |
| Volkov | Modelling study |
| Voysey | Prevalence of variants unknown and suspected to be <50% |
| Waldhorn | Serious risk of bias |
| Wickert | Critical risk of bias |
| Wijtvliet | Clinical outcomes of interest for this LES not reported |
| Williams (2) | Critical risk of bias |
| Young-Xu | Prevalence of variants unknown and suspected to be <50% |
| Zacay | Delayed exclusion – critical risk of bias |
| Zhong | Clinical outcomes of interest for this LES not reported |

**Appendix 2: Glossary**

**AZ**: AstraZeneca

**Alpha**: variant of concern B.1.1.7

**Beta:** variant of concern B.1.351

**Delta:** variant of concern B.1.617.2

**Gamma:** variant of concern P.1

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

**HCW:** Healthcare workers

**LTC:** Long-term care

**LTCF:** Long-term care facility

**MOD**: Moderna

**Obs:** observational study

**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**

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

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

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

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

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

Review question:

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

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

**Critical Appraisal Process**

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

| VE Study Characteristics that may introduce bias | Description |
|---|---|
| **Study design**<br><br>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<br><br>Examples and typical judgement:<br>• test-negative design with a clearly defined symptomatic study population (low)<br>• test-negative design (mixed or unclear study population) or case-control or cohort design or data-linkage with no concerns (moderate)<br>• cross-sectional design or case-control (concerns about whether controls had same access to vaccines/risk of exposure to COVID or unclear) or cohort design (concerns that exposed and non-exposed were not drawn from the same population) (serious) |
| **Method for confirming vaccination** | Questionnaires are prone to recollection bias; Population databases developed for purpose of tracking COVID vaccines minimize this type of bias<br><br>Examples and typical judgement: |

| | |
|---|---|
| ROBINS-I: Bias in classification of interventions | • database linkage study (low)<br>• Questionnaire with confirmation by an additional method (e.g. registry) of at least a subset of study population (moderate)<br>• Questionnaire without confirmation by an additional method (serious)<br>• Estimating vaccination status based on surveillance data alone (critical) |
| **Databases used for retrieval of COVID test results, participant prognostic factors, and clinical outcomes**<br><br>ROBINS-I: Bias in classification of interventions | Databases developed for collecting data on COVID are less prone to bias due to missing information and misclassification<br><br>Examples and typical judgement:<br>• database for non-COVID purpose but with individual level data (moderate)<br>• database for non-COVID purpose without individual level data (serious)<br>• no or unclear description of database type (critical) |
| **Assignment of infection start date**<br><br>ROBINS-I: Bias in classification of interventions | Using date of symptom onset (if within 10 days of testing) as infection start date reduces risk of misclassification bias (e.g., vaccinated participant who is reported as COVID+ may have been infected prior to receiving the vaccine or during non-immune period) and sensitivity of assays decreases over time<br><br>Examples and typical judgement:<br>• using a PCR positive test that was part of an ongoing standardized monitoring system (e.g., within a health network) (low)<br>• using sample date without interview or documented confirmation of symptoms ≤ 10 days (relevant for symptomatic disease only) (serious) |
| **Verification of symptoms**<br><br>ROBINS-I: Bias in classification of interventions | Prospective, standardized collection of symptoms from patients reduces risk of missing information bias; testing within 10 days after symptom onset reduces risk of false-negative COVID test<br><br>Examples and typical judgement:<br>• using sample date without patient report/ documented confirmation of symptoms ≤ 10 days (relevant for symptomatic disease only) (serious)<br>• if symptomatic COVID is not an outcome (no information) |

| | |
|---|---|
| **Accounting for non-immune period (first 14 days after first vaccine dose)**<br><br>ROBINS-I: Bias due to confounding | Reported absence of vaccine effect during non-immune period reduces risk of residual confounding bias<br><br>Example/common case:<br>• presence of an effect during non-immune period or result not reported (moderate)<br>• unclear that non-immune period was considered (serious) |
| **Inclusion of participants with prior COVID infection**<br><br>ROBINS-I: Bias due to confounding | Exclusion (or separate analysis) of participants with prior COVID infection reduces concern about differences in infectivity as well as risk-taking and health-seeking behaviour<br><br>Examples and typical judgement:<br>• inclusion of prior infection status as a covariate in the models (moderate)<br>• previously infected not excluded or analyzed separately (serious) |
| **Accounting for calendar time**<br><br>ROBINS-I: Bias due to confounding (time-varying confounding) | Accounting for calendar time reduces bias due to differences in vaccine accessibility and risk of exposure over time<br><br>Examples and typical judgement:<br>• use of time-varying statistics without explicit mention of adjustment for calendar time (moderate)<br>• not taken into account but short-time frame (e.g. ≤2 months) (serious)<br>• not taken into account and time frame >2 months (critical) |
| **Adjustment for prognostic factors**<br><br>ROBINS-I: Bias due to confounding | Adjustment for prognostic factors for COVID infection, severity of disease, and vaccination, such as age, gender, race, ethnicity, socioeconomic factors, occupation (HCW, LTC), and chronic medical conditions<br><br>Examples and typical judgement:<br>• no or insufficient adjustment for occupation (or number of tests as a surrogate for exposure risk) - exception age>65 or LTCF resident (moderate)<br>• no or insufficient adjustment for socioeconomic factors (or neighborhood or income as a surrogate), race, ethnicity (serious)<br>• no or insufficient adjustment for age (any study population) or chronic medical conditions (LTC)(critical) |
| **Testing frequency**<br><br>ROBINS-I: Bias in measurement of outcomes | Similar frequency of testing between groups reduces risk of bias introduced by detecting asymptomatic infection in one group but not in another (e.g. when only one group undergoes surveillance screening) |

| | |
|---|---|
| | Examples and typical judgement:<br>• no systematic screening but consistent methods for detection in one group vs. the other, e.g., within health networks (moderate)<br>• screening performed for a subset of both study groups (serious)<br>• screening performed routinely in one study group but not in the other (critical) |

**Appendix 6: Detailed description of the narrative summary statement**

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

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

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

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

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