COVID-19 Living Evidence Synthesis #6

(Version 7: 1 June 2021)

Question

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

Findings

We present in Table 1 the key findings about vaccine effectiveness in variants of concern (VOC). Six studies have been added since the previous edition of this living evidence synthesis, all of which are signaled by a last-updated date of 01 June 2021 (highlighted in yellow). New studies for VOC: Alpha [B.1.1.7] (4), Beta [B.1.351] (3), and Gamma [P.1] (1).

Overall, we have moderate quality evidence that BNT162b2 [Pfizer] prevents infection from [VOC Alpha, Beta] and prevents severe disease from VOC Alpha.

We have moderate quality evidence that mRNA-1273 [Moderna] prevents infection from VOC Alpha and low quality evidence that it prevents infection from VOC Beta.

We have moderate certainty evidence that ChAdOx1nCoV-19 [AstraZeneca] prevents infection from VOC Alpha and moderate certainty evidence that it does not prevent infection from VOC Beta.

We have moderate certainty evidence that Johnson & Johnson prevents infection from VOC Beta.

We have moderate certainty evidence that NVX-Co2373 [Novavax] prevents infection from VOC Alpha and Beta.

Methods are presented in Box 1 and Appendices 1-5.

Box 1: Our approach

We retrieved candidate studies and updates to living evidence syntheses on vaccine effectiveness using the following mechanisms: 1) PubMed via COVID-19+ Evidence Alerts; 2) systematic scanning of pre-print servers; 3) updates to the COVID-END inventory of best evidence syntheses; and 4) cross-check with updates from the VESPa team. Each version will include studies and updates to living evidence syntheses identified up to two days before the version release date.

We include studies with clinical outcomes (whether the vaccines prevent infection, severe disease, death, and prevent transmission) and exclude studies that capture only antibody responses. As to the relevance to VOC, we include studies where direct measures are reported, or where reasonable assumptions can be made about the variants prevalent in the jurisdiction at the time of the study.

A full list of studies included, under appraisal, or excluded as non-contributory, is provided as **Appendix 1**.

We extract data from each study in duplicate (McMaster University and University of Ottawa) using the template provided in **Appendix 2**.

We critically appraise each study in duplicate using a simplified version of the ROBINS-I tool as described in **Appendix 3**. The lower the ROBINS-I score, the higher the study quality.

We summarize the evidence by presenting narrative evidence profiles across studies, with or without pooling as appropriate, and rating our confidence in the effect using the GRADE approach for treatment effect (5 domains to downgrade, 3 to upgrade), starting at low confidence for observational evidence. A more detailed explanation of the narrative summary statement is provided in **Appendix 4**.

We update this document every Friday and post it on the COVID-END website. The McMaster/BMJ team maintaining a living evidence synthesis about vaccine efficacy will use our extracted data in their meta-analyses, GRADE assessments, and guideline development. We will incorporate their findings as they become available.

Table 1: Key findings about vaccine effectiveness

Vaccine	Effectiveness	Findings
Pfizer	Overall	Compared to placebo, vaccination with BNT162b2 probably reduces the incidence of symptomatic cases of COVID-19 substantially, although there remains uncertainty about the impact of reducing mortality or severe disease. The evidence for any difference in serious adverse effects is uncertain, although the vaccination probably increases the incidence of any adverse event. Review of RCTs (AMSTAR 10/11); *last search date 2021-05-07;* GRADE evidence profile updated on 2021-01-25
	By variant of concern	
	• Alpha	BNT162b2 provides protection against variant Alpha for the following outcomes 14 days after 1st dose: • 46 to 60% from infection BNT162b2 provides protection against variant Alpha for the following outcomes 7 days after 2nd dose: • 70 to 94% from infection • 90% from symptomatic infection • 92 to 98% from severe disease • 94 to 98% from death (11 Obs, moderate quality of evidence) [1][2][3][9][10][11][15][16][22][23][24]; *last update 2021-06-01*
	• Beta	BNT162b2 provides protection against variant Beta for the following outcomes 35-41 days after 1st dose: • 43% (95 CI, 22 to 59) from symptomatic infection BNT162b2 provides protection against variant Beta for the following outcome 7 days after 2nd dose: • 88% (95% CI, 61 to 96) from symptomatic infection (1 Obs)[24]; *last update 2021-06-01*
	• Gamma	no data
	• Epsilon [B.1.427/B.1.429]	no data
	• R.1	no data
	By special population	
	• HCW, Alpha	BNT162b2 provides protection against variant Alpha for the following outcomes 21 days after 1st dose: • 70% (95% CI, 55 to 85) from infection BNT162b2 provides protection against variant Alpha for the following outcomes 7 days after 2nd dose: • 85 to 96% (95% CI, 74 to 96) from infection • 97% (95% CI, 94 to 99) from symptomatic infection (3 Obs)[12][26][27]; *last update 2021-06-01*
	• LTC, Alpha	BNT162b2 provides protection against variant Alpha for the following outcomes 35-48 days after 1st dose:

		• 70% (aHR 0.3, 95% CI, 0.17 to 0.71) from infection (1 Obs, median age 86)[13];*last update 2021-04-30*
	• Over 80 years, Alpha	BNT162b2 provides protection against variant Alpha for the following outcomes 14 to 28 days after 1st dose: • 71-81% from hospitalization BNT162b2 provides protection against variant Alpha for the following outcomes 14 days after 2nd dose: • 93% (95% CI, 89 to 95) from hospitalization (2 Obs, low quality of evidence)][14] [21]; *last update 2021-05-21*
	• HCW, Beta or Gamma	BNT162b2 provides protection against variant Beta or Gamma for the following outcomes 14 to 42 days after 1st dose: • 37.2% (95% CI, 16.6 to 52.7) from infection BNT162b2 provides protection against variant Beta or Gamma for the following outcome 7 days after 2nd dose: • 79.2% (95% CI, 64.6 to 87.8) from infection (1 Obs)[28]; *last update 2021-06-01*
	• LTC, Beta	BNT162b2 provides protection against variant Beta for the following outcome >28 days after 2 doses: • 50% (95% CI, 34 to 73) from infecton (1 Obs)[25]; *last update 2021-06-01*
	• LTC, R.1	BNT162b2 provides protection against variant R.1 for the following outcomes ≥ 14 days after 2nd dose: • 66.2% (95% CI, 40.5 to 80.8) from infection • 94.4% (95% CI, 44.6 to 99.4) from death (1 Obs); [17] Last update 2021-05-07
Moderna	Overall	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 2021-05-07;* GRADE evidence profile updated on 2021-01-25
	By variant of concern	
	• Alpha	mRNA-1273 provides protection against variant Alpha for the following outcomes 15-41 days after 1st dose: • 58.9 (95% CI, −9.7 to 84.5) from infection • 61% (95% CI, 56 to 66) from symptomatic infection mRNA-1273 provides protection against variant Alpha for the following outcomes 7-15 days after 2nd dose: • 85.7 (95% CI, 67.2 to 93.9) from infection • 90% (95% CI, 88 to 100) from symptomatic infection (2 Obs) [9][24]; *last update 2021-06-01*
	• Beta	mRNA-1273 provides protection against variant Beta for the following outcomes 35-41 days after 1st dose: • 43% (95 CI, 22 to 59) from symptomatic infection

		mRNA-1273 provides protection against variant Beta for the following outcome 7 days after 2nd dose: • 88% (95% CI, 61 to 96) from symptomatic infection (1 Obs)[24]; *last update 2021-06-01*
	• Gamma	no data
	• Epsilon	no data
Astra Zeneca	Overall	Compared to vaccinating with MedACWY (meningitis vaccine), vaccination with ChAd0x1 probably reduces the incidence of asymptomatic cases of COVID-19 as well as the number of positive tests and may reduce severe or critical disease and hospitalizations. The effects on mortality are uncertain, and adverse effects are probably less frequent. (*)Review of RCTs (AMSTAR 10/11); *last search date 2021-05-28;* 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.
	By variant of concern	
	• Alpha	ChAdOx1nCoV-19 provides protection against variant Alpha for the following outcome 21 to 28 after 1st dose: • 65-74% from any infection (2 Obs, moderate to low quality of evidence)[10][11] ChAdOx1nCoV-19 provides protection against variant Alpha for the following outcome after 2 doses: • 70.4% (95% CI, 43.6 to 84.5) from symptomatic infection (1 RCT) [5]; *last updated 2021-04-22*
	• Beta	ChAdOx1nCoV-19 provides protection against variant Beta for the following outcome after 2 doses: • 10.4% (95% CI, -76.8 to 54.8) from mild to moderate disease • no data on protection against severe disease (1 RCT) [4]; *last update 2021-04-14*
	• Gamma	no data
	• Epsilon	no data
	Special populations	
	• LTC, Alpha	ChAdOx1nCoV-19 provides protection against variant Alpha for the following outcomes 35-48 days after 1st dose: • 70% (aHR 0.32, 95% CI, 0.15 to 0.66) from infection (1 Obs)[13]; *last update 2021-04-30*
	• Over 80 years, Alpha	ChAdOx1nCoV-19 provides protection against variant Alpha for the following outcomes 14 to 28 days after 1st dose: • 73-80% from hospitalization

		(2 Obs, low quality of evidence)][14] [21]; *last update 2021-05-21*
Johnson & Johnson	Overall	[Johnson & Johnson's Janssen vaccine] Vaccination with AD26.COV2.S probably reduces the incidence of symptomatic cases of COVID-19 by 66%, 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 2021-05-28*. GRADE evidence profile updated on 2021-05-28 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 the evidence) [8] 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 updated 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)[8]; *last updated 2021-04-22*
	• Gamma	no data
	• Epsilon	no data
Sinovac (Coronavac)	• Overall	[Coronavac vaccine] Compared to placebo, vaccination with CoronaVac probably reduces the incidence of symptomatic cases of COVID-19 by 50%, close to the lowest level deemed effective by the WHO (www.afro.who.int/news/what-covid-19-vaccine-efficacy) and it may substantially reduce the incidence of hospitalization or severe diseases 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 2021-05-07*
	By variant of concern	
	• Alpha	no data
	• Beta	no data
	• Gamma	no data
	• Epsilon	no data
	By special population	

	• HCW, Gamma	CoronaVac provides protection against variant Gamma for the following outcomes ≥14 days after 1st dose: • 35.1% (95% CI, -6.6 to 60.5) from infection • 49.6% (95% CI, 11.3 to 71.4) from symptomatic infection (1 Obs study)[19]; last update 2021-05-07
Sinopharm	• Overall	Synthesis pending. Review of RCTs (AMSTAR /11); last search date 2021-05-13
Novavax	• Overall	[Novavax vaccine] Vaccination with the Novavax vaccine probably reduces the incidence of symptomatic COVID-19 substantially, while it probably increase the risk of any adverse events; its effects on other outcomes are uncertain Review of RCTs (AMSTAR 10/11); last search date 2021-05-28; GRADE evidence profile updated on 2021-05-28
	By variant of concern	
	• Alpha	NVX-CoV2373 provides protection against variant Alpha for the following outcome after 2 doses: • 89.7% (95% CI, 80.2 to 94.6) against infection. • No hospitalizations or deaths in vaccinated group • Post hoc: 86.3% (95% CI, 71.3 to 93.5) against confirmed Alpha variant infection (1 RCT), [20]; last updated 2021-05-21
	• Beta	NVX-CoV2373 provides protection against variant Beta for the following outcome after 7 days after 2nd dose: • 57.7% (95% CI, 25.7 to 75.9) from infection (1 RCT), [18]; last update 2021-05-07

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 6.7): What is the efficacy and effectiveness of available COVID-19 vaccines in general and specifically for variants of concern? Hamilton: Health Information Research Unit, 1 June 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 the same VE as the phase III trial (46-60% 14 days after 1st dose and 92% 7 days after 2nd dose) in a population with an estimated circulation of Alpha. up to 80% against any infection.	Moderate	Cohort Israel, .5 M matched; large population, KM, concordant with trial;2 M excluded (possible overlap with Haas)
2	Haas	BNT162b2 showed the same VE as the phase III trial (91% [>7 days] and against asymptomatic infections [94%], hospitalization [98%] and death [98%], respectively, 14 days after 2nd dose in a population with 94% of Alpha.	Low	Cohort Israel, concordant with trial; effect on death (possible overlap with Dagan) Updated May 14 due to final publication
3	Kustin	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% B.1.135.	Moderate	Case-control Israel, asymmetry in VOC; small sample for Beta (no overlap, CHS cohort).
4	Madhi	Two doses of the ChAdOx1 nCoV-19 vaccine had no efficacy against the Beta variant in preventing mild to-moderate Covid-19.	Moderate	RCT South Africa; VE 20% in seronegative and 10% in seropositive – 75% (95% CI, 9 to 95) after 1 dose before emergence of variant. Underpowered for 20% efficacy
5	Emary	ChAdOx1nCoV-19 (two doses) VE against the Alpha variant was 70.4% (95% CI, 43.6 to 84.5) for Alpha and 81.5% (95% CI, 67.9 to 89.4) for non-Alpha.	Low	RCT UK; neutralization of Alpha 9 times lower
6	Shah	ChAdOx1nCoV-19 reduced infection (and hospitalization) in household contacts of vaccinated HCW by about 30% (HR, 0.70, 95% CI, 0.64 to 0.78); BNT162b2 reduced infection in HCW by about 55% (HR 0.45, 95% CI, 0.42 to 0.49) and hospitalization by 91% (HR 0.16, 95% CI, 0.09 to 0.27)	Moderate	Observational Scotland - (25% of cases had received 2 doses)
7	Thompson	BNT162b2 and mRNA-1273 VE in HCW, first-line responder and essential/frontline workers was 80%	Low	Observational US, multicentric

		(95% CI, 59 to 90) after the first dose and 90% (95% CI, 68 to 97) after the second dose against any infection.		Prospective, standardized, weekly PCR testing; small size. 63% Pfizer, 27% Moderna; larger prevalence of infection in male, Hispanic.
8	Sadoff	For Ad26.COV2.S, VE was 66.9% (95% CI, 59.0 to 73.4) at 14 days and 66.1% (95% CI, 55.0 to 74.8) at 28 days against any infection. 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). VE against VOC Beta was 52.0% and 64.0% at 14 days and 28 days, respectively, and 73.1% for moderate cases and 81.7% for severe cases.	Low	RCT (~40,000) Argentina, Brazil, Chile, Colombia, Mexico, Peru, South Africa, and the United States;
9	Andrejko	BNT162b2 or mRNA-1273 VE was 58.9% (95% CI, −9.7 to 84.5) at 15 days after 1 dose, and 85.7% (67.2 to 93.9) 15 days after 2 dose against any infection.	Moderate	Observational test-negative, case-positive random sampling matched control study. 69% of population at time had variants Alpha., {Epsilon}
10	Glampson	ChAdOx1nCoV-19 or BNT162b2 showed VE 74% (HR 0.26, 95% CI, 0.19 to 0.35) and 78% (HR 0.22, 95% CI, 0.18 to 0.27), respectively, 28 days after first vaccination dose against any infection.	Moderate	Observational retrospective cohort, 2 M eligible for population; 389,587 vaccinated (58% Pfizer, 42 AZ); variants not assessed, but dominant being Alpha at that time.
11	Pritchard	ChAdOx1nCoV-19 or BNT162b2 showed VE of 65% (95% CI, 60 to 70%) 21 days after first dose and 70% (95% CI, 62 to 77%) after second dose against any infection. No difference between vaccines or versus people with previous infection. Same effect for Alpha (dominant) or not Alpha.	Moderate	Observational prospective testing; 370,000 participants, 1.6 M tests infections with evidence of high viral shedding Ct<30 (88% reduction after two doses; 95% CI 80 to 93%; P<0.001) and with self-reported symptoms (90% reduction after two doses; 95% CI 82 to 94%; P<0.001)
12	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 two doses in the study population against any infection.	Low	prospective cohort with standardized testing and adjustment for confounders, HCW, all of England; 23,000, 46 years of age, 84% females.
13	Shrotri	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.	Low	9160 of 10412 frail LTC residents (median 86 years of age), 66% Pfizer, 33% AZ. Prospective testing.

14	Hyams	1st BNT162b2 showed VE 71.4% (95% CI, 43.1 to 86.2). ChAdOx1nCoV-19 1st dose VE 80.4% (95% CI, 36.4 to 94.5) against hospitalization for 80+ 14 days after 1st dose. 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).	Moderate	Test negative case control, Scotland. Small sample, single center, 80+ (median age 86). Adjusted/matched Cox
15	Harris	First dose of BNT162b2 or ChAdOx1 (21 days prior) reduced likelihood of transmission by 40-50% for household contacts of HCW	Moderate	Data-linkage and case-control; will have missed asymptomatic infection
16	Goldberg	Prior infection (in unvaccinated) has similar VE against any infection [94.8%], and severe illness [96.4%] as two doses of BNT162b2	Moderate	Individual-level population database in Israel; likely overlaps with Dagan and Haas
17	Cavanaugh	VE against infection was 66.2% (95% CI, 40.5% to 80.8%) among residents and among HCP was 75.9% (95% CI, 32.5% to 91.4%). VE against hospitalization was 94.4% (95% CI, 73.9% to 98.8%) among residents; no HCP were hospitalized. Three residents died, two of whom were unvaccinated (VE = 94.4%; 95% CI, 44.6% to 99.4%).	Serious	Outbreak analysis; small sample size
18	Shinde	NVX-CoV2372 VE showed VE 50.4% (95% CI, 16.6 to 70.5) against symptomatic infection 7 days after 2nd dose	RCT	4387 participants 39/41 cases Beta
19	Hitchings	One dose of CoronaVac showed VE of 35.1% (95% CI, -6.6 to 60.5) against infection in HCW	Serious	53,176 HCW in Manaus 75% prevalence of Gamma; 776 (28%) of 2797 PCR were used for the case control; infection increased in the first 13 days (Healthcare seeking behaviour, differential test seeking); rate of previous infection high in the population
20	Heath	Two doses of NVX-CoV2373 showed VE 89.7% (95% CI, 80.2 to 94.6) against any infection. No hospitalizations or deaths in vaccinated group.	RCT	15,187 people in UK Post hoc: VE 86.3% (95% CI, 71.3 to 93.5) against Alpha variant

21	Ismail	Two doses of BNT162b2 or ChAdOx1 showed VE 80% (95% CI, 74 to 85) against hospitalization 28 days after 1st dose and 92% (95% CI, 87 to 95%) 14 days after 2nd dose for people 80+.	Moderate	13,907 hospitalized patients in UK; results for age 80+ also reported separately according to vaccine
22	Bernal	BNT162b2 reduced risk of death in 70+ by 44% (95% CI, 32 to 53) after 1st dose and by 69% (95% CI, 31 to 86) after 2nd dose; single dose ChAdOx1 reduced risk of death by 55% (95% CI, 41 to 66)	Low	48,096 cases above age 70+ in England; linked to mortality database; 12.7% BNT162b2 and 8.2% ChAdOx1
23	Chodick	BNT162b2 showed VE 94% (95% CI, 88 to 97) against infection 7-27 days after 2nd dose; 71% (95% CI, 37 to 87) in immunosuppressed	Moderate	Health care organization in Israel; compared time frames to estimate effectiveness against Alpha
24	Chung	BNT162b2 or mRNA-1273 showed VE 61% (95% CI, 56 to 66) against symptomatic infection by 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 Beta or Gamma 14 days after 1st dose and 88% (95% CI, 61 to 96) 7 days after 2nd dose.	Serious	Ontario ICES study; limitations in symptom collection; screening for variants started 2 months into study period; results also reported for age>70
25	Bailly	BNT162b2 showed VE 50% (95% CI, 34 to 73) against infection with Beta >28 days after 2 doses	Moderate	Outbreak in a single LTC in France, all samples genome sequenced; 2 deaths in vaccinated group
26	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	Moderate	Single centre tertiary medical centre in Israel; testing strategy was different between vaccinated and unvaccinated
27	Bianchi	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	Moderate	Single centre medical centre in Italy;
28	Yassi	BNT162b2 (93%) or mRNA-1273 showed VE 37.2% (95% CI, 16.6 to 52.70) against infection by Beta or Gamma 14 to 42 days after 1st dose and 79.2% (95% CI, 64.60 to 87.80) 7 days after 2nd dose	Low	25,558 Canadian HCW; evenly split between Gamma and Beta by end of study period

Section 2: studies under appraisal		
#	**Author**	**Notes**
1		
3		

Section 3: excluded studies			
#	**Author**	**Reason for exclusion**	**Notes**
	Jacobson	Not actionable information, and high risk of bias.	Imprecise information about infection rate, proportion of prevalent variant, amount of missing outcome data.
	Hollinghurst	Serious risk of bias	
	Mor	Moderate risk of bias	Observational USA, multiple LTC; routine screening; no details on testing; not variant of concern

Appendix 2: Glossary

Alpha: variant of concern B.1.1.7

Beta: variant of concern B.1.351

Gamma: variant of concern P.1

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

HCW: Healthcare workers

LTC: Long-term care

Obs: observational study

Vaccine effectiveness (VE): measure of how well a vaccine protects people from becoming infected (For example: VE of 92% means that 92% of people be well protected from becoming infected with COVID and 8% of people will still be at risk of becoming infected with COVID)

Appendix 3: Data-extraction template (under revision)

Vaccine product	BNT = BNT162b2 (Pfizer-BioNTech)
	MOD = mRNA-1273 (Moderna)
	AZ = ChAdOx1-S (AstraZeneca, COVISHIELD)
	JJ = Ad26.COV2 (Janssen [Johnson & Johnson])
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)	gen public/LTC/Households/HCW/Other
Control group	not vaccinated, <7day vacc internal control, none,other
Total (N)	number of all study participants
% female	percent female or NA
LTC	number or NA
HCW	number or NA
Households	number or NA
>80	number older than this age group or unclear or NA
>70	number older than this age group or unclear or NA
>60	number older than this age group or unclear or NA
Notes	about study as a whole
Outcomes	outcomes separated by variant type
Group	group the outcomes in the next few columns applies to: all or subgroup label
Outcomes	confirmed infection/asymptomatic/mild symptomatic/severe symptoms/hosp/ICU/death/biomarkers
1st Dose VE	VE with 95% CI
Days post 1st dose	days post 1st dose when VE measured
2nd Dose VE	VE with 95% CI
Days post 2nd dose	days post 2nd dose when VE measured
Over Study Period	number
Rate per 100 pt years	vaccinated vs control
HR	vaccinated vs control
RR	vaccinated vs control

Biomarkers	antibody titres
PCR-conf	percent PCR confirmed with Ct value if available
NAAT	percent confirmed by NAAT
(repeat above outcome columns for each VARIANT)	
Transmission	infection rates in contacts (overlaps with studies of duration of infectivity)
Viral load	
Detection Frame	
Duration of infectivity	correlation of serial rRT-PCR test results with virus cultures, studies of contracts, modelling studies
Critical appraisal	See appendix 2
Comments	

Appendix 4: Critical appraisal process

We appraise the quality of the individual studies using 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. It also includes identifying all the confounders and co-interventions potentially relevant to the specific field of investigation (listed below). The table below indicates which domains we consider relevant to the VE&VOC field. We focus our assessment on the most relevant domains, but we consider potential bias arising in any of them.

ROBINS- I Domains	Anticipated relevance of the domain to VE & VOC
Bias due to	
Confounding	high relevance
Selection of participants into the study	intermediate relevance
Classification of interventions	low relevance
Deviations from intended intervention	low relevance
Missing data	high relevance
Measurement of outcomes	high relevance
Selection of the reported result	low relevance

Overarching review question:

Participants	People at risk of COVID 19 (usually without but sometimes with previous, previous COVID19 infection)
Intervention	COVID19 Vaccine
Comparator	Unvaccinated people (*)
Outcomes	PCR-diagnosis of COVID 19 infection (**); symptomatic disease; hospital/ICU admission; death

(*) confirmation of specific variant, or evidence the variant was the dominant circulating strain
(**) before-after studies, where the infection rate in the first 2 weeks after the vaccination are used as control are commonly performed and maybe appraised but are open to confounding and bias.

Aim for this study is to assess the effect of assignment to intervention (most vaccine studies will assess patients who received the vaccine)

List the potential confounding domains relevant to all or most studies

Socio-economic status, age, sex, gender, ethnicity, job role, LTC status, HCW status

List co-interventions that could be different between intervention groups and that could impact on outcomes

Use of PPE; self-isolation

Appendix 5: Detailed description of the narrative summary statement

We aim at providing a lay language, concise, standardized summary statement for each combination of vaccine/VOC for which we found evidence. Where more than one study was found, we will provide a summary statements.

We are reporting on the following clinical outcomes: prevention of infection, severe illness, and death, and prevention of transmission.