

## COVID-19 Living Evidence Synthesis #6

(Version 5: 17 May 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. Two studies and one updated one have been added since the previous edition of this living evidence synthesis, all of which are signaled by a last-updated date of 14 May 2021 (highlighted in yellow). One new study reporting the effectiveness of vaccines (Pfizer and AstraZeneca) against transmission of B.1.1.7 to household contacts and another reporting effectiveness of prior infection against re-infection have been added.

Overall, we have moderate certainty that the Pfizer, Moderna, and AZ vaccines prevent infection by VOC B.1.1.7. We have evidence that the Johnson & Johnson vaccine prevents infection by B.1.1.7 and B.1.351, but the degree of certainty is unknown. The AZ vaccine does not prevent infection associated with B.1.351. There remains uncertainty about the impact of any of the vaccines on severe disease, death or prevention of transmission of the VOC.

We present our methods 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 illness, 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	<a href="#">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.</a> Review of RCTs (AMSTAR 10/11); <i>last search date 2021-05-07; GRADE evidence profile updated on 2021-01-25</i>
	By variant of concern	
	• B.1.1.7	BNT162b2 showed the same VE as the phase III trial (46 to 60% 14 days after 1 <sup>st</sup> dose) and 85.7 to 92% 7 days or 70 to 94% 14-21 days after 2 <sup>nd</sup> dose) in a population with an estimated circulation of B.1.1.7. up to 80-94%. Severe disease and death were reduced by 92 to 98% and 94 to 98%, respectively after the 2 <sup>nd</sup> dose. Neutralization effect was 2.4 lower after 2 <sup>nd</sup> dose in a population with >90% B.1.1.7. Ct>30 reduced by 88% and symptomatic episodes reduce by 90%; no difference with previous infection protection (8 studies, low quality of evidence) <a href="#">[1][2][3][9][10][11][15][16]</a> <i>last updated 2021-05-14</i>
	• B.1.351	no data
	• P.1	no data
	• CAL.20C	no data
	By special population	
	• Healthcare workers	BNT162b2 reduced infection rate in HCW by about 55% compared to non vaccinated people (HR 0.45, 95% CI, 0.42 to 0.49) to 80% (95% CI, 59 to 90) after the first dose and 90% (95%, CI 68 to 97) after the second dose; hospitalization after the first dose was reduced by 91% (HR 0.16, 95% CI, 0.09 to 0.27) (2 studies, low quality of evidence) <a href="#">[6][7]</a> <i>last update 2021-04-14</i>
	• HCW, B.1.1.7	A single dose of BNT162b2 vaccine showed VE of 70% (95% CI, 55 to 85) 21 days after first dose and 85% (74 to 96) 7 days after two doses in HCW (median age 46, 84% females) <a href="#">[12]</a> , <i>last update 2021-04-30</i>
	• LTC, B.1.17	VE for BNT162b2 at 35-48 days was (aHR 0.3, 95% CI, 0.17 to 0.71)(median age 86) <a href="#">[13][14]</a> <i>last update 2021-04-30</i>
Moderna	Overall	<a href="#">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.</a> Review of RCTs (AMSTAR 10/11); <i>last</i>

		<i>search date 2021-05-07; GRADE evidence profile updated on 2021-01-25</i>
	By variant of concern	
	• B.1.1.7	mRNA-1273 VE was 58.9 (95% CI, -9.7 to 84.5) 15 days after 1 dose, and 85.7 (95% CI, 67.2 to 93.9) 15 days after 2 dose. (1 study, [9] <i>last updated 2021-04-22</i> )
	• B.1.35.1	no data
	• P.1	no data
	• CAL.20C	no data
Astra Zeneca	Overall	<a href="#">Compared to vaccinating with MedACWY (meningitis vaccine), vaccination with ChAdOx1 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 hospitalisations. The effects on mortality are uncertain, and adverse effects are probably less frequent.</a> (*)Review of RCTs (AMSTAR 10/11); <i>last search date 2021-05-07; 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.</i>
	By variant of concern	
	• B.1.1.7	ChAdOx1nCoV-19 VE in preventing mild to-moderate Covid-19 from the B.1.1.7 variant was 70.4% (95% CI, 43.6 to 84.5) compared to 81.5% (95% CI, 67.9 to 89.4) versus naïve COVID19; neutralization effect was 9 times lower; VE confirmed at 65-74% after one dose in large observational retrospective cohorts (1 RCT, 2 Obs, moderate to low quality of evidence)[5][10][11] <i>last updated 2021-04-22</i>
	• B.1.351	ChAdOx1 nCoV-19 vaccine (two doses) had very low efficacy against the B.1.351 variant in preventing mild to-moderate Covid-19 and there is no data on protection against severe disease (1 RCT).[4] <i>last update 2021-04-14</i>
	• P.1	no data
	• CAL.20C	no data
	Special populations	
	• LTC, B.1.17	VE for ChAdOx1 at 35-48 days was (aHR 0.32, 95% CI, 0.15 to 0.66) (median age 86)[13][14] <i>last update 2021-04-30</i>
Johnson & Johnson	Overall	<a href="#">[Johnson &amp; Johnson's Janssen vaccine] Synthesis pending.</a> Review of RCTs (AMSTAR 8/9); <i>last update 2021-05-07</i> Interim summary, provided by VOC-study group: Ad26.COVS 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). <i>last updated 2021-05-17</i>
	By variant of concern	
	• B.1.1.7	no data
	• B.1.351	<a href="#">VE against VOC 20H/501Y.V2 variant (B.1.351) was 52.0% and 64.0% at 14 days and 28 days for moderate, and 73.1% and 81.7% for severe cases.</a> (1 RCT), [8] <i>last updated 2021-04-22</i>
	• P.1	no data
	• CAL.20C	no data
Sinovac (Coronavac)	• Overall	<a href="#">[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.</a> High quality review of RCTs (AMSTAR 10/11); <i>last search date 2021-05-07</i> ; GRADE evidence profile updated on 2021-05-07
	• By variant of concern	
	• B.1.1.7	no data
	• B.1.351	no data
	• P.1	no data
	• CAL.20C	no data

Links to references are provided in Appendix 1

Iorio A, Little J, Linkins L, Abdelkader W, Bennett D, Lavis JN. COVID-19 living evidence synthesis #6 (version 6.5): What is the efficacy and effectiveness of available COVID-19 vaccines in general and specifically for variants of concern? Hamilton: Health Information Research Unit, 17 May 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	<a href="#">Dagan</a>	BNT162b2 showed the <b>same VE as the phase III trial</b> (46-60% 14 days after 1 <sup>st</sup> dose and 92% 7 days after 2 <sup>nd</sup> dose) <b>in a population with an estimated circulation of B.1.1.7. up to 80%.</b>	Moderate	Cohort Israel, .5 M matched; large population, KM, concordant with trial; 2 M excluded (possible overlap with Haas)
2	<a href="#">Haas</a>	BNT162b2 showed <b>the same VE as the phase III trial (91% [&gt;7 days]</b> and against asymptomatic infections <b>[94%]</b> , hospitalization <b>[98%]</b> and death <b>[98%]</b> , respectively, 14 days after second dose <b>in a population with 94% of B.1.1.7.</b>	Low	Cohort Israel, concordant with trial; effect on death (possible overlap with Dagan) <b>Updated May 14 due to final publication</b>
3	<a href="#">Kustin</a>	BNT162b2 showed <b>lower relative VE (2.4:1)</b> against <b>B.1.1.7.</b> after first dose; and <b>lower VE (8:1)</b> against <b>B.1.351</b> after second dose <b>in a population with &gt;90% of B.1.1.7 and &lt;1% B.1.135</b>	Moderate	Case-control Israel, asymmetry in VOC; small sample for B.1.135 (no overlap, CHS cohort).
4	<a href="#">Madhi</a>	Two doses of the ChAdOx1 nCoV-19 vaccine had <b>no efficacy against the B.1.351</b> 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	<a href="#">Emery</a>	ChAdOx1nCoV-19 (two doses) <b>VE against the B.1.1.7 variant was 70.4%</b> (95% CI, 43.6 to 84.5) for B.1.17 and 81.5% (95% CI, 67.9 to 89.4) for non-B.1.1.7.	Low	RCT UK; neutralization of B.1.1.7 9 times lower
6	<a href="#">Shah</a>	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)	Moderate	Observational Scotland - (25% of cases had received 2 doses)

		and hospitalization by 91% (HR 0.16, 95% CI, 0.09 to 0.27)		
7	<a href="#">Thompson</a>	BNT162b2 and mRNA-1273 VE in HCW, first-line responder and essential/frontline workers was 80% (95% CI, 59 to 90) after the first dose and 90% (95% CI, 68 to 97) after the second dose	Low	Observational US, multicentric Prospective, standardized, weekly PCR testing; small size. 63% Pfizer, 27% Moderna; larger prevalence of infection in male, Hispanic.
8	<a href="#">Sadoff</a>	Ad26.COVS.2.S VE 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. For severe cases, VE was 76.7% (95% CI, 54.6 to 89.1) at $\geq 14$ days and 85.4% (95% CI, 54.2 to 96.9) at $\geq 28$ days). VE against VOC B.1.351 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	<a href="#">Andrejko</a>	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	Moderate	Observational test-negative, case-positive random sampling matched control study. 69% of population at time had variants B.1.1.7., {B.1.427, B.1.429}.
10	<a href="#">Glampson</a>	ChAdOx1nCoV-19 or BNT162b2 showed 74% (HR 0.26, 95% CI, 0.19 to 0.35) and 78% (HR 0.22, 95% CI, 0.18 to 0.27) 28 days after first vaccination dose, compared to unvaccinated subjects.	Moderate	Observational retrospective cohort, 2 M eligible for population; 389,587 vaccinated (58% Pfizer, 42 AZ); variants not assessed, but dominant being B.1.1.7 at that time.
11	<a href="#">Pritchard</a>	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, compared to unvaccinated subjects. No difference between vaccines or versus people with previous infection. Same effect for B.1.1.1.7 (dominant) or not B.1.1.7.	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	<a href="#">Hall (SIREN)</a>	A single dose of BNT162b2 vaccine showed VE of 70% (95% CI, 55 to 85) 21 days after first dose and 85% (95% CI, 74 to 96) 7 days after two doses in the study population.	Low	prospective cohort with standardized testing and adjustment for confounders, HCW, all of England; 23,000, 46 yo, 84% females.
13	<a href="#">Shrotri</a>	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 yo), 66% Pfizer, 33% AZ. Prospective testing.
14	<a href="#">Hyams</a>	First dose of BNT162b2 showed VE 71.4% (95% CI, 46.5 to 58 90.6). ChAdOx1nCoV-19 first dose VE 80.4% (95% CI, 36.4 to 4.5). 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, median age 86. Adjusted/matched Cox
15	<a href="#">Harris</a>	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	<a href="#">Goldberg</a>	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

### Section 2: studies under appraisal

#	Author	Notes
1		
2		
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.

	<a href="#">Hollinghurst</a>	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

**HCW:** Healthcare workers

**LTC:** Long-term care

**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
<b>Study details</b>	
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
<b>Outcomes</b>	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)	
<b>Transmission</b>	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
<b>Critical appraisal</b>	See appendix 2
<b>Comments</b>	

## 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. As a default, we will provide one statement for overall infection prevention and prevention of severe illness (or absence of evidence thereof). Other statements may be added as needed.

We will use the following template whenever possible:

**Vaccine X provides a XX% protection from infection and XX% protection from severe illness due to variant Y [optional subgroup: in people such and such] =>dd days after [first/second] dose. # people, #studies, quality.**

Examples (not real statement, look for real statements in the synopsis):

Example 1: Moderna (mRNA) provides an 84% protection from infection and >90% protection from severe illness due to the B1.1.7. variant two weeks after the second dose. 12,000 people, one study, moderate confidence.

Example 2: AZ provides a 10% protection from infection due to the B.1.351 variant and unknown protection from severe illness two weeks after the first dose. 50,747 people, one study, high confidence.

Example 3: Pfizer (mRNA) provides a 62-84% protection and >90% protection from severe illness from infection due to the B1.1.7. variant two weeks after the first dose. 250,000 people, seven studies, moderate confidence.

The level of protection is provided whenever possible as % reduction of the risk of infection. Complete protection would be 100% protection, complete absence of protection 0%. How much is enough is a judgement call and may vary case by case. Some vaccines provide incomplete protection against the original strain of COVID19; the same level of protection is the maximum expected for each variant.