COVID-19 Living Evidence Synthesis #6

(Version 3: 30 April 2021)

Question

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

Findings

We present in Table 1 the key findings about vaccine effectiveness. Five rows in the table have been updated since the previous edition of this living evidence synthesis, all of which are signaled by a last-updated date of 30 April 2021 (highlighted in yellow). First, the overall certainty of the evidence about the effectiveness of the Johnson & Johnson vaccine has been updated. Second, three new studies about the effectiveness of vaccines (Pfizer and AstraZeneca) against B.1.1.7 in higher risk populations have been added. We have also added rows for a new variant of concern (CAL.20C, otherwise known as B.1.427 & B.1.429), however, no data are yet available for this variant.

Overall, we have moderate confidence that the Pfizer vaccine is effective against VOC B1.1.1.7. We have moderate confidence that the Johnson & Johnson vaccine is effective against B1.351, the Moderna vaccine is effective against the B1.1.7., and that the AZ vaccine is not effective against mild-to-moderate COVID-19 associated with B1.351. We do not have data relating to VOC for other vaccines/variants combinations.

We present our methods in Box 1 and Appendix 1 and Appendix 2.

We present additional details about included studies in Appendix 3.

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) updates to the COVID-END inventory of best evidence syntheses; 3) additions and updates from the VESPa team. We considered studies and updates to living evidence syntheses identified up to 29 April 2021.

We included studies with clinical outcomes (and excluded studies that captured only antibody responses) and where reasonable assumptions could be made about the variants prevalent in the jurisdiction at the time of the study.

Two individuals (one at McMaster University and one at the University of Ottawa) independently extracted data from each study using the data-extraction template provided in Appendix 1.

The same two individuals independently critically appraised each study using a reduced version of the ROBINS-I tool as depicted in Appendix 2. The reduced version includes an assessment of bias in missing data and measurement of outcomes and (separately) an assessment of confounding and outcome selection. It does not include an assessment of selection of participants, classification of interventions, and deviation from intended intervention, which are unlikely to be relevant for the studies being examined.

We present evidence profiles by summarizing evidence across studies, with or without pooling as appropriate, and confidence in the effect using the standard GRADE approach for treatment effect (5 to downgrade, 3 to upgrade), starting at low for observational evidence.

We focus our narrative descriptions on whether the vaccines prevent infection, prevent severe illness and death, and prevent transmission.

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

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. High quality review of RCTs (AMSTAR 10/11); *last update 2021-03-26*
	By variant of concern	
	• B.1.1.7	BNT162b2 showed the same VE as the phase III trial (46-60% 14 days after 1st dose) and 85.7-92% 7 days or 70-94% 14-21 days after 2nd dose) in a population with an estimated circulation of B.1.1.7. up to 80-94%. Neutralization effect was 2.4 lower after 2nd 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 (6 studies, moderate to low quality of the evidence)[1][2][3][11][12][13]*last updated 2021-04-22*
	• B.1.351	There are not yet clinical data, but neutralizing experiments showed a 8 times lower VE BNT162b2 in a population with <1% B.1.351 (1 study, low quality of the evidence)[3] *last update 2021-04-14*
	• P.1	no data
	• CAL.20C	no data
	By special population	
	• Healthcare workers	BNT162b2 was VE in reducing the infection rate in HCW by about 55% (HR 0.45, 95% CI 0.42 – 0.49) to 80% (95% CI 59-90) after the first dose and 90 (95% CI 68-97) after the second dose; hospitalization after the first dose was reduced by 91% (HR 0.16, 95% CI 0.09 – 0.27) (2 studies, moderate to low quality of the evidence) [6][8] *last update 2021-04-14*
	• HCW, B.1.1.7	A single dose of BNT162b2 vaccine showed vaccine effectiveness of 70% (95% CI 55–85) 21 days after first dose and 85% (74–96) 7 days after two doses in HCW (median age 46, 84% females)[14], *last update 2021-04-30*
	• LTC, B.1.17	VE for BNT162b2 at 35-48 days was (aHR 0·35 [0·17, 0·71])(median age 86)[15][16] *last update 2021-04-30*
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. High quality review of RCTs (AMSTAR 10/11); *last update 2021-03-26*
	By variant of concern	
	• B.1.1.7	mRNA-1273 VE was 58.9 (−9.7, 84.5) 15 days after 1 dose, and 85.7 (67.2, 93.9) 15 days after 2 dose. (1 study, moderate quality of the evidence, [11] *last updated 2021-04-22*
	• B.1.35.1	no data
	• P.1	no data
	• CAL.20C	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 hospitalisations. The effects on mortality are uncertain, and adverse effects are rare but serious. (*) High quality review of RCTs (AMSTAR 10/11); *last update 2021-03-26*. (*) judgement on adverse adjusted to account for Vaccine-Induced Prothrombotic Immune Thrombocytopenia (VIPIT).
	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 74.6% (95% CI, 41.6 to 88.9) compared to 84.1% (95% CI, 71 to 91) 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 the evidence)[5][12][13] *last updated 2021-04-22*
	• B.1.351	ChAdOx1 nCoV-19 vaccine (two doses) had no efficacy against the B.1.351 variant in preventing mild to-moderate Covid-19 (1 RCT, moderate quality of the evidence). [4] *last update 2021-04-14*
	• 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 [0·15-0·66] (median age 86)[15][16] *last update 2021-04-30*
Johnson & Johnson	Overall	[Johnson & Johnson's Janssen vaccine] Synthesis pending. High quality review of RCTs (AMSTAR 8/9); *last update 2021-04-23* 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% (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) [10] Rare but serious thrombotic side effects were reported (data not systematically reviewed). *last updated 2021-04-30*
	By variant of concern	
	• B.1.1.7	no data
	• B.1.351	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. (1 RCT, moderate quality of the evidence) [10] *last updated 2021-04-22*
	• P.1	no data
	• CAL.20C	no data
Sinovac (Coronavac)	• Overall	[Coronavac] Synthesis pending. High quality review of RCTs (AMSTAR 8/9); *last update 2021-04-23*
	• By variant of concern	
	• B.1.1.7	no data
	• B.1.351	no data
	• P.1	no data
	• CAL.20C	no data

Note that references are also provided as Appendix 3

Iorio A, Little J, Linkins L, Abdelkader W, Bennett D, Lavis JN. COVID-19 living evidence synthesis #6 (version 6.3): What is the efficacy and effectiveness of available COVID-19 vaccines in general and specifically for variants of concern? Hamilton: Health Information Research Unit, 30 April 2021.

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Appendix 1: Data-extraction template

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 2: Critical-appraisal template

Domain	Judgement	Anticipated direction	VE & VOC
	Low / Moderate / Serious / Critical / NI	Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable	
Bias due to confounding			low relevance
Bias in selection of participants into the study			very low relevance
Bias in classification of interventions			very low relevance
Bias due to deviations from intended intervention			very low relevance
Bias due to missing data			relevant
Bias in measurement of outcomes			relevant
Bias in selection of the reported result			low relevance
Overall			

Appendix 3: Detailed notes about individual studies

Ref	Author	Bottom line	ROBINS-I	Design, Notes
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 B.1.1.7. up to 80%	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 (90% [>7 days] and 94% [14 days] after second dose) against asymptomatic infections and death [91%] in a population with 94% of B.1.1.7.	Low	Cohort Israel, concordant with trial; effect on death (possible overlap with Dagan)
3	Kustin	BNT162b2 showed lower relative VE (2.4:1) against B.1.1.7. after first dose; and lower VE (8:1) against B.1.351 after second dose in a population with >90% of B.1.1.7 and <1% B.1.135	Moderate	C-control Israel, asymmetry in VOC; small sample for B.1.135 (no overlap, CHS cohort).
4	Madhi	Two doses of the ChAdOx1 nCoV-19 vaccine had no efficacy against the B.1.351 variant in preventing mild to-moderate Covid-19	Moderate	RCT South Africa; VE 20% in seronegative and 10% in seropositive – 75% (9-95%) after 1 dose before emergence of variant. Underpowered for 20% efficacy
5	Emary	ChAdOx1nCoV-19 (two doses) VE against the B.1.1.7 variant was 70.4% (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	Shah	ChAdOx1nCoV-19 was VE in reducing the infection rate (and hospitalization) in household of vaccinated HCW by about 30% (HR .70, 95% CI 0.64 – 0.78); BNT162b2 was VE in reducing the infection rate in HCW by about 55% (HR 0.45, 95% CI 0.42 – 0.49) and hospitalization by 91% (HR 0.16, 95% CI 0.09 – 0.27)	Moderate	Obs Scotland - (25% of cases 2 doses)
7	Hollinghurst	ChAdOx1nCoV-19 in people >60 dwelling in LTC reduced infection rate to 1.05%, with 90% of cases	Serious	Obs Wales – 75% cases AZ

		occurring within 4 weeks of vaccination;		
8	Thompson	BNT162b2 and mRNA-1273 VE in HCW, first line responder and essential/frontline workers was 80% (95% CI 59-90) after the first dose and 90 (95% CI 68-97) after the second dose	Low	Obs US, multicentric Prospective, standardized, weekly PCR testing; small size. 63% Pfizer, 27% Moderna; larger prevalence of infection in male, Hispanic.
9	Mor	BNT162b2 or mRNA-1273 VE in LTC reduced cumulative number of confirmed infections by 5.2 per 100 at risk at 7 weeks post vaccination in the early group	Moderate	Obs USA, multiple LTC; routine screening; no details on testing
10	Sadoff	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% (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). 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.	Low	RCT Argentina, Brazil, Chile, Colombia, Mexico, Peru, South Africa, and the United States;
11	Andrejko	BNT162b2 or mRNA-1273 VE was 58.9 (−9.7, 84.5) 15 days after 1 dose, and 85.7 (67.2, 93.9) 15 days after 2 dose	Moderate	Obs test-negative, case-positive random sampling matched control study. 69% of populaton at time had variants B.1.1.7., {B.1.427, B.1.429).
12	Glampson	ChAdOx1nCoV-19 or BNT162b2 showed a 74% (HR 0.26 (0.19-0.35)) and 78% (HR 0.22 (0.18-0.27)) 28 days after first vaccination dose, compared to unvaccinated subjects.	Moderate	Obs 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.
13	Pritchard	ChAdOx1nCoV-19 or BNT162b2 showed VE as infection reduction of 65% (60-70%) 21 days after first dose and 70% (62-77%) after second dose, compared to unvaccinated subjects. No difference between	Moderate	Obs prospective testing; 370,000 participants, 1.6 M tests infections with evidence of high viral shedding Ct<30 (88% reduction after two

		vaccines or versus people with previous infection. Same effect for B.1.1.1.7 (dominant) or not B.1.1.7		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)
14	Hall (SIREN)	A single dose of BNT162b2 vaccine showed vaccine effectiveness of 70% (95% CI 55–85) 21 days after first dose and 85% (74–96) 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.
15	Shrotri	Similar effect sizes were seen for ChAdOx1 (aHR 0·32 [0·15-0·66] and BNT162b2 (aHR 0·35 [0·17, 0·71]) vaccines at 35-48 days.	Low	9160 of 10412 frail LTC residents (median 86 yo), 66% Pfizer, 33% AZ. Prospective testing.
16	Hyams	First dose vaccine effectiveness of BNT162b2 was 71.4% (95% confidence interval [CI] 46.5-58 90.6). ChAdOx1nCoV-19 first dose vaccine effectiveness was 80.4% (95% CI 36.4-94.5). When effectiveness analysis for BNT162b2 was restricted to the period covered by ChAdOx1nCoV-19, the estimate was 79.3% (95% CI 47.0-92.5).	Moderate	Test negative case control, Scotland. Small sample, single center, median age 86. Adjusted/matched Cox