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

CMCM MBMC Montreal Behavioural Medicine Centre

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

COVID-19 Living Evidence Synthesis #10

(Version 10.4: 30th March 2022)

Questions

1. How does the level of vaccine efficacy/ effectiveness (VE) against COVID-19 infection, hospitalisation, and death change over time (>112 days) in individuals who have received a complete primary COVID-19 vaccine series?
2. How does the level of VE against COVID-19 infection, hospitalisation, and death change over time (>84 days) in individuals who have received a complete primary COVID-19 vaccine series plus an additional dose?

Findings

1. A visual summary of the primary series VE against any infections, hospitalisations, and deaths are presented in Tables 1, 4, and 7, respectively. For delta-related outcomes the summaries are presented in Tables 2, 5, and 8; and for omicron-related outcomes in Tables 3, 6, and 9. Figure 1 provides information on cases by variant and Figure 2 provides information on cases by specific vaccine brand
2. A visual summary of the primary series + additional dose VE against any infections and hospitalisations are presented in Tables 10, 11, and 12, respectively. These tables include variant specific information where available.

Methods are presented in Box 1 and in the related appendices.

Overall (from the initiation of this review), 13,344 studies were title and abstract screened, 728 were full-text appraised, and 29 used to complete this summary. The reasons for excluding the 699 studies are reported in **Appendix 6**.

Box 1: Our approach

We retrieved candidate studies and updates to living evidence syntheses on vaccine effectiveness using the following mechanisms: 1) search on the National Institute of Health (NIH) iSearch COVID-19 portfolio and EMBASE; 2) systematic scanning of COVID-END Forum website, McMaster Health Forum website, and citations of systematic reviews on this topic; and 4) cross-check with updates from the VESPa team. We included studies and updates to living evidence syntheses identified up to five 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 and 6**, respectively. A glossary is provided in **Appendix 3**.

Prioritized outcome measures: Infection, hospitalisation, and death.

Data extraction: We prioritised any infection data over symptomatic or asymptomatic and total population data over sub-groups. We extracted data from each study using a standard template with peer-review to confirm information **Appendix 5**. Only data from four of the Health Canada vaccines (BNT162b2, mRNA-1273, ChAdOx1, and Ad26.COV2.S) and only delta and omicron VOC data were extracted for sub-analyses. VOC data was determined directly when reported by study authors.

Critical appraisal: We assessed risk of bias and certainty of evidence. **Risk of bias:** assessed in duplicate for individual studies using an adapted version of ROBINS-I (see **Appendix 4)**.

Summaries: We summarized the evidence by presenting meta-analysed pooled estimates with 95% CIs by 4-week blocks (see **Appendix 2** for details). For meta-analyses, sub-groups were considered as separate cohorts. Where data was insufficient, we provide an average (and range) of the available VE data or point estimate (and 95%CIs) in there was only a single study.

We update this document every 4th Wednesday and post it on the COVID-END website.

Highlights of changes in this version

- Three new studies have been added and one study was updated (marked in blue in **Appendix 1**) that report on the long-term VE of the full vaccine schedule.
- No new studies were included that report on the long-term VEs of additional doses beyond the full vaccine schedule.

- We have included some figures to provide more intuitive visual representations of the aggregated point-estimates.
- We updated our decision trees around how to manage data at the extreme ends of the VE spectrum (e.g., 100% VE, negative VE, and negative CIs). This had a minimal impact on the point estimates, but did change some of the CIs
- We realised we had made a couple of coding errors for some of the cohorts in the previous meta-analyses. This has now been corrected and verified.

Visual representation of data

- **Percentages** indicate the *level of effectiveness* of the COVID-19 vaccines. A VE of 0% indicates no protection and a VE of 100% indicates that the vaccines maximally prevent COVID-19 events (e.g., cases, death, hospitalisations). Meta-analysed point estimates and 95% CIs are provided, along with the number of cohorts contributing to the data. It is possible that any particular study may provide more than one cohort, depending on how they reported the data.
- **Colour** indicates **Level of Certainty** based on the evidence
- In all tables, **days (weeks)** refers to time since the completion of a full vaccine series.

High certainty evidence	Moderate certainty evidence	Low certainty evidence
Pooling of low to moderate risk of bias RCTs or pooling of observational studies with low risk of bias and consistent findings	Single RCT with low to moderate risk of bias or more than one observational study with low to moderate risk of bias and at least partially consistent findings	Single RCT or observational study with serious risk of bias or multiple low to serious risk of bias observational studies with inconsistent findings
At least 10 cohorts represented with at least one CI within 10% of the point estimate	At least 4 cohorts represented with at least one CI within 15% of the point estimate	

Question 1a: VE against COVID-19 infections change over time (>112 days) in individuals who have received a complete primary COVID-19 vaccine series

Table 1: VE against COVID-19 cases* for completed primary series (**all strains**)

	Baseline days (weeks)		Follow-up days (weeks)								
	0-13 (0-2)	**14-42 (2-6)**	**112-139 (12-16)**	**140-167 (16-20)**	**168-195 (20-24)**	**196-223 (24-28)**	**224-251 (28-32)**	**252-279 (32-36)**	**280-307 (36-40)**	**308-335 (40-44)**	**336+ (44+)**
Any vaccine	63% (47-75) 7 cohorts	88% (86-90) 51 cohorts	69% (61-74) 24 cohorts	64% (59-69) 47 cohorts	55% (47-61) 31 cohorts	66% (51-76) 7 cohorts	42% (11-62) 6 cohorts	50% (9-73) 4 cohorts	33% (-66-85) 2 cohorts	-0.3% (-10-10) 1 cohort	17% (3-28) 1 cohort
Any mRNA vaccine	71% (62-78) 5 cohorts	92% (90-93) 37 cohorts	73% (65-80) 18 cohorts	67% (60-73) 34 cohorts	57% (45-65) 22 cohorts	63% (44-76) 7 cohorts	34% (-8-60) 4 cohorts	50% (-10-77) 3 cohorts	33% (-66-85) 2 cohorts	0.3% (-10-10) 1 cohort	17% (3-28) 1 cohort
Any adenovirus	36% (-5-61) 2 cohorts	72% (68-76) 12 cohorts	49% (36-60) 5 cohorts	53% (45-61) 11 cohorts	46% (30-58) 8 cohorts	54% (51-57) 1 cohort		50% (42-57) 1 cohort			
BNT162b2	71% (62-78) 5 cohorts	90% (87-92) 19 cohorts	70% (57-79) 11 cohorts	61% (51-70) 20 cohorts	54% (40-64) 16 cohorts	59% (26-77) 5 cohorts	34% (-8-60) 4 cohorts	40% (-38-78) 2 cohorts	-18% (-26-9) 1 cohort	-0.3% (-10-10) 1 cohort	17% (3-28) 1 cohort
mRNA-1273		94% (92-95) 19 cohorts	79% (72-85) 9 cohorts	75% (65-82) 16 cohorts	71% (50-83) 7 cohorts	73% (71-75) 2 cohorts		65% (62-68) 1 cohort	74% (-12-94) 1 cohort		
ChAdOx1	47% (37-56) 1 cohort	75% (71-79) 9 cohorts	49% (46-51) 2 cohorts	54% (44-63) 8 cohorts	39% (16-56) 5 cohorts						
Ad26.COV2.S	11% (-36-41) 1 cohort	62% (43-74) 3 cohorts	50% (24-67) 3 cohorts	51% (39-61) 3 cohorts	56% (47-64) 3 cohorts	54% (51-57) 1 cohort		50% (42-57) 1 cohort			

* This is a combination of any, symptomatic, and asymptomatic infections. If a study reports any infections this is prioritised over symptomatic or asymptomatic (when reported). If the study reports symptomatic and asymptomatic, then symptomatic is prioritised.

Table 2: VE against COVID-19 cases* for completed primary series (**Delta variant**)

	Baseline days (weeks)		Follow-up days (weeks)								
	0-13 (0-2)	**14-42 (2-6)**	**112-139 (12-16)**	**140-167 (16-20)**	**168-195 (20-24)**	**196-223 (24-28)**	**224-251 (28-32)**	**252-279 (32-36)**	**280-307 (36-40)**	**308-335 (40-44)**	**336+ (44+)**
Any vaccine	71% (64-77) 1 cohort	90% (85-93) 14 cohorts	80% (66-88) 5 cohorts	72% (67-77) 14 cohorts	69% (62-74) 12 cohorts	76% (70-80) 3 cohorts	80% (74-85) 1 cohort	65% (62-68) 1 cohort	74% (-12-94) 1 cohort		
Any mRNA vaccine	71% (64-77) 1 cohort	92% (91-94) 9 cohorts	84% (78-88) 4 cohorts	76% (73-79) 9 cohorts	72% (67-77) 8 cohorts	76% (70-80) 3 cohorts		65% (62-68) 1 cohort	74% (-12-94) 1 cohort		
Any adenovirus		78% (64-87) 3 cohorts		46% (44-48) 3 cohorts	44% (43-44) 2 cohorts						
BNT162b2		92% (90-93) 5 cohorts	88% (85-90) 2 cohorts	70% (68-73) 5 cohorts	68% (64-72) 4 cohorts	80% (75-84) 3 cohorts					
mRNA-1273		94% (92-95) 6 cohorts	82% (78-85) 4 cohorts	78% (76-80) 6 cohorts	76% (74-79) 5 cohorts	73% (71-75) 1 cohort		65% (62-68) 1 cohort	74% (-12-94) 1 cohort		
ChAdOx1		78% (64-87) 3 cohorts		46% (44-48) 3 cohorts	44% (43-44) 2 cohorts						
Ad26.COV2.S											

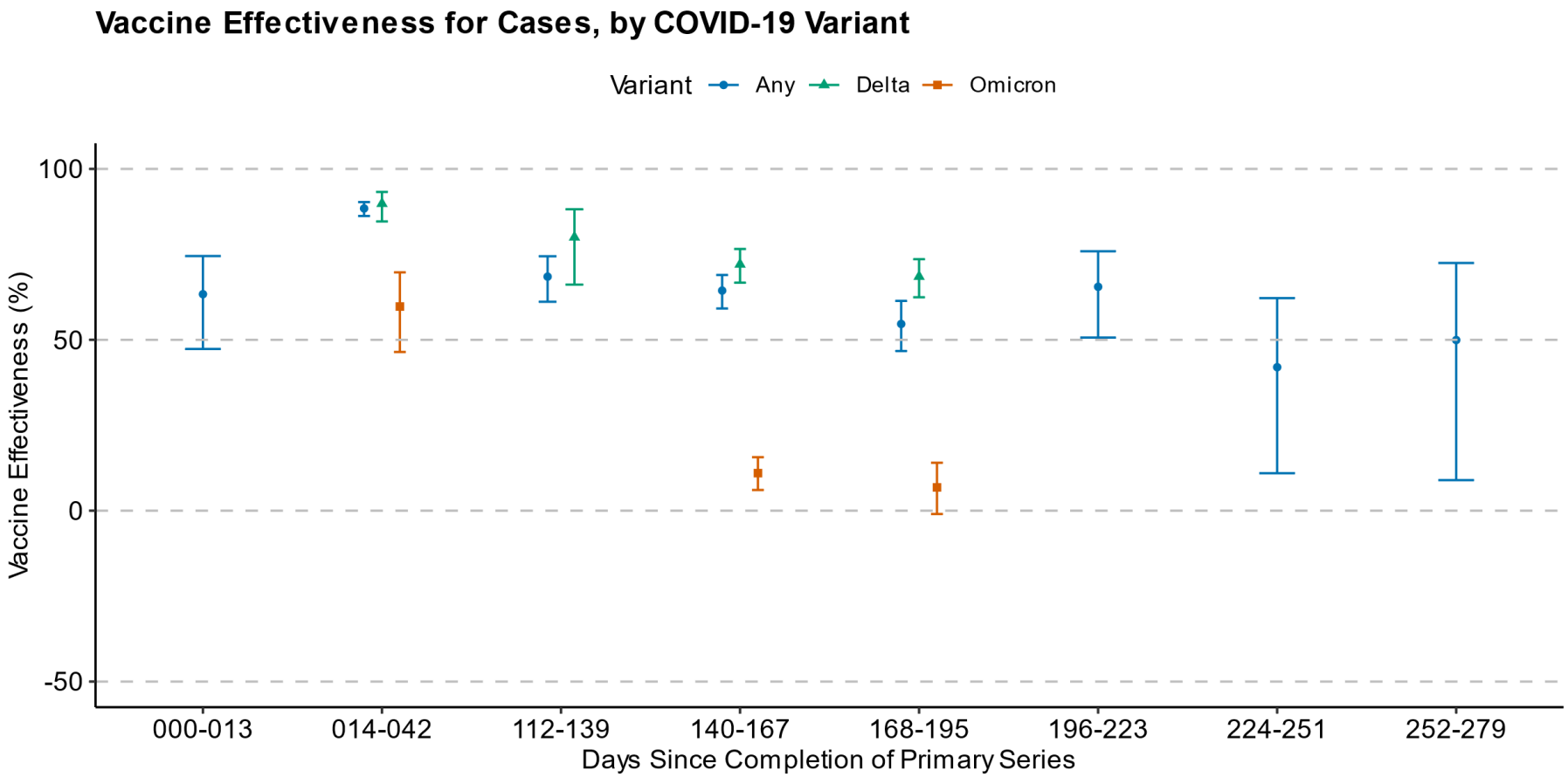
* This is a combination of any, symptomatic, and asymptomatic infections. If a study reports any infections this is prioritised over symptomatic or asymptomatic (when reported). If the study reports symptomatic and asymptomatic, then symptomatic is prioritised.

Table 3: VE against COVID-19 cases* for completed primary series (**Omicron variant**)

	Baseline days (weeks)		Follow-up days (weeks)								
	0-13 (0-2)	**14-42 (2-6)**	**112-139 (12-16)**	**140-167 (16-20)**	**168-195 (20-24)**	**196-223 (24-28)**	**224-251 (28-32)**	**252-279 (32-36)**	**280-307 (36-40)**	**308-335 (40-44)**	**336+ (44+)**
Any vaccine		60% (46-70) 5 cohorts	29% (18-38) 1 cohort	11% (6-16) 5 cohorts	7% (-1-14) 5 cohorts	10% (2-16) 1 cohort	-6% (-13-1) 2 cohorts	2% (-6-9) 1 cohort	-18% (-26 - -10) 1 cohort	-0.3% (-10-10) 1 cohort	17% (3-28) 1 cohort
Any mRNA vaccine		68% (60-75) 3 cohort	29% (18-38) 1 cohort	13% (10-15) 3 cohort	10% (7-14) 3 cohort	10% (2-16) 1 cohort	-8% (-15-1) 1 cohort	2% (-6-9) 1 cohort	-18% (-26-10) 1 cohort	-0.3% (-10-9) 1 cohort	17% (3-28) 1 cohort
Any adenovirus		49% (39-57) 1 cohort		4% (2-6) 1 cohort	-3% (-4- -1) 1 cohort						
BNT162b2		65% (64-67) 2 cohorts	29% (18-38) 1 cohort	12% (10-13) 2 cohorts	10% (5-14) 2 cohorts	10% (2-16) 1 cohort	-8% (-15-1) 1 cohort	2% (-6-9) 1 cohort	-18% (-26- -9) 1 cohort	0% (-10-10) 1 cohort	17% (3-28) 1 cohort
mRNA-1273		75% (71-79) 1 cohort		15% (12-18) 1 cohort	15% (4-25) 1 cohort						
ChAdOx1		49% (39- 57) 1 cohort		4% (2-6) 1 cohort	-3% (-4- -1) 1 cohort						
Ad26.COV2.S											

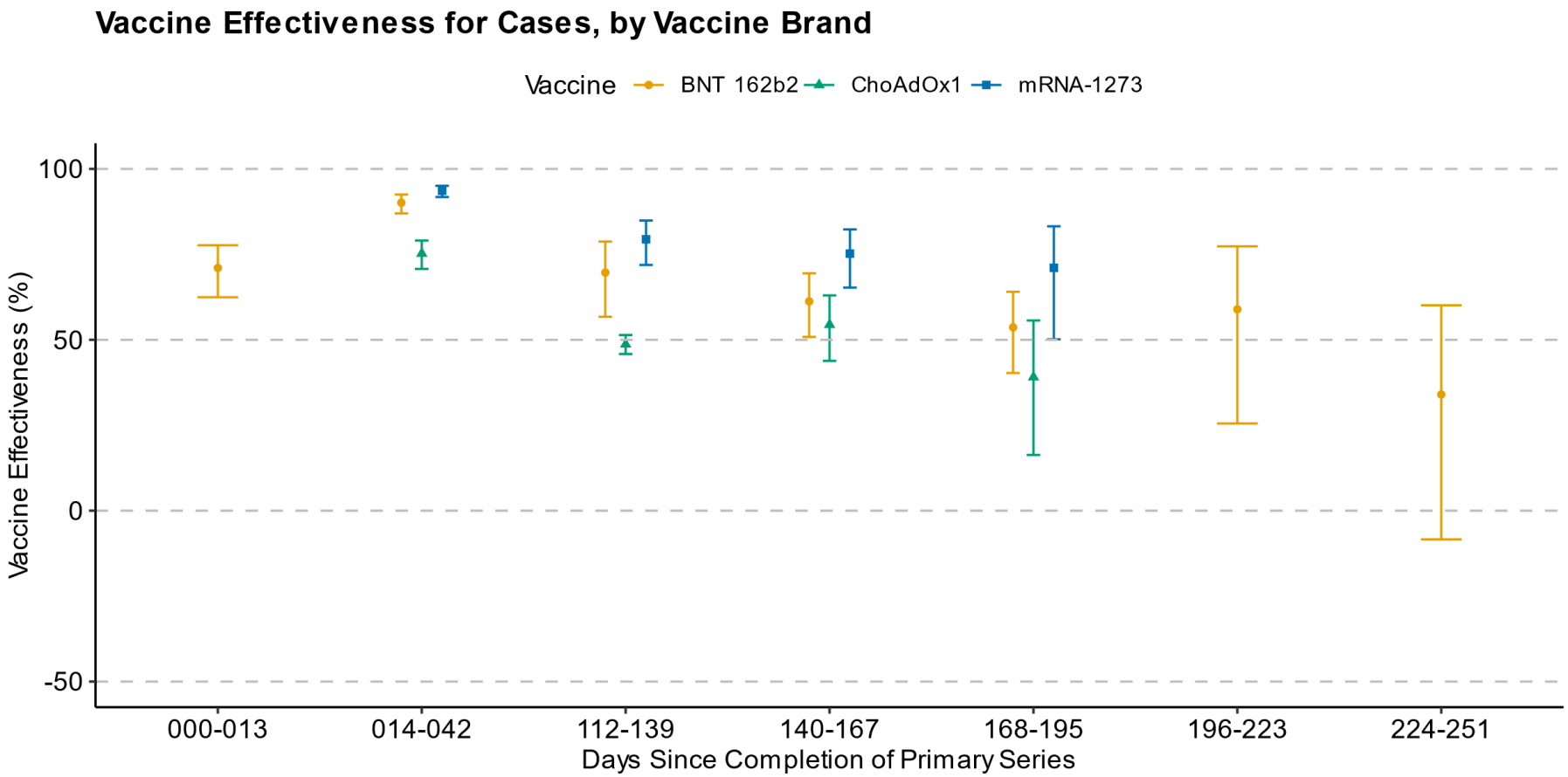
* This is a combination of any, symptomatic, and asymptomatic infections. If a study reports any infections this is prioritised over symptomatic or asymptomatic (when reported). If the study reports symptomatic and asymptomatic, then symptomatic is prioritised.

Figure 1: VE against COVID-19 cases* for any completed primary series by variant (**All**, **Delta**, and **Omicron**)



Only time points with at least 4 cohorts have been included in the figure.
* This is a combination of any, symptomatic, and asymptomatic infections. If a study reports any infections this is prioritised over symptomatic or asymptomatic (when reported). If the study reports symptomatic and asymptomatic, then symptomatic is prioritised.

Figure 2: VE against COVID-19 cases* for specific primary series vaccines (**mRNA-1273**, **ChoAdOx1**, and **BNT 162b2**)



Only time points with at least 4 cohorts have been included in the figure.
* This is a combination of any, symptomatic, and asymptomatic infections. If a study reports any infections this is prioritised over symptomatic or asymptomatic (when reported). If the study reports symptomatic and asymptomatic, then symptomatic is prioritised.

Question 1b: VE against COVID-19 hospitalisations change over time (>112 days) in individuals who have received a complete primary COVID-19 vaccine series

Table 4: VE against COVID-19 hospitalisations for completed primary series (**all strains**)

	Baseline days (weeks)		Follow-up days (weeks)								
	0-13 (0-2)	**14-42 (2-6)**	**112-139 (12-16)**	**140-167 (16-20)**	**168-195 (20-24)**	**196-223 (24-28)**	**224-251 (28-32)**	**252-279 (32-36)**	**280-307 (36-40)**	**308-335 (40-44)**	**336+ (44+)**
Any vaccine		94% (92-95) 28 cohorts	90% (87-92) 13 cohorts	91% (88-93) 26 cohorts	88% (82-92) 6 cohorts	95% (91-97) 1 cohort	88% (85-90) 1 cohort				
Any mRNA vaccine		94% (92-96) 18 cohorts	90% (85-93) 8 cohorts	91% (88-94) 16 cohorts	90% (73-96) 4 cohorts	95% (91-97) 1 cohort	88% (85-90) 1 cohort				
Any adenovirus		89% (76-95) 6 cohorts	81% (73-87) 1 cohort	85% (78-89) 6 cohorts	82% (69-89) 1 cohort						
BNT162b2		95% (92-97) 9 cohorts	93% (89-96) 4 cohorts	92% (89-94) 8 cohorts	95% (76-99) 2 cohorts		88% (85-90) 1 cohort				
mRNA-1273		96% (95-97) 7 cohorts	90% (85-94) 3 cohorts	95% (93-96) 7 cohorts	96% (83-99) 1 cohort	95% (91-97) 1 cohort					
ChAdOx1		92% (79-97) 4 cohorts		85% (80-93) 4 cohorts							
Ad26.COV2.S		79% (71-85) 2 cohorts	81% (73-87) 1 cohort	76% (55-87) 2 cohorts	82% (69-89) 1 cohort						

Table 5: VE against COVID-19 hospitalisations for completed primary series (**Delta variant**)

	Baseline days (weeks)		**Follow-up days (weeks)**								
	0-13 (0-2)	**14-42 (2-6)**	**112-139 (12-16)**	**140-167 (16-20)**	**168-195 (20-24)**	**196-223 (24-28)**	**224-251 (28-32)**	**252-279 (32-36)**	**280-307 (36-40)**	**308-335 (40-44)**	**336+ (44+)**
Any vaccine		94% (94-98) 9 cohorts	91% (91-92) 7 cohorts	91% (86-94) 8 cohorts	87% (75-94) 3 cohorts						
Any mRNA vaccine		97% (92-99) 4 cohorts	93% (87-96) 3 cohorts	89% (77-95) 3 cohorts	90% (8-99) 2 cohorts						
Any adenovirus		95% (95-96) 1 cohort		80% (77-83) 1 cohort							
BNT162b2		98% (94-99) 3 cohorts	97% (92-99) 2 cohorts	92% (90-93) 4 cohorts	98% (91-100) 1 cohort						
mRNA-1273		98% (60-100) 1 cohort	87% (72-94) 1 cohort								
ChAdOx1		95% (95-96) 1 cohort		80% (77-83) 1 cohort							
Ad26.COV2.S											

Table 6: VE against COVID-19 hospitalisations for completed primary series (**Omicron variant**)

	Baseline days (weeks)		**Follow-up days (weeks)**								
	0-13 (0-2)	**14-42 (2-6)**	**112-139 (12-16)**	**140-167 (16-20)**	**168-195 (20-24)**	**196-223 (24-28)**	**224-251 (28-32)**	**252-279 (32-36)**	**280-307 (36-40)**	**308-335 (40-44)**	**336+ (44+)**
Any vaccine		71% (51-83) 1 cohort	58% (38-72) 1 cohort	54% (48-59) 1 cohort							
Any mRNA vaccine		71% (51-83) 1 cohort	58% (38-72) 1 cohort	54% (48-59) 1 cohort							
Any adenovirus											
BNT162b2											
mRNA-1273											
ChAdOx1											
Ad26.COV2.S											

Question 1c: VE against COVID-19 deaths change over time (>112 days) in individuals who have received a complete primary COVID-19 vaccine series

Table 7: VE against COVID-19 deaths for completed primary series (**all strains**)

	Baseline days (weeks)		**Follow-up days (weeks)**								
	0-13 (0-2)	**14-42 (2-6)**	**112-139 (12-16)**	**140-167 (16-20)**	**168-195 (20-24)**	**196-223 (24-28)**	**224-251 (28-32)**	**252-279 (32-36)**	**280-307 (36-40)**	**308-335 (40-44)**	**336+ (44+)**
Any vaccine		94% (91-96) 13 cohorts	76% (38-90) 1 cohort	85% (76-91) 6 cohorts	88% (83-92) 7 cohorts						
Any mRNA vaccine		96% (93-97) 9 cohorts		90% (85-94) 3 cohort	90% (85-93) 6 cohorts						
Any adenovirus		87% (67-95) 6 cohorts	76% (38-90) 1 cohort	77% (63-85) 3 cohorts	84% (74-90) 4 cohorts						
BNT162b2		96% (93-97) 5 cohorts		90% (82-94) 2 cohort	89% (84-93) 3 cohorts						
mRNA-1273		98% (86-99) 2 cohorts		93% (85-97) 1 cohort	95% (90-98) 2 cohorts						
ChAdOx1		95% (93-96) 3 cohorts		85% (76-90) 1 cohort	88% (81-93) 2 cohorts						
Ad26.COV2.S		65% (51-75) 3 cohorts		71% (57-80) 2 cohort	76% (60-86) 2 cohorts						

Table 8: VE against COVID-19 deaths for completed primary series (**Delta variant**)

	Baseline days (weeks)		**Follow-up days (weeks)**								
	0-13 (0-2)	**14-42 (2-6)**	**112-139 (12-16)**	**140-167 (16-20)**	**168-195 (20-24)**	**196-223 (24-28)**	**224-251 (28-32)**	**252-279 (32-36)**	**280-307 (36-40)**	**308-335 (40-44)**	**336+ (44+)**
Any vaccine		97% (90-99) 2 cohorts		89% (80-94) 2 cohorts							
Any mRNA vaccine		99% (97-99) 1 cohort		92% (89-94) 1 cohort							
Any adenovirus		95% (93-96) 1 cohort		85% (76-90) 1 cohort							
BNT162b2		99% (97-99) 1 cohort		92% (89-94) 1 cohort							
mRNA-1273											
ChAdOx1		95% (93-96) 1 cohort		85% (76-90) 1 cohort							
Ad26.COV2.S											

Table 9: VE against COVID-19 deaths for completed primary series (**Omicron variant**)

No data to report

Question 2a: VE against COVID-19 cases change over time (>84 days) in individuals who have received a complete primary COVID-19 vaccine series plus an additional dose

Table 10: VE against COVID-19 cases* for completed primary series and an additional dose

	Baseline days (weeks)		**Follow-up days (weeks)**								
	0-13 (0-2)	**14-42 (2-6)**	**84-111 (8-12)**	**112-139 (12-16)**	**140-167 (16-20)**	**168-195 (20-24)**	**196-223 (24-28)**	**224-251 (28-32)**	**252-279 (32-36)**	**280-307 (36-40)**	**308-335 (40-44)**
Any vaccine											
Any mRNA vaccine											
Any adenovirus											
BNT162b2 - **Omicron**	16 % (1-28) 1 cohort	54 % (47-59) 1 cohort	38 % (29-45) 1 cohort								
mRNA-1273											
ChAdOx1											
Ad26.COV2.S											

* This is a combination of any, symptomatic, and asymptomatic infections. If a study reports any infections this is prioritised over symptomatic or asymptomatic (when reported). If the study reports symptomatic and asymptomatic, then symptomatic is prioritised.

Question 2b: VE against COVID-19 hospitalisations change over time (>84 days) in individuals who have received a complete primary COVID-19 vaccine series plus an additional dose

Table 11: VE against COVID-19 hospitalisations for completed primary series and an additional dose

	Baseline days (weeks)		Follow-up days (weeks)								
	0-13 (0-2)	14-42 (2-6)	84-111 (8-12)	112-139 (12-16)	140-167 (16-20)	168-195 (20-24)	196-223 (24-28)	224-251 (28-32)	252-279 (32-36)	280-307 (36-40)	308-335 (40-44)
Any vaccine											
Any mRNA vaccine – **all strains**		95 % (94-95) 1 cohort	81 % (72-87) 1 cohort								
Any mRNA vaccine – **Delta**		96 % (95-97) 1 cohort	76 % (14-93) 1 cohort								
Any mRNA vaccine – **Omicron**		91 % (88-93) 1 cohort	78 % (67-85) 1 cohort								
Any adenovirus											
BNT162b2											
mRNA-1273											
ChAdOx1											
Ad26.COV2.S											

Question 2c: VE against COVID-19 deaths change over time (>84 days) in individuals who have received a complete primary COVID-19 vaccine series plus an additional dose

Table 12: VE against COVID-19 deaths for completed primary series and an additional dose

No data to report

Narrative overview of findings

1a. Findings for confirmed COVID-19 cases primary series only

A total of 24 studies provided usable baseline and follow-up information with regards to COVID-19 related cases. The meta-analyses indicated that there was a consistent decline in the VE of the vaccines for cases, especially up to 32 weeks post full vaccine schedule. The decline was similar across all vaccines, with the overall VE being slightly higher for any mRNA vs. adenovirus and for mRNA-1273 vs. BNT162b2. With regards to variants, compared to the combined data the patterns of results were similar for the Delta variant. There were only three studies that provided data for Omicron, which showed a notably lower baseline VE compared to Delta and a much more rapid drop in VE over the follow-up period.

1b. Findings for COVID-19 related hospitalisations primary series only

A total of 13 studies provided usable baseline and follow-up information with regards to COVID-19 related hospitalisations. The meta-analyses indicated that there was a great deal of consistency across time in the ability of the vaccines to prevent COVID-19-related hospitalisations, especially across the 28 weeks post receipt of a vaccine series. The results were consistent across vaccines, though mRNA vaccines tended to provide greater protection than adenovirus-based vaccines. With regards to variants, compared to the combined data the patterns of findings were similar for the Delta variant. There was only one study that provided data for Omicron, which showed a lower baseline VE compared to Delta and a graded decrease in VE across the 24 weeks post vaccine series.

1c. Findings for COVID-19 related deaths primary series only

A total of 5 studies provided usable baseline and follow-up information with regards to COVID-19 related deaths. The meta-analyses indicated that there was a great deal of consistency across time in the ability of the vaccines to prevent COVID-19-related deaths, especially across the 24 weeks post receipt of a vaccine series. The results were consistent across vaccines, with minimal differences between mRNA and adenovirus vaccines. Finally, with regards to variants, there was minimal data for the Delta variant (suggesting that VE remained high up to 24 weeks post vaccine series) and no data for the Omicron variant.

2a. Findings for confirmed COVID-19 cases primary series plus additional dose

A total of one study provided usable baseline and follow-up information with regards to confirmed COVID-19 case data (symptomatic cases). The study included members from the general population of Qatar (December 2021 to February 2022) and reported on data for the VE of the BNT162b2 vaccine against Omicron (inferred from Omicron wave – 95% of cases at that time were Omicron). After a small improvement in VE (54%) there was a reduction at 84 days (38%). Of note, this is the same cohort who provided generally lower VE for cases in response to a full vaccine series.

2b. Findings for COVID-19 related hospitalisations primary series plus additional dose

A total of one study provided usable baseline and follow-up information with regards to COVID-19-related hospitalisations. The study included individuals from 10 states in the USA (August 2021 to January 2022) and reported on data for the VE of any mRNA vaccine against any strain, and the Delta and Omicron variants (inferred from variant predominant periods based on state-level surveillance data). In general, 3-dose VE for hospitalisations had a small amount of waning approximately 12+ weeks after administration (from 91-96% to 76-81%) with a 20% drop against Delta and a 13% drop against Omicron. Of note, this study also assessed VE against a full vaccine schedule during the same period and found that 2-dose VE dropped 4% against Delta and 13% against Omicron.

2c. Findings for COVID-19 related deaths primary series plus additional dose
There were no studies that provided usable baseline and follow-up information with regards to COVID-19-related hospitalisations.

Risk of bias (RoB) assessment
The risk of bias data for each individual study is provided in the Supplementary File (10.4_vaccine_waning_adults_RoB_2022-03-30.xlsx). Overall, the risk of bias was serious for the majority of studies due to the lack of adjustment of prognostic factors. Beyond that most items were related low. One study (Young-Xu et al.) was deemed as having a critical RoB due to not accounting for calendar time and was excluded from the analyses.

Strengths and Limitations
Key strengths of the present review include the broad search terms that were included during the initial screening phase, the rigorous methodologies that were employed throughout the review, and validation processes that were included to ensure consistency. In spite of these strengths, there were several limitations that need to be noted. As with any rapid review process, there is a slightly increased possibility that studies might be missed when compared to a full systematic review. However, this was potentially mitigated as we validated our study inclusions against another evidence synthesis team. Due to the turnaround time for the review, we were also limited in the scope of potential sub-groups that could be included and we were not able to extract any immunogenicity data. However, we were able to identify data for several key sub-groups within the extracted studies. The lack of time also meant that we weren't able to contact authors for studies that could have potentially provided data, which means that some studies which had the potential to be included, were excluded (e.g., those that graphed data but did not provide explicit data within the manuscript).

Potential implications for health systems decision-making
Though the current review provides evidence for a *waning in VE for COVID-19 confirmed cases*, it is unclear what might be driving this (e.g., a degradation in immunogenicity, changes in public health measures, or variations in case numbers and general transmission). Contrasting this are *relatively stable VE for COVID-related hospitalisations and deaths*. These patterns seem to be consistent for the Delta variant. However, there is current limited published data on the longer-term impacts of vaccines on Omicron related outcomes, though the initial *data suggests that VE in response to Omicron is lower*.

With regards to long-term waning of an additional vaccine dose. There is currently limited data to provide any notable guidance. The minimal data obtained from two studies indicates that potential waning in VEs for both cases and hospitalisations by 8 weeks post booster dose, with equivalent results for the Delta and Omicron variants.

Given that Omicron has become the dominant variant in Canada, to reduce the transmission of the virus and limit increases in cases, there may be a need to maintain some COVID-19 prevention behaviours, e.g., mask wearing and physical distancing, in individuals who are fully vaccinated with or without an additional dose. Once again, this needs to be considered in the context of the limited number of studies available looking at multiple transmission prevention strategies and a lack of randomised controlled trial evidence on the utility of combinations of prevention measures.

Land Acknowledgements
The Montreal Behavioural Medicine Centre, Concordia University, UQAM, and the CIUSSS-NIM are located on unceded Indigenous lands. The Kanien'kehá:ka Nation is recognized as the custodians of the lands and waters on which these institutions stand today. Tiohtiá:ke commonly known as Montreal is

historically known as a gathering place for many First Nations. Today, it is home to a diverse population of Indigenous and other peoples. We respect the continued connections with the past, present, and future in our ongoing relationships with Indigenous and other peoples within the Montreal community.

SPOR Evidence Alliance operates from the St. Michael's Hospital, Unity Health Toronto which is located on the traditional land of the Huron-Wendat, the Seneca, and the Mississaugas of the Credit. Today, this meeting place is still the home to many Indigenous people from across Turtle Island.

COVID-END is housed within McMaster University which is located on the traditional territories of the Mississauga and Haudenosaunee nations, and within the lands protected by the "Dish With One Spoon" wampum, an agreement to peaceably share and care for the resources around the Great Lakes.

We are grateful to have the opportunity to work on these lands.

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