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 10.7: 22nd June 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?

Visual representation of findings

1. The primary series VE against any infections, hospitalisations, and deaths are presented in Tables 1, 3, and 5, respectively; and for omicron-related outcomes in Tables 2, 4, and 6. Figure 1 provides information on infections by variant and Figure 2 provides information on cases by specific vaccine brand
2. The primary series + additional dose VE against any infections and hospitalisations are presented in Tables 7, 9, and 11, respectively. For omicron-related outcomes in Tables 8, 10, and 12.
3. The primary series + additional dose vs. primary series only OR against any infections and hospitalisations are presented in Tables 13, 15, and 17, respectively. For omicron-related outcomes in Tables 14, 16, and 18.

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

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 7**, 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.

Overall (from the initiation of this review), 14,543 studies were title and abstract screened, 925 were full-text appraised, with 55 initially included, 4 studies were excluded (RoB), leaving 51 that were used to complete this summary. The reasons for excluding the 768 studies are reported in **Appendix 7**.

Highlights of changes in this version

- ***Four*** new studies have been added (marked in blue in **Appendix 1**) that report on the long-term VE of the full vaccine schedule. The information for ***one*** study was updated to reflect the transition from a pre-print to full publication, though no new substantive information was added to the analyses (marked in green in **Appendix 1**).
- ***Two*** new studies have been added (marked in blue in **Appendix 1**) that report on the long-term VEs of additional doses beyond the full vaccine schedule.
- One new study was added (marked in blue in **Appendix 1**) that report on the long-term ORs of additional doses beyond the full vaccine schedule compared to the full vaccine schedule.

- Within the tables we have now included information on Prediction Intervals (PI) as well as confidence intervals. We have also included two measures of heterogeneity, I^2 and σ (details on the meaning of these is provided in **Appendix 2**).
- Delta was removed from the tables for version 10.6 onwards, as such, the last report to include delta data was 10.5 (https://www.mcmasterforum.org/docs/default-source/product-documents/living-evidence-syntheses/covid-19-living-evidence-synthesis-10.5---what-is-the-long-term-effectiveness-of-available-covid-19-vaccines-for-adults.pdf?sfvrsn=8cb53a44_8).

High level summary of outcomes

Primary vaccine series

- For COVID-19 infections, there was a statistically and clinically significantly degradation in VE from 16 weeks onwards after receiving the primary. The level of degradation was consistent with our definition of waning.
- For COVID-19 hospitalisations and mortality, though there is a statistically significant decline in VE, the level of decline is not clinically meaningful, indicated that there doesn't seem to be any evidence of waning over time, up to 32 and 28 weeks, respectively, after receiving the primary vaccine series.
- Data on the Omicron variant indicates that for infections there is insufficient protection at baseline with a further, statistically significant decrease in VE as of 16 weeks post primary series. For hospitalisations, there was insufficient protection at baseline but there didn't seem to be a decrease over time. For mortality, there was insufficient data available to draw any conclusions

Booster dose vs. unvaccinated

- For COVID-19 infections, the available data reflects the Omicron variant, with no other available variant data. The available data indicates that for infections there is insufficient protection at baseline with no statistical decrease in VE up to 20 weeks post booster dose.
- For COVID-19 hospitalisations, there was statistically and clinically significantly degradation in VE from 12 weeks onwards after receiving the booster dose. The level of degradation was consistent with our definition of waning. The Omicron data is consistent with this pattern.
- For COVID-19 mortality, the limited available data would suggest that there isn't clinically significant degradation in VE up to 16 weeks after receiving the booster dose, i.e., no waning. There was insufficient Omicron data to draw any conclusions.

Booster dose vs. primary series

- One study provided data comparing a full schedule vs. a full schedule plus one booster dose for COVID-19 infections. This study found a benefit at baseline of the booster compared to full schedule (OR = 0.34) which had decreased slightly at 16 weeks post booster dose (OR = 0.45). This study only included data captured during the Omicron period.

Visual representation of data

- For Tables 1-12 and Figures 1 and 2, **percentages** indicate the *level of effectiveness* of the COVID-19 vaccines compared to unvaccinated individuals. 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).
- For Tables 13-18, **the number** indicates the *level of effectiveness* of the COVID-19 vaccines compared to individuals who have received a primary series only. An OR of 1.0 indicates no protection of the booster relative to the primary series and an OR of 0 indicates that the booster maximally prevents COVID-19 events (e.g., cases, death, hospitalisations).
- Meta-analysed point estimates and 95% CIs are provided, along with the number of studies (and 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 (see note after the table about colourations of previous versions).
- In all tables, **days (weeks)** refers to time since the completion of a full vaccine series, i.e., since last vaccine.
- For Tables 1-12, the rows translate to:
  - % Vaccine Efficacy;
  - 95% CIs;
  - 95% PI; and
  - # Studies (# cohorts)
- For Tables 13-18, the rows translate to:
  - Odds ratios;
  - 95% CIs;
  - 95% PI; and
  - # Studies (# cohorts).
- We have indicated statistical significance in the tables using the following symbols:
  - † = statistically different from baseline 1 (0-13 days)
  - * = statistically different from baseline 2 (14-42 days)

High certainty evidence	Moderate certainty evidence	Low certainty evidence	Not enough evidence
Pooling of sufficient observational studies (including RCTs with follow-up data) with consistent findings	Pooling of sufficient observational studies (including RCTs with follow-up data) with some consistency in findings	Pooling of sufficient observational studies (including RCTs with follow-up data) but *inconsistent* findings	Pooling of insufficient observational studies (including RCTs with follow-up data) to be able to draw conclusions
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	At least 4 cohorts represented	Less than 4 cohorts reported

It should be noted that previous versions of this report used a slightly different colour scheme to define certainty.

Definition of waning

- There is no formal definition of waning
- The WHO defines preferred levels of initial VE as:
  - VE against symptomatic disease ≥ 70%, with the lower 95% CI ≥ 50%; or
  - VE against severe disease ≥ 90%, with the lower 95% CI ≥ 70%
  - https://www.who.int/publications/m/item/who-target-product-profiles-for-covid-19-vaccines
- In addition, they provides a graded reduction system based on arrows, such that: ↓ = 10 to <20 point reduction in VE; ↓↓ = 20 to <30 point reduction in VE; and ↓↓↓ = ≥ 30 point reduction in VE;
  - https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports
- For the current report we are using the preferred level system, with ***waning defined as***: A statistical reduction in VE from the second baseline (which must meet the preferred levels of initial VE) and one of the following:
  - VE against infection < 70%, with the lower 95% CI < 50%; or
  - VE against hospitalisation or death < 90%, with the lower 95% CI < 70%

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 infections[#] for completed primary series (**all strains**)

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)			
Any vaccine	66%	85%†	62%*	56%*	52%†*	51%*	44%†*	47%*	42%*	45%*	54%*	[49, 51]	[0.47, 0.47]	Yes
	[52, 76]	[81, 88]	[53, 70]	[46, 64]	[40, 61]	[32, 64]	[20, 61]	[20, 64]	[-28, 76]	[-32, 80]	[-19, 83]			
	[-24, 91]	[43, 96]	[-29, 90]	[-40, 88]	[-45, 87]	[-47, 87]	[-54, 85]	[-52, 86]	[-64, 88]	[-65, 89]	[-58, 91]			
	7 (14)	30 (74)	18 (40)	27 (69)	20 (43)	9 (14)	8 (10)	5 (8)	2 (2)	1 (1)	1 (1)			
Any mRNA vaccine	71%	88%†	66%*	58%†*	53%†*	51%†*	42%†*	48%†*	43%*	50%*	58%*	[34, 66]	[0.38, 0.53]	Yes
	[57, 81]	[85, 91]	[56, 74]	[47, 67]	[40, 64]	[33, 65]	[18, 59]	[24, 65]	[-17, 73]	[-14, 78]	[3, 82]			
	[-10, 93]	[56, 97]	[-21, 91]	[-36, 89]	[-43, 87]	[-46, 87]	[-54, 85]	[-50, 87]	[-60, 87]	[-57, 89]	[-49, 91]			
	6 (8)	23 (51)	14 (27)	22 (46)	16 (28)	8 (11)	7 (9)	5 (7)	2 (2)	1 (1)	1 (1)			
Any adenovirus	40%	70%†	52%*	46%*	42%*	59%		55%				[29, 71]	[0.26, 0.40]	Yes
	[8, 61]	[61, 78]	[34, 64]	[30, 59]	[23, 56]	[24, 78]		[16, 76]						
	[-41, 79]	[20, 89]	[-24, 82]	[-31, 80]	[-36, 78]	[-22, 87]		[-28, 86]						
	2 (4)	10 (17)	6 (10)	10 (18)	7 (13)	1 (1)		1 (1)						
BNT162b2	71%	86%†	60%*	51%†*	48%†*	46%†*	41%†*	46%†*	33%†*	45%*	54%*	[24, 76]	[0.29, 0.51]	Yes
	[58, 80]	[82, 90]	[46, 70]	[37, 63]	[31, 60]	[23, 62]	[16, 58]	[17, 64]	[-24, 66]	[-7, 72]	[9, 77]			
	[0, 91]	[55, 96]	[-25, 88]	[-38, 85]	[-42, 84]	[-46, 84]	[-50, 82]	[-47, 84]	[-61, 83]		[-44, 88]			
	5 (7)	15 (24)	9 (14)	17 (27)	12 (19)	5 (6)	6 (7)	3 (4)	1 (1)	1 (1)	1 (1)			
mRNA-1273		92%	77%*	71%*	68%*	56%*	50%*	51%*	66%			[41, 59]	[0.44, 0.53]	Yes
		[88, 94]	[63, 85]	[58, 80]	[47, 80]	[25, 74]	[2, 74]	[-1, 76]	[-51, 94]					
		[67, 98]	[0, 94]	[-17, 93]	[-28, 93]	[-48, 90]	[-57, 89]	[-57, 89]	[-69, 96]					

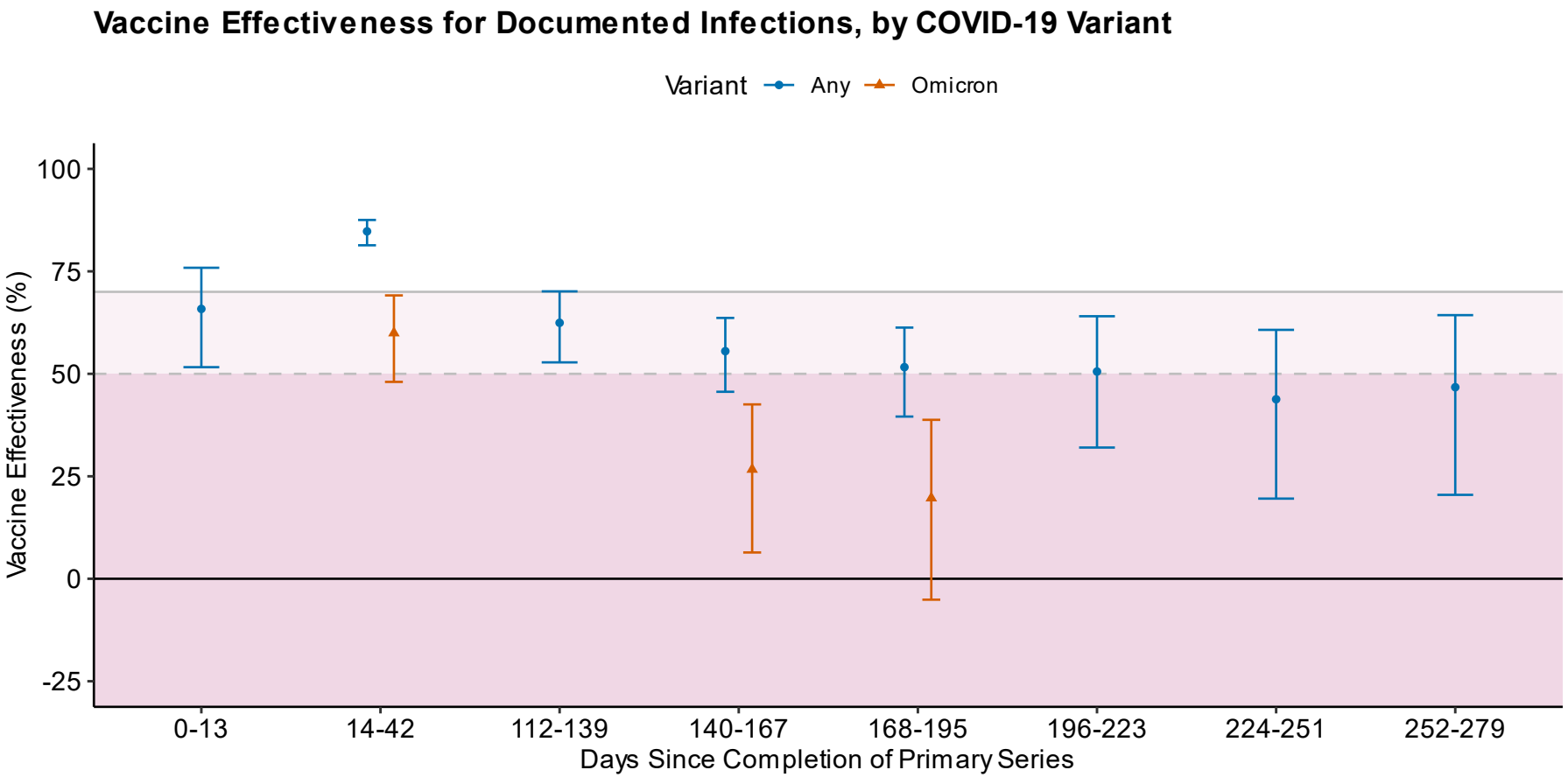
		12 (21)	5 (9)	11 (18)	4 (7)	4 (5)	2 (3)	2 (3)	1 (1)					
ChAdOx1	43%	72%†	53%*	46%*	38%*							[23, 77]	[0.25, 0.46]	Yes
	[7, 65]	[61, 81]	[30, 68]	[23, 62]	[10, 57]									
	[-45, 82]	[16, 91]	[-31, 85]	[-39, 82]	[-47, 80]									
	2 (3)	7 (14)	4 (7)	7 (15)	5 (10)									
Ad26.COV2.S	17%	62%	49%	50%	55%	58%		55%				[53, 45]	[0.21, 0.19]	Yes
	[-51, 66]	[43, 74]	[23, 66]	[27, 65]	[34, 69]	[25, 77]		[17, 75]						
	[-61, 73]	[17, 82]	[-11, 76]	[-7, 77]	[3, 79]	[-1, 83]		[-10, 81]						
	1 (1)	3 (3)	2 (3)	3 (3)	3 (3)	1 (1)		1 (1)						

Table 2: VE against COVID-19 infections[#] for completed primary series (**Omicron variant**)

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)			
Any vaccine	48%	60%†	32%*	27%†*	20%†*	7%†*	10%†*	14%†*	-11%†*	7%†*	23%*	[24, 76]	[0.18, 0.32]	Yes
	[30, 61]	[48, 69]	[6, 52]	[6, 43]	[-5, 39]	[-23, 33]	[-24, 38]	[-23, 43]	[-44, 30]	[-33, 42]	[-20, 53]			
	[-15, 77]	[11, 82]	[-35, 70]	[-38, 67]	[-44, 64]	[-53, 59]	[-52, 61]	[-51, 63]	[-63, 54]	[-56, 62]	[-47, 68]			
	3 (7)	6 (10)	2 (3)	8 (15)	5 (7)	2 (3)	2 (2)	2 (2)	1 (1)	1 (1)	1 (1)			
Any mRNA vaccine	48%	62%	35%*	27%†*	23%†*	20%*	4%†*	16%*	-7%†*	11%†*	26%*	[18, 82]	[0.17, 0.36]	Yes
	[22, 65]	[48, 73]	[6, 56]	[1, 47]	[-8, 45]	[-24, 51]	[-37, 42]	[-23, 46]	[-44, 35]	[-32, 46]	[-19, 56]			
	[-24, 79]	[8, 85]	[-38, 74]	[-43, 70]	[-47, 68]	[-53, 69]	[-60, 63]	[-53, 67]	[-65, 59]	[-57, 66]	[-49, 72]			
	2 (3)	5 (8)	2 (3)	6 (9)	4 (5)	1 (1)	1 (1)	2 (2)	1 (1)	1 (1)	1 (1)			
Any adenovirus	34%	50%		21%	0%							[84, 16]	[0.23, 0.10]	Yes
	[-17, 64]	[-13, 79]		[-22, 51]	[-54, 55]									
	[-44, 76]	[-36, 84]		[-50, 69]	[-67, 67]									
	1 (2)	1 (1)		2 (3)	1 (1)									
BNT162b2	53%	57%	28%	21%†*	11%†*	9%*	-8%†*	1%†*	-18%†*	0%†*	16%*	[68, 32]	[0.20, 0.14]	Yes
	[29, 69]	[41, 70]	[-20, 59]	[-4, 39]	[-24, 40]	[-35, 47]	[-46, 37]	[-41, 42]	[-52, 29]	[-42, 42]	[-32, 52]			
	[5, 77]	[18, 78]	[-37, 68]	[-33, 58]	[-44, 55]	[-49, 58]	[-58, 50]	[-54, 55]	[-62, 44]	[-55, 54]	[-46, 62]			
	1 (2)	3 (3)	1 (1)	4 (5)	2 (2)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)	1 (1)			
mRNA-1273		60%		14%	13%							[95, 5]	[0.44, 0.10]	Yes
		[-37, 90]		[-71, 78]	[-84, 88]									
		[-77, 96]		[-89, 92]	[-93, 94]									
		2 (2)		2 (2)	1 (1)									
ChAdOx1	34%	50%		21%	0%							[84, 16]	[0.23, 0.10]	Yes

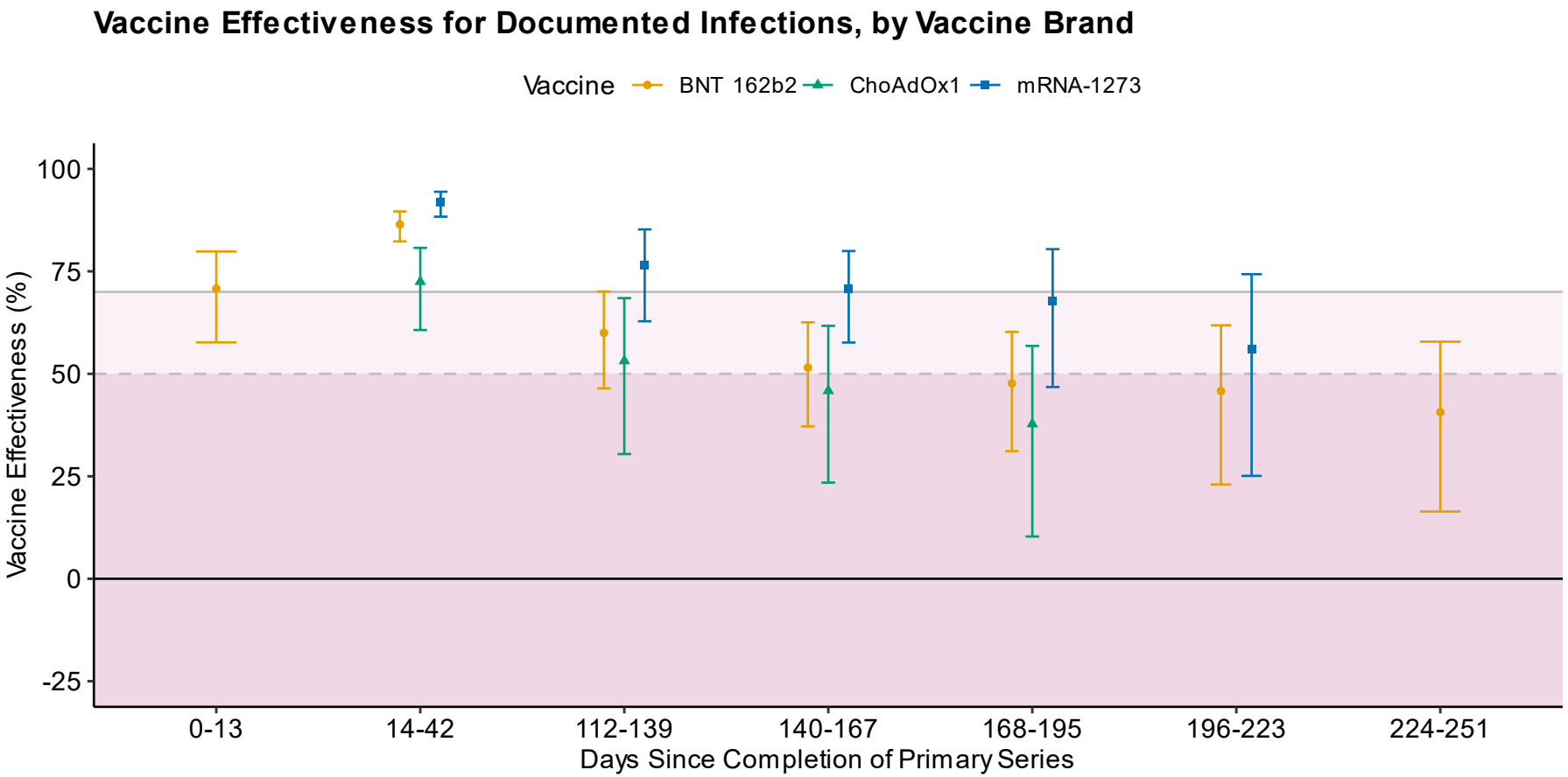
	[-17, 64]	[-13, 79]		[-22, 51]	[-54, 55]									
	[-44, 76]	[-36, 84]		[-50, 69]	[-67, 67]									
	1 (2)	1 (1)		2 (3)	1 (1)									
Ad26.COV2.S														

Figure 1: VE against COVID-19 infections[#] for any completed primary series by variant (**All** and **Omicron**)



Only time points with at least 4 studies have been included in the figure.
The solid line indicates the WHO definition of preferred minimum level of VE and the dotted line is the minimum lower 95%CIs
[#] 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 infections [#] for specific primary series vaccines (**BNT 162b2**, **ChoAdOx1**, and **mRNA-1273**)



Only time points with at least 4 studies have been included in the figure.
The solid line indicates the WHO definition of preferred minimum level of VE and the dotted line is the minimum lower 95%CIs
[#] 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 3: VE against COVID-19 hospitalisations for completed primary series (**all strains**)

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)			
Any vaccine	87%	91%	88%	86%*	82%*	83%	76%*	88%				[44, 54]	[0.56, 0.62]	Yes
	[73, 94]	[87, 93]	[83, 92]	[80, 90]	[72, 88]	[68, 91]	[47, 89]	[49, 97]						
	[22, 98]	[51, 98]	[38, 98]	[24, 97]	[1, 97]	[2, 97]	[-33, 96]	[-7, 99]						
	3 (6)	18 (46)	10 (28)	16 (43)	7 (15)	4 (6)	3 (3)	1 (1)						
Any mRNA vaccine	87%	91%	89%	86%*	84%	83%	77%*	87%				[37, 62]	[0.53, 0.69]	Yes
	[64, 96]	[87, 94]	[83, 93]	[78, 91]	[70, 92]	[67, 92]	[49, 90]	[47, 97]						
	[4, 98]	[48, 99]	[35, 98]	[14, 98]	[0, 98]	[-7, 97]	[-36, 97]	[-16, 99]						
	2 (3)	15 (27)	7 (14)	13 (24)	4 (5)	4 (6)	3 (3)	1 (1)						
Any adenovirus		88%	86%	84%	80%							[50, 47]	[0.47, 0.45]	Yes
		[81, 93]	[76, 92]	[75, 90]	[63, 89]									
		[51, 97]	[41, 97]	[35, 96]	[13, 95]									
		7 (13)	4 (8)	7 (13)	3 (6)									
BNT162b2	88%	93%	90%	86%*	85%*	80%*	79%*	87%				[20, 78]	[0.38, 0.76]	Yes
	[45, 97]	[88, 96]	[81, 94]	[77, 92]	[68, 93]	[57, 90]	[55, 90]	[29, 98]						
	[-17, 99]	[55, 99]	[35, 98]	[16, 98]	[0, 98]	[-25, 97]	[-29, 97]	[-31, 99]						
	1 (1)	10 (14)	4 (6)	9 (13)	3 (4)	3 (4)	3 (3)	1 (1)						
mRNA-1273	92%	94%	96%	92%*	91%	91%	88%	93%				[6, 75]	[0.14, 0.49]	Yes
	[22, 99]	[91, 97]	[92, 98]	[87, 95]	[74, 97]	[82, 95]	[54, 97]	[40, 99]						
	[1, 99]	[82, 98]	[84, 99]	[75, 98]	[59, 98]	[68, 97]	[32, 98]	[23, 99]						

	1 (1)	4 (7)	2 (3)	4 (7)	1 (2)	3 (4)	1 (1)	1 (1)						
ChAdOx1		91%	90%	87%	83%*							[69, 27]	[0.46, 0.29]	Yes
		[86, 95]	[82, 94]	[80, 91]	[68, 91]									
		[71, 97]	[64, 97]	[56, 96]	[38, 95]									
		5 (10)	3 (6)	5 (10)	2 (5)									
Ad26.COV2.S		80%	81%	76%	82%							[73, 0]	[0.32, 0.00]	Yes
		[32, 94]	[8, 96]	[29, 92]	[-10, 97]									
		[-21, 97]	[-35, 98]	[-27, 96]	[-43, 98]									
		2 (2)	1 (1)	2 (2)	1 (1)									

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

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)			
Any vaccine	67%	62%	65%	58%	42%	61%						[81, 0]	[0.20, 0.00]	Yes
	[3, 89]	[51, 71]	[55, 73]	[47, 66]	[3, 65]	[33, 77]								
	[-4, 90]	[37, 77]	[43, 79]	[32, 74]	[-11, 70]	[23, 80]								
	2 (2)	5 (6)	3 (4)	4 (5)	1 (1)	1 (1)								
Any mRNA vaccine	79%	62%	69%	58%		61%						[69, 11]	[0.16, 0.06]	Yes
	[-65, 98]	[50, 71]	[59, 76]	[48, 66]		[35, 77]								
	[-66, 98]	[39, 76]	[50, 80]	[35, 73]		[26, 80]								
	1 (1)	5 (5)	3 (3)	4 (4)		1 (1)								
Any adenovirus		60%	46%	45%										
		[33, 76]	[21, 63]	[-89, 97]										
		1 (1)	1 (1)	1 (1)										
BNT162b2	79%	67%		66%		61%						[0, 94]	[0.00, 0.42]	Yes
	[-97, 100]	[-18, 91]		[-11, 90]		[-63, 94]								
	[-98, 100]	[-68, 97]		[-67, 96]		[-82, 97]								
	1 (1)	2 (2)		2 (2)		1 (1)								
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 5: VE against COVID-19 deaths for completed primary series (**all strains**)

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)			
Any vaccine		91%	89%	80%*	84%							[31, 64]	[0.50, 0.72]	Yes
		[82, 95]	[75, 96]	[62, 90]	[67, 92]									
		[37, 99]	[24, 99]	[-23, 97]	[-7, 98]									
		7 (17)	3 (6)	5 (11)	4 (8)									
Any mRNA vaccine		93%	95%	83%*	88%							[23, 73]	[0.48, 0.86]	Yes
		[84, 97]	[84, 99]	[58, 93]	[70, 95]									
		[38, 99]	[48, 100]	[-37, 98]	[-11, 99]									
		6 (12)	2 (3)	4 (6)	3 (7)									
Any adenovirus		85%	68%	71%	82%							[66, 23]	[0.62, 0.36]	Yes
		[70, 93]	[4, 90]	[39, 86]	[56, 93]									
		[22, 97]	[-52, 95]	[-37, 95]	[-5, 97]									
		5 (8)	2 (3)	4 (5)	2 (4)									
BNT162b2		96%	93%	89%*	90%*							[71, 18]	[0.38, 0.19]	Yes
		[92, 97]	[79, 98]	[80, 94]	[83, 94]									
		[87, 98]	[71, 98]	[67, 96]	[70, 97]									
		4 (6)	1 (1)	3 (3)	2 (4)									
mRNA-1273		98%		93%	95%							[18, 0]	[0.25, 0.00]	Yes
		[89, 100]		[69, 98]	[86, 98]									
		[86, 100]		[62, 99]	[81, 99]									

		2 (3)		1 (1)	1 (2)									
ChAdOx1		94%	82%	79%*	88%							[0, 62]	[0.00, 0.30]	Yes
		[88, 97]	[2, 97]	[63, 89]	[74, 94]									
		[83, 98]	[-13, 97]	[46, 92]	[64, 96]									
		3 (4)	1 (1)	2 (2)	1 (2)									
Ad26.COV2.S		65%	76%	71%	76%							[0, 0]	[0.00, 0.00]	Yes
		[44, 78]	[8, 94]	[50, 83]	[50, 89]									
		[44, 78]	[8, 94]	[50, 83]	[50, 89]									
		3 (3)	1 (1)	2 (2)	2 (2)									

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

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)	336+ (48+)			
Any vaccine		49%	62%	18%										
		[-64, 90]	[-76, 97]	[2, 31]										
		1 (2)	1 (2)	1 (2)										
Any mRNA vaccine		3%	91%	19%										
		[-53, 56]	[19, 99]	[-6, 38]										
		1 (1)	1 (1)	1 (1)										
Any adenovirus		84%	-7%	17%										
		[-22, 98]	[-68, 63]	[-4, 34]										
		1 (1)	1 (1)	1 (1)										
BNT162b2														
mRNA-1273														
ChAdOx1														

Ad26.COV2.S														

Question 2a-1: VE against COVID-19 infections change over time (>84 days) in individuals who have received a complete primary COVID-19 vaccine series plus an additional dose – comparison to unvaccinated

Table 7: VE against COVID-19 infections[#] for completed primary series and an additional dose (**all strains**)

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	84-111 (12-16)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)			
Any vaccine	64%	63%	54%	52%	-30%†*							[25, 75]	[0.31, 0.55]	Yes
	[37, 79]	[44, 76]	[30, 70]	[25, 69]	[-69, 37]									
	[-32, 91]	[-30, 90]	[-44, 88]	[-47, 88]	[-85, 69]									
	2 (4)	8 (15)	7 (13)	6 (11)	1 (1)									
Any mRNA vaccine	64%	63%	54%	53%	-30%†*							[26, 74]	[0.32, 0.55]	Yes
	[36, 79]	[43, 76]	[29, 70]	[25, 70]	[-70, 38]									
	[-33, 91]	[-32, 90]	[-45, 88]	[-47, 88]	[-85, 70]									
	2 (4)	8 (13)	7 (13)	6 (9)	1 (1)									
Any adenovirus		62%		27%										
		[44, 74]		[-42, 69]										
		1 (2)		1 (2)										
BNT162b2	46%	66%	58%	56%	-38%†*							[18, 82]	[0.35, 0.77]	Yes
	[-27, 78]	[32, 83]	[14, 80]	[6, 79]	[-79, 44]									
	[-75, 92]	[-55, 95]	[-64, 94]	[-66, 93]	[-92, 79]									
	1 (2)	6 (11)	4 (9)	4 (5)	1 (1)									
mRNA-1273		54%	32%	38%								[98, 0]	[0.16, 0.00]	Yes
		[24, 72]	[-14, 60]	[-20, 69]										
		[-7, 80]	[-39, 71]	[-40, 77]										

		2 (2)	2 (2)	1 (1)										
ChAdOx1		62%		27%										
		[44, 74]		[-42, 69]										
		1 (2)		1 (2)										
Ad26.COV2.S														

Table 8: VE against COVID-19 infections[#] for completed primary series and an additional dose (**Omicron variant**)

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	84-111 (12-16)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)			
Any vaccine	64%	63%	54%	52%	-30%†*							[25, 75]	[0.31, 0.55]	Yes
	[37, 79]	[44, 76]	[30, 70]	[25, 69]	[-69, 37]									
	[-32, 91]	[-30, 90]	[-44, 88]	[-47, 88]	[-85, 69]									
	2 (4)	8 (15)	7 (13)	6 (11)	1 (1)									
Any mRNA vaccine	64%	63%	54%	53%	-30%†*							[26, 74]	[0.32, 0.55]	Yes
	[36, 79]	[43, 76]	[29, 70]	[25, 70]	[-70, 38]									
	[-33, 91]	[-32, 90]	[-45, 88]	[-47, 88]	[-85, 70]									
	2 (4)	8 (13)	7 (13)	6 (9)	1 (1)									
Any adenovirus		62%		27%										
		[44, 74]		[-42, 69]										
		1 (2)		1 (2)										
BNT162b2	46%	66%	58%	56%	-38%†*							[18, 82]	[0.35, 0.77]	Yes
	[-27, 78]	[32, 83]	[14, 80]	[6, 79]	[-79, 44]									
	[-75, 92]	[-55, 95]	[-64, 94]	[-66, 93]	[-92, 79]									
	1 (2)	6 (11)	4 (9)	4 (5)	1 (1)									
mRNA-1273		54%	32%	38%								[98, 0]	[0.16, 0.00]	Yes
		[24, 72]	[-14, 60]	[-20, 69]										
		[-7, 80]	[-39, 71]	[-40, 77]										
		2 (2)	2 (2)	1 (1)										
ChAdOx1		62%		27%										
		[44, 74]		[-42, 69]										

		1 (2)		1 (2)										
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-1: 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 – comparison to unvaccinated

Table 9: VE against COVID-19 hospitalisations for completed primary series and an additional dose (**all strains**)

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	84-111 (12-16)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)			
Any vaccine	84%	91%†	76%*	68%†*	84%							[50, 44]	[0.34, 0.32]	Yes
	[76, 89]	[86, 94]	[67, 83]	[50, 79]	[55, 94]									
	[54, 94]	[75, 97]	[35, 91]	[8, 89]	[34, 96]									
	4 (9)	3 (5)	6 (13)	4 (6)	1 (1)									
Any mRNA vaccine	85%	92%†	78%*	70%†*	81%							[89, 0]	[0.34, 0.00]	Yes
	[79, 89]	[89, 94]	[73, 83]	[58, 79]	[53, 93]									
	[68, 93]	[83, 96]	[55, 90]	[35, 86]	[41, 94]									
	4 (8)	3 (5)	6 (12)	4 (6)	1 (1)									
Any adenovirus	82%		76%											
	[54, 93]		[72, 80]											
	1 (2)		1 (2)											
BNT162b2	83%	89%	77%	66%*	81%							[85, 0]	[0.30, 0.00]	Yes
	[73, 90]	[77, 94]	[67, 85]	[38, 82]	[51, 93]									
	[61, 93]	[70, 96]	[50, 90]	[15, 87]	[39, 94]									
	2 (4)	1 (1)	3 (5)	2 (2)	1 (1)									
mRNA-1273		90%	84%	77%										
		[87, 93]	[78, 88]	[63, 86]										
		1 (1)	1 (1)	1 (1)										

ChAdOx1	82%		76%											
	[54, 93]		[72, 80]											
	1 (2)		1 (2)											
Ad26.COV2.S														

Table 10: VE against COVID-19 hospitalisations for completed primary series and an additional dose (**Omicron variant**)

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	84-111 (12-16)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)			
Any vaccine	81%	90%†	76%*	67%†*	83%							[54, 39]	[0.32, 0.27]	Yes
	[72, 87]	[85, 93]	[66, 82]	[49, 78]	[54, 94]									
	[51, 93]	[74, 96]	[38, 90]	[12, 87]	[36, 95]									
	4 (7)	3 (5)	6 (11)	4 (6)	1 (1)									
Any mRNA vaccine	85%	91%†	78%*	69%†*	81%							[88, 0]	[0.33, 0.00]	Yes
	[79, 89]	[88, 93]	[72, 82]	[57, 78]	[54, 92]									
	[67, 93]	[81, 96]	[55, 89]	[35, 85]	[43, 94]									
	4 (7)	3 (5)	6 (11)	4 (6)	1 (1)									
Any adenovirus	71%		77%											
	[67, 75]		[72, 81]											
	1 (1)		1 (1)											
BNT162b2	83%	89%	77%	66%*	81%							[85, 0]	[0.30, 0.00]	Yes
	[73, 90]	[77, 94]	[67, 85]	[38, 82]	[51, 93]									
	[61, 93]	[70, 96]	[50, 90]	[15, 87]	[39, 94]									
	2 (4)	1 (1)	3 (5)	2 (2)	1 (1)									
mRNA-1273		90%	84%	77%										
		[87, 93]	[78, 88]	[63, 86]										
		1 (1)	1 (1)	1 (1)										
ChAdOx1	71%		77%											
	[67, 75]		[72, 81]											

	1 (1)		1 (1)											
Ad26.COV2.S														

Question 2c-1: 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 – comparison to unvaccinated

Table 11: VE against COVID-19 deaths for completed primary series and an additional dose (**all strains**)

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	84-111 (12-16)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)			
Any vaccine	82%		84%		71%							[58, 0]	[0.30, 0.00]	Yes
	[73, 88]		[75, 90]		[-40, 95]									
	[60, 92]		[63, 93]		[-48, 96]									
	2 (5)		2 (5)		1 (1)									
Any mRNA vaccine	81%		87%		71%							[0, 0]	[0.00, 0.00]	Yes
	[71, 87]		[81, 91]		[-51, 96]									
	[71, 87]		[81, 91]		[-51, 96]									
	2 (3)		2 (3)		1 (1)									
Any adenovirus	83%		82%											
	[61, 93]		[50, 94]											
	1 (2)		1 (2)											
BNT162b2	82%		68%		71%									
	[70, 89]		[-65, 96]		[-13, 93]									
	1 (1)		1 (1)		1 (1)									
mRNA-1273														

ChAdOx1	83%		82%											
	[61, 93]		[50, 94]											
	1 (2)		1 (2)											
Ad26.COV2.S														

Table 12: VE against COVID-19 deaths for completed primary series and an additional dose (**Omicron variant**)

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	84-111 (12-16)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)			
Any vaccine	77%		83%		71%							[50, 0]	[0.25, 0.00]	Yes
	[58, 87]		[69, 90]		[-56, 96]									
	[43, 90]		[58, 93]		[-61, 97]									
	2 (3)		2 (3)		1 (1)									
Any mRNA vaccine	78%		87%		71%							[12, 0]	[0.11, 0.00]	Yes
	[46, 91]		[72, 94]		[-84, 99]									
	[40, 92]		[68, 95]		[-84, 99]									
	2 (2)		2 (2)		1 (1)									
Any adenovirus	74%		77%											
	[60, 83]		[67, 84]											
	1 (1)		1 (1)											
BNT162b2	82%		68%		71%									
	[70, 89]		[-65, 96]		[-13, 93]									
	1 (1)		1 (1)		1 (1)									
mRNA-1273														
ChAdOx1	74%		77%											
	[60, 83]		[67, 84]											

	1 (1)		1 (1)											
Ad26.COV2.S														

Question 2a-2: OR against COVID-19 infections change over time (>84 days) in individuals who have received a complete primary COVID-19 vaccine series plus an additional dose – comparison to those who have only received the primary series

Table 13: OR against COVID-19 infections[#] for completed primary series and an additional dose vs. those who have only received the primary series (**all strains**)

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	84-111 (12-16)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)			
Any vaccine		0.34		0.45										
		[0.24, 0.49]		[0.24, 0.81]										
		1 (1)		1 (1)										
Any mRNA vaccine		0.34		0.45										
		[0.24, 0.49]		[0.24, 0.81]										
		1 (1)		1 (1)										
Any adenovirus														
BNT162b2		0.34		0.45										
		[0.24, 0.49]		[0.24, 0.81]										
		1 (1)		1 (1)										
mRNA-1273														

ChAdOx1														
Ad26.COV2.S														

Table 14: OR against COVID-19 infections[#] for completed primary series and an additional dose vs. those who have only received the primary series (**Omicron variant**)

	Baseline days (weeks)		Follow-up days (weeks)									I^2 [w/b]	σ [w/b]	MOD
	0-13 (0-2)	14-42 (2-6)	84-111 (12-16)	112-139 (16-20)	140-167 (20-24)	168-195 (24-28)	196-223 (28-32)	224-251 (32-36)	252-279 (36-40)	280-307 (40-44)	308-335 (44-48)			
Any vaccine		0.34		0.45										
		[0.24, 0.49]		[0.24, 0.81]										
		1 (1)		1 (1)										
Any mRNA vaccine		0.34		0.45										
		[0.24, 0.49]		[0.24, 0.81]										
		1 (1)		1 (1)										
Any adenovirus														
BNT162b2		0.34		0.45										
		[0.24, 0.49]		[0.24, 0.81]										
		1 (1)		1 (1)										
mRNA-1273														
ChAdOx1														

Ad26.COV2.S														

Question 2b-2: OR 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 – comparison to those who have only received the primary series

Table 15: OR against COVID-19 hospitalisations for completed primary series and an additional dose vs. primary series only (**all strains**)

No data to report

Table 16: OR against COVID-19 hospitalisations for completed primary series and an additional dose vs. primary series only (**Omicron variant**)

No data to report

Question 2c-2: OR 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 – comparison to those who have only received the primary series

Table 17: OR against COVID-19 deaths for completed primary series and an additional dose vs. primary series only (**all strains**)

No data to report

Table 18: OR against COVID-19 deaths for completed primary series and an additional dose vs. primary series only (**Omicron variant**)

No data to report

Narrative overview of findings

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

A total of 37 studies provided usable baseline and follow-up information with regards to COVID-19 infections. The analyses indicated that VE for infections started to wane 16 weeks up to 40 weeks post full vaccine schedule. With the exception of mRNA-1273, the waning was seen across all vaccines (with variable follow-up times). For mRNA-1273, though there was a statistically significant decline in VE as of 16 weeks post full schedule it didn't reach the level of waning until 28 weeks post full schedule.

With regards to the nine studies reporting Omicron variant data, baseline levels of VE did not meet the WHO minimum preferred level of VE. As of 16 weeks post full schedule there was a further statistical decline in the VE. One study provided a direct comparison between the Omicron BA.1 and BA.2 variants (Kirsebom et al.). Aggregating data across ChAdOx1-S, BNT162b2, and mRNA-1273 vaccines they didn't find a large difference between the variants for VE at 25+ weeks (17.4% vs. 24.3%, respectively).

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

A total of 21 studies provided usable baseline and follow-up information with regards to COVID-19 related hospitalisations. The analyses indicated that there was a statistically significant decease in VE, across time in the ability of the vaccines to prevent COVID-19-related hospitalisations, which was not clinically meaningful. The results were consistent across vaccines. With regards to the seven Omicron variant studies, baseline levels of VE did not meet the WHO minimum preferred level of VE. That being said, there wasn't a statistical decrease in VE across the 20 weeks post vaccine series.

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

A total of seven studies provided usable baseline and follow-up information with regards to COVID-19 related deaths. There was a non-clinically significant, but statistically significant decrease in the ability of the vaccines to prevent COVID-19-related deaths VE for COVID-19 related deaths across the 24 weeks post receipt of a vaccine series. There seemed to be a qualitatively better retention of VE for the mRNA vaccines compared to the adenovirus vaccines, but there was too little data to provide any specific comparisons. With regards to the one study providing Omicron variant data, baseline levels of VE did not meet the WHO minimum preferred level of VE.

2a-1. Findings for confirmed COVID-19 infections primary series plus additional dose – compared to unvaccinated

A total of ten studies provided usable baseline and follow-up information with regards to confirmed COVID-19 infection data. These studies all reported on the Omicron variant. The baseline levels of VE did not meet the WHO minimum preferred level of VE. That being said, there wasn't a statistical decrease in VE across 20 weeks post vaccine series. One study provided a direct comparison between the Omicron BA.1 and BA.2 variants (Kirsebom et al.). Aggregating data across BNT162b2 and mRNA-1273 booster doses, they didn't find a large difference between the variants for VE at 15+ weeks (45.5% vs. 48.4%, respectively).

2b-1. Findings for COVID-19 related hospitalisations primary series plus additional dose – compared to unvaccinated

A total of seven studies provided usable baseline and follow-up information with regards to COVID-19-related hospitalisations. Though there was a statistically significant decrease in VE as of 12 weeks post booster dose, this did not become clinically significant until 16 weeks post booster dose, i.e., the point where waning occurs. A similar pattern was seen for the Omicron variant.

2c-1. Findings for COVID-19 related deaths primary series plus additional dose – compared to unvaccinated

A total of two studies provided usable baseline and follow-up information with regards to COVID-19-related deaths. Though limited, the data indicates that there is no clinical drop in VE as up to 16 weeks post booster dose. A similar pattern was seen for the Omicron variant.

2a-2. Findings for confirmed COVID-19 infections primary series plus additional dose – compared to full vaccine series

One study provided data comparing a full schedule vs. a full schedule plus one booster dose for COVID-19 infections (Richterman et al.). This study found a benefit at baseline of the booster compared to full schedule (OR = 0.34) which had decreased slightly at 16 weeks post booster dose (OR = 0.45). This study only included data captured during the Omicron period.

2b-2. Findings for COVID-19 related hospitalisations primary series plus additional dose – compared to full vaccine series
The was no available data to report on this.

2c-2. Findings for COVID-19 related deaths primary series plus additional dose – compared to full vaccine series
The was no available data to report on this.

Risk of bias (RoB) assessment
The risk of bias data for each individual study is provided in the Supplementary File (les10.7_vaccine_waning_adults_RoB_3_2022-06-22.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. Four studies (Young-Xu et al., Menni et al., Lee et al., and Paranthaman et al.) were deemed as having a critical RoB and were excluded from the analyses. Young-Xu et al., Menni et al., and Lee et al., did to not account for calendar time, Menni et al also used self-reported vaccination and infection data. Finally, Paranthaman et al.) did not account for medical conditions in a long-term care cohort.

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 *long term waning in VE for COVID-19 confirmed infections*, 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, there is *no strong evidence of waning in VEs for COVID-related hospitalisations and deaths*. These patterns seem to be consistent for the Omicron variant. However, the baseline levels of VE did not meet the WHO minimum preferred level of VE, suggesting that the *VE response to the Omicron variant is lower in general*.

With regards to long-term waning of an additional vaccine dose, the majority of the available data is derived from Omicron studies, which indicate that the baseline levels of VE do not meet the WHO minimum preferred level of VE. In spite of that, we still see signs of statistical reductions in VE for cases with relative stability for COVID-19 hospitalisations.

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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The opinions, results, and conclusions are those of the team that prepared the living evidence synthesis, and independent of the Government of Canada, CIHR, PHAC, or FRQS. No endorsement by the Government of Canada, CIHR, PHAC, or FRQS is intended or should be inferred.

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