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 10.5: 27th April 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, 13, and 16, respectively. For delta-related outcomes the summaries are presented in Tables 11, 14, and 17; and for omicron-related outcomes in Tables 12, 15, and 18.

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

Overall (from the initiation of this review), 13,806 studies were title and abstract screened, 796 were full-text appraised, with 41 initially included, 2 studies were excluded (RoB), leaving 39 that were used to complete this summary. The reasons for excluding the 691 studies are reported in **Appendix 7**.

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.

Highlights of changes in this version

- ***Nine*** new studies have been added (marked in blue in **Appendix 1**) and ***one*** study was updated (marked in green in **Appendix 1**) that report on the long-term VE of the full vaccine schedule.
- ***Six*** 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*** study provided information on the longer-term VE of both the primary series and booster dose for Omicron BA.1 vs. Omicron BA.2.

- We have now provided details on the number of studies and number of cohorts (one study may provide information on more than one cohort) for each cell in the tables.

High level summary of outcomes

Primary vaccine series

- For COVID-19 cases, there is a general degradation in VE over time, up to 32 weeks after receiving the primary vaccine series.
- For COVID-19 hospitalisations and mortality, VE is maintained over time, up to 32 and 24 weeks, respectively, after receiving the primary vaccine series.
- Data on the Delta and Omicron variants showed similar patterns, but with a lower initial baseline for Omicron compared to Delta (ca. 50% vs. ca. 80-90%).

Booster dose

- For COVID-19 cases, there is a general degradation in VE from baseline, that was stable across 20 weeks after receiving the booster dose. Of note, this data is all based on the Omicron variant.
- For COVID-19 hospitalisations, VE is maintained up to 20 weeks after receiving the booster dose, which seemed to be consistent for both the Delta and Omicron variants.
- There was limited data for COVID-19 deaths, which suggested that VE is maintained up to 24 weeks after receiving the booster dose, which seemed to be consistent for both the Delta (16 weeks post booster dose) and Omicron variants (24 weeks post booster dose).

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.
- The rows translate to:
  - % Efficacy;
  - 95% CIs; and
  - # Studies (# cohorts).

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	

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

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	**59%** (41 - 71) 6 (11)	**86%** (83 - 88) 25 (68)	**62%** (53 - 69) 16 (38)	**58%** (52 - 63) 24 (64)	**47%** (38 - 56) 16 (39)	**56%** (43 - 66) 6 (10)	**48%** (26 - 64) 7 (9)	**60%** (32 - 76) 3 (6)	**33%** (-66 - 84) 2 (2)	**0%** (-10 - 9) 1 (1)	**16%** (3 - 28) 1 (1)
Any mRNA vaccine	**62%** (35 - 78) 5 (7)	**89%** (86 - 92) 20 (48)	**65%** (54 - 73) 12 (25)	**60%** (53 - 66) 19 (43)	**52%** (40 - 61) 13 (25)	**58%** (43 - 69) 6 (9)	**44%** (19 - 62) 6 (8)	**62%** (27 - 80) 3 (5)	**33%** (-66 - 84) 2 (2)	**0%** (-10 - 9) 1 (1)	**16%** (3 - 28) 1 (1)
Any adenovirus	**36%** (-5 - 61) 1 (2)	**70%** (61 - 76) 10 (17)	**43%** (14 - 62) 6 (10)	**47%** (32 - 59) 9 (16)	**34%** (13 - 50) 7 (13)	**54%** (51 - 57) 1 (1)		**50%** (42 - 57) 1 (1)			
BNT162b2	**71%** (62 - 78) 4 (5)	**88%** (83 - 91) 15 (24)	**63%** (45 - 75) 9 (14)	**54%** (43 - 63) 16 (25)	**49%** (35 - 59) 12 (19)	**56%** (34 - 70) 5 (6)	**48%** (22 - 65) 6 (7)	**62%** (2 - 85) 3 (4)	**-18%** (-26 - -8) 1 (1)	**0%** (-10 - 9) 1 (1)	**16%** (3 - 28) 1 (1)
mRNA-1273		**93%** (89 - 95) 12 (21)	**80%** (73 - 85) 5 (9)	**73%** (61 - 81) 11 (18)	**71%** (51 - 83) 4 (7)	**64%** (46 - 76) 4 (5)	**55%** (16 - 76) 2 (3)	**62%** (53 - 70) 2 (3)	**74%** (-12 - 94) 1 (1)		
ChAdOx1	**47%** (37 - 56) 1 (1)	**72%** (62 - 79) 7 (14)	**39%** (5 - 61) 4 (7)	**46%** (29 - 60) 6 (13)	**26%** (-1 - 45) 5 (10)						
Ad26.COV2.S	**11%** (-36 - 49) 1 (1)	**62%** (43 - 74) 3 (3)	**50%** (24 - 67) 2 (3)	**51%** (39 - 61) 3 (3)	**56%** (46 - 64) 3 (3)	**54%** (51 - 57) 1 (1)		**50%** (42 - 57) 1 (1)			

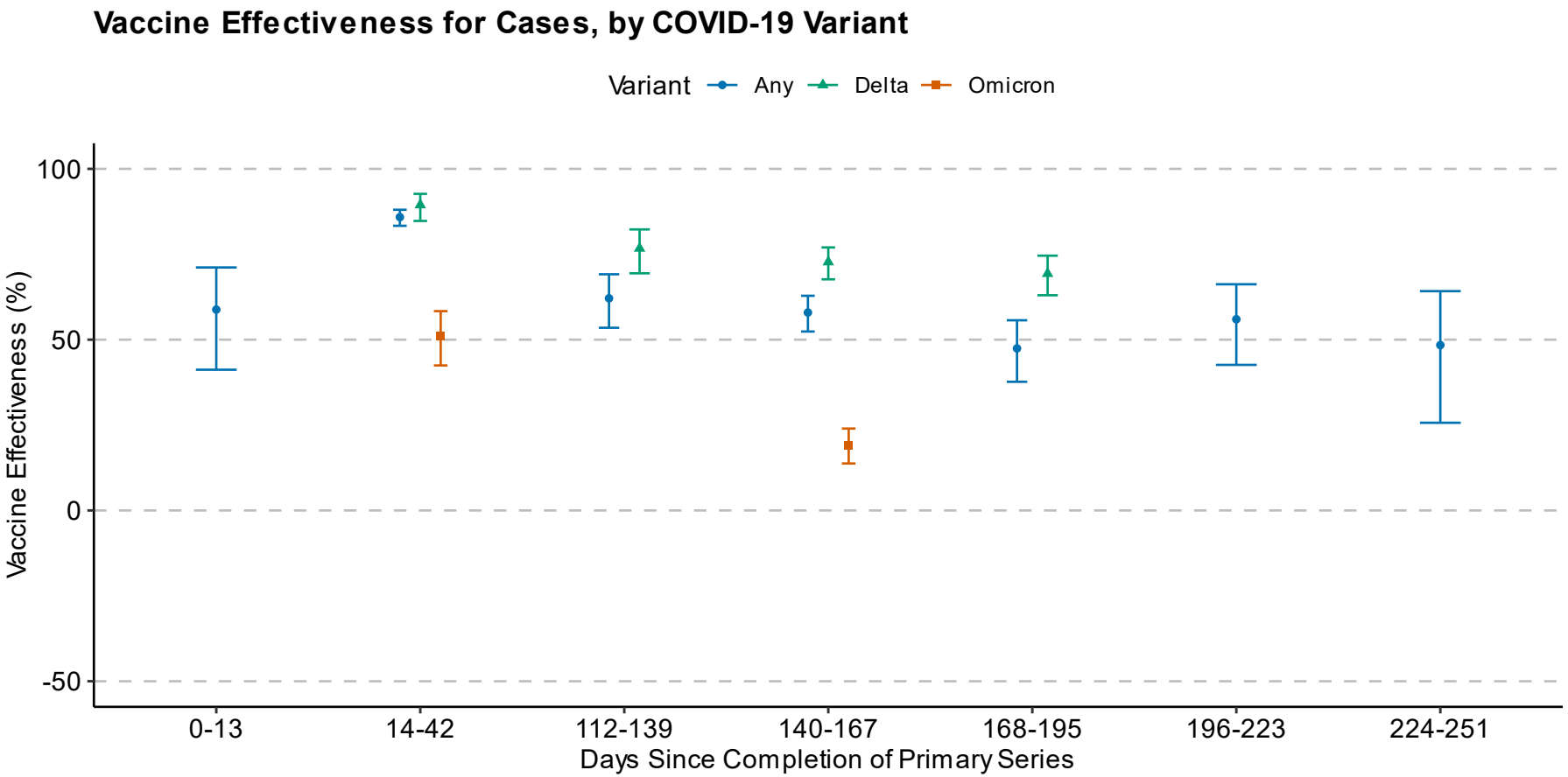
Table 2: VE against COVID-19 cases* for completed primary series (**Delta variant**)

	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%** (63 - 77) 1 (1)	**89%** (85 - 93) 8 (20)	**77%** (69 - 82) 5 (11)	**73%** (68 - 77) 7 (18)	**69%** (63 - 75) 6 (15)	**74%** (72 - 75) 2 (3)	**77%** (74 - 80) 2 (3)	**71%** (61 - 79) 2 (3)	**74%** (-12 - 94) 1 (1)		
Any mRNA vaccine	**71%** (63 - 77) 1 (1)	**92%** (91 - 93) 6 (11)	**76%** (65 - 83) 4 (6)	**76%** (71 - 79) 5 (9)	**74%** (67 - 79) 4 (8)	**74%** (72 - 75) 2 (3)	**76%** (71 - 80) 1 (2)	**71%** (61 - 79) 2 (3)	**74%** (-12 - 94) 1 (1)		
Any adenovirus		**78%** (66 - 85) 3 (5)	**74%** (69 - 77) 1 (2)	**55%** (51 - 58) 3 (5)	**44%** (42 - 46) 2 (4)						
BNT162b2		**91%** (90 - 92) 3 (5)	**84%** (80 - 86) 1 (2)	**74%** (69 - 79) 3 (5)	**74%** (68 - 80) 2 (4)	**79%** (76 - 81) 1 (2)	**79%** (75 - 82) 1 (2)	**79%** (74 - 83) 1 (2)			
mRNA-1273		**94%** (92 - 95) 4 (6)	**83%** (79 - 87) 3 (4)	**79%** (77 - 81) 4 (6)	**76%** (74 - 79) 3 (5)	**66%** (53 - 75) 2 (3)	**68%** (61 - 74) 1 (2)	**62%** (52 - 70) 2 (3)	**74%** (-12 - 94) 1 (1)		
ChAdOx1		**78%** (66 - 85) 3 (5)	**74%** (69 - 77) 1 (2)	**55%** (51 - 58) 3 (5)	**44%** (42 - 46) 2 (4)						
Ad26.COV2.S											

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

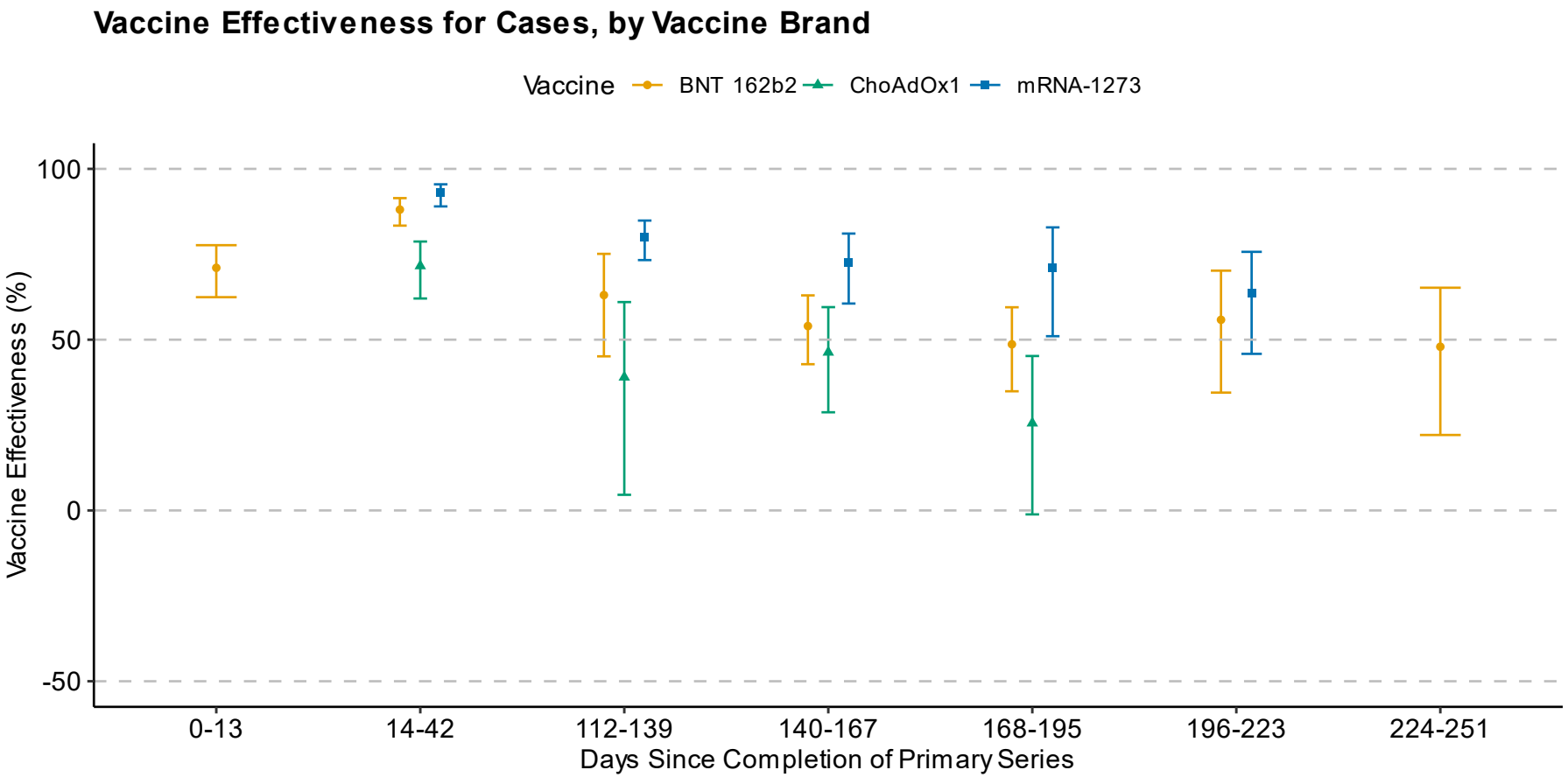
	Baseline days (weeks)		**Follow-up days (weeks)**								
	0-13 (0-2)	**14-42 (2-6)**	**112-139 (12-16)**	**140-167 (16-20)**	**168-195 (20-24)**	**196-223 (24-28)**	**224-251 (28-32)**	**252-279 (32-36)**	**280-307 (36-40)**	**308-335 (40-44)**	**336+ (44+)**
Any vaccine	**50%** (18 - 70) 2 (4)	**51%** (42 - 58) 5 (9)	**14%** (5 - 21) 2 (3)	**19%** (14 - 24) 6 (11)	**7%** (-1 - 14) 3 (5)	**18%** (11 - 24) 2 (3)	**-6%** (-13 - 1) 2 (2)	**2%** (-6 - 9) 1 (1)	**-18%** (-26 - -8) 1 (1)	**0%** (-10 - 9) 1 (1)	**16%** (3 - 28) 1 (1)
Any mRNA vaccine	**24%** (16 - 31) 1 (2)	**53%** (44 - 61) 4 (7)	**14%** (5 - 21) 2 (3)	**13%** (11 - 15) 4 (7)	**10%** (6 - 14) 2 (3)	**10%** (2 - 16) 1 (1)	**-7%** (-15 - 1) 1 (1)	**2%** (-6 - 9) 1 (1)	**-18%** (-26 - -8) 1 (1)	**0%** (-10 - 9) 1 (1)	**16%** (3 - 28) 1 (1)
Any adenovirus		**49%** (39 - 57) 1 (1)		**4%** (2 - 6) 1 (1)	**-3%** (-4 - -1) 1 (1)						
BNT162b2		**56%** (29 - 73) 3 (3)	**28%** (18 - 38) 1 (1)	**10%** (9 - 12) 3 (3)	**10%** (5 - 14) 2 (2)	**10%** (2 - 16) 1 (1)	**-7%** (-15 - 1) 1 (1)	**2%** (-6 - 9) 1 (1)	**-18%** (-26 - -8) 1 (1)	**0%** (-10 - 9) 1 (1)	**16%** (3 - 28) 1 (1)
mRNA-1273		**61%** (3 - 84) 2 (2)		**13%** (12 - 14) 2 (2)	**15%** (4 - 25) 1 (1)						
ChAdOx1		**49%** (39 - 57) 1 (1)		**4%** (2 - 6) 1 (1)	**-3%** (-4 - -1) 1 (1)						
Ad26.COV2.S											

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 studies 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 (**BNT 162b2**, **ChoAdOx1**, and **mRNA-1273**)



Only time points with at least 4 studies 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	**83%** (77 - 87) 2 (4)	**93%** (90 - 94) 17 (45)	**89%** (86 - 91) 10 (29)	**89%** (86 - 91) 15 (42)	**83%** (76 - 88) 7 (15)	**93%** (84 - 97) 3 (4)	**87%** (67 - 95) 3 (3)	**96%** (91 - 98) 1 (1)			
Any mRNA vaccine	**84%** (74 - 90) 1 (1)	**93%** (89 - 96) 14 (26)	**88%** (84 - 92) 7 (15)	**89%** (85 - 92) 12 (23)	**90%** (79 - 95) 4 (5)	**93%** (82 - 97) 3 (4)	**86%** (64 - 95) 3 (3)	**96%** (91 - 98) 1 (1)			
Any adenovirus		**88%** (81 - 93) 7 (13)	**85%** (79 - 90) 4 (8)	**84%** (80 - 87) 7 (13)	**80%** (74 - 85) 3 (6)						
BNT162b2		**95%** (90 - 97) 9 (13)	**93%** (88 - 95) 4 (6)	**90%** (83 - 94) 8 (12)	**89%** (80 - 94) 3 (4)	**90%** (77 - 96) 2 (3)	**88%** (67 - 96) 3 (3)	**96%** (84 - 99) 1 (1)			
mRNA-1273		**96%** (95 - 97) 4 (7)	**96%** (91 - 98) 2 (3)	**95%** (93 - 96) 4 (7)	**94%** (73 - 98) 1 (2)	**94%** (91 - 97) 2 (3)	**91%** (73 - 97) 1 (1)	**95%** (65 - 99) 1 (1)			
ChAdOx1		**91%** (85 - 94) 5 (10)	**88%** (84 - 92) 3 (6)	**85%** (82 - 88) 5 (10)	**80%** (72 - 86) 2 (5)						
Ad26.COV2.S		**79%** (71 - 85) 2 (2)	**81%** (73 - 87) 1 (1)	**76%** (55 - 87) 2 (2)	**82%** (69 - 89) 1 (1)						

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	**83%** (77 - 88) 1 (2)	**95%** (92 - 97) 7 (16)	**93%** (91 - 95) 6 (15)	**92%** (89 - 94) 6 (15)	**88%** (78 - 94) 3 (7)	**95%** (90 - 97) 1 (2)					
Any mRNA vaccine		**96%** (87 - 99) 5 (6)	**93%** (89 - 96) 4 (6)	**91%** (85 - 95) 4 (5)	**96%** (93 - 98) 1 (2)	**95%** (90 - 97) 1 (2)					
Any adenovirus		**92%** (82 - 97) 3 (4)	**94%** (83 - 98) 2 (3)	**84%** (78 - 88) 3 (4)	**90%** (68 - 97) 1 (2)						
BNT162b2		**98%** (95 - 99) 2 (3)	**96%** (95 - 97) 1 (2)	**95%** (91 - 98) 2 (3)	**95%** (91 - 97) 1 (2)	**94%** (88 - 97) 1 (2)					
mRNA-1273		**96%** (88 - 99) 1 (2)	**97%** (96 - 98) 1 (2)	**94%** (92 - 96) 1 (2)	**94%** (65 - 99) 1 (2)	**95%** (81 - 98) 1 (2)					
ChAdOx1		**92%** (82 - 97) 3 (4)	**94%** (83 - 98) 2 (3)	**84%** (78 - 88) 3 (4)	**90%** (68 - 97) 1 (2)						
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	**64%** (0 - 87) 1 (1)	**59%** (52 - 65) 4 (5)	**65%** (53 - 73) 3 (4)	**54%** (51 - 57) 3 (4)	**42%** (25 - 55) 1 (1)						
Any mRNA vaccine		**59%** (51 - 66) 4 (4)	**68%** (58 - 76) 3 (3)	**54%** (51 - 57) 3 (3)							
Any adenovirus		**60%** (33 - 76) 1 (1)	**46%** (21 - 63) 1 (1)	**45%** (-89 - 97) 1 (1)							
BNT162b2		**50%** (34 - 63) 1 (1)		**52%** (47 - 56) 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 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		**92%** (88 - 95) 7 (17)	**82%** (53 - 93) 3 (6)	**78%** (61 - 87) 5 (11)	**88%** (84 - 91) 4 (8)						
Any mRNA vaccine		**94%** (90 - 96) 6 (12)	**93%** (88 - 96) 2 (3)	**84%** (58 - 94) 4 (6)	**89%** (85 - 92) 3 (7)						
Any adenovirus		**86%** (67 - 94) 5 (8)	**61%** (-6 - 85) 2 (3)	**68%** (40 - 83) 4 (5)	**84%** (74 - 90) 2 (4)						
BNT162b2		**95%** (93 - 97) 4 (6)	**93%** (88 - 96) 1 (1)	**89%** (86 - 92) 3 (3)	**89%** (85 - 92) 2 (4)						
mRNA-1273		**98%** (94 - 99) 2 (3)		**93%** (85 - 97) 1 (1)	**95%** (90 - 98) 1 (2)						
ChAdOx1		**94%** (92 - 96) 3 (4)	**77%** (22 - 93) 1 (1)	**79%** (63 - 88) 2 (2)	**88%** (81 - 92) 1 (2)						
Ad26.COV2.S		**65%** (51 - 75) 3 (3)	**76%** (38 - 90) 1 (1)	**71%** (57 - 80) 2 (2)	**76%** (60 - 86) 2 (2)						

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		**95%** (86 - 98) 2 (4)	**85%** (59 - 95) 1 (2)	**83%** (66 - 92) 2 (4)							
Any mRNA vaccine		**97%** (82 - 100) 2 (2)	**92%** (66 - 98) 1 (1)	**87%** (57 - 96) 2 (2)							
Any adenovirus		**91%** (50 - 98) 2 (2)	**77%** (22 - 93) 1 (1)	**79%** (63 - 88) 2 (2)							
BNT162b2		**99%** (97 - 99) 1 (1)		**92%** (89 - 94) 1 (1)							
mRNA-1273											
ChAdOx1		**91%** (50 - 98) 2 (2)	**77%** (22 - 93) 1 (1)	**79%** (63 - 88) 2 (2)							
Ad26.COV2.S											

Table 9: VE against COVID-19 deaths 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		**49%** (-64 - 90) 1 (2)	**62%** (-76 - 97) 1 (2)	**18%** (2 - 31) 1 (2)							
Any mRNA vaccine		**3%** (-53 - 56) 1 (1)	**91%** (19 - 99) 1 (1)	**19%** (-6 - 38) 1 (1)							
Any adenovirus		**84%** (-22 - 98) 1 (1)	**-7%** (-68 - 63) 1 (1)	**17%** (-4 - 34) 1 (1)							
BNT162b2											
mRNA-1273											
ChAdOx1											
Ad26.COV2.S											

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 (**all strains**)

	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	**81%** (63 - 90) 2 (4)	**56%** (47 - 64) 4 (6)	**66%** (36 - 82) 5 (9)	**64%** (19 - 83) 3 (5)	**61%** (53 - 68) 1 (1)						
Any mRNA vaccine	**81%** (63 - 90) 2 (4)	**56%** (47 - 64) 4 (6)	**66%** (36 - 82) 5 (9)	**64%** (19 - 83) 3 (5)	**61%** (53 - 68) 1 (1)						
Any adenovirus											
BNT162b2	**87%** (58 - 96) 1 (2)	**61%** (36 - 76) 3 (3)	**80%** (26 - 95) 3 (4)	**79%** (-40 - 97) 2 (2)	**61%** (53 - 68) 1 (1)						
mRNA-1273		**48%** (47 - 48) 1 (1)	**37%** (35 - 39) 1 (1)	**38%** (33 - 42) 1 (1)							
ChAdOx1											
Ad26.COV2.S											

Table 11: VE against COVID-19 cases* for completed primary series and an additional dose (**Delta variant**)

No data to report

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

	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	**81%** (63 - 90) 2 (4)	**56%** (47 - 64) 4 (6)	**66%** (36 - 82) 5 (9)	**64%** (19 - 83) 3 (5)	**61%** (53 - 68) 1 (1)						
Any mRNA vaccine	**81%** (63 - 90) 2 (4)	**56%** (47 - 64) 4 (6)	**66%** (36 - 82) 5 (9)	**64%** (19 - 83) 3 (5)	**61%** (53 - 68) 1 (1)						
Any adenovirus											
BNT162b2	**87%** (58 - 96) 1 (2)	**61%** (36 - 76) 3 (3)	**80%** (26 - 95) 3 (4)	**79%** (-40 - 97) 2 (2)	**61%** (53 - 68) 1 (1)						
mRNA-1273		**48%** (47 - 48) 1 (1)	**37%** (35 - 39) 1 (1)	**38%** (33 - 42) 1 (1)							
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 13: VE against COVID-19 hospitalisations for completed primary series and an additional dose (**all strains**)

	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	**81%** (75 - 86) 3 (8)	**92%** (89 - 94) 3 (5)	**76%** (68 - 81) 5 (11)	**70%** (56 - 79) 4 (6)	**81%** (67 - 90) 1 (1)						
Any mRNA vaccine	**83%** (78 - 87) 3 (7)	**92%** (89 - 94) 3 (5)	**80%** (76 - 83) 5 (10)	**70%** (56 - 79) 4 (6)	**81%** (67 - 90) 1 (1)						
Any adenovirus	**82%** (54 - 93) 1 (2)		**76%** (72 - 80) 1 (2)								
BNT162b2	**85%** (77 - 90) 2 (5)	**89%** (87 - 90) 1 (1)	**77%** (67 - 84) 3 (5)	**66%** (61 - 71) 2 (2)	**81%** (67 - 90) 1 (1)						
mRNA-1273		**90%** (87 - 93) 1 (1)	**84%** (78 - 88) 1 (1)	**77%** (63 - 86) 1 (1)							
ChAdOx1	**82%** (54 - 93) 1 (2)		**76%** (72 - 80) 1 (2)								
Ad26.COV2.S											

Table 14: VE against COVID-19 hospitalisations for completed primary series and an additional dose (**Delta variant**)

	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	**88%** (84 - 90) 1 (2)	**96%** (95 - 97) 1 (1)	**78%** (62 - 88) 1 (2)	**76%** (14 - 93) 1 (1)							
Any mRNA vaccine	**86%** (82 - 89) 1 (1)	**96%** (95 - 97) 1 (1)	**83%** (74 - 89) 1 (1)	**76%** (14 - 93) 1 (1)							
Any adenovirus	**89%** (87 - 91) 1 (1)		**70%** (45 - 84) 1 (1)								
BNT162b2											
mRNA-1273											
ChAdOx1	**89%** (87 - 91) 1 (1)		**70%** (45 - 84) 1 (1)								
Ad26.COV2.S											

Table 15: VE against COVID-19 hospitalisations for completed primary series and an additional dose (**Omicron variant**)

	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	**76%** (71 - 79) 3 (6)	**91%** (89 - 93) 3 (5)	**75%** (65 - 82) 5 (9)	**69%** (56 - 78) 4 (6)	**81%** (67 - 90) 1 (1)						
Any mRNA vaccine	**83%** (76 - 87) 3 (6)	**91%** (89 - 93) 3 (5)	**80%** (75 - 83) 5 (9)	**69%** (56 - 78) 4 (6)	**81%** (67 - 90) 1 (1)						
Any adenovirus	**71%** (67 - 75) 1 (1)		**77%** (72 - 81) 1 (1)								
BNT162b2	**85%** (77 - 90) 2 (5)	**89%** (87 - 90) 1 (1)	**77%** (67 - 84) 3 (5)	**66%** (61 - 71) 2 (2)	**81%** (67 - 90) 1 (1)						
mRNA-1273		**90%** (87 - 93) 1 (1)	**84%** (78 - 88) 1 (1)	**77%** (63 - 86) 1 (1)							
ChAdOx1	**71%** (67 - 75) 1 (1)		**77%** (72 - 81) 1 (1)								
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 16: VE against COVID-19 deaths for completed primary series and an additional dose (**all strains**)

	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	**82%** (74 - 87) 2 (5)		**84%** (77 - 89) 2 (5)		**71%** (-13 - 93) 1 (1)						
Any mRNA vaccine	**81%** (74 - 86) 2 (3)		**87%** (83 - 90) 2 (3)		**71%** (-13 - 93) 1 (1)						
Any adenovirus	**83%** (61 - 93) 1 (2)		**82%** (50 - 94) 1 (2)								
BNT162b2	**82%** (70 - 89) 1 (1)		**68%** (-65 - 96) 1 (1)		**71%** (-13 - 93) 1 (1)						
mRNA-1273											
ChAdOx1	**83%** (61 - 93) 1 (2)		**82%** (50 - 94) 1 (2)								
Ad26.COV2.S											

Table 17: VE against COVID-19 deaths for completed primary series and an additional dose (**Delta variant**)

	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	**87%** (81 - 91) 1 (2)		**88%** (77 - 94) 1 (2)								
Any mRNA vaccine	**84%** (74 - 90) 1 (1)		**87%** (74 - 94) 1 (1)								
Any adenovirus	**89%** (84 - 92) 1 (1)		**94%** (52 - 99) 1 (1)								
BNT162b2											
mRNA-1273											
ChAdOx1	**89%** (84 - 92) 1 (1)		**94%** (52 - 99) 1 (1)								
Ad26.COV2.S											

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

	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	**77%** (69 - 82) 2 (3)		**82%** (70 - 90) 2 (3)		**71%** (-13 - 93) 1 (1)						
Any mRNA vaccine	**78%** (67 - 86) 2 (2)		**87%** (83 - 90) 2 (2)		**71%** (-13 - 93) 1 (1)						
Any adenovirus	**74%** (60 - 83) 1 (1)		**77%** (67 - 84) 1 (1)								
BNT162b2	**82%** (70 - 89) 1 (1)		**68%** (-65 - 96) 1 (1)		**71%** (-13 - 93) 1 (1)						
mRNA-1273											
ChAdOx1	**74%** (60 - 83) 1 (1)		**77%** (67 - 84) 1 (1)								
Ad26.COV2.S											

Narrative overview of findings

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

A total of 31 studies provided usable baseline and follow-up information with regards to COVID-19 related cases. The 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 (nine studies). Seven studies provided data for Omicron, which showed a notably lower baseline VE compared to Delta (51% vs. 89%) and a much more rapid drop in VE over the follow-up period. 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 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 19 studies provided usable baseline and follow-up information with regards to COVID-19 related hospitalisations. The 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 32 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 (eight studies). There were five study that provided data for Omicron, which showed a lower baseline VE compared to Delta (59% vs. 95%) which was generally consistent 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. The 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 (two studies suggesting that VE remained high up to 24 weeks post vaccine series) and one study for the Omicron variant which indicated a lower baseline VE compared to the Delta variant (49% vs. 95%) and a dramatic reduction in VE up to 20 weeks post vaccine series.

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

A total of six studies provided usable baseline and follow-up information with regards to confirmed COVID-19 case data. These studies all reported on the Omicron variant, there were no studies for the Delta variant. These studies found a significant drop in VE from baseline that was stable up to 20 weeks post booster dose (81% vs 61%). 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 a large difference between the variants for VE at 15+ weeks (45.5% vs. 48.4%, respectively).

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

A total of six studies provided usable baseline and follow-up information with regards to COVID-19-related hospitalisations. In general, these studies showed that VE was maintained up to 20 weeks post booster dose. Similar patters were seen for the Delta (two studies) and Omicron (six studies) variants over the same period.

2c. Findings for COVID-19 related deaths primary series plus additional dose
A total of two studies provided usable baseline and follow-up information with regards to COVID-19-related deaths. In general, these studies suggested that VE may be maintained up to 24 weeks post booster dose. The one Delta variant study showed a similar pattern up to 16 weeks post booster, and two studies indicated the same for the Omicron variant (up to 24 weeks post booster).

Risk of bias (RoB) assessment
The risk of bias data for each individual study is provided in the Supplementary File (les10.5_vaccine_waning_adults_RoB_3_2022-04-27.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. Two studies (Young-Xu et al. and Menni et al.) were deemed as having a critical RoB due to not accounting for calendar time (both) and self-reporting vaccines and infections (Menni) and were 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 VEs 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 response to the Omicron variant 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 the studies indicates that potential waning in VEs for cases by 8 weeks post booster dose (specific to Omicron), but that there was relative stability in VE for hospitalisations and deaths up to 24 weeks post booster, 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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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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