COVID-19 Living Evidence
Synthesis # 8
(Version 8.11: 9 May 2022)

Question

What is the effectiveness of available COVID-19 vaccines for children and adolescents, including variants of concern?

Findings

For vaccine effectiveness in variants of concern (VOC), we present a visual summary of evidence in Table 1 and Table 2.

Methods are presented in Box 1 and in the following appendices:
1) reference list
2) glossary
3) data-extraction template
4) process for assigning variant of concern to studies
5) research question and critical appraisal process
6) detailed description of the narrative summary statement.

Overall, 50 studies were appraised and 21 used to complete this summary. The reasons for excluding the remaining 29 studies are reported in the second section of Appendix 2.

Four new studies have been added since the previous edition of this living evidence synthesis, which is signaled by a last updated date of 09 May 2022 (highlighted in yellow). The new studies included results for VOC Delta and VOC Omicron. Studies for VOC Omicron do not report information by sublineages (BA.1 and BA.2)

Box 1: Our approach

We retrieved candidate studies and updates to living evidence syntheses on vaccine effectiveness using the following mechanisms: 1) PubMed via COVID-19+ Evidence Alerts; 2) systematic scanning of pre-print servers; 3) updates to the COVID-END inventory of best evidence syntheses; and 4) cross-check with updates from the VESPa team. We included studies and updates to living evidence syntheses identified up to two 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**. A glossary is provided in **Appendix 2**.

Prioritized outcome measures: Infection, severe disease (as defined by the study investigators), death, and transmission.

Data extraction: We prioritized variant-confirmed and vaccine-specific data over total study population data (variant assumed and/or vaccine unspecified). We extracted data from each study in duplicate using the template provided in **Appendix 3**. Relevance to VOC is determined directly, when reported by study authors, or indirectly where reasonable assumptions can be made about the variant prevalent in the jurisdiction at the time of the study as described in **Appendix 4**.

Critical appraisal: We assessed risk of bias, direction of effect, and certainty of evidence. **Risk of bias:** assessed in duplicate for individual studies using an adapted version of ROBINS-I. **Direction of vaccine effect:** "prevented" or "protects" was applied to mean estimates or range of mean estimates of effect that are greater than or equal to 50% (the lowest acceptable limit for vaccine effectiveness as determined by WHO). **Certainty of evidence:** assessed for the collection of studies for each vaccine according to variant of concern using a modified version of GRADE. Details of the research question for this synopsis and the critical appraisal process are provided in **Appendix 5**.

Summaries: We summarized the evidence by presenting narrative evidence profiles across studies, with or without pooling, as appropriate. A template for the summary statements used on page 1 under "Findings" and in Table 1 under each VOC is provided in **Appendix 6**.

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

Highlights of changes this report

- New data on Pfizer [BNT162b2] against VOC Delta has been added to Table 1, Table 2 and Table 3 of two serious risk of bias studies (ref 18 and 19)
- New data on Moderna [mRNA-1723] against VOC Delta has been added to Table 1, Table 2 and Table 3 of one serious risk of bias study (ref 19)
- New data on Johnson & Johnson [AD26.COV2.S] against VOC Delta has been added to Table 1, Table 2 and Table 3 of one serious risk of bias study (ref 19)
- New data on Sinovac [CoronaVac] against VOC Omicron has been added to Table 1 and Table 3 of one serious risk of bias study (ref 21)
- We did not find studies in children and adolescents that evaluated the vaccine effectiveness for Omicron VOC by the BA.1 and BA.2 sublineages.

Pfizer/Comirnaty [BNT162b2]

- **VOC Delta**
  - We have low certainty evidence that 1 dose of **BNT162b2 (Pfizer)** prevented infection from VOC **Delta** (range of mean estimates: 56 to 80% - 4 Obs [2][10][17][18]) in adolescents age 12 to 18 years
  - We have moderate certainty evidence that 1 dose of **BNT162b2 (Pfizer)** prevented symptomatic infection from VOC **Delta** (range of mean estimates: 70 to 76% - 3 Obs [5][9][17]) in adolescents age 12 to 18 years
  - We have moderate certainty evidence that 2 doses of **BNT162b2 (Pfizer)** prevented infection from VOC **Delta** (range of mean estimates: 81 to 93% - 7 Obs [1][2][6][9][11][13][17]) in adolescents age 12 to 18 years
  - We have moderate certainty evidence that 2 doses of **BNT162b2 (Pfizer)** prevented symptomatic infection from VOC **Delta** (range of mean estimates: 87 to 97% - 4 Obs [5][9][16][19]) in adolescents age 12 to 18 years
  - We have low certainty evidence that 2 doses of **BNT162b2 (Pfizer)** prevented ICU admission from VOC **Delta** (98% [95% CI, 93 to 99] - 1 Obs [4]), in adolescents age 12 to 18 years
  - We have low certainty evidence that 2 doses of **BNT162b2 (Pfizer)** prevented MIS-C from VOC **Delta** (91% [95% CI, 78 to 97] - 1 Obs [7]), in adolescents age 12 to 18 years

- **VOC Omicron**
  - We have low certainty evidence that 1 dose of **BNT162b2 (Pfizer)** prevented infection from VOC **Omicron** (53.7% [95% CI, 43.3 to 62.2]- 1 Obs [10]) in adolescents age 12 to 17 years
  - We have low certainty evidence that 1 dose of **BNT162b2 (Pfizer)** prevented symptomatic infection from VOC **Omicron** (range of mean estimates: 44 to 53% - 1 Obs [5]) in adolescents age 12 to 17 years
  - We have low certainty evidence that 2 doses of **BNT162b2 (Pfizer)** prevented symptomatic infection from VOC **Omicron** (range of mean estimates: 71 to 83% - 1 Obs [5]) in adolescents age 12 to 17 years
  - We have moderate certainty evidence that 2 doses of **BNT162b2 (Pfizer)** prevented infection from VOC **Omicron** (range of mean estimates: 53 to 59% - 2 Obs [11][13])in adolescents age 12 to 17 years
  - We have low certainty evidence that 3 doses of **BNT162b2 (Pfizer)** prevented symptomatic infection from VOC **Omicron** (81% [95% CI, 59 to 91] - 1 Obs [8]) in adolescents age 16 to 17 years
  - We have low certainty evidence that 3 doses of **BNT162b2 (Pfizer)** prevented symptomatic infection from VOC **Omicron** (62% [95% CI, 49 to 72] - 1 Obs - [16]) in adolescents age 12 to 17 years

Moderna Spikevax [mRNA-1723]

- **VOC Delta**
  - We have low certainty evidence that 2 doses of **mRNA-1723 (Moderna)** prevented symptomatic infection from VOC **Delta** (98% [95% CI, 92 to 99] - 1 Obs [19]) in adolescents age 16 to 19 years

Johnson & Johnson [AD26.COV2.S]

- **VOC Delta**
  - We have low certainty evidence that 2 doses of **AD26.COV2.S (Johnson & Johnson)** prevented symptomatic infection from VOC **Delta** (58% [95% CI, 19 to 79] - 1 Obs [19]) in adolescents age 16 to 19 years

Sinovac [CoronaVac]

- **VOC Omicron**
  - We have low certainty evidence that 1 dose of **CoronaVac** prevented symptomatic infection from VOC **Omicron** (22.3% [95% CI, 19.7 to 24.9] - 1 Obs [21]) in children age 6 to 11 years
  - We have low certainty evidence that 2 doses of **CoronaVac** prevented infection from VOC **Omicron** (38.2% [95% CI, 36.5 to 39.9] - 1 Obs [12]) in children age 3 to 5 years
  - We have low certainty evidence that 2 doses of **CoronaVac** prevented ICU admission from VOC **Omicron** (69% [95% CI, 18.6 to 88.2] - 1 Obs [12]) in children age 3 to 5 years
  - We have low certainty evidence that 2 doses of **CoronaVac** prevented symptomatic infection from VOC **Omicron** (41.5% [95% CI, 34.4 to 47.7] - 1 Obs [21]) in children age 6 to 11 years

Table 1: Visual summary of evidence for COVID-19 vaccines for variants of concern (up to 28 days after 2 doses)

Percentages indicate level of effectiveness from 0% (no effect) to 100% (full protection): ranges of estimated means are provided when ≥ 1 study is available; estimated mean value is provided for single studies

Colour indicates level of certainty based on the evidence*

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 >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

***Note:** From LES 8.9 and afterwards, we are implementing a new colour label to classify the certainty of the evidence. High certainty evidence remains highlighted in green; moderate certainty evidence will be from now on presented in yellow, and the low certainty evidence, in orange.*

Outcome (and vaccine)	Vaccine Effectiveness (2 doses unless otherwise stated) up to 28 days after last dose each combination of vaccine, variant, and outcome				
	Overall	Beta	Gamma	Delta	Omicron

Pfizer	91%			81 - 93%	53 - 59%
Moderna					
CoronaVac					38%
Pfizer				87 - 97%	71 - 83%
Moderna				98%	
CoronaVac					41%
Johnson & Johnson				58%*	
Pfizer					
Moderna					
CoronaVac					
Pfizer				98%	
Moderna					
CoronaVac					69%
Pfizer					
Moderna					
CoronaVac					
Pfizer					
Moderna					
CoronaVac					

*Single dose
**mean estimate of effect less than the lowest acceptable limit for vaccine effectiveness as determined by WHO

Table 2: Visual summary of evidence for COVID-19 vaccines for variant of concern – Delta and Omicron [2 doses > 28 days since last dose; 3 doses: > 1 days since last dose]

Percentages indicate level of effectiveness from 0% (no effect) to 100% (full protection): ranges of estimated means are provided when ≥ 1 study is available; estimated mean value is provided for single studies

Colour indicates level of certainty based on the evidence*

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 >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

***Note:** From LES 8.9 and afterwards, we are implementing a new colour label to classify the certainty of the evidence. High certainty evidence remains highlighted in green; moderate certainty evidence will be from now on presented in yellow, and the low certainty evidence, in orange.*

Outcome (and vaccine)	Variant	Number of doses	Time since Last Dose (days)	Age (years)	Vaccine Effectiveness
Any Infection					
Pfizer	Delta	1	21 to 48	12 to 17	63 to 68
			28 to 56		86.4% (95% CI, 83.5 to 88.7)

			49 to 76		47 to 56
			56 to 84		61.5% (95% CI, 43.5 to 73.7)
			77		29 to 49
		2	35 to 56	12 to 18	90% (95% CI, 67 to 97)
			63 to 84		95% (95% C10, 79 to 99)
			91 to 119		83% (95% CI, 34 to 95)
			35 to 62	16 to 17	92.8% (95% CI, 89.8 to 94.9)
			63		83.7% (95% CI, 75.9 to 89)
			14 to 149	12 to 15	87% (95% CI, 49 to 97)
	Omicron	1	21 to 48	12 to 17	16 to 34
			28 to 56		57.9% (95% CI, 50.9 to 63.9)
			49 to 76		-1 to 17
			77		-13 to -5
			56 to 84		63.7% (95% CI, 59 to 67.9)
		2	14 to 82	5 to 11	31% (95% CI, 9 to 48)
			35 to 62	16 to 17	45.7% (95% CI, 34.8 to 54.7)
			63		23.3% (95% CI, 2.7 to 39.5)
			14 to 149	12 to 15	59% (95% CI, 22 to 79)
Moderna					
CoronaVac					
Symptomatic Infection					
Pfizer	Delta	1	28 to 34	12 to 17	61 to 63%
			35 to 41		56 to 58%
			42 to 55		44 to 54%
			56 to 69		36 to 48%
			70 to 83		35 to 46%
			84 to 104		29 to 53%
			105	16 to 17	30.9% (95% CI, 25.4 to 36.0)
		2	35 to 69	16 to 17	91.5% (95% CI, 89.9 to 93.0)
			70		83.7% (95% CI, 72.0 to 90.5)
			14 to 149	12 to 17	85 to 92%
			60 to 119		96% (95% CI, 94 to 97)
			31 to 60	12 to 19	87 to 93%
			61 to 90		86 to 92%
			91 to 120		82 to 92%
	Omicron	1	28 to 34	12 to 17	33 to 42%
			35 to 41		36 to 49%
			42 to 55		29 to 40%
			56 to 69		23 to 27%

			70 to 83		16 to 27%
			84		17 to 26%
			105	16 to 17	12.5% (95% CI, 96.9 to 17.8)
		2	7 to 59	12 to 17	51% (95% CI, 38 to 61)
			14 to 149		34 to 45%
			60 to 119		31% (95% CI, 20 to 41)
			35 to 69	16 to 17	49.5% (95% CI, 45.7 to 53.0)
			70		22.6% (95% CI, 14.5 to 29.9)
		3	7	16 to 17	81% (95% CI, 59 to 91)
			0 to 60	12 to 17	56% (95% CI, 34 to 70)
			7		62% (95% CI, 49 to 72)
Moderna	Delta	2	31 to 60	16 to 19	91% (95% CI, 87 to 94)
			61 to 90		85% (95% CI, 82 to 88)
			91 to 120		85% (95% CI, 87 to 87)
CoronaVac					
Johnson & Johnson	Delta	1	31 to 60	16 to 19	52% (95% CI, 27 to 69)
			61 to 90		63% (95% CI, 43 to 75)
			91 to 120		58% (95% CI, 45 to 68)
Transmission					
Pfizer					
Moderna					
CoronaVac					
ICU Admission					
Pfizer					
Moderna					
CoronaVac					
MIS-C					
Pfizer	Delta	2	28	12 to 18	91% (78 to 97)
Moderna					
CoronaVac					
Severe Disease (may include death for some studies)					
Pfizer					
Moderna					
CoronaVac					
Death					
Pfizer					
Moderna					
CoronaVac					

Table 3: Key findings about vaccine effectiveness

Vaccine	Effectiveness	Findings
Pfizer/ BioNTech **Comirnaty** **[BNT162b2]**	**Delta** At least 14 days after 1st dose & At least 7 days after 2nd dose	BNT162b2 provided protection against VOC Delta for the following outcomes at least 14 days after 1st dose in adolescents age 12 to 18: ● 56 to 80% from infection (RME) (4 Obs - [2][10][17][18]) ● 70 to 76% from symptomatic infection(RME) (2 Obs - [5][9]) BNT162b2 provided protection against VOC Delta for the following outcomes at 0 to 27 days after 1st dose in adolescents age 12 to 15: ● 14.2% (95% CI, - 25.6 to 41.4) against hospitalization (1 Obs - [5]) BNT162b2 provided protection against VOC Delta for the following outcomes at 0 to 27 days after 1st dose in adolescents age 16 to 17: ● 64.6% (95% CI, 40.7 to 78.9) from hospitalization (1 Obs - [5]) BNT162b2 provided protection against VOC Delta for the following outcomes at least 7 days after 2nd dose in adolescents age 12 to 18: ● 81 to 93% against infection (RME) (7 Obs -[1][2][6][9][11][13][17]) ● 87 to 97% against symptomatic infection (RME) (4 Obs -[5][9][16][19]) BNT162b2 provided protection against VOC Delta for the following outcomes at least 14 days after 2nd dose in adolescents age 12 to 18: ● 94% (95% CI, 90 to 96) from hospitalization (1 Obs - [4]) ● 98% (95% CI, 93 to 99) from ICU admission (1 Obs - [4]) (13 Obs) [1][2][4][5][6][9][10][11][13][16][17][18][19]; *last update 2022-05-09*
	Delta >30 days after 1st dose	BNT162b2 provided protection against infection by VOC Delta the following number of days after 1st dose in adolescents age 12 to 17: ● 86.4% (95% CI, 83.5 to 88.7) – at 28 to 56 days (1 Obs - [10]) ● 61.5% (95% CI, 43.5 to 73.7) – at 56 to 84 days (1 Obs - [10]) ● 63 to 68% (RME) – at 21 to 48 days (1 Obs - [13]) ● 47 to 56% (RME) – at 49 to 76 days (1 Obs - [13]) ● 29 to 49% (RME) – at least 77 days (1 Obs - [13]) BNT162b2 provided protection against symptomatic infection by VOC Delta the following number of days after 1st dose in adolescents age 12 to 17: ● 61 to 63% (RME) – at 28 to 34 days (1 Obs - [5]) ● 56 to 58% (RME) – at 35 to 41 days (1 Obs - [5]) ● 44 to 54% (RME) – at 42 to 55 days (1 Obs - [5]) ● 36 to 48% (RME) – at 56 to 69 days (1 Obs - [5]) ● 35 to 46% (RME) – at 70 to 83 days (1 Obs - [5]) ● 29 to 53% (RME) – at 84 to 104 days (1 Obs - [5]) BNT162b2 provided protection against symptomatic infection by VOC Delta the following number of days after 1st dose in adolescents age 16 to 17: ● 30.9% (95% CI, 25.4 to 36.0) – at least 105 days (1 Obs - [5])

		BNT162b2 provided protection against hospitalization by VOC Delta the following number of days after 1st dose in adolescents age 12 to 17: ● 76 to 83% (RME) - at least 28 days (1 Obs - [5]) (3 Obs) [5][10][13]; *last update 2022-04-11*
	Delta >30 days after 2nd dose	BNT162b2 provided protection against infection by VOC Delta for the following number of days after 2nd dose in adolescents age 12 to 18: ● 90% (95% CI, 67 to 97) - at 35 to 56 days (1 Obs - [9]) ● 83% (95% CI, 34 to 95) - at 34 to 95 days (1 Obs - [9]) ● 95% (95% CI, 79 to 99) - at 79 to 99 (1 Obs - [9]) BNT162b2 provided protection against infection by VOC Delta for the following number of days after 2nd dose in adolescents age 12 to 15: ● 87% (95% CI, 49 to 97) - at 14 to 149 days (1 Obs - [11]) BNT162b2 provided protection against infection by VOC Delta for the following number of days after 2nd dose in adolescents age 16 to 17: ● 92.8% (95% CI, 89.8 to 94.9) - at 35 to 62 days (1 Obs - [13]) ● 83.7% (95% CI, 75.9 to 89) - at least 63 days (1 Obs - [13]) BNT162b2 provided protection against MIS-C by VOC Delta the following number of days after 2nd dose in adolescents age 12 to 18: ● 91% (95% CI, 78 to 97) - at least 28 days, Median 84 days (IQR 51–122) (1 Obs - [7]) BNT162b2 provided protection against symptomatic infection by VOC Delta for the following number of days after 2nd dose in adolescents age 16 to 17: ● 91.5% (95% CI, 89.9 to 93.0) - at 35 to 69 days (1 Obs - [5]) ● 83.7% (95% CI, 72.0 to 90.5) - at least 70 days (1 Obs - [5]) BNT162b2 provided protection against symptomatic infection by VOC Delta for the following number of days after 2nd dose in adolescents age 12 to 17: ● 85 to 92% (RME) - at 14 to 149 days (1 Obs - [8]) 96% (95% CI, 94 to 97) - at 60 to 119 days (1 Obs - [16]) BNT162b2 provided protection against symptomatic infection by VOC Delta for the following number of days after 2nd dose in adolescents age 12 to 19: ● 87 to 93% (RME) - at 31 to 60 days (1 Obs - [19]) ● 86 to 92% (RME) - at 61 to 90 days (1 Obs - [19]) ● 82 to 92% (RME) - at 91 to 120 days (1 Obs - [19]) BNT162b2 provided protection against hospitalization by VOC Delta for the following number of days after 2nd dose in adolescents age 12 to 18: ● 93% (95% CI, 89 to 95)- at 14 to 154 days (1 Obs - [13]) (8 Obs) [5][7][8][9][11][13][16][19]; *last update 2022-05-09*
	Omicron At least 14 days after 1st dose	BNT162b2 provided protection against VOC Omicron for the following outcomes at least 14 days after 1st dose in adolescents age 12 to 17: ● 53.7% (95% CI, 43.3 to 62.2) from infection (1 Obs - [10])

	& At least 7 days after 2nd dose	● 44 to 53% (RME) from symptomatic infection (1 Obs - [5]) BNT162b2 provided protection against VOC Omicron for the following outcomes at least 14 days after 2nd dose in adolescents age 12 to 17: ● 53 to 59% (RME) from infection (2 Obs - [11][13]) BNT162b2 provided protection against VOC Omicron for the following outcomes at least 7 days after 2nd dose in adolescents age 12 to 17: ● 71 to 83% from symptomatic infection (RME) (1 Obs - [5]) BNT162b2 provided protection against VOC Omicron for the following outcomes at least 14 days after 2nd dose in children age 5 to 11: ● 68% (95% CI, 42 to 82) from hospitalization (1 Obs - [15]) (5 Obs) [5][10][11][13][15]; *last update 2022-04-11*
	Omicron Any time frame after 3rd dose	BNT162b2 provided protection against VOC Omicron for the following outcomes at least 7 days after 3rd dose in adolescents age 16 to 17: 81% (95% CI, 59 to 91) from symptomatic infection (1 Obs - [8]) BNT162b2 provided protection against Symptomatic infection by VOC Omicron the following number of days after 3rd dose in adolescents age 12 to 17: ● 56% (95% CI, 34 to 70) – at 0 to 6 days (1 Obs - [16]) ● 62% (95% CI, 49 to 72) – at least 7 days (1 Obs - [16]) (2 Obs) [8][16]; *last update 2022-04-25*
	Omicron >30 days after 1st dose	BNT162b2 provided protection against infection by VOC Omicron the following number of days after 1st dose in adolescents age 12 to 17: ● 57.9% (95% CI, 50.9 to 63.9) – at 28 to 56 days (1 Obs - [10]) ● 63.7% (95% CI, 59 to 67.9) – at 56 to 84 days (1 Obs - [10]) ● -1 to 17 (RME) – at 49 to 76 days (1 Obs - [13]) ● -13 to 5 (RME) – at least 77 days (1 Obs - [13]) ● 16 to 34 (RME) – at 21 to 48 days (1 Obs - [13]) BNT162b2 provided protection against symptomatic infection by VOC Omicron the following number of days after 1st dose in adolescents age 12 to 17: ● 33 to 42% (RME) – at 28 to 34 days (1 Obs - [5]) ● 36 to 49% (RME) – at 35 to 41 days (1 Obs - [5]) ● 29 to 40% (RME) – at 42 to 55 days (1 Obs - [5]) ● 23 to 27% (RME) – at 56 to 69 days (1 Obs - [5]) ● 16 to 27% (RME) – at 70 to 83 days (1 Obs - [5]) ● 17 to 26% (RME) – at least 84 days (1 Obs - [5]) BNT162b2 provided protection against symptomatic infection by VOC Omicron the following number of days after 1st dose in adolescents age 16 to 17: ● 12.5% (95% CI, 6.9 to 17.8) – at least 105 days (1 Obs - [5]) (3 Obs) - [5][10][13]; *last update 2022-04-11*
	Omicron	BNT162b2 provided protection against infection by VOC Omicron for the following number of days after 2nd dose in children age 5 to 11:

	>30 days after 2nd dose	● 31% (95% CI, 9 to 48) - at 14 to 82 days (1 Obs - [11]) BNT162b2 provided protection against infection by VOC Omicron for the following number of days after 2nd dose in adolescents age 12 to 15: ● 59% (95% CI, 22 to 79) - at 14 to 149 days (1 Obs - [11]) BNT162b2 provided protection against infection by VOC Omicron for the following number of days after 2nd dose in adolescents age 16 to 17: ● 45.7% (95% CI, 34.8 to 54.7) - at 35 to 62 days (1 Obs - [13]) ● 23.3% (95% CI, 2.7 to 39.5) - at least 63 days (1 Obs - [13]) BNT162b2 provided protection against symptomatic infection from VOC Omicron for the following number of days after 2nd dose in adolescents age 16 to 17: ● 49.5% (95% CI, 45.7 to 53) - at 35 - 69 days (1 Obs - [5]) ● 22.6% (95% CI, 14.5 to 29.9) - at least 70 days (1 Obs - [5]) BNT162b2 provided protection against symptomatic infection by VOC Omicron for the following number of days after 2nd dose in children age 5 to 11: ● 51% (95% CI, 30 to 65) - at 14 to 67 days (1 Obs - [8]) BNT162b2 provided protection against symptomatic infection by VOC Omicron for the following number of days after 2nd dose in adolescents age 12 to 17: ● 51% (95% CI, 38 to 61) - at 7 to 59 days (1 Obs - [16]) ● 34 to 45% (RME) - at 14 to 149 days (1 Obs - [8]) ● 31% (95% CI, 20 to 41) - at 60 to 119 days (1 Obs - [16]) BNT162b2 provided protection against hospitalization by VOC Omicron for the following number of days after 2nd dose in adolescents age 12 to 18: ● 43% (95% CI, -1 to 68) - at 14 to 67 days (1 Obs - [15]) (6 Obs) [5][8][11][13][15][16]; *last update 2022-04-25*
Moderna **Spikevax** **[mRNA-1723]**	**Delta** At least 14 days after 1st dose & At least 7 days after 2nd dose	mRNA-1723 provided protection against VOC Delta for the following outcomes at least 14 days after 2nd dose in adolescents age 16 to 19: ● 98% (95% CI, 92 to 99) from symptomatic infection-(1 Obs - [19]) (1 Obs) [19]; *last update 2022-05-09*
	Delta >30 days after 2nd dose	mRNA-1723 provided protection against symptomatic infection by VOC Delta for the following number of days after 2nd dose in adolescents age 16 to 19: ● 91% (95% CI, 87 to 94) - at 31 to 60 days (1 Obs - [19]) ● 85% (95% CI, 82 to 88) - at 61 to 90 days (1 Obs - [19]) ● 85% (95% CI, 82 to 87)- at 91 to 120 days (1 Obs - [19]) (1 Obs) [19]; *last update 2022-05-09*

AstraZeneca [ChAd0x1] **Vaxzevria** **Serum Institute of India [Covishield]***	VOC	No data
Johnson & Johnson [AD26.COV2.S]*	**Delta** Up to 30 days after dose	AD26.COV2.S provided protection against VOC Delta for the following outcomes at least 14 days after dose in adolescents age 16 to 19: ● 58% (95% CI, 19 to 79) from symptomatic infection-(1 Obs - [19]) (1 Obs) [19]; *last update 2022-05-09*
	Delta >30 days after dose	AD26.COV2.S provided protection against symptomatic infection by VOC Delta for the following number of days after dose in adolescents age 16 to 19: ● 52% (95% CI, 27 to 69) - at 31 to 60 days (1 Obs - [19]) ● 63% (95% CI, 43 to 75) - at 61 to 90 days (1 Obs - [19]) ● 58% (95% CI, 45 to 68)- at 91 to 120 days (1 Obs - [19]) (1 Obs) [19]; *last update 2022-05-09*
Sinovac [CoronaVac]	**Omicron** At least 14 days after 1st dose & At least 7 days after 2nd dose	CoronaVac provided protection against VOC Omicron for the following outcomes at least 14 days after 1st dose in children age 6 to 11: ● 22.3% (95% CI, 19.7 to 24.9) from symptomatic infection-(1 Obs - [21]) CoronaVac provided protection against VOC Omicron for the following outcomes at least 14 days after 2nd dose in children age 3 to 5: ● 38.2% (95% CI, 36.5 to 39.9) from infection-(1 Obs - [12]) ● 64.6% (95% CI, 49.6 to 75.2) from hospitalization-(1 Obs - [12]) ● 69% (95% CI, 18.6 to 88.2) from ICU admission-(1 Obs - [12]) CoronaVac provided protection against VOC Omicron for the following outcomes at least 14 days after 2nd dose in children age 6 to 11: ● 41.5% (95% CI, 34.4 to 47.7) from symptomatic infection-(1 Obs - [21]) (2 Obs) [12][21]; *last update 2022-05-09*
Sinopharm (Wuhan) [WIV04]* **Sinopharm (Beijing) [HBO2] [BBIBP-CorV]***	VOC	No data
Novavax [NVX-CoV2373]*	VOC	No data
FBRI	VOC	No data

[EpiVacCorona]*		
Bharat Biotech [Covaxin] [BBV152]*	VOC	No data
Gamaleya [Sputnik V] [Gam-COVID-Vac]*	VOC	No data

Studies Covering Time Frame for More than One VOC		
Vaccine	**Effectiveness**	**Findings**
Pfizer/ BioNTech **Comirnaty** **[BNT162b2]**	Overall	BNT162b2 provided protection for the following outcomes at least 14 days after 1st dose in adolescents age 12 to 15: ● 67% (95% CI, 50 to 78) from infection (1 Obs - [3]) ● 100% (95% CI, 100 to 100) from hospitalization (1 Obs - [3]) BNT162b2 provided protection for the following outcomes at least 7 days after 2nd dose in adolescents age 12 to 15: ● 91% (95% CI, 88 to 93) from infection (1 Obs - [3]) ● 81% (95% CI, -55 to 98) from hospitalization (1 Obs - [3]) (1 Obs) [3]; *last update 2021-12-13*
	Delta to Omicron At least 14 days after 1st dose & At least 7 days after 2nd dose	BNT162b2 provided protection against VOC Delta to Omicron for the following outcomes at least 14 days after 1st dose in adolescents age 12 to 17: ● 38% (95% CI, -51 to 79) from hospitalization (1 Obs – [14]) BNT162b2 provided protection against VOC Delta to Omicron for the following outcomes at least 14 days after 1st dose in children age 4 to 11: ● 32% (95% CI, -49 to 72) from hospitalization (1 Obs – [14]) BNT162b2 provided protection against VOC Delta to Omicron for the following outcomes at least 14 days after 1st dose in children and adolescents age 4 to 17: ● 37% (95% CI, -13 to 67) from hospitalization (1 Obs – [14]) BNT162b2 provided protection against VOC Delta to Omicron for the following outcomes at least 7 days after 2nd dose in adolescents age 16 to 17: ● 90.7% (95% CI, 87.4 to 93.1) from infection (1 Obs - [13]) BNT162b2 provided protection against VOC Delta to Omicron for the following outcomes at least 14 days after 2nd dose in adolescents age 12 to 18: ● 82 to 83% (RME) from hospitalization (1 Obs - [15]) BNT162b2 provided protection against VOC Delta to Omicron for the following outcomes at least 14 days after 2nd dose in adolescents age 12 to 17: ● 59% (95% CI, 23 to 82) from hospitalization (1 Obs - [14]) BNT162b2 provided protection against VOC Delta to Omicron for the following outcomes at least 14 days after 2nd dose in adolescents age 4 to 17:

		● 59% (95% CI, 23 to 79) from hospitalization (1 Obs - [14]) (3 Obs) [13][14][15]; *last update 2022-04-11*
	Delta to Omicron >30 days after 1st dose	BNT162b2 provided protection against infection by VOC Delta Omicron the following number of days after 1st dose in adolescents age 12 to 17: ● 62 to 65 (RME) – at 21 to 48 days (1 Obs - [13]) ● 48 to 57 (RME) – at 49 to 76 days (1 Obs - [13]) ● 48 to 70 (RME) – at least 77 days (1 Obs - [13]) (1 Obs) - [13]; *last update 2022-04-11*
	Delta to Omicron >30 days after 2nd dose	BNT162b2 provided protection against infection by VOC Delta to Omicron for the following number of days after 2nd dose in adolescents age 16 to 17: ● 92.3% (95% CI, 82.9 to 96.6) - at 35 to 62 days (1 Obs - [13]) ● 87.8% (95% CI, 78.8 to 92.9) - at least 63 days (1 Obs - [13]) BNT162b2 provided protection against hospitalization by VOC Delta to Omicron for the following number of days after 2nd dose in children age 5 to 11: ● 74% (95% CI, -35 to 95) - at 14 to 67 days (1 Obs - [8]) BNT162b2 provided protection against hospitalization by VOC Delta to Omicron for the following number of days after 2nd dose in adolescents age 12 to 17: ● 92 to 94% (RME) - at 14 to 149 days (1 Obs - [8]) BNT162b2 provided protection against symptomatic infection by VOC Delta to Omicron for the following number of days after 2nd dose in children age 5 to 11: ● 46% (95% CI, 24 to 61) - at 14 to 67 days (1 Obs - [8]) BNT162b2 provided protection against symptomatic infection by VOC Delta to Omicron for the following number of days after 2nd dose in adolescents age 12 to 17: ● 76 to 83% (RME) - at 14 to 149 days (1 Obs - [8]) (2 Obs) [8][13]; *last update 2022-04-11*
	Delta to Omicron Any time frame after 3rd dose	BNT162b2 provided protection against VOC Delta to Omicron for the following outcomes at least 7 days after 3rd dose in adolescents age 16 to 17: ● 86% (95% CI, 73 to 93) from symptomatic infection (1 Obs - [8]) (1 Obs) [8]; *last update 2022-03-14*

Links to references are provided in Appendix 1

Pan American Health Organization/World Health Organization. Pharmacovigilance for COVID-19 Vaccines. https://covid-19pharmacovigilance.paho.org

*****As of the date of publication, these vaccines have not been approved for the population of children and adolescents.

Flórez ID[1,2], Velásquez-Salazar P[1], Martínez JC[1], Linkins L[3], Abdelkader W[3], Iorio A[3], Lavis J[3], Patiño-Lugo DF[1]. COVID-19 living evidence synthesis #8 (version 11): What is the effectiveness of available COVID-19 vaccines in children and adolescents in general and specifically for variants of concern? Evidence and Deliberation Unit for Decision Making (UNED), University of Antioquia & Health Information Research Unit (HIRU), McMaster University, 9 May 2022.

To help Canadian decision-makers as they respond to unprecedented challenges related to the COVID-19 pandemic, COVID-END in Canada is preparing rapid evidence responses like this one. The development and continued updating of this living evidence synthesis has been funded by the Canadian Institutes of Health Research (CIHR) and the Public Health Agency of Canada. The opinions, results, and conclusions are those of the team that prepared the living evidence synthesis, and independent of the Government of Canada, CIHR and the Public Health Agency of Canada. No endorsement by the Government of Canada, CIHR or Public Health Agency of Canada is intended or should be inferred.

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Appendix 1: Summary of Study Findings and Appraisals

Section 1: included studies				
Ref	**Author**	**Bottom line**	**ROBINS-I***	**Design, Notes**
*Note: ROBINS-I score risk of bias: Low risk of bias indicates high quality				
1	Glatman-Freedman	BNT162b2 showed VE 91.5% (95% CI, 88.2 to 93.9) against infection at least 8 days after 2nd dose in adolescents age 12 to 15 years. There were no deaths in either group.	Serious	Population cohort in Israel of adolescents age 12 to 15 years; 2,034,591 vaccinated person-days and 13,623,714 unvaccinated person-days; time and setting for VOC Delta *Included in LES 8.1*
2	Reis	BNT162b2 showed VE 59% (95% CI, 52 to 65) against infection 14 to 20 days after 1st dose in adolescents age 12 to 18. BNT162b2 showed VE 90% (95% CI, 88 to 92) against infection 7 to 21 days after 2nd dose in adolescents age 12 to 18.	Moderate	Case-control study in Israel; 94,354 vaccinated matched to 94,354 unvaccinated adolescents age 12 to 18; time and setting for VOC Delta *Included in LES 8.1*
3	Tartof	BNT162b2 showed VE 67% (95% CI, 50 to 78) against infection and VE 100% (95% CI, 100 to 100) against hospitalization at least +14 days after 1st dose in adolescents age 12 to 15 years. BNT162b2 showed VE 91% (95% CI, 88 to 93) against infection and VE 81% (95% CI, -55 to 98) against hospitalization at least +7 days after 2nd dose in adolescents age 12 to 15 years.	Moderate	Retrospective Cohort in USA of 3,436,957 Kaiser Permanente Southern California (KPSC) healthcare system members ≥12 years of age between Dec 14, 2020 – Aug 8, 2021. The cohort included 122,779 adolescents age 12 to 15 years. The primary exposure was being fully vaccinated, defined as receiving 2 doses of BNT162b2 with ≥ 7 days after the second dose. Over the study period, 28.4% of 9,147 specimens sent for whole genome sequencing (WGS) and viral lineage designation were Delta. *Included in LES 8.1* *last update 2022-01-04*
4	Olson	BNT162b2 showed VE 94% (95% CI, 90 to 96) against hospitalization at least +14 days after 2nd dose in adolescents age 12 to 18 years. BNT162b2 showed VE 95% (95% CI, 88 to 97) in adolescents age 12 to 15 years and VE 94% (95% CI, 88 to 97) in	Moderate	Test-negative study in U.S of adolescents age 12 to 18 years between Jun 1–Oct 25, 2021; 299 fully vaccinated (receipt of 2 doses of BNT162b2 vaccine, with the second dose administered ≥14 days before illness onset), 55 partially

		adolescents age 16 to 18 years against hospitalization at least +14 days after 2nd dose. BNT162b2 showed VE 98% (95% CI, 93 to 99) against ICU admission at least +14 days after 2nd dose in adolescents age 12 to 18 years.		vaccinated (had received only one dose of vaccine or who had received a second dose less than 14 days before illness onset) and 868 unvaccinated (no receipt of any COVID-19 vaccine before illness onset), time and setting for VOC Delta. *Included in LES 8.2* *last update in LES 8.3*
5	Powell	BNT162b2 showed after 1st dose VE 74.5% (95% CI, 73.2 to 75.6) at 14-20 days, VE 63.4% (95% CI, 61.7 to 65.1) at 28-34 days, VE 47.5% (95% CI, 44.9 to 49.9) at 56-69 days, and VE 53.1% (95% CI, 41.6 to 62.4) at least 84 days, in adolescents age 12 to 15 years against infection. (VOC Delta) BNT162b2 showed after 1st dose VE 49.6% (95% CI, 43.9 to 54.8) at 14-20 days, VE 42.1% (95% CI, 36.7 to 46.9) at 28-34 days, VE 22.5% (95% CI, 19.1 to 25.8) at 56-69 days, and VE 17.2% (95% CI, 12.0 to 22.1) at least 84 days, in adolescents age 12 to 15 years against infection. (VOC Omicron) BNT162b2 showed after 1st dose VE 75.9% (95% CI, 74.3 to 77.3) at 14-20 days, VE 60.6% (95% CI, 58.1 to 62.9) at 28-34 days, VE 36.3% (95% CI, 33.1 to 39.3) at 56-69 days, VE 29.3% (95% CI, 25.9 to 32.6) at 84-104 days, and VE 30.9% (95% CI, 25.4 to 36.0) at least 105 days, in adolescents age 16 to 17 years against infection. (VOC Delta) BNT162b2 showed after 1st dose VE 51.4% (95% CI, 42.7 to 58.8) at 14-20 days, VE 33% (95% CI, 18.6 to 44.9) at 28-34 days, VE 26.6% (95% CI, 17.4 to 34.8) at 56-69 days, VE 20.5% (95% CI, 13.0 to 27.3) at 84-104 days, and VE 12.5% (95% CI, 6.9 to 17.8) at least 105 days, in adolescents age 16 to 17 years against infection. (VOC Omicron) BNT162b2 showed after 2nd dose VE 93.2% (95% CI, 81.5 to 97.5) at 7-13 days	Moderate	Test-negative case-control design in England of adolescents age 12-17 years from week 37, 2021 onwards; there were 617,259 eligible tests for 12-15-year-olds and 225,670 for 16-17-year-olds. Symptomatic 12-15-year-olds and 16-17-year-olds with PCR-confirmed SARS-COV-2 infection was compared with vaccination status in symptomatic adolescents in the same age-groups who had a negative SARS-COV-2 PCR test. All cases prior to week 48 were defined as Delta, unless S gene target failure (SGTF), genotyping or sequencing information confirmed otherwise. Tests were defined as Omicron from week 48 onwards using SGTF, genotyping or sequencing information. *Included in LES 8.2* *Updated in LES 8.6* *Link Updated in LES 8.8*

		and VE 87.2% (95% CI, 73.7 to 93.8) at least 14 days in adolescents age 12 to 15 years against infection. (VOC Delta) BNT162b2 showed after 2nd dose VE 83.1% (95% CI, 78.2 to 86.9) at 7-13 days and VE 73% (95% CI, 66.4 to 78.3) at least 14 days in adolescents age 12 to 15 years against infection. (VOC Omicron) BNT162b2 showed after 2nd dose VE 93.1% (95% CI, 91.6 to 94.4) at 7-13 days, VE 96.1% (95% CI, 95.2 to 96.8) at 14-34 days, VE 91.5% (95% CI, 89.9 to 93.0) at 35-69 days, and VE 83.7% (95% CI, 72.0 to 90.5) at least 70 days in adolescents age 16 to 17 years against infection. (VOC Delta) BNT162b2 showed after 2nd dose VE 76.1% (95% CI, 73.4 to 78.6) at 7-13 days, VE 71.3% (95% CI, 69.3 to 73.1) at 14-34 days, VE 49.5% (95% CI, 45.7 to 53.0) at 35-69 days, and VE 22.6% (95% CI, 14.5 to 29.9) at least 70 days in adolescents age 16 to 17 years against infection. (VOC Omicron) BNT162b2 showed after 1st dose VE 14.2% (95% CI, -25.6 to 41.4) at 0-27 days, and VE 83.4% (95% CI, 54.0 to 94.0) at least 28 days in adolescents age 12 to 15 years against hospitalization. (VOC Delta) BNT162b2 showed after 1st dose VE 64.6% (95% CI, 40.7 to 78.9) at 0-27 days, and VE 76.3% (95% CI, 61.1 to 85.6) at least 28 days in adolescents age 16 to 18 years against hospitalization. (VOC Delta)		
6	Lutrick	BNT162b2 showed VE 92% (95% CI, 79 to 97) against infection at least +14 days after 2nd dose in adolescents age 12 to 17 years.	Moderate	Prospective cohort in Arizona, of 243 adolescents aged 12–17 years between Jul 25 - Dec 4, 2021; 21,693 vaccinated person-days and 4,288 unvaccinated person-days; time and setting for VOC Delta. *Included in LES 8.3*

7	Zambrano	BNT162b2 showed VE 91% (95% CI, 78 to 97) against MIS-C at least +28 days after 2nd dose in adolescents age 12 to 18 years.	Moderate	Test-negative case-control design in 24 pediatric hospitals in 20 states of U.S among hospitalized patients aged 12–18 years between Jul 1–Dec 9, 2021; 283 participants; VE was assessed by comparing the odds of antecedent vaccination in 102 patients with MIS-C (case patients) and 181 patients in two groups of hospitalized controls (test-negative and syndrome-negative) matched to case-patients; time and setting for VOC Delta. *Included in LES 8.3*
8	Klein	BNT162b2 showed after 2nd dose VE 74% (95% CI, -35 to 95) at 14-67 days, in children age 5 to 11 years against hospitalization. (VOC Delta to Omicron) BNT162b2 showed after 2nd dose VE 92% (95% CI, 79 to 97) at 14-149 days, in adolescents age 12 to 15 years against hospitalization. (VOC Delta to Omicron) BNT162b2 showed after 2nd dose VE 94% (95% CI, 87 to 97) at 14-149 days, in adolescents age 16 to 17 years against hospitalization. (VOC Delta to Omicron) BNT162b2 showed after 2nd dose VE 46% (95% CI, 24 to 61) at 14-67 days, in children age 5 to 11 years against symptomatic infection. (VOC Delta to Omicron) BNT162b2 showed after 2nd dose VE 83% (95% CI, 80 to 85) at 14-149 days, in adolescents age 12 to 15 years against symptomatic infection. (VOC Delta to Omicron) BNT162b2 showed after 2nd dose VE 76% (95% CI, 71 to 80) at 14-149 days, in adolescents age 16 to 17 years against symptomatic infection. (VOC Delta to Omicron)	Serious	Test-negative case-control design in 10 states of the U.S among 39,217 emergency department (ED) and urgent care (UC) encounters and 1,699 hospitalizations among persons aged 5–17 years with COVID-19–like illness during April 9, 2021– January 29, 2022. VE was estimated comparing the odds of a positive SARS-CoV-2 test result between vaccinated (received at least 2 doses ≥14 days earlier or 3 doses ≥7 days earlier) and unvaccinated (received no doses) patients; time and setting for VOC Delta and VOC Omicron. *Included in LES 8.7*

		BNT162b2 showed after 3rd dose VE 86% (95% CI, 73 to 93) at least 7 days, in adolescents age 16 to 17 years against symptomatic infection. (VOC Delta to Omicron) BNT162b2 showed after 2nd dose VE 92% (95% CI, 89 to 94) at 14-149 days, in adolescents age 12 to 15 years against symptomatic infection. (VOC Delta) BNT162b2 showed after 2nd dose VE 85% (95% CI, 81 to 89) at 14-149 days, in adolescents age 16 to 17 years against symptomatic infection. (VOC Delta) BNT162b2 showed after 2nd dose VE 51% (95% CI, 30 to 65) at 14-67 days, in children age 5 to 11 years against symptomatic infection. (VOC Omicron) BNT162b2 showed after 2nd dose VE 45% (95% CI, 30 to 57) at 14-149 days, in adolescents age 12 to 15 years against symptomatic infection. (VOC Omicron) BNT162b2 showed after 2nd dose VE 34% (95% CI, 8 to 53) at 14-149 days, in adolescents age 16 to 17 years against symptomatic infection. (VOC Omicron) BNT162b2 showed after 3rd dose VE 81% (95% CI, 59 to 91) at least 7 days, in adolescents age 16 to 17 years against symptomatic infection. (VOC Omicron)		
9	Oliveira	BNT162b2 showed after 1st dose VE 74% (95% CI, 18 to 92) at least 14 days, in adolescents age 12 to 18 years against infection. (VOC Delta) BNT162b2 showed after 2nd dose VE 90% (95% CI, 79 to 95) at least 14 days, VE 91% (95% CI, 33 to 99) at 7-28 days, VE 90% (95% CI, 67 to 97) at 35-56 days, VE 95% (95% CI, 79 to 99) at 63-84 days, and VE 83% (95% CI, 34 to 95) at 91-119 days, in adolescents age 12 to 18 years against infection. (VOC Delta)	Moderate	Matched case-control study in Connecticut (US) of 542 adolescents aged 12-18 years, including 186 case participants and 356 matched control participants, between Jun 1 - Aug 15, 2021; time and setting for VOC Delta. *Included in LES 8.8*

		BNT162b2 showed after 2nd dose VE 93% (95% CI, 81 to 97) at least 14 days, in adolescents age 12 to 18 years against symptomatic infection. (VOC Delta)		
10	Molteni	BNT162b2 showed after 1st dose VE 80.4% (95% CI, 78.5 to 82.2) at 14-30 days, VE 86.4% (95% CI, 83.5 to 88.7) at 1-2 months (28 to 56 days), and VE 61.5% (95% CI, 43.5 to 73.7) at 2-3 months (56 to 84 days), in adolescents age 12 to 17 years against infection. (VOC Delta) BNT162b2 showed after 1st dose VE 53.7% (95% CI, 43.3 to 62.2) at 14-30 days, VE 57.9% (95% CI, 50.9 to 63.9) at 1-2 months (28 to 56 days), and VE 63.7% (95% CI, 59 to 67.9) at 2-3 months (56 to 84 days), in adolescents age 12 to 17 years against infection. (VOC Omicron)	Serious	Prospective cohort in the United Kingdom using data from the Covid Symptom Study (CSS), of 101,076 adolescents aged 12-17 years, between Aug 05, 2021–Feb 14, 2022; time and setting for VOC Delta to VOC Omicron. In the article, the effectiveness is presented as an adjusted relative risk reduction obtained by $RRR = (RR - 1) * 100$, in the present report it is transformed for the reader's understanding. *Included in LES 8.8*
11	Fowlkes	BNT162b2 showed after 2nd dose VE 81% (95% CI, 51 to 93) at least 14 days, and VE 87% (95% CI, 49 to 97) at 14-149 days, in adolescents age 12 to 15 years against infection. (VOC Delta) BNT162b2 showed after 2nd dose VE 31% (95% CI, 9 to 48) at 14-82 days, in children age 5 to 11 years against infection. (VOC Omicron) BNT162b2 showed after 2nd dose VE 59% (95% CI, 24 to 78) at least 14 days, and VE 59% (95% CI, 22 to 79) at 14-149 days, in adolescents age 12 to 15 years against infection. (VOC Omicron)	Moderate	Prospective cohort in four states of US (Arizona, Florida, Texas, and Utah), of 1,364 participants between Jul 2021–Feb 2022; the PROTECT cohort included 1,052 children aged 5–11 years and 312 adolescents aged 12–15 years that were tested weekly for SARS-CoV-2; viral whole genome sequencing was assessed, time and setting for VOC Delta to VOC Omicron. *Included in LES 8.8*
12	Araos	CoronaVac showed VE 38.2% (95% CI, 36.5 to 39.9) against infection, VE 64.6% (95% CI, 49.6 to 75.2) against hospitalization and VE 69% (95% CI, 18.6 to 88.2) against ICU admission at least +14 days after 2nd dose in children age 3 to 5 years. (VOC Omicron)	Moderate	Population based cohort in Chile, of 490,694 children aged 3–5 years, between Dec 06, 2021 - Feb 26, 2022; to estimate the effectiveness of the complete primary immunization schedule (two doses, 28 days apart) of an inactivated SARS-CoV-2 vaccine, CoronaVac; time and setting for VOC Omicron. *Included in LES 8.8*

13	Veneti	BNT162b2 showed after 1st dose VE 67.9 % (95% CI, 64.0 to 71.4) at 21-48 days, VE 55.8% (95% CI, 52.7 to 58.8) at 49-76 days, and VE 48.8% (95% CI, 46 to 51.5) at least 77 days, in adolescents age 12 to 15 years against infection. (VOC Delta) BNT162b2 showed after 1st dose VE 62.6 % (95% CI, 56.2 to 68) at 21-48 days, VE 47.3% (95% CI, 40 to 53.8) at 49-76 days, and VE 29.3% (95% CI, 20.4 to 37.1) at least 77 days, in adolescents age 16 to 17 years against infection. (VOC Delta) BNT162b2 showed after 2nd dose VE 90.8% (95% CI, 89.1 to 92.3) at 7-34 days, VE 92.8% (95% CI, 89.8 to 94.9) at 35-62 days, and VE 83.7% (95% CI, 75.9 to 89) at least 63 days, in adolescents age 16 to 17 years against infection. (VOC Delta) BNT162b2 showed after 1st dose VE 16.2 % (95% CI, -2.4 to 31.3) at 21-48 days, VE -1.3% (95% CI, -22.4 to 16.2) at 49-76 days, and VE -12.8% (95% CI, -21.7 to -4.6) at least 77 days, in adolescents age 12 to 15 years against infection. (VOC Omicron) BNT162b2 showed after 1st dose VE 33.7% (95% CI, -88.3 to 5.1) at 21-48 days, VE 16.8% (95% CI, -87.3 to 27.1) at 49-76 days, and VE -5.3% (95% CI, -32.9 to 16.6) at least 77 days, in adolescents age 16 to 17 years against infection. (VOC Omicron) BNT162b2 showed after 2nd dose VE 53.1% (95% CI, 42.6 to 61.7) at 7-34 days, VE 45.7% (95% CI, 34.8 to 54.7) at 35-62 days, and VE 23.3% (95% CI, 2.7 to 39.5) at least 63 days, in adolescents age 16 to 17 years against infection. (VOC Omicron) BNT162b2 showed after 1st dose VE 65 % (95% CI, 62.3 to 67.6) at 21-48 days,	Moderate	Population-based cohort in Norway, of 372,179 adolescents aged 12-17 years, between Aug 25, 2021 – Jan 16, 2022; to estimate BNT162b2 one dose effectiveness for individuals 12-15 years old and one or two doses effectiveness for individuals 16-17 years old against SARS-CoV-2 infections; time and setting for VOC Delta to Omicron. *Included in LES 8.9*

		VE 57.3% (95% CI, 54.4 to 60) at 49-76 days, and VE 70.2% (95% CI, 45.9 to 83.6) at least 77 days, in adolescents age 12 to 15 years against infection. (VOC Delta to Omicron) BNT162b2 showed after 1st dose VE 61.5 % (95% CI, 57.1 to 65.5) at 21-48 days, VE 48% (95% CI, 43.3 to 52.4) at 49-76 days, and VE 47.5% (95% CI, 39 to 54.9) at least 77 days, in adolescents age 16 to 17 years against infection. (VOC Delta to Omicron) BNT162b2 showed after 2nd dose VE 90.7% (95% CI, 87.4 to 93.1) at 7-34 days, VE 92.3% (95% CI, 82.9 to 96.6) at 35-62 days, and VE 87.8% (95% CI, 78.8 to 92.9) at least 63 days, in adolescents age 16 to 17 years against infection. (VOC Delta to Omicron)		
14	Simmons	BNT162b2 showed after 1st dose VE 32% (95% CI, -49 to 72) at least 14 days in children age 4 to 11 years against hospitalization. (VOC Delta to Omicron) BNT162b2 showed after 1st dose VE 38% (95% CI, -51 to 79) at least 14 days in adolescents age 12 to 17 years against hospitalization. (VOC Delta to Omicron) BNT162b2 showed after 1st dose VE 37% (95% CI, -13 to 67) at least 14 days in children and adolescents age 4 to 17 years against hospitalization. (VOC Delta to Omicron) BNT162b2 showed after 2nd dose VE 59% (95% CI, 23 to 82) at least 14 days in adolescents age 12 to 17 years against hospitalization. (VOC Delta to Omicron) BNT162b2 showed after 2nd dose VE 59% (95% CI, 23 to 79) at least 14 days in children and adolescents age 4 to 17 years against hospitalization. (VOC Delta to Omicron)	Serious	Age and time-matched nested case-control design in Ontario, Canada of 1,441 pediatric and adolescent patients aged 4-17 years, between May 28, 2021-Jan 10, 2022; to estimate the effectiveness of one and two mRNA vaccine doses at preventing hospitalization; time and setting for VOC Delta to VOC Omicron. *Included in LES 8.9*
15	Price	BNT162b2 showed after 2nd dose VE 93% (95% CI, 89 to 95) at 2–22 weeks in adolescents age 12 to 18 years against hospitalization. (VOC Delta)	Serious	Test-negative case-control design in 23 states of the U.S among 2,812 adolescents aged 12–18 years between Jul 1,

		BNT162b2 showed after 2nd dose VE 96% (95% CI, 90 to 98) at least 14 days in adolescents age 12 to 18 years against critical COVID-19. (VOC Delta) BNT162b2 showed after 2nd dose VE 43% (95% CI, -1 to 68) at 2–22 weeks in adolescents age 12 to 18 years against hospitalization. (VOC Omicron) BNT162b2 showed after 2nd dose VE 68% (95% CI, 42 to 82) at least 14 days, in children age 5 to 11 years against hospitalization. (VOC Omicron) BNT162b2 showed after 2nd dose VE 79% (95% CI, 51 to 91) at least 14 days in adolescents age 12 to 18 years against critical COVID-19. (VOC Omicron) BNT162b2 showed after 2nd dose VE 83% (95% CI, 77 to 88) at least 14 days in adolescents age 12 to 15 years against hospitalization. (VOC Delta to Omicron) BNT162b2 showed after 2nd dose VE 82% (95% CI, 74 to 88) at least 14 days in adolescents age 16 to 18 years against hospitalization. (VOC Delta to Omicron)		2021– Feb 17, 2022. VE against Covid-19 leading to hospitalization and against critical Covid-19 was estimated comparing odds ratios of antecedent vaccination (fully vaccinated vs. unvaccinated) in case patients as compared with controls; time and setting for VOC Delta and VOC Omicron. *Included in LES 8.9*
16	Buchan	BNT162b2 showed after 2nd dose VE 97% (95% CI, 94 to 99) at 7-59 days, and VE 96% (95% CI, 94 to 97) at 60-119 days in adolescents age 12 to 17 years against symptomatic infection. (VOC Delta) BNT162b2 showed after 2nd dose VE 51% (95% CI, 38 to 61) at 7-59 days, and VE 31% (95% CI, 20 to 41) at 60-119 days in adolescents age 12 to 17 years against symptomatic infection. (VOC Omicron) BNT162b2 showed after 3rd dose VE 56% (95% CI, 34 to 70) at 0-6 days, and VE 62% (95% CI, 49 to 72) at least 7 days in adolescents age 12 to 17 years against symptomatic infection. (VOC Omicron)	Moderate	Test-negative case-control design in Ontario, Canada among adolescents aged 12–17 years during Nov 22, 2021– Mar 6, 2022, including 9,902 Omicron-positive cases with 19,953 test-negative controls, and 502 Delta-positive Cases with 17,930 test-negative controls. VE against symptomatic infection and severe outcomes (i.e., hospitalization or death) was estimated over time since second or third dose receipt of BNT162b2; time and setting for VOC Delta and VOC Omicron, Delta outcomes were assessed prior to Jan 2, 2022. *Included in LES 8.10*

		BNT162b2 showed after 2nd dose VE 100% at 7-59 days, and VE 100% at 60-119 days in adolescents age 12 to 17 years against severe outcomes. (VOC Delta) (there were no cases of patients that presented severe outcomes) BNT162b2 showed after 2nd dose VE 76% (95% CI, -10 to 95) at 7-59 days, and VE 83% (95% CI, 55 to 93) at 60-119 days in adolescents age 12 to 17 years against severe outcomes. (VOC Omicron)		
17	Kildegaard	BNT162b2 showed after 1st dose VE 62% (95% CI, 59 to 65) at 0-20 days in adolescents age 12 to 17 years against infection. (VOC Delta) BNT162b2 showed after 2nd dose VE 93% (95% CI, 93 to 94) at 0-59 days in adolescents age 12 to 17 years against infection. (VOC Delta)	Serious	Population-based cohort in Denmark, of adolescents aged 12-17 years, who were vaccinated before or on 1 October 2021; vaccine effectiveness was assessed in 229,799 adolescents after a first dose and 175,176 after a second dose of BNT162b2; time and setting for VOC Delta. *Included in LES 8.10*
18	Chadeau-Hyam round 15 final report	BNT162b2 showed after 1st dose VE 56.2% (95% CI, 41.3 to 67.4) at least 14 days in adolescents age 12 to 17 years against infection. (VOC Delta)	Serious	Surveillance study in England; 100,112 participants, including 14,974 (14.96%) adolescents aged 12 to 17 years; vaccine effectiveness was assessed after a first BNT162b2 dose comparing swab positivity among vaccinated and unvaccinated individuals; time and setting for VOC Delta. *Included in LES 8.11*
19	Britton	BNT162b2 showed after 2nd dose VE 97% (95% CI, 95 to 98) at 14 days, VE 94% (95% CI, 94 to 95) at 14 - 60 days, VE 96% (95% CI, 95 to 97) at 14 – 30 days, VE 93% (95% CI, 92 to 94) at 31 - 60 days, VE 92% (95% CI, 91 to 93) at 61 - 90 days and VE 90% (95% CI, 88 to 91) at 91-120 days in adolescents age 12 to 15 years against symptomatic infection. (VOC Delta) BNT162b2 showed after 2nd dose VE 94% (95% CI, 92 to 95) at 14 days, VE 90% (95% CI, 89 to 91) at 14 - 60 days,	Serious	Test-negative case-control design in U.S with data from 6884 US COVID-19 testing sites in the pharmacy-based Increasing Community Access to Testing platform, including 180,112 laboratory-based SARS-CoV-2 nucleic acid amplification tests form adolescents aged 12–19 years during Mar 13, – Oct 17, 2021; time and setting for VOC Delta. *Included in LES 8.11*

		VE 94% (95% CI, 92 to 95) at 14 – 30 days, VE 87% (95% CI, 85 to 89) at 31 - 60 days, VE 86% (95% CI, 84 to 87) at 61 - 90 days and VE 82% (95% CI, 80 to 83) at 91-120 days in adolescents age 16 to 19 years against symptomatic infection. (VOC Delta) mRNA-1273 showed after 2nd dose VE 99% (95% CI, 96 to 99) at 14 days, VE 94% (95% CI, 92 to 96) at 14 - 60 days, VE 98% (95% CI, 92 to 99) at 14 – 30 days, VE 91% (95% CI, 87 to 94) at 31 - 60 days, VE 85% (95% CI, 82 to 88) at 61 - 90 days and VE 85% (95% CI, 82 to 87) at 91-120 days in adolescents age 16 to 19 years against symptomatic infection. (VOC Delta) AD26.COV 2.S showed after dose VE 52% (95% CI, 6 to 75) at 14 days, VE 54% (95% CI, 38 to 70) at 14 - 60 days, VE 58% (95% CI, 19 to 79) at 14 – 30 days, VE 52% (95% CI, 27 to 69) at 31 - 60 days, VE 63% (95% CI, 46 to 75) at 61 - 90 days and VE 58% (95% CI, 45 to 68) at 91-120 days in adolescents age 16 to 19 years against symptomatic infection. (VOC Delta)		
20	Dorabawila	BNT162b2 showed after 2nd dose VE 68% (95% CI, 63 to 72) at Dec. 13-19, VE 57% (95% CI, 48 to 52) at Dec. 20-26, VE 50% (95% CI, 48 to 52) at Dec. 27-Jan 2, VE 48% (95% CI, 47 to 50) at Jan. 3-9, VE 34% (95% CI, 31 to 36) at Jan. 10-16, VE 20% (95% CI, 16 to 23) at Jan. 17-23 and VE 12% (95% CI, 6 to 16) at Jan. 24-30 in children age 5 to 11 years against infection. (VOC Delta to Omicron) BNT162b2 showed after 2nd dose VE 85% (95% CI, 84 to 86) at Nov. 29- Dec 05, VE 82% (95% CI, 81 to 83) at Dec. 6-12, VE 66% (95% CI, 64 to 67) at Dec. 13-19, VE 57% (95% CI, 56 to 58) at Dec. 20-26, VE 55% (95% CI, 54 to 56) at Dec. 27-Jan 2, VE 53% (95% CI, 52 to 54) at Jan. 3-9, VE 50% (95% CI, 48 to 51) at Jan. 10-16, VE 50% (95% CI, 48 to	Serious	Data-linkage study in New York state, U.S; that included 1,539,762 person days of children aged 5-11 years and 151,005 person days of children aged 12-17 years, to estimate BNT162b2 vaccine effectiveness against COVID cases and hospitalizations during Dec, 2021- Jan, 2022; time and setting for VOC Omicron. *Included in LES 8.11*

		52) at Jan. 17-23 and VE 51% (95% CI, 48 to 54) at Jan. 24-30 in adolescents age 12 to 17 years against infection. (VOC Delta to Omicron) BNT162b2 showed after 2nd dose VE 100% (95% CI, -189 to 100) at Dec. 13-19, VE 73% (95% CI, -7 to 97) at Dec. 20-26, VE 82% (95% CI, 45 to 96) at Dec. 27-Jan 2, VE 74% (95% CI, 36 to 96) at Jan. 3-9, VE 68% (95% CI, 28 to 91) at Jan. 10-16, VE 46% (95% CI, -15 to 77) at Jan. 17-23 and VE 48% (95% CI, -12 to 75) at Jan. 24-30 in children age 5 to 11 years against hospitalization. (VOC Delta to Omicron) BNT162b2 showed after 2nd dose VE 94% (95% CI, 76 to 99) at Nov. 29- Dec 05, VE 95% (95% CI, 64 to 100) at Dec. 6-12, VE 85% (95% CI, 63 to 95) at Dec. 13-19, VE 78% (95% CI, 63 to 88) at Dec. 20-26, VE 74% (95% CI, 61 to 84) at Dec. 27-Jan 2, VE 74% (95% CI, 63 to 82) at Jan. 3-9, VE 75% (95% CI, 64 to 86) at Jan. 10-16, VE 75% (95% CI, 61 to 83) at Jan. 17-23 and VE 73% (95% CI, 53 to 87) at Jan. 24-30 in adolescents age 12 to 17 years against hospitalization. (VOC Delta to Omicron)		
21	Florentino	CoronaVac showed after 1st dose VE -6.83% (95% CI, -11.07 to -2.76) at 0 – 13 days, and VE 22.3% (95% CI, 19.7 to 24.9) at least 14 days in children age 6 to 11 years against symptomatic infection. (VOC Omicron) CoronaVac showed after 2nd dose VE 35% (95% CI, 27.7 to 41.5) at 0 – 13 days, and VE 41.5% (95% CI, 34.4 to 47.7) at least 14 days in children age 6 to 11 years against symptomatic infection. (VOC Omicron) CoronaVac showed after 1st dose VE 27.8% (95% CI, -4.04 to 52) at 0 – 13 days, and VE 40% (95% CI, 18.4 to 56.8) at least 14 days in children age 6 to 11 years against severe COVID-19. (VOC Omicron)	Serious	Test-negative case-control design in Brazil, including 194,258 tests among children aged 6–11 years during Jan 21, 2022 – April 19, 2022, to assess CoronaVac effectiveness against infection and severe disease (hospitalization or death); time and setting for VOC Omicron. *Included in LES 8.11*

		CoronaVac showed after 2nd dose VE 69.2% (95% CI, 11.7 to 93.6) at 0 – 13 days, and VE 63.5% (95% CI, 5.8 to 90) at least 14 days in children age 6 to 11 years against severe COVID-19. (VOC Omicron)		

Section 2: excluded studies		
Author	**Reason for exclusion**	**Version of exclusion**
Tang	Did not report the vaccine effectiveness in <18 years	*Excluded in LES 8.1*
Naleway	Did not report results according to vaccine type	*Excluded in LES 8.1*
Chadeau-Hyam round 14	Vaccine effectiveness not reported	*Excluded in LES 8.1*
de Gier	Did not report results according to vaccine type	*Excluded in LES 8.2*
Delahoy	Did not report results according to vaccine type	*Excluded in LES 8.2*
Lin	Did not report the vaccine effectiveness in <18 years	*Excluded in LES 8.2**
McLean	Did not report the vaccine effectiveness in <18 years	*Excluded in LES 8.2*
Chung	Did not report the vaccine effectiveness in <18 years, Did not report results according to vaccine type	*Excluded in LES 8.3**
Fisman	Did not report the vaccine effectiveness in <18 years	*Excluded in LES 8.3*
Lyngse	Did not report results according to vaccine type	*Excluded in LES 8.3*
Prunas	Critical risk of bias	*Excluded in LES 8.3*
Chiew	Critical risk of bias	*Excluded in LES 8.3*
Elliot	Critical risk of bias	*Excluded in LES 8.4*
New York State Department of Health	Did not report results according to vaccine type	*Excluded in LES 8.4*
Andeweg	Did not report results according to vaccine type	*Excluded in LES 8.5*
Jalali	Did not report results according to vaccine type	*Excluded in LES 8.5**
Choe	Critical risk of bias	*Excluded in LES 8.6*
Madhi	Did not report the vaccine effectiveness in <18 years	*Excluded in LES 8.6*
De Serres	Did not report results according to vaccine type	*Excluded in LES 8.7*
Nyberg	Did not report results according to vaccine type	*Excluded in LES 8.7*
Hoeg	Clinical outcomes of interest for this LES not reported	*Excluded in LES 8.7*
Levi	Did not report results according to vaccine type	*Excluded in LES 8.7*
Nygaard	Critical risk of bias	*Excluded in LES 8.8*
Chemaitelly	Did not report the vaccine effectiveness in <18 years	*Excluded in LES 8.8*
AlHosani	Did not report the vaccine effectiveness in <18 years	*Excluded in LES 8.8*
Ng	Vaccine effectiveness not reported	*Excluded in LES 8.8*
Petrie	Did not report the vaccine effectiveness in <18 years	*Excluded in LES 8.10*
González	Critical risk of bias	*Excluded in LES 8.11*

Carazo	Did not report results according to vaccine type	*Excluded in LES 8.11*

* For this studies links have been updated after their exclusion

Some studies excluded in previous reports due to critical risk of bias (Chadeu-Hyam et al., Britton et al., and Dorabawila et al.) were reassessed and upgraded as serious RoB and included in LES 8.11.

Appendix 2: Glossary (revised 13 Jan 2022)

AZ: AstraZeneca

Alpha: variant of concern B.1.1.7

Beta: variant of concern B.1.351

Delta: variant of concern B.1.617.2

Gamma: variant of concern P.1

Epsilon: variant of concern B.1.427/B.1.429

MIS-C: Multisystem inflammatory syndrome in children

MOD: Moderna

Obs: observational study

OR: odds ratio

PF: Pfizer

RME: range of mean estimates across 2 or more studies

VE (Vaccine effectiveness): measure of how well a vaccine protects people from getting the outcome of interest in real-world practice (For example: VE of 92% against infection means that 92% of people will be protected from becoming infected with COVID and 8% of people will still be at risk of becoming infected with COVID)

VET: vaccine effectiveness against transmission

VOC: variant of concern

VOI: variant of interest

Appendix 3: Data-extraction template (revised 13 Jan 2022)

Vaccine product	
Source	First author of study
Link	DOI or PubMed ID
Date published	in format YYYY/MM/DD or preprint
Country	
Funding	public or industry
Study details	
Study type	RCT/cohort/data-linkage/test-negative/case-control/other
Surveillance	routine screening Y or N
Intervention	Pfizer/Comirnaty [BNT162b2]/Moderna/Spikevax [mRNA-1273]/AstraZeneca/Vaxzevria [ChAdOx1]/Johnson & Johnson [AD26.COV2.S]/Sinovac [CoronaVac]/Sinopharm (Wuhan) [WIV04]/Novavax [NVX-CoV2373]/FBRI [EpiVacCorona]/Bharat Biotech [Covaxin] [BBV152]/Gamaleya [Sputnik V] [Gam-COVID-Vac]
Dose and timing	
Control group	not vaccinated, <7day vaccinated internal control, none, other
Total (N)	number of all study participants
Female	number or %
< 12 years	number or %
≥ 12 years	number or %
Outcomes	outcomes separated by VOC type
Outcomes	confirmed infection/asymptomatic/mild symptomatic/severe symptoms/hospitalized/ICU/death/MIS-C
1st Dose VE	VE with 95% CI
Days post 1st dose	days post 1st dose when VE provided
2nd Dose VE	VE with 95% CI
Days post 2nd dose	days post 2nd dose when VE provided
Rates per X person-days/years	vaccinated vs control
HR	vaccinated vs control
RR	vaccinated vs control
Adjusted	Regression, stratification, matching and associated variables
Transmission	infection rates in unvaccinated contacts of vaccinated individuals
Critical appraisal	See Appendix 5

Appendix 4: Process for assigning Variant of Concern to studies

A Variant of Concern is considered to be the dominant (≥50%) strain in a study if any of the following conditions apply:
i) the authors make a statement about prevalence of VOC during the study time frame
ii) time and setting of the study is consistent with a VOC being dominant according to the following open tracking sources:

Nextstrain. Real-time tracking of pathogen evolution. https://nextstrain.org/
Outbreak Info. https://outbreak.info/location-reports

Appendix 5: Research question and critical appraisal process (revised 13 Jan 2022)

Review question:

Participants	People aged under 18 years at risk of COVID-19 (usually without but sometimes with previous COVID-19 infection)
Intervention	COVID-19 Vaccine
Comparator	Unvaccinated children and adolescents (*)
Outcomes	PCR-diagnosis of COVID-19 infection; symptomatic disease; hospital/ICU admission; death; transmission; MIS-C

(*) Eligible studies must have a comparison group (unvaccinated; non-immune period; time since vaccination; 2 doses vs 3 doses); before-after studies, where the infection rate in the first 2 weeks after the vaccination are used as control are commonly performed and may be appraised

Key exclusion criteria

Studies that address the question of interest but from which the information of children cannot be separated from that of adults.
Comparison of one vaccine vs another (e.g., relative effectiveness) is not eligible.
Studies reporting only antibody responses are excluded.

Critical Appraisal Process

We appraise the quality of the individual studies using an adapted version of ROBINS-I. This tool classifies the Risk of Bias of a study as **Low, Moderate, Serious, Critical, or No Information**. Low Risk of Bias indicates High Quality, and Critical Risk of Bias indicates Very Low (insufficient) Quality. ROBINS-I appraises 7 bias domains and judges each study against an ideal reference randomized controlled trial. To improve the utility of ROBINS-I for assessing studies reporting vaccine effectiveness, we have focused on study characteristics that introduce bias as reported in the vaccine literature. (WHO. Evaluation of COVID-19 vaccine effectiveness. Interim Guidance. 17 March 2021). Studies rated as "critical" risk of bias will not be included in the Summary statements on Page 1-2 (exception: if limited data available for an outcome for a VOC). An overall judgement of "serious" or "critical" is given when the study is judged to be at serious or critical risk of bias in at least one domain or "serious" in 3 separate ROBINS-I domains.

VE Study Characteristics that may introduce bias	Description
Study design ROBINS-I: Bias in selection of participants into study	In cohort studies, people who get vaccinated may differ in health-seeking behaviour from people who do not get vaccinated; using a test-negative study design minimizes this type of bias Examples and typical judgement: ● test-negative design with a clearly defined symptomatic study population (low) ● test-negative design (mixed or unclear study population) or case-control or cohort design or data-linkage with no concerns (moderate) ● cross-sectional design or case-control (concerns about whether controls had same access to vaccines/risk of exposure to COVID or unclear) or cohort design (concerns that exposed and

	non-exposed were not drawn from the same population) (serious)
Method for confirming vaccination ROBINS-I: Bias in classification of interventions	Questionnaires are prone to recollection bias; Population databases developed for purpose of tracking COVID vaccines minimize this type of bias <u>Examples and typical judgement</u>: ● database linkage study (low) ● Questionnaire with confirmation by an additional method (e.g., registry) of at least a subset of study population (moderate) ● Questionnaire without confirmation by an additional method (serious) ● Estimating vaccination status based on surveillance data alone (critical)
Databases used for retrieval of COVID test results, participant prognostic factors, and clinical outcomes ROBINS-I: Bias in classification of interventions	Databases developed for collecting data on COVID are less prone to bias due to missing information and misclassification <u>Examples and typical judgement</u>: ● database for non-COVID purpose but with individual level data (moderate) ● database for non-COVID purpose without individual level data (serious) ● no or unclear description of database type (critical)
Assignment of infection start date ROBINS-I: Bias in classification of interventions	Using date of symptom onset (if within 10 days of testing) as infection start date reduces risk of misclassification bias (e.g., vaccinated participant who is reported as COVID+ may have been infected prior to receiving the vaccine or during non-immune period) and sensitivity of assays decreases over time <u>Examples and typical judgement</u>: ● using a PCR positive test that was part of an ongoing standardized monitoring system (e.g., within a health network) (low) ● using sample date without interview or documented confirmation of symptoms ≤ 10 days (relevant for symptomatic disease only) (serious)
Verification of symptoms ROBINS-I: Bias in classification of interventions	Prospective, standardized collection of symptoms from patients reduces risk of missing information bias; testing within 10 days after symptom onset reduces risk of false-negative COVID test <u>Examples and typical judgement</u>: ● using sample date without patient report/ documented confirmation of symptoms ≤ 10 days (relevant for symptomatic disease only) (serious) ● if symptomatic COVID is not an outcome (no information)
Accounting for non-immune period (first 14 days after first vaccine dose)	Reported absence of vaccine effect during non-immune period reduces risk of residual confounding bias <u>Example/common case</u>:

ROBINS-I: Bias due to confounding	• presence of an effect during non-immune period or result not reported (moderate) • unclear that non-immune period was considered (serious)
Inclusion of participants with prior COVID infection ROBINS-I: Bias due to confounding	Exclusion (or separate analysis) of participants with prior COVID infection reduces concern about differences in infectivity as well as risk-taking and health-seeking behaviour Examples and typical judgement: • inclusion of prior infection status as a covariate in the models (moderate) • previously infected not excluded or analyzed separately (serious)
Accounting for calendar time ROBINS-I: Bias due to confounding (time-varying confounding)	Accounting for calendar time reduces bias due to differences in vaccine accessibility and risk of exposure over time Examples and typical judgement: • use of time-varying statistics without explicit mention of adjustment for calendar time (moderate) • not taken into account but short-time frame (e.g., ≤2 months) (serious) • not taken into account and time frame >2 months (critical)
Adjustment for prognostic factors ROBINS-I: Bias due to confounding	Adjustment for prognostic factors for COVID infection, severity of disease, and vaccination, such as age, gender, race, ethnicity, socioeconomic factors, occupation (HCW, LTC), and chronic medical conditions Examples and typical judgement: • no or insufficient adjustment for occupation (or number of tests as a surrogate for exposure risk) -exception age>65 or LTCF resident (moderate) • no or insufficient adjustment for socioeconomic factors (or neighborhood or income as a surrogate), race, ethnicity (serious) • no or insufficient adjustment for age (any study population) or chronic medical conditions (LTC)(critical)
Testing frequency ROBINS-I: Bias in measurement of outcomes	Similar frequency of testing between groups reduces risk of bias introduced by detecting asymptomatic infection in one group but not in another (e.g., when only one group undergoes surveillance screening) Examples and typical judgement: • no systematic screening but consistent methods for detection in one group vs. the other, e.g., within health networks (moderate) • screening performed for a subset of both study groups (serious) • screening performed routinely in one study group but not in the other (critical)

Appendix 6: Detailed description of the narrative summary statement (revised 13 Jan 2022)

We include studies with the following clinical outcomes: prevention of infection, MIS-C, severe disease (as defined by the study investigators), hospitalization, death, and prevention of transmission. These outcomes were selected because they are less susceptible to bias, or they are important for parents and patients. If data are not available for these specific outcomes, but are available for symptomatic infection, data for these additional outcomes are provided temporarily.

We aim at providing a lay language, standardized summary statement for each combination of vaccine and VOC for which we found evidence.

Where more than one study was found, we will provide a summary statement with a **range of the estimates across the studies**.

Where a single study provided data, we will provide the **estimate plus 95% confidence interval** for that study. As additional studies are added, the estimate plus confidence interval will be replaced by a range as described above.

In the summaries, "prevented" or "protects" will be applied to mean estimates or range of mean estimates that are greater than or equal to 50%.

Appendix 7: Table 1b. Visual summary of evidence for COVID-19 vaccines overall and for variants of concern (Moderate to Low Risk of Bias Studies compared to All studies)

Top yellow row = moderate or low ROB studies only
Bottom orange row = serious ROB studies only

Outcome (and vaccine)	Vaccine Effectiveness (2 doses unless otherwise stated) for each combination of vaccine, variant, and outcome					
	Overall	**Alpha**	**Beta**	**Gamma**	**Delta**	**Omicron**
Any Infection						
Pfizer	91% (1 Obs – ref 3)				81 to 92% (5 Obs – ref 2,6,9,11, 13)	59% (1 Obs – ref 11)
	Same single study				91.5 - 93% (2 Obs - ref 1,17)	53.1% (1 Obs - ref 13)
Moderna						
CoronaVac						38% (1 Obs – ref 12)
						Same single study
Symptomatic Infection						
Pfizer					87 to 97% (3 Obs - ref 5,9,16)	71 to 83% (1 Obs - ref 5)
					94 - 96% (1 Obs - ref 19)	Same single study
Moderna					Same single study	
					98% (1 Obs - ref 19)	
CoronaVac						Same single study
						41% (1 Obs - ref 21)
Johnson & Johnson					Same single study	
					58% * (1 Obs - ref 19)	
Transmission						
Pfizer						
Moderna						
CoronaVac						
ICU Admission						
Pfizer					98% (1 Obs - ref 4)	
					Same single study	
Moderna						
CoronaVac						69% (1 Obs – ref 12)

						Same single study
Severe Disease (may include death for some studies)						
Pfizer						
Moderna						
CoronaVac						
Death						
Pfizer						
Moderna						
CoronaVac						

**mean estimate of effect less than the lowest acceptable limit for vaccine effectiveness as determined by WHO

Notes:
Comparing Table 1 with Table 1b allows you to see whether it is an RCT or multiple Obs studies that determined the "moderate certainty of evidence" rating on Table 1