



Unidad de Evidencia y Deliberación para la toma de decisiones UNED



COVID-19 Living Evidence <u>Synthesis # 8</u>

(Version 8.10: 25 April 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 <u>visual</u> <u>summary of evidence in Table 1</u> and <u>Table 2</u>.

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) <u>detailed description of the narrative</u> <u>summary statement</u>.

Overall, 47 studies were appraised and 17 used to complete this summary. The reasons for excluding the remaining 30 studies are reported in the second section of Appendix 2.

Three new studies have been added since the previous edition of this living evidence synthesis, which is signaled by a last updated date of 25 April 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 and Table 2 of one moderate risk of bias study (ref 16) and one serious risk of bias study (ref 17)
- New data on Pfizer [BNT162b2] against VOC Omicron has been added to Table 1 and Table 2 of one moderate risk of bias study (ref 16)
- 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: 59 to 80% 3 Obs [2][10][17]) in adolescents age 12 to 18 years
- We have moderate certainty evidence that <u>1 dose</u> 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% 3 Obs [5][9][16]) in adolescents age 12 to 18 years
- We have low certainty evidence that <u>2 doses</u> 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 <u>1 dose</u> 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 <u>1 dose</u> 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 <u>2 doses</u> 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 <u>2 doses</u> of **BNT162b2 (Pfizer)** prevented infection from VOC **Omicron** (range of mean estimates: 53 to 59% 2 Obs [<u>11</u>][<u>13</u>])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 <u>3 doses</u> 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

Sinovac [CoronaVac]

• VOC Omicron

• We have low certainty evidence that <u>2 doses</u> of **CoronaVac** prevented infection from VOC **Omicron** (38.2% [95% CI, 36.5 to 39.9] - 1 Obs [<u>12</u>]) in children age 3 to 5 years

We have low certainty evidence that <u>2 doses</u> 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

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

Percentages indicate <u>level of effectiveness</u> 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 single RCT with low to moderate single RCT or observational risk of bias RCTs or pooling risk of bias or >one observational study with serious risk of bias of observational studies with study with low to moderate risk of or multiple low to serious risk low risk of bias and bias and at least partially of bias observational studies with inconsistent findings consistent findings consistent 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	Vaccine Effectiveness (2 doses unless otherwise stated)					
(and vaccine)	up to 28 days after last dose each combination of vaccine, variant, and					
			outo	come		
	Overall	Alpha	Beta	Gamma	Delta	Omicron
Any Infection						
Pfizer	91%				81 - 93%	53 - 59%
Moderna						
CoronaVac						38%
Symptomatic I	nfection					
Pfizer					87 - 97%	71 - 83%
Moderna						
CoronaVac						
Transmission						
Pfizer						
Moderna						
CoronaVac						
ICU Admission	n					
Pfizer					98%	
Moderna						
CoronaVac						69%
Severe Disease	(may includ	le death for s	ome studies)			
Pfizer						
Moderna						
CoronaVac						
Death						
Pfizer						

Moderna			
CoronaVac			

^{*}Single dose

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 <u>level of effectiveness</u> 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 <u>level of certainty</u> based on the evidence*

High certainty evidence Moderate certainty evidence Low certainty evidence single RCT with low to moderate pooling of low to moderate single RCT or observational risk of bias RCTs or pooling risk of bias or >one observational study with serious risk of bias study with low to moderate risk of of observational studies with or multiple low to serious risk low risk of bias and bias and at least partially of bias observational studies consistent findings with inconsistent findings consistent 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	Variant		Time since Last	Age (years)	Vaccine Effectiveness
(and vaccine)		of doses	Dose (days)		
Any Infection	n				
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

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

			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					
Symptoma	atic Infection	ļ	I.		
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)
	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)
			<mark>7</mark>		62% (95% CI, 49 to 72)
Moderna					
CoronaVac					
Transmiss	sion		1		
Pfizer					
Moderna					
CoronaVac					

ICU Admiss	ion				
Pfizer					
Moderna					
CoronaVac					
MIS-C					
Pfizer	Delta	2	28	12 to 18	91% (78 to 97)
Moderna					
CoronaVac					
Severe Disea	se (may i	nclude de	ath for some studies	s)	
Pfizer					
Moderna					
CoronaVac					
Death					
Pfizer					
Moderna					
CoronaVac					

Table 3: Key findings about vaccine effectiveness

Vaccine	Effectiveness	Findings
Pfizer/	Delta	BNT162b2 provided protection against VOC Delta for the
BioNTech		following outcomes at least 14 days after 1st dose in adolescents age
	At least 14 days	12 to 18:
Comirnaty	after 1st dose	• 59 to 80% from infection (RME) (3 Obs - [2][10][17])
	&	• 70 to 76% from symptomatic infection(RME) (2 Obs - [5][9])
[BNT162b2]	At least 7 days	BNT162b2 provided protection against VOC Delta for the
	after 2 nd dose	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 <u>2nd dose</u> 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) (3 Obs -[5][9][16])
		BNT162b2 provided protection against VOC Delta for the
		following outcomes at least 14 days after 2 nd 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])
		● (11 Obs) [1][2][4][5][6][10][11][13][16][17]; last update 2022-04-25

Delta	BNT162b2 provided protection against infection by VOC Delta
Della	the following number of days after 1st dose in adolescents age 12 to
>30 days after 1 st	17:
dose	
dose	• 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 1^{st} 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	BNT162b2 provided protection against infection by VOC Delta for
	the following number of days after 2 nd dose in adolescents age 12 to
>30 days after 2 nd	18:
dose	• 90% (95% CI, 67 to 97) - at 35 to 56 days (1 Obs - [2])
	• 83% (95% CI, 34 to 95) - at 34 to 95 days (1 Obs - [2])
	• 95% (95% CI, 79 to 99) - at 79 to 99 (1 Obs - [2])
	BNT162b2 provided protection against infection by VOC Delta for
	the following number of days after 2 nd 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 2 nd 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 2 nd 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 - [Z])
	BNT162b2 provided protection against symptomatic infection by
	VOC Delta for the following number of days after 2 nd dose in
	adolescents age 16 to 17:
	• 91.5% (95% CI, 89.9 to 93.0) - at 35 to 69 days (1 Obs - [5])

1	
Omicron At least 14 days after 1st dose & At least 7 days after 2nd dose	● 83.7% (95% CI, 72.0 to 90.5) - at least 70 days (1 Obs - [3]) BNT162b2 provided protection against symptomatic infection by VOC Delta for the following number of days after 2 nd 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 hospitalization by VOC Delta for the following number of days after 2 nd dose in adolescents age 12 to 18: ● 93% (95% CI, 89 to 95)- at 14 to 154 days (1 Obs - [13]) (7 Obs) [5][7][8][2][1][13][16]; last update 2022-04-25 BNT162b2 provided protection against VOC Omicron for the following outcomes at least 14 days after 1 st dose in adolescents age 12 to 17: ● 53.7% (95% CI, 43.3 to 62.2) from infection (1 Obs - [3]) BNT162b2 provided protection against VOC Omicron for the following outcomes at least 14 days after 2 nd dose in adolescents age 12 to 17: ● 53 to 59% (RME) from symptomatic infection (1 Obs - [3]) BNT162b2 provided protection against VOC Omicron for the following outcomes at least 14 days after 2 nd 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 2 nd 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 2 nd 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	BNT162b2 provided protection against VOC Omicron for the following outcomes at least 7 days after 3 rd dose in adolescents age 16 to 17:
after 3 rd dose	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 3 rd 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	BNT162b2 provided protection against infection by VOC
>30 days after 1st	Omicron the following number of days after 1st dose in adolescents
>30 days after 1 st dose	age 12 to 17: • 57.9% (95% CI, 50.9 to 63.9) − at 28 to 56 days (1 Obs - [10])
4000	• 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])

		DNTT1/01-01-1 1
		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 2^{nd} dose in
	>30 days after 2 nd	children age 5 to 11:
	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 2 nd 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 2 nd 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 2^{nd}
		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 2 nd 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 2 nd 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 2 nd dose in
		adolescents age 12 to 18:
		• 43% (95% CI, -1 to 68) - at 14 to 67 days (1 Obs - [15])
		(6 Obs) [<u>5][8][11][13][15][16]</u> ; last update <mark>2022-04-25</mark>
Moderna	VOC	No data
-		

Spikevax		
P		
[mRNA-1723]		
AstraZeneca [ChAd0x1]	VOC	No data
Vaxzevria		
Serum Institute of India [Covishield]*		
Johnson & Johnson [AD26.COV2.S]*	VOC	No data
Sinovac [CoronaVac]	Omicron At least 14 days after 1 st dose & At least 7 days after 2 nd dose	CoronaVac provided protection against VOC Omicron for the following outcomes at least 14 days after 2 nd 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]) (1 Obs) [12]; last update 2022-03-28
Sinopharm (Wuhan) [WIV04]* Sinopharm (Beijing) [HBO2] [BBIBP-CorV]*	VOC	No data
Novavax [NVX- CoV2373]*	VOC	No data
FBRI [EpiVacCorona] *	VOC	No data
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/	Overall	BNT162b2 provided protection for the following outcomes at least	
BioNTech		14 days after 1 st dose in adolescents age 12 to 15:	
		• 67% (95% CI, 50 to 78) from infection (1 Obs - [3])	

Comirnaty		• 100% (95% CI, 100 to 100) from hospitalization (1 Obs - [3])
		BNT162b2 provided protection for the following outcomes at least
[BNT162b2]		7 days after 2 nd dose in adolescents age 12 to 15:
[21(110202]		• 91% (95% CI, 88 to 93) from infection (1 Obs - [3])
		, , , , , , , , , , , , , , , , , , , ,
		• 81% (95% CI, -55 to 98) from hospitalization (1 Obs - 3)
	Direct	(1 Obs) [3]; last update 2021-12-13
	Delta to	BNT162b2 provided protection against VOC Delta to Omicron for
	Omicron	the following outcomes at least 14 days after 1st dose in adolescents
		age 12 to 17:
	At least 14 days	• 38% (95% CI, -51 to 79) from hospitalization (1 Obs – [14])
	after 1 st dose	BNT162b2 provided protection against VOC Delta to Omicron for
	&	the following outcomes at least 14 days after 1st dose in children age
	At least 7 days	4 to 11:
	after 2 nd dose	• 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 2 nd 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 2 nd 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 2 nd 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 2 nd 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	BNT162b2 provided protection against infection by VOC Delta
	Omicron	Omicron the following number of days after 1st dose in adolescents
		age 12 to 17:
	>30 days after 1st	• 62 to 65 (RME) – at 21 to 48 days (1 Obs - [13])
	dose	• 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	BNT162b2 provided protection against infection by VOC Delta to
	Omicron	Omicron for the following number of days after 2 nd dose in
		adolescents age 16 to 17:
	>30 days after 2 nd	• 92.3% (95% CI, 82.9 to 96.6) - at 35 to 62 days (1 Obs - [13])
	dose	· · · · · · · · · · · · · · · · · · ·
	dose	• 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 2 nd 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 2 nd 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 2^{nd}	
	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 2^{nd}	
	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	BNT162b2 provided protection against VOC Delta to Omicron for	
Omicron	the following outcomes at least 7 days after 3rd dose in adolescents	
	age 16 to 17:	
Any time f		
after 3 rd do	se (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 P¹, Martínez JC¹, Linkins L³, Abdelkader W³, Iorio A³, Lavis J³, Patiño-Lugo DF¹. COVID-19 living evidence synthesis #8 (version 10): 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, 25 April 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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¹ Faculty of Medicine, University of Antioquia, Colombia

² School of Rehabilitation Science, McMaster University, Canada

³ Faculty of Health Sciences, McMaster University, Canada

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	k of bias indica	ites high quality
1	Glatman- Freedman	BNT162b2 showed VE 91.5% (95% CI, 88.2 to 93.9) against infection at least 8 days after 2 nd 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 persondays and 13,623,714 unvaccinated person-days; time and setting for VOC Delta <i>Included in LES 8.1</i>
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 <i>Included in LES 8.1</i>
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	<u>Olson</u>	BNT162b2 showed VE 94% (95% CI, 90 to 96) against hospitalization at least +14 days after 2 nd 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

	Т	,		1
		adolescents age 16 to 18 years against hospitalization at least +14 days after 2 nd		vaccinated (had received only one dose of vaccine or who had
		dose.		received a second dose less than
		dosc.		14 days before illness onset) and
		BNT162b2 showed VE 98% (95% CI, 93		868 unvaccinated (no receipt of
		to 99) against ICU admission at least +14		any COVID-19 vaccine before
		days after 2 nd dose in adolescents age 12		illness onset), time and setting
		to 18 years.		for VOC Delta.
		to 16 years.		Included in LES 8.2
				last update in LES 8.3
5	Powell	BNT162b2 showed after 1st dose VE	Moderate	Test-negative case-control
	1 OWCII	74.5% (95% CI, 73.2 to 75.6) at 14-20	Moderate	design in England of
		days, VE 63.4% (95% CI, 61.7 to 65.1) at		adolescents age 12-17 years
		28-34 days, VE 47.5% (95% CI, 44.9 to		from week 37, 2021 onwards;
		49.9) at 56-69 days, and VE 53.1% (95%		there were 617,259 eligible tests
		CI, 41.6 to 62.4) at least 84 days, in		for 12-15-year-olds and 225,670
		adolescents age 12 to 15 years against		for 16-17-year-olds.
		infection. (VOC Delta)		Symptomatic 12-15-year-olds
		miccion. (voc Deita)		and 16-17-year-olds with PCR-
		BNT162b2 showed after 1st dose VE		confirmed SARS-COV-2
		49.6% (95% CI, 43.9 to 54.8) at 14-20		infection was compared with
		days, VE 42.1% (95% CI, 36.7 to 46.9) at		vaccination status in
		28-34 days, VE 22.5% (95% CI, 19.1 to		symptomatic adolescents in the
		25.8) at 56-69 days, and VE 17.2% (95%		same age-groups who had a
		CI, 12.0 to 22.1) at least 84 days, in		negative SARS-COV-2 PCR
		adolescents age 12 to 15 years against		test.
		infection. (VOC Omicron)		All cases prior to week 48 were
		iniccion. (VOC Officion)		defined as Delta, unless S gene
		BNT162b2 showed after 1st dose VE		target failure (SGTF),
		75.9% (95% CI, 74.3 to 77.3) at 14-20		genotyping or sequencing
		days, VE 60.6% (95% CI, 58.1 to 62.9) at		information confirmed
		28-34 days, VE 36.3% (95% CI, 33.1 to		otherwise. Tests were defined as
		39.3) at 56-69 days, VE 29.3% (95% CI,		Omicron from week 48
		25.9 to 32.6) at 84-104 days, and VE		onwards using SGTF,
		30.9% (95% CI, 25.4 to 36.0) at least 105		genotyping or sequencing
		days, in adolescents age 16 to 17 years		information.
		against infection. (VOC Delta)		Included in LES 8.2
		agamet intection. (***CODEIIa)		Updated in LES 8.6
		BNT162b2 showed after 1st dose VE		Link Updated in LES 8.8
		51.4% (95% CI, 42.7 to 58.8) at 14-20		п по Сримии и про 0.0
		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 2 nd dose VE		
		93.2% (95% CI, 81.5 to 97.5) at 7-13 days		
		75.470 (7570 C1, 61.5 to 97.5) at 7-15 days		

		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 <u>2nd dose</u> 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 2 nd 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)		
		miceuon. (VOC Delta)		
		BNT162b2 showed after 2 nd 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)		
		DNT14 (21-2 -1 1 - 6 1 st -1 V/E		
		BNT162b2 showed after 1 st 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)		
		DNT-1/212 1 1 5 48 1 175		
		BNT162b2 showed after 1 st 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.		
	T 1	(VOC Delta)	3.5 1	D
6	<u>Lutrick</u>	BNT162b2 showed VE 92% (95% CI, 79	Moderate	Prospective cohort in Arizona,
		to 97) against infection at least +14 days		of 243 adolescents aged 12–17
		after 2 nd dose in adolescents age 12 to 17		years between Jul 25 - Dec 4,
		years.		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 2 nd 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 syndromenegative) matched to casepatients; time and setting for VOC Delta. <i>Included in LES 8.3</i>
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 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 3 rd 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 2 nd 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 2 nd 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 2 nd 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 2 nd 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 2 nd 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 3 rd 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 1 st dose VE	Moderate	Matched case-control study In
		74% (95% CI, 18 to 92) at least 14 days,		Connecticut (US) of 542
		in adolescents age 12 to 18 years against		adolescents aged 12-18 years,
		infection. (VOC Delta)		including 186 case participants
				and 356 matched control
		BNT162b2 showed after 2 nd dose VE		participants, between Jun 1 -
		90% (95% CI, 79 to 95) at least 14 days,		Aug 15, 2021; time and setting
		VE 91% (95% CI, 33 to 99) at 7-28 days,		for VOC Delta.
		VE 90% (95% CI, 67 to 97) at 35-56		Included in LES 8.8
		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)		

		BNT162b2 showed after 2 nd dose VE 93% (95% CI, 81 to 97) at least 14 days, in adolescents age 12 to 18 years against		
10	<u>Molteni</u>	symptomatic infection. (VOC Delta) BNT162b2 showed after 1 st 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 1 st dose VE	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
		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)		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. <i>Included in LES 8.8</i>
11	Fowlkes	BNT162b2 showed after 2 nd 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 2 nd 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 2 nd dose VE 59% (95% CI, 24 to 78) at least 14 days,	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. <i>Included in LES 8.8</i>
		and VE 59% (95% CI, 22 to 79) at 14- 149 days, in adolescents age 12 to 15 years against infection. (VOC Omicron)		
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 2 nd 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	<u>Veneti</u>	BNT162b2 showed after 1st dose VE	Moderate	Population-based cohort in
		67.9 % (95% CI, 64.0 to 71.4) at 21-48		Norway, of 372,179 adolescents
		days, VE 55.8% (95% CI, 52.7 to 58.8) at 49-76 days, and VE 48.8% (95% CI, 46		aged 12-17 years, between Aug 25, 2021 – Jan 16, 2022; to
		to 51.5) at least 77 days, in adolescents		estimate BNT162b2 one dose
		age 12 to 15 years against infection.		effectiveness for individuals 12-
		(VOC Delta)		15 years old and one or two
		BNT162b2 showed after 1 st dose VE 62.6 % (95% CI, 56.2 to 68) at 21-48		doses effectiveness for individuals 16-17 years old against SARS-CoV-2 infections;
		days, VE 47.3% (95% CI, 40 to 53.8) at		time and setting for VOC Delta
		49-76 days, and VE 29.3% (95% CI, 20.4		to Omicron.
		to 37.1) at least 77 days, in adolescents		Included in LES 8.9
		age 16 to 17 years against infection. (VOC Delta)		
		BNT162b2 showed after 2 nd 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 1 st 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 1 st 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 <u>2nd dose</u> 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 1 st dose VE 65		
		% (95% CI, 62.3 to 67.6) at 21-48 days,		

14	Simmons	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) 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 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 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)	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
		BNT162b2 showed after 2 nd 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)		
15	Price	BNT162b2 showed after 2 nd 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 2 nd 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 2 nd 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 2 nd dose VE		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. <i>Included in LES 8.9</i>
		68% (95% CI, 42 to 82) at least 14 days, in children age 5 to 11 years against hospitalization. (VOC Omicron)		
		BNT162b2 showed after 2 nd 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 2 nd 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 2 nd 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)		
16	<u>Buchan</u>	BNT162b2 showed after 2 nd 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)	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,
		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)		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
		BNT162b2 showed after 3 rd 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)		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. <i>Included in LES 8.10</i>

		BNT162b2 showed after 2 nd 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 2 nd 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. <i>Included in LES 8.10</i>

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		
<u>Naleway</u>	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*		
<u>McLean</u>	Did not report the vaccine effectiveness in <18 years	Excluded in LES 8.2		
Chadeau-Hyam round 15 final report	Critical risk of bias	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*		
<u>Fisman</u>	Did not report the vaccine effectiveness in <18 years	Excluded in LES 8.3		
<u>Lyngse</u>	Did not report results according to vaccine type	Excluded in LES 8.3		
<u>Prunas</u>	Critical risk of bias	Excluded in LES 8.3		
Chiew	Critical risk of bias	Excluded in LES 8.3		

<u>Elliot</u>	Critical risk of bias	Excluded in LES 8.4	
New York State	Did not report results according to vaccine type	Excluded in LES 8.4	
Department of Health			
Andeweg	Did not report results according to vaccine type	Excluded in LES 8.5	
<u>Jalali</u>	Did not report results according to vaccine type	Excluded in LES 8.5*	
<u>Choe</u>	Critical risk of bias	Excluded in LES 8.6	
<u>Britton</u>	Critical risk of bias	Excluded in LES 8.6	
<u>Madhi</u>	Did not report the vaccine effectiveness in <18 years	Excluded in LES 8.6	
<u>Dorabawila</u>	Critical risk of bias	Excluded in LES 8.6	
<u>De Serres</u>	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	
<u>Hoeg</u>	Clinical outcomes of interest for this LES not reported	Excluded in LES 8.7	
<u>Levi</u>	Did not report results according to vaccine type	Excluded in LES 8.7	
<u>Nygaard</u>	Critical risk of bias	Excluded in LES 8.8	
Chemaitelly	Did not report the vaccine effectiveness in <18 years	Excluded in LES 8.8	
<u>AlHosani</u>	Did not report the vaccine effectiveness in <18 years	Excluded in LES 8.8	
Ng	Vaccine effectiveness not reported	Excluded in LES 8.8	
<u>Petrie</u>	Did not report the vaccine effectiveness in <18 years	Excluded in LES 8.10	

^{*} For this studies links have been updated after their exclusion

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
Tartesparies	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**. <u>Low Risk of Bias indicates High Quality, and Critical Risk of Bias indicates Very Low (insufficient) Quality</u>. 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	Description
Characteristics that	
may introduce bias	
Study design	In cohort studies, people who get vaccinated may differ in health-
	seeking behaviour from people who do not get vaccinated; using a
ROBINS-I: Bias in	test-negative study design minimizes this type of bias
selection of participants	
into study	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	Questionnaires are prone to recollection bias; Population databases		
vaccination	developed for purpose of tracking COVID vaccines minimize this		
, , , , , , , , , , , , , , , , , , , 	type of bias		
ROBINS-I: Bias in	type of blas		
classification of	Examples and typical judgement:		
interventions	 database linkage study (low) 		
interventions	 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)		
Databassassadfan	\ /		
Databases used for	Databases developed for collecting data on COVID are less prone		
retrieval of COVID test	to bias due to missing information and misclassification		
results, participant			
prognostic factors, and	Examples and typical judgement:		
clinical outcomes	• database for non-COVID purpose but with individual level data		
DODDIC I D' '	(moderate)		
ROBINS-I: Bias in	• database for non-COVID purpose without individual level data		
classification of	(serious)		
interventions	no or unclear description of database type (critical) University of the second		
Assignment of	Using date of symptom onset (if within 10 days of testing) as		
infection start date	infection start date reduces risk of misclassification bias (e.g.,		
DODD IO I D'	vaccinated participant who is reported as COVID+ may have been		
ROBINS-I: Bias in	infected prior to receiving the vaccine or during non-immune		
classification of	period) and sensitivity of assays decreases over time		
interventions			
	Examples and typical judgement:		
	• 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		
Vanification of	disease only) (serious)		
Verification of	Prospective, standardized collection of symptoms from patients		
symptoms	reduces risk of missing information bias; testing within 10 days after		
DODING L. Diag in	symptom onset reduces risk of false-negative COVID test		
ROBINS-I: Bias in classification of	Examples and typical judgements		
interventions	Examples and typical judgement:		
micryemions	• using sample date without patient report/ documented		
	confirmation of symptoms ≤ 10 days (relevant for symptomatic		
	disease only) (serious) of symptometric COVID is not an outcome (no information)		
A accounting for man	if symptomatic COVID is not an outcome (no information) Percented absence of varging offset during non impure period.		
Accounting for non-	Reported absence of vaccine effect during non-immune period		
immune period (first 14	reduces risk of residual confounding bias		
days after first vaccine	E 1- /		
dose)	Example/common case:		

ROBINS-I: Bias due to	presence of an effect during non-immune period or result not			
confounding	reported (moderate)			
T 1	• unclear that non-immune period was considered (serious)			
Inclusion of participants with prior COVID infection	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			
ROBINS-I: Bias due to	Examples and typical judgement:			
confounding	• inclusion of prior infection status as a covariate in the models (moderate)			
	• previously infected not excluded or analyzed separately (serious)			
Accounting for	Accounting for calendar time reduces bias due to differences in			
calendar time	vaccine accessibility and risk of exposure over time			
ROBINS-I: Bias due to	Examples and typical judgement:			
confounding (time-	• use of time-varying statistics without explicit mention of			
varying confounding)	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	Adjustment for prognostic factors for COVID infection, severity of			
prognostic factors	disease, and vaccination, such as age, gender, race, ethnicity, socioeconomic factors, occupation (HCW, LTC), and chronic			
ROBINS-I: Bias due to	medical conditions			
confounding				
	 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	Similar frequency of testing between groups reduces risk of bias introduced by detecting asymptomatic infection in one group but			
ROBINS-I: Bias in	not in another (e.g., when only one group undergoes surveillance			
measurement of	screening)			
outcomes				
	 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 <u>range of the</u> estimates across the studies.

Where a <u>single study</u> provided data, we will provide the <u>estimate plus 95% confidence interval</u> 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			T	T	1	1
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 I	nfection					
Pfizer					87 to 97% (3 Obs - ref 5,9,16)	71 to 83% (1 Obs - ref 5)
					Same single study	Same single study
Moderna						
CoronaVac						
Transmission			1	T	T	T
Pfizer						
Moderna						
CoronaVac						
ICU Admission	n T		I	1	000/	I
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 so	me 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