Coversheet on evidence assessment by ATAGI using the GRADE framework for updated formulation COVID-19 vaccine in people aged 6 months and over

A summary of the use of the GRADE approach in the development of ATAGI and Australian Immunisation Handbook recommendations for a single dose of the updated formulation COVID-19 vaccine following a previous dose in the last 6–12 months compared to no updated formulation COVID-19 vaccine dose following a previous dose in the last 6–12 months in people aged 6 months and over

Background

- In early 2021 ATAGI made recommendations on the COVID-19 vaccine rollout in Australia for adolescents, adults, and older adults.
- In January 2022, the rollout extended to children aged 5 to 11 years and later extended to under 5 years in August 2022.
- In 2023, bivalent COVID-19 vaccines for primary vaccination were approved. ATAGI preferred these vaccines for vaccination against COVID-19, and recommendations for further doses were revised based on risk conditions and COVID-19 epidemiology.
- Later in 2023, monovalent Omicron XBB.1.5 formulation of Comirnaty and Spikevax COVID-19 vaccines were approved by the Therapeutics Good Administration (TGA) and are currently preferred over original and bivalent vaccines.
- Vaccination remains the most important measure to protect those at risk of severe disease from COVID-19. Currently, COVID-19 vaccines are recommended every 6–12 months for older adults and adults with severe immunocompromise due to their increased risk of severe COVID-19.
- The purpose of this GRADE was to investigate whether people aged 6 months and over should receive a single further dose of an updated formulation COVID-19 vaccine to protect from severe disease from COVID-19, and from this, to inform future recommendations for COVID-19 vaccination.

Research questions

1. Should people aged 6 months and over receive a single dose of the updated formulation COVID-19 vaccine following a previous dose in the last 6–12 months?

Table 1: Population, Intervention, Comparator, Outcomes (PICO) – A single dose of the updated formulation COVID-19 vaccine vs no COVID-19 vaccine dose, people aged 6 months and over

Population	People aged 6 months and over
Intervention	Single dose of an updated formulation COVID-19 vaccine (monovalent Omicron XBB.1.5 formulation of Comirnaty or Spikevax COVID-19 mRNA vaccine) following a previous dose between 6 and 12 months prior
Comparator	No dose of an updated formulation COVID-19 vaccine (monovalent Omicron XBB.1.5 formulation of Comirnaty or Spikevax COVID-19 mRNA vaccine) following a previous dose between last 6 to 12 months prior
Outcomes	*Critical* • Vaccine effectiveness against COVID-19-related hospitalisation • Vaccine effectiveness against COVID-19-related death • Vaccine effectiveness against long COVID-19 • Serious adverse events (SAE) (any and vaccine-related) • Adverse event of special interest (AESI): myocarditis (with or without pericarditis) occurring within 42 days from vaccination *Important* • Solicited local adverse events within 7 days after the receipt of each dose of vaccine or placebo e.g.: pain, erythema, swelling, axillary swelling • Solicited systemic adverse events within 7 days after the receipt of each dose of vaccine or placebo e.g.: fever, headache, fatigue, myalgia, arthralgia, nausea/vomiting, chills, diarrhoea, joint or muscle pain, dizziness, decreased appetite, irritability

Literature search

The literature search was completed on 12 January 2024 to identify all publications evaluating VE of a dose of the updated formulation COVID-19 vaccine for PICO 1. The citations were included for review if they met the following criteria:

- *Study design:* Eligible primary studies were included according to the following hierarchy:
  - systematic reviews and meta-analyses of randomised controlled trials (RCTs)
  - randomised controlled trials and quasi-randomised trials
  - non-randomised comparative studies (e.g., prospective or retrospective cohort studies, case-control studies)
- *Publication date:* Vaccine effectiveness: 1January 2023 –13 February 2024
- *Population:* 6 months and over
- *Intervention:* A single dose of updated formulation COVID-19 vaccine following a previous dose within the last 6–12 months
- *Comparator:* No dose of updated formulation COVID-19 vaccine following a previous dose within the last 6–12 months
- *Outcomes:* Vaccine effectiveness

The literature search was completed on 12 January 2024 to identify all publications evaluating safety of a dose of the updated formulation COVID-19 vaccine for PICO 1. The citations were included for review if they met the following criteria:

- Study design: Eligible primary studies were included according to the following hierarchy:
  - systematic reviews and meta-analyses of randomised controlled trials (RCTs)
  - randomised controlled trials and quasi-randomised trials
  - non-randomised comparative studies (e.g., prospective or retrospective cohort studies, case–control studies)
  - non-comparative observational studies (e.g., single-arm cohorts, surveillance studies) – included only for outcomes where comparative evidence is not available, particularly for safety signals.
- *Publication date:* Published anytime
- *Population:* 6 months and over
- *Intervention:* A single dose of COVID-19 vaccine following a previous dose within the last 6–12 months
- *Comparator:* No dose of COVID-19 vaccine following a previous dose within the last 6–12 months
- *Outcomes:* Safety

The literature search retrieved a total of 1897 (vaccine effectiveness (VE)) and 469 (myocarditis (MI)) unique citations, of which 4=VE, 1=MI, 7=safety met the pre-defined inclusion criteria. The study characteristics and RoB of each individual study are presented in appendix A Table A1 and Table A2. For detailed search strategy refer to appendix B.

Four observational studies reporting short term VE of a single dose of updated formulation COVID-19 vaccine against hospitalisation were identified, two among elderly and two among individuals of ages 18 years and above. These studies are from Netherland, Denmark, and the USA. No publications for VE of a single dose of updated formulation COVID-19 vaccine against COVID-19-related death and long COVID were identified. The June 2023 COVID-19 vaccine safety report published by the Therapeutic Goods Administration (TGA) was included to report the rates of MI in Australian males and females after 'all dose' and after 'second doses' of mRNA and protein subunit COVID-19 vaccines. Adverse event profile safety outcome data were used from seven RCTs conducted in high and middle–income countries. Adverse events of special interest (AESI) and safety outcomes for the updated formulation COVID-19 vaccine are extrapolated from the phase 3 clinical trials of the original and earlier formula COVID-19 vaccines (compared to placebo), as these data were not available for the updated formulation COVID-19 vaccine.[1] This is in line with regulatory agencies, such as the TGA, which approved the updated formulation COVID-19 vaccines by extrapolating safety data from large phase 3 clinical trials of the original and earlier formula COVID-19 vaccines.

Inclusion criteria and rationale

Table 2: Rationale for PICO and inclusion criteria

PICO	Rationale
Study type RCT, observational study, meta-analysis	Vaccine effectiveness studies were preferred, particularly nationwide studies which included a large and diverse population. For safety outcomes, large population-based database-based studies were preferred. However, large clinical trial data was acceptable for inclusion if it met the other criteria.
Population People aged ≥6 months	1. People aged ≥6 months were the selected population as that is the age of lowest registration approved by TGA for COVID vaccination in Australia.

	2. Currently infants, children and adolescents are not routinely recommended a COVID-19 dose; however, to keep the PICO relevant for any future GRADEs or recommendations targeting any age group, a broad age group was selected proactively.
Intervention A single dose of updated formulation COVID-19 vaccine following a previous dose between 6 and 12 months prior	Updated formulation vaccines (e.g. XBB.1.5-based formulation, JN.1-based formulation) are now preferred over other older formulation COVID-19 vaccines in Australia.
Comparator No single dose of updated formulation COVID-19 vaccine following a previous dose between 6 and 12 months prior	This comparator was used as it was most relevant to the most recent ATAGI recommendations regarding further doses for COVID-19 vaccination.
Outcomes	Included outcomes as stated above in Table 1 as these represent the severe outcomes that those at risk of severe disease from COVID-19 should be protected from by COVID-19 vaccination. Less severe outcomes, such as VE against COVID-19 infection, were excluded as the priority of recommendations is to protect people from severe outcomes of COVID-19 and also given most of the population has had exposure to COVID-19 through previous vaccination, natural infection or hybrid immunity.
	Ranking of importance discussed in many iterations with portfolio leads and ATAGI full panel.
	General framework (depending on outcomes measured in studies available): *Critical* • Vaccine effectiveness against COVID-19-related hospitalisation • Vaccine effectiveness against COVID-19-related death* • Vaccine effectiveness against long COVID-19* • Serious adverse events (SAE) (any and vaccine-related) • Adverse event of special interest (AESI): myocarditis (with or without pericarditis) occurring within 42 days from vaccination *Important* • Solicited local adverse events within 7 days after the receipt of each dose of vaccine or placebo eg; pain, erythema, swelling, axillary swelling • Solicited systemic adverse events within 7 days after the receipt of each dose of vaccine or placebo eg: fever, headache, fatigue, myalgia, arthralgia, nausea/vomiting, chills, diarrhoea, joint or muscle pain, dizziness, decreased appetite, irritability *Note: some outcomes may be missing in GRADE projects due to no data from available included studies.
Effect size for VE and safety	Effectiveness: <20=trivial, 20-49= small, 50-79= moderate, 80+= large effect Safety: <10= trivial, 10-25= small, 25-49=moderate, 50+= large effect. Where effect sizes differed between dose 1 and dose 2 of the vaccine, ATAGI adopted a conservative approach and reported the larger effect size.

Abbreviations: AE, adverse events; AESI, adverse event of special interest; CI, confidence interval; RCT, randomised controlled trial; SAE, serious adverse events; VE, vaccine effectiveness.

Risk of bias assessment

Risk of Bias (RoB) assessment was carried out on all included studies by two assessors using ROB 2.0 and ROBINS-I for RCT and comparative observational studies, respectively. Refer to Appendix A for RoB and ROBINS-I rating of included studies. Risk of bias domains are assessed in relation to the effect of assignment to intervention (intention-to-treat effect), as required by the ROBINS-I tool.

Appendix A

Table A1: Risk of Bias assessment for comparative, observational studies using ROBINS-I

Study	Outcome	Confounding	Selection	Intervention classification	Deviations from intervention	Missing data	Measurement of outcomes	Selection of the reported results	Overall bias
van Werkhoven et al, 2024[2] Retrospective cohort study (screening method)	VE against COVID-19-related hospitalisation	Low	Moderate	Low	Low	Moderate	Moderate	Moderate	Moderate
Hansen et al, 2024[3] Prospective cohort study (short-term)	VE against COVID-19-related hospitalisation	Low	Moderate	Low	Low	Low	Low	Low	Moderate
DeCuir et al, 2024[4] Test-negative, case-control design	VE against COVID-19-related hospitalisation	Low	Low	Low	Low	Low	Low	Low	Low
Tartof et al, 2024[5] Test-negative, case-control design	VE against COVID-19-related hospitalisation	Low	Moderate	Low	Low	Low	Low	Low	Moderate
TGA COVID-19 vaccine safety report, June 2023[15]	AESI: myocarditis (with or without pericarditis) occurring within 42 days from vaccination	Low	Moderate	Low	Low	Low	Low	Low	Moderate*

Abbreviations: AE=adverse event; AESI=adverse event of special interest; ROBINS-I=Risk of Bias In Non-randomised Studies - of Interventions; TGA=Therapeutic Goods Administration; VE=vaccine effectiveness.

* The TGA report was rated as moderate risk of bias from the ROBINS-I risk of bias assessment, due to potential risk of bias in the domain of selection as there was no prespecified criteria for the selection. This risk of bias domain for the AESI outcome in the GRADE summary of findings and evidence profile tables was not downgraded as the TGA included nationwide data, and is the largest and most appropriate study to use to evaluate this outcome.

Table A2: Risk of bias assessment for randomised controlled trials using ROB 2.0

Study	Outcome	Domain 1: Risk of bias arising from the randomisation process	Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Domain 3: Missing outcome data	Domain 4: Risk of bias in measurement of the outcome	Domain 5: Risk of bias in selection of the reported result	Overall risk of bias
Munoz et al 2023[6]	Safety	Low	Low	Low	Low	Low	Low
Walter et al 2022[7]	Safety	Low	Low	Low	Low	Low	Low
Anderson et al 2022[8]	Safety	Low	Low	Low	Low	Low	Low
Creech et al 2022[9]	Safety	Low	Low	Low	Low	Low	Low
Frenck et al 2021[10]	Safety	Low	Low	Low	Low	Low	Low
Ali et al 2021[11]	Safety	Low	Low	Low	Low	Low	Low
Polack et al, 2020[12] Thomas et al 2021[13]	Safety	Low	Low	Low	Low	Low	Low
Baden et al, 2021[14] El Sahly et al 2021[15]	Safety	Low	Low	Low	Low	Low	Low
Áñez et al 2023[16]	Safety	Low	Low	Low	Low	Low	Low
Dunkle, 2021[17]	Safety	Low	Low	Low	Low	Low	Low
Heath 2021[18], 2023[19]	Safety	Low	Low	Low	Low	Low	Low

Abbreviations: AE=adverse event; ROBINS-I=Risk of Bias In Non-randomised Studies - of Interventions.

Appendix B: Search Strategy

Vaccine effectiveness

Ovid MEDLINE: COVID-19 mRNA vaccines – outcomes including GP presentation, Hospitalisation, Death and Long COVID (as at 12.01.24)

Database: MEDLINE(R) All including Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946-12 January 2024>

Search Strategy:

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1 exp COVID-19/ (251636)

2 ('2019 nCoV$' or 2019-nCoV$ or 2019nCoV$ or 'n CoV$' or n-CoV$ or nCoV$).tw. (3285)

3 ('covid 19' or covid-19 or covid19).tw. (340520)

4 exp SARS-CoV-2/ (163906)

5 ("Severe Acute Respiratory Syndrome Coronavirus 2" or "Severe Acute Respiratory Syndrome Coronavirus-2" or "SARS coronavirus 2" or "SARS coronavirus-2").tw. (34846)

6 ('SARS CoV2' or SARS-CoV2 or SARSCoV2 or SARS-CoV-2).tw. (117459)

7 1 or 2 or 3 or 4 or 5 or 6 (393288)

8 exp Immunization/ (213178)

9 exp Immunization Programs/ (16205)

10 exp Vaccines/ (283284)

11 (immuni$ or vaccin$).tw. (688952)

12 8 or 9 or 10 or 11 (790781)

13 7 and 12 (69024)

14 exp COVID-19 Vaccines/ (24750)

15 13 or 14 (69302)

16 (Pfizer$ or BioNTech$ or Moderna$).tw. (7507)

17 15 and 16 (3908)

18 exp mRNA Vaccines/ (5357)

Ovid EMBASE: COVID-19 mRNA vaccines – outcomes including GP presentation, Hospitalisation, Death and Long COVID (as at 12.01.24)

Database: Embase <1974 to 2024 January 10>

Search Strategy:

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1 exp coronavirus disease 2019/ (376952)

2 ('2019 nCoV$' or 2019-nCoV$ or 2019nCoV$ or 'n CoV$' or n-CoV$ or nCoV$).tw. (4204)

3 ('covid 19' or covid-19 or covid19).tw. (385826)

4 exp Severe acute respiratory syndrome coronavirus 2/ (107339)

5 ("Severe Acute Respiratory Syndrome Coronavirus 2" or "Severe Acute Respiratory Syndrome Coronavirus-2" or "SARS coronavirus 2" or "SARS coronavirus-2").tw. (35191)

6 ('SARS CoV2' or SARS-CoV2 or SARSCoV2 or SARS-CoV-2).tw. (137124)

7 1 or 2 or 3 or 4 or 5 or 6 (476085)

8 exp immunization/ (383919)

9 exp vaccine/ (422516)

10 (immuni$ or vaccin$).tw. (815430)

11 8 or 9 or 10 (967637)

12 7 and 11 (92572)

13 exp SARS-CoV-2 vaccine/ (43791)

14 12 or 13 (93531)

15 (Pfizer$ or BioNTech$ or Moderna$).tw. (51299)

16 14 and 15 (9113)

17 exp RNA vaccine/ (18585)

18 ((rna or mrna or (messenger adj1 rna)) adj3 vaccin$).tw. (12584)

19 17 or 18 (22987)

19 ((rna or mrna or (messenger adj1 rna)) adj3 vaccin$).tw. (9771)	20 14 and 19 (20145)
20 18 or 19 (11796)	21 exp bnt 162 vaccine/ (318)
21 15 and 20 (9840)	22 (BNT162b2$ or tozinameran$ or comirnaty$).tw. (7893)
22 exp BNT162 Vaccine/ (3726)	23 exp elasomeran/ (6860)
23 (BNT162b2$ or tozinameran$ or comirnaty$).tw. (5072)	24 (mRNA-1273$ or elasomeran$ or spikevax$).tw. (4360)
24 exp 2019-nCoV Vaccine mRNA-1273/ (871)	25 21 or 22 or 23 or 24 (12743)
25 (mRNA-1273$ or elasomeran$ or spikevax$).tw. (1914)	26 16 or 20 or 25 (22409)
26 22 or 23 or 24 or 25 (6357)	27 exp general practice/ (86008)
27 17 or 21 or 26 (12024)	28 exp general practitioner/ (121026)
28 exp General Practice/ (78981)	29 ((general or family) adj3 (practice$ or practitioner$)).tw. (75797)
29 exp General Practitioners/ (10969)	30 exp hospitalization/ (548126)
30 ((general or family) adj3 (practice$ or practitioner$)).tw. (114841)	31 hospital$.tw. (2601504)
31 exp Hospitalization/ (297187)	32 exp hospital emergency service/ (10271)
32 hospital$.tw. (1667542)	33 (emergency adj2 (department$ or room$ or ward$ or attend$ or present$)).tw. (249385)
33 exp Emergency Service, Hospital/ (101176)	34 (urgent adj3 care).tw. (7363)
34 (emergency adj2 (department$ or room$ or ward$ or attend$ or present$)).tw. (157709)	35 exp mortality/ (1405595)
35 (urgent adj3 care).tw. (4607)	36 exp death/ (2046481)
36 exp Mortality/ (425557)	37 (mortalit$ or death$ or fatal$ or case-fatal$ or lethal$ or died).tw. (3193274)
37 exp Death/ (166561)	38 exp long COVID/ (6572)
38 (mortalit$ or death$ or fatal$ or case-fatal$ or lethal$ or died).tw. (2228980)	39 "post COVID-19 syndrome".tw. (600)
39 exp Post-Acute COVID-19 Syndrome/ (2864)	40 "post acute COVID-19 syndrome".tw. (255)
40 "post COVID-19 syndrome".tw. (478)	41 (("post acute" or "post-acute" or postacute) adj2 (COVID$ or "SARS CoV2" or SARS-CoV2 or SARSCoV2 or SARS-CoV-2)).tw. (880)
41 "post acute COVID-19 syndrome".tw. (206)	42 (post-acute adj1 sequelae adj2 (COVID$ or "SARS CoV2" or SARS-CoV2 or SARSCoV2 or SARS-CoV-2)).tw. (745)
42 (("post acute" or "post-acute" or postacute) adj2 (COVID$ or "SARS CoV2" or SARS-CoV2 or SARSCoV2 or SARS-CoV-2)).tw. (678)	43 PASC.tw. (990)
43 (post-acute adj1 sequelae adj2 (COVID$ or "SARS CoV2" or SARS-CoV2 or SARSCoV2 or SARS-CoV-2)).tw. (543)	44 ("long COVID$" or long-COVID$ or longCOVID$).tw. (4775)

44 PASC.tw. (699) 45 ("long COVID$" or long-COVID$ or longCOVID$).tw. (3721) 46 (("long term" or "long-term" or longterm) adj2 (COVID$ or "SARS CoV2" or SARS-CoV2 or SARSCoV2 or SARS-CoV-2)).tw. (482) 47 (("long haul$" or "long-haul$" or longhaul$) adj2 (COVID$ or "SARS CoV2" or SARS-CoV2 or SARSCoV2 or SARS-CoV-2)).tw. (122) 48 ((protract$ or extend$ or sustain$ or persist$ or prolong$ or continu$ or chronic$ or ongoing) adj2 (COVID$ or "SARS CoV2" or SARS-CoV2 or SARSCoV2 or SARS-CoV-2) adj2 (symptom$ or sequela$ or illness$ or syndrome$)).tw. (389) 49 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 (4053226) 50 27 and 49 (2923) 51 limit 50 to yr="2023" (926) 52 remove duplicates from 51 (923)	45 (("long term" or "long-term" or longterm) adj2 (COVID$ or "SARS CoV2" or SARS-CoV2 or SARSCoV2 or SARS-CoV-2)).tw. (577) 46 (("long haul$" or "long-haul$" or longhaul$) adj2 (COVID$ or "SARS CoV2" or SARS-CoV2 or SARSCoV2 or SARS-CoV-2)).tw. (171) 47 ((protract$ or extend$ or sustain$ or persist$ or prolong$ or continu$ or chronic$ or ongoing) adj2 (COVID$ or "SARS CoV2" or SARS-CoV2 or SARSCoV2 or SARS-CoV-2) adj2 (symptom$ or sequela$ or illness$ or syndrome$)).tw. (530) 48 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 (6019652) 49 26 and 48 (7269) 50 limit 49 to yr="2023" (2269) 51 remove duplicates from 50 (2240)
Cochrane Central Register of Controlled Trials Issue 1 of 12, January 2024 (via Wiley): **COVID-19 mRNA vaccines – outcomes including GP presentation, Hospitalisation, Death and Long COVID (as at 12.01.24)** ID Search Hits #1 MeSH descriptor: [COVID-19] explode all trees 5024 #2 (2019 NEXT nCoV OR 2019nCoV OR "n CoV" OR nCoV):ti,ab,kw 403 #3 ("covid 19" OR "covid-19" OR covid19):ti,ab,kw 17989 #4 MeSH descriptor: [SARS-CoV-2] 1 tree(s) exploded 0 #5 ("Severe Acute Respiratory Syndrome Coronavirus 2" OR "Severe Acute Respiratory Syndrome Coronavirus-2" OR "SARS coronavirus 2" OR "SARS coronavirus-2"):ti,ab,kw 2082 #6 ("SARS CoV2" OR "SARS-CoV2" OR SARSCoV2 OR "SARS-CoV-2"):ti,ab,kw 840 #7 #1 OR #2 OR #3 OR #4 OR #5 OR #6 18265 #8 MeSH descriptor: [Immunization] explode all trees 6981 #9 MeSH descriptor: [Immunization Programs] explode all trees 307	

#10	MeSH descriptor: [Vaccines] explode all trees 16164	
#11	(vaccin* OR immunis* OR immuniz*):ti,ab,kw 34224	
#12	#8 OR #9 OR #10 OR #11 34419	
#13	#7 AND #12 2895	
#14	MeSH descriptor: [COVID-19 Vaccines] explode all trees 501	
#15	#13 OR #14 2895	
#16	(Pfizer* OR BioNTech* OR Moderna*):ti,ab,kw 3276	
#17	#15 AND #16 206	
#18	MeSH descriptor: [mRNA Vaccines] explode all trees 122	
#19	((rna OR mrna OR (messenger NEAR/1 rna)) NEAR/3 vaccin*):ti,ab,kw 597	
#20	#18 OR #19 633	
#21	#15 AND #20 475	
#22	MeSH descriptor: [BNT162 Vaccine] explode all trees 83	
#23	(BNT162b2* OR tozinameran* OR comirnaty*):ti,ab,kw 301	
#24	MeSH descriptor: [2019-nCoV Vaccine mRNA-1273] explode all trees 41	
#25	(mRNA-1273* OR elasomeran* OR spikevax*):ti,ab,kw 164	
#26	#22 OR #23 OR #24 OR #25 393	
#27	#17 OR #21 OR #26 665	
#28	MeSH descriptor: [General Practice] explode all trees 3051	
#29	MeSH descriptor: [General Practitioners] explode all trees 498	
#30	((general OR family) NEAR/3 (practice* OR practitioner*)):ti,ab,kw 15722	
#31	MeSH descriptor: [Hospitalization] explode all trees 22793	
#32	hospital*:ti,ab,kw 239043	
#33	MeSH descriptor: [Emergency Service, Hospital] explode all trees 3369	
#34	(emergency NEAR/2 (department* OR room* OR ward* OR attend* OR present*)):ti,ab,kw 16920	
#35	(urgent NEAR/3 care):ti,ab,kw 612	

#36 MeSH descriptor: [Mortality] explode all trees 21899 #37 MeSH descriptor: [Death] explode all trees 8082 #38 (mortalit* OR death* OR fatal* OR case-fatal* OR lethal* OR died):ti,ab,kw 185901 #39 MeSH descriptor: [Post-Acute COVID-19 Syndrome] explode all trees 87 #40 "post COVID-19 syndrome":ti,ab,kw 62 #41 "post acute COVID-19 syndrome":ti,ab,kw 114 #42 (("post acute" OR "post-acute" or postacute) NEAR/2 (COVID* OR "SARS CoV2" OR "SARS-CoV2" OR SARSCoV2 or "SARS-CoV-2")):ti,ab,kw 141 #43 (post-acute NEAR/1 sequelae NEAR/2 (COVID* OR "SARS CoV2" OR SARS-CoV2 OR SARSCoV2 OR SARS-CoV-2)):ti,ab,kw27 #44 PASC:ti,ab,kw 59 #45 ((long NEAR/1 COVID*) OR long-COVID* OR longCOVID*):ti,ab,kw 369 #46 (("long term" OR "long-term" OR longterm) NEAR/2 (COVID* OR "SARS CoV2" OR SARS-CoV2 OR SARSCoV2 OR SARS-CoV-2)):ti,ab,kw 22 #47 ((long NEAR/1 haul*) OR long-haul* OR longhaul*):ti,ab,kw NEAR/2 (COVID* OR "SARS CoV2" OR SARS-CoV2 OR SARSCoV2 OR SARS-CoV-2):ti,ab,kw 14 #48 ((protract* OR extend* OR sustain* OR persist* OR prolong* OR continu* OR chronic* OR ongoing) NEAR/2 (COVID* OR "SARS CoV2" OR SARS-CoV2 OR SARSCoV2 OR SARS-CoV-2) NEAR/2 (symptom* OR sequela* OR illness* OR syndrome*)):ti,ab,kw 49 #49 #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 391969 #50 #27 AND #49 116 #51 #50 with Cochrane Library publication date Between Jan 2023 and Dec 2023 24 DSR – 0 CENTRAL – 24	

Safety

Ovid MEDLINE: COVID-19 mRNA vaccines and myocarditis/pericarditis (as at 17.01.24)	**Ovid EMBASE: COVID-19 mRNA vaccines and myocarditis/pericarditis (as at 17.01.24)**
Database: MEDLINE(R) All including Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946-current>	Database: Embase <1974 to 2024 January 12>
Search Strategy:	Search Strategy:
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1 exp COVID-19/ (251975)	1 exp coronavirus disease 2019/ (378282)
2 ('2019 nCoV$' or 2019-nCoV$ or 2019nCoV$ or 'n CoV$' or n-CoV$ or nCoV$).tw. (3286)	2 ('2019 nCoV$' or 2019-nCoV$ or 2019nCoV$ or 'n CoV$' or n-CoV$ or nCoV$).tw. (4226)
3 ('covid 19' or covid-19 or covid19).tw. (340977)	3 ('covid 19' or covid-19 or covid19).tw. (387325)
4 exp SARS-CoV-2/ (164026)	4 exp Severe acute respiratory syndrome coronavirus 2/ (107712)
5 ("Severe Acute Respiratory Syndrome Coronavirus 2" or "Severe Acute Respiratory Syndrome Coronavirus-2" or "SARS coronavirus 2" or "SARS coronavirus-2").tw. (34892)	5 ("Severe Acute Respiratory Syndrome Coronavirus 2" or "Severe Acute Respiratory Syndrome Coronavirus-2" or "SARS coronavirus 2" or "SARS coronavirus-2").tw. (35286)
6 ('SARS CoV2' or SARS-CoV2 or SARSCoV2 or SARS-CoV-2).tw. (117633)	6 ('SARS CoV2' or SARS-CoV2 or SARSCoV2 or SARS-CoV-2).tw. (137604)
7 1 or 2 or 3 or 4 or 5 or 6 (393829)	7 1 or 2 or 3 or 4 or 5 or 6 (478042)
8 exp Immunization/ (213247)	8 exp immunization/ (384990)
9 exp Immunization Programs/ (16206)	9 exp vaccine/ (423578)
10 exp Vaccines/ (283376)	10 (immuni$ or vaccin$).tw. (817289)
11 (immuni$ or vaccin$).tw. (689388)	11 8 or 9 or 10 (969829)
12 8 or 9 or 10 or 11 (791243)	12 7 and 11 (92999)
13 7 and 12 (69138)	13 exp SARS-CoV-2 vaccine/ (44012)
14 exp COVID-19 Vaccines/ (24780)	14 12 or 13 (93964)
15 13 or 14 (69416)	15 (Pfizer$ or BioNTech$ or Moderna$).tw. (51376)
16 (Pfizer$ or BioNTech$ or Moderna$).tw. (7508)	16 14 and 15 (9173)
17 15 and 16 (3909)	17 exp RNA vaccine/ (18697)
18 exp mRNA Vaccines/ (5361)	18 ((rna or mrna or (messenger adj1 rna)) adj3 vaccin$).tw. (12652)
19 ((rna or mrna or (messenger adj1 rna)) adj3 vaccin$).tw. (9785)	19 17 or 18 (23120)
	20 14 and 19 (20252)

20 18 or 19 (11813) 21 15 and 20 (9857) 22 exp BNT162 Vaccine/ (3728) 23 (BNT162b2$ or tozinameran$ or comirnaty$).tw. (5076) 24 exp 2019-nCoV Vaccine mRNA-1273/ (871) 25 (mRNA-1273$ or elasomeran$ or spikevax$).tw. (1914) 26 22 or 23 or 24 or 25 (6361) 27 17 or 21 or 26 (12042) 28 exp Myocarditis/ (17460) 29 myocardi$.tw. (440133) 30 exp Pericarditis/ (12601) 31 pericardi$.tw. (49021) 32 myopericardi$.tw. (928) 33 28 or 29 or 30 or 31 or 32 (488555) 34 27 and 33 (793)	21 exp bnt 162 vaccine/ (322) 22 (BNT162b2$ or tozinameran$ or comirnaty$).tw. (7942) 23 exp elasomeran/ (6913) 24 (mRNA-1273$ or elasomeran$ or spikevax$).tw. (4387) 25 21 or 22 or 23 or 24 (12824) 26 16 or 20 or 25 (22539) 27 exp myocarditis/ (40755) 28 myocardi$.tw. (621658) 29 exp pericarditis/ (24169) 30 pericardi$.tw. (68236) 31 myopericardi$.tw. (1440) 32 27 or 28 or 29 or 30 or 31 (695443) 33 26 and 32 (1549)
Cochrane Library Central Register of Controlled Trials (CENTRAL) - Issue 1 of 12, January 2024 (via Wiley): COVID-19 mRNA vaccines and myocarditis/pericarditis (as at 17.01.24) ID Search Hits #1 MeSH descriptor: [COVID-19] explode all trees 5024 #2 (2019 NEXT nCoV OR 2019nCoV OR "n CoV" OR nCoV):ti,ab,kw 404 #3 ("covid 19" OR "covid-19" OR covid19):ti,ab,kw 17999 #4 MeSH descriptor: [SARS-CoV-2] 1 tree(s) exploded 0 #5 ("Severe Acute Respiratory Syndrome Coronavirus 2" OR "Severe Acute Respiratory Syndrome Coronavirus-2" OR "SARS coronavirus 2" OR "SARS coronavirus-2"):ti,ab,kw 2082 #6 ("SARS CoV2" OR "SARS-CoV2" OR SARSCoV2 OR "SARS-CoV-2"):ti,ab,kw 840 #7 #1 OR #2 OR #3 OR #4 OR #5 OR #6 18275 #8 MeSH descriptor: [Immunization] explode all trees 6981	

#9	MeSH descriptor: [Immunization Programs] explode all trees	307
#10	MeSH descriptor: [Vaccines] explode all trees	16164
#11	(vaccin* OR immunis* OR immuniz*):ti,ab,kw	34229
#12	#8 OR #9 OR #10 OR #11	34424
#13	#7 AND #12	2896
#14	MeSH descriptor: [COVID-19 Vaccines] explode all trees	501
#15	#13 OR #14	2896
#16	(Pfizer* OR BioNTech* OR Moderna*):ti,ab,kw	3277
#17	#15 AND #16	206
#18	MeSH descriptor: [mRNA Vaccines] explode all trees	122
#19	((rna OR mrna OR (messenger NEAR/1 rna)) NEAR/3 vaccin*):ti,ab,kw	597
#20	#18 OR #19	633
#21	#15 AND #20	475
#22	MeSH descriptor: [BNT162 Vaccine] explode all trees	83
#23	(BNT162b2* OR tozinameran* OR comirnaty*):ti,ab,kw	301
#24	MeSH descriptor: [2019-nCoV Vaccine mRNA-1273] explode all trees	41
#25	(mRNA-1273* OR elasomeran* OR spikevax*):ti,ab,kw	164
#26	#22 OR #23 OR #24 OR #25	393
#27	#17 OR #21 OR #26	665
#28	MeSH descriptor: [Myocarditis] explode all trees	169
#29	myocardi*:ti,ab,kw	52213
#30	MeSH descriptor: [Pericarditis] explode all trees	111
#31	pericardi*:ti,ab,kw	2039
#32	myopericardi*:ti,ab,kw	13
#33	#28 OR #29 OR #30 OR #31 OR #32	53904
#34	#27 AND #33	7

References

Should people aged 6 months and above receive a single dose of the updated formulation COVID-19 vaccine following a previous dose within the last 6–12 months?

1. Austraian Government Department of Health, disability and ageing. TGA adopts Access Consortium guidance for fast-tracking authorisations of modified COVID-19 vaccines for variants. 2021. Available from: https://www.tga.gov.au/news/news-articles/tga-adopts-access-consortium-guidance-fast-tracking-authorisations-modified-covid-19-vaccines-variants? (Accessed 15/03/2024).
2. van Werkhoven CH, Valk A-W, Smagge B, et al. Early COVID-19 vaccine effectiveness of XBB. 1.5 vaccine against hospitalisation and admission to intensive care, the Netherlands, 9 October to 5 December 2023. *Eurosurveillance* 2024;29:2300703. Available from: https://pubmed.ncbi.nlm.nih.gov/38179623/.
3. Hansen CH, Moustsen-Helms IR, Rasmussen M, et al. Short-term effectiveness of the XBB. 1.5 updated COVID-19 vaccine against hospitalisation in Denmark: a national cohort study. *The Lancet Infectious Diseases* 2024;24:e73-e4. Available from: https://pubmed.ncbi.nlm.nih.gov/38190834/.
4. DeCuir J. Interim Effectiveness of Updated 2023–2024 (Monovalent XBB. 1.5) COVID-19 Vaccines Against COVID-19–Associated Emergency Department and Urgent Care Encounters and Hospitalization Among Immunocompetent Adults Aged≥ 18 Years—VISION and IVY Networks, September 2023–January 2024. *MMWR Morbidity and Mortality Weekly Report* 2024;73. Available from: https://www.cdc.gov/mmwr/volumes/73/wr/mm7308a5.htm.
5. Tartof SY, Slezak JM, Frankland TB, et al. BNT162b2 XBB1. 5-adapted vaccine and COVID-19 hospital admissions and ambulatory visits in US adults. *medRxiv* 2023:2023.12. 24.23300512. Available from: https://scholar.google.com/scholar?hl=en&as_sdt=0%2C5&q=BNT162b2+XBB1.5-adapted+Vaccine+and+COVID-19+Hospital+Admissions+and+Ambulatory+Visits+in+US+Adults&btnG=#d=gs_cit&t=1729730775546&u=%2Fscholar%3Fq%3Dinfo%3AoZXw6PPCmvsJ%3Ascholar.google.com%2F%26output%3Dcite%26scirp%3D0%26hl%3Den.
6. Muñoz FM, Sher LD, Sabharwal C, et al. Evaluation of BNT162b2 Covid-19 vaccine in children younger than 5 years of age. *New England Journal of Medicine* 2023;388:621-34. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa2211031.
7. Walter EB, Talaat KR, Sabharwal C, et al. Evaluation of the BNT162b2 Covid-19 vaccine in children 5 to 11 years of age. *New England Journal of Medicine* 2022;386:35-46. Available from: https://pubmed.ncbi.nlm.nih.gov/34752019/.
8. Anderson EJ, Creech CB, Berthaud V, et al. Evaluation of mRNA-1273 vaccine in children 6 months to 5 years of age. *New England Journal of Medicine* 2022;387:1673-87. Available from: https://pubmed.ncbi.nlm.nih.gov/36260859/.
9. Creech CB, Anderson E, Berthaud V, et al. Evaluation of mRNA-1273 Covid-19 vaccine in children 6 to 11 years of age. *New England Journal of Medicine* 2022;386:2011-23. Available from: https://pubmed.ncbi.nlm.nih.gov/35544369/.
10. Frenck Jr RW, Klein NP, Kitchin N, et al. Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. *New England Journal of Medicine* 2021;385:239-50. Available from: https://pubmed.ncbi.nlm.nih.gov/34043894/.
11. Ali K, Berman G, Zhou H, et al. Evaluation of mRNA-1273 SARS-CoV-2 vaccine in adolescents. *New England Journal of Medicine* 2021;385:2241-51. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa2109522.
12. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *New England Journal of Medicine* 2020;383:2603-15. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa2034577.
13. Thomas SJ, Moreira Jr ED, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine through 6 months. *New England Journal of Medicine* 2021;385:1761-73. Available from: https://pubmed.ncbi.nlm.nih.gov/34525277/.
14. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *New England Journal of Medicine* 2021;384:403-16. Available from: https://pubmed.ncbi.nlm.nih.gov/33378609/.
15. El Sahly HM, Baden LR, Essink B, et al. Efficacy of the mRNA-1273 SARS-CoV-2 vaccine at completion of blinded phase. *New England Journal of Medicine* 2021;385:1774-85. Available from: https://pubmed.ncbi.nlm.nih.gov/34551225/.
16. Áñez G, Dunkle LM, Gay CL, et al. Safety, immunogenicity, and efficacy of the NVX-CoV2373 COVID-19 vaccine in adolescents: a randomized clinical trial. *JAMA network open* 2023;6:e239135-e. Available from: https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2804216.
17. Dunkle LM, Kotloff KL, Gay CL, et al. Efficacy and safety of NVX-CoV2373 in adults in the United States and Mexico. *New England Journal of Medicine* 2022;386:531-43. Available from: https://pubmed.ncbi.nlm.nih.gov/34910859/.
18. Heath PT, Galiza EP, Baxter DN, et al. Safety and efficacy of NVX-CoV2373 Covid-19 vaccine. *New England Journal of Medicine* 2021;385:1172-83. Available from: https://pubmed.ncbi.nlm.nih.gov/34910859/.
19. Heath PT, Galiza EP, Baxter DN, et al. Safety and efficacy of the NVX-CoV2373 coronavirus disease 2019 vaccine at completion of the placebo-controlled phase of a randomized controlled trial. *Clinical Infectious Diseases* 2023;76:398-407. Available from: https://pubmed.ncbi.nlm.nih.gov/36210481/.
15. Australian Government Therapeutic Goods Administration. COVID-19 vaccine safety report - 29-06-2023. 2023. Available from: https://www.tga.gov.au/news/covid-19-vaccine-safety-reports/covid-19-vaccine-safety-report-29-06-2023 (Accessed 15/03/2024)