Booster review Dec 22

7 December 2022
Prepared for ATAGI COVID-19 Working Group

s47F

NCIRS
National Centre for Immunisation Research and Surveillance

Outline

- Vaccine coverage update
- Other NITAG bivalent booster recommendations
- Summary of recent VE studies incl BA.4/5
- Supply update

- *For reference:*
  - additional slides detailing VE studies
  - previous VE slides from October booster discussion

Coverage update – 1 Dec 22

		Months since last vaccination as at 01/12/2022			
Current Age	Totals	0 - 2 months	3 - 5 months	6 - 11 months	12+ months
0-4 years	876	491	149	122	114
5-11 years	1,142,231	20,481	66,847	1,054,054	849
12-15 years	1,023,713	5,679	17,974	315,018	685,042
16-19 years	1,120,750	13,634	40,369	479,575	587,172
20-29 years	3,262,997	36,146	108,634	1,657,880	1,460,337
30-39 years	3,619,228	81,974	323,589	1,824,361	1,389,304
40-49 years	3,189,116	88,792	398,088	1,609,181	1,093,055
50-59 years	3,066,466	118,721	702,585	1,484,582	760,578
60-69 years	2,724,877	109,437	773,522	1,438,617	403,301
70-79 years	1,992,386	50,742	398,819	1,379,082	163,743
80-89 years	888,719	21,193	174,923	631,047	61,556
90+ years	206,500	5,774	40,721	143,902	16,103
Total	22,237,859	553,064	3,046,220	12,017,421	6,621,154
Total Cumulative Distribution		2.5%	16.2%	70.2%	100.0%
Total Distribution		2.5%	13.7%	54.0%	29.8%

There has been an increase of approximately 2.8 million individuals who last received a COVID-19 vaccination greater than 12 months ago since the report from data as at the 20th of October.

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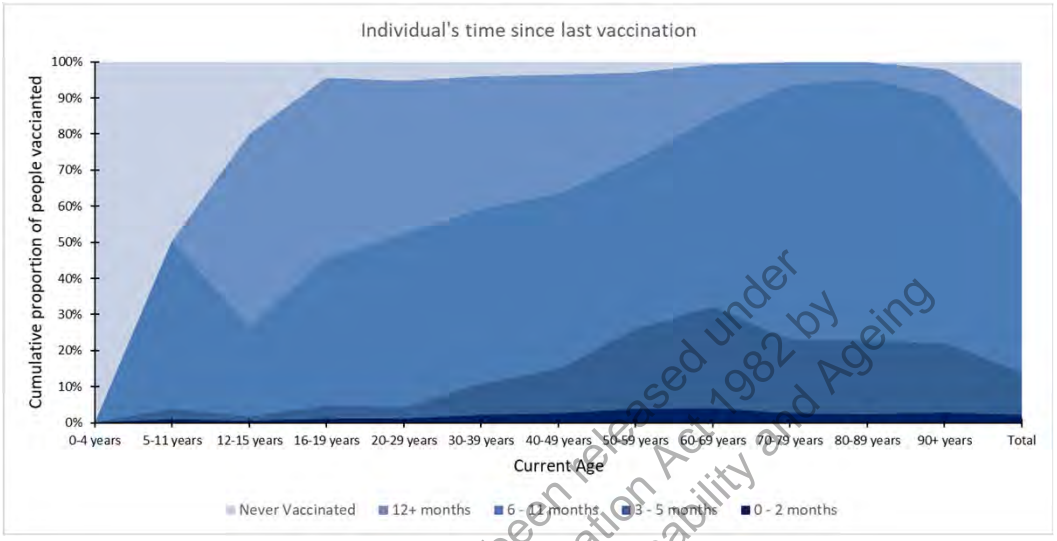
Coverage update - 1 Dec 22



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Coverage update – 1 Dec 22

Current Age	June 2021 ERP Population	Third Dose Eligible Population as of 01/12/2022	Fourth Dose Eligible Population as of 01/12/2022	% Received 1 Dose	% received 2 or more doses	% Eligible received 3 or more doses (16+)	% Eligible received 4 or more doses (30+)	% Total received 3 or more doses (16+)	% Total received 4 or more doses (30+)
0-4 years	1,509,959	N/A	N/A	0.1%	0.0%	N/A	N/A	N/A	N/A
5-11 years	2,269,663	N/A	N/A	50.3%	40.0%	N/A	N/A	N/A	N/A
12-15 years	1,279,387	N/A	N/A	80.0%	75.1%	N/A	N/A	N/A	N/A
16-19 years	1,171,248	1,096,556	N/A	95.7%	93.8%	41.2%	N/A	38.6%	N/A
20-29 years	3,445,415	3,185,440	N/A	94.7%	92.5%	55.0%	N/A	50.9%	N/A
30-39 years	3,767,007	3,549,308	2,189,502	96.1%	94.3%	62.6%	14.5%	59.0%	8.4%
40-49 years	3,304,535	3,148,842	2,237,748	96.5%	95.3%	71.7%	20.2%	68.3%	13.7%
50-59 years	3,162,061	3,035,570	2,396,218	97.0%	96.0%	79.4%	35.1%	76.2%	26.6%
60-69 years	2,745,168	2,696,375	2,341,142	99.3%	98.3%	87.1%	58.1%	85.6%	49.6%
70-79 years	1,953,968	1,977,043	1,830,505	102.0%	101.2%	92.8%	78.2%	93.9%	73.2%
80-89 years	868,712	882,409	828,776	102.3%	101.6%	94.1%	80.4%	95.6%	76.7%
90+ years	210,956	203,482	190,803	97.9%	96.5%	94.2%	79.7%	90.9%	72.1%
Total	25,688,079	19,775,025	12,014,694	86.6%	84.3%	72.3%	43.5%	55.7%	20.3%

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Coverage update – 1 Dec 22

227,566 doses of Moderna Bivalent Omicron BA.1 have been administered in Australia, with 204,020 having been administered as a 3rd or 4th dose.

* Bivalent brands in the final table includes only doses of Moderna Bivalent Omicron BV1 vaccines as a proportion of total doses administered to individuals in the noted vaccination dose.

% of total number of episodes	Dose number	
	3	4
Current Age	Bivalent brand*	Bivalent brand*
0-4 years	0.0%	0.0%
5-11 years	0.0%	0.0%
12-15 years	0.1%	0.4%
16-19 years	0.3%	7.6%
20-29 years	0.3%	8.9%
30-39 years	0.2%	9.2%
40-49 years	0.1%	8.4%
50-59 years	0.1%	6.3%
60-69 years	0.1%	3.3%
70-79 years	0.0%	0.9%
80-89 years	0.0%	0.7%
90+ years	0.0%	0.6%
% of Total Number of Episodes	0.1%	3.5%

Other NITAGs – bivalent booster recommendations

NITAG	Recommendation
UK JCVI	Moderna BA.1 (18+), Pfizer BA.1 (12+) and Pfizer BA.4/5 (12+) approved. Booster dose recommended to existing Autumn booster recommendations (50+, high risk 5+), 3 months after previous dose. Silent on number of previous boosters.
USA ACIP	Moderna BA.4/5 (18+) and Pfizer BA.4/5 (5+) approved. Booster dose recommended for people aged ≥5 years, 2 months after previous dose regardless of number of previous boosters. Monovalent boosters no longer approved.
Canada NACI	Moderna BA.1 and BA.4/5 (18+), Pfizer BA.4/5 (12+) approved. Bivalent booster recommended for ≥65y & high risk ≥12 years, and offered for all 12-64y, 3-6 months after last dose or infection regardless of number of previous boosters
Europe ECDC /EMA	Moderna BA.1 and BA.4/5 (12+), Pfizer BA.1 and BA.4/5 (12+) approved. ECDC and EMA advise that these boosters be directed as a priority to people at risk (60+ and high risk/pregnant) ≥3 months after last dose.
Germany STI KO	Pfizer BA.1 and BA.4/5 recommended for all booster vaccinations in people aged ≥12 years, bivalent preferred over monovalent, 6 months after last dose or infection 1st booster for all ≥12 years, 2nd only for at risk (60+, high risk 12+), 3rd booster for "very old", immunocomp.
Israel MoH	Moderna BA.4/5 (6+) and Pfizer BA.4/5 (5+) approved. Recommended as a booster dose for 65+, high risk, HCW, pregnant. Available for anyone aged ≥12 years, 3 months after previous dose or infection

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Other NITAGs – bivalent booster recommendations (Southern Hemisphere)

NITAG	Recommendation
Chile Ministerio de Salud / CAVEI	Pfizer Bivalent Original+Omicron [strain not specified] approved. Moderna bivalent supply agreement. Chile have moved to an 'Annual COVID-19 Immunisation Program', which began on 7 October 2022 with the bivalent mRNA vaccines preferred. Rollout occurred in order of priority/risk groups and then time since last dose. The only requirement for inclusion will be to have completed the primary series [two initial doses or a single CanSino dose], and to comply with minimum interval requirements [16 weeks/4 months after the primary series, or 24 weeks/6 months since the booster dose].
Argentina Ministerio de Salud / CoNaIn	No bivalent vaccines approved. Booster dose recommended for people aged 18 years and older or 12 years and older who are immunocompromised, 4 months since previous dose regardless of previous doses. This is a strong recommendation for people aged 50 years and older and people with risk factors.
Peru MINSA (bivalent press release)	Pfizer-BioNTech Bivalent Omicron BA.4/BA.5 to be available from January 2023 in Peru. Rollout to begin with priority risk groups, beginning with people aged 60 years and older. Committee of Experts advised the bivalent vaccine could then be administered as a single booster dose annually [advice subject to change]. The second booster is available to people aged: 18 years and older [5 months from previous], 60 years and older [4 months from previous], people with immunocompromise and immunosuppression [5 months from previous], healthcare workers [5 months from previous].
South Africa Department of Health	No bivalent vaccines. First booster available to people aged 18 years and older, 90 days after second dose or 60 days after Janssen dose. Second booster available to people aged 50 years and older [90 days after first booster], people 18 years and older with Janssen first dose [90 days after first booster]. Third booster available to people aged 50 years and older who received Janssen as first dose [120 days after 2nd booster, must be Pfizer].
Brazil Anvisa	Pfizer-BioNTech Bivalent Original/Omicron BA.1 and Pfizer Original/Omicron BA.4/BA.5 approved as booster dose for 12 years and older. No further information.

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Update on vaccine effectiveness

UK HSA – 1 Dec 2022

Bivalent (Original/Omicron BA.1)

Incremental VE against hospitalisation (**autumn booster)**

- Offered to those in clinical risk groups and those aged 50 years and older from September 2022
- Estimated as relative to someone who is ≥6 months post **≥2nd** dose
- ≥14 days post booster VE = 57% (95% C.I.: 48- 65%)

Monovalent vaccines

Incremental 4-dose VE against hospitalisation (**spring booster**)

- Offered to those at risk and those aged 75 years and older
- Estimated relative to 25-39 weeks (~6mo) post a **3rd** dose

Dose	Interval (weeks)	Vaccine effectiveness (95% CI)
3	25 to 39 weeks	Baseline
	40+ weeks	-7.1 (-31.0 to 12.5)
4	0 to 6 days	46.5 (37.7 to 54.2)
	7 to 13 days	45.6 (36.4 to 53.4)
	2 to 4 weeks	58.8 (54.1 to 63.0
	5 to 9 weeks	50.1 (45.6 to 54.2)
	10 to 14 weeks	35.9 (30.2 to 41.1)
	15 to 19 weeks	21.1 (11.6 to 29.5)
	20+ weeks	10.8 (-6.2 to 25.1)

- Incremental bivalent VE is almost equivalent to incremental monovalent 4th dose VE (57% vs 59%) (Yellow boxes)
- Incremental protection from a monovalent 4th dose, relative to 25-39 weeks after a 3rd dose is lost by ~ 20 weeks post dose 4
- No waning data yet for bivalent vaccines

UK HSA - https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1121345/vaccine-surveillance-report-week-48-2022.pdf

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Link-Gelles et al (MMWR – 22 Nov 2022

Study design: Cohort study (n[NAAT tests]=360,626)
Observation period: September 14–November 11, 2022
Results:

- Absolute benefit of **BA.4/5** booster similar regardless of number of prior doses (table 2)
- When stratified by age, number of doses and time since last monovalent dose (table 3):
  - Relative VE was greater the longer it had been since the last dose
  - Relative VE was also higher for those who had received fewer monovalent doses

TABLE 2. Absolute vaccine effectiveness against symptomatic SARS-CoV-2 infection for a single bivalent mRNA COVID-19 booster dose received after 2, 3, or 4 doses of monovalent vaccine compared with no doses, by age group and number of monovalent COVID-19 vaccine doses — Increasing Community Access to Testing program, United States, September–November 2022

	Absolute VE (95% CI), by no. of monovalent doses received before the bivalent vaccine dose			
Age group, yrs	2 doses	3 doses	4 doses*	≥2 doses
18–49	41 (31–49)	43 (39–46)	NA	43 (39–46)
50–64	50 (35–61)	25 (17–33)	28 (20–34)	28 (22–33)
≥65	32 (9–49)	19 (8–29)	23 (15–30)	22 (15–29)

TABLE 3. Relative vaccine effectiveness of a single bivalent mRNA COVID-19 booster dose against symptomatic SARS-CoV-2 infection* received after 2, 3, or 4 monovalent vaccine doses, by age group, number of monovalent COVID-19 vaccine doses received, and interval since last monovalent dose — Increasing Community Access to Testing program, United States, September–November 2022

	Relative VE (95% CI), by no. of monovalent doses received†			
Age group, yrs/mos since receipt of most recent monovalent dose	2 doses	3 doses	4 doses§	≥2 doses
18–49				
2–3	45 (31–56)	24 (14–33)	NA	30 (22–37)
4–5	47 (35–57)	41 (35–47)	NA	43 (38–48)
6–7	42 (30–52)	47 (42–52)	NA	46 (41–50)
≥8	53 (45–60)	58 (56–61)	NA	56 (53–58)
50–64				
2–3	—	15 (−4–31)	33 (24–41)	31 (24–38)
4–5	44 (18–62)	31 (18–42)	36 (29–43)	36 (30–41)
6–7	46 (22–62)	36 (25–45)	40 (32–47)	38 (32–43)
≥8	61 (49–70)	51 (45–55)	NA	48 (45–51)
≥65				
2–3	—	—	32 (23–40)	28 (19–35)
4–5	—	21 (1–36)	36 (29–42)	33 (27–39)
6–7	—	14 (−6–30)	40 (33–46)	36 (29–41)
≥8	45 (27–58)	42 (35–48)	NA	43 (39–46)

Link-Gelles et al - https://www.cdc.gov/mmwr/volumes/71/wr/mm7148e1.htm

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Summary on new VE studies since October update

- 6 new studies reported on waning since the Oct update:
  - **3 and 4 dose waning summary from new studies**
    - UK study showed protection against hospitalisation is well-maintained post dose 3 (~75% at ≥40 weeks); USA study showed waning of 3 doses against hospitalisation after 3 months ~ 39%) (UK HAS; Adams et al)
    - Proportion who have severe outcomes (ICU admission or death) if hospitalised remains higher in unvaccinated > primary only > than primary + 1st/2nd booster (Adams et al)
    - Those with immunocompromising conditions had greatest incidence of severe outcomes (hospitalisation with pneumonia and/or all-cause death) compared to other high-risk groups (aged ≥65 years or high-risk non-immunocompromising conditions) (Kelly et al)
    - Waning from natural infection is slower than for vaccine induced immunity (Chemaitelly et al (b))
    - Studies are citing being unable to estimate VE against severe outcomes due to too few cases in 4 dose and comparator groups (2/3 dose or natural infection) (Canetti et al; Adams et al)

Summary on new VE studies since October update

- **Adolescent waning summary from new studies**
  - Some waning occurs in those with 2 doses + infection. Protection against symptomatic infection in populations with hybrid immunity is well-maintained (Powell et al)
  - Waning in children (aged 5-11 years) occurs more rapidly than for adolescents (aged 12-17 years), likely due to smaller dose (10ug vs 30ug) (Chemaitelly et al (a))
  - Studies are citing being unable to estimate VE against severe outcomes due to too few cases with such outcomes (Powell et al; Chemaitelly et al (a))

Studies on VE are slowing – authors cite slower uptake of vaccines, countries no longer offering free PCR test (UK), fewer people reporting RAT test results, high primary series coverage, fewer cases of severe disease

Supply update

Supply update

Which vaccines will run out?

- *Moderna ancestral will no longer be available from 5 January. Currently only available in very small amounts.*
- *AstraZeneca will no longer be available from the end of March.*
- *Moderna BA.1 bivalent will currently not be available from May however this is subject to Government decision on a new agreement.*

Any supply issues with BA.1 bivalent?

- *Moderna BA.1 bivalent will currently not be available from May however this is subject to Government decision on a new agreement.*
- *No supply issues for Pfizer BA.1 bivalent.*

Anticipated supply issues with BA.4/5?

- *No known supply issues, currently expected to arrive late Q1 and Pfizer supply agreement is flexible enough that we should be able to switch from BA.1 to BA.4/5 once it is available.*

Additional slides – detailed slides on VE studies

3 and 4 dose VE waning

UK HSA – 1 Dec 2022

Monovalent vaccines

Absolute VE against hospitalisation

- Protection against hospitalisation in those aged over 65 is well-maintained at 40 weeks in those who have had 2 or 3 doses

Over 65		At least 2 days stay with a respiratory code in primary diagnosis field	At least 2 days stay with either oxygen, ventilation or ICU and a respiratory code in primary diagnosis field
	Interval (weeks)	VE	VE
Dose 1	4+	47.1 (38.9 to 54.1)	52.6 (25.2 to 69.9)
Dose 2	2 to 14	80.2 (72.9 to 85.6)	86.1 (64.5 to 94.5)
	15 to 24	54.5 (41.1 to 64.8)	83.0 (63.7 to 92.1)
	25 to 39	50.5 (44.7 to 55.8)	60.0 (44.2 to 71.4)
	40+	53.7 (49.1 to 57.9)	65.0 (52.5 to 74.2)
Booster	2 to 4	89.5 (87.8 to 91.0)	92.4 (88.1 to 95.2)
	5 to 9	86.4 (85 to 87.6)	89.0 (85.5 to 91.7)
	10 to 14	83.0 (81.5 to 84.3)	87.0 (83.4 to 89.8)
	15 to 19	78.4 (76.6 to 80.1)	79.1 (73.3 to 83.7)
	20 to 24	71.4 (68.9 to 73.6)	73.0 (65.2 to 79.1)
	25 to 39	63.1 (60.1 to 66.0)	66.8 (57.2 to 74.3)
	40+	60.7 (53.7 to 66.6)	75.4 (47.7 to 88.4)

UK HSA - https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1121345/vaccine-surveillance-report-week-48-2022.pdf

Canetti et al (NEJM – 1 Dec 2022) – Israel, Waning of 4 dose VE against infection in HCWs

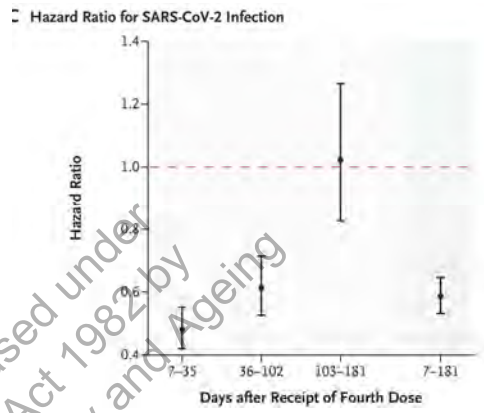
Study design: Prospective cohort study (n = 11,176), excluding people with previous infection

Observation period: Not available – Omicron period

Outcomes: Relative VE – 4 dose to 3 dose from hazard ratios for SARS-CoV-2 infection adjusting for age, sex, and professional role; calendar time was used as the time scale to account for differences in the prevalence of infection over time

Results: Relative VE against infection

- 52% (95% CI, 45 to 58) 1-5 weeks post dose 4
- −2% (95% CI, −27 to 17) 15 to 26 weeks (~6mo) post dose 4
- Unable to estimate VE against severe outcomes as no cases of severe outcomes occurred



Canetti et al - https://www.nejm.org/doi/full/10.1056/NEJMc2211283?query=featured_coronavirus

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Adams et al (BMJ – 11 Oct) – USA, primary series and booster VE doses against hospitalisations

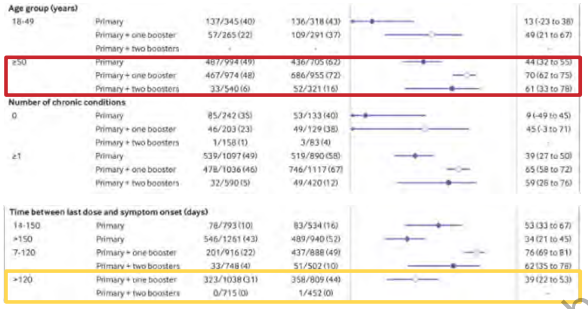
Study design: IVY Network – TNCC

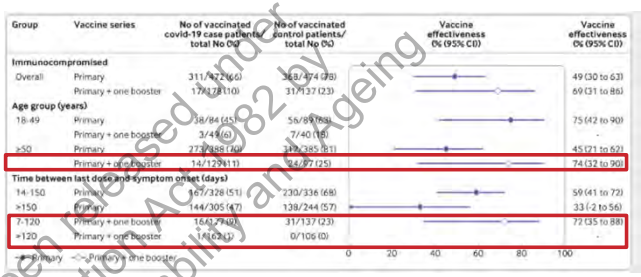
Observation period: 26 December 2021 to 30 June 2022

Outcomes: VE against hospitalisation based on adjusted odds ratio

Results: VE against hospitalisation

- VE against hospitalisation wanes post dose 3
- Unable to estimate waning of 4 dose VE
- No estimates of 2nd booster (i.e. 5th dose) in people with immunocompromise
- Of those who were hospitalized those who were unvaccinated had poorer outcomes (ICU admission and/or death) compared to those who had primary series. Those who had a first or second booster had fewer severe outcomes again.





5th Dose VE for IC patients was not able to estimated as no patients took up this dose

Adams et al - https://www.bmj.com/content/379/bmj-2022-072065

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Kelly et al (JAMA – 11 Oct 2022) – USA, Incidence of hospitalisation post 3 doses in VHA facility residents

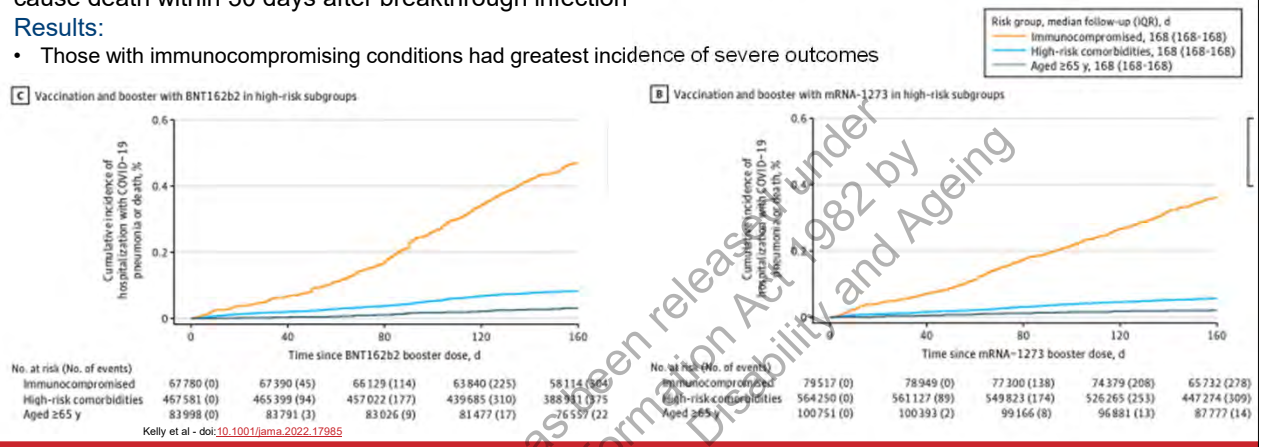
Study design: retrospective cohort study of adults receiving care at VHA facilities, median age 71 years, 93% participants were classified as high-risk populations (70% were high-risk non-immunocompromising co-morbid conditions)

Observation period: 24 week follow-up until 30 May 2022

Outcomes: symptomatic infection, hospitalisation with any diagnosis of COVID-19 pneumonia and/or all-cause death within 30 days after breakthrough infection

Results:

- Those with immunocompromising conditions had greatest incidence of severe outcomes



Kelly et al - doi:10.1001/jama.2022.17985

Waning of VE in adolescents

Powell et al (The Lancet – 24 Nov 2022) – England, 1,2 & 3 dose and natural infection/hybrid immunity against symptomatic infection in adolescents aged 12-17 years

Study design: TNCC (n = 1,161,704 SARS-CoV-2 PCR tests);
Observation period: 9 Aug 2021 to **31 March 2022**
Outcomes:

- VE and hybrid immunity against WT, Alpha, Delta and Omicron symptomatic infection

Results: VE against BA.1/BA.2

- Those *without previous* hx of infection have *greater waning*
- Those with *hybrid immunity* have *greater protection* than those without hx of infection
- Some waning occurs in those with 2 doses + infection, but protection is well-maintained

	No previous infection	Previous wildtype infection before vaccination	Previous alpha infection before vaccination	Previous delta infection before vaccination	Previous omicron infection before vaccination	Previous delta infection after vaccination	Previous omicron infection after vaccination
Unvaccinated	..	32·7% (27·7 to 37·4)	36·6% (32·9 to 40·1)	52·4% (50·9 to 53·8)	59·3% (46·7 to 69·0)	52·4% (50·9 to 53·8)	59·3% (46·7 to 69·0)
Dose one, Pfizer							
0–1 week	15·2% (9·9 to 20·1)	69·2% (55·9 to 78·5)	77·6% (69·5 to 83·6)	79·3% (76·7 to 81·6)	..	..	..
2–14 weeks	18·8% (17·2 to 20·3)	85·3% (83·7 to 86·8)	81·5% (80·0 to 82·9)	78·8% (77·9 to 79·5)	79·6% (44·9 to 92·4)	51·2% (28·4 to 66·8)	..
15–24 weeks	17·9% (14·9 to 20·7)	73·4% (67·2 to 78·4)	69·5% (64·5 to 73·8)	67·2% (63·7 to 70·3)	..	65·9% (60·5 to 70·6)	85·5% (77·5 to 90·6)
25–39 weeks	12·8% (−1·6 to 25·1)	67·8% (24·1 to 86·3)	66·7% (35·2 to 82·9)	55·8% (17·2 to 76·4)	..	77·2% (67·5 to 84)	90·2% (75·9 to 96·0)
≥40 weeks	14·7% (−19·9 to 55·4)	..	..	..	..	..	..
Dose two, Pfizer							
0–1 week	52·2% (50·4 to 53·9)	87·4% (83·5 to 90·4)	84·9% (81·3 to 87·8)	82·1% (80·1 to 83·9)	..	86·1% (82·3 to 89·1)	95·5% (85·3 to 98·6)
2–14 weeks	64·5% (63·6 to 65·4)	84·7% (82·6 to 86·5)	85·5% (84·0 to 86·9)	83·5% (82·5 to 84·5)	..	86·5% (85·1 to 87·8)	91·2% (80·0 to 96·1)
15–24 weeks	29·8% (24·9 to 34·2)	53·4% (32·7 to 67·7)	64·3% (52·4 to 73·3)	75·5% (65·6 to 82·5)	..	65·9% (55·2 to 74·1)	96·4% (84·4 to 99·1)
25–39 weeks	19·4% (11·7 to 26·4)	28·9% (−15·5 to 56·3)	63·6% (46·0 to 75·5)	..	..	76·1% (65·3 to 83·6)	..
≥40 weeks	25·7% (−4·2 to 47·0)	..	..	..	..	..	..
Booster dose, any mRNA vaccine							
0–1 week	55·1% (50·7 to 59·1)	77·7% (55·7 to 88·8)	82·2% (68·1 to 90·1)	89·5% (81·7 to 94·0)	..	87·0% (78·8 to 92·0)	..
2–14 weeks	62·9% (60·5 to 65·1)	79·8% (70·4 to 86·3)	79·6% (71·4 to 85·5)	80·7% (71·1 to 87·1)	..	90·1% (86·6 to 92·7)	..
15–24 weeks	33·6% (14·6 to 48·3)	..	..	..	..	..	..

Data are point estimate (95% CI).

Table 4: **Protection from combinations of vaccination and previous infection with wildtype, alpha, delta, and omicron BA.1 and BA.2 variants of SARS-CoV-2 against omicron BA.1 and BA.2 variant infection by time since vaccination**

adjusted for in logistic regression models for age, sex, index of multiple deprivation quintile, ethnic group, geographical region (National Health Service region), period (calendar week of test), clinical risk group status (a separate flag for those aged 16 years or older and younger than 16 years), and clinically extremely vulnerable (if aged 16 years or older)

Powell et al - https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00729-0/fulltext

ATAGI COVID-19 WG

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s47B(a)

Chemaitelly et al (a) (The Lancet – 17 Nov 2022) – Qatar, VE against infection in children and adolescents (aged 5-17 years)

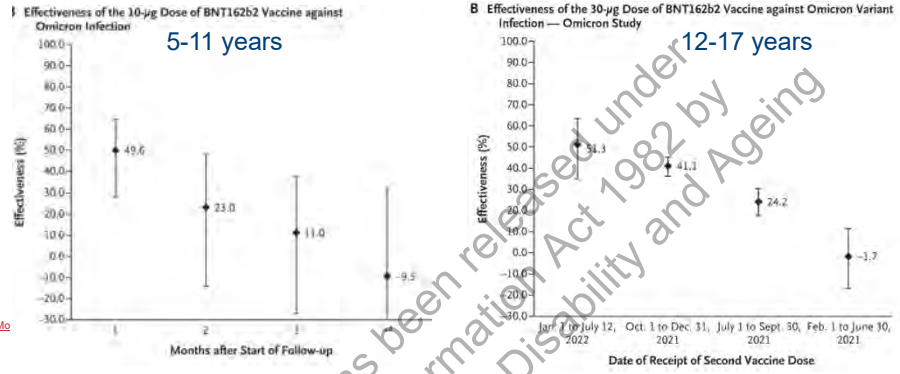
Study design: Three matched, retrospective cohort studies emulating randomized target trials; ≥80% had no co-morbidities

Observation period: 1 February 2021 to 12 July 2022

Outcomes: Hazard ratio against infection and severe disease; VE = (1-HR)*100

Results:

- More rapid waning against infection in children aged 5-11 years compared to adolescents aged 12-17 years
- Too few severe, critical, or fatal cases of Covid-19 were observed for us to estimate the vaccine effectiveness against severe Covid-19 – only 2 cases in unvaccinated group progressed to severe or critical COVID-19



Chemaitelly et al - https://www.nejm.org/doi/full/10.1056/NEJMoa2210058?query=featured_coronavirus

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Natural infection vs Vaccination

Chemaitelly et al (b) (The Lancet – 1 Dec 2022) – Qatar, Natural infection vs mRNA vaccine against re-infection/infection and severe COVID-19

Study design: two matched retrospective cohort studies (n[matched-pairs]=434,097); 9% of Qatar's population is aged over 50 years (92% of study population were aged under 50 years; ≥80% of study participants had no-comorbidities

Observation period: 28 Feb 2020 to 12 May 2022

Outcomes: Hazard ratio

- VE against SARS-CoV-2 infection (PCR or RAT)
- VE against severe, critical, or fatal COVID-19
- Sensitivity analyses for age (≥50 years and sex)

Results:

- Natural infection protection against re-infection is greater than vaccine protection against infection**
- Waning against infection is faster for vaccine protection compared to natural infection
- For severe outcomes – only small numbers for those who had natural infection and those who were vaccinated, so unable to draw clear conclusions

	Natural infection versus BNT162b2 vaccination study		Natural infection versus mRNA-1273 vaccination study	
	Natural infection cohort	BNT162b2-vaccinated cohort	Natural infection cohort	mRNA-1273-vaccinated cohort
Total follow-up, person-weeks	1 985 243	1 921 539	1 374 220	1 338 649
Incidence rate of infection, per 10 000 person-weeks	18·1 (17·5–18·7)	37·1 (36·2–37·9)	16·7 (16·1–17·4)	32·0 (31·0–33·0)
Unadjusted HR for SARS-CoV-2 infection	0·48 (0·46–0·50)	1 (ref)	0·51 (0·49–0·54)	1 (ref)
Adjusted HR for SARS-CoV-2 infection*	0·47 (0·45–0·48)	1 (ref)	0·51 (0·49–0·54)	1 (ref)
Unadjusted HR for severe, critical, or fatal COVID-19†	0·25 (0·08–0·77)	1 (ref)	0·27 (0·06–1·32)	1 (ref)
Adjusted HR for severe, critical, or fatal COVID-19*†	0·24 (0·08–0·72)	1 (ref)	0·24 (0·05–1·19)	1 (ref)

95% CIs for HRs and incidence rate are shown in parentheses. HR=hazard ratio. *Cox regression analysis adjusted for sex, 10-year age group, ten nationality groups, comorbidity count (table 1), and timing of primary infection or first-dose vaccination. †Severe, critical, and fatal COVID-19 cases were defined according to WHO guidelines.[10,11]

Table 2: HRs for the incidence of SARS-CoV-2 infection and severe, critical, and fatal COVID-19

**Population of Qatar is not generalizable to an Australian context, however study provides evidence that natural infection is an additional immunizing event that provides protection from severe outcomes and may reduce rate of waning

Chemaitelly et al - https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(22)00287-7/fulltext

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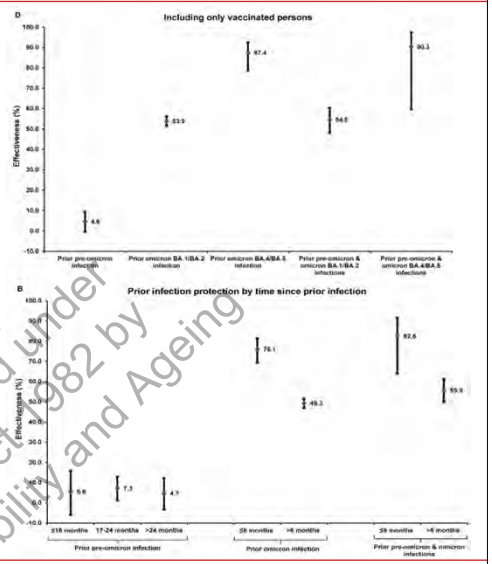
s47B(a)

Additional slides - VE data previously presented for Oct Booster discussion

Protection from past infection

Chemaitelly et al (Pre-print MedRxiv): Protection against reinfection with SARS-CoV-2 omicron BA.2.75* sublineage

- BA.2.75* (predominantly BA.2.75.2) became the dominant sublineage in Qatar by Sept 10, 2022
- A test-negative, case-control study design evaluated protection against BA.2.75 from prior COVID variant infections
- Pre-omicron infections showed no protection against subsqunent BA.2.75 in vaccinated individuals (4.6% [95%CI: -0.5; 9.5]) and minor protection in unvaccinated individuals (12.3% [95% CI 1.7; 21.7])
- Protection from prior BA.4/5 infection (87.4% [95% CI: 78.7 92.5]) was greater than prior BA.1/2 (53.9% [95% CI: 51.5 to 56.3]) infection against BA.2.75 but additional pre-omicron infections showed no further benefit
- Protection from prior infection waned after 6 months for previous omicron variants



https://www.medrxiv.org/content/10.1101/2022.10.29.22281606v1.full.pdf

Hansen et al (The Lancet): Risk of Reinfection, Vaccine Protection, and Severity of Infection with the BA.5 Omicron Subvariant: A Danish Nation-Wide Population-Based Study (18 October 2022)

- Danish adults (≥18 years old) with COVID-19 RT-PCR results from 10 April 2022 to 30 June, 2022
- Previous COVID-19 infections increased relative protection against both BA.5 and BA.2 in vaccinated individuals
- Prior omicron infection produced greater relative protection against reinfection than delta or alpha infection
- Prior omicron infections also protected against hospitalisation due to reinfections
  - Hospitalisation from BA.5 infection: 96.4% (95%CI: 74.2; 99.5)
  - Hospitalisation from BA.2 infection: 91.2% (95%CI: 76.3; 96.7)

Relative protection in triple vaccinated (mRNA vaccines) individuals and previous COVID-19 infection

	Cases	Controls	OR	Adjusted OR*	Estimated protection
Protection against infection with BA.5					
Previous omicron infection					
Exposed	210 (2·4%)	33 972 (19·0%)	0·106 (0·092–0·121)	0·073 (0·063–0·084)	92·7% (91·6–93·7)
Unexposed	8468 (97·6%)	144 697 (81·0%)	1	1	..
Previous delta infection					
Exposed	65 (0·8%)	3336 (2·3%)	0·333 (0·261–0·427)	0·266 (0·207–0·343)	73·4% (65·7–79·3)
Unexposed	8468 (99·2%)	144 697 (97·7%)	1	1	..
Previous alpha infection					
Exposed	58 (0·7%)	1878 (1·3%)	0·528 (0·406–0·686)	0·388 (0·296–0·509)	61·2% (49·1–70·4)
Unexposed	8468 (99·3%)	144 697 (98·7%)	1	1	..
Protection against infection with BA.2					
Previous omicron infection					
Exposed	192 (0·7%)	33 972 (19·0%)	0·028 (0·024–0·032)	0·029 (0·025–0·034)	97·1 (96·6–97·5)
Unexposed	29 100 (99·3%)	144 697 (81·0%)	1	1	..
Previous delta infection					
Exposed	100 (0·3%)	3336 (2·3%)	0·149 (0·122–0·182)	0·158 (0·129–0·193)	84·2 (80·7–87·1)
Unexposed	29 100 (99·7%)	144 697 (97·7%)	1		..
Previous alpha infection					
Exposed	98 (0·3%)	1878 (1·3%)	0·259 (0·212–0·318)	0·262 (0·214–0·322)	73·8 (67·8–78·6)
Unexposed	29 100 (99·7%)	144 697 (98·7%)	1	1	..

Hansen et. Al. - https://www.thelancet.com/action/showPdf?pii=S1473-3099%2822%2900595-3

Waning of dose 3 and 4 vaccine effectiveness against hospitalisation and death

Waning of vaccine effectiveness following a 2nd booster dose

- 1st and 2nd booster (dose 3 & 4) provide an initial boost in protection against all outcomes – likely similar for 5th dose but no VE data yet

- Early evidence that a 2nd booster (dose 4) VE:
  - vs hospitalisation for >60 years **may** start to wane by 4 months
  - vs death for >80 **may** start to wane by 3-5 months
- Little dose 4 data on other at-risk groups

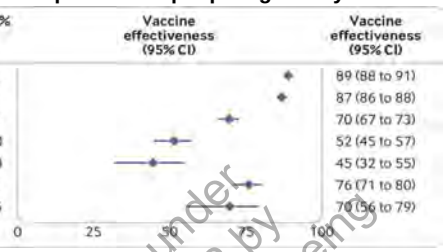
- Dose 2 vs severe illness (hospitalisation or death) is maintained for at least 6-8 months in adults 40 years or younger
- Some studies show a large initial increase in protection against severe illness from dose 3 that wanes
  - Follow-up beyond 6 months demonstrates a sustained incremental improvement until at least 9 months

- Absolute rates of hospitalisation and death are incrementally smaller with each subsequent dose

3 Oct 2022: Ferdinands et al (BMJ) – USA-Vision, VE vs hospitalisation

Absolute vaccine effectiveness (%) against covid-19-associated hospital admissions by time since vaccination and age group, restricted to omicron period and people aged 65 years or

Vaccination status	No	Covid-like illness controls (col %)	Covid-19 cases (col %)	Row %	Vaccine effectiveness (95% CI)	Vaccine effectiveness (95% CI)
3-dose vaccinated <2 months	3514	3225 (6.5)	289 (2.8)	8.2		89 (88 to 91)
3-dose vaccinated 2 to <4 months	9000	8304 (16.7)	696 (6.8)	7.7		87 (86 to 88)
3-dose vaccinated 4 to <6 months	9290	8652 (17.4)	638 (6.2)	6.9		70 (67 to 73)
3-dose vaccinated 6 to <8 months	4969	4473 (9.0)	496 (4.8)	10.0		52 (45 to 57)
3-dose vaccinated ≥8 months	881	749 (1.5)	132 (1.3)	15.0		45 (32 to 55)
4-dose vaccinated <2 months	1927	1780 (3.6)	147 (1.4)	7.6		76 (71 to 80)
4-dose vaccinated 2 to <4 months	323	286 (0.6)	37 (0.4)	11.5		70 (56 to 79)



col% - column percentage. Unvaccinated people >65 years accounted for 46% of admissions, and people >65 with 1-2 doses accounted for 30% of admissions

- Test-negative case control (PCR only), December 2021 to August 2022
- Absolute VE vs hospitalisation of 70% [56-79%] between 2 and 4 months post dose 4
- Sub-analysis of people with likely IC, but for post dose 3 and 7 days post dose 4, no data for post dose 5

https://www.bmj.com/content/379/bmj-2022-072141 Page 33

13 July 2022: Nordstrom et al (Lancet Region Health) – Swiss national database, VE vs all-cause death >80 years

- Relative VE vs **all-cause** death 71% [69-72%] during the first 3 months
- Falls to 54% [48-60%] between 3 and 5 months

- Indicates VE vs death from COVID may start waning by 5 months
- Confounded by relationship between vaccine-seeking behaviour and death

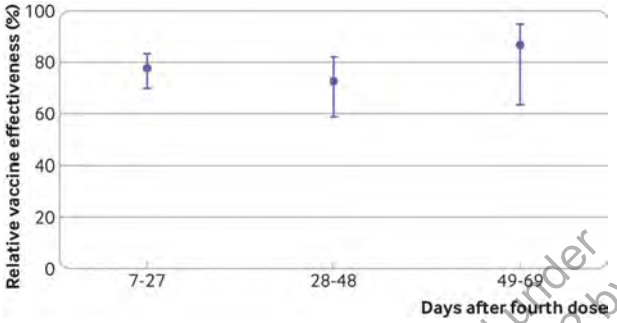
- Did an analysis of LTCF residents, however:
  - results not statistically significant
  - Population already at increased risk of non-COVID death (i.e. already a lower proportion of all-cause deaths to prevent from COVID, which decreased the VE estimate markedly)

	Fourth-dose group		Third-dose group		Relative vaccine effectiveness (95% CI)	
	Deaths	Deaths/100,000 person-days	Deaths	Deaths/100,000 person-days	Adjusted for age and baseline date	Fully adjusted*
7-60 days, total cohort (*N* = 365,249)	2040	17·4	2659	45·3	64 (62-66)	71 (69-72)
Men (*N* = 151,823)	887	17·9	1195	50·5	67 (65-70)	71 (69-74)
Women (*N* = 213,426)	1153	17·0	1464	41·8	62 (59-65)	70 (68-72)
Age >85 years (*N* = 186,451)	1520	25·2	1957	66·4	64 (62-67)	71 (69-73)
Age ≤85 years (*N* = 178,798)	520	9·1	702	24·0	65 (61-69)	70 (67-74)
>4 months since vaccination in the third-dose group (*N* = 134,831)	859	18·5	1353	80·6	78 (77-80)	79 (77-81)
≤4 months since vaccination in the third-dose group (*N* = 230,418)	1181	16·6	1306	31·2	50 (46-54)	61 (58-64)
>4 months since vaccination in the fourth-dose group (*N* = 308,446)	1815	18·3	2298	46·3	63 (61-66)	71 (69-72)
61-143 days, total remaining cohort (*N* = 243,880)	757	4·8	297	7·8	46 (38-53)	54 (48-60)

***Table 4*: Relative vaccine effectiveness of the fourth dose against all-cause mortality in individuals aged 80 years and older by number of days after the fourth dose, and according to sex, age, and time passed since vaccination.**
CI=confidence interval.
* Adjusted for age, baseline date, sex, born in Sweden, and residence in long-term care facility.

https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(22)00162-4/fulltext Page 34

Gazit et al (BMJ – 24/5/22) – Israel, 4th dose VE against hospitalisation or death in those aged ≥60 years



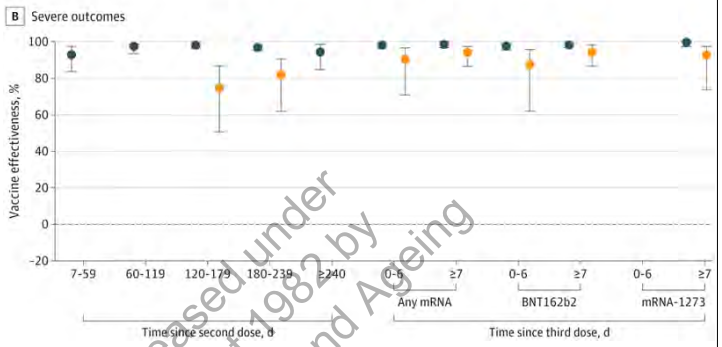
- TNCC (PCR only), health district database, 69,623 participants had received 3 doses (19,211 with at least 1 positive test) and 27,876 participants had received 4 doses (11,520 with at least 1 positive test)
- Short follow-up time of 2-month (10 weeks): 10 January to 13 March, 2022
- Results:
  - *Relative VE of a fourth dose against severe covid-19 was maintained at a high level (>72%)*
  - *Hospitalisation (including death): 331 in 3-dose cohort, 163 in 4-dose cohort (<1% of study population)*
  - *Deaths: 77 in 3-dose cohort, 23 in 4-dose cohort, over two months (<0.15% of study population)*

22-Sept: Buchan et al (JAMA) – Ontario, Canada, mRNA 2 and 3 dose VE Against Omicron or Delta Symptomatic Infection and Severe Outcomes

Study design: TNCC; N = 134,435 aged ≥18 years;
mean age 36-43 years
Vaccine: mRNA and ChAdOx1 (primary only)
Obs period: 6 to 25 December 2021
Outcomes: Absolute VE from adjusted odds ratio for severe outcomes (hospitalisation or death) associated with infection

Results:

- Long term 2-dose VE maintains protection against severe outcomes
- 3rd dose provides some additional protection against severe disease



Buchan et al - doi:10.1001/jamanetworkopen.2022.32760

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23-Sept: Ridgway et al (JAMA) – USA, Relative 3 vs 2 Doses of mRNA COVID-19 Vaccine by Time Since Booster Dose against Hospitalisation

Study design: Multi-centre case-control study; N(cases) = 3062, N(controls) =12,248; **mean age ~70 years**; 4% prior infection; median time from D2 to hospitalisation 305 days, median time from D3 to hospitalisation 231-235 days

Vaccine: mRNA

Obs period: 1 October 2021 to 26 July 2022

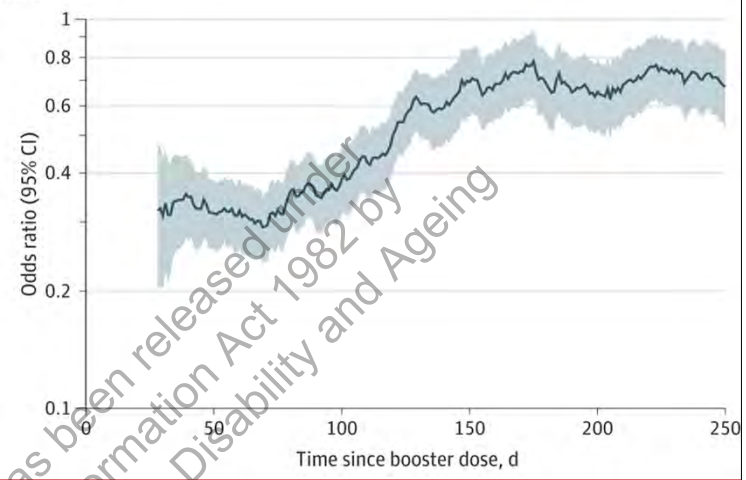
Outcomes: Relative 3 dose vs 2 dose VE against hospitalisation

Results:

- Overall VE = 59% (54 to 63)
- By time since booster:
  - <50 days = 76%
  - 50-100 days = 76%
  - ≥150 days 28 %

Ridgeway et al - doi:10.1001/jama.2022.17811

Figure. Odds of Hospitalization for COVID-19 After 3 vs 2 Doses of mRNA COVID-19 Vaccine by Time Since Booster Dose



Other relevant VE studies

Ferdinands et al (BMJ - 3 Oct 2022) – USA, 3 and 4 dose VE against hospitalisation

Study design: TNCC (Vision Network); immunocompetent adults >18 years; N= 259,006; median age 69 years; 23% had an immunocompromising condition

Vaccine: monovalent mRNA vaccines

Obs period: 17 January 2021 to 12 July 2022

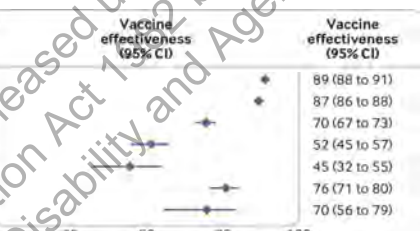
Outcomes: Absolute 3 and 4 dose VE against hospitalisation; VE = (1-OR)*100

Results:

- Absolute VE against hospitalisation 2-4 months post D4 for people aged ≥65 years = 70% (56-79%)
- Unvaccinated people aged>65 years accounted for 46% of admissions and <2% for 4 doses
- People >65 with 1-2 doses accounted for 30% of admissions
- Absolute VE against hospitalisation in younger age groups post dose 2 and 3 were not significantly different to those aged ≥65 years

Table 1: Absolute vaccine effectiveness (%) against covid-19-associated hospital admissions by time since vaccination and age group, restricted to omicron period and people aged ≥65

Vaccination status	No	Covid-like illness controls (col %)	Covid-19 cases (col %)	Row %	Vaccine effectiveness (95% CI)
3-dose vaccinated <2 months	3514	3225 (6.5)	289 (2.8)	8.2	89 (88 to 91)
3-dose vaccinated 2 to <4 months	9000	8304 (16.7)	696 (6.8)	7.7	87 (86 to 88)
3-dose vaccinated 4 to <6 months	9290	8652 (17.4)	638 (6.2)	6.9	70 (67 to 73)
3-dose vaccinated 6 to <8 months	4969	4473 (9.0)	496 (4.8)	10.0	52 (45 to 57)
3-dose vaccinated ≥8 months	881	749 (1.5)	132 (1.3)	15.0	45 (32 to 55)
4-dose vaccinated <2 months	1927	1780 (3.6)	147 (1.4)	7.6	76 (71 to 80)
4-dose vaccinated 2 to <4 months	323	286 (0.6)	37 (0.4)	11.5	70 (56 to 79)



Ferdinands et al: https://www.bmj.com/content/379/bmj-2022-072141

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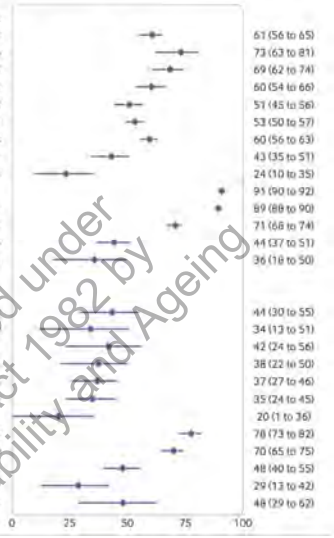
3 Oct 2022: Ferdinands et al (BMJ) – USA-Vision, VE vs hospitalisation

Vaccine effectiveness (%) against covid-19-associated hospital admissions by time since vaccination and immunocompromise status, restricted to omicron period.

Vaccination status	No	Covid-like illness controls (Col %)	Covid-19 cases (Col %)	Row %	Vaccine effectiveness (95% CI)
No likely immunocompromising condition					
Unvaccinated	25215	17 350 (29.3)	7865 (57.3)	31.2	
Partially vaccinated	2583	2202 (3.7)	381 (2.8)	14.8	61 (56 to 65)
2-dose vaccinated <2 months	324	280 (0.5)	44 (0.3)	13.6	73 (63 to 81)
2-dose vaccinated 2 to <4 months	869	724 (1.2)	145 (1.1)	16.7	69 (62 to 74)
2-dose vaccinated 4 to <6 months	1315	1063 (1.8)	252 (1.8)	19.2	60 (54 to 66)
2-dose vaccinated 6 to <8 months	2012	1555 (2.6)	457 (3.3)	22.7	51 (45 to 56)
2-dose vaccinated 8 to <10 months	4378	3179 (5.4)	1199 (8.7)	27.4	53 (50 to 57)
2-dose vaccinated 10 to <12 months	4771	3849 (6.5)	922 (6.7)	19.3	60 (56 to 63)
2-dose vaccinated 12 to <14 months	3076	2812 (4.8)	264 (1.9)	8.6	43 (35 to 51)
2-dose vaccinated ≥14 months	1654	1430 (2.4)	224 (1.6)	13.5	24 (10 to 35)
3-dose vaccinated <2 months	4164	3837 (6.5)	327 (2.4)	7.9	91 (90 to 92)
3-dose vaccinated 2 to <4 months	9089	8499 (14.4)	590 (4.3)	6.5	89 (88 to 90)
3-dose vaccinated 4 to <6 months	8644	8130 (13.7)	514 (3.7)	5.9	71 (68 to 74)
3-dose vaccinated 6 to <8 months	4187	3742 (6.3)	445 (3.2)	10.6	44 (37 to 51)
3-dose vaccinated ≥8 months	624	530 (0.9)	94 (0.7)	15.1	36 (18 to 50)
Any likely immunocompromising condition					
Unvaccinated	5830	4482 (22.3)	1348 (37.6)	23.1	
Partially vaccinated	812	688 (3.4)	124 (3.5)	15.3	44 (30 to 55)
2-dose vaccinated <4 months	377	298 (1.5)	79 (2.2)	21.0	34 (13 to 51)
2-dose vaccinated 4 to <6 months	453	371 (1.8)	82 (2.3)	18.1	42 (24 to 56)
2-dose vaccinated 6 to <8 months	679	554 (2.8)	125 (3.5)	18.4	38 (22 to 50)
2-dose vaccinated 8 to <10 months	1437	1098 (5.5)	339 (9.5)	23.6	37 (27 to 46)
2-dose vaccinated 10 to <12 months	1630	1339 (6.7)	291 (8.1)	17.9	35 (24 to 45)
2-dose vaccinated ≥12 months	1478	1341 (6.7)	137 (3.8)	9.3	20 (1 to 36)
3-dose vaccinated <2 months	1352	1212 (6.0)	140 (3.9)	10.4	78 (73 to 82)
3-dose vaccinated 2 to <4 months	3055	2751 (13.7)	304 (8.5)	10.0	70 (65 to 75)
3-dose vaccinated 4 to <6 months	3508	3159 (15.7)	349 (9.7)	9.9	48 (40 to 55)
3-dose vaccinated ≥6 months	2241	2039 (10.1)	202 (5.6)	9.0	29 (13 to 42)
4-dose vaccinated ≥7 days	700	638 (3.2)	62 (1.7)	8.9	48 (29 to 62)



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Surie et al (MMWR – 21 Sept 2022) – USA, 2,3 & 4 Dose VE against hospitalisation during BA.1/BA.2 and BA.4/BA.5 Omicron periods

Study design: TNCC (IVY Network); immunocompetent adults >18 years; N= 4730; median age 65-69 years

Vaccine: monovalent mRNA vaccines

Obs period: December 26, 2021-August 31, 2022

Outcomes: Absolute 2 and 3 or 4 dose VE against hospitalisation; VE = (1-OR)*100

Results:

- 3 dose VE did not wane faster for BA.4/BA.5 ~30-40%points
- No significant differences in VE for any dose between the two sub-variant periods
- Unvaccinated people accounted for 32% of hospital admissions vs 5 % for 4 doses

TABLE 2. Effectiveness of monovalent mRNA vaccines against COVID-19–associated hospitalization during the BA.1/BA.2 and BA.4/BA.5 predominant periods of SARS-CoV-2 Omicron variant circulation* among immunocompetent adults — IVY Network, 21 hospitals in 18 U.S. states,† December 26, 2021–August 31, 2022

Group/No. of doses	Interval from last vaccine dose to illness onset, days§	Median interval (IQR) from last vaccine dose to illness, days	Vaccinated case-patients, no./total no. (%)	Vaccinated control-patients, no./total no. (%)	Adjusted VE, % (95% CI)¶
BA.1/BA.2 period					
2	≥14	277 (216–341)	533/1,242 (43)	483/918 (53)	39 (26–49)
	14–150	111 (87–130)	62/771 (8)	79/514 (15)	63 (46–75)
	>150	290 (241–351)	471/1,180 (40)	404/839 (48)	34 (20–46)
3	≥7	145 (92–190)	432/1,141 (38)	694/1,129 (61)	69 (62–74)
	7–120	80 (55–100)	167/876 (19)	393/828 (47)	79 (74–84)
	>120	180 (154–208)	265/974 (27)	301/736 (41)	41 (23–55)
4	≥7	26 (16–39)	25/734 (3)	41/476 (9)	61 (29–78)
	7–120	26 (16–39)	25/734 (3)	41/476 (9)	61 (29–78)
	>120	—	—	—	—
BA.4/BA.5 period					
2	≥14	428 (324–468)	131/317 (41)	181/336 (54)	41 (17–57)
	14–150	102 (77–123)	3/189 (2)	13/168 (8)	83 (35–96)
	>150	430 (329–471)	128/314 (41)	168/323 (52)	37 (12–55)
3	≥7	233 (196–267)	232/418 (56)	232/387 (60)	31 (7–49)
	7–120	74 (33–110)	13/199 (7)	24/179 (13)	60 (12–81)
	>120	237 (204–269)	219/405 (54)	208/363 (57)	29 (3–48)
4	≥7	69 (54–103)	63/249 (25)	102/257 (40)	60 (36–75)
	7–120	66 (51–85)	56/242 (23)	95/250 (38)	61 (37–76)
	>120	131 (126–137)	7/193 (4)	7/162 (4)	—

Limitation: Problem here is >18 without age-stratified analyses, and longer f/u (esp over big Omi waves) may have accentuated misclassification errors with higher pi past infection in control cohort. Both would decrease VE estimate for our target age group

Surie et al. MMWR

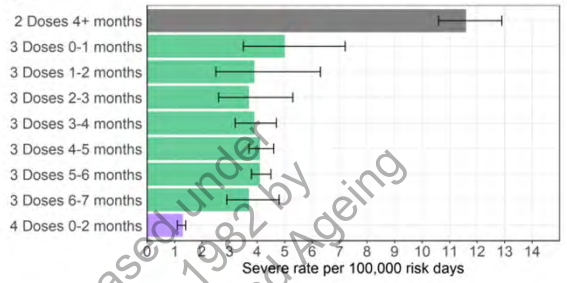
s47B(a)

Amir et al (Preprint – 5 May 2022) – Israel, 4th Dose BNT62b2 VE against Omicron (BA.1&BA.2) severe disease

- Inclusion of younger age groups probably decreases VE despite even lower absolute rates of hosp/death.

- Cohort study (N=1,445,615), aged ≥60 years (~54%)
- Obs period: January 16, 2022, to March 12, 2022
- Outcomes: Severe illness = ≤14 days post confirmed infection NIH definition as a resting respiratory rate of more than 30 breaths per minute, an oxygen saturation of less than 94% while breathing ambient air, or a ratio of partial pressure of arterial oxygen to fraction of inspired oxygen of less than 300)
- Adjusted rate ratios
  - *3 dose vaccinated persons 6-7 months after their third dose were 3.1 times (rVE ~68%) less likely to develop severe disease than those who had received their second dose ≥4 months ago*
  - *4 dose vaccinated persons were 2.9 times (rVE ~66%) less likely to develop severe disease than those who had received their third dose 6-7 months prior*
  - *4 dose vaccinated persons were 8.9 times (rVE ~89%) less likely to develop severe disease than those who had received their second dose ≥4 months prior*

Figure 3. Adjusted rates of severe illness per 100,000 risk days obtained from Poisson regression analysis for the study period January 16, 2022, to March 12, 2022, adjusted for age category (60-69, 70-79, 80+), gender, sector, and exposure (based on the epidemiological week).



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Amir et al - https://www.medrxiv.org/content/10.1101/2022.05.04.22274647v1

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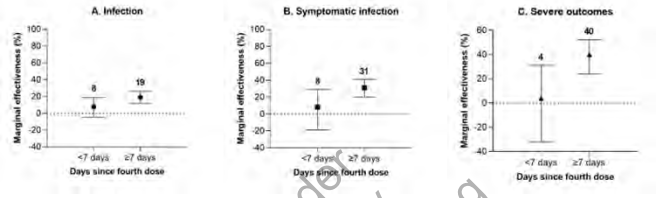
s47B(a)

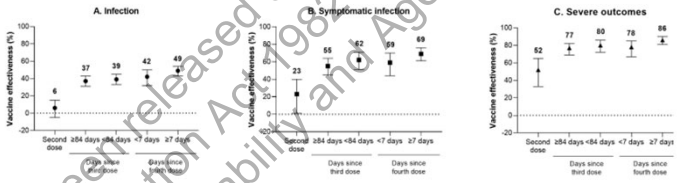
Grewel et al (Preprint – 1 June 2022 [accepted in BMJ not yet published]) – Canada, 4th dose VE in LTCF residents against Omicron infection, symptomatic infection and severe disease

- TNCC, Data linkage study of LTCF residents (≥60 years) N = 46,849 (Negative Controls) 9,957 (Omicron cases)
- Obs period: 30 Dec 2021 to 2 March 2022
- 97% 4th doses were mRNA-1273
- Absolute VE against severe disease is relatively well maintained
  - 3rd Dose ≥84 days = 77% (95%CI 69-82%)"
  - 4th Dose ≥7 days = 86% (95%CI 81-90%)
- Among 3 dose recipients those who received 3 doses of mRNA-1273 or 2 doses of BNT161b2 + 1 dose of mRNA-1273 had greater protection than 3 doses of BNT162b2

Marginal VE of 4th dose vs ≥84 days post dose 3



Absolute VE of 4th Dose vs 2 and 3 doses



Grewel et al- https://www.medrxiv.org/content/10.1101/2022.04.15.22273846v2

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s47B(a)

Bar-On et al (Preprint – 1/2/22) – Israel, VE of a 4th dose (2nd booster) of Pfizer against infection and severe disease

- 4th doses began in Israel 2 Jan 2022 in >60y.o., HCW, high risk popⁿ at least 4m from 3rd dose.
- Study: **>60y.o. Pfizer vaccine**
- 15-29 Jan 2022
- Outcomes: confirmed COVID-19 (PCR/RAT) and severe illness in 4th dose @ ≥12d vs:
  - 3rd dose recipients
  - 4th dose @ 3-7d.
- Adjusted for age group (60-69, 70-79, and 80+ years), sex, and demographic group, calendar date

	Cases (person-days at risk)			Rate Ratio (95% CI)		Adjusted rate difference per 100,000 person-days at risk (95% CI)	
	3rd dose only	3-7 days after 4th dose	12+ days after 4th dose	3rd dose only vs. 12+ days after 4th dose	3-7 vs. 12+ days after 4th dose	3rd dose only vs. 12+ after 4th dose	3-7 vs. 12+ days after 4th dose
Confirmed Infections	42,693 (7,603,132)	5,945 (1,264,767)	9,071 (3,421,826)	2.0 [2.0, 2.1]	1.9 [1.8, 2.0]	279 [271, 287]	234 [219, 247]
Severe illness	195 (4,277,639)	55 (1,023,355)	13 (980,984)	4.3 [2.4, 7.6]	4.0 [2.2, 7.5]	3.8 [2.8, 4.8]	3.5 [2.1, 5.1]

- 2x lower rate of infection (**rate difference** of 279 per 100,000 person-days) in 4th dose vs 3rd dose recipients.
- 4.3x lower rate of severe illness in 4th dose vs 3rd dose recipients. Rate difference 3.8 per 100,000 person-days

Bar-On et al - https://www.medrxiv.org/content/10.1101/2022.02.01.22270232v1

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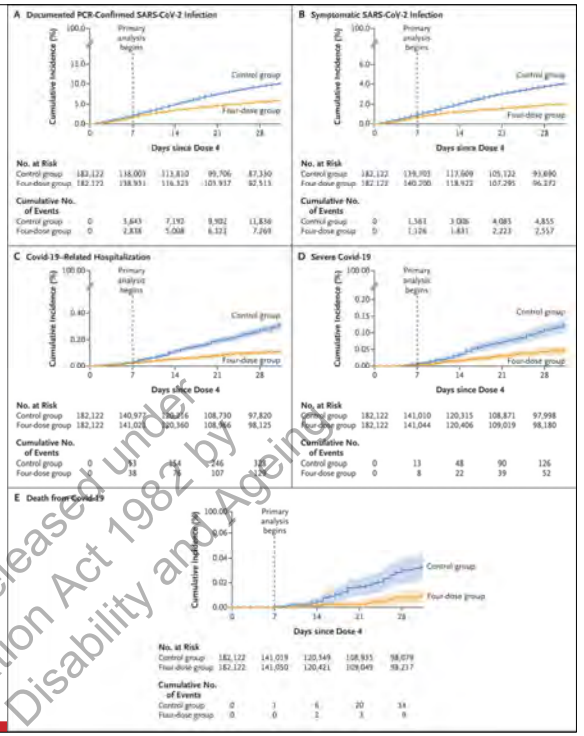
Magen et al (NEJM – 28/4/22), Israel, 4 Dose VE in those aged ≥60 years

- Comparison of 4-doses with individuals who received their 3rd dose ≥4 months ago
- Relative VE 14-30 days post dose 4
  - COVID-19 related hospitalisation: 72% (95% CI, 63 to 79),
  - Severe COVID-19: 64% (95% CI, 48 to 77), and
  - Death from COVID-19: 76% (95% CI, 48 to 91).
- Absolute difference in risk 7 to 30 after a fourth vaccine dose(three doses vs. four doses):
  - Covid-19–related hospitalization:180.1 cases per 100,000 persons (95% CI, 142.8 to 211.9)
  - Severe Covid-19: 68.8 cases per 100,000 persons (95% CI, 48.5 to 91.9)



Magen et al - https://www.nejm.org/doi/full/10.1056/NEJMoa2201688

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AIR-MADIP Vaccine Effectiveness Study Collaboration - preliminary findings

s47F

Collaborative analysis involving:
NCIRS, UNSW, ANU, UniSA, Bond University, Health Economics and Research Division, Health Protection

Aims and methods

- **Aim:** To estimate the effectiveness of COVID-19 vaccines against COVID-19 mortality considering time since receipt of dose, vaccine brand and pandemic period in Australian adults
- Primary outcome: COVID-19 mortality as defined by ABS
- Study population: 2021 Census population who are present in AIR-MADIP spine
- Analyses focus on two Omicron 'waves': B.A.1/2 (1 Jan – 31 May 2022); B.A.4/5 (1 June – 30 Sept 2022)

Methods (continued)

- Retrospective cohort methods: Competing risks analysis for cause-specific mortality with exposure (vaccination) as a time-varying covariate
- Due to few deaths in younger age groups **analyses focus on 65+ years**
- Analyses adjusted for: age, sex, jurisdiction of residence, household equivalised income, co-morbidities (based on Rx risk score), number of GP visits in year prior to study entry, receipt of influenza vaccination in 2021
- Vaccine effectiveness can be estimated by formula: 1-aHR x 100%

Page 3

Characteristics of cohort aged 65+ years at start of each analysis period

	1 Jan-30 May 2022 Omicron B.A.1/2	1 Jun-30 Sept 2022 Omicron B.A.4/5
Number people in analyses	3.8 million	3.8 million
Mean age	74.6 years	74.6 years
% female	53%	53%
% ≥3 comorbidities	50%	50%
% ≥12 GP visits in last year	32%	31%
% received flu vaccine in 2021	72%	72%
COVID-19 vaccine doses received, N		
0	195,000	170,000
1	36,000	10,500
2	2,700,000	320,000
3	900,000	2,010,000
4	1,500	1,300,000
Number of COVID-19 deaths during follow-up	**3250**	**2690**

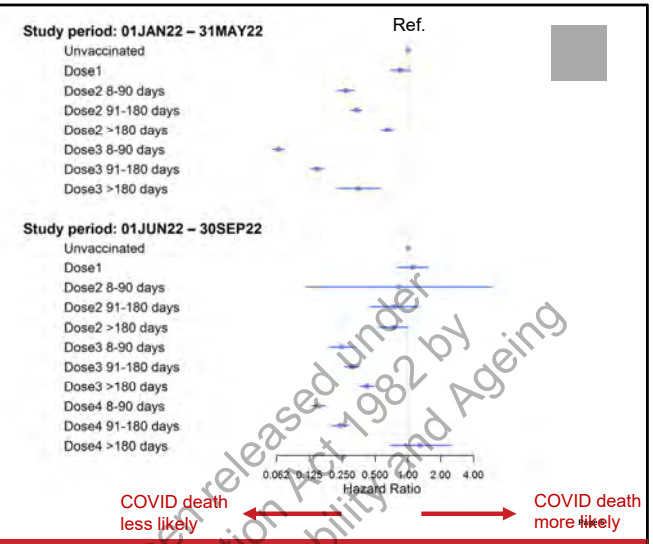
Numbers in table are rounded to enable disclosure; some individuals received 5 COVID-19 vaccine doses but numbers too small to disclose

Page 4

Preliminary hazard ratios for COVID-19 death by vaccine dose and time since receipt 65+ years

(Vaccine effectiveness estimated by 1-aHR x 100%)

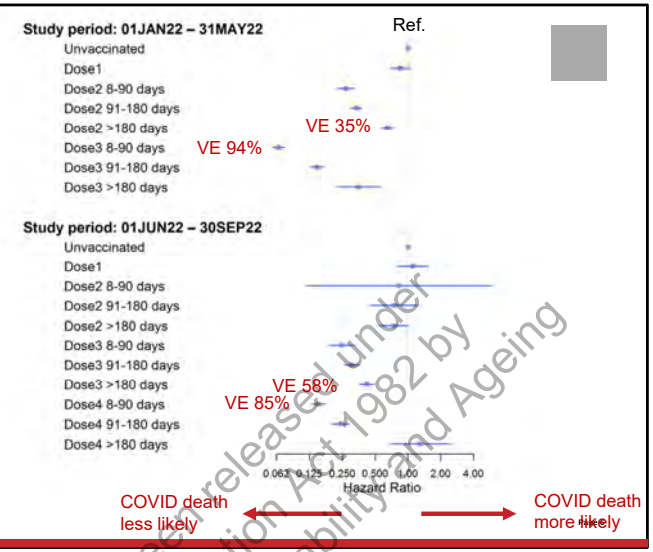
Hazard ratios adjusted for age, sex, jurisdiction, household income, co-morbidities, GP visits, 2021 flu vaccine receipt



Preliminary hazard ratios for COVID-19 death by vaccine dose and time since receipt 65+ years

(Vaccine effectiveness estimated by 1-aHR x 100%)

Hazard ratios adjusted for age, sex, jurisdiction, household income, co-morbidities, GP visits, 2021 flu vaccine receipt



Initial conclusions

- Vaccine effectiveness against COVID-19 mortality wanes after receipt although in most cases there was some residual protection (compared to unvaccinated individuals) even by 6 months post receipt
- During Omicron B.A.1/2 three vaccine doses substantially increased protection against death compared to unvaccinated people and those who had two doses
- During Omicron B.A.4/5 each additional dose increased protection against death from COVID-19 but the risk reduction was less with each additional dose; this is potentially due to increasing 'natural' immunity in the population (i.e. unvaccinated and vaccinated, reducing relative 'gap' in immunity)
- Small numbers of those receiving 4 doses more than 6 months ago make interpretation of these results uncertain but suggest substantial waning VE; possible low levels hybrid immunity in this group

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Continuing work . . .

- Analyses in population resident in aged care – priority group (completed)
- All-cause mortality outcome
- Analyses can be readily updated to include current COVID-19 wave once deaths incorporated (~2-3 month delay on deaths), other datasets slower to update (e.g. new aged care admissions)
- Analyses can be updated to include ICU data (dependent on how current)
- Analyses can be modified with different intervals and reference group

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Acknowledgements

- NCIRS: s47F
- s47F
-
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- HERD: s47E(c), s47F
- Health Protection: s47E(c), s47F

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Comparative effectiveness of COVID-19 vaccines against SARS-CoV-2 infection

s47F

An NCIRS NSW Health Collaboration

Rationale and aim

- Limited data directly comparing effectiveness of vaccine types
- Most data involves mRNA vaccines, some comparisons with adenoviral vector vaccines, no data on protein subunit vaccines
- Most individuals received BNT162b2 mRNA (Pfizer Comirnaty) or ChAdOx1 nCov-19 (Astrazeneca) for their primary course; mRNA-1273 (Moderna Spikevax) available from October 2021, NVX-CoV2373 (Novavax) from February 2022
- Aim: to compare effectiveness of different vaccine types for prevention of SARS-CoV-2 infection during Omicron BA1/2 period in NSW

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Methods

- Used AIR linked to COVID-19 notifications in NSW (Greater Sydney & HNE), as well as deaths (for censoring)
- Study population limited to those aged 18+ years
- Compared rates of COVID-19 notification according to receipt of vaccine dose and brand
- Focus on comparisons of primary or booster dose, and time since receipt (14-63 days)
- Period of analysis 1 March – 27 May 2022 (Omicron BA.1/2)
- Statistical methods used Cox regression, time-varying vaccination status

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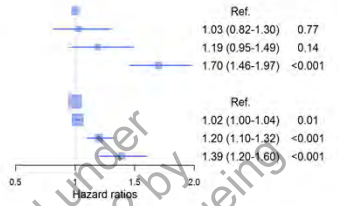
Results

	Number of infections	%PCR confirmed	Person Years	Person-time rate (per 100-Person-Year) (95% CI)	Adjusted HRs (95% CI)	P value
Primary course; dose 2 14-63 days						
BNT162b2 mRNA	635	49%	1530	42 (36; 49)	Ref.	
mRNA-1273	84	45%	193	43 (28; 67)	1.03 (0.82-1.30)	0.77
ChAdOx-1 nCov-19	83	46%	185	45 (29; 69)	1.19 (0.95-1.49)	0.14
NVX-CoV2373	231	53%	410	56 (43; 73)	1.70 (1.46-1.97)	<0.001
Booster; dose 3 14-63 days						
BNT162b2 mRNA	73,373	50%	122,731	60 (59; 61)	Ref.	
mRNA-1273	19,517	48%	31,083	63 (61; 64)	1.02 (1.00-1.04)	0.01
ChAdOx-1 nCov-19	503	51%	899	56 (47; 66)	1.20 (1.10-1.32)	<0.001
NVX-CoV2373	187	58%	271	69 (53; 91)	1.39 (1.20-1.60)	<0.001



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Summary

- Data suggest relatively higher effectiveness of mRNA COVID-19 vaccines than either viral vector and protein subunit vaccines
- Data generally consistent with immunological data
- Potential uncontrolled confounding (populations receiving NVX/AZ may differ in ways we can't measure from those receiving mRNA)
- Sample size small (particularly for primary course analysis) so unable to compared severe disease outcomes

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COVID-19 WG
2023 Booster Policy Framework

21 December 2022

Prepared by NCIRS for ATAGI COVID-19 Working Group

s47F

Overview

1. 2023 booster policy framework

2. Provisional recommendations

3. Additional slides:
   - Further review of studies assessing risk of severe breakthrough COVID-19 among vaccinated +/- boosted populations
   - Additional VE study (Tenforde et al, MMWR Dec 16 2022)

PICO summary

Population	People in Australia who have completed primary vaccination against COVID-19 at least 3 months ago, grouped into the following target popuations: • High risk adults • Healthy adults • High risk people aged < 18 years • Healthy people aged < 18 years
Intervention	COVID-19 vaccine booster dose of either: • Ancestral-based vaccine • BA.1 bivalent vaccine • ?BA.4/5 bivalent vaccine
Comparisons	• People who have completed primary vaccination +/- booster(s) against COVID-19 whose last dose was at least 2 months ago (based on relevant studies) • People who have completed primary vaccination +/- booster(s) with ancestral based vaccine (vs bivalent vaccines)
Outcome	Protection against serious illness, hospitalisation and death from COVID-19

Policy Questions

1. Should additional COVID-19 booster dose(s) be recommended in 2023 for:
   - High risk adults?
   - Healthy adults?
   - High risk people aged <18 years?
   - Healthy people aged <18 years?
2. What should be the timing of the published advice?
3. What should be the interval from most recent dose/prior infection?
4. Should there be a brand-agnostic or preferential recommendation based on vaccine composition (bivalent vs ancestral; vaccine platform)?

1. Should additional booster dose(s) be recommended in 2023?

Considerations	Summary of evidence/discussion
Is there evidence of an increase in serious illness/hospitalisations from COVID-19?	*FluCAN, Vic, QLD and NSW data 21.12.22* Evidence of increased circulation of SARS-CoV-2 in Australia in late 2022: Epidemic situational reports
Evidence of waning immunity from 3rd/4th doses	NCIRS VE Update 7 Dec • Protection from 3rd/4th ancestral doses wanes within several months Coverage update 7 Dec (slides 3-6) • By early 2023, majority of population will be > 6 months since their last dose, and >30% over 12 mo • Many <18 years will be approaching 1.5 years since their last dose
Benefits & harms • How much additional protection will a booster dose offer? • Duration of additional protection? • What are the potential harms to the individual?	NCIRS VE Update 7 Dec, AIR-MADIP data 21 Dec, FluCAN data 21 Dec • Bivalent booster or 4th dose of monovalent booster offers additional protection against serious illness from COVID-19 • Protection from 4th monovalent dose wanes by ~5mo • No data on waning from bivalent booster or on 5th doses • Safe & well tolerated; no evidence of adverse effects from imprinting

Prepared by NCIRS for ATAGI COVID-19 WG 21 Dec 2022 Page 5

1. Should additional booster dose(s) be recommended in 2023?

Consideration	Summary of evidence/discussion
Which population group(s) should receive a booster dose?	*Review of risk factors for severe breakthrough COVID-19 among vaccinated population (see **Additional slides**) and earlier review April 2022* • Older age and medical comorbidities represent highest ongoing risk Review of other NITAG recommendations Dec 7 (slide 7-8) and coverage update (slides 3-6) • Most countries recommend for older adults; several are permissive for younger/healthy groups • Most Australians are > 6 months since their last dose of a COVID-19 vaccine. Many young healthy people are >12 months and may be ~1.5 years since last dose
Will any group(s) require multiple booster doses?	NCIRS VE update • Evidence of waning rVE from additional booster after several months Discussion: Benefit of preparing individuals for possible future doses by foreshadowing in next advice
Values: how does the population perceive the importance of booster doses?	Coverage update 7 Dec, Sentiment update 21 Dec (LINK) Good uptake of 3rd/4th doses among older adults Evidence of 'vaccine fatigue' - reduced uptake of 4th dose from eligible population groups vs 3rd dose
Acceptability: what factors may make additional recommendation more acceptable?	Sentiment update – ATAGI #89, 21 Dec Preference for simple messaging & to avoid 'reactive' policies Preference to discontinue numbering doses
Feasibility & resource use • Adequate supply? • How will vaccine be rolled out?	Supply update 7 Dec (LINK): Anticipated adequate supply of ancestral (Pfizer, Novavax) and bivalent (Pfizer BA.1) vaccines. BA.4/5 TBA ?Primary care/pharmacy capacity Co-administration with influenza vaccine may make more feasible/improve update due to fewer health service visits required

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1. Should additional booster dose(s) be recommended in 2023?

Provisional recommendations:

- Yes, an additional booster dose is warranted and feasible
- Regardless of number of prior doses
- ?Recommended for age 50+ and adults with medical risk factors for severe COVID-19
- ?Permissive approach for healthy aged 18+
- ?Permissive approach for people <18 years with risk factors for serious illness

s47B(a)

2. What should be the timing of the published advice?

Considerations	Summary of evidence/discussion
Timing in relation to COVID-19 wave	• No clear evidence of seasonality (to predict next wave)
Timing in relation to periods of health system stress	• Likely increased health system demand during winter season; beneficial to boost population immunity before then • Timing of influenza season has been less predictable in recent seasons
Timing in relation to other vaccination programs	• Logistical benefits to coincide with influenza vaccination program
Framing of the booster	• Preference to avoid dose numbering • Support for naming in relation to season

Provisional recommendation
Defer until early 2023 – not recommended in response to current wave
Frame as 'autumn booster'
Flag in initial advice that:
- Some high risk groups may require an additional dose later in the year
- Advice may changed based on new variants or vaccines

3. What should be the interval from most recent dose/prior infection?

Considerations	Summary of evidence/discussion
When does protection from booster doses wane?	VE update • Incremental benefit from ancestral booster doses wanes within several months • No data on bivalent booster vaccines
Feasibility of confirming infection	Confirmation of infection will become more challenging since payment to private providers for PCR will cease in 2023
What has been the consensus of other NITAGs?	NITAG recommendations summary (slides 7-8) Most NITAGs recommend 3-6 month interval from last dose

Provisional recommendation
Next booster dose should be 6 months from last dose or confirmed infection.

4. Brand-agnostic vs preferential recommendation?

Considerations	Summary of evidence/discussion
Comparison of ancestral vs bivalent booster vaccines	*VE brand comparison 21 Dec* *NCIRS presentation Moderna BA.4/5 - Feb 23* No published direct head-to-head VE comparisons Nab titres against Omicron sublineages higher from bivalent than ancestral; rVE estimates are similar (UK HSE) All 3 shown to provide additional protection against serious illness from Omicron sublineages
Acceptability	Comms update at ATAGI #89; *Sentiment update 21 Dec* Clear preference for simple messaging
Adequate supply of ancestral vs bivalent vaccines?	Supply update – 7 Dec Anticipated adequate supply of Pfizer ancestral, Pfizer BA.1 and Pfizer BA.4/5 Moderna ancestral and BA.1 may run out

Provisional recommendations

Any COVID-19 vaccine that is registered for use as a booster, noting bivalent vaccines only registered for use in people aged 18 and older.

Provisional recommendations

2023 Autumn booster advice:

- ATAGI recommends an additional COVID-19 booster dose for all adults aged 50 and older, and adults with medical risk factors for severe COVID-19 from 6 months after the most recent dose or confirmed SARS-CoV-2 infection, and regardless of the number of prior doses received.
- Healthy adults aged 18-50 *?and people aged <18 with risk factors for severe COVID-19* can consider an additional dose after discussion with their healthcare provider.
- ATAGI recommends vaccination with any COVID-19 vaccine that is registered for use as a booster, noting bivalent vaccines are currently only registered for use in people aged 18 and older.
- The booster dose can be co-administered with influenza or other vaccines.
- Further advice will be provided in coming months. High risk groups may be recommended to have an additional booster dose later in the year.

s47B(a)

Additional slides:

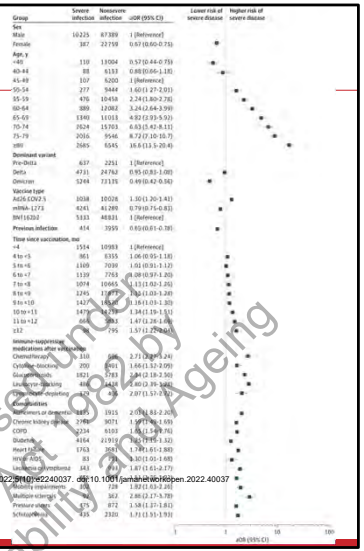
Further review of risk factors for severe breakthrough infection with SARS-CoV-2

Summary

- Risk factors for severe breakthrough COVID-19 in vaccinated (including boosted) populations include:
  - Older age – strongest association (strong evidence)
  - Medical comorbidities, particularly immunocompromise (strong evidence)
  - Longer time since last dose (weak evidence)
- Severe illness remains rare among young healthy vaccinated people

USA, Dec 2020 – Feb 2022: Risk factors for severe breakthrough infection in veterans

- Retrospective cohort study of 110,760 US veterans
- Association between severe disease and exposures estimated using logistic regression
- Figure 2 (at right): risk of severe vs nonsevere breakthrough infections
- Strongest association with risk of severe disease after vaccination was older age
- Other risk factors identified: immunosuppression, chronic conditions associated with end-organ disease
- Receipt of a booster dose reduced the odds of severe disease (aOR 0.50; 95% CI 0.44 – 0.57)



Vo AD, La J, Wu JT, et al. Factors Associated With Severe COVID-19 Among Vaccinated Adults Treated in US Veterans Affairs Hospitals. *JAMA Netw Open*. 2022;5(10):e2240037. doi:10.1001/jamanetworkopen.2022.40037

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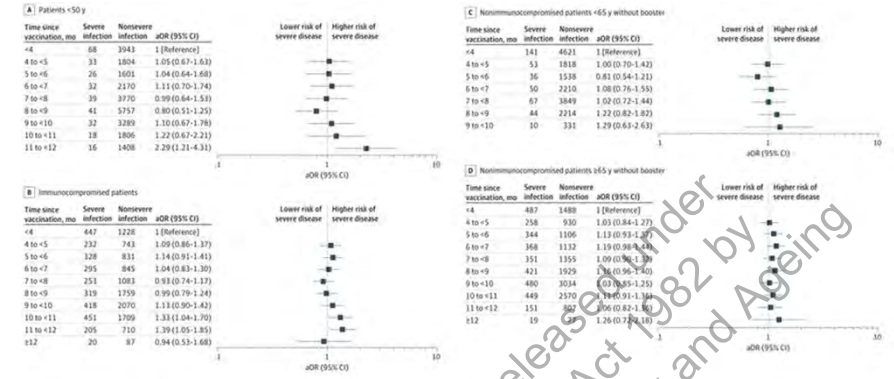
USA, Dec 2020 – Feb 2022: Risk factors for severe breakthrough infection in veterans



A Patients <50 y

Time since vaccination, mo	Severe infection	Nonsevere infection	aOR (95% CI)
<4	68	3941	1 [Reference]
4 to <5	33	1804	1.05 (0.67-1.63)
5 to <6	26	1601	1.04 (0.64-1.68)
6 to <7	32	2170	1.11 (0.70-1.74)
7 to <8	39	3770	0.99 (0.64-1.53)
8 to <9	41	5757	0.80 (0.51-1.25)
9 to <10	32	3289	1.10 (0.67-1.78)
10 to <11	18	1806	1.22 (0.67-2.21)
11 to <12	16	1408	2.29 (1.21-4.31)

B Immunocompromised patients

Time since vaccination, mo	Severe infection	Nonsevere infection	aOR (95% CI)
<4	447	1228	1 [Reference]
4 to <5	232	743	1.09 (0.86-1.37)
5 to <6	128	831	1.14 (0.91-1.41)
6 to <7	295	845	1.04 (0.83-1.30)
7 to <8	253	1083	0.93 (0.74-1.17)
8 to <9	319	1759	0.99 (0.79-1.24)
9 to <10	418	2070	1.13 (0.90-1.42)
10 to <11	451	1709	1.33 (1.04-1.70)
11 to <12	205	710	1.39 (1.05-1.85)
≥12	20	87	0.94 (0.53-1.68)

C Nonimmunocompromised patients <65 y without booster

Time since vaccination, mo	Severe infection	Nonsevere infection	aOR (95% CI)
<4	141	4621	1 [Reference]
4 to <5	53	1818	1.00 (0.70-1.42)
5 to <6	36	1538	0.81 (0.54-1.21)
6 to <7	50	2210	1.08 (0.76-1.55)
7 to <8	67	3849	1.02 (0.72-1.44)
8 to <9	44	2214	1.22 (0.82-1.82)
9 to <10	10	331	1.29 (0.63-2.63)

D Nonimmunocompromised patients ≥65 y without booster

Time since vaccination, mo	Severe infection	Nonsevere infection	aOR (95% CI)
<4	487	1488	1 [Reference]
4 to <5	258	930	1.03 (0.84-1.27)
5 to <6	344	1106	1.13 (0.93-1.37)
6 to <7	368	1132	1.19 (0.98-1.44)
7 to <8	351	1355	1.09 (0.90-1.32)
8 to <9	421	1929	1.16 (0.96-1.40)
9 to <10	480	3034	1.03 (0.85-1.25)
10 to <11	449	2570	1.10 (0.91-1.33)
11 to <12	151	987	1.06 (0.82-1.36)
≥12	19	87	1.26 (0.72-2.18)

Vo AD, La J, Wu JT, et al. Factors Associated With Severe COVID-19 Among Vaccinated Adults Treated in US Veterans Affairs Hospitals. *JAMA Netw Open*. 2022;5(10):e2240037. doi:10.1001/jamanetworkopen.2022.40037

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Jan-March 22 (Omicron era): Evaluation of Risk Factors for Postbooster Omicron COVID-19 Deaths in England

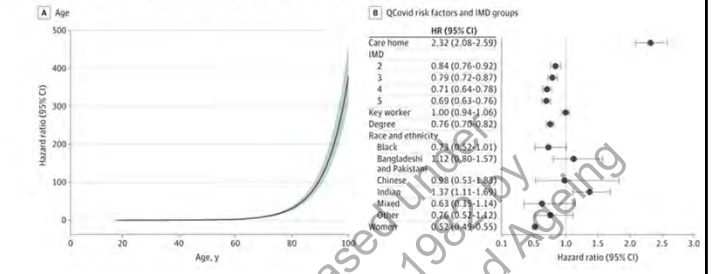
Data linkage study combining ONS public health data with electronic health records

Population: 19,473,570 people aged 18-100 who had completed primary vaccination + mRNA booster ≥ 14 days prior to 31 Dec 2021

Outcome: time to death involving COVID-19 from 1 Jan – 16 March 2021

Findings: Age was the most important risk factor. Other high risk groups included people with SCID, haematological/bone marrow cancer, dementia

Figure. Risk Factors for Death From COVID-19 After Receiving a Booster

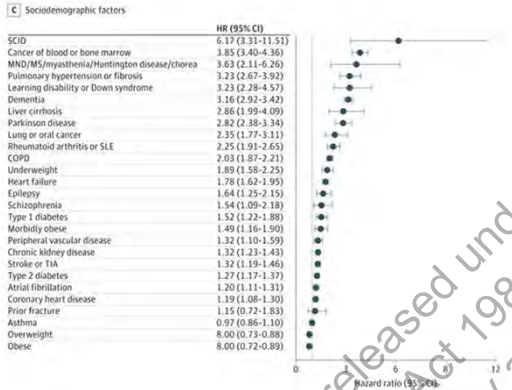


Nafilyan, Vahé, et al. "Evaluation of risk factors for postbooster Omicron COVID-19 deaths in England." *JAMA Network Open* 5.9 (2022): e2233446-e2233446.

Prepared by NCIRS for ATAGI COVID-19 WG 21 Dec 2022

Page 16

Jan-March 22 (Omicron era): Evaluation of Risk Factors for Postbooster Omicron COVID-19 Deaths in England (continued)



Open 5.9 (2022): e2233446-e2233Nafilyan, Vahé, et al. "Evaluation of risk factors for postbooster Omicron COVID-19 deaths in England." *JAMA Network* 446

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Additional slide:
VE update 21 Dec 2022

rVE of bivalent booster against ED/UC presentation

- TNCC study with 78,303 ED/UC encounters in individuals with COVID-19 like illness
- Presented VE relative to monovalent vaccination by interval since last dose; and absolute VE vs unvaccinated
- Relative VE was higher with increased time since last monovalent dose

TABLE 2. Bivalent booster COVID-19 vaccine effectiveness* against laboratory confirmed COVID-19–associated emergency department and urgent care encounters and hospitalizations among immunocompetent adults aged 18 years — nine states,† September–November 2022

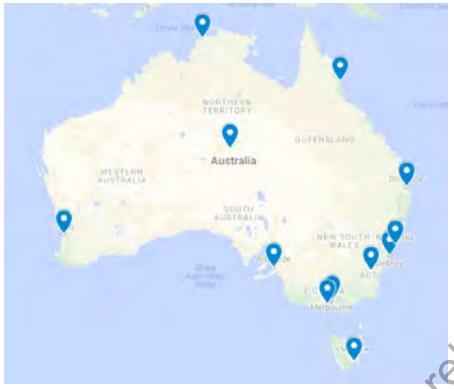
mRNA dosage pattern	Total	Median interval since last dose, days (IQR)	VE % (95% CI)
ED/UC encounters			
Relative VE			
Only MV doses, last dose 2–4 mos earlier	5,668	115 (91–134)	Ref
BV booster dose, ≥7 days earlier	3,905	25 (16–37)	31 (19–41)
Only MV doses, last dose 5–7 mos earlier	6,891	184 (166–209)	Ref
BV booster dose, ≥7 days earlier	3,905	25 (16–37)	42 (32–50)
Only MV doses, last dose 8–10 mos earlier	14,220	294 (273–312)	Ref
BV booster dose, ≥7 days earlier	3,905	25 (16–37)	53 (45–60)
Only MV doses, last dose ≥11 mos earlier	23,477	459 (365–542)	Ref
BV booster dose, ≥7 days earlier	3,905	25 (16–37)	50 (43–57)
Absolute VE			
Unvaccinated	24,142	NA	Ref
BV booster dose, ≥7 days earlier	3,905	25 (16–37)	56 (49–62)
Hospitalizations			
Relative VE			
Only MV doses, last dose 2–4 mos earlier	—§	—	—
BV booster dose, ≥7 days earlier	—	—	—
Only MV doses, last dose 5–7 mos earlier	1,819	178 (164–201)	Ref
BV booster dose, ≥7 days earlier	783	23 (14–34)	38 (13–56)
Only MV doses, last dose 8–10 mos earlier	2,655	294 (273–313)	Ref
BV booster dose, ≥7 days earlier	783	23 (14–34)	42 (19–58)
Only MV doses, last dose ≥11 mos earlier	4,595	472 (362–556)	Ref
BV booster dose, ≥7 days earlier	783	23 (14–34)	45 (25–60)
Absolute VE			
Unvaccinated	8,092	NA	Ref
BV booster dose, ≥7 days earlier	783	23 (14–34)	57 (41–69)

Tenforde MW, Weber ZA, Natarajan K, et al. Early Estimates of Bivalent mRNA Vaccine Effectiveness in Preventing COVID-19–Associated Emergency Department or Urgent Care Encounters and Hospitalizations Among Immunocompetent Adults — VISION Network, Nine States, September–November 2022. MMWR Morb Mortal Wkly Rep. ePub: 16 December 2022. DOI: http://dx.doi.org/10.15585/mmwr.mm7151e1.

FluCAN – vaccine status

s47F

FluCAN-PAEDS 2012-22



22 hospitals (incl 6 paediatric hospitals)

17 hospitals used for surveillance

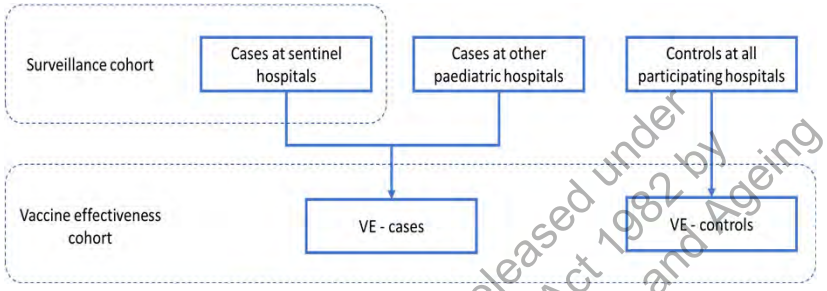
All states/territories

Metropolitan/regional
Temperate/tropical

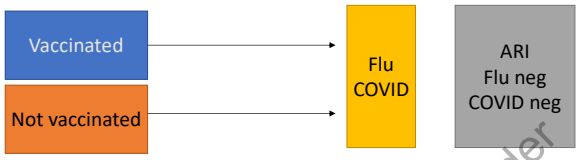
>14% of national bed capacity

(TSANZ/ASID collaboration 2009)

Study design



Incidence density test-negative

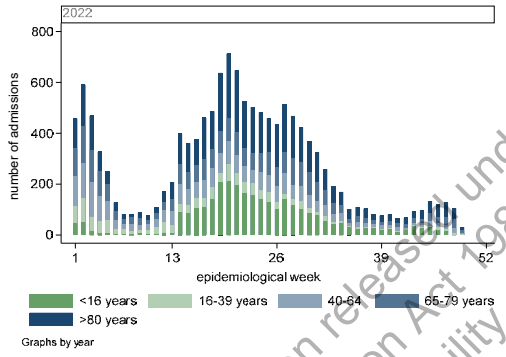


"Exposure"

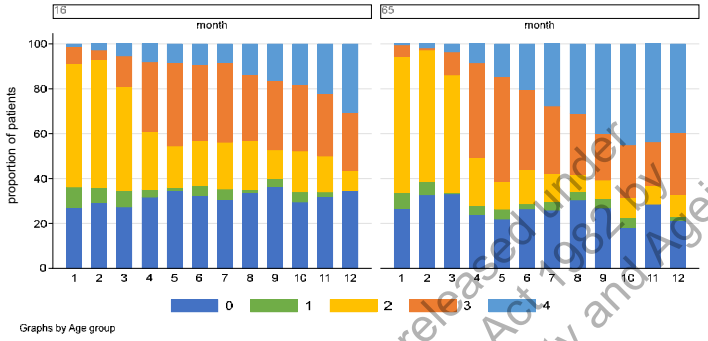
"Outcome"

Case = influenza or COVID
Control = non influenza/COVID ILI matched for date of presentation
Case/control status assigned when test result known
Adjust for confounders

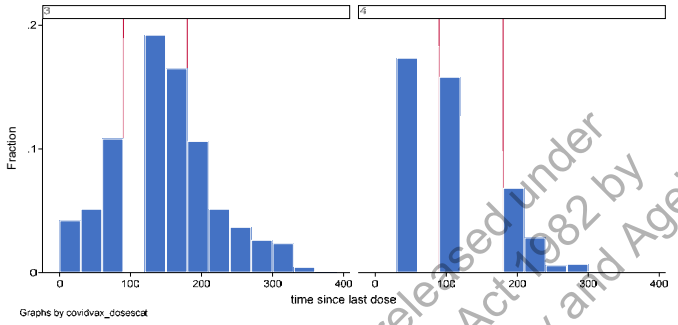
Cases by week in 2022



Vaccine status of cases in 2022, by age group

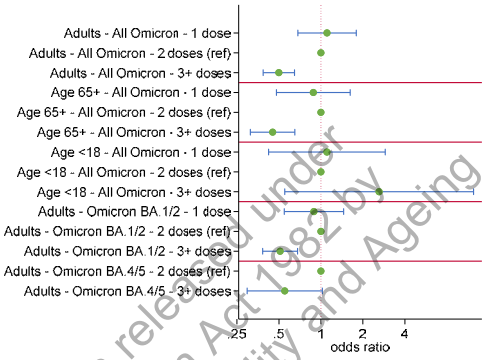


Time since last dose (3rd and 4th doses) in cases

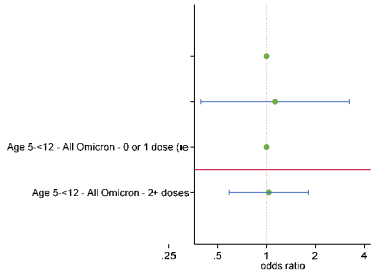


Hospitalisation with COVID and vaccine doses

- Substantial additional protection with 3 doses vs 2 doses
- Similar in elderly
- Similar in BA.1/2 vs BA.4/5



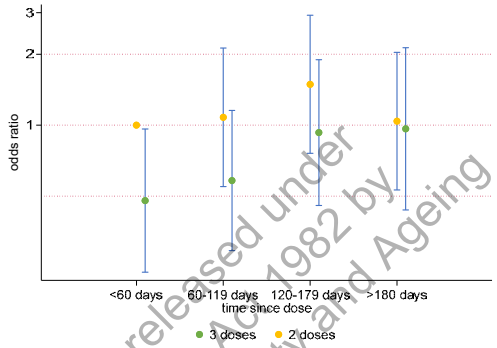
Paediatric COVID VE



- Adjusted for month and risk factors, stratified by age group
- No detectable protective effect against hospitalisation
- Small numbers – interpret with caution

Hospitalisation with COVID and time since last dose

- Small numbers when divided by time since last dose
- Higher risk of hospitalisation after 2 doses (vs 3 doses)
- Evidence of waning protection after 3 doses



Summary

- Three waves in 2022 consistent with other surveillance data
  - Shift to older people in most recent wave
- In hospitalised cases, 20% of younger adults and 40% of older adults have received dose 4 (half more than 90 days prior to admission)
- VE difficult to estimate
  - Protective effect of 3+ doses vs 2 doses evident
  - Waning of 3rd dose protection

COVID-19 Epidemiology and Vaccination in Victoria

Victorian Department of Health

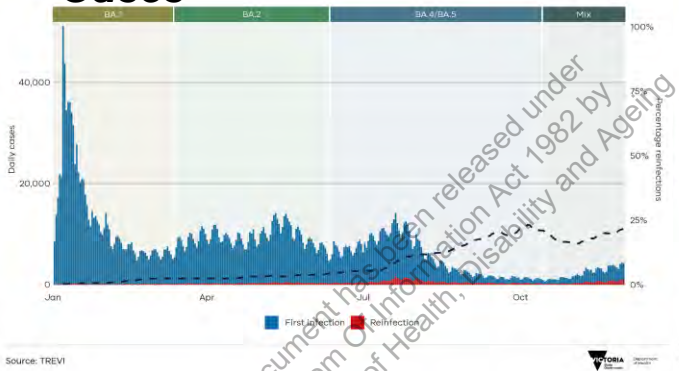
NOT FOR DISTRIBUTION
COMMITTEE IN CONFIDENCE: ATAGI

VICTORIA State Government | Department of Health

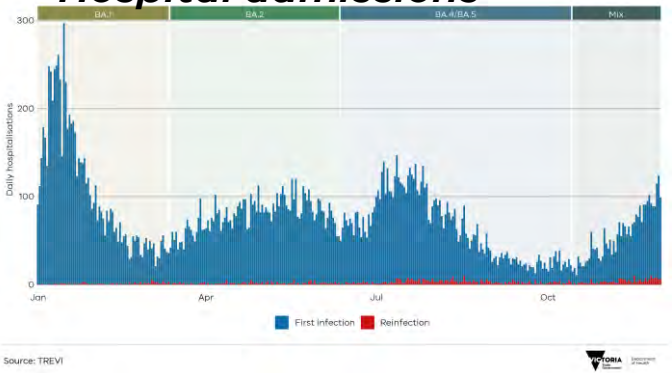
COVID-19 in Victoria in 2022

- There have been multiple COVID waves in 2022 with the largest wave in January.
- Reinfections rose to 19% of cases in the latest wave but the true rate is much higher due to low rates of testing and reporting.
- From 1 Jan to 30 Nov 2022, there were 25,505 COVID-19 hospital admissions (59% aged 65+) in Victoria.
- 4,470 deceased cases had a date of death between 1 Jan and 30 Nov 2022.
- In hospital mortality rate has remained high but largely stable throughout 2022.
- Long COVID data is not actively collected in Victoria. Estimates from the literature indicate that 5-10% of cases in Australia reported symptoms persisting for more than 3 months.

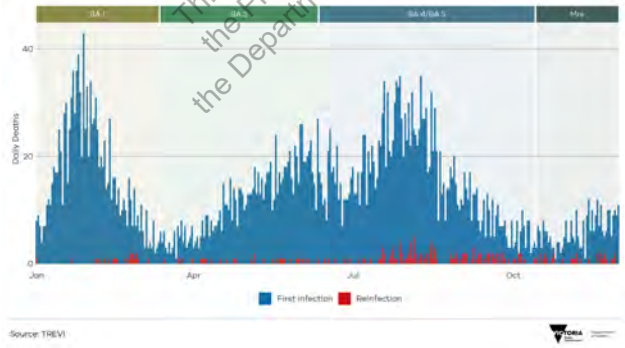
Cases



Hospital admissions



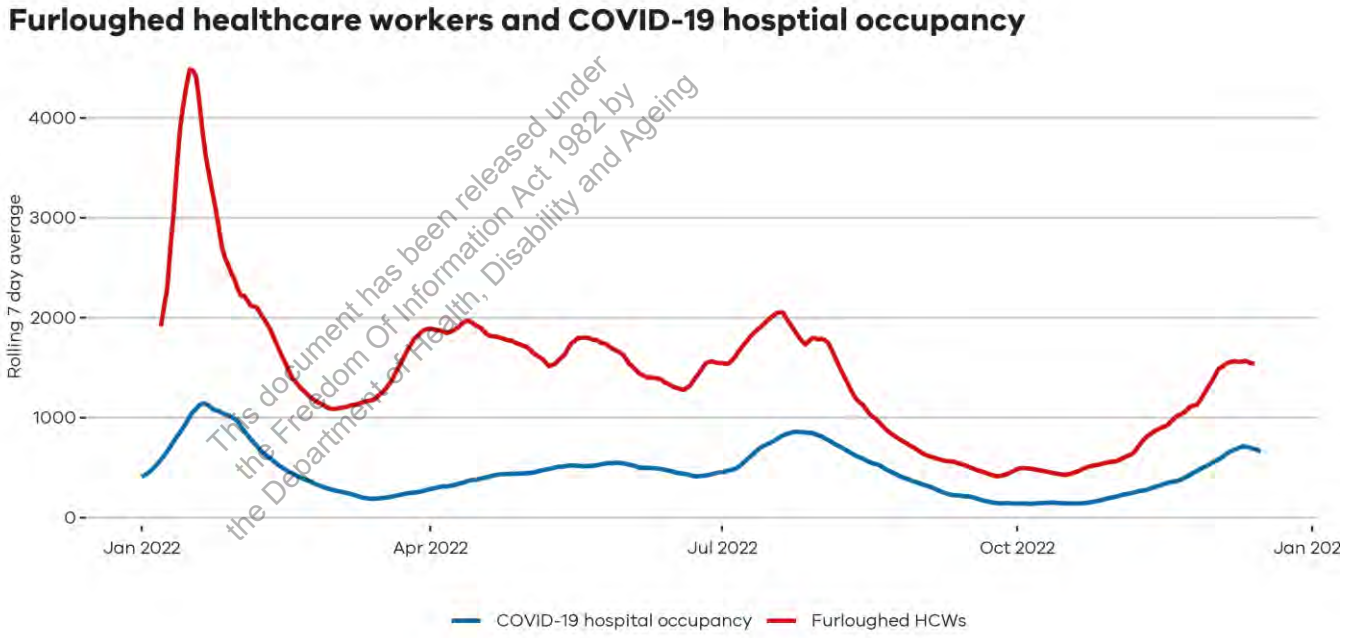
Deaths



Mortality in Hospitalised Cases

Healthcare Worker furlough in 2022

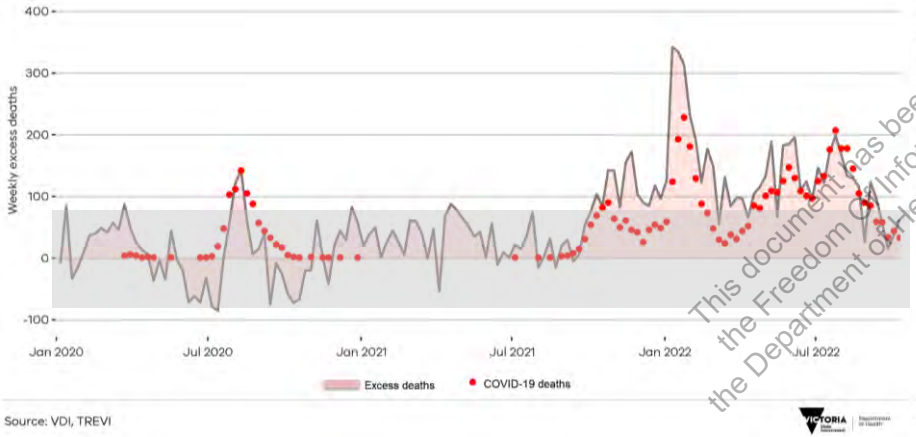
Healthcare Worker furlough numbers* have fluctuated in line with COVID waves in Victoria. The impact of this is substantial as workers are furloughed when system pressure is at its greatest.



*HCW furlough numbers shown do not differentiate reason for absence but does include diagnosis and expose. Victoria is no longer able to capture diagnoses linked to occupation but total furlough numbers.

Excess Deaths in Victoria

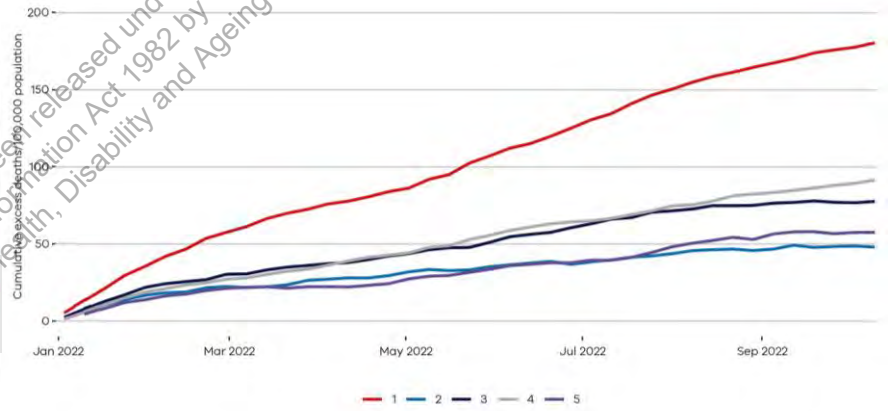
Excess deaths in Victoria with COVID-19 deaths superimposed



Source: VDI, TREVI

Cumulative excess deaths in Victoria by socio-economic status quintile

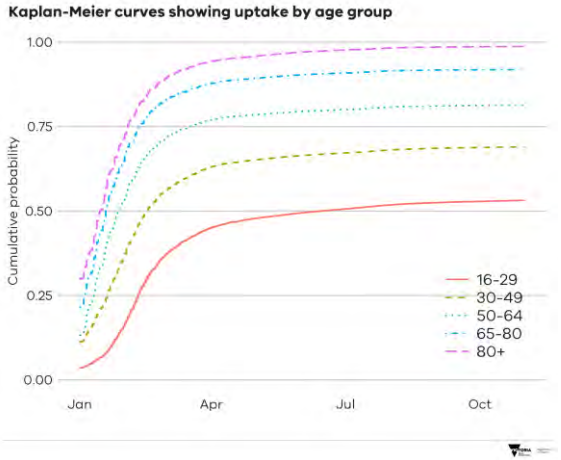
1 being the quintile with greatest relative social disadvantage

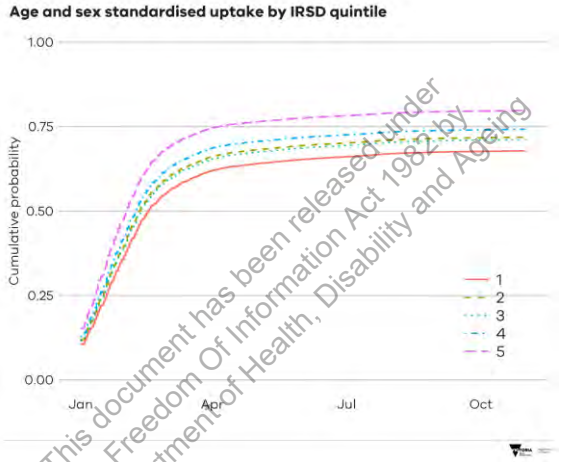


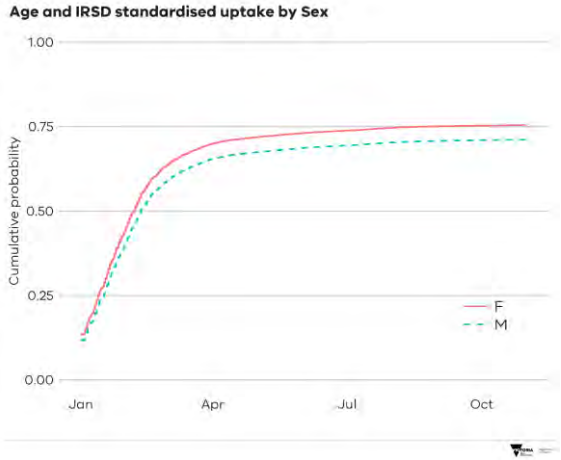
Source: VDI

- **From 1 January 2022 to 13 October 2022, estimated excess deaths in Victoria were 86 excess deaths per 100,000 population (17% above expected).**
- The close alignment of excess deaths and COVID-19 death counts suggest excess deaths in Victoria were largely explained by COVID-19 associated mortality.
- Excess death rates were higher in areas of lower socioeconomic disadvantage.

COVID-19 Vaccine Uptake in Victoria: 3rd dose

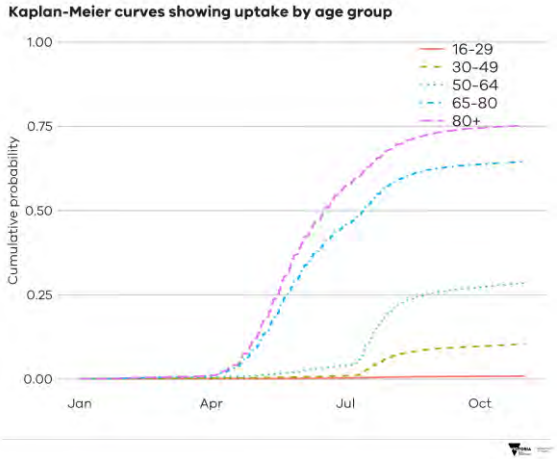


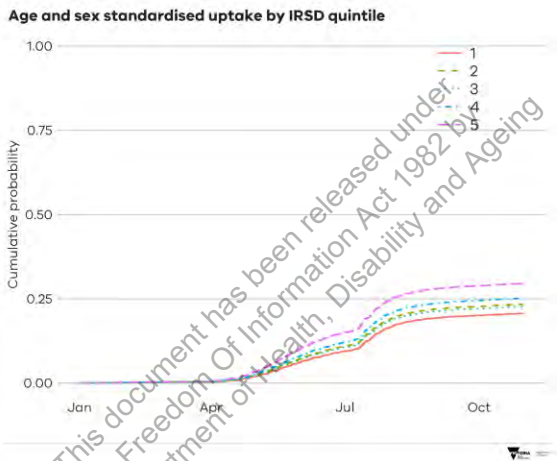


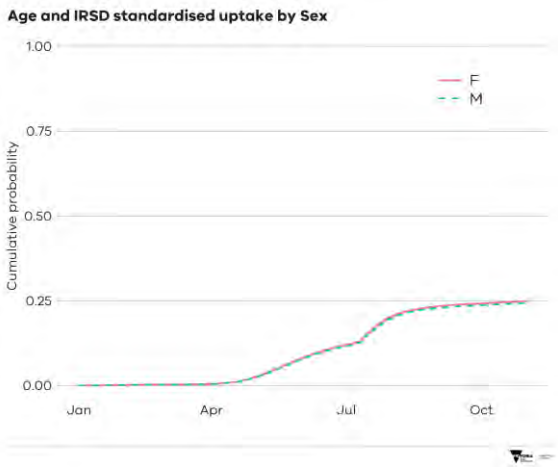


- Factors affecting third dose uptake include:
  - People living in areas of greater social disadvantage are less likely to have a third dose
  - Males are less likely than females to have a third dose
  - Older Victorians are more likely to have a third dose

COVID-19 Vaccine Uptake in Victoria: 4th dose







Uptake determinants were similar to those for third dose with more marked differences by age group due to eligibility criteria.

Descriptive – COVID Hospitalisations

The table below shows COVID hospital and ICU admissions in Victoria in 2022. Time at risk^ allows for comparisons between ages and vaccination rates accounting for difference in group size over time.

- Both three and four doses saw considerably lower rates of hospitalisation and ICU compared to two doses but were similar to one another. This analysis does not account for the effect of waning or risk factor differences between population groups such as comorbidities.
- Older age is associated with higher rates of hospitalisation and ICU across all vaccination levels.

Dose	Age group	Hospitalisation (n)	ICU admission (n)	Time at risk^ (person years)	Hosp rate* (95% CI)	ICU rate* (95% CI)
2	16-29	744	28	472,080	16 (15, 17)	0.59 (0.39, 0.86)
2	30-49	1,291	61	590,825	22 (21, 23)	1.03 (0.79, 1.33)
2	50-64	1,039	76	249,675	42 (39, 44)	3.04 (2.4, 3.81)
2	65+	3,577	179	164,867	217 (210, 224)	10.86 (9.32, 12.57)
3	16-29	376	11	409,125	9 (8, 10)	0.27 (0.13, 0.48)
3	30-49	1,164	39	859,365	14 (13, 14)	0.45 (0.32, 0.62)
3	50-64	1,327	84	608,878	22 (21, 23)	1.38 (1.1, 1.71)
3	65+	5,053	152	486,583	104 (101, 107)	3.12 (2.65, 3.66)
4	16-29	18	*n<5*	3,420	53 (31, 83)	NA
4	30-49	111	7	47,864	23 (19, 28)	1.46 (0.59, 3.01)
4	50-64	299	14	89,302	33 (30, 37.5)	1.57 (0.86, 2.63)
4	65+	2,539	84	285,439	89 (86, 92)	2.94 (2.35, 3.64)

Victoria, 1st of Jan to 1st of Nov 2022
* Events per 10,000 person years at risk

^Time at risk calculates the total for the group in the data period. For a given subject and dose started at date of dose administration or start of study period, whichever occurred later, and ended at next dose administration date, end of study period or date of death, whichever occurred first.

Descriptive – COVID attributable mortality

The table below shows COVID mortality in Victoria in 2022. Time at risk^ allows for comparisons between ages and vaccination rates accounting for difference in group size over time.

- Both three and four doses saw considerably lower rates of death compared to two doses. This analysis does not account for the effect of waning or risk factor differences between population groups such as comorbidities.
- Older age is associated with higher rates of death across all vaccination levels.

Dose	Age group	Death (n)	Time at risk^ (person years)	Mortality rate* (95% CI)
2	16-29	8	472,080	0.17 (0.07, 0.33)
2	30-49	29	590,825	0.49 (0.33, 0.7)
2	50-64	61	249,675	2.44 (1.87, 3.14)
2	65+	904	164,867	54.83 (51.32, 58.53)
3	16-29	*n<5*	409,125	NA
3	30-49	21	859,365	0.24 (0.15, 0.37)
3	50-64	99	608,878	1.63 (1.32, 1.98)
3	65+	1,292	486,583	26.55 (25.12, 28.04)
4	16-29	*n<5*	3,420	NA
4	30-49	*n<5*	47,864	NA
4	50-64	16	89,302	1.79 (1.02, 2.91)
4	65+	898	285,439	31.46 (29.44, 33.59)

Victoria, 1st of Jan to 1st of Nov 2022

* Events per 10,000 person years at risk

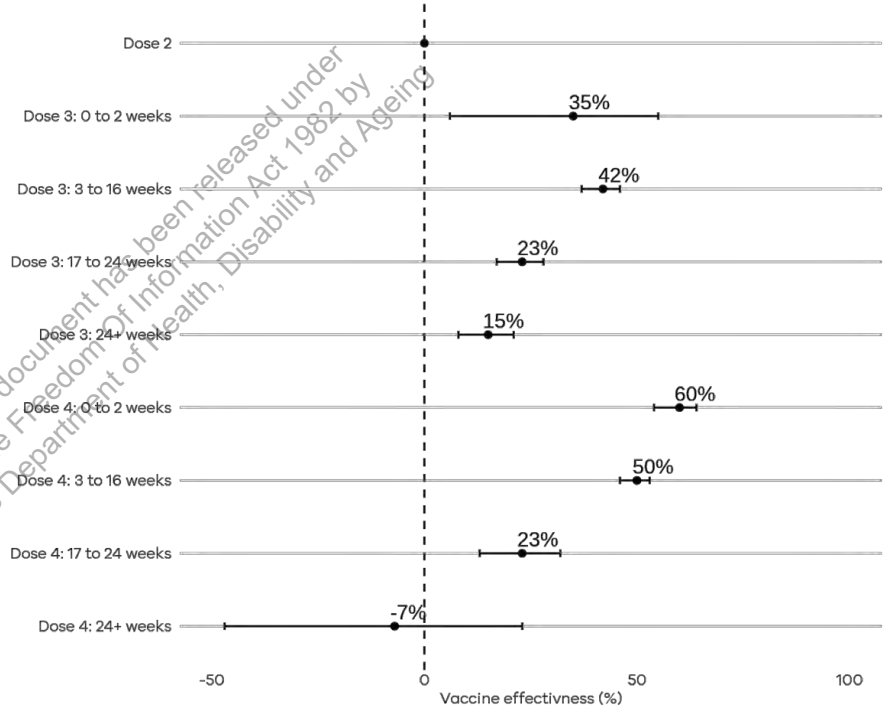
^Time at risk calculates the total for the group in the data period. For a given subject and dose started at date of dose administration or start of study period, whichever occurred later, and ended at next dose administration date, end of study period or date of death, whichever occurred first.

Vaccine Effectiveness: modelled in Victoria

Based on Cox-regression modelling of Victorian data, the instantaneous risk of hospitalisation for persons aged 60+ was significantly reduced for people that received three and four doses

However, the protective effect of booster doses progressively waned as time from administration passed

- Beyond six months from administration the relative effectiveness (rVE) of the third dose was 15% (95% CI:7% to 21%).
- The rVE for a four dose beyond six months from administration was not significant at a p = 0.05 level.



Waning Immunity in Victoria

A significant proportion of Victorians are more than 180 days from their last recorded immune event (infection or vaccination).

Over two thirds of the most at risk group (65+ years) have not had an infection notified or a vaccine in the last 180 days.

- While this proportion is an upper bound estimate due to low case ascertainment, it will increase substantially in the coming months as a majority of this group received their fourth vaccine dose before the end of July 2022.

Of age groups in Victoria 16 or older, 16 to 29 year-olds have the highest proportion without a recent immune event.

120 days			
Age group	**Victorians without a recent immune event**	**Population (from AIR)**	**Proportion with waned immunity**
16-29	1,121,742	1,185,018	95%
30-49	1,657,949	1,814,819	91%
50-64	1,000,468	1,131,047	89%
65+	1,005,732	1,105,291	91%

180 days			
Age group	**Victorians without a recent immune event**	**Population (from AIR)**	**Proportion with waned immunity**
16-29	1,017,000	1,185,018	86%
30-49	1,384,423	1,814,819	76%
50-64	700,878	1,131,047	62%
65+	760,797	1,105,291	69%

Conclusions

- COVID-19 continues to pose a significant public health challenge in Victoria. It is highly likely that Victoria will continue to experience regular waves of COVID-19 transmission, hospitalisations and deaths for the next few years.
- The protective effect of booster doses against severe outcomes is significant but wanes over time, with the 6-month efficacy of 3rd and 4th doses close to that provided by 2 doses.
- Third and fourth dose vaccination levels are lower for males, people living in areas of disadvantage and for Aboriginal Victorians. Areas of greater social disadvantage have seen a disproportionate rate of COVID-19 mortality and excess mortality in 2022.
- The vast majority (74%) of Victorian adults have not had their most recent vaccine dose or a recorded COVID-19 infection in the last 6 months. There has been good uptake of a boosters for those greatest at risk.

<u>Based on local and external evidence (slides 13 and 14) Victoria asks ATAGI to:</u>

- Consider broadening the goal of the vaccination program in Australia to include vaccination as a tool used in combination with other strategies to reduce infection and Long COVID, not only severe disease. Vaccination should be coupled with intensified engagement and communication and it is readily deployable as part of a multi-layered mitigation strategy.
- Urgently consider a recommendation of a **booster dose every 6 months** (currently using an updated bivalent vaccine) for cohorts at greatest risk of severe disease (>50 years) and healthcare workers.

Appendix

Evidence from external sources to support additional vaccination

Bivalent effectiveness	Hospitalisation	Symptomatic infection
BA.4/BA.5 bivalent booster	**65+ years:** VE 73-84% against hospitalisation compared to monovalent booster or no vax (last booster received 2 – 12+ months ago, respectively) **18+ years:** VE 42% compared with ≥2 monovalent vaccines received 8-10 months earlier **Study period:** Sept 8- Nov 30 2022: BA.4/BA.5 and BA.1/BQ1.1 predominant *CDC data Dec 16	**65+ years:** rVE of booster compared to **≥2 monovalent doses at 2-3 months and ≥8 months**: 28% and 43%, respectively **50 – 64 years:** rVE (As above) 31% and 48% respectively **18 – 49 years:** rVE (As above) 30% and 56% **Study period:** Sept 14 – Nov 11 2022: BA.4/BA.5 and BA.1/BQ1.1 predominant *CDC data Dec 2
BA.1 bivalent booster	**50+ years:** VE 57% against hospitalisation compared with ≥2 vaccine doses received ≥6 months earlier **Study period:** Sept 2022: BA.4/BA.5 and sublineages predominant *UK Gov data Dec 1	

International recommendations on regular booster doses	
Israel	**Regular bivalent booster doses** at least 3 months since last vaccination **Recommended cohorts:** • Aged 65 years and over • At-risk groups for severe illness (https://corona.health.gov.il/en/testing-lobby/risk-groups/) • Healthcare workers • Caregivers of those belonging to at-risk groups
Canada	**Regular bivalent booster doses** at least 6 months since last vaccination/COVID-19 infection **Recommended cohorts:** • Aged 65 years and over • ≥ 12 years and at increased risk of severe illness

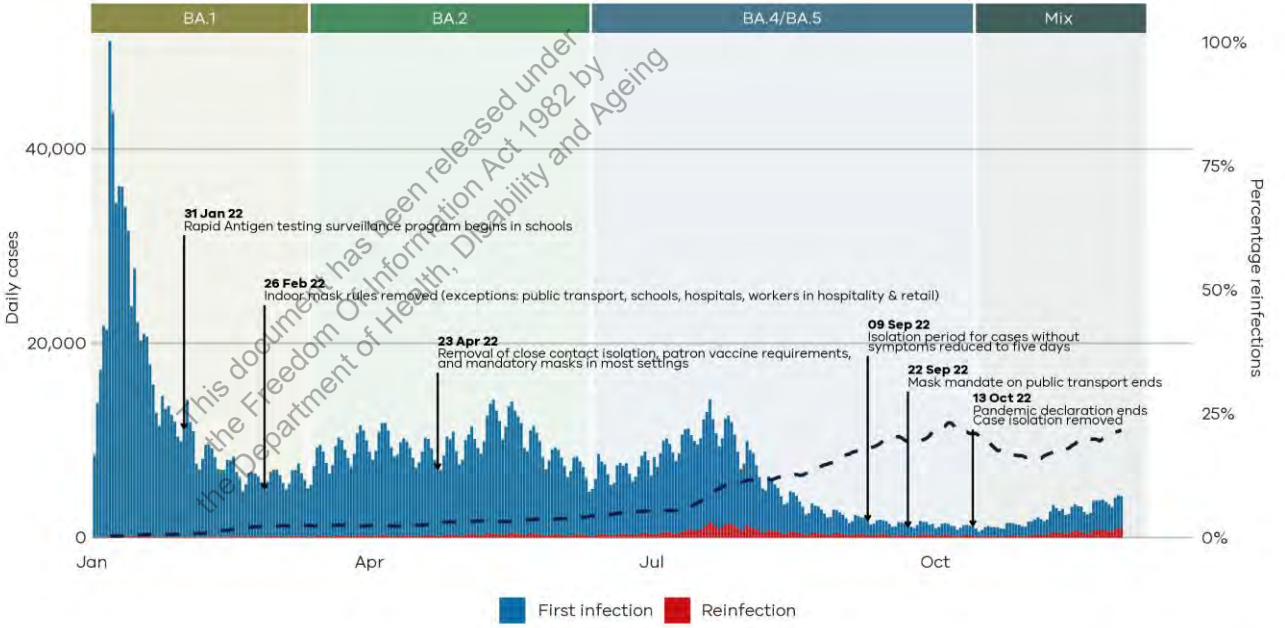
Long COVID - Evidence from external sources to support additional vaccination

Numerous studies have found that vaccination reduces likelihood of Long COVID and post COVID complications.

Author	Key Findings
Azzolini et al	Higher vaccine doses associated with reduced risks. 42% of unvaxxed, 30% single dose, 17% double, 15% triple dose had long covid.
Taquet et al	Vaxxed had 30% lower risks of death/resp failure, 28% less ventilator, 25% less ICU, 19% less blood disorders.
Al-Aly et al	Vaxxed had 35% lower deaths, 53% lower stroke, 51% lower heart disease, 40% lower lung disease
Arjun et al	2 doses had between 2.05 to 2.32 odds of getting long COVID.
Senjam et al	2 doses had between 35% to 45% lower risks of long COVID.
Kuodi et al	2 doses had 36% to 73% lower risks for most long COVID symptoms. >60 yo, 2 doses were 68% more likely to fully recover.
Simon et al	Receiving a dose before infection had 78% reduced odds of any long COVID symptom and 88% reduced odds of more than 1 long COVID symptom.
Ayoubkhani et al	Any symptom: First dose 12.8% reduced odds, then uncertain trajectory Second dose 8.8% reduced odds, then 0.8% per week Severe symptom: First dose 12.3% reduced odds, then uncertain trajectory Second dose 9.1% reduced odds, then 0.55% per week
Tran et al	16.6% vaxxed had full recovery vs 7.5% controls 38.9% had neg impacts vs 46.4% controls 5.7% of vaxxed reported serious side effects after vax
Arnold et al	14.3% of symptom worsened in unvaxxed vs 5.6% vaxxed 15.4% of symptom improved in unvaxxed vs 23.2% vaxxed
Gaber et al	72% had immediate but self-limiting effects Weeks after vax, 21% improved, 67% no change, 12% worsened
Scherlinger et al	31% of vaxxed worsened, 21.8% of vaxxed improved Vax impact lasted >2weeks for 67.8%.
Strain et al	56% to 66% improved, 12% to 19% worsened. 50% of cases who worsened had improved after a few days, likely vax rxn.
Simon et al	0 to 4 weeks – 61.8% reduced odds of any symptom, 4 to 8 weeks 46.5% reduced odds, 8 to 12 weeks 25.3% reduced odds.

COVID-19 Cases in Victoria in 2022

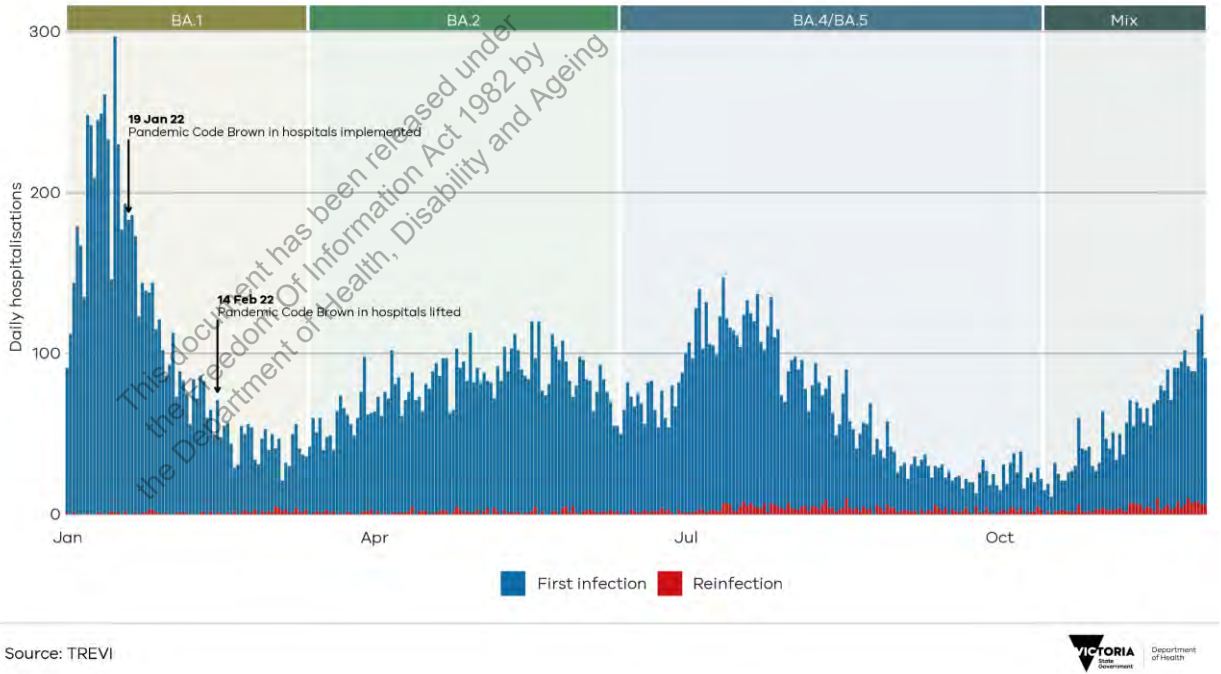
- **2,557,066 cases were notified to the department in 2022 to 30 November.**
- Case ascertainment has likely fallen across the year and the true number of infections may be 7 to 10 times higher.
- Reinfections are estimated to make up approximately 19% of cases in the current wave, however changes in case ascertainment over time and testing/reporting behaviours lead to a high level of uncertainty. Additionally, the reinfection definition changed multiple times.



Source: TREVI

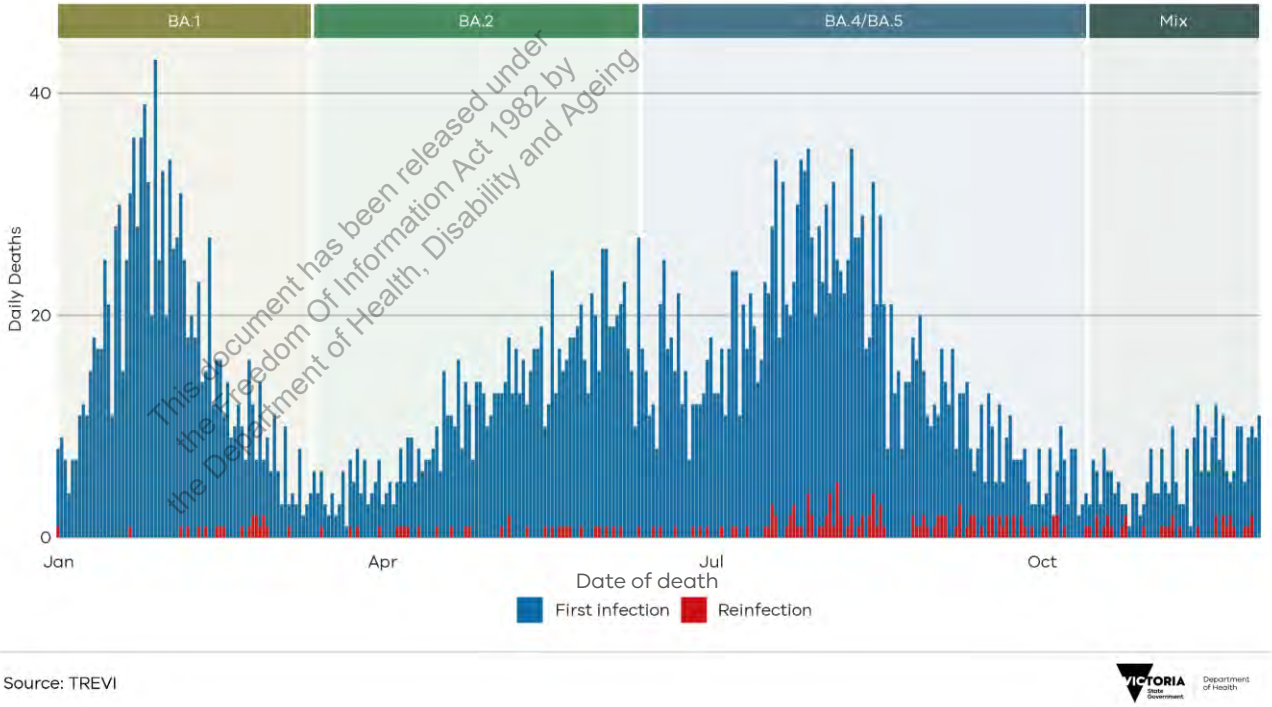
COVID-19 Hospital admissions in Victoria in 2022

- **The highest number of hospital admissions was seen in January in the Omicron wave.**
- Older Victorians aged 65+ comprised the majority (59%) of hospital admissions. This age group had the highest hospitalisation cumulative incidence per population (13.9 per 1,000 population in 2022).
- Adults under 65 and children had substantially lower hospitalisation incidence.



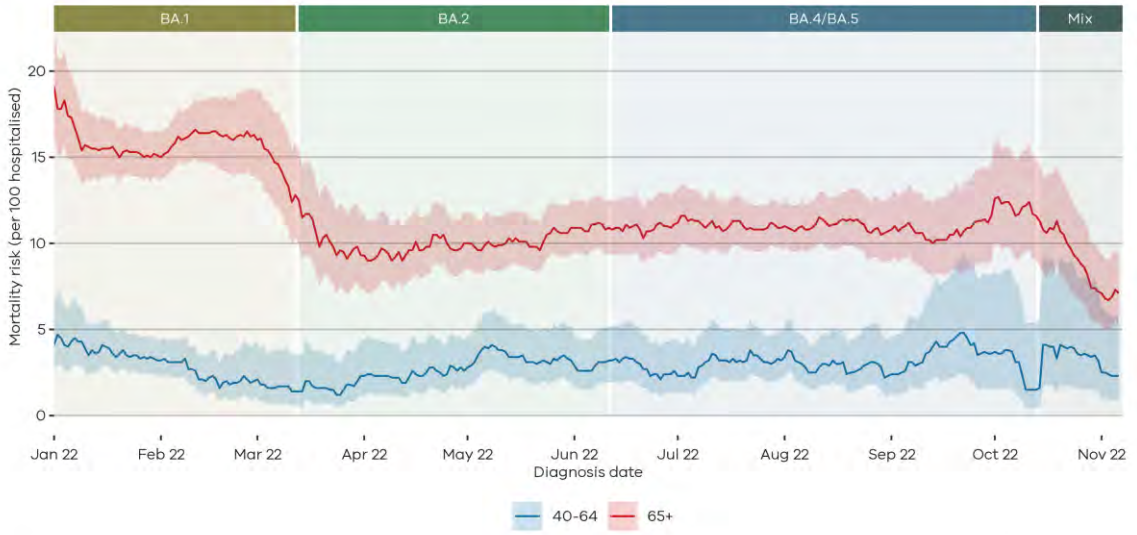
COVID-19 Deaths in Victoria in 2022

- **In 2022 to 30 November, there have been 4,470 attributable to COVID-19**
- The majority of these deaths were aged 65 years and older (93%)
- 44% of these deaths were known to be aged care residents
- 4.5% of these deaths were reported as reinfections



COVID-19 Mortality in Hospitalised Cases in 2022

- **In hospital mortality has remained largely stable throughout 2022 to date.**
- Hospitalised patient mortality is a preferred measure as it is less subject to variable case ascertainment, however it is sensitive to changes in admission criteria and patient demographics



Source: TREVI

Vaccine uptake

Age group	Dose 1^	Dose 2^	Dose 3^	Dose 4^
0-4	0% (+0.01%)	0% (+0.00%)	0% (+NA)	NA (+NA)
5-11	63% (+0.16%)	48% (+0.25%)	0% (+0.01%) Low eligibility	0% (+0.00%)
12-15	100% (+0.03%)	98% (+0.08%)	2% (+0.05%)	0% (+0.00%)
16-29	94% (+0.03%)	92% (+0.02%)	53% (+0.30%)	1% (+0.12%)
30-49	98% (+0.02%)	97% (+0.01%)	68% (+0.16%)	12% (+0.97%)
50-64	99% (+0.03%)	98% (+0.01%)	81% (+0.10%)	32% (+1.56%)
65+	100% (+0.03%)	100% (+0.01%)	92% (+0.07%)	70% (+0.89%)

^ Current vaccination coverage (change in coverage in last 30 days)

Likelihood of receiving a third dose of COVID vaccine

There are significant differences between the characteristics of Victorians receiving a third dose (conditional on receiving a second dose):

Older Victorians were more likely to receive a third dose

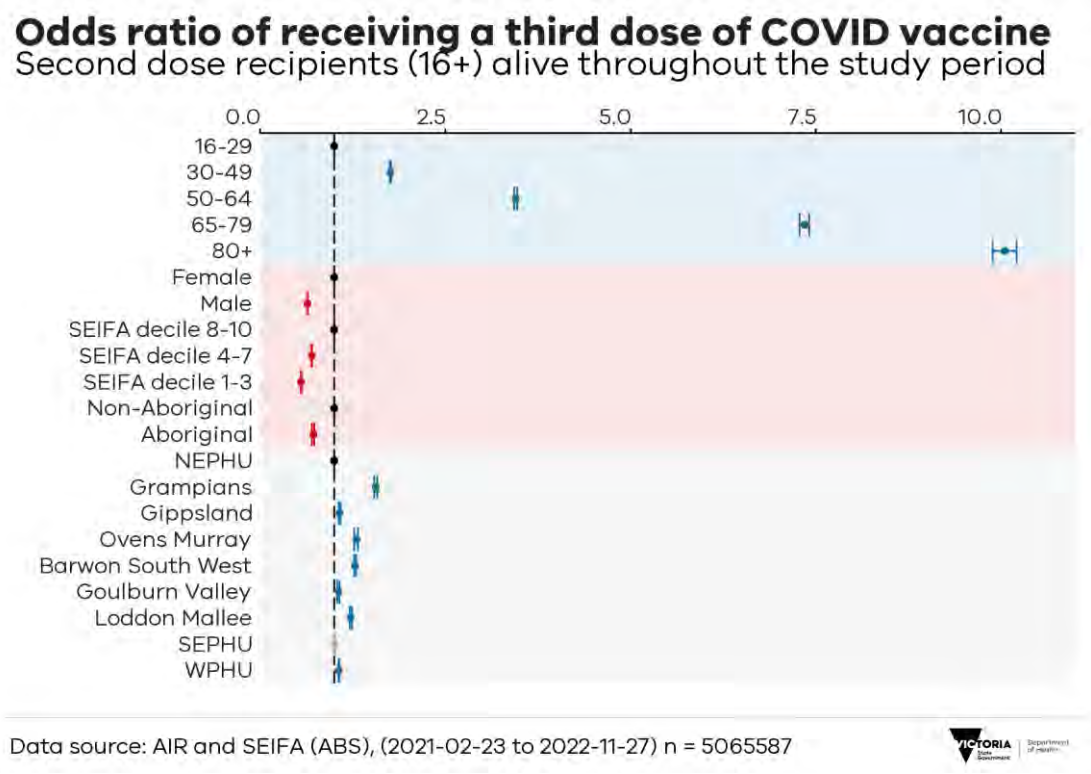
- 1.8 times more likely for 30-49 year old's
- 3.5 times more likely for 50-64 year old's
- 7.4 times more likely for 65-79 year old's
- 10 times more likely to 80+ year old's

Males were 36% less likely to receive a third dose

Victorians from lower SEIFA deciles were less likely to receive a third dose

- 30% less likely for SEIFA deciles 4-7
- 45% less likely for SEIFA deciles 1-3

Aboriginal Victorians were 29% less likely to receive a third dose.



Note: data only includes individuals vaccinated with a second dose over 120 days ago

Likelihood of receiving a fourth dose of COVID vaccine given receipt of a third dose

There are significant differences between the characteristics of Victorians receiving a fourth dose (conditional on receiving a third dose):

Older Victorians were more likely to receive a fourth dose

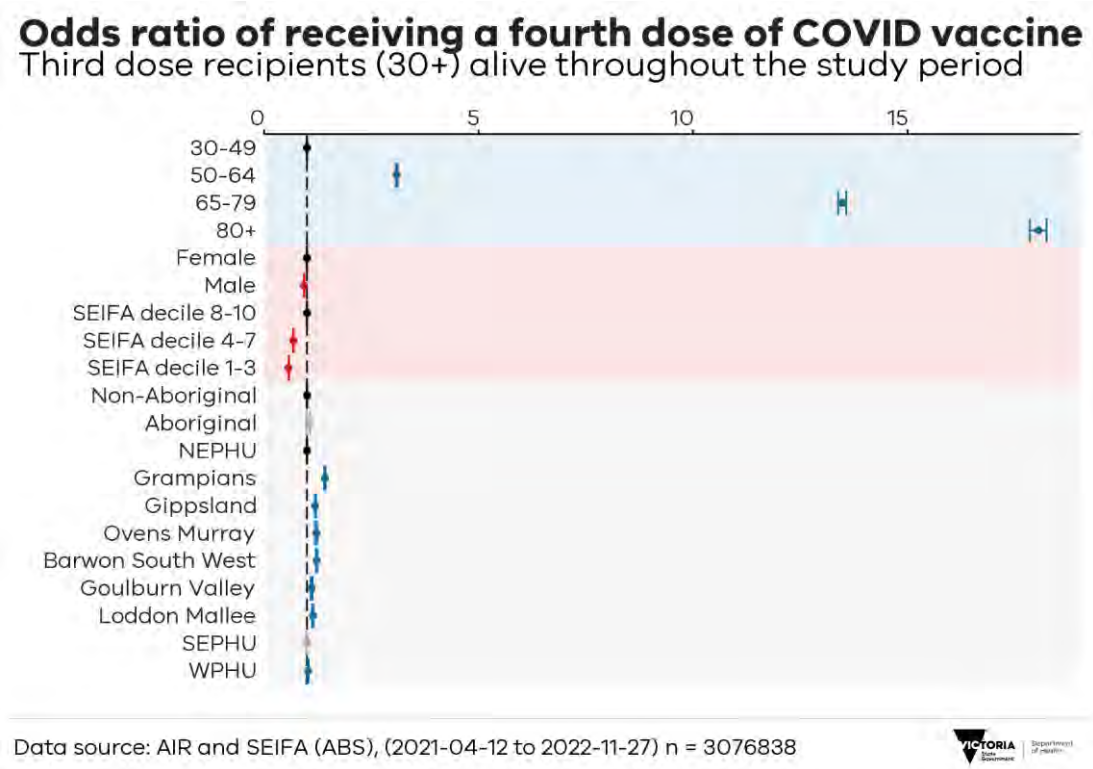
- 3.1 times more likely for 50-64 year olds
- 13.5 times more likely for 65-79 year olds
- 18 times more likely for 80+ year olds

Males were 7% less likely to receive a fourth dose

Victorians from lower SEIFA deciles were less likely to receive a fourth dose

- 32% less likely for SEIFA deciles 4-7
- 43% less likely for SEIFA deciles 1-3

Aboriginal Victorians were equally likely to receive a fourth dose given they received a third dose.



Note: data only includes individuals vaccinated with a third dose over 120 days ago

rVE methods

Study type: retrospective cohort study.

Study population: Victorians aged 60yo and above with 2, 3 or 4 doses of a COVID-19 vaccine.

Study period: 1 Apr 2022 to 15 Oct 2022.

Data sources: AIR, Victorian Admitted Episodes Dataset (VAED), TREVI, ABS. Multistage deterministic data linkage.

Statistical analysis: Cox proportional hazards model. Outcome variable was Covid-19 hospitalisation or death. Explanatory variables were vaccination status, age, sex, IRSD and history of hospitalisation. Individuals enrolled at start of study period and left truncated on date of second dose. Observations were right censored at time of fourth dose or end of study period, whichever occurred first. Vaccination was treated as a time-varying covariate.

$$H(t,x) = h_0(t)exp^{\beta_1 Age + \beta_2 Sex + \beta_3 Dose_3 + \beta_2 HistHosp + \beta_5 IRSD}$$

Relative vaccine effectiveness was calculated as (1 – aHR) * 100 %.

Limitations: Selection bias arising from non-random censoring (i.e. at time of fifth dose)? Confounding effect of comorbidities and occupation only partially accounted for.

rVE Results

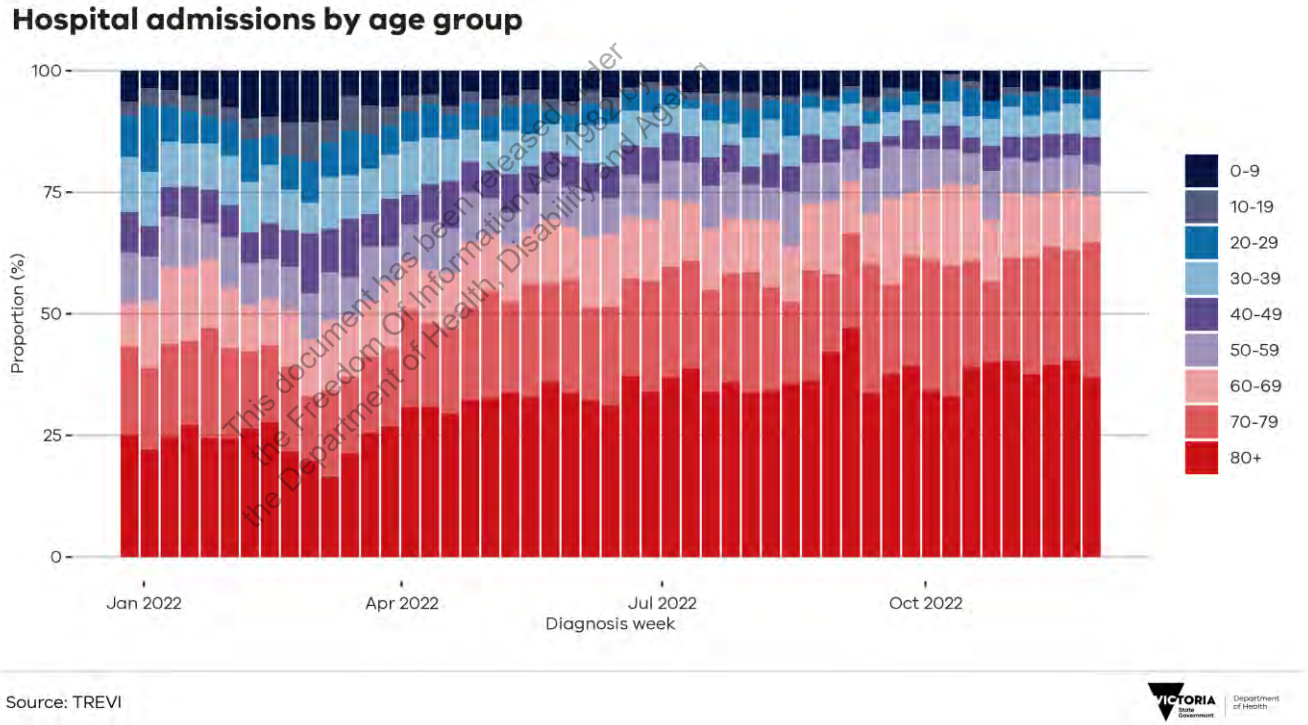
Number of severe outcome events (hospitalisation or death), person years and adjusted hazard ratios by vaccine dose and time from dose administration.

Vaccination status	N (events)	Person Years	Adjusted Hazard Ratio* (95% CI)
Dose 2	1418	69,476	Ref.
Dose 3: 0 to 2 weeks	29	2060	0.652 (0.452 to 0.943)
Dose 3: 3 to16 weeks	1358	110,947	0.582 (0.536 to 0.631)
Dose 3: 7 to 24 weeks	1857	99,738	0.77 (0.718 to 0.827)
Dose 3: 24+ weeks	1163	77,055	0.853 (0.787 to 0.926)
Dose 4: 0 to 2 weeks	302	27,385	0.403 (0.356 to 0.457)
Dose 4: 3 to 16 weeks	2133	174,133	0.503 (0.469 to 0.539)
Dose 4: 17 to 24 weeks	423	47,876	0.768 (0.679 to 0.868)
Dose 4: 24+ weeks	41	3483	1.066 (0.773 to 1.47)

*** Adjusted for age, sex, socioeconomic status and recent history of hospitalisation.**

Age distribution of hospitalisations over time

Older Victorians (aged 60+ years) comprised the majority of hospital admissions in 2022 (to 30 November).



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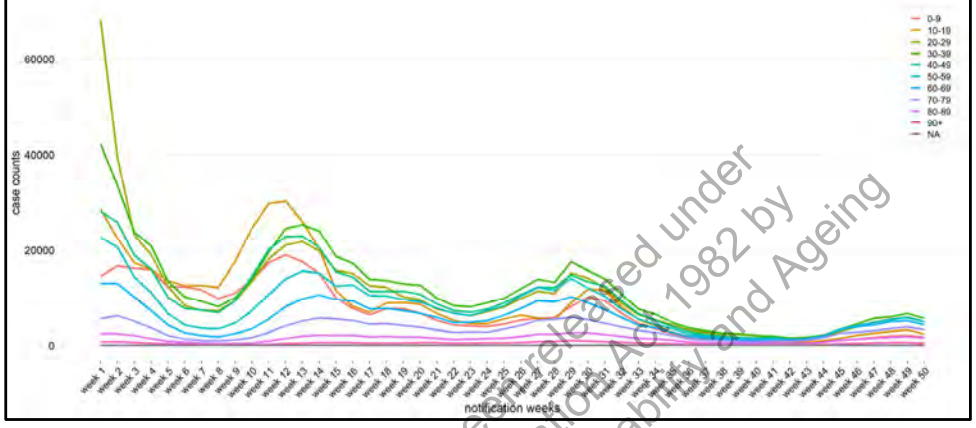
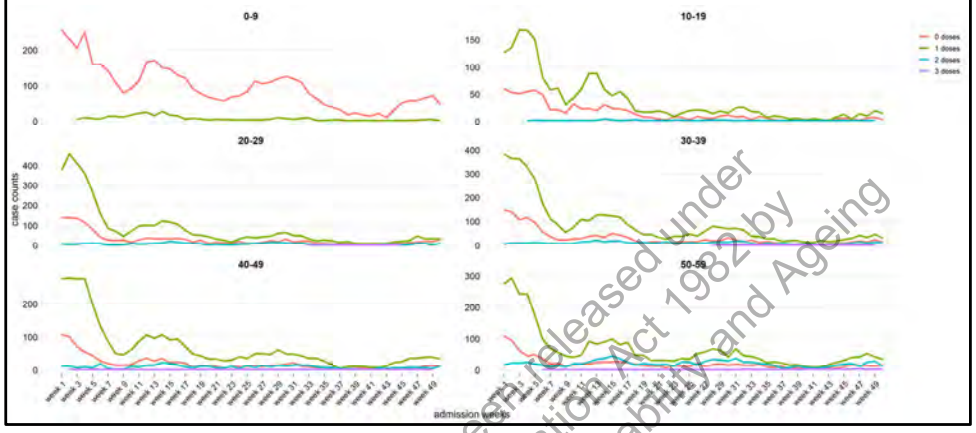
Weekly notifications by 10-year age group, NSW 02 Jan to 14 Dec 2022



Hospitalisations by 10-year age group and vaccination status



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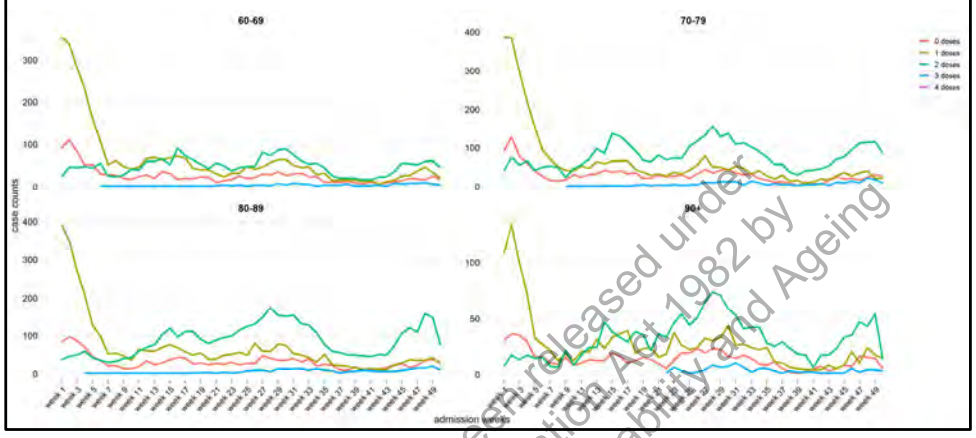
Hospitalisations by 10-year age group and vaccination status



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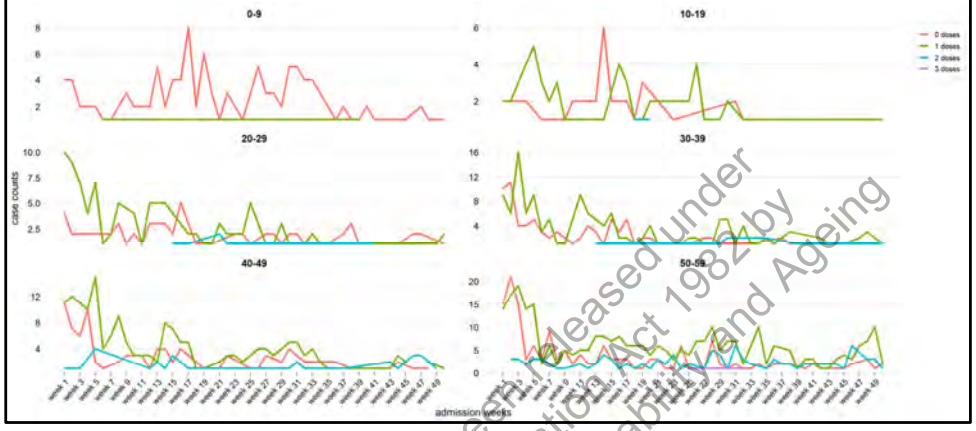
ICU admissions by 10-year age group and vaccination status



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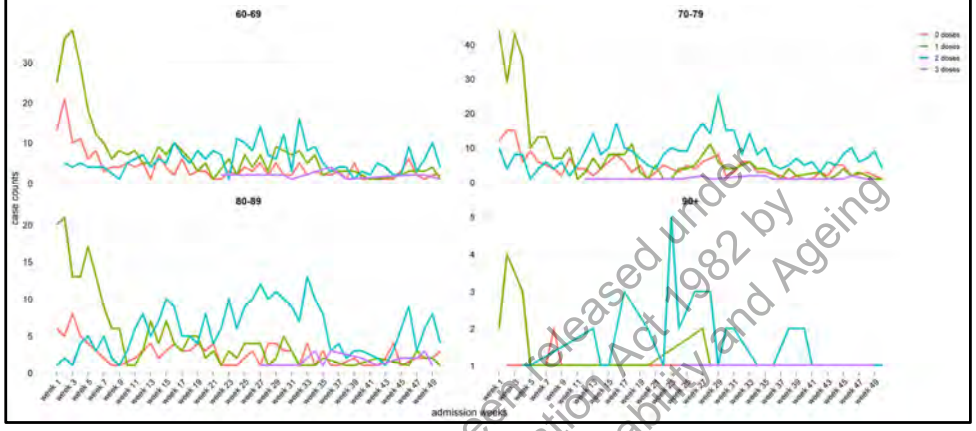
ICU admissions by 10-year age group and vaccination status



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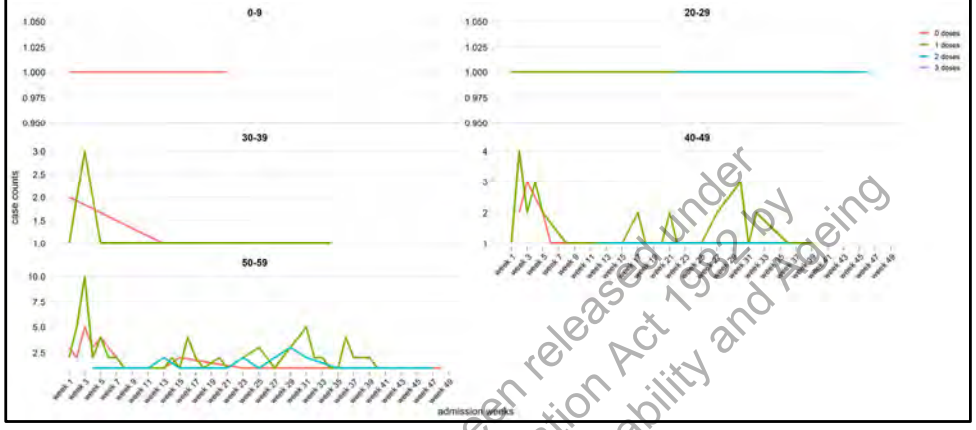
Deaths by 10-year age group and vaccination status



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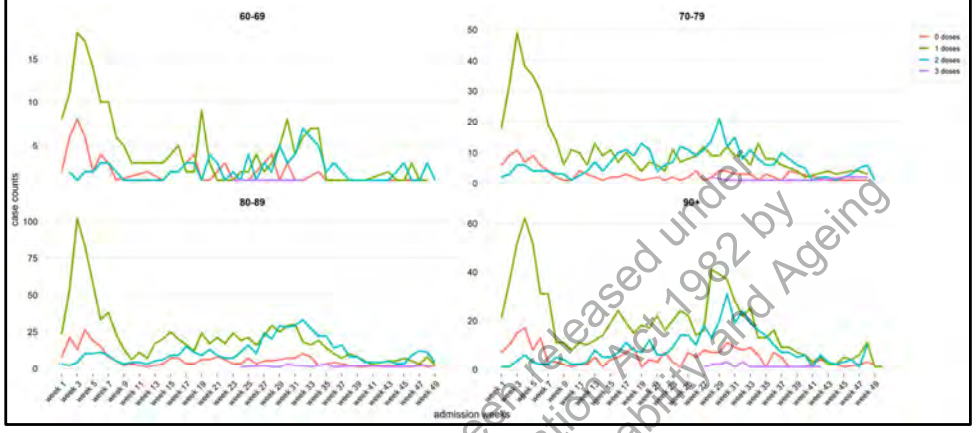
Deaths by 10-year age group and vaccination status



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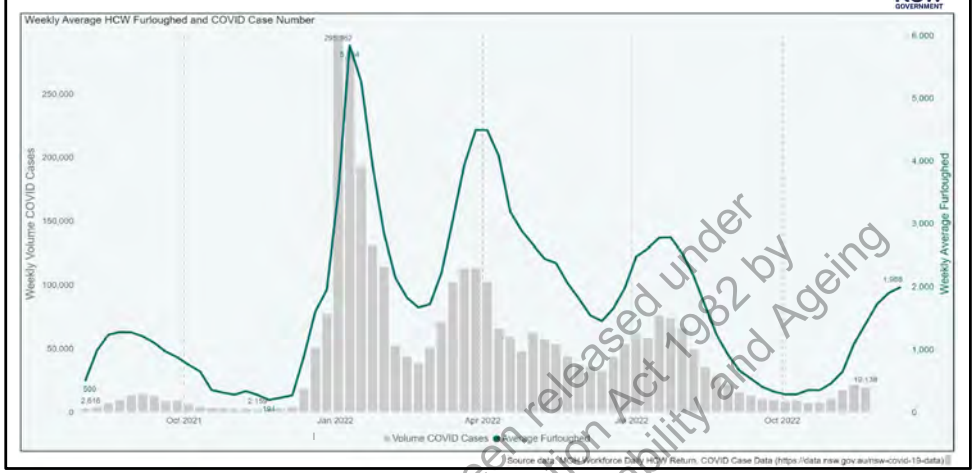
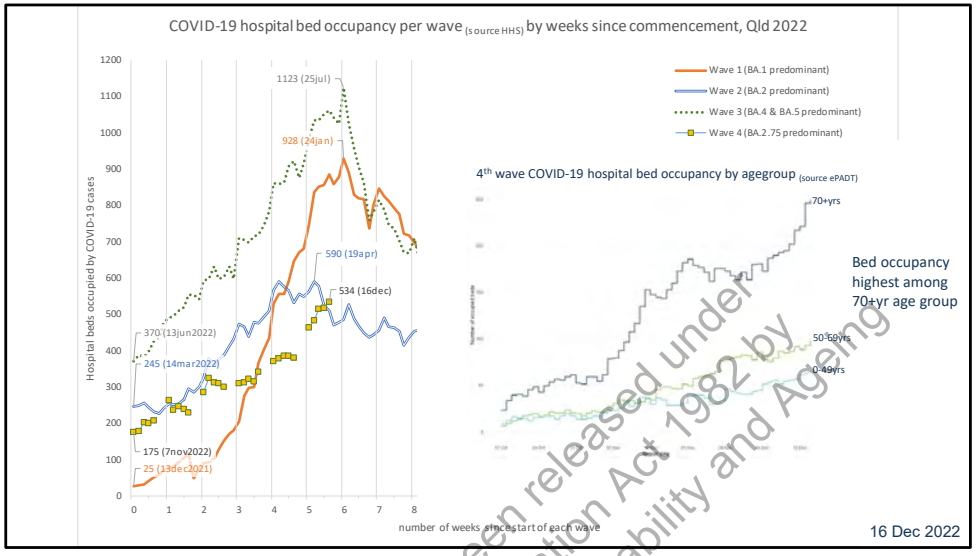
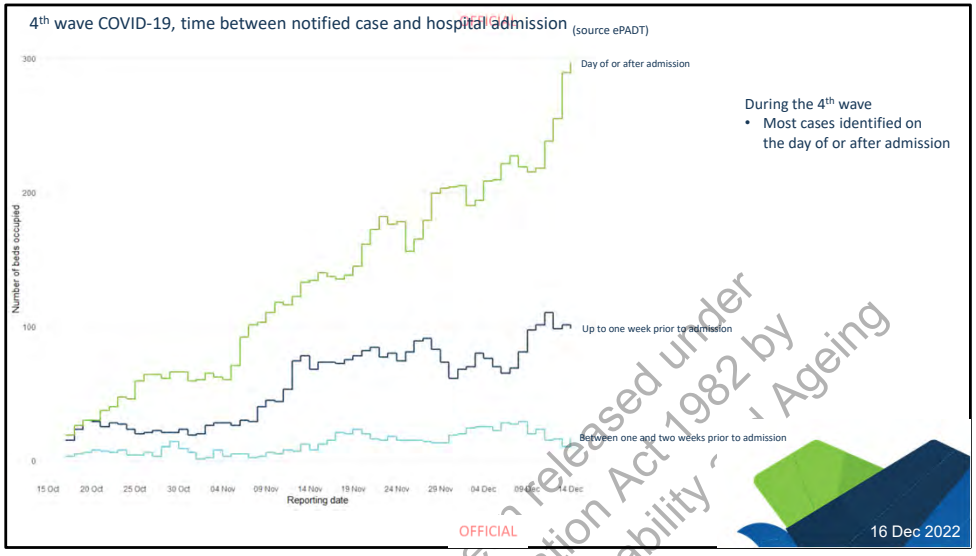
NSW HCW furloughing trends

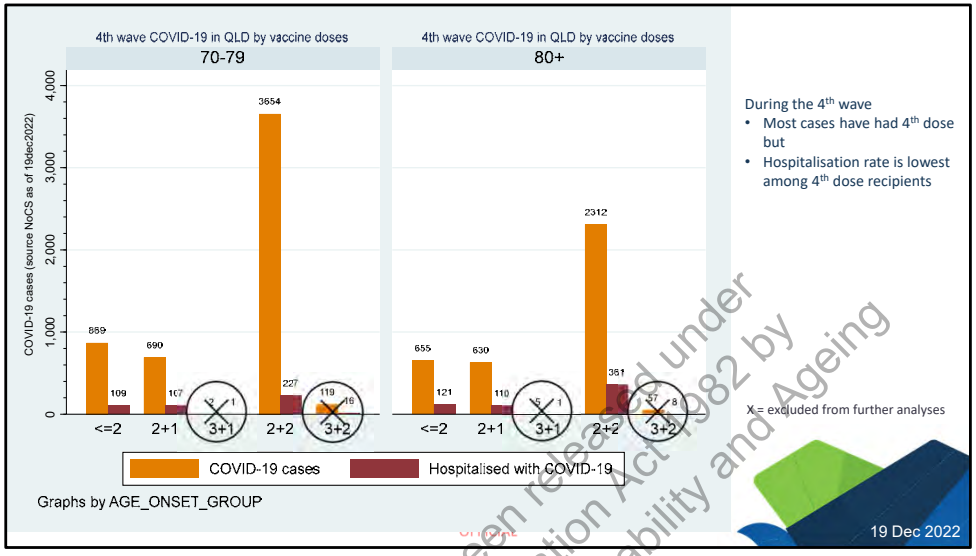


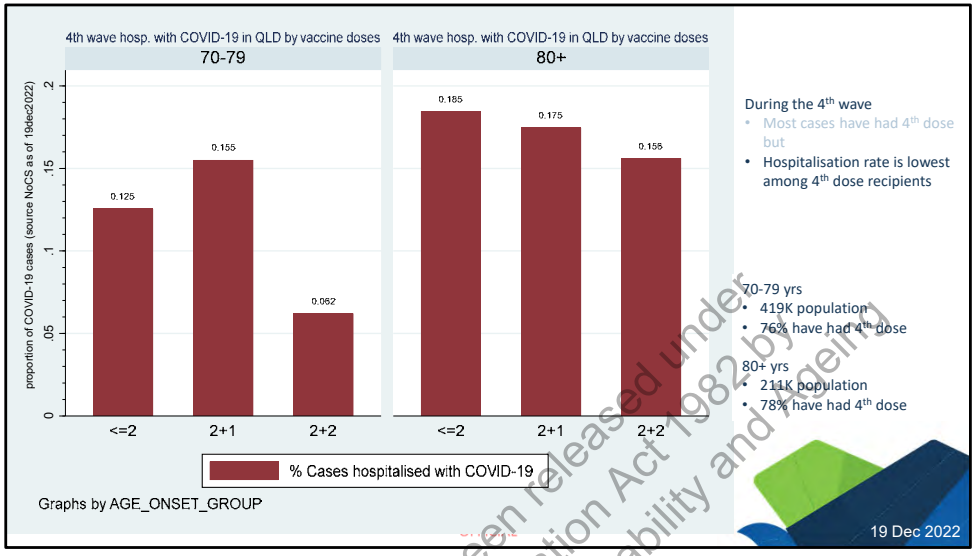
Data limitations

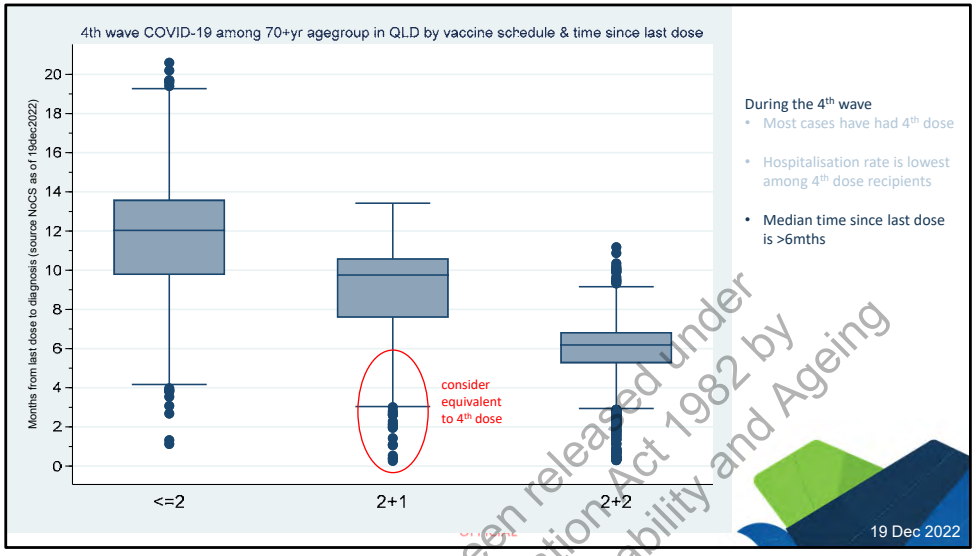
- Data is from Notifiable Conditions Information Management System and has not been linked to other sources
- Hospitalisation and ICU admissions data where the only positive test is a RAT are not imported into NCIMS
- Case vaccination data where the only positive test is a RAT are not imported into NCIMS
- There is no distinction between people admitted to hospital or ICU due to COVID or with COVID
- Additional vaccination data may be obtained with linking to the AIR
- Data indicative of trends only and should not be used to assess outcomes related to vaccine efficacy or clinical severity











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Primary Question

Among notified cases aged 70+ years during the 4th wave, what is the effectiveness of a 4th dose (or equivalent) in preventing

a) hospitalisation with COVID-19 as an outcome?

predictors included in logistic regression model
- Age80+, sex, test type (PCR vs RAT)
- excluded
  RACF resident, reinfection,
  time since last dose (<6m vs 6m or more)

- 10% if had 4th dose $_{617/6170}$ vs 16% if not $_{418/2640}$
- **VE 33% (95%CI 22%,42%)**
  OR_{adj} 0.67 (95%CI 0.58,0.78)

b) death with COVID-19 within 28 days?

predictors included in logistic regression model
- Age80+
- excluded
  RACF resident, reinfection,
  time since last dose (<6m vs 6m or more),
  sex, test type (PCR vs RAT)

- 0.5% if had 4th dose $_{29/6170}$ vs 0.8% if not $_{20/2640}$
- **VE 32% (95%CI -20%,62%)**
  OR_{adj} 0.68 (95%CI 0.38,1.20)

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19 Dec 2022

Logistic regression — Number of obs = 8,775; LR chi2(4) = 97.89; Prob > chi2 = 0.0000; Log likelihood = -5300.7578; Pseudo R2 = 0.0091

dose4th	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
hosp	.6718531	.0497712	-5.37	0.000	.5810545	.7768403
Age80	.8638442	.0416624	-3.03	0.002	.785928	.949485
female	.8895868	.04211	-2.47	0.013	.8107657	.9760707
PCR	.803458	.0411077	-4.28	0.000	.7267964	.8882057
_cons	3.125333	.1423962	25.01	0.000	2.858341	3.417266

Logistic regression — Number of obs = 8,810; LR chi2(2) = 22.33; Prob > chi2 = 0.0000; Log likelihood = -5368.0038; Pseudo R2 = 0.0021

dose4th	Odds Ratio	Std. Err.	z	P>|z|	[95% Conf.	Interval]
deaths	.6761245	.197741	-1.34	0.181	.381138	1.19942
Age80	.810782	.0382372	-4.45	0.000	.7391978	.8892985
_cons	2.557591	.0788023	30.48	0.000	2.407712	2.716799

Note: _cons estimates baseline odds.

COVID ATAGI#95

ATAGI 95 meeting

16/06/2023

Prepared by:
s47F

NCIRS
National Centre for Immunisation Research and Surveillance

Holding statement

- Aim is to reiterate the importance of a booster in older or high-risk adults who haven't yet received one in 2023
- No new advice. 'Advice regarding the need for further doses will be issued as required.'
- Questions:
  - Move away from the term 'booster' and refer to as 'dose' instead? DW/KG
  - 'recommend' people follow previous advice, or 'strongly recommend'? AC/KG

Plan for ATAGI #96

- NITAG summary of 2023 booster strategies
- XBB monovalent vaccine composition recommendations (WHO/EMA/FDA)

- Update on waning vaccine effectiveness of COVID-19 boosters
  - Presentation from s47F, NCIRS Population Health

- Summary of relevant NNDSS data (hospitalisations, ICU admissions, deaths in older adults over the past 6 months) to identify highest risk cohort

- Any other information that members would like presented (e.g. SPRINT-SARI data)?

AIR-MADIP COVID-19 Vaccine Effectiveness Study Collaboration

s47F

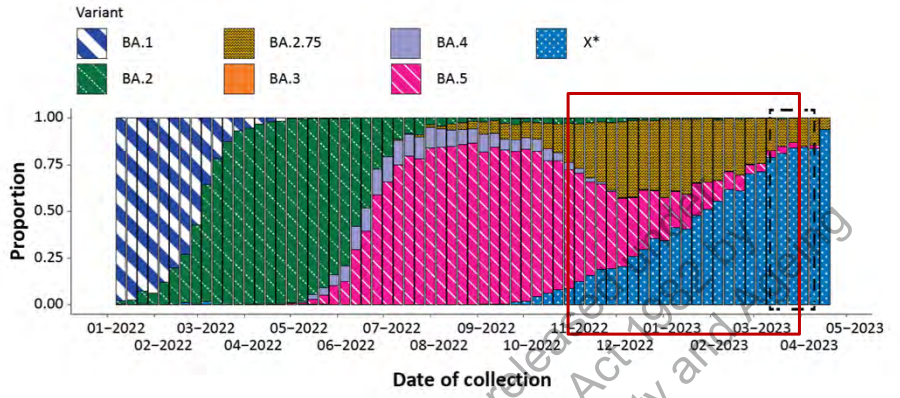
Collaborative analysis involving:
NCIRS, UNSW, ANU, UniSA, Bond University, Health Economics and Research Division, Health Protection

Update on COVID-19 vaccine effectiveness

- Primary outcome: COVID-19 mortality as defined by ABS from death certification
- Study population: 2021 Census population who are present in AIR-MADIP spine,
- Analyses focus on calendar periods approx. corresponding to Omicron 'waves':
  - B.A.1/2 (1 Jan – 31 May 2022);
  - B.A.4/5 (1 June – 30 Nov 2022);
  - **Recombinant (1 Nov 2022 – 31 Mar 2023)**
- Retrospective cohort methods: Survival analysis for cause-specific mortality and all-cause mortality with exposure (vaccination) as a time-varying covariate;
- Due to fewer deaths in younger age groups **analyses focus on 65+ years**
- Analyses adjusted for: age, sex, jurisdiction of residence, household equivalised income, co-morbidities (based on Rx risk score), number of GP visits in year prior to study entry, receipt of influenza vaccination in 2021 or 2022

Page 2

Figure 7: Omicron sub-lineage proportions in Australia since 1 January 2022 by sample collection date [a, b, c]



Comm Dis Intell

Page 3

COVID-19 vaccine effectiveness by dose, time since receipt and pandemic wave

Age 65+ years

	Rate (per 100-PY) (95% CI)	VE (%) (95%CI)
01JAN22 – 31MAY22		
Unvaccinated	0.929 (0.812; 1.063)	ref
Dose2 8-90 days	0.279 (0.217; 0.359)	72.7 (67.8; 76.9)
Dose2 91-180 days	0.326 (0.285; 0.373)	65.9 (61.7; 69.7)
Dose2 >180 days	0.927 (0.794; 1.082)	34.0 (25.5; 41.6)
Dose3 8-90 days	0.070 (0.060; 0.081)	93.4 (92.6; 94.2)
Dose3 91-180 days	0.164 (0.141; 0.191)	85.1 (82.9; 86.9)
Dose3 >180 days	1.139 (0.536; 2.417)	63.4 (42.9; 76.6)
Dose4 8-90 days	0.094 (0.058; 0.151)	92.6 (90.0; 94.5)
Dose4 >90 days	0.386 (0.053; 2.831)	73.3 (16.8; 91.4)
01JUN22 – 30NOV22		
Unvaccinated	0.490 (0.399; 0.601)	ref
Dose2 8-90 days	1.218 (0.471; 3.149)	13.9 (-36.6; 45.7)
Dose2 91-180 days	0.595 (0.337; 1.051)	21.8 (-4.3; 41.4)
Dose2 >180 days	0.209 (0.162; 0.269)	49.6 (41.0; 56.9)
Dose3 8-90 days	0.232 (0.142; 0.381)	74.9 (67.5; 80.6)
Dose3 91-180 days	0.207 (0.172; 0.248)	68.6 (63.9; 72.7)
Dose3 >180 days	0.205 (0.172; 0.245)	56.0 (49.6; 61.6)
Dose4 8-90 days	0.134 (0.114; 0.156)	84.3 (82.0; 86.2)
Dose4 91-180 days	0.094 (0.078; 0.113)	74.7 (70.7; 78.2)
Dose4 >180 days	0.128 (0.086; 0.189)	56.3 (44.0; 65.9)

Vaccine effectiveness adjusted for age, sex, jurisdiction, household income, co-morbidities, GP visits, 2022 flu vaccine receipt

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4445191

Page 4

s47B(a)

COVID-19 vaccine effectiveness by time since booster (3rd, 4th, 5th dose) receipt, 65+ years

01NOV22-31MAR23	Person-time rate (per 100-Person Year)	VE (%) (95%CI)
Unvaccinated	0.268 (0.205; 0.351)	ref
Dose2	0.109 (0.078; 0.154)	46.3(32.8; 57.1)
Booster 8-90 days	0.059 (0.033; 0.105)	74.7 (64.9; 81.7)
Booster 91-180 days	0.123 (0.100; 0.150)	62.9 (55.1; 69.4)
Booster 181-270 days	0.134 (0.117; 0.153)	59.1 (51.2; 65.6)
Booster >270 days	0.091 (0.076; 0.110)	52.9 (43.5; 60.8)
(events=2,015)		
(Person-time=1,673,073)		

COVID-19 mortality rate in unvaccinated population aged 65+ years per 100 p-years

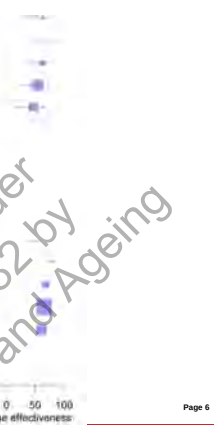
Jan – May 22 0.93
Jun – Nov 22 0.49
Nov 22 – Mar 23 0.27

Vaccine effectiveness adjusted for age, sex, jurisdiction, household income, co-morbidities, GP visits, 2022 flu vaccine receipt

Page 5

COVID-19 vaccine effectiveness by time since booster receipt 65+ years

01NOV22-31MAR23	Person-time rate	
Age group 65-74 yo	**(per 100-Person Year)**	**VE (%) (95%CI)**
Unvaccinated	0.044 (0.020; 0.095)	ref
Dose2	0.013 (0.005; 0.034)	63.5 (31.9; 80.4)
Booster 8-90 days	NC	78.6 (37.2; 91.3)
Booster 91-180 days	0.027 (0.015; 0.050)	61.8 (33.6; 78.0)
Booster 181-270 days	0.029 (0.020; 0.044)	54.4 (24.2; 72.6)
Booster >270 days	0.026 (0.016; 0.042)	43.4 (11.9; 67.4)
(events=240)		
(Person-time=923,983)		
Age group 75+ yo		
Unvaccinated	0.616 (0.464; 0.817)	ref
Dose2	0.296 (0.206; 0.426)	49.2 (35.5; 60.0)
Booster 8-90 days	0.116 (0.064; 0.210)	78.3 (69.4; 84.7)
Booster 91-180 days	0.244 (0.198; 0.302)	68.4 (61.3; 74.2)
Booster 181-270 days	0.247 (0.215; 0.284)	65.1 (56.3; 71.2)
Booster >270 days	0.179 (0.147; 0.219)	60.5 (52.0; 67.5)
(events=1,800)		
(Person-time=749,091)		

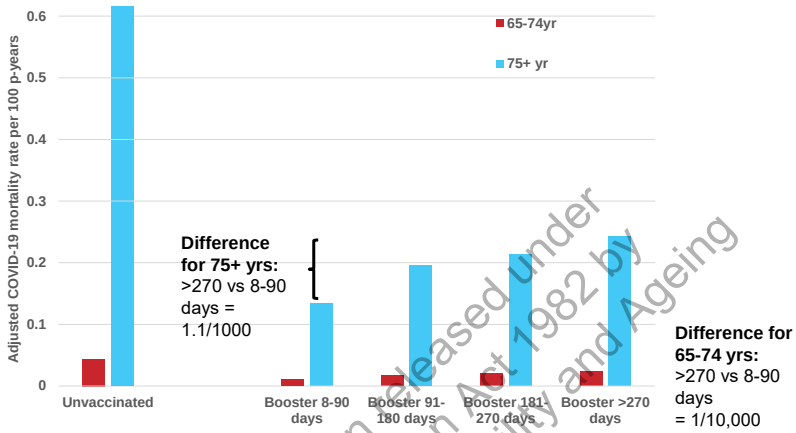


Influenza mortality estimates from modelling in 65+ years: 0.016 per 100p-years

Vaccine effectiveness adjusted for age, sex, jurisdiction, household income, co-morbidities, GP visits, 2022 flu vaccine receipt

Page 6

Adjusted COVID-19 mortality rates by time since booster dose



Difference for 75+ yrs: >270 vs 8-90 days = 1.1/1000

Difference for 65-74 yrs: >270 vs 8-90 days = 1/10,000

Page 7

Interpretation

- Vaccine effectiveness in Nov 22 – Mar 23 suggests waning VE of booster doses against COVID-19 mortality is still observed but differences less
- In adults 75+ years estimated difference in COVID-19 mortality is about 1.1/1000 person-years between those boosted 8-90 days vs 270+ days
- Small numbers who received bivalent boosters in the Nov 22-Mar 23 period but early analyses in Australian population suggest protection against COVID-19 mortality may be higher compared to monovalent, this is consistent with international studies
- Data limitations:
  - no hospitalisation data so benefits may differ for this outcome
  - no updated aged care data
  - co-morbidity data is based on risk score so unable to look at specific groups

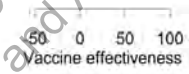
Page 8

COVID-19 vaccine effectiveness by time since booster receipt and booster type, 65+ years

01NOV22-31MAR23 Age group 65+ yo	Person-time rate (per 100-Person Year)	VE (%) (95% CI)
Unvaccinated	0.268 (0.205; 0.351)	ref
Dose2	0.109 (0.078; 0.154)	46.2 (32.7; 57.0)
Other booster 8-90 days	0.079 (0.040; 0.154)	71.7 (59.0; 80.5)
Other booster >90 days	0.119 (0.108; 0.131)	58.1 (50.6; 64.5)
Bivalent booster 8-90 days	0.014 (0.005; 0.041)	79.6 (64.0; 88.5)
Bivalent booster >90 days	NC	NC

(events=2,015)

(Person-time=1,673,073)



Comparing bivalent booster 8-90 days to monovalent booster 8-90 days
rVE = 28% (-37% to 62%)

Vaccine effectiveness adjusted for age, sex, jurisdiction, household income, co-morbidities, GP visits, 2022 flu vaccine receipt

Page 9

ATAGI Booster Policy Review: July 2023

12/07/2023

Prepared by:
s47F

Acknowledgement: Professor s47F

NCIRS
National Centre for Immunisation Research and Surveillance

Policy Question

- Should a *second* 2023 booster dose be recommended or considered for any population group/s?

- Policy options
  - No change & reinforce the recommendation for a single 2023 booster

  - Recommend/consider for previously defined high-risk groups
    - ≥ 65 years
    - Adults with medical risk conditions

  - Recommend/consider for a more select group
    - e.g. ≥ 75 years
    - ?-Adults with medical risk conditions

Background

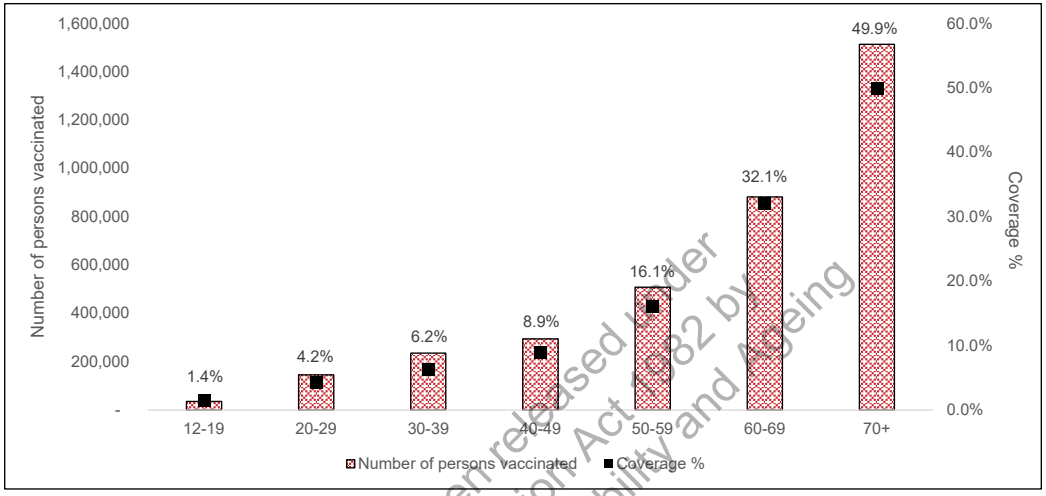
- ATAGI 2023 booster advice issued in February 2023
  - In August some individuals may be ≥ 6 months post 2023 booster dose
- Age remains the most significant risk factor for severe illness
- Strong evidence supporting hybrid immunity
- BA.4/5 vaccines most likely to be used for any additional booster doses
- Monovalent XBB.1.5 vaccines are anticipated – timing not known but unlikely for many months

Coverage update

s47B(a)

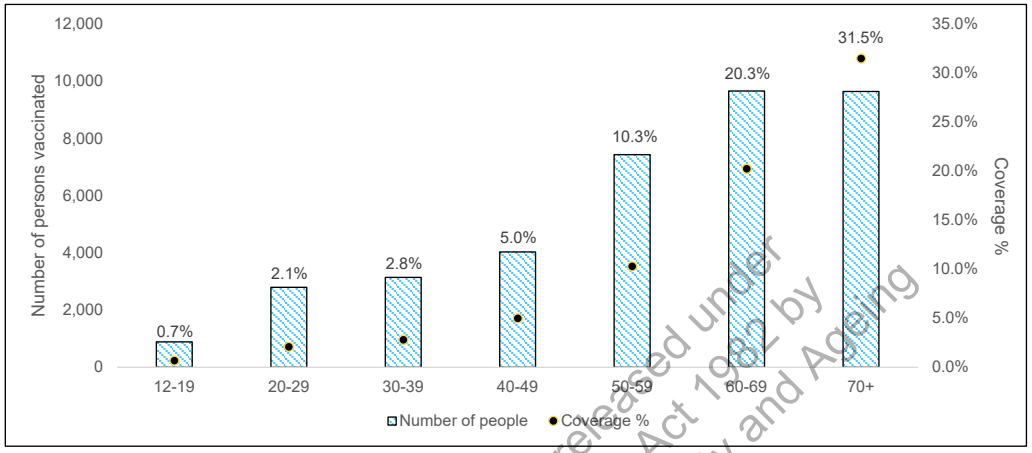
Percentage of persons with at least 1 bivalent dose (aged 12+) over Estimated Residential population

Total 16.5%



Data supplied by National COVID-19 Vaccine Program Division | Health Resourcing Group, Australian Government, Department of Health and Aged Care
Source: Australian Immunisation Register as at 11:59pm 05/07/2023

First Nations Percentage of persons with at least 1 bivalent dose (12+) over AIR First Nations Population



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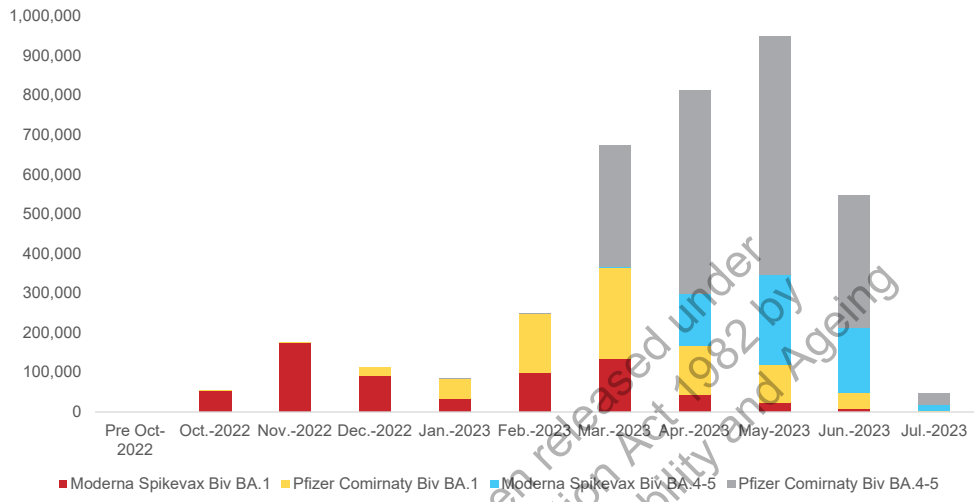
Source: Australian Immunisation Register as at 11:59pm 05/07/2023

Prepared by NCIRS for ATAGI #96

Page 6

Bivalent doses administered by month and brand to persons 12+



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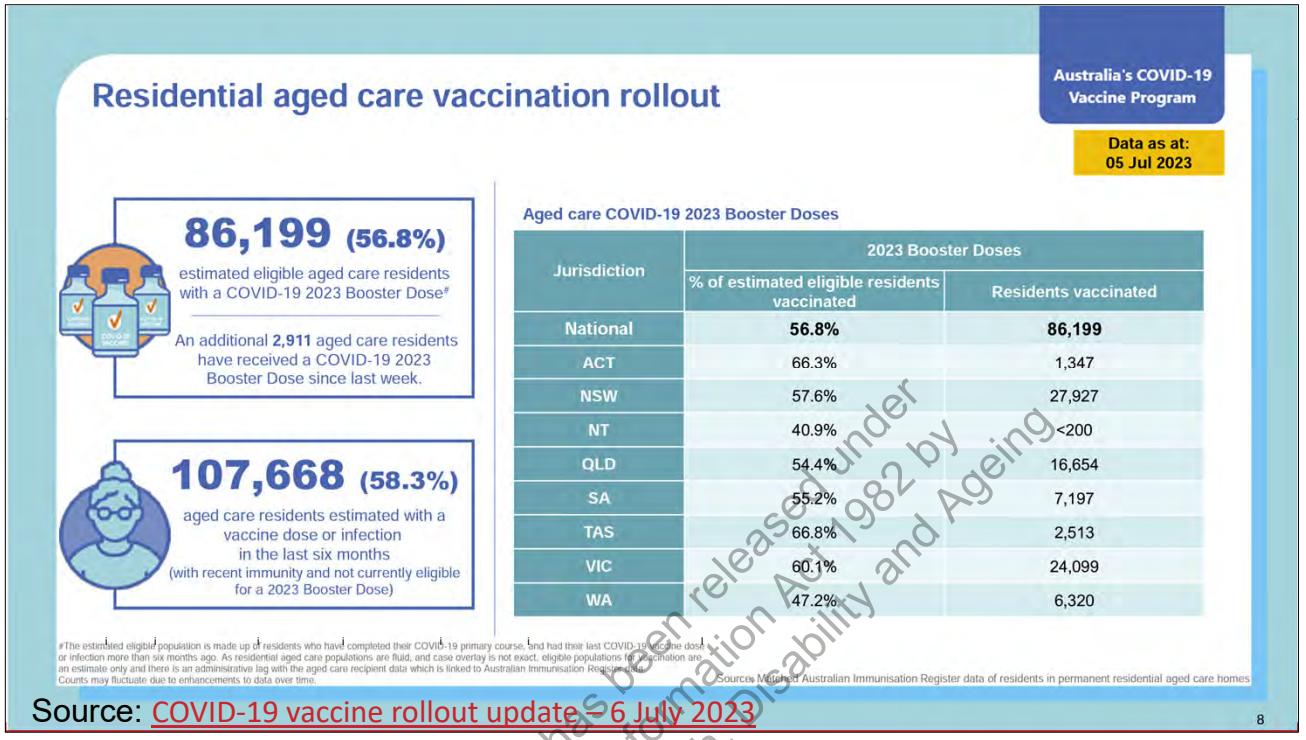
Source: Australian Immunisation Register as at 11:59pm 05/07/2023

Prepared by NCIRS for ATAGI #96

Page 7



Source: COVID-19 vaccine rollout update – 6 July 2023

NITAG Summary

NITAG Summary

- Large variation in recommended ages for booster doses
- Most suggest a minimum interval of 6 months from last dose
- Many no longer refer to a minimum interval after last infection
- Only ACIP specifically recommends at least 1 bivalent dose be received
- All still recommend booster doses for people with immunocompromise and medical conditions, however age cut-offs vary

s47B(a)

NITAG Summary – additional boosters

NITAG/Authority	Recommended age (years)	Severe IC (years)	At-risk medical	Other	'Can consider age (years)	Minimum interval (months)	Last updated
ACIP	• ≥6 (receive at least 1 bivalent booster) • ≥65 (additional dose after 1st updated booster)	≥6 months (additional dose ≥2 months after 1st updated booster)	Nil			• ≥2 months since last dose • ≥4 months since last updated dose	June 2023
JCVI	≥75 (and anticipates another dose in 6 months' time)	≥5	Nil	Aged care residents		'around 6 months' since last dose only	April 2023
EMA	≥60 (if XBB becomes available, recommends 1 dose for all ≥5)	≥6 months	Yes	Pregnancy, healthcare workers		≥3 or 4 months since last dose only	June 2023
NACI	≥80 ≥65 if infection naive	≥18	Nil	Aged care residents, long-term care homes		≥6 since last infection or dose	March 2023
NZ	≥65 ≥50 (Māori and Pacific people)	≥12	≥16 (12-15 additional booster dose on prescription)	Aged care and disability care facilities, pregnancy with high-risk conditions, serious mental health issues, disability	≥30	≥6 since last infection or dose	May 2023
ATAGI (current)	≥65 ≥50 (First Nations people)	≥18	≥18		≥18 ≥5 at-risk	≥6 since last infection or dose	Feb 2023

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s47B(a)

WHO SAGE Roadmap for COVID-19 vaccination in the Omicron era

- Advice from the 20-23 March 2023 meeting:
  - A **longer interval** (**12 months after the previous dose**) is recommended for **additional booster doses** (beyond the first booster) for **high-priority-use groups**, while maintaining a **6-month interval** for the **oldest age groups**, for older adults with multiple significant comorbidities, and for adults, adolescents and children above 6 months with moderate or severe immunocompromising conditions.
  - Additional boosters beyond the first booster are **no longer routinely recommended** for the **medium priority**-use group.
  - A booster dose is **recommended during pregnancy** if the last dose was given **more than 6 months earlier**; ideally, the dose should be given in the middle of the second trimester.
  - Additional booster doses are recommended for **frontline health workers 12 months after the last dose**.
  - **Healthy children and adolescents**: First booster dependent on country context; additional booster doses are **not routinely recommended**.

WHO (23 March 2023). Strategic Advisory Group of Experts on Immunization (SAGE) - March 2023 – Meeting highlights and final report: https://www.who.int/news-room/events/detail/2023/03/20/default-calendar/sage_meeting_march_2023

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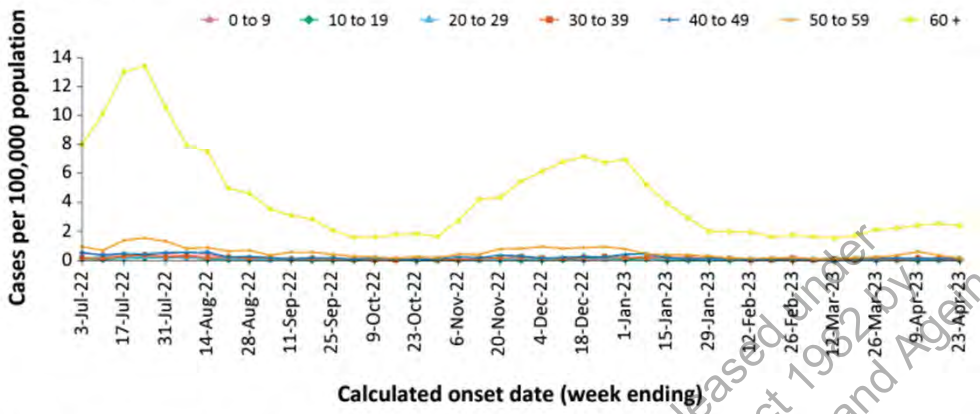
s47B(a)

NNDSS review

COVID-19 Epidemiology Report 74 – selected figures

2023 · Volume 47
Communicable Diseases Intelligence
COVID-19 Australia: Epidemiology Report 74
Reporting period ending 7 May 2023
COVID-19 Epidemiology and Surveillance Team

Figure 4: Age-specific rates of COVID-19 cases admitted to ICU or died, by date of onset, Australia, 27 June 2022 to 23 April 2023[a,b]



a Source: NNDSS extract from 17 May 2023 for cases with an illness onset from 27 June 2022 to 23 April 2023; cases with an illness onset in the last two weeks (27 March–7 May 2023) were excluded to account for the delay between onset and development of severe illness. The Australian Capital Territory did not supply hospitalisation data from 12 November to 24 November 2022 due to technical reasons.

b Population data based on Australian Bureau of Statistics (ABS) Estimated Resident Population (ERP) as at June 2022.

https://doi.org/10.33321/cdi.2023.47.33

NCIRS NNDSS analysis

- NNDSS data extracted: Date of diagnosis 23rd Oct- 2022 to 1st April 2023 (4th Omicron Wave)
- COVID-19 cases: Included confirmed + probable cases
- Rates/100,000 reported
- Denominator - ABS: June 2022 population data
- Age groups: 65-69, 70-74, 75-79, 80-84, >/=85

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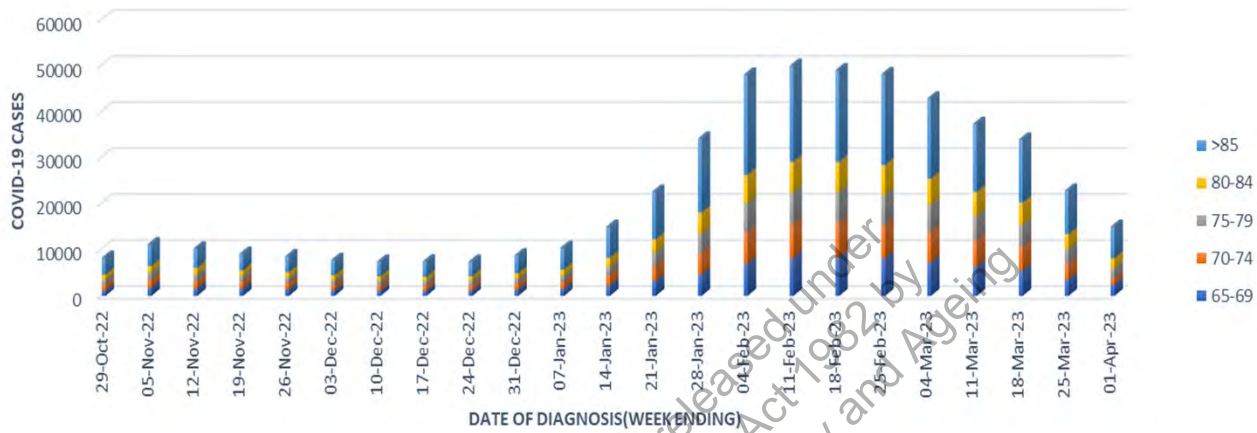
COVID-19 Cases (23rd Oct 2022-1st Apr 2023)



NNDSS data extracted: Date of diagnosis 23rd Oct- 2022 to 1st April 2023 (4th Omicron Wave)

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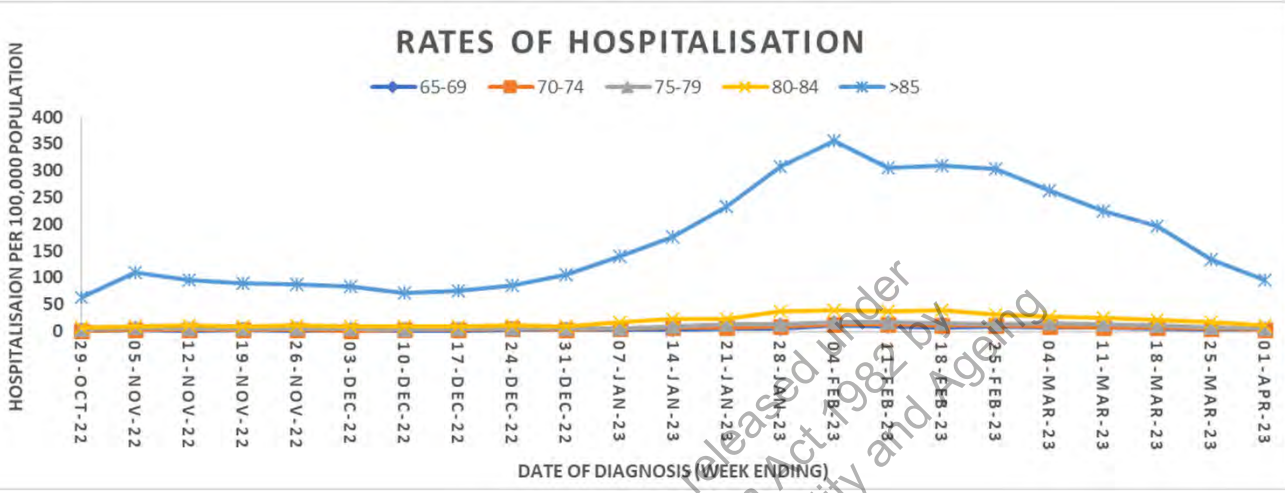
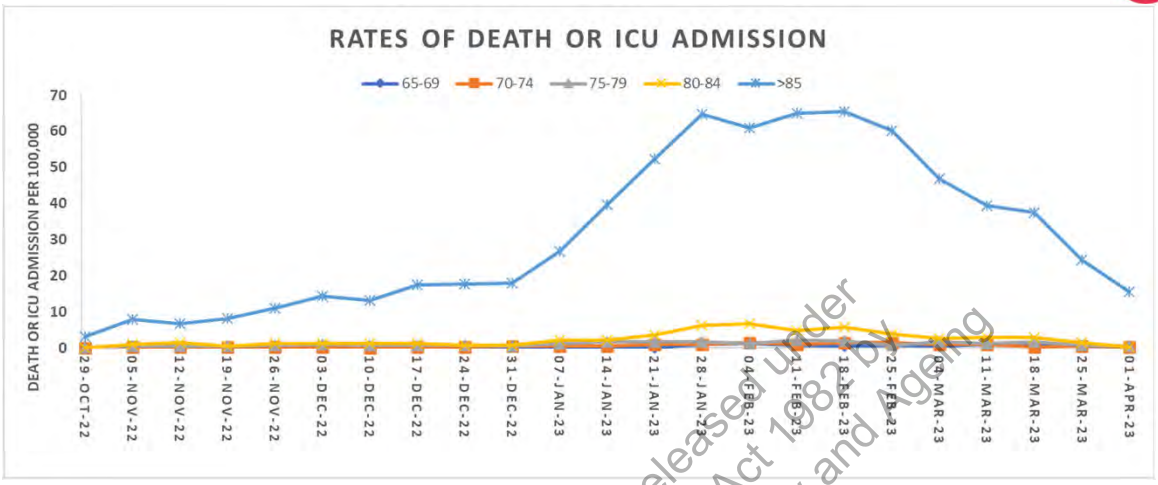
Rates of Hospitalisation by Age Groups and Epi Weeks



NNDSS data extracted: Date of diagnosis 23rd Oct- 2022 to 1st April 2023 (4th Omicron Wave)

Page 17

Rates of Death or ICU Admission by Age Groups and Epi Weeks



NNDSS data extracted: Date of diagnosis 23rd Oct- 2022 to 1st April 2023 (4th Omicron Wave)

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Rates per 100,000 and Proportion of Hospitalisation ICU admission and Death

Age groups	Hospitalisation			ICU admission			Death		
	N	Rates	Proportion (%)	N	Rates	Proportion (%)	N	Rates	Proportion(%)
18-49	3707	33.13	1.08	154	1.38	0.05	10	0.09	0.00
50-59	1717	53.90	1.07	107	3.36	0.07	14	0.44	0.01
60-64	819	54.94	1.21	44	2.95	0.07	9	0.60	0.01
>/=65	28657	646.41	**5.52**	1485	33.50	**0.29**	3443	77.66	**0.66**
65-69	1318	101.29	1.58	106	8.15	0.13	29	2.23	0.03
>/=70	27339	872.87	**6.28**	1379	44.03	**0.32**	3414	109.00	**0.78**
70-74	1559	136.37	2.03	128	11.20	0.17	52	4.55	0.07
>/=75	25780	1296.20	**7.21**	1251	62.90	**0.35**	3362	169.04	**0.94**

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s47B(a)

COVID-19 Epidemiology Report 74 – selected figures

Table 7: COVID-19 associated case fatality rates, among cases notified to NNDSS, by age group and date of onset, 1 January 2020 to 23 April 2023[a,b,c,d]

Age group (years)	1 March – 23 April 2023	Fourth Omicron wave 24 October 2022 – 28 February 2023	Third Omicron wave 15 June – 23 October 2022	Omicron to date 15 December 2021 – 23 April 2023	Delta 16 June – 14 December 2021	Pandemic to date 1 January 2020 – 23 April 2023
0–9	0.00%	0.00%	< 0.05%	< 0.05%	< 0.05%	< 0.05%
10–19	< 0.05%	< 0.05%	< 0.05%	< 0.05%	< 0.05%	< 0.05%
20–29	< 0.05%	< 0.05%	< 0.05%	< 0.05%	< 0.05%	< 0.05%
30–39	< 0.05%	< 0.05%	< 0.05%	< 0.05%	0.06%	< 0.05%
40–49	< 0.05%	< 0.05%	< 0.05%	< 0.05%	0.18%	< 0.05%
50–59	0.06%	0.06%	< 0.05%	< 0.05%	0.65%	0.05%
60 +	1.11%	1.08%	1.04%	1.01%	6.13%	1.12%
Australia	**0.35%**	**0.33%**	**0.21%**	**0.16%**	**0.71%**	**0.18%**

a Source: NNDSS, extract from 17 May 2023 for deaths with an illness onset date to 23 April 2023.

b To account for the lag between illness onset and the development of severe illness, cases with an onset date in the last two weeks have been excluded from calculations of the case fatality rate.

c A value of 0.00% indicates that no COVID-19 associated fatalities occurred during the indicated period for the specified age group.

d Crude case fatality rates which reflect number of deaths as a proportion of reported COVID-19 cases during specific periods, noting these rates are likely overestimated due to underreporting of cases.

https://doi.org/10.33321/cdi.2023.47.33

s47B(a)

Queensland Health

What proportion of older population hospitalised with COVID-19 is fully/partially vaccinated?

(ie had 2023 dose/dose in last 6 months)

ATAGI meeting
prepared by Prof Ross Andrews
05 July 2023
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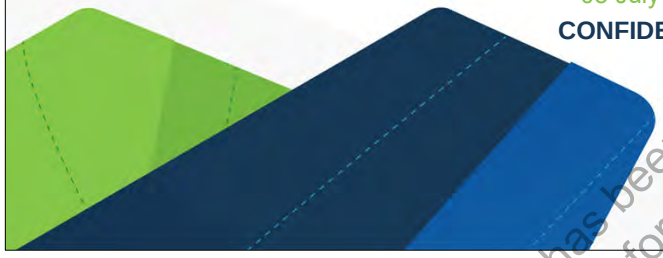
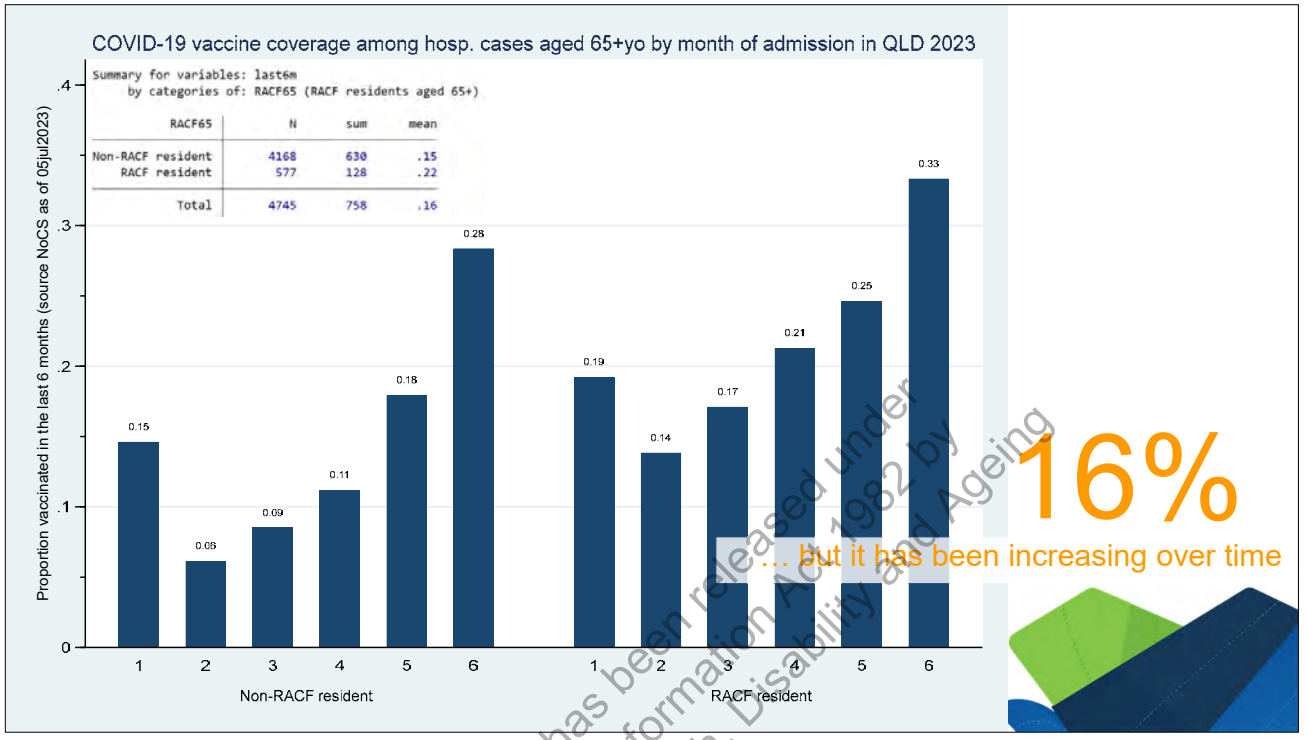
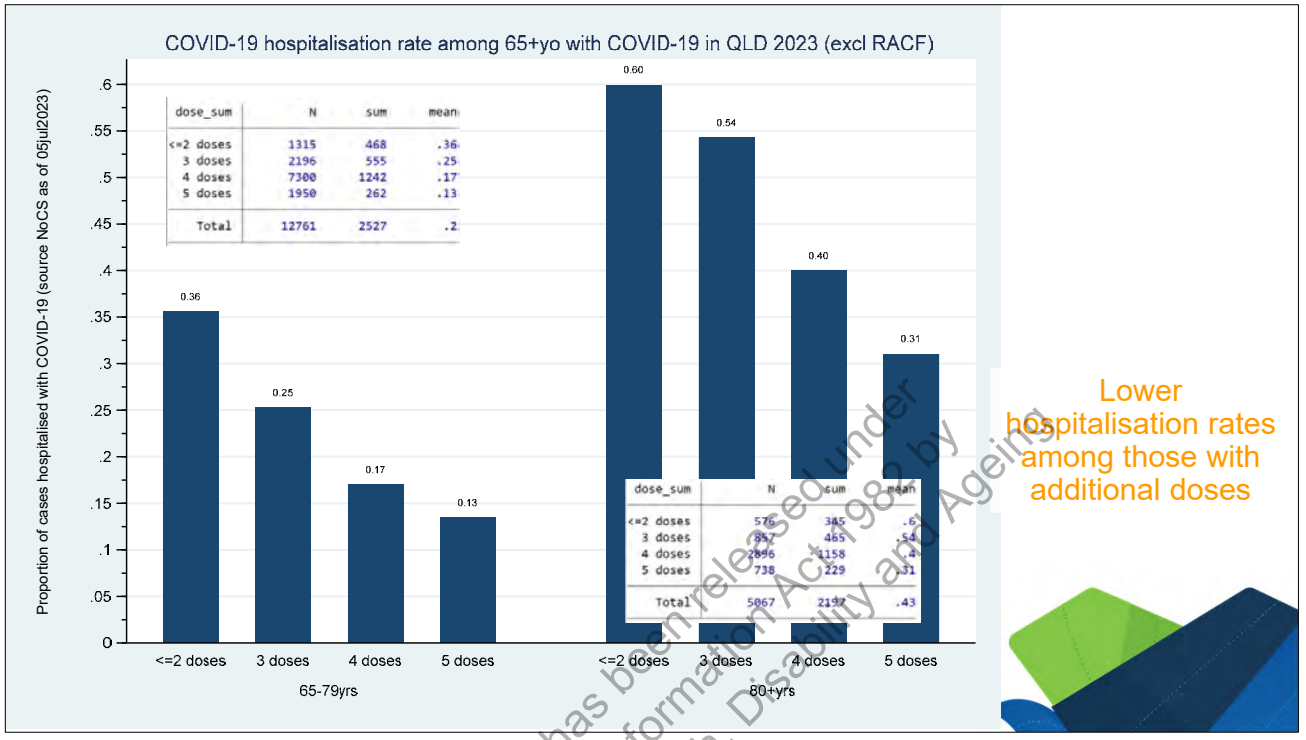


Queensland Government

s47B(a)





Evidence to Recommendation Framework

Evidence to Recommendation Framework

Criteria	Evidence
Is the problem of public health importance?	Rates of hospitalisation, ICU admission and death remain low among children and healthy adults under 65 years. Highest rates in 75+, particularly 85+ for hospitalisation/death.
Benefits	Absolute benefit is small for individuals with hybrid immunity or recent infection/vaccination. ?Greater benefit for older adults/those with medical risk conditions
Potential harms	Theoretical concerns re: imprinting Rare risk of serious AEFI

s47B(a)

[redacted]

Evidence to Recommendation Framework

Criteria	Evidence
Values: are the benefits large relative to the potential harms?	
Acceptability	Evidence of reduced vaccine uptake over time, presumed due to vaccine fatigue, and other factors (e.g. perceived need etc)
Resource use	Adequate supply of BA.4/5 vaccines – not a limitation
Feasibility	Not a limitation – but unclear what uptake might be; focus is on benefit being for individual protection in highest risk group/s Single dose prefilled syringes available Consider influence of current guidance on next year's program/timing - in future may be more feasible to recommend an annual dose co-administered with influenza vaccine;

s47B(a)

Proposed policy position

- Adults aged ≥ 65 may consider a second 2023 booster dose. This would be of most benefit if:
  - ≥ 6 months since last dose or infection
  - Older age within this group (e.g. >75/80/85)
  - No known history of prior infection
  - ?No previous bivalent vaccine dose

- Alternatives:
  - Include adults with medical risk conditions e.g. severe IC?
  - Raise age limit e.g. to 75?

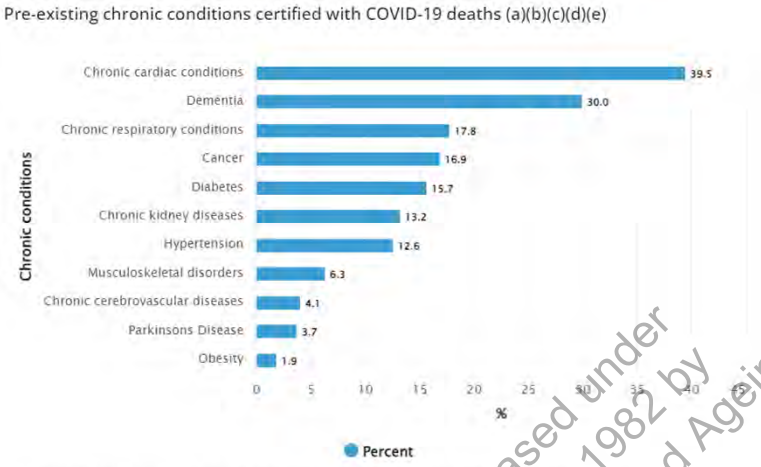
- Reiterate previous guidance to encourage uptake in those previously recommended who have not yet received a 2023 COVID-19 booster

s47B(a)

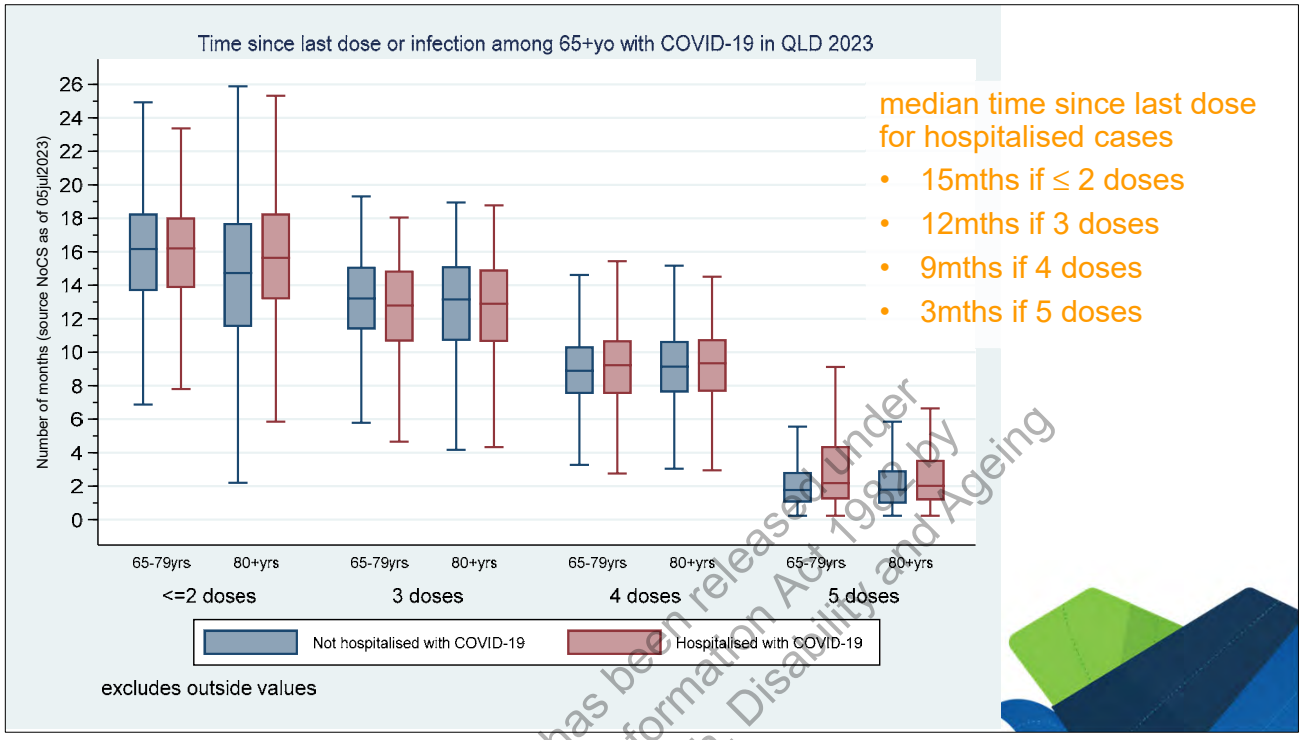
Additional policy questions

- Advice for:
  - Adults with medical risk conditions
  - Pregnant women

Additional slides



https://www.abs.gov.au/articles/covid-19-mortality-australia-deaths-registered-until-28-february-2023



s47B(a)

```
. logistic hosp dose5th Age80 Cases_FN male RACF65 i.dose_sum if COLLECT_DATE>=d(01jan2023) & COLLECT_DATE<=d(30jun2023)
> & AgeYrs>=65 & AgeYrs<. & (vaxmths!=. | VACCINATION_STATUS=="Not vaccinated") & disease=="Covid"
note: 5.dose_sum omitted because of collinearity

Logistic regression                             Number of obs     =     21,823
                                                LR chi2(7)        =    1785.95
                                                Prob > chi2       =     0.0000
Log likelihood = -11270.302                     Pseudo R2         =     0.0734

------------------------------------------------------------------------------
        hosp | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    dose5th |   .2925859   .0194533   -18.48   0.000     .2568379    .3333094
      Age80 |   2.798627   .0993009    29.00   0.000     2.610614     3.00018
   Cases_FN |   1.637598   .1557242     5.19   0.000     1.359139    1.973107
       male |   1.533956   .0506728    12.95   0.000     1.437786    1.636558
     RACF65 |    .298279    .015093   -23.91   0.000     .2701168    .3293774
            |
   dose_sum |
   3 doses |   .6452016   .0373901    -7.56   0.000     .5759269    .7228089
   4 doses |   .3911049   .0197139   -18.62   0.000     .3543136    .4317165
   5 doses |          1  (omitted)
            |
      _cons |   .4490892   .0225028   -15.98   0.000     .4070812    .4954323
------------------------------------------------------------------------------
Note: _cons estimates baseline odds.
```


preliminary analysis suggests

VE 71% (95CI 67%, 74%)

- 4th dose effective albeit 3 mths since last dose
- analyses using hazard ratios are underway

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What proportion of older population hospitalised with COVID-19 is fully/partially vaccinated?

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ATAGI meeting
prepared by Prof Ross Andrews
05 July 2023
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16%

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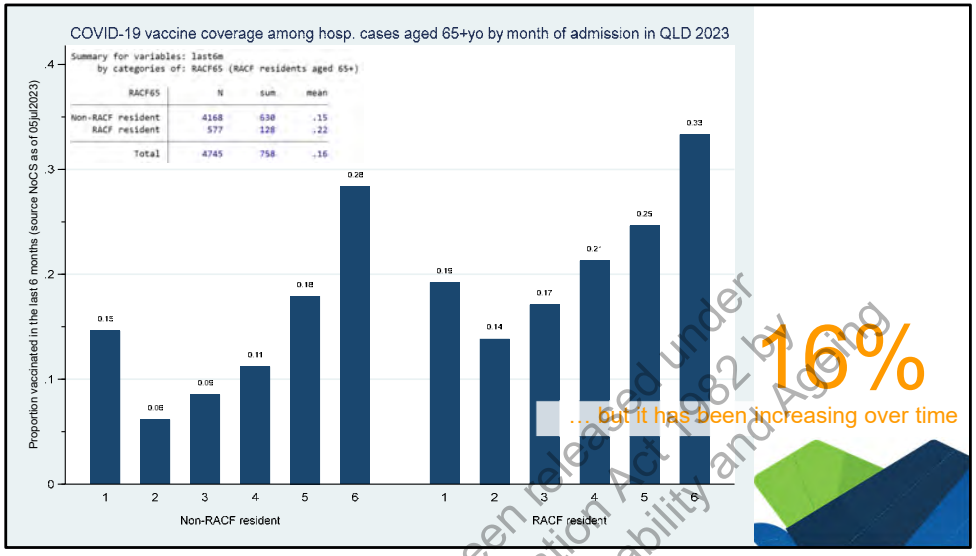
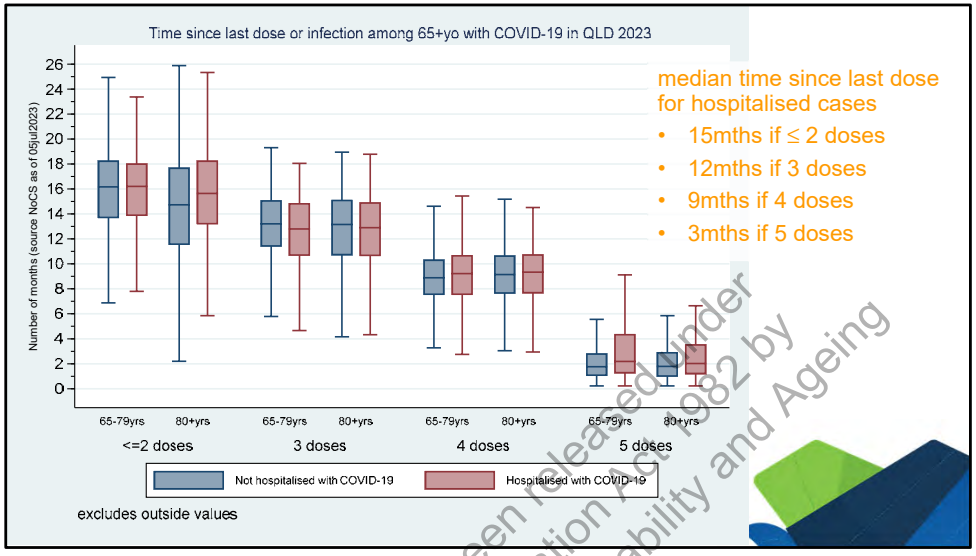
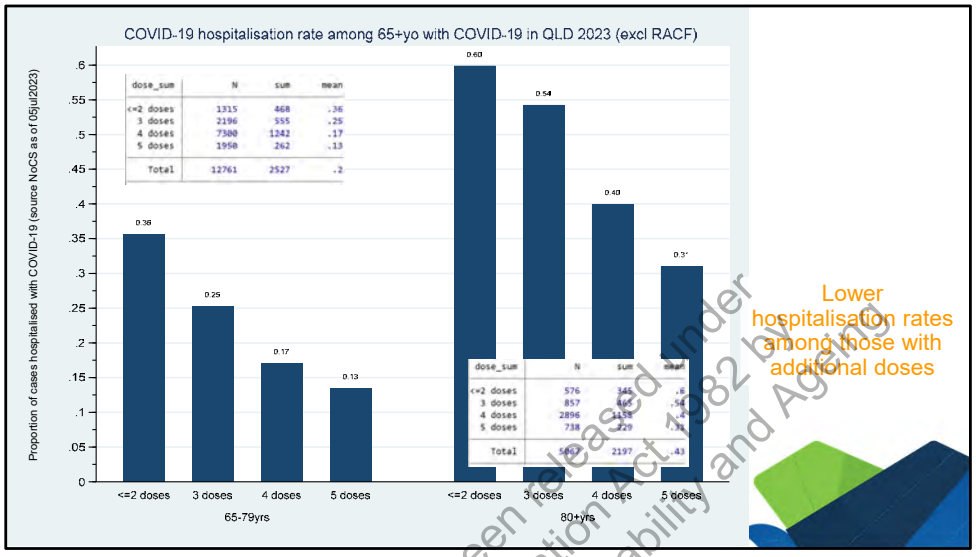




No apparent difference between hosp and non hosp cases



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                                                Prob > chi2       =     0.0000
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------------------------------------------------------------------------------
        hosp | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     dose5th |   .2925859   .0194533   -18.48   0.000     .2568379    .3333094
       Age80 |   2.798627   .0993009    29.00   0.000     2.610614     3.00018
    Cases_FN |   1.637598   .1557242     5.19   0.000     1.359139    1.973107
        male |   1.533956   .0506728    12.95   0.000     1.437786    1.636558
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            |
    dose_sum |
    3 doses |   .6452016   .0373901    -7.56   0.000     .5759269    .7228089
    4 doses |   .3911049   .0197139   -18.62   0.000     .3543136    .4317165
    5 doses |          1  (omitted)
            |
       _cons |   .4490892   .0225028   -15.98   0.000     .4070812    .4954323
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```

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preliminary analysis suggests

VE 71% (95CI 67%, 74%)

- 4th dose effective albeit 9 mths since last dose
- analyses using hazard ratios are underway

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AUSTRALIAN TECHNICAL ADVISORY GROUP ON IMMUNISATION
102nd MEETING
15-16 February 2024

Agenda Paper
Sponsor: Michelle Giles

AGENDA ITEM 11 & 12
COVID-19 Policy Settings 2014 & ATAGI COVID-19 Annual Statement

---

Recommendations
That member:

1. **DISCUSS and ENDORSE** further dose recommendations for 2024 as drafted in the COVID-19 Annual Statement (Attachment A) (to be released with the annual flu statement)

Issues for Discussion

- 6-monthly doses recommended for adults aged ≥75 years
- 12-monthly doses for adults aged 18 to 74 years with severe immunocompromise. Can **consider** a dose every 6 months.
- 12-monthly doses for all adults aged 65 to 74 years
- Adults aged 18–64 years with conditions that increase the risk of severe COVID-19 who are not severely immunocompromised may **consider** a dose every 12 months

Background

ATAGI has previously iterated the further dose COVID-19 vaccination recommendations in February and September 2023. With changing epidemiology, burden of disease, and vaccine effectiveness, ATAGI is meeting to discuss any changes to recommendations for 2024. Vaccine coverage, burden of disease, vaccine effectiveness data, and recommendations of other NITAGs will be reviewed, with a particular focus on groups at high-risk of sever disease.

Previously XBB.1.5-containing vaccines were preferred for primary and booster doses over other COVID-19 vaccines for people aged ≥5 years. In late December 2023 it has been approved for use in children aged 6 months – <5 years and supply is anticipated in coming months.

Next Steps

- NCIRS to finalise annual statement and update Handbook chapter and other relevant resources with final endorsement by chairs.
- On-going monitoring of immunogenicity, safety and vaccine effectiveness data
- Literature review of high-risk conditions that may be removed from the current chapter list
- GRADE assessment

Attachments:
Attachment A: Draft 2024 COVID-19 Annual Statement

Age recommendations for a primary dose of COVID-19 vaccine

Prepared by NCIRS

s47F

Aim

- Wide range of age groups recommended for a primary dose by other NITAGs:
  - from ≥ 6 months (USA) to no primary doses (only annual doses for ≥ 65 years and at-risk groups; France, Denmark)
- disease burden is low in children, adolescents, and young adults

- Review:
  - national coverage data
  - burden of disease in Australia
  - vaccine effectiveness vs severe disease (hospitalisation and death)
  - NITAG recommendations
  - evidence to recommendation framework

- Discuss and endorse a policy position

Policy options

Healthy children and adolescents aged 5-17 years:

1. are recommended to have a primary course (current advice)

OR

2. are not recommended to receive COVID-19 vaccine
(+/- permissive language)

Summary 1/2

- Poor vaccine uptake in children and adolescents aged 5-15 years in 2023 (1.4% of children turning 5)
- Coverage between 41% and 94%, depending on age cohort
- Nearly all vaccines in people aged 5 to 18 years were given greater than 12 months ago

- Burden of disease remains low in 2023 in children aged 5-18 years:
  - case fatality rate remains <0.05%
  - 20 ICU admissions and 3 deaths recorded nationally by PAEDS
  - no ICU admissions or deaths in unvaccinated children who had no comorbidities
  - at least 210 hospitalisations, but likely many more

Summary 2/2

- Vaccine effectiveness vs hospitalisation in early Omicron era:
  - similar relative protection to adults (approximately 68-75%)
  - lower absolute protection (rates of hospitalisation >10 times greater in >80 years, compared to 15-19 years)
- Vaccine effectiveness vs death in early Omicron era:
  - Counts too small to calculate relative risk
  - Less than 1 death per 100,000 children and adolescents for unvaccinated and vaccinated

Coverage summary: most children and adolescents aged 5-15 years did not get vaccinated in 2023

- 1.4% of all children who turned 5 this year received the recommended dose between 1 January and 31 October 2023

- 3.4% of unvaccinated children and adolescents aged 5-15 years received their first over the last 12 months
- 50% of unvaccinated adolescents aged 16-18 years received their first over the last 12 months

- Coverage between 41% and 94%, depending on age cohort

Vaccine coverage

In confidence: AIR coverage data

- 1.4% of 5-year-olds received their first dose between 1 January and 31 October 2023

The data has been sourced as of the 8 November 2023.

The following filters have been applied:

1. Encounter date between 1/1/2023 – 31/10/2023
2. Number of doses = 1
3. Date of birth greater than or equal to 1/1/2028 i.e., those turning 5 this year

June 2021 ERP has been used of those aged 5 years to calculate the unvaccinated cohort i.e., June 2021 ERP – Vaccinated.

Received 1 dose (turned 5 this year)	June 2021 ERP (Aged 5 years)	Unvaccinated
4,479	321,002	316,523

Source: Australian Immunisation Register as at 11:59pm 8/11/2023

Caveat:
The above data contains sensitive information which should only be use for the purpose that it is indented (ATAGI Meeting). Please do not utilise this data for any other use.
The data is not for further distribution either within the department or externally without prior written approval from the National COVID-19 Vaccine Program Division.

Most eligible children aged 5-15 did not get vaccinated in 2023 (In confidence: AIR coverage data)

Age cohort (as at 31 October 2023) (years)	Vaccinated between 1 Nov 2022 and 31 Oct 2023 (last 12 months) (% of unvaccinated population)	Unvaccinated as at 31 Oct 2022	Change in cohort coverage 31 Oct 2022 to 31 Oct 2023 (last 12 months) (%)
5-11	38,778 (3%)	1,337,608	+1.7% (41% to 43%)
12-15	18,779 (5%)	343,728	+1.4% (73% to 75%)
16-18	34,026 (50%)	68,232	+4.2% (92% to 96%)
All 5-18	**91,583 (5%)**	**1,749,568**	**+2.1% (60% to 63%)**

- Most unvaccinated 5-15-year-olds as of November 2022 did not get vaccinated over the last 12 months
- Half of unvaccinated 16-18-year-olds did get vaccinated, possibly due to entering workplaces or educational institutions that required COVID-19 vaccination

- Cohort coverage proportional to age; nearly all doses were received greater than 12 months ago

Burden of disease

Burden of disease summary: low rates and absolute counts of severe disease in children aged 5 to 17 years

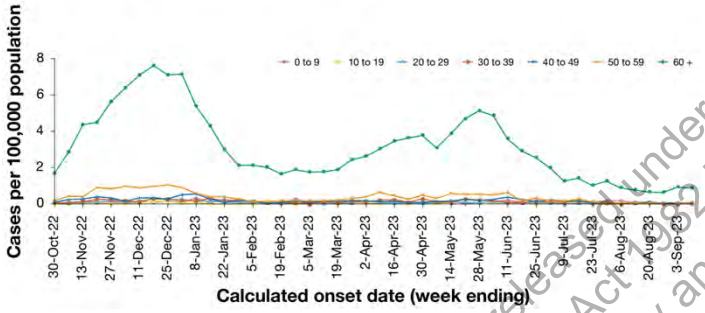
- NNDSS data:
  - ICU admission remains very rare
  - Case fatality rates remains <0.05%

- PAEDS data, 1 Jan to 31 Oct 2023:
  - 20 ICU admissions and 3 deaths between 1 Jan and 31 Oct 2023 where COVID-19 could not be excluded as a contributing or causative factor
  - 4 ICU admissions and 1 death were in unvaccinated children and adolescents
  - No ICU admissions or deaths in unvaccinated children with no comorbidities

- PIMS-TS (MIS-C) 1 Jan to 30 Sept 2023:
  - At most 9 additional ICU admissions and no deaths; at least 19 hospitalisations

Children and adolescents have very low rates of ICU admission and death

Figure 4: Age-specific weekly rates of COVID-19 cases admitted to ICU or died, by date of onset, Australia, 24 October 2022 to 10 September 2023[a,b]



- ICU admission and death rates remain very low
- Case fatality rates among individuals aged 19 or younger have remained <0.05% throughout the pandemic

CDI epidemiology report 79. Available at: https://www1.health.gov.au/internet/main/publishing.nsf/Content/99424DA2A5F3A488CA2589BA0019141B/$File/covid_19_australia_epidemiology_report_79_reporting_period_ending_24_september_2023.pdf

UKHSA: Adolescent risk much lower than elderly

Figure 1a: hospitalisation rates by age and risk group status

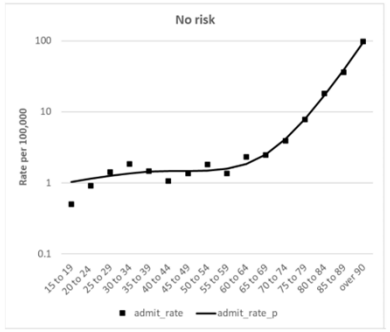
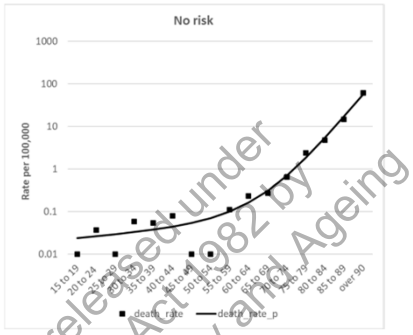


Figure 1c: death



https://www.gov.uk/government/publications/covid-19-autumn-2023-vaccination-programme-jcvi-advice-26-may-2023

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PAEDS

- PAEDS is a national sentinel paediatric hospital surveillance system
- Aims to differentiate clinical from incidental COVID-19
- Many hospitalisations from COVID-19 would have occurred outside this network and have not been captured
- Nearly all ICU admissions and in-hospital deaths in Australia would have been captured
- Cannot calculate proportions; the total at-risk populations are not identified by PAEDS

Vaccine Effectiveness

Piechotta et al, 2023 (meta-analysis published in Lancet Child Adolesc Health) children aged 5–11 years

- **Database**:COVID-19 L·OVE (living overview of evidence) platform up to Jan 23, 2023
- **Vaccines**: Pfizer original, Pfizer original and BA.4/5, Moderna original, Moderna (original and BA.1)
- **N:** 6 studies of hospitalisation (3,058,480 children) and 4 studies of death (2,869,874 children) during Omicron period
- **Hospitalisation**
  - **moderate certainty: 'moderate risk of bias'**
  - VE of 2 dose: 75·3% (95% CI: 68·0–81·0) at median of 2-3 months
  - prevented 32-38 hospitalisations per 100,000 doses: 47 unvaccinated vs 9-15 vaccinated hospitalisations per 100,000 children (based on case control studies – does not
- **Death**
  - **low certainty: 'very serious imprecision'**
  - counts too low to calculate vaccine effectiveness (at median 27 days)
  - no deaths in 1,081,881 vaccinated with 2 doses versus 3 deaths in 1,787,993 unvaccinated children observed

https://www.thelancet.com/action/showPdf?pii=S2352-4642%2823%2900078-0

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Li et al, 2023 (meta-analysis published in Journal of Infection) children and adolescents aged 3 to 18 years

- Published as a letter to the editor
- **Databases**: MEDLINE, EMBASE, and Cochrane CENTRAL, November 1, 2021, and November 30, 2022
- **Vaccines**: Pfizer, Moderna, and CoronaVac; formulations not stated
- **N** = 3 studies of hospitalisation in children, 5 studies of hospitalisations in adolescents; 2,288,162 people
- Age definitions not reported; children presumably 3-11 years and adolescents 12-18 years
- **VE against hospitalization from Omicron (median time point not reported)**:
- children 71.0% (95% CIs: 63.3–78.6)
- adolescents 70.2% (95% CIs: 48.3–92.0)
- absolute rates not reported

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NITAG Summary

NITAG Summary

- Age recommendation for primary dose:
  - **Based on disease burden**: SAGE
  - **≥ 6 months**: US ACIP
  - **≥ 5 years**:
    - UK JCVI
    - Canada NACI (discretionary recommendation for ≥ 6 months)
    - NZ
  - **≥ 18 years**: Germany STIKO
  - **No primary dose** for unvaccinated people: France, Denmark, Norway (annual dose for ≥65 years and at-risk only; discretionary for everyone)

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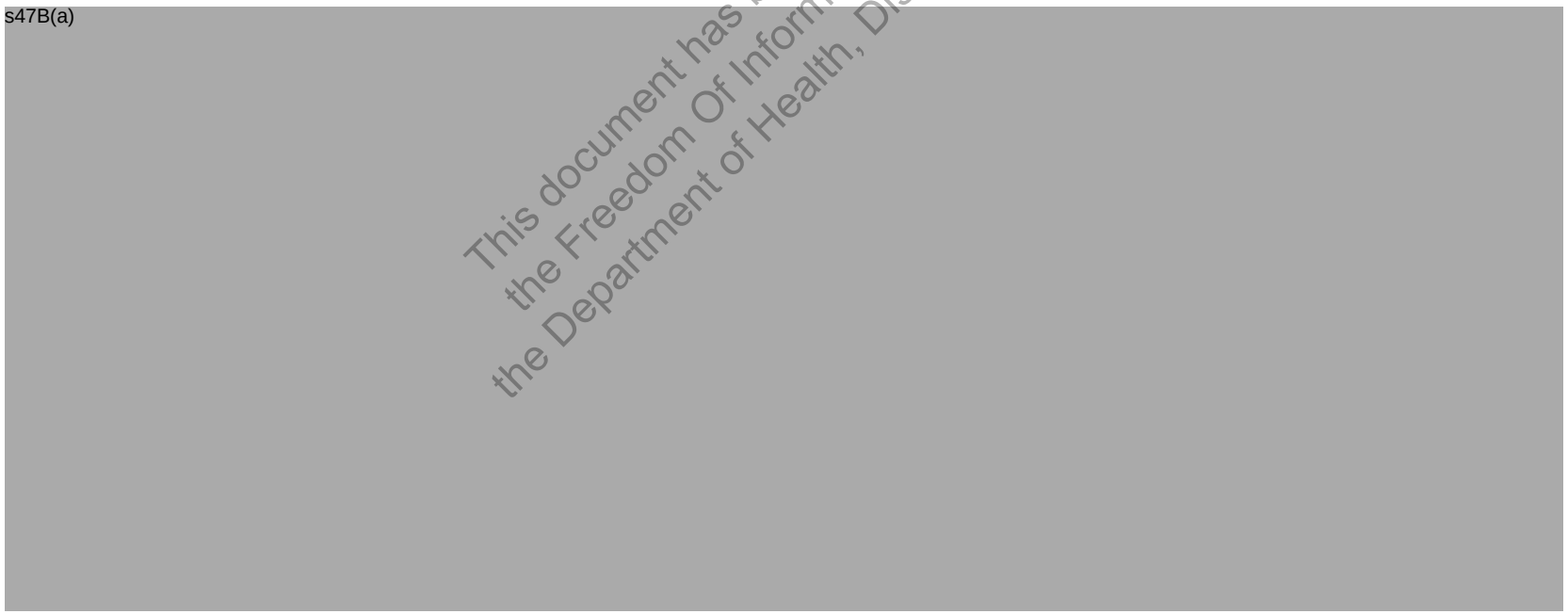

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Evidence to recommendation

Criteria	Evidence
Is the problem of public health importance?	• Burden of disease in Aus is low in children and adolescents • High level of population immunity developed over the past few years
Benefits	• May improve vaccine fatigue and uptake in other programs (e.g., annual flu, school vx programs) • May improve access to the workforce for older adolescents (where mandates are in place) • Prevention of very rare risks of harm • Less product required
Potential harms	• Very safe vaccine in children and young adolescents. Small benefits achievable with negligible risk. • Myocarditis risk unclear older adolescents following a primary dose in context of widespread past infection
Values	• Those with vaccine fatigue would probably value no primary course recommendation • Those who want themselves or child vaccinated cannot access one in the absence of private market supply
Acceptability	• Most individuals and parents are not getting vaccinated and will likely accept a 'no primary series' recommendation • Minority of people and parents (some of those currently getting vaccinated) may not accept restriction of access to vaccine
Resource use	• No anticipated supply limitations • Increased short-term wastage (if stock not donated elsewhere)
Feasibility	• Infrastructure already in place

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Policy options

Healthy children and adolescents aged 5-17 years:

1. are recommended to have a primary course (current advice)

OR

2. are not recommended to receive COVID-19 vaccine (+/- permissive language)

Back up slides

In confidence: DOHAC vaccination coverage data

From department: 'The data has been sourced from our records as of the 8 November 2023. This is the earliest snapshot that we have available. I have then applied a filter to the measures of Encounter Date <=31/10/2023. Encounter dates can be changed and added in retrospect so while we try to produce data that we have recorded on the day our current system cannot accommodate daily snapshots outside of what we produce for our regular public and internal reporting. The numbers below will be very close to what we had in the system on 31/10/2023 but not exact.'

Source: Australian Immunisation Register as at 11:59pm 8/11/2023

Age Cohort	Unvaccinated (no lifetime doses)*	1 or more lifetime dose	Last dose within the last 12 months
0 to 4 years	1,508,741	1,218	936
5 to 11 years	1,298,830	970,833	38,778
12 to 15 years	324,949	954,438	18,779
16 to 18 years	36,370	842,053	34,026
Total	3,168,890	2,768,542	92,519

*Unvaccinated (no lifetime doses) is calculated by subtracting the June 2021 ERP by those with 1 or more lifetime dose.

Caveat:
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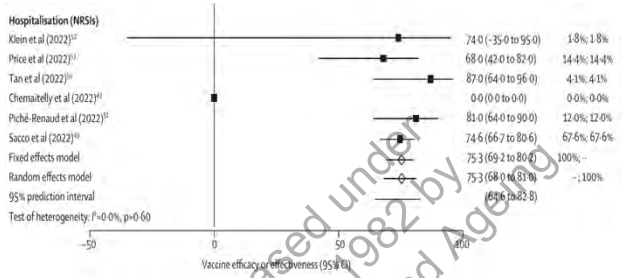
Piechotta et al, 2023 (Published: Meta-analysis in Lancet Child Adolesc Health) children aged 5–11 years

- **Database**:COVID-19 L·OVE (living overview of evidence) platform up to Jan 23, 2023
- **Vaccines**: mRNA vaccines BNT162b2 (Pfizer-BioNTech), BNT162b2 Bivalent, mRNA-1273 or mRNA-1273.214
- **N:** 6 studies of hospitalisation and 2 studies of death in Omicron period
- **Hospitalisation**: VE of 2 dose: 75·3% (95% CI: 68·0–81·0)
- **Death:** Crude event rates in unvaccinated children: <1/100 000 children, and no events for vaccinated children



Vaccine effectiveness outcomes against omicron hospitalistion. A vaccine effectiveness estimate greater than 0% favours vaccination. NRSI=non-randomised study of intervention.

https://www.thelancet.com/action/showPdf?pii=S2352-4642%2823%2900078-0

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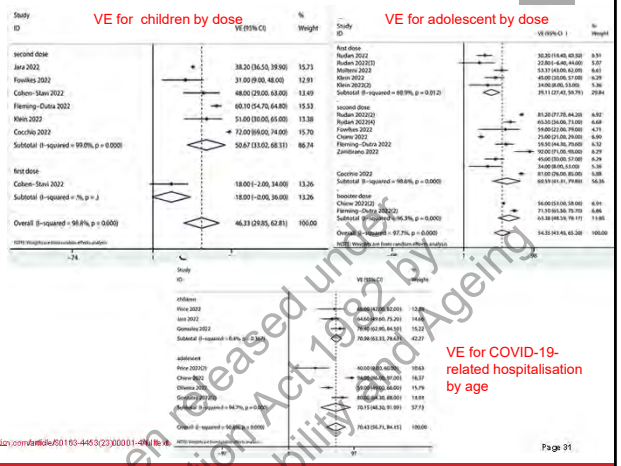
Li et al, 2023 (Published: Meta-analysis in Journal of Infection) children and adolescents

- **Databases**: MEDLINE, EMBASE, and Cochrane CENTRAL, November 1, 2021, and November 30, 2022
- **N=** 14, 3793,543 patients
- **Overall, VE**: children with Omicron infection 46.33% (95% CIs: 29.85–62.81) vs 54.35% (95% CIs: 43.49–65.20)
- **VE among children**: 18% (95% CIs: 0–36) of the **1st dose vs 2nd dose** 50.67% (95% CIs: 33.02–68.31)
- **VE among adolescent**: 39.11% (95% CIs: 27.43–50.79, < 0.05) of the **1st dose vs 2nd dose** 60.59% (95% CIs: 41.31–79.86
- **VE against hospitalisation**: children 70.98% (95% CIs: 63.33–78.63, vs adolescents 70.17% (95% CIs: 48.30–91.99)

VE for children by dose

VE for adolescent by dose



VE for COVID-19-related hospitalisation by age

Prepared by NCIRS for ATAGI #101

https://www.journalofinfection.com/article/S0163-4453(23)00081-8/fulltext

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ATAGI 2024 COVID-19 Vaccines Recommendations

Date: 15 February 2024

Prepared by NCIRS

NCIRS
National Centre for Immunisation Research and Surveillance

Aim

- Land 2024 policy settings for further dose advice
- Check changes to list of risk conditions

- Publish as a COVID-19 annual statement alongside flu and RSV

- Review coverage, burden of disease, VE vs serious illness, and other NITAG recommendations

Proposed 2024 policy positions

- These recommendations will be reviewed annually (or earlier if new evidence emerges or epidemiology changes):

- ATAGI **recommends** COVID-19 vaccination for the following groups:
  - Adults aged ≥75 years, should receive a dose every 6 **months**
  - Adults aged 65–74 years should receive a dose every **12 months** (remove 'can consider every 6 months')
  - Adults aged 18—74 years with severe immunocompromise should receive a dose every **12 months**, and can **consider** a dose every 6 months based on individual preferences and risk-benefit assessment

- The following groups can **consider** a COVID-19 vaccine every **12 months**, based on an individual risk-benefit assessment:
  - All other adults aged ≥18 years , including those with medical conditions that may increase their risk of severe COVID-19 (remove active 12-monthly recommendation for at-risk groups)
  - Children and adolescents aged 5 – <18 years with severe immunocompromise

Evidence summary

- 48% of adults 65-74 years received at least 1 dose in 2023
- 17% of adults aged ≥75 years received 2 doses in 2023 (66% received at least 1 dose)
- At most, 30% of RAC residents received 2 doses in 2023 (68% received at least 1 dose)

- National hospitalisations, ICU admissions, and deaths remain greatest in adults aged ≥75 years, followed by adults aged 65-74 years
- Victorian adults ≥65 years, especially ≥75 years, who did not receive a vaccine in 2023 were more likely to develop severe disease
- Limited evidence on vaccine effectiveness in people with at-risk medical conditions

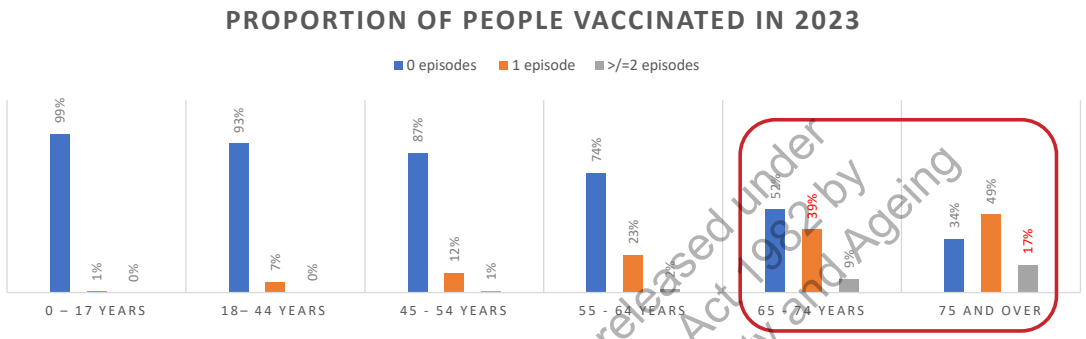
- XBB.1.5 VE studies emerging (short follow-up times of 2-4 weeks): 63%-77% vs hospitalisation, 73% vs ICU admission, mostly in adults aged ≥ 60 years

- Most NITAGs do not recommend adults 65-74 years receive or consider a 6-monthly dose
- Most NITAGs recommend adults aged 18-74 with at-risk medical conditions receive a yearly dose; some have signalled they plan to narrow the membership of this group

Coverage update

DoHAC data: Number of COVID-19 doses in 2023 by age group

- Most adults aged ≥75 and 65-74 years did not receive the recommended doses in 2023
- 48% of adults 65-74 years received at least 1 dose in 2023
- 17% of adults aged ≥75 years received 2 doses in 2023 (66% received at least 1 dose)



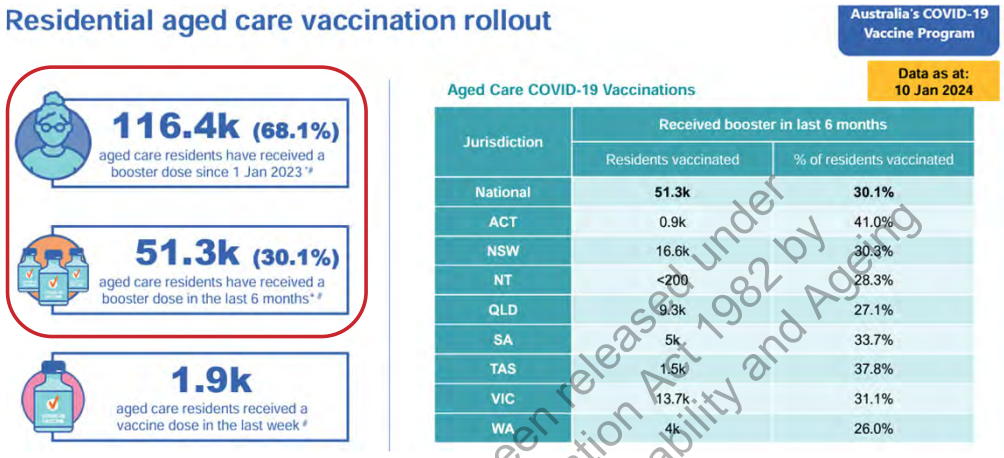
Data source: Australian Immunisation Register as at 11:59pm 30/01/2024
Only episodes with an encounter date between 01-Jan-2023 and 31-Dec-2023 are included
Number of episodes in 2023 are the number of doses received in 2023 and are NOT part of a persons dosing sequence (e.g. those that have received 0 doses in 2023 may have received doses 1 and 2 in previous years)
0 episodes is calculated by subtracting 2021 ERP from total doses administered in 2023

Prepared by NCIRS for ATAGI #102

Page 6

Residential aged care vaccination rollout

- Although higher uptake than their community counterparts, most aged care residents did not receive the recommended 2nd 2023 dose between Sep and Dec



Jurisdiction	Received booster in last 6 months	
	Residents vaccinated	% of residents vaccinated
National	**51.3k**	**30.1%**
ACT	0.9k	41.0%
NSW	16.6k	30.3%
NT	<200	28.3%
QLD	9.3k	27.1%
SA	5k	33.7%
TAS	1.5k	37.8%
VIC	13.7k	31.1%
WA	4k	26.0%

https://www.health.gov.au/sites/default/files/2024-01/covid-19-vaccine-rollout-update-12-january-2024.pdf

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Burden of Disease

Burden of Disease Summary

- JN.1 is becoming more prominent
- High immune escape potential; no indication of increase in severity of disease

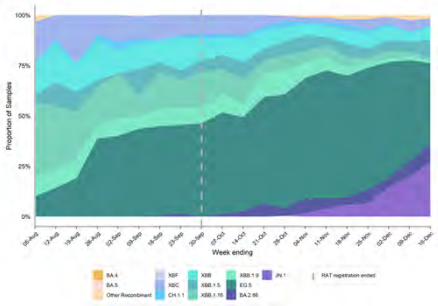
- Rates of NNDSS-captured hospitalisation, ICU admissions, and death decreasing over time (to October 2023)
- Adults ≥65 years continue to over-represent severe disease burden

- Victorian adults ≥65 years, especially ≥75 years, who did not receive a vaccine in 2023 were more likely to develop severe disease
- No method currently available to S&T to stratify by at-risk medical conditions

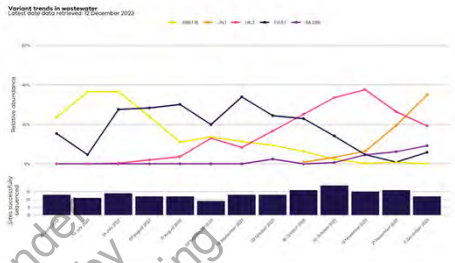
Prepared by NCIRS for ATAGI #102

Local Burden: NSW, Tasmania, VIC

Figure 9. Estimated distribution of COVID-19 sub-lineages in the community, 05 August 2023 to 16 December 2023.



NSW: 6th Jan 2024: EG.5 continues to dominate circulating sub-lineages and the proportion sequenced as JN.1 is increasing.



Tasmania: 31st Dec 2023: Among 138 samples, 49 (36%) were JN, 47 (35%) were HK and 10 (7%) were HV.

VIC Dec 2023: Dominated by Omicron XBB recombinant sublineages. JN.1 is most prevalent single subvariant

https://www.health.nsw.gov.au/Infectious/covid-19/Documents/respiratory-surveillance-20240106.pdf
https://www.health.tas.gov.au/sites/default/files/2024-01/fortnightly-respiratory-surveillance-report-to_31_december_2023.pdf
https://www.health.vic.gov.au/sites/default/files/2023-12/victorian-covid-19-surveillance-report-22-december-2023_0.pdf

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JN.1-Global burden

- WHO has now classified it as a separate variant of interest.
- Current vaccines will continue to protect against severe disease and death from JN.1.
- CDC: subvariant JN.1 made up about an estimated 15% to 29 % of cases in the United States as of 8 December.
- The countries reporting the largest proportion of JN.1 sequences are
  - France (20.1%, 1552 sequences),
  - United States of America (14.2%, 1072 sequences),
  - Singapore (12.4%, 934 sequences),
  - Canada (6.8%, 512 sequences),
  - United Kingdom (5.6% 422 sequences),
  - Sweden (5.0%, 381 sequences).

Table 1: Global proportions of SARS-CoV-2 Variants, week 44 to week 48 of 2023

Lineage	Countries§	Sequences§	2023-44	2023-45	2023-46	2023-47	2023-48
VOIs							
XBB.1.5*	128	316 888	8.2	7.9	8.6	7.4	7.3
XBB.1.16*	119	103 516	9.8	9.0	6.6	5.6	4.2
EG.5*	93	343 675	53.7	54.1	51.7	46.5	36.3
BA.2.86*	49	5 972	4.4	4.8	5.8	7.1	5.9
JN.1*	41	7 344	3.3	5.3	10.1	16.7	27.1
VUMs							
DV.7*	40	4 635	1.2	0.9	0.9	1.0	0.6
XBB*	143	90 441	2.3	2.0	1.8	1.2	1.0
XBB.1.9.1*	118	85 640	6.7	5.4	5.5	4.3	3.3
XBB.1.9.2*	95	37 764	1.7	1.1	0.7	0.5	0.2
XBB.2.3*	107	34 573	3.5	3.4	2.5	2.3	1.6
Unassigned	95	155 778	3.4	4.2	4.2	6.4	11.9

§ Number of countries and sequences are since the emergence of the variants
* Includes descendant lineages, except those specified on the table. For example, XBB* does not include XBB.1.5, XBB.1.16, EG.5, XBB.1.9.1, XBB.1.9.2, and XBB.2.3.

https://www.who.int/docs/default-source/coronaviruse/18122023_jn.1_ire_clean.pdf

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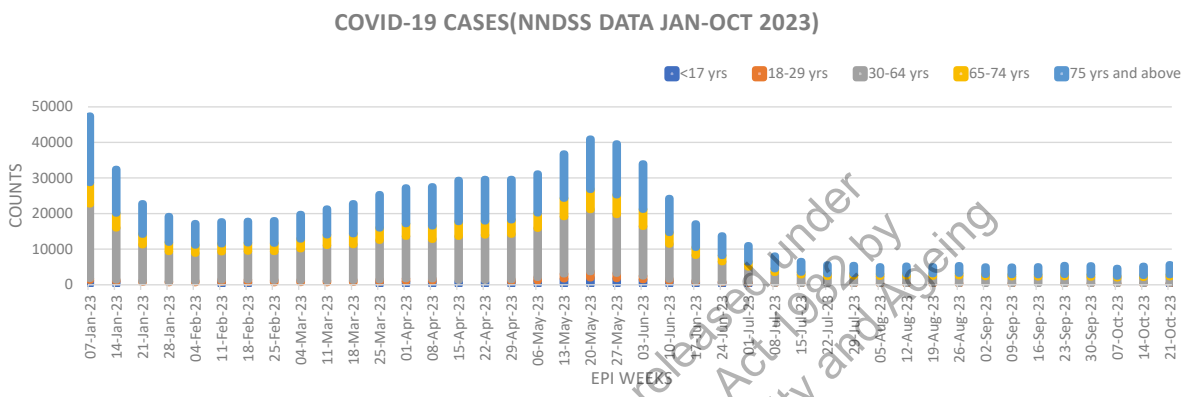
[redacted]

COVID-19 Cases

- Case notifications have dropped overtime, probably due to lower rates of testing



NNDSS data 1st Jan 2023-21ST Oct 2023
COVID-19 cases: Included confirmed + probable cases

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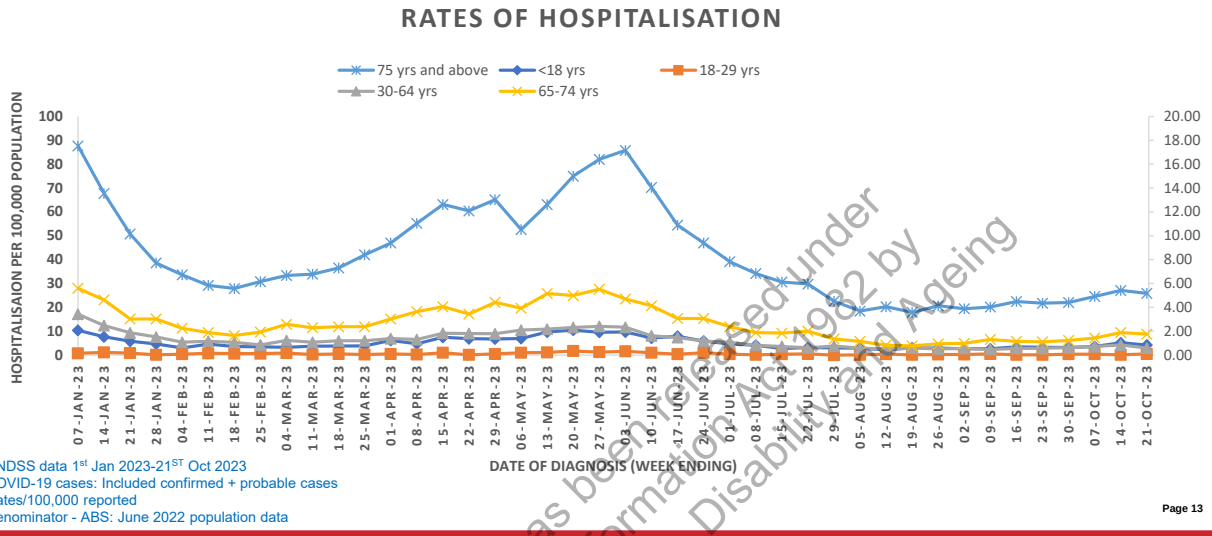
Rates of Hospitalisation by Age Groups and Epi Weeks

- Rates of hospitalisation in adults aged ≥75 years remains much greater than other age groups



NNDSS data 1st Jan 2023-21ST Oct 2023
COVID-19 cases: Included confirmed + probable cases
Rates/100,000 reported
Denominator - ABS: June 2022 population data

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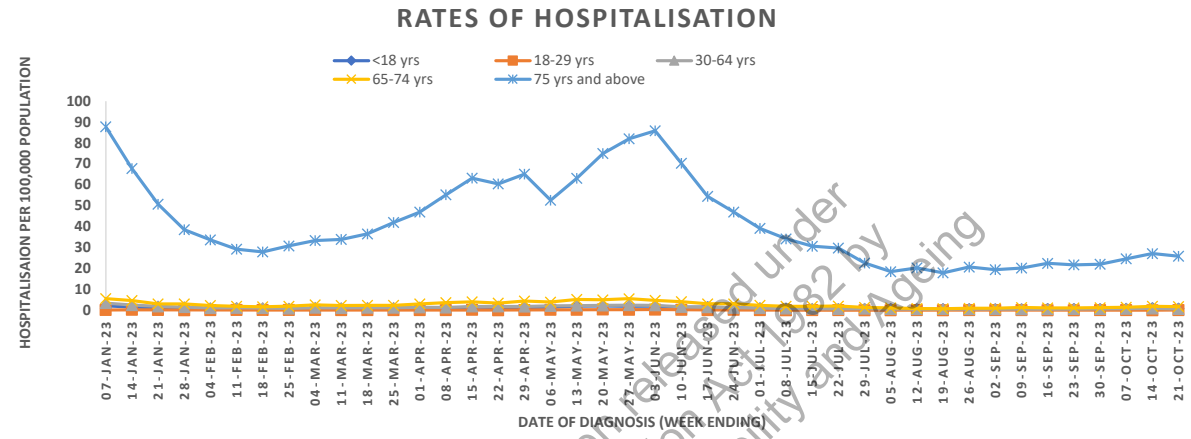
s47B(a) [redacted]

Rates of Hospitalisation by Age Groups and Epi Weeks

- Rates of hospitalisation in adults aged ≥75 years remains much greater than other age groups



NNDSS data 1st Jan 2023-21ST Oct 2023
COVID-19 cases: Included confirmed + probable cases
Rates/100,000 reported
Denominator - ABS: June 2022 population data

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Rates/100,000 and proportion of hospitalisation, ICU admission, and deaths by age group, 1 Jan to 21 Oct 2023

- Rates of hospitalisation, ICU admission, and death remain much higher in adults aged ≥ 65 years, especially ≥ 75 years
- The higher rate in <18 is likely due to over-representation of incidental COVID-19 (when compared to jurisdictional data)

Age groups (yrs)	Hospitalisation			ICU admission			Death		
	N	Rates	Proportion of all hospitalisations among cases (%)	N	Rates	Proportion of all ICU admission among cases (%)	N	Rates	Proportion of all deaths among cases (%)
<18	2435	42.7	8.4	69	1.2	0.2	77	1.3	0.3
18-29	189	4.7	1.0	14	0.3	0.1	1	0.0	0.0
30-64	6257	52.9	1.9	354	3.0	0.1	37	0.3	0.0
65-74	2710	110.9	2.7	207	8.5	0.2	64	2.6	0.1
75 and above	34855	1752.5	12.0	1839	92.5	0.6	4128	207.5	1.4

NNDSS data 1st Jan 2023-21ST Oct 2023
COVID-19 cases: Included confirmed + probable cases
Rates/100,000 reported
Denominator - ABS: June 2022 population data

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Table 7: COVID-19 associated case fatality rates among cases notified to NNDSS, by age group and date of onset, 1 January 2020 to 10 September 2023 [a,b,c,d]

Age group (years)	Omicron to date 15 December 2021 – 10 September 2023	Delta 16 June – 14 December 2021	Pandemic to date 1 January 2020 – 10 September 2023
0–9	< 0.05%	< 0.05%	< 0.05%
10–19	< 0.05%	< 0.05%	< 0.05%
20–29	< 0.05%	< 0.05%	< 0.05%
30–39	< 0.05%	0.06%	< 0.05%
40–49	< 0.05%	0.18%	< 0.05%
50–59	< 0.05%	0.65%	0.05%
60+	1.09%	6.13%	1.19%
Unknown	0.00%	0.00%	0.00%
Australia	**0.18%**	**0.71%**	**0.20%**

a Source: NNDSS, extract from 11 October 2023 for deaths with an illness onset date to 10 September 2023.
b To account for the lag between illness onset and the development of severe illness, cases with an onset date in the last two weeks have been excluded from calculations of the case fatality rate.
c A value of 0.00% indicates that no COVID-19 associated fatalities occurred during the indicated period for the specified age group.
d Crude case fatality rates which reflect number of deaths as a proportion of reported COVID-19 cases during specific periods. Note, the current crude case fatality rates are likely overestimated due to changes in case ascertainment and increased underreporting of non-severe cases.

https://www1.health.gov.au/internet/main/publishing.nsf/Content/99424DA2A5F3A488CA2589BA0019141B/$File/covid_19_australia_epidemiology_report_79_reporting_period_ending_24_september_2023.pdf

s47B(a)

Jurisdictional Data

Jurisdictional severe disease data by vaccine status (confidential)

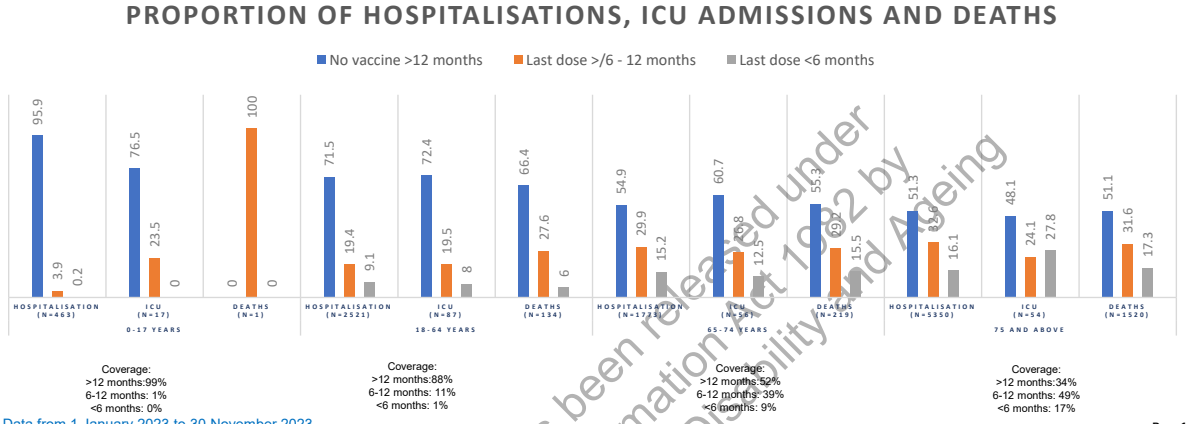
- Attempted to collate jurisdictional data, stratified by vaccine status

- Victoria and Northern Territory kindly provided data. Thanks to:
  - s47F and team (NT)
  - s47F and team (VIC)

- NSW was unable to provide reliable data by vaccine status
- WA and QLD attempted to provide data but did not have capacity to deliver prior to meeting

Victoria: Proportion of Hospitalisations, ICU Admissions, and Deaths from clinical COVID-19 by age

- Adults ≥65 years, especially ≥75 years, who did not receive a vaccine in 2023 were more likely to develop severe disease
- Effect of a 6-monthly dose in adults ≥75 years less clear from these data
- Probable confounding by individuals with at-risk medical conditions over-representing vaccinated cohorts
- Far fewer hospitalisations in <18 years compared to NNDSS data (which probably included many incidental cases)



Coverage:
>12 months:99%
6-12 months: 1%
<6 months: 0%

Coverage:
>12 months:88%
6-12 months: 11%
<6 months: 1%

Coverage:
>12 months:52%
6-12 months: 39%
<6 months: 9%

Coverage:
>12 months:34%
6-12 months: 49%
<6 months: 17%

- Data from 1 January 2023 to 30 November 2023

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s47B(a)

Victoria: Proportion of Hospitalisations, ICU Admissions, and Deaths from clinical COVID-19 by age

PROPORTION OF HOSPITALISATIONS, ICU ADMISSIONS AND DEATHS

Coverage:
>12 months:99%
6-12 months: 1%
<6 months: 0%

Coverage:
>12 months:88%
6-12 months: 11%
<6 months: 1%

Coverage:
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<6 months: 9%

Coverage:
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- Data from 1 January 2023 to 30 November 2023

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s47B(a)

Coverage:
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Coverage:
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Coverage:
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<6 months: 17%

Prepared by NCIRS for ATAGI #96

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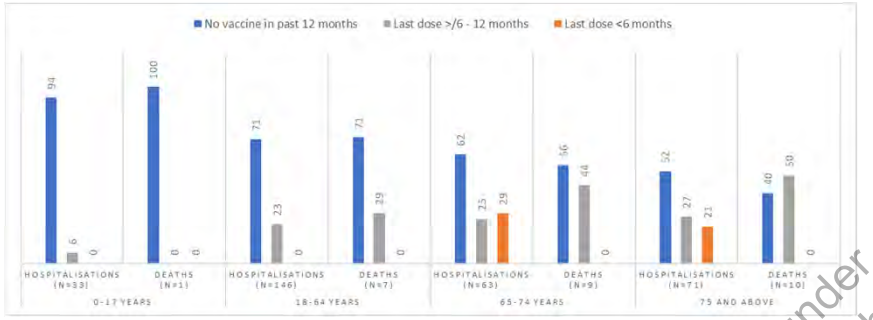

Coverage:
>12 months:99-100%
6-12 months: 0-1%
<6 months: 0-0.4%

Coverage:
>12 months:91-96%
6-12 months: 2-5%
<6 months: 1-3%

Coverage:
>12 months:65%
6-12 months: 20%
<6 months: 14%

Coverage:
>12 months:53-55%
6-12 months: 23-24%
<6 months: 21-22%

In confidence: NT: Proportion of hospitalisations, ICU admissions, and deaths from COVID-19 by age group

- No ICU admission during the period of interest
- Small absolute numbers, difficult to interpret

Prepared by NCIRS for ATAGI #102

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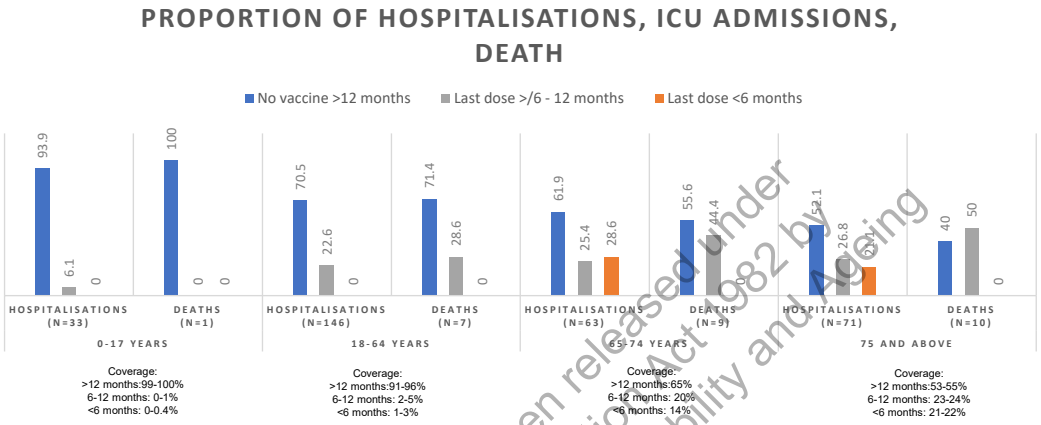
NT: Proportion of Hospitalisations, ICU Admissions, and Deaths from COVID-19 by Age Cohort

- Less NT residents aged ≥65 years received a vaccine within the last 12 months compared to the national average
- More NT residents aged ≥65 years received a vaccine within the last 6 months (unclear if 1 or 2 doses total for 2023)
- Small absolute numbers, difficult to interpret



Coverage:
>12 months:99-100%
6-12 months: 0-1%
<6 months: 0-0.4%

Coverage:
>12 months:91-96%
6-12 months: 2-5%
<6 months: 1-3%

Coverage:
>12 months:65%
6-12 months: 20%
<6 months: 14%

Coverage:
>12 months:53-55%
6-12 months: 23-24%
<6 months: 21-22%

- National coverage data not representative of NT coverage historically
- NT population over-representation of First Nations people
- No ICU admission during period of interest
- The vaccination coverage is current as of 30 Jan 2024

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VE studies of XBB.1.5 vaccines (preprints/published)

VE studies

Study year	Study design and sample size	Vaccine	Findings
Tartof et al, Dec 2023 US	Test-negative case-control study 4232 cases, 19,775 controls, median age of 54 years	BNT162b2 XBB1.5-adapted vaccine vs no XBB1.5-adapted vaccine Received BNT162b2 XBB1.5-adapted vaccine a median of 30 days ago (Oct 11-Dec10, 2023)	VE against hospitalisation: 63% VE against ED/UC: 58% VE against outpatient: 58% Compared to the unvaccinated, those who had received only older versions of COVID-19 vaccines did not show significantly reduced risk of COVID-19 outcomes, including hospital admission.
Werkhoven et al,Dec 2023 Netherland	Screening 2050 hospitalisations including 92 ICU admissions, >60 years old	XBB.1.5 vs at least one previous COVID-19 vaccination VE anytime after 7 days of vaccination (Sep 25 till 5 Dec 2023)	VE against hospitalisation: 70.7% VE against ICU admission: 73.3%
Hansen et al, The Lancet, Jan 2024 Denmark	Cohort 442 247 people were vaccinated, 65 and above age	XBB.1.5 vs at least one previous COVID-19 vaccination Followed up from day 7 after vaccination for an average of 9·9 days (Oct 8 and Oct 26, 2023)	VE against hospitalisation: 77%

https://www.medrxiv.org/content/10.1101/2023.12.24.23300512.abstract
Https://www.medrxiv.org/content/10.1101/2023.12.12.23299855v1
Https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(23)00746-6/fulltext

NITAG Summary

Recommendations for previously vaccinated adults aged 65-74 years

- Over a 12-month period, current recommendations have seen/will see:

- 1 dose for all adults aged 65-74 years (proposed ATAGI position)
  - STIKO (updated May 2023): for all adults ≥ 60 years, 'every 12 months'
  - JCVI (updated October 2023)

- 1 dose for adults aged 65-74 years, can consider a 6-monthly dose (current ATAGI position):
  - NACI (updated Jan 2024)

- 2 doses for adults 65-74 years
  - ACIP (updated Oct 2023): for all ≥6 months old

Recommendations for previously vaccinated adults aged 18-74 years at-risk of severe COVID-19 (without severe immunocompromise)

- Over a 12-month period, current recommendations have seen/will see:
- Can consider 1 dose (proposed ATAGI position)
- Recommended 1 dose per year (current ATAGI position):
  - JCVI (updated October 2023): notes this group is too broad; recommendation was made to keep program simple; narrowing of 'at-risk' populations in the future
  - STIKO (updated May 2023)
  - NACI (updated Jan 2024): high-risk individuals can consider a second dose
- Recommended 2 doses per year:
  - ACIP (updated September 2023): everyone ≥ 6 months, bivalent and XBB.1.5

Evidence to Recommendations

EtR: Previously vaccinated adults aged 65-74 years: recommended 1 dose (remove 'consider' a second dose)

Criteria	Evidence
Is the problem of public health importance?	Yes. Adults aged 65-74 years remain at greater risk of severe disease than their younger peers
Benefits	Reduce vaccine fatigue, especially where needing to 'consider' a dose
Potential harms	There may be a small, but significant, increase in protection against severe disease if given 6-monthly
Value	Evidence of reduced vaccine uptake over time, presumed due to vaccine fatigue
Acceptability	Some individuals may appreciate not having to decide about value of an additional dose; others may disapprove that their access to an additional dose has been removed
Resources	Plentiful supply of vaccines
Feasibility	Relatively simple to implement (infrastructure already in place)

Previously vaccinated adults 18-65 years at-risk of severe COVID-19 (without severe IC): Consider 1 dose (remove active rec)

Criteria	Evidence
Is the problem of public health importance?	Although many medical conditions have been shown to historically increased risk of severe disease, it is unclear whether this remains the case in the context of Omicron and hybrid immunity. Age is a greater risk factor.
Benefits	Simplification of the program (all adults ≥18 years can consider a dose every 12 months)
Potential harms	Vaccine fatigue, especially where needing to 'consider' a dose Some people who may benefit from a 12-monthly dose might not be recommended one
Value	Some members of this group may be very health-conscious and motivated, others may reflect broader population: less interest in vaccine recommendations over time, evidence of reduced vaccine uptake
Acceptability	Access to vaccination would remain; special interest groups may disapprove of a 'downgrade' in recommendations (though these groups have not been representative of their constituents in the past)
Resources	Adequate supply of vaccines – not a limitation
Feasibility	Relatively simple to implement (infrastructure already in place)

Proposed 2024 policy positions

- These recommendations will be reviewed annually (or earlier if new evidence emerges or epidemiology changes):

- ATAGI **recommends** COVID-19 vaccination for the following groups:
  - Adults aged ≥75 years, should receive a dose every 6 **months**
  - Adults aged 65–74 years should receive a dose every **12 months** (remove 'can consider every 6 months')
  - Adults aged 18—74 years with severe immunocompromise should receive a dose every **12 months**, and can **consider** a dose every 6 months based on individual preferences and risk-benefit assessment

- The following groups can **consider** a COVID-19 vaccine every **12 months**, based on an individual risk-benefit assessment:
  - All other adults aged ≥18 years , including those with medical conditions that may increase their risk of severe COVID-19 (remove active 12-monthly recommendation for at-risk groups)
  - Children and adolescents aged 5 – <18 years with severe immunocompromise

List of risk conditions that may be associated with severe COVID-19 - modifying existing conditions

Category	Example medical conditions	COVID-19	FLU	RSV
		THESE COLUMNS WILL NOT BE IN THE COVID-19 STATEMENT – FOR ATAGI REVIEW ONLY, TO COMPARE WITH FLU/RSV		
Cardiac disease	Congenital heart disease, congestive heart failure, coronary artery disease	Y	Y	Y
Chronic respiratory conditions	Severe asthma*, cystic fibrosis, bronchiectasis, suppurative lung disease, chronic obstructive pulmonary disease, chronic emphysema	Y	Y	Y
Immunocompromising conditions	Immunocompromise due to disease or treatment, asplenia or splenic dysfunction , HIV infection, malignancy, solid organ transplant, haematopoietic stem cell transplant	Y	Y	Y
Chronic metabolic conditions	Type 1 or 2 diabetes ~~requiring medication~~, chronic metabolic disorders	Y	Y	Y
Chronic kidney disease Stage 4 and 5		Y	Y	Y
Haematological disorders	Haemoglobinopathies	Y	Y	N
Chronic liver disease	Cirrhosis, autoimmune hepatitis, non-alcoholic fatty liver disease, alcoholic liver disease	Y	Y [recommended not funded, therefore not in statement]	?
Obesity		Y (BMI ~~≥40~~ ≥30kg/m^2)	Y BMI ≥30kg/m^2	?

List of risk conditions that may be associated with severe COVID-19 - substitution of existing conditions

Category	Rationale for removal	COVID-19	FLU	RSV
~~Severe underweight with BMI <16.5 kg/m²~~	very small group; those that are medically unstable could arguably come under 'chronic metabolic disorder	Y	N	N
~~Disability with significant or complex health needs or multiple comorbidities that increased the risk of severe COVID-19 / complex multi-system disorders)~~	Proposing to remove or at least re-word (see below), since this is not a 'medical condition' used in any other ATAGI guidance Substitute with conditions below and conditions on the existing list	Y	N	N

Category	Example medical conditions	COVID-19	FLU	RSV
Chronic neurological conditions	Hereditary and degenerative CNS diseases, seizure disorders, spinal cord injuries, neuromuscular disorders, neurological disabilities	N	Y	Y
Chromosomal abnormality	Trisomy 21 (ACIP and JCVI both specifically list)	Y (as an example medical condition)	N	N

Additional slides

Co-administration with flu vaccines: No studies in children

Study year	Study design and sample size	Vaccine	Findings
Gonen et al 2023, Isreal	Cohort study, HCW, Reactogenicity: 588 Immunogenicity: 151	Influvac Tetra (Abbott) influenza vaccine (2022/2023), the Omicron BA.4/BA.5–adapted bivalent (Pfizer/BioNTech) vaccine, or both	Compared with COVID-19 vaccination alone, the risk of systemic symptoms: (odds ratio, 0.82; 95% CI, 0.43-1.56)in co-admin GMT in the coadministration group: 0.84 (95% CI, 0.69-1.04) times lower vs COVID-19 vaccine–alone group.
Wagenhäuser et al, 2023. Germany	1231 HCW, 249 coadmin group	Quadrivalent influenza and COVID-19 booster vaccination (BNT162b2mRNA / mRNA-1273)	BNT162b2mRNA coadministration, the median anti-SARS-CoV-2-spike IgG: 1560.7 BAU·mL−1 (IQR 1078.0–2493.6 BAU·mL−1), compared to 1955.1 BAU·mL−1 (IQR 1234.6–3022.9 BAU·mL−1) in BNT162b2mRNA-only vaccinated. mRNA-1273 coadministration, a median of 1891.1 BAU·mL−1 (IQR 1068.2–3324.0 BAU·mL−1) was observed, in contrast to 2709.8 BAU·mL−1 (IQR 1735.4–4001.2 BAU·mL−1) for mRNA-1273-only vaccinated. No safety concerns
Moro et al, 2023, USA	2,449 reports of adverse events July 1, 2021–June 30, 2022, adults	mRNA COVID-19 and seasonal inactivated influenza vaccines	Most common AEs among non-serious reports were injection site reactions (193; 14.5%), headache (181; 13.6%), and pain (171; 12.8%). The most common AEs among reports classified as serious were dyspnea (38; 14.9%), COVID-19 infection (32; 12.6%), and chest pain (27; 10.6%).
Ramsay et al, 2023, Australia	RCT, 248, FluVID	mRNA COVID-19 and seasonal inactivated influenza vaccines	142 BNT162b2 booster dose one and 43 BNT162b2 booster dose two recipients, the posterior median risk difference for moderate/severe adverse events following SIV versus placebo: 13% (95% credible interval [CrI] −0.03 to 0.27) and 13% (95%CrI −0.37 to 0.12), respectively. 18 mRNA1273 booster dose one and 35 mRNA1273 booster dose two recipients, the posterior median risk difference of moderate/severe adverse events following influenza vaccine versus placebo: 6% (95%CrI −0.29 to 0.41) and −4% (95%CrI −0.30 to 0.23), respectively
Dulfer et al, 2023, Netherland	RCT, 154, TACTIC study	Vaxigrip Tetra and BNT162b2 COVID-19 booster	Anti-S IgG GMCs for the co-administration and reference group were 1684 BAU/ml and 2435 BAU/ml, respectively. Concurrent vaccination did not meet the criteria for non-inferiority (estimate −0.1791, 95% CI −0.3680 to −0.009831) and antibodies showed significantly lower neutralization capacity compared to the reference group. Reported side-effects were mild and did not differ between study groups.
Hause et al, 2022, USA	September 22, 2021, through May 1, 2022, through v-safe, 981 099 persons aged 12 years or older	COVID-19 mRNA booster and seasonal influenza vaccines	Respondents who simultaneously received influenza and Pfizer-BioNTech booster vaccines (aOR, 1.08; 95% CI, 1.06-1.10) or influenza and Moderna booster vaccines (aOR, 1.11; 95% CI, 1.08-1.14) were slightly more likely to report any systemic reaction in the week following simultaneous vaccination than respondents who received only a COVID-19 mRNA vaccine booster.

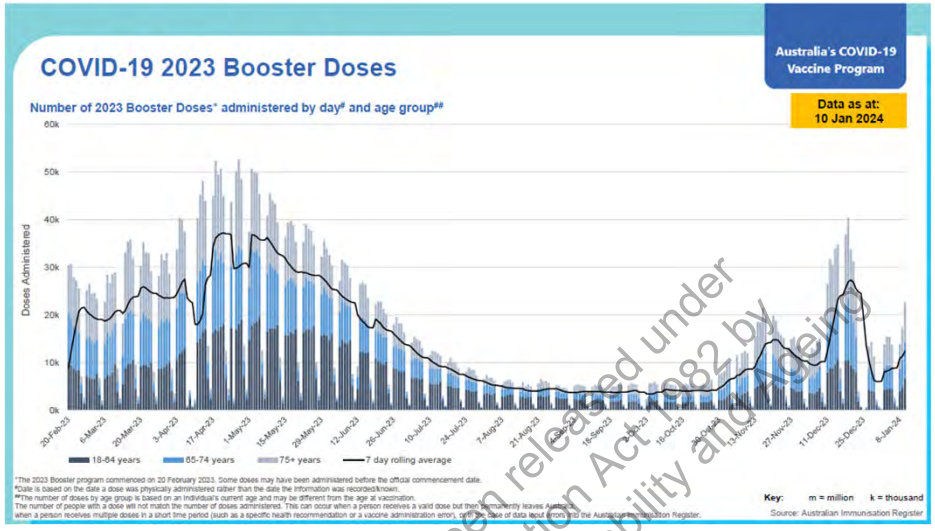
https://jamanetwork.com/journals/jamanetworkopen/article-abstract/2809119 , https://erj.ersjournals.com/content/61/1/2201390, https://www.sciencedirect.com/science/article/pii/S0264410X23000166?casa_token=RGaNetFEPj8AAAAA:hmtyn_M0Y1zIzEGHn_y93QSaqhg8vw40aOHGpiZjcO9UKVj4vHWUo

s47B(a)

Updated Primary Dose Recommendations

- Single primary dose of COVID-19 vaccine
  - Adults aged 18 years or older not immunocompromised
  - Children and adolescents aged 5 years to <18 years who are at high risk of severe COVID-19 but not immunocompromised
- 2 primary doses, 8 weeks apart, and can consider a third primary dose, 8 weeks after dose 2:
  - Children, adolescents and adults aged 5 years or older with severe immunocompromise
  - Children aged 6 months to <5 years who are at increased risk of severe COVID-19 (including severe immunocompromise)
- Children and adolescents aged less than 18 years are no longer recommended a primary dose unless they are at increased risk of severe COVID-19

2023 Booster Doses-COVID-19 Vaccine Rollout Dated 10 Jan 2024

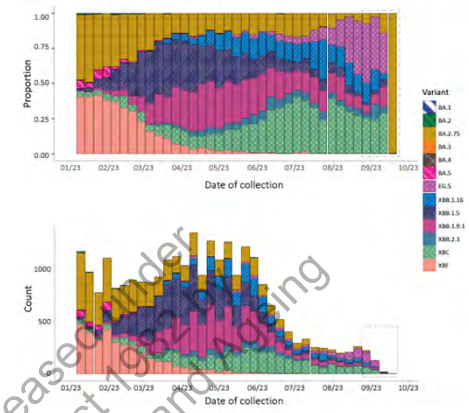


https://www.health.gov.au/sites/default/files/2024-01/covid-19-vaccine-rollout-update-12-january-2023.pdf

Omicron in Australia, Communicable Diseases Intelligence 2023, report 79

- Of the 462 sequences uploaded to AusTrakka between 28 August and 24 September 2023:
- 94.6% (437/462) were recombinant or recombinant sub-lineages;
- 5.2% (24/462) were BA.2.75 sub-sub lineages; and
- One sequence (0.2%,1/462 belonged to a BA.5 sub-lineage.
- No other BA.1, BA.3 or BA.4 Omicron sublineages were identified..

Figure 8: Omicron sub-lineage in Australia since 1 January 2023 by sample collection date, showing (A) proportions and (B) count per week[a,b,c]



a Sequences in Australkka aggregated by epidemiological week.
b The dashed box indicates the distribution of sequences collected within the reporting period.
c Proportions in Figure 8A may not be representative when sequence numbers are small; refer to Figure 8B. Data for earlier epidemiological weeks may change between reporting periods as sequences with older collection dates are uploaded. These numbers are not equivalent to number of cases, as there are many cases which may not be sequenced. Non-VOI and non-VUM Omicron sub-lineages have been removed from current lineages BA.1, BA.2, BA.3, BA.4 and BA.5.

https://www1.health.gov.au/internet/main/publishing.nsf/Content/99424DA2A5F3A488CA2589BA0019141B/$File/covid_19_australia_epidemiology_report_79_reporting_period_ending_24_september_2023.pdf

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Total number of Omicron sequences in Australia: CDGN, 4th Dec 2023

- ^ the number (and percentage) of sequences within the preceding 4 week (28 day) period
  ~ Inclusive of all XBB* sub-lineages

https://www.cdgn.org.au/variants-of-concern

Total # sequences in AusTrakka		# sequences (% in reporting period)^		# sequences in previous two reporting periods (% in reporting period)^			
		04/12/2023		06/11/2023		29/10/2023	
Variants of Concern (VOC)		#	%	#	%	#	%
B.1.1.529	34	0	0	0	0	0	0
BA.1	26272	0	0	0	0	0	0
BA.2	57044	356	44.8%	45	5.2%	26	4.1%
BA.3	3	0	0	0	0	0	0
BA.4	5052	0	0	0	0	0	0
BA.5	43203	0	0	0	0	0	0
Recombinant	35497	438	55.2%	813	94.6%	613	95.6%
Total	167105	794		859		641	
Variants of Interest (VOI)							
XBB.1.5 + sub-lineages	5782	34	4.3%	52	6.1%	49	7.6%
XBB.1.16	4571	22	2.8%	102	11.9%	69	10.8%
EG.5 (XBB.1.9.2.5)	4449	321	40.4%	438	51.0%	310	48.3%
JN.1	449	251	31.6%	-	-	-	-
BA.2.86	805	351	44.2%	-	-	-	-
Variants under monitoring (VUM)							
Recombinant							
XBB + all sub-lineages	23973	408	51.4%	720	83.8%	524	81.7%
XBB.1.9.1, XBB.1.9.2 + sub-lineages	9824	338	42.6%	509	59.3%	360	56.2%
XBB.2.3	1408	8	1.0%	35	4.1%	20	3.1%
XBC	4539	17	2.2%	85	4.1%	86	13.4%
DV.7	119	5	0.06%	88			
Omicron BA.2							
BA.2.75 + sub-lineages	14577	5	0.06%	16	1.9%	12	1.9%
CH.1.1 + sub-lineages	4465	5	0.06%	16	1.9%	12	1.9%

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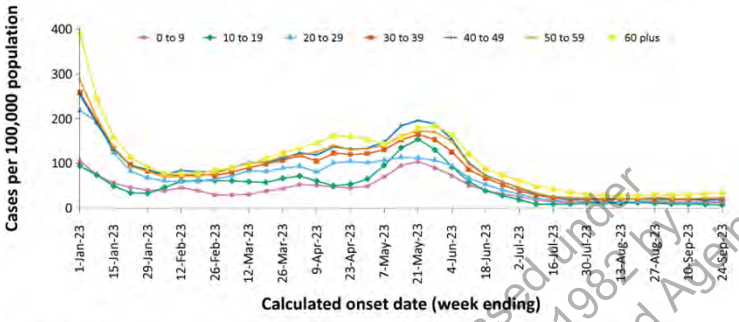
s47B(a)

COVID-19 Epidemiology Report 79 – selected figures

Figure 2: Confirmed and probable COVID-19 notification weekly rates for ten-year age groups by date of onset, Australia, 26 December 2022 – 24 September 2023[a,b]



a Source: NNDSS extract from 11 October 2023 for cases with an illness onset from 26 December 2022 to 24 September 2023.

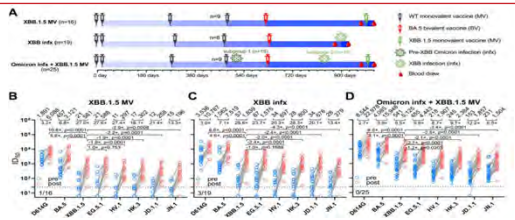
b Population data based on Australian Bureau of Statistics (ABS) Estimated Resident Population (ERP) as at June 2022.

https://www1.health.gov.au/internet/main/publishing.nsf/Content/99424DA2A5F3A488CA2589BA0019141B/$File/covid_19_australia_epidemiology_report_79_reporting_period_ending_24_september_2023.pdf

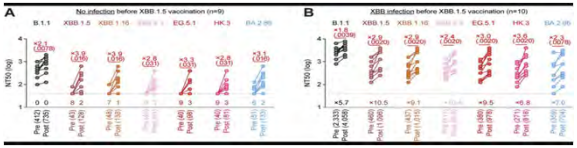
NCIRS NNDSS analysis

- NNDSS data extracted: Date of diagnosis 1st Jan to the latest 23rd Oct 2023(Epi week ending: 28th Oct)
- COVID-19 cases: Included confirmed + probable cases
- Rates/100,000 reported
- Denominator - ABS: June 2022 population data
- Age groups: <18, 18-<30, 30-<65, 65-<75, 75 and above

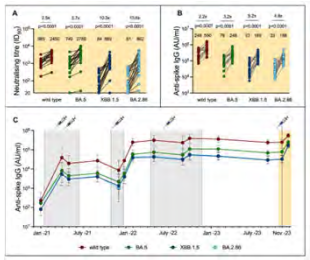
Immunogenicity studies



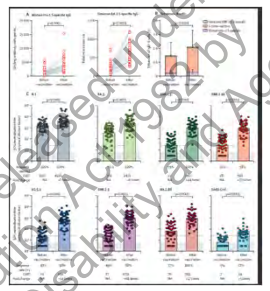
Guo et al, Dec 2023: XBB vaccine to uninfected individuals boosted serum virus-neutralization antibodies against not only XBB.1.5 (27.0-fold) and the currently dominant EG.5.1 (27.6-fold) but also key emergent viruses like HV.1, HK.3, JD.1.1, and JN.1 (13.3-to-27.4-fold).



Kosugi et al Nov 2023: XBB vaccine sera with prior infection efficiently (1.8-to 3.6-fold) boosted antiviral humoral immunity against all variants tested. In the case of the XBB vaccine sera without prior infection, vaccine induced antiviral activity (2.1-to 3.9-fold) against all variants.



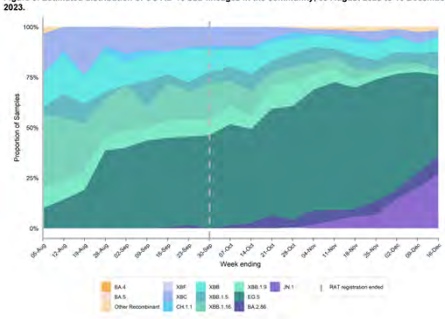
Marking et al, Dec 2023: Increase in neutralisation of all variants tested following the XBB vaccine. GMT to XBB.1.5 increased more than 10 times two weeks post vaccination (84 to 869).



Stankov et al Nov 2023: omicron XBB.1.5 vaccination resulted in 2·9-fold increase in anti-S IgG and a 3·6-fold increase in omicron anti-S IgG. After vaccination, percentage of RBD-binding MBCs expanded significantly (mean frequency 0·88%) a 100% response rate at baseline for B.1pp, 91% for BA.5pp, 55% for XBB.1.5pp, 43% for EG.5.1pp and 77% for BA.2.86pp

Epidemiological weeks 52-01, ending 6th Jan 2024: Estimated distribution of COVID-19 sub-lineages in the NSW community

Figure 9. Estimated distribution of COVID-19 sub-lineages in the community, 05 August 2023 to 16 December 2023.



EG.5 continues to dominate circulating sub-lineages and the proportion sequenced as JN.1 is increasing. Insufficient samples were sequenced to update the graph beyond 16 December 2023.

https://www.health.nsw.gov.au/Infectious/covid-19/Documents/respiratory-surveillance-20240106.pdf

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Respiratory Surveillance Report: Tasmania (31st Dec 2023)

COVID-19 variants identified by whole genome sequencing in Tasmania:

- During the last four weeks (from 03 December to 24 December 2023), a total of 138 samples were sequenced.
- Among the viruses that were genotyped, the majority of variants characterized were Omicron recombinant XBB or BA.2 sub-lineages.
- Among 138 samples, 49 (36%) were JN, 47 (35%) were HK and 10 (7%) were HV.

https://www.health.tas.gov.au/sites/default/files/2024-01/fortnightly-respiratory-surveillance-report-to_31_december_2023.pdf

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Respiratory Surveillance Report: Victoria (Dec 2023)

Current indicators show high levels of COVID-19 activity in Victoria.

The emergence of JN.1 in Victoria is expected to contribute to prolonged high levels of COVID-19 activity through December and January.

Daily numbers last 12 weeks

The number of people in hospital with COVID-19 increased this week with a daily average of 306, up from 266 last week. The current average remains high compared to recent months but remains below the most recent peak in May/June.

The **7-day average of ICU patients declined this week** (15 to 13).

Quantitative wastewater measures indicate there are high COVID-19 viral loads in Victorian wastewater. Metropolitan wastewater catchments have shown increased levels in the most recent samples, while regional quantitative wastewater levels continue to remain high.

Higher levels of SARS-CoV-2 in wastewater suggest higher prevalence of COVID-19 infections in the community.

(Plot shows metro median relative quantitative levels of COVID-19 in wastewater)

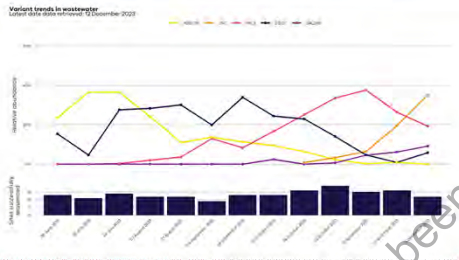
Deaths in the most recent 28-day period (08/11/2023 – 05/12/2023) have continued to increase, compared to the prior 28-day period (11/10/2023 – 07/11/2023), with a current 28-day total of 183. Increases and decreases in the reporting of deaths attributable to COVID-19 tend to lag waves of infections and hospitalisations by several weeks.

(Note that reporting periods for deaths are lagged by 2 weeks to allow for delays in data collection)

Following rapid growth in recent weeks, **JN.1 (a sublineage of BA.2.86) is now the most prevalent single subvariant in Victorian wastewater samples** and is being closely monitored.

A mix of Omicron recombinant sublineages continue to make up the majority of variant share in Victoria.

Globally EG.5 and subvariants remain the most prevalent variant of interest. However, of most concern is **JN.1, which remains the fastest growing variant worldwide.**



The polyclonal representation of SARSCoV-2 subvariants across Victoria continues to be dominated by Omicron XBB recombinant sublineages.
Analysis of wastewater samples can help us understand which SARS-CoV-2 variants are currently circulating in Victoria.
In the past there have been waves of infections and hospitalisations when a new variant or subvariant has spread quickly relative to the others.
There are a number of closely related sublineagescirculating in Victoria. Only the most detected variants have been displayed here.

chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.health.vic.gov.au/sites/default/files/2023-12/victorian-covid-19-surveillance-report-22december-2023_0.pdf
file:///C:/Users/anana/Downloads/consolidated-surveillance-report-13-october-2023.pdf

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Tartof et al, Preprint medRxiv 28th Dec 2023: US, BNT162b2 XBB1.5-adapted Vaccine and COVID-19 Hospital Admissions and Ambulatory Visits, Adults

- **Study design**: Test-negative case-control study,
- **Objectives**:Compare the odds of BNT162b2 XBB1.5- adapted vaccine receipt between COVID-19 cases and test-negative controls among adults in the Kaiser Permanente Southern California health system between October 11 and December 10, 2023
- **Analysis**: Regression
- **Vaccine**: BNT162b2 XBB1.5-adapted vaccine compared to not receiving an XBB1.5-adapted vaccine
- **Past history of infection**: Regardless of prior COVID-19 vaccination or SARS-CoV-2 infection history
- **Outcomes**: COVID-19 hospital admissions, emergency department (ED) and urgent care (UC) encounters, and outpatient visits.
- **Results**: 4232 cases, 19,775 controls, median age of 54 years
- Adjusted ORs for testing positive for SARS-CoV-2 among those who received BNT162b2 XBB1.5-adapted vaccine a median of 30 days ago (vs not having received an XBB1.5-adapted vaccine of any kind) were 0.37 (95% CI: 0.20–0.67, VE(63%) for COVID-19 hospitalization, 0.42 (0.34–0.53) Ve(58%) for ED/UC visits, and 0.42 (0.27–0.66) VE(58%) for outpatient visits.
- Compared to the unvaccinated, those who had received only older versions of COVID-19 vaccines did not show significantly reduced risk of COVID-19 outcomes, including hospital admission.

https://www.medrxiv.org/content/10.1101/2023.12.24.23300512v1

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Werkhoven et al, Preprint medRxiv 13th Dec 2023: Netherlands, VE of XBB.1.5 vaccine against hospitalisation and ICU admission, ≥60 years old

- **Study design**: Screening
- **Objectives**: e 2023 seasonal VE among persons aged 60 years and older (birth year 1962 or before) with at least one previous COVID-19 vaccination. Study period: 9 October and 5 December 2023
- **Analysis**: VE and 95% confidence intervals (95%CI), logistic regression model, with vaccination status as dependent variable and the covariate-specific logit of seasonal dose received in the population as offset. The exponentiated intercept of this model is interpreted as the relative risk (RR), and VE is calculated as (1-RR) x 100%
- **Vaccine**: XBB.1.5 vs at least one previous COVID-19 vaccination
- **Past history of infection:** not reported
- **Outcomes**: COVID-19 hospital admissions, emergency department (ED) and urgent care (UC) encounters, and outpatient visits.
- **Results**: 2050 hospitalisations including 92 ICU admissions. VE against hospitalisation: 70.7% (95% CI: 66.6; 74.3), VE against ICU admission: 73.3% (95% CI: 42.2; 87.6).

https://www.medrxiv.org/content/10.1101/2023.12.12.23299855v1

Guo et al, Preprint bioRxiv 6th Dec 2023: US, XBB.1.5 monovalent mRNA vaccine booster elicits robust neutralizing antibodies against emerging SARS-CoV-2 variants

Study design: Cohort

Methods: Sera examined by anti-nucleoprotein (NP) ELISA to determine status of prior SARS-CoV-2 Serum samples from 60 individuals across three different cohorts were collected. The three cohorts were

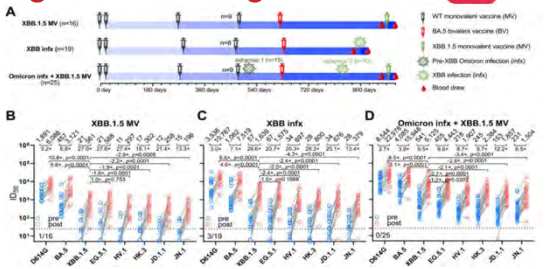
- 1) No recorded SARS-CoV-2 infections who received an XBB.1.5 monovalent vaccine booster ("XBB.1.5 MV");
- 2) Recent XBB infection who did not receive an XBB.1.5 vaccine booster ("XBB infx"); and
- 3) Prior Omicron infection who also received an XBB.1.5 monovalent vaccine booster ("Omicron infx + XBB.1.5 MV")

Objectives: Neutralizing antibody responses induced by XBB.1.5 mRNA vaccines against currently circulating and newly emerged subvariants

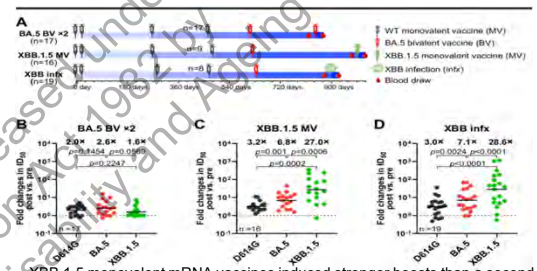
Results: 78% females, mean age 49.7 years. Sera collected an average of 26 days pre and post XBB.1.5 vaccination or XBB infection. infection. Monovalent mRNA vaccine (XBB.1.5 MV) to uninfected individuals boosted serum virus-neutralization antibodies significantly against not only XBB.1.5 (27.0-fold) and the currently dominant EG.5.1 (27.6-fold) but also key emergent viruses like HV.1, HK.3, JD.1.1, and JN.1 (13.3-to-27.4-fold).

In individuals previously infected by an Omicron subvariant, serum neutralizing titers were boosted to highest levels (1,504-to-22,978) against all viral variants tested.

https://www.biorxiv.org/content/10.1101/2023.11.26.568730v2



Neutralizing antibody titers before and after an XBB.1.5 mRNA booster, XBB infection, or both.



XBB.1.5 monovalent mRNA vaccines induced stronger boosts than a second BA.5 bivalent mRNA vaccine.

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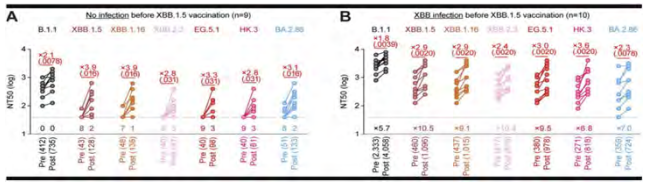
Kosugi et al, Preprint bioRxiv 30th Nov 2023: Japan, Antiviral humoral immunity against SARS-CoV-2 Omicron subvariants induced by XBB.1.5 monovalent vaccine in infection-naïve and XBB-infected individuals

- **Study design:** Cohort
- **Methods**: two types of sera from individuals vaccinated with the XBB.1.5 vaccine; those who had not been previously infected with SARS-CoV-2(N=9) and those who had been infected with XBB subvariants prior to XBB.1.5 vaccination (N=10). We collected sera before and 3-4 weeks after vaccination, and then performed a neutralization assay using these sera and pseudoviruses.
- **Objectives**: Antiviral humoral immunity against SARS-CoV-2 Omicron subvariants induced by XBB.1.5 monovalent vaccine
- **Results**:XBB.1.5 vaccine sera with prior XBB infection efficiently (1.8-to 3.6-fold) boosted antiviral humoral immunity against all variants tested with statistical significance.
- In the case of the XBB.1.5 vaccine sera without prior infection, XBB.1.5 vaccine also induced efficiently antiviral activity (2.1-to 3.9-fold) against all variants tested with statistical significance.
- In sera collected prior to XBB.1.5 vaccination, the 50% neutralization titer of sera from the XBB-infected cohort was 5.7-to 10.4-fold higher than that of sera from the infection-naïve cohort.
-



The neutralization activity induced by XBB.1.5 monovalent vaccine

https://www.biorxiv.org/content/10.1101/2023.11.29.569330v1

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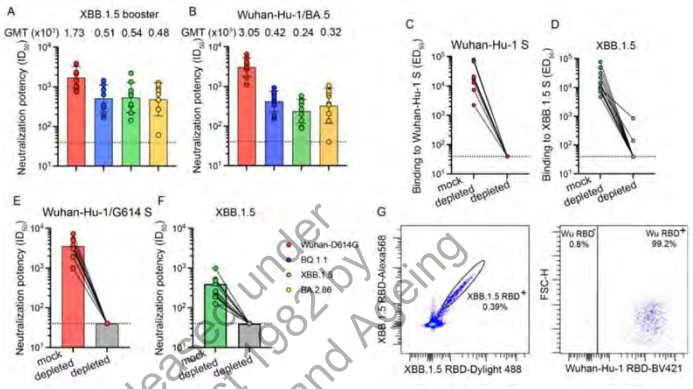
s47B(a)

Tortorici et al, Preprint bioRxiv 30th Nov 2023: US, Persistent immune imprinting after XBB.1.5 COVID vaccination in humans

- **Study design:** Cohort
- **Methods**: Collected plasma from individuals who had previously received multiple vaccine doses with or without known infection. Vesicular stomatitis virus (VSV) pseudotyped with the Wuhan-Hu-1/D614G S, BQ.1.1 S, XBB.1.5 S or the BA.2.86 S to assess the potency and breadth of plasma neutralizing antibodies in this cohort and compare them with plasma collected upon receipt of the bivalent Wuhan-Hu-1/BA.5 vaccine booster.
- **Objectives**: humoral immunity elicited upon receipt of an XBB.1.5 S mRNA vaccine booster
- **Results**:Neutralizing activity was highest against the Wuhan-Hu-1/G614 S VSV with geometric mean titers (GMTs) of 1,700 and 3,000 after receiving the XBB.1.5 S and the Wuhan-Hu-1/BA.5 S bivalent vaccine boosters, respectively. GMTs against BQ.1.1, XBB.1.5 and BA.2.86 S VSV were 510, 540 and 480 (after XBB.1.5 S vaccination) or 420, 240 and 320 (after bivalent vaccination), respectively.



Immune imprinting dominates the immune response elicited upon XBB.1.5 S mRNA booster vaccination in humans.

https://www.biorxiv.org/content/10.1101/2023.11.28.569129v1.full

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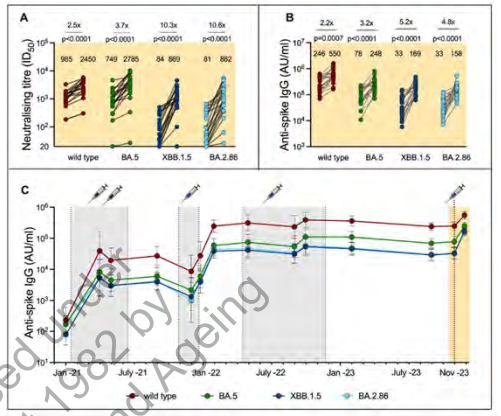
s47B(a)

Marking et al, Preprint: bioRxiv 21st Dec 2023: Sweden, Humoral immune responses to the monovalent XBB.1.5-adapted BNT162b2 mRNA booster

- **Study design:** ongoing observational Covid-19 Immunity (COMMUNITY) cohort study
- **Methods**: humoral responses in 24 individuals who were vaccinated with 30 µg of the monovalent XBB.1.5-adapted BNT162b2 mRNA booster vaccine in November 2023. Serological assessments at four-month intervals since April, 2020. Pseudotyped virus-based neutralisation assay was used
- **Objectives**: Humoral immune responses to the monovalent XBB.1.5-adapted BNT162b2 mRNA booster
- **Results**: (18/20) had received four or more vaccine doses prior to the monovalent XBB.1.5 booster, 18/20 had at least one confirmed prior SARS-CoV-2 infection, and the median age was 64. A significant increase in neutralisation of all variants tested following the XBB.1.5 vaccine. Geometric mean neutralising ID50 titres (GMT) to XBB.1.5 increased more than 10 times two weeks post vaccination (84 to 869).
- Importantly, neutralising titres to BA.2.86 were boosted with a similar magnitude (81 to 862)
- Binding antibody titres to all variants tested also increased significantly following XBB.1.5 vaccination, with relatively larger increases observed towards XBB.1.5 and BA.2.86 compared to wild type and BA.5



Monovalent XBB.1.5-adapted BNT162b2 booster vaccination elicits robust cross-neutralizing antibody responses.

https://www.biorxiv.org/content/10.1101/2023.12.21.572575v1.full

DoHAC data: Number of COVID-19 doses in 2023 by age group

	0 – 17 years		18– 44 years		45 to 54 years		55 to 64 years		65 to 74 years		75 and over	
	N	Proportion	N	Proportion	N	Proportion	N	Proportion	N	Proportion	N	Proportion
0 episodes	5,600,060	99.14%	8,788,476	93.01%	2,834,469	86.90%	2,246,043	74.48%	1,258,639	51.86%	635,324	**33.67%**
1 episode	37,816	0.67%	629,228	6.66%	400,929	12.29%	703,228	23.32%	956,872	39.43%	921,345	**48.83%**
2 episodes	10,370	0.18%	30,371	0.32%	25,917	0.79%	65,742	2.18%	210,001	8.65%	327,803	**17.37%**
3 or more episodes	110	0.00%	748	0.01%	274	0.01%	519	0.02%	1,404	0.06%	2,391	**0.13%**

Data source: Australian Immunisation Register as at 11:59pm 30/01/2024
Only episodes with an encounter date between 01-Jan-2023 and 31-Dec-2023 are included
Number of episodes in 2023 are the number of doses received in 2023 and are NOT part of a persons dosing sequence (e.g. those that have received 0 doses in 2023 may have received doses 1 and 2 in previous years)
0 episodes is calculated by subtracting 2021 ERP from total doses administered in 2023

- Most adults aged ≥75 and 65-74 years did not receive the recommended doses in 2023

Victoria Health

Counts of hospitalisations, ICU admissions, and deaths from COVID-19 from 1 January 2023 to 30 November 2023 by age cohort

	No vaccine > 12 months			Last dose >/= 6 months to 12 months			Last dose < 6 months		
Age Cohort	Hosp	ICU	Deaths	Hosp	ICU	Deaths	Hosp	ICU	Deaths
<0.5	167	5	0	0	0	0	0	0	0
0.5-<5	179	6	0	0	0	0	0	0	0
5-<12	50	1	0	10	3	0	0	0	0
12-<18	48	1	0	8	1	1	1	0	0
18-<30	292	1	3	40	2	0	6	0	0
30-<65	1511	62	86	449	15	37	223	7	8
65-<75	974	34	121	530	15	64	269	7	34
75-<85	1485	20	301	952	9	170	465	14	78
>/=85	1257	6	475	792	4	311	399	1	185

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NT Health

	No vaccine > 12 months			Last dose >/= 6 months to 12 months			Last dose < 6 months		
Age Cohort	Hosp	ICU	Deaths	Hosp	ICU	Deaths	Hosp	ICU	Deaths
<0.5	4		0	0		0	0		0
0.5-<5	22		0	0		0	0		0
5-<12	4		0	1		0	0		0
12-<18	1		1	1		0	0		0
18-<30	7		0	1		0	0		0
30-<65	96		5	32		2	10		0
65-<75	39		5	16		4	8		0
75-<85	24		0	11		4	10		0
>/=85	13		4	8		1	5		1

The vaccination coverage is current as of today 30 Jan 2024. There was no denominator for <6 months so I divided 1 year old by half.

NITAGs Recommendations for Further Doses

NITAGs	Further doses
WHO	Adult over 75 years, adult over 50/60 with comorbidities, immunocompromised individuals (6-12 months revaccination) Adult over 50/60 yrs, adults with comorbidities, healthcare workers (12 months revaccination) Single dose in each pregnancy
US	Up-to date with new vaccine and people who are moderately or severely immunocompromised may get additional doses of updated COVID-19 vaccines (2 or more months after the last recommended COVID-19 vaccine)
JCVI	Committee considered if, as part of the precautionary response, the autumn 2023 cohorts should be expanded and if any already eligible cohorts should be revaccinated. Committee agreed that those who had already received a COVID-19 vaccine in September and October 2023 did not need a second vaccine dose this winter.
NACI	For those previously vaccinated but who did not receive an XBB.1.5 vaccine, a dose of XBB.1.5 is recommended 6 months following previous vaccination or infection. Starting in the spring of 2024, adults 65 years and above, adult residents of long-term care homes, and individuals 6 months of age and older who are moderately to severely immunocompromised may receive an additional dose of XBB.1.5 COVID-19 vaccine
STIKO	Persons aged ≥ 60 years, persons aged 6 months or older with an underlying disease associated with an increased risk of severe COVID-19, persons of any age with an increased occupational risk of infection in health care and nursing settings with direct patient or resident contact, as well as family members and close contacts of individuals in whom a protective immune response (at least 12 months after the last known antigen exposure)
Hongkong	Aged 50 or above (including elderly living in residential care homes), adults aged 18 to 49 with underlying comorbidities, persons aged 6 months or above with immunocompromising conditions, pregnant women, healthcare workers (at least six months after the last dose/infection)
Norway	Adults aged 65 years and above, and residents in nursing homes, adults aged 18-64 years who are in a risk group, adolescents aged 12-17 years with severe underlying conditions, children aged aged from 6 months up to, and including, 11 years with severe underlying conditions if the child's doctor considers it necessary, pregnant women in their second and third trimesters (following groups should take a booster dose of coronavirus vaccine before the autumn/ winter season 2023/2024)

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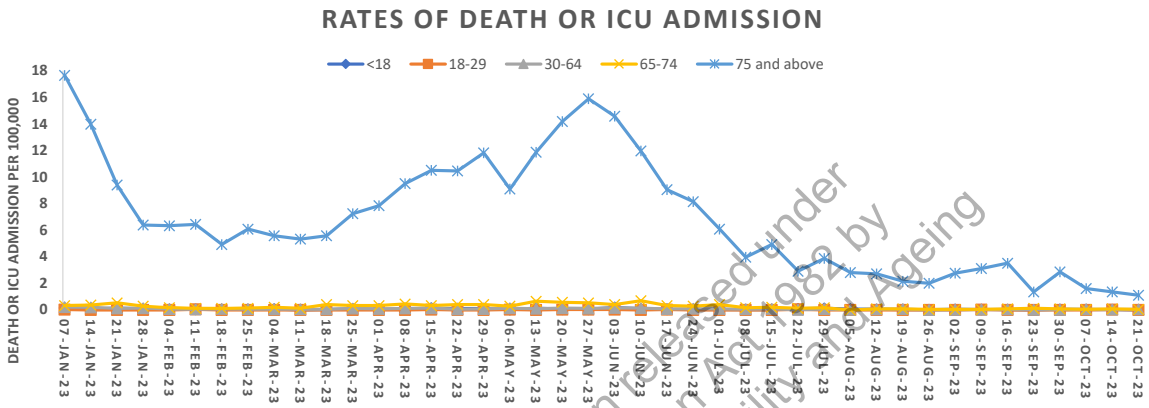
Rates of Death or ICU Admission by Age Groups and Epi Weeks

- Rates of ICU admission or death in adults aged ≥75 years remains much greater than other age groups



NNDSS data 1st Jan 2023-21ST Oct 2023
COVID-19 cases: Included confirmed + probable cases
Rates/100,000 reported
Denominator - ABS: June 2022 population data

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Single primary dose of COVID-19 vaccine

Prepared by NCIRS

s47F

Aim

- Many NITAGs have moved to single primary dose recommendation with the introduction of the XBB.1.5-containing variant vaccines

- Past infection commonplace: first immunising event in lieu of a dose
- Simplification of program recommendations

- Recap evidence reviewed at ATAGI#98 (available in full in 'back-up slides' section)
- NITAG summary
- Evidence to recommendation framework
- Endorse a policy position

Policy options

People without severe immunocompromise:

1. two-dose primary course for ≥ 5 years (current)
2. single dose primary series for ≥ 6 months
3. single dose primary series for ≥ 5 years
    A. children aged 6 months to 4 years: 3 primary Pfizer doses (current)
    B. children aged 6 months to 4 years: 2 primary Pfizer doses

People with severe immunocompromise:

1. 1 additional primary dose
2. specify 3 primary doses

Summary

- Limited immunogenicity and vaccine effectiveness data suggest 1 primary dose and a past infection is as effective as 2 primary doses and no past infection in adults and children aged ≥ 5 years

- Evidence gaps:
  - 1-dose vs 2-dose primary series in context of past infection
  - 1 dose in children aged 6 months to 4 years
  - 1 dose in people with severe immunocompromise

- Most NITAGs recommend:
  - a single primary dose for 'healthy' people ≥ 5 years
  - an additional dose (optional or recommended) for people with severe immunocompromise (resulting in 1 less dose than current)
  - existing primary course doses for children aged 6 months to 4 years (including severe immunocompromise); i.e., no dose reduction

Summary of Evidence: Immunogenicity studies

- Total: N=12 studies, healthcare workers (n=10, sample size:50-475), adolescents(n=2, sample size 10-419)
- Study period 2020-2021 (2 studies 2022), Vaccination: mRNA

- Different immunological outcomes (Antibody titres, IgG and humoral response, IgA antibodies, Interferon-gamma (IFNγ) production by SARS-CoV-2-specific CD4+ and CD8+ T cells)
- Antibody responses: measured at different point in times (14 days, 4 weeks, 8 weeks)

- **Among adolescent**:
  - Antibody responses to the first vaccine dose in individuals with prior infection is equal to or exceeds the antibody titers found in naïve individuals after the second dose

- **Among adults**:
  - Individuals with previous COVID-19 infection generate strong humoral and cellular responses to one dose of COVID vaccine compared to those with no previous infection
  - Spike-specific IgG antibody levels and ACE2 antibody binding inhibition responses elicited by a single vaccine dose in individuals with prior infection were similar to those seen after two doses of vaccine in individuals without prior infection

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Summary: Vaccine effectiveness vs severe disease (single dose + past infection)

- **Adults**:
  - 1 study (2023, n = 2500)[1] evaluating VE vs ICU, intubation, and death (mRNA and others) of 1 dose among individuals with past infection and reported >90% risk reduction if infected prior to vaccination, and >80% risk reduction if vaccinated prior to a past infection.
  - Median time since vaccination/past infection not reported

- **Children and adolescent**:
  - 1 systematic review, 4 additional NRSIs; data from 2020-2023; mRNA vaccines
  - Single dose with past history of infection (73%-86%[2-6]) provided the same VE vs severe disease compared to two dose primary with no past infection (63%-85%[2-6]) at one month post dose
  - Wide
  - Data on waning are limited

Prepared by NCIRS for ATAGI #101

1 https://www.frontiersin.org/articles/10.3389/fpubh.2023.1146059/full
2 https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(23)00272-4/fulltext#:~:text=Interpretation,more%20effective%20than%20monovalent%20boosters.
3 https://www.thelancet.com/journals/laninf/article/
4 https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2797311
5 https://pubmed.ncbi.nlm.nih.gov/36623827/
6 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10065234

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NITAG summary: individuals aged ≥ 5 years (without severe immunocompromise)

- Primary course recommendations:
  - WHO SAGE/EMA: based on disease burden, cost-effectiveness and other health or program priorities and opportunity costs
  - US ACIP (≥6 months) (June 2023): 1 dose
  - UK JCVI (September 2023): 1 dose
  - Canada NACI (October 2023): 1 dose
  - Germany STIKO (≥18 years) (July 2023): 2 doses

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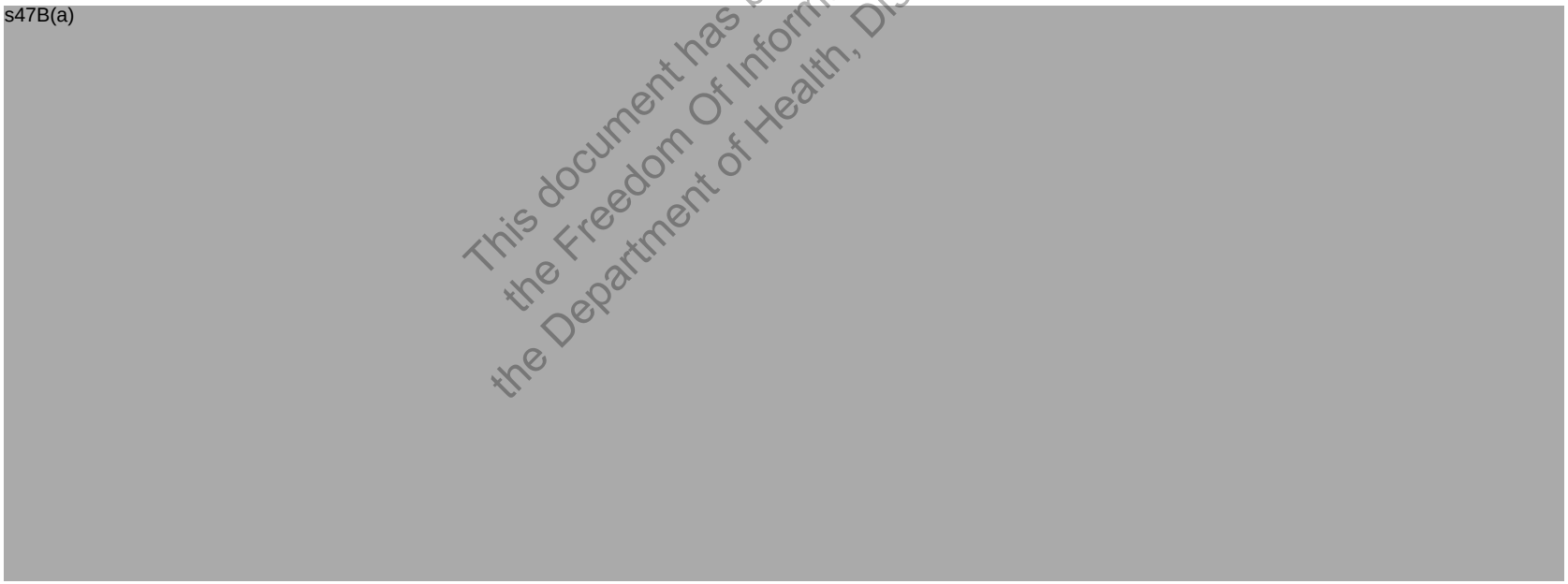

Evidence gaps

- No direct data on immunogenicity or protection against severe disease in:
  - single vs 2-dose primary course with past infection
  - single or 2-dose primary course in children aged 6 months to 4 years
  - single or 2-dose primary course in people with severe immunocompromise

NITAG summary: aged 6 months to 4 years at-risk (but without severe immunocompromise)

- Pfizer original strain and XBB.1.5 formulations are/will be registered for use as a 3-dose primary series in this age group
- Primary course recommendations have all been maintained:
  - US ACIP (October 2023): 3 doses
  - UK JCVI (September 2023): 2 doses
  - Canada NACI (October 2023): 3 doses
  - Germany STIKO (July 2023): 2 doses, 3rd at physician discretion

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NITAG summary: severely immunocompromised

- Primary course recommendations:

- Aged ≥ 5 years
  - optional additional dose: ACIP (2 doses), JCVI (2 doses), STIKO (3 doses)
  - additional dose recommended: NACI (2 doses)

- Aged 6 months to 4 years
- Recommendations regarding an additional dose have been maintained:
  - optional additional dose: ACIP (4 doses), JCVI (3 doses), STIKO (3 doses)
  - additional dose recommended: NACI (4 doses)
  - (current ATAGI: additional dose is not recommended)

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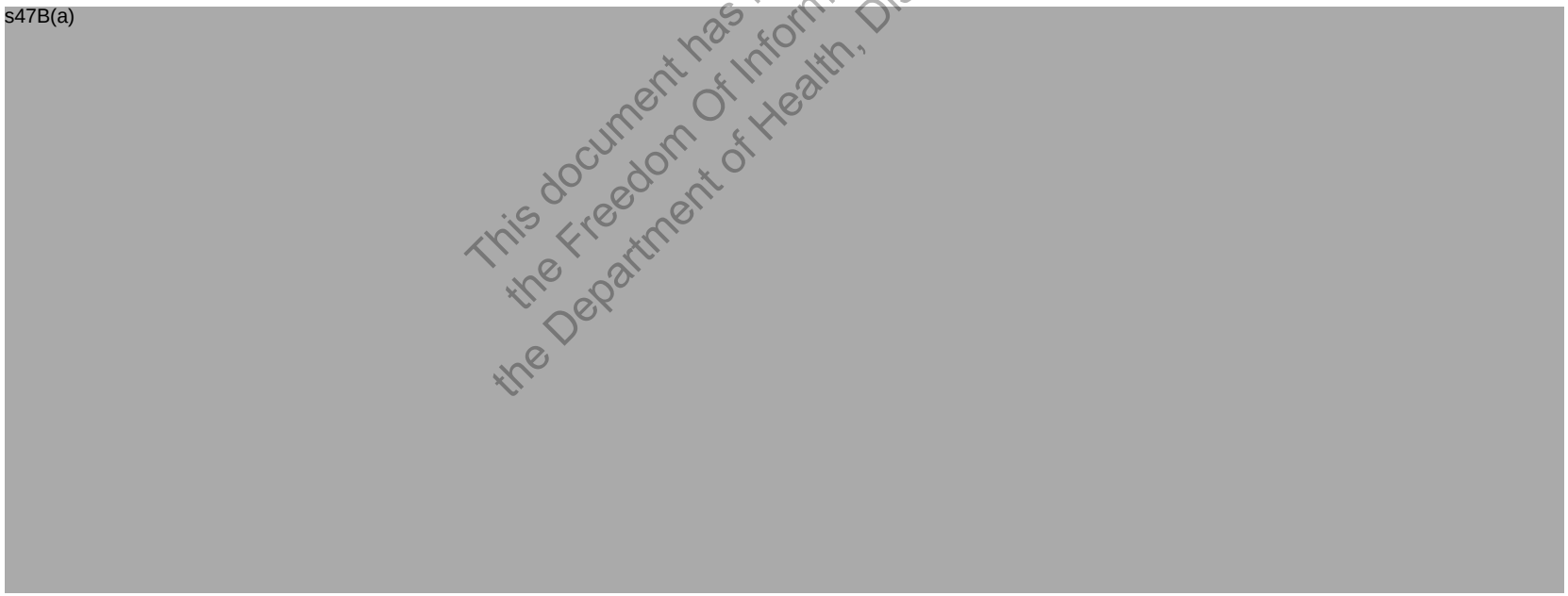

Evidence to Recommendation Framework

Criteria	Evidence
Is the problem of public health importance?	• COVID-19 continues to cause severe disease and death, especially in those aged 65 years and older and those with at-risk medical conditions
Benefits	• Single primary dose in context of widespread hybrid immunity is probably equivalent to two primary doses earlier in the pandemic • Single dose may reduce the risk of myocarditis in younger people (though unknown, as may be 2nd immunising event) • Single dose makes program simpler to communicate • Less product required
Potential harms	• Limited evidence; two primary doses may provide better protection than a single dose in the context of widespread infection • The observed equivalency of protection may wane faster following a single primary dose
Values	• Single primary dose may decrease degree of vaccine fatigue and hesitancy
Acceptability	• Most people and parents would find a single primary dose acceptable • Some may not accept restricted access to a second dose, but is offset by further dose availability if an at-risk population
Resource use	• Plentiful supply of vaccines • Single dose recommendation may result in higher short-term wastage of vaccines (if not donated overseas)
Feasibility	• Infrastructure and processes well established

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Policy options

People without severe immunocompromise:

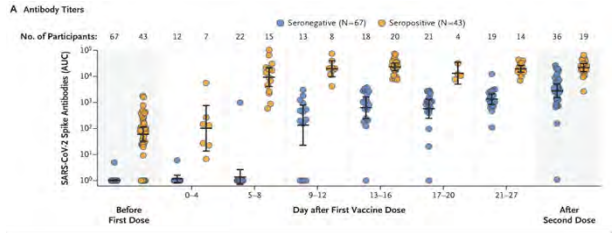
1. two-dose primary course for ≥ 5 years (current)
2. single dose primary series for ≥ 6 months
3. single dose primary series for ≥ 5 years
    A. children aged 6 months to 4 years: 3 primary Pfizer doses (current)
    B. children aged 6 months to 4 years: 2 primary Pfizer doses

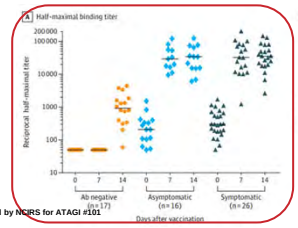
People with severe immunocompromise:

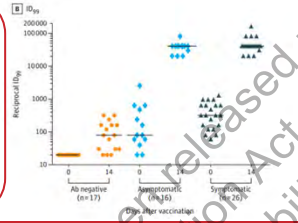
1. 1 additional primary dose
2. specify 3 primary doses

ATAGI#98 data presentation (September 2023)

Immunogenicity Studies: Adults







1: A:quantitative SARS-CoV-2 spike antibody titers (assessed by means of enzyme-linked immunosorbent assay and expressed as AUC

2: A: 7-14 days following vaccination, both groups with prior infection +single vaccine dose: higher peak IgG titers than the antibody (Ab)-negative group. B: Live virus neutralization ID99 (the 99% inhibitory dose, the dilution at which 99% of cells were protected). At 14 days, both groups: higher neutralization titers than the Ab-negative group.

https://www.nejm.org/doi/10.1056/NEJMc2101667?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed
https://pubmed.ncbi.nlm.nih.gov/33646292/

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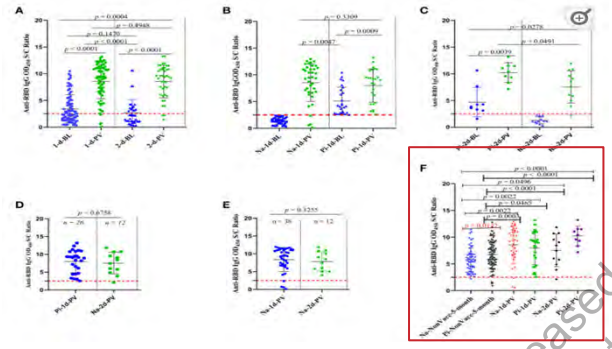
Immunogenicity Studies: Children/Adolescents



Levels of anti-RBD IgG comparison between (A) schoolchildren (n = 80) 1 dose vs 2 doses; (B) 1 dose of the BNT vaccine with and without a baseline pre-existing anti-RBD IgG antibodies; (C): 2 doses of the BNT vaccine with and without a baseline pre-existing anti-RBD IgG antibodies; (D): 1 dose baseline pre-existing anti-RBD IgG antibodies vs SARS-CoV-2-infection-naïve 2 doses; (E): 1 dose with baseline pre-existing anti-RBD IgG vs 2 doses without a baseline pre-existing anti-RBD IgG antibodies: (F): unvaccinated schoolchildren with and without anti-RBD IgG antibodies at baseline or 5-month follow-up vs schoolchildren who received one or two doses with or without a baseline pre-existing anti-RBD IgG

https://pubmed.ncbi.nlm.nih.gov/37398668/

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Adults, Children and Adolescents with Past infection: Omicron-Limited data

Study ID, year	n	Outcomes VE (95%CI)
Adults		
Montes-Gonzalez et al, 2023 Mexico	Severe COVID-19 (n=2,078) paired 1:4 with subjects with reinfection without severe COVID-19 (n=8,312)	Reinfection+ at least 1 dose: a >90% reduction in the risk of severe COVID-19
Children and adolescents		
Lin et al, 2023 US	n=1 368 721, age </=11 yrs	**5-11 years** **Primary vaccination vs unvaccinated** (hospitalisation/death): 73·3% (8·3–92·3) at 1 month and waned afterwards. **Previous infection vs no previous infection**: (hospitalisation/death): **5-11 yrs**: 83·8% (59·1–93·6) at 3 months, 76·2% (49·4–88·8) at 6 months, and 64·9% (34·9–81·1) at 9 months. **0-4 yrs:** 61·4% (29·4–78·9) at 3 months, 58·4% (32·2–74·5) at 6 months, and 55·1% (31·1–70·8) at 9 months
Gazit et al, 2023 Israel	163 812 individuals: 120 721 children, 43 091 adolescents	**1 dose in convalescent children and adolescents vs had a previous infection but unvaccinated** BA.1 and BA.2: adolescents: 54% [50 to 57] , children: 71% [67 to 73] BA.4 and BA.5: adolescents 8% [-18 to 29]), children 12% [-6 to 27]
Carazo et al, 2022 Canada	224 007 case participants and 472 432 control adolescents	VE of prior infection: hospitalisation: 81% (66%-89%) and One dose hybrid: 86% (77%-99%) Two dose hybrid: 94% (91%-96%) Three dose hybrid: 97% (94%-99%) without signs of waning

https://www.frontiersin.org/articles/10.3389/fpubh.2023.1160569/full
https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(22)00273-4/fulltext#:~:text=Interpretation,more%20effective%20than%20monovalent%20boosters.
https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(22)00273-4/fulltext#:~:text=Interpretation,more%20effective%20than%20monovalent%20boosters.
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2792431

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Children and Adolescents without Past Infection : Omicron

Study ID, year	n	Outcomes VE (95%CI)
Children or adolescents		
Gao et al, 2023 Review	88 studies (2-18 yrs), Jan 2020, to Oct 2022 mRNA vaccines and inactivated vaccines.	**Fully vaccinated vs Partially vaccinated** VE against severe infection: 1 dose : 42.87% [95% (CI) = 27.09%-58.65%], 2 dose : 63.33% (95% CI = 52.09%-74.56%) VE against hospitalisation: 1 dose: 72.74% (95% CI = 51.48%-94.01%) and 2 dose: 82.78% (95% CI = 75.78%-89.78%)
Simmons et al, 2023 Canada	62 hospitalized and 27,674 non-hospitalized SARS-CoV-2 cases mRNA vaccine	Adolescents: 1 dose: 10%(aOR: 0.90[95% CI: 0.05, 5.83]), 2 doses:: 85% (aOR = 0.15; 95% CI: [0.04, 0.53]; p<0.01) Children, 1 dose: VE: 79% (aOR = 0.21; 95% CI: [0.03, 0.77]

https://pubmed.ncbi.nlm.nih.gov/36723827/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10065234/

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Bobrovitz et al: (Published 18 Jan 2023, Infectious disease: Review previous SARS-CoV-2 Infection and Hybrid Immunity against the Omicron Variant and Severe Disease, Omicron, Adults

- Jan 2020-Jun 2022
- Previous infection (n=11)
- Hybrid immunity (n=15)
- Multiple types of vaccination

- VE of previous infection against hospital admission or severe disease:
- 74·6% (95% CI 63·1–83·5) at 12 months.

- VE of hybrid immunity against hospital admission or severe disease:
  - 97·4% (95% CI 91·4–99·2) at 12 months with primary series vaccination
  - 95·3% (81·9–98·9) at 6 months with the first booster vaccination after the most recent infection or vaccination.

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00801-5/fulltext

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Lee et al: Preprint: Aug 23: Canada: Protection: COVID-19 Vaccination, Prior SARS-CoV-2 Infection, or Hybrid Immunity against Omicron-Associated Severe Outcomes

- Test-negative design
- PCR-tested adults aged >50
- Vaccine: 96% mRNA vaccines
- 18,526 cases (Omicron-associated severe outcomes) 90,778 test-negative controls
- Vaccinated: prior infection vs no infection: greater protection against severe outcomes:
  - BA.1/BA.2-predominant
  - BA.4/BA.5-predominant
  - **Not significant** at most time points during the **BQ/XBB-predominant** period

			Time Since Last Immunogenic Event (Dose or Prior Infection)				
Period	Dose	Value	3 months	6 months	9 months	12 months	15 months
BA.1/BA.2-predominant	Second	Estimate	82 (62, 92)	73 (60, 81)	65 (44, 78)	58 (21, 78)	52 (-7, 78)
		p-value	**<0.001**	**<0.001**	**<0.001**	**0.008**	0.07
	Third	Estimate	72 (54, 82)	73 (47, 86)	-*	-*	-*
		p-value	**<0.001**	**<0.001**	-*	-*	-*
BA.4/BA.5-predominant	Second	Estimate	-*	73 (42, 87)	79 (63, 88)	82 (69, 90)	85 (70, 92)
		p-value	-*	**<0.001**	**<0.001**	**<0.001**	**<0.001**
	Third	Estimate	58 (1, 82)	62 (45, 74)	65 (49, 75)	66 (43, 80)	-*
		p-value	**0.047**	**<0.001**	**<0.001**	**<0.001**	-*
	Fourth	Estimate	61 (31, 77)	53 (7, 77)	49 (-28, 79)	-*	-*
		p-value	**0.001**	**0.03**	0.13	-*	-*
BQ/XBB-predominant	Second	Estimate	-*	-*	48 (-20, 78)	42 (0, 66)	36 (4, 58)
		p-value	-*	-*	0.13	0.05	**0.03**
	Third	Estimate	-*	4 (-57, 41)	18 (-16, 41)	26 (-1, 46)	33 (4, 53)
		p-value	-*	0.88	0.26	0.06	**0.03**
	Fourth	Estimate	4 (-57, 42)	0 (-51, 34)	-2 (-74, 40)	-4 (-101, 46)	-*
		p-value	0.86	0.99	0.94	0.91	-*
	Fifth	Estimate	42 (-4, 68)	71 (32, 88)	81 (45, 93)	-*	-*
		p-value	0.07	**0.004**	**0.002**	-*	-*

* Not reported due to insufficient data or unstable estimate (95% confidence interval width exceeded 150 percentage points).

Marginal protection against Omicron-associated severe outcomes from documented prior SARS-CoV-2 infection among vaccinated individuals, stratified by period of Omicron sublineage predominance, number of COVID-19 vaccine doses received, and time since last immunogenic event (either COVID-19 vaccine dose or prior SARS-CoV-2 infection)

https://www.medrxiv.org/content/10.1101/2023.08.24.23294503v1

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