Immunisation Coalition ASM 2023

COVID-19: A View From ATAGI

Professor Katie Flanagan

Declaration of interests

- Member of ATAGI and Co-Chair ATAGI COVID-19 Vaccine Working Group
- Previously on Vaccine Advisory Boards for Seqiris and Sanofi-Pasteur
- President of the Australasian Society for Infectious Diseases
- This is my own personal perspective and not necessarily that of ATAGI or ASID

ATAGI Structure and Role

Membership

- 15 voting members
- 7 *ex-officio* members representing DoH, TGA, NCIRS, NIC, CDNA, PBAC

Role

- Provide technical advice to the Minister for Health and Aged Care
- Advice to research organisations via the department on research priorities
- Advise PBAC on vaccine effectiveness and use in Australia
- Produce National Immunisation Handbook
- Consult with the National Immunisation Committee (NIC) on AIH content and implementation
- Consult with CDNA and ACV re implementation of policy and procedures, vaccine safety

- Supported by National Centre for Immunisation Research and Surveillance (NCIRS) whose members attend the meetings

Australian COVID-19 Vaccine Program

- Most complex immunisation program developed and delivered in Australian history
- Development involved some different processes compared to normal in the pandemic setting
- Extensive collaboration invloving multiple government departments and rapid decision-making:
  National Cabinet; National COVID-19 Coordination Commission; Gov COVID-19 Taskforce; Advisory Committee on Vaccines (ACV); Australian Technical Advisory Group on Immunisation (ATAGI); Therapeutic Goods Administration (TGA); Science and Industry Technical Advisory Gp (SITAG); Natl Centre for Imm Research & Surveillance (NCIRS)

	Usual Process	COVID Vaccine Process
Initiation of process	Sponsor application to TGA and PBAC	Australian government with advice from SITAG Direct discussions with manufacturers
Regulatory decisions	TGA with advice from ACV	TGA with advice from ACV
Purchasing decisions	Australian Government with advice from PBAC	Australian Government with advice from SITAG
Clinical and technical information	Statements from ATAGI with support from NCIRS	Multiple providers including ATAGI statements, NCIRS, training materials contracted by Commonwealth
Program implementation	Immunisation Branch in conjunction with jurisdictions	COVID vaccine Taskforce in conjunction with jurisdictions

Adapted from Blyth et al. Key steps in our journey to a COVID-19 vaccine program. MJA 2021.

ATAGI Structure for COVID-19 Program Planning

- To manage the workload required to develop policy, support implementation logistics and monitor safety of emerging COVID-19 vaccines

Aug 2020-Dec 2021

- 3 expert working groups (ATAGI and non-ATAGI expert members) supported by ATAGI Co-Chairs Chris Blyth and Allen Cheng and reporting to ATAGI and COVID-19 Exec
  - **Prioritisation** (led by Katie Flanagan)
  - **Implementation** (led by Robyn Gibbs)
  - **Safety & Confidence** (led by Nigel Crawford)

Jan 2022 onwards

- 2 groups

  ATAGI COVID-19 Working Group (whole of ATAGI attends)
  - Co-Led by Katie Flanagan and Michelle Giles
  - Meet weekly to fortnightly

  COVID-19 Safety Group
  - Led by Tony Korman
  - Meet fortnightly

- Technical support provided by NCIRS
- An ATAGI COVID-19 Executive has supported the working groups throughout the pandemic

The COVID-19 Vaccine Program

- Aim 1: reduce **serious illness** and **death**, and, where possible, disease transmission
- Aims 2-5: equity; promote trust, establish a COVID-19 vaccine NIP; maintain essential services

- Key determinants of initial COVID-19 vaccine program strategy:
  - Vaccine supply (initially limited to priority populations)
  - Vaccine characteristics (particularly storage)
  - Local epidemiology (suppression/elimination vs 3rd wave)

- Initially advised that vaccination be strongly encouraged but not mandatory but over time mandates were introduced widely

- Early unknowns – effect in real world (non-clinical trial) setting, effect on transmission, effectiveness in multiple potentially at-risk populations – elderly, immunocompromised, severe disability, pregnant women

ATAGI COVID-19 Vaccine Program Outputs

- Multiple versions of the clinical guidance supported by National Centre for Immunisation Research and Surveillance (NCIRS)
  - Version 1 when Pfizer approved
  - Updated when AZ approved, Pfizer approved for 12-15 year olds, Moderna approved, Moderna for 12-15 year olds, Pfizer recommended for <50 yrs then <60 yrs, Boosts in immunocompromised, TTS signal, Myocarditis / pericarditis signal etc……
  - Multiple iterations required with at least monthly updates
  - Will soon be incorporated into Australian Immunisation Handbook as a living guideline (bypassing NHMRC approval process)
- All associated documents e.g. consent forms, information sheets updated each time
- Developed the guidance and documents for vaccine administration
- Multiple tools, decision aids e.g. pregnancy, immunocompromised, autoimmune diseases
- Liaison with specialist colleges and societies e.g. ASCIA, RANZCOG, CSANZ
- Weekly ATAGI safety monitoring meetings, Taskforce meetings, CMO meetings and statements

Australian Technical Advisory Group on Immunisation (ATAGI) recommended COVID-19 vaccines and doses

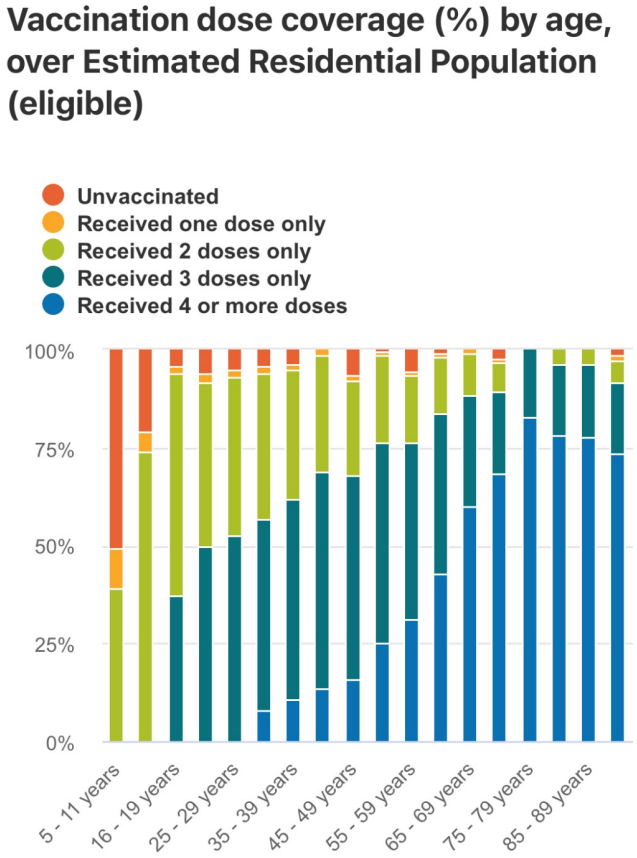
The table below summarises the ATAGI recommendations relating to COVID-19 vaccines for the **general population**. Please read corresponding footnotes for important guidance.

Information for severely immunocompromised individuals, and special populations is located on the following pages.

GENERAL POPULATION					
GROUP	**VACCINE**	**PRIMARY COURSE**	**VACCINE**	**FIRST BOOSTER**	**SECOND BOOSTER**
5 years	Pfizer (COMIRNATY) (Orange)[1] Moderna (SPIKEVAX) (Blue/Purple)[2]	FIRST DOSE → SECOND DOSE	*Not recommended.*[6]		
6 – 11 years	Pfizer (COMIRNATY) (Orange)[1]	FIRST DOSE → SECOND DOSE	*Not recommended.*[6]		
12 – 15 years	Pfizer (COMIRNATY) (Purple)[3] Novavax (NUVAXOVID)[4]	FIRST DOSE → SECOND DOSE	*Not recommended.*[7]		
16 – 17 years	Pfizer (COMIRNATY) (Purple)[3] Novavax (NUVAXOVID)[4]	FIRST DOSE → SECOND DOSE	Pfizer (COMIRNATY) (Purple)[3,8] *[Novavax (NUVAXOVID)]*[4,9]	FIRST BOOSTER *3 months after Primary Course.*	*Not recommended.*
18 – 29 years	Pfizer (COMIRNATY) (Purple)[3] Novavax (NUVAXOVID)[4] AstraZeneca (VAXZEVRIA)[5]	FIRST DOSE → SECOND DOSE	Pfizer (COMIRNATY) (Purple)[3,10] Moderna (SPIKEVAX Bivalent)[10,11] Pfizer (COMIRNATY Bivalent)[10,12] Novavax (NUVAXOVID)[4,10] AstraZeneca (VAXZEVRIA)[5,10]	FIRST BOOSTER *3 months after Primary Course.*	*Not recommended.*[13]
30 – 49 years	Pfizer (COMIRNATY) (Purple)[3] Novavax (NUVAXOVID)[4] AstraZeneca (VAXZEVRIA)[5]	FIRST DOSE → SECOND DOSE	Pfizer (COMIRNATY) (Purple)[3,10] Moderna (SPIKEVAX Bivalent)[10,11] Pfizer (COMIRNATY Bivalent)[10,12] Novavax (NUVAXOVID)[4,10] AstraZeneca (VAXZEVRIA)[5,10]	FIRST BOOSTER *3 months after Primary Course.*	CONSIDER SECOND BOOSTER *From 3 months after Booster.*[14]
50 years+	Pfizer (COMIRNATY) (Purple)[3] Novavax (NUVAXOVID)[4] AstraZeneca (VAXZEVRIA)[5]	FIRST DOSE → SECOND DOSE	Pfizer (COMIRNATY) (Purple)[3,10] Moderna (SPIKEVAX Bivalent)[10,11] Pfizer (COMIRNATY Bivalent)[10,12] Novavax (NUVAXOVID)[4,10] AstraZeneca (VAXZEVRIA)[5,10]	FIRST BOOSTER *3 months after Primary Course.*	SECOND BOOSTER *From 3 months after Booster.*

Future Planning Considerations

COVID-19 Vaccination Rates in Australia

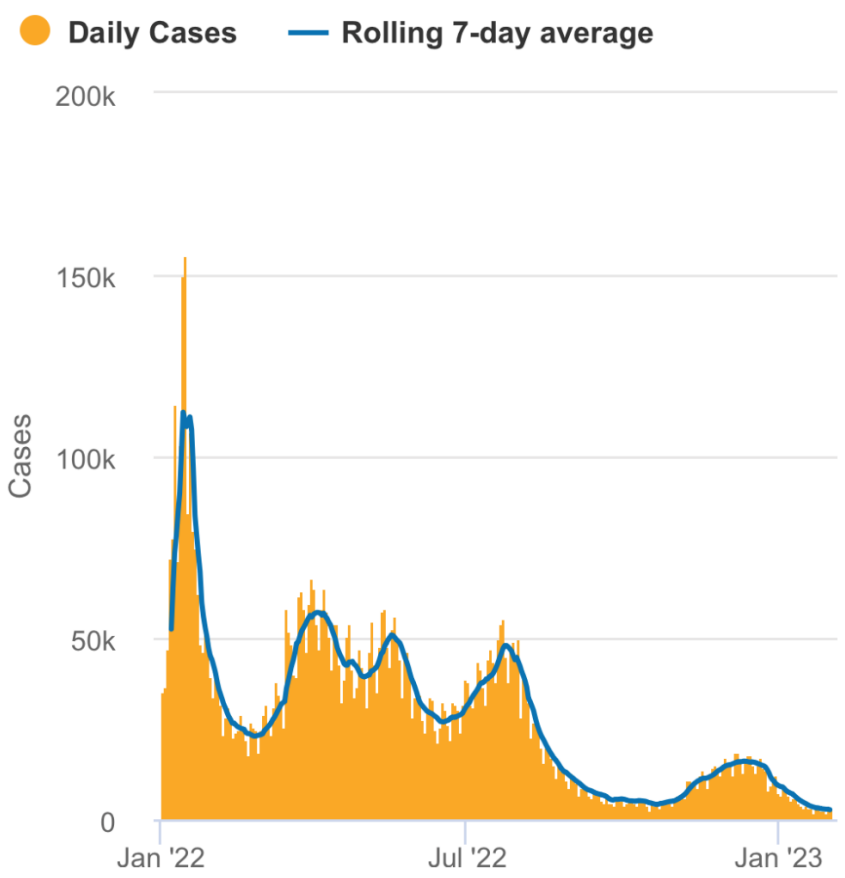


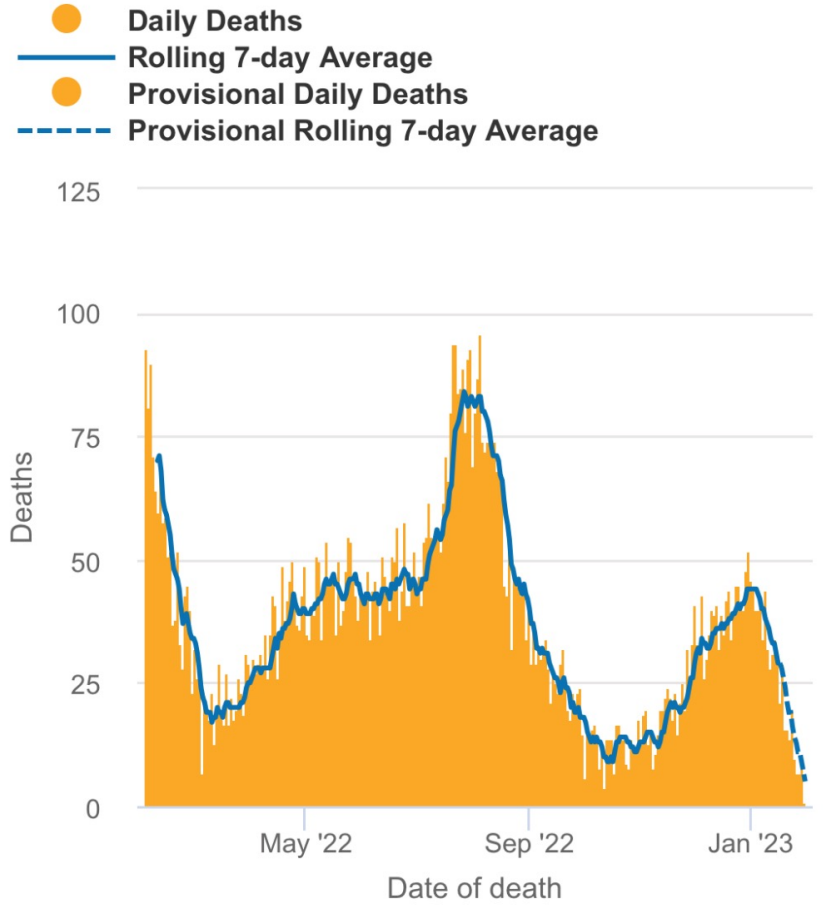
Highly vaccinated population, particularly in the vulnerable older age groups

Very few unvaccinated over the age of 16 years

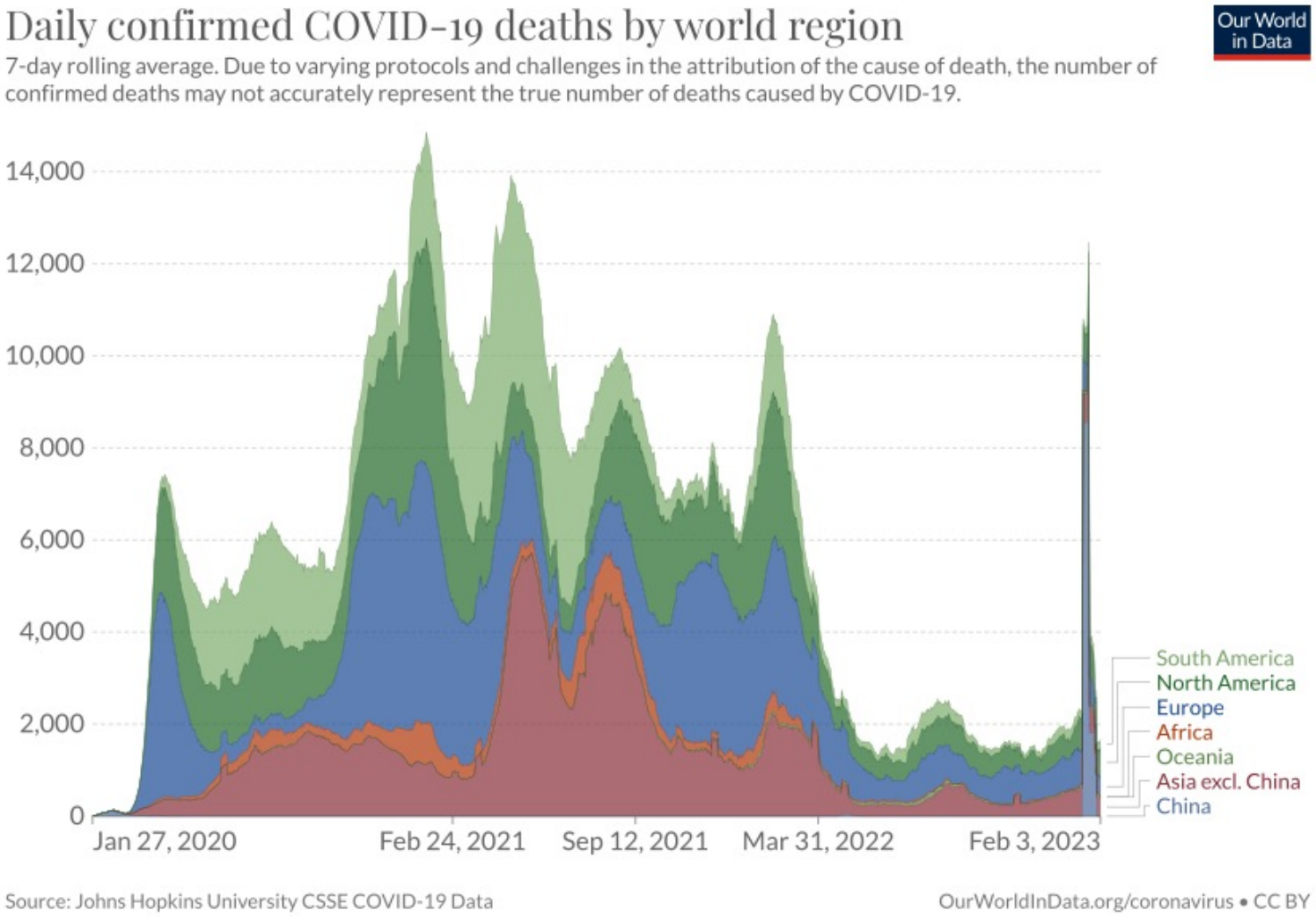
Increasing number of people now >6 months since their last vaccine dose

Current COVID-19 Situation in Australia

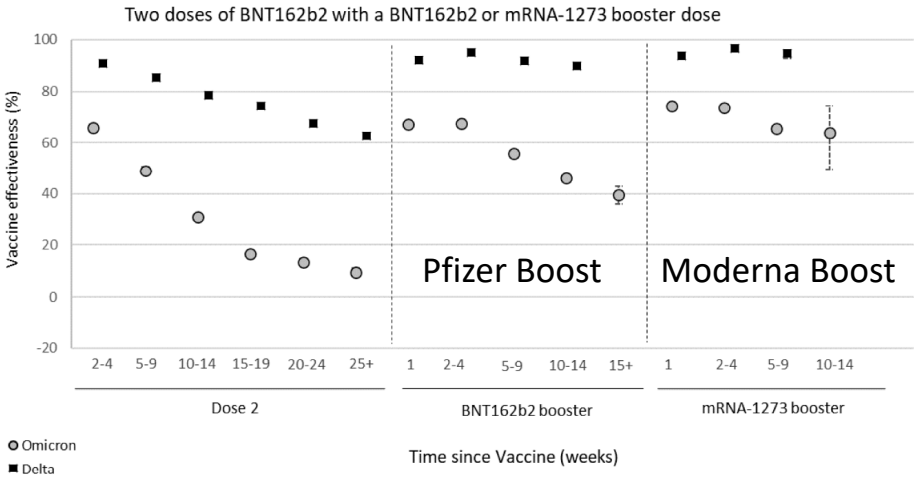




Death Rates Declining with Each Wave



Waning of Immunity

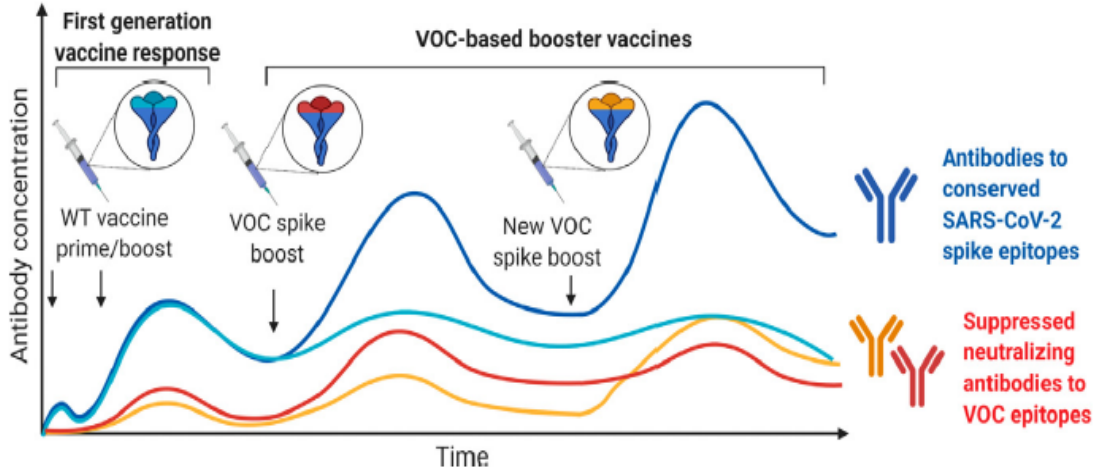


Symptomatic infection. *UK HSA report*

- Australia has a highly vaccinated population
- High rates of infection (as evidenced by national serosurveys showing 65% of population infected and up to 90% of children by Aug 2022)
- Vaccine-induced immunity wanes over time
- Protection against any infection wanes rapidly (several months)
- Protection against severe disease, hospitalisation and death is maintained at reasonable levels to at least 12 months
- Incremental benefit of boosters is decreasing

Hybrid Immunity & Immune Imprinting

- Hybrid immunity is the immunity obtained from vaccination plus one or more infections
- Hybrid immunity is superior to infection alone or vaccination alone
- Most people's initial exposure via vaccination or infection was to pre-Omicron strains raising issue of immune imprinting
- Pre-Omicron immunity predominates with variant vaccine immunisation in those with prior immunity to other strains, but Omicron-specific immunity is also induced



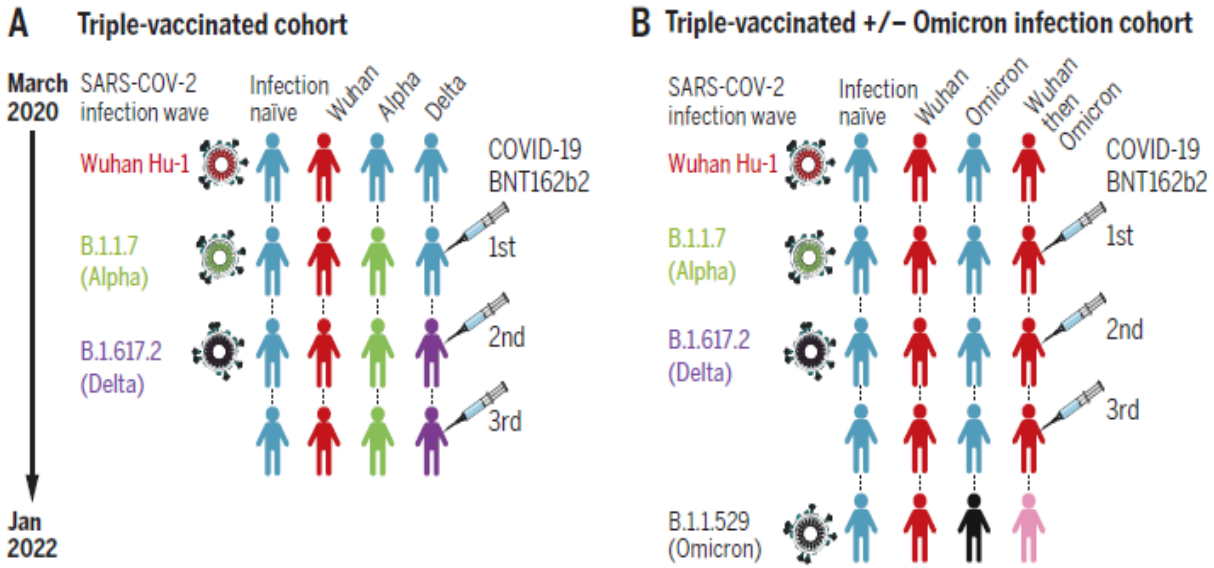
- *Blue conserved epitope is preferentially boosted each time at expense of variant epitope responses (red and yellow) limiting response to variants*
- *Can apply to natural infection or variant vaccines*

Wheatley et al, Trends in Immunol 2021; 42(11): 956

Key Variables

Hybrid Immunity will be influenced by:

- Vaccines used, timing and number of doses
- Variants causing infection, timing in relation to vaccination
- Severity of infection
- Host susceptibility factors including age, co-morbidities and medication
- Everybody's immune experience is different so predicting impact of vaccination at an individual level is no longer possible



Reynolds et al. Immune boosting by B.1.1.529 (Omicron) depends on previous SARS-CoV-2 exposure. Science 2022; 377(6603): eabq1841

Considerations in the Australian Context?

- High vaccination rates of a predominantly COVID naïve population
- High levels of post-vaccination infection, predominantly with Omicron
- Our immune memory has now been laid down
- Vaccinating a broadly naïve population prevented the initial immune imprinting from Wuhan or VOCs (which may ablate / decrease Omicron immunity)

Adults

- If vaccinated with ≥2 doses plus infection then good sustained protection against severe disease and death
- Omicron protection enhanced by subsequent boosters

Children ≤15 yrs

- A fully vaccinated and prior-infected child would have good protection against severe outcomes to which they are not very susceptible in the first place
- May even be better protected than boosted adults
- Little added value in offering them further boosters

Bivalent vs Ancestral Vaccines

- Current ATAGI advice:
  - No preference for Ancestral vs Bivalent vaccines
  - Bivalent not recommended for primary vaccination (no data)
- Evidence that BA.4/5 bivalent induces superior nAbs to BA.4/5 and newer subvariants (e.g. BQ.1.1, XBB) and similar / slightly higher ancestral strain nAbs cf Ancestral vaccines
- Similar safety profile cf Ancestral vaccines
- Clinical benefit uncertain but some evidence emerging of slightly superior clinical effectiveness of BA.4/5 cf Ancestral and Bivalent BA.1 vaccines
- Ancestral mRNA vaccines being phased out globally

Vaccine	TGA Approved as Booster	ATAGI recommended
Pfizer Bivalent BA.1 + Ancestral	Yes ≥18 years	Yes ≥18 years
Pfizer Bivalent BA.4/5 + Ancestral	Yes ≥12 years	Under evaluation
Moderna Bivalent BA.1 + Ancestral	Yes ≥18 years	Yes ≥18 years
Moderna Bivalent BA.4/5 + Ancestral	Under evaluation	Under evaluation

Other NITAG 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. No preference for bivalent boosters over ancestral vaccines.
USA ACIP	Moderna BA.4/5 (6+ months) and Pfizer BA.4/5 (6+ months) approved. Bivalent not authorised as primary series, except for children 6m-4y who may receive Pfizer BA.4/5 as the third dose in the primary series following two monovalent doses. Booster dose recommended for people aged ≥6 months (except those 6m-4y who received 3 doses primary Pfizer), 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 (5+) approved. Note: Pfizer Original/BA.1 (12+ years) approved but not in use. Bivalent booster recommended for ≥65y & high risk ≥5 years, and offered for all 5-64y, 3-6 months after last dose or infection regardless of number of previous boosters Strong NACI recommendation that bivalent Omicron-containing mRNA COVID-19 vaccines are the preferred booster products for the authorised age groups.
Europe ECDC / EMA	Moderna BA.1 (6+) and BA.4/5 (12+), Pfizer BA.1 (12+) and BA.4/5 (5+) approved. ECDC and EMA advise that these boosters be directed as a priority to people at risk (60+ and high risk (5+)/pregnant) and healthcare workers ≥3 months after last dose.
Germany STIKO	Moderna BA.1 and BA.4/5 (30+), and Pfizer BA.1 (12+) and BA.4/5 (5+) approved. Recommended for all booster vaccinations in people aged ≥5 years, bivalent preferred over monovalent, 6 months after last dose or infection. 1st booster for all ≥12 years and in children ≥5 years with pre-existing medical conditions or immunocompromise, 2nd only for at risk (60+, high risk 12+), 3rd booster for "very old", immunocomp
WHO SAGE	Variant-containing vaccines should not be used as the primary series. Current data not sufficient to support issuance of any preferential recommendation for bivalent variant-containing boosters over ancestral-virus-only boosters. WHO recommends any WHO EUL COVID-19 vaccines or authorised mRNA bivalent variant-containing vaccines can be used for booster vaccination. 1st booster: all 12+, particularly to highest priority-use groups, interval 4–6 months after primary series. For countries considering second boosters, WHO recommends a targeted approach with focusing second boosters for all older persons, all persons with moderately and severely immunocompromising conditions, and adults with comorbidities that put them at higher risk of severe disease, as well as for pregnant women and health workers, 4–6 months after the previous dose.

The Future COVID-19 Vaccine Program

- Future not certain, but current vaccines likely to provide reasonable protection against future variants that do not yet exist
- Particularly protection against severe disease and death which should last for at least 12 months
- The more closely related the variant to which an individual has been exposed, and the more recent the exposure, the better the protection
- Boosters do work although incremental benefit is declining
- Intermittent boosters are likely to be required in the future – hopefully annually rather than chasing waves – particularly for the more vulnerable (older, immunocompromised etc)
- Chasing variants with variant vaccines not practical or necessary
- Future COVID vaccines are being designed to overcome immune imprinting effects by being more epitope-specific, focus on conserved regions and mucosal vaccines to induce mucosal immunity

It’s Been a Rollercoaster Ride for ATAGI
But
Is Finally Slowing Down!