COVID-19 Update

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Medical Director and Principal Investigator, Nucleus Network

Immunisation Coalition Director and Scientific Advisory Board Member

Disclosures

- Principal Investigator on numerous vaccine clinical trials
  - including the following SARS-CoV-2 vaccines;
    - UQ
    - Novavax
    - Serum Institute of India
    - Symvivo
    - Tetherex
    - Sanofi (mRNA and protein)
  - And many Influenza and RSV vaccine studies
    - Including with Moderna and Novavax
- Speaker Honoraria includes Seqirus, Novartis, Gilead, Sanofi and Janssen
- Medical Advisory Board Memberships including AstraZeneca, GSK, MSD and Pfizer

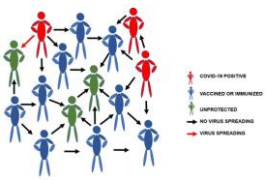
Outline

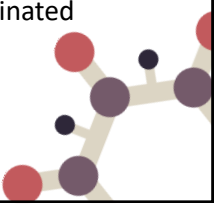
- Case numbers
- Variants
- Vaccination
  - Boosters
    - Including “Winter Booster”
  - Children
  - 2nd Generation Vaccines
- Therapies

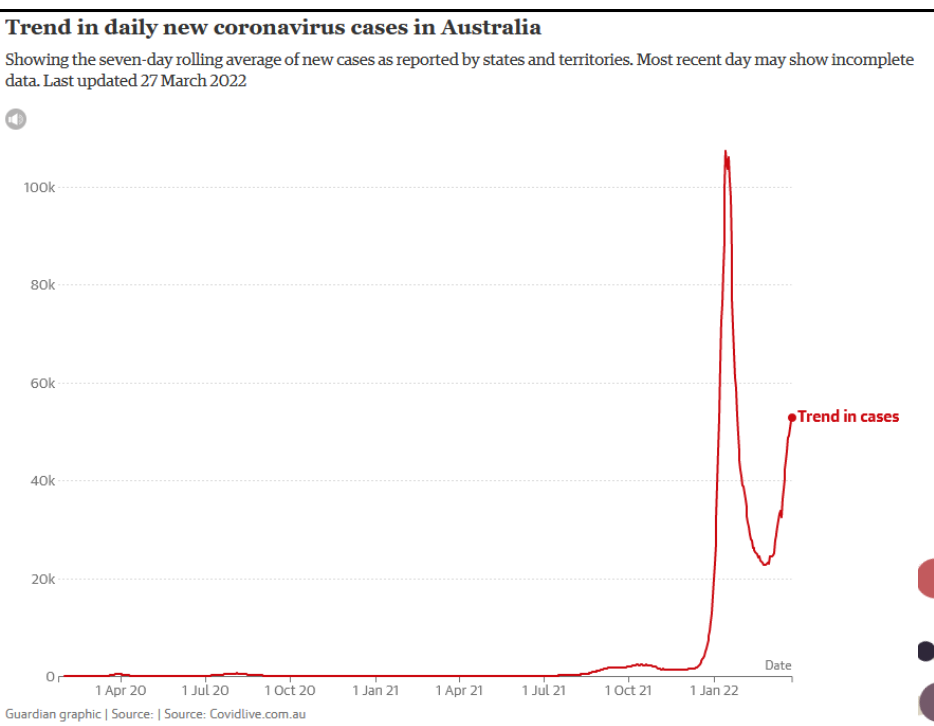
Case numbers

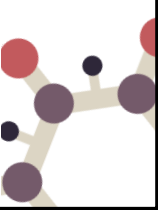
Why do so many cases occur in vaccinated individuals

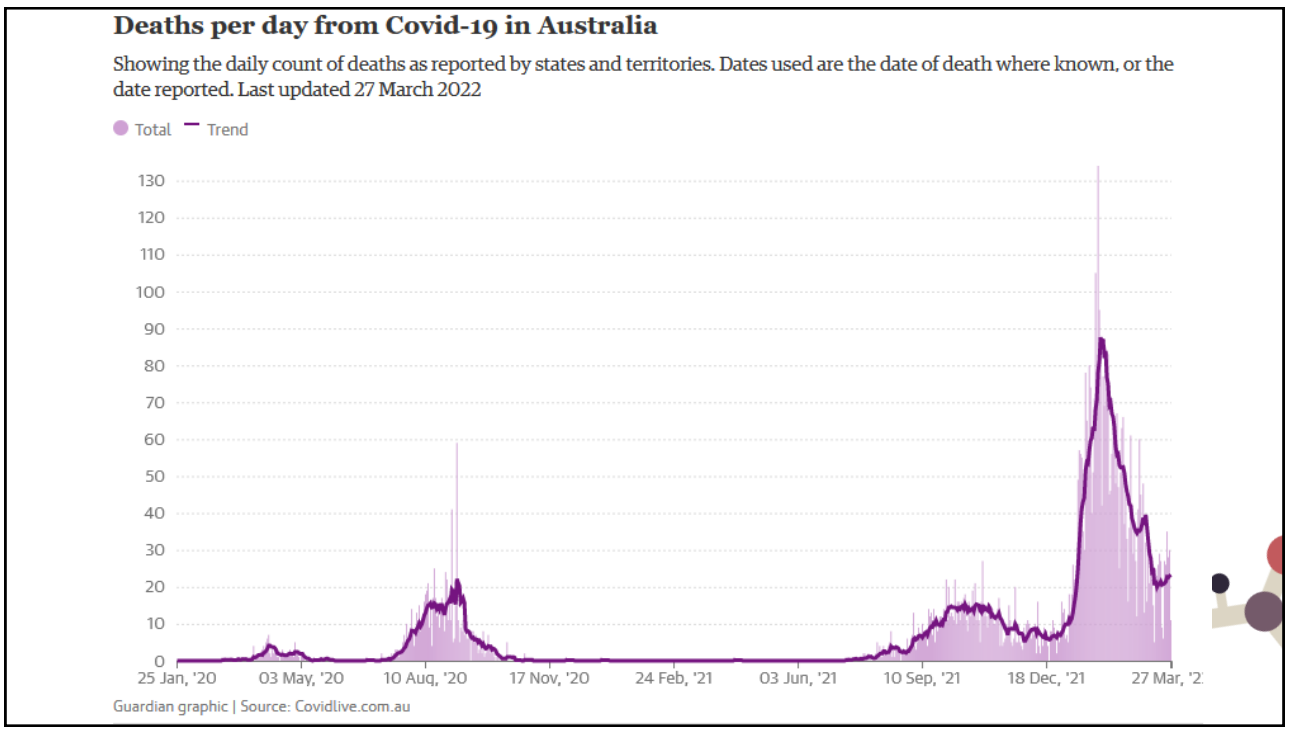
- Vaccine (fully vaccinated) highly effective
  - Reduction of transmission likely ~50%
    - So can still get infected
  - 2 dose protection from infection against Omicron is reduced
- If number of people vaccinated high, then even though the number infected goes down, numbers higher in vaccinated than unvaccinated
  - A recognised paradox
- Fully vaccinated (or up to date) infected people;
  - Less likely to pass it on
  - Less likely to get symptoms
  - Much less likely to get really sick
    - So benefits of vaccination should remain abundantly clear
- Risk of infection may also be increased in vaccinated people relative to their unvaccinated vulnerable counterparts
  - Not required to continue other mitigation strategies e.g. less likely to wear a mask
  - Their perception of risk goes down (appropriately) so less likely to social distance etc
  - Allowed to move around more freely
    - So not comparing like with like

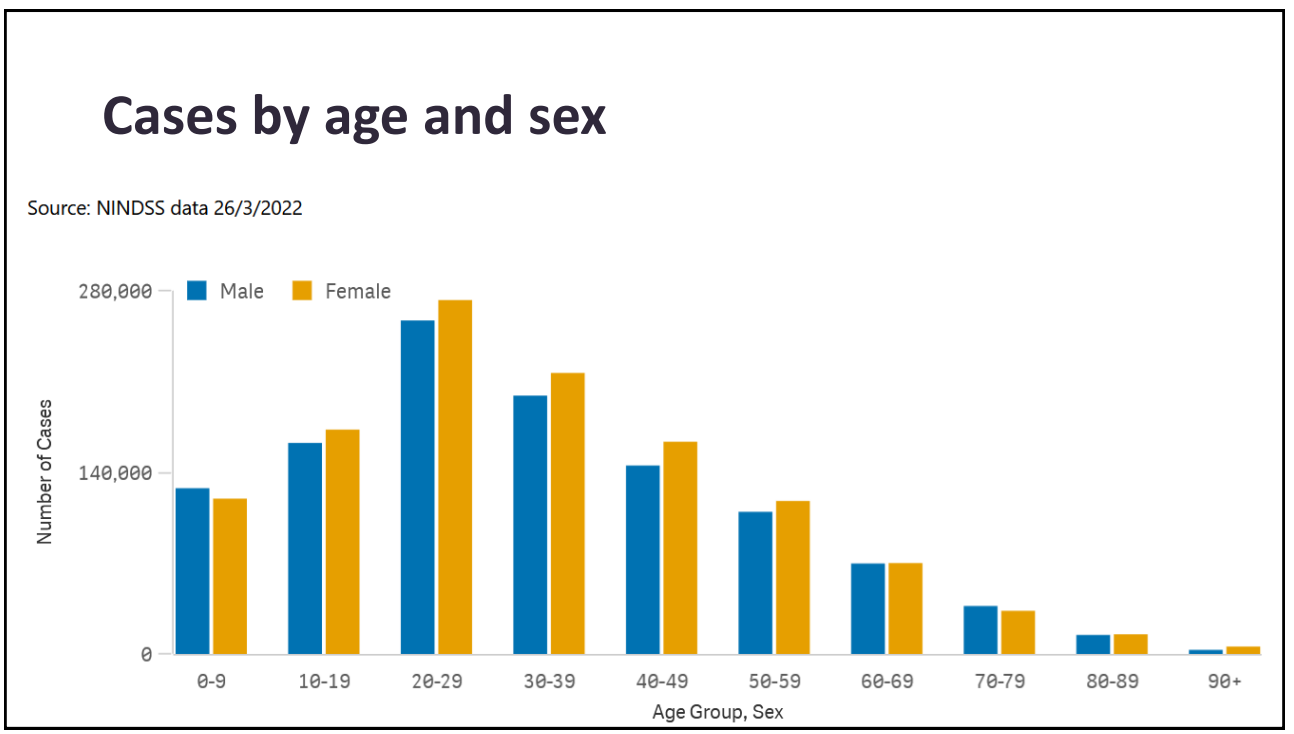






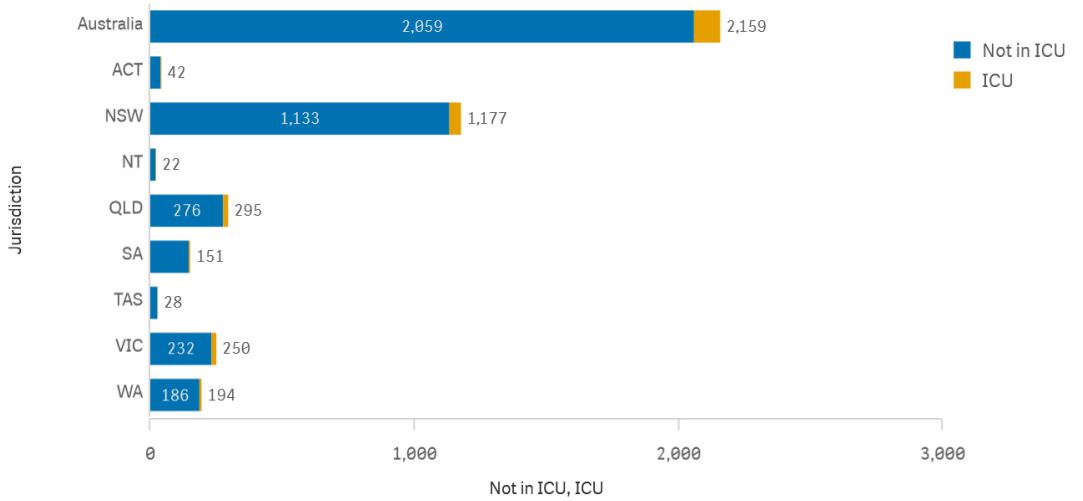



Deaths per day from Covid-19 in Australia
Showing the daily count of deaths as reported by states and territories. Dates used are the date of death where known, or the date reported. Last updated 27 March 2022
Total
Trend
130
120
110
100
90
80
70
60
50
40
30
20
10
0
25 Jan, '20
03 May, '20
10 Aug, '20
17 Nov, '20
24 Feb, '21
03 Jun, '21
10 Sep, '21
18 Dec, '21
27 Mar, '2
Guardian graphic | Source: Covidlive.com.au


Cases by age and sex
Source: NINDSS data 26/3/2022
Male
Female
280,000
140,000
0
Number of Cases
0-9
10-19
20-29
30-39
40-49
50-59
60-69
70-79
80-89
90+
Age Group, Sex

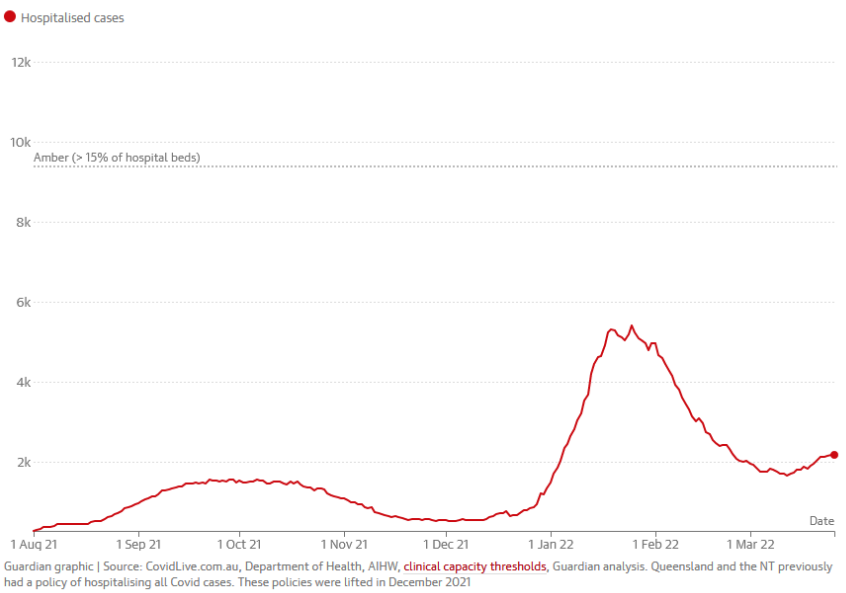
Current cases in hospital

Source: Department of Health, States & Territories Report 26/3/2022



Covid cases hospitalised in Australia v hospital capacity impact thresholds

Showing the number of people hospitalised with Covid over time, along with the federal government's clinical capacity thresholds that indicate when action is required. The 'amber' or 15% hospital capacity threshold indicates 'targeted adjustments' are required or in progress, while the 'red' threshold of 30% - currently not shown - indicates a 'harder or wider' response is required. Last updated 26 March 2022.



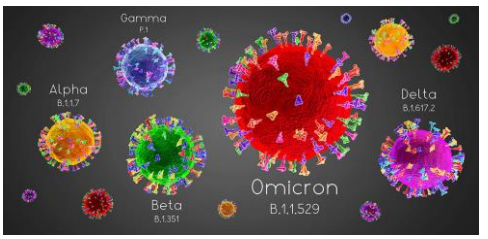
Guardian graphic | Source: CovidLive.com.au, Department of Health, AIHW, clinical capacity thresholds, Guardian analysis. Queensland and the NT previously had a policy of hospitalising all Covid cases. These policies were lifted in December 2021

So why are cases going up again

- Viral factors
  - BA.2
    - More infectious
- Mitigation strategies reduced
  - Most states have reduced public health and social measures
    - Changes in mask wearing rules
    - Changes in close contact definitions and management
    - Caps on numbers largely abolished
- Behavioural factors
  - Schools back (compared to BA.1 wave)
  - Many large events have returned
  - People are moving about more
  - Floods
- Host factors
  - Declining immunity, particularly in highest risk
  - Waning protection following infection in prior wave
- Perception of risk
  - Perhaps below where it needs to be to maintain baseline level of control

Variants

Variants of Concern

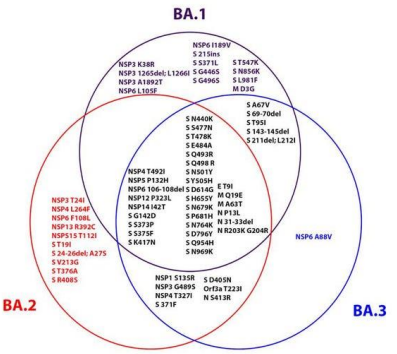


- All living cells have errors when reproducing
  - Higher organisms are good at repairing these errors
  - Viruses (and bacteria) are not so good at fixing them, so mutations are common
    - SARS-CoV-2 actually mutates relatively slowly as far as viruses go
- These mutations often result in a loss of "fitness" and just simply fade away
- When they confer a benefit, the new strain or variant can take over and replace the previous one
- When the variant appears to be more harmful to us via changes in transmissibility, clinical presentation and severity, or if they impact on countermeasures, including diagnostics, therapeutics and vaccines
  - Variant of concern
- While some may be more infectious, and vaccine efficacy may be reduced, no strain as yet that vaccines do not protect us from
  - Do not know for certain that disease severity will continue to decline
- Will continue to emerge

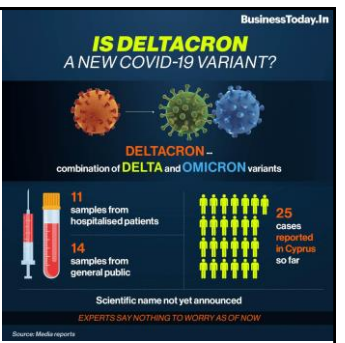
WHO label	Lineage + additional mutations	Country first detected (community)	Spike mutations of interest	Year and month first detected	Impact on transmissibility	Impact on immunity	Impact on severity	Transmission in EU/EEA
Beta	B.1.351	South Africa	K417N, E484K, N501Y, D614G, A701V	September 2020	Increased (v) (1)	Increased (v) (2, 3)	Increased (v) (4, 5)	Community
Gamma	P.1	Brazil	K417T, E484K, N501Y, D614G, H655Y	December 2020	Increased (v) (6)	Increased (v) (7)	Increased (v) (5)	Community
Delta	B.1.617.2	India	L452R, T478K, D614G, P681R	December 2020	Increased (v) (8)	Increased (v) (9-11)	Increased (v) (10, 12)	Community
Omicron	B.1.1.529	South Africa and Botswana	(x)	November 2021	Increased (v) (13, 14)	Increased (v) (15-21)	Reduced (v) (22-27)	Dominant

Omicron

- Omicron (BA.1.1.529 or BA.1) first reported in South Africa on 24th November 2021
  - Variant of concern 26th November 2021
  - Large number of mutations (~72), with over 30 in the spike protein
  - Probably 3 to 4 times more infectious than Delta
    - Multiplies in the upper airways maybe 70 times faster
  - Reduced protection from vaccination (with 2 doses that is)
    - Reduced protection from infection
    - Still good protection from severe disease
    - Restored with third dose
      - Back up to over 80's
  - Shorter incubation period (~3 days)
  - Less severe but not correct to say its "mild"
    - Lower rates of hospitalisations, ICU admissions and death (~40-80%)
- BA.2 (Subvariant)
  - First found in the Philippines
  - More infectious, probably around 30-50% more
  - Taking over in many countries
  - No more severe



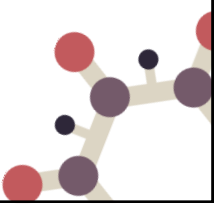
Deltacron



- Recombinant of Delta and Omicron
- Most information coming out of France
  - Also found in Denmark, Netherlands, USA, UK, Brazil
  - Although the France/Denmark/Netherlands version a little different to the USA/UK version
- Not taking over in the area's its been found
- Many speculate properties more similar to Omicron than Delta
  - Hasn't picked up the worst of both
- Not unexpected
  - High rates of infection
  - High rates of sequencing
  - Low vaccine rates in many parts of the world still

Variant Specific Boosters

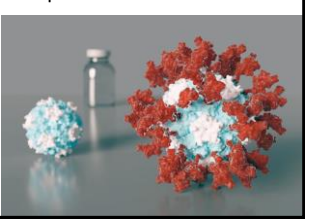
- Given the majority of vaccines in use currently are essentially "plug and play" platforms
  - Relatively easy to develop variant specific boosters
- Established pathway to roll them out
  - Neutralising antibody studies sufficient
  - No clinical trials required
- Timelines suggested to be around 8 to 10 weeks
- Most companies have developed variant specific boosters to all significant VOC
  - Alpha, Beta, Gamma, Delta and Omicron
- Given efficacy of original vaccines, with a booster, no need to deploy
  - Yet



Healthed

Variant Proof Vaccines

- A number of vaccines are under development with the intention of being less susceptible to reduced protection against new emerging variants
- More specifically targeting the receptor binding domain (RBD) as opposed to other area's (or entire) spike protein is thought to reduce chance of protection being reduced
  - ~5 candidates
    - Icosavax and Serum Institute of India in clinical trials in Brisbane
- A true variant proof vaccine or even a pan or universal coronavirus vaccine would be ideal
  - Have never achieved for an endemic virus
  - Approaches include
    - Using the mRNA platform to target a large number of different parts of the virus or even multiple coronaviruses
    - Mosaic RBD nanoparticle that combines multiple RBD's
    - Targeting S2 of spike protein that links S1 to the virus, more conserved
    - Ferritin nanoparticle
      - Walter Reed Army Institute of Research
      - Has 24 sides so can combine multiple spike or other proteins into a nanoparticle

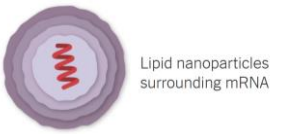


Vaccines

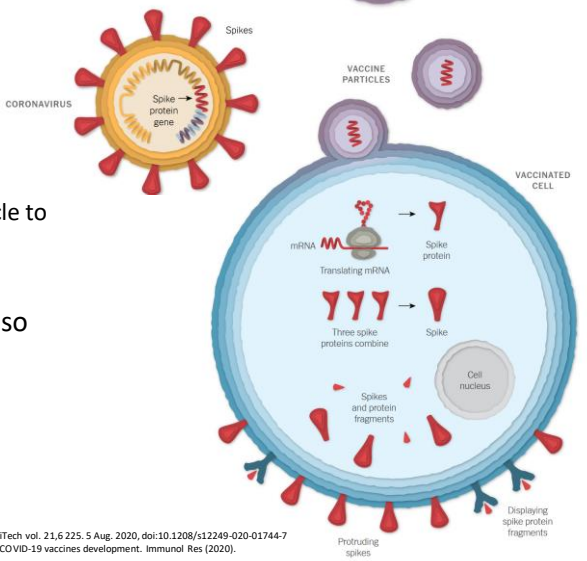
Australian COVID-19 Vaccine Supply

- 4 vaccine supply deals (total 169.8 million doses)
  1. BioNTech/Pfizer
     - Provisionally approved 25 January 2021
     - 10+10+20 million doses
  2. Oxford/AstraZeneca
     - Provisionally approved 16 February 2021
     - 53.8 million doses
       - Initially 30 million to be manufactured onshore
       - Added another 20 million doses on 11 December 2021
  3. University of Queensland
     - Abandoned
       - Diagnostic interference
     - Clamp "2.0" underway
  4. Moderna
     - Provisionally approved in Australia 9 August 2021
     - 25 million doses
       - 10 million in 2021
       - 15 million updated variant booster 2022
  5. Novavax
     - Provisionally approved 20 January 2022
     - 51 million doses

Nucleic acid-mechanism of action

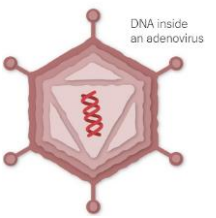


- mRNA:
  - Instruction to make proteins
  - Cellular machinery (ribosome) translates these instructions into proteins
  - In this case, the protein is the spike protein
- Given mRNA is inherently unstable
  - Need to be coated in oily bubble or lipid nanoparticle to prevent degradation
    - Allergy risk
  - Need to be kept very cold
- The mRNA helps to boost the immune response so no adjuvant required
  - But still require multiple doses
- Fast, but not previously licenced technology
- Safe
- Issues include myocarditis and allergy risk



- Wang, Jieliang et al. "The COVID-19 Vaccine Race: Challenges and Opportunities in Vaccine Formulation." AAPS PharmSciTech vol. 21,6 225. 5 Aug. 2020, doi:10.1208/s12249-020-01744-7
- Calina, D., Sarkar, C., Arsene, A.L. et al. Recent advances, approaches and challenges in targeting pathways for potential COVID-19 vaccines development. Immunol Res (2020).
- NCIRS Vaccine Platforms: http://ncirs.org.au/vaccine-platforms

Viral vector-mechanism of action



- Gene for the target, (spike protein), inserted into a benign unrelated virus
  - In this case most commonly an Adenovirus
    - Oxford-AstraZeneca is a modified chimpanzee adenovirus ChAdOx1
  - The virus is capable of entering cells but not replicating
    - Typically, some are able to replicate
  - Once inside, DNA to mRNA to protein
    - Spike protein produced
  - The vector virus also aids in the generation of an immune response, so no adjuvant required
    - And typically potent cellular and humoral responses generated
    - Relatively reactogenic
  - However, pre-existing or newly generated immunity against the vector may impact efficacy

- Wang, Jieliang et al. "The COVID-19 Vaccine Race: Challenges and Opportunities in Vaccine Formulation." AAPS PharmSciTech vol. 21,6 225. 5 Aug. 2020, doi:10.1208/s12249-020-01744-7
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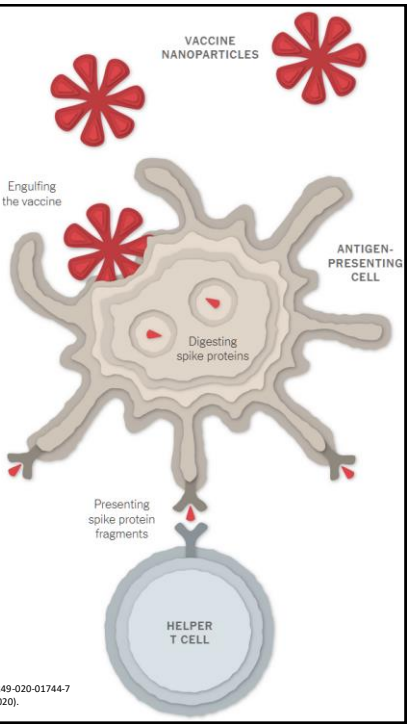
Protein-mechanism of action

- Target antigen produced in laboratory
  - Now often associated with additional technologies
    - Nanoparticles/Virus Like Particles/Molecular Clamp etc
  - Pro's: Easy to manufacture (from sequence), no live virus, well established platform, specifically targeting essential antigens can reduce reactogenicity
  - Con's: can have high production costs, often require adjuvant and or multiple doses



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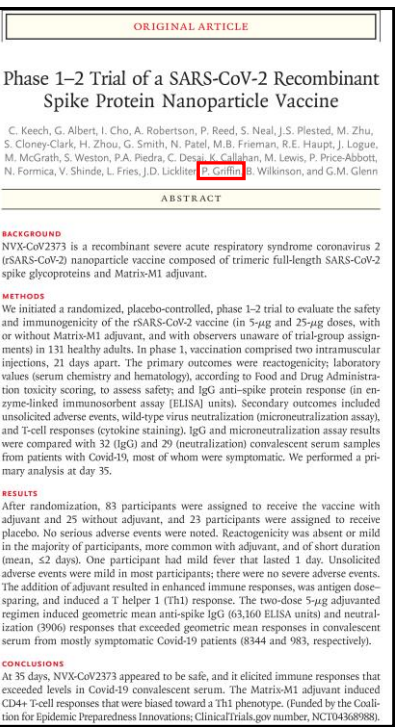
Novavax NVX-CoV2373

- Novavax NVX-CoV2373
  - Recombinant Spike protein nanoparticle with matrix M adjuvant
    - 2 doses, 21 days apart
    - Stable at standard refrigeration temperatures
  - First vaccine to commence human trials in southern hemisphere, 26th May 2020
    - Principal Investigator
  - Phase 3 commenced September 24 2020
  - Authorised in Indonesia on the 2nd Nov
  - Approved and now in use in Australia



ORIGINAL ARTICLE

Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine

C. Keech, G. Albert, I. Cho, A. Robertson, P. Reed, S. Neal, J.S. Plested, M. Zhu, S. Cloney-Clark, H. Zhou, G. Smith, N. Patel, M.B. Frieman, R.E. Haupt, J. Logue, M. McGrath, S. Weston, P.A. Piedra, C. Desai, K. Callahan, M. Lewis, P. Price-Abbott, N. Formica, V. Shinde, L. Fries, J.D. Lickliter, P. Griffin, B. Wilkinson, and G.M. Glenn

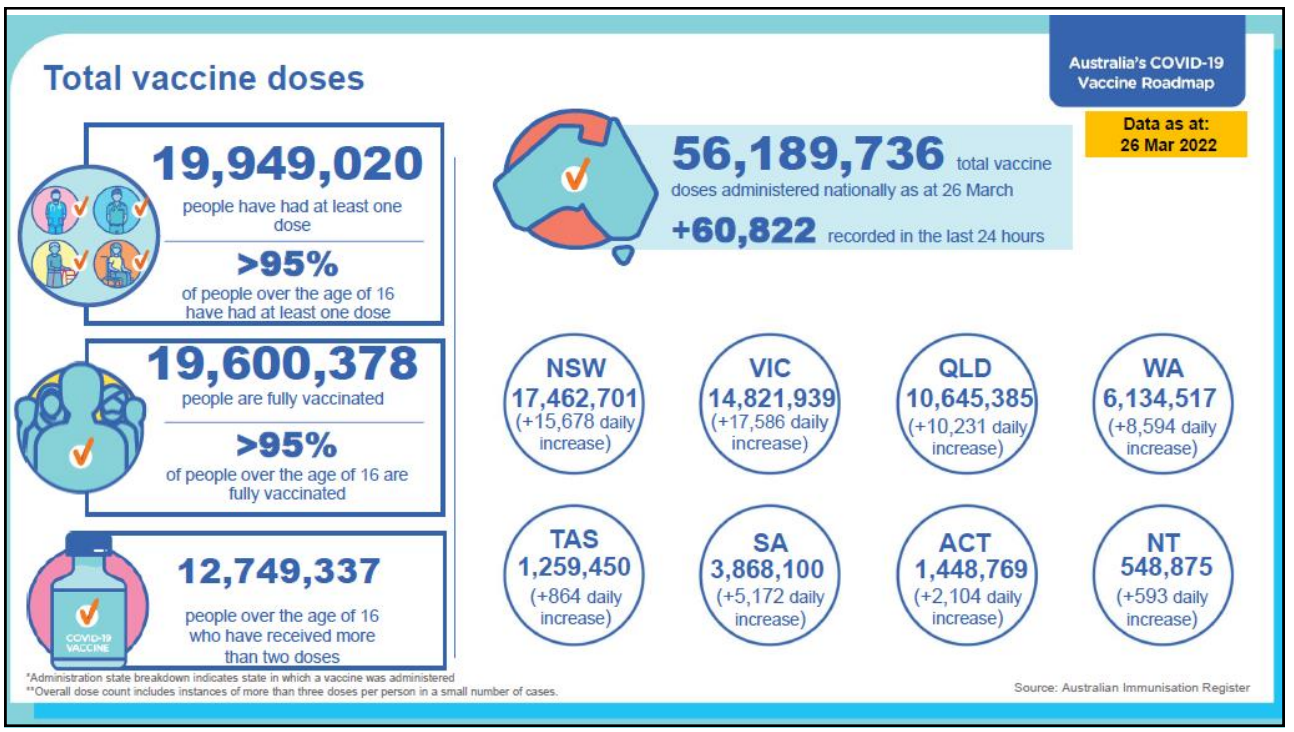
ABSTRACT

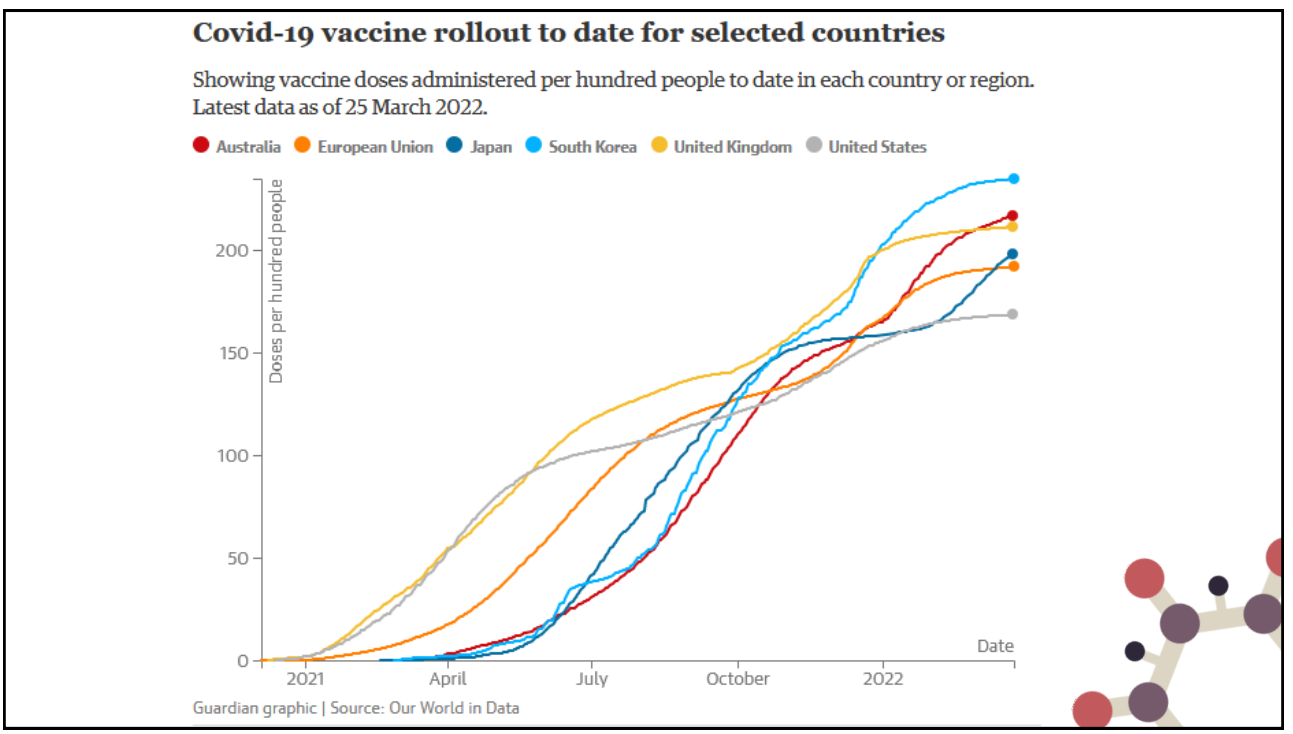
BACKGROUND
NVX-CoV2373 is a recombinant severe acute respiratory syndrome coronavirus 2 (rSARS-CoV-2) nanoparticle vaccine composed of trimeric full-length SARS-CoV-2 spike glycoproteins and Matrix-M1 adjuvant.

METHODS
We initiated a randomized, placebo-controlled, phase 1–2 trial to evaluate the safety and immunogenicity of the rSARS-CoV-2 vaccine (in 5-μg and 25-μg doses, with or without Matrix-M1 adjuvant, and with observers unaware of trial-group assignments) in 131 healthy adults. In phase 1, vaccination comprised two intramuscular injections, 21 days apart. The primary outcomes were reactogenicity; laboratory values (serum chemistry and hematology), according to Food and Drug Administration toxicity scoring, to assess safety; and IgG anti–spike protein response (in enzyme-linked immunosorbent assay [ELISA] units). Secondary outcomes included unsolicited adverse events, wild-type virus neutralization (microneutralization assay), and T-cell responses (cytokine staining). IgG and microneutralization assay results were compared with 32 (IgG) and 29 (neutralization) convalescent serum samples from patients with Covid-19, most of whom were symptomatic. We performed a primary analysis at day 35.

RESULTS
After randomization, 83 participants were assigned to receive the vaccine with adjuvant and 25 without adjuvant, and 23 participants were assigned to receive placebo. No serious adverse events were noted. Reactogenicity was absent or mild in the majority of participants, more common with adjuvant, and of short duration (mean, ≤2 days). One participant had mild fever that lasted 1 day. Unsolicited adverse events were mild in most participants; there were no severe adverse events. The addition of adjuvant resulted in enhanced immune responses, was antigen dose–sparing, and induced a T helper 1 (Th1) response. The two-dose 5-μg adjuvanted regimen induced geometric mean anti-spike IgG (63,160 ELISA units) and neutralization (3906) responses that exceeded geometric mean responses in convalescent serum from mostly symptomatic Covid-19 patients (8344 and 983, respectively).

CONCLUSIONS
At 35 days, NVX-CoV2373 appeared to be safe, and it elicited immune responses that exceeded levels in Covid-19 convalescent serum. The Matrix-M1 adjuvant induced CD4+ T-cell responses that were biased toward a Th1 phenotype. (Funded by the Coalition for Epidemic Preparedness Innovations; ClinicalTrials.gov number, NCT04368988).


Total vaccine doses
Australia's COVID-19 Vaccine Roadmap
Data as at: 26 Mar 2022
19,949,020
people have had at least one dose
>95%
of people over the age of 16 have had at least one dose
19,600,378
people are fully vaccinated
>95%
of people over the age of 16 are fully vaccinated
12,749,337
people over the age of 16 who have received more than two doses
56,189,736 total vaccine doses administered nationally as at 26 March
+60,822 recorded in the last 24 hours
NSW 17,462,701 (+15,678 daily increase)
VIC 14,821,939 (+17,586 daily increase)
QLD 10,645,385 (+10,231 daily increase)
WA 6,134,517 (+8,594 daily increase)
TAS 1,259,450 (+864 daily increase)
SA 3,868,100 (+5,172 daily increase)
ACT 1,448,769 (+2,104 daily increase)
NT 548,875 (+593 daily increase)
*Administration state breakdown indicates state in which a vaccine was administered
**Overall dose count includes instances of more than three doses per person in a small number of cases.
Source: Australian Immunisation Register


Covid-19 vaccine rollout to date for selected countries
Showing vaccine doses administered per hundred people to date in each country or region.
Latest data as of 25 March 2022.
Australia
European Union
Japan
South Korea
United Kingdom
United States
Doses per hundred people
200
150
100
50
0
Date
2021
April
July
October
2022
Guardian graphic | Source: Our World in Data

Some Major Milestones in Our Rollout

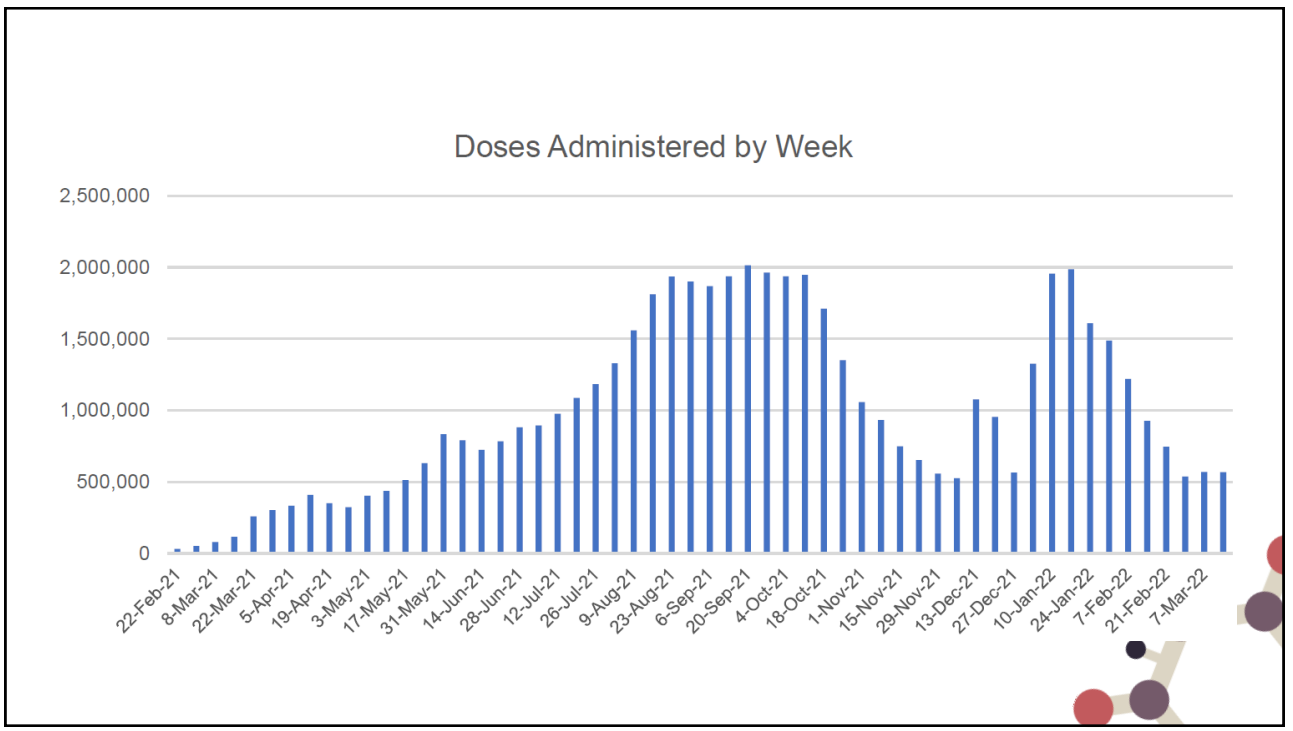
- First case in Australia: 25th January 2020
- Vaccine approvals
  - Pfizer provisionally approved Jan 25, 2021
  - AstraZeneca provisionally approved Feb 16, 2021
- First big variant: UK/B.1.1.7 (alpha) arrives in Australia, Feb, 21
- Rollout commenced Feb 22
  - 1a: Front line and aged care
  - 1b: 22nd March: elderly (>70), vulnerable, other HCW, indigenous
- Adverse events: TTS
  - Early March: reports of clotting and European countries suspending AZ
  - ATAGI released statements on the 16th and 19th of March
    - No change to use
  - ATAGI recommend Pfizer for under 50's from the 8th of April
- Pregnancy: ATAGI and RANZCOG recommend vaccine in pregnancy, 9th of June
- AZ updated to over 60's from 17th June
- Another variant: Delta: hits Australia, mid June
  - 13th July: reconsider using AZ in younger in an outbreak setting, shorten interval (4 to 8)

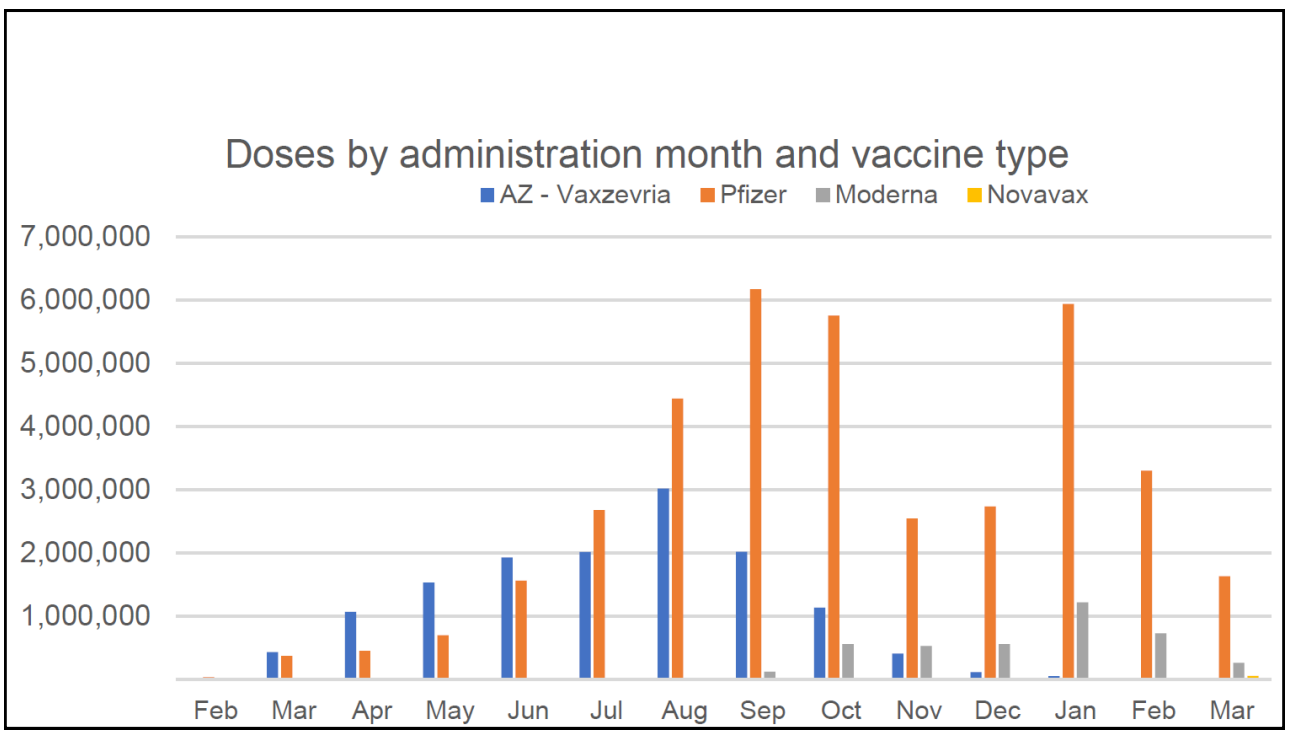
First dose AZ 19th March

Some Major Milestones in Our Rollout

- Children
  - Remote, vulnerable children 12 and older recommended from 2nd August
    - All adolescents from 12 years of age recommended from 27th August
  - Pfizer commenced dosing 5 to 11 y.o.a Jan 10th, 2022
  - Moderna approved for 6 to 11 y.o.a Feb 17th , 2022
- Third dose recommended for severely immunocompromised from October 8th
- Omicron
  - First reported 24th November, 21
  - In Australia within 3 days
  - Successive shortening of booster interval
    - To 4 months from January 4
    - Shortly after to 3 months
- Now 4th dose "winter booster" recommendation

My children vaccinated
Dose 1: January 10th 2022
Dose 2: Mar 11th 2022


Doses Administered by Week
2,500,000
2,000,000
1,500,000
1,000,000
500,000
0
22-Feb-21
8-Mar-21
22-Mar-21
5-Apr-21
19-Apr-21
3-May-21
17-May-21
31-May-21
14-Jun-21
28-Jun-21
12-Jul-21
26-Jul-21
9-Aug-21
23-Aug-21
6-Sep-21
20-Sep-21
4-Oct-21
18-Oct-21
1-Nov-21
15-Nov-21
29-Nov-21
13-Dec-21
27-Dec-21
10-Jan-22
24-Jan-22
7-Feb-22
21-Feb-22
7-Mar-22


Doses by administration month and vaccine type
AZ - Vaxzevria
Pfizer
Moderna
Novavax
7,000,000
6,000,000
5,000,000
4,000,000
3,000,000
2,000,000
1,000,000
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Jan
Feb
Mar

- But we still have a long way to go.....

Aboriginal and Torres Strait Islander peoples
Number of people vaccinated

Data as at: 22 Mar 2022
Updated weekly

Australia's COVID-19 Vaccine Roadmap

435,465
people over the age of 16 have had at least one dose

84.0%
of people over the age of 16 have had at least one dose

413,329
people over the age of 16 are fully vaccinated

79.7%
of people over the age of 16 are fully vaccinated

People aged 12 – 15 years

48,488	42,163
68.3%	59.4%
At least one dose	Fully vaccinated

178 Aboriginal community controlled health services (ACCHS)

0#	50	27	44	12	3	21	21
ACT	NSW	NT	QLD	SA	TAS	VIC	WA

Medicare Address State##	Individuals Dose 1	Individuals Dose 1 %	Individuals Dose 2	Individuals Dose 2 %
Australian Capital Territory	4,826	91.2%	4,705	88.9%
New South Wales	134,554	86.6%	131,266	84.5%
Northern Territory	42,190	89.2%	39,740	84.0%
Queensland	114,999	81.0%	108,745	76.6%
South Australia	19,741	79.4%	18,169	73.1%
Tasmania	13,896	88.4%	13,429	85.4%
Victoria	35,245	89.6%	34,372	87.4%
Western Australia	53,111	84.8%	47,861	76.4%
Unknown/Other Territories	16,903	65.2%	15,042	58.0%
Totals	435,465	84.0%	413,329	79.7%

Source: Australian Immunisation Register

*Identifying as Aboriginal and Torres Strait Islander is optional and the estimated population may be under reported.
**Includes all Aboriginal and Torres Strait Islander peoples who have received a vaccination, not limited to those administered in an ACCHS setting
#ACCHS in the ACT are currently operating as a Commonwealth Vaccine Clinics so not included to avoid double counting
##The above table includes all identified Aboriginal and Torres Strait Islander people who are aged 16 and above by their state of residence.

Residential aged care vaccination rollout

Residential aged care facilities status

100% Commonwealth facilities visited (2,537 planned sites)

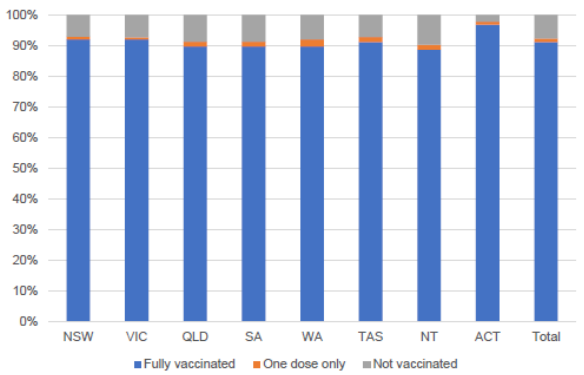
174,536 People fully vaccinated

176,706 People with at least one dose

Australia's COVID-19 Vaccine Roadmap

Data as at: 24 Mar 2022 Updated weekly

Aged care resident vaccinations



Aged care worker vaccinations

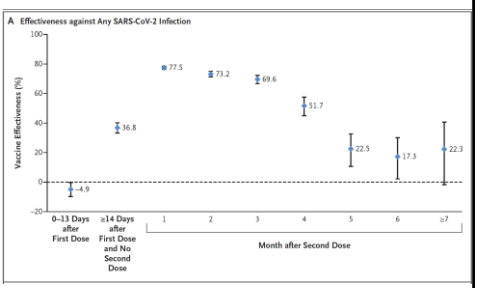
Jurisdictions	Total workers with at least one dose	Workers fully vaccinated	% Workers with at least one dose	% Workers fully vaccinated
NSW	78,130	78,121	98.7%	98.7%
VIC	66,398	66,397	96.9%	96.9%
QLD	48,462	48,455	98.7%	98.7%
SA	26,362	26,342	97.7%	97.6%
WA	23,583	23,580	98.1%	98.1%
TAS	7,676	7,676	100.0%	100.0%
NT	844	844	100.0%	100.0%
ACT	3,038	3,038	99.9%	99.9%
Total	254,493	254,453	98.1%	98.1%

Source: My Aged Care Portal vaccination progress
*Status updates are provided by facilities at least once per week. Reporting is updated Monday to Friday to encompass different facility updates being made on different days.
Data is sourced directly from Aged Care Service Providers and is not drawn or closely aligned with data from AIR due to inconsistencies and potential lags in uploading of records.

Boosters

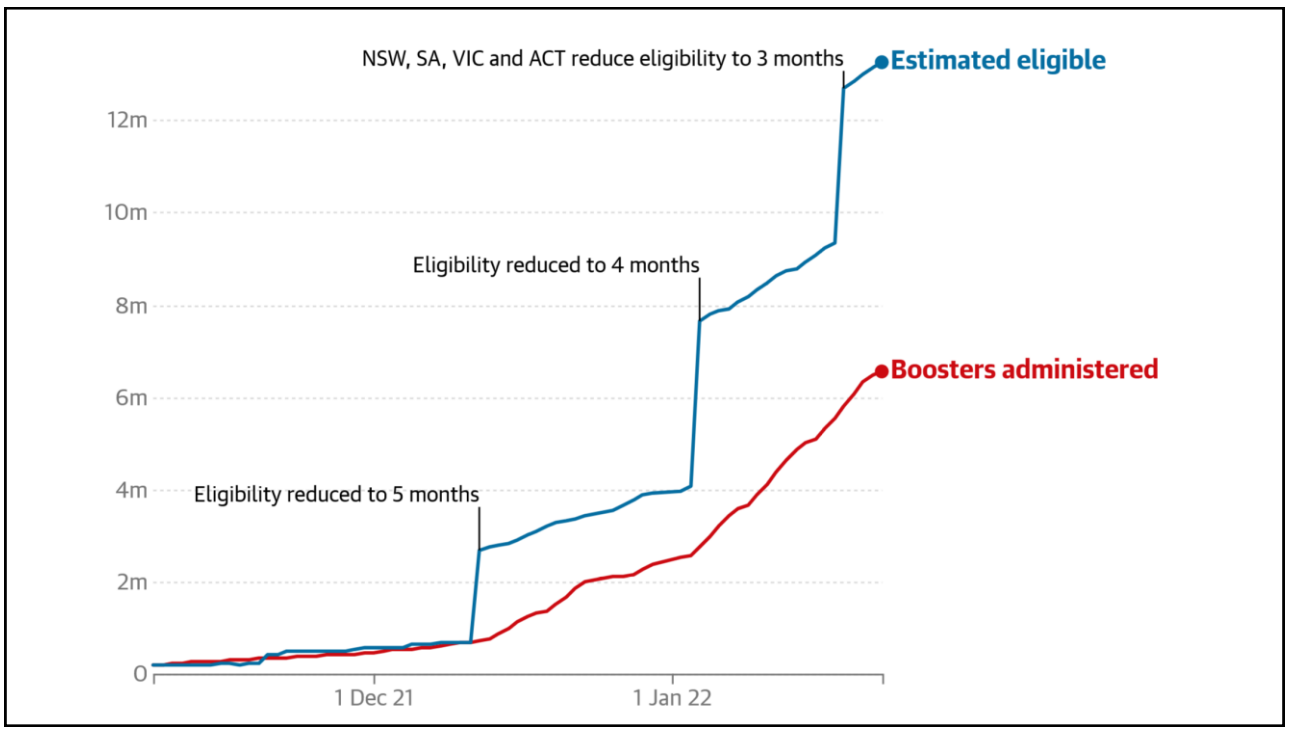
Boosters

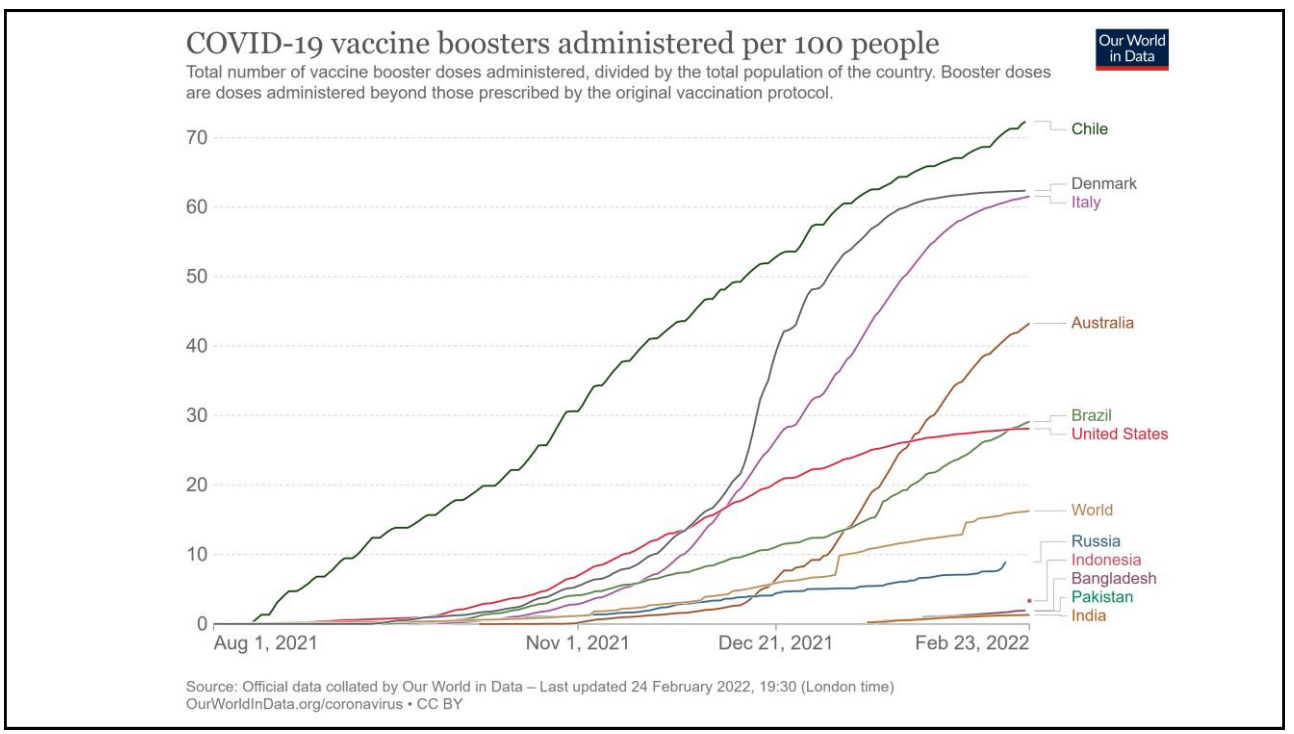
- Even before Omicron, protection known to reduce over time
  - Antibody levels shown to fall
  - Reduction in protection against infection following vaccination over time, particularly from 6 months
  - Protection against transmission from infected vaccinated individuals also appears to wane over time
  - Severe disease protection wanes to a lesser degree
- TGA approval for Pfizer COVID-19 vaccine booster dose, 27th October
  - 18 years and over
  - ≥ 6 months from completion of primary course
  - Highest priority groups
    - Risk for severe COVID-19
    - Increased occupational risk



Boosters

- Other vaccines for boosters
  - AstraZeneca able to be used for some time (adverse reaction to mRNA e.g. anaphylaxis/myocarditis)
    - Officially approved as booster 8th Feb, 2022
  - Moderna approved for use as booster 12th Dec, 2021
  - Novavax will likely also be available soon
- Omicron (late November 2021)
  - Partial immune evasion
    - Protection from 2 doses reduced
  - Booster able to address
    - Interval successively reduced
      - Now 3 months
    - Possibly at cost of reduction of longevity of protection


NSW, SA, VIC and ACT reduce eligibility to 3 months
Estimated eligible
12m
10m
Eligibility reduced to 4 months
8m
Boosters administered
6m
4m
Eligibility reduced to 5 months
2m
0
1 Dec 21
1 Jan 22


COVID-19 vaccine boosters administered per 100 people
Total number of vaccine booster doses administered, divided by the total population of the country. Booster doses are doses administered beyond those prescribed by the original vaccination protocol.
Our World in Data
70
60
50
40
30
20
10
0
Chile
Denmark
Italy
Australia
Brazil
United States
World
Russia
Indonesia
Bangladesh
Pakistan
India
Aug 1, 2021
Nov 1, 2021
Dec 21, 2021
Feb 23, 2022
Source: Official data collated by Our World in Data – Last updated 24 February 2022, 19:30 (London time)
OurWorldInData.org/coronavirus • CC BY

Boosters Moving Forward

- Will likely need to be regular
  - Longer term intervals hard to know just yet
  - The more boosters required and the shorter the interval, the lower our probability of achieving sufficient coverage
    - Also threatens to create greater inequity
  - May be addressed by second (or later) generation vaccines
    - Longer lasting protection
  - Heterologous boosting also may be a solution
    - Optimum combination still to be determined
- In the future, may be combined with flu
- Boosters will be used moving forward to address
  - Waning protection
  - New variants
  - Epidemiology e.g. increased transmission/severity

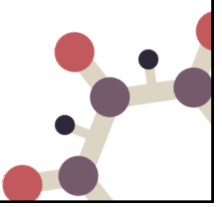
Winter Booster

- Announced 25th March
- Aim to increase vaccine protection before winter for select groups
  - High risk severe illness
  - Likely to have relatively reduced protection
    - Due to their risk group
    - Prioritised for primary vaccination
- These groups include
  - Adults aged 65 years and older
  - Residents of aged care or disability care facilities
  - People aged 16 years and older with severe immunocompromise
    - as defined in the ATAGI statement on the use of a 3rd primary dose of COVID-19 vaccine in individuals who are severely immunocompromised
  - Aboriginal and Torres Strait Islander people aged 50 years and older
- When
  - 4 months or longer from 3rd booster dose
  - 4 months from confirmed SARS-CoV-2 infection if after booster dose
  - Rollout in April, likely coinciding with the influenza vaccine program
- Which
  - mRNA preferred
  - Vaxzevria (AZ) can be used if mRNA contraindicated or declined
  - Nuvaxovid (Novavax) can be used if no other vaccines considered suitable

Box 1: People with the following immunocompromising conditions and therapies for which a 3rd primary dose is recommended

N.B. This list is not exhaustive. Clinicians may use their judgement for conditions or medications that are not listed, and which are associated with severe immunocompromise.

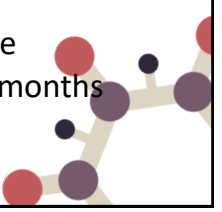
- Active haematological malignancy
- Non-haematological malignancy with current active treatment (e.g. chemotherapy, whole body irradiation)
- Solid organ transplant with immunosuppressive therapy
- Haematopoietic stem cell transplant (HSCT) recipients or chimeric antigen receptor T-cell (CAR-T) therapy within 2 years of transplantation.
  - These patients require *revaccination with 3 additional doses* of COVID-19 vaccine, irrespective of doses given prior to transplantation, commencing generally ≥3-6 months after their transplant after discussion with their treating specialist.
  - Those beyond 2 years from transplant should discuss with their treating specialist about the need for a 3rd dose.
- Immunosuppressive therapies including:
  - High dose corticosteroid treatment equivalent to >20mg/day of prednisone for ≥14 days in a month, or pulse corticosteroid therapy.
  - Multiple immunosuppressants where the cumulative effect is considered to be severely immunosuppressive.
  - Selected conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDS):
    - including mycophenolate, methotrexate (≥10 mg/week), leflunomide, azathioprine (≥ 1mg/kg day), 6-mercaptopurine (≥ 0.5mg/kg/day), alkylating agents (e.g. cyclophosphamide, chlorambucil), and systemic calcineurin inhibitors (e.g. cyclosporin, tacrolimus).
    - excluding hydroxychloroquine or sulfasalazine when used as monotherapy.
  - Biologic and targeted therapies anticipated to reduce the immune response to COVID-19 vaccine. Refer to **Table 1** below for examples. However, clinicians may use their judgement for medications which are not listed.
- Primary immunodeficiency including combined immunodeficiency and syndromes, major antibody deficiency (e.g. common variable immune deficiency (CVID) or agammaglobulinemia), defects of innate immunity (including phagocytic cells), defects of immune regulation, complement deficiencies and phenocopies of primary immunodeficiencies.
- Advanced or untreated HIV with CD4 counts <250/μL or those with a higher CD4 count unable to be established on effective anti-retroviral therapy.
  - a 3rd primary dose is not required for people living with HIV, receiving ART with CD4 counts ≥250/μL.
- Long term haemodialysis or peritoneal dialysis.



Healthed

Definitions

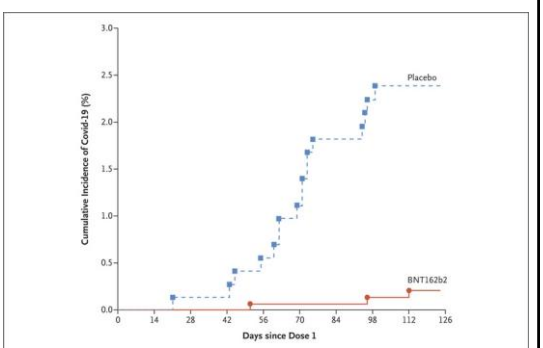
- Fully vaccinated no longer preferred term
- Instead “up-to-date”
- Change made to serve as basis for policies for the public health management of the COVID-19 pandemic
- All individuals 16 years and over are recommended to receive a booster from 3 months following completion of primary course
  - This is required to maintain “up-to-date” status
  - 3 months from completion of primary course is the “due date”
- Individuals 16 years of age and over will be considered “overdue” if booster not received within 6 months of completing primary schedule
- Children/adolescents 5 to 15 years are up to date after primary course
- If you have had confirmed COVID-19, can defer next dose for up to 4 months however this is not necessarily recommended



Children

Children 5 to 11 years

- Pfizer clinical trial results published in NEJM (Nov 9)
  - 10 µg dose chosen from phase 1 (16 children in each group)
    - Adult is 30 µg
    - Same 3 week interval
  - 1517 children received IP in phase 2-3 study
    - Efficacy 90.7%
  - Adverse events
    - Fatigue (34%/39%)
    - Headache (22%/28%)
    - Myalgia (9%/12%)
    - More redness and swelling at injection site than adults
    - But, overall fewer and milder AE's than teens or adults
    - No myocarditis, pericarditis, hypersensitivity, or anaphylaxis



Efficacy End Point	SARS-CoV-2 Infection Status	BNT162b2		Placebo		Vaccine Efficacy (95% CI)
		No. of participants with event (total no.)	Surveillance time (no. at risk)	No. of participants with event (total no.)	Surveillance time (no. at risk)	
			1000 person-yr		*1000 person-yr*	%
Covid-19 ≥7 days after second dose	Without evidence of previous infection	3 (1305)	0.322 (1273)	16 (663)	0.159 (637)	90.7 (67.7–98.3)
Covid-19 ≥7 days after second dose	With or without evidence of previous infection	3 (1450)	0.353 (1398)	16 (736)	0.176 (704)	90.7 (67.4–98.3)

Children 5 to 11 years

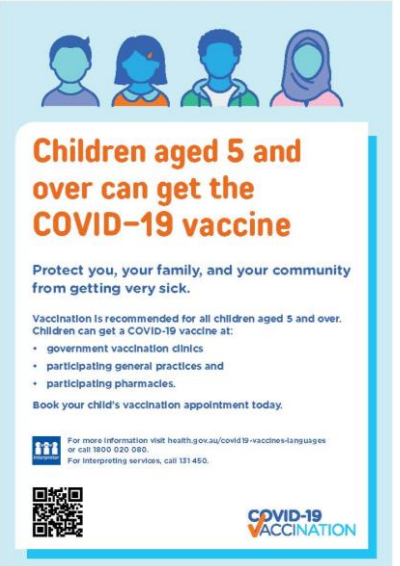
- Vulnerable children 12 to 15 recommended from 2nd August
  - All adolescents from 12 recommended from the 27th August
- Provisional determination by the TGA for 5 to 11 year old's on the 13th of October
  - Able to apply to vary approval to include this group
- Pfizer approved in the USA on the 29th of October for 5 to 11 year olds
- Pfizer approved in Australia on the 10th December
  - Administration commenced January 10th 2022
- Moderna approved for 6 to 11 y.o.a on 17th Feb

Children 5 to 11 years

- Balance between many factors including
  - Covid typically mild in younger children
    - However, Multi-system inflammatory syndrome in children (MIS-C) reported
      - Over 5000 cases in the USA with over 40 deaths
  - Many say it will increase ability to attend school
    - However, modelling suggests “test and stay” approach using RAT’s means only positive students need to be sent home and schools need not be closed
  - Clinical trials show the vaccine is safe
    - Large numbers of children receiving the vaccine in the USA means we could review that real world experience before approving here
      - Approximately 900 000 children received the vaccine in the USA in the first week alone
- Other issues
  - Consent issues
  - Reduction in benefit for individual children as overall rate of eligible adults and teens increases
  - Travel and other restrictions on the unvaccinated

Uptake in Children in Australia

- While rates for older age groups are promising
  - 16+ second dose: 95.06%
  - 12+ second dose: 94.2%
  - 18+ booster 63.53%
- Uptake in children is concerning
  - 5 to 11 first dose: 52.08%
  - 5 to 11 second dose: 23.8%
  - Particularly given over 95% of 5 year olds have received childhood vaccinations
- Challenges include
  - Difficulties with appointments
  - Supply issues
  - Anxiety
  - Misinformation



2nd Generation Vaccines

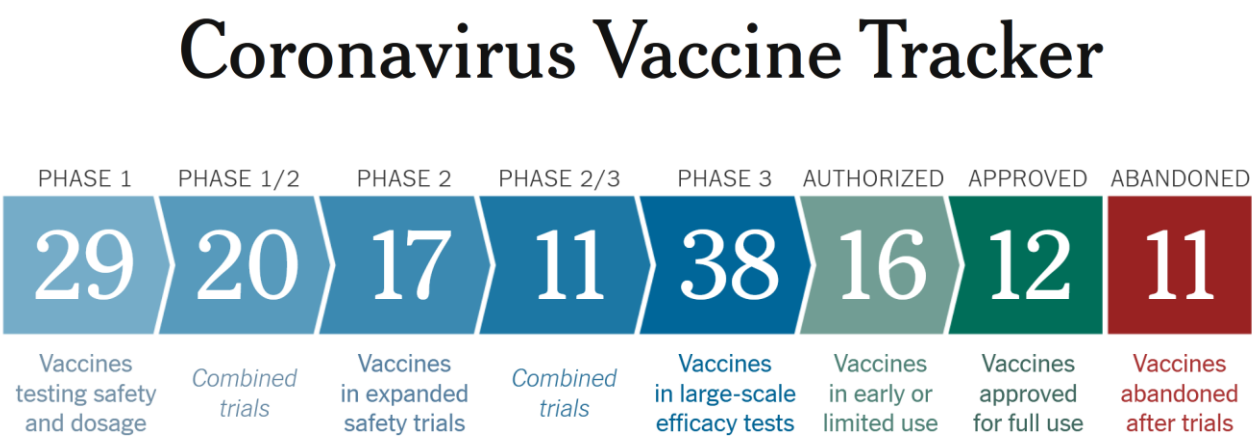
New vaccines:

Why we need to continue to develop COVID-19 vaccines

- No question currently available vaccines are impressive in terms of safety and efficacy
  - However not perfect
- Desirable properties of a perfect vaccine include
  - Single dose
    - Perhaps even not IM
  - Long lasting, ideally lifelong, protection
  - High efficacy in all outcome measures
    - Severe disease but also transmission blocking
  - No, or very few, adverse effects
  - Thermal stability
    - Room temperature ideally
  - Long term stability
  - Ease of manufacture
    - Low dose, easier to scale manufacturing
  - Ease of administration
    - Not needle and syringe
  - Less susceptible to changes from emerging variants
    - Pan Coronavirus vaccine, conserved regions

Healthed

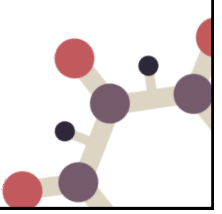
Coronavirus Vaccine Tracker: Feb 18, 2022

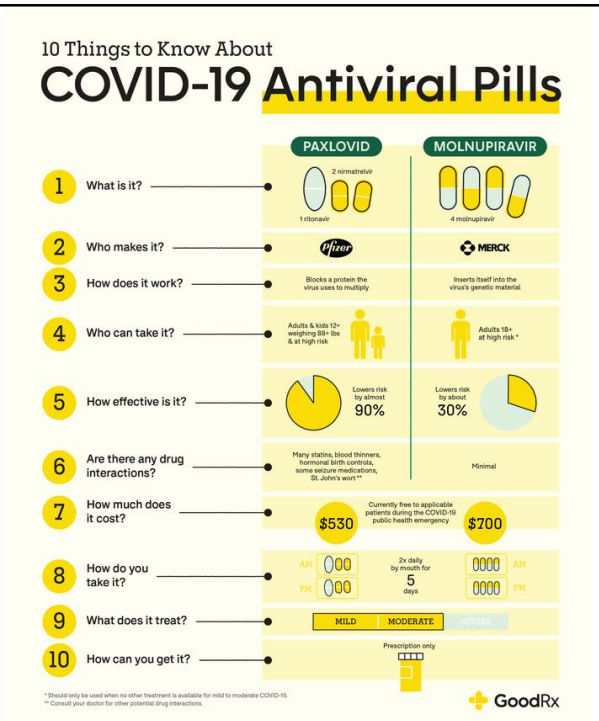


Therapies

Therapies

- Rapidly changing landscape
- IV
  - Early: Sotrovimab
  - Later: Remdesivir (Severe, hospitalised)
    - Also can be used early, outpatient but this is limited in Australia to date
- Oral
  - Paxlovid
  - Molnupiravir
- Pre-exposure
  - Evusheld





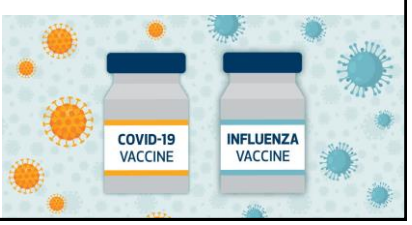
What about for people that can't respond to vaccination

- Estimated 2% of the global population increased risk due to an inability to develop an adequate response to a COVID-19 vaccine.
  - Inherent immune compromise
  - Immune suppressing treatment for autoimmune or inflammatory conditions, preventing rejection of transplanted organs or treating malignant conditions.
- These groups also some of the highest risk from adverse outcomes from infection.
- Many approaches to address under investigation including pre-exposure prophylaxis using antibodies or antivirals
  - First approved in Australia is Evusheld
    - combination of two long-acting monoclonal antibodies
      - tixagevimab and cilgavimab
    - Challenge linking patients who will benefit to access

Other respiratory viruses

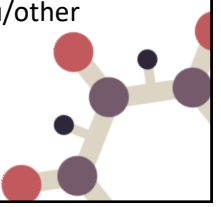
COVID and Flu

- Flu cases low during pandemic
  - Measures to mitigate COVID-19 highly effective for Flu
    - Particularly closing of international border
  - With low case numbers and low vaccination rates
    - Population susceptibility highest for some time
  - With re-opening of international borders and relaxation of other mitigation strategies, Flu will return
- Initially an arbitrary recommendation of separating COVID and Flu vaccines by 2 weeks, then 1 week
- Evidence suggested both could be co-administered without safety concerns or compromising immunogenicity
- Now many candidates combining both into single vaccine
  - Novavax
    - NVX-CoV2373 with NanoFlu
  - Moderna
    - COVID, Flu and RSV combined
- Plan to try and have available for next year



COVID and Flu

- Going to take a significant change in strategy to address Flu
  - Rapid antigen tests only for COVID-19 at this stage
  - Reduced reliance on PCR based testing has led to reduced capability
  - COVID-19 not yet in many respiratory viral panels so needs to be ordered separately
  - Many stories of people with symptoms who are doing multiple RAT's that are negative so they continue as normal
  - Likely to be more scrutiny of flu vaccine than previously
  - A modest flu year with a little covid→strain on health care system
- Recommendations
  - Depending on epidemiology at the time, need to look to test for COVID-19 and Flu/other respiratory viruses
  - Need to encourage people to isolate more on symptoms, even if negative RAT
  - Need to strongly encourage Flu vaccines
    - Likely to coincide with 4th dose recommendations



Conclusion

- Cases are taking off again for a number of reasons
  - not seeing increases in severe disease (yet)
- We are very fortunate to have developed a number of safe and highly effective vaccines against SARS-CoV-2 in record time
  - Using basically every known platform and many new platforms never before approved for use
  - Now approved from 5 years of age
- Uptake in Australia has been impressive, but there is still work to be done
  - Boosters/Children/Vulnerable Groups
- Many new candidates under investigation
  - Hopefully with properties to address limitations of currently available vaccines
    - Including reduced protection against variants
  - Including novel mechanisms and routes of administration
  - Combination vaccines
- While clearly here to stay, given the tools now at our disposal, particularly vaccination, but also therapies (including oral) and antibodies for prophylaxis, our ability to control this virus is now at a very high level