

CVRN Networking Event: COVID and the Heart

Prof Anthony Cunningham

The COVID-19 Vaccines in Australia

Director, Centre for Virus Research, University of Sydney



NSW CARDIOVASCULAR
RESEARCH NETWORK

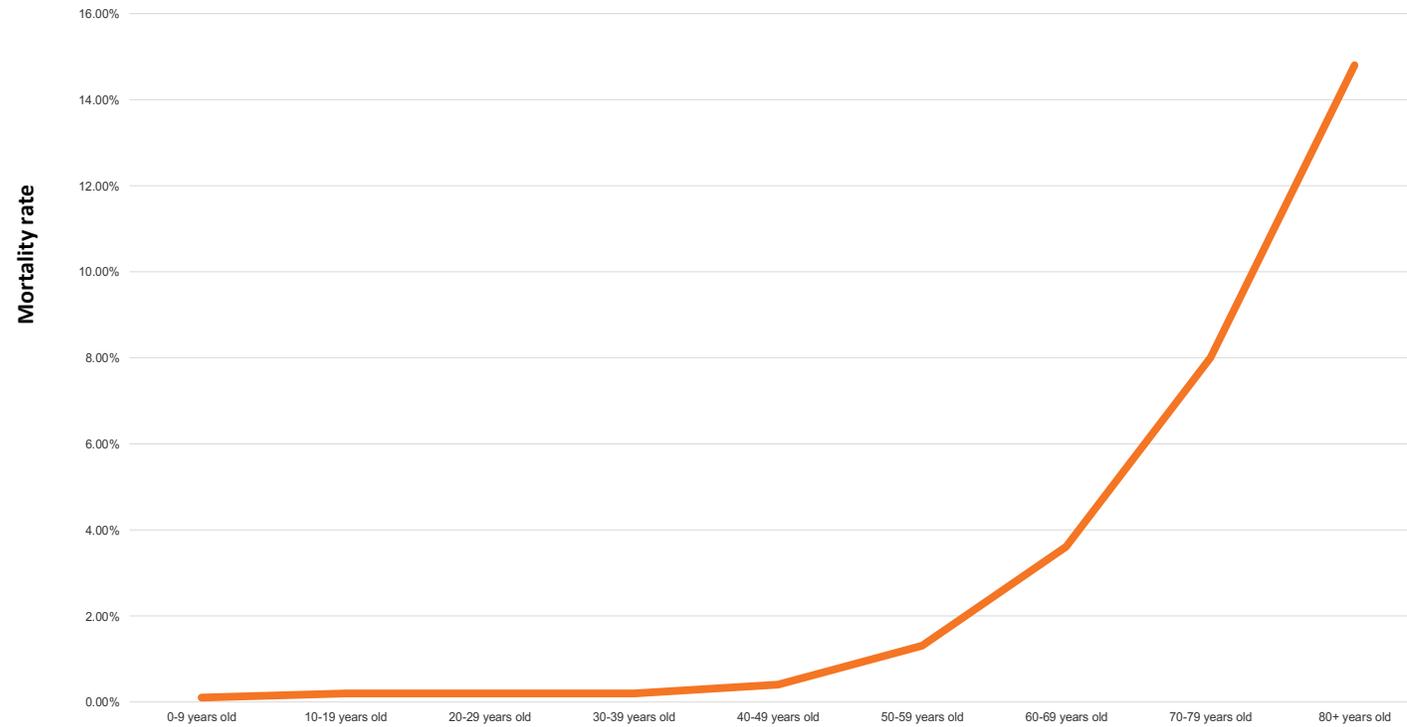
COVID Vaccines: An update

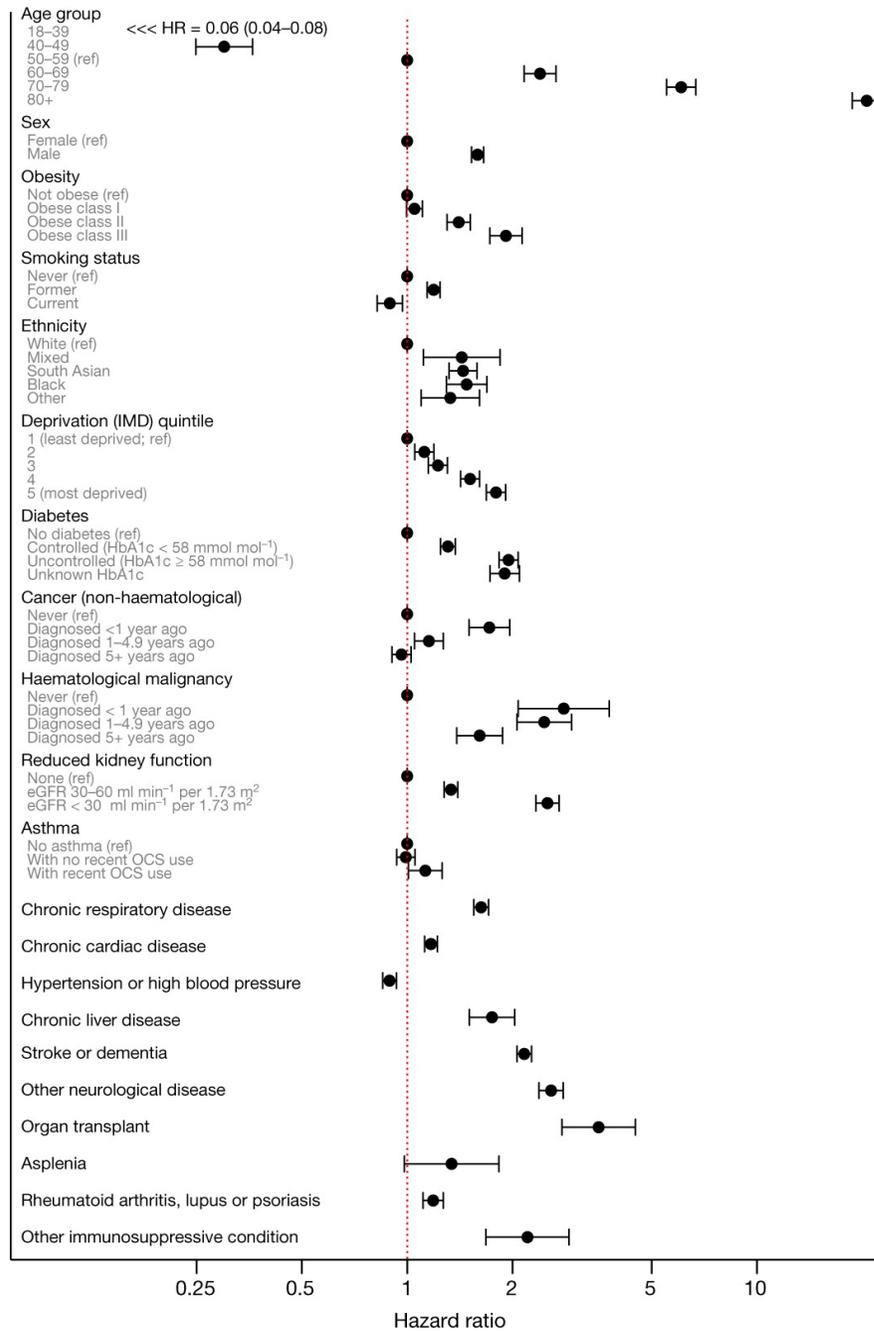
Tony Cunningham

Centre for Virus Research, Westmead Institute for Medical Research
and The University of Sydney



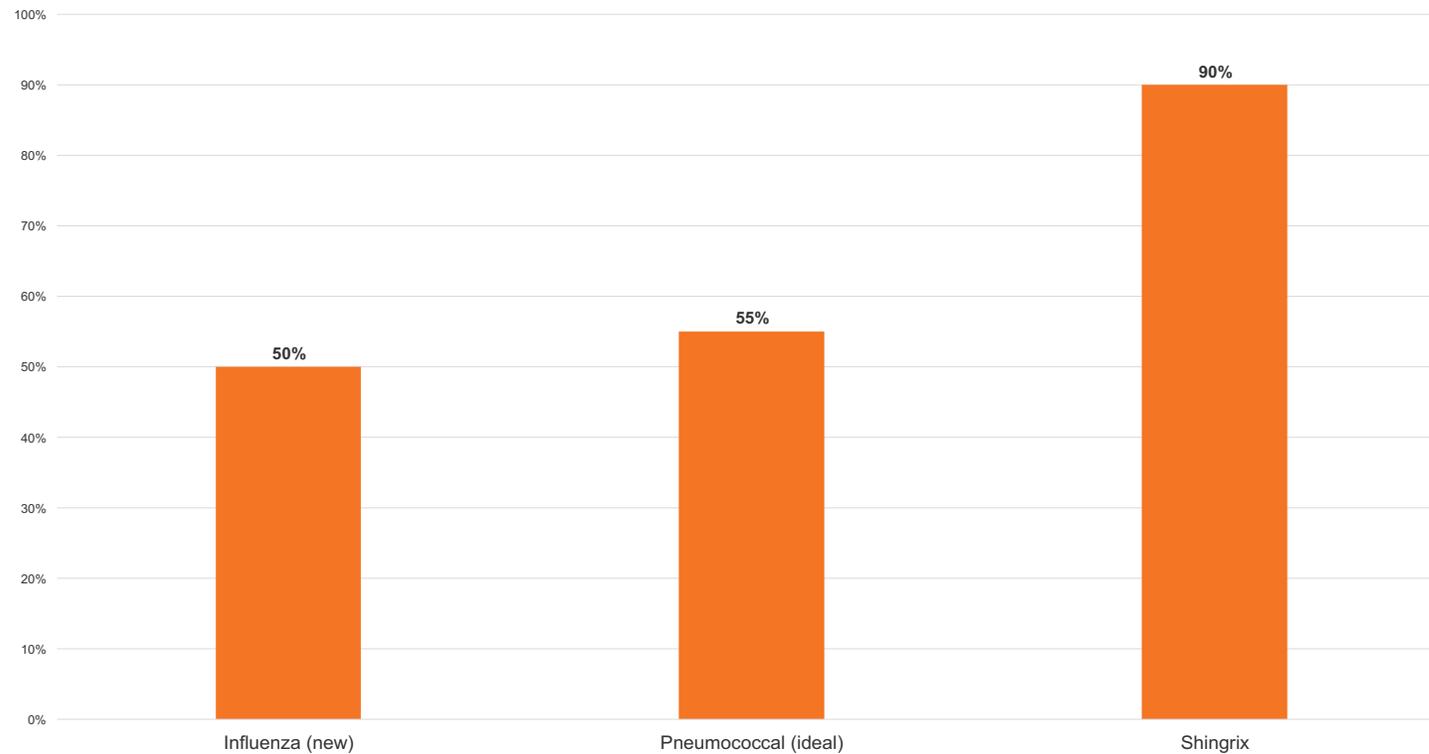
Mortality of COVID-19 climbs in the ageing



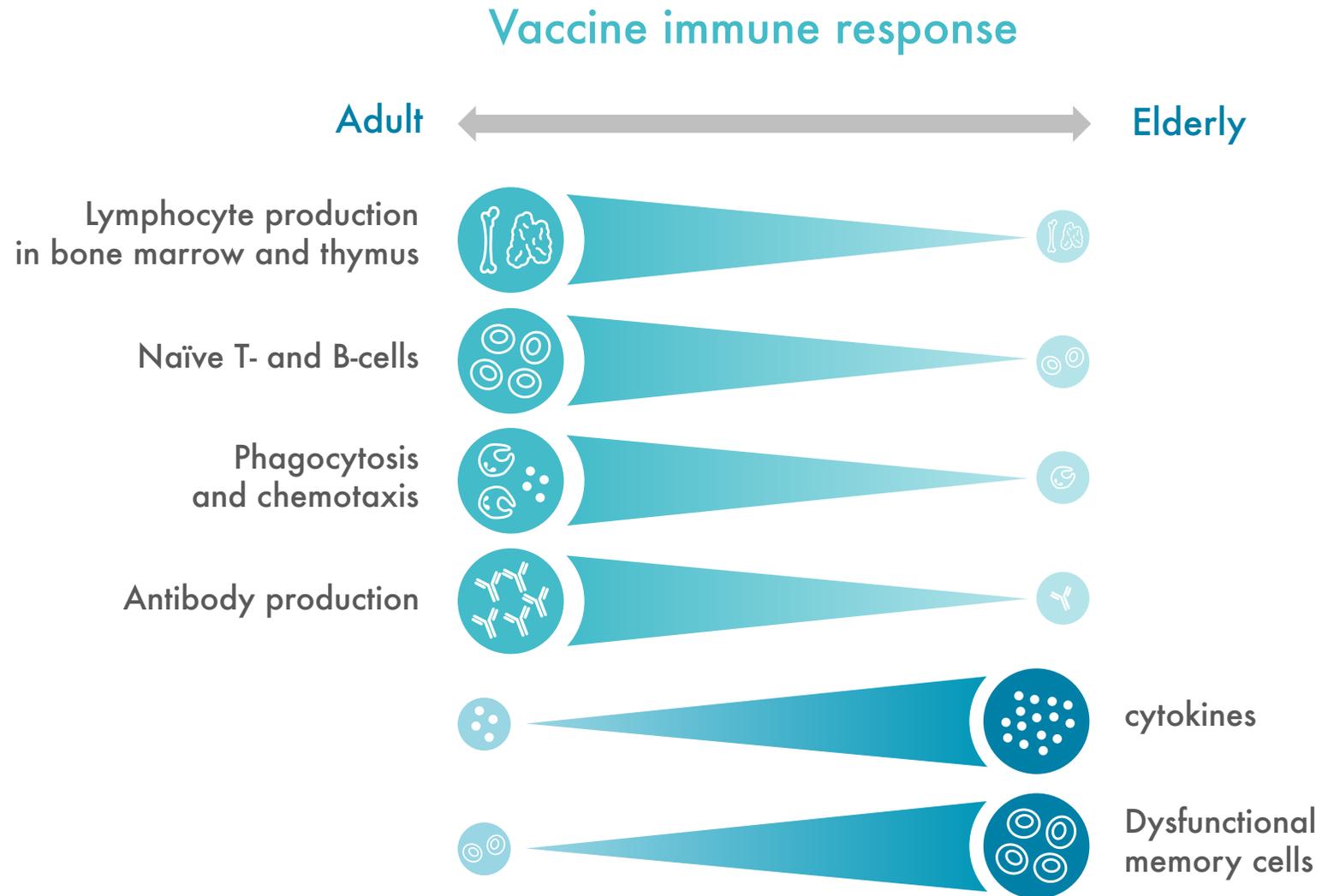


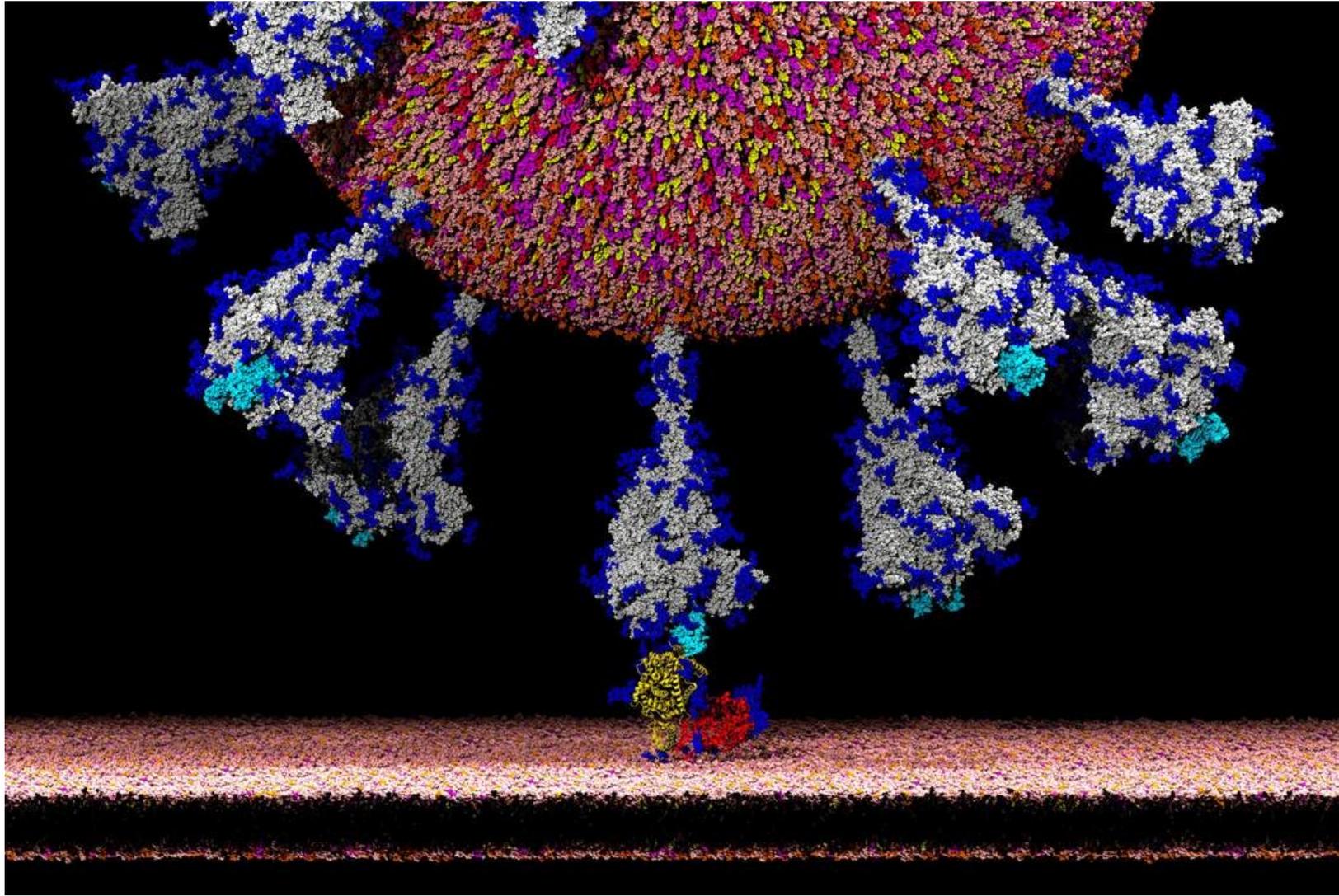
Factors associated with
COVID19 related death
using OPENSafely-
17million, UK

Vaccine efficacy for ageing people (>65 years)

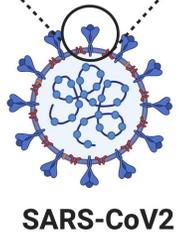
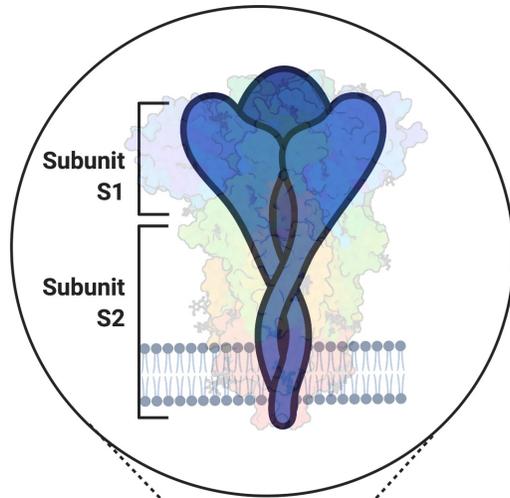


Vaccine response decreases with ageing

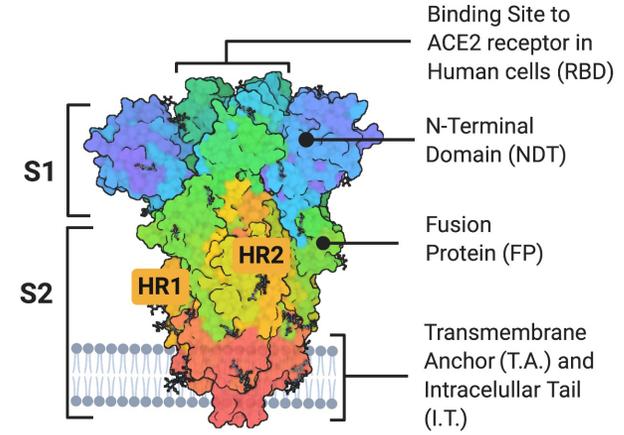




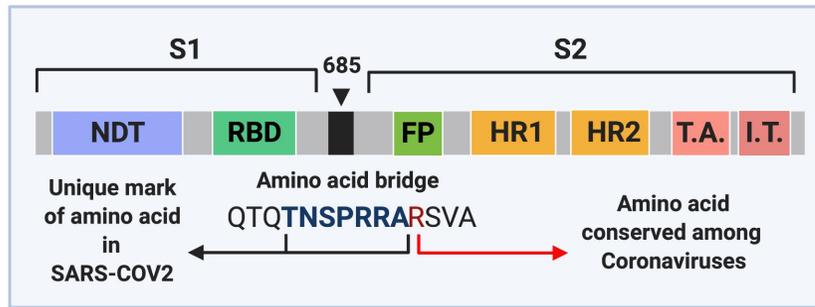
**Virus spike protein
Diagram**



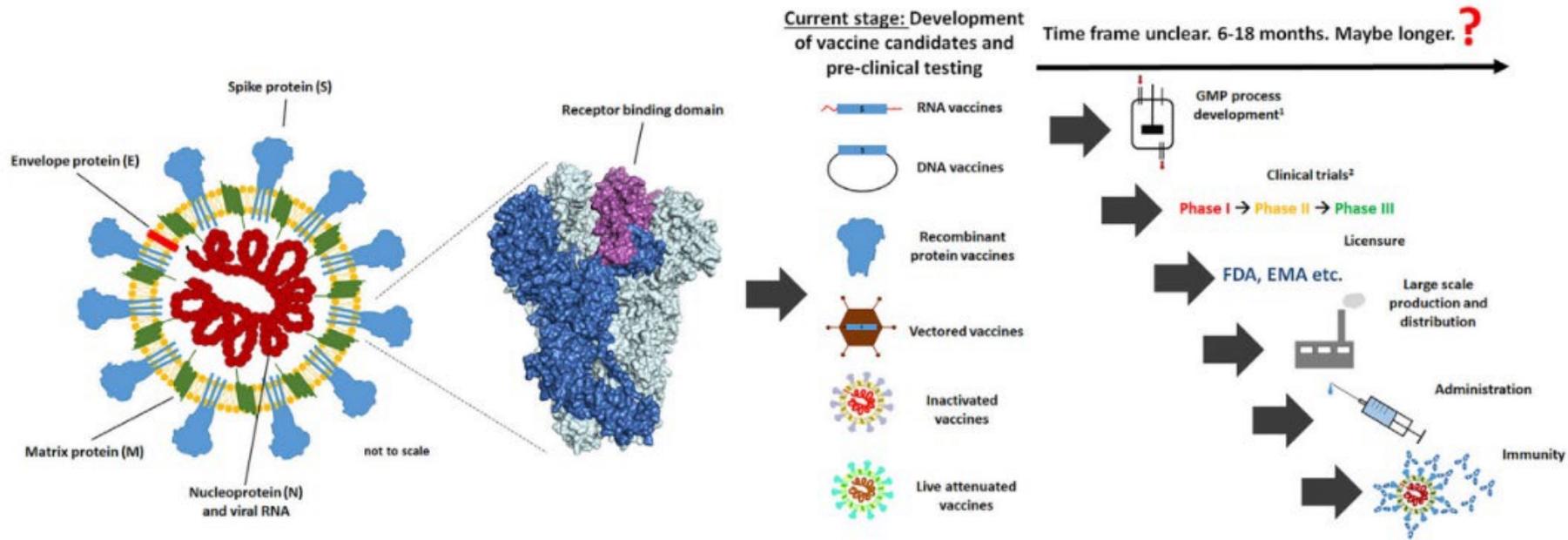
**Virus spike protein
Crystallographic structure seen by electron microscopy
(PDB ID: 6VXX-PDB)**



Primary Structure

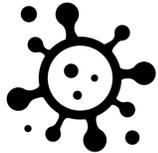


SARS-CoV-2 Vaccines: development pathway



Developer	How It Works	Phase	Status
 Pfizer-BioNTech	mRNA	23	Approved in several countries. Emergency use in U.S., E.U., other countries.
 Moderna	mRNA	3	Approved in Switzerland. Emergency use in U.S., E.U., other countries.
 Gamaleya	Ad26, Ad5	3	Early use in Russia. Emergency use in other countries.
 Oxford-AstraZeneca	ChAdOx1	23	Approved in Brazil. Emergency use in U.K., E.U., other countries.
 CanSino	Ad5	3	Approved in China. Emergency use in Mexico, Pakistan, Hungary.
 Johnson & Johnson	Ad26	3	Emergency use in U.S., E.U., other countries.
 Vector Institute	Protein	3	Early use in Russia.
 Novavax	Protein	3	
 Sinopharm	Inactivated	3	Approved in China, U.A.E., Bahrain. Emergency use in other countries.
 Sinovac	Inactivated	3	Approved in China. Emergency use in other countries.
 Sinopharm-Wuhan	Inactivated	3	Approved in China. Limited use in U.A.E.
 Bharat Biotech	Inactivated	3	Emergency use in India, other countries.

PFIZER / BioNTech



Mechanism
mRNA



**Trial
size**
44,000



Efficacy
95%



Australian doses
40 million

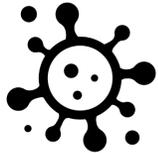


**Doses per
person**
2, 21 days apart



**Storage
temperature**
-70° C

ASTRA-ZENECA / OXFORD



Mechanism
Viral vector



**Trial
size**
65,000



Efficacy
82%



Australian doses
50.8 million

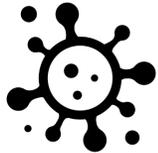


Doses per person
2, 12 weeks apart



**Storage
temperature**
2° C - 8° C

Novavax



Mechanism
Spike protein



**Trial
size**
45,000



Efficacy
90%



Australian doses
51 million



**Doses per
person**
2, 21 days apart



**Storage
temperature**
2° C - 8° C

SOURCE: BLOOMBERG

IN CONVERSATION FROM THE LAB

Common Side Effects



**Pain at site of
injection**



Fatigue



Headache



**Muscle aches
and pain**



Joint pain



**Fever and
chills**

**Transient (2 days):
Pfizer>AZ
2nd>1st**

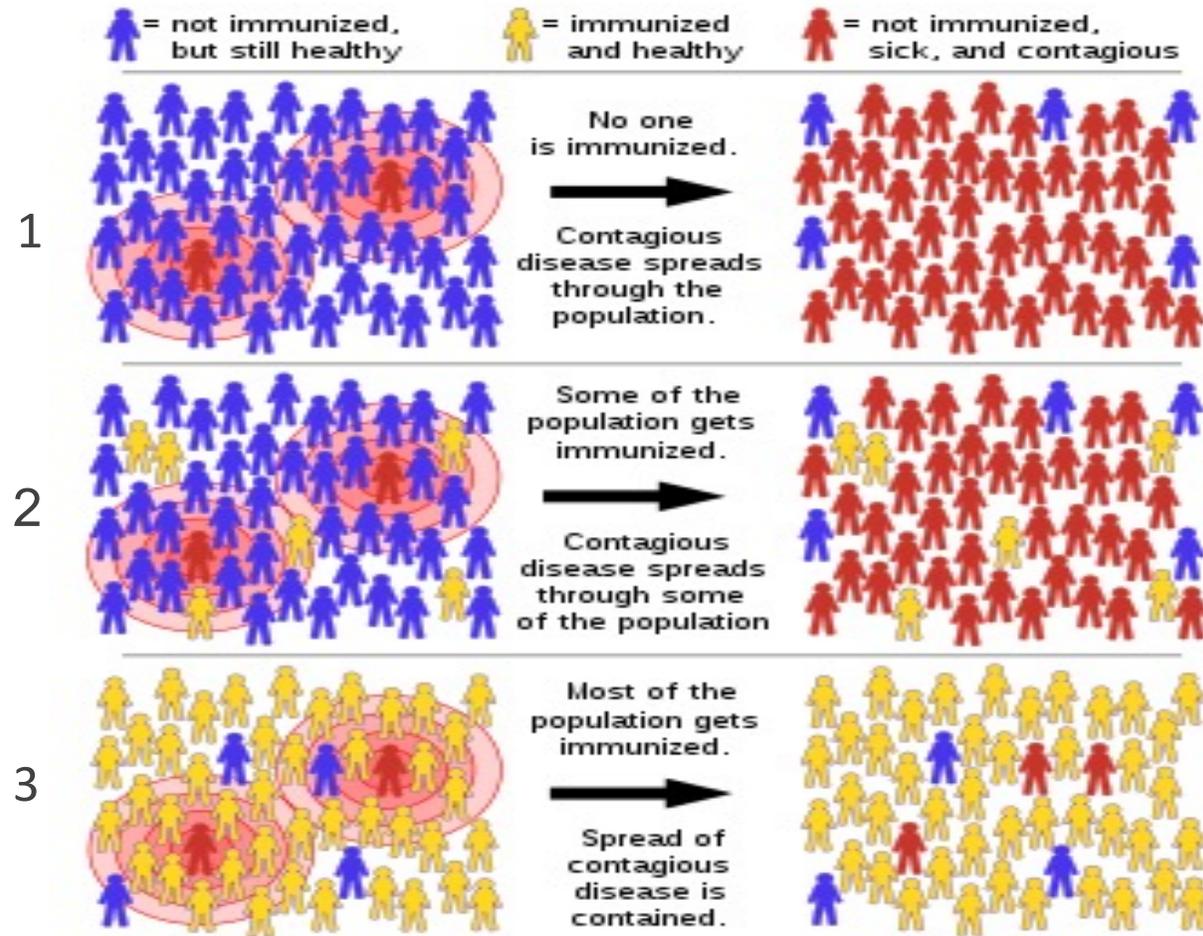
Rare serious side effects

- Anaphylaxis
 - Pfizer 2.7/million; Moderna: 2.3/million
 - vast majority first 30 mins, so observe, EpiPen available
- Thrombosis-Thrombocytopenia syndrome
 - Astra-Zeneca ? 4/million; Johnson & Johnson: ? 1/million
 - cerebral or splanchnic venous thrombosis, thrombocytopenia
 - AZ: 25% mortality
 - pathogenesis; antibody to PF4 + another antigen (?SARS-CoV-2 spike, ?Adenoviral) -> platelet activation
 - Diagnosis: platelet activation
 - Treatment: immunoglobulin, non heparin, non warfarin anticoagulants
 -

Aims of COVID vaccine deployment

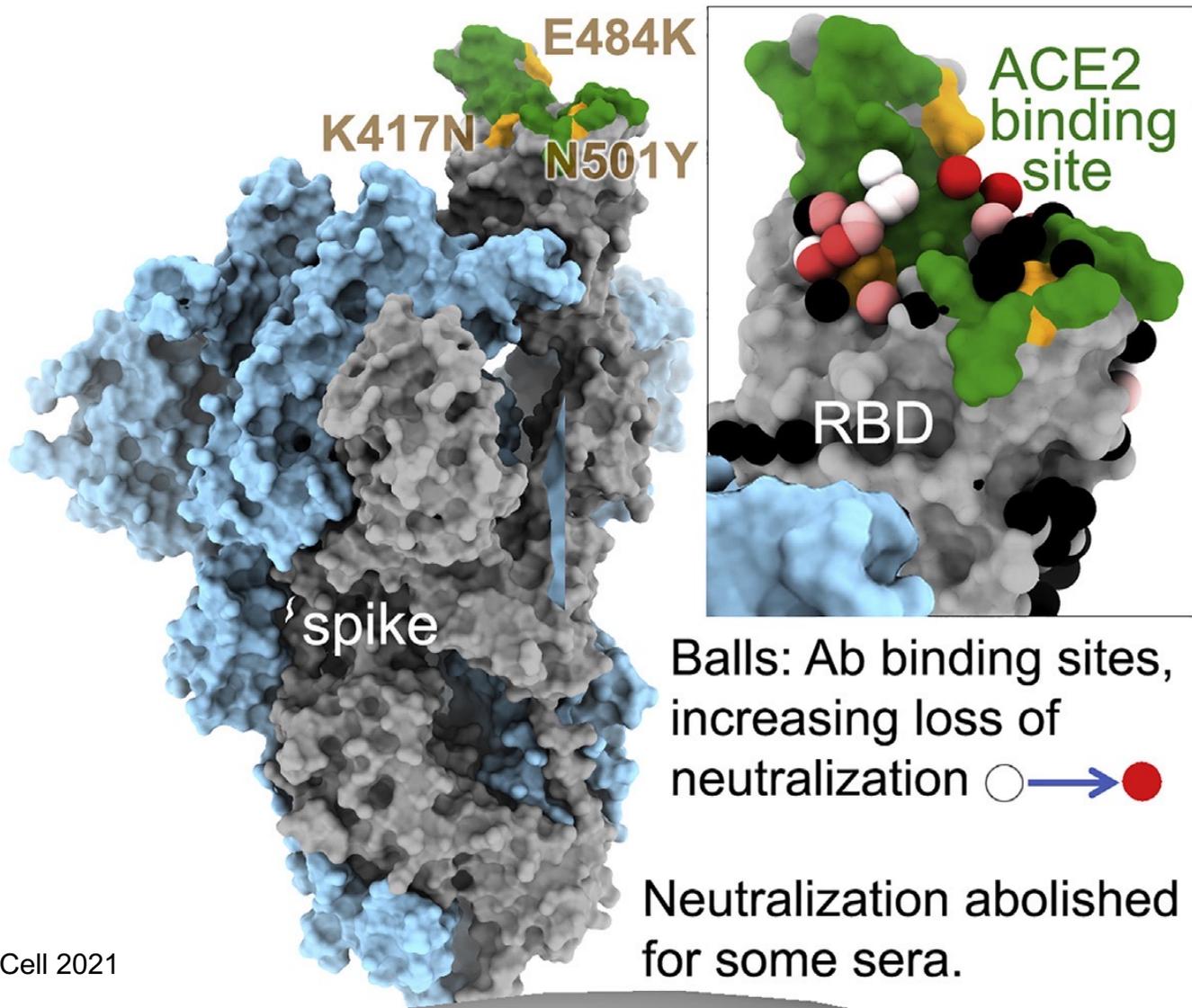
- Prevent death and hospitalization
- Protect healthcare workers
- Prevent spread out of quarantine (depends on efficacy against spread)
- Protect those in aged care facilities
- Prevent spread out of aged care facilities
- Protect the vulnerable in the community:
 - ageing (>70 YOA)
 - immunocompromised (eg transplant patients)
 - indigenous etc.
- Economic including travel

Prevention of spread by vaccines depends on 'herd immunity'



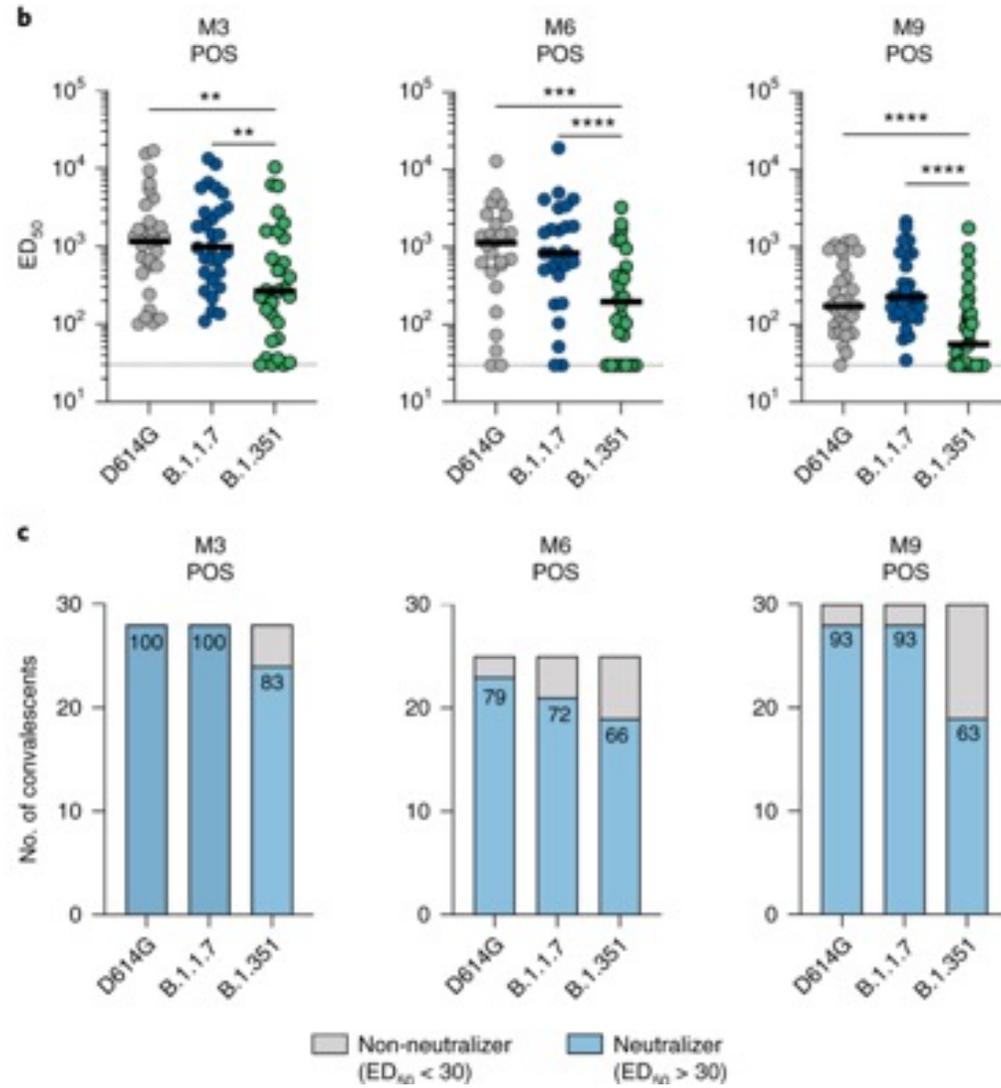
Vaccines for COVID-19: recent developments

- **Effectiveness of vaccines in the field** (after second dose):
 - against hospitalization/symptomatic disease:
 - Pfizer: 85-92% (Scotland/UK/Israel)
 - Astra Zeneca: 94% (28-34 days post first dose, Scotland)
 - in those >70 YOA: 79%
- **Effectiveness against spread:** Pfizer: 85% (7d after second dose)
- **Durability of vaccine effectiveness:** unknown
- **New variants able to evade some vaccines**
 - UK B1.117, South Africa B1.351, Brazil P1, India 1.617



Zhou D et al Cell 2021

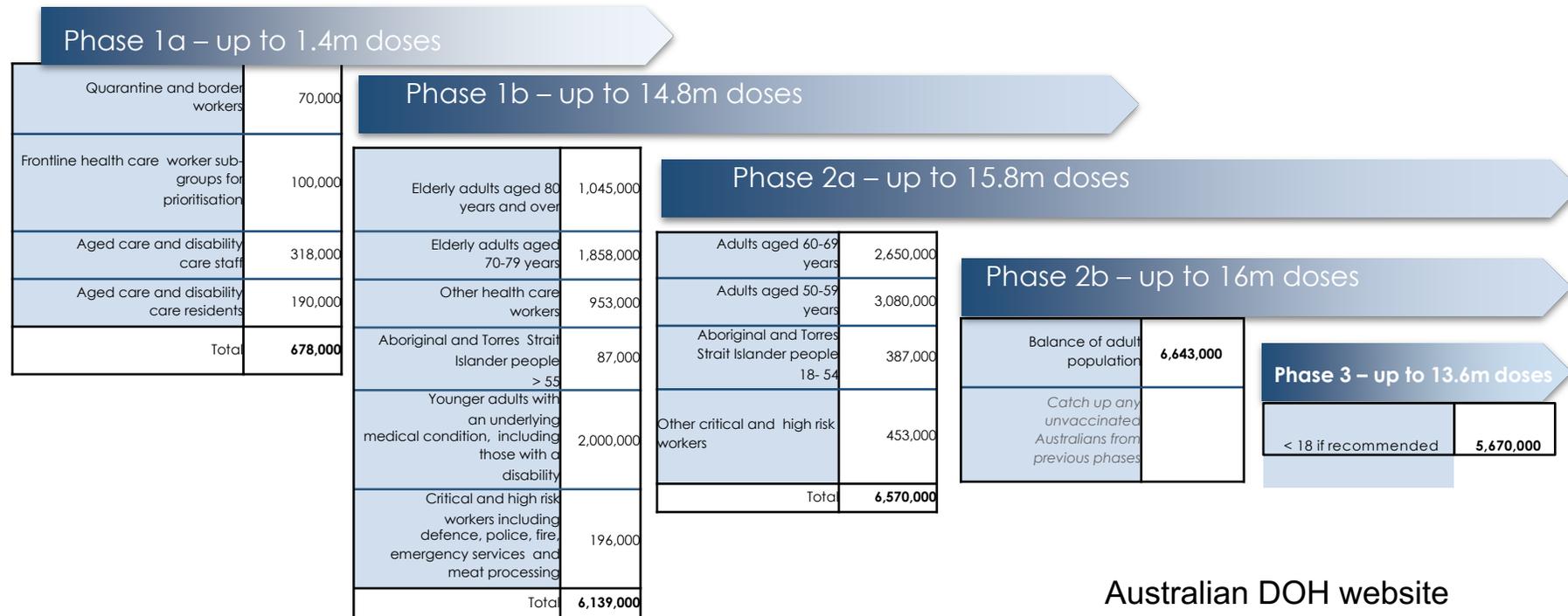
SARS-CoV-2
B.1.351



COVID vaccine efficacy with new variants

- UK B1.117: efficacy of AZ, Pfizer, Moderna unchanged
- B1.351: Novavax 90-> 60%
 - AZ: ?10%
 - Pfizer 0 vs 6!

Australian COVID-19 vaccine roll-out strategy



Australian DOH website

Population numbers are current estimates for each category.

Recent Changes: Phase 2A advanced; AZ for <50 YOA, Pfizer preferred for <50YOA

Problems with current vaccine rollout and preparing for new vaccines

- Supply- international
 - national (need greater diversity of vaccine type production. Including RNA)
- Vaccine refusal (~5%)
- 'vaccine hesitancy' 15-20% (exacerbated by rapid COVID vaccine devt.)
- Communications –needs professional approach to reduce vaccine hesitancy

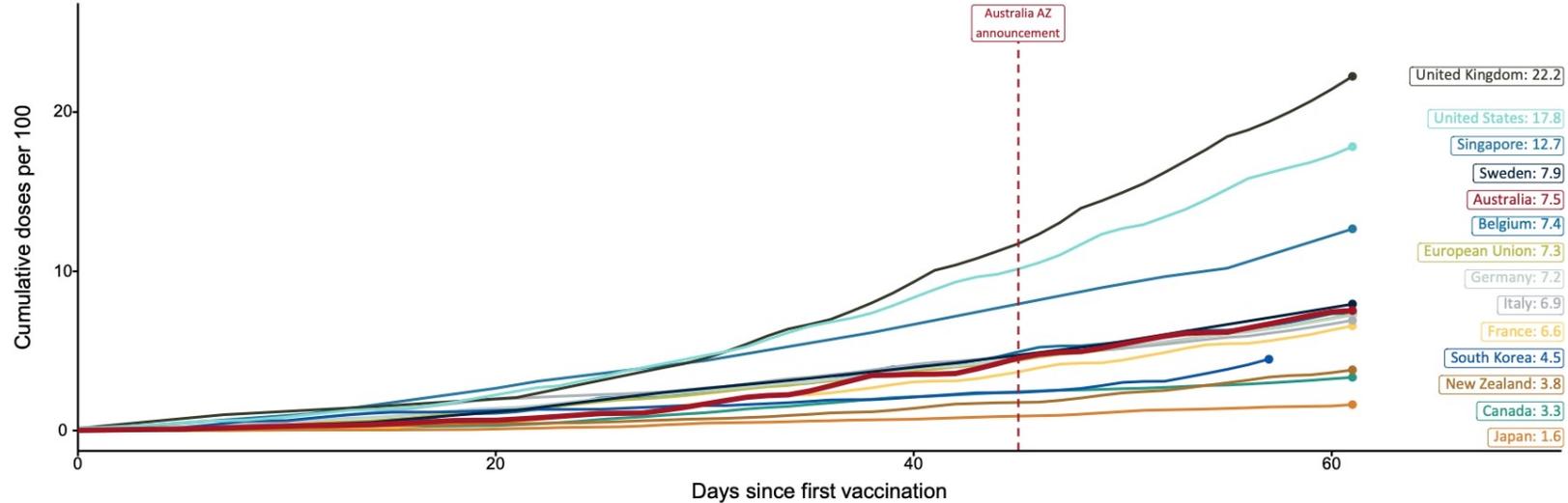
International comparisons at equivalent stages of rollout

Data as at:
24 Apr 2021

Australia's COVID-19
Vaccine Roadmap

Cumulative doses administered (24 Apr): **1,933,892**

The x-axis is truncated at the length of Australia's vaccination program. Some countries started later and some countries do not have daily data points so the closest day to AUS's we have data for is used. Israel excluded as it is beyond scale of the graph



Source: Department of Health (Australia), Our World in Data (international)
Latest data: 24 April

Immunity to SARS-CoV2

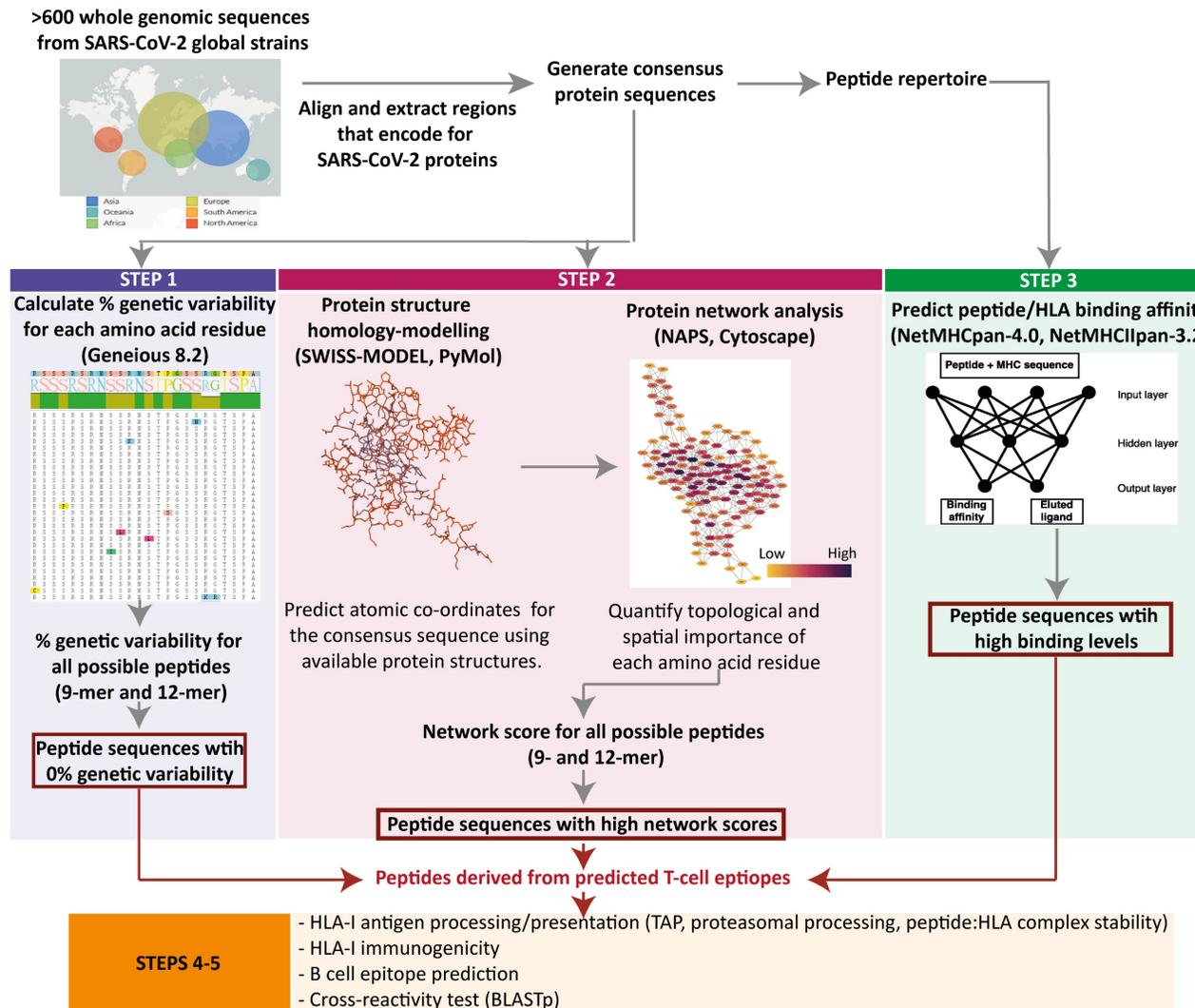
- Neutralizing antibody
 - major importance, need PC3 lab -> PC2 tests
 - exact level required for immunity unknown
- T cells important in
 - duration of immunity
 - protection in the ageing
 - broadening response to new variants?
- Problems: False negative tests (Nab, T cells, with variants)
 - cross reactivity with other coronaviruses (common cold ~40%)

SARS-CoV-2 T cell Immunogenicity studies

NSW, WIMR

- Comparing level and duration of immunogenicity in ageing (>60 YOA) with younger subjects
 - using a highly specific peptide pool which avoids variant strains and seasonal coronaviruses
 - natural COVID-19 over 2 years (NSW MOH)
 - after immunization: COVALIA phase I/II trial of DNA candidate
 - 150 subjects, 18 months
 - NSW VIIM study: Pfizer rollout
 - T and B cell immunogenicity
 - Sydney wide collaborative,
 - over 2 years,
 - effectiveness against new strains

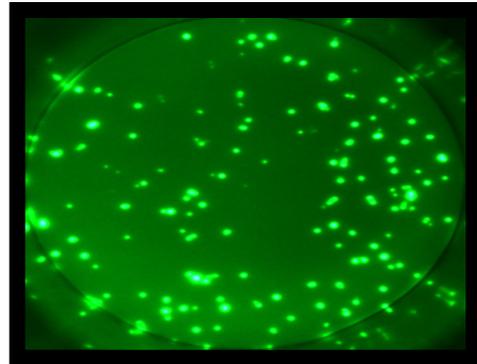
A highly specific SARS-CoV-2 T cell peptide pool for immunogenicity studies and vaccines



Fluorospot T cell responses in PBMCs from convalescent donors

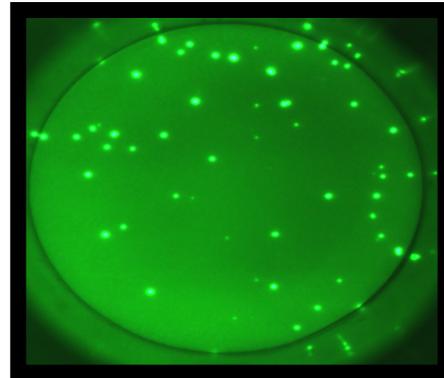
Donor A

>1 month
post-
recovery



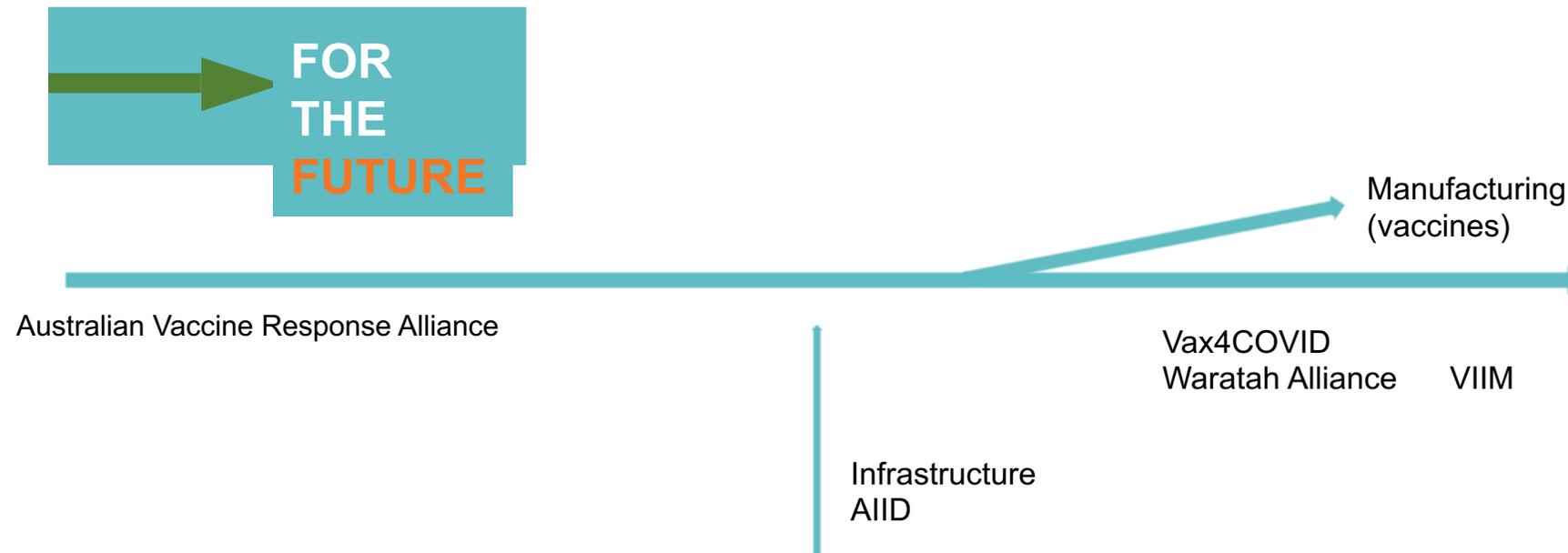
Donor B

>3 months
post-
recovery



Vaccines for COVID-19

Current State/National Networking Initiatives



VIIM = Vaccine, Infection & Immunology Collaborative Research Group of NSW

AIID = Australian Institutes of infectious Diseases

COVID has galvanized action on adult vaccines in Australia

- **For duration of COVID-19 pandemic and for next pandemic**
- Government support for vaccine manufacture
- Enhanced national and state govt research funding
- State and national vaccine trial alliances
- Vaccine development collaborative consortia
- ?expanded vaccine manufacturing centres
- Enhanced and networked vaccine surveillance

- Accelerated vaccine licensure processes

- Enhanced Australian Immunization register
- Enhanced vaccine safety surveillance after licensure

Challenges

- **New strains and quarantine**
 - immunizing the world to reduce new strain variation
 - reduce aerosol transmission in quarantine
 - monitor new strains
 - deploy new vaccines, check immunogenicity
- **Vaccine rollout and hesitancy**
 - investigate rare side effects and if vaccine related, manage
 - maintain public confidence by transparent, accurate and timely communication, listen to vaccine psychology experts
- **The next pandemic**

