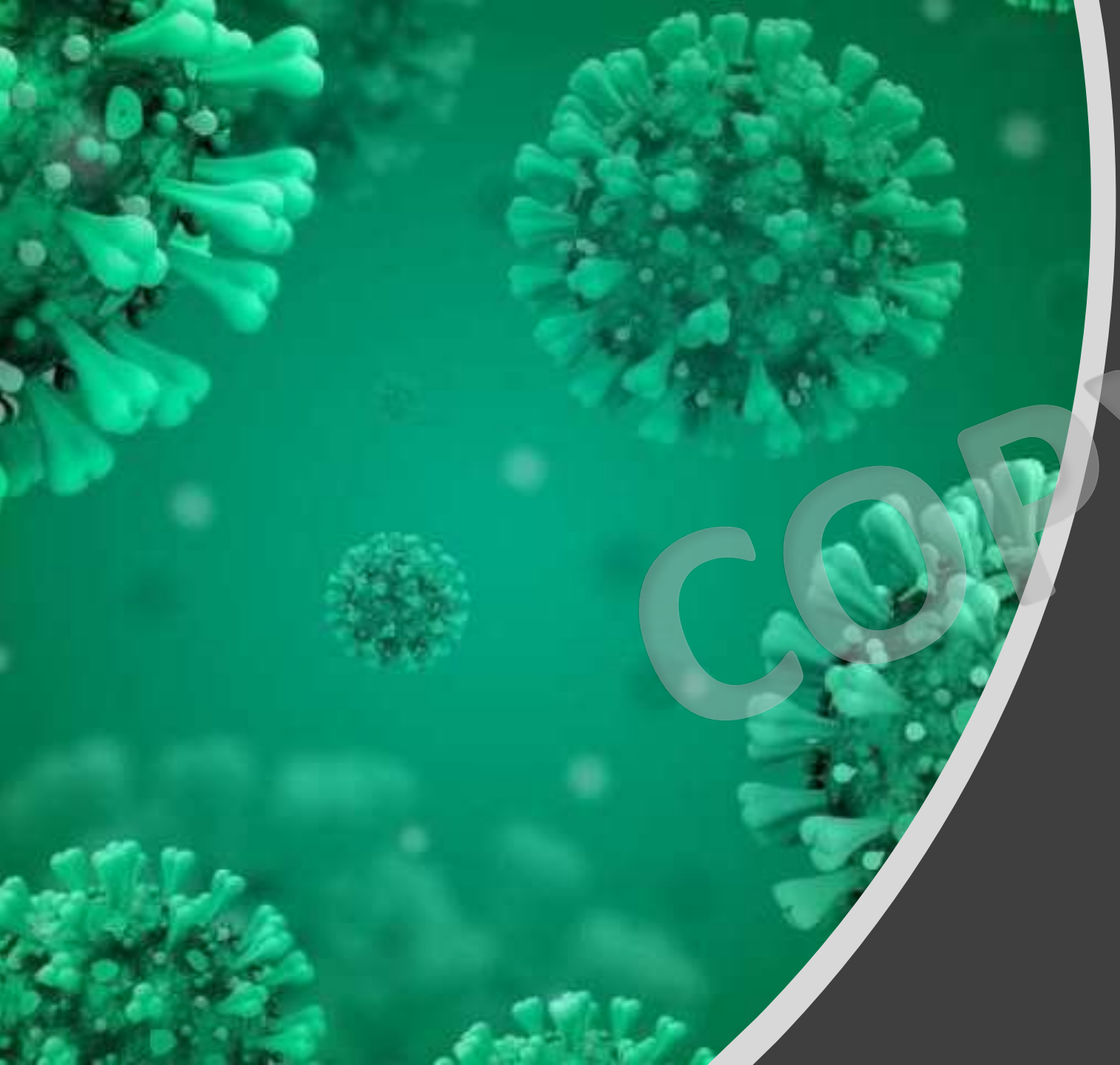


The COVID-19 Vaccine Landscape in 2021

Professor Katie Flanagan

Head of Infectious Diseases, LGH, Tasmania
Director of Tasmanian Vaccine Trial Centre
Clinical Professor, UTAS
Adjunct Professor, RMIT
Adjunct Assoc Prof, Monash University

Declarations

- Member of the Australian Technical Advisory Group on Immunisation (ATAGI)
- Lead of ATAGI COVID-19 Vaccine Utilisation and Prioritisation Working Group
- Previous advisory board member for Seqiris and Sanofi Pasteur
- Note these are my views and not necessarily those of ATAGI

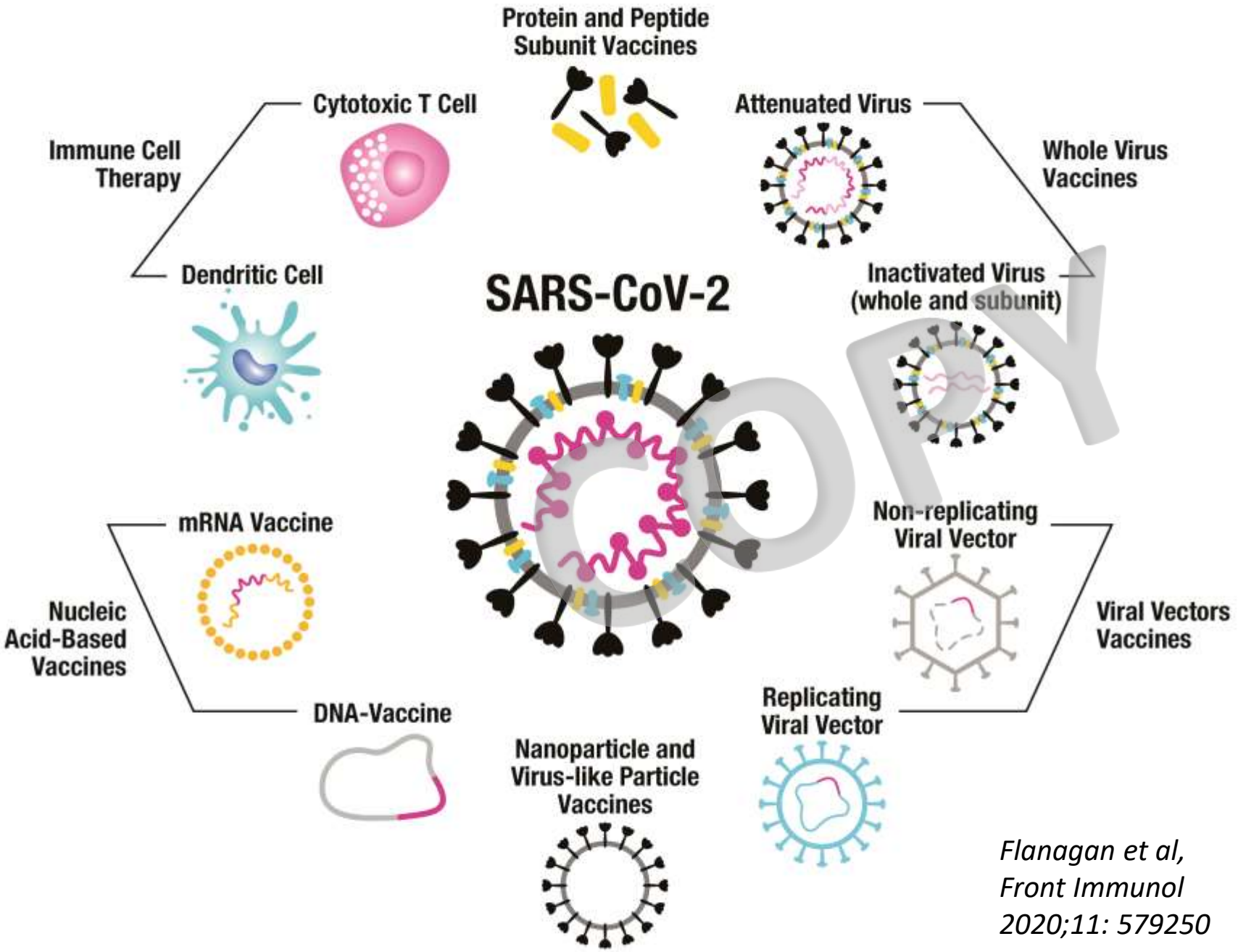
Global Overview

Over 100 million documented cases of COVID-19

Over 2 million deaths

173 vaccine candidates in pre-clinical development

64 in clinical trials



SARS-CoV-2 Vaccine Platforms

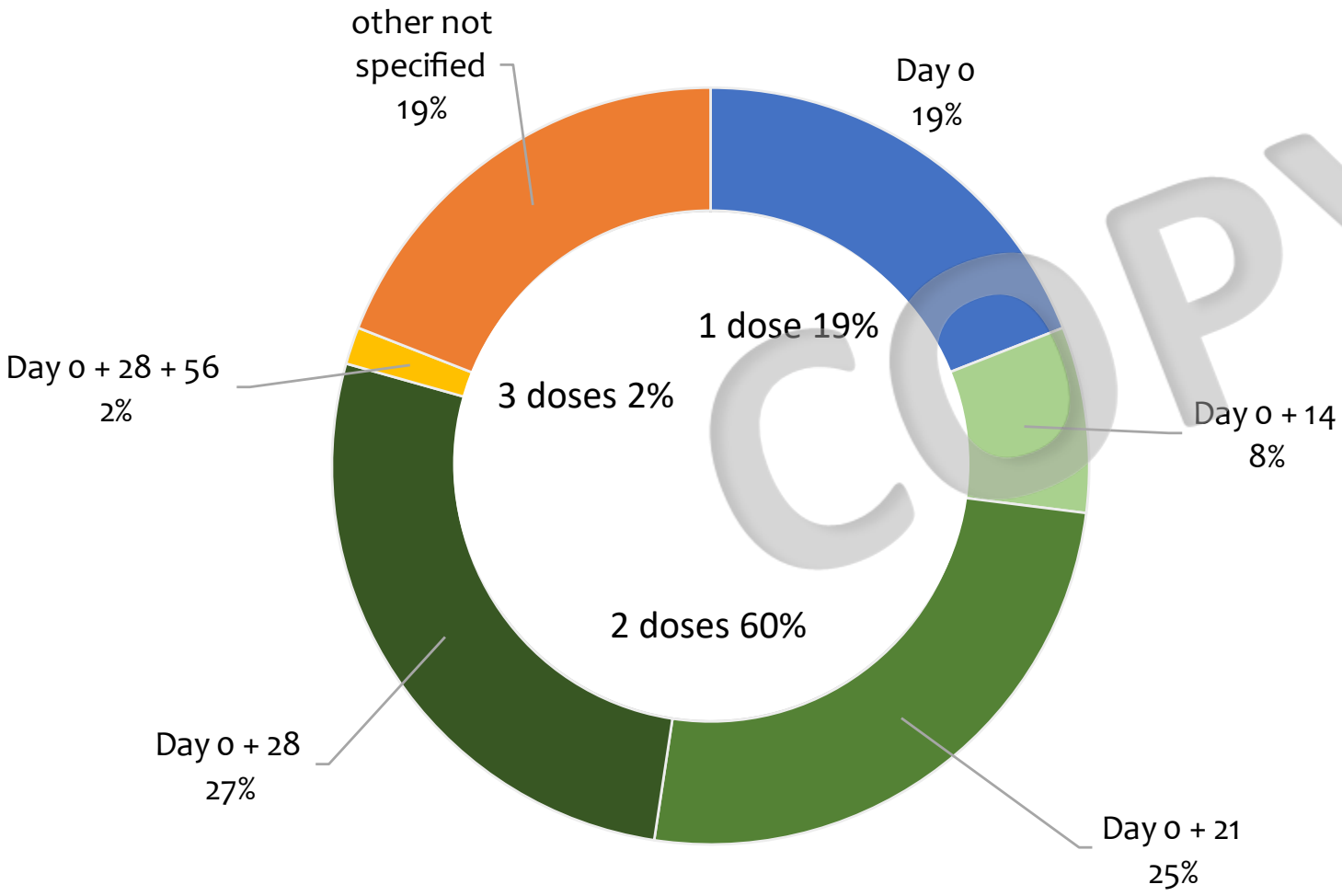
Flanagan et al, Front Immunol 2020;11: 579250

Platforms in Clinical Trials

VACCINE PLATFORM	Number in Pre-Clinical Trials	Number in Clinical Trials
Live attenuated virus	2	1
Inactivated whole virus	12	9
Protein / peptide subunit	60	20
Non-replicating viral vectors (VVnr + APC)	21 (0)	10 (1)
Replicating viral vectors (VVnr + APC)	19 (0)	3 (2)
DNA	16	8
RNA	23	7
Virus like particle (VLP)	16	2
Live attenuated bacterial vector Replicating bacterial vector	2 1	0 0

https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

COVID-19 Vaccines in Clinical Trials



Route	Number	Percent
Injectable	53	84%
Intramuscular	*48*	*76%*
Intradermal	*3*	*5%*
Subcutaneous	*2*	*3%*
Oral	2	3%
No data	8	13%

Twenty one Candidates in Phase 2/3 or Phase 3 Clinical Trials

Platform	N	Details
Inactivated Virus	5	Sinovac; Sinopharm; Bharat Biotech (BBV152); Inst Med Biol/Chinese Acad Sci; Kazakhstan Res Inst (QazCovid-in)
Protein Subunit	5	Novavax NVX-CoV2373 (S+Matrix M); Anhui/Chinese Acad Sci; Clover (SCB2019 S-timer+ASO3 or CpG1018+Alum); Medigen/Dynavax/NIAID (MVC-COV1901 with CpG1018); COVAXX/United Biomed (Multiepitope RBD UB-612)
RNA	3	Pfizer/BioNTech (BNT162) [Comirnaty]; Moderna (mRNA1273); Curevac (CVnCoV)
VVnr	4	AZ/UnivOxford (ChAdOx1/AZD1222) [Covishield], Janssen (Ad26COV2.S), Gameleya (rAd26-S/rAd5-S, Gam-COVID-Vac); CanSino/Beijing Inst Biotech (Ad5)
DNA	3	Zydus Cadila (nCov); Inovio (INO-4800+electroporation); AnGes/Takara/Osaka (AG0301-COVID19)
VLP	1	Medicago (CoVLP)

COVID-19 Vaccines in Clinical Trials in Australia

Platform	Vaccine	Developer / Manufacturer	Details
Protein	COVAX-19	Flinders Uni / Vaxine	Phases 1 and 2 ongoing - Adelaide
Pro	TRIALS ABANDONED DUE TO FALSE POSITIVE HIV RESULTS		ne
Protein	NVX-CoV2373 S-protein + Matrix M	Novavax	Phase 1 published Phases 2 and 3 ongoing including multiple sites in Australia
Protein	S-trimer	Clover	Phase 1 published - Perth. Phase 2/3 commenced.
VLP (with SpyTag 'superglue')	RBD-SARS-CoV-2 HBsAg	SpyBiotech/SII/Accelagen	Phase 1/2 - Melbourne
DNA needle free delivery	COVIGEN	Technovalia/Univ of Sydney	Phase 1a/b - Sydney
DNA oral vaccine	Symvivo	bacTRL-Spike-1	Phase 1 - Brisbane

Interim Phase 3 Trial Results

Candidate	Trial Details	1° Endpoint	Priority Population Data / Notes	Reference
BNT1621b RNA BioNTech/Pfizer	N=43,661 2 doses @ 0 and 4wks	95% efficacy against symptomatic disease from 7d after dose 2 (COVID naïve)	94% efficacy in those >65 yrs and those with prior COVID Consistent protection across age, gender, race, ethnicity 1 severe case in vaccine recipient	NEJM 10 Dec 2020
mRNA-1273 RNA NIH/Moderna	N=30,000 2 doses @ 0 and 4wks	94.1% efficacy against symptomatic disease	No severe disease in vaccinated gp 37% participants from racial / ethnic minorities	NEJM 30 Dec 2020
AZD1222 Chimp adenovirus Astra Zeneca	N=10,000 (Brazil) 2 doses @ 0 and 4wks N=12,390 (UK) ½ dose then full 4wks	70.4% combined efficacy Brazil 64% efficacy from 14d after dose 2 UK 90% efficacy from 14d after dose 2	No hospitalisation/severe disease in vaccine recipients Small numbers in >56y gp and those with co-morbidities so cannot assess efficacy Greater efficacy with greater dosing interval	The Lancet 08 Dec 2020
Janssen Ad26.COV2.S	N=43,783	66% overall against mod/severe 28d after vaccination 72% in US, 66% in Latin Am, 57% in S Africa	Single shot vaccine, good efficacy across age groups 85% efficacy against severe disease 100% efficacy against hospitalisation and death	Not published
Gamaleya Sputnik V Ad26 / Ad5	N=21,977 >18yrs	91.6% effective from 21 days after dose 1	>90% effective in all age strata, 11% >60yrs, 98.5% white	The Lancet 02 Feb 2021
Novavax S+Matrix M NVX-CoV2373	N=15,000 (UK) N=4,400 (S Africa)	UK 89.3% efficacy against PCR+ symptomatic disease in 18-84y olds (COVID naïve); S Africa 60.1% efficacy in HIV- and 49.4% in HIV+	No severe cases in UK vaccinated, 27% >65yrs, poorer efficacy against variant strains and those with HIV infection, $^{1}/_{3}^{rd}$ had prior COVID-19	Not published

Warning

- The released phase 3 results are interim
- Duration of protection and rate of immunity waning unknown
- Priority populations under-represented and some not at all (pregnant women, severely immunosuppressed)
- No data about effects on disease transmission
- Real world efficacy may not be the same as observed in a clinical trial
- Rare side effects may be missed

Australian COVID Vaccine Program

	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

SITAG = Science and Industry Technical Advisory Gp, ACV = Advisory Committee on Vaccines, NCIRS = Natl Centre for Imm Research & Surveillance

Australian Government Commitment

Population ~25 million

Platform	Vaccine	Developer Company	Pre-purchase Doses	Approval Status	Notes
Chimp adeno	AZD1222	Oxford Uni / Astra Zeneca	53.8 million	PD with TGA	Local manufacturing ongoing at CSL 6m in fridge
mRNA	BNT162b1	BioNTech/ Pfizer	10 million	PA with TGA	Import only -70℃ storage / dry ice for shipping, 5d in fridge
Protein	NVX-CoV2373	Novavax	51 million	PD with TGA	Import only Fridge storage
Human adeno	Ad26.COV2.S	Janssen	In negotiation	PD with TGA	Can be single dose Fridge storage
Pr					
Government has also invested in Gavi's COVAX Facility allowing them to purchase COVID-19 vaccines as they become available for up to 50% of the Australian population Also supports vaccine access for low-income countries					

TRIALS ABANDONED DUE TO FALSE POSITIVE HIV RESULTS

PD = Provisional determination to be eligible to apply for provisional registration
PA = Provisional approval – valid for 2 years

Coalition for Epidemic Preparedness Innovations (CEPI) and COVAX

Founding members: BMGF, World Economic Forum, Wellcome Trust, India Dept of Biotech, Gov of Norway

CEPI

- Launched 2017 to deal with worldwide threat of epidemic outbreaks including Disease X
- Not-for-profit independent legal organisation hosted by Norwegian Inst for Public Health
- Consensus that new and sustainable partnership models needed for product development
- Scientific advisory committee of independent experts
- Working with global health authorities and vaccine developers to support COVID-19 vaccine development
- Advancing 9 frontrunner candidate vaccines across the platforms
- Works from discovery to development/licensing/manufacturing to delivery/stockpiling
- Global access negotiated upfront to ensure equitability

COVAX Facility

- Co-led by Gavi, CEPI and WHO as part of the Access to COVID-19 Tools Accelerator
- Global risk-sharing for procurement and equitable distribution of COVID-19 vaccines
- Richer countries pay and LMICs don't
- All participating countries get equal access to the vaccines once developed
- Aiming for 2 billion doses by end of 2021 (7.7 billion people in world)
- The only way many poorer countries would be able to afford COVID-19 vaccines

Worldwide Rollout

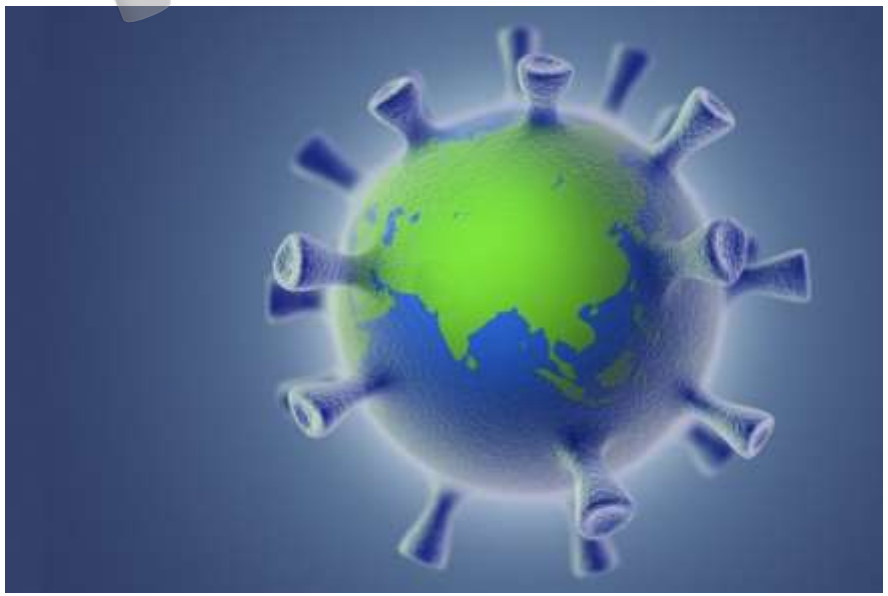
- 7 vaccines now available for public use:
  - 2 RNA – Pfizer, Moderna
  - 2 viral vector – Astra Zeneca/Oxford, Gameleya Sputnik V
  - 3 inactivated virus – Sinovac, CanSino, Sinopharm
- China and Russia commenced their programs in the absence of phase 3 efficacy data (Sinopharm 79% efficacy, Sinovac 50% efficacy)
- More than 104 million doses now given across 66 countries
- >4 million doses currently being delivered daily

https://www.Bloomberg.com/graphics/covid-vaccine-tracker-global-distribution

Country	Candidates (date approved)	Program Start	Doses Given	Doses / 100 people
China	CanSino (29/06/20) Sinopharm (28/08/20), Sinovac (28/08/20)	29/06/20 28/08/20	24,000,000	1.71
UK	Pfizer/BioNTech (MHRA 2/12/20) AstraZeneca (MHRA 30/12/20)	8/12/20 Pfizer 4/1/20 AZ	10,143,511	15.19
USA	Pfizer/BioNTech (FDA EU 11/12/20) Moderna (FDA EU 18/12/20)	14/12/20 Pfizer 21/12/20 Moderna	33,713,182	10.26
Israel	Pfizer/BioNTech (20/12/20) Moderna (5/1/20)	19/12/20	5,051,363	55.8
Canada	Pfizer/BioNTech (9/12/20) Moderna (23/12/20)	14/12/20	984,195	2.62
France	Pfizer/BioNTech (EMA 21/12/20)	27/12/20	1,609,272	2.48
Germany	Pfizer/BioNTech (EMA 21/12/20)	27/12/20	2,586,997	3.11

New Variants and Vaccine Immune Escape

- **Pfizer/BioNTech BNT1621b** (mRNA)
  - Neutralises the UK COVID-19 variant B117 *in vitro*
- **Novavax NVX-CoV2373** (Protein/Matrix M)
  - Phase 3 trials showed 86% efficacy against new UK variant 501Y.V1 (50% of cases) (cf 96% efficacy against wild-type strain)
  - 60.1% efficacy against S African variant 501Y.V2 if HIV- and 49.4% if combine HIV- and HIV+ groups
  - Currently making vaccines for variants, will commence clinical trials Q2 this year
- **Janssen Ad26.COV2.S** (viral vector)
  - Protects against multiple variants including S African B13551 lineage (501Y.V2)



Next-Generation Vaccines

- >200 vaccines in the pipeline including
  - oral and intranasal vaccines
  - novel delivery systems e.g. electroporation device
  - Vaccines based on COVID-19 proteins other than spike which may be less susceptible to mutation e.g. nucleoprotein
- First generation vaccines will not be perfect
- Multiple companies are already developing their next-generation vaccines
- New vaccines will have to cater for emerging mutant strains
- Novel immune potentiators and delivery technologies being investigated
- Planned trials to combine vaccines in a prime-boost strategy e.g. AZD1555 / Sputnik V; RNA prime/Viral vector boost
- Moderna investigating developing a COVID-19/influenza combined vaccine

Summary

- 7 vaccines deployed worldwide and 4 million doses being administered daily
- Provisional approvals based on interim phase 3 safety and efficacy analyses
- Many using new platforms never licensed for human vaccintion
- Australian Government have procured several vaccines using different platforms but only Pfizer vaccine currently licensed by TGA
- Plans to start vaccinating in late Feb 2021 in a Federally coordinated plan
- Many new vaccines on the horizon including oral, inhaled options
- First-generation vaccines will not be perfect and future vaccines will need to protect against emerging COVID variant strains