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COVID-19 Vaccination and Boosters

The ALUMNI REFRESHER VACCINOLOGY COURSE (ARVAC) 2023

6-8 June 2023; Morning session

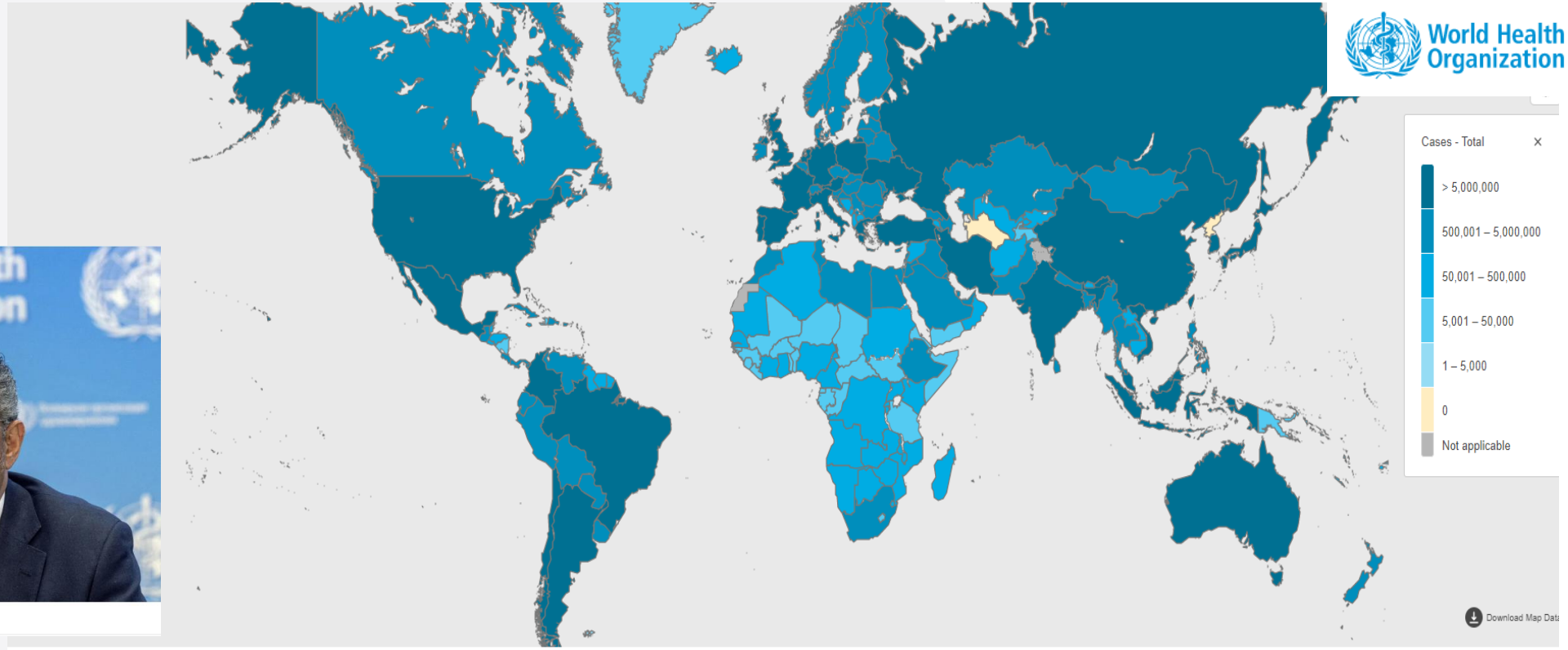
13-15 June 2023; Afternoon session

Dr. Melanie Saville, Executive Director – *Vaccine Research & Development, CEPI*

7 June & 14 June 2023

Facts and figures about the COVID 19 pandemic and vaccination

The World Health Organization declares an end to the Covid-19 global health emergency.



5th May 2023 COVID-19 public health emergency of international concern declared over

Globally, as of **4:16pm CEST, 3 May 2023**, there have been **765,222,932 confirmed cases** of COVID-19, including **6,921,614 deaths**, reported to WHO. As of **3 May 2023**, a total of **13,347,114,071 vaccine doses** have been administered.

https://covid19.who.int/

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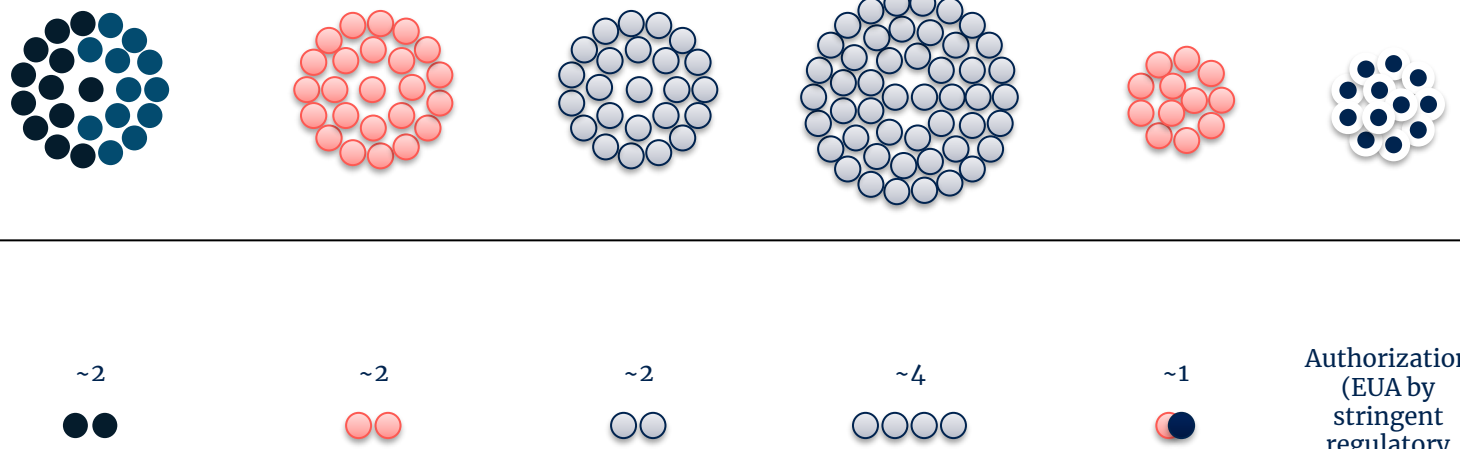
Agenda

- Speed of development of SARS CoV-2 vaccines
- Vaccine development to deployment
- Efficacy of vaccines over time
- Variants and variant vaccine approaches
- Mucosal delivery to impact transmission
- SARS CoV2 vaccine recommendations
- Conclusions

COVID-19 Vaccines were developed and deployed at record speed and scale

Vaccine development then and now, months

	Preclinical, including toxicity, technology development	Phase I: Safety and immunology	Phase II: Proof-of-concept study	Phase III: Large-scale safety and efficacy trials	Filing	Registration	
Sample baseline scenario[1], (after multiple years of research)	~12-24	~12-24	~24	~36-48	~12	~12	**~10 years**
Sample accelerated timeline[2], (based on previous SARS/MERS research) *Development was simultaneous rather than sequential. Clinical phases were continued after subsequent steps were initiated*	~2	~2	~2	~4	~1	Authorization (EUA by stringent regulatory authority)	**326 days**



1. Timelines can vary widely based on disease and trial designs
2. Patient safety was paramount despite the condensed timeline

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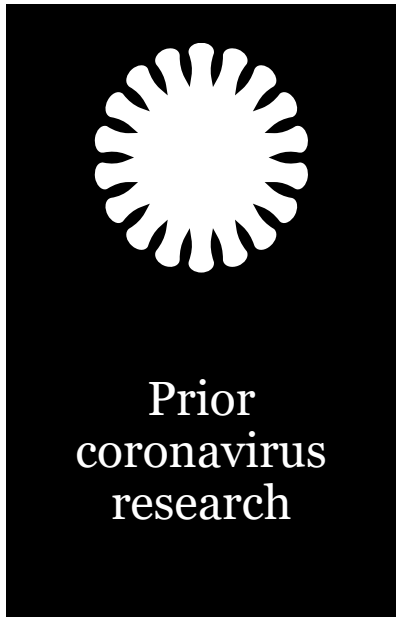
Prior research was an important factor to be able to move so fast



We were able to respond quickly to COVID-19 due to:

1. Prior research and development in two closely related coronaviruses, SARS and MERS

2. Decades of development of **the mRNA platform**, allowing for fast, adaptable and highly scalable vaccine development —a step change from traditional biological manufacturing.

11 SARS-CoV-2 vaccines obtained WHO EUL

	RNA	Viral vector	Inactivated*	Protein-based
Monovalent (Wuhan strain)	Pfizer BIONTECH moderna	AstraZeneca OXFORD janssen Infectious Diseases & Vaccines SERUM INSTITUTE OF INDIA PVT. LTD Cyrus Poonawalla Group 康希诺生物 CanSinoBIO	Sinopharm / BIBP sinovac BHARAT BIOTECH	NOVAVAX SERUM INSTITUTE OF INDIA PVT. LTD Cyrus Poonawalla Group
Bivalent booster (Original/Omicron BA.1, BA.4-5)**	Pfizer BIONTECH			

Source:https://extranet.who.int/pqweb/sites/default/files/documents/Status_COVID_VAX_12January2023.pdf

**Supply of Bharat Vaccine suspended.*

***Variant-containing vaccines (Bivalent Pfizer Vaccine) have not yet received regulatory approval as primary series, only for boosters. WHO SAGE, though, issued a permissive statement on primary use on an off-label basis.*

J&J and CanSino vaccines are administered as single-dose primary series.

Many WHO EUL'ed vaccines were distributed through COVAX, a CEPI co-founded end-to-end initiative for global equitable access to COVID-19 vaccines

11 Vaccines

CEPI-led R&D support enabled access to a portfolio of **11** vaccines/candidates across **4** technology platforms

1.8b doses

COVAX has shipped over **1.9b** vaccine doses, out of which **1.6B** to AMC countries (92 LMICs)

39 Days

COVAX made it possible for the first vaccine deliveries in LMICs to take place within **39** days from introduction in the first few high-income countries

COVAX

ONE WORLD PROTECTED

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Gavi The Vaccine Alliance

unicef

World Health Organization

>100 countries

COVAX assessed and supported the roll-out planning process in **>100** countries with the development of National Deployment and Vaccination Plans (NDVP)

Global allocation

The fair and equitable allocation mechanism was established across partners, ready in time to allocate doses globally

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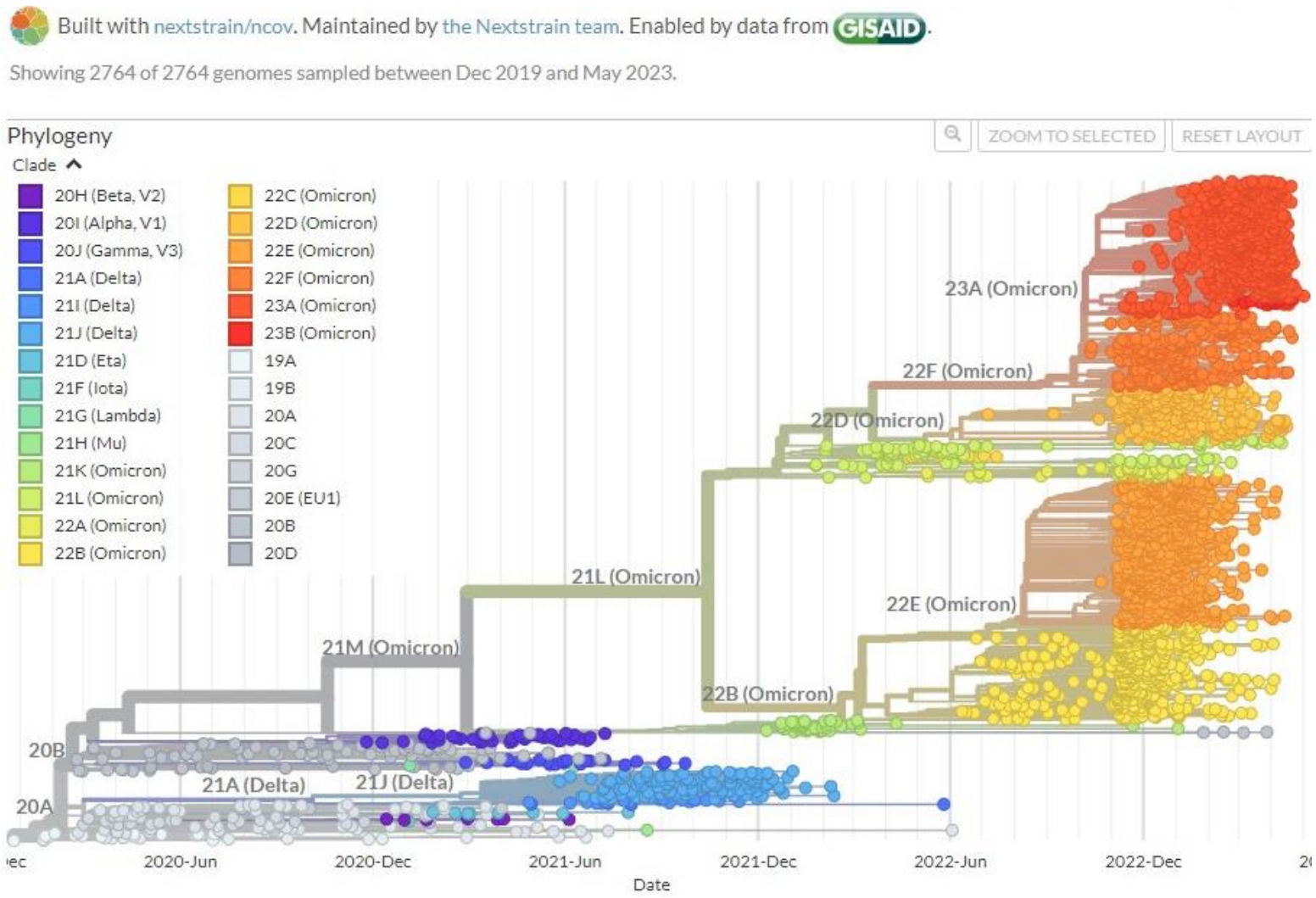
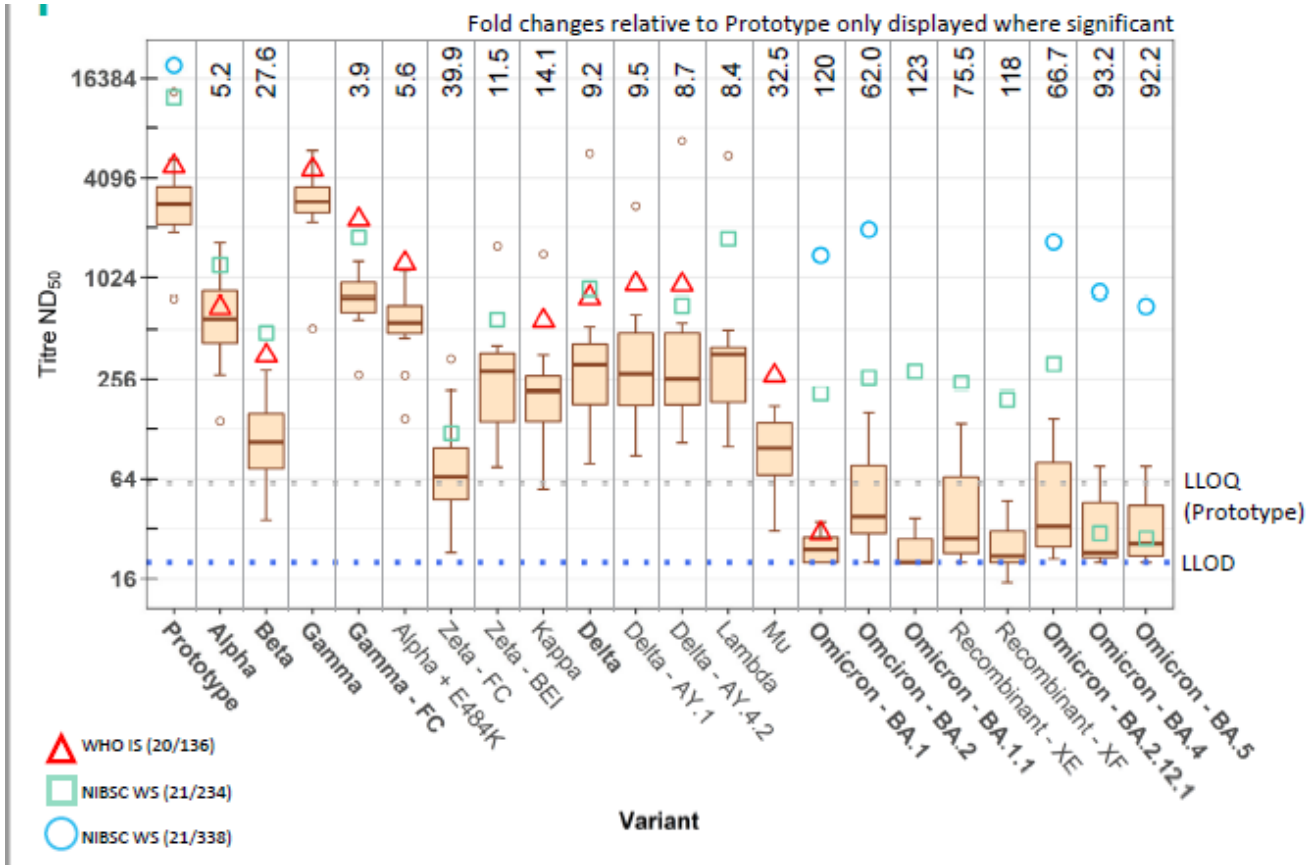
Evolution of variants over time

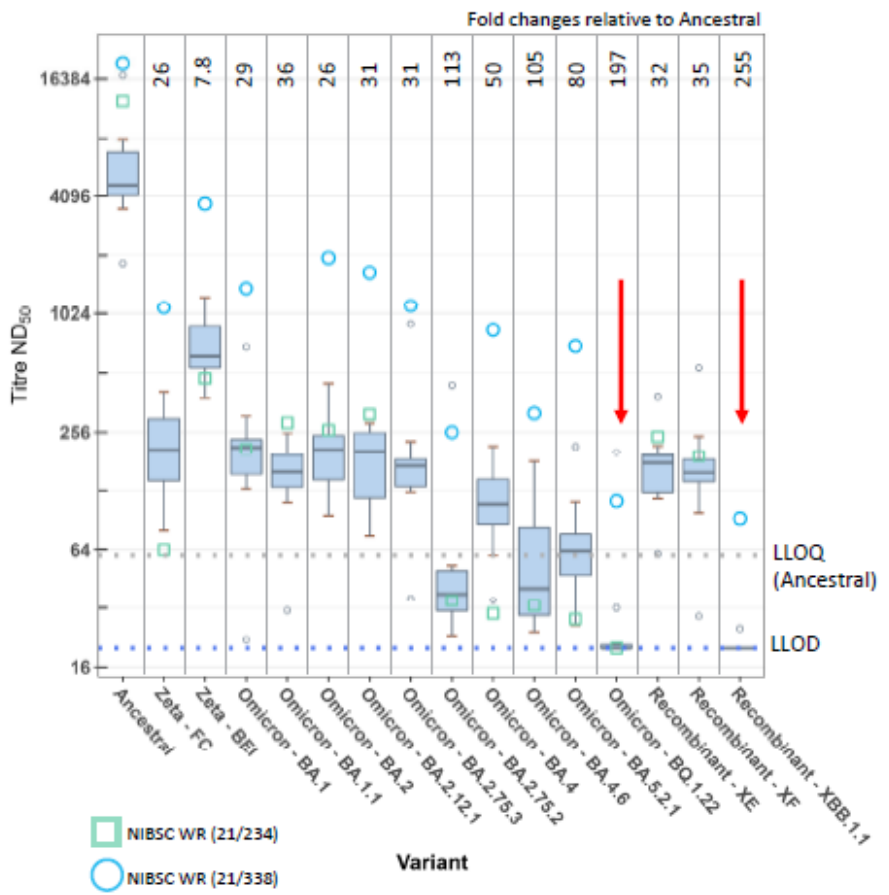


Agility Program: Impact of SARS-CoV-2 variants on *in vitro* neutralization

Convalescent panel (pre-variant)



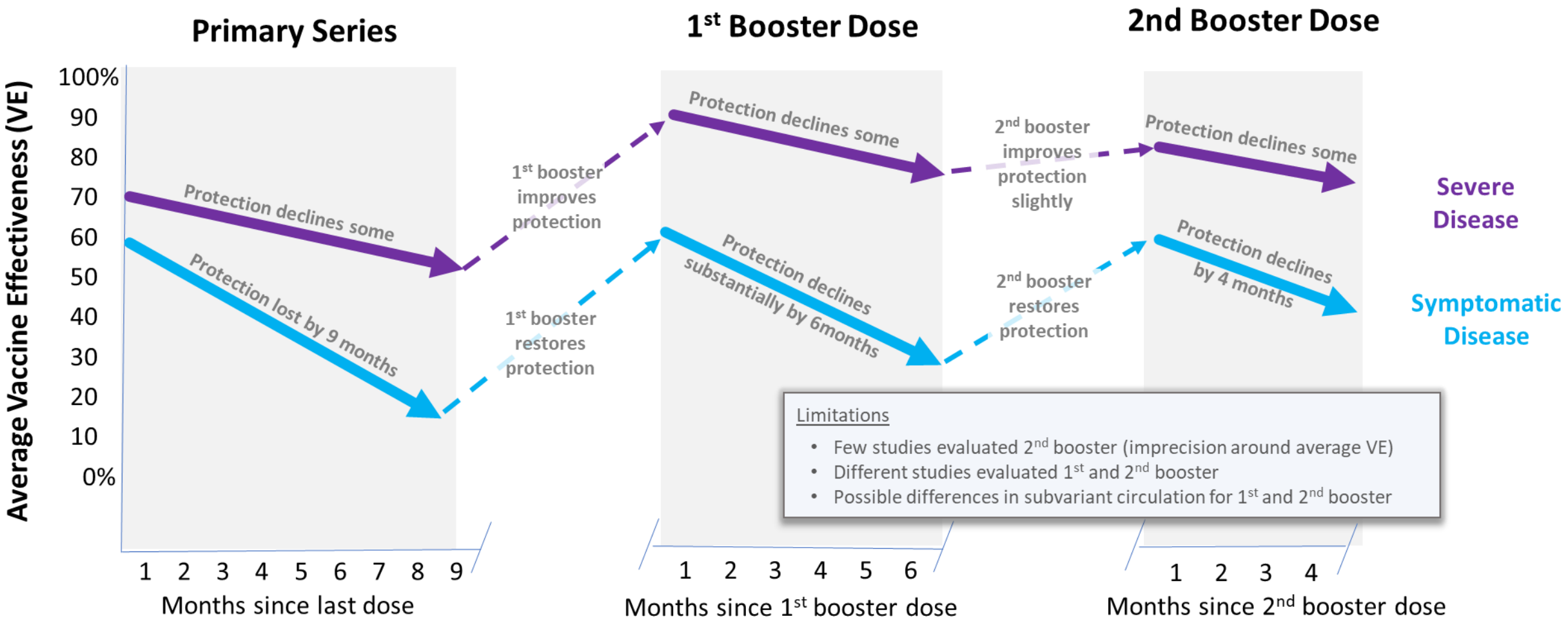
Vaccine Panel (3 vaccinations)



https://epi.tghn.org/covax-overview/enabling-sciences/agility_epi/#ref1

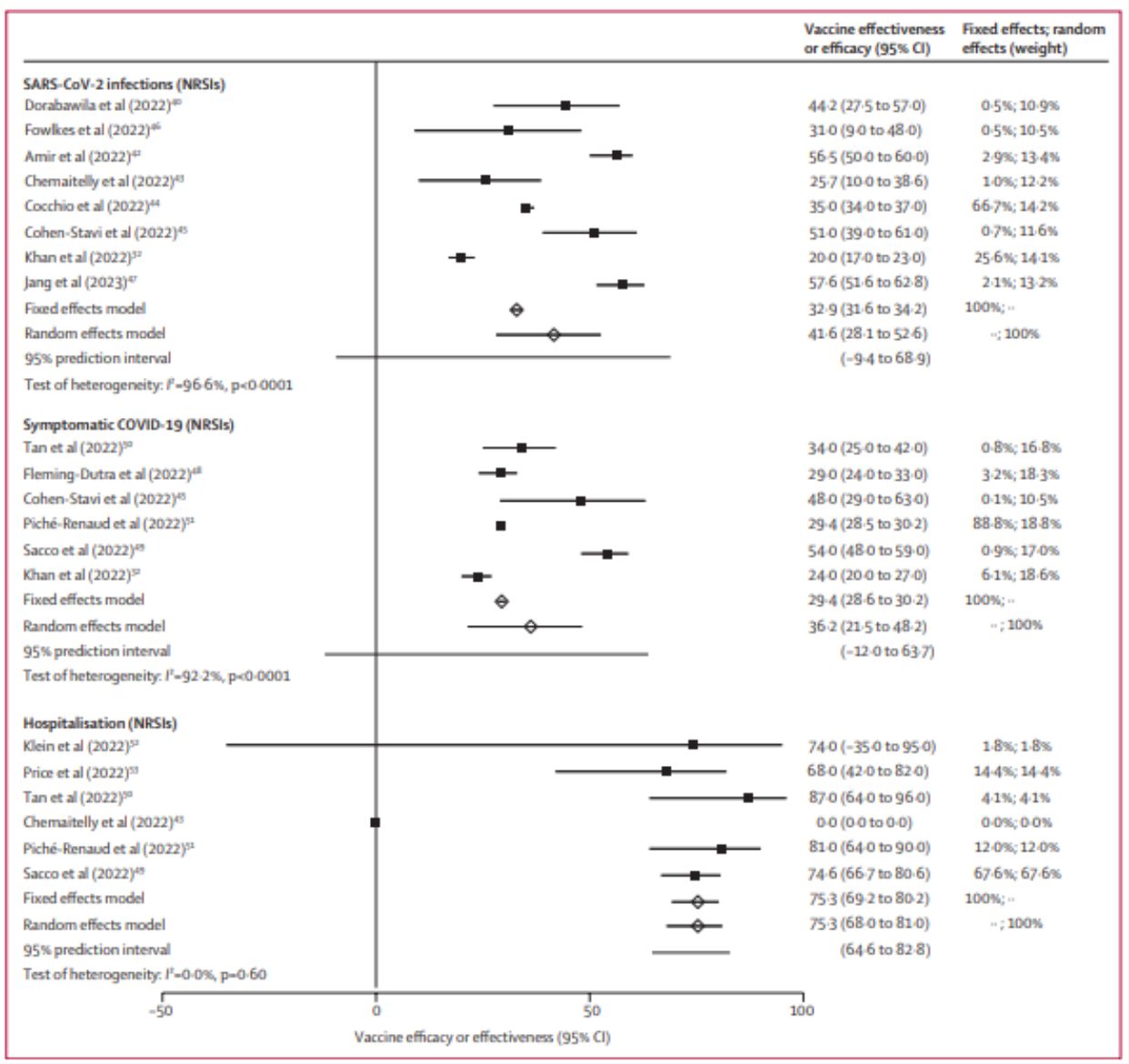
Waning of vaccine effectiveness and emergence of immune-evading variants posed challenges to achieving herd immunity, despite increasing global coverage

Summary of COVID-19 VE against Omicron over time (ancestral strain vaccines)



[10] From meta-regression by JHU/IVAC, Methods in Feikin D, et al, Lancet 2022, doi: 10.1016/S0140-6736(22)00152-0

mRNA vaccine effectiveness against Omicron in Children 5-11ys (systematic review)



- Modest protection against infection and symptomatic disease
- Protection against hospitalization
- Frequent mainly mild reactogenicity

Piechotta et al 18th April 2023 online https://www.thelancet.com/action/showPdf?pii=S2352-4642%2823%2900078-0

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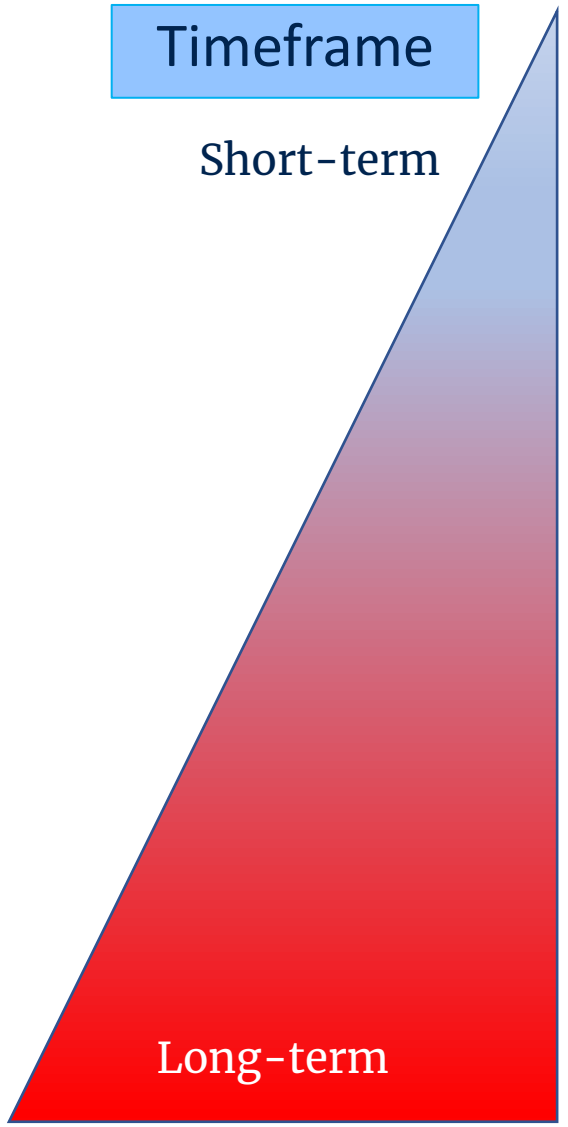
Approach to broad protection

Optimal use of current vaccines
Primary regimen + booster
Mix & match

Variants of current vaccines
Strain adaptation
Bivalent

SARS-CoV-2 "variant-proof" vaccines
Broadly protective ACE-2 sarbecovirus
Breadth of coverage: Multivalent; mosaic; chimera; conserved epitopes
Breadth of immune response: Effector Abs, T cells, memory cells, mucosal

Broadly protective coronavirus vaccines
Broadly protective sarbecovirus
Broadly protective betacoronavirus
Pan-coronavirus



Omicron triggered new wave of variant specific vaccine development in addition to broadly protective vaccine development

Late stage Ph2/3 or Ph3

- Pfizer BA1 Omicron
- Moderna BA1 Omicron
- Novavax BA1 Omicron
- Pfizer Beta
- Moderna Beta
- Moderna Delta, Beta
- Moderna Delta
- Valneva
- Sinovac Omicron
- Sinopharm Omicron v1
- Sinopharm Omicron v2
- Abogen BA4/5 Omicron
- Sanofi / GSK Beta + Wuhan
- AstraZeneca Beta
- HIPRA Alpha + Beta
- Sinocelltech Alpha + Beta

Registration

- Moderna BA1 Omicron + Wuhan
- Moderna BA4/5 Omicron + Wuhan
- Sinopharm Wuhan, Beta, Kappa
- Pfizer BA4/5 Omicron + Wuhan
- Sanofi / GSK Beta

* Based on publicly available information from vaccine candidates based on variants

TAG-CO-VAC monitoring the uncertainties of further viral evolution and impact of boosters on vaccine-induced protection

Vaccine booster	Severe disease	Symptomatic disease	Breadth	Neutralizing Ab
Index vaccines	High protection	Decline over time	Less breadth, X reactivity	Low neuts
BA1 bivalent	High protection	Modest increase, decline over time	Increased breadth, X reactivity	Lower neuts against BQ.1/XBB.1
BA4/5 bivalent	High protection	Modest increase, decline over time	Increased breadth, X reactivity	Higher neuts against BQ.1/XBB.1

Potential role for imprinting?
Future boosters – bivalent/monovalent? Frequency?

Source: https://www.who.int/news/item/14-04-2023-report-of-the-meeting-of-the-who-technical-advisory-group-on-covid-19-vaccine-composition-(tag-co-vac)-held-on-16-17-march-2023

Further virus evolution is likely; therefore, world needs to monitor the evolution of SARS-CoV-2 and develop more broadly protective Vx approaches

Virus continues to evolve

Severity reduces over time

Spikes in transmission possible

Periodic boosting for high-risk groups likely

Season pattern of peaks in temperate zones may emerge

The current trajectory of the pandemic indicates that **virus will continue to evolve** but **cause less severe disease** with possible surges in infections that will **require periodic booster doses** of the vaccine to protect the highest priority group.

Assuming that status quo does not worsen (no new Variant of Concern identified, relatively stable/declining numbers on key metrics, health systems broadly coping, vaccines remain effective)

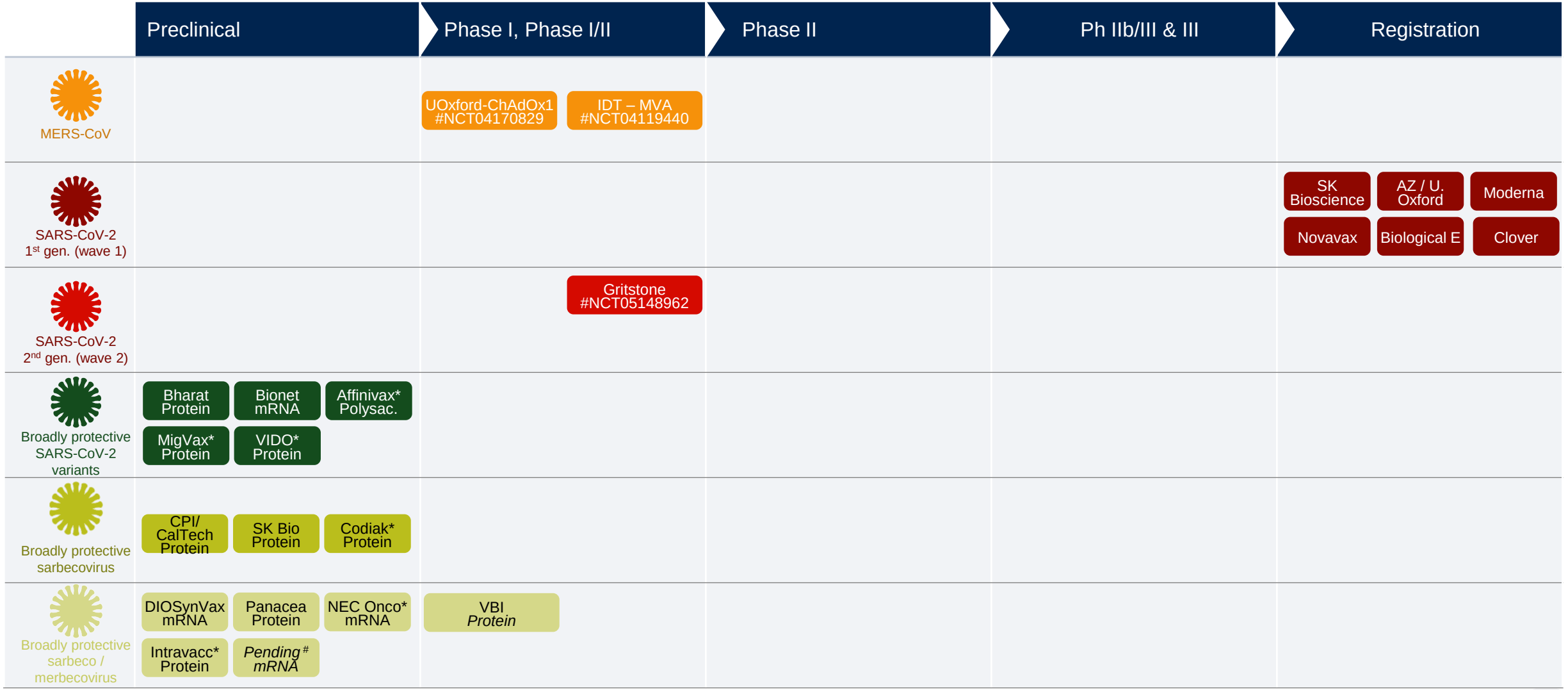
https://cdn.who.int/media/docs/default-source/immunization/sage/2023/march-2023/sage_march_2023_meeting_highlights.pdf?sfvrsn=a8e5be9_4

Portfolio composition | Active CEPI-funded coronavirus R&D pipeline overview

February 2023

As of Jan 2023, the COVID-19 (SARS-CoV-2) vaccine landscape constituted more than 570 vaccine candidates, with more than 140 vaccine candidates targeting variants. Of the 44 vaccines that have reached registration, five are variant-adapted vaccines. The MERS vaccine development landscape constituted 39 candidates predominantly in preclinical phase, where CEPI is funding front runner projects.

Below shows the CEPI-funded coronavirus Active R&D pipeline including MERS, COVID-19 (SARS-CoV-2) and broadly protective candidates.



*Seed funded projects # Pending signature

SARS-CoV-2 Mucosal Vaccine Development Landscape

February 2023

Mucosal immunity could potentially improve protection against both infection and transmission of SARS-CoV-2

	Preclinical	Phase I	Phase II	Phase III	Registration
Viral vector	U. Lancaster; Insitut Pasteur; NIAID; IAVI; U. Erlangen-Nuremberg; InvVax; U. McMaster; U. Tsinghua; IMCAS; Webond; U. Virginia; Rokote Labs	CyanVac LLC; AstraZeneca / Oxford; Tetherex / Moat Bio; iosBio	Mt Sinai / CastleVax; Vaxart		Bharat Bio / U. Washington; Gamaleya; Cansino
RNA	Moderna; Esperovax				
DNA	U. Stanford; AIOVA; MBF Therapeutic				
Protein-based	UNSAM; CUA; MIT; NIAID; U.Sydney; AuraVax; Flow Pharma; Intravacc; U. Leiden; U. Maryland; Loval Tech; AlbuVAX; Oragenics; Shionogi; Iconovo; U. Ghent; ConserV; U. Tianjin; Immophron; CCBJIC; Vaxine; U. Oxford; WestVac; Mymetics; Wuhan Institute; UASLP; Migvax	VaxForm; Blue Willow; ACM Bio Lab; Intravacc; Yisheng Bio; Oravax	CIGB		Razi Institute
Inactivated and Live attenuated		Meissa Liv.; Symvivo Liv.		Codagenix / SII Liv.	Beijing Wantai Liv.

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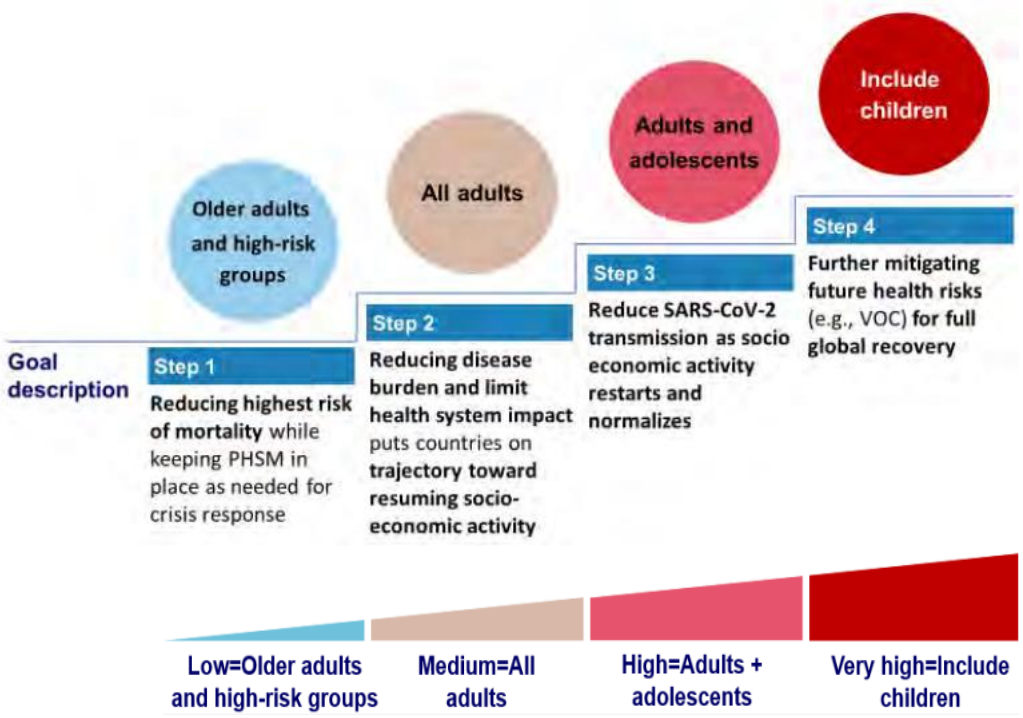
- Dropper
- Sprayer / Inhaler
- Other / unknown
- Tablet delivery
- Lung target confirmed e.g., use nebulizing device

WHO Vaccine policy recommendations have evolved in response to Omicron, hybrid immunity, easing of supply constraints, and availability of bivalent Vx

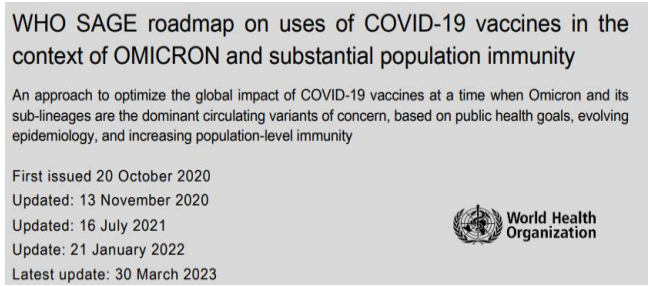
WHO SAGE published its **first Vaccine prioritization roadmap in 2020** when the supply of COVID-19 vaccines was scarce, and the impact of transmission and deaths were higher on health and socio-economic systems.



https://cdn.who.int/media/docs/default-source/immunization/sage/covid/global-covid-19-vaccination-strategic-vision-for-2022_sage-yellow-book.pdf?sfvrsn=4827ec0d_7

In light of Omicron and high population-level immunity due to infection and vaccination (and increasing vaccine supply, decreasing demand), **SAGE revised the roadmap** for prioritizing the use of COVID-19 vaccines **in 2023**.

- **Primary Series + 2 boosters for High Priority** Group (elderly, adults with comorbidities, immunocompromised, healthcare workers)
- **Primary Series + 1 booster for Medium Priority** Group (healthy adults and children/ adolescent with comorbidities)
- **Primary series + 1 booster for Low Priority** Group (healthy children and adolescents) ***only* within country context**, including disease burden in this age group, cost-effectiveness, other health or programmatic priorities, and opportunity costs;


WHO SAGE roadmap on uses of COVID-19 vaccines in the context of OMICRON and substantial population immunity

An approach to optimize the global impact of COVID-19 vaccines at a time when Omicron and its sub-lineages are the dominant circulating variants of concern, based on public health goals, evolving epidemiology, and increasing population-level immunity

First issued 20 October 2020
Updated: 13 November 2020
Updated: 16 July 2021
Update: 21 January 2022
Latest update: 30 March 2023

World Health Organization

https://www.who.int/publications/i/item/WHO-2019-nCoV-Vaccines-SAGE-Roadmap

Conclusions

- COVID-19 vaccines reached emergency use in record time – first vaccine available in just 326 days
- Need for booster vaccines for durability and evolving variant protection
- Protection against severe disease remains high with benefit in Adults and children
- mRNA is the platform of choice to ‘keep up’ with variants
- Next generation vaccines are focusing on breadth of protection and potential transmission blocking potential
- The PHEIC is over but COVID19 continues to evolve – vaccine strategies will also need to evolve

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