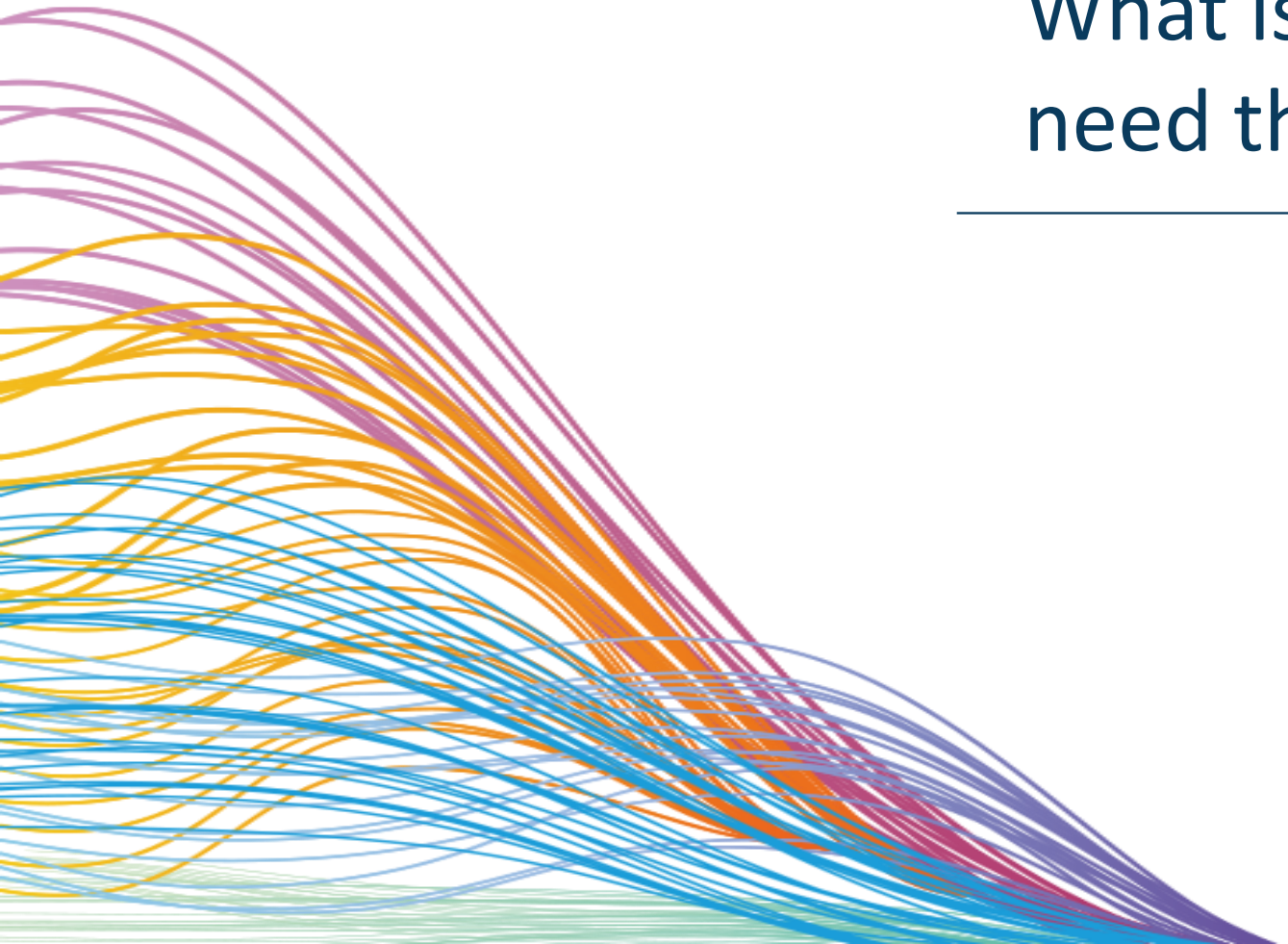
ACTaccelerator
ACCESS TO COVID-19 TOOLS

Hosted by World Health Organization



Variant vaccines:
What is the state of R&D, do we need them, and who decides?

Member State Briefing – 3 February 2022

Dr. Soumya Swaminathan

COVID-19 advisory group pathway to informed decisions

Strong, multidisciplinary mechanism of external experts for evidence-based decision making

Aim: Monitor & assess SARS-CoV-2 variants and evaluate their impact on countermeasures, including vaccines, therapeutics, diagnostics or effectiveness of public health and social measures.

Virus

Monitoring & surveillance

TAG-Virus Evolution (VE)

- determines where variants are circulating
- Advises on VOI or VOC determination based on variants' alteration in:
  - transmission or disease characteristics or
  - impact on vaccines, therapeutics, diagnostics or
  - effectiveness of public health and social measures

Vaccine Products

Research & evidence assessment

Vax Research Expert Group

- methods standardization for vaccine development and assessment

Vax Effectiveness WG

- assesses and supports VE and impact studies

Regulatory TAG

- Advises on EUL of vaccines through evidence-based assessment

TAG-CO-VAC

- determines if changes to vaccine composition are needed through evidence-based assessment

Vaccine implementation

Policy

SAGE

- recommends policies and strategies on vaccine use and immunization programmes through evidence-based assessment

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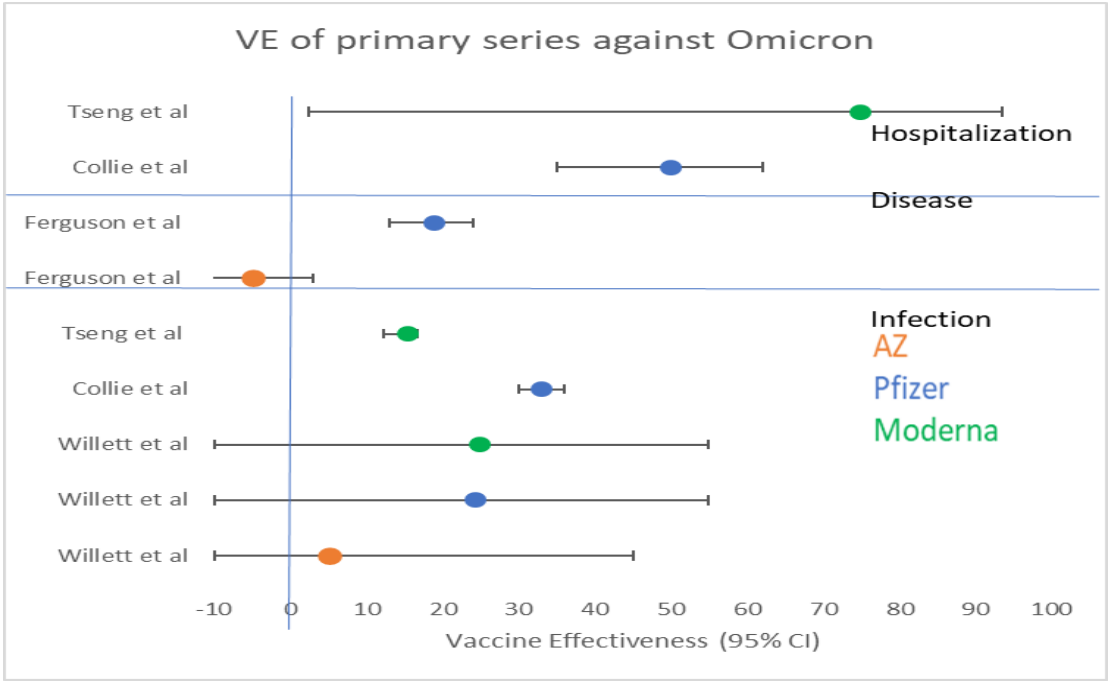
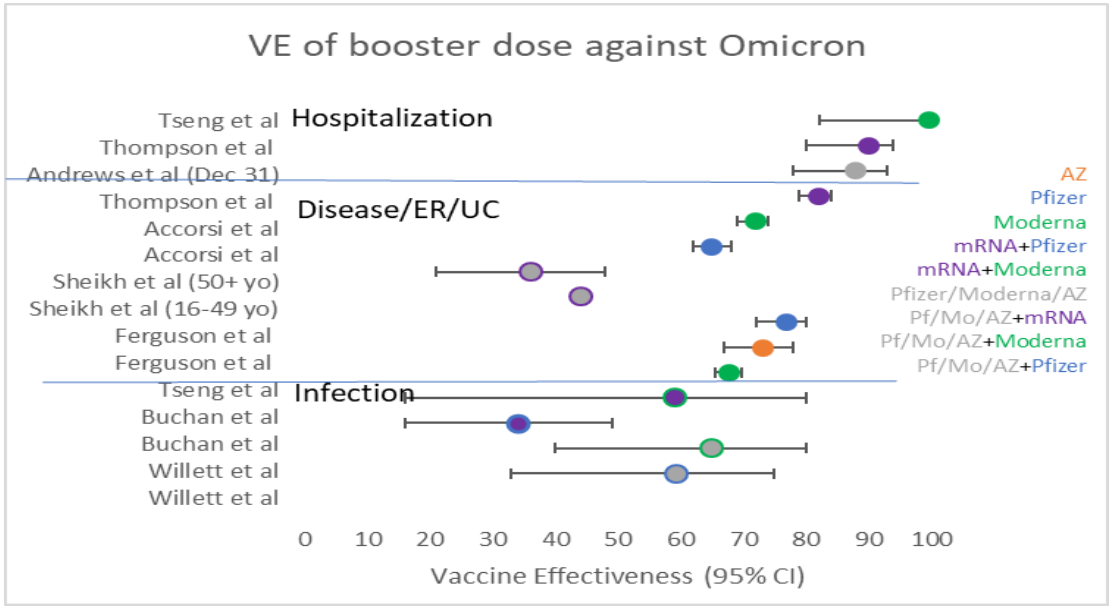
Vaccine Effectiveness against Omicron:

- **Primary Series**
  - 5 studies with VE estimates 2+ weeks after primary series
  - Only 2 looking at hospitalization
- **Booster Dose**
  - 10 studies with VE estimates 1-2 weeks post booster dose*
  - Only 3 looking at hospitalization
  - 1 study evaluated VE in immunocompromised
    - 3 doses of Moderna VE=21.7 (0.0-45.0)
- Almost all studies provide comparison of performance Delta to Omicron → Omicron VEff always lower than Delta





*(2 not graphed because they provide relative VE comparing 3 to 2 dose recipients, not unvaccinated)

How well do current vaccines work against Omicron? (1/2)

Context of the vaccine performance evidence

- **Lab studies** numerous and supportive, but their predictive link to performance limited
  - **51 neutralization studies** show a 14-35 fold **reduction in neutralization**, much larger compared to other VOCs (improved with booster, but still lower than Delta)
  - **10 cellular immunity studies** show that **T-cell immunity largely preserved against Omicron**
- **Veff data is limited** geographically and on the vaccines studied – plus methodological constraints, so no single study should be relied on alone
  - **22 real world studies with limited** g**eographic/epidemiologic** representation
    - Canada, Denmark, Qatar, South Africa, UK, USA (i.e. 1 country in Africa, 0 in South America, Asia)
  - Data is mainly from **mRNA vaccines**, or **mixed regimens:** No Veff studies to date from inactivated or protein vaccines
  - Evidence to address **waning** over time is still too preliminary
  - Studies on **transmission,** a critical outcome, are very difficult to conduct – are largely inferred from studies of infection

How well do current vaccines work against Omicron? (2/2)

Key take-aways are emerging from growing body of evidence

- VEff remains **high** (following primary & booster) against the **severe disease** end of the spectrum, but….
- **Lower against Omicron** than Delta, for all outcomes, and….
- Greater reduction against **infection** than severe disease outcomes, but…
- **Boosters** make a substantial difference in vaccine performance against Omicron (though still below Delta)

Need to keep monitoring the situation to **understand VEff of all the vaccines in use**, to understand **if there is true waning of the booster dose**, and if the **protection against hospitalization and severe outcomes remains sufficient.**

WHO consultation on COVID vaccines research: Why do we need a pan-sarbecovirus vaccine?

January 28 2022, organized by WHO R&D Blueprint

Main conclusions

- Structural similarity between sarbecoviruses should enable development of a pan-sarbecovirus vaccine.
- Pan-sarbecovirus vaccines may have a better chance of blocking transmission and facilitating herd immunity, and are expected to be more durable.
- A variety of strategies may induce broader immune responses. These include different antigen presentation strategies as well as inclusion of additional antigens.
- Current vaccines, due to broadly acting responses, are working well against severe disease. Major benefit of next generation vaccines could be in reducing infection and transmission.
- Continued investment in R&D is critical. Equity and access are essential.
- While we deal with the pandemic, preparing platforms for the next variant or virus is key.

COVAX

CEPI Gavi The Vaccine Alliance unicef World Health Organization

State of vaccine R&D and approaches to variants

Dr. Melanie Saville

3rd February 2022

‘Variant Vaccines’ – *what is the state of R&D?*
What approaches are being considered?

Optimize use of current vaccines
Regimen/booster
Mix and match

↓

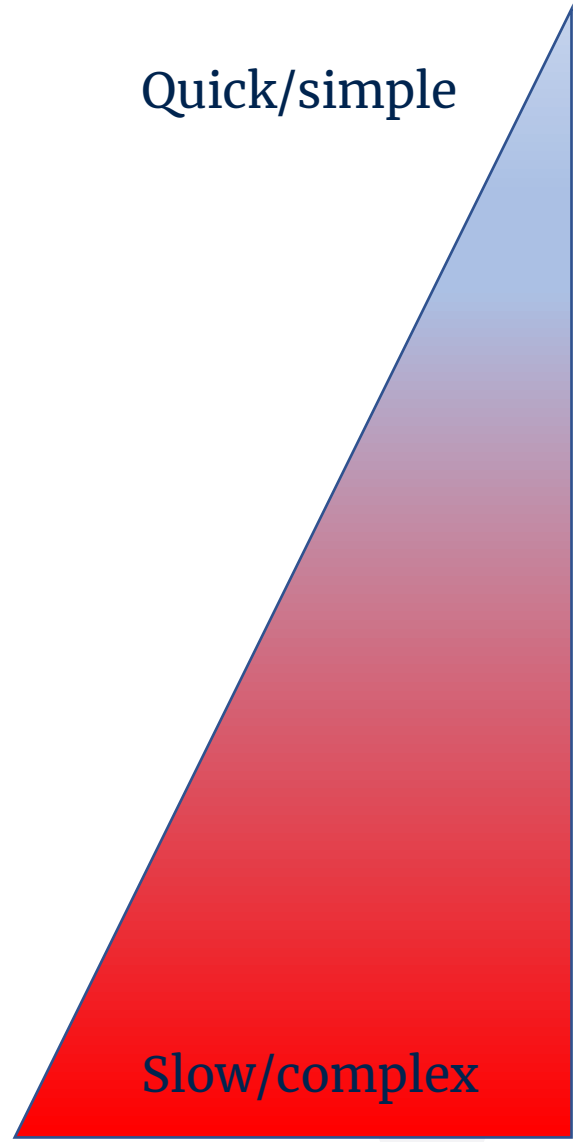
Variants of current vaccines
Strain change
multivalent

↓

Next generation broad protection SARS-CoV 2
Protect against existing and future variants

↓

Universal Coronavirus
Broadly protective beta coronavirus
Pan coronavirus

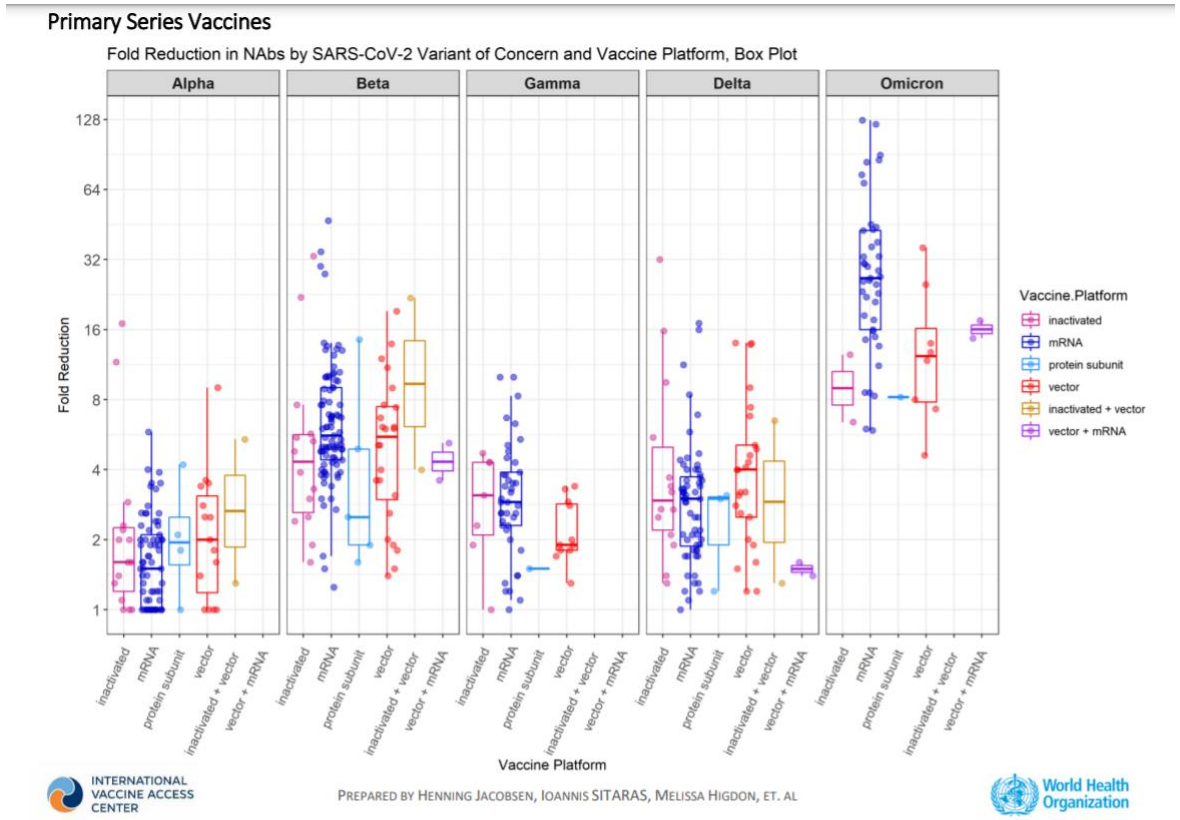


Fold reductions in neutralizing antibodies by vaccine platform and variant

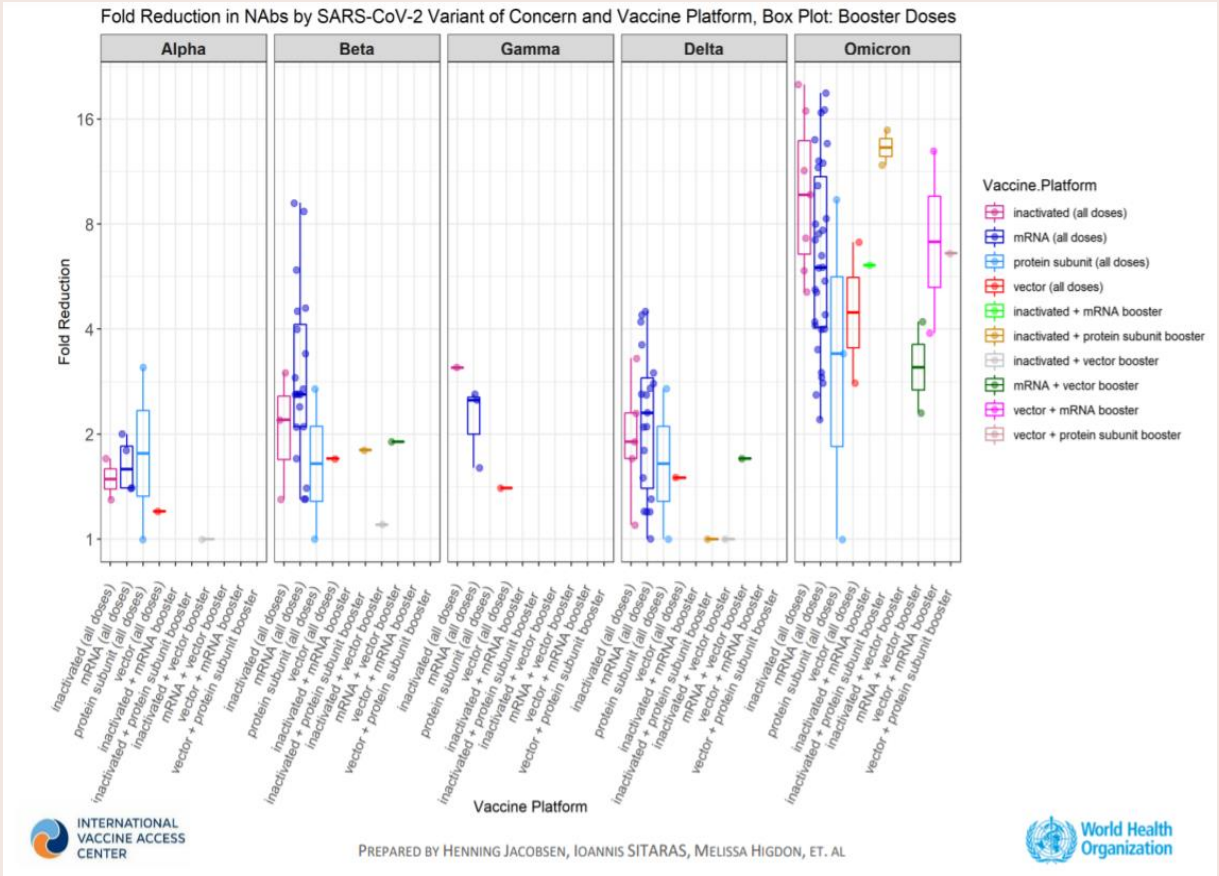
Neutralization data suggest large drop against Omicron for all vaccines

- Improves somewhat with booster dose
- More preserved cellular immunity

Primary series (excludes boosters)



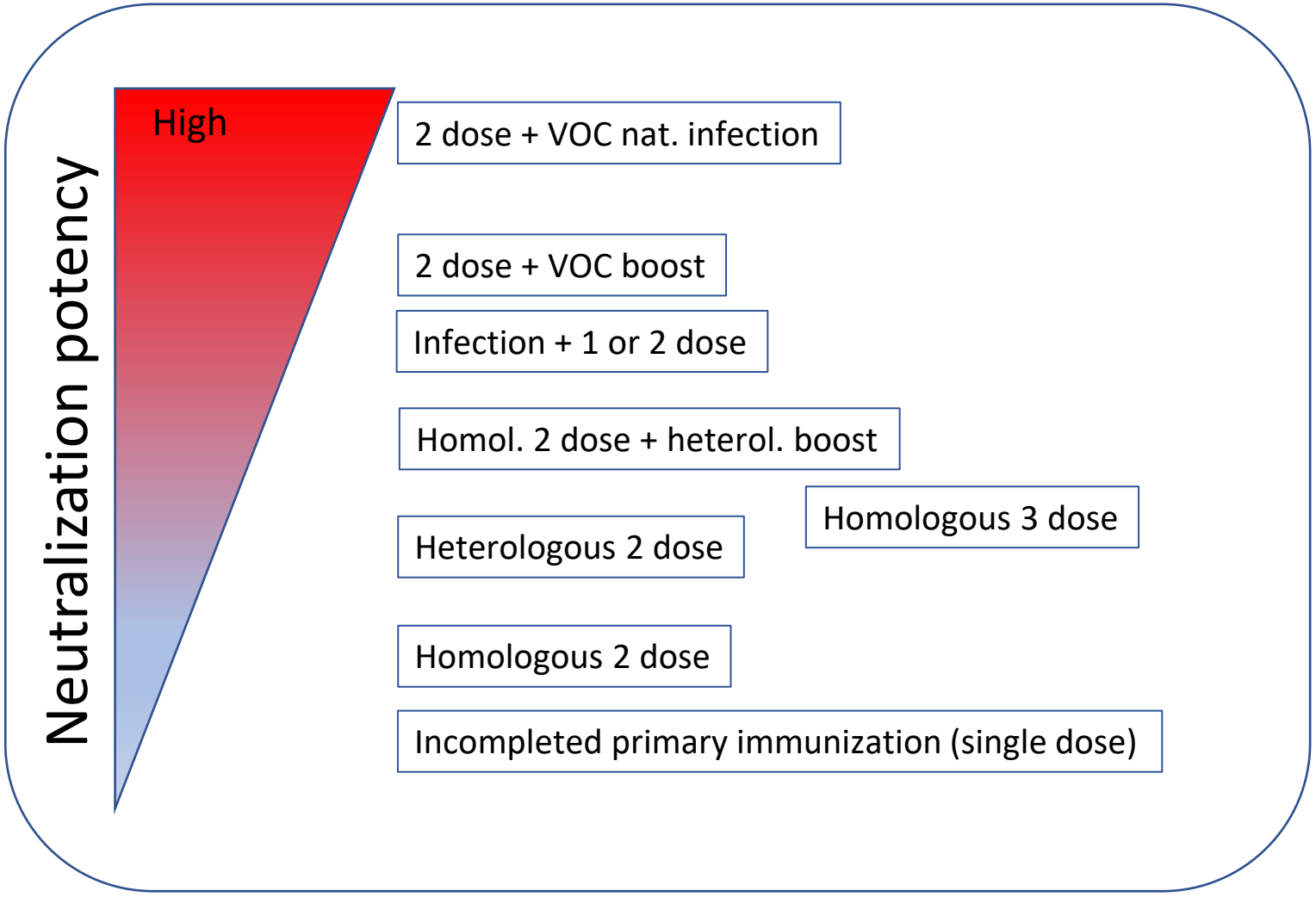
Booster doses



https://view-hub.org/sites/default/files/2022-01/Neutralization%20Plots_0.pdf
https://view-hub.org/sites/default/files/2022-01/Neutralization%20Plots_0.pdf

More and more data becoming available: But what do they tell us?

Potential for improving cross-neutralization against Omicron with existing vaccines

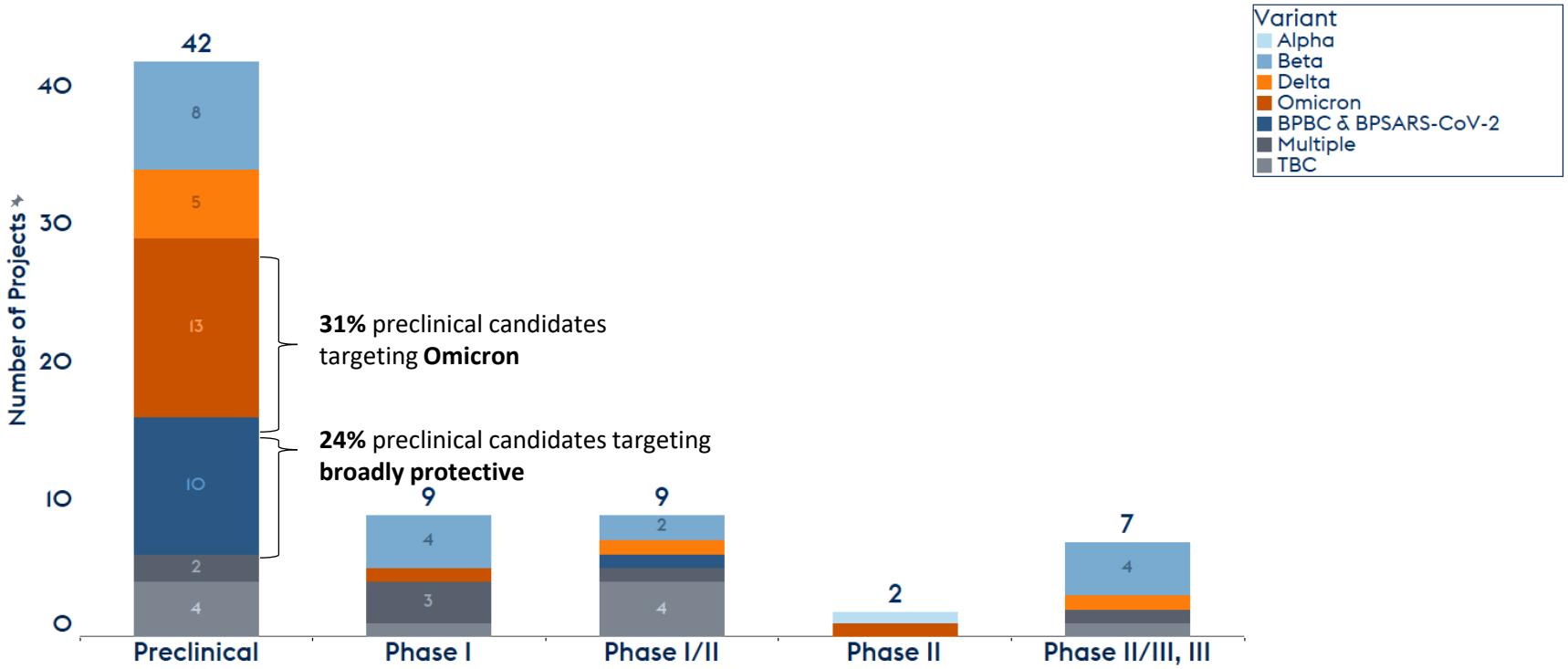


Caveat

Limited data is currently available
Need to link with effectiveness data which remains limited

COVID-19 current vaccine development pipeline - Variants

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



* Includes only broadly protective Betacoronavirus (BPBC) and broadly protective SARS-CoV-2 (BP-SARS-CoV-2) projects currently under assessment by CEPI

Variant R&D activities in COVAX R&D portfolio and from most advanced licensed COVID-19 vaccines

- All CEPI's COVID 19 partners are developing variant constructs
- >50% have manufactured variant clinical trial material
- Preclinical data on most variant vaccines

Developer	Region	Tech	Variant activities and progress
AZ	UK	Adeno vector	Delta, others
Novavax	US	Protein	Beta, Omicron
Clover	China	Protein	Delta
BioE	India	Protein	Beta, Delta, Omicron
SK	S. Korea	Protein	Beta, SARS-CoV broadly protective
Zerun	China	Protein	Beta, Chimera
Gritstone	US	saRNA	Beta, Omicron
VBI	Canada	Viral vector	Beta
Pfizer/BioNTech	US	mRNA	Omicron: Phase II immuno trial
Moderna	US	mRNA	Omicron: Phase II

Non CEPI funded

Calls for broadly protective SARS-CoV-2/ Sarbeco vaccines

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

Universal Coronavirus Vaccines — An Urgent Need

David M. Morens, M.D., Jeffery K. Taubenberger, M.D., Ph.D., and Anthony S. Fauci, M.D.

NIAD portfolio – plan to fund up to $43M

University of Wisconsin, Madison

Project Title: PanCorVac (Center for Pan-Coronavirus Vaccine Development)

Grant: 1 P01AI165077-01

Brigham and Women's Hospital, Boston

roject Title: Discovering Durable Pan-Coronavirus Immunity

Grant: 1 P01AI165072-01

Duke University, Durham, North Carolina

Project Title: Design and Development of a Pan-Betacoronavirus Vaccine

Grant: 1 P01AI158571-01A1

CEPI

Call for Proposals:

Broadening protection against SARS-COV-2 and new broadly protective Betacoronavirus candidate vaccines

CEPI portfolio – plan to fund up to $200M

Developer	Region	Technology
BioNetAsia	Thailand	mRNA/VLP
SK Bio	S. Korea	Protein nano-particle
Zerun/ Walvax	China	Protein
Under DD		Protein vaccine
Seed funding		
MigVax	Israel	Protein vaccine
VIDO	Canada	Protein vaccine
Affinivax	US	Protein on poly saccharide backbone

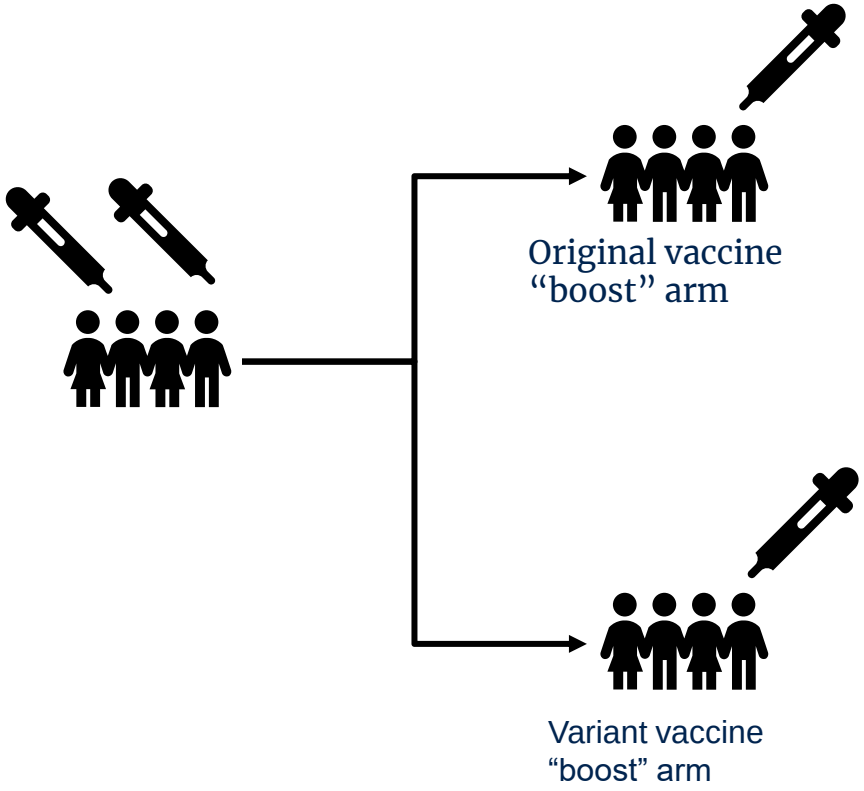
CEPI

First CEPI partnerships for Broad coronavirus vaccines will be announced shortly

Regulatory requirements for variant vaccine

Population

First or second “boost” to homologous or heterologous primary series
(No prior Covid-19 infection)



Neutralizing antibody titres

Original virus neut assay	Variant virus neut assay
❶ Original vaccine “boost” arm samples against original strain	❷ Original vaccine “boost” arm samples against variant strain
	❸ Variant vaccine “boost” arm samples against variant strain

Guidelines (Feb 2021)

- **Primary analysis**
  - nAb GMT ❶ *vs.* ❸
  - Non-inferiority
  - The lower bound of the 95% CI around the GMT ratio ≥0.67
- **Secondary Analysis**
  - nAb GMT ❷ *vs.* ❸
  - Superiority
  - Lower bound of the 95% confidence interval around the GMT ratio >1

Note:

- Links to efficacy data but relevance of comparison back to original strain
- Comparison using different assays

Discussion at RAG (Dec 2021) and ICMRA (Jan 2022)

- **Primary Analysis**
  - nAb GMT ❷ *vs.* ❸
  - Superiority
- **Descriptive**
  - Neuts *vs.* other VoCs

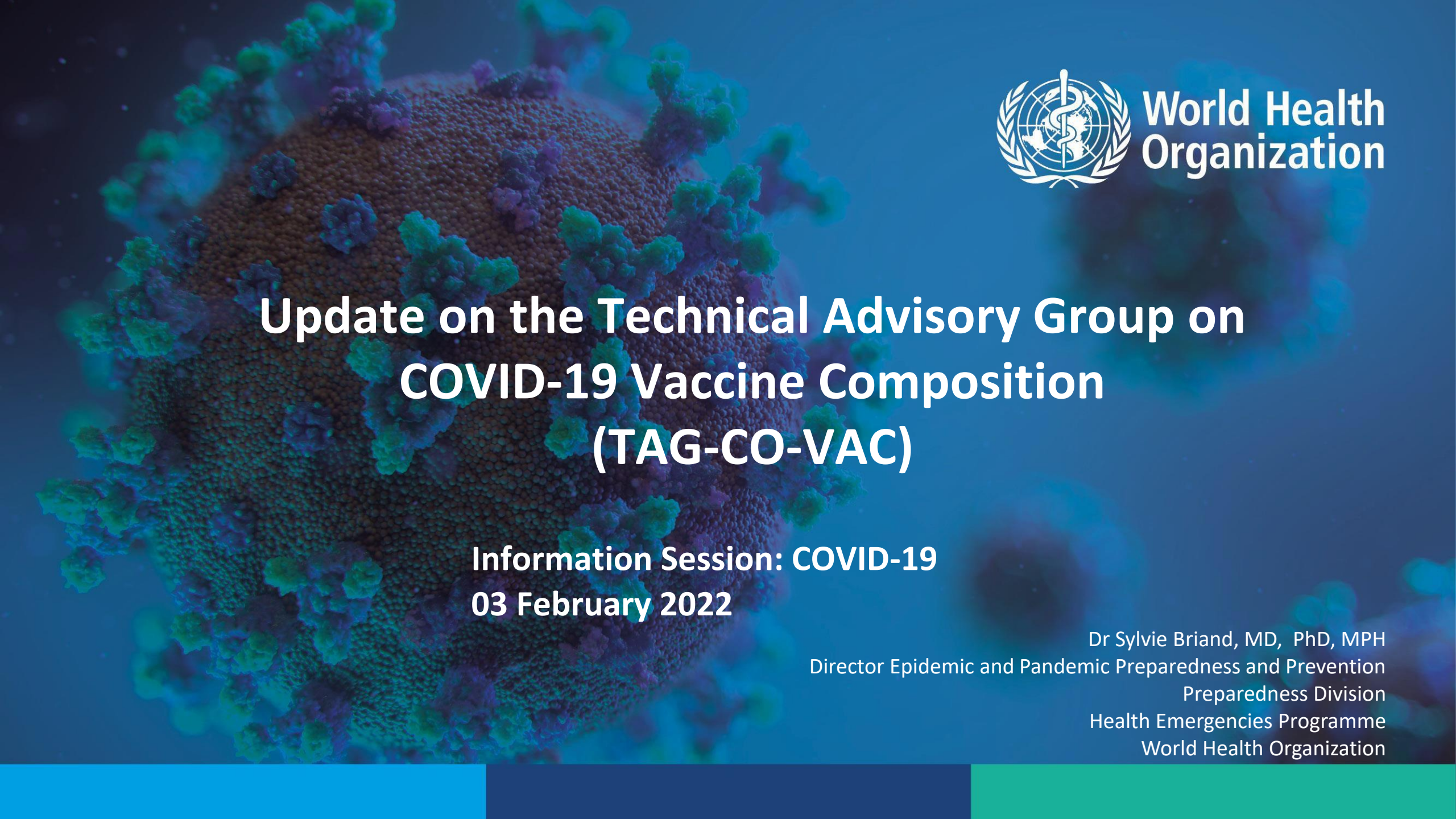
Regulatory considerations

Evolving environment in virus exposure and vaccine roll out raises additional regulatory questions for second generation vaccines

- What are the regulatory requirements for
  - New booster only vaccines?
  - New variant vaccines?
  - Chimeric vaccines (broadly protective)?
  - Multivalent vaccines?

Developers should continue to progress variant development programmes

- Generates experience for the developer
  - Platform experience – eventual elimination of clinical data requirements
  - Streamline and accelerate development – *c.f.* 100 days



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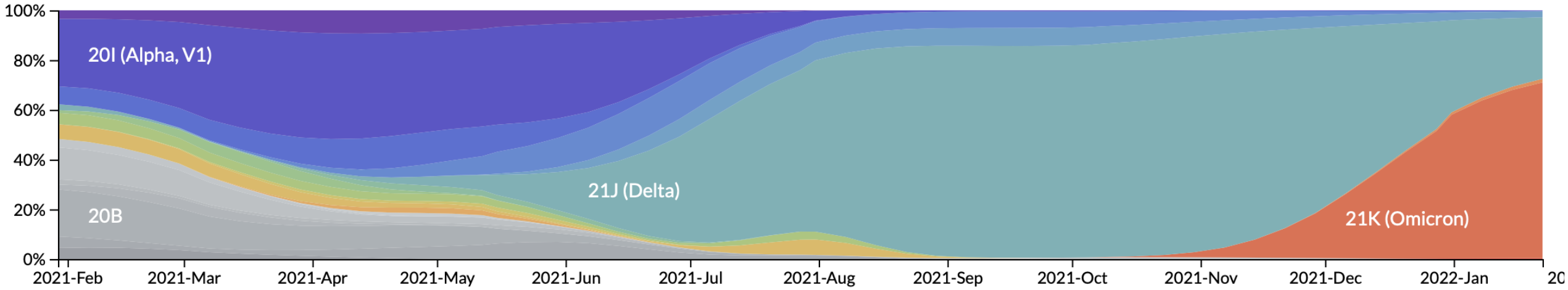
Update on the Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC)

Information Session: COVID-19
03 February 2022

Dr Sylvie Briand, MD, PhD, MPH
Director Epidemic and Pandemic Preparedness and Prevention
Preparedness Division
Health Emergencies Programme
World Health Organization

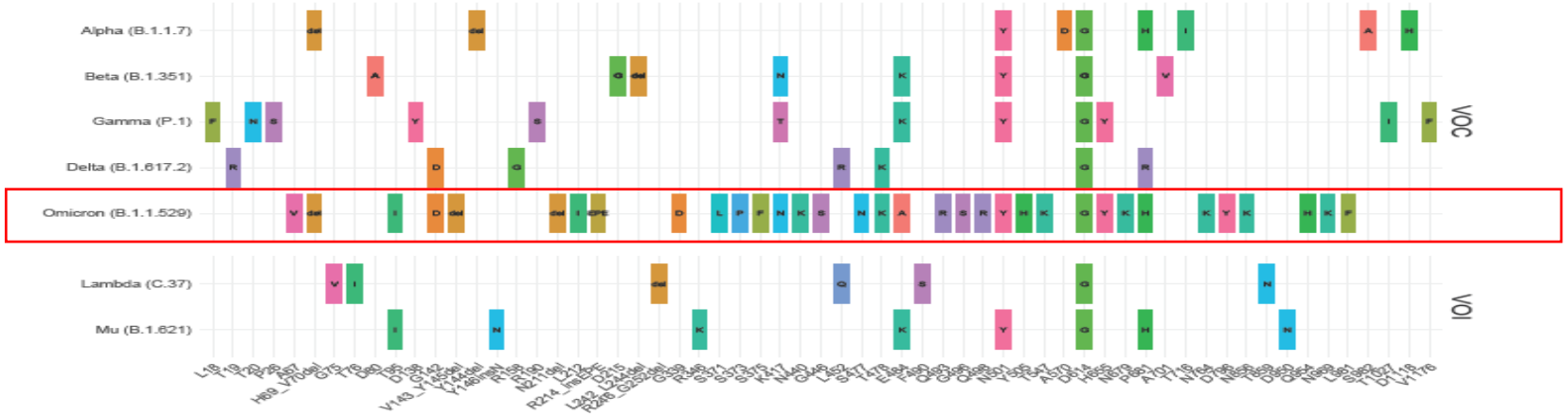
Evolution of SARS-CoV-2

Frequencies (colored by Clade)



Source: Nextstrain

Amino acid changes in the spike protein of VOC and VOI



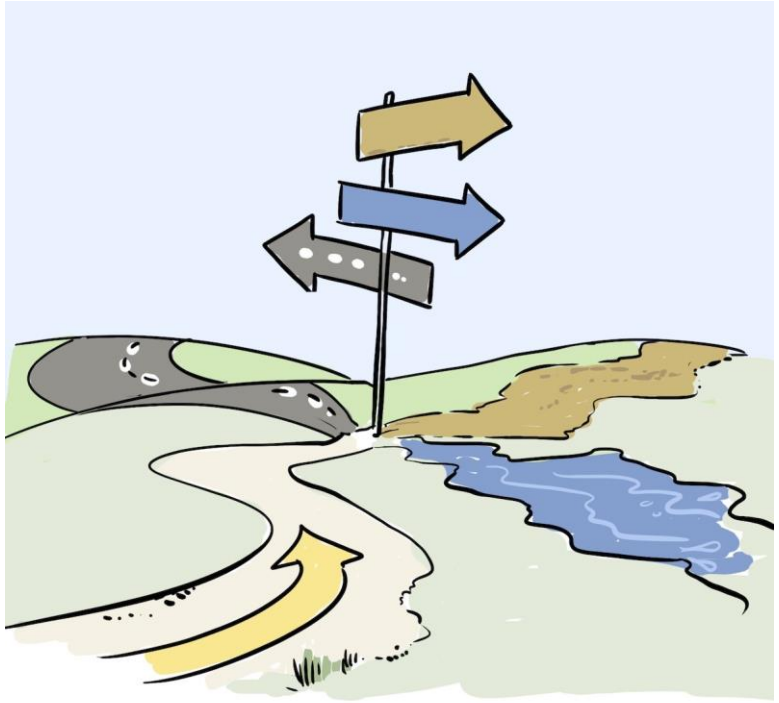
Omicron

World Health Organization

Three potential scenarios used for planning

Scenario N°1: 5th endemic coronavirus

SARS-CoV-2 remains highly contagious but causes mild illness in the majority of cases. The virus can be grouped with the 4 other coronaviruses that circulate endemically. This scenario is not unrealistic, but it may take many years to be realized.



Scenario N°2: “Flu-Like”

The disease presents itself as recurring epidemics when the conditions of transmission are favorable (similar to seasonal influenza). Since the population has basic immunity, severe forms of the disease are observed only in people at risk. It will be important to continue to vaccinate at-risk groups and adopt preventive measures when transmission is high.

Scenario 3: Ongoing pandemic through new VOCs

A new variant emerges evading acquired immunity and resulting in a large number of cases. The health system is overloaded and therefore there are more deaths. The situation is very similar to what was experienced at the beginning of 2020 in many regions of the world.

World Health Organization

Technical Advisory Group on COVID-19 Vaccine Composition

Functions of the TAG-CO-VAC

- Make recommendations to WHO on the methods to assess the impact of VOCs on vaccines
- Provide interpretation of available evidence on the effect of VOCs on vaccines, including but not limited to vaccine effectiveness
- Recommend to WHO, for each COVID-19 vaccine platform, adaptations (if any) needed so that vaccines continue to safely provide WHO-recommended levels of protection against VOCs.

Credits: Kanta Subbarao, TAG-CO-VAC Chair

World Health Organization

Two-step decision making process

When would the TAG-CO-VAC recommend a change in vaccine composition?

Change(s)

- in the virus
- In the epidemiology
- in vaccine performance

What information would be needed?

- Virologic, epidemiologic, clinical, antigenic VE data
- Do the data exist or does it need to be generated? If so, who can do this?
- Regional vs global data?

1. CHANGE?
What features of a newly emerged VOC prompt consideration of change in vaccine strain composition?

2. WHAT ?
What specific “strain” should be recommended in updated composition?

BETTER VACCINE

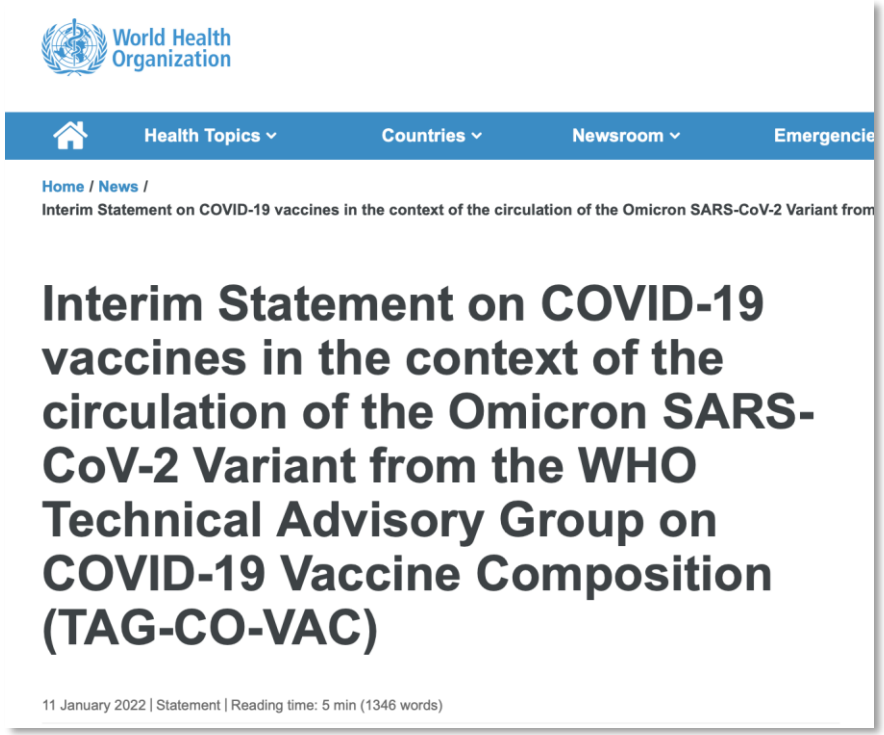
Credits: Kanta Subbarao, TAG-CO-VAC Chair

World Health Organization

TAG-CO-VAC statement on COVID-19 Vaccines – 11 Jan 2022 (1)

Key messages

- Indicates **protection against severe disease and death is more likely to be preserved** by current COVID-19 vaccines for the Omicron variant.
- Urges the world to **accelerate broader access to primary vaccination**, particularly for groups at greater risk.
- Stresses vaccination strategies based on repeated **booster doses** of the original vaccine composition is unlikely to be appropriate or sustainable.
- Calls for the development of COVID-19 vaccines that have high impact on prevention of **infection and transmission.**
- Specifies until such vaccines are available and as the virus continues to evolve, **the composition of current COVID-19 vaccines may need to be updated** to ensure WHO-recommended levels of protection.



Link to the TAG-CO-VAC statement

Endorsement by the International Coalition of Medicines Regulatory Authorities (ICMRA)

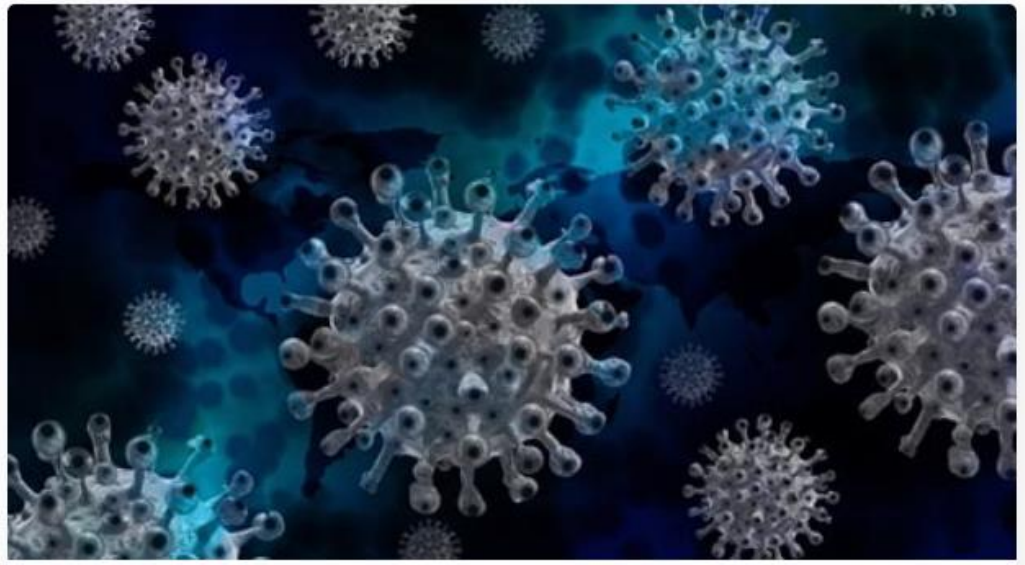
World Health Organization

TAG-CO-VAC statement on COVID-19 Vaccines – 11 Jan 2022 (2)

Options to consider

- a **monovalent vaccine** that elicits an immune response against the predominant circulating variant(s), although this option faces the challenge of the rapid emergence of SARS-CoV-2 variants and the time needed to develop a modified or new vaccine;
- a **multivalent vaccine** containing antigens from different SARS-CoV-2 VOCs;
- a **pan SARS-CoV-2 vaccine**: a more sustainable long-term option that would effectively be variant-proof.

The TAG-CO-VAC is considering the strain composition of COVID-19 vaccines, and **encourages vaccine developers to gather data on a small scale on the breadth and magnitude of immune response for monovalent and multivalent vaccines against VOCs** – this data would then be considered in a broader decision-making framework on vaccine composition.



28 January 2022 13:00 – 19:00 CET

WHO consultation on COVID vaccines research: Why do we need a pan-sarbecovirus vaccine?

Link to registration and agenda of the consultation (R&D Blueprint)

World Health Organization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Organization
Thank You