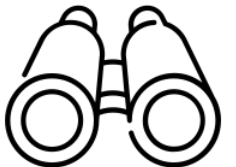


Update on COVID-19 vaccines

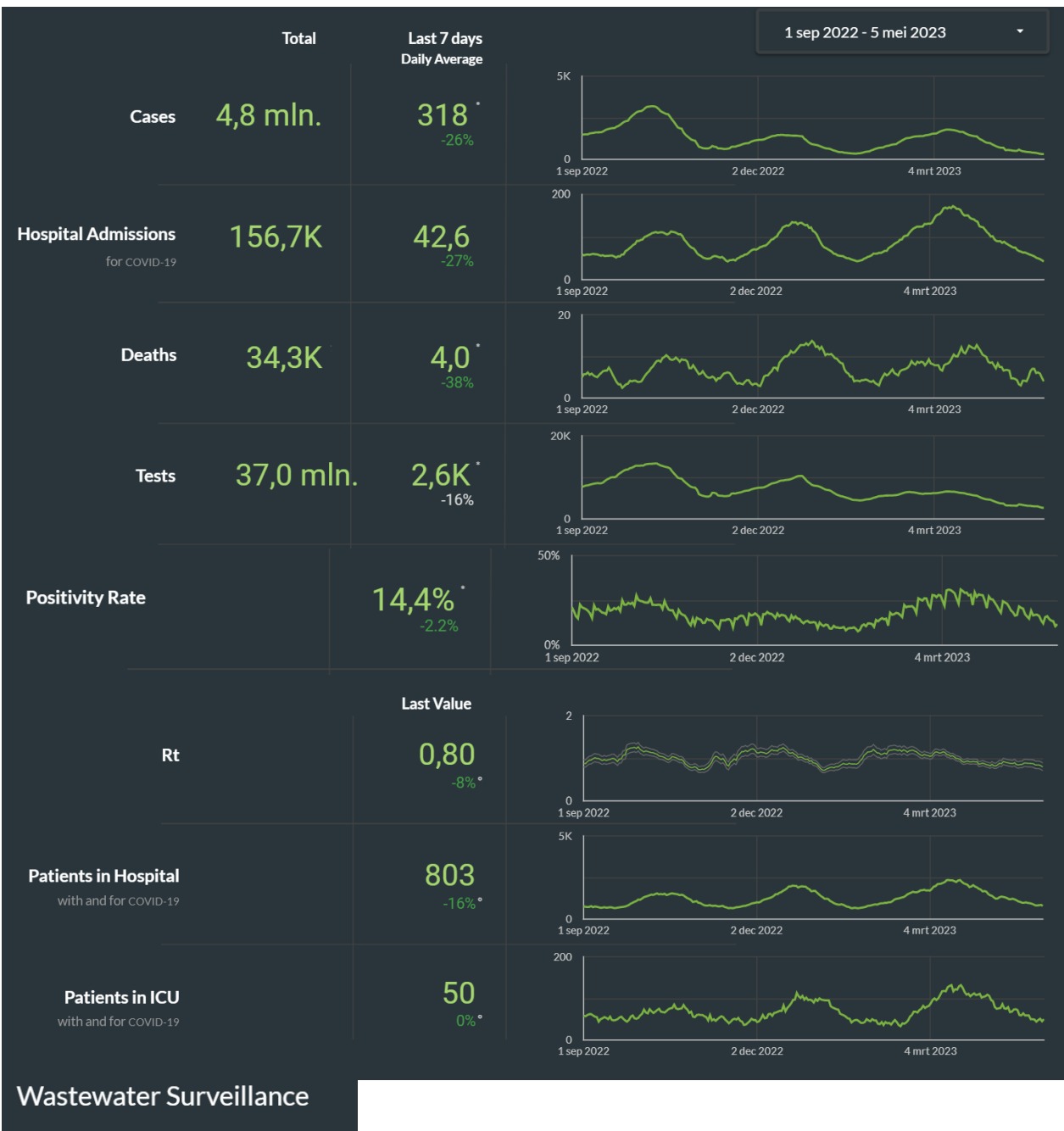
Overview

1. What is the current epidemiological and virological situation and how will SARS-CoV-2 further evolve?
2. Which vaccines are available and are the booster vaccines still protective against (severe) COVID-19?
3. How to prepare for the next respiratory season? A new booster shot needed?
4. Novel COVID-19 vaccines on the horizon?



1. What is the current epidemiological and virological situation and how will SARS-CoV-2 further evolve?





W.H.O. Ends Global Health Emergency Designation for Covid

The decision has little practical effect but is a significant moment in the struggle against a virus that has killed millions and upended lives throughout the world.

Give this article



51

May 5, 2023

The WHO Director-General concurs with the advice offered by the Committee regarding the ongoing COVID-19 pandemic. He determines that COVID-19 is now an established and ongoing health issue which no longer constitutes a public health emergency of international concern (PHEIC).



Tedros Adhanom Ghebreyesus, the W.H.O. director general, in Geneva last month.

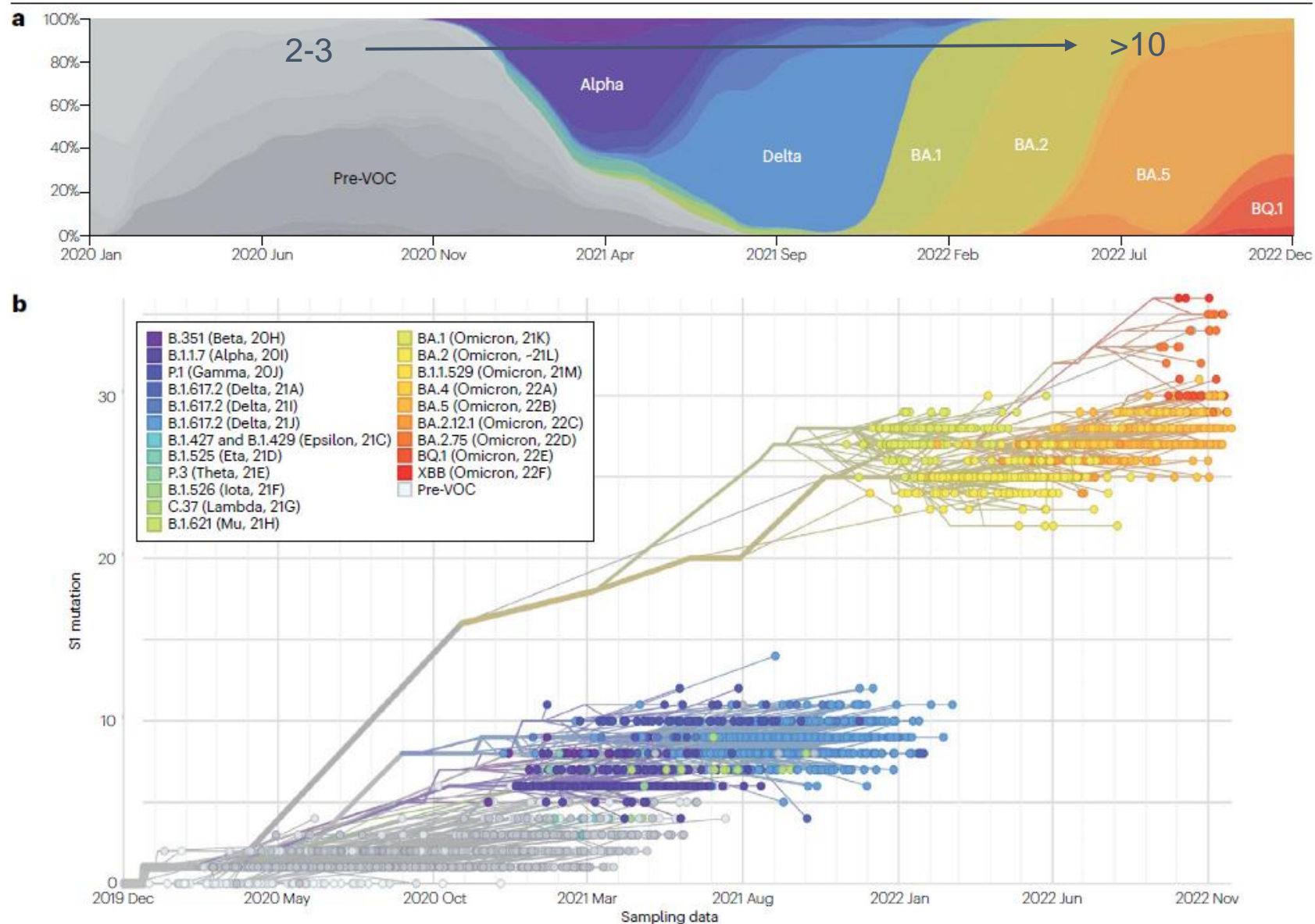
Fabrice Coffrini/Agence France-Presse — Getty Images

5 May 2023:
an end has come to 1.191 days of
public health emergency of international concern

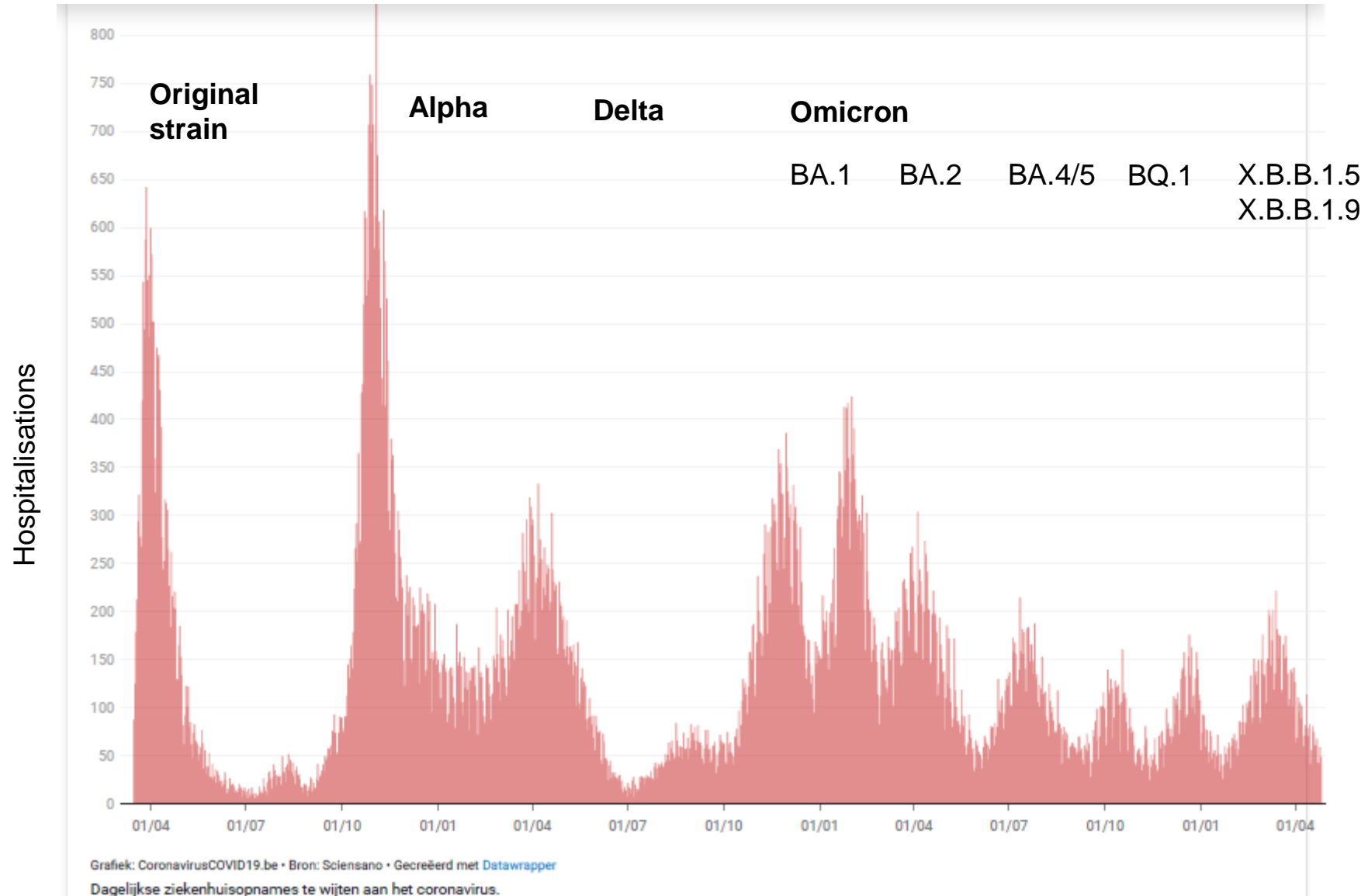
The pandemic is not over yet.

The evolution of SARS-CoV-2 (Jan 2020 – Dec 2022)

R0



COVID-19 waves in Belgium and SARS-CoV-2 variants

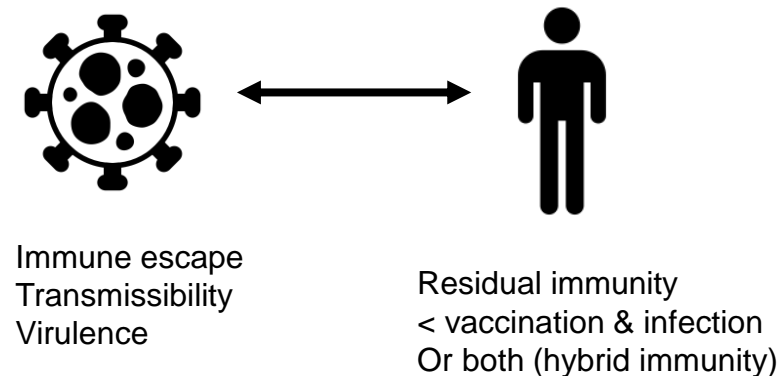


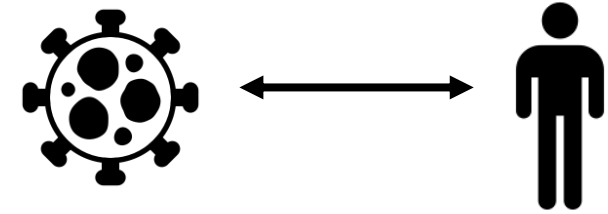
The evolution of SARS-CoV-2

Peter V. Markov^{1,2}✉, Mahan Ghafari³, Martin Beer⁴, Katrina Lythgoe³, Peter Simmonds⁵, Nikolaos I. Stilianakis^{1,6}
& Aris Katzourakis⁷✉

Possible future scenarios

- **Scenario 1: ‘drift like’ evolution within the omicron lineage**
Hybrid (vaccine + infection) immunity protects well against severe disease
A new wave of infection every ~4 months?
Eventually a more regular seasonal pattern?
- **Scenario 2: ‘shift like’ evolution**
Emergence of a new variant which evades immunity
Potentially more virulent than omicron
- **Other scenario’s:**
recombination between different viruses, spillover from animal reservoir, ...





The evolution of SARS-CoV-2

Peter V. Markov^{1,2}✉, Mahan Ghafari³, Martin Beer⁴, Katrina Lythgoe³, Peter Simmonds⁵, Nikolaos I. Stilianakis^{1,6}
& Aris Katzourakis⁷✉

“The virus will **likely become endemic** (=regular seasonal fluctuations and no out-of-season peaks), a process that could take **years to decades**.”

“The eventual **infection prevalence and disease burden** will depend on the rate of emergence of **antigenically distinct** lineages, **our ability to roll out and update vaccines**, and **the future trajectory of virulence**.”

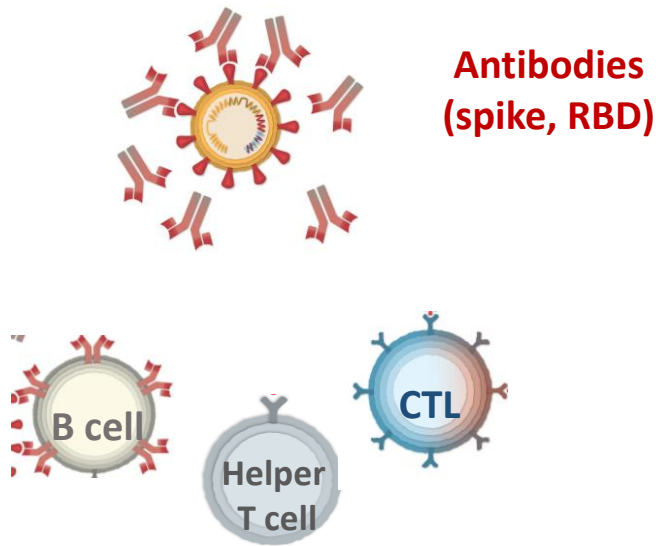
“**The highly multifactorial and stochastic nature of the evolutionary process** will always keep the future trajectory of the virus essentially **unknown** in many of its crucial details.”

“Meanwhile, **focusing on the epidemiology of the pathogen**, it is important to bear in mind that **the transition** from a pandemic to future endemic existence of SARS-CoV-2 is **likely to be long and erratic**, rather than a short and distinct switch, and that **endemic SARS-CoV-2** is by far **not a synonym for safe infections, mild COVID-19 or a low population mortality and morbidity burden**.”

2. Which vaccines are available and are the booster vaccines still effective against (severe) COVID-19?

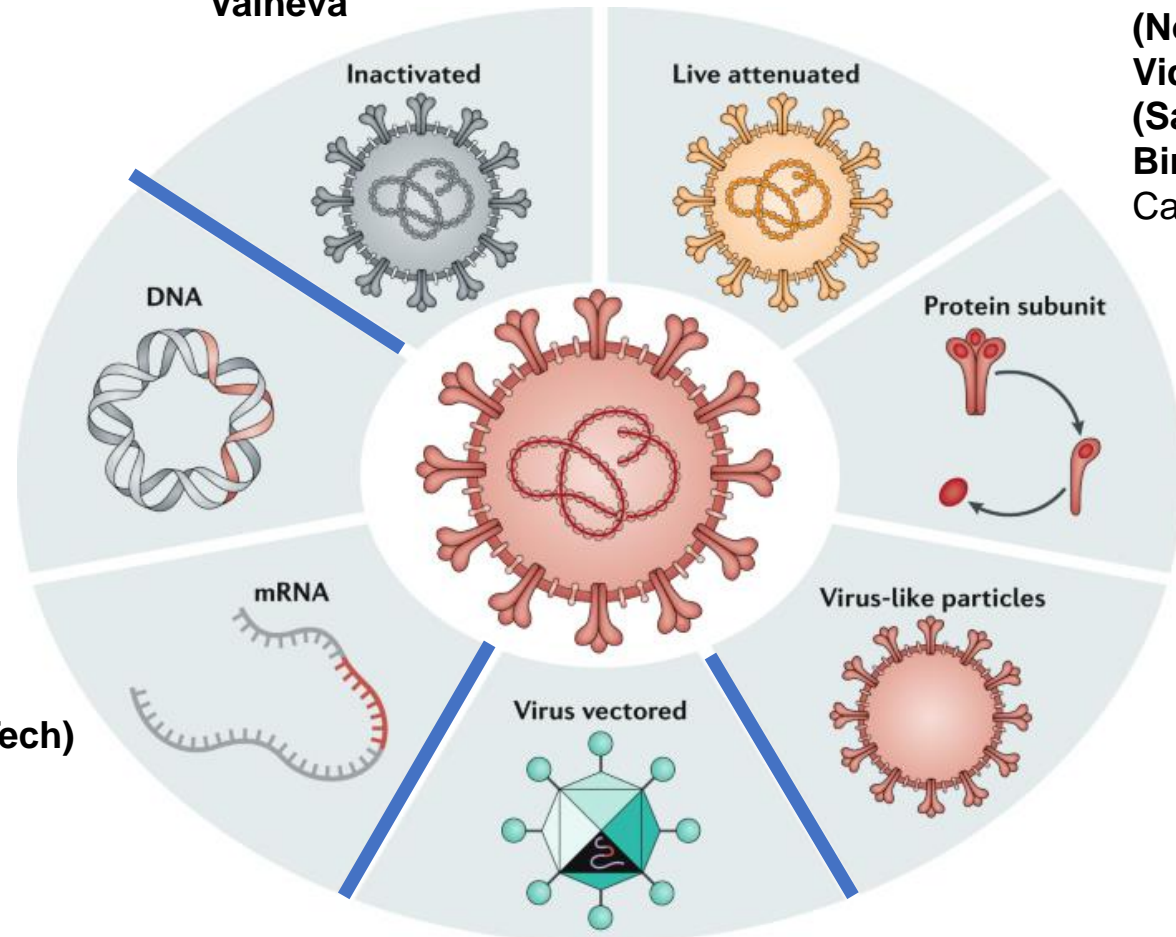


SARS-CoV-2 vaccines: different strategies aiming at inducing humoral and cellular immunity



**Comirnaty
(Pfizer/BioNTech)
Spikevax
(Moderna)**

**Sinovac
Sinopharm
Valneva**



**Nuvaxovid
(Novavax)
VidPrevtyn beta
(Sanofi Pasteur GSK)
Bimervax (HIPRA)
CanSino Biologicals**

**Vaxzevria (Oxford/AstraZeneca)
Jcovden (Johnson&Johnson)
Sputnik V
CanSino**

8 EMA licenced COVID-19 vaccines

Overview of COVID-19 vaccines in Belgium

mRNA-vaccins

PER MERKNAAM	PER GROEPSNAAM	plaatsbepaling	alles openvouwen
Comirnaty (Pfizer)		Monovalent vaccine	
Comirnaty Original/Omicron BA.1 (Pfizer)		Bivalent vaccine	
Comirnaty Original/Omicron BA.4-5 (Pfizer)		Bivalent vaccine	
Spikevax (Moderna)		Monovalent vaccine	
Spikevax bivalent Original/Omicron BA.1 (Moderna)		Bivalent vaccine	

Comirnaty:

30 µg (12+)
10 µg (5-11)
3 µg (6 months – 3 years)

Spikevax:

100 µg (12+ priming)
50 µg (6-11 years, booster for 30+)

Vectorvaccins

PER MERKNAAM	PER GROEPSNAAM	plaatsbepaling	alles openvouwen
Jcovden (Janssen-Cilag)			
Vaxzevria (AstraZeneca)			

Jcovden and Vaxzevria

not in use anymore
Lower vaccine effectiveness
Very low risk of vaccine-induced
thrombotic thrombocytopenia (VITT)

Subunitvaccins

PER MERKNAAM	PER GROEPSNAAM	plaatsbepaling	alles openvouwen
Nuvaxovid (Novavax)			
VidPrevryn Beta (Sanofi Belgium)			

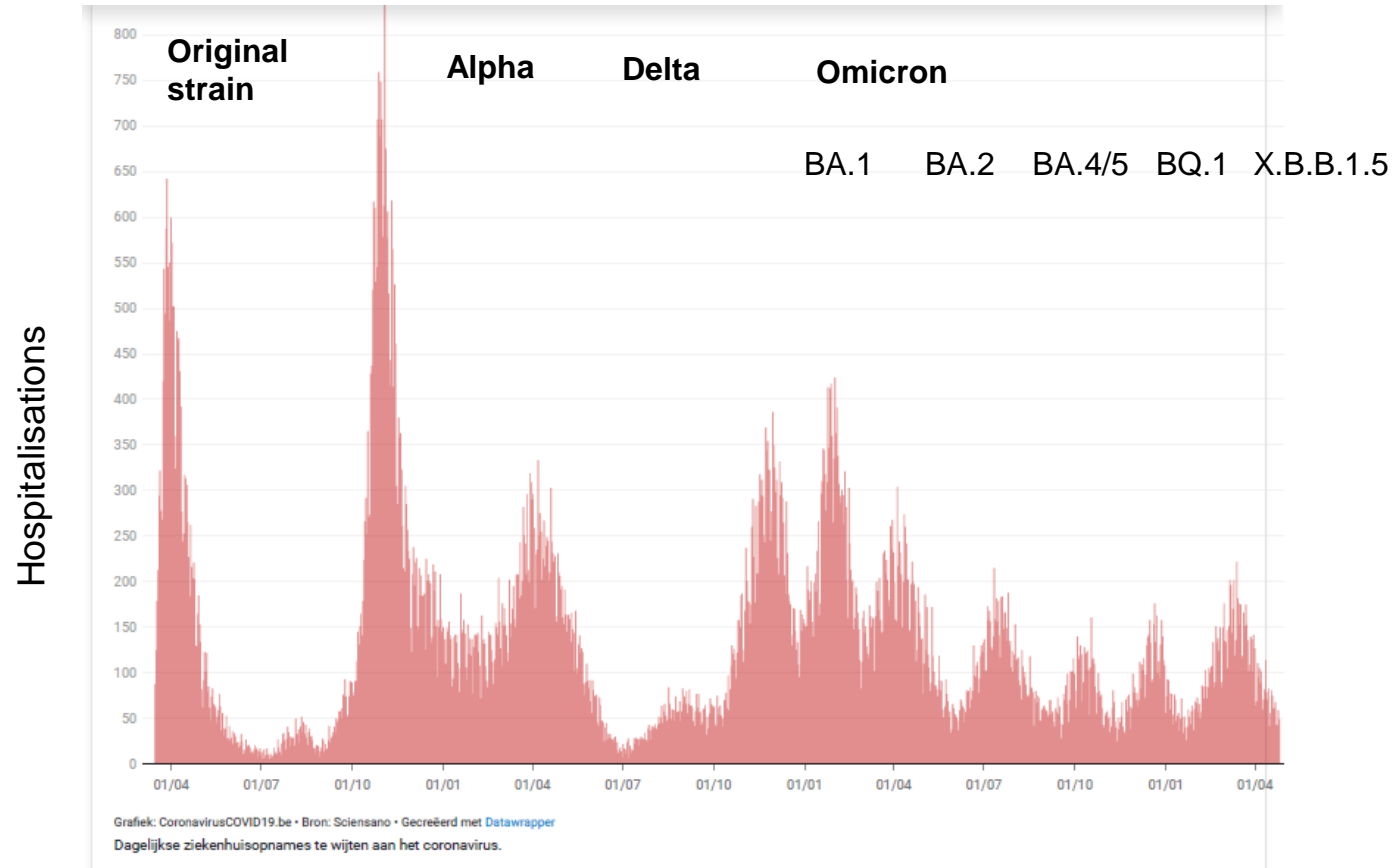
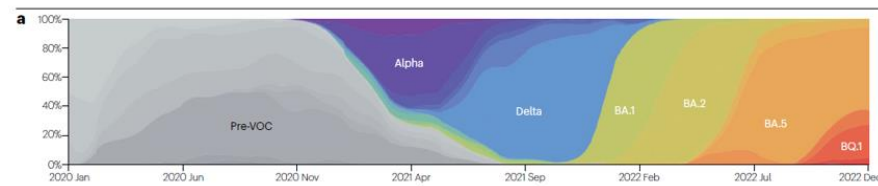
Nuvaxovid:

For people intolerant to mRNA vaccines

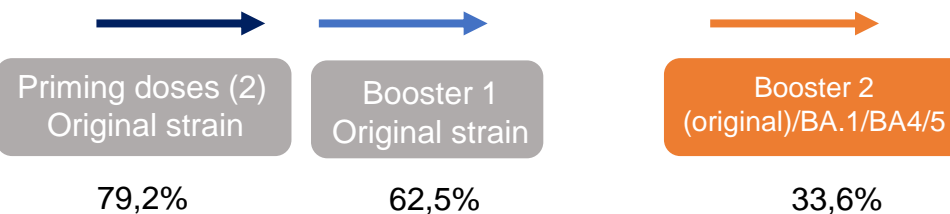
Vidprevryn Beta:

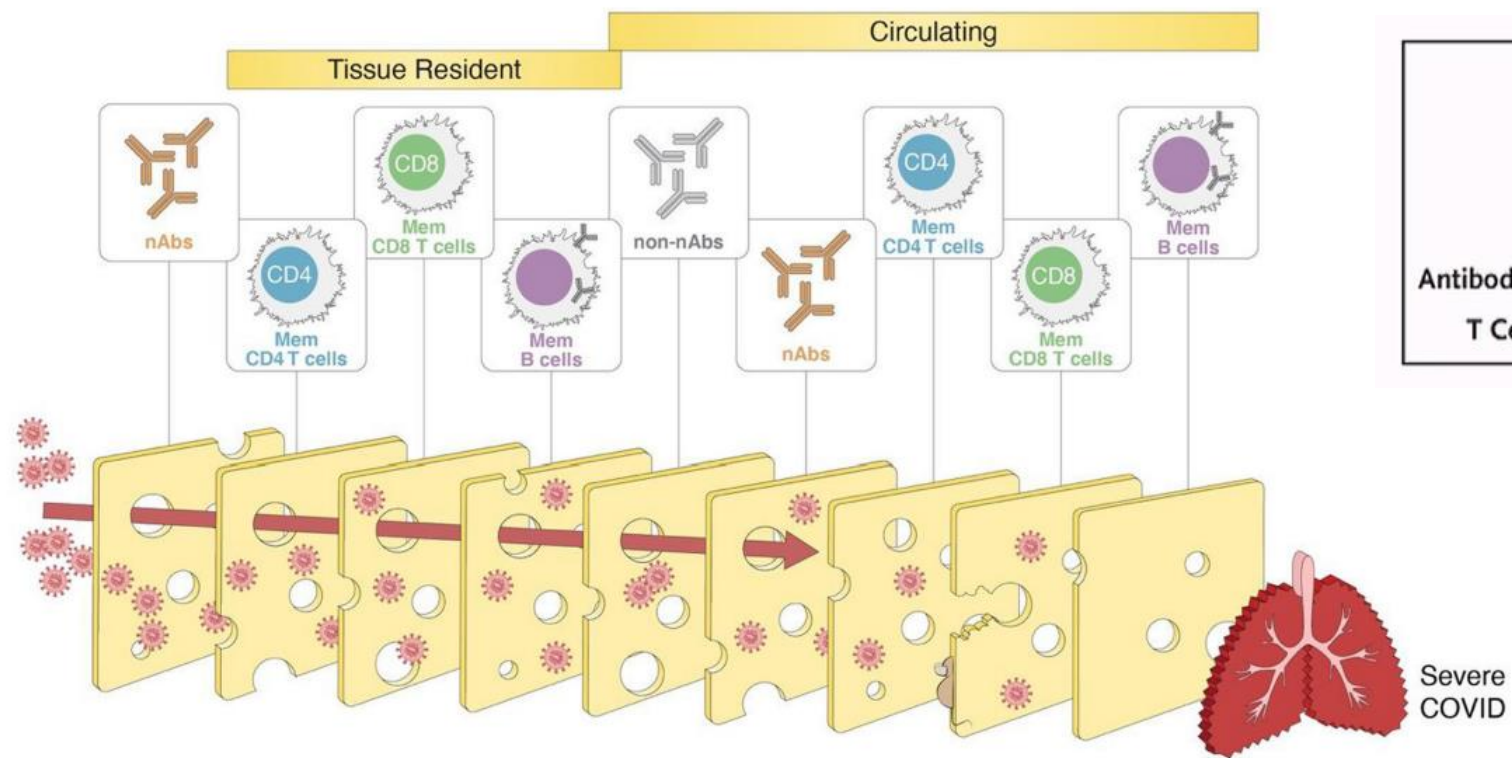
Only approved as booster vaccine

Vaccination campaigns and uptake rates in Belgium



Vaccination uptake in Belgium






COVID disease severity 				
	Asymptomatic Infection	Symptomatic Infection	Severe Disease, Hospitalization	Death
Antibodies	++++	+++	++	++
T Cells	+	++	++++	++++

FIGURE 3 Layered defenses against SARS-CoV-2, or the “Swiss cheese” model of immunity. Multiple types of adaptive immunity with diverse mechanisms and locations likely provide layers of defense against COVID-19. Conceptually, layered defenses are like a “Swiss cheese model”: even though each layer is imperfect, all together they make it highly unlikely that the pathogen breaches all of the layers of defense. Graphic inspired by the masking and public health layered defenses Swiss cheese model of Ian M. Mackay

Are booster vaccines still doing the job?

Study design:



- **Immunogenicity results:** neutralising antibodies (nAb) and binding IgG antibodies (ELISA)



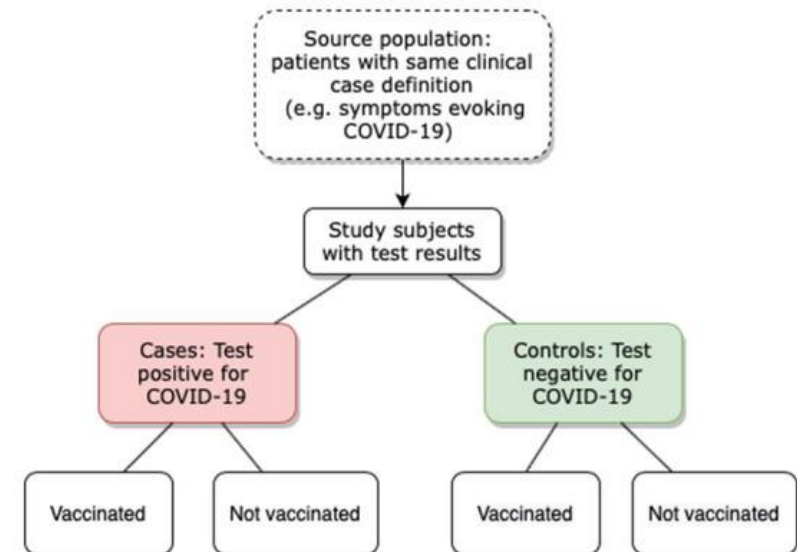
- **Vaccine efficacy:** Randomised controlled trials (RCT)



- **Vaccine effectiveness (VE):** Real world evidence (e.g. test-negative case-control study design)
 - $VE = 1 - \left(\frac{\text{odds of vaccination in a test positive case}}{\text{odds of vaccination in a test negative control}} \right)$

Outcomes:

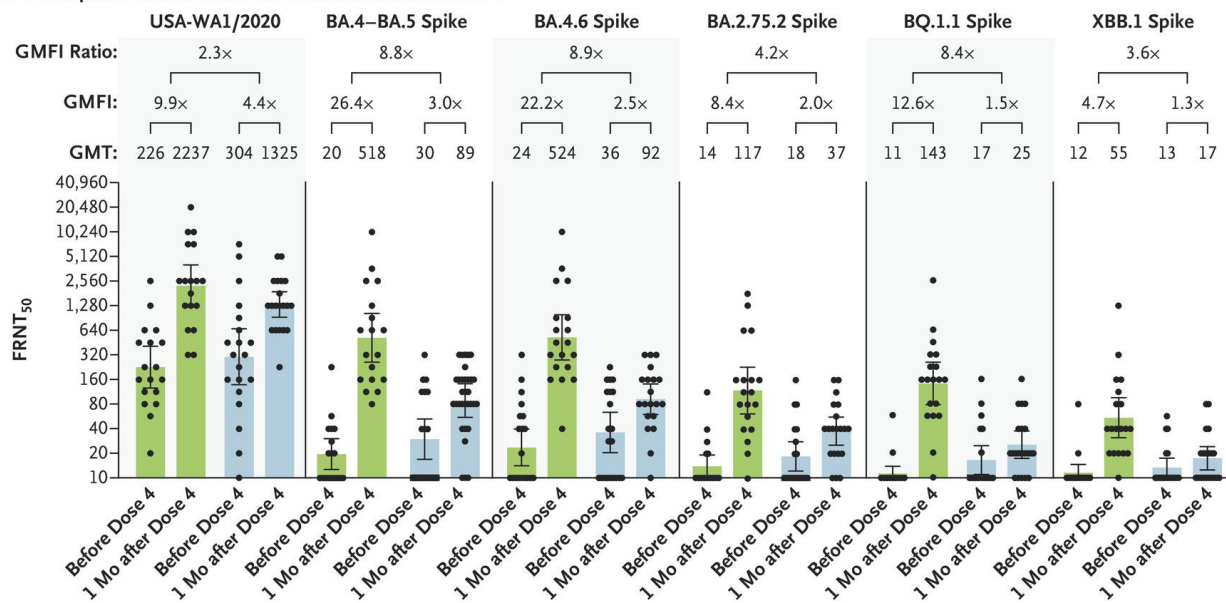
- Serious infections: hospitalisations, ICU admission
- Mild infections: not possible anymore since community testing has halted



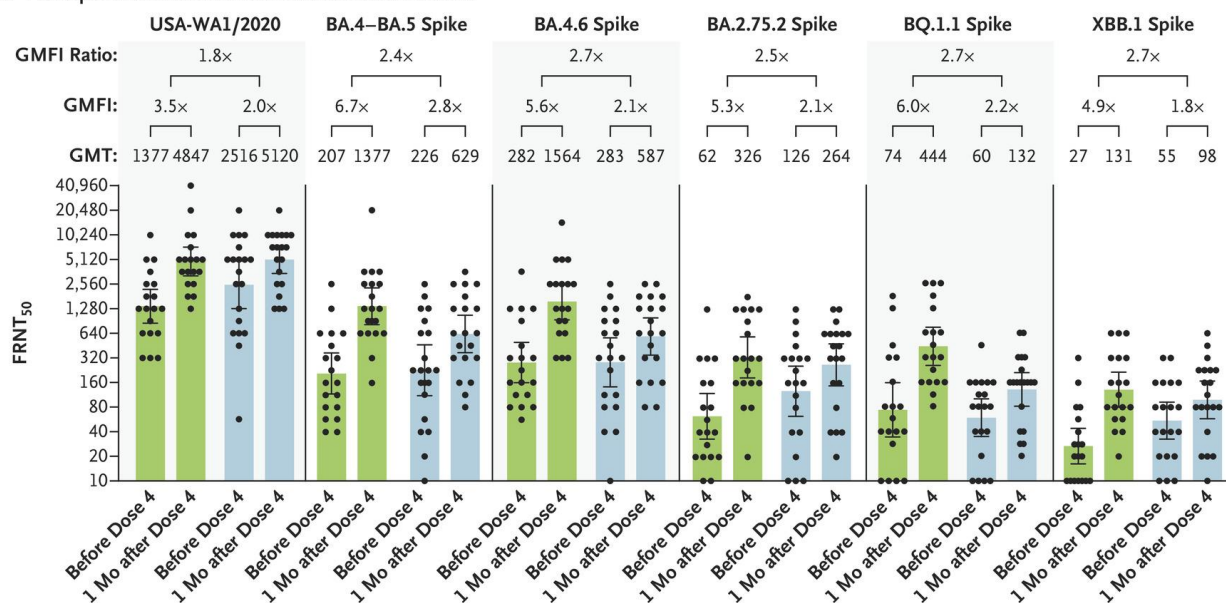


■ Bivalent vaccine ■ Monovalent vaccine

A Participants without SARS-CoV-2 Infection before Dose 4



B Participants with SARS-CoV-2 Infection before Dose 4



CORRESPONDENCE

Neutralization of BA.4–BA.5, BA.4.6, BA.2.75.2, BQ.1.1, and XBB.1 with Bivalent Vaccine

Design

- 3 doses of BNT162b2
- 4th dose: BNT162b2 (monovalent) vs original + BA.4/5 vaccine (bivalent)

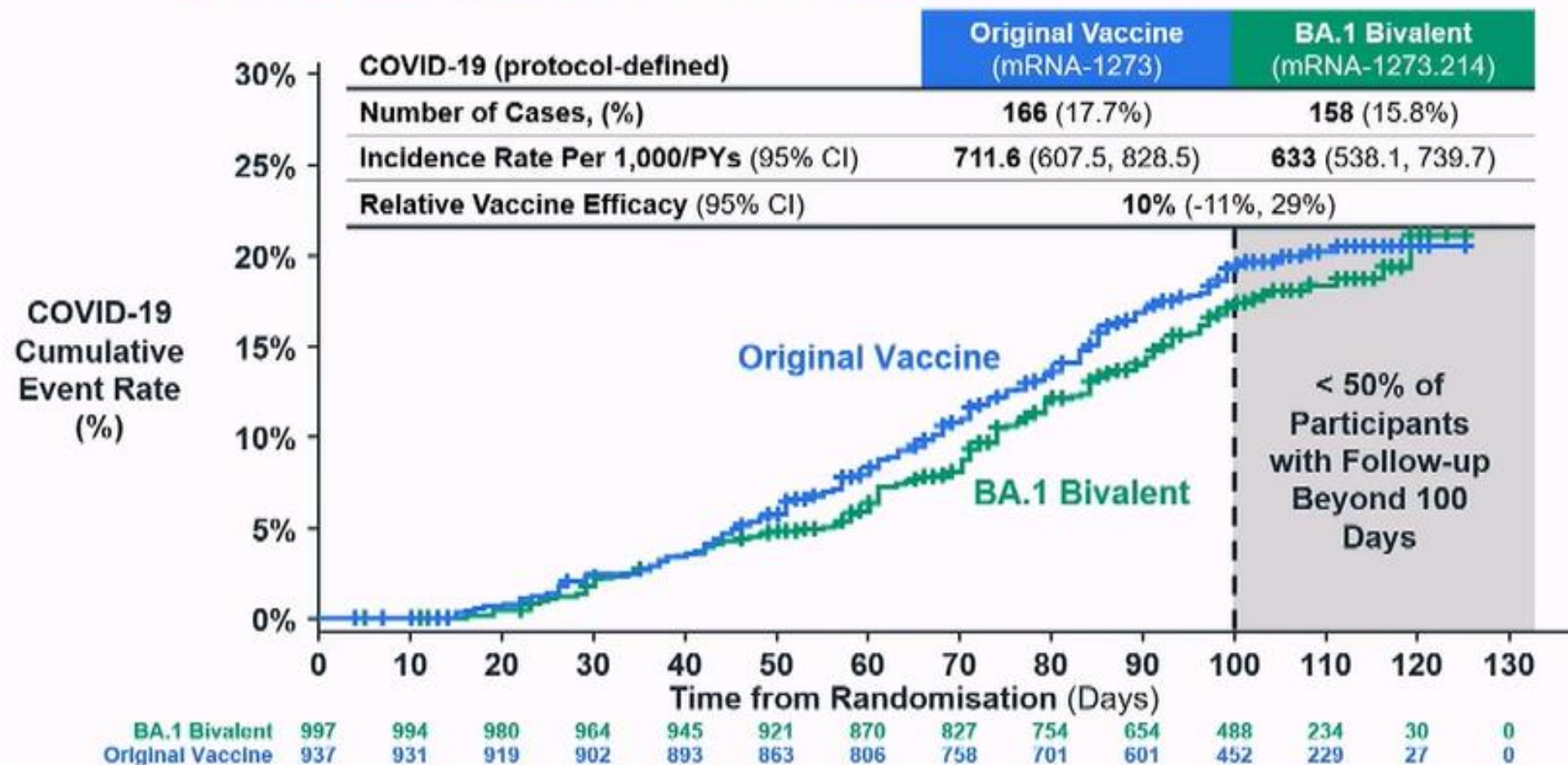
Results

- BA.5 bivalent vaccine elicits better neutralisation against the newly emerged omicron sublineages than the monovalent vaccine
- Infection history: higher and broader neutralisation against ongoing omicron sublineages after BA.5 bivalent booster
- Most recent variants (B.Q.1.1, XBB.1) exhibit greatest evasion against vaccine-elicited neutralization



Numerically Lower Incidence Rate of COVID-19 Following the Omicron BA.1 Bivalent Booster

Part 2: Primary Case Definition – Per Protocol Set for Efficacy

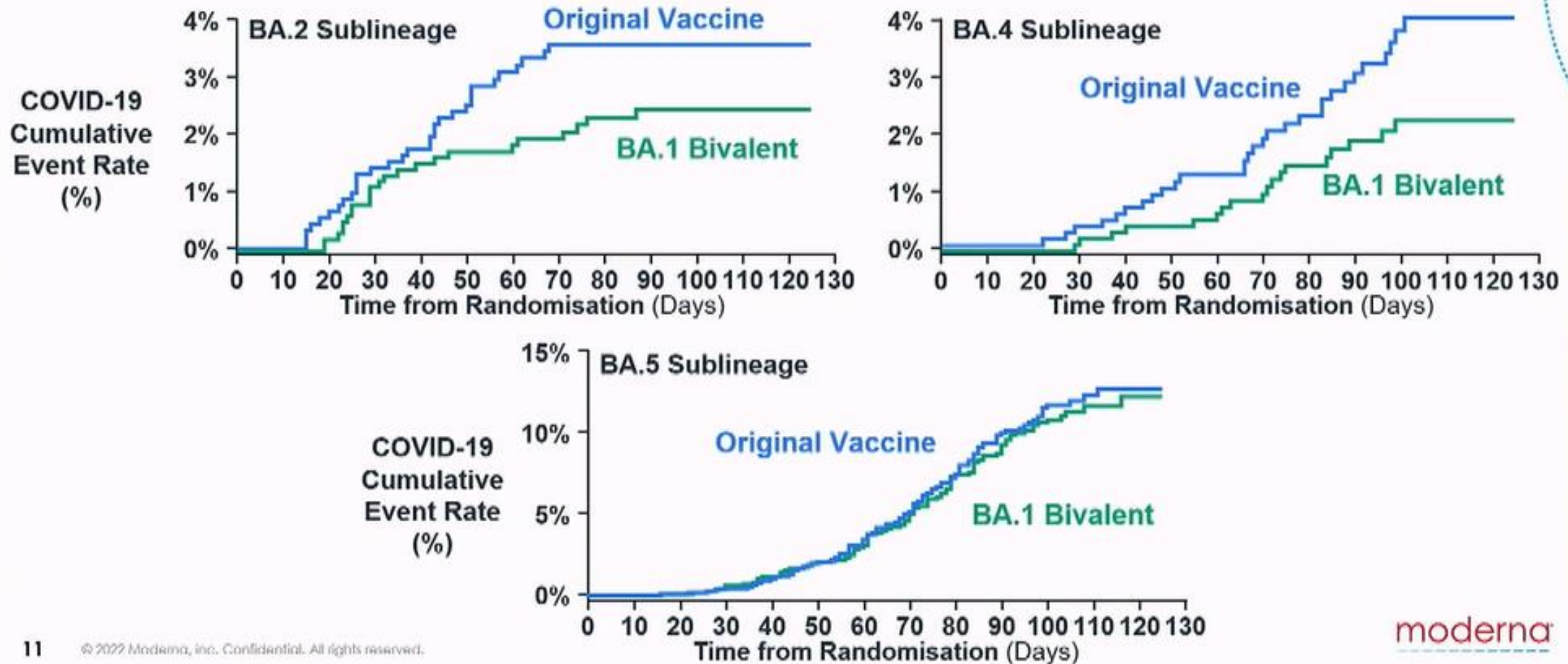


moderna

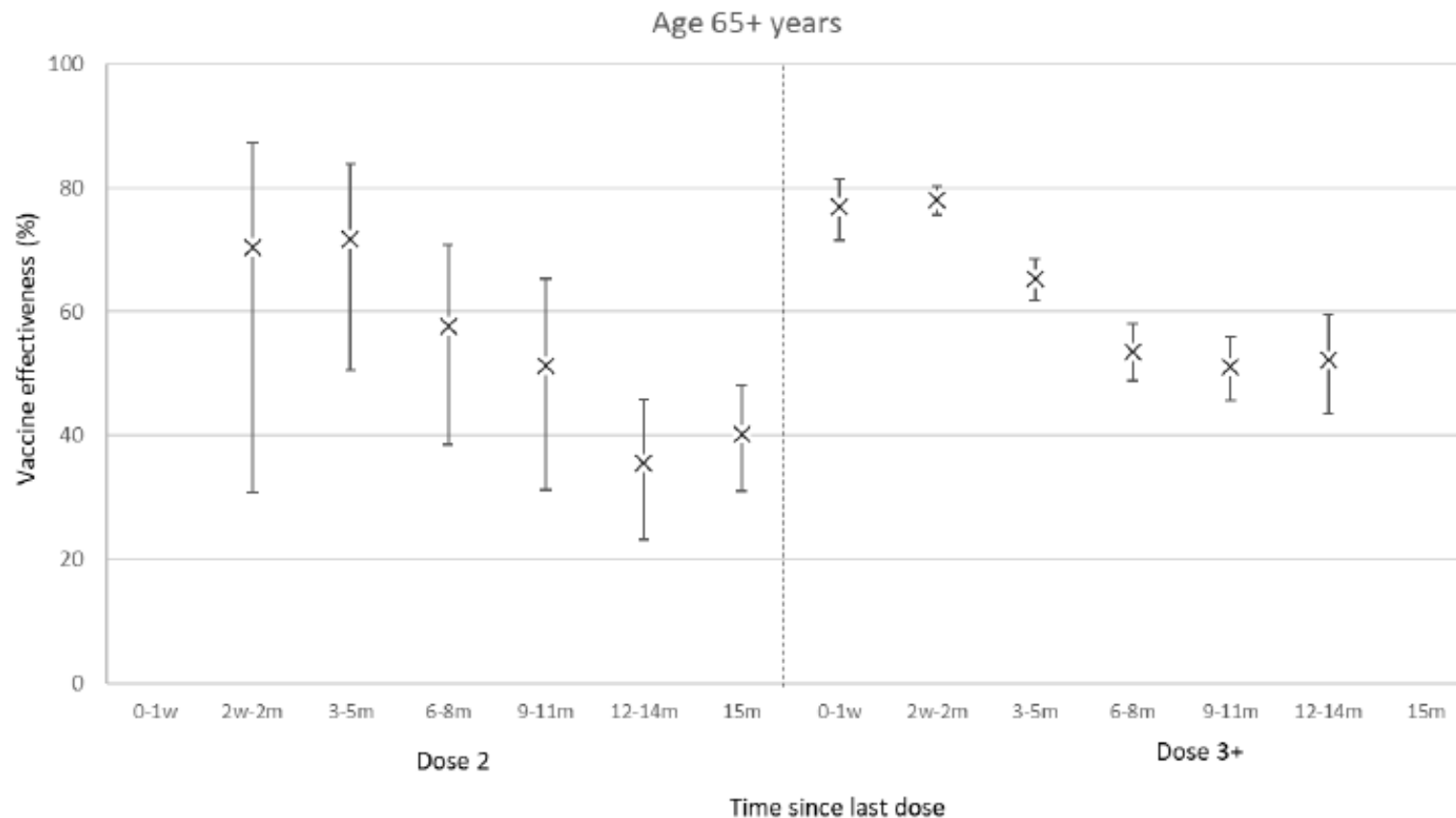


Variant-Containing Booster Vaccines Closely Matched to Circulating Variants May Provide Improved Benefit

Part 2: Primary Case Definition – Per Protocol Set for Efficacy – Exploratory Analysis



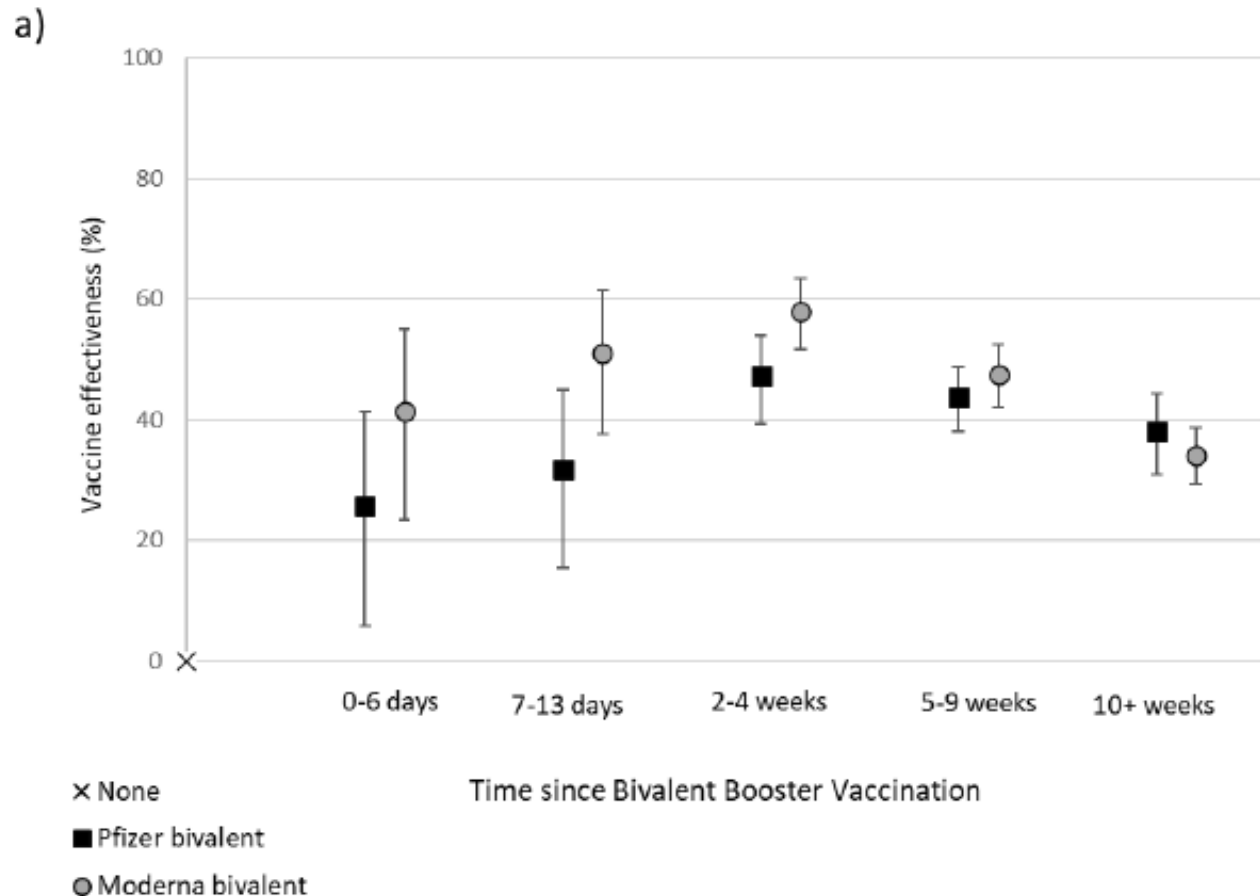
VE against COVID-19 hospitalization of monovalent vaccines



At least 3 doses of monovalent vaccine still provide (modest) protection (50%) against severe disease after 1 year

in a period of BA.5, BQ.1, CH.1.1. and XBB.1.5 circulation in the UK

iVE against COVID-19 hospitalization of BA.1 bivalent vaccine



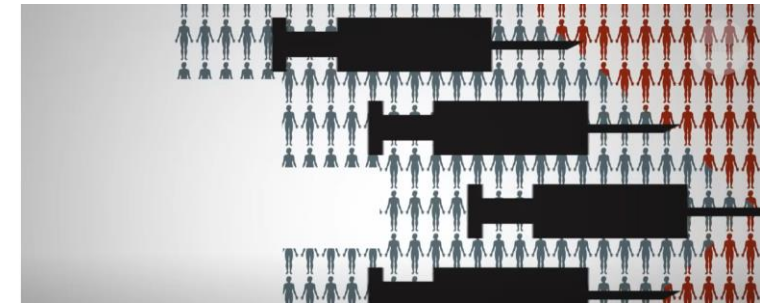
- Incremental vaccine effectiveness (iVE) of BA.1 bivalent booster versus comparator group who received 2 or 3 doses of monovalent vaccine (last dose > 6 months ago).
- A bivalent booster increases protection to appx. 75%
- Similar results for BA4/5 bivalent booster
- VE against newer omicron variants seem lower (BQ.1, XBB.1.5), low numbers

in a period of BA.5, BQ.1, CH.1.1. and XBB.1.5 circulation in the UK

3. How to prepare for the next respiratory season? A new booster shot needed?



Basic principles of the 2023 autumn COVID-19 booster campaign



- **Target:** optimizing personal protection to prevent severe COVID-19
- **Target groups:**
 - Older adults (60 or 65+)
 - Younger individuals with increased vulnerability (immunocompromised, chronic conditions of heart, lung, ...)
 - Health care workers
- Co-administration with **influenza vaccine** possible
- Administered by **GP and pharmacists** (not in vaccination centers)
- **Which vaccine?** mRNA vaccine (some subunit vaccines)
- Vaccine composition?

Is another vaccine update needed?

- All boosters boost protection against serious disease
- Neutralising antibody titers are higher when there is a close antigenic match between the vaccine strain and the circulating variants
- The most recent variants (X.B.B.1.5, 1.9, 1.16) display more immune evasion
- Since Feb 2022: >98% of genetic sequences are of the omicron lineage
→ do we still need the original strain?

→ Vaccine will probably be updated, strain selection expected to be communicated by FDA and EMA mid June 2023.



4. Novel COVID-19 vaccines on the horizon



2 minute read · April 11, 2023 8:37 PM GMT+2 · Last Updated 24 days ago



U.S. spending \$5 billion to speed up development of new COVID vaccines

Reuters



[1/2] Vials and syringes are seen in front of displayed U.S. flag in this illustration photo taken March 16, 2021. REUTERS/Dado Ruvic/Illustration

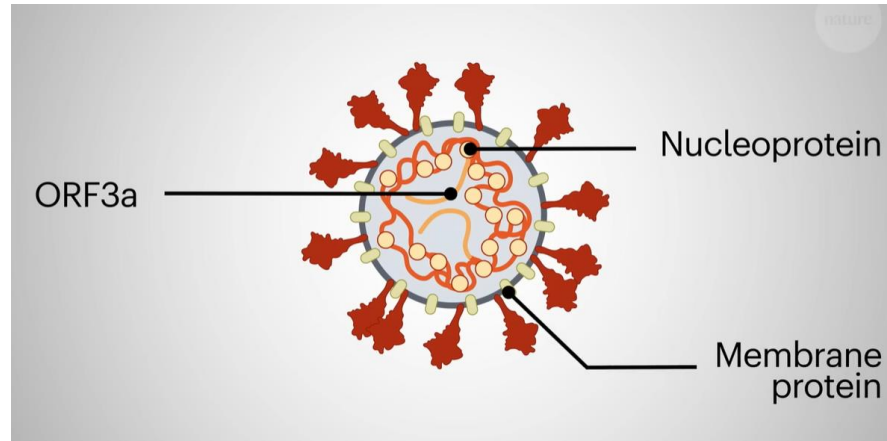
< 1 2 >

WASHINGTON, April 10 (Reuters) - The U.S. government is spending over \$5 billion on an effort to speed up the development of new COVID-19 vaccines and treatments, a Department of Health and Human Services (HHS) spokesperson and a Biden administration official said on Monday.

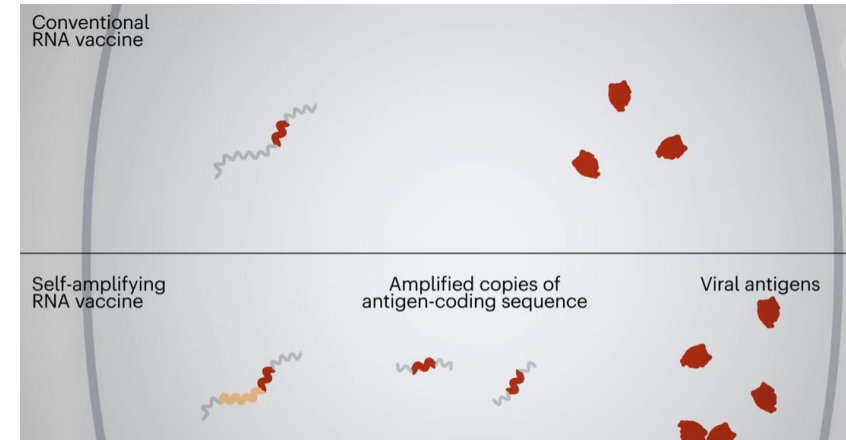
Project NextGen

- Need for novel vaccines which induce broader and longer lasting immunity - 'variant proof vaccines'
- Ideally, this vaccine would also protect against milder disease and transmission

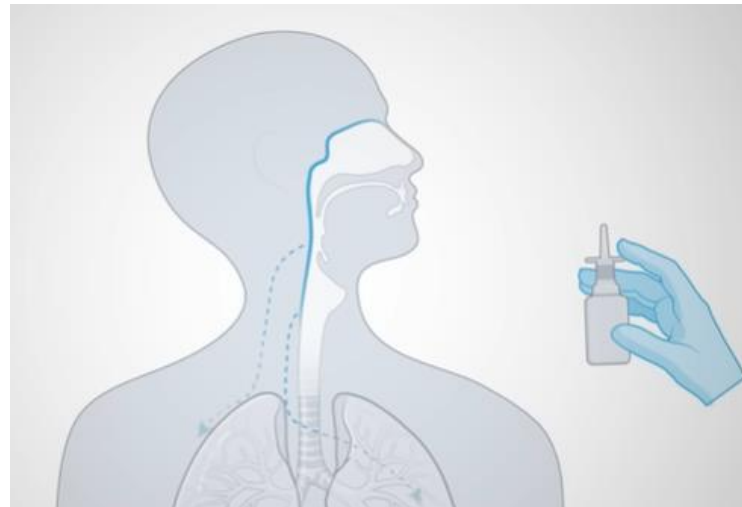
Novel approaches for next generation SARS-CoV-2 vaccines



T cell vaccines (conserved epitopes)



Self-amplifying mRNA vaccines (SAM)



Intranasal vaccines (mucosal immunity)

Conclusions

- Vaccines have had a major impact on the course of the pandemic
- Emerging variants of the SARS-CoV-2 virus have increased transmissibility and immune evasion capacities
- The currently available vaccines provide protection against serious disease, but protection wanes over time
- Focus of future booster campaigns is protection of vulnerable individuals
- Updating the vaccine might optimize protection
- **Continued surveillance (virus evolution, viral activity and vaccine effectiveness) remains of utmost importance.**

Conclusions

“While the emergency of COVID-19 may be over, COVID-19 is not. The biggest mistake we could make is to dismantle the surveillance systems that have been put in place.”

Maria Van Kerkhove, COVID-19 technical lead WHO.
ESPID Opening Lecture, 9 May 2023



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