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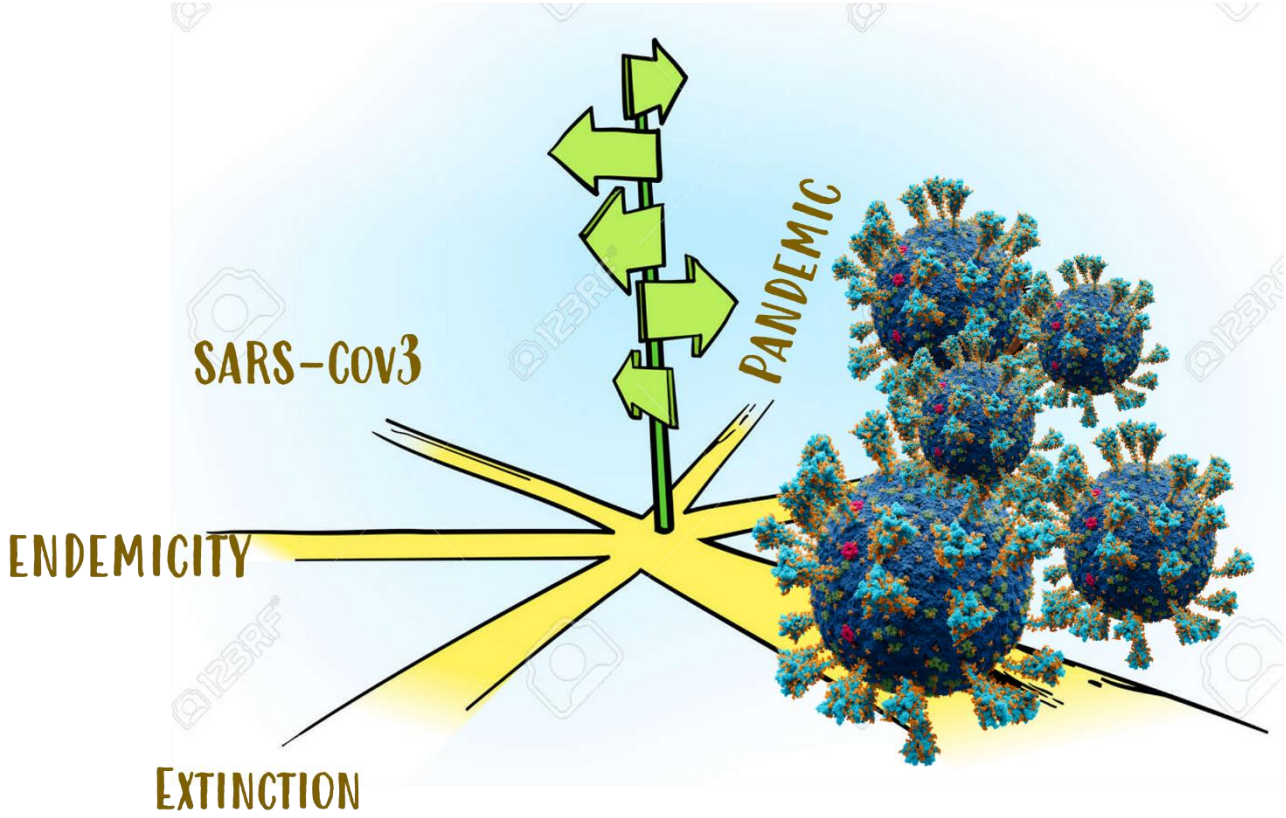
SARS-COV-2. ¿Y AHORA QUÉ?



¿Qué nos espera?

Dr. Jose Gómez Rial
Servicio de Inmunología
Hospital Clínico Universitario Santiago
Grupo de Investigación en Vacunas GENVIP
@gomez_rial5

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Declaración de potenciales conflictos de interés

Desarrollo parte de mi actividad profesional en el GRUPO DE INVESTIGACIÓN EN VACUNAS GENVIP y en la UNIDAD DE ENSAYOS CLINICOS DE VACUNAS PEDIATRICAS del HOSPITAL CLÍNICO UNIVERSITARIO DE SANTIAGO DE COMPOSTELA:

He recibido honorarios por conferencias de Pfizer, Moderna, AstraZeneca, GSK, Sanofi y MSD.

He recibido honorarios por asesoría científica de Pfizer, Moderna, GSK, Sanofi y MSD.

He recibido ayudas de investigación de Sanofi, GSK, MSD, Pfizer y Novartis.

Participo en ensayos clínicos de vacunas de Sanofi, MSD, Pfizer, Roche, Medimmune, Novartis, Ablynx, Janssen y GSK.

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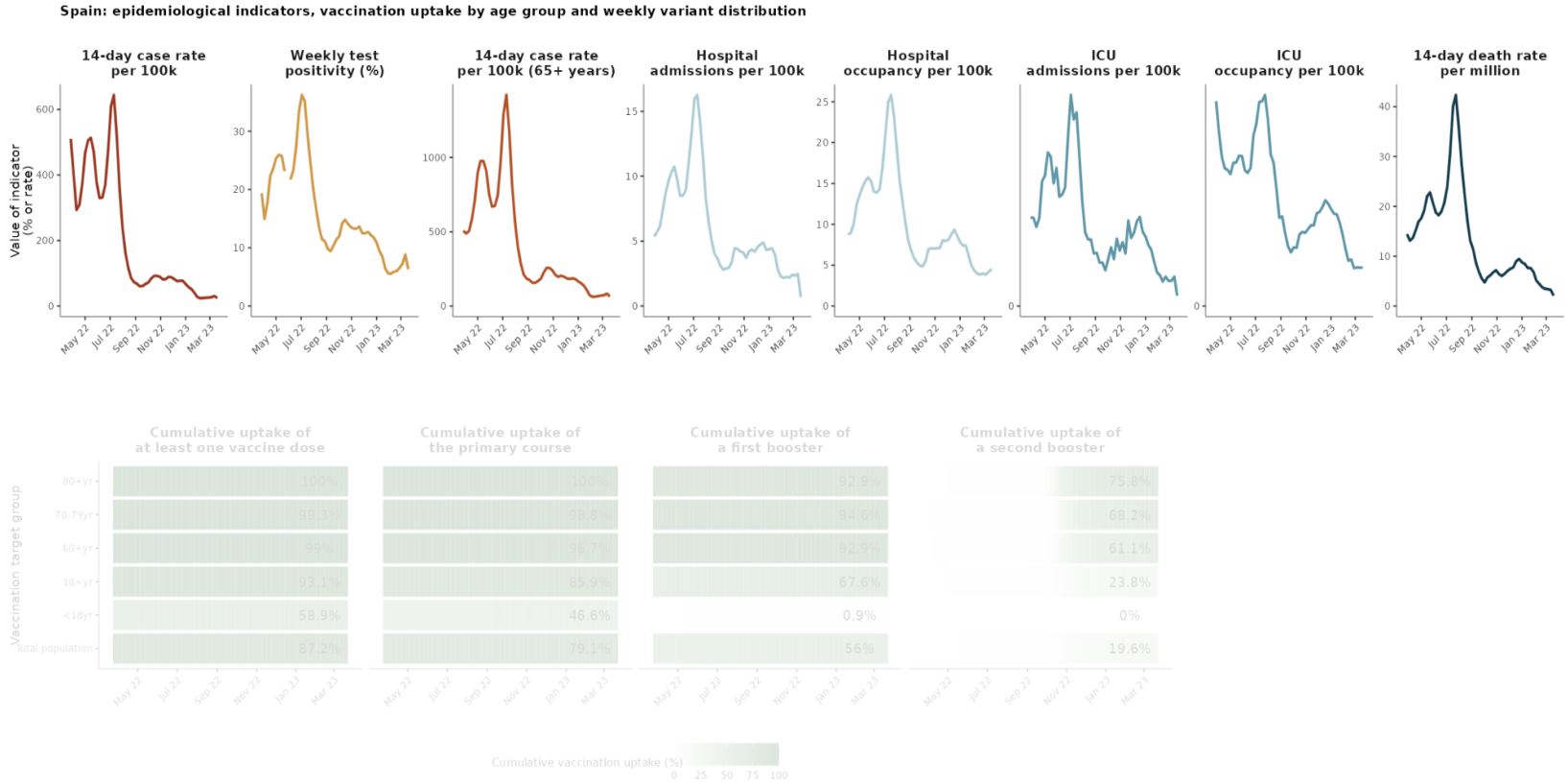
Country overview report: week 11 2023

Produced on 24 March 2023 at 11.30

GENVIP fidis

Spain

Indicator summary | Cases, deaths and testing | Hospital and ICU | Vaccine uptake | LTCF surveillance | Data completeness



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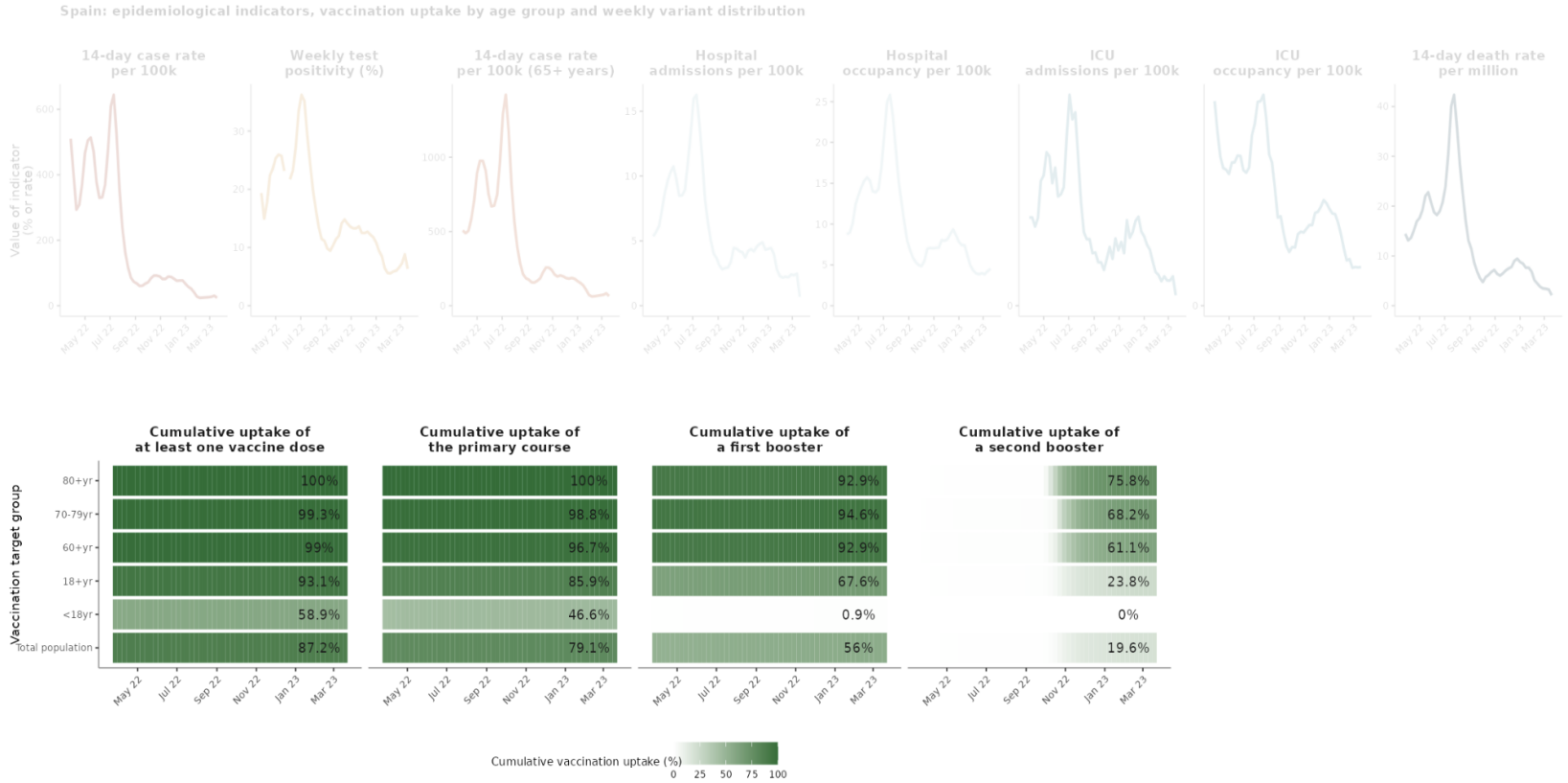

Source: ECDC database compiled from public online sources: Hospital occupancy:
GISAID: Variants:
TESSy COVID-19: 14-day case notification rate, Test positivity (%), 14-day case rate, Hospital admissions, ICU admissions, ICU occupancy, 14-day death rate, Vaccination uptake

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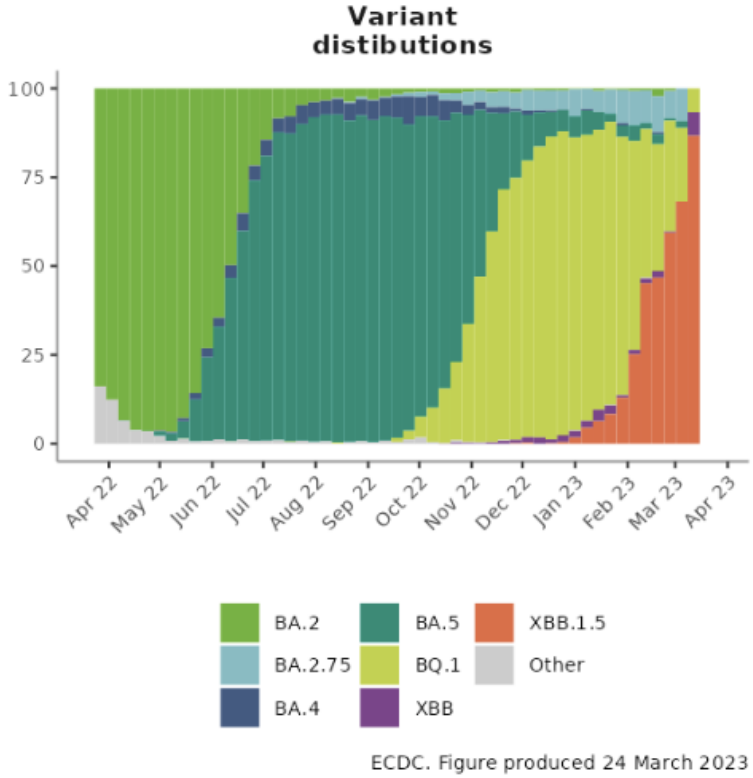

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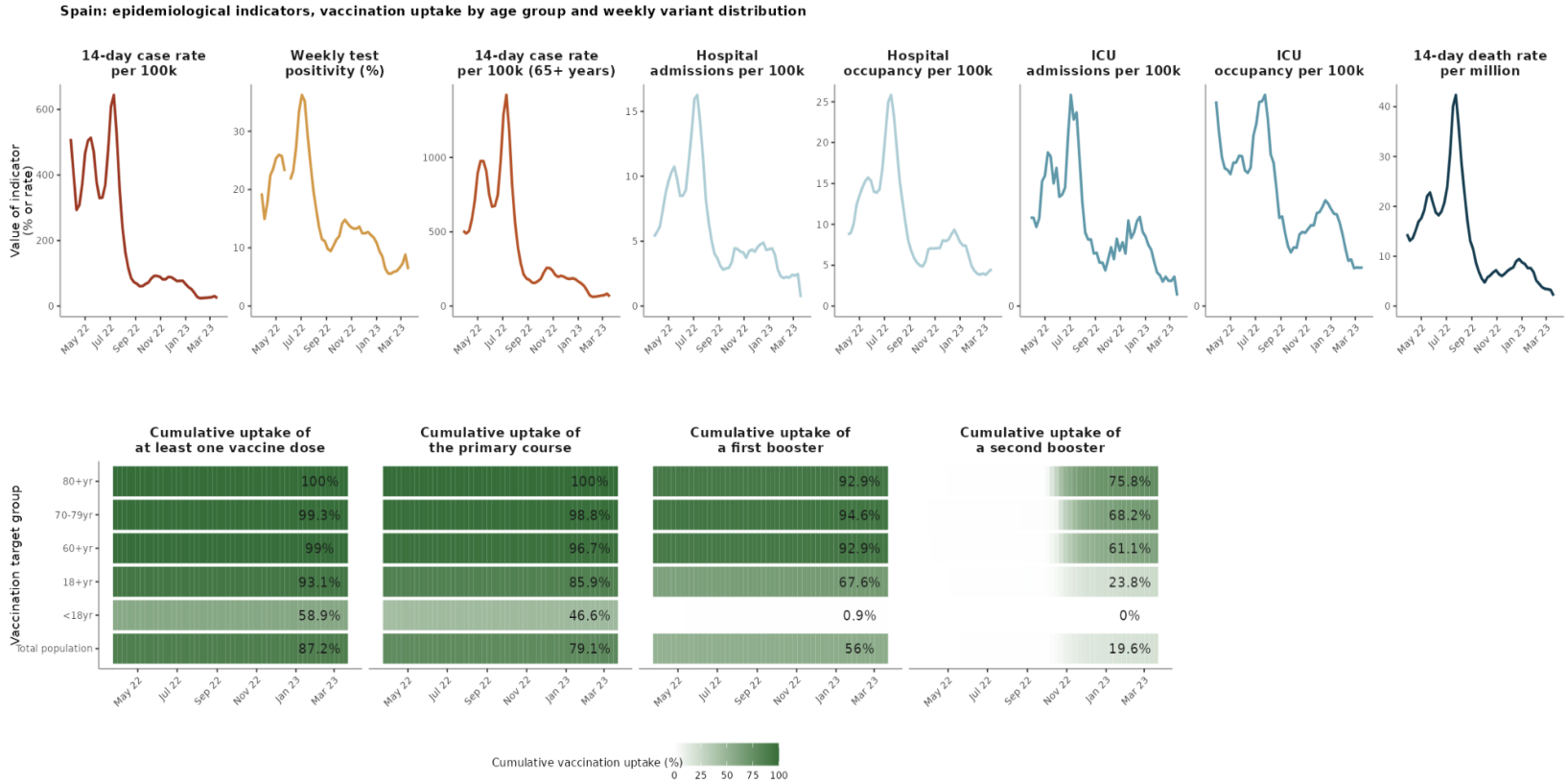

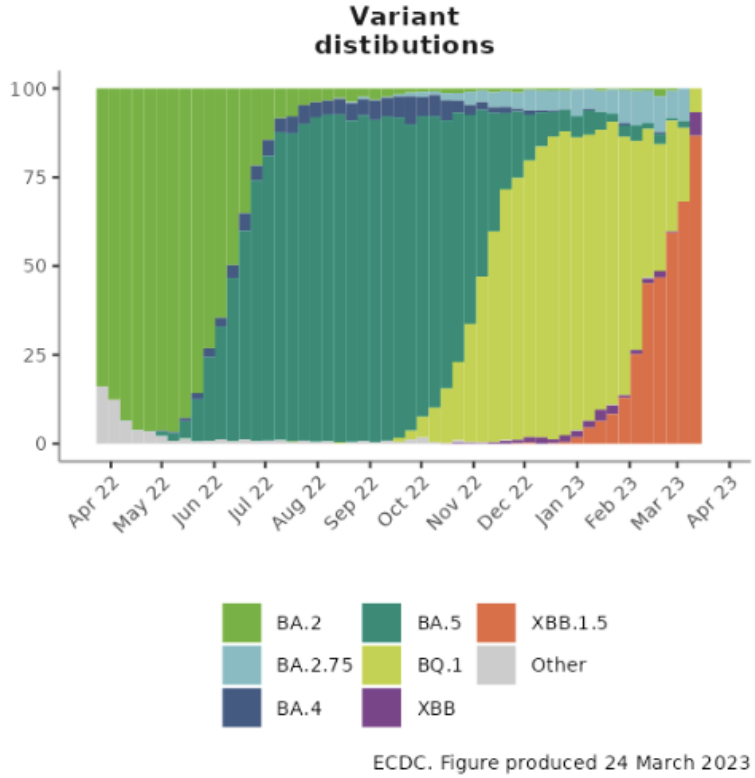

ECDC. Figure produced 24 March 2023

Source: ECDC database compiled from public online sources: Hospital occupancy:
GISAID: Variants:
TESSy COVID-19: 14-day case notification rate, Test positivity (%), 14-day case rate, Hospital admissions, ICU admissions, ICU occupancy, 14-day death rate, Vaccination uptake

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Country overview report: week 11 2023

Produced on 24 March 2023 at 11.30

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Distribution of variants of concern (VOCs) and variants of interest (VOIs)

- Among the seven countries with an adequate volume of sequencing or genotyping for weeks 9–10 (27 February to 12 March 2023), the estimated distribution of variants of concern (VOC) or of interest (VOI) was 54.4% (49.6–66.4% from six countries) for XBB.1.5, 16.8% (5.9–51.7% from seven countries) for BA.2.75, 14.3% (10.5–20.3% from five countries) for XBB, 11.7% (10.5–19.9% from six countries) for BQ.1, 1.6% (1.1–45.5% from seven countries) for BA.5, 1.1% (0.8–2.8% from three countries) for BA.2 and 0.2% (0.1–0.8%, 6 detections from three countries) for BA.4.

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Country overview report: week 11 2023

Produced on 24 March 2023 at 11.15

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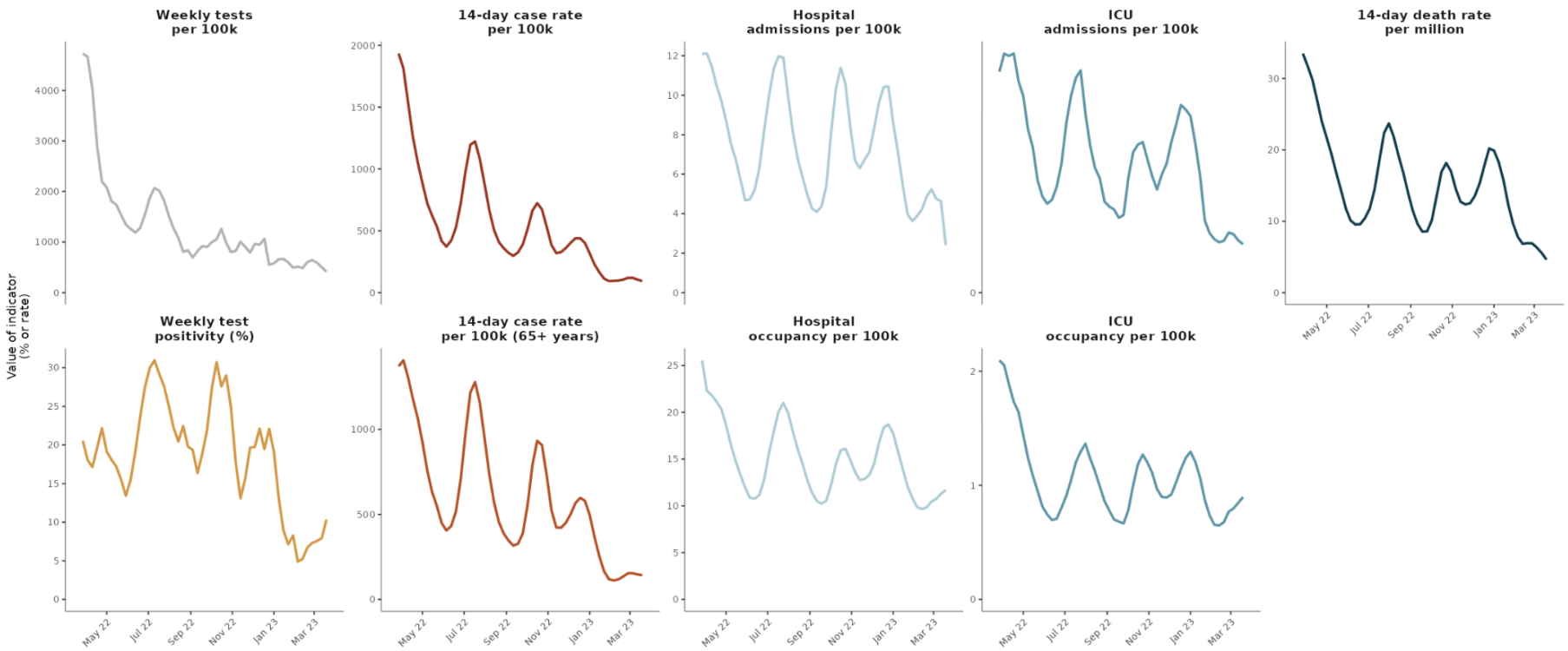
Summary table | **Indicator summary** | Cases, deaths and testing | Hospital and ICU | Recent trends by indicator and country

EU/EEA: epidemiological indicators



ECDC. Figure produced 24 March 2023
Pooled data from Member States (n = 14 for week 11): Hospital occupancy, ICU admissions;
Pooled data from Member States (n = 15 for week 11): ICU occupancy;
Pooled data from Member States (n = 16 for week 11): Hospital admissions;
Pooled data from Member States (n = 26 for week 11): Tests, Test positivity (%);
TESSy COVID-19: 14-day case notification rate, 14-day death rate;
TESSy COVID-19 (n = 27 for week 11): 14-day case rate

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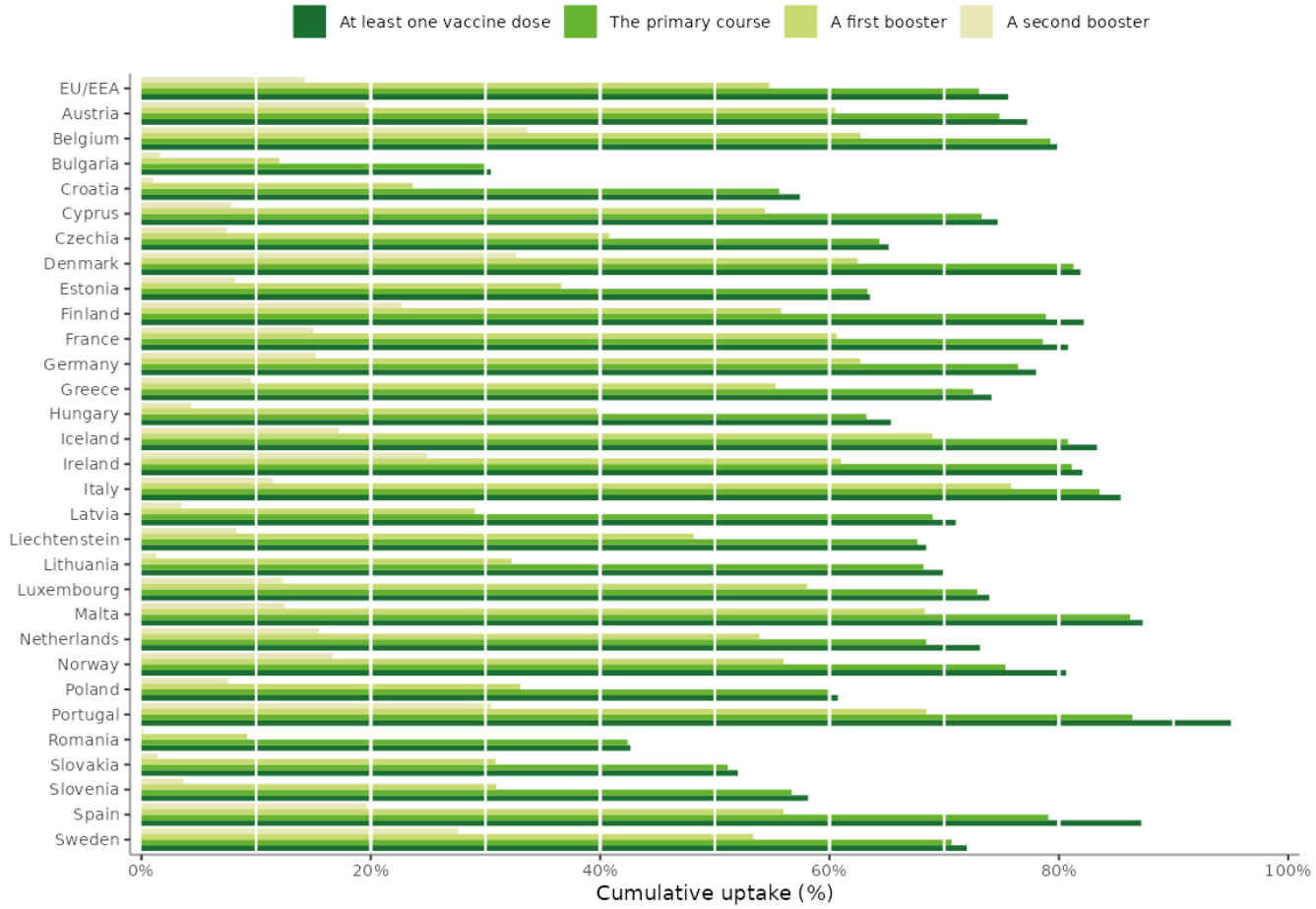
Cumulative vaccine uptake among the total population, week 11 2023

EU/EEA values based on pooled data from 30 countries reporting at least one dose administered and with available population data for the target group



Country overview report: week 11 2023

Target group	Indicator	Cumulative uptake (%)	Country range (%)	Number of countries
The total population	At least one vaccine dose	75.6	30.5 - 95.0	30
The total population	The primary course	73.0	30.1 - 86.4	30
The total population	A first booster	54.7	9.2 - 75.8	30
The total population	A second booster	14.2	0.2 - 33.6	30
18+yr	At least one vaccine dose	84.8	36.3 - 100.0	30
18+yr	The primary course	82.4	35.8 - 96.4	30
18+yr	A first booster	65.4	11.3 - 87.1	30
18+yr	A second booster	17.3	0.2 - 42.0	30
<18yr	At least one vaccine dose	26.7	2.4 - 58.9	30
<18yr	The primary course	24.2	2.3 - 50.1	30
<18yr	A first booster	1.8	0.2 - 20.4	29
60+yr	At least one vaccine dose	92.4	38.9 - 100.0	30
60+yr	The primary course	91.2	38.5 - 100.0	30
60+yr	A first booster	84.9	13.3 - 100.0	30
60+yr	A second booster	35.5	0.4 - 86.7	30
Healthcare workers	At least one vaccine dose	95.3	29.4 - 100.0	16
Healthcare workers	The primary course	90.4	29.0 - 100.0	16
Healthcare workers	A first booster	67.0	6.0 - 100.0	14
Healthcare workers	A second booster	11.9	1.1 - 49.7	13

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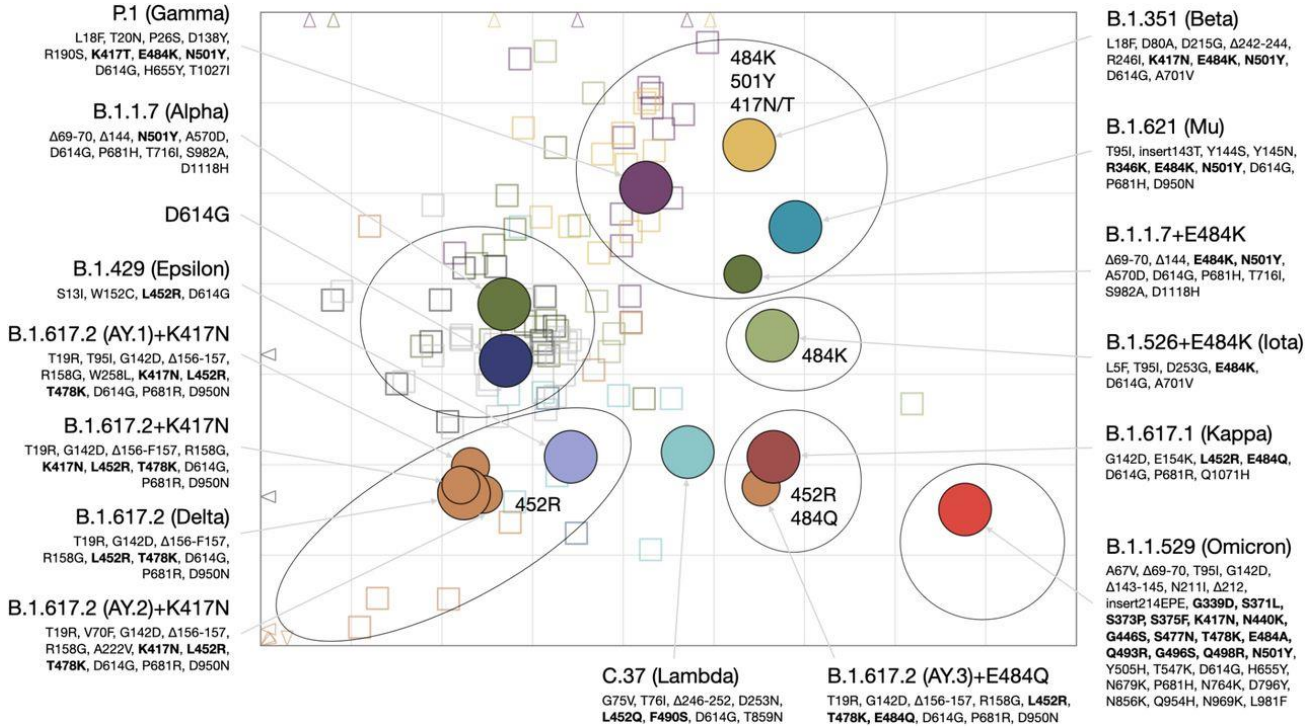
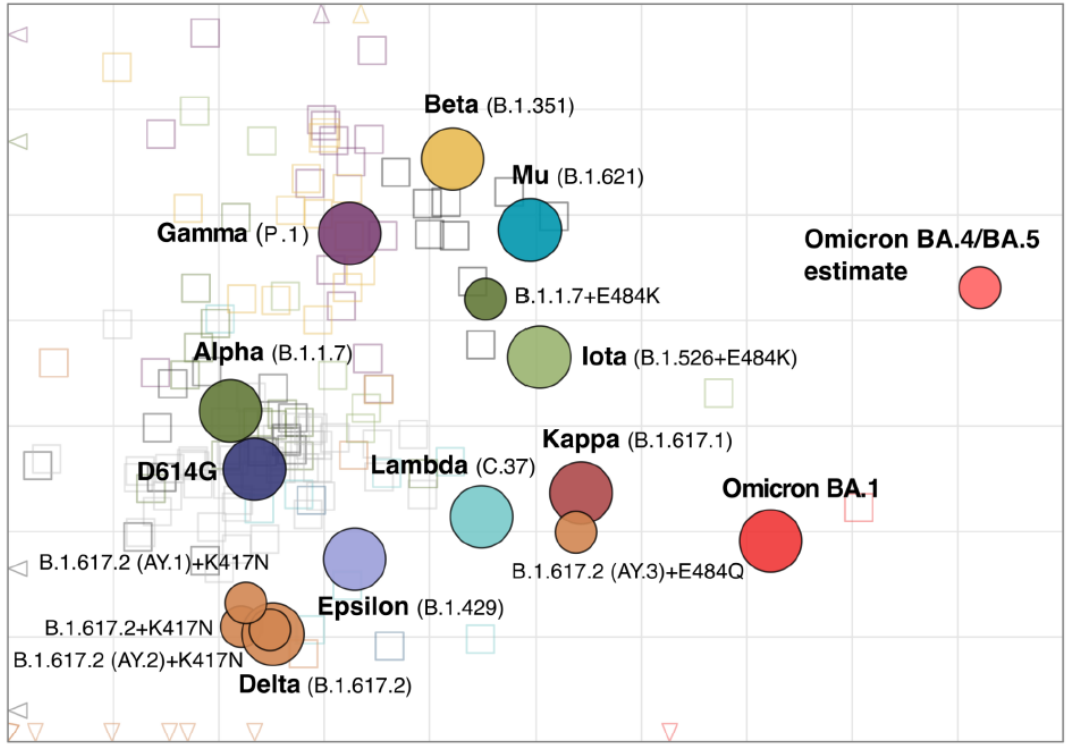
How much is COVID-19 mutating now?

Mapping SARS-CoV-2 antigenic relationships and serological responses

https://doi.org/10.1101/2022.01.28.477987;





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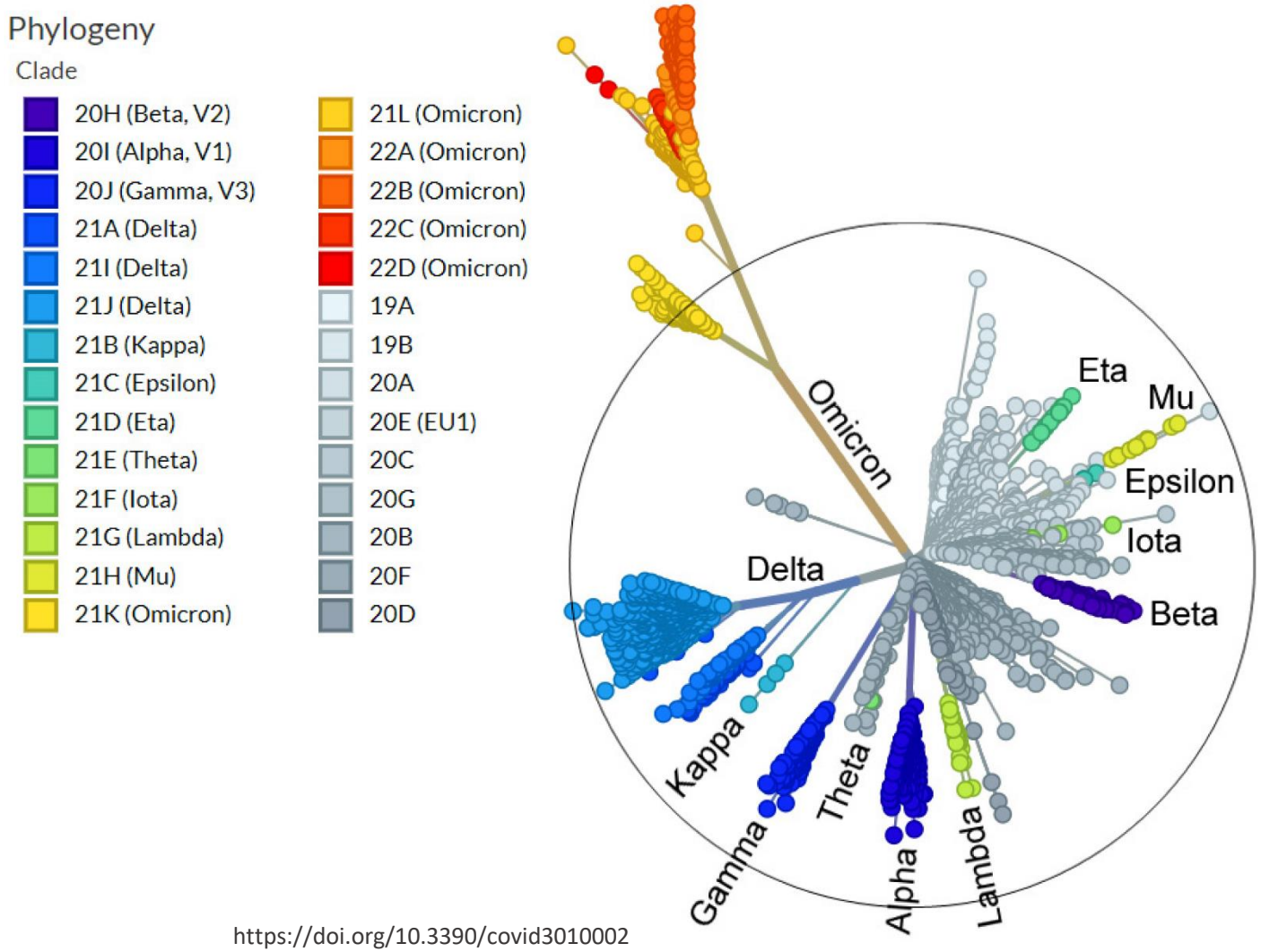
COVID

MDPI

Article

The Difference in Wave Dynamics between SARS-CoV-2 Pre-Omicron and Omicron Variant Waves

Franz Konstantin Fuss [1,*], Yehuda Weizman [1,2] and Adin Ming Tan [1,3]



https://doi.org/10.3390/covid3010002

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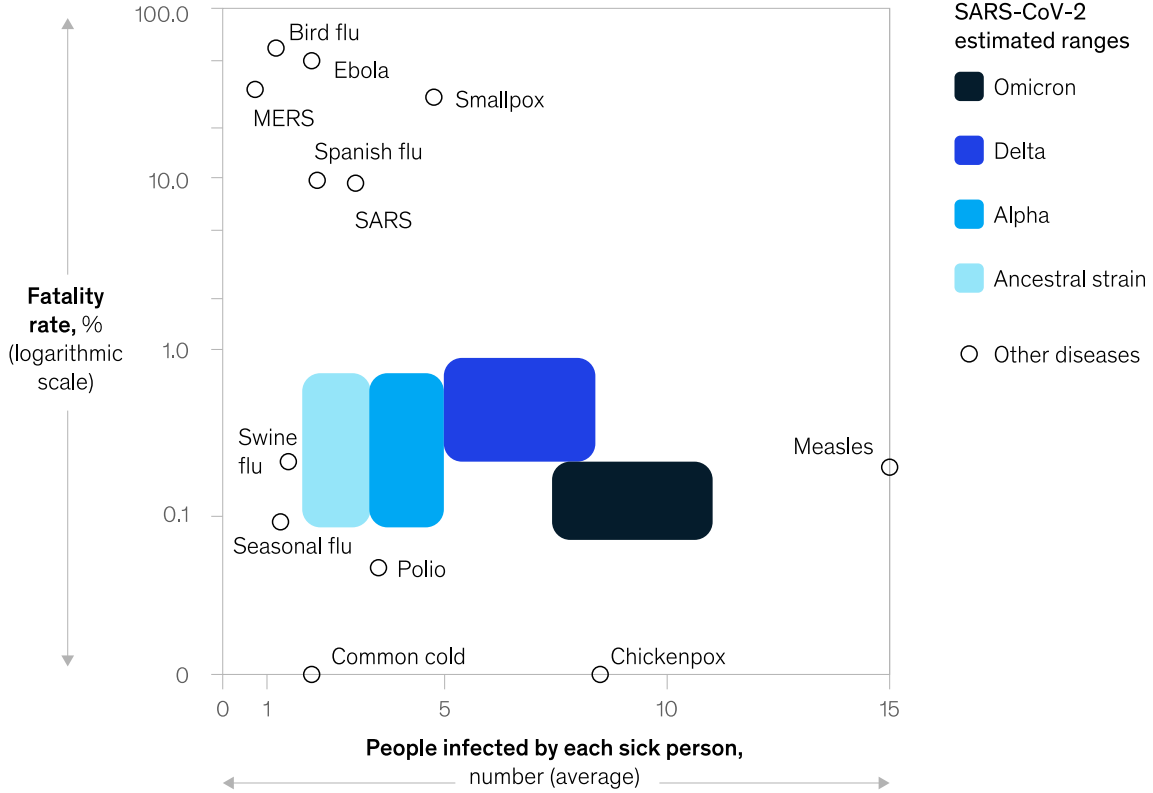
SARS-Cov2 Variants: Fatality rate and transmission numbers

Omicron is more infectious than other common viruses, and less fatal than Delta.

Disease fatality and infection rates[1]



[1]Average case-fatality rates and transmission numbers are shown. Estimates of case-fatality rates can vary. The preliminary estimates for the new coronavirus are shown in the SARS-CoV-2 ancestral-strain area.
Source: *New York Times*, Ancestral, Alpha, Delta, Omicron CFR, Omicron RO

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Cell

Article

Alarming antibody evasion properties of rising SARS-CoV-2 BQ and XBB subvariants

Authors

Qian Wang, Sho Iketani, Zhiteng Li, ..., Aubree Gordon, Lihong Liu, David D. Ho

Correspondence

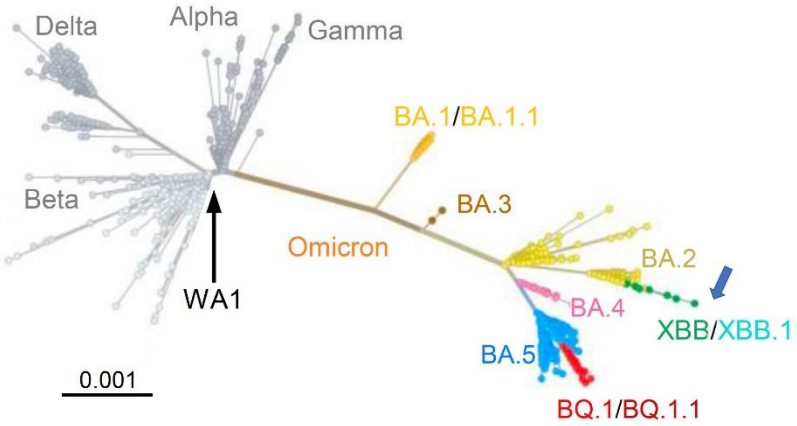
ll3411@cumc.columbia.edu (L.L.), dh2994@cumc.columbia.edu (D.D.H.)

In brief

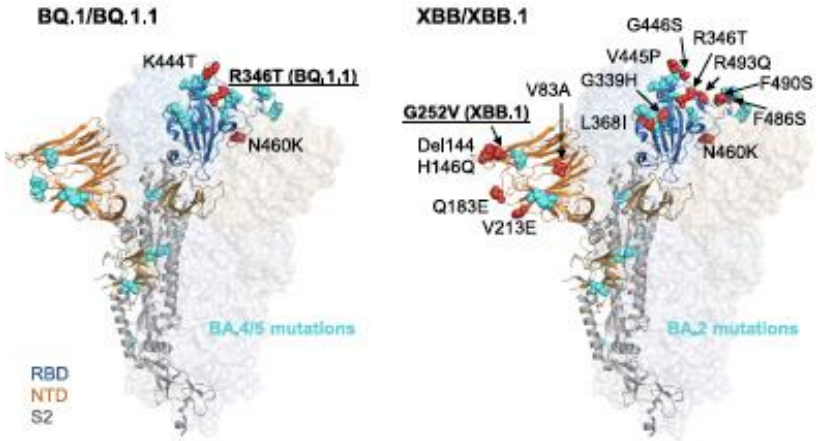
Recent BQ and XBB subvariants of SARS-CoV-2 demonstrate dramatically increased ability to evade neutralizing antibodies, even those from people who received the bivalent mRNA booster or who are immunized and had previous breakthrough Omicron infection. Additionally, both BQ and XBB are completely resistant to bebtelovimab, meaning there are now no clinically authorized therapeutic antibodies effective against these circulating variants.

Highlights

- BQ.1, BQ.1.1, XBB, and XBB.1 are the most resistant SARS-CoV-2 variants to date
- Serum neutralization was markedly reduced, including with the bivalent booster
- All clinical monoclonal antibodies were rendered inactive against these variants
- The ACE2 affinity of these variants were similar to their parental strains



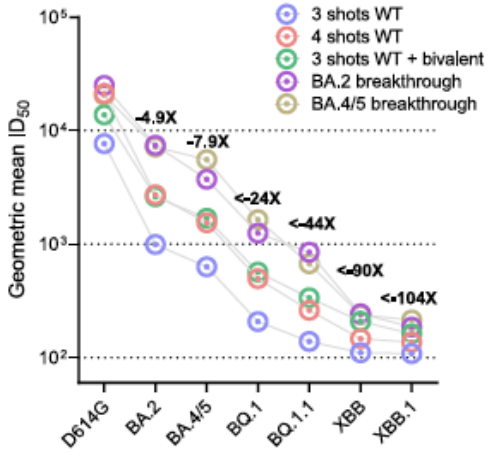
Key mutations found in BQ and XBB subvariants



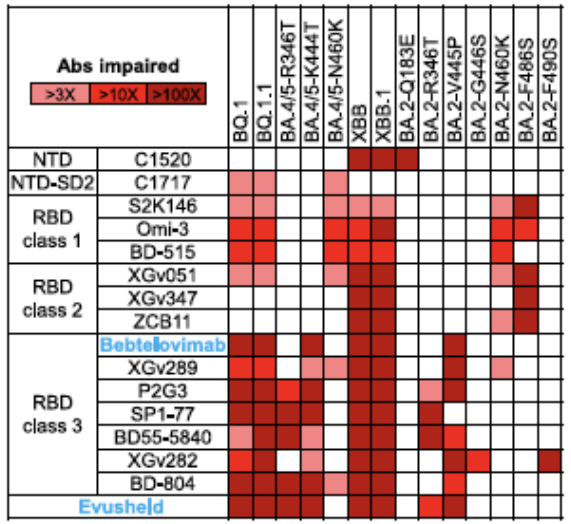
Viral receptor affinity

Subvariants	K_D tested by SPR (nM)
BA.4/5	0.61
BQ.1	0.62
BQ.1.1	0.56
BA.2	0.95
XBB	2.00
XBB.1	2.06

Neutralization by sera from 5 cohorts



Neutralization by monoclonal Abs



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Cell

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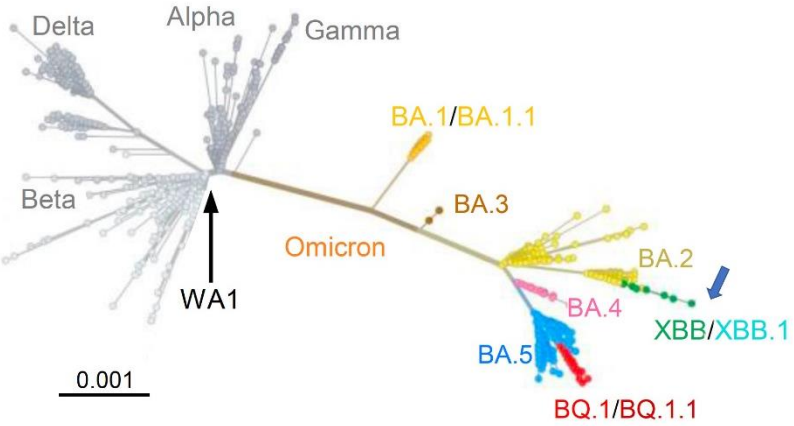

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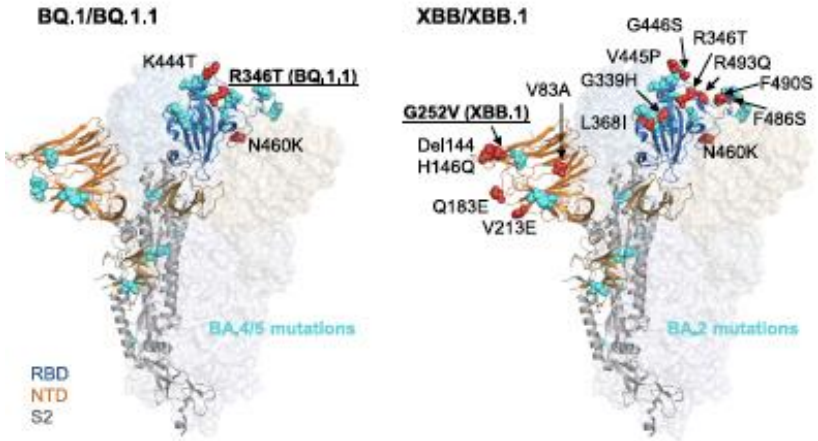

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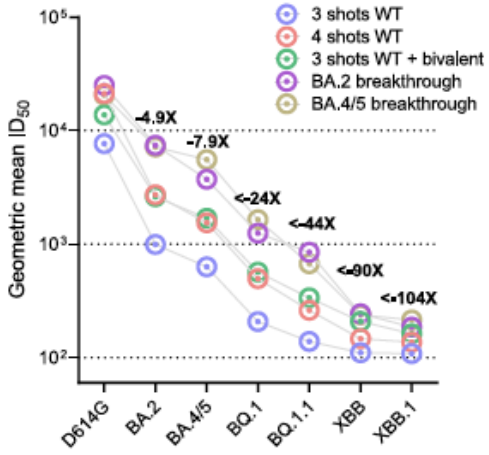
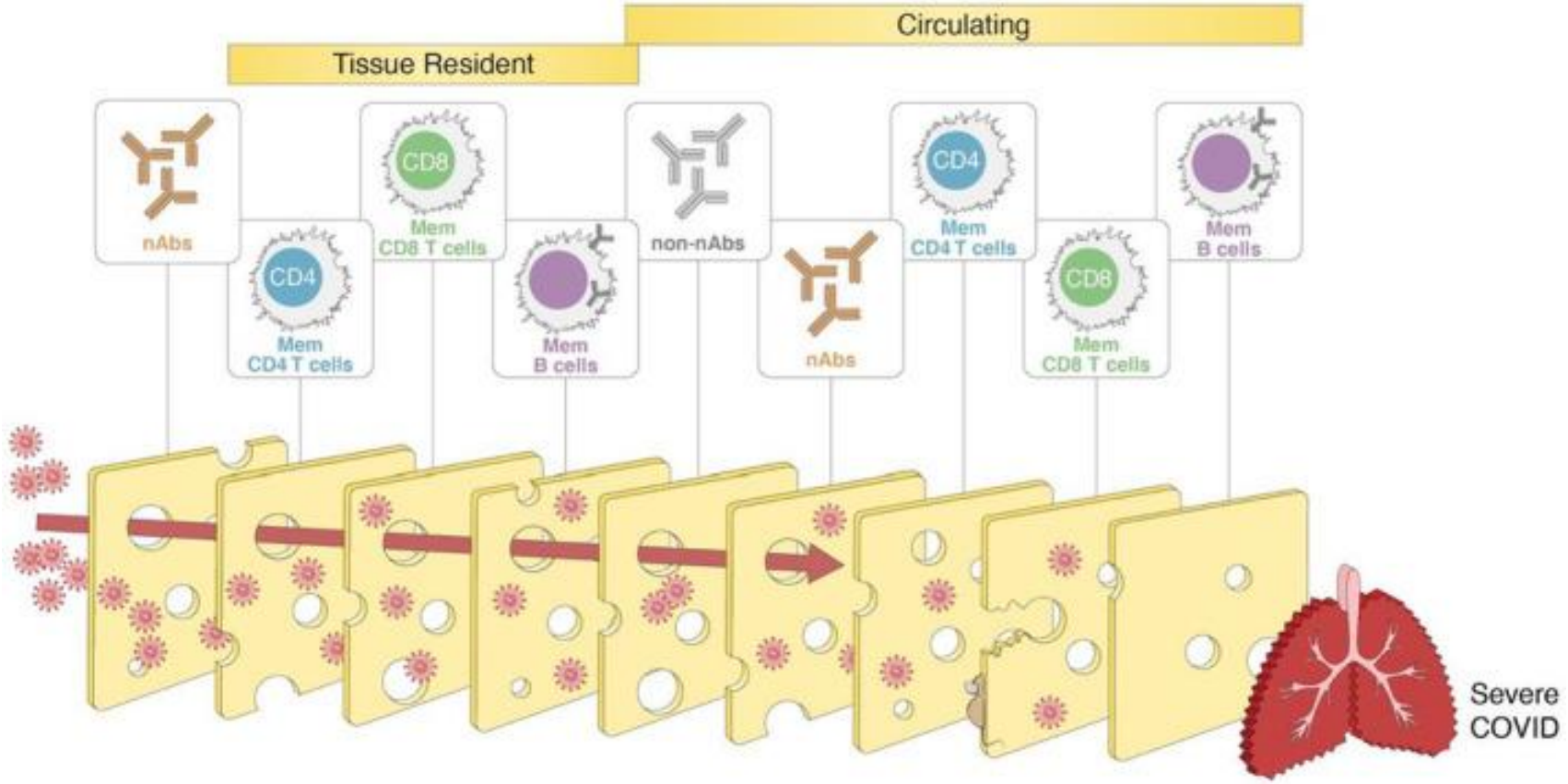


Neutralization by monoclonal Abs

Abs impaired (>3X, >10X, >100X)		BQ.1	BQ.1.1	BA.4/5-R346T	BA.4/5-K444T	BA.4/5-N460K	XBB	XBB.1	BA.2-Q183E	BA.2-R346T	BA.2-V445P	BA.2-G446S	BA.2-N460K	BA.2-F486S	BA.2-F490S
NTD	C1520						■	■	■						
NTD-SD2	C1717	■	■			■									
RBD class 1	S2K146	■	■			■	■	■					■	■	
	Omi-3	■	■			■	■	■					■	■	
	BD-515	■	■			■	■	■					■	■	
RBD class 2	XGv051	■	■			■	■	■					■	■	
	XGv347						■	■					■	■	
	ZCB11						■	■					■	■	
RBD class 3	Bebtelovimab	■	■		■		■	■		■					
	XGv289	■	■	■	■		■	■		■			■		
	P2G3	■	■	■	■		■	■	■	■					
	SP1-77	■	■	■	■		■	■	■	■					
	BD55-5840	■	■	■	■		■	■	■	■					
	XGv282	■	■		■	■	■	■		■	■	■			■
	BD-804	■	■	■	■	■	■	■		■	■				
Evusheld		■	■	■	■		■	■		■	■				

Will an annual shot be enough?



D Goldblatt et al. Correlates of protection against SARS-Cov2 infection and COVID-19 disease. Immunol Rev 2022 Jun 5

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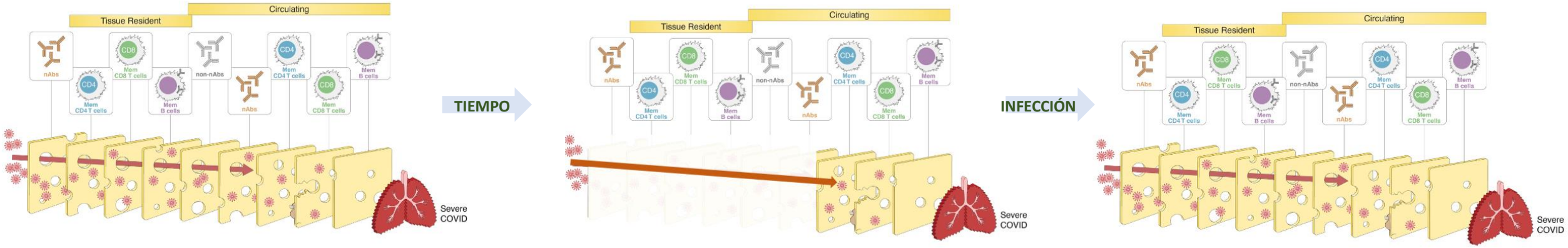
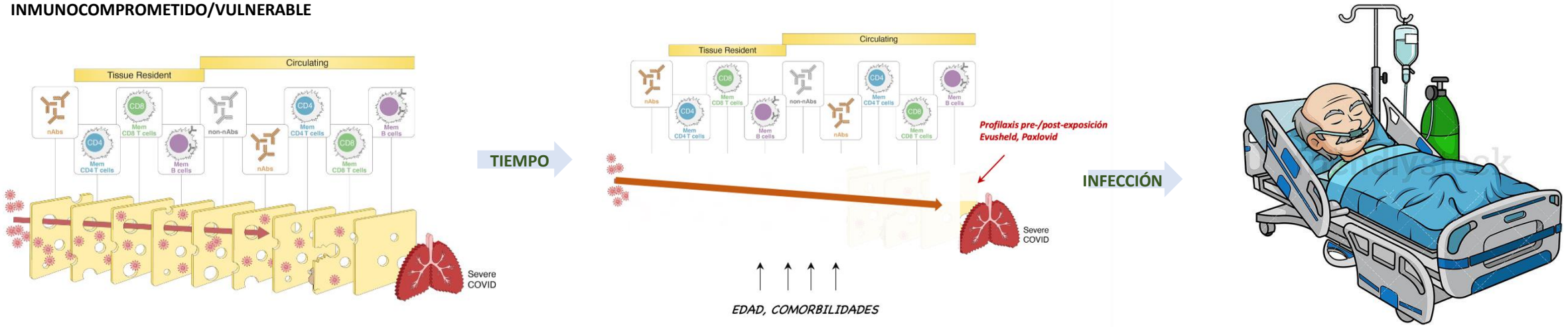
INMUNOCOMPETENTE



INMUNOCOMPROMETIDO/VULNERABLE



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Organización Mundial de la Salud

Temas de salud | Países | Centro de prensa | Emergencias

Acceso / Comunicados de prensa / El SAGE actualiza la guía de vacunación contra la COVID-19

El SAGE actualiza la guía de vacunación contra la COVID-19

- Priorizar el acceso al *booster* a grupos de riesgo
- Dosis en un plazo de 6 a 12 meses desde la ultima dosis
- Revisar recomendación según escenario epidemiológico

28 de marzo de 2023 | Comunicado de prensa

Tras su reunión celebrada del 20 al 23 de marzo, el Grupo de Expertos en Asesoramiento Estratégico (SAGE) sobre inmunización de la OMS revisó la hoja de ruta para priorizar el uso de las vacunas contra la COVID-19, a fin de reflejar el impacto provocado por la variante ómicron y el alto nivel de inmunidad de la población debido a la infección y la vacunación.

La hoja de ruta mantiene la prioridad del SAGE de proteger a las poblaciones expuestas a un mayor riesgo de muerte y enfermedad grave a causa de la infección por SARS-CoV-2, y sigue destacando la necesidad de preservar la resiliencia de los sistemas de salud. De nuevo, la hoja de ruta compara la relación costoeficacia de vacunar contra la COVID-19 a las personas en menor riesgo, es decir, los niños y adolescentes sanos, con la de otras intervenciones de salud. Además, incluye recomendaciones revisadas sobre las dosis de refuerzo adicionales y acerca del intervalo de tiempo entre los refuerzos. También analiza el efecto actual de las vacunas por lo que respecta a la reducción de las afecciones posteriores a la COVID-19, pero las pruebas empíricas sobre el alcance de su impacto son inconsistentes.

«Se ha actualizado la hoja de ruta para reflejar que una gran parte de la población está vacunada, se ha infectado previamente por COVID-19, o bien ambas cosas. La hoja de ruta revisada vuelve a enfatizar la importancia de vacunar, incluso con refuerzos adicionales, a quienes aún están en riesgo de enfermedad grave, que son principalmente adultos mayores y personas con afecciones subyacentes», declaró la presidenta del SAGE, la Dra. Hanna Nohynek. «Los países deben tener en cuenta su contexto particular cuando decidan si siguen vacunando a los grupos de riesgo bajo, como los niños y adolescentes sanos, sin que ello suponga comprometer la administración de las vacunas rutinarias, que tan importantes son para la salud y el bienestar de este grupo de edad».

La versión revisada de la hoja de ruta establece tres grupos de prioridad para la vacunación contra la COVID-19: alta, media y baja. La definición de estos grupos se basa principalmente en el riesgo de enfermedad grave y muerte, y tiene en cuenta cuestiones como la eficacia de la vacuna, la relación costoeficacia, los factores programáticos y la aceptación por parte de la comunidad.

El grupo de prioridad alta incluye a las personas mayores, a los adultos jóvenes que padecen comorbilidades importantes (por ejemplo, diabetes y cardiopatías), a las personas con afecciones de inmunodeficiencia (por ejemplo, personas que viven con el VIH y receptores de trasplantes), incluidos los niños de 6 meses o más, a las personas embarazadas y al personal de salud de primera línea.

Con respecto al grupo de prioridad alta, el SAGE recomienda administrar una dosis de refuerzo adicional en un plazo de 6 o 12 meses tras la última dosis, dependiendo de factores como la edad y las afecciones de inmunodeficiencia. Cualquier recomendación sobre la vacuna contra la COVID-19 solo es válida durante un tiempo determinado, y únicamente se refiere al escenario epidemiológico actual. En consecuencia, no se debe interpretar que se recomienda administrar dosis de refuerzo adicionales cada año de manera continuada. El objetivo es ayudar a los países a planificar a corto y medio plazo.

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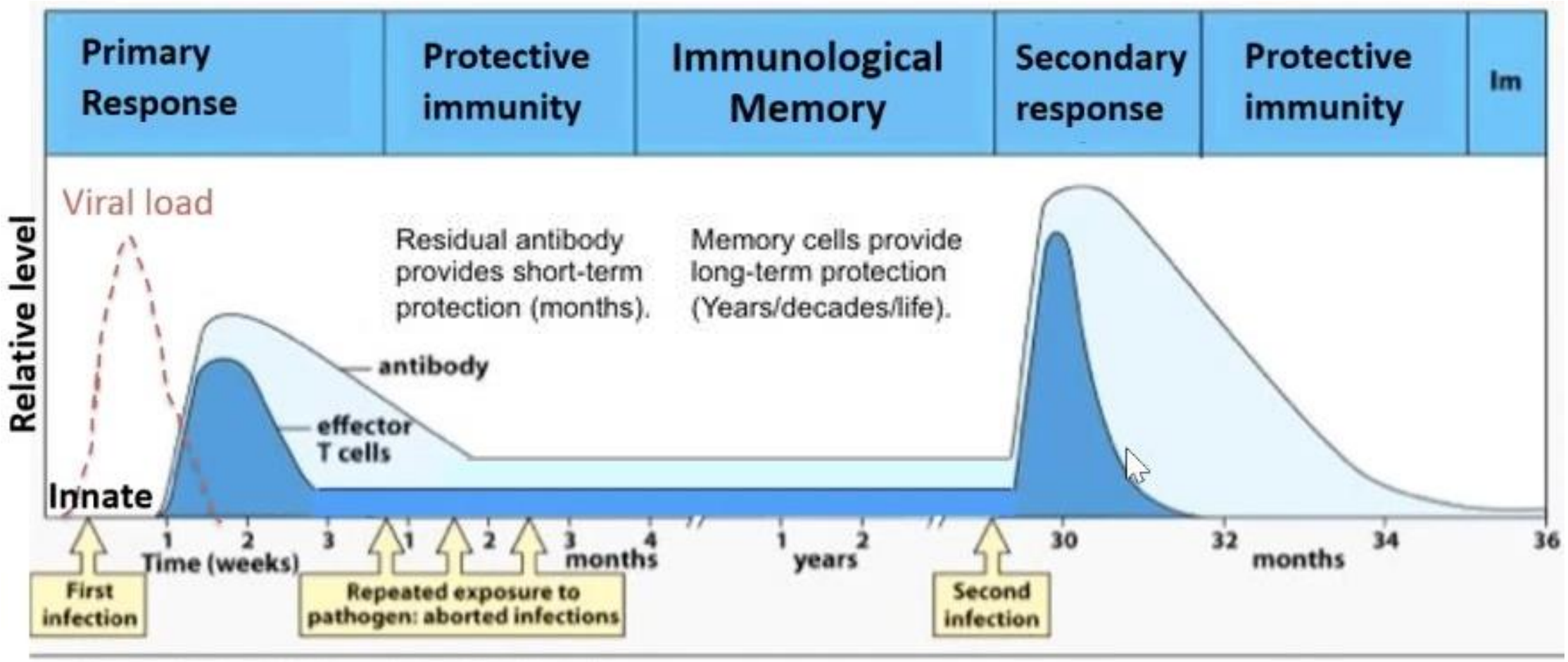
INMUNIDAD PROTECTORA vs MEMORIA INMUNOLÓGICA



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Adapted from: Parham P. The Immune System 4th Ed Garland Science (2015)

Adapted from: Parham P. The Immune System 4th Ed Garland Science (2015)

INMUNIDAD MUCOSAL vs SISTÉMICA

Inmunidad NO Esterilizante

Inmunidad Esterilizante

Injectable vs. mucosal vaccine

	Circulating IgG and IgM	Secretory IgA	Systemic cellular response	Mucosal cell-mediated response	Negative preexisting antibody effect
Injectable – not live	+++	+/–	++	+/–	+/–
Injectable – live	+++	+/–	+++	+/–	+++
Mucosal – live	+++	+++	+++	+++	+++

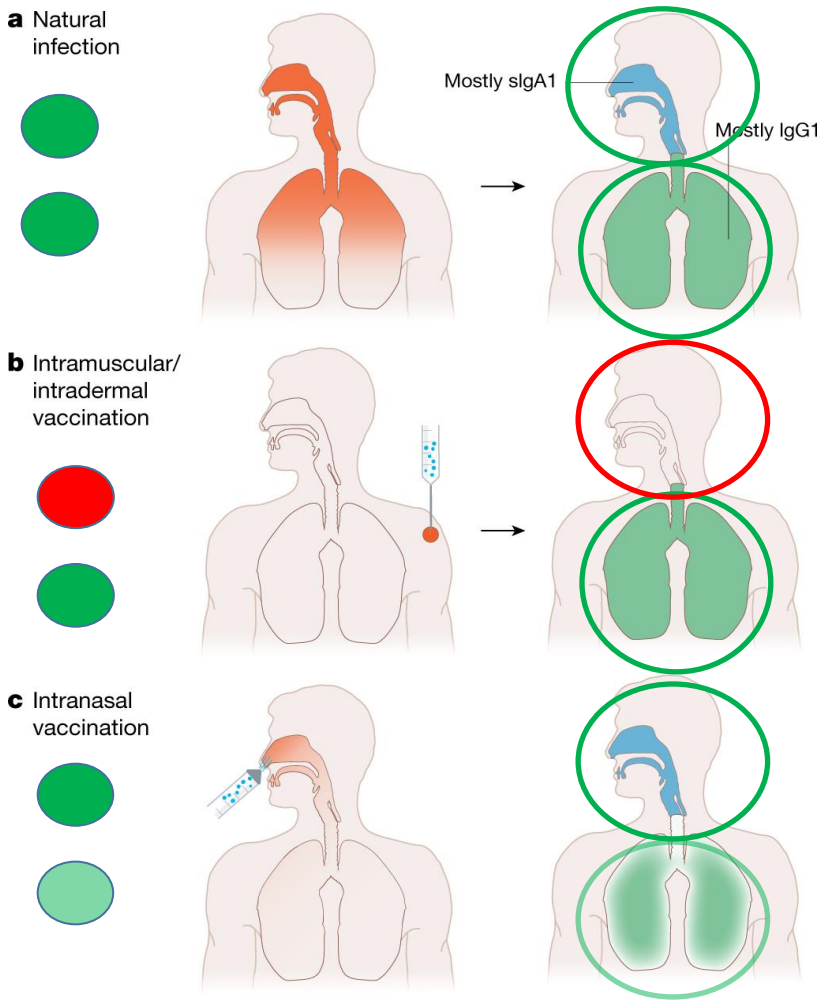
MDedge News

Source: Dr. Harrison

Harrison´s Principles of Internal Medicine 20e. J Larry Jameson et al McGraw Hill

Review

SARS-CoV-2 vaccines in development



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Nature | Vol 586 | 22 October 2020

Fig. 2 | Mucosal and systemic immune responses to natural infection with respiratory viruses and to vaccination. The lower human respiratory tract is thought to be mostly protected by IgG (IgG1 is most prevalent), the main type of antibody in serum, which is transported into the lung. The upper respiratory

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Tolerability and immunogenicity of an intranasally-administered adenovirus-vectored COVID-19 vaccine: An open-label partially-randomised ascending dose phase I trial

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eBioMedicine 2022;85: 104298
Published online 10 October 2022
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Summary

Background Intranasal vaccination may induce protective local and systemic immune responses against respiratory pathogens. A number of intranasal SARS-CoV-2 vaccine candidates have achieved protection in pre-clinical challenge models, including ChAdOx1 nCoV-19 (AZD1222, University of Oxford / AstraZeneca).

Methods We performed a single-centre open-label Phase I clinical trial of intranasal vaccination with ChAdOx1 nCoV-19 in healthy adults, using the existing formulation produced for intramuscular administration.

Thirty SARS-CoV-2 vaccine-naïve participants were allocated to receive 5×10^9 viral particles (VP, n=6), 2×10^{10} VP (n=12), or 5×10^{10} VP (n=12). Fourteen received second intranasal doses 28 days later. A further 12 received non-study intramuscular mRNA SARS-CoV-2 vaccination between study days 22 and 46.

To investigate intranasal ChAdOx1 nCoV-19 as a booster, six participants who had previously received two intramuscular doses of ChAdOx1 nCoV-19 and six who had received two intramuscular doses of BNT162b2 (Pfizer / BioNTech) were given a single intranasal dose of 5×10^{10} VP of ChAdOx1 nCoV-19.

Objectives were to assess safety (primary) and mucosal antibody responses (secondary).

Findings Reactogenicity was mild or moderate. Antigen-specific mucosal antibody responses to intranasal vaccination were detectable in a minority of participants, rarely exceeding levels seen after SARS-CoV-2 infection. Systemic responses to intranasal vaccination were typically weaker than after intramuscular vaccination with ChAdOx1 nCoV-19. Antigen-specific mucosal antibody was detectable in participants who received an intramuscular mRNA vaccine after intranasal vaccination. Seven participants developed symptomatic SARS-CoV-2 infection.

Interpretation This formulation of intranasal ChAdOx1 nCoV-19 showed an acceptable tolerability profile but induced neither a consistent mucosal antibody response nor a strong systemic response.

Funding AstraZeneca.

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NEWS | 03 November 2022

Intranasal COVID-19 vaccine fails to induce mucosal immunity

Nature Medicine **explores the latest translational and clinical research news, with a clinical trial of an intranasal ChAdOx1 vaccine.**

Added value of this study

We present a first-in-human study of intranasal COVID-19 vaccination with an adenovirus-vectored vaccine. Reactogenicity was acceptable at all doses but immunogenicity was insufficient to warrant further development of the current formulation / device combination.

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Pandemic to endemic: Where does one end and the other begin?

Epidemic disease

Sudden increase in cases spreading through a large population

Pandemic disease

Sudden increase in cases across several countries, continents or the world

Endemic disease

Constantly present in a population or region, with relatively low spread

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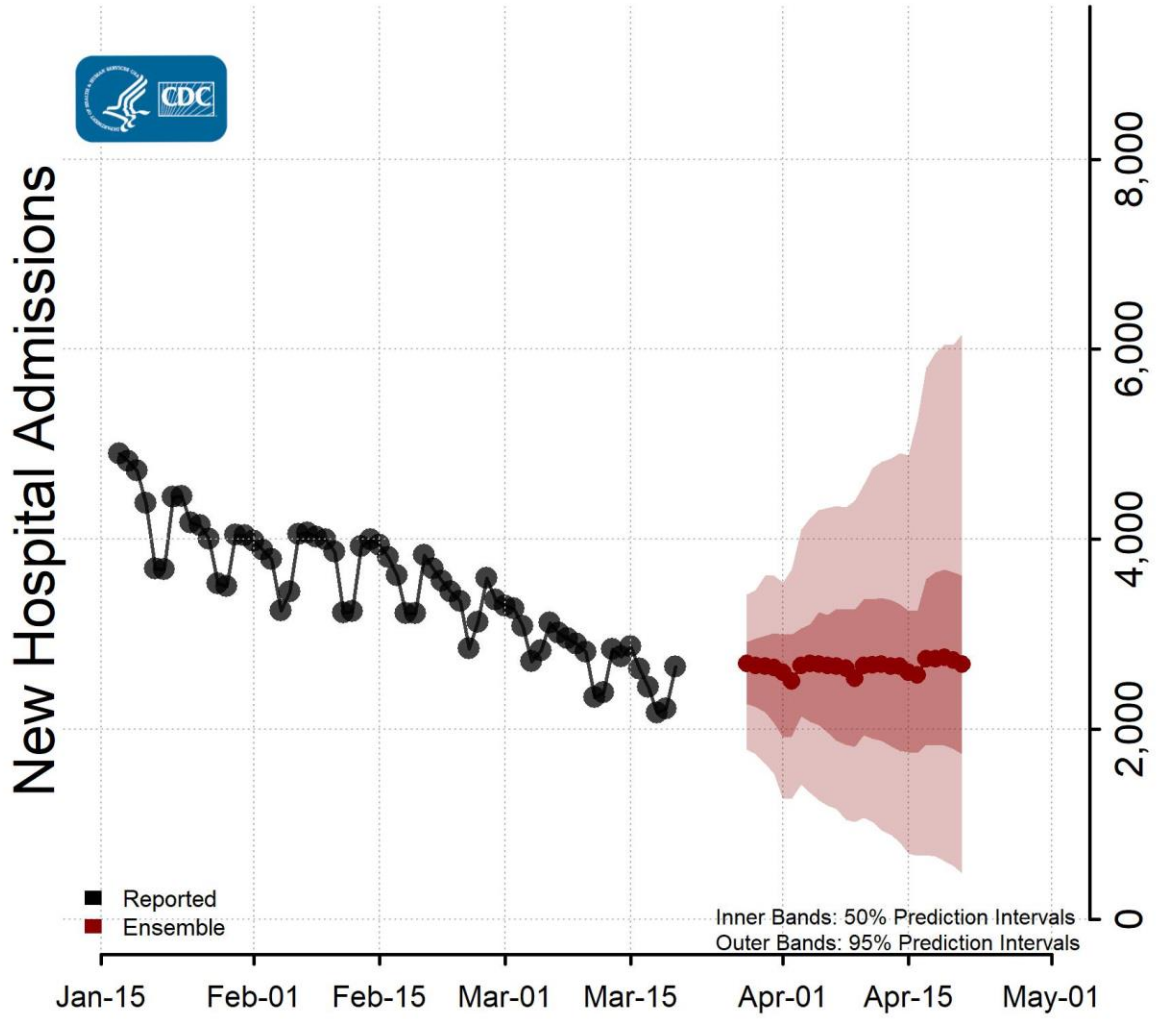
National Forecast

27 March 2023



https://www.cdc.gov/coronavirus/2019-ncov/science/forecasting/hospitalizations-forecasts.html

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Here are three example scenarios for a new dominant variant of COVID-19.

Three example COVID-19 scenarios

‘Milder-cron’

Description:
New variant spreads rapidly but causes only mild disease in the vast majority of cases

Infectiousness: High

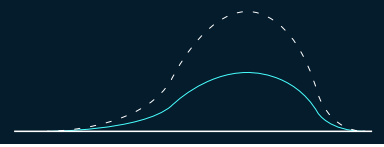
Immune evasion:
Evasion of prior immunity, including from Omicron infections

Average severity:
Significantly lower than Omicron

Cases during initial wave:
Similar to recent wave

Hospitalizations during initial wave:
Significantly lower than recent wave

Hospitalizations
(illustrative)



‘Omicron’s twin’

Description:
New variant evades prior immunity, including from Omicron, but otherwise has similar characteristics

Infectiousness: High

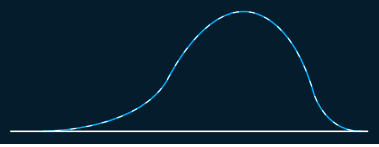
Immune evasion:
Evasion of prior immunity, including from Omicron infections
Up-to-date vaccinations protect against severe disease

Average severity:
Similar to Omicron

Cases during initial wave:
Similar to recent wave

Hospitalizations during initial wave:
Similar to recent wave

Hospitalizations
(illustrative)



‘Delta-cron’

Description:
New variant is as transmissible/ immune evasive as Omicron but as severe as Delta

Infectiousness: High

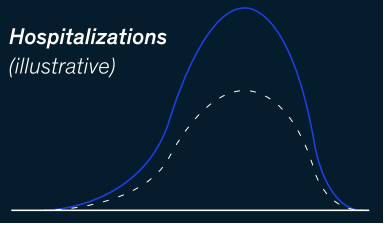
Immune evasion:
Evasion of prior immunity, including from Omicron infections
Up-to-date vaccinations protect against severe disease

Average severity:
Similar to Delta

Cases during initial wave:
Similar to recent wave

Hospitalizations during initial wave:
Higher than recent wave, which was the worst so far in most places

Hospitalizations
(illustrative)



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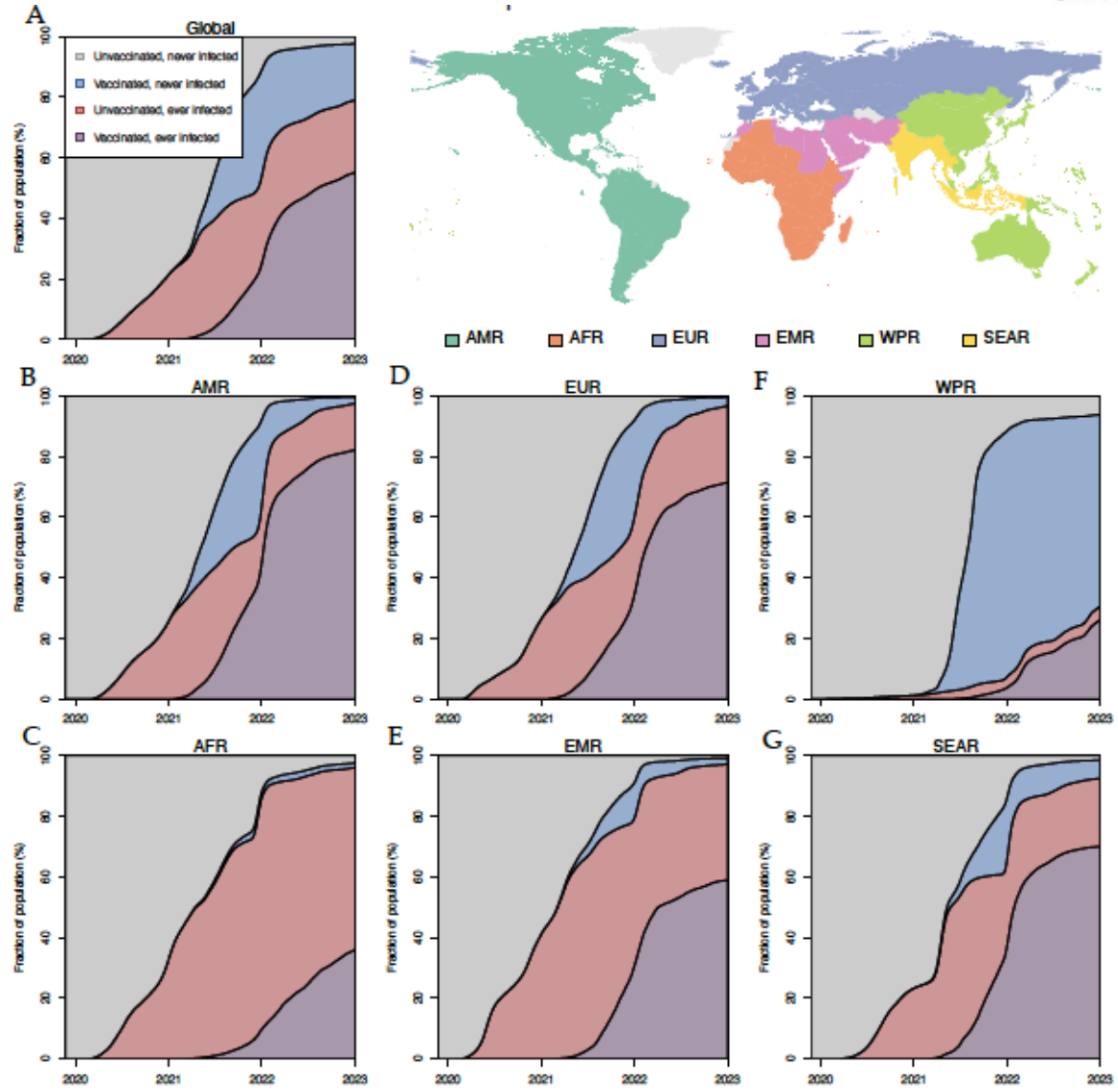
medRxiv preprint doi: https://doi.org/10.1101/2023.03.07.23286952; this version posted March 8, 2023.

Forecasting the trajectory of the COVID-19 pandemic into 2023 under plausible variant and intervention scenarios: a global modelling study

Corresponding author: Robert C. Reiner, Jr., PhD, bcreiner@uw.edu

Interpretation

As infection-derived and vaccine-conferred protection wanes, we expect infections to rise, but as most of the world's population has some level of immunity to SARS-CoV-2 as of December 12, 2022, all but the most pessimistic forecasts in this analysis do not predict a massive global surge by June 30, 2023. Paradoxically, China, due to its lower levels of population immunity and effective vaccination will likely experience substantial numbers of infections and deaths that, due to its large population size, will adversely affect the global toll. This could be substantially mitigated by existing intervention options including masking, vaccination, health-care preparedness, and effective antiviral compounds for those at most at risk of poor outcomes. While still resulting in morbidity and mortality, this endemic transmission provides protection from less transmissible variants and particularly protects against sub-lineages of the more severe pre-Omicron variants. In the scenarios where a new variant does emerge and spread globally, however, the speed of this spread may be too fast to rely on even the most quickly developed mRNA vaccines to provide protection soon enough. Existing vaccines and boosters have played an important role in increasing immunity worldwide, but the continued contribution of mask usage (both past and future) in the prevention of infection and death cannot be understated. The characteristics of future COVID-19 variants are inherently difficult to predict, and our forecasts do show considerable differences in outcomes as a function of these variant properties. Given the uncertainty surrounding what type of variant will next emerge, the world would be wise to remain vigilant in 2023 as we move to the next phase of the COVID-19 pandemic.



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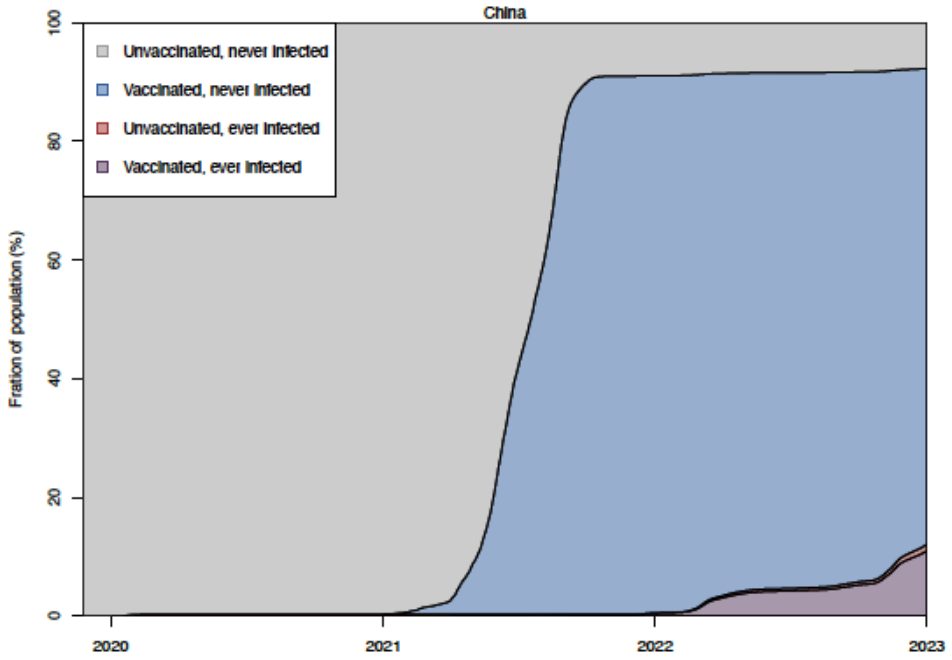

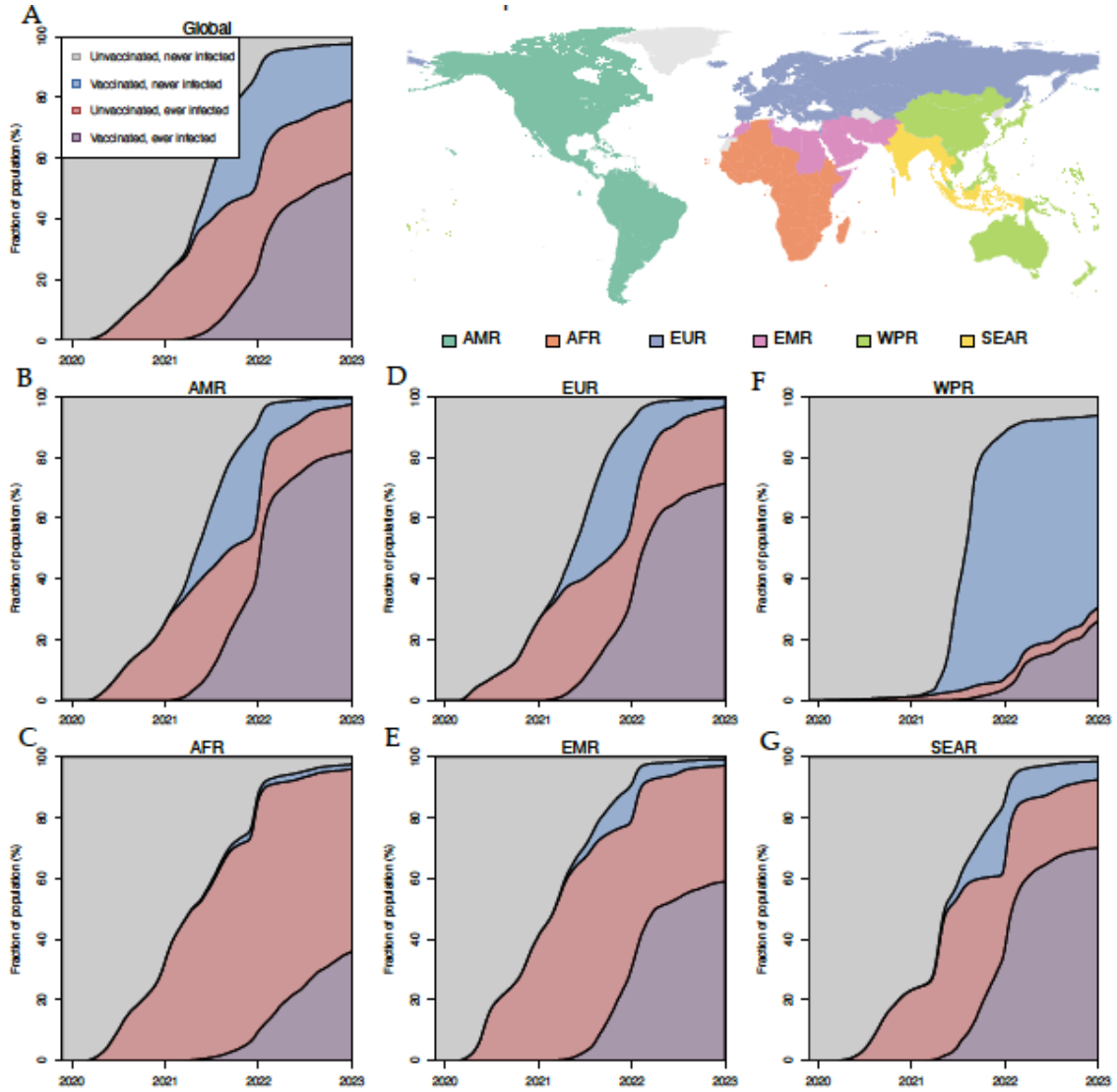

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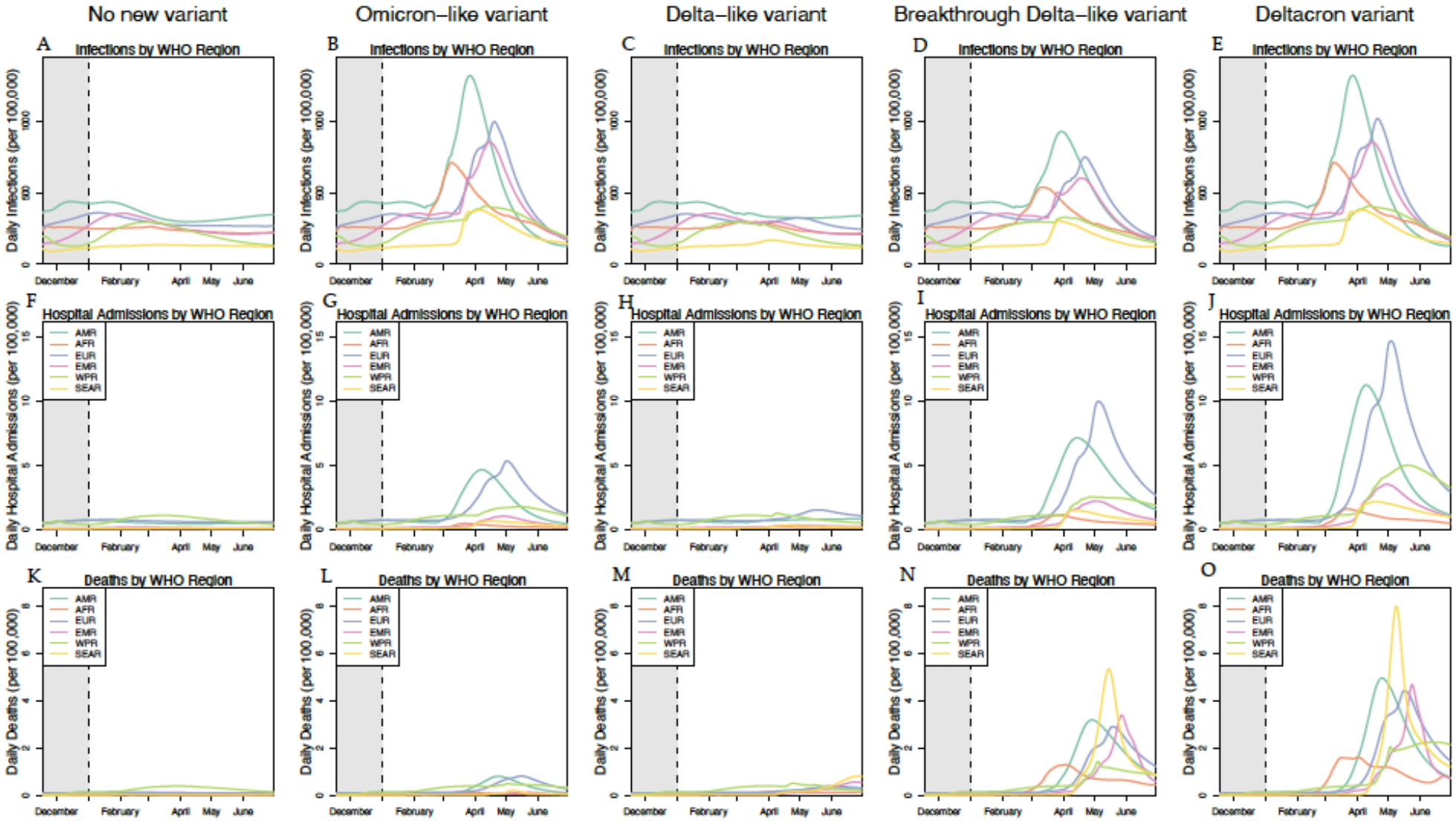

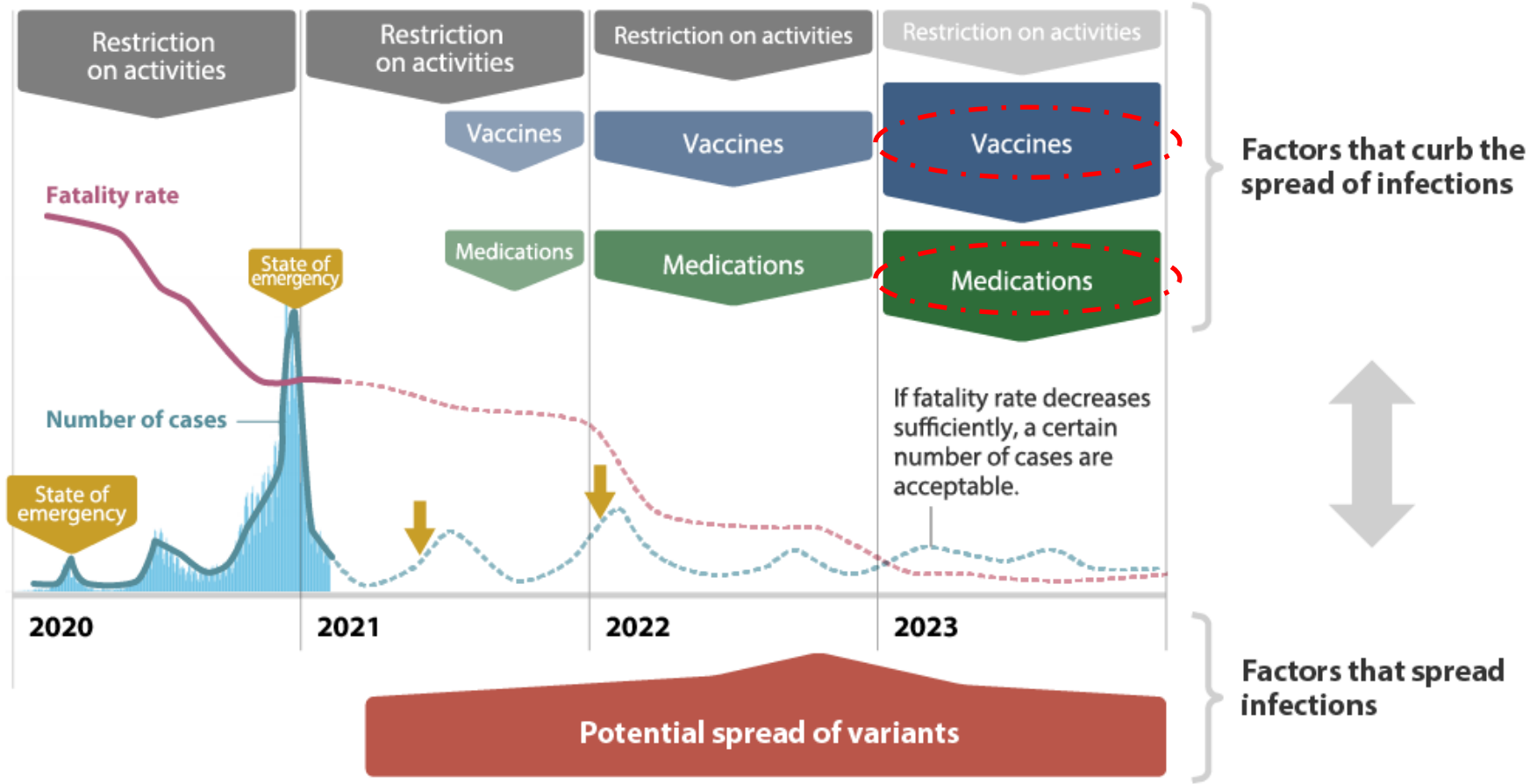

Activities are restricted when the number of cases increases.

* The dotted lines are merely illustrative and not based on actual predictions for the future number of cases and fatalities.

Source: Mitsubishi Research Institute, Inc.

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Public health surveillance for COVID-19

Interim guidance

22 July 2022

World Health Organization

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VIGILANCIA EPIDEMIOLOGICA

https://www.who.int/publications/i/item/WHO-2019-nCoV-SurveillanceGuidance-2022.2

Key points

Surveillance for COVID-19 remains critical to ending the COVID-19 emergency worldwide and informing public health actions to limit the spread of SARS-CoV-2 and reduce morbidity, mortality and impact.

The World Health Organization (WHO) continues to recommend maintaining and strengthening surveillance to achieve the core surveillance objectives for COVID-19. This should include:

- **early warning** for changes in epidemiological patterns
- **monitoring trends** in morbidity and mortality
- **monitoring burden of disease on health care capacity** (health and care workers, hospitalizations and intensive care unit admissions)
- **incorporating strategic and geographically representative genomic surveillance** to monitor circulation of known variants of concern (VOCs) and allow for early detection of new variants of concern, circulation of SARS-CoV-2 in potential animal reservoirs and changes in virological patterns.

In addition, WHO continues to recommend Member States with the capacity to carry out enhanced surveillance activities and conduct special studies to:

- **describe and monitor SARS-CoV-2 infection in high-risk groups** who continue to be at the highest risk of exposure or severe disease
- **characterize new variants,** including aspects of their severity, transmissibility, immune escape and the impact of countermeasures
- **better understand post COVID-19 condition (long COVID),** including the role of immunity and risk factors.

WHO recommends that the following remain priority groups and settings for SARS-CoV-2 surveillance:

- **priority groups:** Individuals older than 60 years, individuals with immunocompromising diseases or taking immunosuppressive medications, people with multiple co-morbidities, pregnant women and unvaccinated individuals
- **priority settings:** environments where there is a higher chance that people belonging to priority groups might stay for extended periods of time in close proximity with each other, such as in closed settings, long-term care facilities and nursing homes.

COVID-19 surveillance reporting variables from Member States to WHO include:

- **daily cases and deaths,** as per International Health Regulations (IHR 2005) requirements
- **required weekly reporting** to WHO of detailed surveillance variables
  - age and sex of probable and confirmed cases and deaths
  - cases and deaths among health and care workers
  - number of new cases admitted for hospitalization and to an intensive care unit (ICU)
  - number of persons tested with a nucleic acid amplification test (NAAT) and other testing methods.
- **variants of concern (VOCs) and variants of interest (VOIs)**: date of detection of first case and weekly relative prevalence (based on representative sampling)
- **vaccination**: doses administered; number of persons vaccinated with a primary series and booster.

What is new in this version:

- updated WHO case definitions (see the Annex), contact definitions, priority groups and settings in line with the latest contact tracing and quarantine guidance
- updates of core and enhanced surveillance objectives and methods in various settings, including environmental and animal surveillance
- updated guidance on surveillance of SARS-CoV-2 variants, including the integration of sampling for genomic surveillance in SARS-CoV-2 testing strategies
- updates of COVID-19 surveillance reporting requirements to WHO, which includes the addition of new ICU admissions for COVID-19 treatment.

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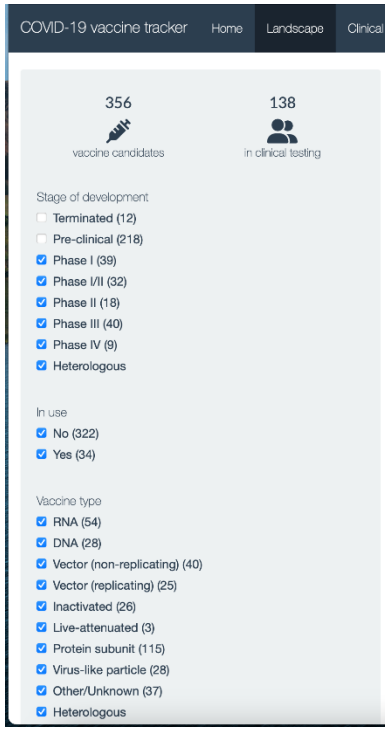
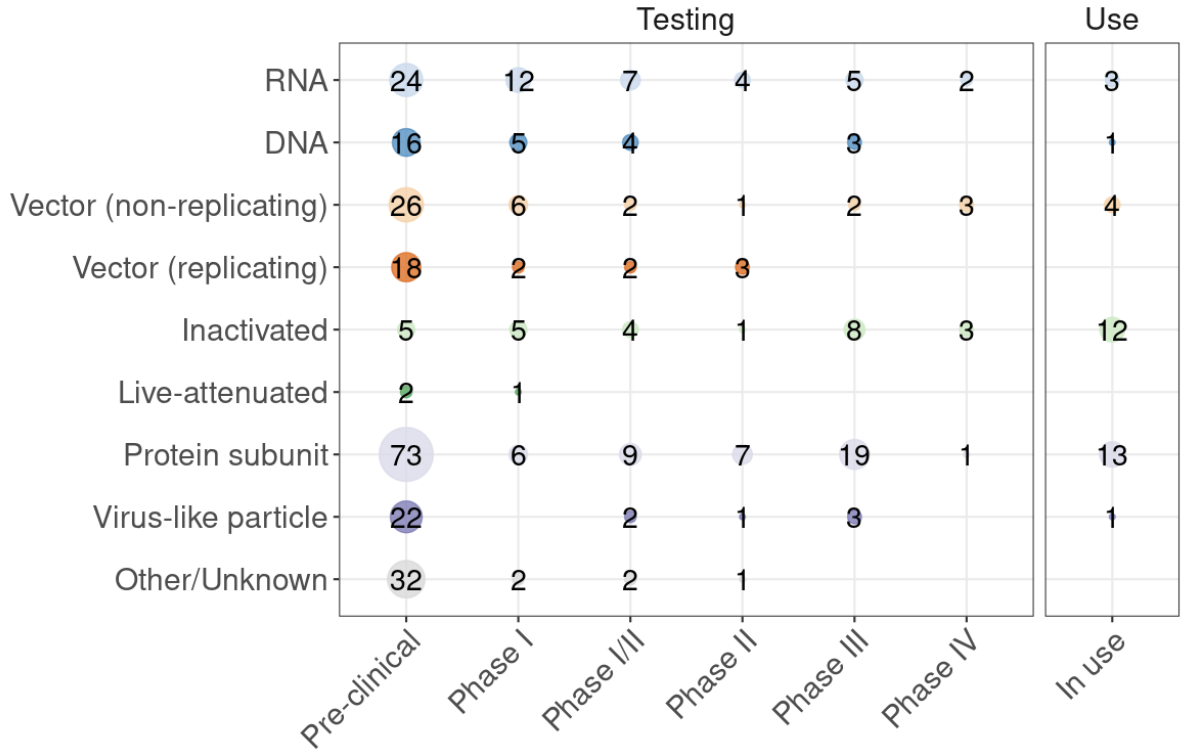
VACUNAS



Full pipeline | Summary



Candidates listed above as being in phase III include several undergoing combined phase II/III trials.

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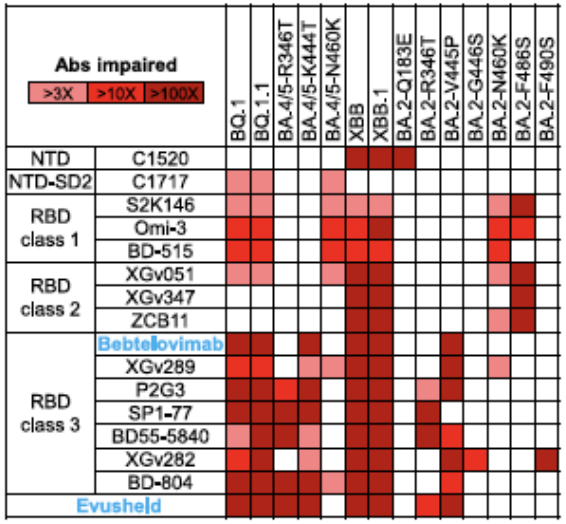
TRATAMIENTOS

- **Neutralization by monoclonal Abs**



02/11/2022	Bebtelovimab (460KB) (reissued August 5 and October 27, 2022) Letter Granting EUA Amendment (March 30, 2022) (216KB) Letter Granting EUA Amendment (September 16, 2022) (194KB) Letter Granting EUA Amendment (November 4, 2022) (310KB) FDA Announces Bebtelovimab is Not Currently Authorized in Any US Region (November 30, 2022) ASPR and FDA Statement on Shelf-Life Extension of Bebtelovimab (October 28, 2022)	Bebtelovimab is not currently authorized in any U.S. region due to the high frequency of circulating SARS-CoV-2 variants that are non-susceptible to bebtelovimab. Therefore, bebtelovimab may not be administered for treatment of COVID-19 under the Emergency Use Authorization until further notice by the Agency.	Healthcare Providers (763KB) (updated November 4, 2022) Patients, Parents, and Caregivers (245KB)(updated November 4, 2022) • Spanish (141KB) Frequently Asked Questions on the Emergency Use Authorization of Bebtelovimab (1.01MB) CDER Scientific Review Documents Supporting EUA	FRN EUA March 22, 2022
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TRATAMIENTOS

Table 2a. Therapeutic Management of Nonhospitalized Adults With Mild to Moderate COVID-19 Who Do Not Require Supplemental Oxygen

Last Updated: December 28, 2022

Patient Disposition	Panel's Recommendations
All Patients	• All patients should be offered symptom management (**AIII**). • The Panel **recommends against** the use of **dexamethasone**[a] or **other systemic corticosteroids** in the absence of another indication (**AIIb**).
Patients Who Are at High Risk of Progressing to Severe COVID-19[b]	*Preferred therapies. Listed in order of preference:* • **Ritonavir-boosted nirmatrelvir (Paxlovid)**[c,d] (**AIIa**) • **Remdesivir**[d,e] (**BIIa**) *Alternative therapy. For use when the preferred therapies are not available, feasible to use, or clinically appropriate:* • **Molnupiravir**[d,f,g] (**CIIa**)

Each recommendation in the Guidelines receives 2 ratings that reflect the strength of the recommendation and the quality of the evidence that supports it. See Guidelines Development for more information.

[a] There is currently a lack of safety and efficacy data on the use of dexamethasone in outpatients with COVID-19. Using systemic glucocorticoids in outpatients with COVID-19 may cause harm.

[b] For a list of risk factors, see the CDC webpage Underlying Medical Conditions Associated With Higher Risk for Severe COVID-19. When deciding whether to prescribe antiviral treatment to a patient who has been vaccinated, clinicians should be aware of the conditions associated with a high risk of disease progression. These conditions include older age, a prolonged amount of time since the most recent vaccine dose (e.g., >6 months), and a decreased likelihood of an adequate immune response to vaccination due to a moderate to severe immunocompromising condition or the receipt of immunosuppressive medications. The number and severity of risk factors also affects the level of risk.

[c] Ritonavir-boosted nirmatrelvir has significant drug-drug interactions. Clinicians should carefully review a patient's concomitant medications and evaluate potential drug-drug interactions. See Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications for more information.

[d] If a patient requires hospitalization after starting treatment, the full treatment course can be completed at the health care provider's discretion.

[e] Administration of remdesivir requires an IV infusion once daily for 3 days.

[f] Molnupiravir appears to have lower efficacy than the other options recommended by the Panel. Therefore, it should be considered when the other options are not available, feasible to use, or clinically appropriate.

[g] The Panel **recommends against** the use of **molnupiravir** for the treatment of COVID-19 in pregnant patients unless there are no other options and therapy is clearly indicated (**AIII**).

Key: CDC = Centers for Disease Control and Prevention; IV = intravenous; the Panel = the COVID-19 Treatment Guidelines Panel

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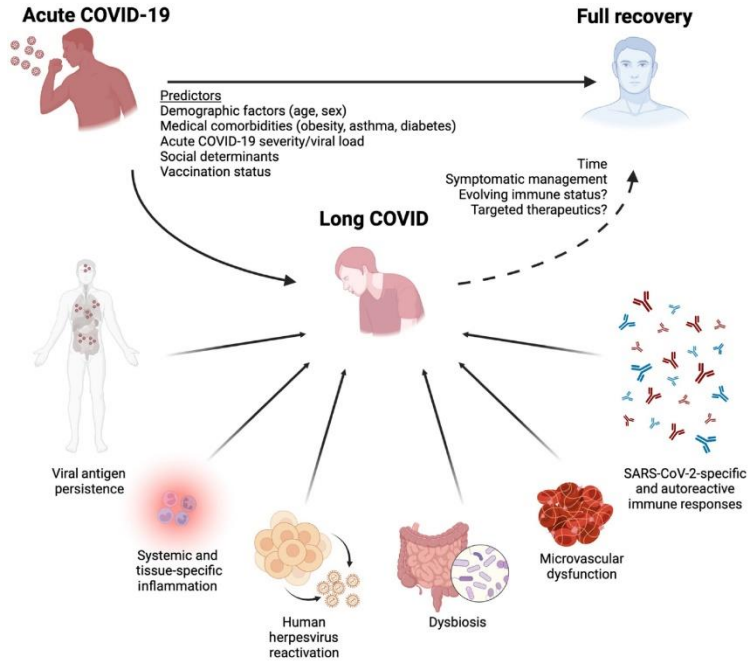
COVID PERSISTENTE



Mental Health
- Anxiety
- Depression
- Sleep problems
- Substance abuse

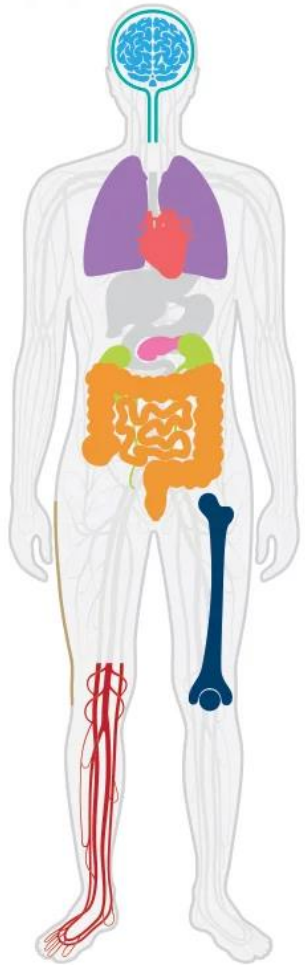
Respiratory System
- Cough
- Low blood oxygen
- Shortness of breath

Kidney
- Acute kidney injury
- Chronic kidney disease

Gastrointestinal
- Diarrhea
- Acid reflux
- Constipation

Skin Disorders
- Rash
- Hair loss

Blood Disorders
- Anemia
- Blood clots



Nervous System
- Stroke
- Headaches
- Memory problems
- Loss of smell and taste

Cardiovascular
- Arrhythmia
- Palpitations
- Heart failure
- Acute coronary disease

Metabolic/Endocrine
- Obesity
- Diabetes
- High cholesterol

Musculoskeletal
- Joint pain
- Muscle weakness

General
- Fatigue
- Malaise
- Mitochondrial dysfunction

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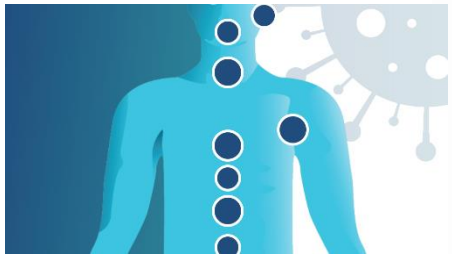
VIGILANCIA EPIDEMIOLOGICA

VACUNAS

TRATAMIENTOS



COVID PERSISTENTE

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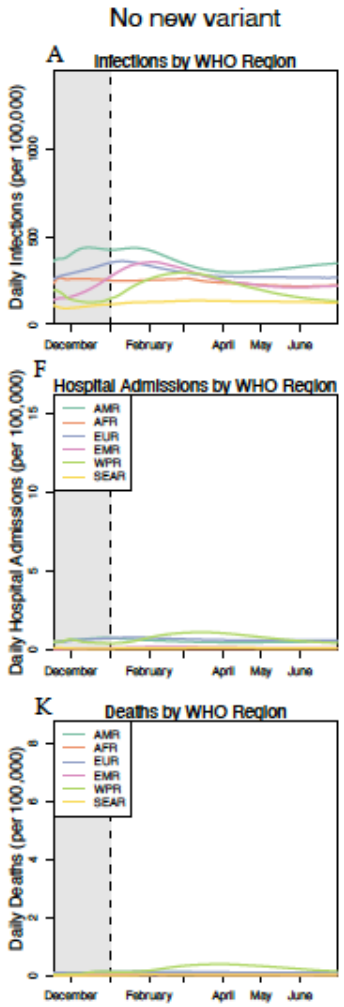
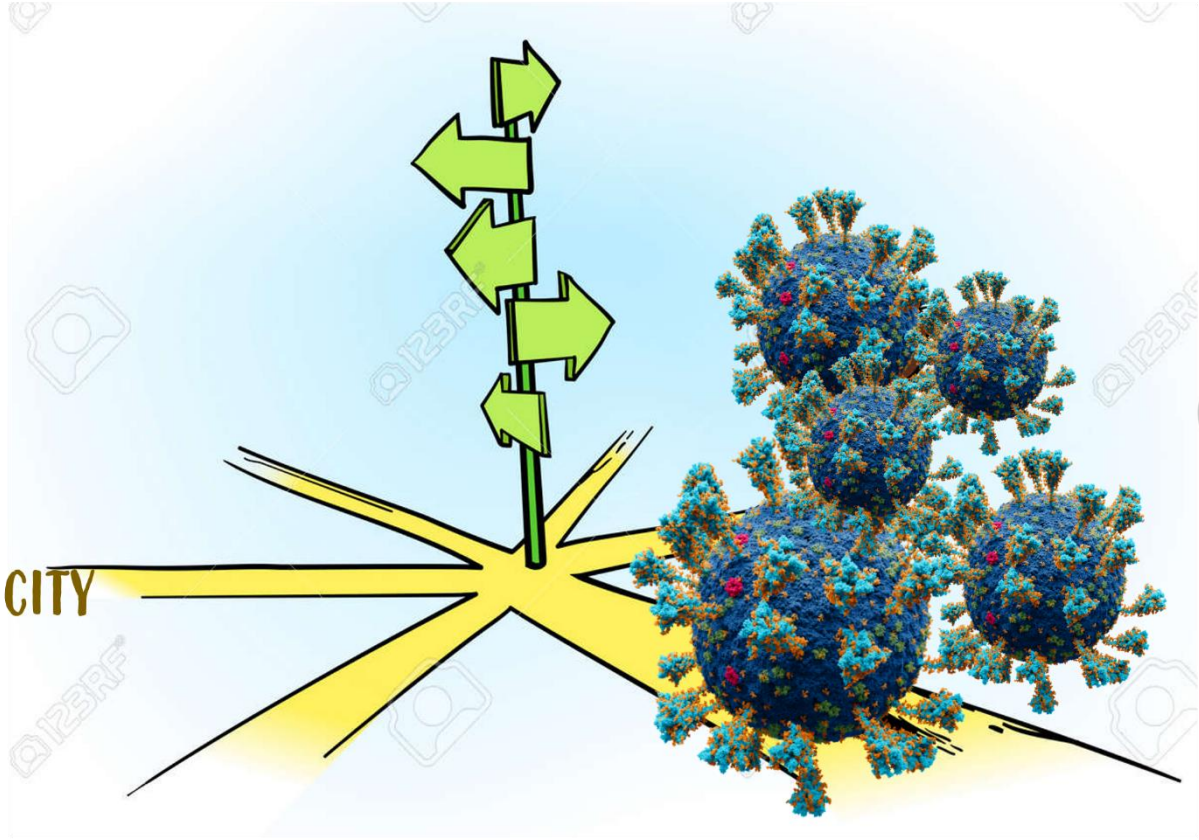
SARS-COV-2. ¿Y AHORA QUÉ?





¿Qué nos espera?

@gomez_rial5