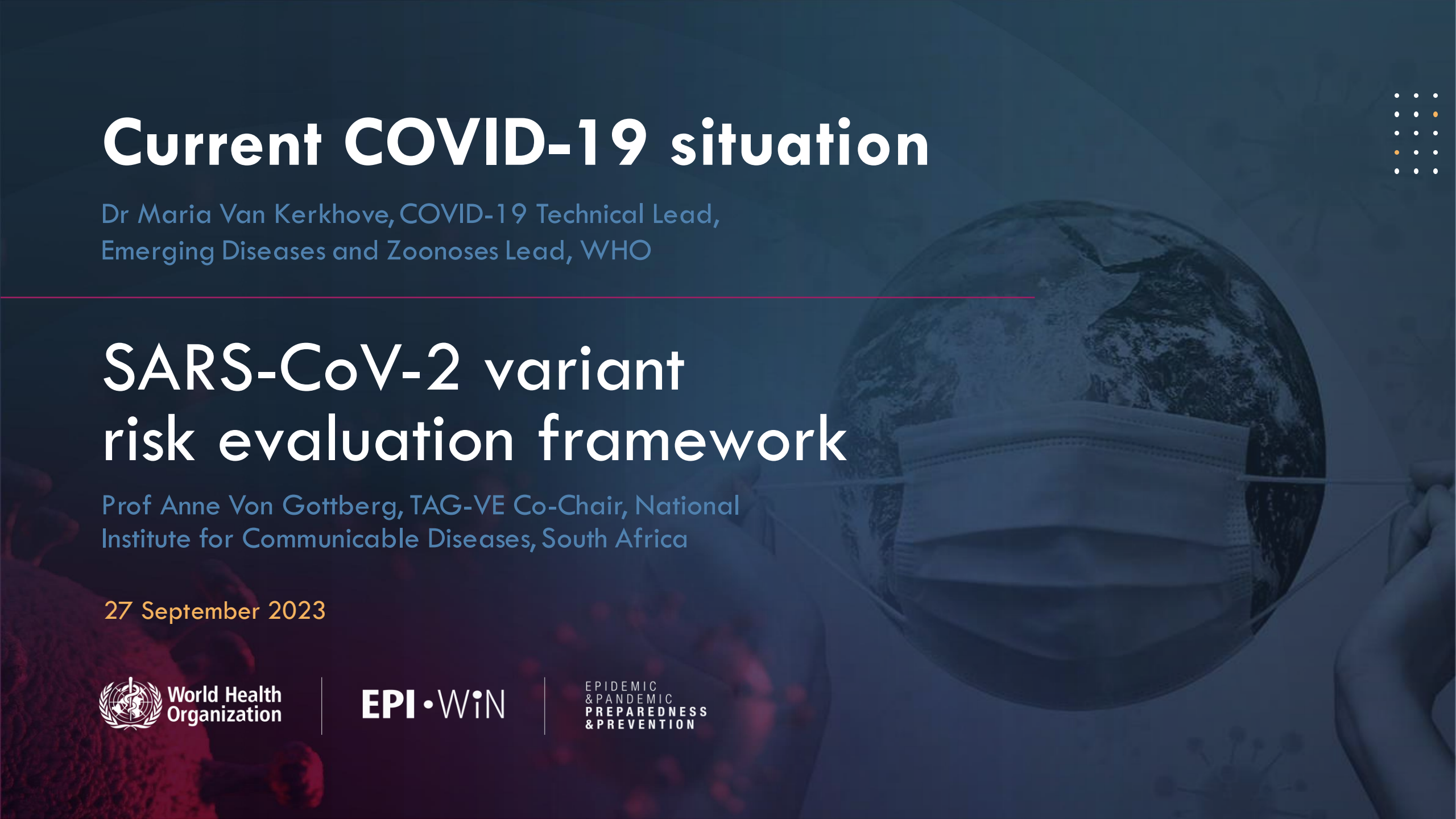
Current COVID-19 situation

Dr Maria Van Kerkhove, COVID-19 Technical Lead,
Emerging Diseases and Zoonoses Lead, WHO

SARS-CoV-2 variant risk evaluation framework

Prof Anne Von Gottberg, TAG-VE Co-Chair, National Institute for Communicable Diseases, South Africa

27 September 2023



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Current COVID-19 situation

Maria Van Kerkhove, WHO

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Public Health Emergency of International Concern:
COVID-19

30 January 2020

5 May 2023

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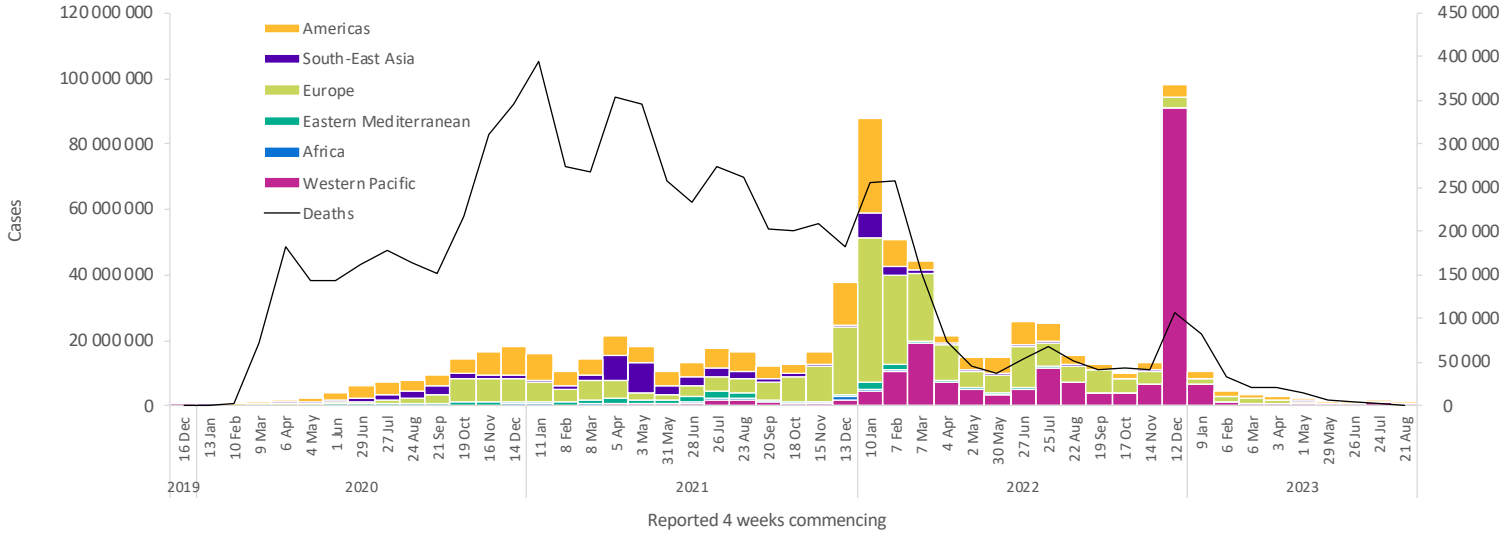
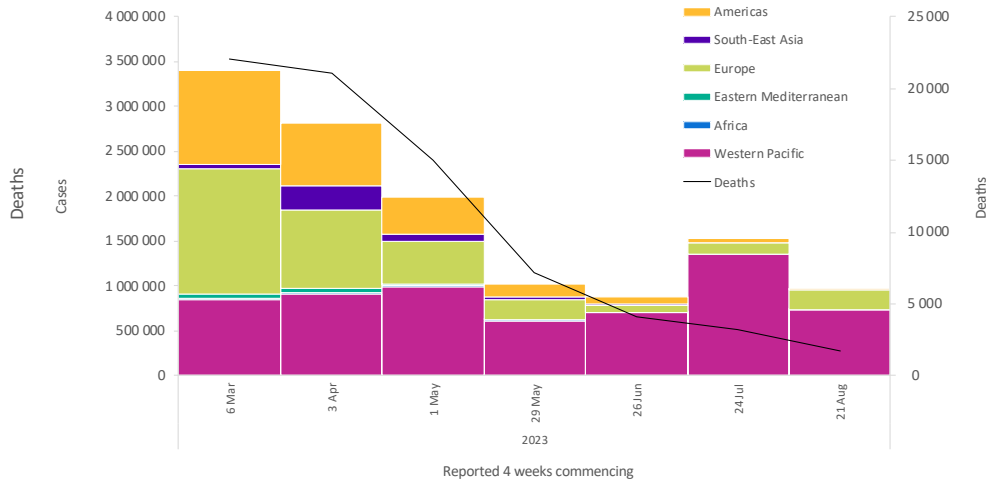
While the PHEIC is over, the public health threat posed by COVID-19 is not

Cases reported to WHO as of 17 September 2023

- New cases : > 977 000 reported by 93/234 countries
- New deaths: ~ 1700 reported by 40/234 countries
- Cumulative cases: > 770 Million
- Cumulative deaths: > 6.9 Million





Starting from the week commencing on 11 September 2023, the source of the data from the Region of the Americas was switched to the aggregated national surveillances, received through the COVID-19, Influenza, RSV and Other Respiratory Viruses program in the Americas. Data have been included retrospectively since 31 July 2023. For more information regarding COVID-19 in the Americas, please access the link: https://www.paho.org/en/topics/influenza-and-other-respiratory-viruses.

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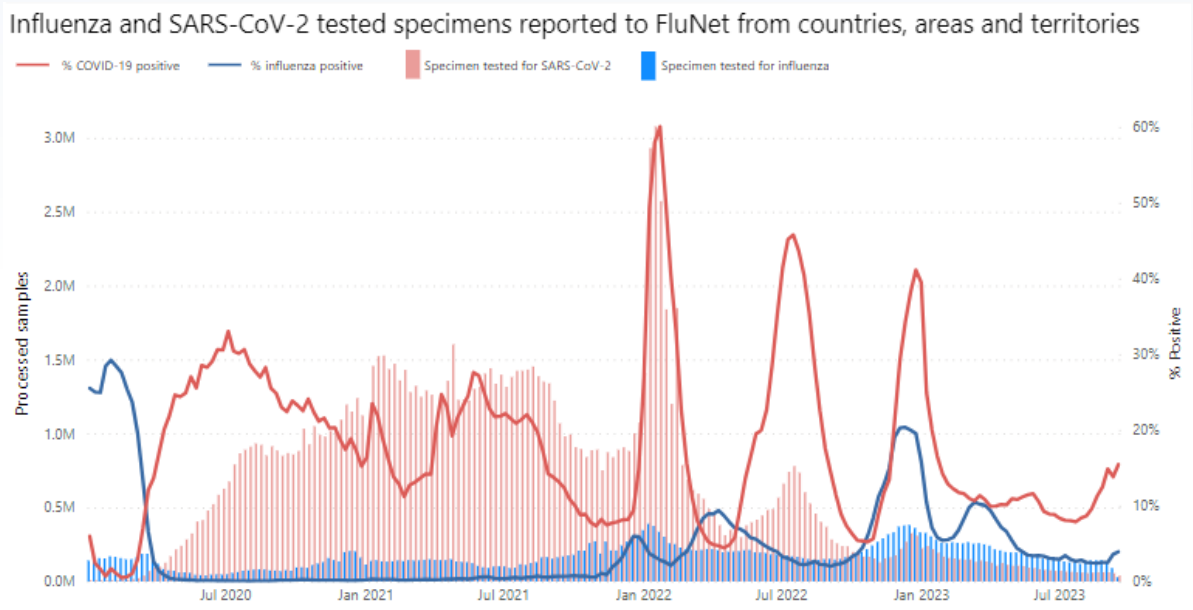
Newly reported and cumulative COVID-19 confirmed cases and deaths, by WHO region

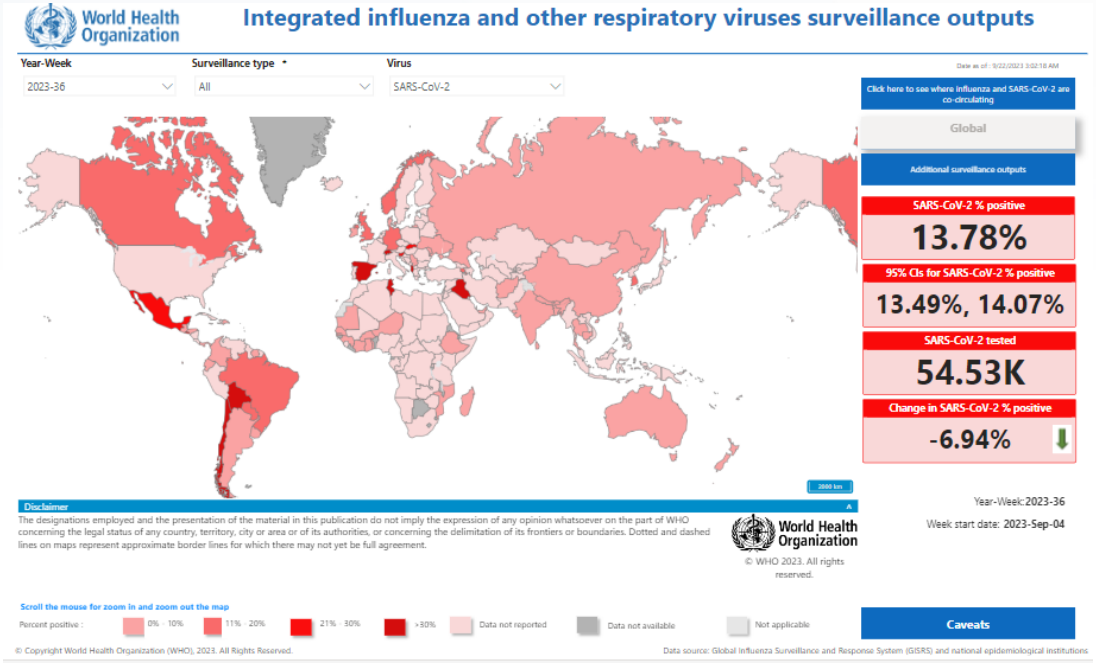
As of 17 September 2023

WHO Region	New cases in last 28 days (%)	Change in new cases in last 28 days *	Cumulative cases (%)	New deaths in last 28 days (%)	Change in new deaths in last 28 days *	Cumulative deaths (%)
Western Pacific	737 111 (75%)	-46%	207 262 442 (27%)	535 (32%)	-46%	416 969 (6%)
Europe	211 403 (22%)	75%	276 117 561 (36%)	871 (51%)	-39%	2 248 538 (32%)
Americas	22 890 (2%)	-47%	193 254 876 (25%)	141 (8%)	-81%	2 959 361 (43%)
South-East Asia	3 214 (<1%)	-29%	61 204 332 (8%)	126 (7%)	85%	806 778 (12%)
Eastern Mediterranean	2 757 (<1%)	-10%	23 390 996 (3%)	19 (1%)	-44%	351 414 (5%)
Africa	435 (<1%)	-49%	9 547 425 (1%)	3 (<1%)	-50%	175 426 (3%)
Global	**977 810 (100%)**	**-36%**	**770 778 396 (100%)**	**1 695 (100%)**	**-48%**	**6 958 499 (100%)**

- **Percent change in the number of newly confirmed cases/deaths in the past 28 days, compared to 28 days prior. Data from previous weeks are updated continuously with adjustments received from countries*
- Starting from the week commencing on 11 September 2023, the source of the data from the Region of the Americas was switched to the aggregated national surveillances, received through the COVID-19, Influenza, RSV and Other Respiratory Viruses program in the Americas. Data have been included retrospectively since 31 July 2023. For more information regarding COVID-19 in the Americas, please access the link: https://www.paho.org/en/topics/influenza-and-other-respiratory-viruses.

Integrated respiratory disease surveillance: expanded Global Influenza Surveillance and Response System (e-GISRS)





Source: [WHO's integrated dashboard provided by the Global Influenza Programme]

28-day change in new hospitalizations and ICU admissions by WHO region

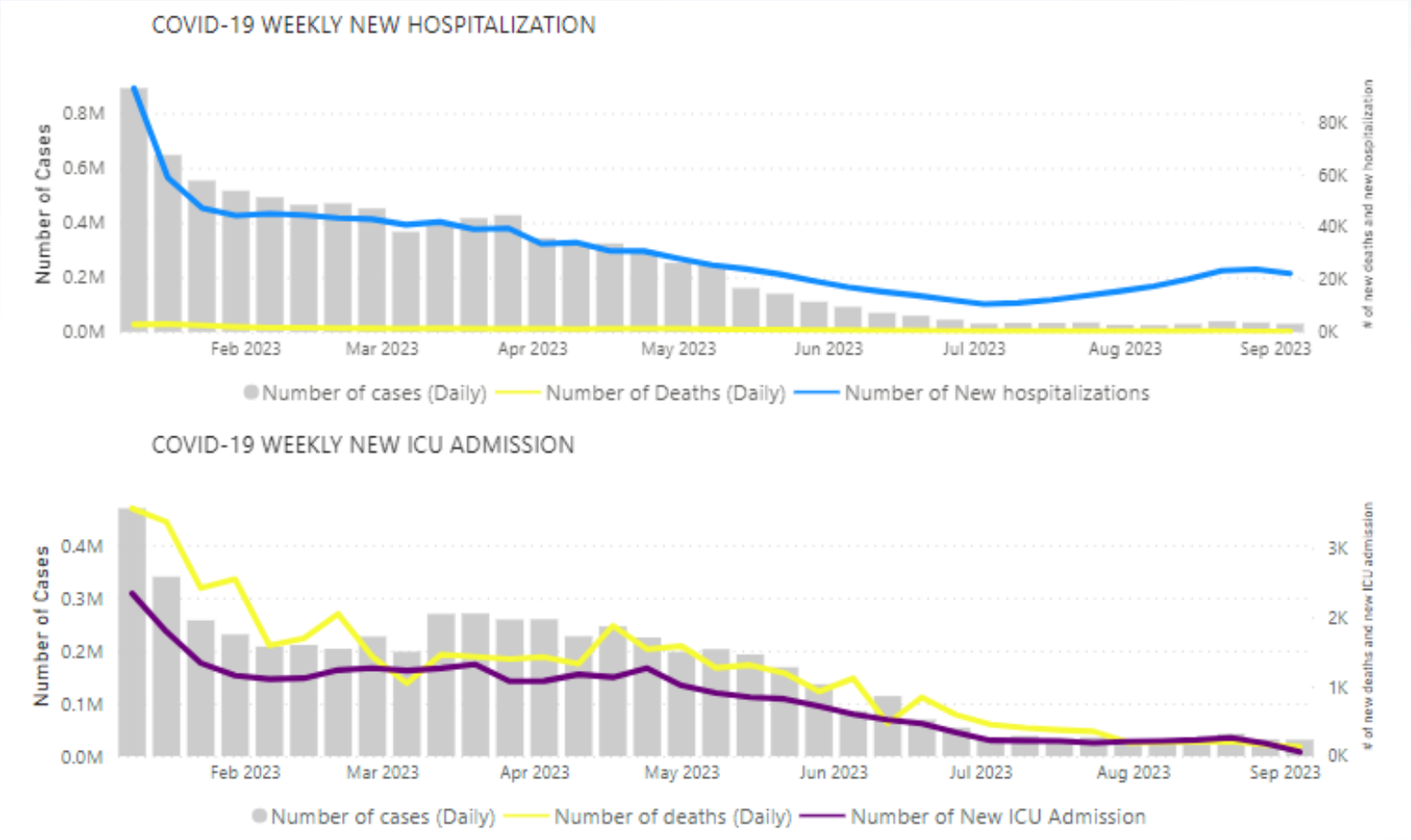
14 August to 10 September 2023 compared to 17 July to 13 August 2023

Region	New hospitalizations from countries that reported consistently in the last and previous 28 days			New ICU admissions from countries that reported consistently in the last and previous 28 days		
	Number of countries (percentage)	Number of new hospitalizations	Percent change*	Number of countries (percentage)	Number of new ICU admission	Percent change*
Africa	0/50 (<1%)	NA	NA	0/50 (<1%)	N/A	N/A
Americas	11/56 (20%)	76 908	+266	9/56 (16%)	38	+3%
Eastern Mediterranean	0/22 (<1%)	NA	N/A	0/22 (<1%)	N/A	N/A
Europe	8/61 (13%)	8717	+43%	8/61 (13%)	248	+43%
South-East Asia	2/10 (20%)	98	-94%	1/10 (10%)	4	-60%
Western Pacific	1/35 (3%)	2276	-17%	2/35 (9%)	62	-41%
Global	**22/234 (9%)**	87 999	**+55%**	**19/234 (8%)**	**352**	**+8%**

*To compare the last 28 days and the previous 28-day period, the table includes only those countries that consistently reported data for both periods.
**N/A denotes 'not available,' while N/D represents 'not definable'.

Global COVID-19 weekly trends in reported hospitalizations and ICU admissions

Data reported to WHO as of 10 September 2023



Number of countries that reported new hospitalizations at least once in 2023

68/234 (29%)

Number of countries that reported new ICU admissions at least once in 2023

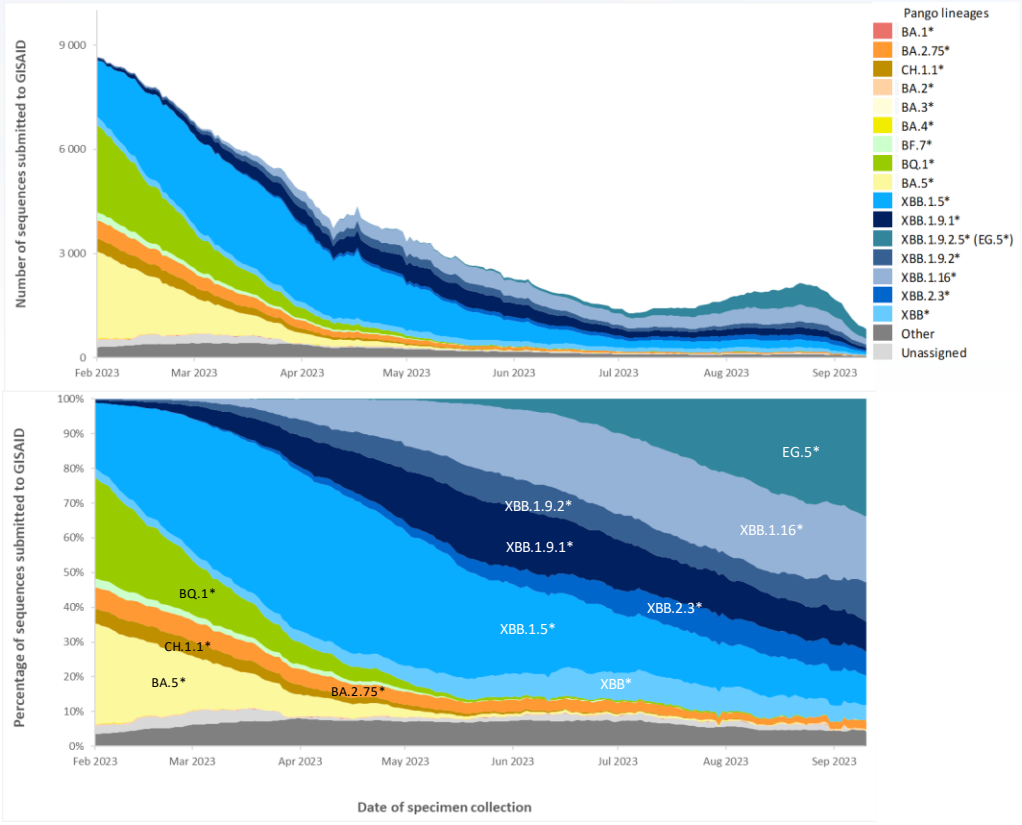
42/234 (17%)

Note: Recent weeks are subject to reporting delays and data might not be complete, note to interpret the data with caution. Cases included in grey bars in the graph are only from countries reporting hospitalizations or ICU admissions, respectively.

Circulation of SARS-CoV-2 variants

as of 25 September 2023

Number and percentage of SARS-CoV-2 sequences, 1 February to 10 September 2023



Figures by WHO, data from GISAID.org, extracted on 25 September 2023.

- § Number of countries and sequences are since the emergence of the variants
- * Includes descendant lineages, except those individually specified elsewhere in the table. For example, XBB* does not include XBB.1.5, XBB.1.16, EG.5, XBB.1.9.1, XBB.1.9.2, and XBB.2.3
- + "Other" represents other circulating lineages excluding the VOI, VUMs, BA.1*, BA.2*, BA.3*, BA.4*, BA.5*. Due to delays in or retrospective assignment of variants, caution should be taken when interpreting the prevalence of the "Other" category.
- ǂ Prevalence for BA.2.86 cannot be calculated due to the very small numbers of sequences.
- The VOI and the VUMs that have shown increasing trends are highlighted in orange, those that have remained stable are highlighted in blue, while those with decreasing trends are highlighted in green.

Genomic sequencing of circulating SARS-CoV-2

Globally, from 28 August to 24 September 2023 (28 days), 21 773 SARS-CoV-2 sequences were shared through GISAID.

Variants of Interest (VOIs)*, as of 30 August 2023

- XBB.1.5
- XBB.1.16
- EG.5

Variants Under Monitoring (VUMs)*, as of 30 August 2023

- BA.2.75
- CH.1.1
- XBB
- XBB.1.9.1
- XBB.1.9.2
- XBB.2.3
- BA.2.86

Global weekly prevalence of SARS-CoV-2 VOIs and VUMs, Week 32 to 36, 2023§

Lineage	Countries§	Sequences§	2023-32	2023-33	2023-34	2023-35	2023-36
VOIs							
XBB.1.5*	125	287491	12.0	10.7	9.7	9.8	8.6
XBB.1.16*	120	69600	23.5	22.4	21.3	21.3	18.9
EG.5*	73	31905	25.9	28.1	30.2	30.5	33.6
VUMs							
BA.2.75*	128	128180	1.7	1.6	1.7	2.0	2.7
BA.2.86ǂ							
CH.1.1*	99	41367	0.1	0.1	0.1	0.0	0.0
XBB*	136	76999	6.2	5.9	5.2	4.7	4.1
XBB.1.9.1*	114	65528	10.3	9.8	9.5	9.9	8.7
XBB.1.9.2*	92	34137	6.3	7.6	8.4	8.7	11.2
XBB.2.3*	89	19158	7.7	7.1	7.1	7.4	6.9
Unassigned	92	149746	1.3	1.5	1.6	0.8	0.1
Other+	211	6778535	4.6	4.7	4.7	4.4	4.7

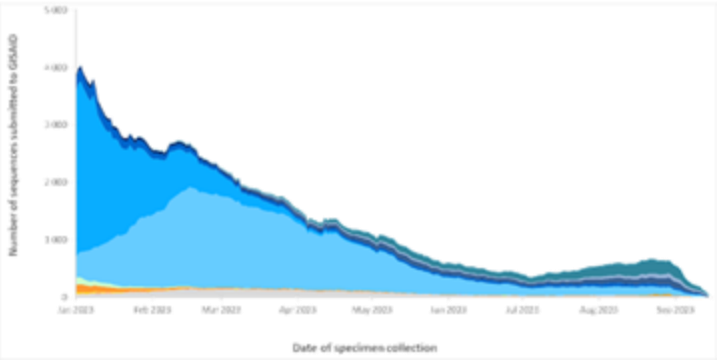
Variants trends by region

AFRO

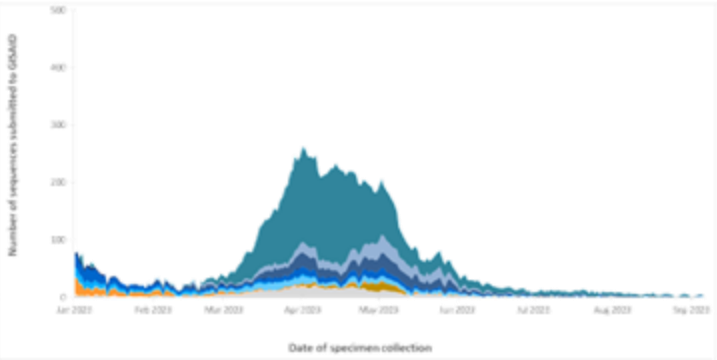
EMRO

EURO

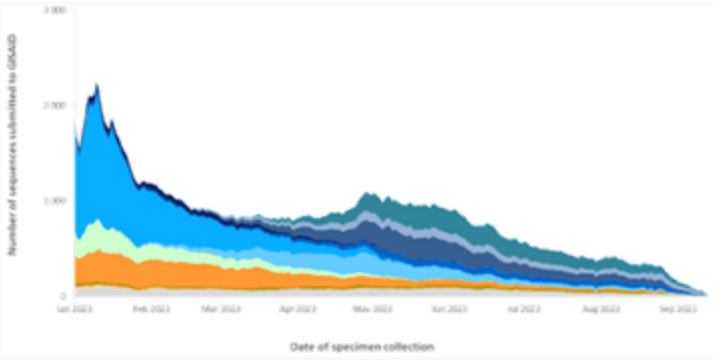
PAHO



SEARO



WPRO

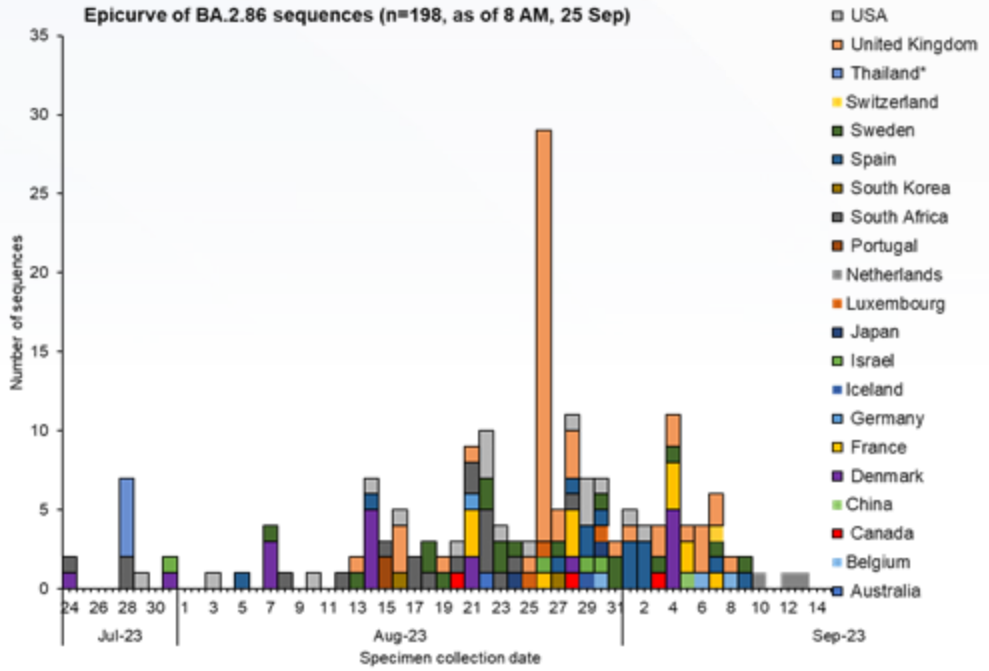


Note: Y-axis is different by regions.

Countries detecting VUM BA.2.86*

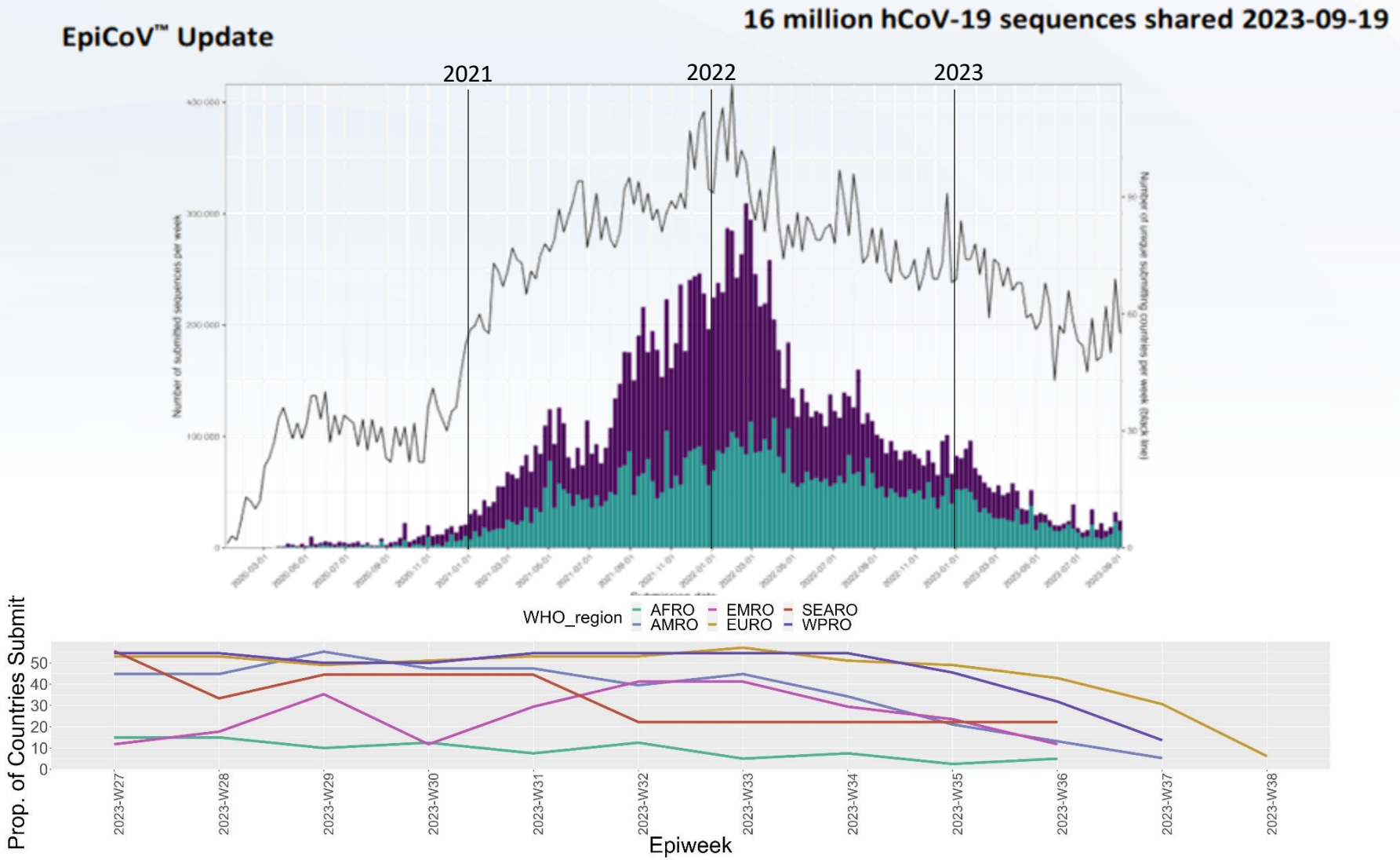
As of 8:00AM CEST, 25 September 2023

Country	Region	Sequences	Host	Source	Earliest specimen date
United Kingdom	EURO	53	Human	GISAID	13-Aug-23
Denmark	EURO	27	Human	GISAID	24-Jul-23
Sweden	EURO	18	Human	GISAID	7-Aug-23
Spain	EURO	16	Human	GISAID	5-Aug-23
France	EURO	13	Human	GISAID	21-Aug-23
Israel	EURO	4	Human	GISAID	31-Jul-23
Belgium	EURO	3	Human	GISAID	30-Aug-23
Luxembourg	EURO	3	Human	GISAID	25-Aug-23
Netherlands	EURO	3	Human	GISAID	10-Sep-23
Portugal	EURO	2	Human	GISAID	15-Aug-23
Germany	EURO	1	Human	GISAID	21-Aug-23
Iceland	EURO	1	Human	GISAID	29-Aug-23
Switzerland	EURO	1	Human	GISAID	7-Sep-23
South Africa	AFRO	19	Human	GISAID	24-Jul-23
United States of America	PAHO	19	Human	GISAID	29-Jul-23
Canada	PAHO	4	Human	GISAID	20-Aug-23
Thailand	SEARO	5	Environment	GISAID	28-Jul-23
Japan	WPRO	2	Human	GISAID	24-Aug-23
Republic of Korea	WPRO	2	Human	GISAID	16-Aug-23
Australia	WPRO	1	Human	GISAID	22-Aug-23
China	WPRO	1	Human	GISAID	5-Sep-23
Total		**198**			

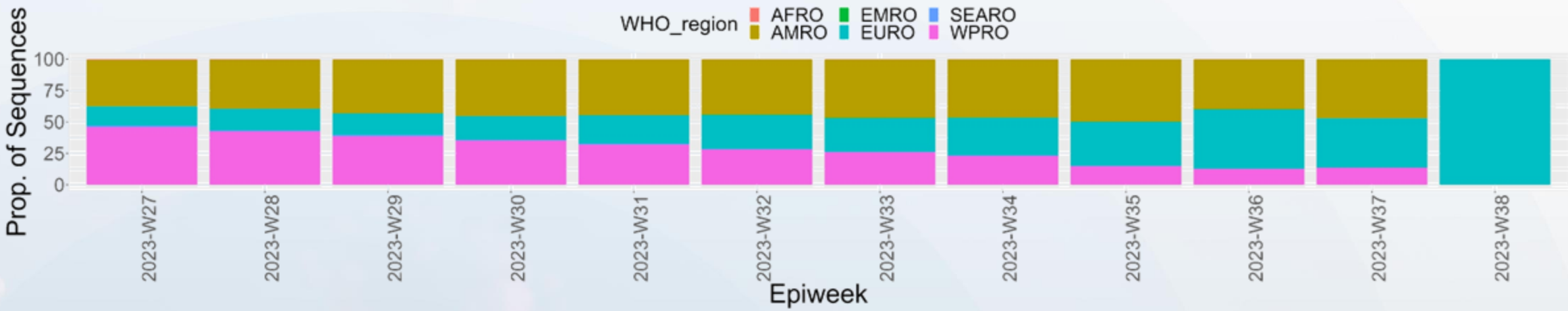


- 21 countries in 5 WHO regions have reported at least one sample of BA.2.86
- Limited information in epi / clinical presentation
- More cases/samples (both human and environment) were reported through EBS

Sequences shared through GISAID and the proportion of countries submitting sequences by WHO region

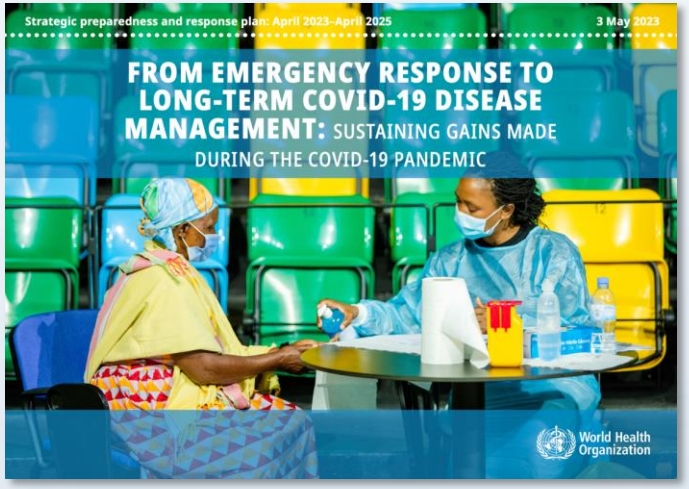


Sequence Contribution Proportion by Region



The majority of sequences are submitted by countries in three regions: AMRO, EURO, and WPRO

Successfully Transitioning from Emergency Response to Long-Term Sustained COVID-19 Disease Management



OBJECTIVES:

- To reduce and control the incidence of SARS-CoV-2 infections to minimize severe disease and reduce impacts on the health care system.
- To prevent, diagnose and treat COVID-19 to reduce mortality, morbidity, and long-term sequelae.
- To support Member States transition from a crisis response to an integrated longer-term, strengthened and sustainable COVID-19 programs.

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WHO advisory groups related to variants and vaccination

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 which variants warrant further investigation
- Assesses public health risk posed by emerging variants
- Assesses whether variants have altered phenotypic characteristics

Vaccine

Research, evidence assessment

TAG-CO-VAC

- Assesses the impact of variants on current COVID-19 vaccines and whether changes to vaccine composition needed

Vax Research Expert Group
methods for vaccine development & assessment

Vax Effectiveness WG
assesses & supports VE and impact studies

Regulatory TAG
advises on EUL of vaccines through evidence-based assessment

Vaccine impact

Policy

SAGE

- advises on vaccination policies, as well as immunization strategies and delivery programmes

Standing recommendations for COVID-19 issued by the Director-General in accordance with the IHR (2005)

9 August 2023

A. States Parties are recommended to revise and implement, as appropriate, national COVID19 plans and policies that take into account the WHO COVID-19 Strategic Preparedness and Response Plan April 2023- April 2026 (…).

B. States Parties are recommended to sustain collaborative surveillance5 for COVID-19, in order to provide a basis for situational awareness and risk assessment and the detection of significant changes in virus characteristics, virus spread, disease severity and population immunity

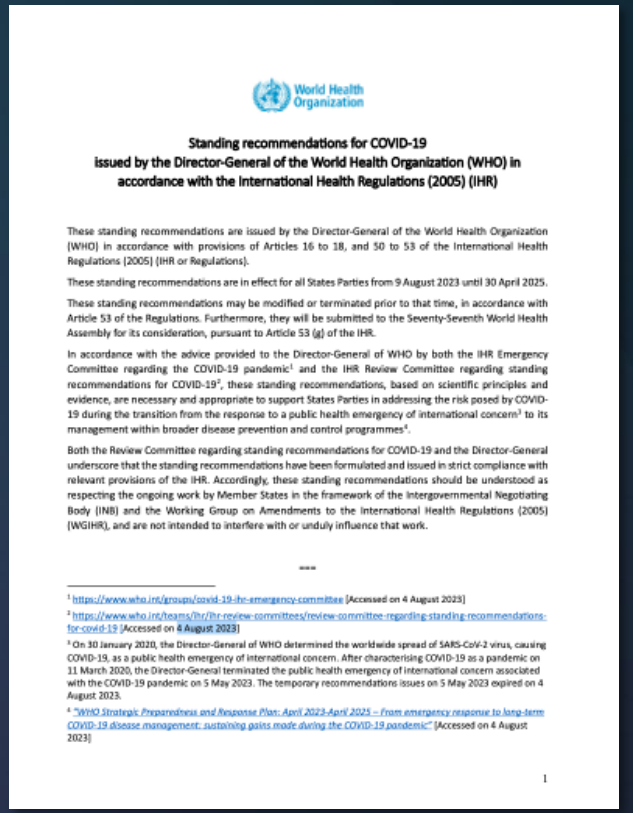
C. States Parties are recommended to continue reporting COVID-19 data (…) and vaccine effectiveness data to WHO or in open sources so that WHO can understand and describe the epidemiological situation and variant landscape, perform global risk assessments and work with expert networks and relevant WHO Advisory Groups

D. States Parties are recommended to continue to offer COVID-19 vaccination based on both, the recommendations of the WHO Strategic Advisory Group of Experts on Immunization (SAGE) and on national prioritization informed by cost benefit reviews. Vaccine delivery should be appropriately integrated into health services.

E. States Parties are recommended to continue to initiate, support, and collaborate on research to generate evidence for COVID-19 prevention and control, with a view to reduce the disease burden of COVID-19

F. States Parties are encouraged to continue deliver optimal clinical care for COVID-19, appropriately integrated into all levels of health services, including access to proven treatments and measures to protect health workers and caregivers as appropriate

G. States Parties are encouraged to continue to work towards ensuring equitable access to safe, effective and quality-assured medical countermeasures for COVID-19.



World Health Organization

Standing recommendations for COVID-19
issued by the Director-General of the World Health Organization (WHO) in accordance with the International Health Regulations (2005) (IHR)

These standing recommendations are issued by the Director-General of the World Health Organization (WHO) in accordance with provisions of Articles 16 to 18, and 50 to 53 of the International Health Regulations (2005) (IHR or Regulations).

These standing recommendations are in effect for all States Parties from 9 August 2023 until 30 April 2025.

These standing recommendations may be modified or terminated prior to that time, in accordance with Article 53 of the Regulations. Furthermore, they will be submitted to the Seventy-Seventh World Health Assembly for its consideration, pursuant to Article 53 (g) of the IHR.

In accordance with the advice provided to the Director-General of WHO by both the IHR Emergency Committee regarding the COVID-19 pandemic[1] and the IHR Review Committee regarding standing recommendations for COVID-19[2], these standing recommendations, based on scientific principles and evidence, are necessary and appropriate to support States Parties in addressing the risk posed by COVID-19 during the transition from the response to a public health emergency of international concern[3] to its management within broader disease prevention and control programmes[4].

Both the Review Committee regarding standing recommendations for COVID-19 and the Director-General underscore that the standing recommendations have been formulated and issued in strict compliance with relevant provisions of the IHR. Accordingly, these standing recommendations should be understood as respecting the ongoing work by Member States in the framework of the Intergovernmental Negotiating Body (INB) and the Working Group on Amendments to the International Health Regulations (2005) (WGIHR), and are not intended to interfere with or unduly influence that work.

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[1] https://www.who.int/groups/covid-19-ihr-emergency-committee [Accessed on 4 August 2023]

[2] https://www.who.int/teams/ihr/ihr-review-committees/review-committee-regarding-standing-recommendations-for-covid-19 [Accessed on 4 August 2023]

[3] On 30 January 2020, the Director-General of WHO determined the worldwide spread of SARS-CoV-2 virus, causing COVID-19, as a public health emergency of international concern. After characterising COVID-19 as a pandemic on 11 March 2020, the Director-General terminated the public health emergency of international concern associated with the COVID-19 pandemic on 5 May 2023. The temporary recommendations issues on 5 May 2023 expired on 4 August 2023.

[4] *"WHO Strategic Preparedness and Response Plan: April 2023-April 2025 – From emergency response to long-term COVID-19 disease management: sustaining gains made during the COVID-19 pandemic"* [Accessed on 4 August 2023]

1

https://www.who.int/publications/m/item/standing-recommendations-for-covid-19-issued-by-the-director-general-of-the-world-health-organization-(who)-in-accordance-with-the-international-health-regulations-(2005)-(ihr)

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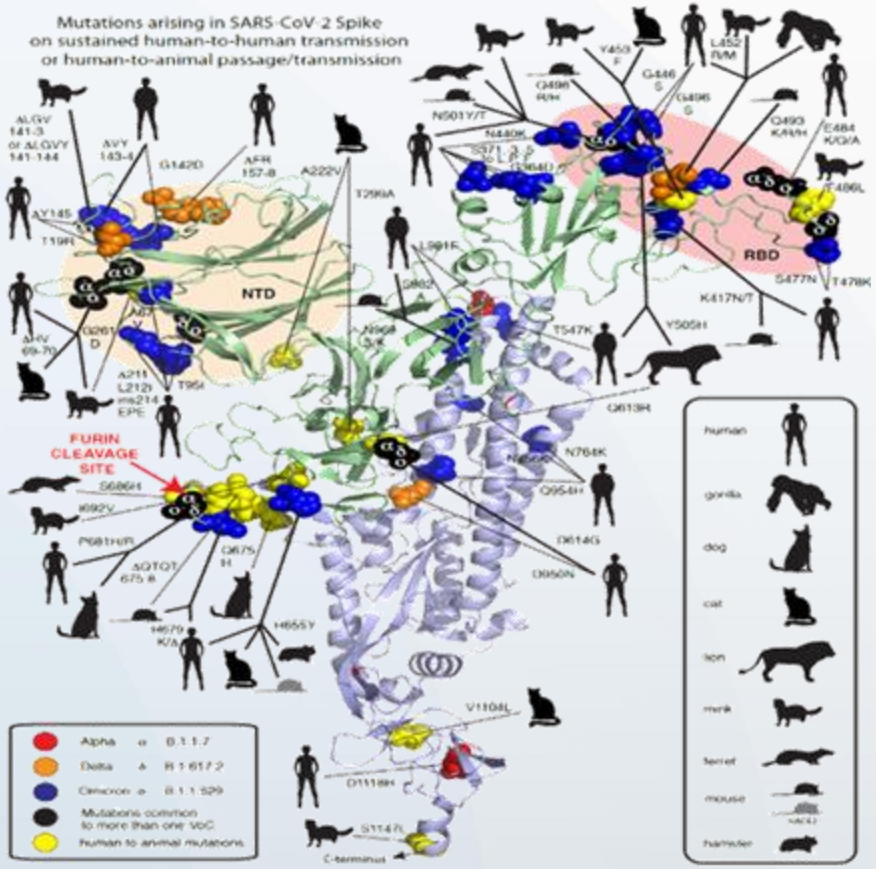
SARS-CoV-2 variant risk evaluation framework

Anne Von Gottberg

World Health Organization | EPI•WiN | EPIDEMIC & PANDEMIC PREPAREDNESS & PREVENTION

SARS-CoV-2 will continue to evolve

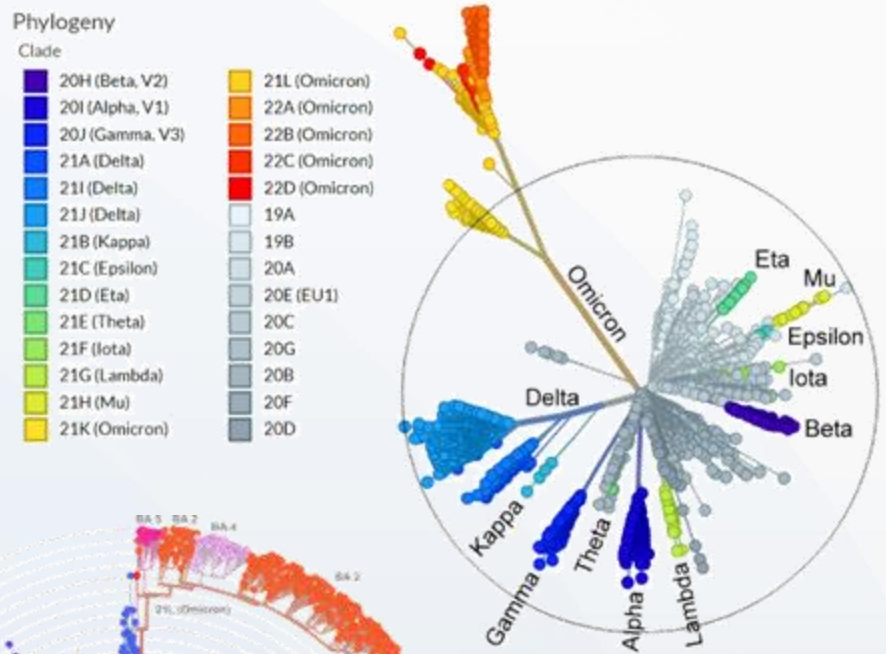
- Potential drivers of emergence of genetically divergent SARS-CoV-2 variants
  - Transmission and prolonged human-human transmission in areas with limited surveillance and sequencing
  - Viral adaptation following prolonged circulation in susceptible animals
  - Recombination of SARS-CoV-2 with other coronaviruses in animals or humans
  - Persistent SARS-CoV-2 infection in an immunocompromised

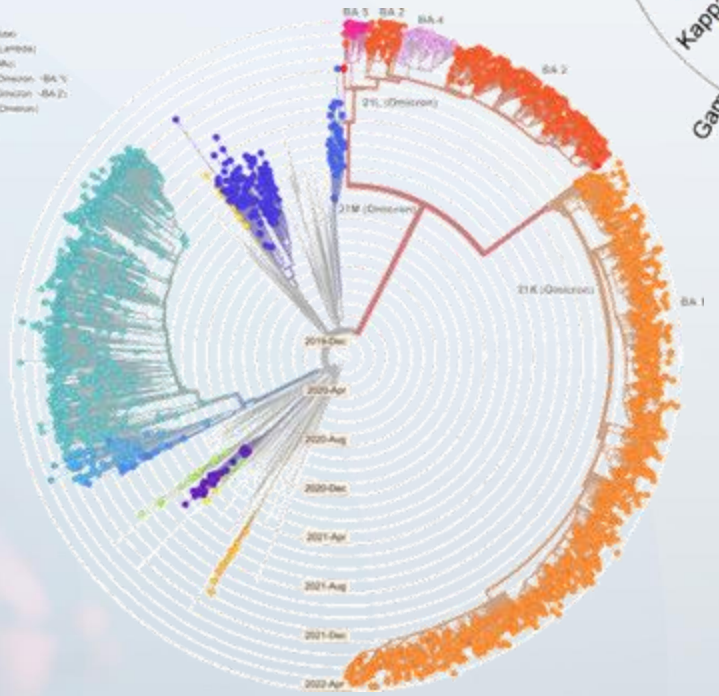


Omicron

Many lineages, One family

- Different, yet similar
  - Wide spectrum of mutations and sub-lineages
  - All lineages far more similar to each other than to pre-Omicron lineages
    - High immune escape
    - Upper airway tropism
    - Lower severity, esp with prior immunity





Shreshtha, Med Virol 2022 and Fuss, COVID 2023

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Global prevalence of SARS-CoV-2 VOIs and VUMs

Lineage	Countries[§]	Sequences[§]	2023-32	2023-33	2023-34	2023-35	2023-36
VOIs							
XBB.1.5*	125	287 491	12.0	10.7	9.7	9.8	8.6
XBB.1.16*	120	69 600	23.5	22.4	21.3	21.3	18.9
EG.5*	73	31 905	25.9	28.1	30.2	30.5	33.6
VUMs							
BA.2.75*	128	128 180	1.7	1.6	1.7	2.0	2.7
BA.2.86[ǂ]	21	198					
CH.1.1*	99	41 367	0.1	0.1	0.1	0.0	0.0
XBB*	136	76 999	6.2	5.9	5.2	4.7	4.1
XBB.1.9.1*	114	65 528	10.3	9.8	9.5	9.9	8.7
XBB.1.9.2*	92	34 137	6.3	7.6	8.4	8.7	11.2
XBB.2.3*	89	19 158	7.7	7.1	7.1	7.4	6.9
Unassigned	92	149 746	1.3	1.5	1.6	0.8	0.1
Other[+]	211	6 778 535	4.6	4.7	4.7	4.4	4.7

+ "Other" represents other circulating lineages excluding the VOI, VUMs, BA.1*, BA.2*, BA.3*, BA.4*, BA.5*. Due to delays in or retrospective assignment of variants, caution should be taken when interpreting the prevalence of the "Other" category.

Initial and updated risk evaluation of variants

Indicators:

1. Growth Advantage
2. Immune Escape
3. Disease/Clinical severity

Public health risk for each indicator:

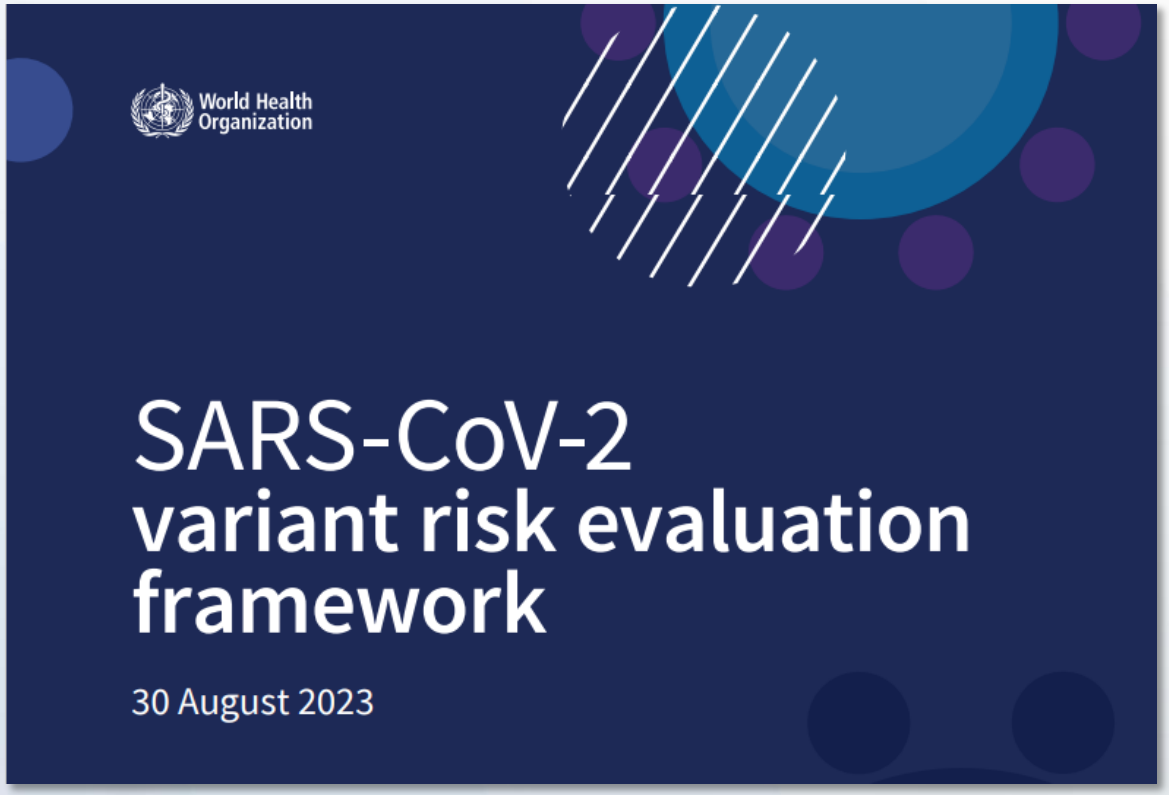
Low, Moderate and High

Confidence in the Assessment:

Low, Moderate and High

Assessments:

1. Rapid (0-4 Weeks)
2. Comprehensive (4-12 Weeks)



SARS-CoV-2 variant risk evaluation framework, 30 August 2023 (who.int)

Current WHO process to track variants

GISAID covSPECTRUM

Step 1:

Any variant showing an early signal of growth advantage and significant spread is eligible to become a variant under monitoring (VUM); alternatively, a variant with an unusually large number of mutations including in antigenic sites and evidence of community spread can also become a VUM, even if sequences are too few to estimate growth advantage.

Step 2:

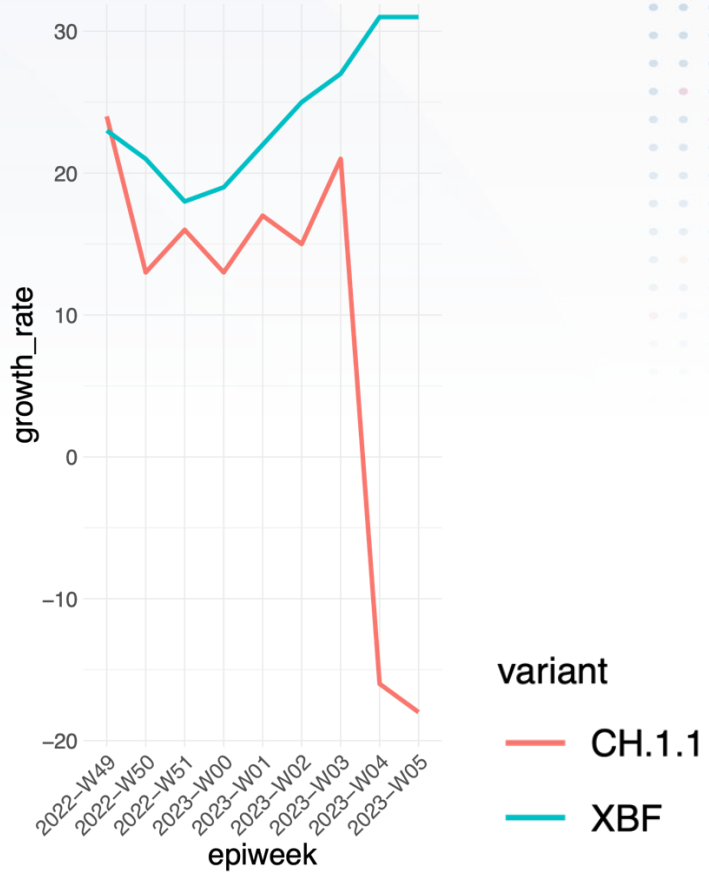
If growth advantage is suspected to be able to lead to global predominance, advice from TAG-VE is solicited and an initial risk evaluation that looks at various indicators (i.e. mainly immune escape, growth advantage and severity, but also impact on therapeutics and diagnostics) is initiated. The risk evaluation is updated as new data emerges.

Tracking SARS-CoV-2 variants (who.int)

Example of early signal of growth advantage (step 1)

Oceania

nextstrainClade	2022-W50	2022-W51	2023-W00	2023-W01	2023-W02	2023-W03	2023-W04	2023-W05
21L (BA.2)	0.82	1.11	1.17	0.92	0.83	0.38	0.83	0.00
22A (BA.4)	0.22	0.07	0.21	0.00	0.10	0.00	0.00	0.00
22B (BA.5)	13.09	12.41	7.46	6.93	4.24	2.63	2.50	8.33
22D (BA.2.75)	44.69	43.46	39.87	42.65	40.85	44.09	46.67	41.67
22E (BQ.1)	21.97	19.54	18.23	17.20	15.62	17.07	13.33	16.67
22F (XBB)	2.89	1.93	2.03	1.84	2.59	3.19	9.17	0.00
23A (XBB.1.5)	0.22	0.82	0.21	0.75	1.34	3.19	6.67	0.00
recombinant	16.09	20.65	30.81	29.72	34.44	29.46	20.83	33.33



WHO-TAG-VE Risk Evaluation EG.5 (step 2)

Overall assessment	**Low**	
Indicator	**Level of risk**	**Level of confidence**
Growth advantage	Moderate	High
Antibody escape	Moderate	Moderate
Severity and clinical considerations	Low	Low

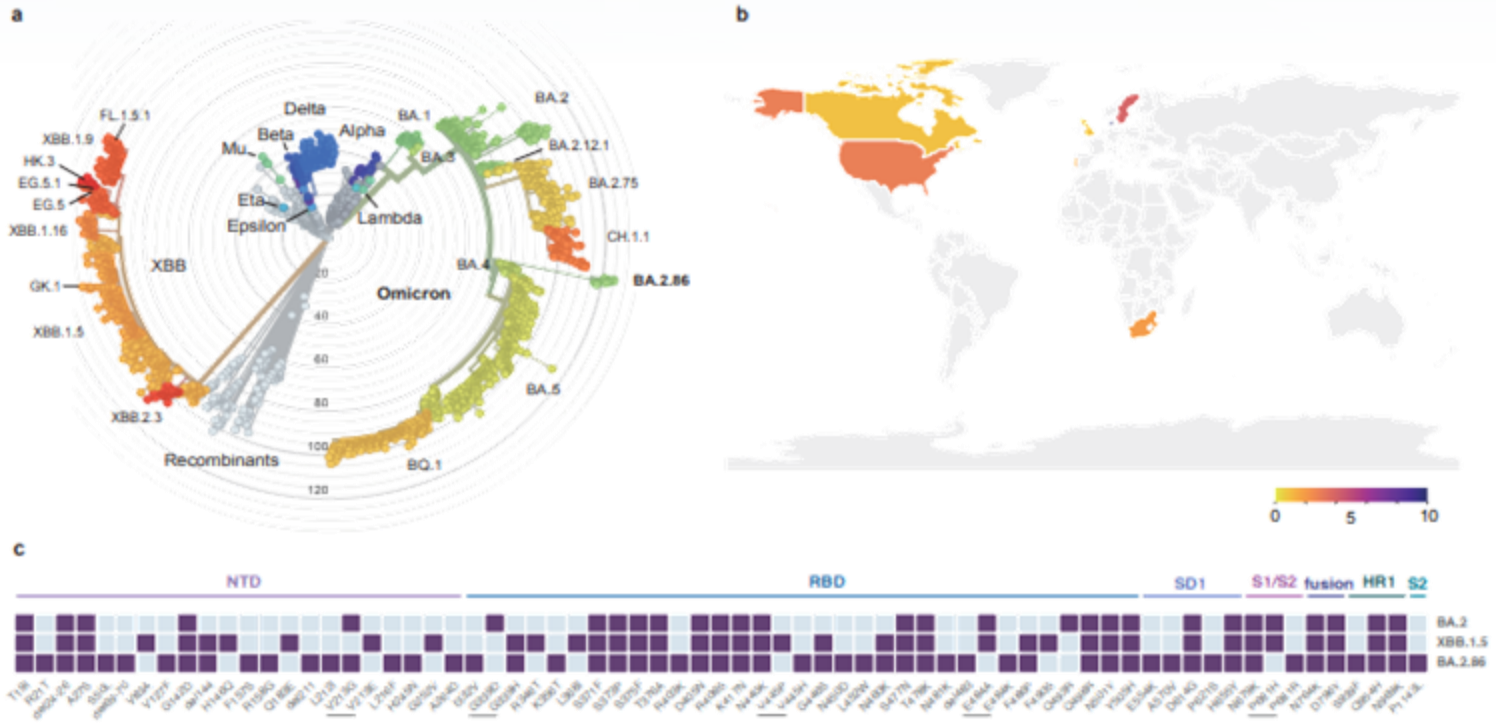
WHO-TAG-VE Risk Evaluation EG.5 (step 2)

- **Updated risk evaluation release:**
  21 September 2023 (Initial risk evaluation released on 09 August 2023)
- **Data:**
  31 712 sequences of EG.5 from 71 countries (excluding low coverage sequences). The largest portion of EG.5 sequences are from the United States of America (25.2%, 7979 sequences), China (18.4%, 5826 sequences), and Japan (10.2%, 3241 sequences).
- **Overall Assessment:** Available evidence does not suggest that EG.5 has additional public health risks relative to the other currently circulating Omicron descendent lineages.

eg5-risk-evaluation.pdf (who.int)

- **Confidence in the Assessment:** Low: due to the prevailing unreliability of reporting and non-representative availability of sequencing, additional data outlined in this risk evaluation are needed for a more comprehensive evaluation of the risk posed by EG.5.
- **Recommendations:**
  - Neutralization assays using human sera representative of the affected community(ies) and XBB.1.5 live virus isolates (2-4 weeks).
  - Comparative assessment to detect changes in rolling or ad hoc indicators of severity (4-12 weeks)

BA.2.86: a new highly mutated variant under monitoring

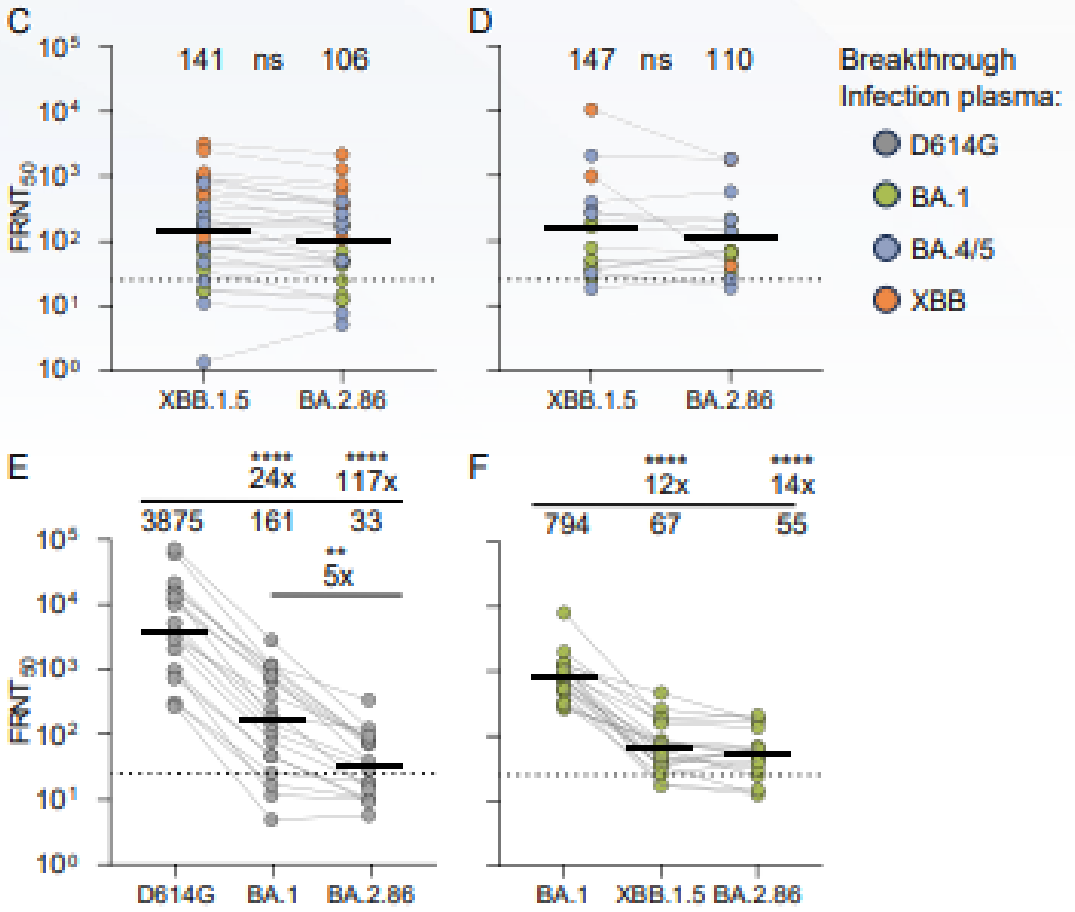


- >20 mutations in the spike as compared to XBB.1.5, including many in the RBD
- Significant evolutionary jump as compared to BA.2
- Not part of the XBB family of viruses, as opposed to vast majority of currently circulating variants (eg EG.5, XBB.1.5 etc)

Yang et al 2023 bioxriv, https://www.biorxiv.org/content/10.1101/2023.09.01.555815v1

Phenotypic characterization of BA.2.86: Neutralization

- BA.2.86 did not have significantly more escape than Omicron XBB.1.5 from neutralizing immunity elicited by infection of Omicron subvariants ranging from BA.1 to XBB, either by infection alone or as breakthrough infection in vaccinated individuals.

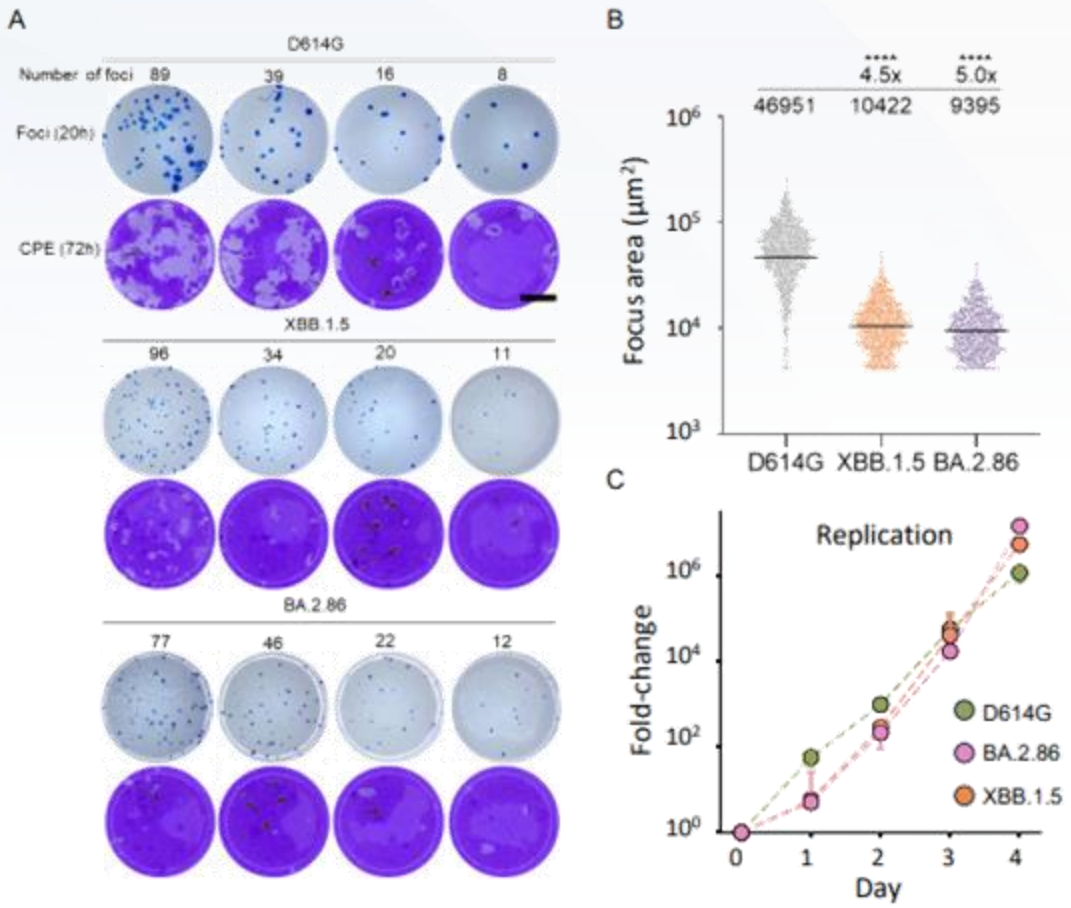


Khan et al, medxriv 2023, Evolution and neutralization escape of the SARS-CoV-2 BA.2.86 subvariant (medrxiv.org)

Phenotypic characterization of BA.2.86: Virus Properties

- No substantial difference in viral properties in cell culture relative to XBB.1.5.
- Both BA.2.86 and XBB.1.5 produced infection foci of similar size, had similar cytopathic effect (both lower than ancestral SARS-CoV-2), and had similar replication dynamics.

Khan et al, medxriv 2023, Evolution and neutralization escape of the SARS-CoV-2 BA.2.86 subvariant (medrxiv.org)



Summary

- EG.5 and its descendent lineages are the most reported variants globally, with a prevalence of around 30%. An updated risk evaluation for EG.5 was published on 21 September 2023 with the overall risk evaluation assessed to be low.
- This is followed by XBB.1.16 and its descendant lineages, which have been steadily decreasing in prevalence for a number of weeks, following the same trend as XBB.1.5
- On 17 August 2023, WHO designated BA.2.86 as a Variant Under Monitoring (VUM) due to the large number (>30) of spike gene mutations it carries.
  - As of 25 September 2023, there have been 198 new samples of BA.2.86 from 21 countries shared through GISAID. Samples are mainly from the WHO European Region.
  - However, information in epidemiology and clinical presentation is still limited, challenging to appropriately evaluate the risk of BA.2.86 on public health.

Acknowledgements

- WHO COVID-19 EMST
- Technical Advisory Groups and Scientific Advisory Groups supporting WHO, especially TAG-VE and TAG-CO-VAC
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