Current COVID-19 situation

Dr Maria Van Kerkhove, WHO

Overview of SARS-CoV-2 circulating variants

Dr Lorenzo Subissi, WHO

TAG-VE and variant risk assessment

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8 Feb 2023

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Current COVID-19 situation

Maria Van Kerkhove

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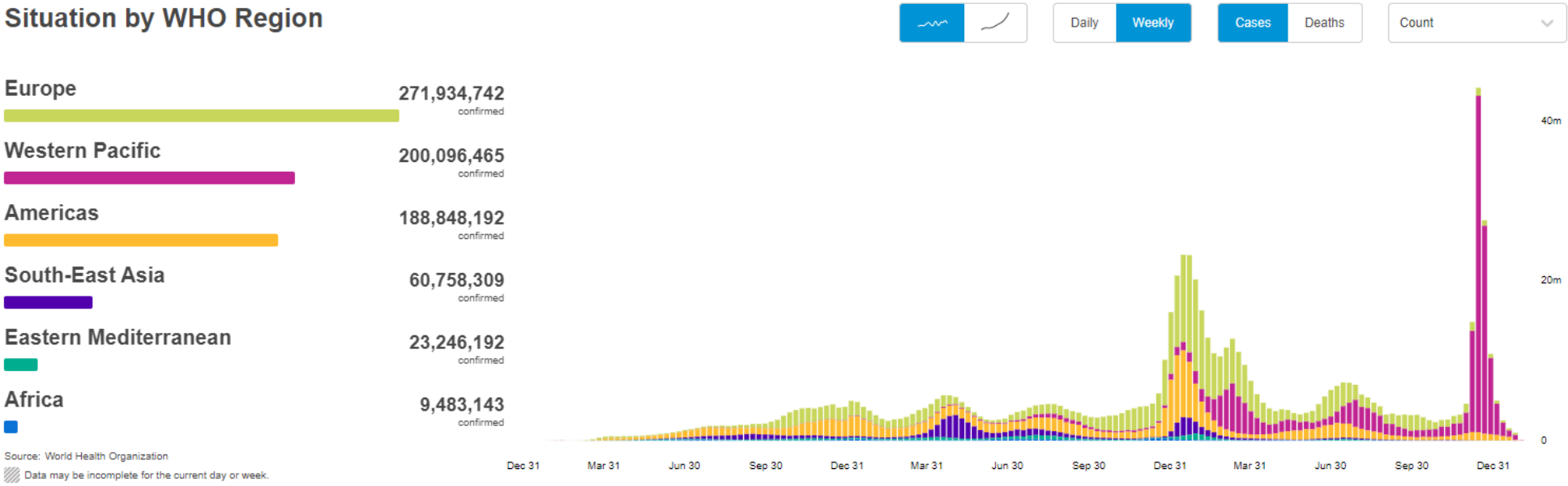
Global COVID-19 trends in reported cases and deaths

Cases reported to WHO as of 5 February 2023

- **New cases: > 1.3 Million**
- **New deaths: > 13 000**
- **Cumulative cases: > 754 Million**
- **Cumulative deaths: > 6.8 Million**

Situation by WHO Region



NOTE: Prior to 8 December 2022, cases from China (excl. Hong Kong SAR, Macao SAR, and Taiwan) were limited to symptomatic cases. From 9 December 2022 to 22 January 2023, all positive nucleic acid tests are reported as confirmed cases. Prior to 8 December 2022, deaths from China were defined as deaths directly caused by COVID-19 respiratory failure. Beginning 9 December, deaths from China are defined as deaths occurring in hospitals due to COVID-19 respiratory failure or COVID-19 infection combined with other underlying diseases.

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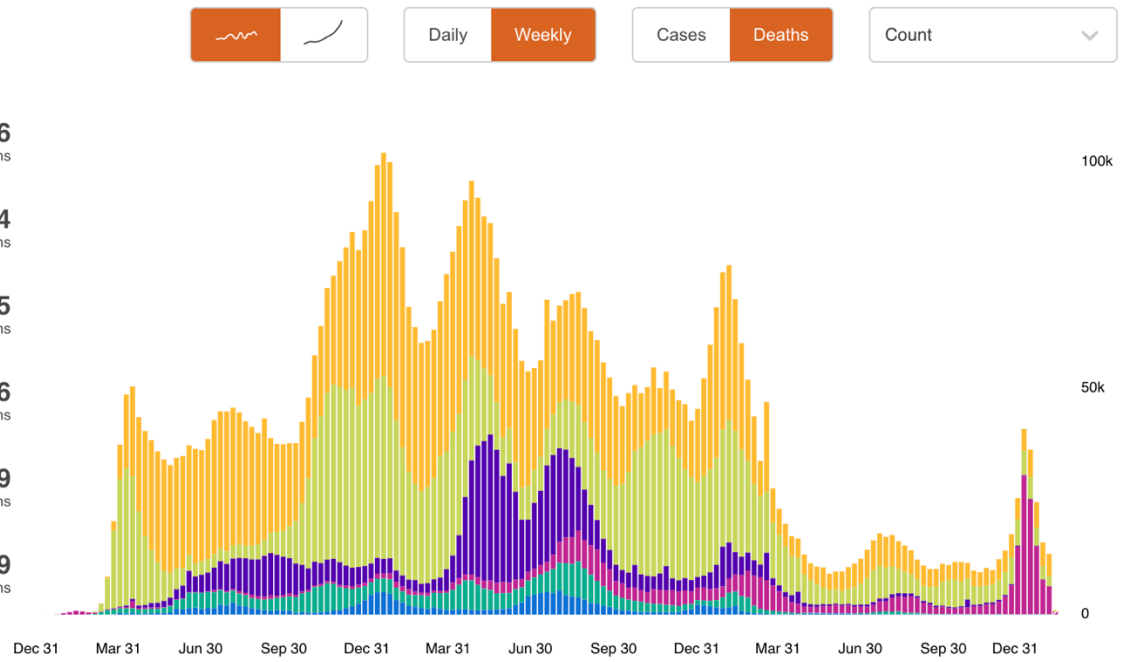
Situation by WHO Region

Americas	2,918,916 deaths
Europe	2,184,634 deaths
South-East Asia	803,725 deaths
Western Pacific	398,306 deaths
Eastern Mediterranean	349,379 deaths
Africa	175,259 deaths

Source: World Health Organization

Data may be incomplete for the current day or week.



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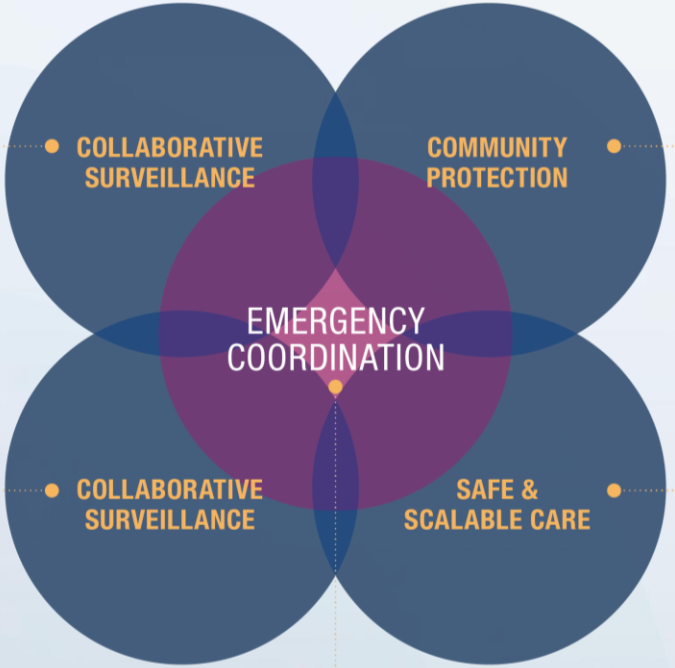
Critical areas of work/support for COVID-19 that continues

- Integrated disease surveillance
- Laboratories & diagnostics
- Public health intelligence



- Risk communication & infodemic management
- Environmental & population interventions
- Social welfare & economic protection

- Fast-track research and development
- Scalable manufacturing
- Coordinated supply chain & equitable access

- Emergency clinical care
- Health worker & patient protection
- Maintain essential health services

- Health emergency workforce
- National action plans for prevention preparedness & readiness
- Rapid alert & response coordination

* Additional Information Slides at the end

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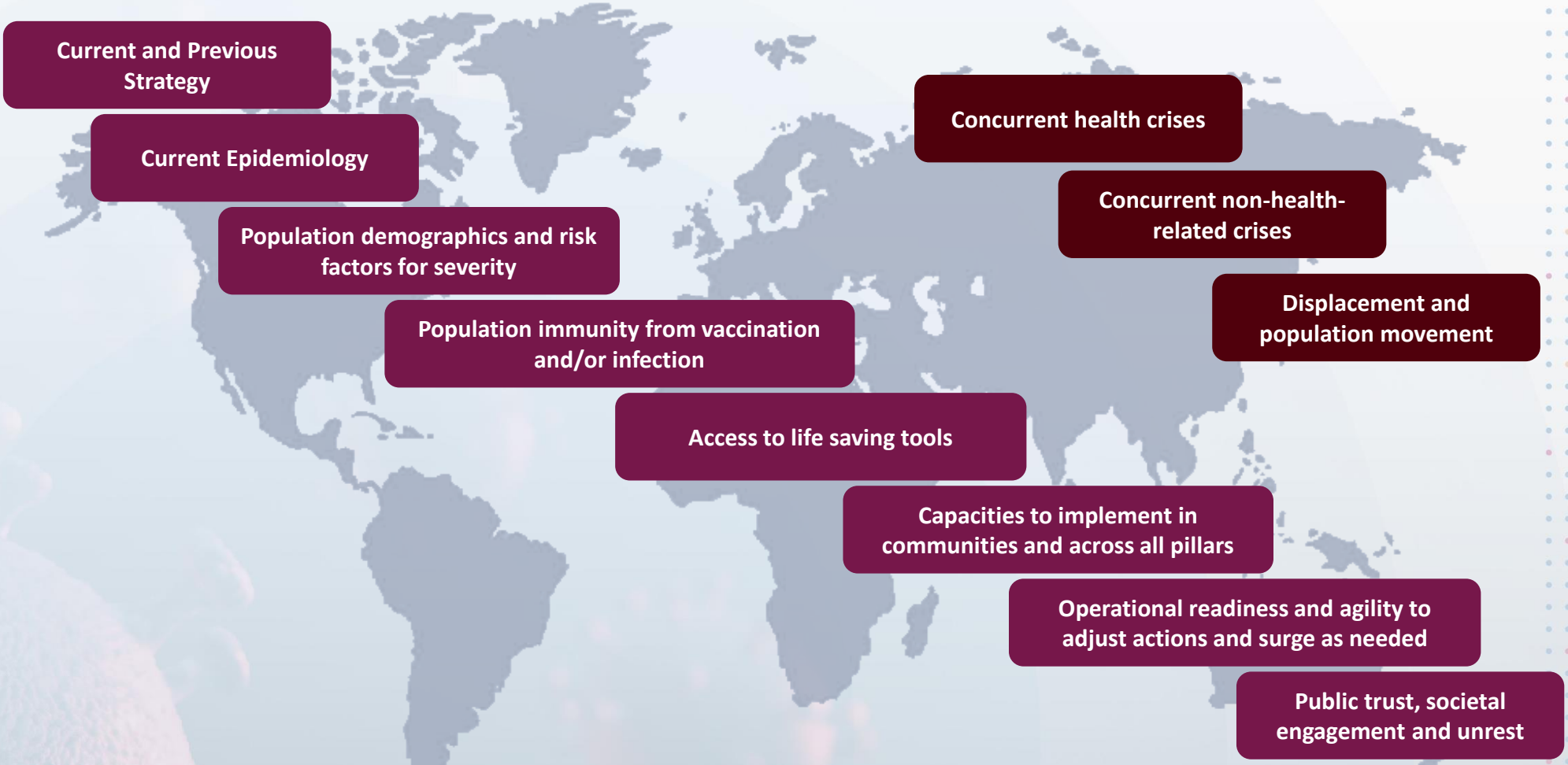
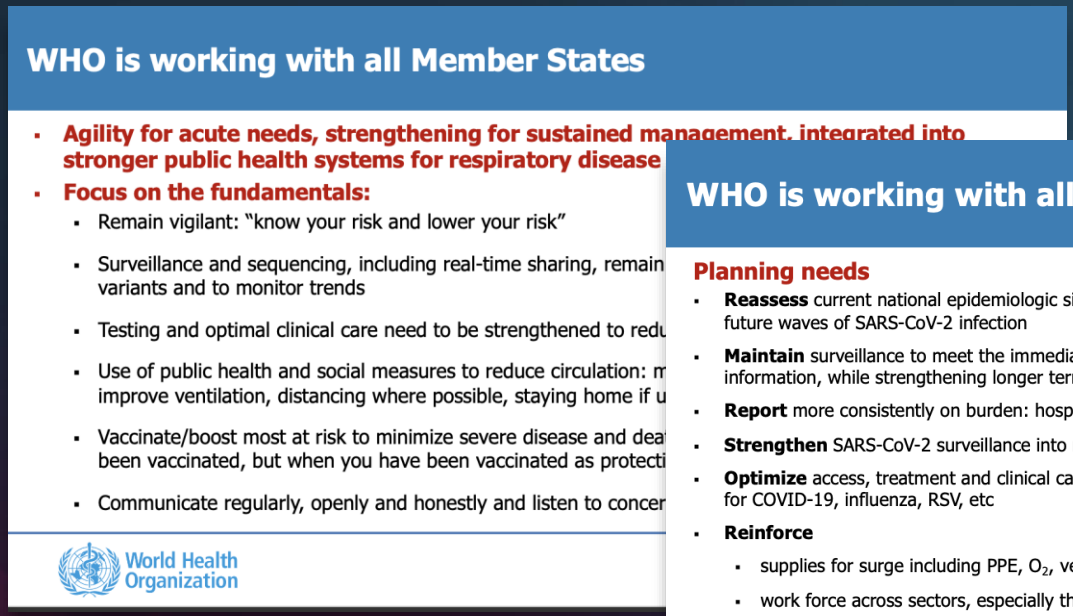
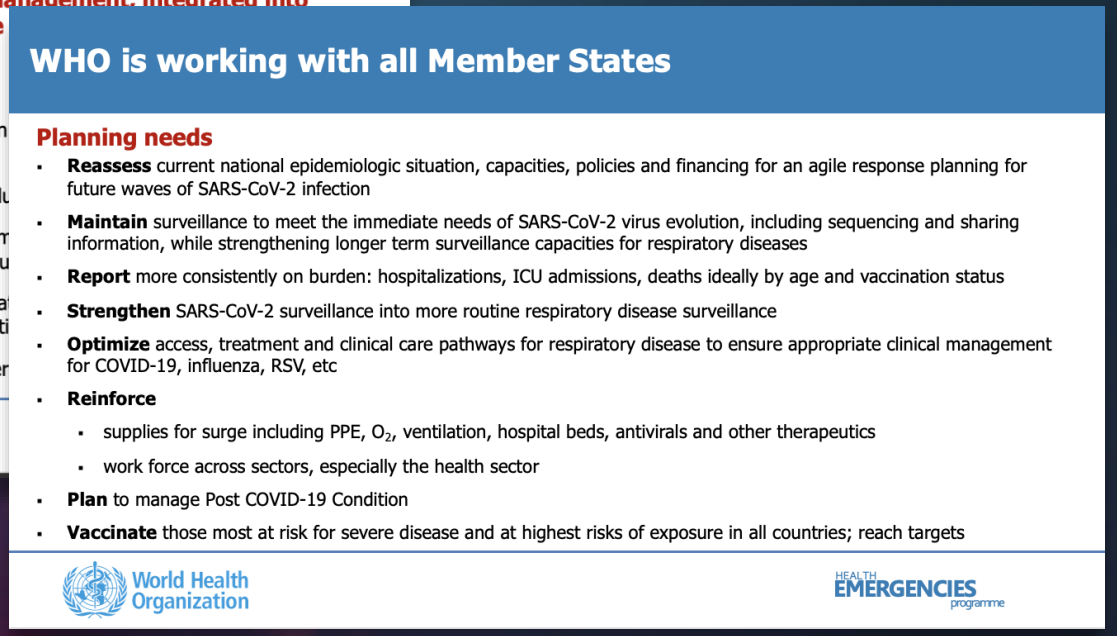
Countries face different situations, challenges & scenarios for ending the emergency phase & for transitioning to sustained COVID-19 management



WHO is working with all Member States to end the Emergency and achieve longer term COVID-19 management





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Overview of SARS-CoV-2 circulating variants

Lorenzo Subissi

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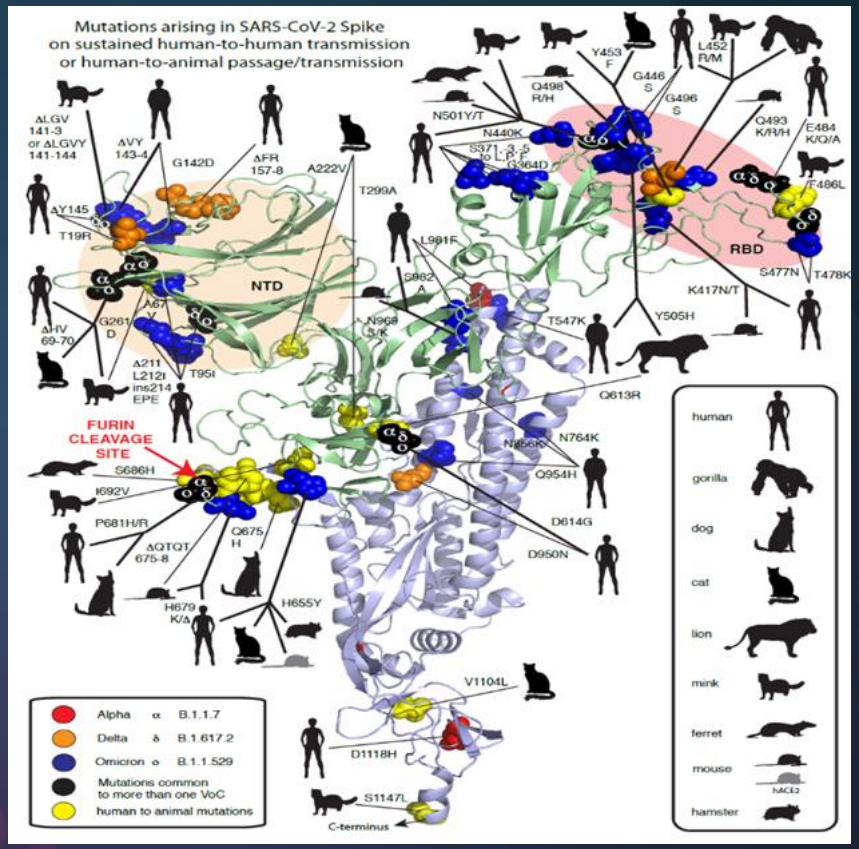
SARS-CoV-2 will continue to evolve

- **Potential drivers of emergence of genetically divergent SARS-CoV-2 variants**
  - Uncontrolled 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



Telenti A et al., Nature. 2021

Current WHO process to track variants

Step 1:

- Any variant showing an early signal of growth advantage and significant spread is eligible to become to be tracked more closely (e.g. Omicron subvariants under monitoring)

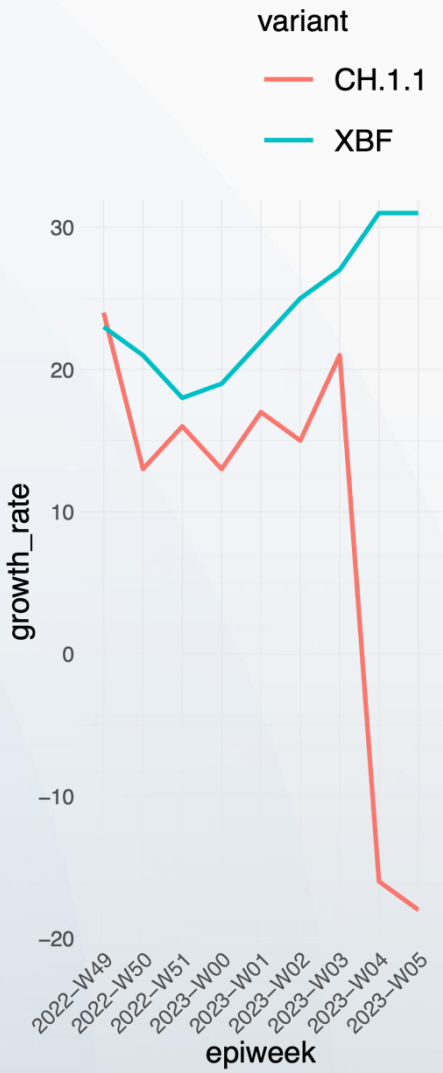
Step 2:

- If growth advantage is suspected to be able to lead to global predominance, advice from TAG-VE is solicited and a rapid risk assessment (RRA) is initiated. RRA is updated as new data emerges.

Example of early signal of growth advantage (step 1)

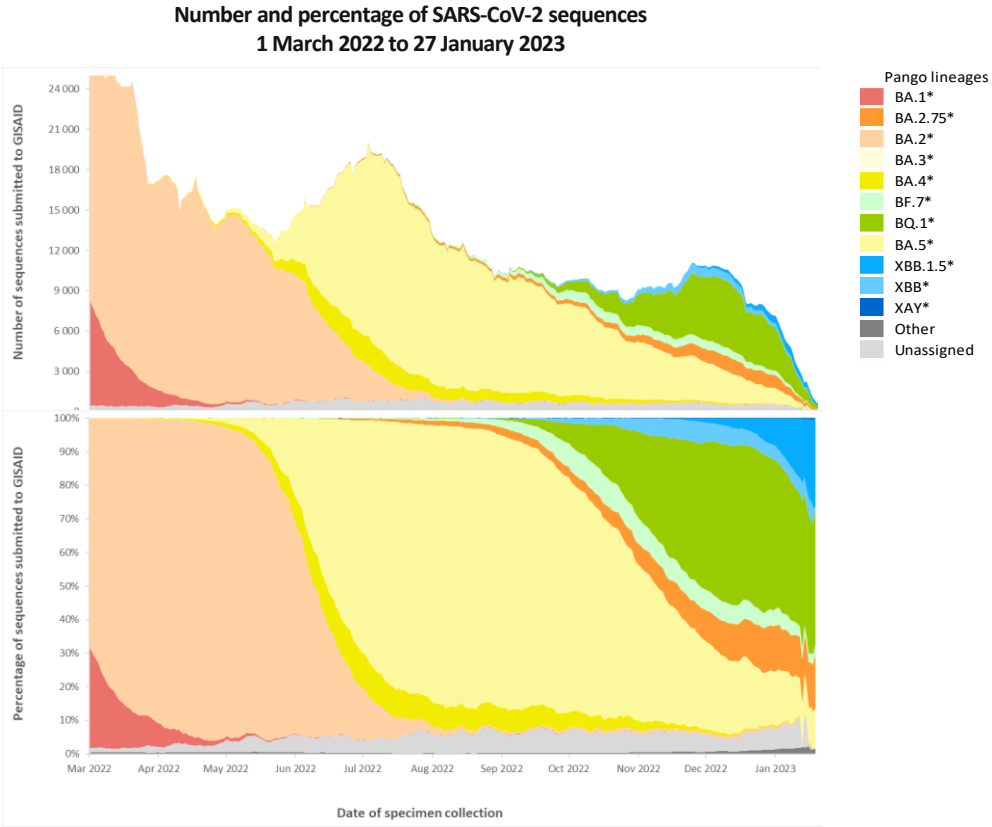
Oceania

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



Global circulation of SARS-CoV-2 variants

As of 6 February 2023



Figures by WHO, data from GISAID.org, extracted on 6 February 2023.
* indicates descendent lineages are included

- Globally, from 6 Jan to 6 Feb 2023, 90 096 SARS-CoV-2 sequences were shared through GISAID
- Omicron accounts for 99.6% of the total.

  Epi Week 3 (16 to 22 Jan 2023)

  vs **Week 51** (19 to 25 Dec 2022)

BA.5* prevalence	53.9% (74.2%)
BA.2* prevalence	12% stable trend
Pooled recombinant variants	24.6% (8.8%) mostly due to XBB.1.5 (17.7%)

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Omicron subvariants under monitoring

variant	mutations	sequences	countries	Growth Advantage (cov-spectrum)	Growth Advantage (tfpscanner)
BQ.1.1	BA.5 + Spike: R346T, K444T, N460K	196,416	106	25%	5%
XBB	Recombinant of BA.2.10.1 and BA.2.75 sublineages, i.e. BJ1 and BM.1.1.1, with breakpoint in S1.	63,479	99	25%	NA
XBB.1.5	XBB + Spike: S486P	23,544	62	67%	30%
BF.7	BA.5 + Spike: R346T	84,381	96	13%	-14%
BA.2.75	BA.2 + Spike: K147E, W152R, F157L, I210V, G257S, D339H, G446S, N460K, R493Q	107,089	108	15%	NA
CH.1.1	BA.2.75 + Spike R346T, K444T, L452R, F486S	20,212	74	35%	19%
XBF	Recombinant of BA.5.2.3 and CJ.1 (BA.2.75.3 sublineage)	4,996	43	29%	25%

Summary

- BA.5 and its descendant lineages are the dominating variants circulating globally, with a prevalence of over 50% at present
- There is some heterogeneity in dominant variants across regions
- Virus has not stabilized into predictable pattern of evolution.
  - More variants are expected with increased growth rate and immune escape, no certainty on change of severity.
  - Some recombinants have been detected throughout the pandemic, however current attention on XBB.1.5.
  - With waning immunity, breakthrough and reinfections will occur.
- Declining and unrepresentative surveillance and sequencing is making it more difficult to rapidly assess known and detect new variants/recombinants.
- Smart (representative) surveillance and sequencing remains critical at this stage of the pandemic.

TAG-VE and variant risk assessment

Anurag Agrawal

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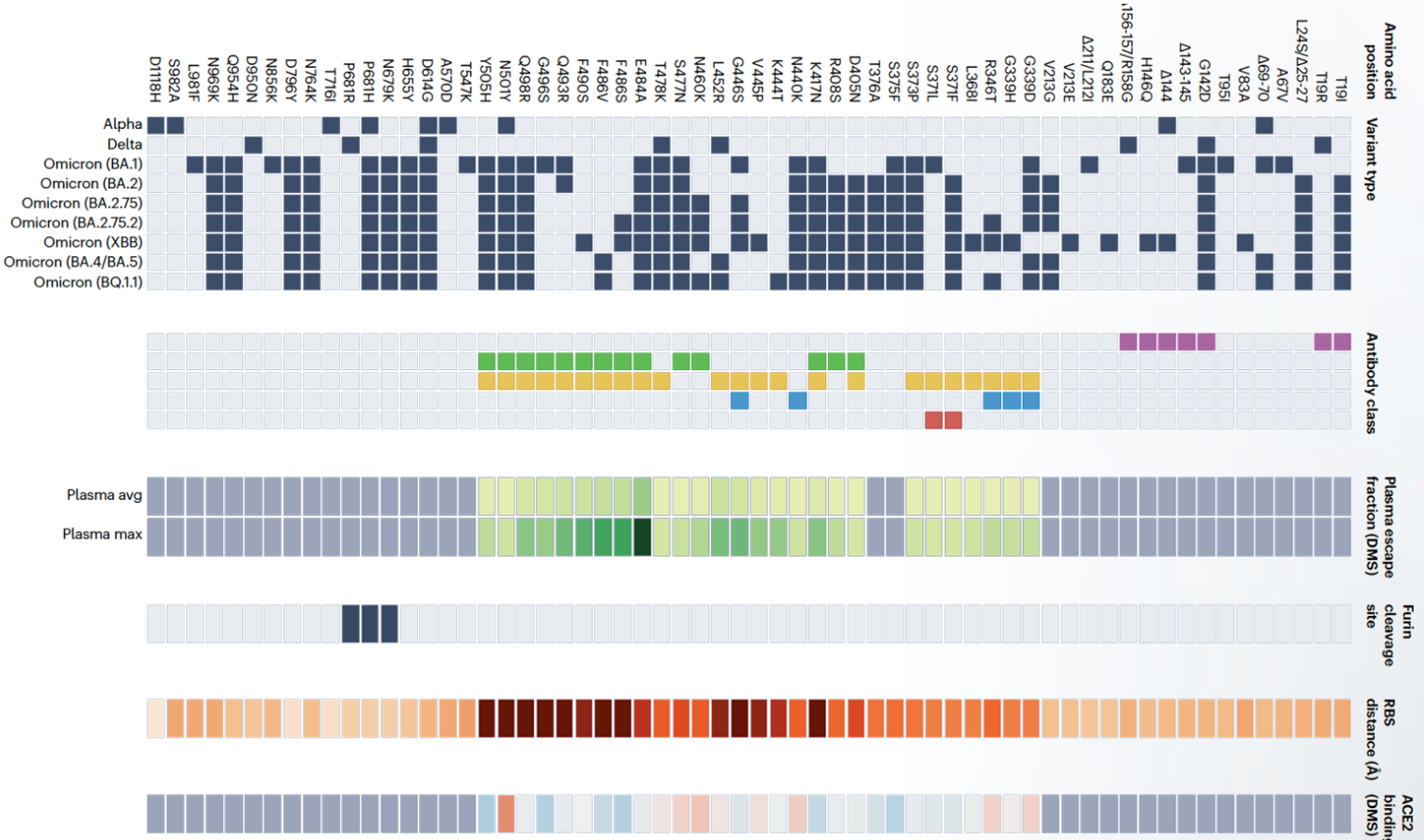
Amino acid substitutions or deletions in selected SARS-CoV-2 variants of concern



Carabelli, Nature Reviews Microbiology, 2023

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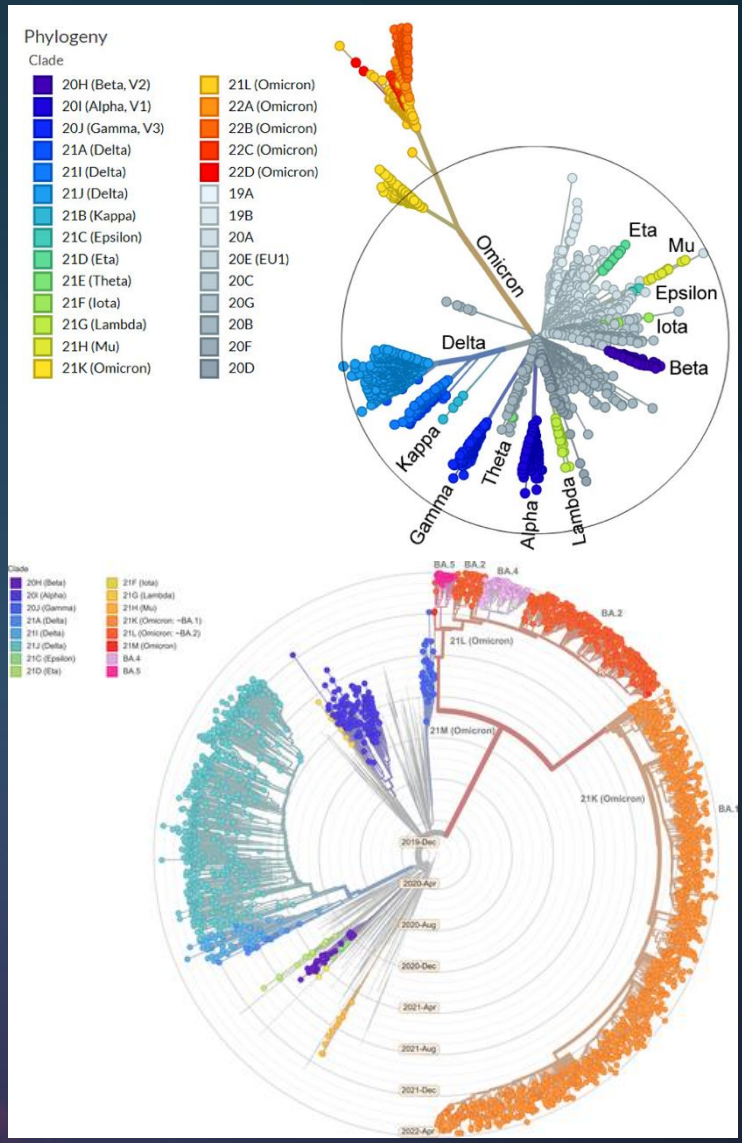
Omicron

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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Rapid risk assessment of variants

	Rapid indicators: 0-4 weeks	Confidence in the assessment		
		LOW	**MODERATE**	**HIGH**
Growth advantage	Evidence of a growth advantage likely to lead to global predominance A. An increase in variant specific Rt B. Logistic growth (compared to currently circulating variant) (Nb variants with subnational-limited growth are not assessed)	All data derived from one country	At least two models; data from two countries not linked by close travel	At least two models and at least three countries in three regions, over more than two weeks
Immune escape	• Genomic (predictive) and structural biology assessment • Pseudovirus neutralization using vaccinee sera or pre-banked population serosurveys • Reinfection rate through a cohort study or surveillance system • Signals from outbreak investigations [Rapid VE is unlikely by 28 days so the rapid RA cannot reach high confidence].	One indicator (reinfection, neutralization or structural model)	Two indicators including neutralization data	[rapid VE]
Severity and clinical considerations	• Change in a rolling surveillance metric for severity synchronized with increase in variant e.g. • infection hospitalization ratio • indicators from sentinel hospital network (e.g. surveillance of severe acute respiratory infections) • comparison of admission trends with previous variants • change in the demographic profile of who is admitted to hospital • Change in clinical phenotype • Major tests/therapeutics issues	One metric, one country	Multiple metrics, one country OR same method in multiple countries	Multiple metrics, multiple countries in multiple regions
Risk assessment	Including overall view of threat in the wider context, confidence level in the assessment, and identification of urgent priority work.			

Indicators:

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

Confidence Assessment:

Low, Moderate and High

Assessments:

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

WHO-TAG-VE Risk Assessment XBB.1.5

- **Updated RRA release:** 23 January 2023 (First RRA released on 11 January 2023)
- **Data:**
  - 8931 sequences of the Omicron XBB.1.5 from 54 countries (excluding low coverage sequences). Most from the USA (75.0%), the UK (9.9%), Canada (3.0%), Denmark (2.0%), Germany (1.5%), Ireland (1.3%) and Austria (1.3%).
- **Overall Assessment:** Available information does not suggest that XBB.1.5 has additional public health risks relative to the other currently circulating Omicron subvariants.
- **Confidence in the Assessment:** Moderate (updated from Low)
- **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)

WHO-TAG-VE Risk Assessment XBB.1.5

	Indicator	Confidence in the assessment
Growth advantage	In the USA, XBB1.5 is increasing in many regions (the prevalence of XBB.1.5 in some regions is predicted to be 80%, while in others, 20-50%). In the UK, growth advantage relative to BQ.1.1 was estimated to 38.9%, with high uncertainty due to the small number of sequenced XBB.1.5 cases. ECDC has reported growth of XBB.1.5 in several countries, including Iceland where it has increased to 8.7% in week 2 of 2023. *In silico* analysis reported that the mutation S:F486S (present in XBB.1) abrogated the local hydrophobic interaction with ACE-2 while 486P (present in XBB.1.5) restored it. The amino acid change to 486P contributes to higher ACE-2 binding affinity, and suggests a mechanism for XBB.1.5 to have a higher growth advantage as compared to its parent lineage XBB.1.	Moderate
Antibody escape	Using pseudotyped virus neutralization assays, XBB.1.5 is shown to be as immune evasive as XBB.1, one of the Omicron subvariants with the highest immune escape to date. Antibody titers against XBB.1 were mostly absent in individuals with a history of vaccination with the index vaccine (2-4 doses), were higher in those who recently received a bivalent (BA.5) vaccine booster, and highest in individuals with hybrid immunity. There are currently no data on real world vaccine effectiveness against severe disease or death.	Moderate
Severity and clinical considerations	Severity assessments in human populations are ongoing. The number of cases associated with XBB.1.5 is still low and thus clinical severity cannot yet be confidently assessed. XBB.1.5 does not carry any known mutation(s) associated with potential changes in severity (such as S:P681R).	Low
Risk assessment	Based on its genetic characteristics and growth rate estimates, XBB.1.5 is likely to contribute to increases in case incidence globally. There is moderate-strength evidence for increased risk of transmission and immune escape. From reports by several countries, no early signals of increases in severity have been observed. The number of cases associated with XBB.1.5 is still low and thus severity cannot yet be confidently assessed. **Taken together, available information does not suggest that XBB.1.5 has additional public health risks relative to the other currently circulating Omicron descendent lineages.**	

“The more things change, the more they remain the same.

Plus ça change, plus c’est la même chose.

Jean-Baptiste Alphonse Karr