ACT-A Dx

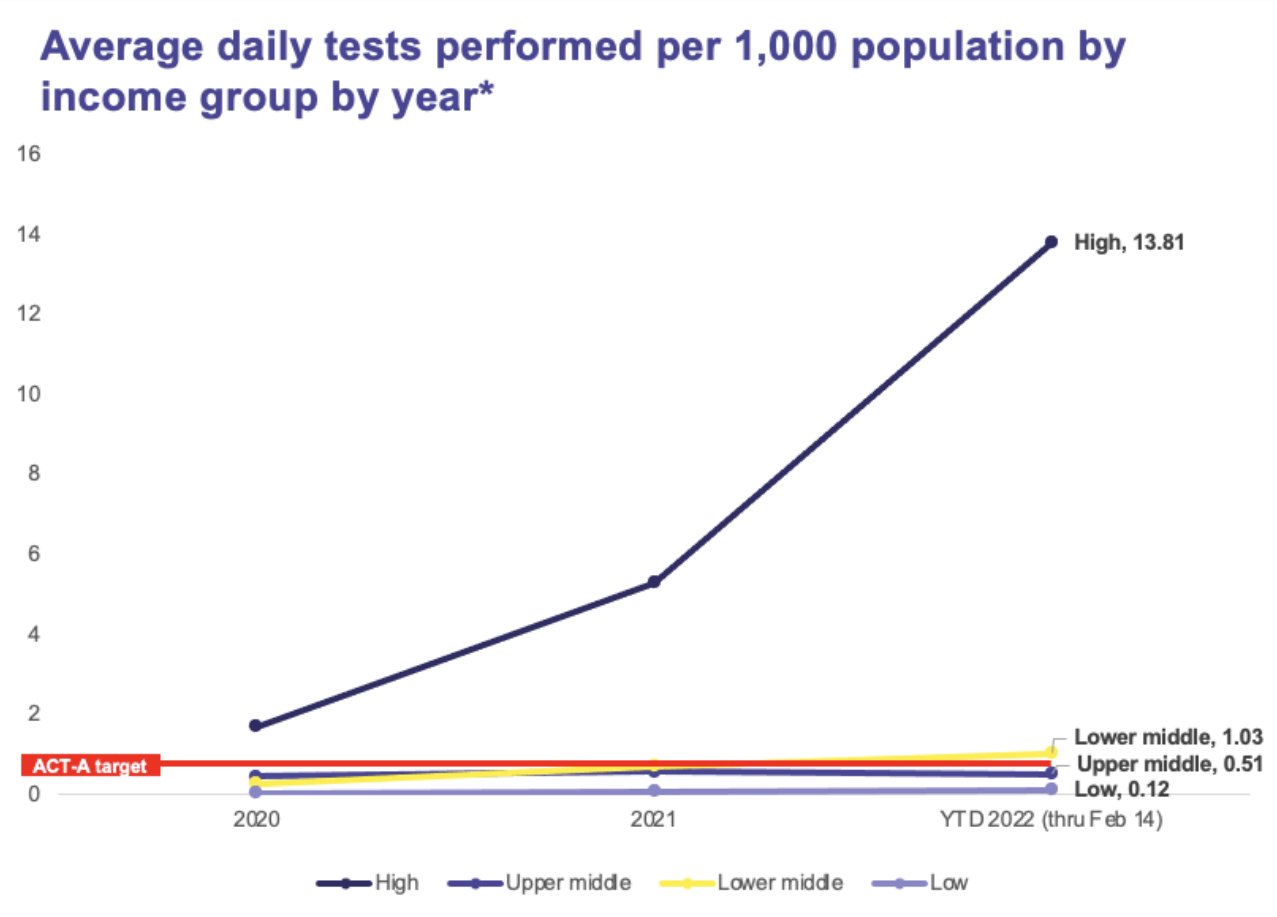
Member State Meeting

17th February 2022

#UnitedAgainstCoronavirus

#StrongerTogether | #GlobalResponse | #GlobalGoalUnite

Despite availability of COVID tests, there is continued inequity in testing rates



Testing Rates and the ACT-A Target

- The global ACT-A target is 1 test/1,000 population/day
- **LICs and LMICs continue to test at a fraction of HICs test rates**.
- As of Feb 2022 (tests/1,000 people/day):
  - High-income countries: **13.80**
  - Upper middle-income countries: **0.51**
  - Lower middle-income countries: **1.03**
  - Low-income countries: **0.12**

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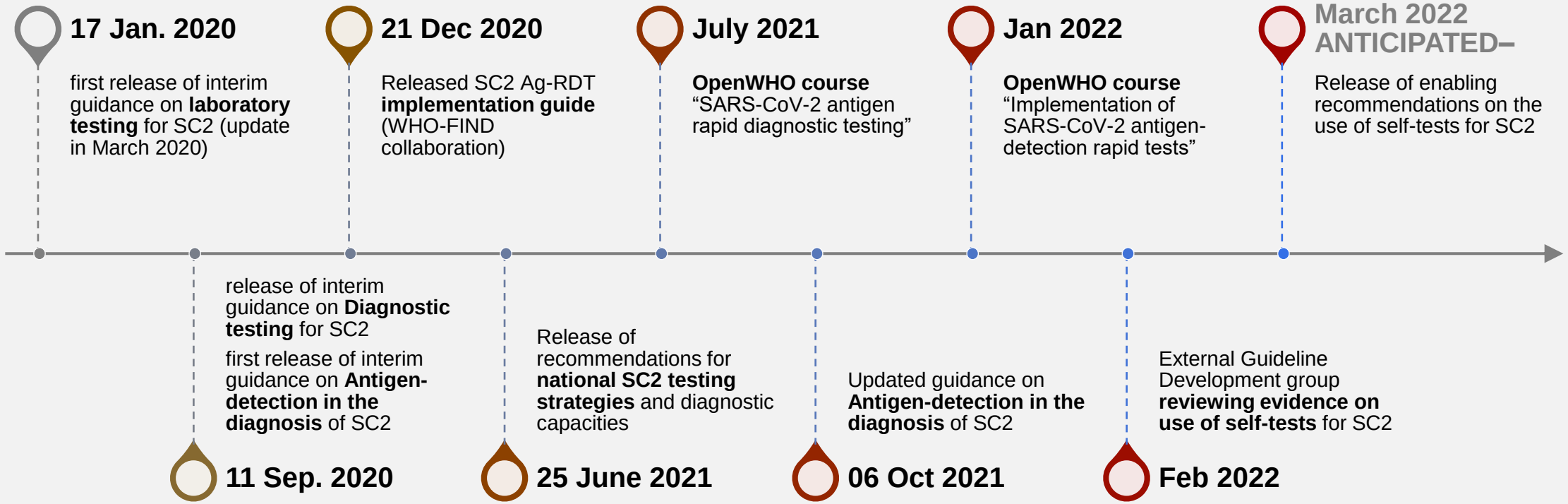
**FIND Test Tracker with data reflected as of 14th Feb 2022*

Adoption Issues for COVID Testing Mirror Broader Health Challenges

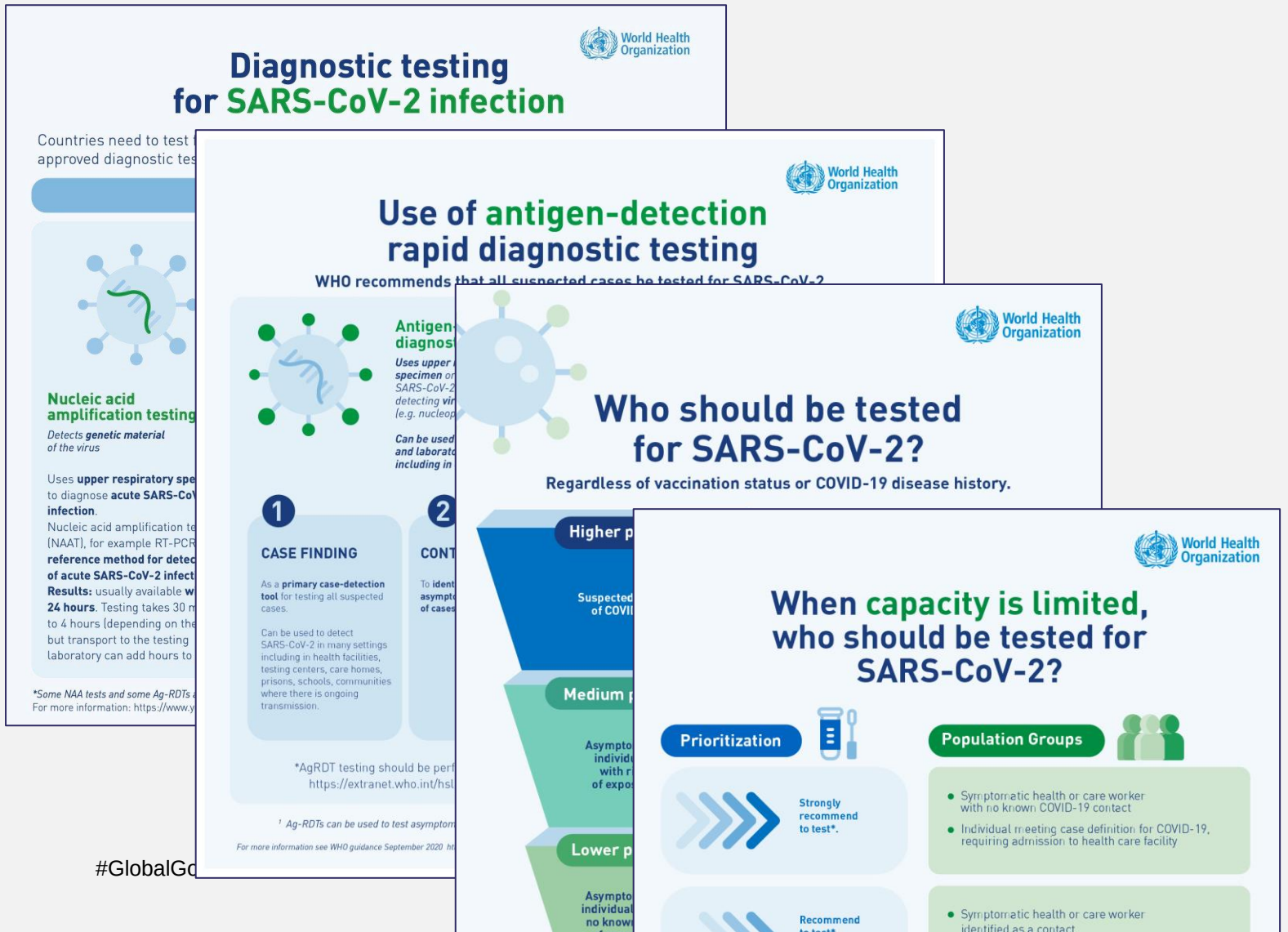
- Lack of **funding**
- Challenges in **supply chain and limited availability of access to tests beyond health facilitates**
- **Regulatory review** and approval
- **Variable perceptions of importance / utility in testing** among stakeholders and general population
- **Restrictive eligibility / case-definition** criteria for testing
- **In-country governance** and financing structures
- Inadequate **health workforce** and health system capacity
- **Political will and competing priorities**, especially vaccines
- **Lack of accessibility** to testing for individuals related to lack of testing facilities in area, travel required to get tested, high prices of tests, and lack of knowledge about where to get tested

Source: ACT-A Analysis

Timeline of WHO guidance for diagnostic testing for SARS-CoV-2



WHO has released 5 infographics to facilitate access to impactful testing services



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World Health Organization

Why is testing for SARS-CoV-2 important?

Test should be reliable, accurate, affordable, accessible and provide results rapidly*

Results of testing are important for a number of reasons:

- Enables individuals to know if they are infected
- Ensures appropriate clinical care and support to individuals
- Prevents transmission by empowering individuals to protect their families and communities
- Enables a better understanding of where the virus is circulating to inform the COVID-19 response

Examples of where testing can be done:

- Health care facilities, clinics, health centers, and pharmacies
- Community-based testing sites, such as walk-through or drive-through centers, through outreach
- Specific settings, including to protect vulnerable populations, in closed communities, as part of sentinel surveillance, etc.
- At home

** National programs may choose to implement and adjust testing strategies based on local epidemiology, capacities and overall goals. For additional information, visit: https://who.int/covid-19 and https://www.who.int/publications/i/item/WHO-2019-nCoV-lab-testing-2021.1-eng*

The WHO pipeline of tests for EUL approval

IVD products	Nucleic acid	Antigens	Antibodies
EOI	69	62	41
Awaiting dossier	2	4	ON HOLD
Dossier received	16	31	
• Pre-screening	3	0	
• Screening	4	15	
• Under assessment	9	16	
In renewal process	23	3	1
Not Renewed	1*	0	0
EUL listed	24 (-1)	5	1
EUL not accepted	28	21	10

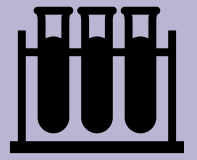
*withdrawn

WHO EUL processes are being modified to account for urgent needs

- **Increasing capacity of teams** through collaborations with national regulatory agencies
- **Revised EUL procedures** are being developed in order **to expedite assessment & listing times**
- **Early triage of incomplete dossier** in order to focus limited resources on more promising dossiers
- **Revising scope & prioritization of EUL eligible tests**
  - i.e. stop accepting applications for IVDs not considered high priority for procurement
  - i.e. inclusion of SARS CoV-2 Ag RDT self-tests, once supporting WHO guidance is published

Now is the time for scaling diagnostics

Political engagement with diagnostics; continued focus and prioritization of funding lab systems in order to increase testing rates and enhance sequencing services



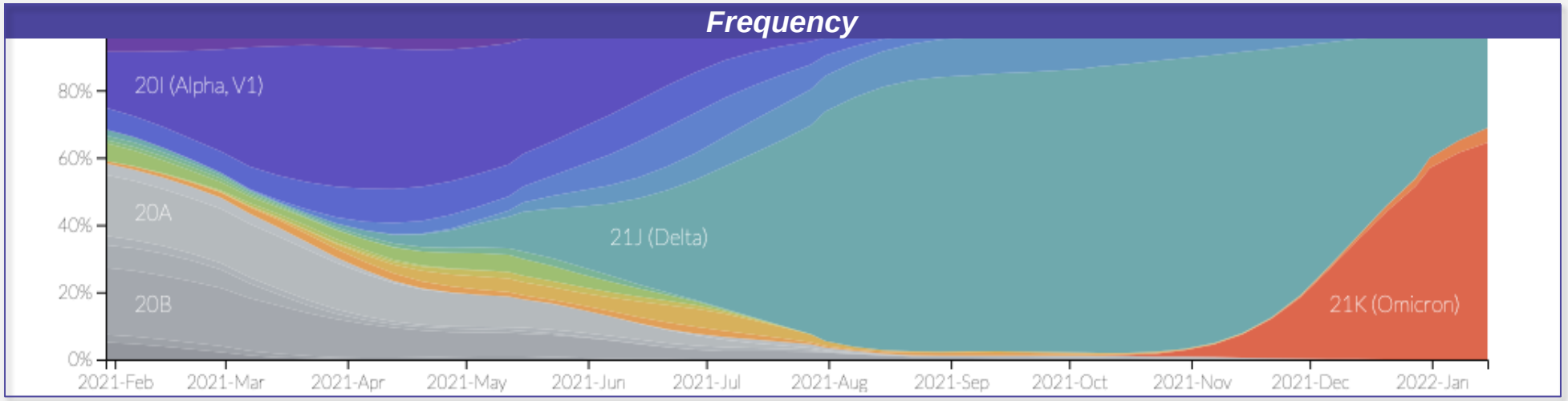
Leap forward in technology development, accessibility and affordability with a focus on increasing funding and research attention

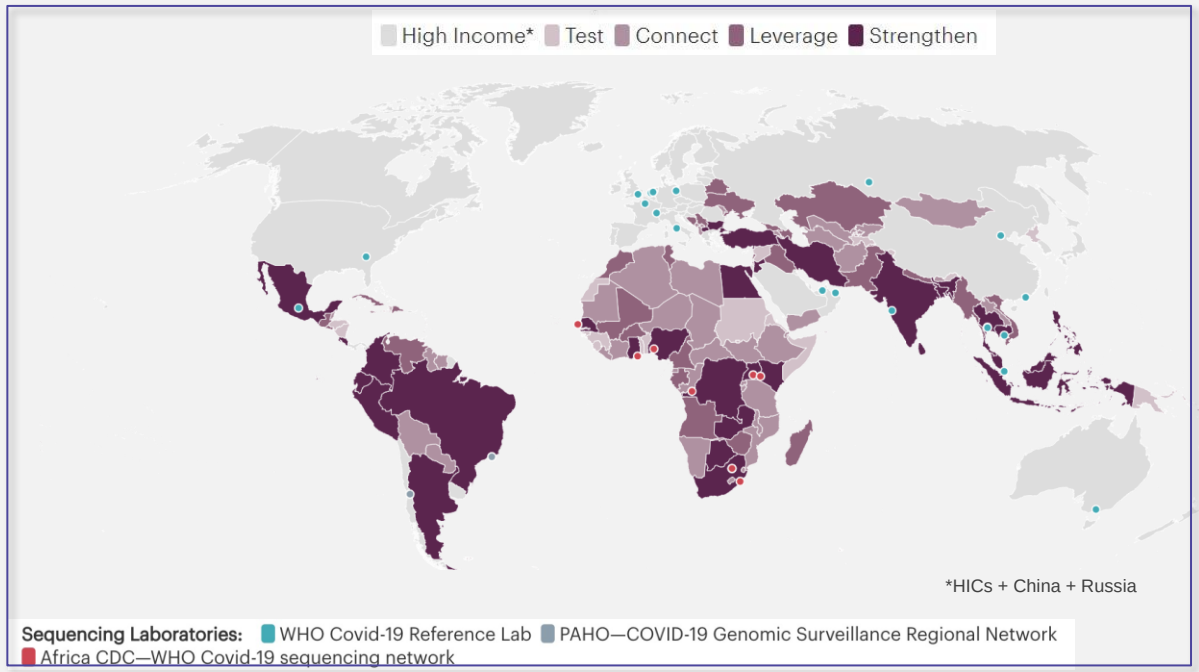
Preparing for the next threat by strengthening health systems, workforce and governance structures thereby improving rapid development and deployment for the next pandemic threat, including the G7 100-day agenda

Focused interest on local manufacturing to support manufacturing equity, driven by the spotlight on fragile supply chains

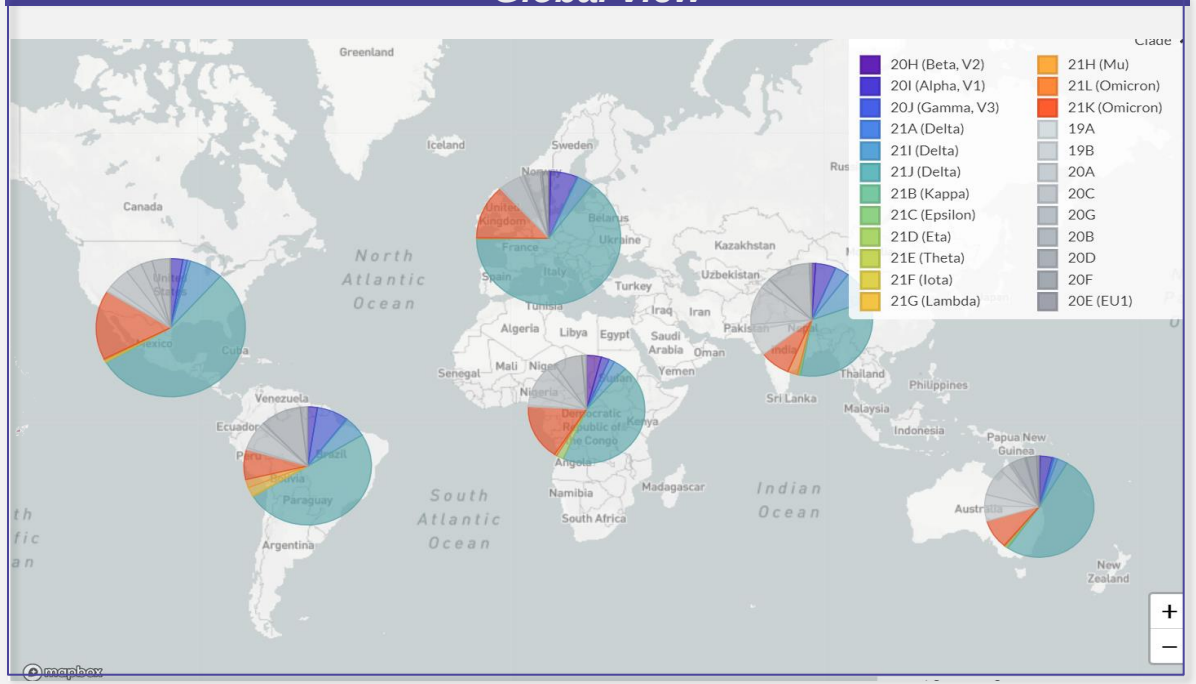
New variants are a global concern: sequencing capacity

Frequency





Global View



Source: GISAID, Feb 2021 to Jan 2022

Effectiveness of Dx tools against Omicron

- ***Ag-RDT:*** **All widely used Ag-RDTs can detect Omicron infections.** However, a **lower analytic sensitivity** of Ag RDTs to Omicron (cultured virus) compared to earlier variants has been observed in many labs

- ***Ag-RDT*****: Discrepant results on whether oral or nasal (NP/OP) swabs are better samples** for the detection of Omicron

- ***Ag-RDT*****: Current Ag-RDT guidance for Covid-19 testing should remain in place, including sample type** – no need for change at the moment

- ***PCR***: The use of **S gene target failure as a proxy marker to screen for Omicron should be interpreted with great caution,** largely due to emergence of BA.2 sub-variant. Omicron **surveillance should be via sequencing**

Disclaimer: list of studies are not exhaustive

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Summary: analytical studies for key SARS-CoV-2 Ag-RDTs

Independent Studies

	Manufacturer	Test name	Regulatory	Manufacturer claim*	Ref	Sample size	Delta	Sample size	Omicron	Impact of Omicron
1	Abbott	**Panbio**	WHO EUL	No expected impact (In silico)	1	18	3.03 *10^6 PFU/mL	17	3.34 *10^6 PFU/mL	↘
					2	4	6.0 $\log^{10}$RNA cp/mL	4	6.0 $\log^{10}$RNA cp/mL	No impact
2	Abbott	**BinaxNOW**	FDA EUA	No Impact (analytical/clinical studies)	3	30	Ct = 25	32	Ct = 27	↘
3	SD Biosensor	**Standard Q**	WHO EUL	No expected impact (In silico)	1	18	3.03 *10^6 PFU/mL	17	3.94 *10^6 PFU/mL	↘
					2	4	6.0 $\log^{10}$RNA cp/mL	4	6.0 $\log^{10}$RNA cp/mL	No impact
4	ACON biotech	**Flowflex**	FDA EUA	No expected impact (In silico)	1	18	3.03 *10^6 PFU/mL	17	2.73 *10^6 PFU/mL	↗
5	PMC	**Sure Status**	WHO EUL	No expected impact (In silico)	1	18	2.43 *10^6 PFU/mL	17	4.27 *10^6 PFU/mL	↘
6	Wondfo	**2019-nCoV Antigen test**	FDA EUA	No expected impact (In silico)	1	18	3.34 *10^6 PFU/mL	17	3.64 *10^6 PFU/mL	↘

↘ Ability to detect Omicron lower (worse LOD)

↗ Ability to detect Omicron higher (better LOD)

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* Manufacturers claim as per evidence submitted to FIND testing database Jan 2022

References: [1] Bekliz et al, 2021 (pre-print) / [2] Deerain et al., 2021 / [3] Kanjilal et al., 2021 (pre-print)

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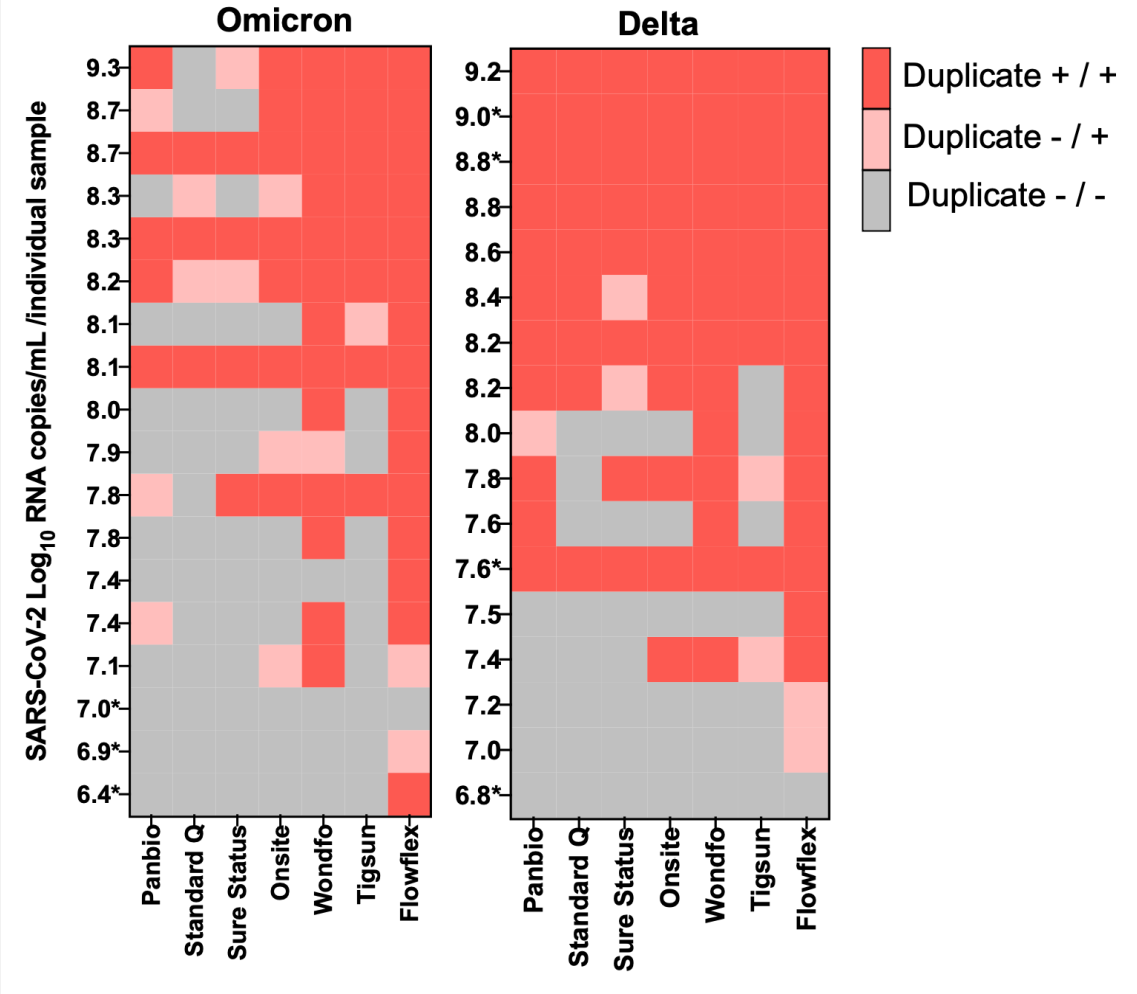
Hôpitaux Universitaires Genève

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE

Performance with clinical specimens

Clinical sensitivity of 7 Ag RDTs on Omicron (n=18) and Delta (n=17) breakthrough infections



Nasopharyngeal specimen, first 5 days post-symptom onset;

RNA viral load, days post symptom onset and infectious virus presence did not differ significantly between the groups

Performance of Ag RDT vs PCR against Omicron

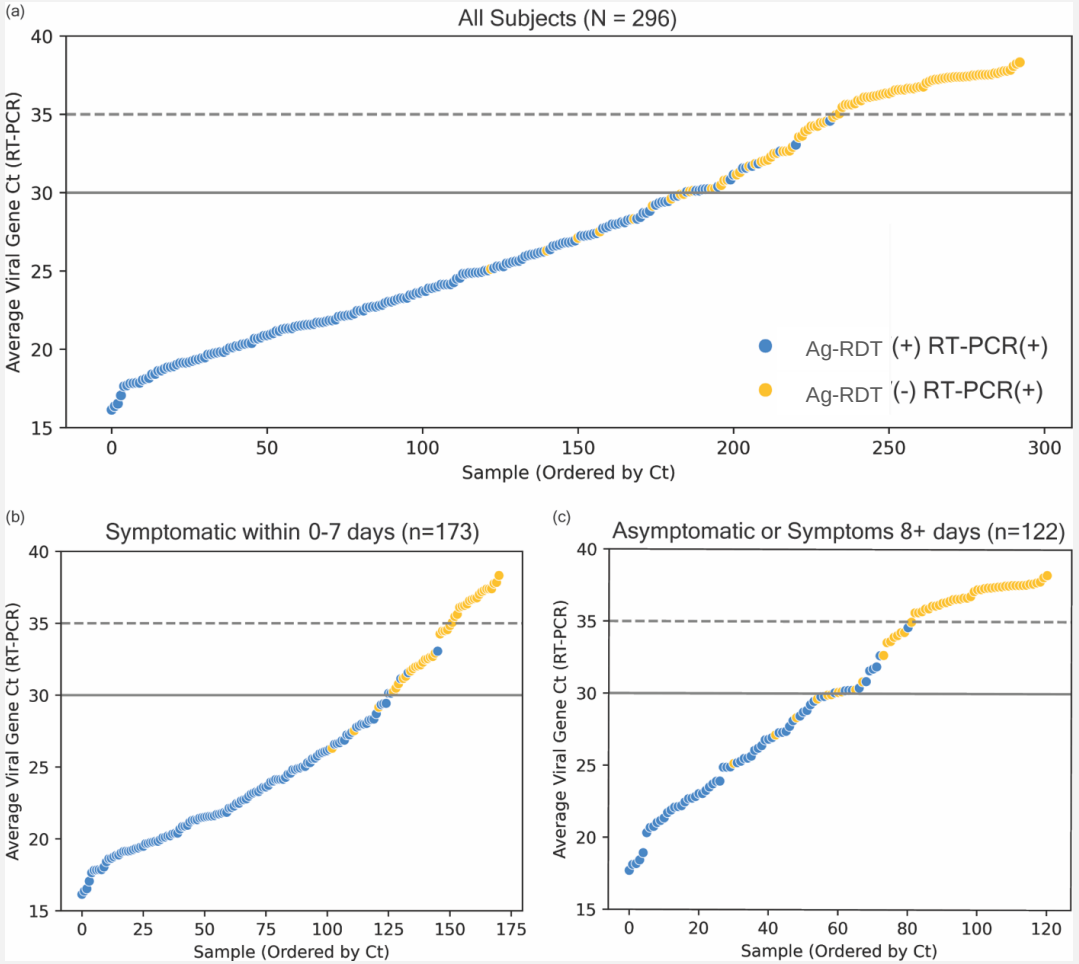


Figure. 731 consecutive walk-up subjects at a San Francisco community testing center were tested by nasal swab on 3-4 January 2022. 296 of 6731 subjects were positive for SARS-CoV-2 (test positivity rate = 40.5%, and 98.5% were shown to have infection Omicron variant. (Adapted from Schrom *et al.*[1]).

Decreasing viral load

Ct value	**Sensitivity** (95% C.I.) vs Omicron[1]	**Sensitivity** (95% C.I.) vs prior variants[2,3]	
		Pre-Delta[2]	Delta[3]
All Ct values	**65.2%** (60-70%)	**77.4%** (72-82%)	**74.0%** (64-82%)
<35	**82.1%** (77-87%)	**81.2%** (76-86%)	
<30	**95.2%** (92-98%)	**95.8%** (92-98%)	

1. *Schrom et al., 12 Jan 2022. Available at: medRxiv preprint. doi: https://doi.org/10.1101/2022.01.08.22268954*
2. *Pollock et al., J Clin Microbiol. 2021 May; 59(5): e00083-21. doi: https://doi.org/10.1128/JCM.00083-21*
3. *Frediani et al., Sci Rep 11, 14604 (2021). doi: https://doi.org/10.1038/s41598-021-94055-1*

Differences between saliva and nasal swabs
Limited data and discordant results

[PCR Data] Marais et al., 2021 (Groote Schuur Hospital Covid testing centre, Cape Town

"The current standard of care for diagnosis using swabs of the nasal or nasopharyngeal mucosa may be **suboptimal for the Omicron variant**."

[PCR vs RDTs] Adamson et al., 2022 (occupational cohorts, New York and San Francisco)

*"A subgroup (n=5) who received daily saliva PCR, nasal swab PCR, and nasal swab rapid antigen testing showed **viral load peaked in saliva 1-2 days before nasal tests**"*

[PCR Data] Schrom et al., 2022 (outdoor testing site, San Francisco)

"Our data argue against replacing nasal swabs with throat swabs for diagnosis"

[Ag RDT Data] Eckerle et al., 2022 (outpatient testing centre, HUG)

*Prospective clinical study - **Preliminary results (unpublished)** **showed no higher sensitivity of Ag RDTs on OP (oropharyngeal) compared to NP (nasopharyngeal),** as well as a lower Ct in saliva samples compared to NP and OP.*

PCR testing: S gene test failure (SGTF) and Omicron sub lineages

- The Omicron **variant has three sub-lineages:** BA.1, BA.2* and BA.3. Overall, BA.1 is the dominant sub-lineage globally but BA.2 is increasing in particular countries
- A **minority of Omicron sequences (including all BA.2) lack the genetic deletion in the spike protein** which produces S-gene test failure in some PCR tests
- This **deletion is also found in other VOCs** (e.g., Alpha and subsets of Gamma and Delta)

The use of S gene target failure as a proxy marker to screen for Omicron should be interpreted with caution. Confirmation by sequencing should be made at least for a subset of samples

- **PCR-based screening assays** (e.g., Single Nucleotide Polymorphism genotyping) **may be useful proxy markers depending on the setting**

 *BA.2 has been designated a variant under investigation in the UK, based on increasing numbers of BA.2 sequences identified both domestically and internationally.

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