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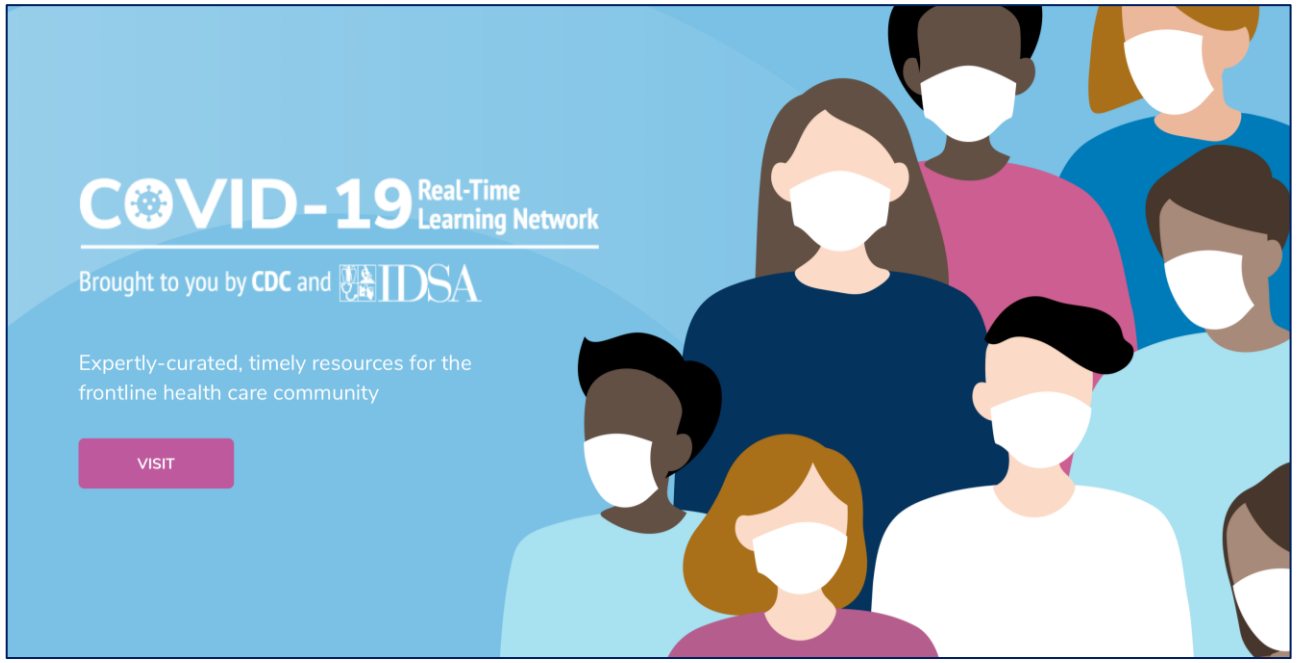
COVID-19 Real-Time Learning Network



Specialty Society Collaborators:

- American Academy of Family Physicians
- American Academy of Pediatrics
- American College of Emergency Physicians
- American College of Physicians
- American Geriatrics Society
- American Thoracic Society
- Pediatric Infectious Diseases Society
- Society for Critical Care Medicine
- Society for Healthcare Epidemiology of America
- Society of Hospital Medicine
- Society of Infectious Diseases Pharmacists

With funding from the Centers for Disease Control and Prevention, IDSA has launched the COVID-19 Real Time Learning Network, an online community that brings together information and opportunities for discussion on latest research, guidelines, tools and resources from a variety of medical subspecialties around the world.

www.COVID19LearningNetwork.org

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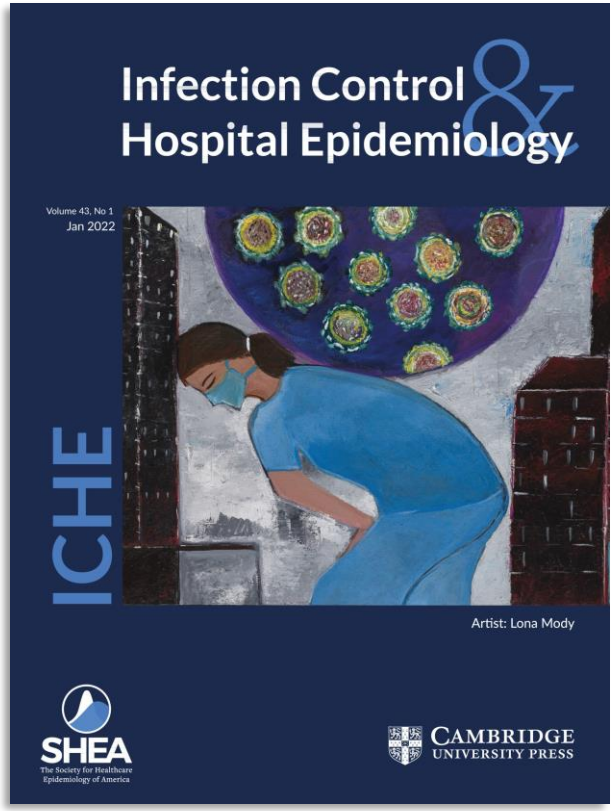
ICHE Journal – Fast Tracking COVID Article Submissions



Infection Control & Hospital Epidemiology publishes scientifically authoritative, clinically applicable, peer-reviewed research on control and evaluation of the transmission of pathogens in healthcare institutions and on the use of epidemiological principles and methods to evaluate and improve the delivery of care. Major topics covered include infection control practices, surveillance, antimicrobial stewardship, cost-benefit analyses, resource use, occupational health, and regulatory issues.

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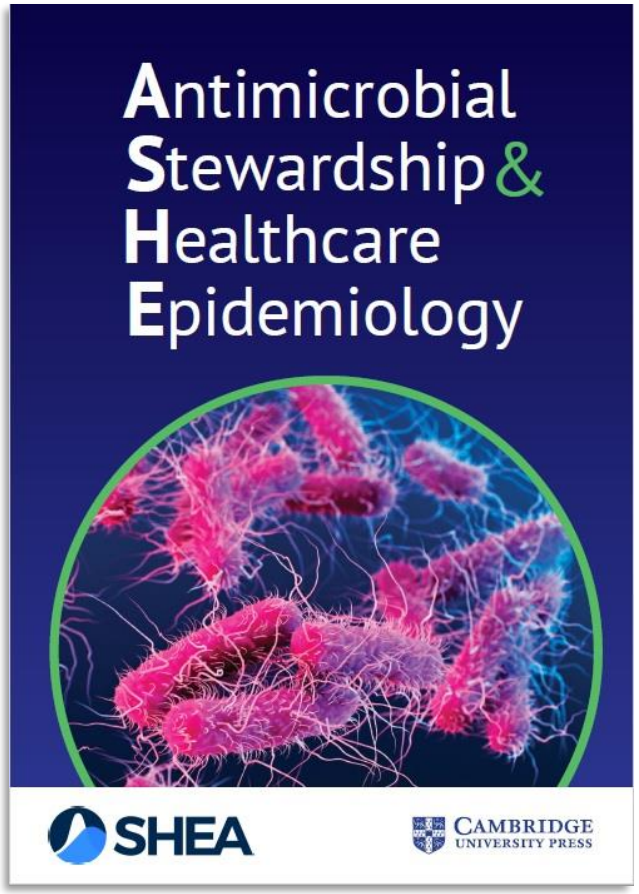

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SHEA Webinar

COVID-19 Town Hall Round 83

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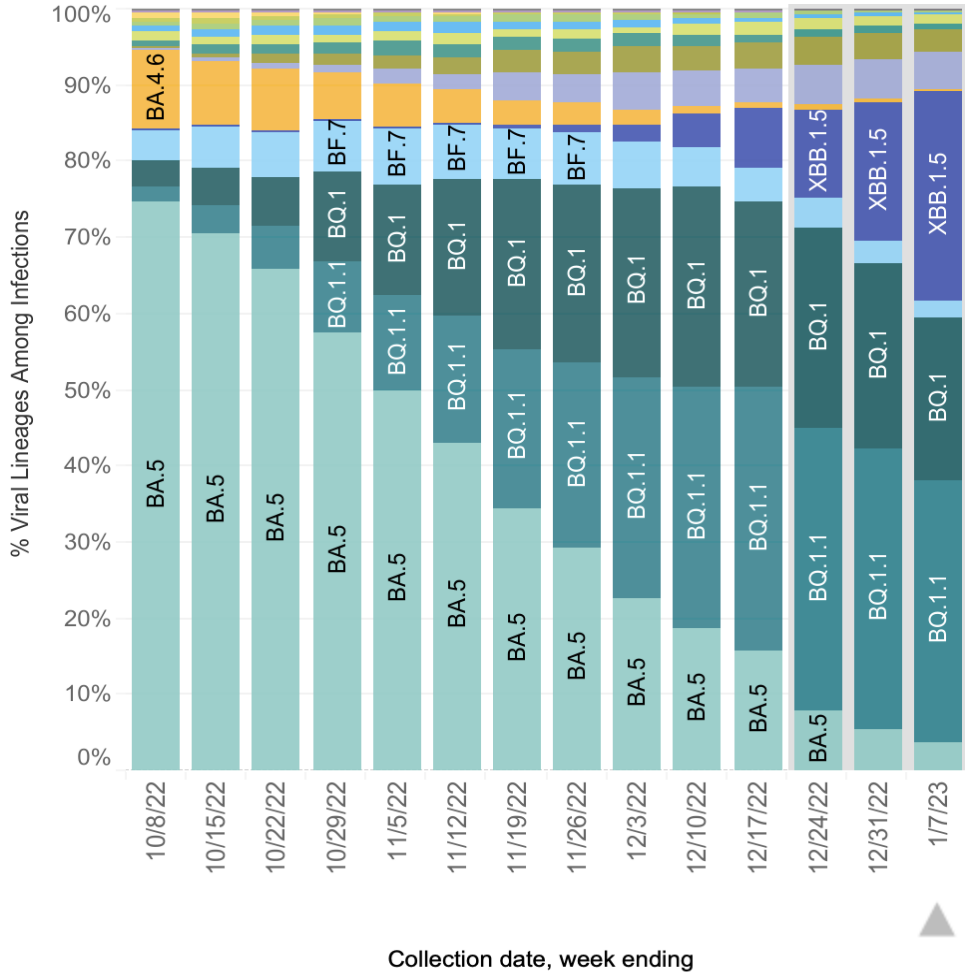
House Keeping Items

- Technical difficulties? Visit: https://support.zoom.us
- Webinar recording, PowerPoint presentation, and references available LearningCE’ s Rapid Response Program
- Streaming Live on SHEA's Facebook page
- Zoom Q&A and Chat

SHEA Town Hall 83
Overview

SARS-CoV-2 Variants, US, CDC

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BQ.1.1	VOC	34.4%	26.7-43.0%
	XBB.1.5	VOC	27.6%	14.0-46.5%
	BQ.1	VOC	21.4%	16.1-27.7%
	XBB	VOC	4.9%	4.0-6.1%
	BA.5	VOC	3.7%	2.7-5.0%
	BN.1	VOC	3.0%	2.1-4.1%
	BF.7	VOC	2.2%	1.6-3.0%
	BA.2.75	VOC	1.3%	0.9-2.0%
	BA.5.2.6	VOC	0.7%	0.5-0.9%
	BA.2	VOC	0.3%	0.2-0.5%
	BF.11	VOC	0.3%	0.2-0.4%
	BA.4.6	VOC	0.2%	0.2-0.3%
	BA.2.75.2	VOC	0.1%	0.1-0.1%
	BA.4	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.2.12.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.1%



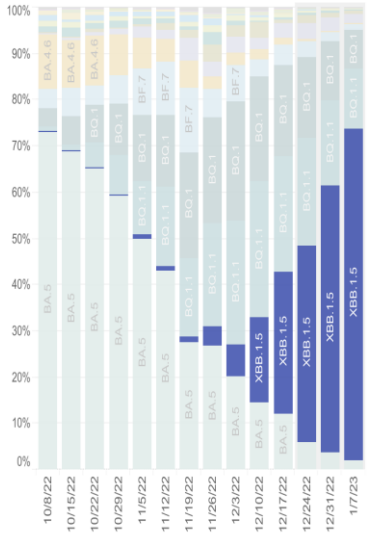
* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.

** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates

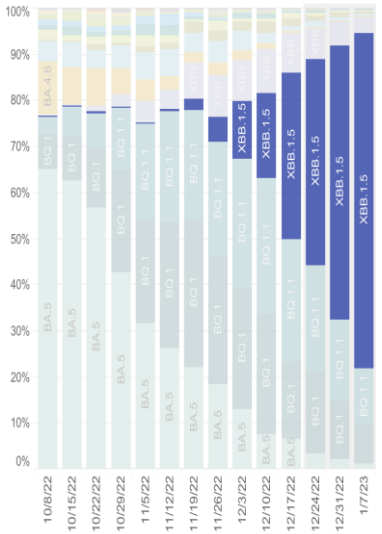
\# BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. Except BA.2.12.1, BA.2.75, BA.2.75.2, BN.1,XBB and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Except BF.7, BF.11, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. Except XBB.1.5, sublineages of XBB are aggregated to XBB. For all the lineages listed in the above table, their sublineages are aggregated to the listed parental lineages respectively. Previously, XBB.1.5 was aggregated to XBB. Lineages BA.2.75.2, XBB, XBB.1.5, BN.1, BA.4.6, BF.7, BF.11, BA.5.2...

https://covid.cdc.gov/covid-data-tracker/#variant-proportions

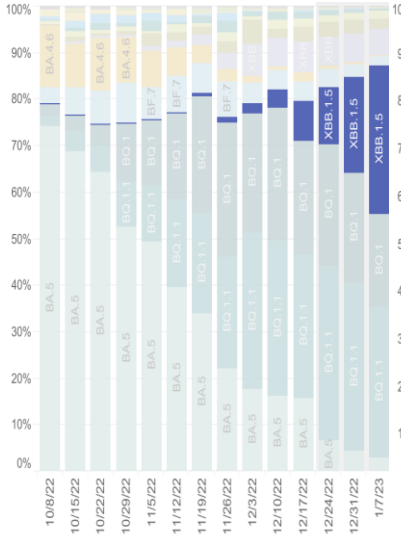
XBB 1.5 SARS-CoV-2 Variant, by Regions, CDC



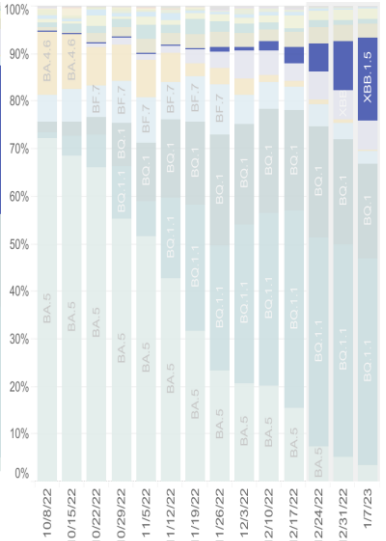
Region 1
(CT, ME, MA, NH, RI, VT)



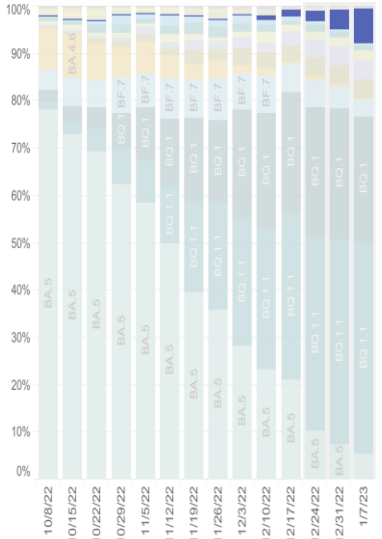
Region 2
(NJ, NY, PR, VI),



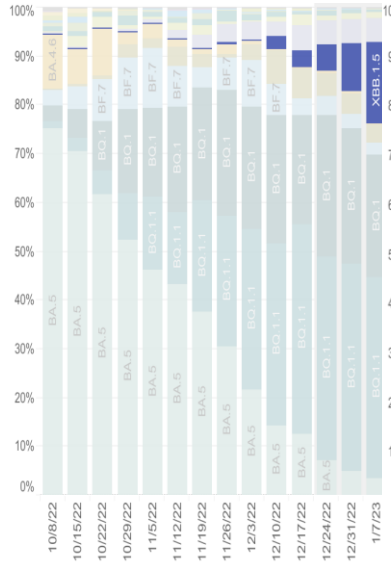
Region 3
(DE, DC, MD, PA, VA, WV),



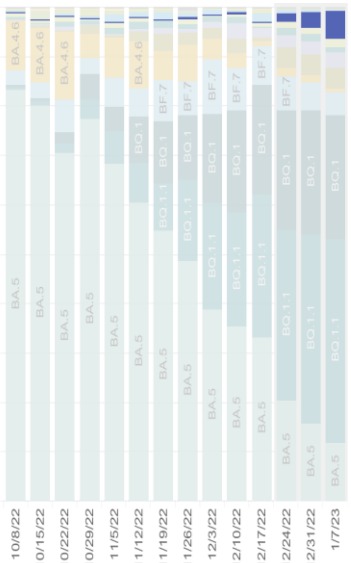
Region 4
(AL, FL, GA, KY, MS, NC, SC, TN),



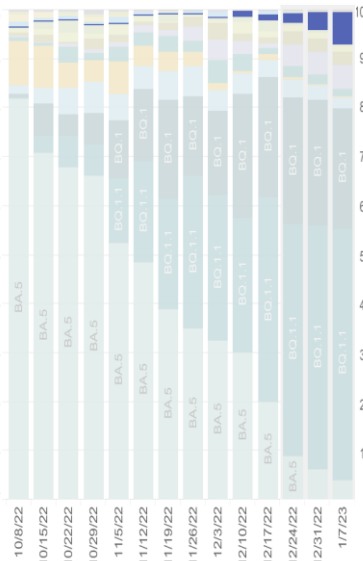
Region 5
(IL, IN, MI, MN, OH, WI),



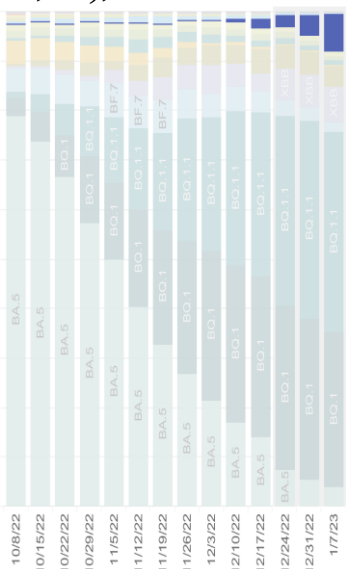
Region 6
(AR, LA, NM, OK, TX)



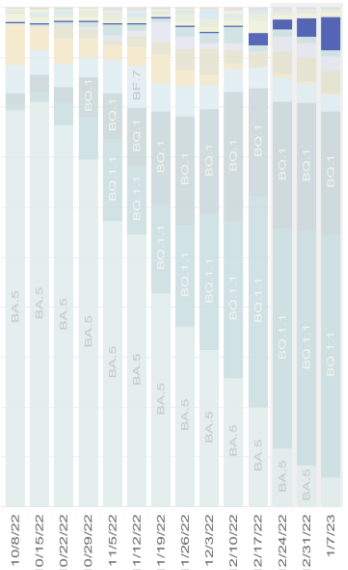
Region 7
(IA, KS, MO, NE)



Region 8
(CO, MT, ND, SD, UT, WY)



Region 9
(AZ, CA, HI, NV, Pacific Isl)

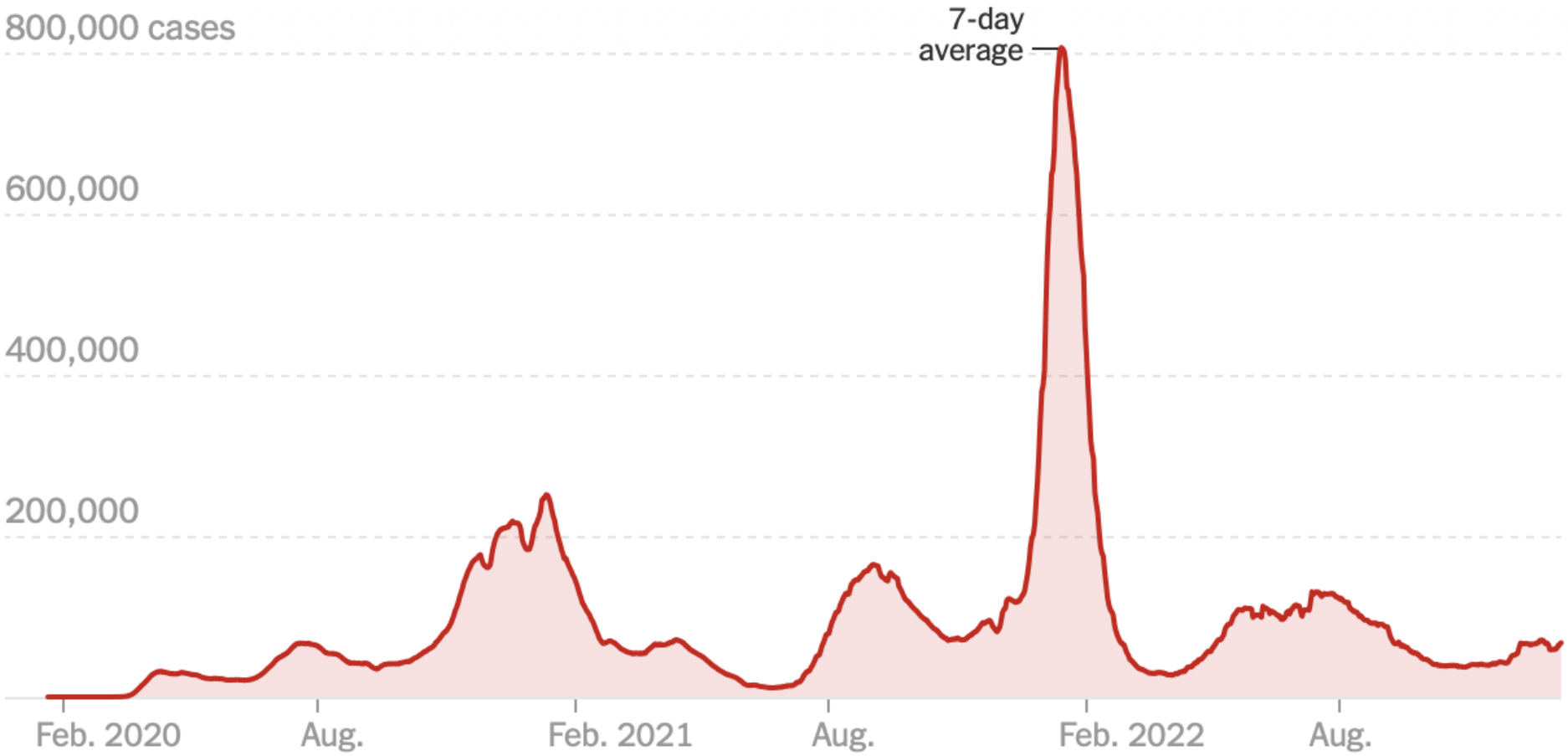


Region 10
(AK, ID, OR, WA)

https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Reported COVID-19 Cases in the United States

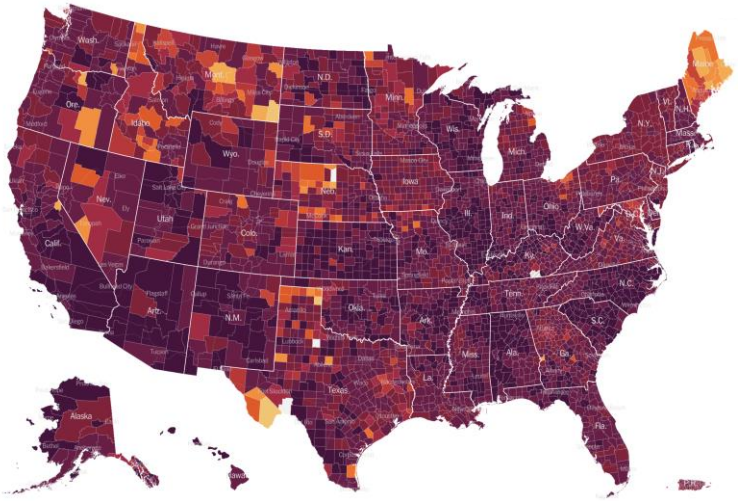
Cumulative Cases – 101,235,080



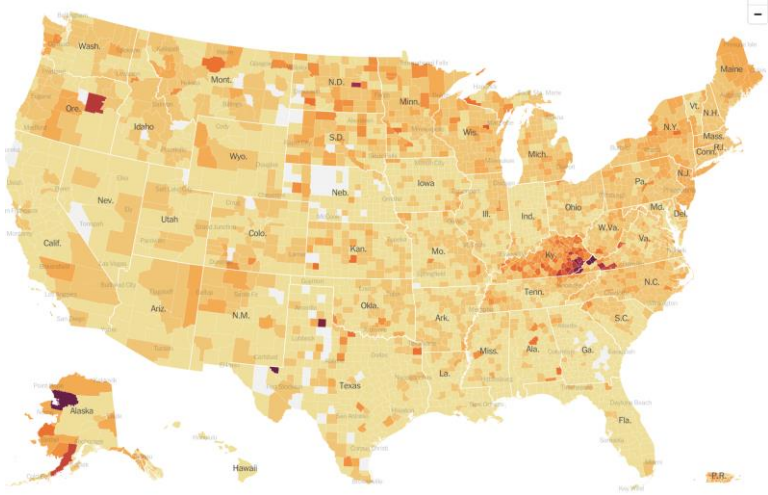
Cases decreased by 4% from two weeks earlier

Sources: New York Times 1-7-2023; Johns Hopkins Coronavirus Resource Center: https://coronavirus.jhu.edu/region/united-states 1-7-2023

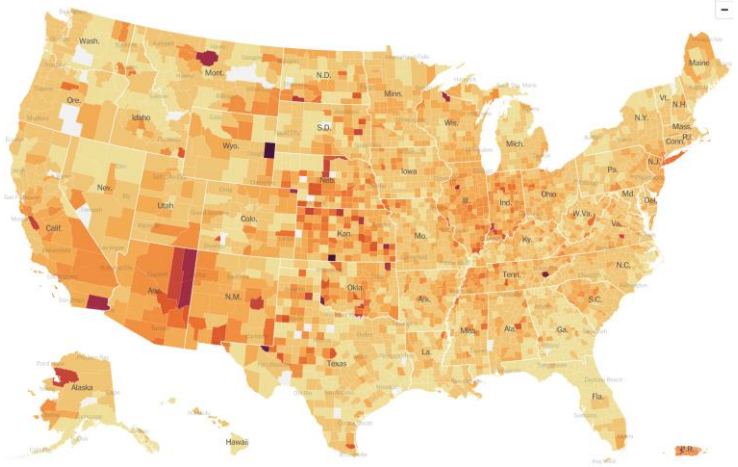
US COVID-19 HOTSPOTS



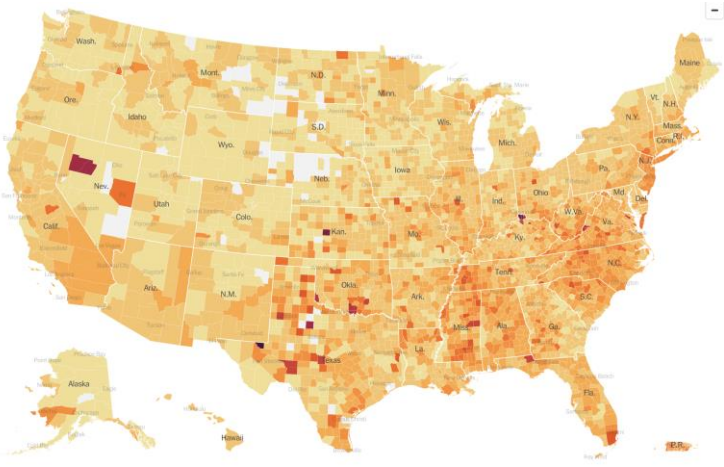
February 6, 2022



October 9, 2022



December 10, 2022



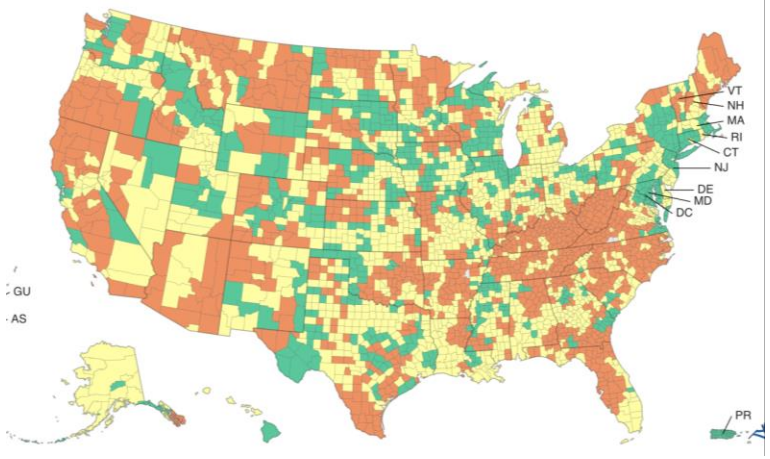
January 7, 2023

Average daily cases per 100,000 people in past week

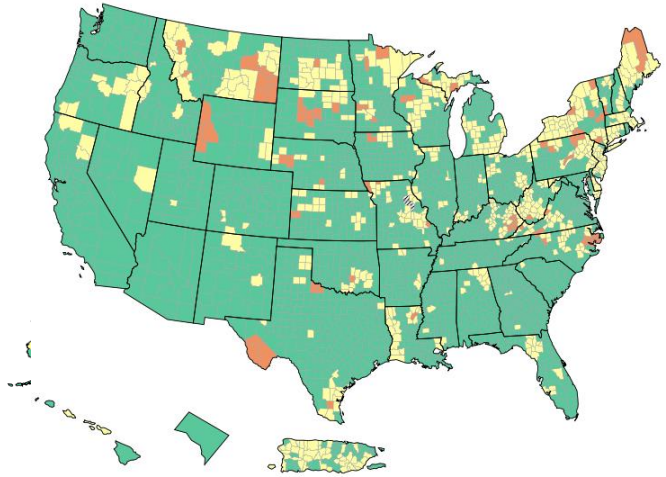
10 30 50 70 100 250 Few or no cases

Source: New York Times 1-7-2023

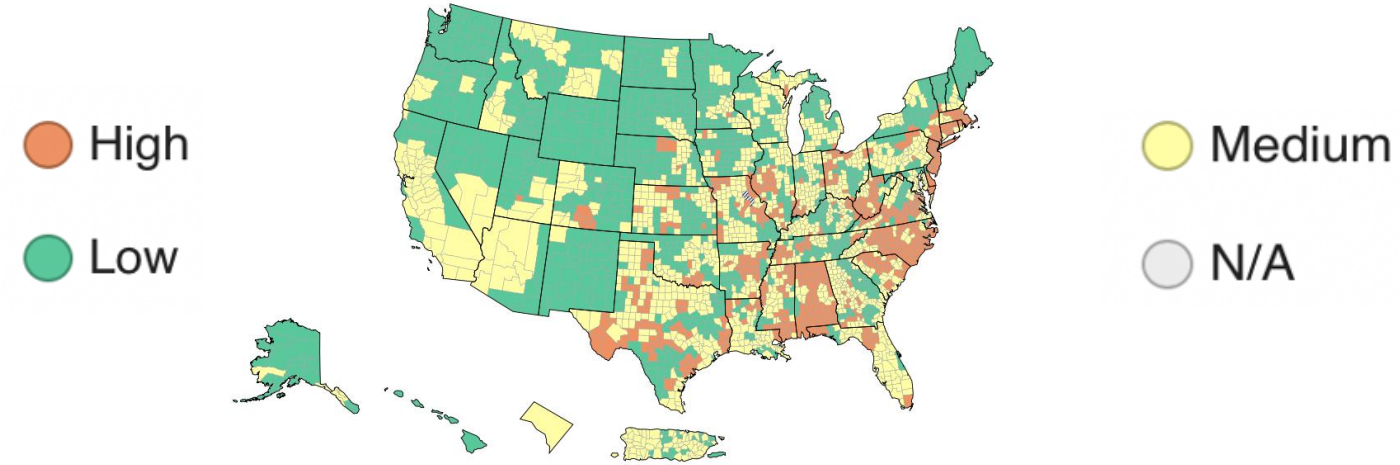
CDC COVID-19 COMMUNITY LEVELS



February 27, 2022



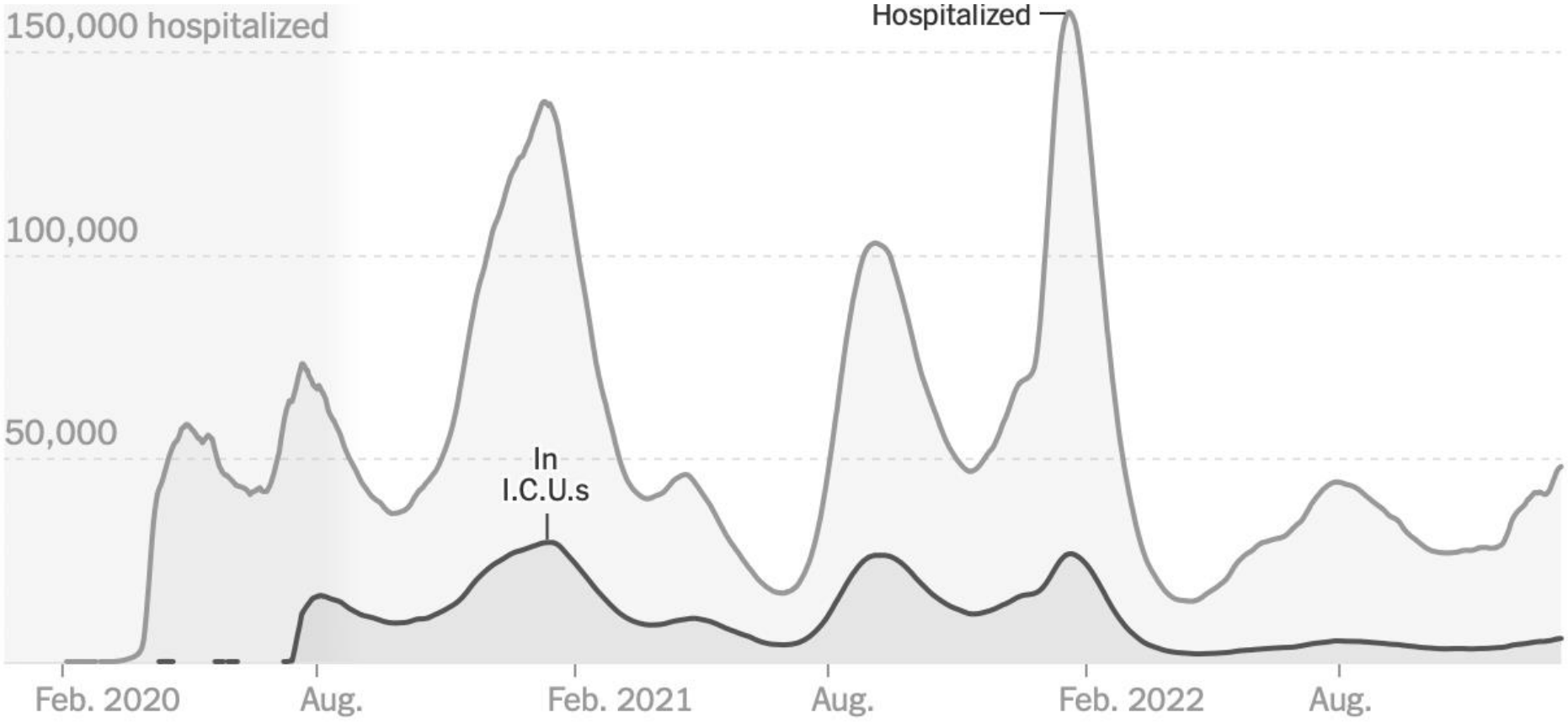
October 9, 2022



January 7, 2023

Source – https://covid.cdc.gov/covid-data-tracker/#county-view?list_select_state=all_states&list_select_county=all_counties&data-type=CommunityLevels&null=CommunityLevels

HOSPITALIZATIONS AND ICU ADMISSIONS FOR COVID-19 IN THE UNITED STATES



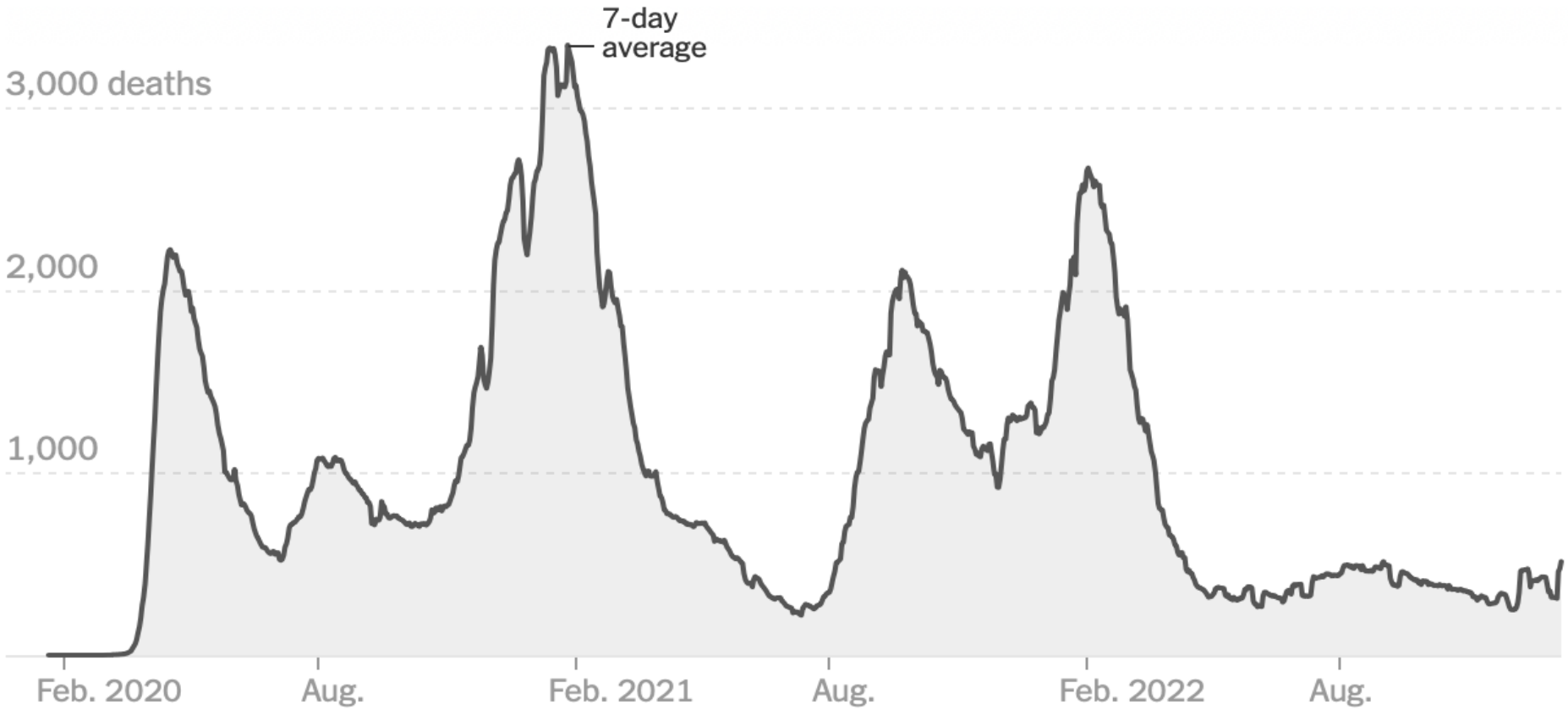
Hospitalizations increased 16% from two weeks earlier

ICU hospitalizations increased 15% from two weeks earlier

Source: New York Times 1-7-23

COVID-19 Deaths in the United States

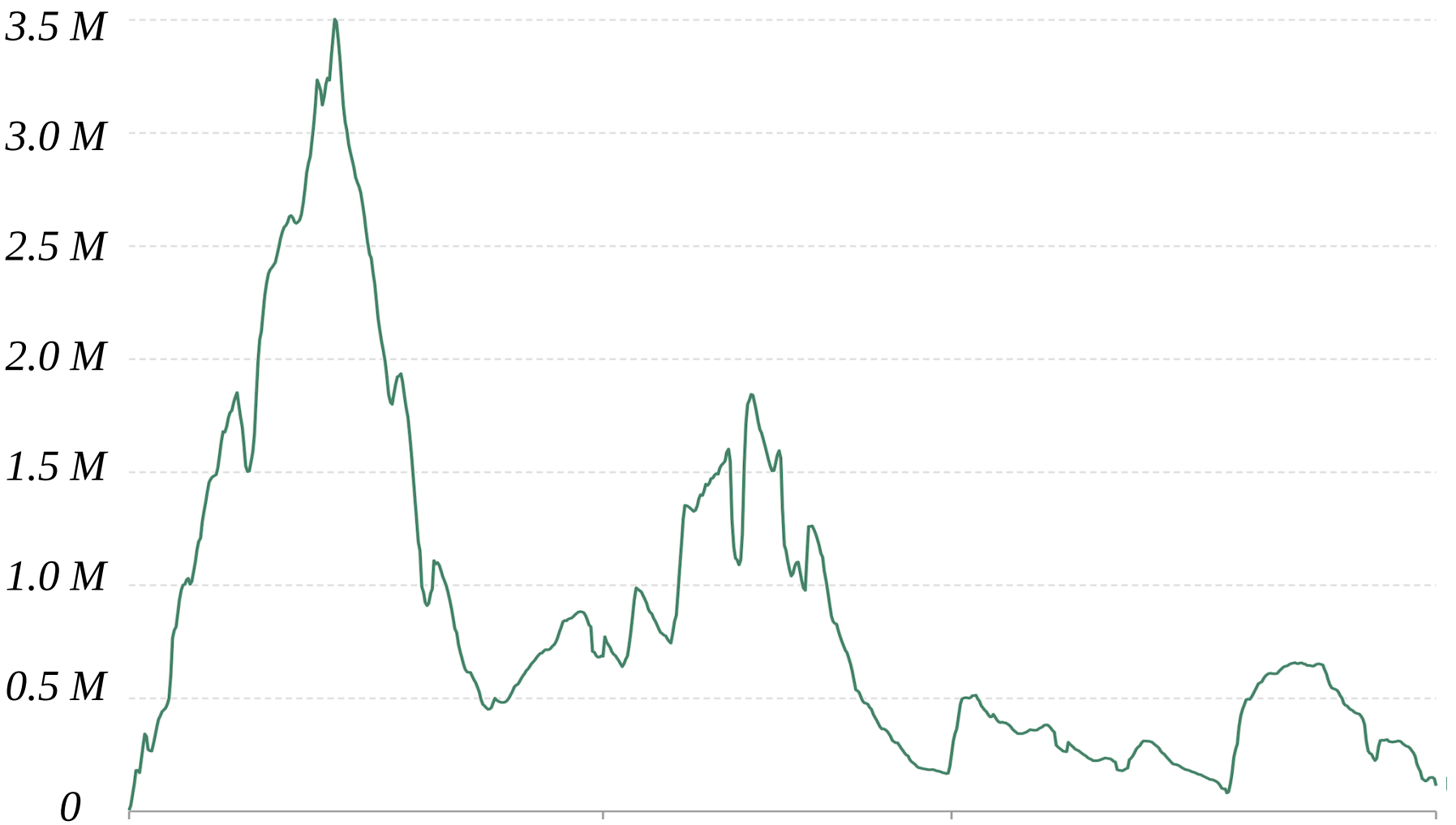
Cumulative Deaths – 1,096,489



20% increase from two weeks earlier

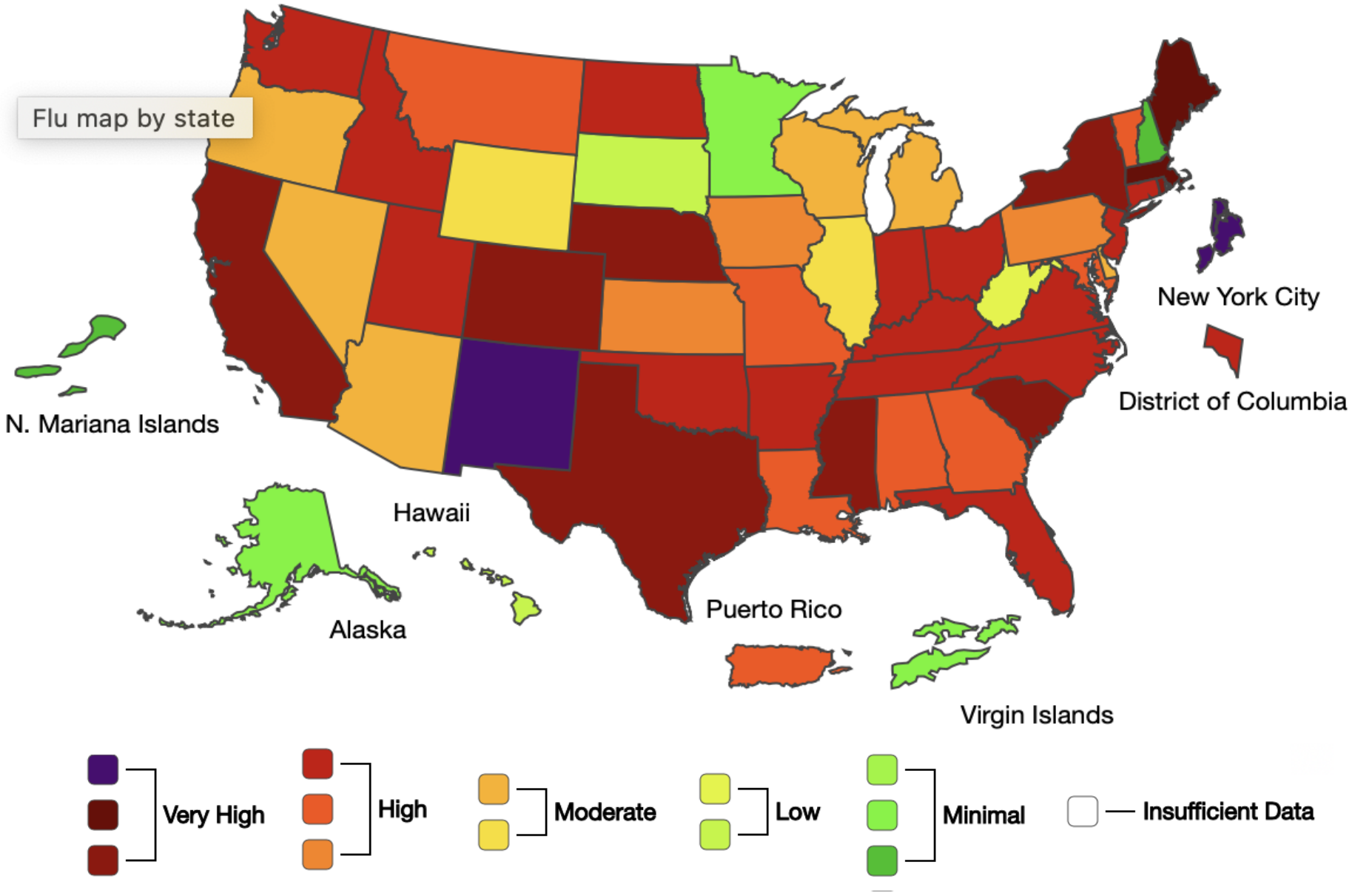
Sources: New York Times 1-7-23,; Johns Hopkins Coronavirus Resource Center: https://coronavirus.jhu.edu/region/united-states 1-7-23

DAILY COVID-19 VACCINATIONS IN THE UNITED STATES



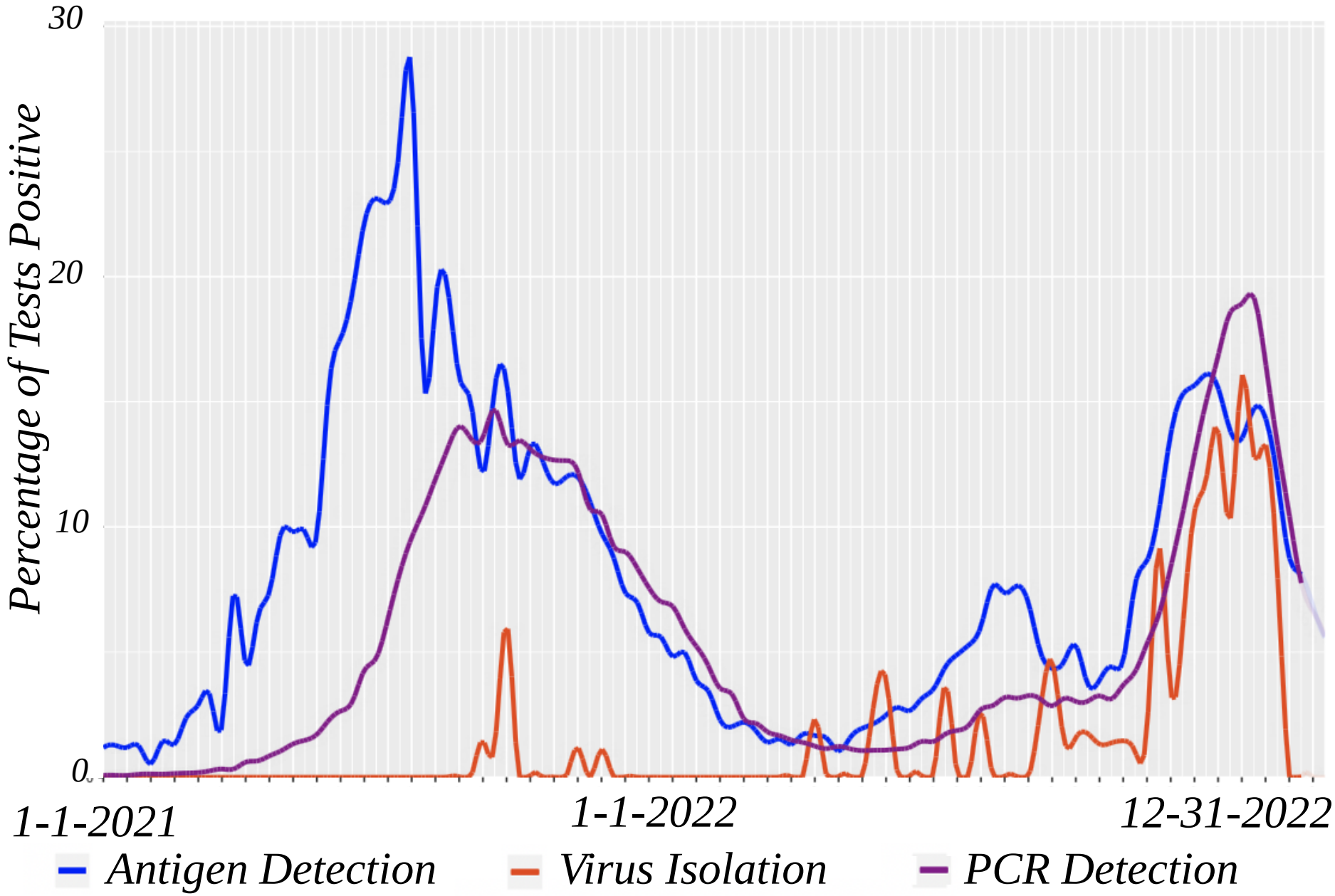
Source: Our World in Data 1-7-22

Influenza Activity by State in the United States



Source: CDC https://www.cdc.gov/flu/weekly/usmap.htm 1-7-23

RSV Activity in the United States



Source: CDC https://www.cdc.gov/surveillance/nrevss/rsv/natl-trend.htm 1-6-23

INFLUENZA 2022 -2023

- Influenza activity remains high in the US but was declining before the holiday season.
- The effect of holiday travel and holiday events is yet to be determined, but will likely increase transmission at least transiently
- Through the end of 2022:
  - Approximately 20 million Americans have had influenza this season.
  - More than 210,000 people have been hospitalized with influenza.
  - The cumulative hospitalization rate is more than four times higher than it has been at this point in the season in more than a decade.
  - 13,000 people have already died this season from influenza.
- Of those that have been typed, a significant majority of cases (78%) have been caused by Influenza A $H_3N_{2;}$ 22% by Influenza A $H_1N_{1..}$
- That number is already more than twice the 9 million cases that occurred during the entire 2021-22 influenza season.
- CDC Director Rochelle Walensky has emphasized that this year's flu vaccine is a very good match for the strains circulating in the US.

Source: https://www.cdc.gov/flu/weekly/index.htm;

This Week's Emerging Infectious Disease News

1. *A letter to the **New England Journal** described a small study that demonstrated benefit of the bivalent booster against the most recently emerging variants.*
2. *A study published in the **New England Journal** found the experimental Chinese antiviral VV116 to be noninferior to Nirmatrelvir–Ritonavir for the oral treatment of COVID-19..*
3. *A **Nature Medicine** study found reduced bivalent booster protection against newly emerging sub-variants and that prior infection plus the bivalent booster provided the broadest protection.*
4. *A research letter in **JAMA** compared COVID-19 and excess all-cause mortality in the US, in the 10 most- and least-vaccinated states, and in 20 peer Organization for Economic Cooperation and Development (OECD) countries during the Delta and Omicron waves.*
5. *A paper in **JAMA Oncology** found oncology patients to be at higher risk for breakthrough infection and complications of COVID and that a third (booster) dose of vaccine was associated with decreased risk.*
6. *A large VA Study published in **MedRXiv** (not yet peer reviewed) found that administration of nirmatrelvir plus ritonavir (Paxlovid) was associated with a decreased risk for long-COVID.*
7. *An open-label clinical trial published in **Nature Cancer** found that that administration of convalescent/vaccinated plasma may improve COVID-19 outcomes in patients with cancer who are unable to intrinsically generate an adequate immune response.*
8. *A **JAMA Internal Medicine** paper found COVID-19-associated hospitalization rates to be 10.5 times higher in unvaccinated persons and 2.5 times higher in vaccinated persons with no booster dose, respectively, compared with those who had received a booster dose.*
9. *A large study in the **American Journal of Public Health** conducted in Indiana found significantly lower rates of all-cause ED visits, hospitalizations, and mortality in those vaccinated, raising questions about the wisdom of reliance on natural immunity when safe and effective vaccines are available.*
10. A **JAMA** multicenter trial evaluated 180-Day outcomes for critically ill COVID-19 patients; those treated with IL-6 receptor antagonists and antiplatelet agents had more favorable outcomes; those treated with hydroxychloroquine or Kaletra had high probabilities of harm.

References available in the chat

Panelists:

Dr. David Henderson
NIH Consultant

Dr. Tara Palmore
George Washington University School of Medicine & Health Sciences

Dr. Marci Drees
ChristianaCare

Dr. Kristina Bryant
University of Louisville

Dr. David Weber
UNC School of Medicine

COVID-19 UPDATE: FOCUS ON XBB SUBLINEAGES

David J. Weber, MD, MPH, FIDSA, FSHEA, FRSM (London)
Sanders Distinguished Professor of Medicine, Pediatrics and Epidemiology
Associate Chief Medical Officer
Medical Director, Hospital Epidemiology
University of North Carolina, Chapel Hill, NC

UNC SCHOOL OF MEDICINE

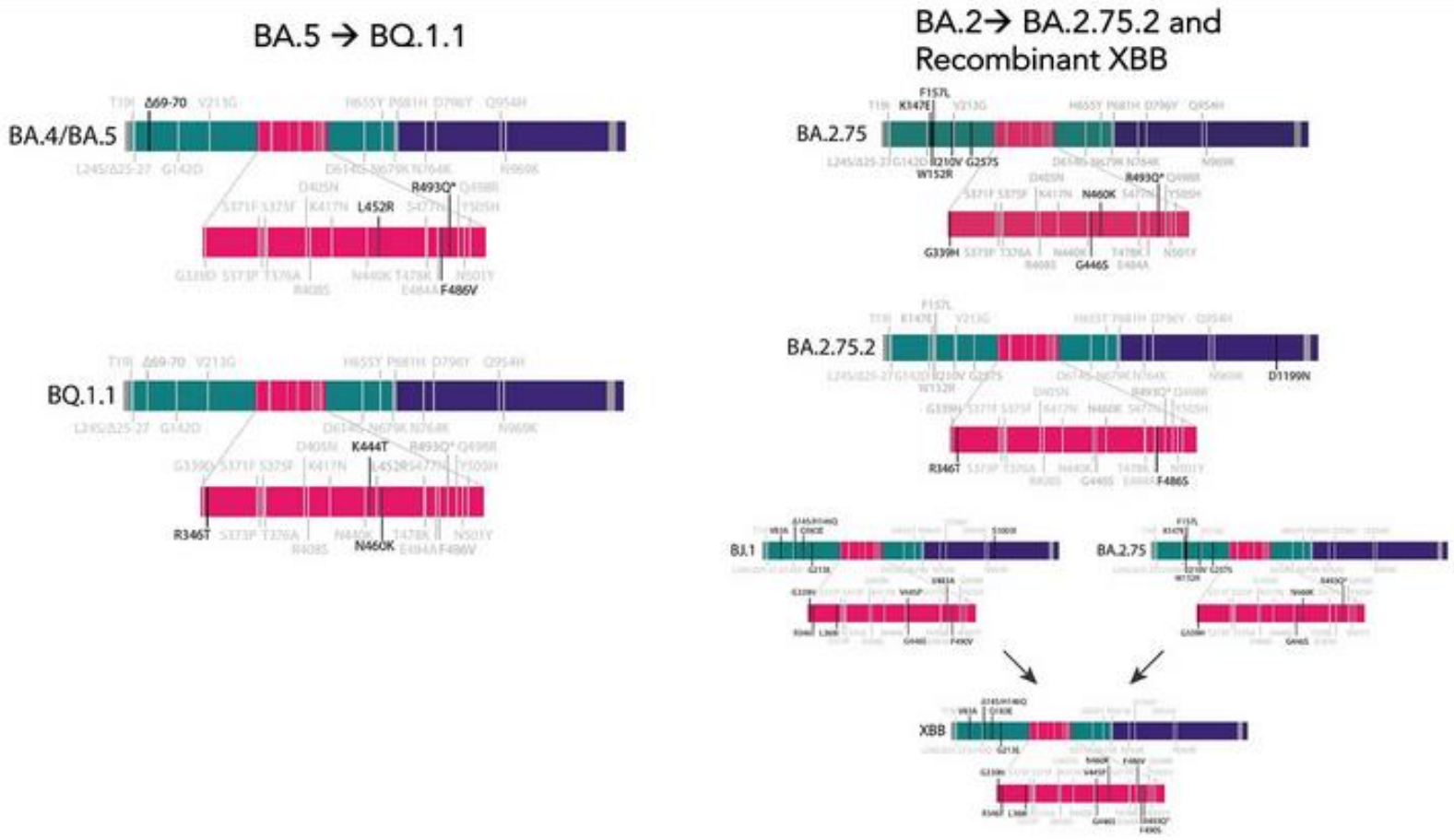
Disclosures: Consultancy; Pfizer, Merck, Sanofi, PDI, BD, Germitec, Wellair
All drugs/vaccines issues discussed consistent with FDA approvals or authorizations

SARS-CoV-2 Variants: Current Summary

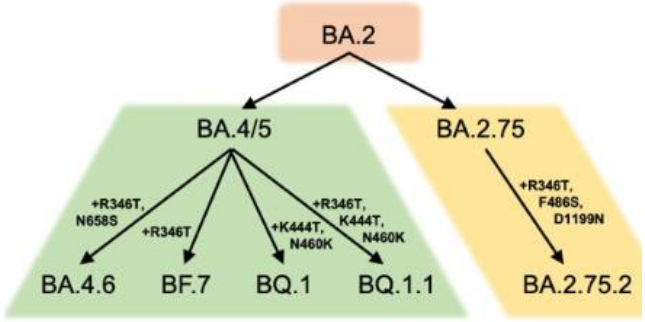
- XBB.1 first reported from India in August 2022; XBB.1.5 first reported from US (NY, CT) in late October 2022
- Epidemiology, US
  - The sublineages BQ.1, BQ.1.1, XBB and XBB.1.5 carry an additional spike mutation in a key antigenic site (i.e. R346T); these sublineages show a significant growth advantage over other circulating Omicron sublineages in many settings
  - Rapid increase of XBB.1 and XBB.1.5 – subvariant with greatest escape from vaccines and natural immunity (also not impacted by Evusheld or Bebtelovimab); similar severity of disease
  - XBB.1.5 = effective Ro, 1.6; 40% higher than any other sublineage (https://www.cnn.com/2023/01/03/health/covid-variant-xbb-explainer/index.html)
- XBB.1: Recombinant of BA.2.10.1 and BA.2.75 sublineages; evidence pointing at a higher reinfection risk, as compared to other circulating Omicron sublineages
- Alternative therapy to monoclonal antibodies: Remdesivir (IV x 3 days) {Remdesivir resistance report in 2 kidney transplant recipients}^
- Best evidence suggests that antivirals (e.g., Remdesivir, Paxlovid, Molnupivir) retain activity against all variants
- Bivalent COVID-19 vaccine elicits lower neutralizing antibodies to XBB than other SARS-CoV02 variants and Omicron sublineages but is superior to monovalent vaccines including persons who have had 2 boosters (i.e., 4 doses)
- Only ~15% of Americans 5+ have received bivalent booster; ~33% of persons 65 years and older

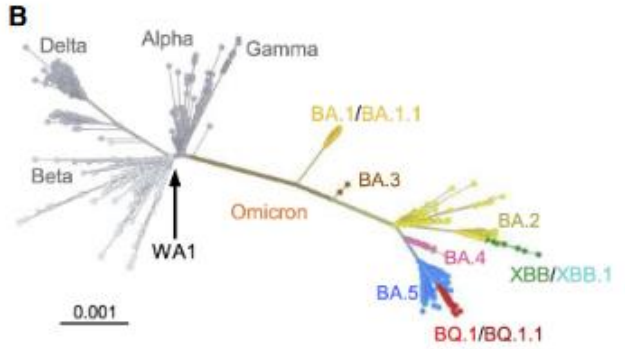
^Hogan JI, et al. Clin Infect Dis 2022;Sept 26,ciac769

EVOLUTION OF NEW SARS-CoV-2 VARIANTS



XBB is a recombinant of BA.2.10.1 and BA.2.75





https://erictopol.substack.com/p/a-booster-is-your-best-shot-now

Qu P, et al. https://www.biorxiv.org/content/10.1101/2022.10.19.512891v1.full.pdf

Wang Q, et al. Cells 2023;186, 1-8

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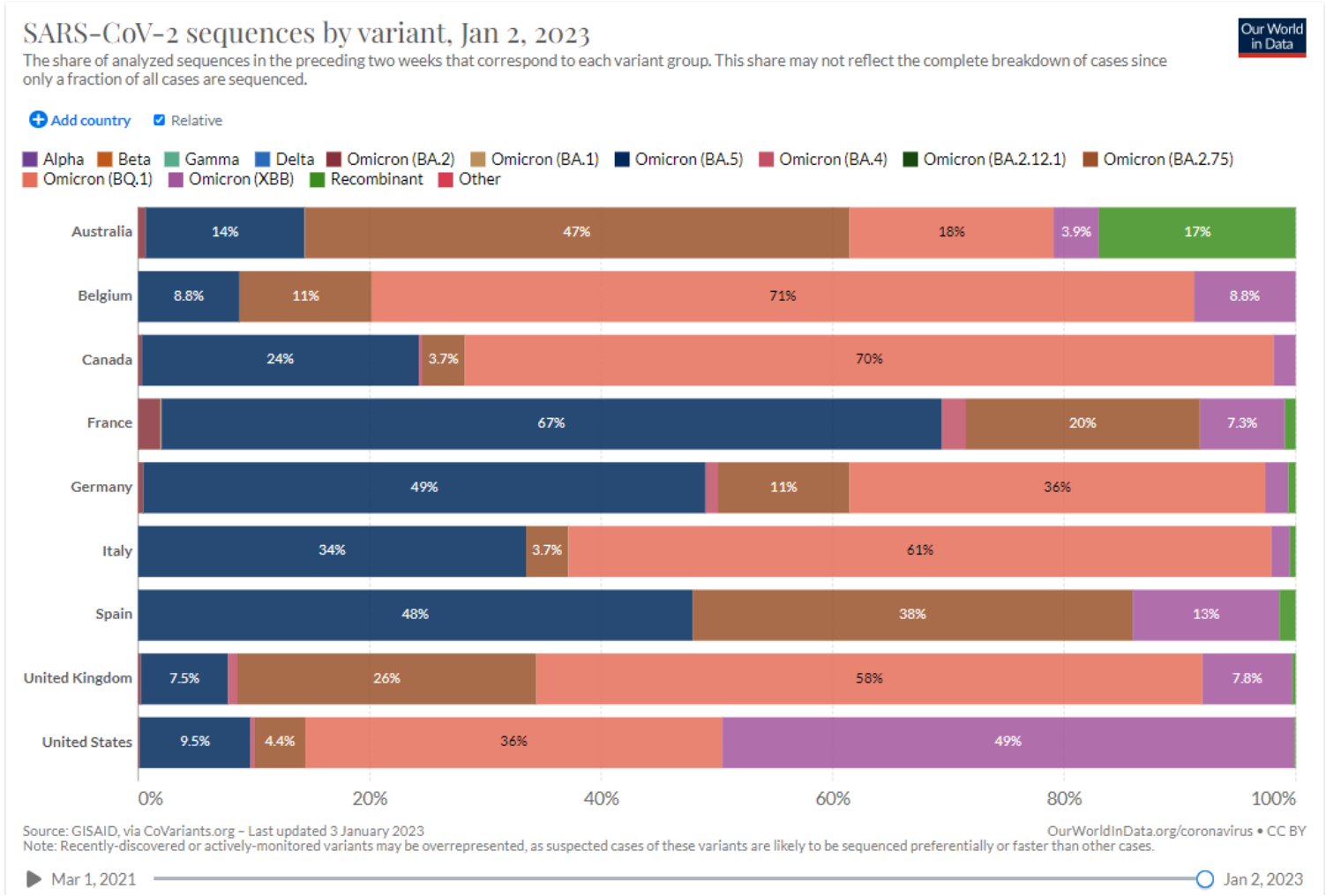
COVID-19 VARIANTS, WORLDWIDE



https://ourworldindata.org/coronavirus

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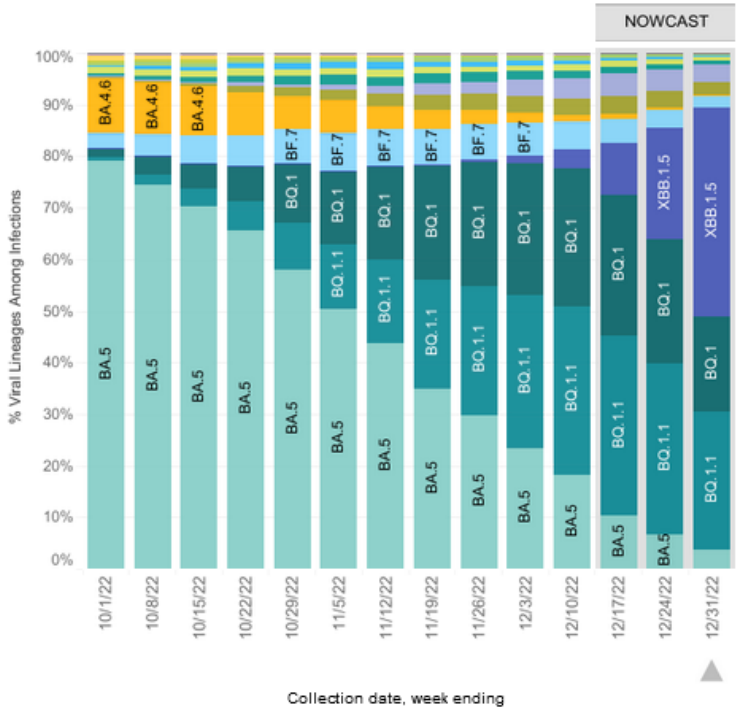
COVID-19 VARIANTS, US

United States: 12/25/2022 – 12/31/2022 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	XBB.1.5	VOC	40.5%	22.7-61.0%
	BQ.1.1	VOC	26.9%	18.9-36.5%
	BQ.1	VOC	18.3%	12.5-25.9%
	BA.5	VOC	3.7%	2.6-5.2%
	XBB	VOC	3.6%	2.5-5.0%
	BN.1	VOC	2.4%	1.6-3.5%
	BF.7	VOC	2.1%	1.4-3.1%
	BA.2.75	VOC	0.9%	0.5-1.4%
	BA.5.2.6	VOC	0.6%	0.4-0.9%
	BA.4.6	VOC	0.3%	0.2-0.5%
	BA.2	VOC	0.3%	0.2-0.5%
	BF.11	VOC	0.3%	0.2-0.4%
	BA.2.75.2	VOC	0.1%	0.1-0.2%
	BA.4	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.2.12.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

United States: 9/25/2022 – 12/31/2022



* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
\# BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. Except BA.2.12.1, BA.2.75, BA.2.75.2, BN.1,XBB and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Except BF.7, BF.11, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. Except XBB.1.5, sublineages of XBB are aggregated to XBB. For all the lineages listed in the above table, their sublineages are aggregated to the listed parental lineages respectively. Previously, XBB.1.5 was aggregated to XBB. Lineages BA.2.75.2, XBB, XBB.1.5, BN.1, BA.4.6, BF.7, BF.11, BA.5.2.6 and BQ.1.1 contain the spike substitution R346T.

Multiple sublineages escape from monoclonal antibody prophylaxis (i.e., Evusheld) and treatment (i.e., bebtelovimab) including BQ.1., BQ.1.1, XBB.1, XBB.1.5

https://covid.cdc.gov/covid-data-tracker/#variant-proportions

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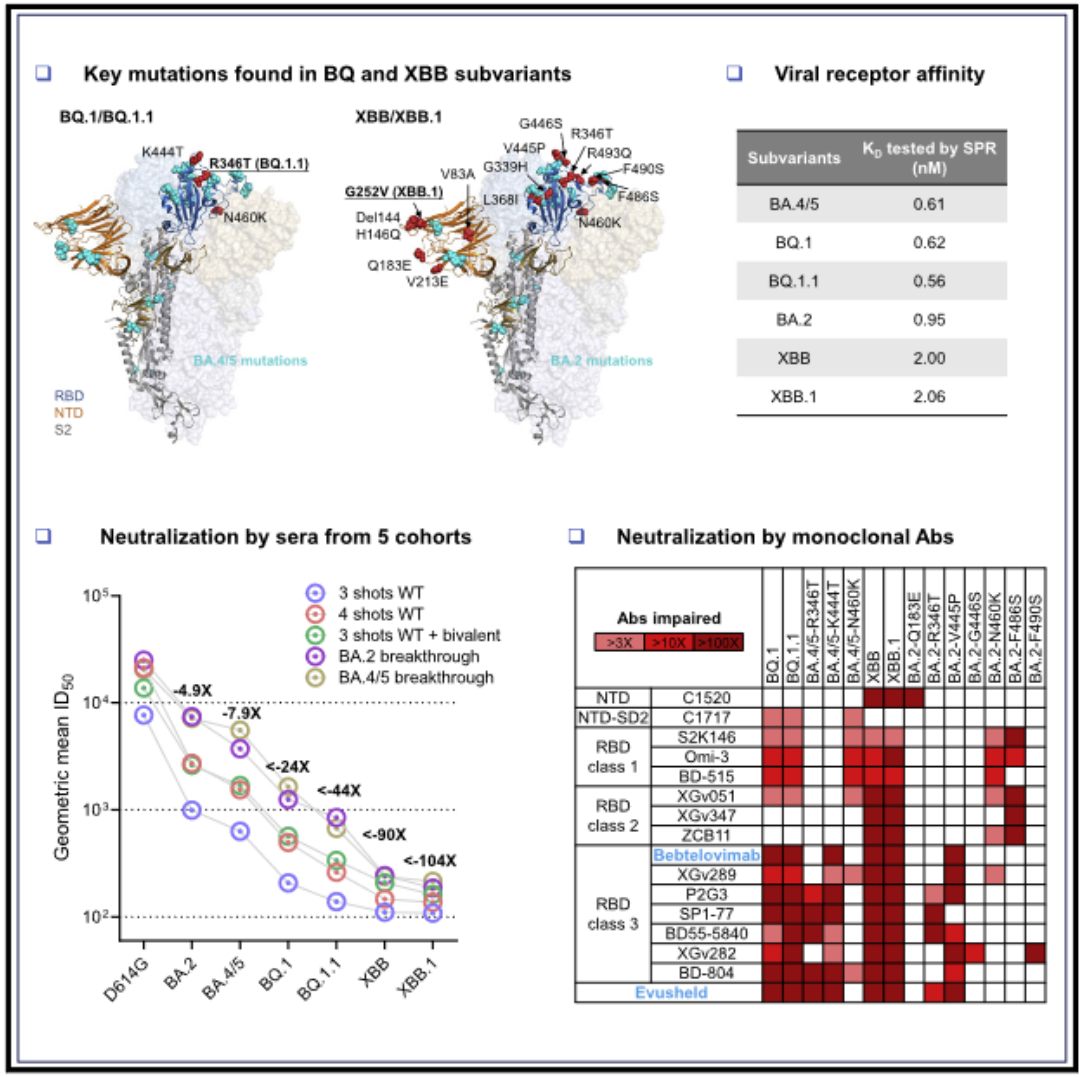
Alarming antibody evasion properties of rising SARS-CoV-2 BQ and XBB subvariants

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

Graphical abstract



Wang Q, et al. Cell 2023;186, 1-8

Enhanced transmissibility of XBB.1.5 is contributed by both strong ACE2 binding and antibody evasion

SARS-CoV-2 recombinant subvariant XBB.1.5 is growing rapidly in the United States, carrying an additional Ser486Pro substitution compared to XBB.1 and outcompeting BQ.1.1 and other XBB sublineages. The underlying mechanism for such high transmissibility remains unclear. Here we show that XBB.1.5 exhibits a substantially higher hACE2-binding affinity compared to BQ.1.1 and XBB/XBB.1. Convalescent plasma samples from BA.1, BA.5, and BF.7 breakthrough infection are significantly evaded by both XBB.1 and XBB.1.5, with XBB.1.5 displaying slightly weaker immune evasion capability than XBB.1. Evusheld and Bebtelovimab could not neutralize XBB.1/XBB.1.5, while Sotrovimab remains weakly reactive and notably, SA55 is still highly effective. The fact that XBB.1 and XBB.1.5 showed comparable antibody evasion but distinct transmissibility suggests enhanced receptor-binding affinity would indeed lead to higher growth advantages. The strong hACE2 binding of XBB.1.5 could also enable its tolerance of further immune escape mutations, which should be closely monitored.

Yue C, et al https://www.biorxiv.org/content/10.1101/2023.01.03.522427v2.full.pdf

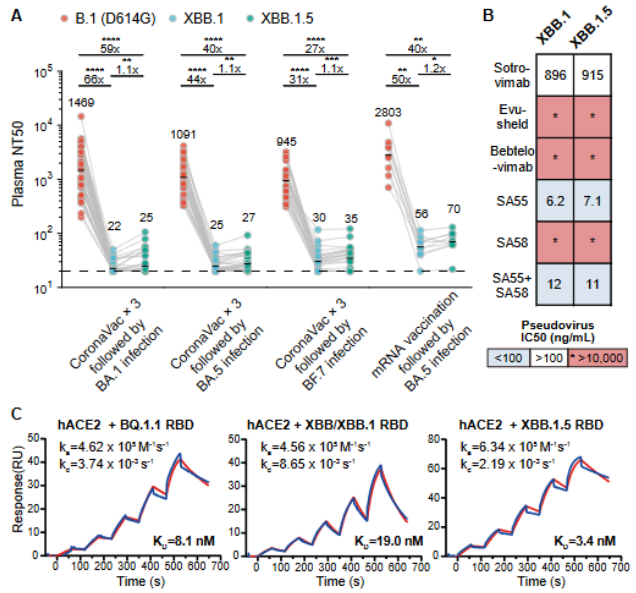


Figure 1 | XBB.1.5 exhibits enhanced hACE2 binding with strong antibody evasion

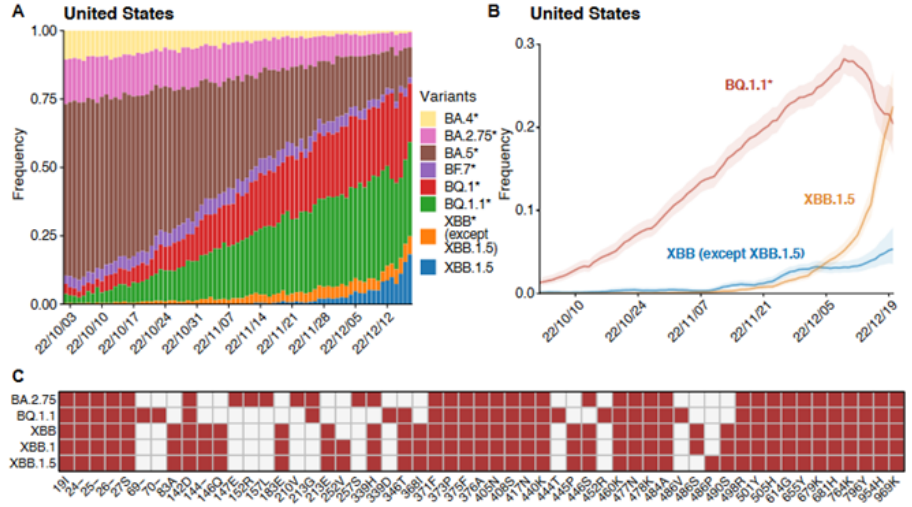


Figure S1 | XBB.1.5 exhibited growth advantage compared to other evasive strains

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

B

Fold change in IC_{50}		NTD	NTD-SD2	SD1	RBD Class 1				RBD Class 2				RBD Class 3											RBD Class 4	
		C1520	C1717	S3H3	S2K146	Omi-3	Omi-18	BD-515	XGv051	XGv347	ZCB11	COV2-2196	LY-CoV1404	XGv289	XGv264	S309	P2G3	SP1-77	BD55-5840	XGv282	BD-804	35B5	COV2-2130	10-40	Evusheld
Relative to BA.4/5	BQ.1	1.4	-3.2	-1.4	-6.5	-38	-10	-34	-3.2	1.2	<-2.1	NA	<-7668	-11	-206	-1.2	-729	-3538	-3.9	-22	<-520	NA	<-472	-4.1	<-284
	BQ.1.1	-2.3	-5.3	-1.8	-5.9	-36	-14	-37	-3.8	-1.0	<-2.1	NA	<-7668	-27	<-4173	-4.2	<-4532	<-1922	<-1125	-105	<-520	NA	<-472	-4.1	<-284
	BA.4/5-R346T	-1.2	1.5	-1.5	1.1	1.2	1.3	1.6	1.2	1.6	1.9	NA	1.2	-1.2	-1.3	-3.4	-19	<-1922	-163	-1.1	<-520	NA	<-472	-2.1	<-284
	BA.4/5-K444T	-1.1	1.8	1.5	-1.2	1.4	1.2	1.6	1.2	-1.4	1.3	NA	<-7668	-4.3	-114	-1.1	-564	-770	-4.3	-6.3	<-520	NA	<-472	-2.9	<-284
	BA.4/5-N460K	-1.6	-5.6	-1.2	-6.0	-57	-15	-43	-3.1	1.1	<-2.1	NA	-1.3	-9.3	-1.1	-1.8	-1.2	-1.7	-1.3	-1.9	-6.4	NA	-1.4	-4.1	-1.8
Relative to BA.2	XBB	<-6340	-1.5	-1.0	-8.0	-78	-92	-45	<-7195	<-3250	<-847	<-5.2	<-6861	<-150	<-3190	2.4	<-4687	<-1626	<-739	<-8886	<-266	<-12	<-1123	-1.1	<-530
	XBB.1	<-6340	-1.2	-1.2	-6.8	-112	-119	-65	<-7195	<-3250	<-847	<-5.2	<-6861	<-150	<-3190	2.1	<-4687	<-1626	<-739	<-8886	<-266	<-12	<-1123	-1.1	<-530
	BA.2-V83A	1.5	1.6	1.1	-1.3	-1.3	-1.4	-1.2	-1.7	-1.0	-1.1	-1.6	1.1	-1.0	1.4	1.3	-1.1	-1.1	-1.4	-1.2	-1.2	-1.5	-1.2	-1.1	-1.3
	BA.2-Del144	-1.1	1.1	1.4	1.1	-1.0	1.2	1.1	-1.1	1.3	1.5	-2.1	1.4	1.1	1.5	1.8	1.1	1.2	-1.0	1.3	1.2	2.4	-1.1	1.0	-1.1
	BA.2-H146Q	2.0	1.6	1.5	-1.2	1.3	1.2	1.3	-1.6	1.5	1.2	-1.5	-1.1	1.2	1.3	1.3	-1.2	-1.1	-1.4	1.6	-1.2	-1.3	-1.0	1.0	-1.0
	BA.2-Q183E	-204	1.8	-1.2	-1.2	-1.2	-1.3	-1.1	-1.4	-1.0	-1.1	-1.6	-1.0	-1.0	1.2	1.3	-1.1	-1.3	-1.5	-1.4	1.3	-1.2	-1.3	-1.1	-1.2
	BA.2-V213E	-1.1	1.4	1.2	-1.1	1.1	1.4	1.2	-1.2	1.2	2.1	-1.1	1.2	1.4	1.2	1.2	1.3	-1.0	-1.0	1.4	1.4	-1.5	-1.0	1.1	-1.0
	BA.2-G252V	1.3	-1.0	1.2	-1.1	1.2	1.2	1.4	-1.1	1.2	1.5	-1.2	1.1	1.4	1.3	1.5	-1.1	1.2	1.2	1.3	1.2	-1.1	-1.2	<-1.1	-1.4
	BA.2-G339H	1.4	1.2	-1.1	-1.2	-1.3	-1.1	-1.0	-1.6	1.4	1.2	-2.0	-1.1	-1.7	1.4	2.8	1.1	-1.2	-3.0	-1.7	-1.3	1.3	-1.3	1.0	-1.2
	BA.2-R346T	-1.7	1.5	1.3	1.6	1.6	1.7	1.8	1.1	1.7	1.7	-1.1	-1.2	1.4	-1.2	-1.7	-3.1	<-1626	-107	-1.1	-3.0	<-12	<-1123	1.1	-79
	BA.2-L368I	-1.9	1.2	-1.2	-1.0	1.5	1.2	1.3	-1.2	2.3	1.8	-1.4	1.1	2.2	1.3	1.4	1.2	1.1	-1.6	1.6	1.4	2.6	1.1	2.7	-1.0
	BA.2-V445P	1.4	1.3	-1.2	1.1	1.7	1.4	1.3	-1.4	1.5	1.5	-1.2	<-6861	<-150	-364	1.9	<-4687	-1.2	-11	<-8886	-42	1.7	<-1123	1.4	-166
	BA.2-G446S	-1.0	1.5	1.3	1.3	1.7	1.4	1.4	-1.0	-1.0	1.5	-1.4	-1.4	2.6	-1.2	1.2	-1.0	1.7	-1.1	-19	1.5	-1.2	-1.9	1.5	-1.5
	BA.2-N460K	-1.0	-2.4	1.3	-4.7	-51	-2.6	-29	-4.9	-1.2	-6.2	1.1	1.1	-5.3	-1.0	-1.1	-1.1	-1.8	-1.2	-1.2	-1.5	-2.4	-1.5	<-1.1	-1.3
	BA.2-F486S	-1.3	-1.2	1.9	<-358	-38	-2.1	-1.4	<-7195	<-3250	<-847	<-5.2	1.5	1.4	1.2	1.4	1.2	1.1	1.5	-1.3	-1.6	-2.7	-1.2	<-1.1	-1.2
	BA.2-F490S	1.3	1.3	1.1	1.3	-2.2	1.4	1.6	1.2	-1.3	-1.0	1.7	1.2	2.3	1.5	1.5	1.3	1.1	1.3	<-8886	-1.3	<-12	-1.5	1.6	1.2
	BA.2-R493Q	-2.1	1.7	-1.5	5.4	2.5	-1.1	1.9	2.3	2.6	7.0	56	-1.0	1.5	1.7	-1.3	1.2	-1.1	-1.6	9.8	3.9	-1.4	-1.1	2.6	2.3

>10	>3	<-3	<-10	<-100

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Figure 3. Resistance of Omicron subvariants to monoclonal antibody neutralization

(A) Footprints of NTD- and RBD-directed antibodies tested are outlined, and mutations within BQ.1, BQ.1.1, XBB, and XBB.1 are highlighted in red.

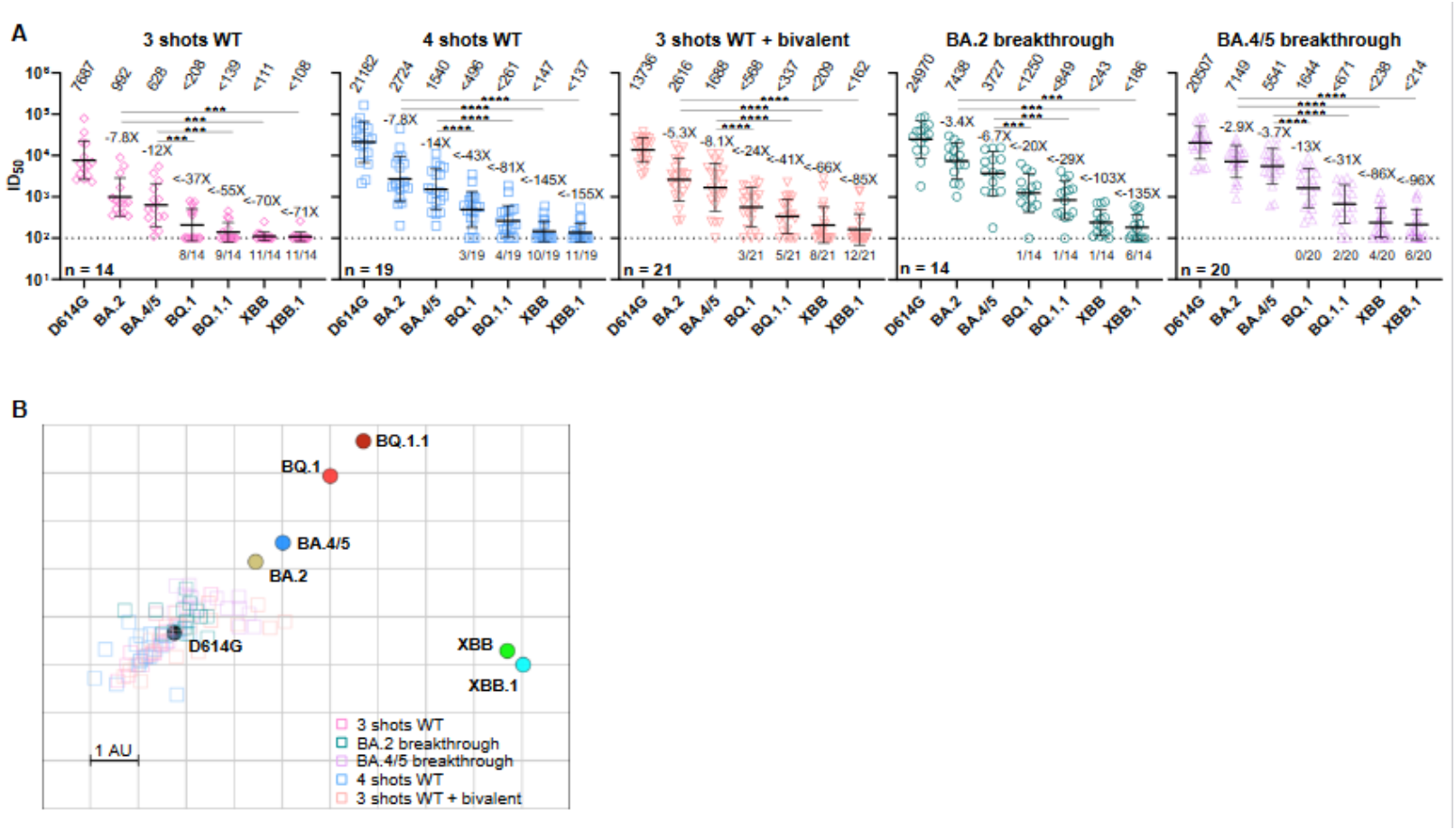
(B) The fold changes in neutralization IC_{50} values of BQ.1, BQ.1.1, XBB, XBB.1, and the individual mutants compared with BA.4/5 or BA.2, with resistance colored red and sensitization colored green. The raw IC_{50} values are shown in Figure S2.

Evusheld = COV2-2196 + COV2-2130; Bebtelovimab = LY-CoV1404

UNC SCHOOL OF MEDICINE

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

The SARS-CoV-2 Omicron variant continues to evolve, with new BQ and XBB subvariants now rapidly expanding in Europe/US and Asia, respectively. As these new subvariants have additional spike mutations, they may possess altered antibody evasion properties. Here, we report that neutralization of BQ.1, BQ.1.1, XBB, and XBB.1 by sera from vaccinees and infected persons was markedly impaired, including sera from individuals who were boosted with a WA1/BA.5 bivalent mRNA vaccine. Compared to the ancestral strain D614G, serum neutralizing titers against BQ and XBB subvariants were lower by 13-81-fold and 66-155-fold, respectively, far beyond what had been observed to date.



Wang Q, et al. https://www.biorxiv.org/content/10.1101/2022.11.23.517532v1

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Neutralization against BA.2.75.2, BQ.1.1, and XBB Bivalent Booster

- Study tested We tested serum samples obtained from participants who had received either one or two monovalent boosters or the bivalent booster to determine the neutralization efficiency of the booster vaccines against wild-type (WA1/2020) virus and primary isolates of omicron subvariants BA.1, BA.5, BA.2.75.2, BQ.1.1, and XBB using an in vitro, live-virus focus reduction neutralization test (FRNT).
- Results: In the cohort that received the BA.5-containing bivalent booster, the neutralizing activity against all the omicron subvariants as compared with that against WA1/2020 was better than in the other two cohorts (Fig. 1C). The FRNT50 GMTs were 2481 against WA1/2020, 618 against BA.1, 576 against BA.5, 201 against BA.2.75.2, 112 against BQ.1.1, and 96 against XBB. The results in this cohort correspond with neutralization titers against BA.1 and BA.5 that were 4 times as low as that against WA1/2020 and neutralization titers against BA.2.75.2, BQ.1.1, and XBB that were 12 to 26 times as low as that against WA1/2020. Persons who received either one or two monovalent Covid-19 vaccine boosters had much lower neutralization activity against omicron subvariants (especially against BA.2.75.2, BQ.1.1, and XBB, which contain the predicted escape mutation R346T) than that against the WA1/2020 strain.

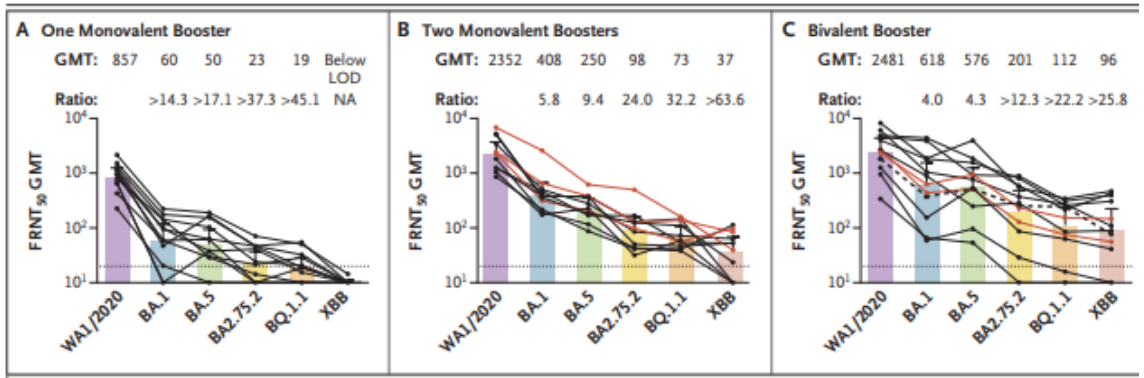


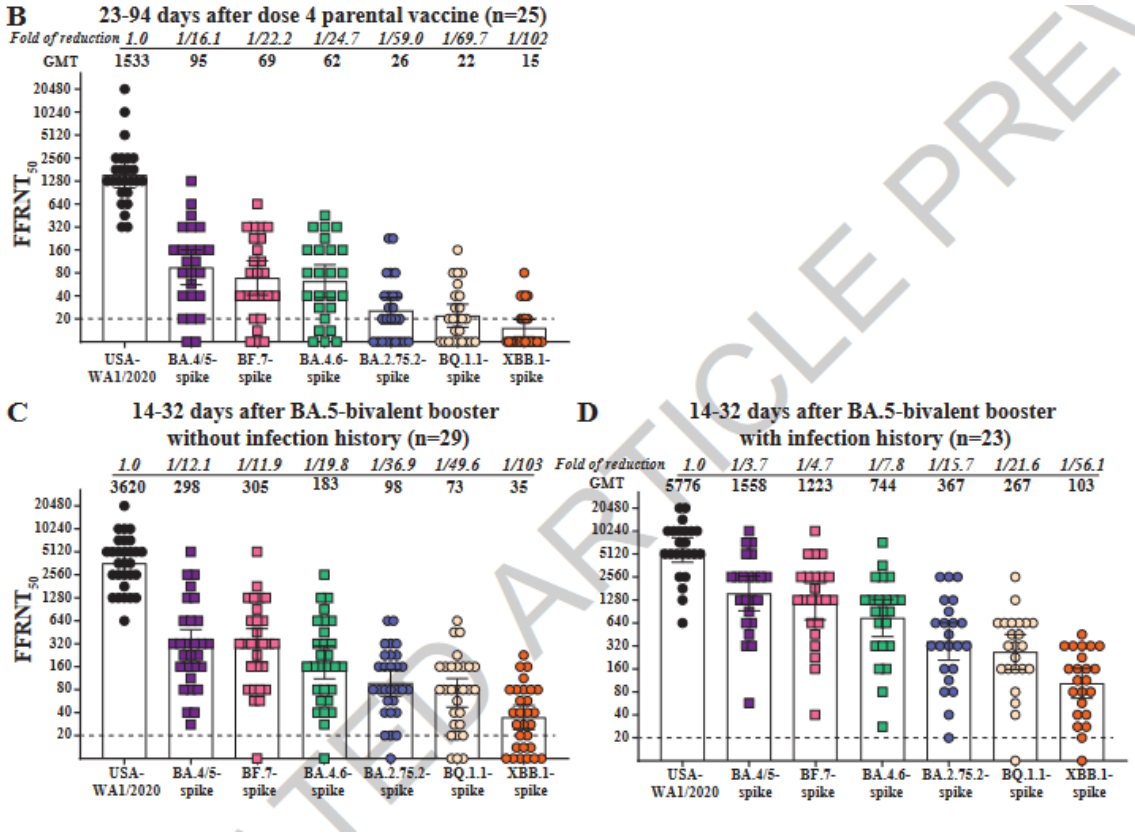
Figure 1. Neutralizing Responses against the WA1/2020 Strain and Omicron Subvariants.

Shown is the neutralization activity against the WA1/2020 strain of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the omicron subvariants BA.1, BA.5, BA.2.75.2, BQ.1.1, and XBB in 12 participants who received one monovalent booster (Panel A), in 11 participants who received two monovalent boosters (Panel B), and in 12 participants who received the updated bivalent booster (Panel C). The focus reduction neutralization test ($FRNT_{50}$ [the reciprocal dilution of serum that neutralizes 50% of the input virus]) geometric mean titer (GMT) of neutralizing antibodies against the WA1/2020 strain and each omicron subvariant is shown at the top of each panel, along with the ratio of the neutralization GMT against the WA1/2020 strain to that against each omicron subvariant. The connecting lines between the variants represent matched serum samples. The horizontal dotted lines represent the limit of detection of the assay ($FRNT_{50}$ GMT 20). The red lines in Panels B and C indicate the participants who reported previous SARS-CoV-2 infection, and the dashed line in Panel C indicates one participant who received two monovalent boosters before the bivalent booster. The colored bars represent the $FRNT_{50}$ GMT among the participants in the cohort, and the I bars indicate 95% confidence intervals, which were not adjusted for multiplicity and may not be used for hypothesis testing. LOD denotes limit of detection, and NA not applicable.

Davis-Gardner ME, et al. NEJM 2022;22 December

Low neutralization of SARS-CoV-2 Omicron BA.2.75.2, BQ.1.1, and XBB.1 by parental mRNA vaccine or a BA.5-bivalent booster

ABSTRACT: The newly emerged SARS-CoV-2 Omicron sublineages, including the BA.2-derived BA.2.75.2 and the BA.5-derived BQ.1.1 and XBB.1, have accumulated additional spike mutations that may affect vaccine effectiveness. Here we report neutralizing activities of three human serum panels collected from individuals 23-94 days after dose 4 of a parental mRNA vaccine, 14-32 days after a BA.5-bivalent-booster from individuals with 2-4 previous doses of parental mRNA vaccine, or 15-32 days after a BA.5-bivalent-booster from individuals with previous SARS-CoV-2 infection and 2-4 doses of parental mRNA vaccine. The results showed that a BA.5-bivalent-booster elicited a high neutralizing titer against BA.4/5 measured at 14- to 32-day post-boost; however, the BA.5-bivalent-booster did not produce robust neutralization against the newly emerged BA.2.75.2, BQ.1.1, or XBB.1. Previous infection significantly enhanced the magnitude and breadth of BA.5-bivalent-booster-elicited neutralization. Our data support a vaccine update strategy that future boosters should match newly emerged circulating SARS-CoV-2 variants



Kurhade C, et al. Nature Medicine
file:///C:/Users/dweber/Downloads/s41591-022-02162-x_reference.pdf

Early Estimates of Bivalent mRNA Vaccine Effectiveness in Preventing COVID-19–Associated ED or Urgent Care Encounters and Hospitalizations Among Immunocompetent Adults, VISION Network, Nine States, Sept.–Nov. 2022

TABLE 2. Bivalent booster COVID-19 vaccine effectiveness* against laboratory confirmed COVID-19–associated emergency department and urgent care encounters and hospitalizations among immunocompetent adults aged 18 years — nine states,† September–November 2022

mRNA dosage pattern	Total	Negative SARS-CoV-2 test result, no. (%)	Positive SARS-CoV-2 test result, no. (%)	Median interval since last dose, days (IQR)	VE % (95% CI)
ED/UC encounters					
Relative VE					
Only MV doses, last dose 2–4 mos earlier	**5,668**	5,131 (91)	537 (9)	115 (91–134)	Ref
BV booster dose, ≥7 days earlier	**3,905**	3,658 (94)	247 (6)	25 (16–37)	31 (19–41)
Only MV doses, last dose 5–7 mos earlier	**6,891**	6,166 (89)	725 (11)	184 (166–209)	Ref
BV booster dose, ≥7 days earlier	**3,905**	3,658 (94)	247 (6)	25 (16–37)	42 (32–50)
Only MV doses, last dose 8–10 mos earlier	**14,220**	12,543 (88)	1,677 (12)	294 (273–312)	Ref
BV booster dose, ≥7 days earlier	**3,905**	3,658 (94)	247 (6)	25 (16–37)	53 (46–60)
Only MV doses, last dose ≥11 mos earlier	**23,477**	20,694 (88)	2,783 (12)	459 (365–542)	Ref
BV booster dose, ≥7 days earlier	**3,905**	3,658 (94)	247 (6)	25 (16–37)	50 (43–57)
Absolute VE					
Unvaccinated	**24,142**	21,102 (87)	3,040 (13)	NA	Ref
BV booster dose, ≥7 days earlier	**3,905**	3,658 (94)	247 (6)	25 (16–37)	56 (49–62)
Hospitalizations					
Relative VE					
Only MV doses, last dose 2–4 mos earlier	—§	—	—	—	—
BV booster dose, ≥7 days earlier	—	—	—	—	—
Only MV doses, last dose 5–7 mos earlier	**1,819**	1,652 (91)	167 (9)	178 (164–201)	Ref
BV booster dose, ≥7 days earlier	**783**	734 (94)	49 (6)	23 (14–34)	38 (13–56)
Only MV doses, last dose 8–10 mos earlier	**2,655**	2,422 (91)	233 (9)	294 (273–313)	Ref
BV booster dose, ≥7 days earlier	**783**	734 (94)	49 (6)	23 (14–34)	42 (19–58)
Only MV doses, last dose ≥11 mos earlier	**4,595**	4,147 (90)	448 (10)	472 (362–556)	Ref
BV booster dose, ≥7 days earlier	**783**	734 (94)	49 (6)	23 (14–34)	45 (25–60)
Absolute VE					
Unvaccinated	**4,092**	3,658 (89)	434 (11)	NA	Ref
BV booster dose, ≥7 days earlier	**783**	734 (94)	49 (6)	23 (14–34)	57 (41–69)

Tenforde MW, et al. MMWR 2022;71:16 December 2022

Early Estimates of Bivalent mRNA Vaccine Effectiveness in Preventing COVID-19–Associated Hospitalization Among Immunocompetent Adults Aged ≥65 Years, IVY Network, 18 States, September 8–November 30, 2022

What is already known about this topic? - Immunity from monovalent COVID-19 mRNA vaccination wanes over time. A bivalent COVID-19 mRNA booster dose is recommended for all eligible persons; however, little is known about its effectiveness against COVID-19 hospitalization.

What is added by this report? - Among immuno-0competent adults aged ≥65 years hospitalized in the multistate IVY Network, a bivalent booster dose provided 73% additional protection against COVID-19 hospitalization compared with past monovalent mRNA vaccination only.

What are the implications for public health practice? - To maximize protection against severe COVID-19 this winter season, all eligible persons, especially adults aged ≥65 years, should receive a bivalent booster dose and consider additional prevention strategies, including masking in indoor public spaces.

Surie D, et al. MMWR 2022;71:16 December 2022

TABLE 2. Effectiveness of a bivalent COVID-19 mRNA booster dose against COVID-19–associated hospitalization among immunocompetent adults aged ≥65 years — IVY Network, 22 hospitals,* 18 states, September 8, 2022–November 30, 2022

Characteristic	Received BV vaccine dose, by case status, n/N (%)		Median interval† from last vaccine dose to illness onset (IQR), days	Adjusted VE, % (95% CI)§
	Case-patients	Control patients		
Absolute VE (BV booster dose versus no vaccine)				
Unvaccinated (Ref)	—	—	NA	—
BV booster dose¶ ≥7 days before illness onset	20/101 (20)	59/121 (49)	29 (15–45)	84 (64–93)
Relative VE (BV booster dose versus MV-only, by interval since last dose)				
≥2 MV-only mRNA doses, last dose ≥2 mos before illness onset (Ref)	—	—	305 (168–377)	—
BV booster dose ≥7 days before illness onset	20/300 (7)	59/355 (17)	29 (15–45)	73 (52–85)
≥2 MV-only mRNA doses, last dose 2–5 mos before illness onset (Ref)			137 (111–155)	—
BV booster dose ≥7 days before illness onset	20/82 (24)	59/155 (38)	29 (15–45)	—**
≥2 MV-only mRNA doses, last dose 6–11 mos before illness onset (Ref)	—	—	304 (258–333)	—
BV booster dose ≥7 days before illness onset	20/155 (13)	59/176 (34)	29 (15–45)	78 (57–89)
≥2 MV-only mRNA doses, last dose ≥12 mos before illness onset (Ref)	—	—	528 (386–575)	—
BV booster dose ≥7 days before illness onset	20/103 (19)	59/142 (42)	29 (15–45)	83 (63–92)

Paxlovid Associated with Decreased Hospitalization Rate Among Adults with COVID-19 — US, April–September 2022

What is already known about this topic? - Nirmatrelvir-ritonavir (Paxlovid) is an outpatient antiviral medication recommended for adults with mild-to-moderate COVID-19 who have elevated risk of severe illness.

What is added by this report? - Among U.S. adults diagnosed with COVID-19, including those with previous infection or vaccination, persons who were prescribed Paxlovid within 5 days of diagnosis had a 51% lower hospitalization rate within 30 days after diagnosis than those who were not prescribed Paxlovid.

What are the implications for public health practice? Paxlovid should be offered to eligible adults irrespective of vaccination status, especially in groups with the highest risk for severe COVID-19 outcomes, such as older adults and those with multiple underlying health conditions

TABLE 2. Adjusted hazard ratios for COVID-19–associated hospitalization based on Paxlovid prescription receipt (exposure) — Cosmos,* United States, April–September 2022

Characteristic	Adjusted HR (95% CI)†	No. of participants	No. hospitalized	Events per 100,000 person-days		
				Overall	Exposed§	Unexposed§
Total	**0.49 (0.46–0.53)**	**693,084**	**5,229**	**25.31**	**15.88**	**29.05**
COVID-19 vaccination status¶						
Vaccinated (≥3 mRNA doses)	**0.50 (0.45–0.55)**	310,196	2,126	**22.98**	14.30	27.87
Vaccinated (2 mRNA doses)	**0.50 (0.42–0.58)**	149,498	1,086	**24.37**	16.37	26.92
Unvaccinated	**0.50 (0.43–0.59)**	170,789	1,477	**29.05**	19.60	31.08
UHC**						
0	**0.89 (0.58–1.36)**	52,592	106	**6.73**	6.51	6.83
1	**0.57 (0.45–0.71)**	200,116	503	**8.40**	6.46	9.03
≥2	**0.47 (0.44–0.51)**	440,376	4,620	**35.29**	20.56	41.57
Previous infection††						
No	**0.48 (0.44–0.51)**	589,147	4,715	**26.86**	16.12	31.53
Yes	**0.76 (0.60–0.98)**	103,937	514	**16.56**	13.54	17.20
Immunocompromised§§						
No	**0.49 (0.45–0.53)**	628,706	3,770	**20.09**	12.61	23.03
Yes	**0.50 (0.44–0.58)**	64,378	1,459	**77.01**	45.99	90.49
Month of COVID-19 diagnosis						
Apr 2022	**0.54 (0.40–0.71)**	60,001	450	**25.16**	17.77	26.71
May 2022	**0.57 (0.48–0.67)**	139,062	979	**23.61**	17.06	25.88
Jun 2022	**0.51 (0.43–0.60)**	143,706	1,006	**23.48**	15.02	26.76
Jul 2022	**0.46 (0.40–0.53)**	184,153	1,432	**26.09**	15.65	30.94
Aug 2022	**0.44 (0.38–0.51)**	166,162	1,362	**27.52**	15.60	32.93
Age group, yrs						
18–49	**0.59 (0.48–0.71)**	275,930	886	**10.73**	6.99	11.68
50–64	**0.40 (0.34–0.48)**	211,940	1,032	**16.30**	7.90	20.10
≥65	**0.53 (0.48–0.58)**	205,214	3,311	**54.56**	29.72	68.80
By age group, yrs						
18–49						
Vaccinated (≥3 mRNA doses)	**0.75 (0.53–1.06)**	84,054	178	**7.07**	6.10	7.46
Vaccinated (2 mRNA doses)	**0.53 (0.35–0.82)**	70,159	198	**9.43**	6.20	10.16
Unvaccinated	**0.54 (0.39–0.76)**	97,637	417	**14.29**	9.09	15.13
1 UHC	**0.91 (0.58–1.44)**	109,620	157	**4.78**	4.11	4.91
≥2 UHC	**0.54 (0.43–0.67)**	166,310	729	**14.67**	8.35	16.54
50–64						
Vaccinated (≥3 mRNA doses)	**0.41 (0.30–0.55)**	98,699	284	**9.61**	5.28	12.11
Vaccinated (2 mRNA doses)	**0.46 (0.33–0.63)**	47,111	265	**18.84**	10.96	21.89
Unvaccinated	**0.38 (0.27–0.53)**	45,154	355	**26.39**	12.43	30.35
No UHC	**1.11 (0.46–2.68)**	32,519	25	**2.56**	2.87	2.46
1 UHC	**0.30 (0.17–0.55)**	53,493	109	**6.80**	2.45	8.72
≥2 UHC	**0.40 (0.33–0.48)**	125,928	898	**23.91**	11.04	30.26
≥65						
Vaccinated (≥3 mRNA doses)	**0.51 (0.46–0.57)**	127,443	1,664	**44.02**	24.51	57.35
Vaccinated (2 mRNA doses)	**0.53 (0.43–0.65)**	32,228	623	**65.58**	36.83	78.59
Unvaccinated	**0.58 (0.47–0.72)**	27,998	705	**85.92**	52.75	96.15
No UHC	**0.84 (0.51–1.36)**	20,073	81	**13.50**	10.34	15.49
1 UHC	**0.63 (0.47–0.85)**	37,003	237	**21.47**	13.66	26.77
≥2 UHC	**0.51 (0.47–0.56)**	148,138	2,993	**68.58**	37.33	85.48

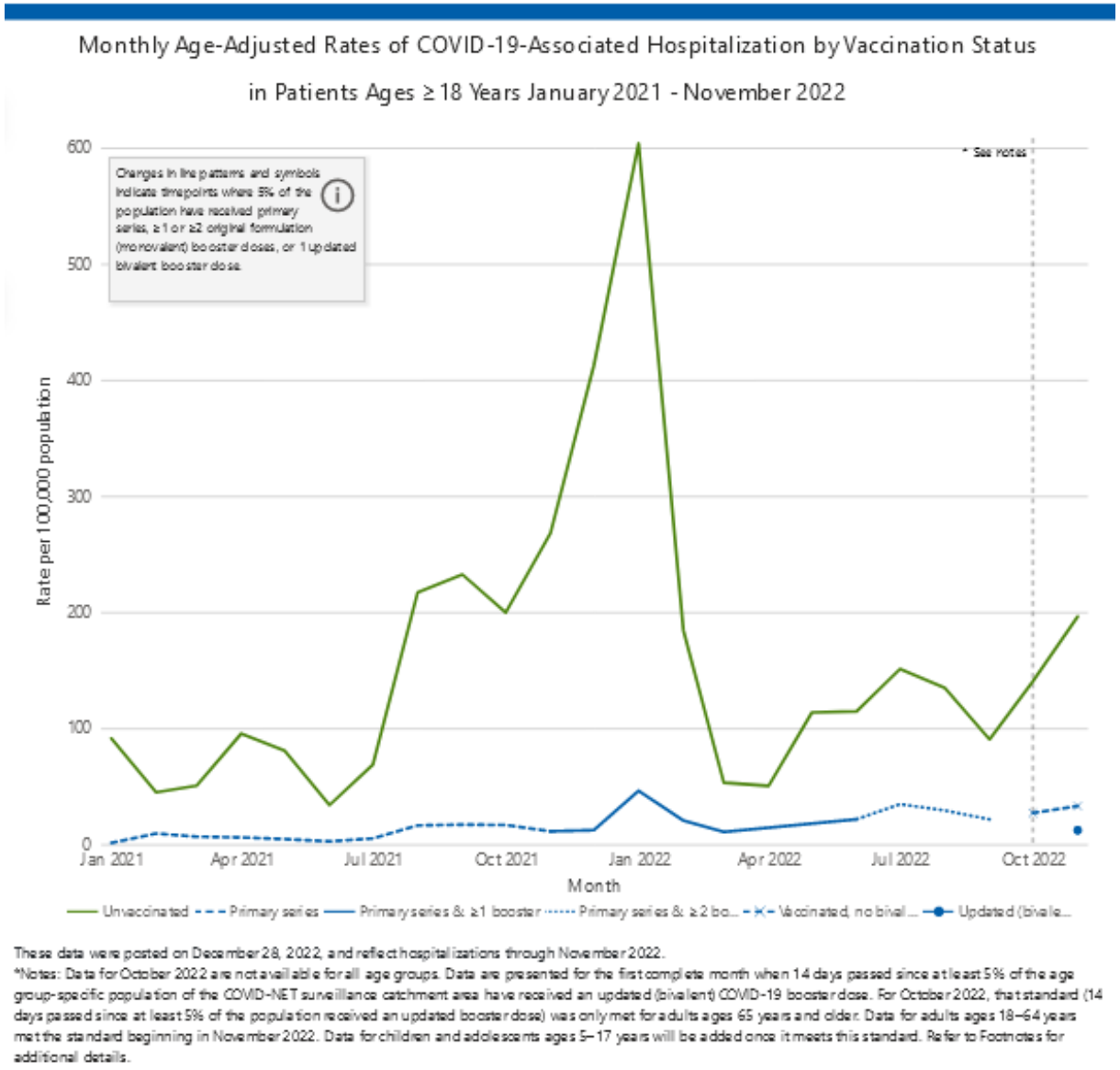
UHC = underlying health condition

Rates of laboratory-confirmed COVID-19 hospitalizations by vaccination status, CDC

In November 2022, compared to adults ages 18 years and older who received an updated COVID-19 bivalent booster dose, monthly rates of COVID-19-associated hospitalizations were **16.0x Higher in Unvaccinated** and **2.7x Higher in Vaccinated Adults without an updated booster.***

29.9x Higher in Unvaccinated Adults Ages 18-49 Years	**13.6x** Higher in Unvaccinated Adults Ages 50-64 Years	**13.5x** Higher in Unvaccinated Adults Ages 65 Years and Older
3.2x Higher in Adults Ages 18-49 Years Vaccinated but Without an Updated booster	**2.9x** Higher in Adults Ages 50-64 Years Vaccinated but Without an Updated booster	**2.5x** Higher in Adults Ages 65 Years and Older Vaccinated but Without an Updated booster

https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination



These data were posted on December 28, 2022, and reflect hospitalizations through November 2022.
*Notes: Data for October 2022 are not available for all age groups. Data are presented for the first complete month when 14 days passed since at least 5% of the age group-specific population of the COVID-NET surveillance catchment area have received an updated (bivalent) COVID-19 booster dose. For October 2022, that standard (14 days passed since at least 5% of the population received an updated booster dose) was only met for adults ages 65 years and older. Data for adults ages 18–64 years met the standard beginning in November 2022. Data for children and adolescents ages 5–17 years will be added once it meets this standard. Refer to Footnotes for additional details.