SHEA

The Society for Healthcare Epidemiology of America

SAFE HEALTHCARE FOR ALL

Music:
www.bensound.com

The Rapid Response Podcasts

COVID-19 Updates: What We Know Now

Releases monthly

Newest Episodes:

- Monkeypox
- Long COVID

COVID-19 Allies in Infection Prevention

LEARNINGCE SHEA Online Education Center

LearningCE.shea-online.org

SHEA

SAFE HEALTHCARE FOR ALL

Music: www.bensound.com

SHEA COVID-19 Resources:

SHEA/CDC Outbreak Response Training Program (ORTP)

This program is designed to give US hospital epidemiologists who oversee infection control programs the skills, knowledge, and tools to provide effective leadership during facility-level outbreaks and large-scale public health emergencies.

- Simulations
- Tools Kits
- On-demand Webinars
- On-demand Workshop Sessions
- Expert Guidance on Incident Management and HICs, Crisis Strategies, Communication Guidance and Much More

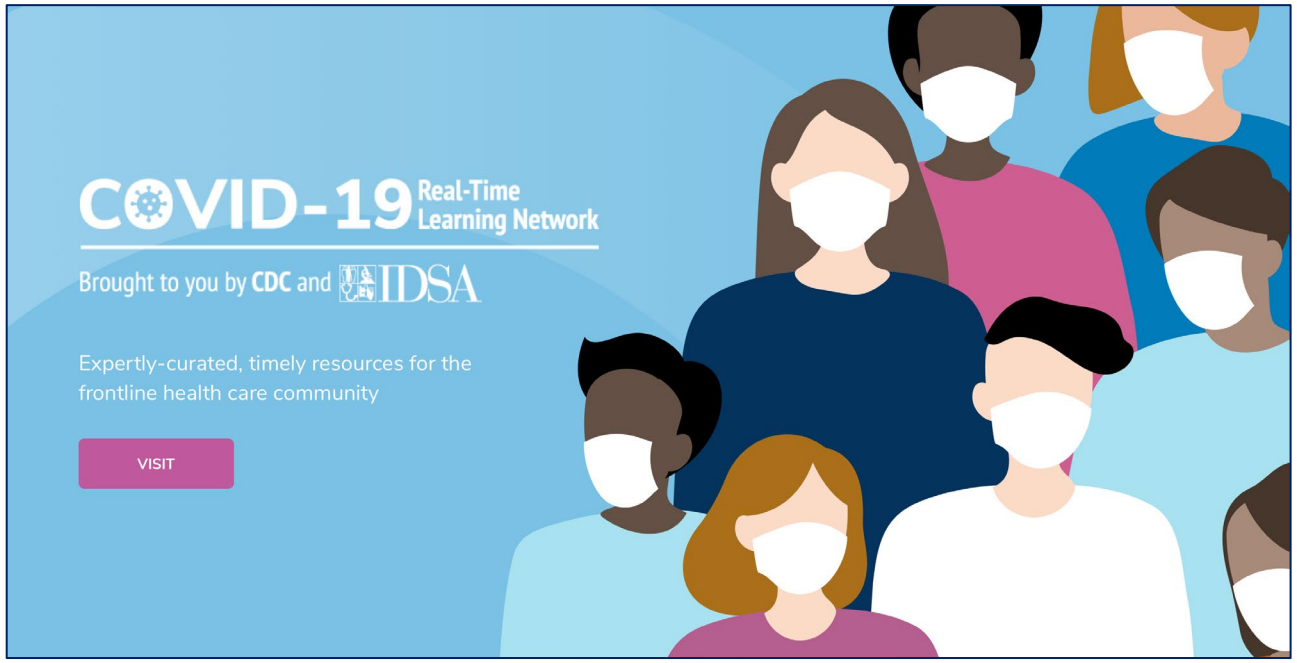
www.ortp.shea-online.org

SHEA

SAFE HEALTHCARE FOR ALL

Music:
www.bensound.com

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

@RealTimeCOVID19 | #RealTimeCOVID19

SHEA

SAFE HEALTHCARE FOR ALL

Music:
www.bensound.com

WE'VE UPDATED ALL MODULES!

The SHEA Prevention Course in HAI Knowledge and Control (Prevention CHKC) is online, interactive, and designed to give frontline personnel what they need to know to prevent healthcare-associated infections (HAIs).

Access for **FREE** using promo code

TOWNHALL

at checkout!

Prevention

PreventionCHKC.org

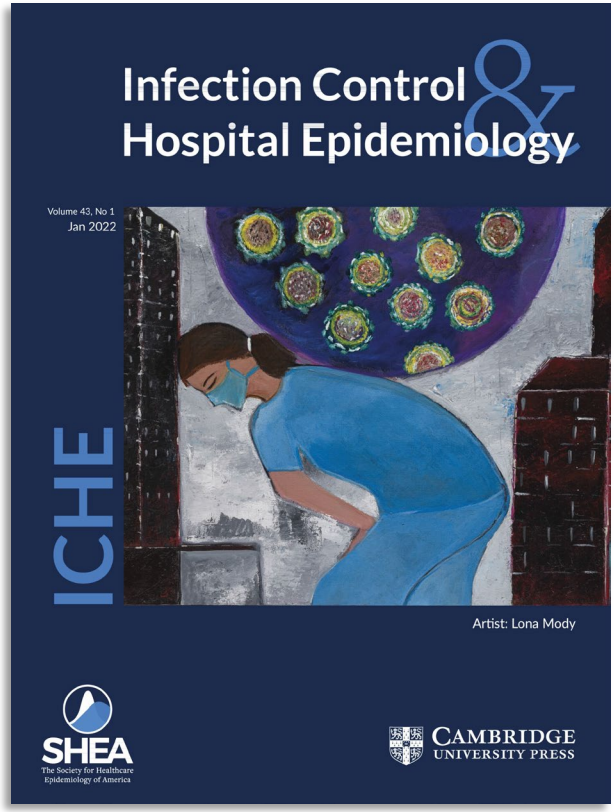
LearningCE SHEA ONLINE EDUCATION CENTER

SHEA

SAFE HEALTHCARE FOR ALL

Music: www.bensound.com

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.

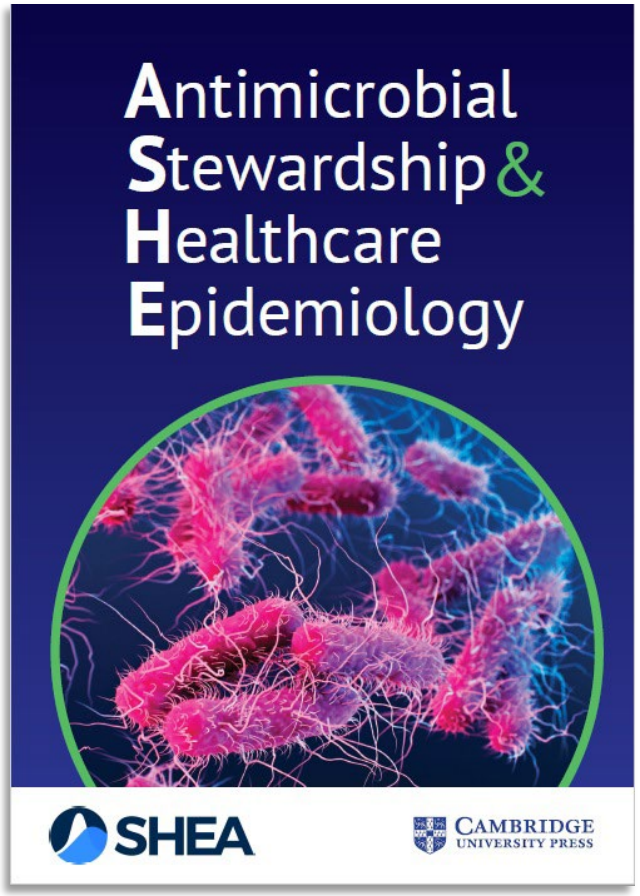
www.cambridge.org/iche

SHEA

SAFE HEALTHCARE FOR ALL

Music:
www.bensound.com

ASHE JOURNAL



High quality articles across the full spectrum of antimicrobial stewardship and healthcare epidemiology.

Exceptional author experience through constructive peer review, competitive turnaround times, immediate online publication, a streamlined production process, and social media promotion.

Global, **open access journal**, bringing the widest possible impact, reach and discoverability of your research.

www.cambridge.org/ashe

SHEA

SAFE HEALTHCARE FOR ALL

Music:
www.bensound.com

SHEA SPRING

SEE YOU NEXT YEAR!

We hope to see you in Seattle, Washington for SHEA Spring 2023 April 12-14.

SHEA Webinar

COVID-19 Town Hall Round 81

Music:
www.bensound.com

In Case of Technical Difficulties:

- **Audio:**
  - Select one form of audio only (computer speakers or telephone connection)
  - For full participation, you will need to join by computer

- **If you are having trouble joining:**
  - Use the emailed invitation to join via the URL, or call in with the provided phone numbers

- https://support.zoom.us

Webinar Recording Access:

LEARNINGCE
SHEA
Online Education Center

This webinar will be recorded and uploaded to LearningCE's [Rapid Response Program]

LIVE

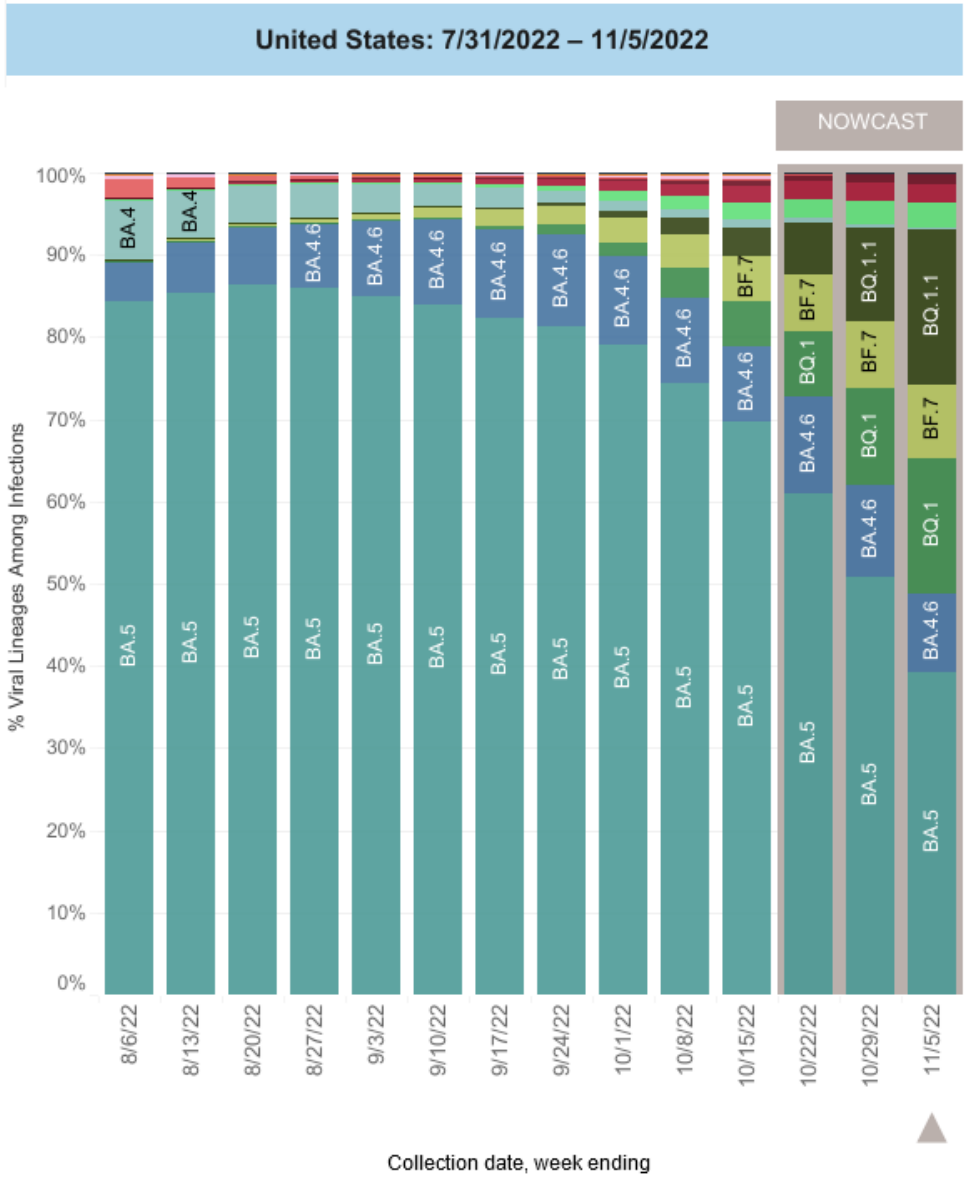
Streaming Live on SHEA's Facebook page

Useful Features:

- **Chat**: Talk to each other or ask SHEA Staff questions if you are having technical difficulties
- **Q&A**: Type in your question to be read aloud by SHEA Staff and answered by the Panelists

SHEA Town Hall 81
Overview

SARS-CoV-2 Variants, US, CDC



United States: 10/30/2022 – 11/5/2022 NOWCAST

USA

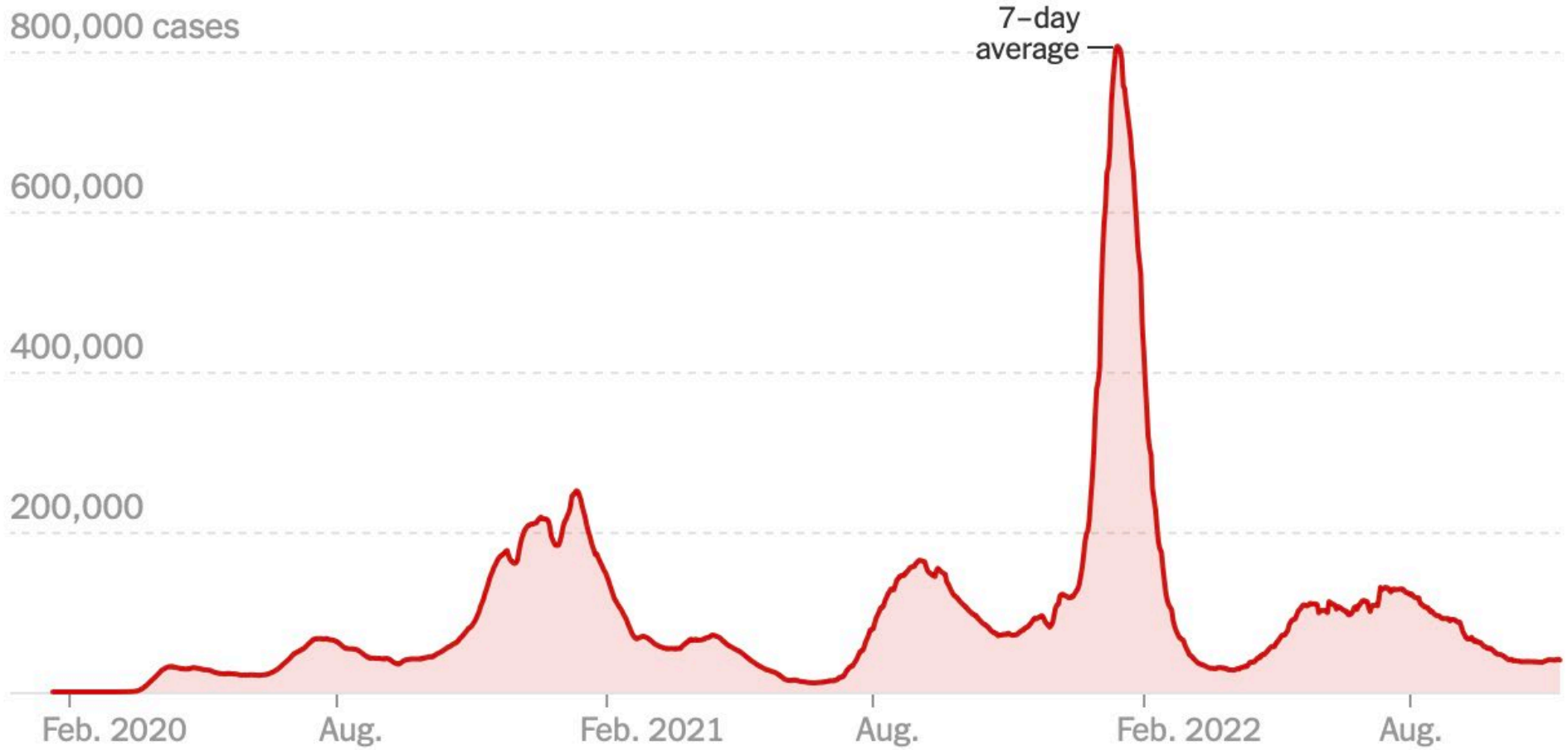
WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	39.2%	36.2-42.3%
	BQ.1.1	VOC	18.8%	15.7-22.4%
	BQ.1	VOC	16.5%	13.6-20.0%
	BA.4.6	VOC	9.5%	8.6-10.5%
	BF.7	VOC	9.0%	7.9-10.1%
	BA.5.2.6	VOC	3.1%	2.5-3.7%
	BA.2.75	VOC	2.3%	1.9-2.8%
	BA.2.75.2	VOC	1.3%	0.9-1.7%
	BA.4	VOC	0.2%	0.2-0.3%
	BA.1.1	VOC	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%
	BA.2	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.1%	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 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, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. For all the lineages listed in the above table, their sublineages are aggregated to the listed parental lineages respectively. Previously, BA.5.2.6 were aggregated with BA.5. Lineages BA.2.75.2, BA.4.6, BF.7, BA.5.2.6 and BQ.1.1 contain the spike substitution R346T.

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

Reported COVID-19 Cases in the United States

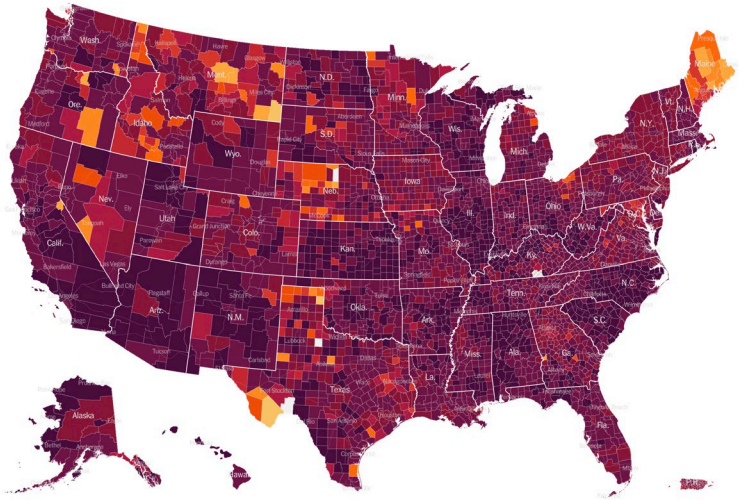
Cumulative Cases – 97,995,355



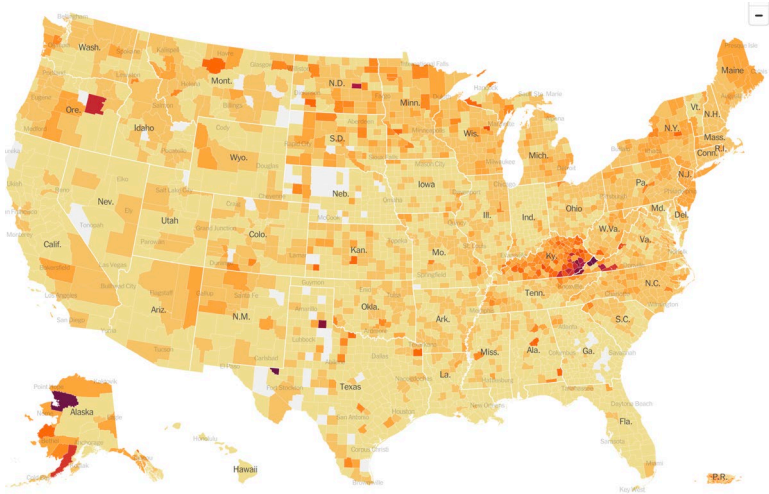
Cases increased by 7% from two weeks earlier

Sources: New York Times 11-13-22; Johns Hopkins Coronavirus Resource Center: https://coronavirus.jhu.edu/region/united-states 11-13-2022

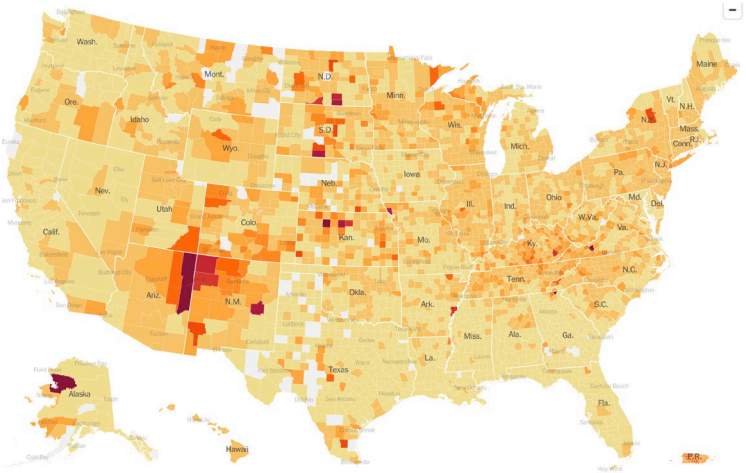
US COVID-19 HOTSPOTS



February 6, 2022



October 9, 2022



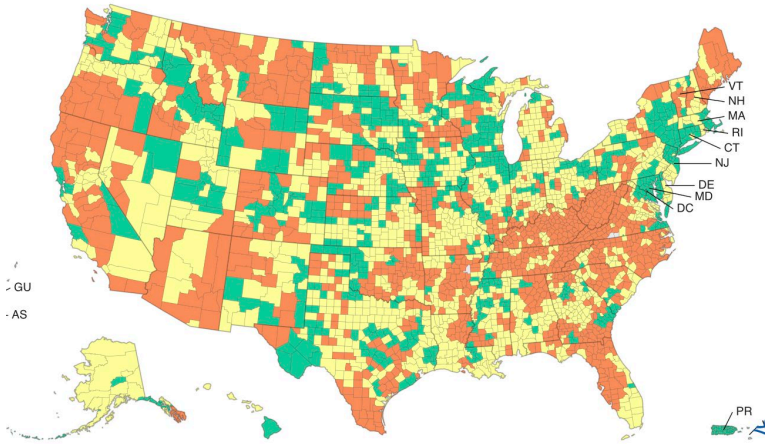
November 18, 2022

Average daily cases per 100,000 people in past week

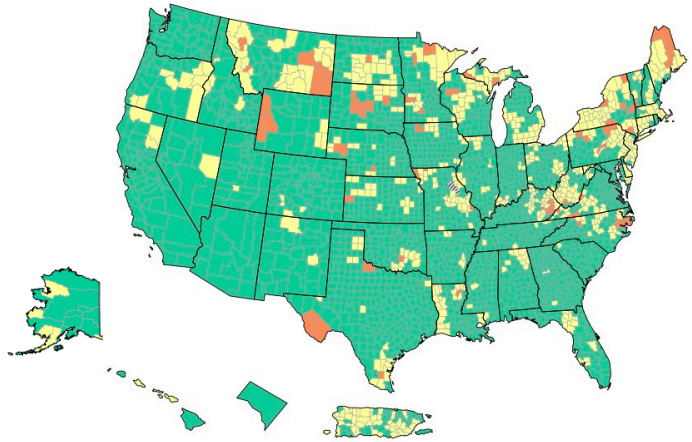
10 30 50 70 100 250 Few or no cases

Source: New York Times 11-12-2022

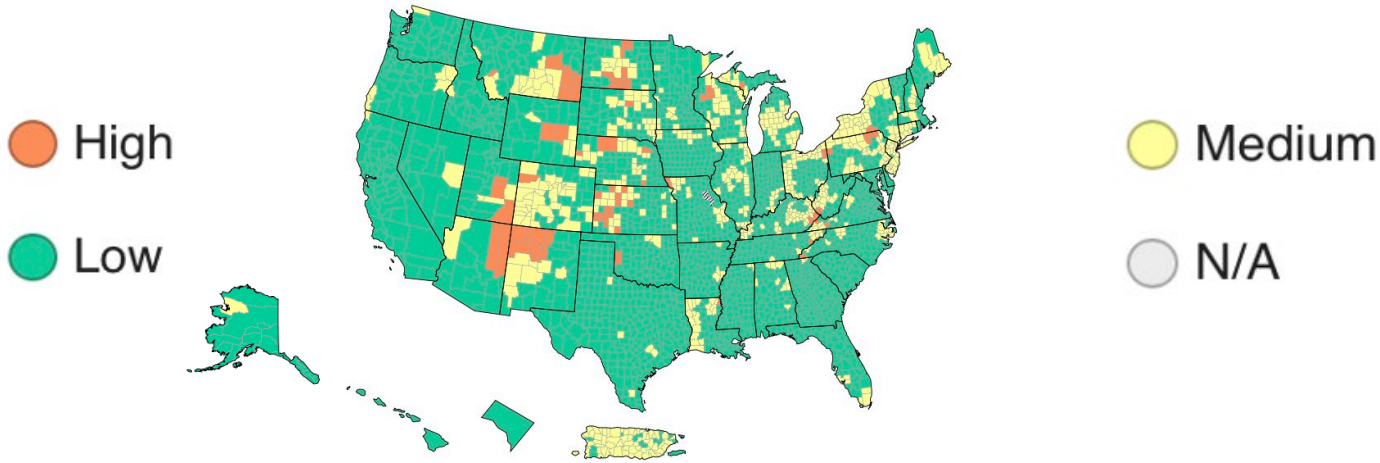
CDC COVID-19 COMMUNITY LEVELS



February 27, 2022



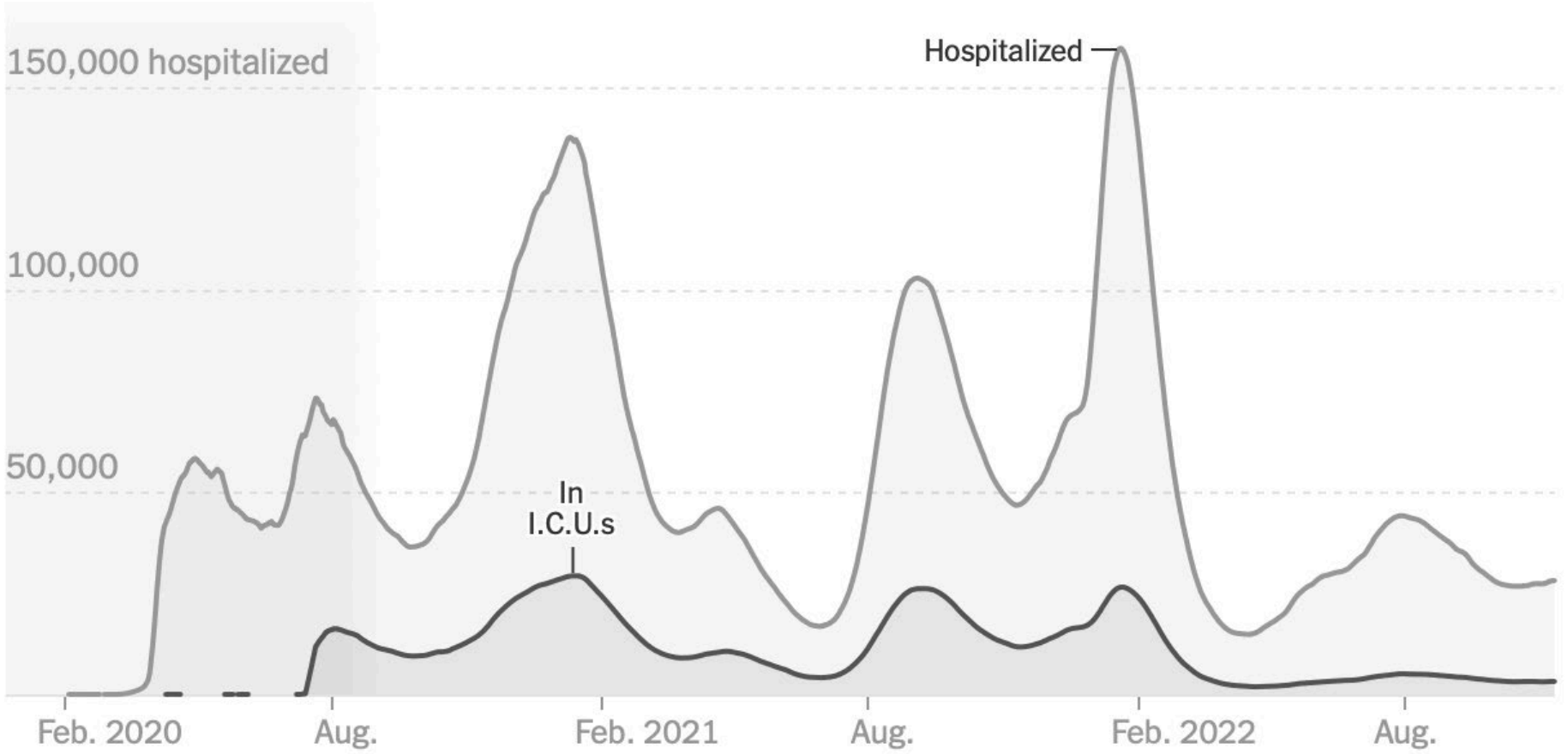
October 9, 2022



November 12, 2022

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

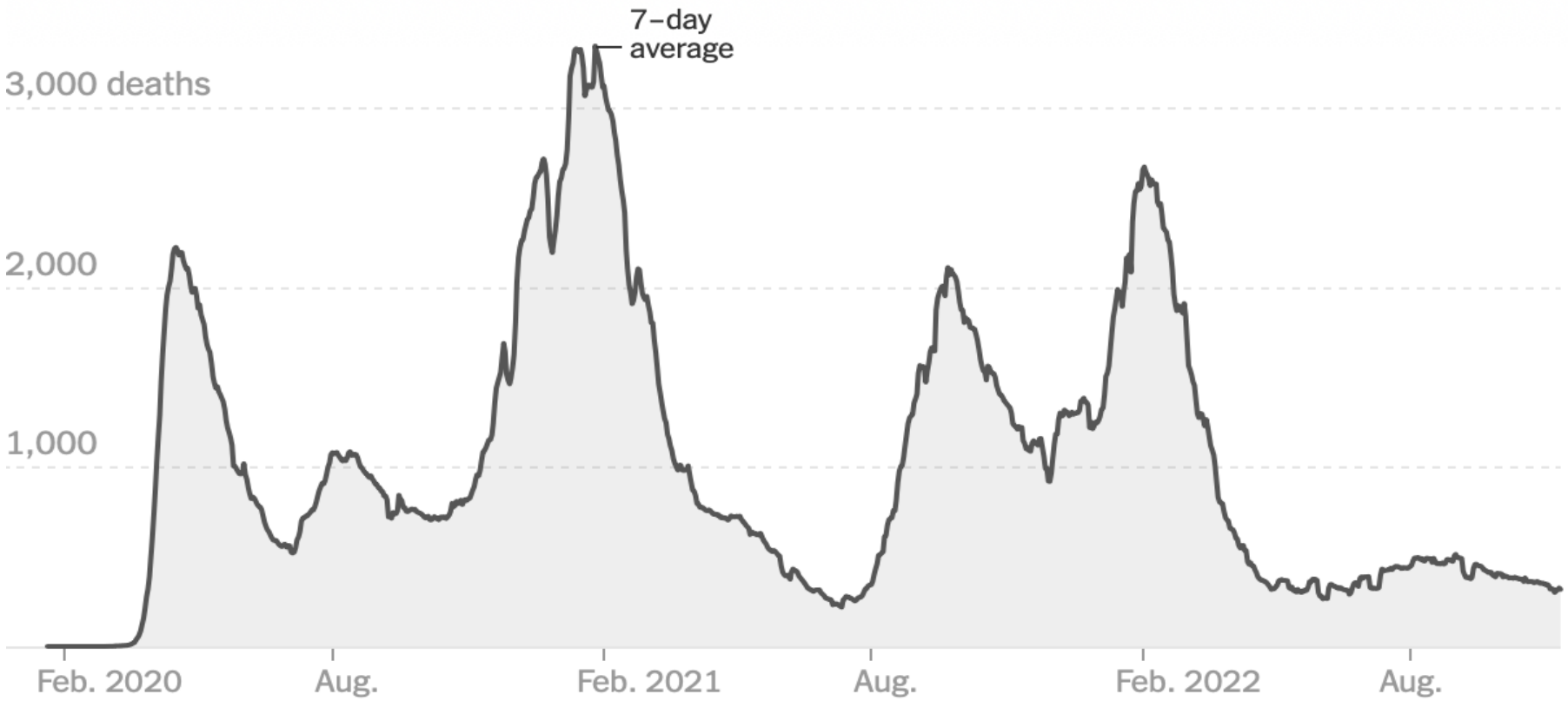


Hospitalizations increased 3 % from two weeks earlier
ICU hospitalizations incfeased 1% from two weeks earlier

Source: New York Times 11-13-22

COVID-19 Deaths in the United States

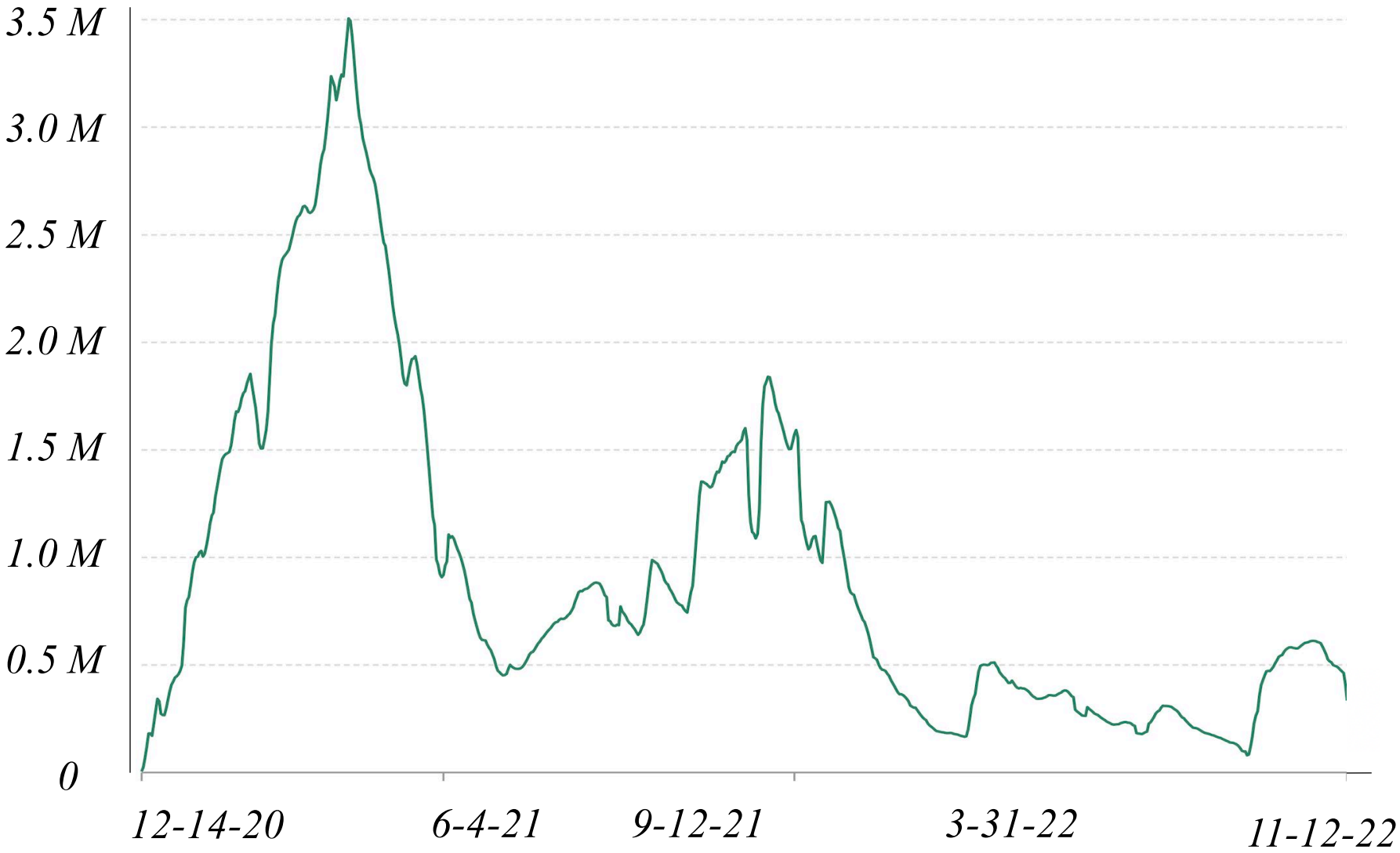
Cumulative Deaths – 1,074,484



10 % decrease from two weeks earlier

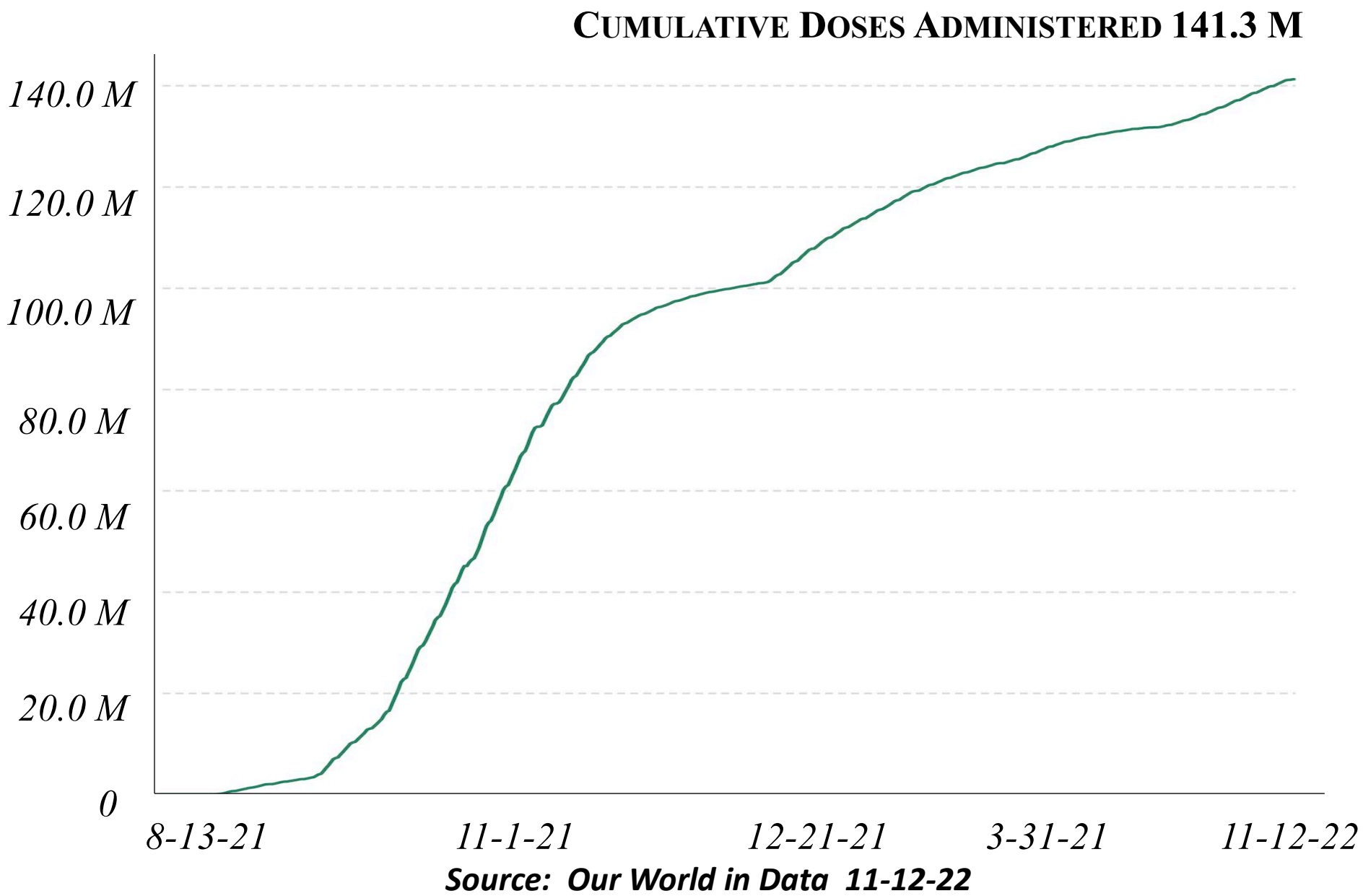
Sources: New York Times 11-13-22,; Johns Hopkins Coronavirus Resource Center: https://coronavirus.jhu.edu/region/united-states 11-13-2022

DAILY COVID-19 VACCINATIONS IN THE UNITED STATES



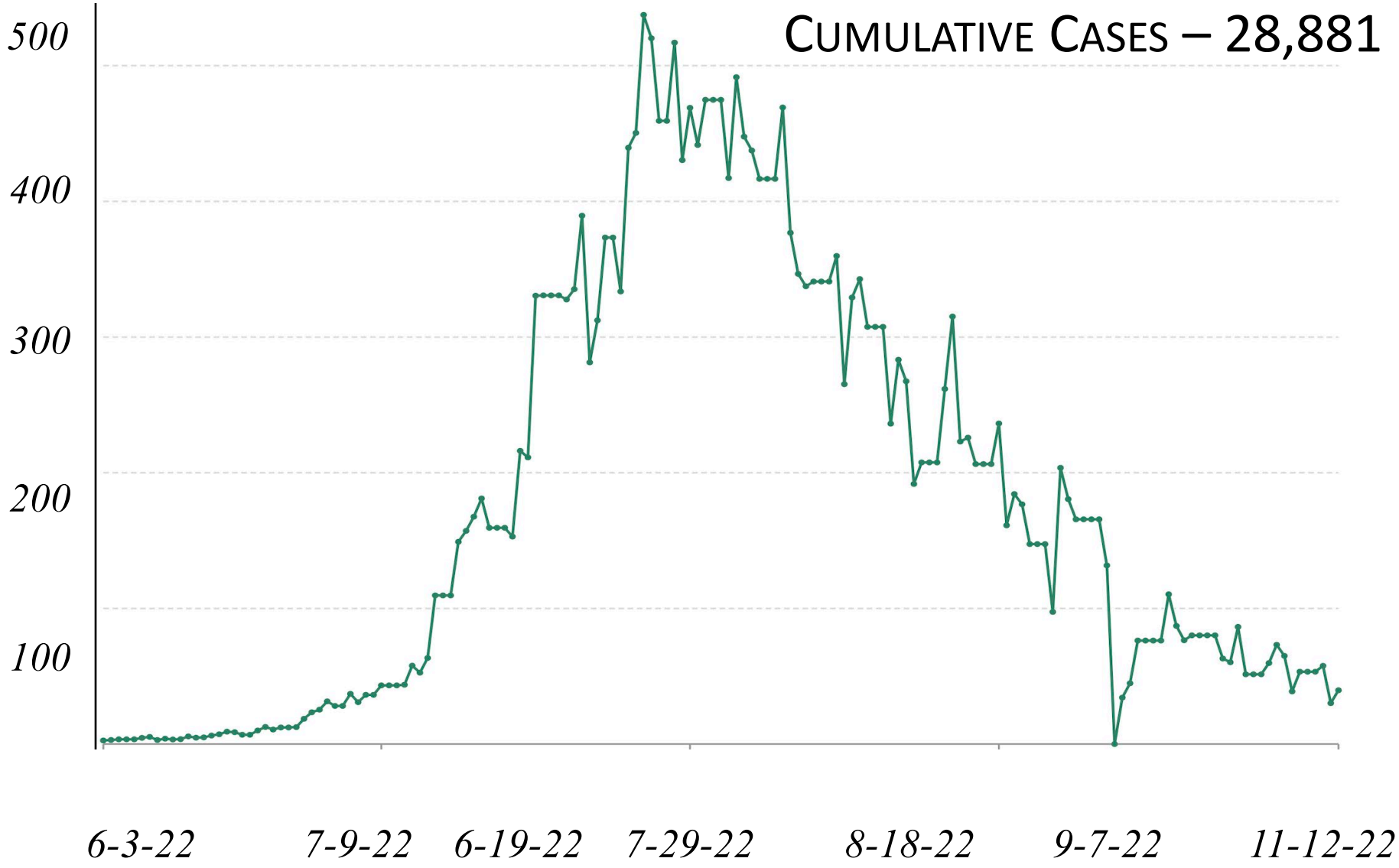
Source: Our World in Data 11-12-22

COVID-19 Booster Doses in the United States



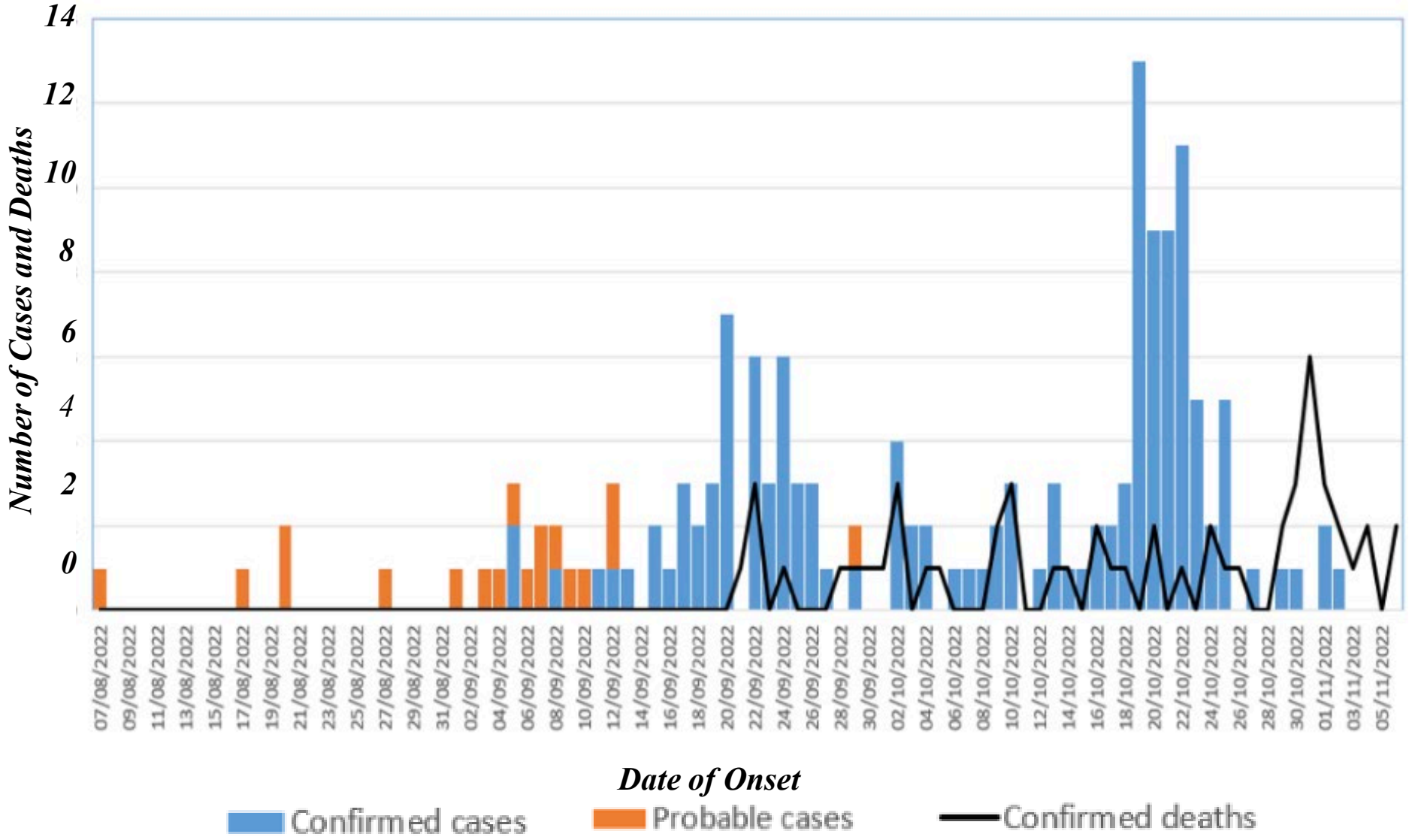
Source: Our World in Data 11-12-22

MONKEYPOX OUTBREAK CURVE: DAILY CASES, UNITED STATES



Source: CDC and Our World in Data 11-12-22

ONGOING EBOLA VIRUS DISEASE OUTBREAK, UGANDA



Source: WHO: https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON423

This Week's Emerging Infectious Disease News

1. *A **British Medical Journal** news feature comments on the so-called "triple epidemic" facing the US this fall and winter*
2. *A **JAMA** news article compares the pediatric epidemic of RSV to the COVID pandemic and relates what physicians need to know about the RSV surge.*
3. *A **New England Journal** paper demonstrated that lifting of masking requirements was associated with an additional 44.9 COVID-19 cases/1000 students and staff during the 15 weeks following lifting the masking requirement – an editorial supports the conclusions.*
4. *Another **New England Journal** paper found that in two high-risk imprisoned populations that mRNA vaccination and previous infection were effective against omicron infection, with lower protection among those infected before the period of delta predominance .*
5. *Another **New England Journal** paper found that administration of two 25-µg doses of the Moderna vaccine to children 6 months to 5 years of age was safe and elicited immune responses that were noninferior to those found in young adults .*
6. *A **Cell** paper provided potential explanations for the pathophysiology of 'brain fog' following COVID .*
7. *A **JAMA Network Open** paper evaluated maternal and cord blood levels of antibody levels after COVID-19 vaccination or infection .*
8. *A **Science Immunology** paper describing a macaque model of COVID-19 vaccine-elicited CD8+ T cells, demonstrated that CD8+ T cells contribute substantially to vaccine protection against SARS-CoV-2.*
9. *Data from a **Clinical Infectious Disease** paper suggested that pre-booster antibody levels could be used to optimally time boosters.*
10. *The **WHO** website summarizes the status of the Ebola virus disease outbreak in Uganda..*
11. *An article in **The Atlantic** underscores the rationale for staying "up-to-date" with COVID boosters, emphasizing that it isa not a good time to be a "booster-slacker".. **References available in the chat***

Panelists:

Dr. David Henderson
NIH Consultant

Dr. Sarah Haessler
Baystate Health

Dr. Kristina Bryant
University of Louisville

Dr. David Weber
UNC School of Medicine

UPDATE: SARS-CoV-2 SUBLINEAGES: EPIDEMIOLOGY AND IMPACT

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

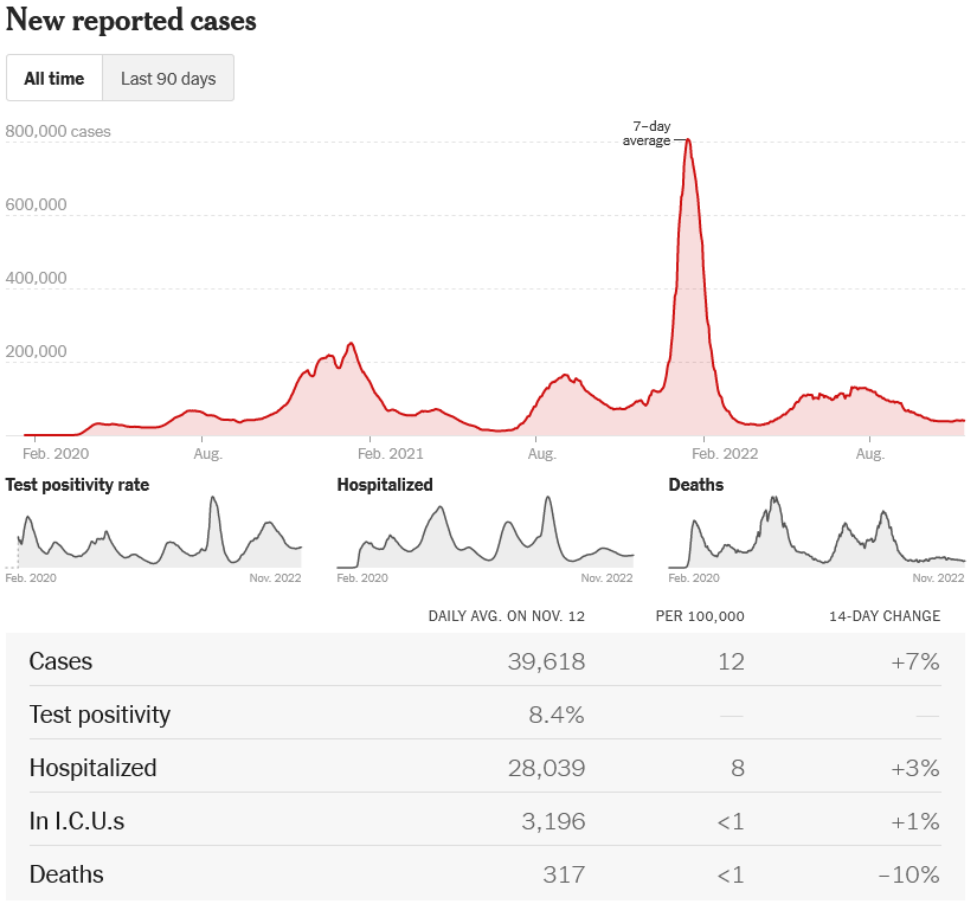
SARS-CoV-2 Variants: Current Summary

- Epidemiology, US
  - Stable frequency of BA.4.6
  - Rapid increase of BQ.1, BQ.1.1, and BF.7
  - The sublineage BQ.1.1 carries an additional spike mutation in a key antigenic site (i.e. R346T); BQ.1 is showing a significant growth advantage over other circulating Omicron sublineages in many settings*
- XBB: Recombinant of BA.2.10.1 and BA.2.75 sublineages; early evidence pointing at a higher reinfection risk, as compared to other circulating Omicron sublineages *
- Escape from monoclonal prophylaxis and/or therapy (current frequency of sublineages, US, CDC)
  - Evusheld escape, ~53% (BQ.1, BQ1.1, BA.4.6, BA.5.2.6, BA.2.75.2)
  - Bebteluvimab escape, ~47% (BQ.1, BQ.1.1, BA5.6.2)
  - Alternative therapy = 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 likely exhibit modestly improved activity against BQ sublineages compared to the monovalent ancestral vaccine

*https://www.who.int/news/item/27-10-2022-tag-ve-statement-on-omicron-sublineages-bq.1-and-xbb
^Hogan JI, et al. Clin Infect Dis 2022;Sept 26,ciac769

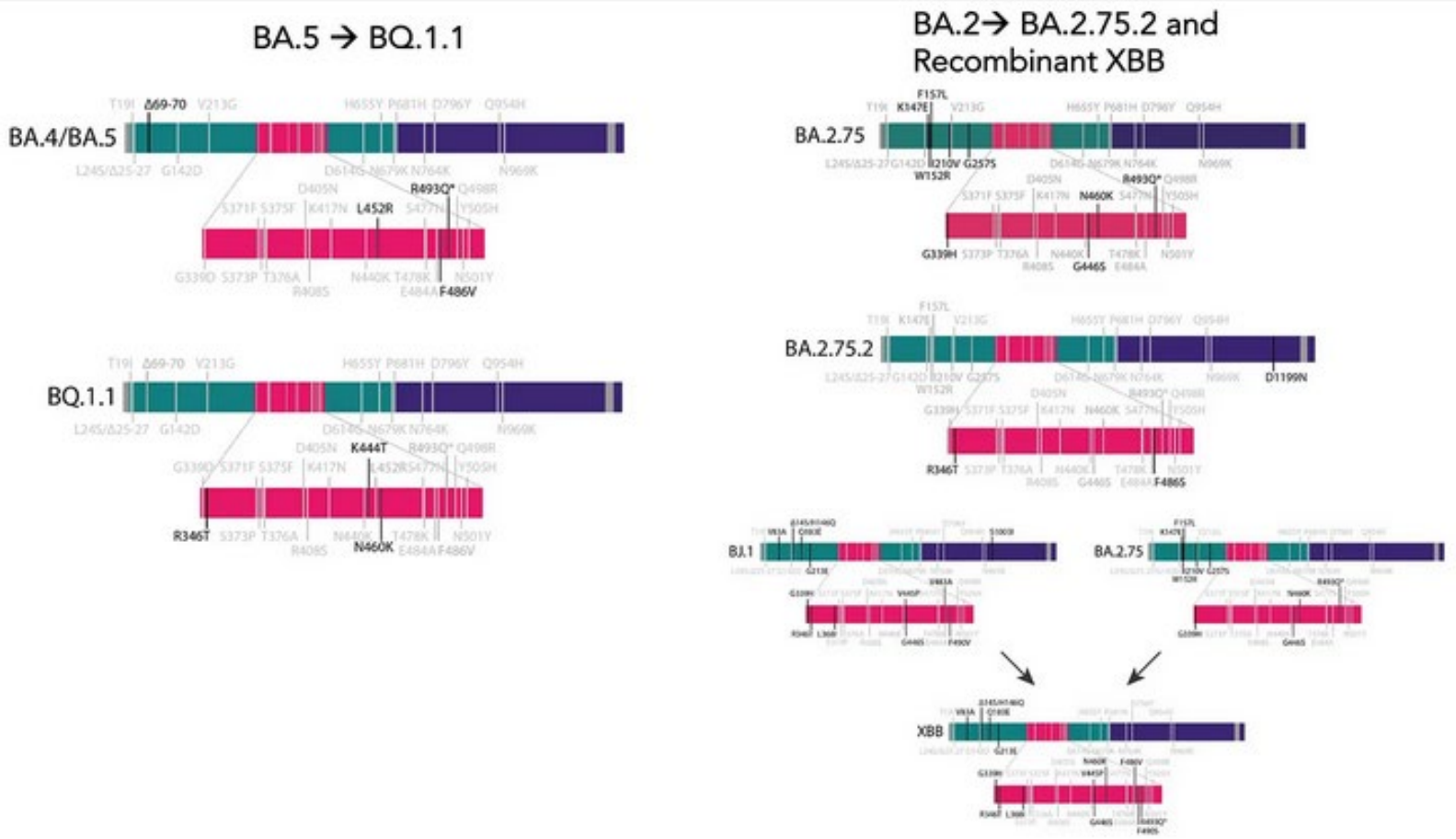
COVID-19: UPDATE, 11/13

- Cases and hospitalizations continue to rise nationwide, driven in part by a growing outbreak in the Southwest.
- The nation's most rapid growth in hospitalizations with the virus is clustered in that region, with Arizona, Colorado, Nevada and New Mexico all seeing hospitalization counts increase by more than 30 percent in the past two weeks. Cases in those states are on a similar upward climb, particularly in New Mexico.
- By contrast, daily deaths from the coronavirus are decreasing. Death counts have fallen by 9 percent nationally in recent weeks, to about 325 per day.

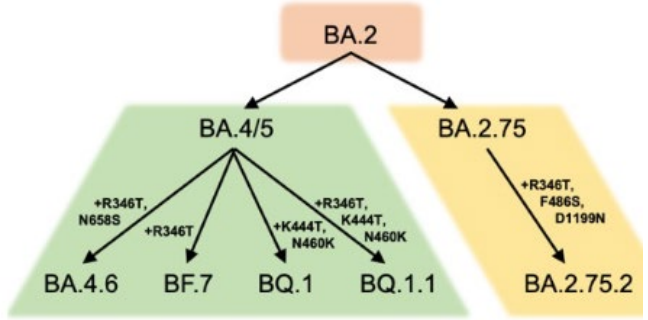


https://www.nytimes.com/interactive/2021/us/covid-cases.html

EVOLUTION OF NEW SARS-CoV-2 VARIANTS



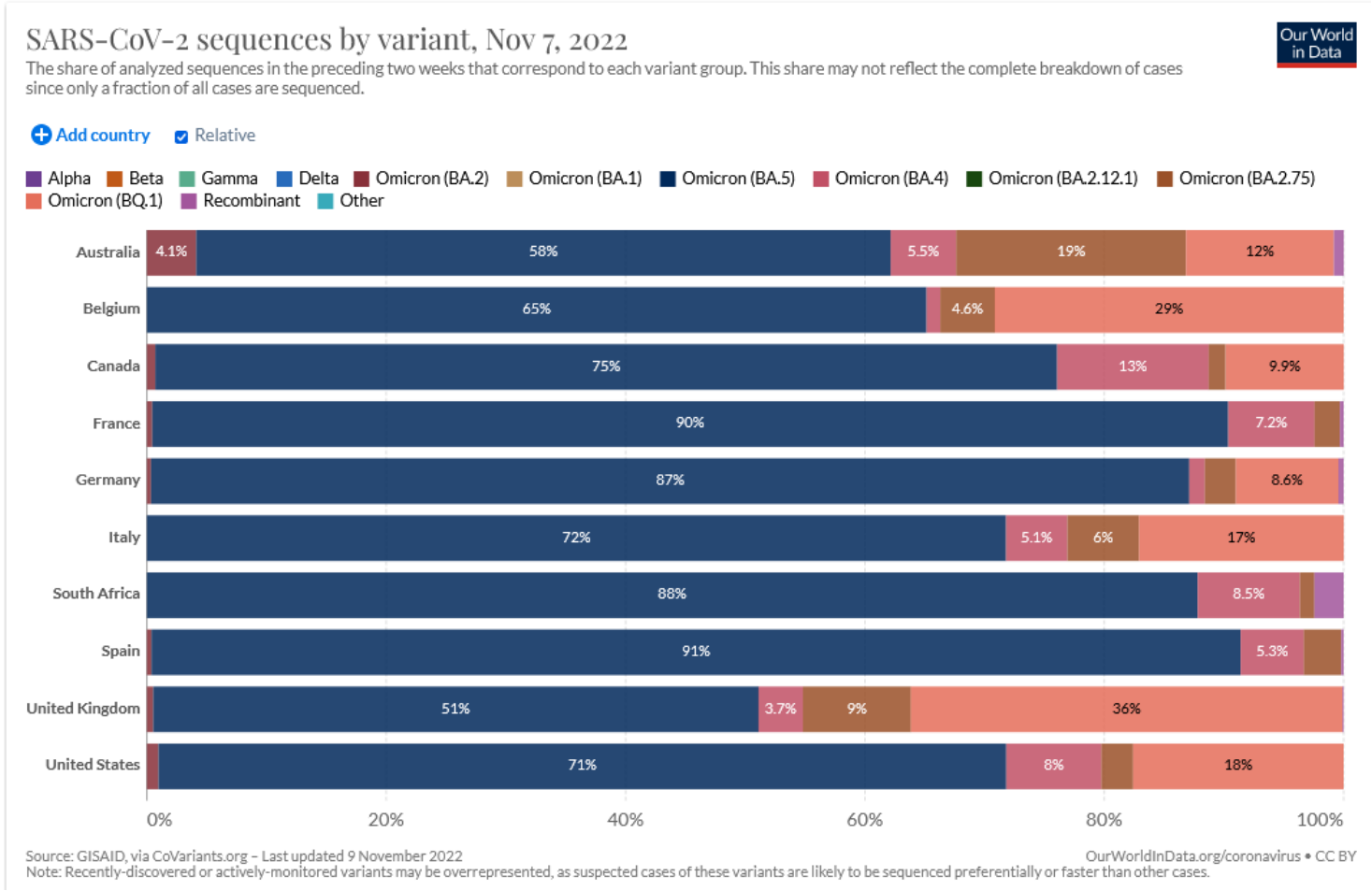
XBB is a recombinant of BA.2.10.1 and BA.2.75



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

UNC SCHOOL OF MEDICINE

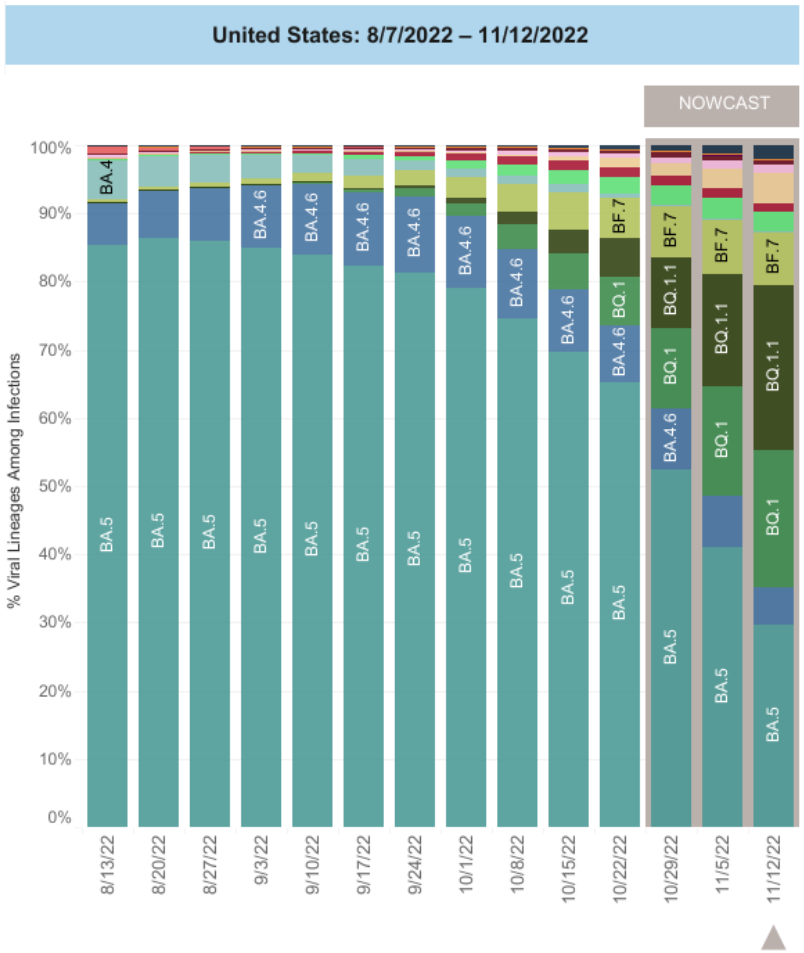
COVID-19 VARIANTS, WORLDWIDE



https://ourworldindata.org/coronavirus

UNC SCHOOL OF MEDICINE

COVID-19 VARIANTS, US



United States: 11/6/2022 – 11/12/2022 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	29.7%	27.2-32.3%
	BQ.1.1	VOC	24.1%	21.3-27.3%
	BQ.1	VOC	20.1%	17.2-23.4%
	BF.7	VOC	7.8%	6.8-9.0%
	BA.4.6	VOC	5.5%	5.0-6.2%
	BN.1	VOC	4.3%	3.0-6.2%
	BA.5.2.6	VOC	2.9%	2.5-3.4%
	BA.2	VOC	1.3%	0.8-1.9%
	BA.2.75	VOC	1.2%	1.0-1.5%
	BA.2.75.2	VOC	0.9%	0.6-1.2%
	BA.4	VOC	0.1%	0.1-0.1%
	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*		2.0%	1.1-3.3%

* 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 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, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. For all the lineages listed in the above table, their sublineages are aggregated to the listed parental lineages respectively. Previously, BN.1 was aggregated with BA.2.75. Lineages BA.2.75.2, BN.1, BA.4.6, BF.7, BA.5.2.6 and BQ.1.1 contain the spike substitution R346T.

Evusheld escape, ~53%
(BQ.1, BQ1.1, BA.4.6, BA.5.2.6, BA.2.75.2)

Bebteluvimab escape, ~47%
(BQ.1, BQ.1.1, BA5.6.2)

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

UNC SCHOOL OF MEDICINE

Spread of the SARS-CoV-2 Omicron variant sub-lineage BQ.1 in the EU/EEA, 21 October 2022

- BQ.1, including its sub-lineages, has been designated as Variant of Interest (VOI) by ECDC as of 20 October 2022. Based on modelling estimates, it is expected that by mid-November to beginning of December 2022, more than 50% of SARS-CoV-2 infections will be due to BQ.1/BQ.1.1. By the beginning of 2023, more than 80% of SARS-CoV-2 cases are expected to be due to BQ.1/BQ.1.1.
- The observed increase in the growth rate of BQ.1 is probably driven mainly by immune escape. This variant and its sub-lineages will probably contribute to a further increase in cases of COVID-19 in the EU/EEA in the coming weeks and months. The extent of the increase in COVID-19 cases will depend on various factors, including immune protection against infection influenced by the timing and coverage of COVID-19 vaccination regimes, and the extent, timing and variant landscape of previous SARS-CoV-2 pandemic waves. Based on limited available data, there is no evidence of BQ.1 being associated with a greater infection severity than the circulating variants BA.4/BA.5.
- Countries should remain vigilant for signals of BQ.1 emergence and spread; maintain sensitive and representative testing and genomic surveillance with timely sequence reporting and strengthen sentinel surveillance systems (primary care ILI/ARI and SARI).
- Countries should continue to monitor COVID-19 case rates - especially in people aged 65 years and older - and severity indicators such as hospitalizations, ICU admissions, ICU occupancy and death.
- Improving COVID-19 vaccine uptake of the primary course and first booster dose remains a priority for all eligible individuals that are not up-to-date with the recommended schedule. For the time being, for current autumn/winter vaccination campaigns, an additional booster dose should also be offered, prioritizing individuals who are at risk of progression to severe disease, such as older adults (e.g. above 60 years of age), immunocompromised individuals and those with underlying medical conditions, and pregnant women. Residents and staff in long-term care facilities, as well as healthcare workers should also be considered among priority groups.

https://www.ecdc.europa.eu/en/publications-data/spread-sars-cov-2-omicron-variant-sub-lineage-bq1-eueea

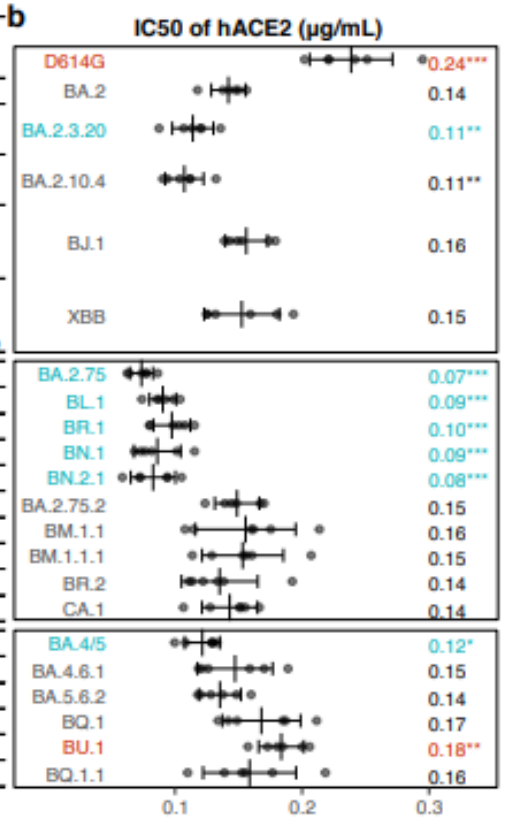
IMPACT OF NEW VARIANTS ON MONOCLONAL THERAPIES

a

Pango lineages	REGN 10933	REGN 10987	REGN10933 +10987	COV2-2196	COV2-2130	COV2-2196+2130	BRII-196	BRII-198	BRII-196+198	S309	DXP-604	LY-CoV 1404	SA58	SA55	SA55+ SA58	Additional RBD mutations
BA.2	*	590	821	4312	6.3	8.2	8530	8990	8610	852	219	0.9	5.1	7.2	7.8	
BA.2.3.20	121	*	199	15	*	26	14	*	24	897	181	9.7	20	4.6	7.8	K444R+N450D+L452M +N460K+R493Q
BA.2.10.4	*	*	*	*	289	501	2109	7990	3984	706	6348	1.3	4.3	4.9	5.0	G446S+F486P+R493Q +S494P
BJ.1	*	*	*	3076	*	5985	7609	*	*	709	166	*	8163	3.7	8.6	D339H+R346T+L368I+ V445P+G446S+V483A +F490V
XBB	*	*	*	*	*	*	*	*	*	963	*	*	8805	5.3	9.8	D339H+R346T+L368I+ V445P+G446S+N460K +F486S+F490S+R493Q
BA.2.75	278	*	410	119	352	121	1730	6622	3861	672	5920	2.2	246	4.3	9.6	
BL.1	260	*	511	93	*	174	1251	*	3075	508	7193	2.8	7975	6.3	10	R346T
BR.1	319	*	679	117	*	170	1992	*	3160	564	6689	*	1616	5.9	9.7	L452R+K444M
BN.2.1	390	*	701	59	303	109	4101	*	8444	6979	8901	1.7	4960	5.7	9.4	K356T+F490S
BN.1	344	*	599	70	*	166	3683	*	7791	*	6012	3.3	8295	4.9	9.0	R346T+K356T+F490S
BA.2.75.2	*	*	*	*	*	*	*	*	*	852	*	3.0	6922	5.9	9.7	R346T+F486S
BM.1.1	*	*	*	*	*	*	*	*	*	879	*	2.3	8823	5.2	8.9	R346T+F486S
BM.1.1.1	*	*	*	*	*	*	*	*	*	956	*	1.9	8082	4.8	10.5	R346T+F486S+F490S
BR.2	*	*	*	*	*	*	*	*	*	921	*	2.6	7263	4.7	10.5	R346T+L452R+F486I
CA.1	*	*	*	*	*	*	*	*	*	897	*	3.2	6927	6.0	11.5	R346T+L452R+F486S
BA.4/5	*	520	709	*	23	40	7124	*	*	1055	6264	0.8	3.9	5.0	4.5	
BA.4.6.1	*	2338	5402	*	*	*	4763	*	7809	4456	4634	1.2	50	4.8	9.9	R346T
BA.5.6.2	*	*	*	*	*	*	4636	*	7883	1408	5892	1662	58	5.1	8.9	K444T
BQ.1	*	*	*	*	*	*	*	*	*	1709	*	1905	44	6.6	9.2	K444T+N460K
BU.1	*	*	*	*	*	*	*	*	*	1082	*	26	56	5.3	10.5	K444M+N460K
BQ.1.1	*	*	*	*	*	*	*	*	*	5581	*	*	900	5.9	10.3	R346T+K444T+N460K

Pseudovirus IC50 (ng/mL): <100 | 100~1,000 | >1,000

b



Bebtoluvimab = LY-CoV 1404; Evusheld = COV2-2196+COV2-2130

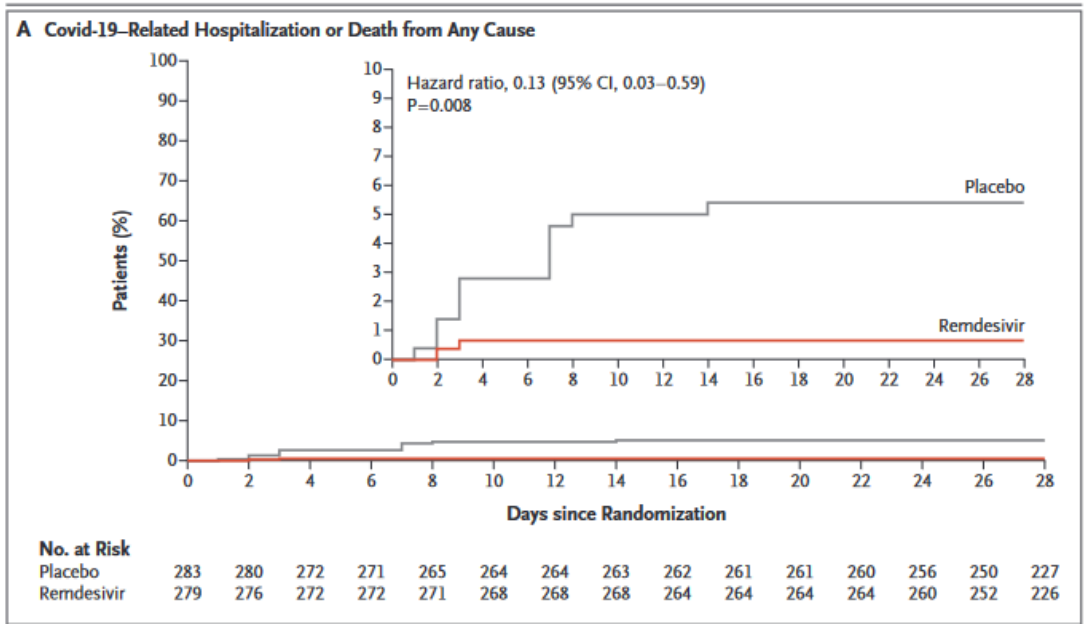
Cao Y, et al. https://www.biorxiv.org/content/10.1101/2022.09.15.507787v3

UNC SCHOOL OF MEDICINE

Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients

- Methods: RCT of non-hospitalized patients with Covid-19 who had symptom onset within the previous 7 days and who had at least one risk factor for disease progression (age ≥60 years, obesity, or certain coexisting medical conditions). Patients were randomized to IV remdesivir (200 mg on day 1 and 100 mg on days 2 and 3) or placebo.
- Results: Covid-19–related hospitalization or death from any cause occurred in 2 patients (0.7%) in the remdesivir group and in 15 (5.3%) in the placebo group (hazard ratio, 0.13; 95% confidence interval [CI], 0.03 to 0.59; P = 0.008). A total of 4 of 246 patients (1.6%) in the remdesivir group and 21 of 252 (8.3%) in the placebo group had a Covid-19–related medically attended visit by day 28 (hazard ratio, 0.19; 95% CI, 0.07 to 0.56).
- Conclusion: 3 day course of remdesivir resulted in 87% lower risk of hospitalization or death

Gottlieb RL, et al. NEJM 2022;386:305 (Jan 27)



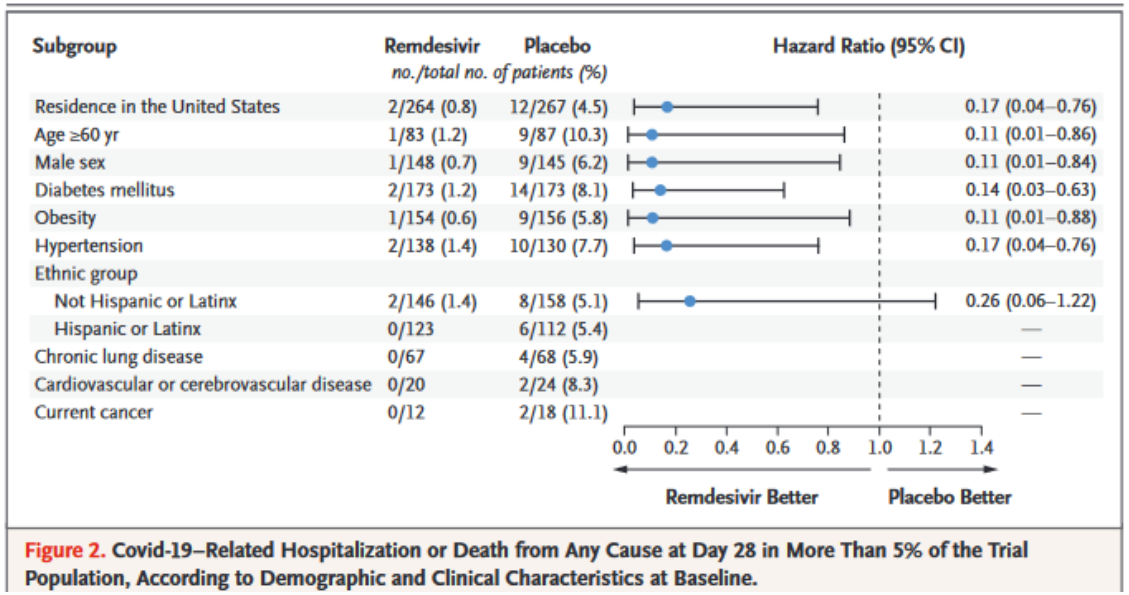


Figure 2. Covid-19–Related Hospitalization or Death from Any Cause at Day 28 in More Than 5% of the Trial Population, According to Demographic and Clinical Characteristics at Baseline.

Efficacy of Antiviral Agents against the Omicron Subvariant BA.2.75

Table 1. Efficacy of Monoclonal Antibodies and Antiviral Drugs against Omicron Subvariants in Vitro*

WHO Label (Pango Lineage): Virus Strain	Neutralization Activity of Monoclonal Antibody†								Viral Susceptibility to Drug‡		
	REGN10987, Imdevimab	REGN10933, Casirivimab	COV2-2196, Tixagevimab	COV2-130, Cilgavimab	S309, Sotrovimab Precursor	LY-CoV1404, Bebtelovimab	REGN10987 plus REGN10933	COV2-2196 plus COV2-2130	GS-441524, Remdesivir§	EIDD-1931, Molnupiravir¶	PF-07321332, Nirmatrelvir‖
	nanograms per milliliter								*micromoles*		
Ancestral strain (A): SARS-CoV-2/ UT-NC002-1T/ Human/2020/Tokyo	4.36 ±0.96	2.42 ±0.93	1.91 ±0.95	5.36 ±1.21	32.80 ±11.22	1.40 ±0.79	2.23 ±0.42	6.47 ±2.31	0.98 ±0.30	0.59 ±0.11	1.71 ±0.29
Omicron (BA.2): hCoV-19/Japan/UT-NCD1288-2N/2022	958.28 ±363.87	>50,000	4374.21 ±1483.72	21.59 ±8.57	>50,000	6.09 ±0.67	968.50 ±58.35	43.22 ±8.16	1.32 ±0.21	0.25 ±0.08	1.69 ±0.66
Omicron (BA.5): hCoV-19/Japan/TY41-702/2022	174.37 ±52.55	>50,000	>50,000	54.02 ±20.29	6240.39 ±1883.65	2.43 ±1.26	192.91 ±82.50	123.65 ±55.81	0.45 ±0.09	0.23 ±0.07	1.50 ±0.34
Omicron (BA.2.75): hCoV-19/Japan/ TY41-716/2022	>50,000	1153.19 ±104.61	122.31 ±67.08	101.71 ±53.24	28,536.48 ±6444.42	6.21 ±2.80	1811.78 ±600.23	34.19 ±7.60	1.52 ±0.42	0.90 ±0.18	1.78 ±0.35

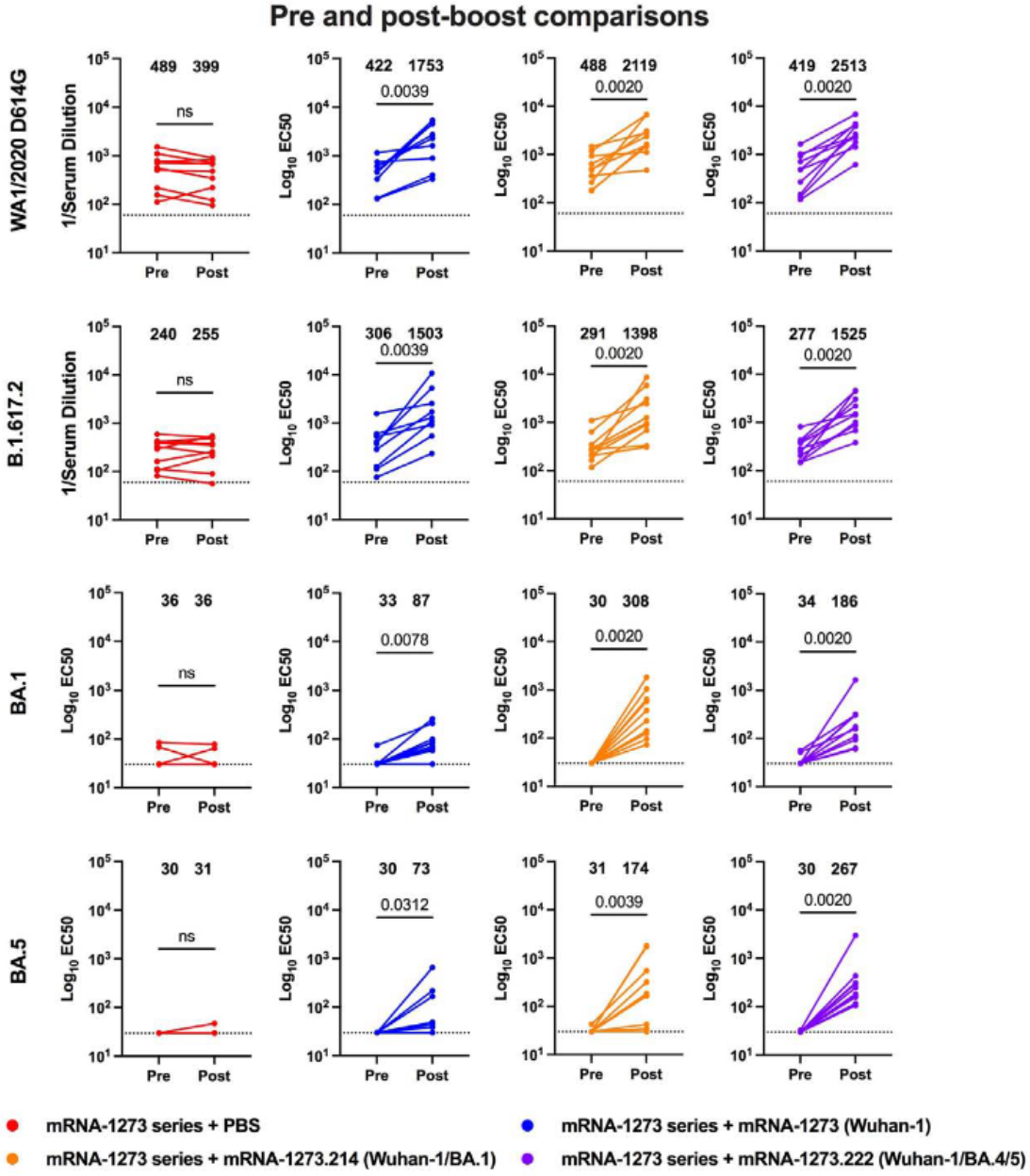
* Plus–minus values are means ±SD. The antibodies used in this analysis were produced in the authors' laboratories and are not identical to the commercially available products. SARS-CoV-2 denotes severe acute respiratory syndrome coronavirus 2, and WHO World Health Organization.
† The individual monoclonal antibodies were tested at a starting concentration of 50,000 ng per milliliter as a 50% focus reduction neutralization test titer. The monoclonal antibody combinations were tested at a starting concentration of 10,000 ng per milliliter for each antibody.
‡ The values presented are the 50% inhibitory concentration of the mean micromole value of triplicate reactions.
§ GS-441524 is the main metabolite of remdesivir, an RNA-dependent RNA polymerase inhibitor.
¶ EIDD-1931 is the active form of molnupiravir, an RNA-dependent RNA polymerase inhibitor.
‖ PF-07321332, nirmatrelvir, is an inhibitor of the main protease, also called 3-chymotrypsin-like protease, of SARS-CoV-2.

Takashita E, et al. NEDJM 2022;387:1236 (29 September)

UNC SCHOOL OF MEDICINE

Bivalent SARS-CoV-2 mRNA vaccines increase breadth of neutralization and protect against the BA.5 Omicron variant in mice

We evaluated the immunogenicity and protective efficacy of two, recently authorized, bivalent COVID-19 vaccines that contain two mRNAs encoding Wuhan-1 and either BA.1 (mRNA-1273.214) or BA.4/5 (mRNA-1273.222) spike protein. When administered to mice as a booster at 7 months after the primary vaccination series with mRNA-1273, the bivalent vaccines induced broadly neutralizing antibody responses. Whereas the majority of anti-Omicron receptor binding domain antibodies in serum induced by mRNA-1273, mRNA-1273.214, and mRNA-1273.222 boosters cross-reacted with the antecedent Wuhan-1 spike antigen, the mRNA-1273.214 and mRNA-1273.222 bivalent vaccine boosters also induced unique BA.1 and BA.4/5-specific responses, respectively. Although boosting with parental or bivalent mRNA vaccines substantially improved protection against BA.5 compared to mice receiving two vaccine doses, the levels of infection, inflammation, and pathology in the lung were lowest in animals administered the bivalent mRNA vaccines. Thus, boosting with bivalent Omicron-based mRNA-1273.214 or mRNA-1273.222 vaccines enhances immunogenicity and confers protection in mice against a currently circulating SARS-CoV-2 strain.



Scheaffer SM, et al. Nature Medicine;20 October 2022

5 Lab Studies Assessing the Bivalent BA.5 Booster vs the Original Booster

Lab	Assay	Bivalent vs. BA.5 Compared to Original	Bivalent vs. BQ.1.1 Compared to Original
Ho	Pseudovirus	Minimal difference	Not assessed
Barouch	Pseudovirus	1.3-fold increase	Not assessed
Suthar	Live virus	4-fold improved	~10-fold increased (vs 1 booster)
Shi	Pseudovirus	3-fold improved	Low, but 3-fold GMT
Barouch	Pseudovirus	No difference	Modest ~1.2-fold increase

Wang Q, Ho DD. https://www.biorxiv.org/content/10.1101/2022.10.22.513349v1.full.pdf
Davis-Gardner ME, Suthar MS. https://www.biorxiv.org/content/10.1101/2022.10.31.514636v1
Kurhade C, p-Y Shi. https://www.biorxiv.org/content/10.1101/2022.10.31.514580v1
Collier Ai-ris Y, Barouch DH. https://www.biorxiv.org/search/bivalent%252Bcovid%252Bvaccine

Eric Topol. Ground Truths

Antibody responses to Omicron BA.4/BA.5 bivalent mRNA vaccine booster shot

The SARS-CoV-2 Omicron variant and its numerous sub-lineages have exhibited a striking ability to evade humoral immune responses induced by prior vaccination or infection. The Food and Drug Administration (FDA) has recently granted Emergency Use Authorizations (EUAs) to new bivalent formulations of the original Moderna and Pfizer mRNA SARS-CoV-2 vaccines that target both the ancestral strain as well as the Omicron BA.4/BA.5 variant. Despite their widespread use as a vaccine boost, little is known about the antibody responses induced in humans. Here, we collected sera from several clinical cohorts: individuals after three or four doses of the original monovalent mRNA vaccines, individuals receiving the new bivalent vaccines as a fourth dose, and individuals with BA.4/BA.5 breakthrough infection following mRNA vaccination. Using pseudovirus neutralization assays, these sera were tested for neutralization against an ancestral SARS-CoV-2 strain, several Omicron sub-lineages, and several related sarbecoviruses. At ~3-5 weeks post booster shot, individuals who received a fourth vaccine dose with a bivalent mRNA vaccine targeting BA.4/BA.5 had similar neutralizing antibody titers as those receiving a fourth monovalent mRNA vaccine against all SARS-CoV-2 variants tested, including BA.4/BA.5. Those who received a fourth monovalent vaccine dose had a slightly higher neutralizing antibody titers than those who received the bivalent vaccine against three related sarbecoviruses: SARS-CoV, GD-Pangolin, and WIV1. When given as a fourth dose, a bivalent mRNA vaccine targeting Omicron BA.4/BA.5 and an ancestral SARS-CoV-2 strain did not induce superior neutralizing antibody responses in humans, at the time period tested, compared to the original monovalent vaccine formulation.

Wang Q, et al. https://doi.org/10.1101/2022.10.22.513349

Low neutralization of SARS-CoV-2 Omicron BA.2.75.2, BQ.1.1, and XBB.1 by 4 doses of parental mRNA vaccine or a BA.5-bivalent booster

Here we report neutralizing activities of three human serum panels collected from individuals 1-3 months after dose 4 of parental mRNA vaccine (post-dose-4), 1 month after a BA.5-bivalent-booster (BA.5-ivalent-booster), or 1 month after a BA.5-bivalent-booster with previous SARS-CoV-2 infection (BA.5-bivalent-booster-infection). Post-dose-4 sera neutralized USA-WA1/2020, BA.5, BF.7, BA.4.6, BA.2.75.2, BQ.1.1, and XBB.1 SARS-CoV-2 with geometric mean titers (GMTs) of 1533, 95, 69, 62, 26, 22, and 15, respectively; BA.5-bivalent-booster sera improved the GMTs to 3620, 298, 305, 183, 98, 73, and 35; BA.5-bivalent-booster-infection sera further increased the GMTs to 5776, 1558,1223, 744, 367, 267, and 103. Thus, although BA.5-bivalent-booster elicits better neutralization than parental vaccine, it does not produce robust neutralization against the newly emerged Omicron BA.2.75.2, BQ.1.1, and XBB.1. Previous infection enhances the magnitude and breadth of BA.5-bivalent-booster-elicited neutralization.

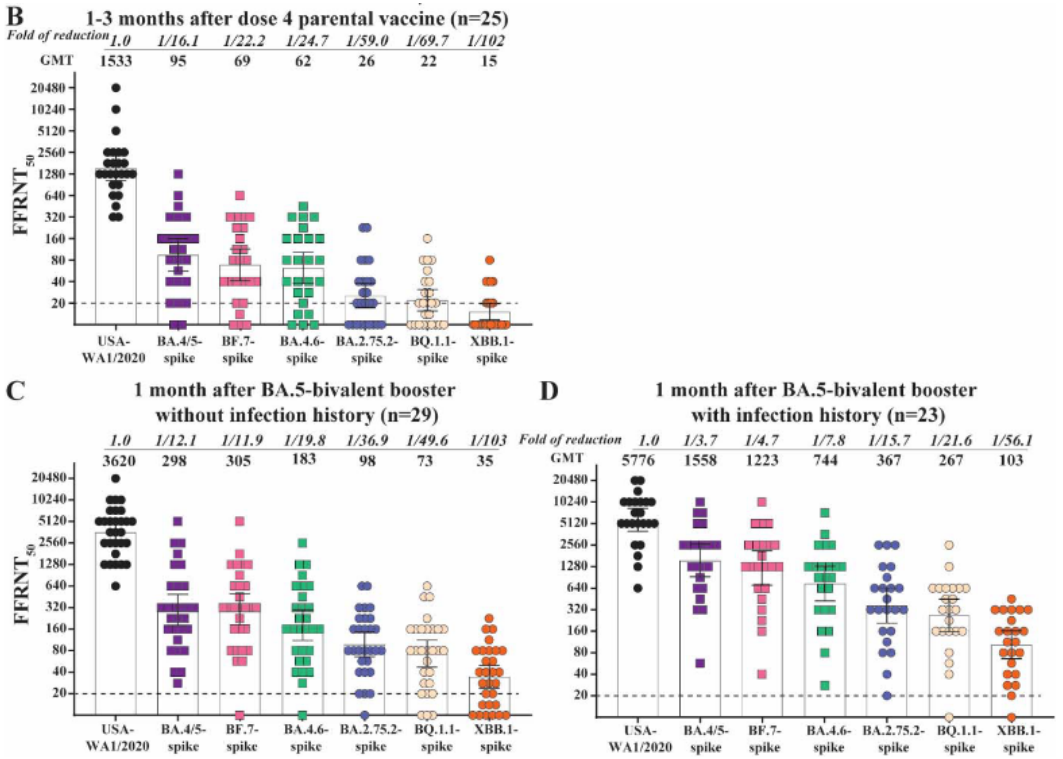
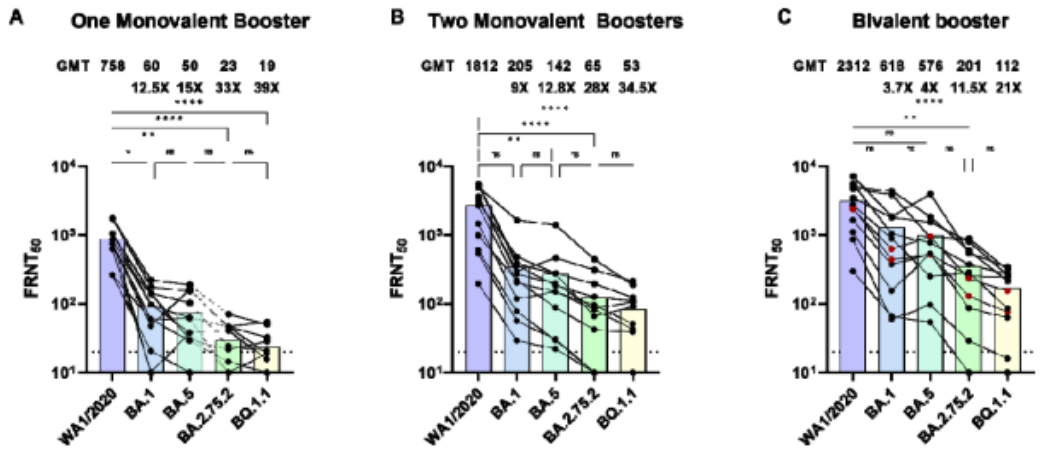


Figure 1. Neutralization of Omicron sublineages after 4 doses of parental mRNA vaccine or a BA.5-bivalent-booster

Karhade C, Shi Y-P, et al. https://www.biorxiv.org/content/10.1101/2022.10.31.514580v1.full.pdf

mRNA bivalent booster enhances neutralization against BA.2.75.2 and BQ.1.

Using a live virus neutralization assay, we evaluated serum samples from individuals who had received either one or two monovalent boosters or the bivalent booster to determine neutralizing activity against wild-type (WA1/2020) virus and Omicron subvariants BA.1, BA.5, BA.2.75.2, and BQ.1.1. In the one monovalent booster cohort, relative to WA1/2020, we observed a reduction in neutralization titers of 9-15-fold against BA.1 and BA.5 and 28-39-fold against BA.2.75.2 and BQ.1.1. In the BA.5-containing bivalent booster cohort, the neutralizing activity improved against all the Omicron subvariants. Relative to WA1/2020, we observed a reduction in neutralization titers of 3.7- and 4-fold against BA.1 and BA.5, respectively, and 11.5- and 21-fold against BA.2.75.2 and BQ.1.1, respectively. These data suggest that the bivalent mRNA booster vaccine broadens humoral immunity against the Omicron subvariants.



Neutralizing responses against WA1/2020, BA.1, BA.5, BA.2.75.2, and BQ.1.1

Davis-Gardner ME, et al. https://doi.org/10.1101/2022.10.31.514636