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The Society for Healthcare Epidemiology of America

SAFE HEALTHCARE FOR ALL

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The Rapid Response Podcast

COVID-19 Updates: What We Know Now

Releases monthly

Newest Episodes:

- Monkeypox
- Long COVID

LEARNINGCE SHEA Online Education Center

LearningCE.shea-online.org

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SHEA COVID-19 Resources:

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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.

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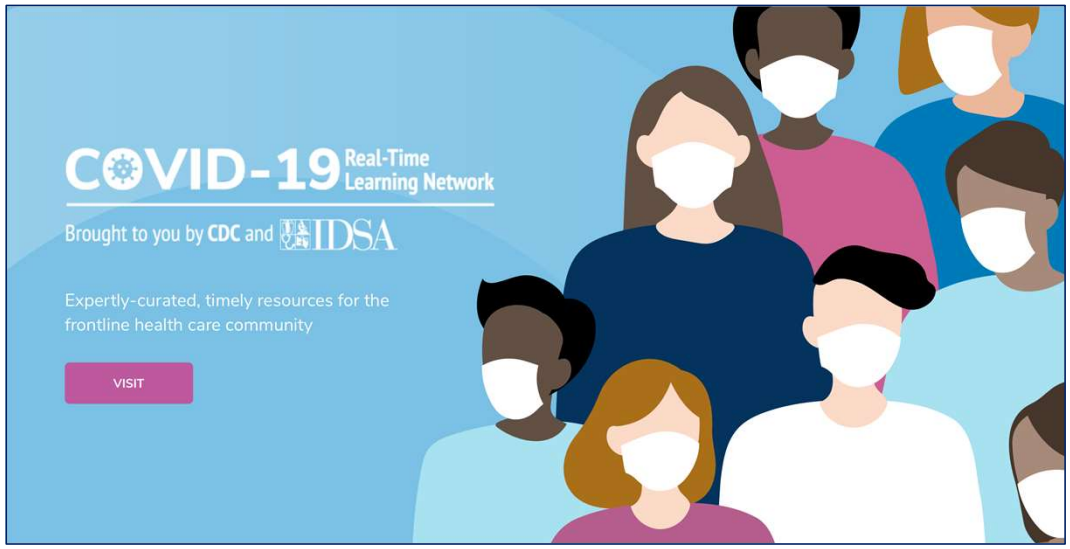
COVID-19 Real-Time Learning Network



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

@RealTimeCOVID19 | #RealTimeCOVID19

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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).

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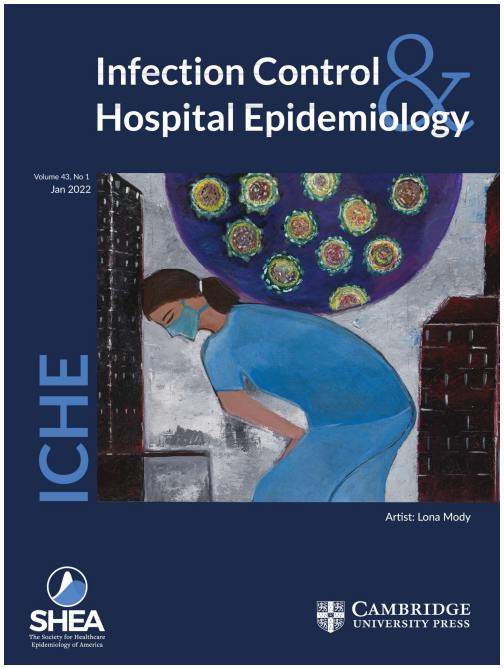
ICHE Journal – Fast Tracking COVID Article Submissions



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.

www.cambridge.org/iche

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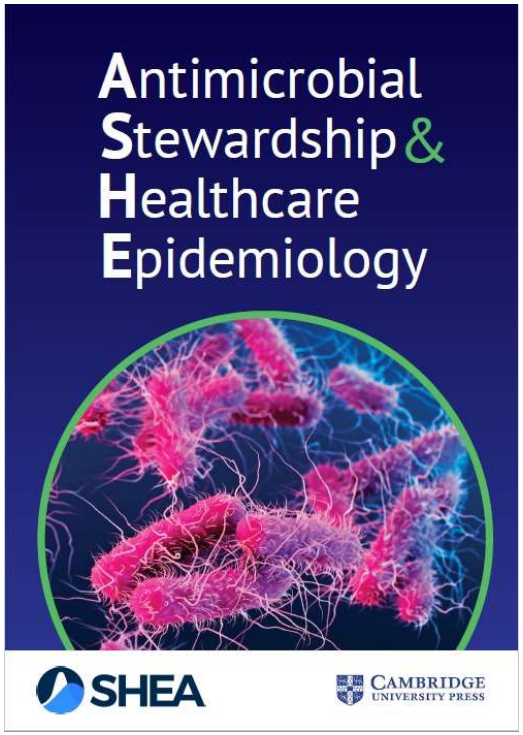
ASHE JOURNAL



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SHEA SPRING

SEE YOU NEXT YEAR!

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


IDWeek
Save the Date
Registration is open!
Join Us LIVE in Washington, DC
Oct. 19-23, 2022

SHEA Webinar

COVID-19 Town Hall Round 77

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

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  - Use the emailed invitation to join via the URL, or call in with the provided phone numbers

- https://support.zoom.us

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Streaming Live on SHEA's Facebook page

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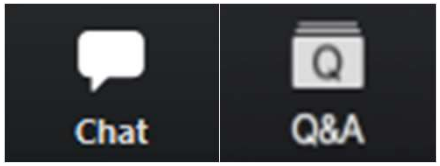
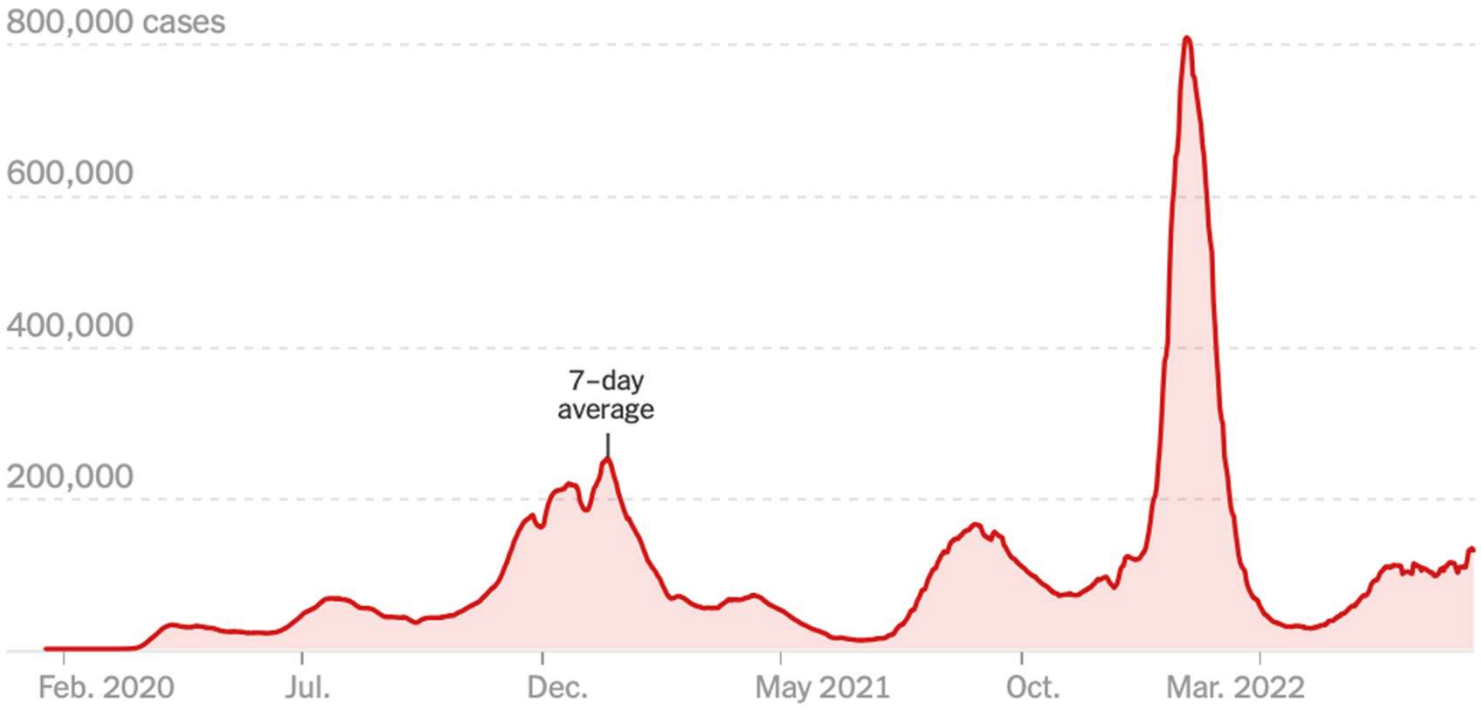


- **Chat**: Talk to each other or ask SHEA Staff questions if you are having technical difficulties
- **Q&A**: Type in your question to be read aloud by SHEA Staff and answered by the Panelists

REPORTED COVID-19 CASES IN THE UNITED STATES

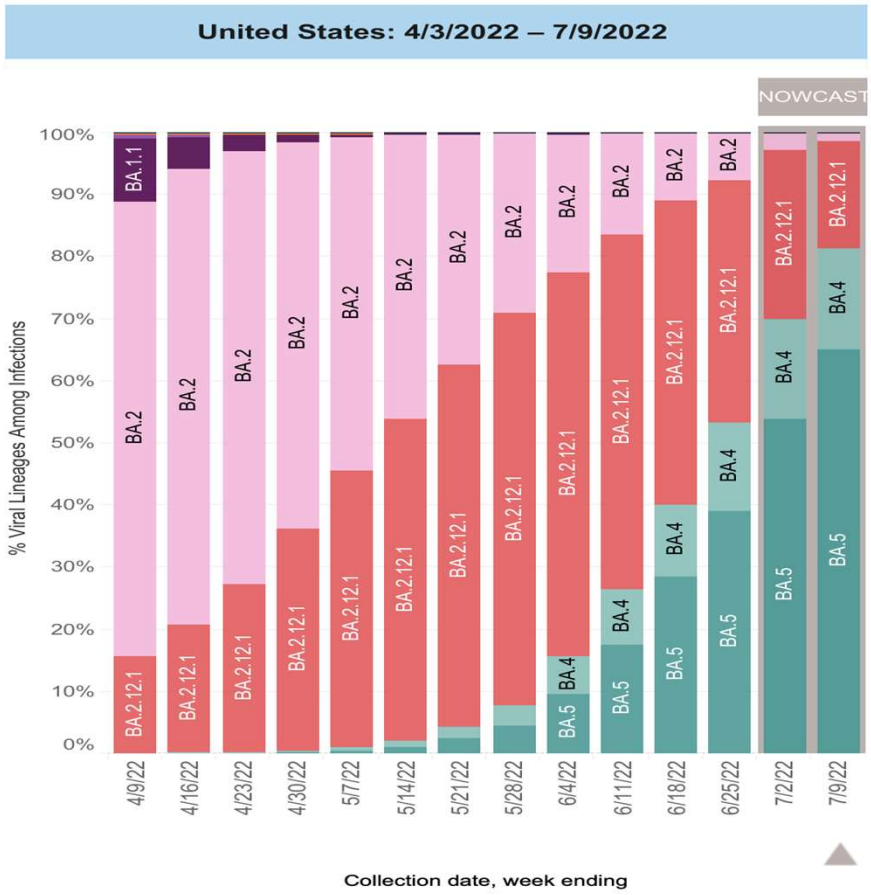
Cumulative Cases – 89,295,542



Cases increased by 14% from two weeks earlier

Source: New York Times 7-17-22

SARS-CoV-2 VARIANTS, US, CDC



United States: 7/3/2022 – 7/9/2022 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	65.0%	62.2-67.7%
	BA.2.12.1	VOC	17.3%	15.7-19.0%
	BA.4	VOC	16.3%	14.5-18.3%
	BA.2	VOC	1.4%	1.3-1.6%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.1.1	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%

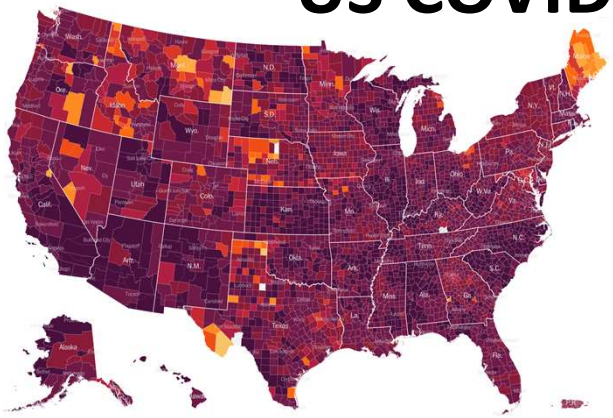
* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.

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

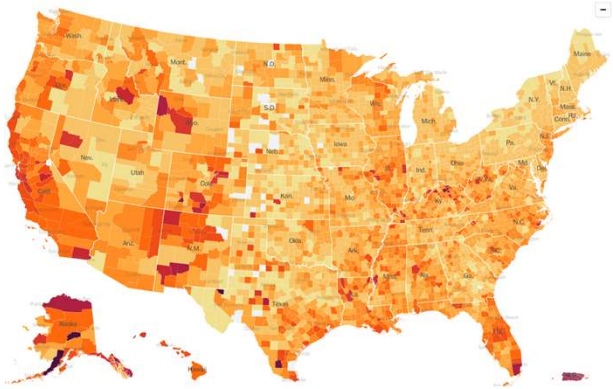
AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. For regional data, BA.1.1 and its sublineages are also aggregated with B.1.1.529, as they currently cannot be reliably called in each region. Except BA.2.12.1, BA.2 sublineages are aggregated with BA.2. BA.5.1 is aggregated with BA.5.

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

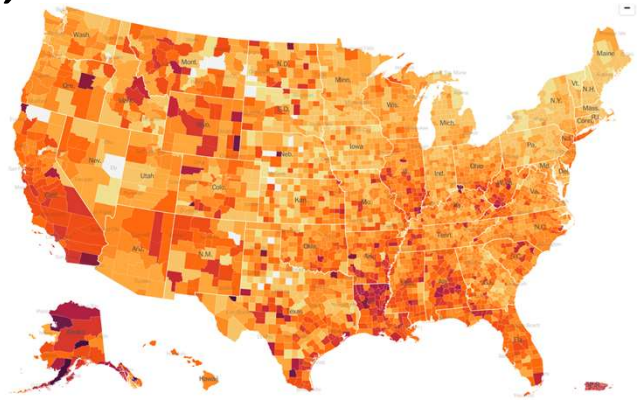
US COVID-19 HOTSPOTS



February 6, 2022



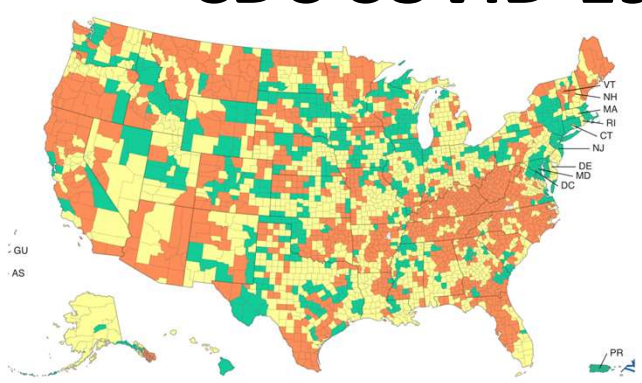
June 26, 2022



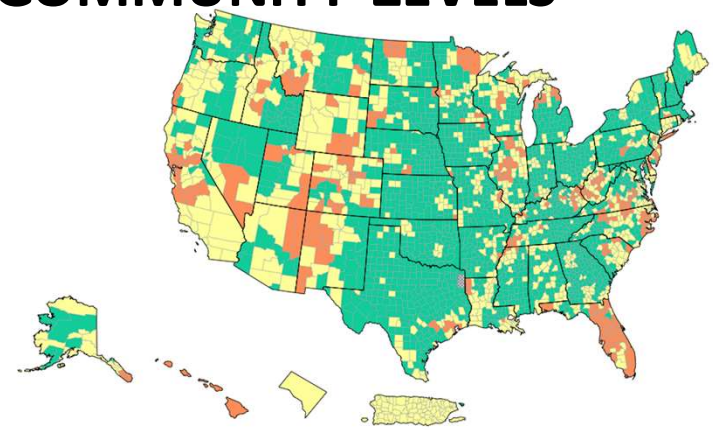
July 17, 2022

Source: New York Times 7-17-2022

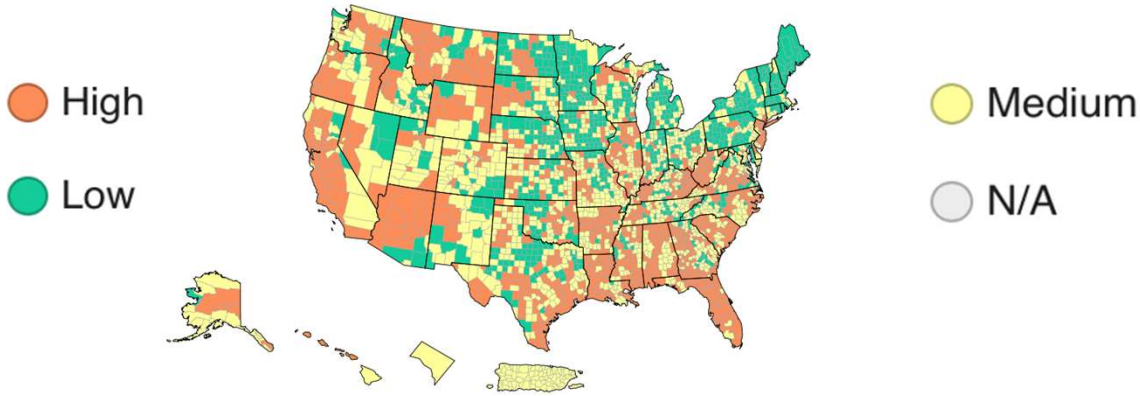
CDC COVID-19 COMMUNITY LEVELS



February 27, 2022



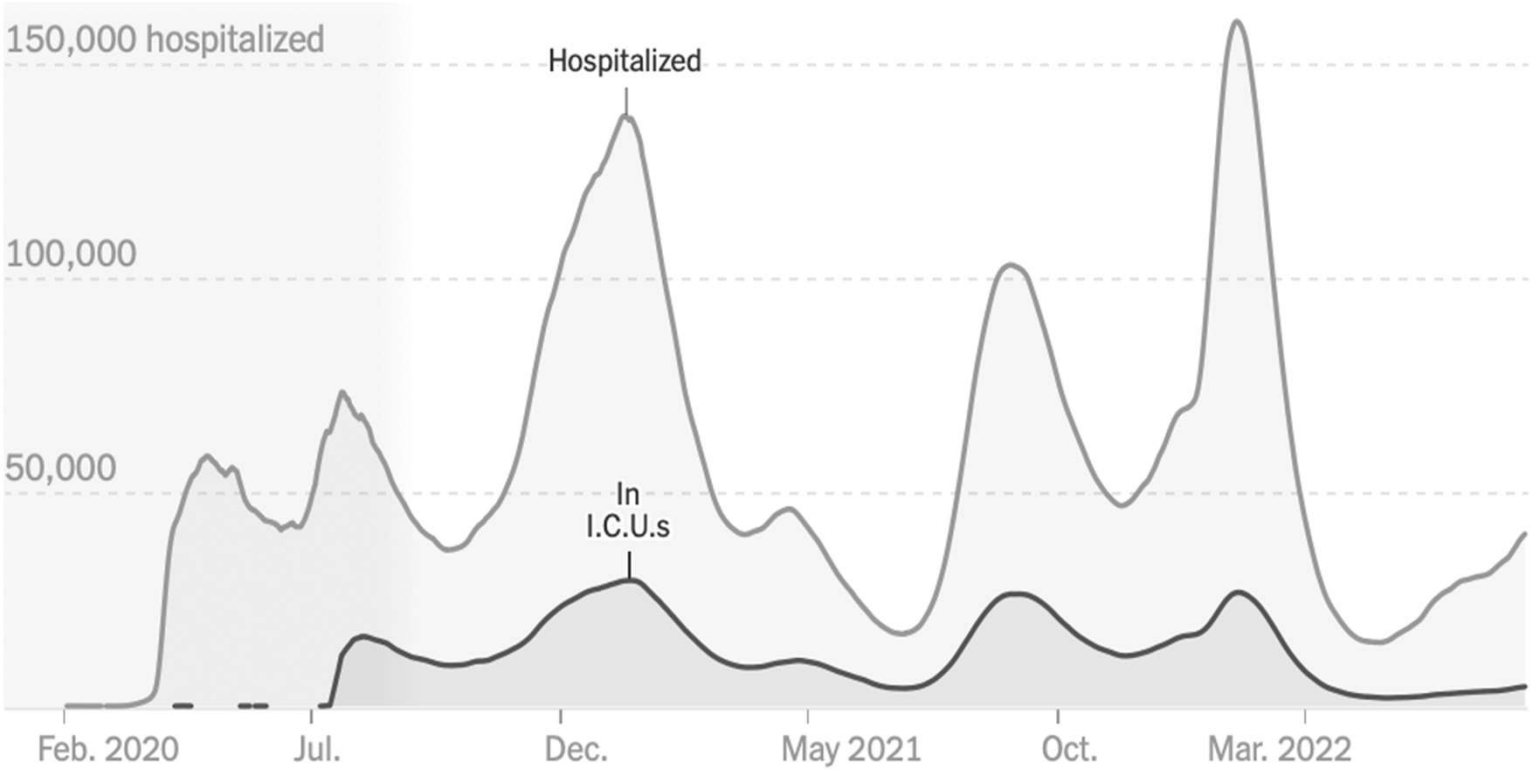
June 26, 2022



July 17, 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

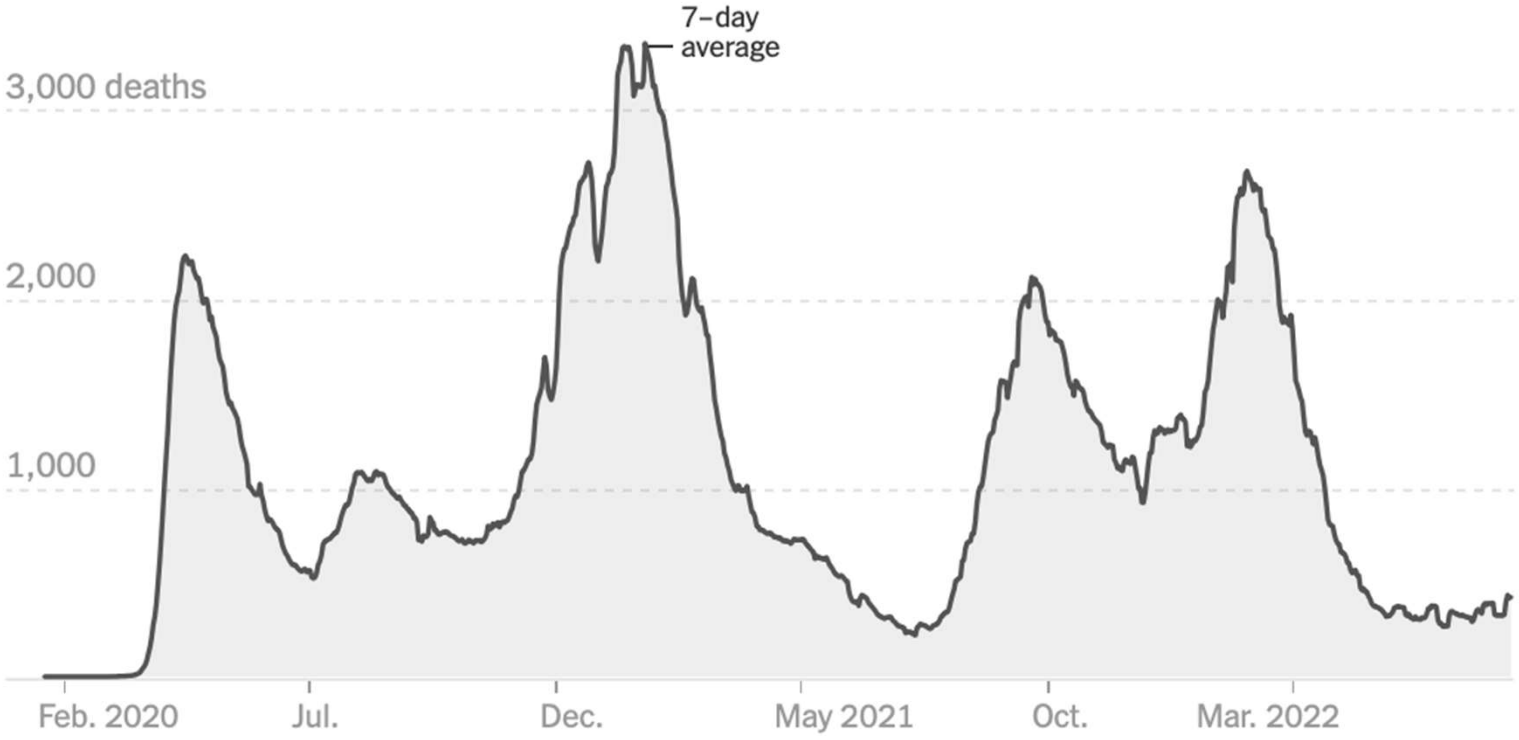


Hospitalizations increased 20 % from two weeks earlier

Source: New York Times 7-17-22

COVID-19 DEATHS IN THE UNITED STATES

Cumulative Deaths – 1,020,198



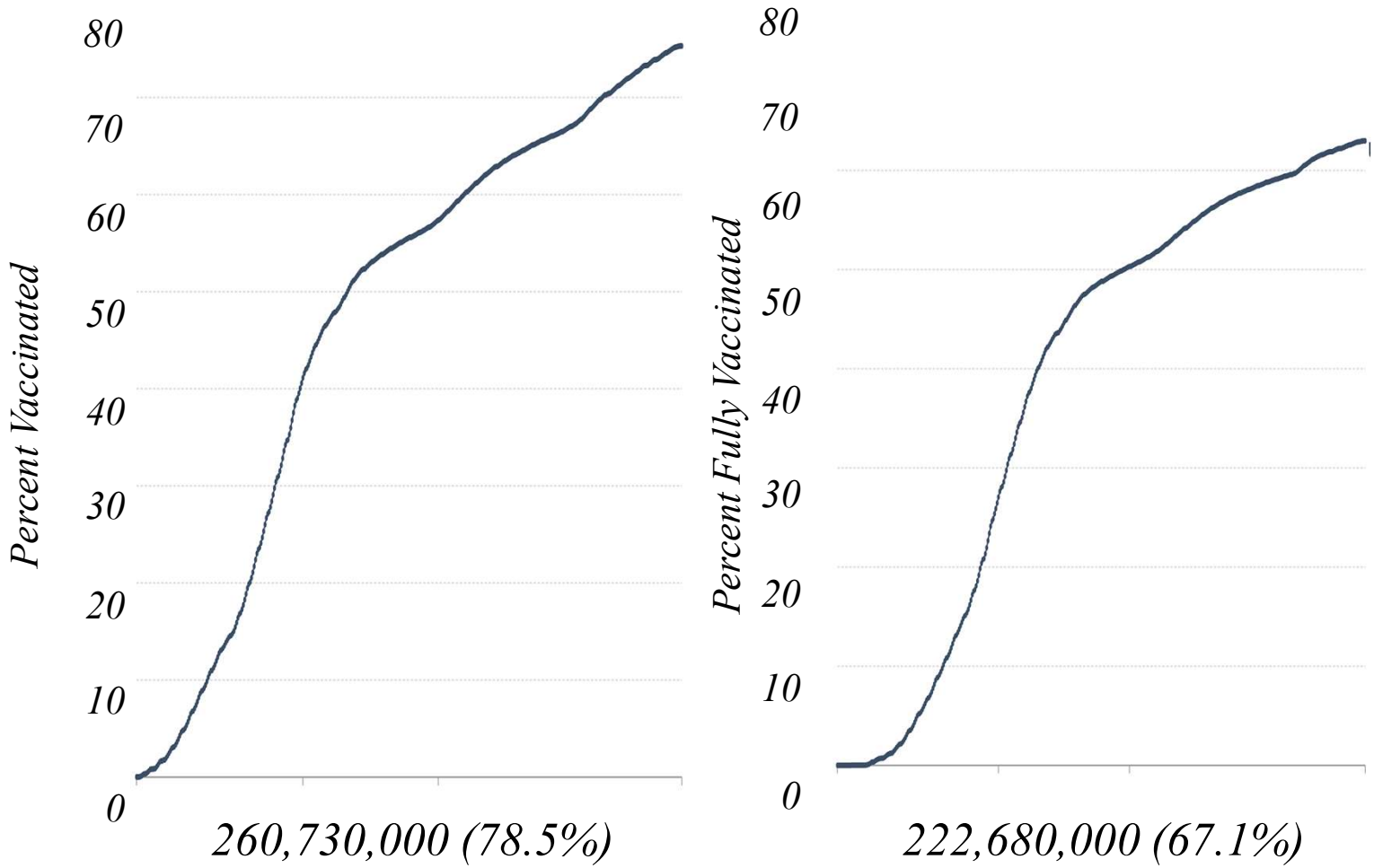
8 % increase from two weeks earlier

Source: New York Times 7-17-22

DAILY COVID-19 VACCINATIONS IN THE UNITED STATES

Source: Our World in Data 7-16-22

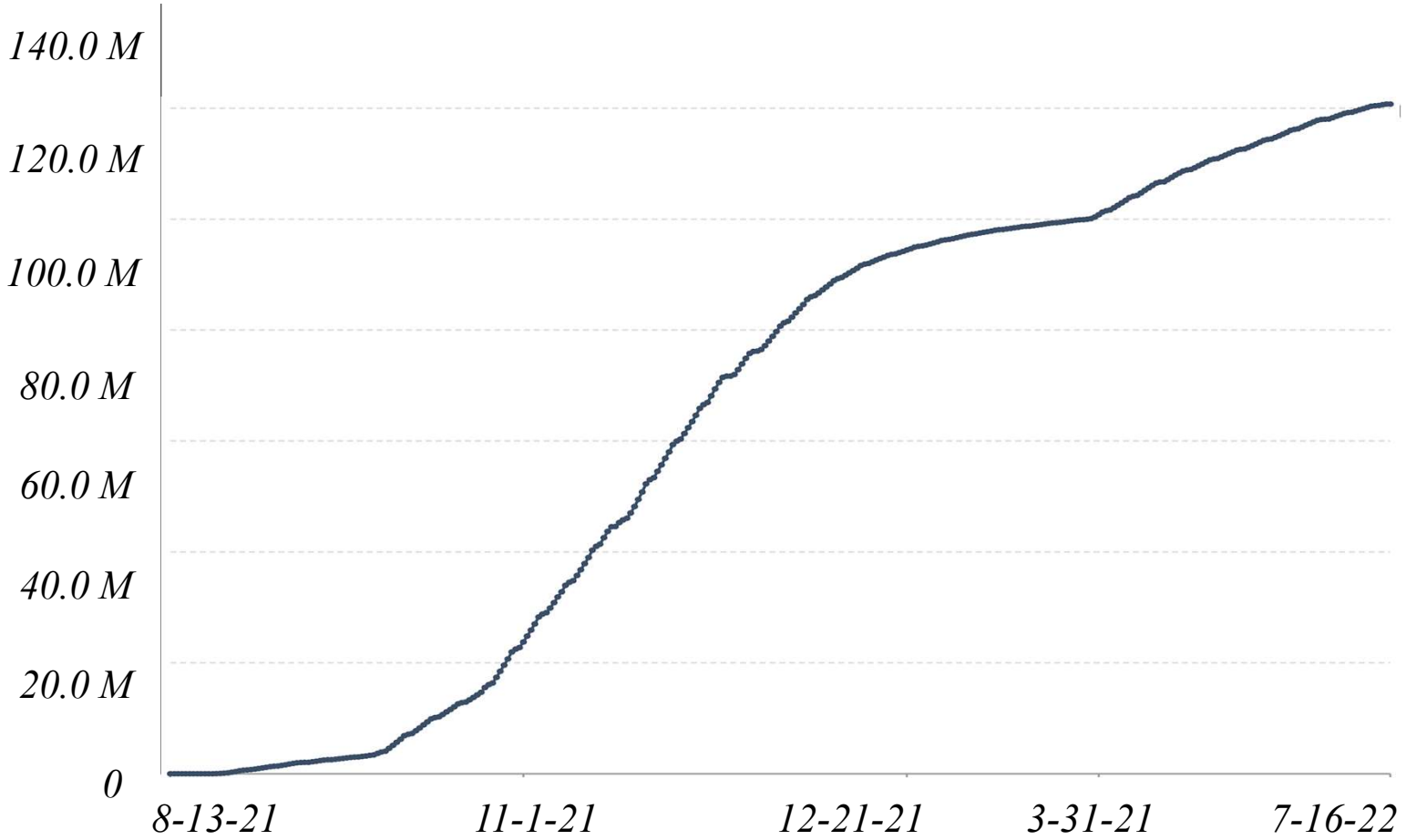
COVID-19 VACCINATIONS IN THE UNITED STATES



Source: Our World in Data 7-16-22

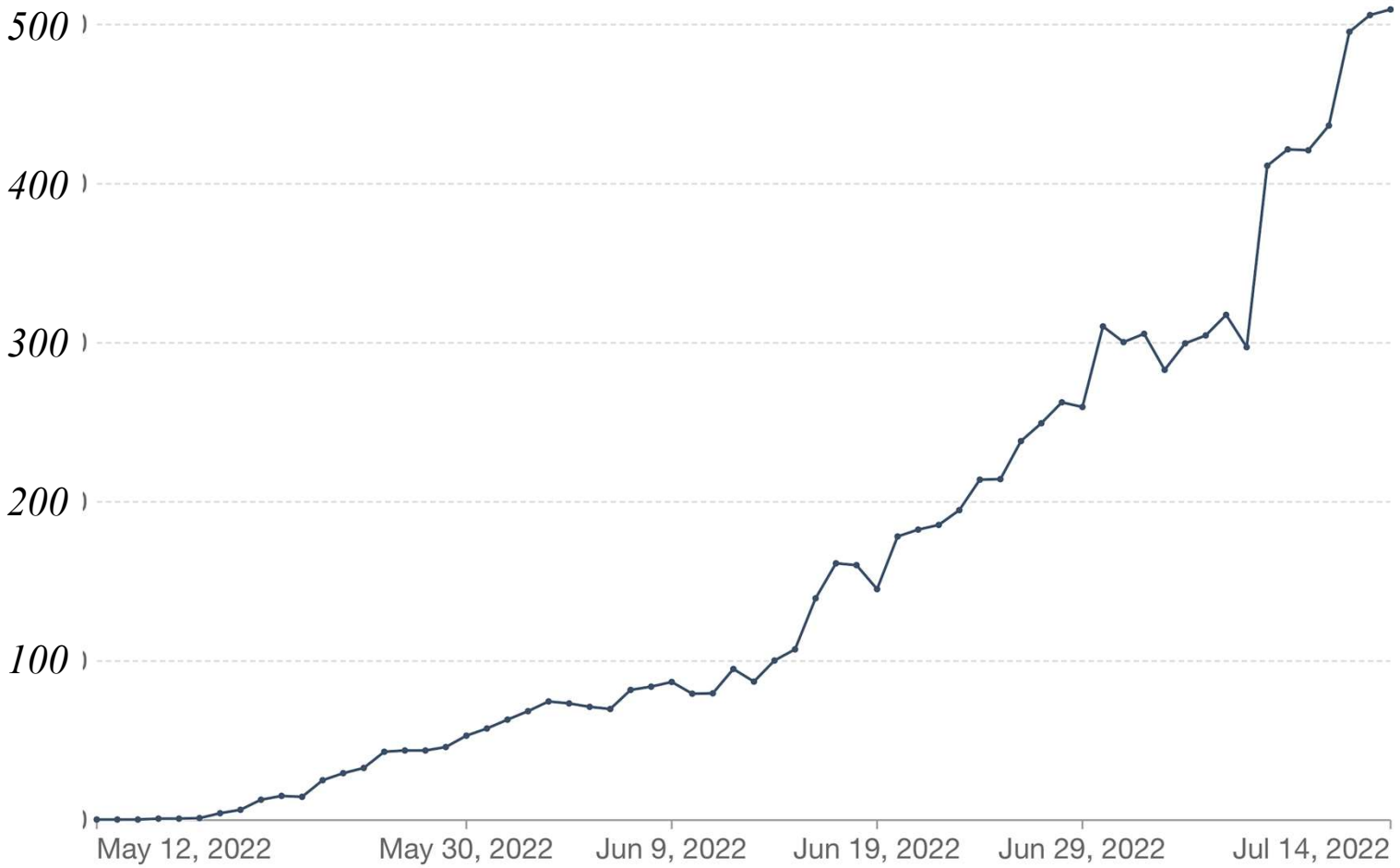
COVID-19 Booster Doses in the United States

Cumulative Doses Administered 125.25 M



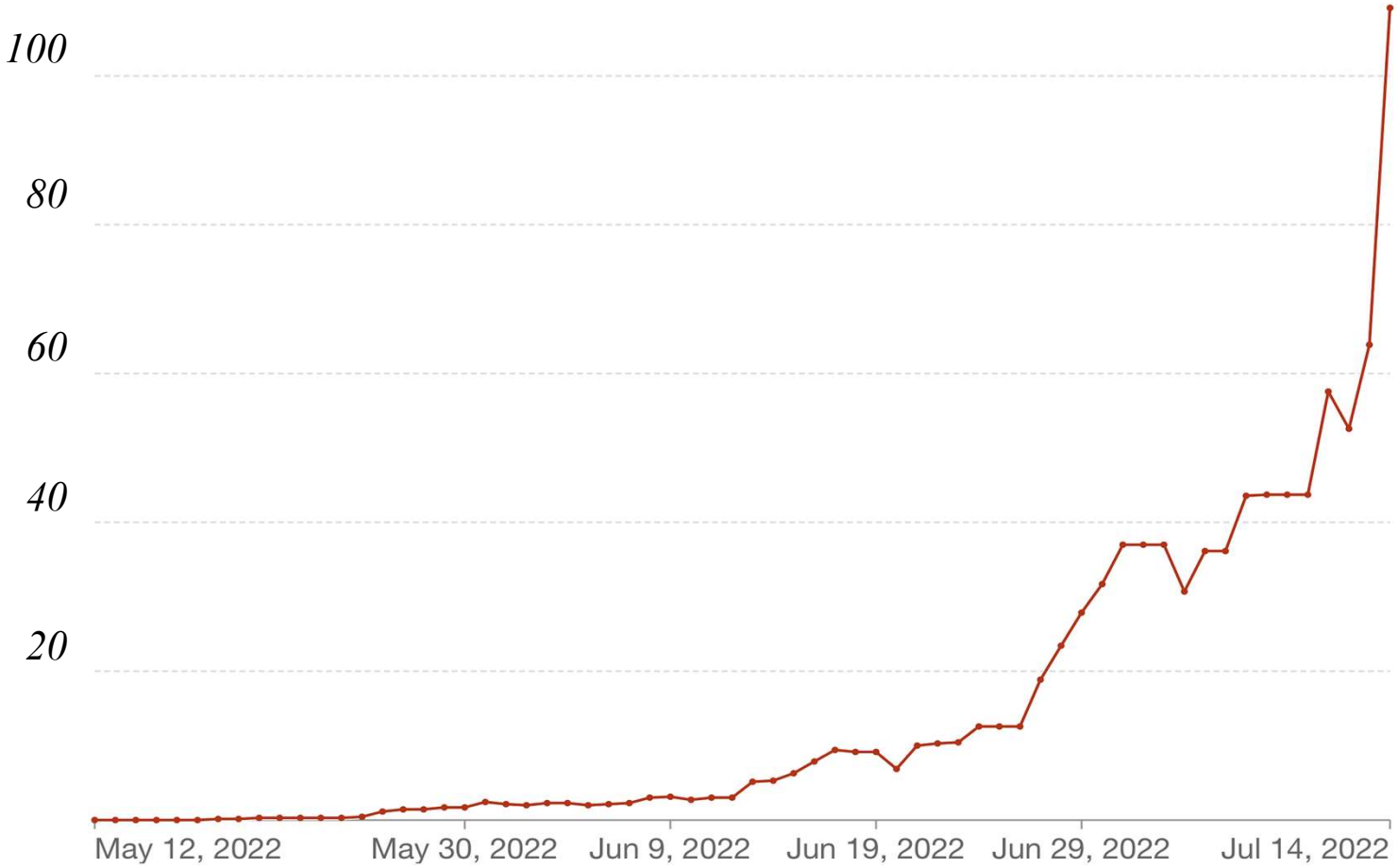
Source: Our World in Data 7-16-22

MONKEYPOX OUTBREAK: DAILY CASES, WORLDWIDE



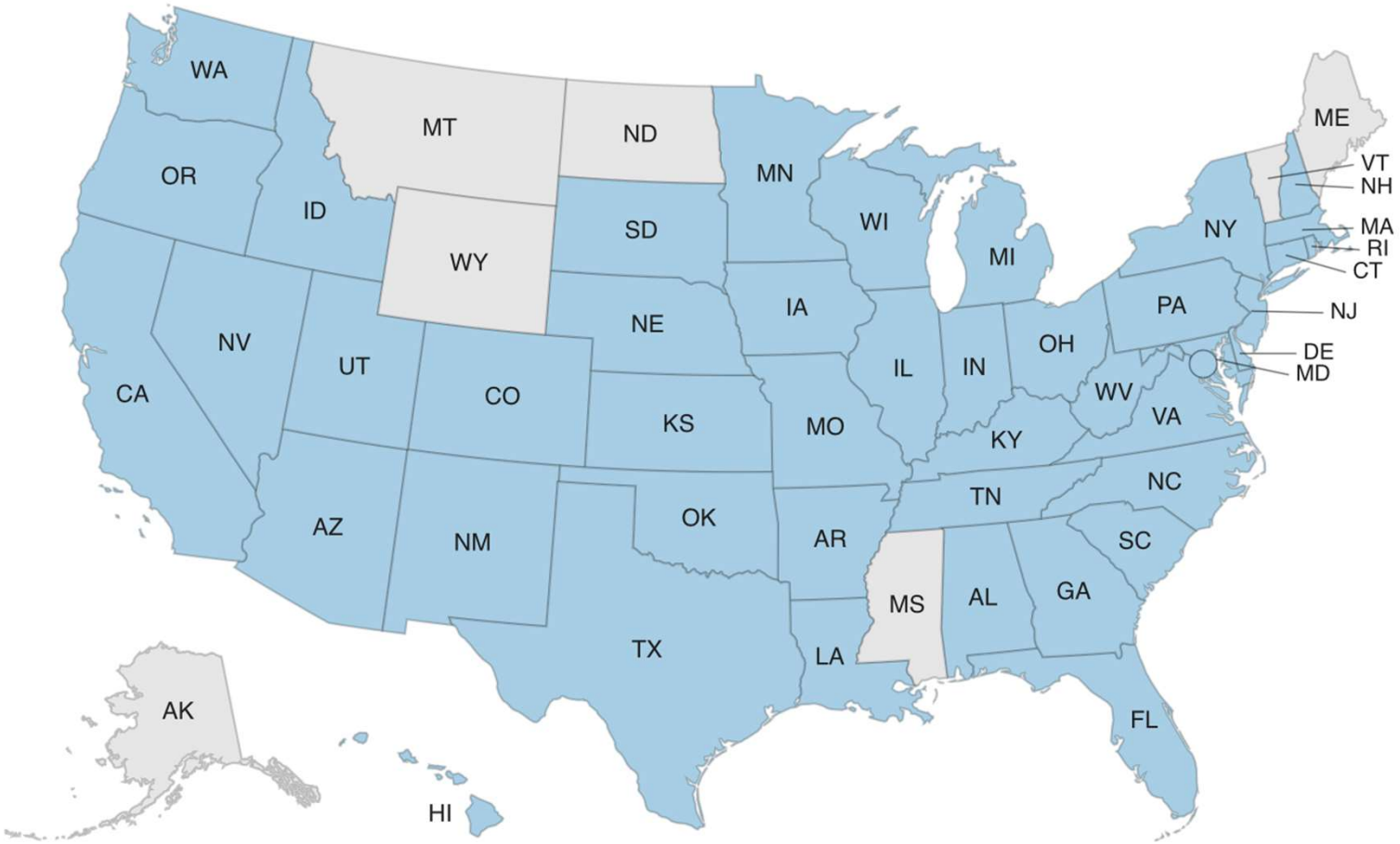
Our World in Data - https://ourworldindata.org/monkeypox

MONKEYPOX OUTBREAK CURVE: DAILY CASES, US



Our World in Data - https://ourworldindata.org/monkeypox

2022 Monkeypox Outbreak, US



https://www.cdc.gov/poxvirus/monkeypox/response/2022/index.html

This Week's Pandemic and Epidemic News

1. *Current administration considering offering second COVID booster to all adults.*
2. *FDA recommended inclusion of omicron BA.4/5 component for COVID-19 vaccine booster doses to be administered this fall.*
3. *FDA grants emergency use authorization to the Novavax vaccine.*
4. *Collateral damage – CDC issued a special report documenting a substantial increase in multidrug-resistant organism infections and deaths in the US during the pandemic.*
5. *A **New England Journal** letter reported COVID vaccination during pregnancy was not associated with increased risk for clinically serious acute adverse events.*
6. *The **New England Journal** published a thoughtful review of vaccine hesitancy that emphasizes both the importance of health care providers offering support and encouragement to their patients as well as the importance of listening carefully to each patient's perspective.*
7. *A **JAMA Network Open** modelling study estimated that COVID-19 vaccination prevented 27 million SARS-CoV-2 infections, 1.6 million COVID-19 hospitalizations, and 235 000 COVID-19 deaths from December 1, 2020, to September 30, 2021.*
8. *An accompanying editorial in **JAMA Network Open** notes that vaccines that should have been able to reduce deaths by up to 94% only managed to prevent 58% of deaths.*
9. *CDC and Our World in Data Monkeypox Situation Summaries..*

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

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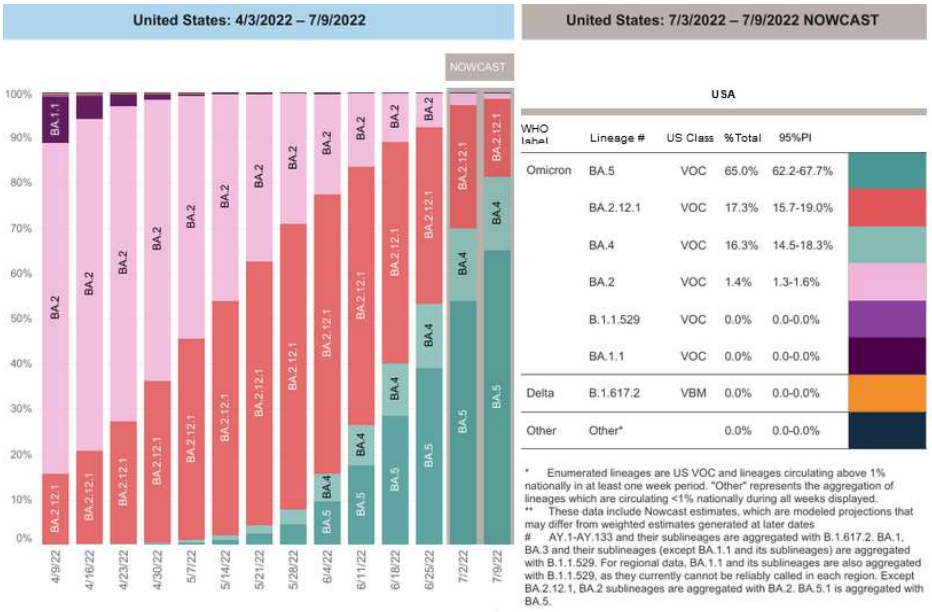
COVID-19 UPDATE: FOCUS ON NEW VARIANTS, BA.4 AND BA.5

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

UNC SCHOOL OF MEDICINE

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

VARIANT PROPORTIONS, US



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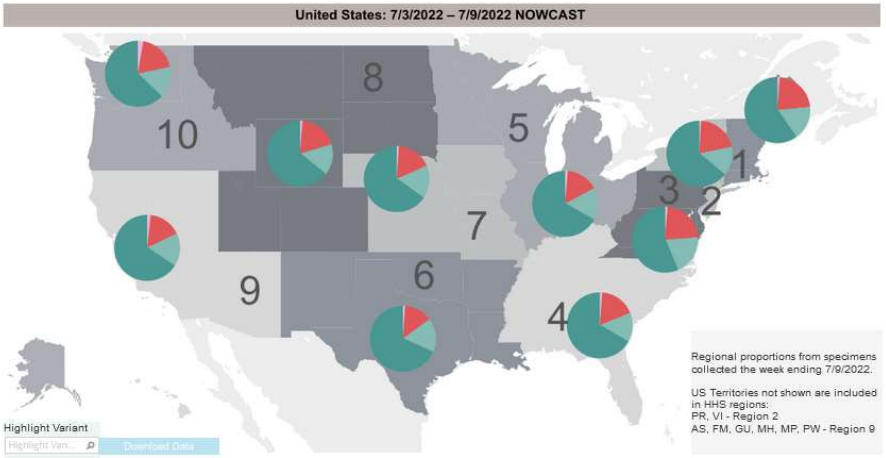
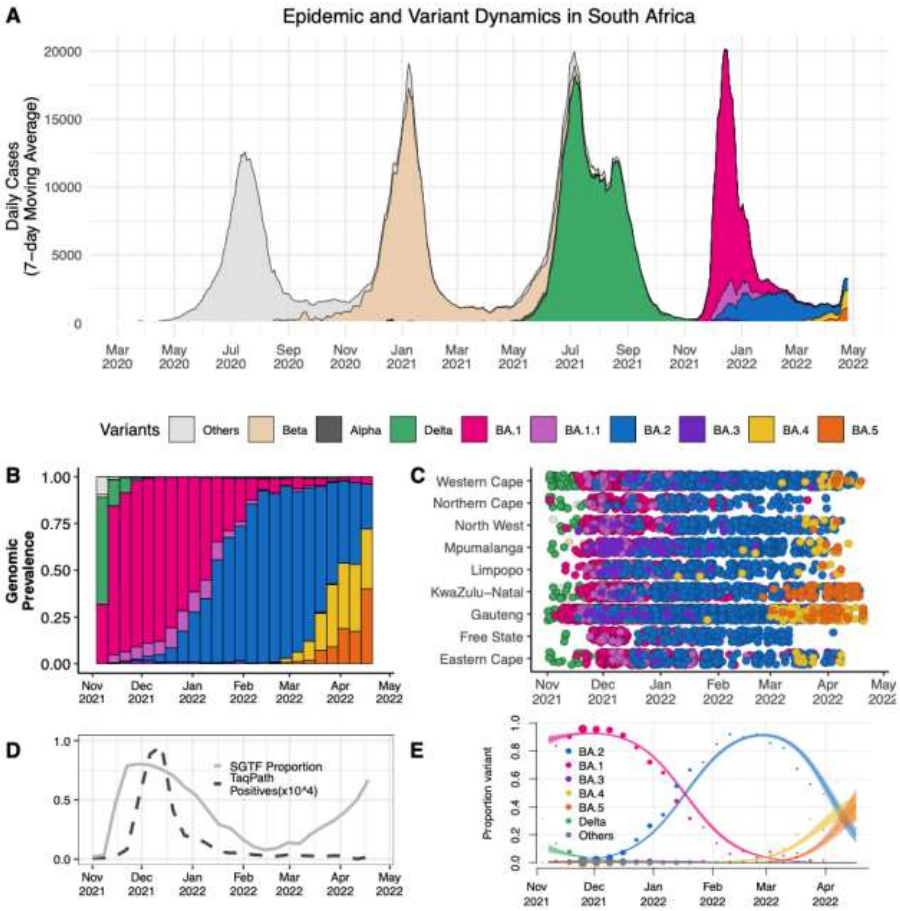
# AY.1-AY.133 and their sublineages are aggregated with B.1.617.2. BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. For regional data, BA.1.1 and its sublineages are also aggregated with B.1.1.529, as they currently cannot be reliably called in each region. Except BA.2.12.1, BA.2 sublineages are aggregated with BA.2. BA.5.1 is aggregated with BA.5.



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

Continued Emergence and Evolution of Omicron in SA: New BA.4 and BA.5 lineages

- Assessment new lineages BA.4 and BA.5, South Africa
- Results: The spike proteins of BA.4 and BA.5 are identical, and comparable to BA.2 except for the addition of 69-70del, L452R, F486V and the wild type amino acid at Q493. BA.4 and BA.5 have rapidly replaced BA.2, reaching more than 50% of sequenced cases in South Africa from the first week of April 2022 onwards. Using a multinomial logistic regression model, we estimate growth advantages for BA.4 and BA.5 of 0.08 (95% CI: 0.07-0.09) and 0.12 (95% CI: 0.09 - 0.15) per day respectively over BA.2 in South Africa. {this growth advantage is similar to that observed for BA.2 over BA.1.}
- Reasons for growth advantage: (i) an increase in its intrinsic transmissibility relative to other variants, (ii) an increase relative to other variants in its capacity to infect, and be transmitted from, previously infected and vaccinated individuals or (iii) both. Given that the transmission advantage becomes apparent approximately four months from the start of the Omicron wave, it is plausible that waning immunity (particularly that acquired from BA.1 infection) is an important contributory factor.



Tegally H, et al. https://krisp.org.za/manuscripts/MEDRXIV-2022-274406v1-deOliveira.pdf

SARS-CoV-2 Outcomes; Omicron lineages BA.4 and BA.5 compared with previous waves

- Goal: Assess the clinical severity of Omicron BA.4/BA.5 infection with BA.1 and earlier variant infections, South Africa
- Methods: Public sector patients aged ≥20 years with lab-confirmed COVID-19;1-21 May 2022 (BA.4/BA.5 wave) and equivalent prior wave periods. We compared the risk between waves of (i) death and (ii) severe hospitalization/ death (all within 21 days of diagnosis) using Cox regression
- Among 3,793 patients from the BA.4/BA.5 wave and 190,836 patients from previous waves the risk of severe hospitalization/ death was similar in the BA.4/BA.5 and BA.1 waves (adjusted hazard ratio [aHR] 1.12; 95% confidence interval [CI] 0.93; 1.34). Both Omicron waves had lower risk of severe outcomes than previous waves. Prior infection (aHR 0.29, 95% CI 0.24; 0.36) and vaccination (aHR 0.17; 95% CI 0.07; 0.40 for boosted vs.no vaccine) were protective.

	Outcome = death not adjusted for vaccination and prior infection		Outcome = death adjusted for vaccination and prior infection		Outcome = severe hospitalization[a]/death not adjusted for vaccination or prior diagnosed infection		Outcome = severe hospitalization[a]/death adjusted for vaccination or prior diagnosed infection	
	Adjusted[b] HR	95% CI	Adjusted HR	95% CI	Adjusted[b] HR	95% CI	Adjusted HR	95% CI
Male sex (vs. female)	1.40	1.34; 1.45	1.40	1.34; 1.45	1.27	1.23; 1.31	1.26	1.22; 1.30
Age (vs. 20-39 years)								
40-49 years	2.54	2.30; 2.81	2.57	2.33; 2.84	2.00	1.87; 2.15	2.04	1.90; 2.19
50-59 years	5.46	4.99; 5.97	5.56	5.08; 6.08	3.42	3.21; 3.65	3.50	3.28; 3.74
60-69 years	12.55	11.47; 13.73	12.88	11.77; 14.10	6.39	5.97; 6.83	6.56	6.13; 7.01
≥70 years	23.19	21.15; 25.43	23.93	21.82; 26.24	10.35	9.65; 11.09	10.65	9.94; 11.42
Comorbidities (vs. comorbidity absent)								
diabetes	2.01	1.92; 2.10	2.01	1.93; 2.10	1.97	1.89; 2.04	1.98	1.91; 2.06
hypertension	1.08	1.03; 1.13	1.07	1.02; 1.12	1.18	1.14; 1.23	1.17	1.13; 1.22
chronic kidney disease	1.90	1.80; 2.00	1.90	1.81; 2.00	1.63	1.56; 1.70	1.63	1.56; 1.70
chronic pulmonary disease / asthma	0.98	0.93; 1.04	0.99	0.93; 1.04	1.18	1.13; 1.23	1.19	1.14; 1.24
previous tuberculosis	1.30	1.20; 1.40	1.28	1.19; 1.38	1.25	1.17; 1.33	1.23	1.16; 1.31
current tuberculosis	2.53	2.20; 2.91	2.44	2.13; 2.81	2.89	2.59; 3.23	2.79	2.50; 3.11
HIV	1.60	1.48; 1.72	1.60	1.49; 1.72	1.54	1.45; 1.64	1.54	1.45; 1.64
Number of admissions in district in week of diagnosis (vs <1/3 of maximum)								
1/3 to <2/3	1.11	1.05; 1.17	1.12	1.06; 1.18	1.03	0.98; 1.08	1.04	0.99; 1.09
≥2/3	1.12	1.05; 1.20	1.13	1.06; 1.21	1.05	0.99; 1.11	1.06	1.00; 1.12
Prior diagnosed SARS CoV-2 infection								
Yes (vs none)			0.51	0.42; 0.63			0.29	0.24; 0.36
Vaccination (vs. None)[c]								
single dose Ad26.COV2.S			0.24	0.18; 0.33			0.26	0.21; 0.32
two doses (Ad26.COV2.S and/or BNT162b2)			0.36	0.31; 0.42			0.37	0.33; 0.42
boosted (≥ 3doses Ad26.COV2.S and/or BNT162b2)			0.06	0.01; 0.40			0.17	0.07; 0.40
Wave period (dominant variant)								
wave 1 (ancestral)	2.08	1.90; 2.28	1.30	1.17; 1.44	N/A[a]		N/A[a]	
wave 2 (Beta)	2.35	2.16; 2.57	1.47	1.34; 1.62	2.06	1.93; 2.20	1.28	1.20; 1.38
wave 3 (Delta)	2.58	2.37; 2.81	1.75	1.59; 1.92	2.16	2.03; 2.29	1.44	1.35; 1.54
wave 4 (Omicron BA.1)	Ref		Ref		Ref		Ref	
wave 5 (Omicron BA.4/BA.5)	0.93	0.72; 1.20	1.16	0.90; 1.50	0.90	0.75; 1.08	1.12	0.93; 1.34

Davies MA, et al. medRxiv 2022 Jul 1;2022.06.28.22276983

Protection of SARS-CoV-2 natural infection against reinfection with the Omicron BA.4 or BA.5 subvariants

Table 3. Effectiveness of previous SARS-CoV-2 infection in preventing reinfection with the Omicron BA.4 or BA.5 subvariants using A) S-gene "target failure" infections diagnosed between May 7, 2022 and July 4, 2022, and B) all SARS-CoV-2 infections diagnosed between June 8, 2022 and July 4, 2022, when BA.4 and BA.5 dominated incidence.

Type of analysis	Cases† (SARS-CoV-2-positive tests)			Controls† (SARS-CoV-2-negative tests)			Effectiveness in % (95% CI)‡
	Median interval between previous infection and SARS-CoV-2 test (IQR) in days	Previous infection (n)	No previous infection (n)	Median interval between previous infection and SARS-CoV-2 test (IQR) in days	Previous infection (n)	No previous infection (n)	
Primary analyses							
A) Analysis using SGTF status as a proxy for BA.4 or BA.5							
Effectiveness against symptomatic BA.4 or BA.5 infection*							
Pre-omicron previous infection	542 (455-713)	21	164	498 (427-699)	77	525	15.1 (-47.1 to 50.9)
Omicron previous infection	169 (166-175)	13	164	167 (159.5-173)	140	525	76.1 (54.9 to 87.3)
Effectiveness against any BA.4 or BA.5 infection							
Pre-omicron previous infection	473 (427-628)	125	1,267	460 (410-620)	551	4,273	28.3 (11.4 to 41.9)
Omicron previous infection	166 (154-173)	87	1,267	163 (150-171)	1,328	4,273	79.7 (74.3 to 83.9)
B) Analysis using any infection during BA.4 and BA.5 dominance							
Effectiveness against symptomatic BA.4 or BA.5 infection*							
Pre-omicron previous infection	490 (438-685)	107	1,080	476 (430-670.5)	444	3,119	40.0 (23.9 to 52.7)
Omicron previous infection	167 (161-171)	45	1,080	164 (155-171)	982	3,119	89.6 (85.5 to 92.6)
Effectiveness against any BA.4 or BA.5 infection							
Pre-omicron previous infection	480 (435-647.5)	528	5,683	470 (429-652)	2,559	19,125	34.1 (26.9 to 40.5)
Omicron previous infection	167 (159-174)	289	5,683	163 (154-171)	5,367	19,125	83.8 (81.6 to 85.8)
Sensitivity analyses adjusting for vaccination status in conditional logistic regression							
A) Analysis using SGTF as a proxy for BA.4 or BA.5							
Effectiveness against symptomatic BA.4 or BA.5 infection*							
Pre-omicron previous infection	542 (455-713)	21	164	498 (427-699)	77	525	14.9 (-47.5 to 50.9)
Omicron previous infection	169 (166-175)	13	164	167 (159.5-173)	140	525	76.1 (54.9 to 87.3)
Effectiveness against any BA.4 or BA.5 infection							
Pre-omicron previous infection	473 (427-628)	125	1,267	460 (410-620)	551	4,273	28.6 (11.8 to 42.2)
Omicron previous infection	166 (154-173)	87	1,267	163 (150-171)	1,328	4,273	79.7 (74.4 to 84.0)
B) Analysis using any infection during BA.4 and BA.5 dominance							
Effectiveness against symptomatic BA.4 or BA.5 infection*							
Pre-omicron previous infection	490 (438-685)	107	1,080	476 (430-670.5)	444	3,119	40.3 (24.3 to 52.9)
Omicron previous infection	167 (161-171)	45	1,080	164 (155-171)	982	3,119	89.6 (85.5 to 92.6)
Effectiveness against any BA.4 or BA.5 infection							
Pre-omicron previous infection	480 (435-647.5)	528	5,683	470 (429-652)	2,559	19,125	34.9 (27.8 to 41.2)
Omicron previous infection	167 (159-174)	289	5,683	163 (154-171)	5,367	19,125	84.0 (81.8 to 85.9)

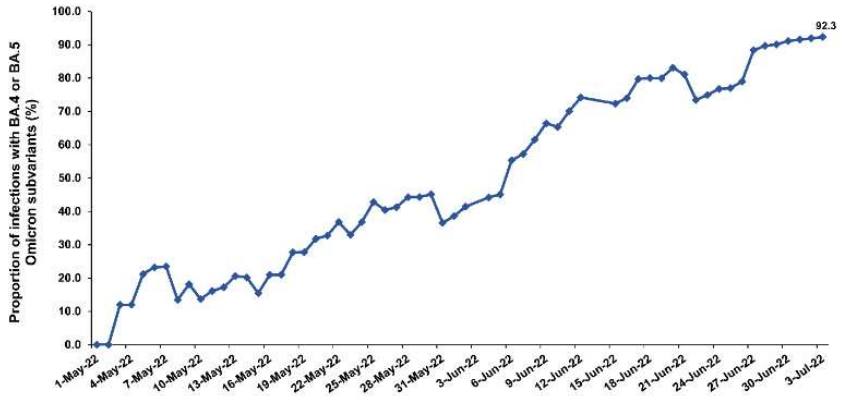
CI denotes confidence interval, IQR interquartile range, PCR polymerase chain reaction, RA rapid antigen, SARS-CoV-2 severe acute respiratory syndrome coronavirus 2, and SGTF S-gene "target failure".
*A symptomatic infection was defined as a SARS-CoV-2 PCR or RA test conducted because of clinical suspicion due to presence of symptoms compatible with a respiratory tract infection.
†Cases and controls were exact matched one-to-five by sex, 10-year age group, nationality, comorbid condition count, calendar week of test, method of testing (PCR or RA), and reason for testing.
‡Effectiveness of previous infection in preventing reinfection was estimated using the test-negative, case–control study design.[2]

Altarawneh HN, et al https://www.medrxiv.org/content/10.1101/2022.07.11.22277448v1

Protection of SARS-CoV-2 natural infection against reinfection with the Omicron BA.4 or BA.5 subvariants

- Study estimates the effectiveness of previous infection with SARS-CoV-2 in preventing reinfection with Omicron BA.4/BA.5 subvariants using a test-negative, case–control study design. Cases (SARS-CoV-2-positive test results) and controls (SARS-CoV-2-negative test results) were matched according to sex, 10-year age group, nationality, comorbid condition count, calendar week of testing, method of testing, and reason for testing (5/7/22-7/4/22).
- Effectiveness of a previous pre-Omicron infection against symptomatic BA.4/BA.5 reinfection was 15.1% (95% CI: -47.1-50.9%), and against any BA.4/BA.5 reinfection irrespective of symptoms was 28.3% (95% CI: 11.4-41.9%). Effectiveness of a previous Omicron infection against symptomatic BA.4/BA.5 reinfection was 76.1% (95% CI: 54.9-87.3%), and against any BA.4/BA.5 reinfection was 79.7% (95% CI: 74.3-83.9%). Sensitivity analyses adjusting for vaccination status confirmed study results. Protection of a previous infection against BA.4/BA.5 was lower than that against BA.1/BA.2, consistent with BA.4/BA.5's greater capacity for immune-system evasion than that of BA.1/BA.2.

Figure 1. Proportion of SARS-CoV-2 Omicron infections that are with the BA.4 or BA.5 subvariants versus with the BA.2 subvariant, the only other subvariant of appreciable presence in Qatar between May 1, 2022 and July 3, 2022. BA.4 or BA.5 subvariant status was proxied as an S-gene "target failure" (SGTF) status in the PCR testing conducted using the TaqPath COVID-19 Combo Kit (Thermo Fisher Scientific, USA[24]).



Altarawneh HN, et al
https://www.medrxiv.org/content/10.1101/2022.07.11.22277448v1

BA.2.12.1, BA.4 and BA.5 escape antibodies elicited by Omicron infection

- SARS-CoV-2 Omicron sublineages BA.2.12.1, BA.4 and BA.5 exhibit higher transmissibility over BA.2. Study showed that BA.2 sublineages, including A.2.12.1 and BA.2.13, exhibit increased ACE2-binding affinities compared to BA.1; while BA.4/BA.5 displays the weakest receptor-binding activity due to F486V and R493Q reversion. Importantly, compared to BA.2, BA.2.12.1 and BA.4/BA.5 exhibit stronger neutralization evasion against the plasma of 3-dose vaccinees and, most strikingly, of vaccinated BA.1 convalescents. As for therapeutic NAbs, LYCoV1404 (Bebtelovimab) and COV2-2130 (Cilgavimabcan) still effectively neutralize BA.2.12.1 and BA.4/BA.5, while the S371F, D405N and R408S mutations carried by BA.2/BA.4/BA.5 sublineages would undermine most broad sarbecovirus Nabs.
- Results indicate that Omicron can evolve mutations to specifically evade humoral immunity elicited by BA.1 infection. The continuous evolution of Omicron poses great challenges to SARS-CoV-2 herd immunity and suggests that BA.1-derived vaccine boosters may not be ideal for achieving broad-spectrum protection.

Bebtelovimab

Evusheld

IC50 (ng/mL)	LY-CoV016	LY-CoV555	LY-CoV1404	REGN 10933	REGN 10987	COV2-2196	COV2-2130	BRII-196	BRII-198	S309	DXP-604	ADG-2	S2K146	SA58 (BD55-5840)	SA55 (BD55-5514)	LY-CoV016+ LY-CoV555	REGN10933+ REGN10987	COV2-2196+ COV2-2130	BRII-196+ BRII-198	SA55+SA58
D614G	32	15	0.7	5.6	5.7	1.6	2.5	53	1239	74	11	11	17	0.9	11	20	5.0	2.1	81	2.1
BA.1	*	*	0.6	*	*	5419	3007	7118	1171	361	285	979	11	4.4	1.7	*	*	491	1890	3.2
BA.1.1	*	*	1.8	8912	*	4764	*	6324	*	314	198	991	17	4.5	3.0	*	*	8090	*	3.3
BA.2	*	*	0.9	*	590	4312	6.3	8530	8990	918	219	*	20	12	7.2	*	821	8.2	8610	7.8
BA.3	*	*	1.1	*	*	5609	11	7833	1687	972	259	6226	16	8.1	7.1	*	*	19	2190	6.4
BA.2.13	*	*	1.0	9221	417	3591	6.6	6902	*	700	148	*	16	4.9	5.9	*	699	7.1	*	4.8
BA.2.12.1	*	*	0.8	*	499	5521	11	7620	*	989	201	*	13	5.0	5.2	*	714	18	*	5.0
BA.4/BA.5	*	*	0.9	*	520	*	23	7124	*	792	6264	*	221	3.9	5.0	*	709	40	*	4.5
SARS-CoV-1	*	*	*	*	*	*	*	*	*	31	*	1.7	108	5.6	4.4	*	*	*	*	4.6
Pangolin-GD	1125	6.8	8.6	157	84	17	*	13	*	*	7.4	5.0	14	296	5.7	10	98	27	33	7.7
RaTG13	*	*	*	*	*	*	*	16	*	*	1.1	*	3.9	*	38	*	*	*	29	49

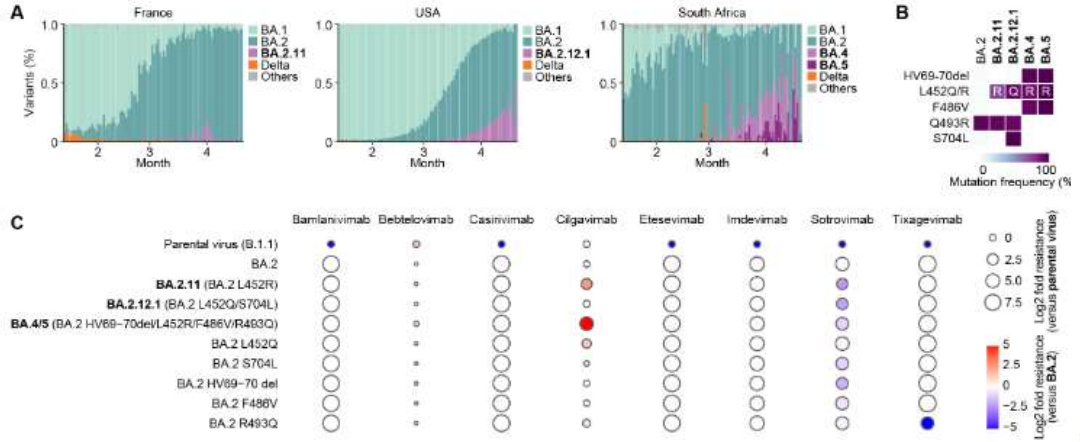
COV2-2196 = tixagevimab + COV2130 = Cilgavimab (Evusheld); LYCoV1404 = Bebtlovimab

Cao Y, et al. Nature

UNC SCHOOL OF MEDICINE

Sensitivity of novel SARS-CoV-2 Omicron subvariants, BA.2.11, BA.2.12.1,1 BA.4 and BA.5 to therapeutic monoclonal antibodies

- Background: Omicron BA.2.11, BA.2.12.119 and BA.4/5 subvariants are becoming dominant in France, US and South Africa, respectively.
- Study goal: Assess the sensitivity of these new Omicron subvariants (BA.2.11, BA.2.12.1 and BA.4/5) to eight therapeutic monoclonal antibodies (bamlanivimab, bebtelovimab, casirivimab, cilgavimab, etesevimab, imdevimab, sotrovimab and tixagevimab).
- Results: Although cilgavimab is antiviral against BA.2, BA.4/5 exhibits higher resistance to this antibody compared to BA.2. Bamlanivimab, casirivimab, tesevimab, imdevimab and tixagevimab were not functional against BA.2. Bebtelovimab was ~2-fold more effective against BA.2 and all Omicron subvariants tested than the parental virus. Omicron subvariants bearing L452R substitution including BA.2.11 and BA.4/5 were more sensitive to sotrovimab than BA.2. Cilgavimab was also antiviral against BA.2, while the L452R/; BA.4/5 exhibited ~30-fold more resistance to cilgavimab compared to BA.2



Yamasoba D, et al.
https://doi.org/10.1101/2022.05.03.490409

UNC SCHOOL OF MEDICINE

Augmented neutralisation resistance of emerging omicron subvariants BA.2.12.1, BA.4, and BA.5

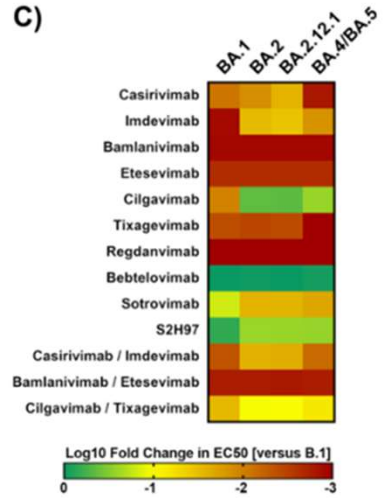
- Methods: We analysed neutralisation of BA.2.12.1 and BA.4/BA.5 by monoclonal antibodies and antibodies induced on vaccination or infection, making use of S-protein-bearing reporter viruses, which represent an adequate surrogate model.
- Results: Bebtelovimab (LY-CoV1404) neutralised all subvariants tested with similarly high efficacy. Patients infected with BA.1 or BA.2: Neutralisation of BA.2.12.1 was similar to that of BA.2, whereas A.4/BA.5 neutralisation was markedly reduced compared with BA.2 and BA.2.12.1. We identified that BA.1 and BA.2 evaded neutralisation by antibodies that were induced on triple BNT162b2 (Pfizer-BioNTech) vaccination with similar efficiency (ie, 4·3-times reduced neutralisation for BA.1 and 4·2-times reduced neutralisation for BA.2 compared with B.1), as expected, whereas evasion by BA.2.12.1 (ie, 6·1-times reduced neutralisation compared with B.1) and particularly BA.4/BA.5 (ie, 8·1-times reduced neutralisation compared with B.1) was more efficient. A similar tendency was also observed for samples taken from individuals who had been triple vaccinated with BNT162b2 with subsequent BA.1 or BA.2 breakthrough infection

Arora P, et al. Lancet ID 2022;28 June

	B.1	BA.1	BA.2	BA.2.12.1	BA.4/BA.5
Casirivimab	12.1	1456	938	480	>5000
Imdevimab	11.8	>5000	415	345	844
Bamlanivimab	11.3	>5000	>5000	>5000	>5000
Etesevimab	22.2	>5000	>5000	>5000	>5000
Cilgavimab	21.7	2036	48.9	47.7	83.4
Tixagevimab	5.1	1253	1460	1322	>5000
Regdanvimab	2.9	>5000	>5000	>5000	>5000
Bebtelovimab	3.7	3.1	3.9	3.1	4.1
Sotrovimab	77.5	501	3060	3032	3840
S2H97	1269	1849	4958	4893	4771
Casirivimab / Imdevimab	6.6	1469	267	293	966
Bamlanivimab / Etesevimab	16.9	>5000	>5000	>5000	>5000
Cilgavimab / Tixagevimab	7.6	269	70.9	71.9	117

EC50 [ng/ml]

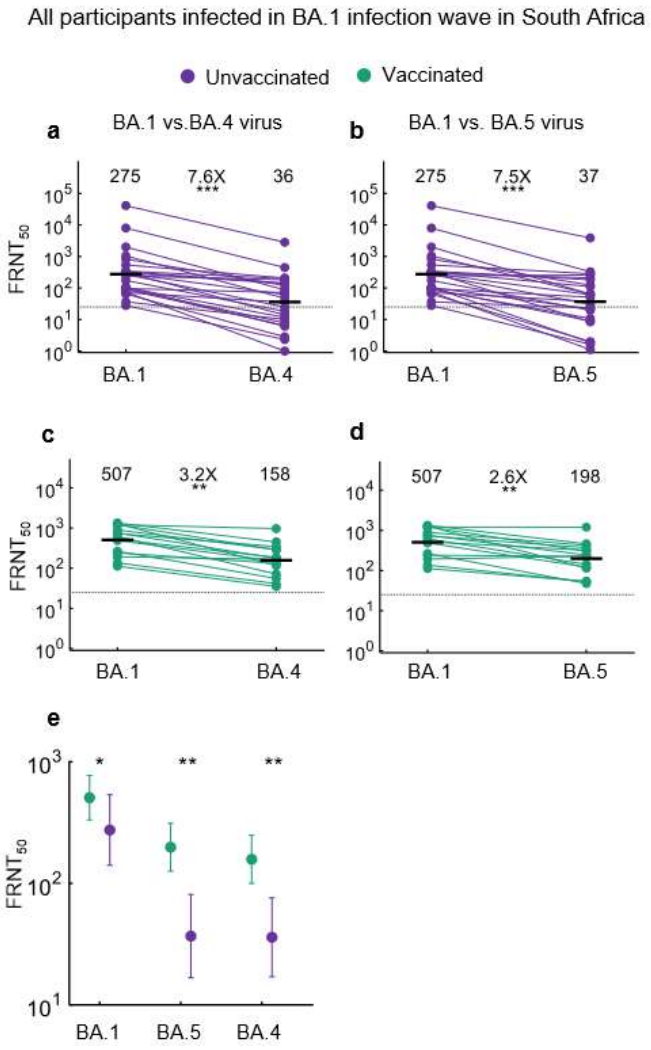
C)



Omicron sub-lineages BA.4/BA.5 escape BA.1 infection elicited neutralizing immunity

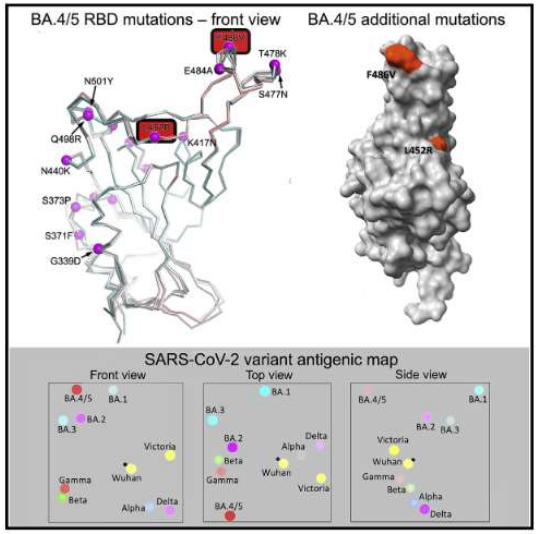
- Methods: We isolated live BA.4 and BA.5 viruses and tested them against neutralizing immunity elicited to BA.1 infection in participants who were Omicron/BA.1 infected but unvaccinated (n=24) and participants vaccinated with Pfizer or J&J vaccines with breakthrough Omicron/BA.1 infection (n=15).
- Results: In unvaccinated individuals, FRNT50, the inverse of the dilution for 50% neutralization, declined from 275 for BA.1 to 36 for BA.4 and 37 for BA.5, a 7.6 and 7.5-fold drop, respectively. In vaccinated BA.1 breakthroughs, FRNT50 declined from 507 for BA.1 to 158 for BA.4 (3.2-fold) and 198 for BA.5 (2.6-fold). Absolute BA.4 and BA.5 neutralization levels were about 5-fold higher in this group versus unvaccinated BA.1 infected participants
- Conclusion: The observed escape of BA.4 and BA.5 from BA.1 elicited immunity is more moderate than of BA.1 against previous immunity. However, the low absolute neutralization levels for BA.4 and BA.5, particularly in the unvaccinated group, are unlikely to protect well against symptomatic infection. This may indicate that, based on neutralization escape, BA.4 and BA.5 have potential to result in a new infection wave.

Khan K, et al, https://doi.org/10.1101/2022.04.29.22274477

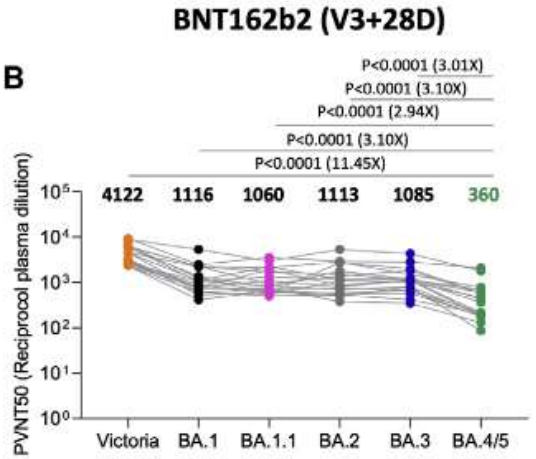


Antibody escape of SARS-CoV-2 Omicron BA.4 and BA.5 from vaccine and BA.1 serum

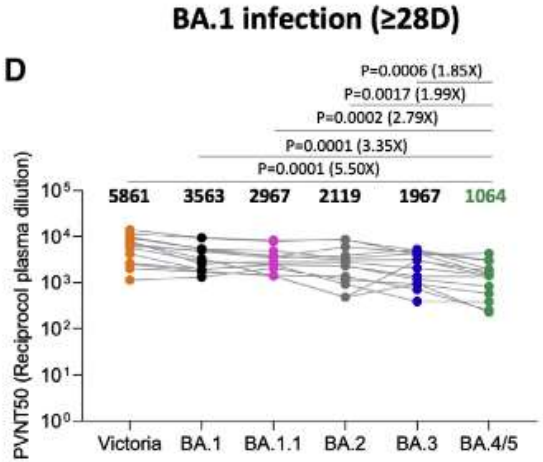
- BA.4/5 resist neutralization by triple-dosed vaccinee serum more than BA.1 and BA.2
- BA.1 vaccine breakthrough serum shows reduced neutralization of BA.4/5
- Activity of SARS-CoV-2 therapeutic antibodies against BA.4/5 is reduced
- L452R and F486V mutations both make major contributions to BA.4/5 escape



Tuekprakhon A, et al.
Cell 2022;185:2422 (July 7)



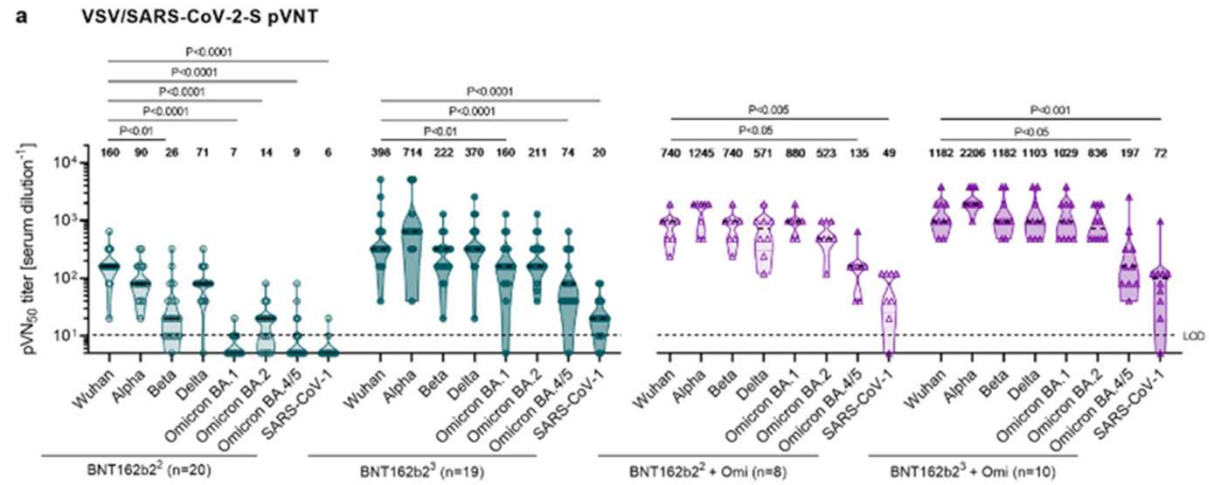
B. IC50 values for the indicated viruses using serum obtained from vaccinees 28 days following their after the third dose of Pfizer BNT162b2 (n = 19)

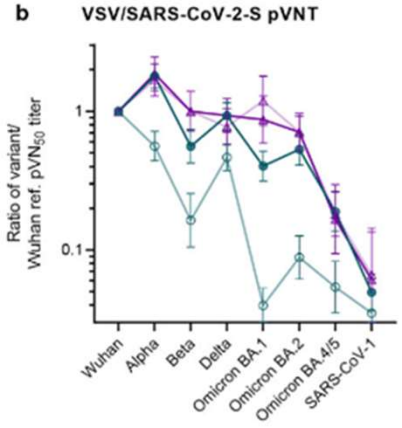


D. Serum from volunteers suffering break-through BA.1 infection taken late, i.e., R28 days from symptom onset (median 45 days) n = 14.

Omicron BA.1 breakthrough infection drives cross-variant neutralization and memory B cell formation against conserved epitopes

- We report that Omicron BA.1 breakthrough infection in BNT162b2-vaccinated individuals resulted in strong neutralizing activity against Omicron BA.1, BA.2 and previous SARS-CoV-2 VOCs, but not against the Omicron sublineages BA.4 and BA.5.



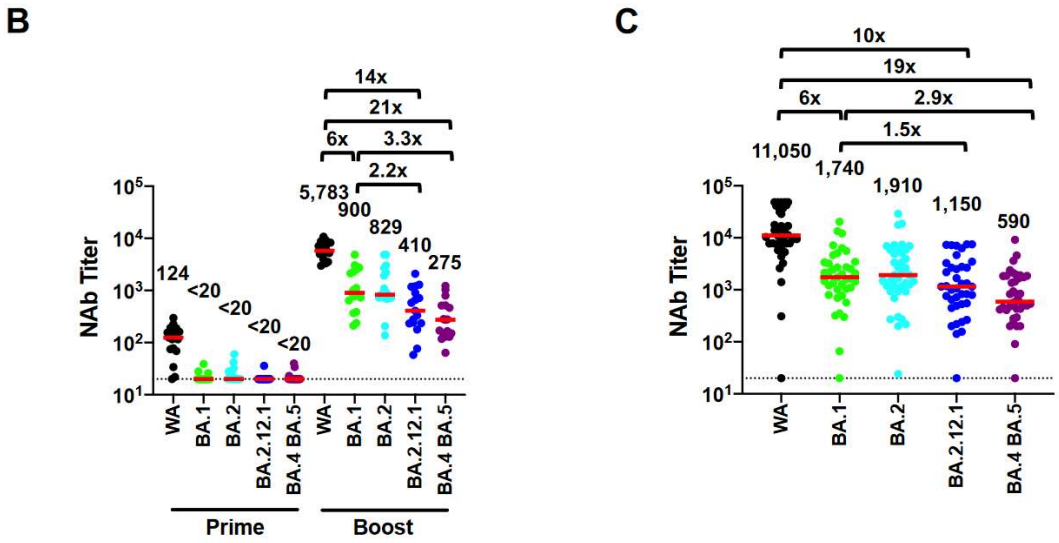


Geometric mean ratio	Alpha	Beta	Delta	Omi BA.1	Omi BA.2	Omi BA.4/5	SARS-CoV-1
BNT162b2² (n=20)	0.56	0.16	0.46	0.04	0.09	0.05	0.04
BNT162b2³ (n=19)	1.79	0.56	0.93	0.40	0.53	0.19	0.05
BNT162b2² + Omi (n=8)	1.68	1.00	0.77	1.19	0.71	0.18	0.07
BNT162b2³ + Omi (n=8)	1.87	1.00	0.93	0.87	0.71	0.17	0.06

Quandt J, et al
Science Immunology 2022;2 June

Neutralization Escape by the SARS-CoV-2 Omicron Variants BA.2.12.1 and BA.4/BA.5

- Our data show that BA.2.12.1 and BA.4/BA.5 substantially escape NAbs induced by both vaccination and infection. Moreover, BA.4/BA.5 NAb titers, and to lesser extent BA.2.12.1 NAb titers, were lower than BA.1 and BA.2 NAb titers, suggesting that the SARS-CoV-2 Omicron variant has continued to evolve with increasing neutralization escape.



B. Neutralizing antibody (NAb) titers by a pseudovirus neutralization assay in individuals 6mo following initial BNT162b2 vaccination (Prime) and 2wk following BNT162b2 boost (Boost). C. NAb titers in individuals following infection with BA.1 or BA.2. All were vaccinated except for the one individual with negative NAb titers. NAb responses were measured against the SARS-CoV-2 WA1/2020, Omicron BA.1, BA.2, BA.2.12.1, and BA.4/BA.5 variants. Medians (red bars) are depicted and shown numerically with fold differences

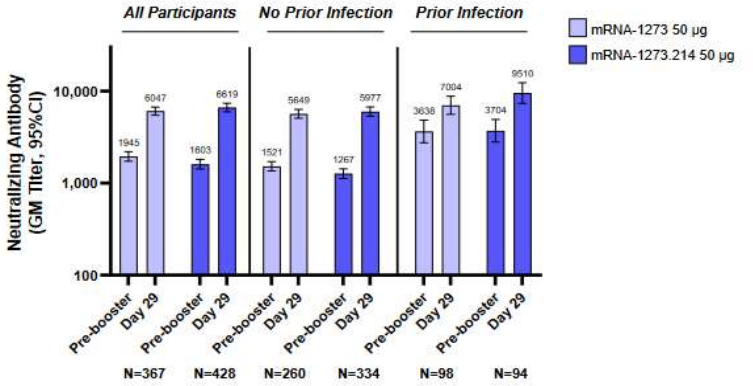
Hachmann NP, et al.
https://www.medrxiv.org/content/10.1101/2022.05.16.22275151v1

A Bivalent Omicron-containing Booster Vaccine Against Covid-19

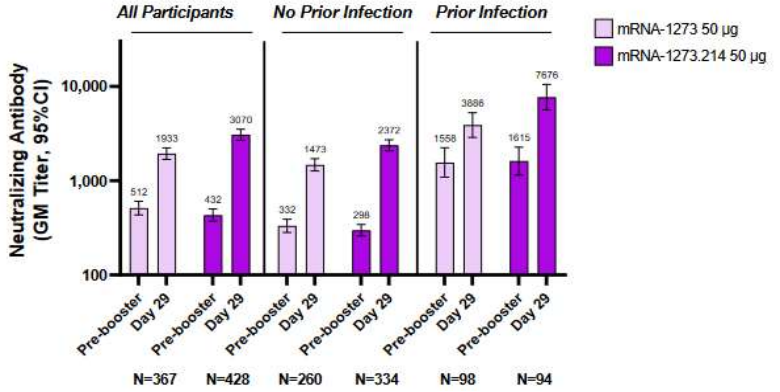
- Methods: In this ongoing, phase 2/3 trial, the 50-µg bivalent vaccine mRNA-1273.214 (25-µg each ancestral Wuhan-Hu-1 and omicron B.1.1.529 spike SARS-CoV-2 mRNAs) was compared to the authorized 50-µg mRNA-1273 booster in adults who previously received 2-dose primary series of 100-µg mRNA-1273 and a first booster dose of 50-µg mRNA-1273 at least 3 months prior.
- Results: In participants with no prior SARS-CoV-2 infection, observed omicron neutralizing antibody geometric mean titers (GMTs [95% confidence interval]) after the mRNA-1273.214 and mRNA-1273 booster doses, were 2372.4 (2070.6−2718.2) and 1473.5 (1270.8−1708.4) respectively and the model-based GMT ratio (97.5% confidence interval) was 1.75 (1.49−2.04). mRNA-1273.214 50-µg induced a potent neutralizing antibody response against omicron subvariants BA.4/BA.5. GMT, fold-rise compared to pre-booster level in subjects without prior SARS-CoV-2 against BA.4 and BA.5 was 6.3 (5.7-6.9)

Figure 3: Observed Neutralizing Antibody Titers Against Ancestral SARS-CoV-2 (D614G) and Omicron after 50-µg of mRNA-1273.214 and mRNA-1273 Administered as Second Booster Doses

A. Ancestral SARS-CoV-2 (D614G)

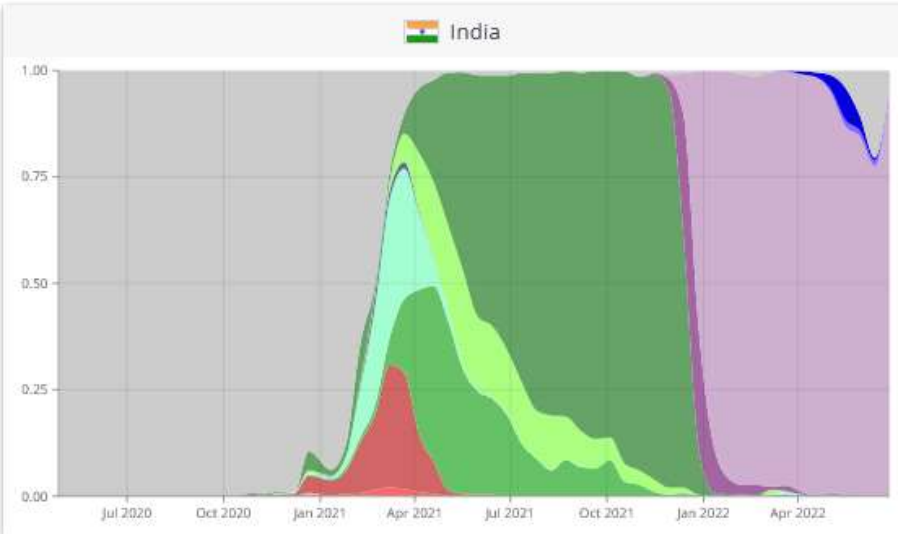


B. Omicron

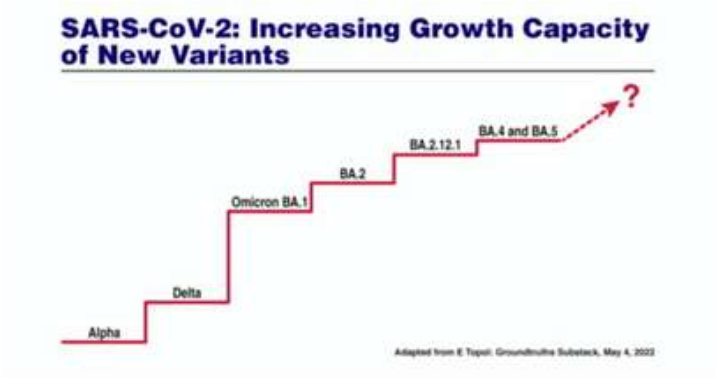


Chalkias S et al. https://www.medrxiv.org/content/10.1101/2022.06.24.22276703v1.full.pdf

OMICRON BA.2.75



- ~25% of cases in India; outcompeting BA.5
- Rare cases in US (CA, NC, IL, TX, WI, WA); cases reported from 14 countries
- 9 mutations in spike region compared to B.A.2 and 11 changes compared to BA.5 – may aid in immune evasion



H Covid-19 Response Team

CONCLUSIONS: BA.4 AND BA.5

- BA.4 and BA.5 now the predominant Omicron variants in US and UNC-MC; expected to dominate COVID-19 infections
- Likely derived from BA.2; the spike proteins of BA.4 and BA.5 are identical, and comparable to BA.2 except for the addition of 69-70del, L452R, F486V and the wild type amino acid at Q493
- BA.4 and BA.5 have a growth advantage over other Omicron variants, likely due to escape from immunity conferred by prior infection and vaccines
- Clinical course and severity similar to BA.1 and BA.2
- Prior infection with Delta (or earlier variant) provides poor protection against reinfection; prior infection with BA.1 or BA.2 provides better, but incomplete protection against reinfection
- Vaccine superior to prior infection for protection against infection; 3 (or 4) doses of an mRNA vaccine superior to 2 doses
- Vaccine better at preventing serious disease than preventing infection
- Evusheld and bebtelovimab continue to remain effective for pre-exposure prophylaxis and treatment (but reduced activity)
- Antivirals (Paxlovid and Molnupivir) remain effective against all COVID-19 variants including BA.4 and BA.5
- Prediction: Continued moderate to high transmission in the community (cases undercounted); continued (or increased) levels of hospitalizations and deaths over the next weeks/months
- Future: Moderna and Pfizer expect to have bivalent vaccines (i.e., include an Omicron variant) available in the Fall

Nightmare on Chestnut St: Monkeypox in a HCP

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SHEA Town Hall

July 17,2022

9pm Phone Call

- Received a call from a supervisor that a HCP (in training) with direct patient contact had monkeypox
- Had worked with patients and was in close quarters with multiple other types of HCP daily while symptomatic for 2 weeks
- Had also sought care as a patient multiple times in two of our ED's and our employee health department while symptomatic

Decision point #1: Launch exposure investigation in the middle of the night or wait until morning?

Decision 1: Both

- Immediate 3-way call with the HCP and training program supervisor
  - Obtained thorough history from HCP: exactly where was he and what did he do at work since symptom onset?
- Immediately notified Chief Physician Executive, Hospital President and Medical Director of Employee Health
- Put infrastructure in place for emergency work group using modified incident command structure to perform massive exposure work up with plans to launch at 6 am

Details….Where was he? What did he do?

- 6/28-HCP is notified that swab of skin lesion is positive for orthopox

----------→going backward in time:

- 6/12: MSM Sexual exposure (receptive) while on a weekend away
- 6/14: Back to work
  - Worked with patients, care teams, nurses, physicians, other people in training program daily for subsequent two weeks
  - Always wore a mask (mandatory), ate alone
  - Has one roommate who is also a HCP in training
- 6/14 -6/23 sore throat minimal with peritonsillar erythema and no cervical lymphadenopathy
- 6/16 –fever and chills: employee health visit, testing for COVID-19 (-), cleared to RTW
- 6/16 – 1st lesion, lower abdomen
- 6/17 – Sought care in our ED for testicular swelling: underwent ultrasound and physical examination
- 6/19- Returned to ED: assessed by triage nurse, underwent vitals and COVID testing (negative)left due to long wait time
- 6/20 - Sought care in another of our ED's: underwent ultrasound and physical examination
- 6/23 – 2nd & 3rd lesions noted at Left thigh and Left infra-areolar region; covered by clothing. Developed Rectal pain
- 6/24 – Rash/lesions progressed: more lesions at abdomen/trunk; covered by clothing; Proctitis worsened with mucous per rectum.
- 6/25 –Walked through ED , decided wait was too long so left without being seen and went to sleep on a couch in a breakroom-no use of blankets or pillows. Lesions all covered by clothing
- 6/26 –Developed hand and forearm lesions. Day off from work. Received text from sex partner notifying him of monkeypox exposure
- 6/27 --Covered exposed lesions on hands with Band-Aids, came to work, left at noon to get testing for Monkeypox
- 6/28-received positive result

How bad is this?

- HCP in training who had direct contact with patients & coworkers, and was a patient himself
- Two weeks of potential exposures
- Three separate considerations:
  - Were patients exposed?
  - Were coworkers exposed?
  - Were HCP who cared for him in the ED and EHS exposed?
- Need to protect privacy of HCP
  - Vulnerable position
  - Stigmatizing disease

Next Steps: Establish Modified incident command response team

- Get the right people in the room:
  - EHS, Hospital Epi, Infection Prevention, supervisor, DPH by conf call
  - Determine tasks, assign duties
- Get the right people on the phone:
  - Hospital leadership
  - Public Affairs/communications
  - IT to help pull data and activate employee symptom monitoring app
  - Pharmacy for vaccine management
  - EVS-clean common areas

Decision Point # 2:Determine exact exposure definition

- Define what constitutes an exposure
  - CDC Definition: “Direct contact with lesion material or from exposure to respiratory secretions“[1]
    - Exactly what does that mean?
      - Patients, coworkers, HCP’s, the couch and other workspaces, the roommate?
      - Droplet, contact, fomites?
  - CDC definition: Lesions are contagious “until all lesions have crusted, those crusts have separated, and a fresh layer of healthy skin has formed”[1]
    - Exactly what does that mean?
      - If the skin under the separated scabs is still pink, is it still contagious?
      - Does contact with a HCP whose lesions are covered count towards exposures?

1. https://www.cdc.gov/poxvirus/monkeypox/clinicians/infection-control-healthcare.html

Next Steps continued

- Prepare to generate lists of exposed people
- There could be hundreds…Where do you find that information?
  - Patient lists: Patient assignment lists, notes in EHR vs. all patients on a unit
  - Employee schedules: coworkers who worked with the source
  - ED and EHS HCP who cared for him: EHR notes
- Prepare scripts for exposure notifications
- Prepare talking points for managers
- Prepare to mitigate fallout/panic

Decision point #3: Who is considered exposed?

- Key definitions needed to determine who to consider exposed
  - Thank you to MA DPH for the following definitions:

1) Respiratory exposure=
   - >3 hrs unmasked <6 feet apart
2) Contact exposure=
   - Direct contact with lesion fluid or mucous membranes while not wearing full PPE
     - Defined as eye protection, N95, gown & gloves
   - Lesions covered by clothing, bandages or gloves= no exposures
3) Fomites= couch, workspaces/computers are not exposures

Were patients exposed?

- The HCP wore a mask consistently with patients
- All lesions were covered by clothing
- The day that lesions were present on hands, he did not examine patients

- THEREFORE: NO PATIENTS WERE EXPOSED

- whew

Were coworkers exposed?

- The HCP wore a mask consistently while in the hospital and with colleagues in shared work spaces
- The HCP ate alone
- Fomites such as the couch, computers and phones were not considered to be sources of exposures
- All lesions were covered at all times

THEREFORE: NO COLLEAGUES WERE CONSIDERED EXPOSURES

Whew…

Were HCP who cared for him exposed?

- 3 ED visits, 2 EHS visits

Degree of Exposure: High	Monitoring PEP – Recommended
Degree of Exposure: Intermediate	Monitoring PEP– Informed clinical decision making recommended on an individual basis to determine whether benefits of PEP outweigh risks
Degree of Exposure: Low/Uncertain	Monitoring PEP– None
Degree of Exposure: No Risk	Monitoring– None PEP – None

https://www.cdc.gov/poxvirus/monkeypox/clinicians/monitoring.html

Were HCP who cared for him exposed?

- HCP who examined or performed and ultrasound on his genitals while not wearing appropriate PPE were classified as **High risk exposures**
- HCP who did not examine or perform an ultrasound on his genitals while not wearing appropriate PPE were classified as **low risk exposures**
- All other people in the ED or EHS (patients, HCP not involved in his care) were classified as **no risk**

- Total exposures:
  - 5 High risk
  - 19 low risk

Management of exposed HCP

- 5 high risk HCP plus roommate were offered Jynneos vaccine if within 14 days of exposure
  - 4 HCP plus roommate accepted vaccine
  - Shipped from DPH to our pharmacy (both doses in the series)
- All: Twice daily symptom check
  - Repurposed our employee COVID-19 app to enable Monkeypox symptom self-attestation through day 21 after exposure
- Tracked by EHS
- Defined non-compliant as missing two attestations
  - Employee contacted by EHS
  - Taken off schedule until compliant

- Worried well during follow up period: examined HCP with pimples and poison ivy
- Exposure period is over: no HCP or roommate Monkeypox transmissions

Communications & messaging

- Tough decision: Communication to the whole organization or only to involved departments?
  - Worked with senior leadership to determine that sensitive case required targeted communication to ED staff only
  - Communication also included education on clinical presentation and to increase index of suspicion
- RCA-missed diagnosis, learning opportunity
  - ID now fielding many calls to evaluate rashes in ED

Return to work

- What exactly does “crusts have separated, and a fresh layer of healthy skin has formed” mean?
  - Worked with DPH for more precise definition
    - This means that all scabs have fallen off and no open skin remains. Pink skin underneath is OK/not contagious
  - EHS and an Associate Hospital Epi Assessed HCP in controlled setting last week
    - All lesions completely healed
    - Returned to work

Lessons Learned

- We were guarding the front door, but our first case was already in the house:
  - Ensure EHS is prepared with tools to manage HCP exposures, follow up, ability to vaccinate, messaging about presenteeism
- Monkeypox symptoms are non-specific until rash appears. Presenting as STI in current outbreak. EPIDEMIOLOGIC RISK is very important.
- Educate, Educate, Educate: ED, Urgent Care, Primary Care, Sexual health clinics. What to look for, what to do
- COVID-19 mandatory mask policy saved us from a massive monkeypox exposure!!
- DPH-key partner for determining exposures and management