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The Society for Healthcare Epidemiology of America

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The Rapid Response Podcast

COVID-19 Updates: What We Know Now

Releases monthly

Newest Episodes:

- Back to School
- BA.4, BA.5 Updates

LEARNINGCE SHEA Online Education Center

LearningCE.shea-online.org

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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.

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www.ortp.shea-online.org

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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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PreventionCHKC.org

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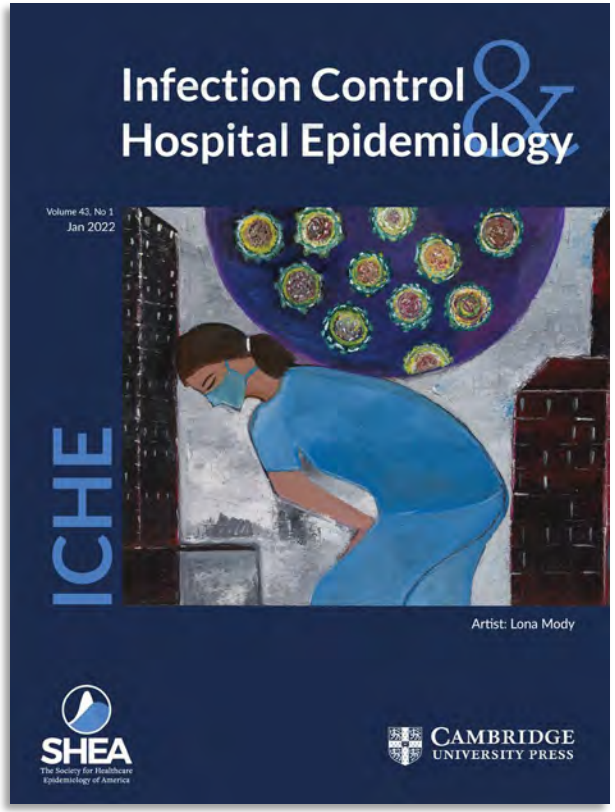
ICHE Journal – Fast Tracking COVID Article Submissions



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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ASHE JOURNAL

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IDWeek
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Registration is open!
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Oct. 19-23, 2022

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In Case of Technical Difficulties:

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  - 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:

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

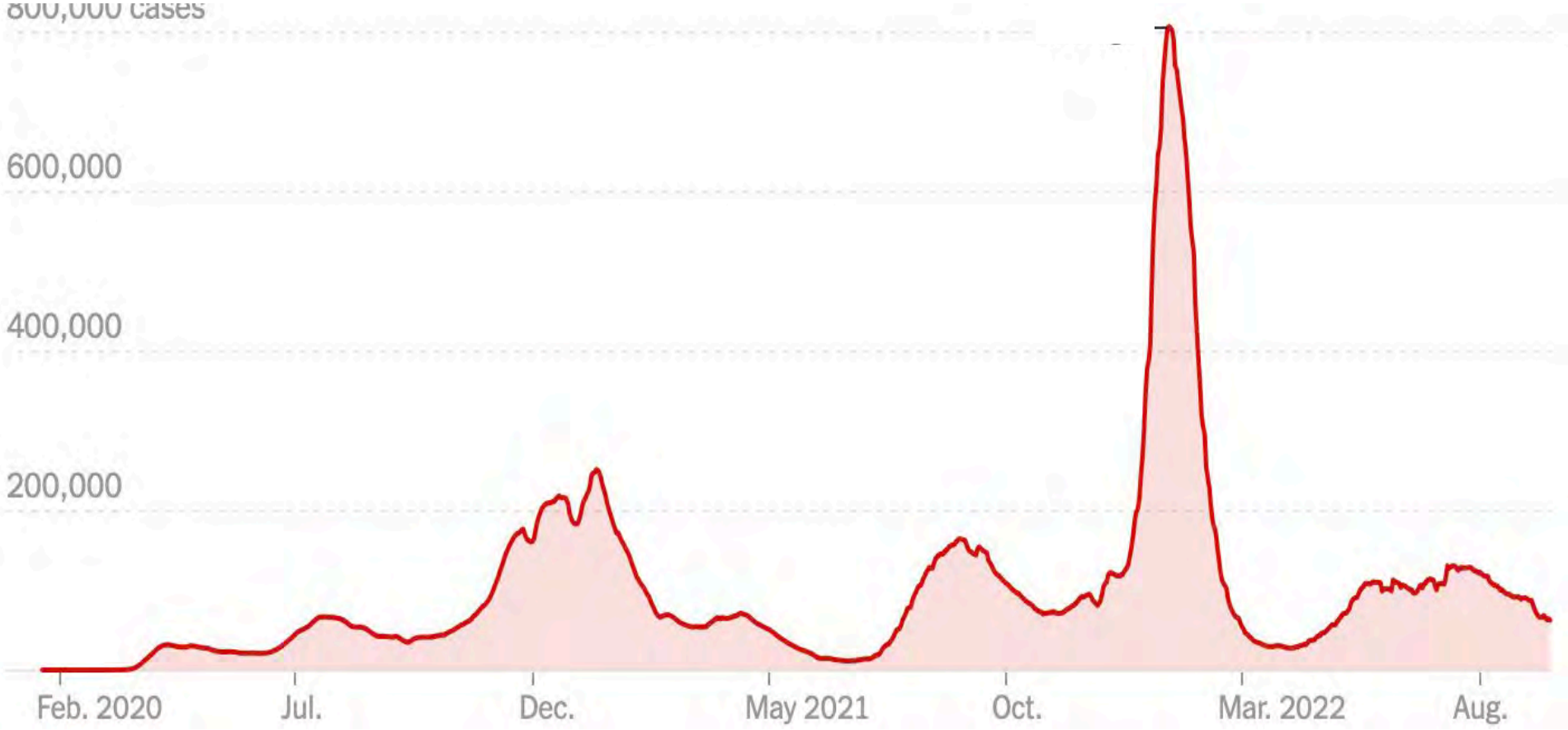
Streaming Live on SHEA's Facebook page

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

Reported COVID-19 Cases in the United States

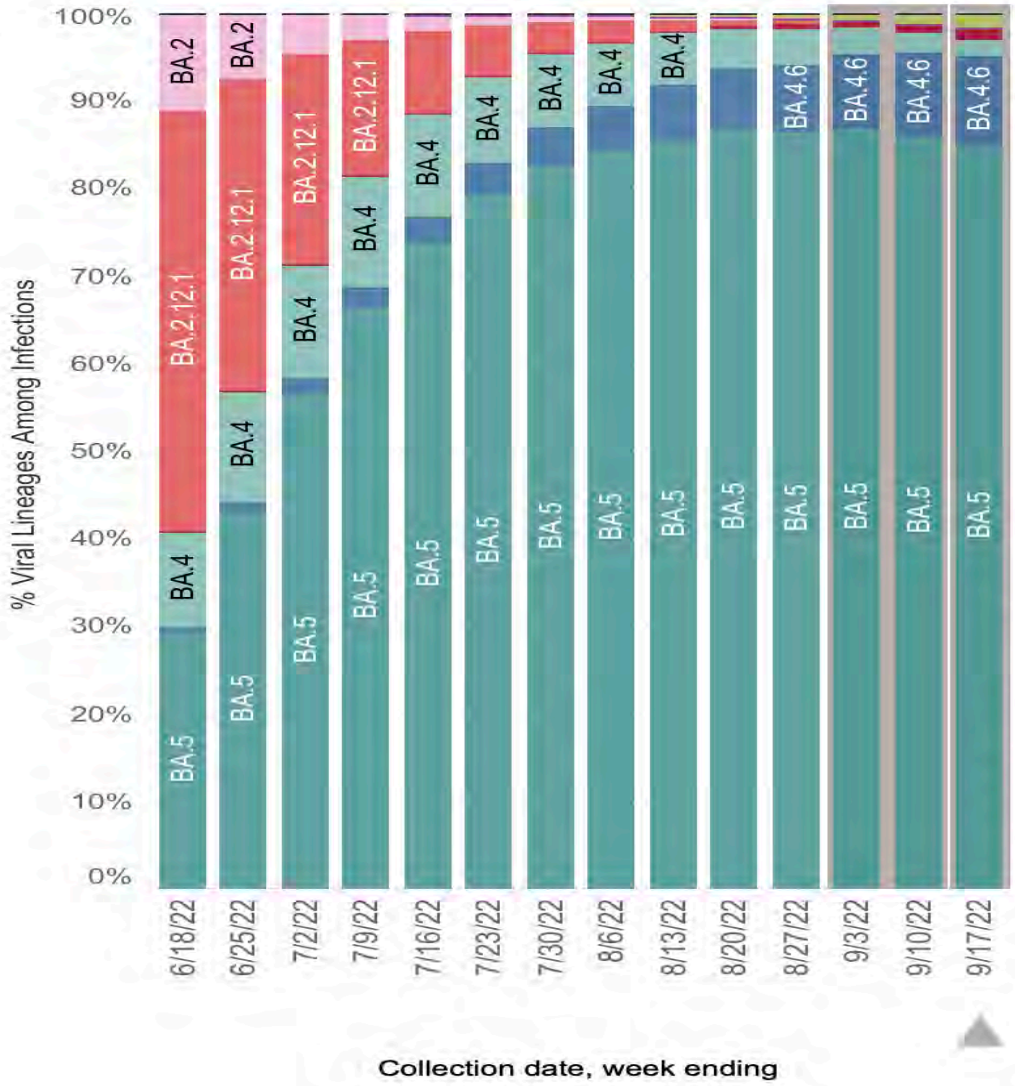
Cumulative Cases – 95,442,102



Cases decreased by 29% from two weeks earlier

Source: New York Times 9-18-22

SARS-CoV-2 Variants, US, CDC



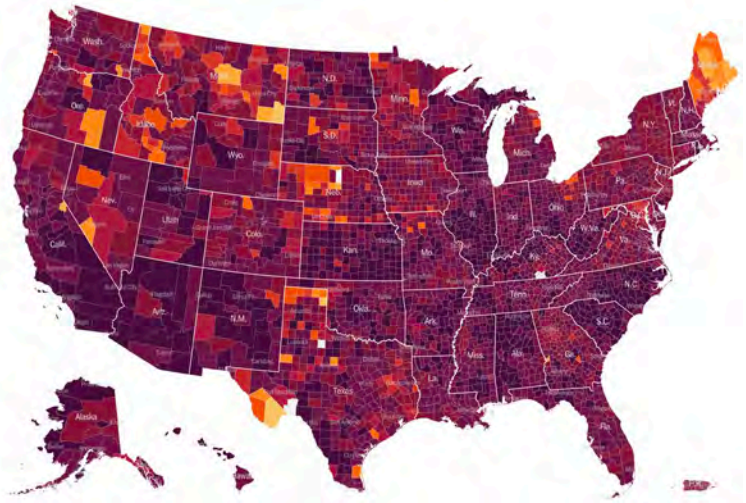
USA

WHO label	Lineage #	US Class	%Total	9.
Omicron	BA.5	VOC	84.8%	83.2
	BA.4.6	VOC	10.3%	9.1-
	BA.4	VOC	1.8%	1.6-
	BF.7	VOC	1.7%	1.2-
	BA.2.75	VOC	1.3%	0.8-
	BA.2.12.1	VOC	0.0%	0.0-
	BA.2	VOC	0.0%	0.0-
	B.1.1.529	VOC	0.0%	0.0-
	BA.1.1	VOC	0.0%	0.0-
Delta	B.1.617.2	VBM	0.0%	0.0-
Other	Other*		0.0%	0.0-

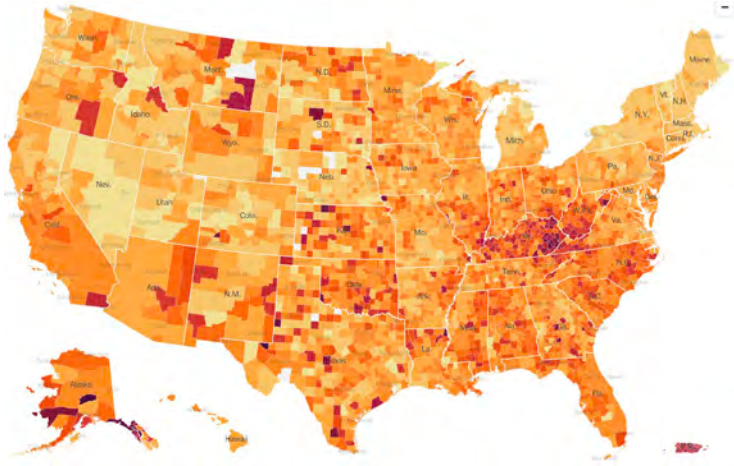
* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ 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. Except BA.2.12.1, BA.2.75 and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of..

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

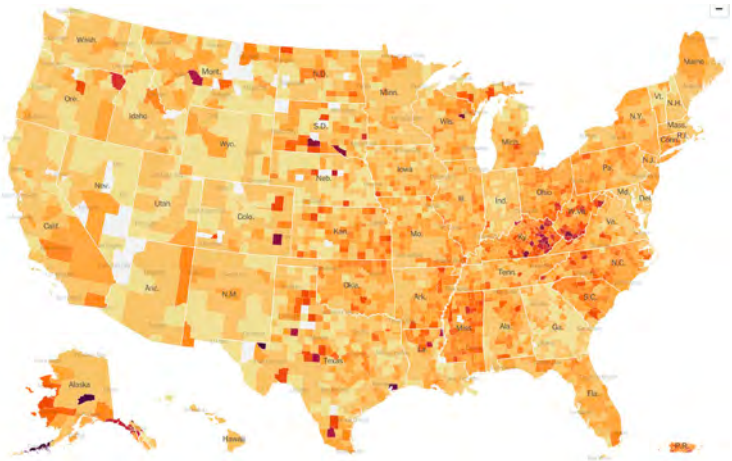
US COVID-19 HOTSPOTS



February 6, 2022



August 14, 2022



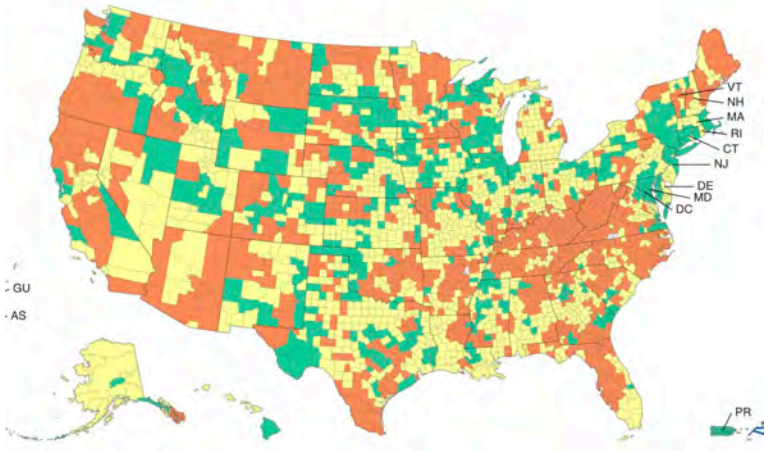
September 18, 2022

Average daily cases per 100,000 people in past week

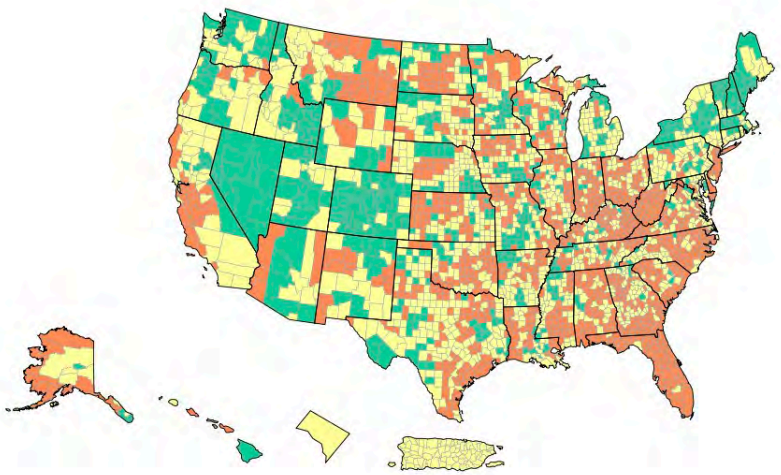
10 30 50 70 100 250 Few or no cases

Source: New York Times 9-18-2022

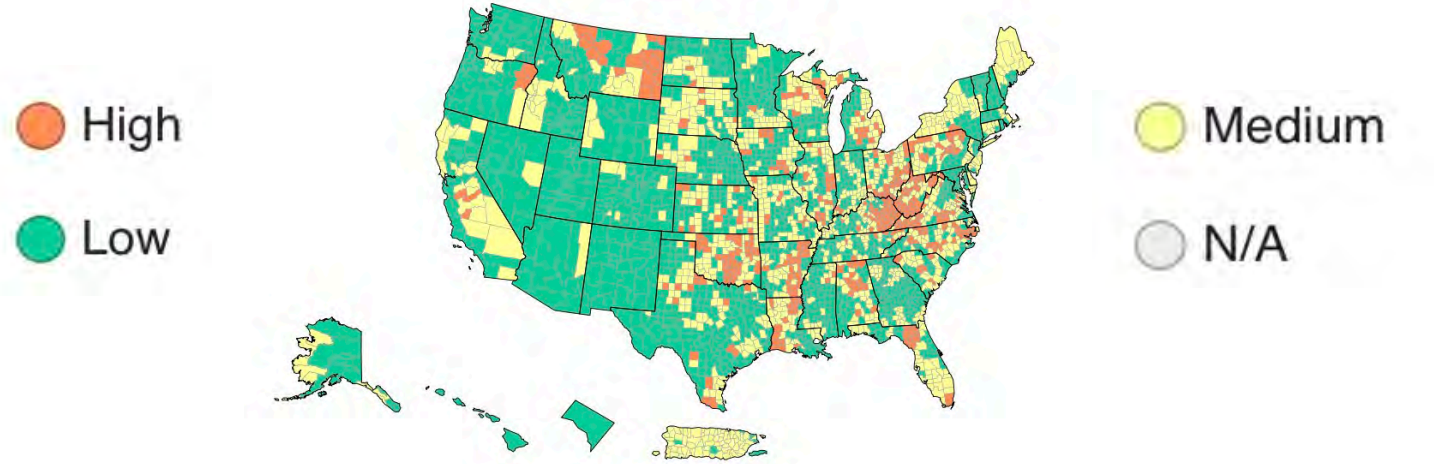
CDC COVID-19 COMMUNITY LEVELS



February 27, 2022



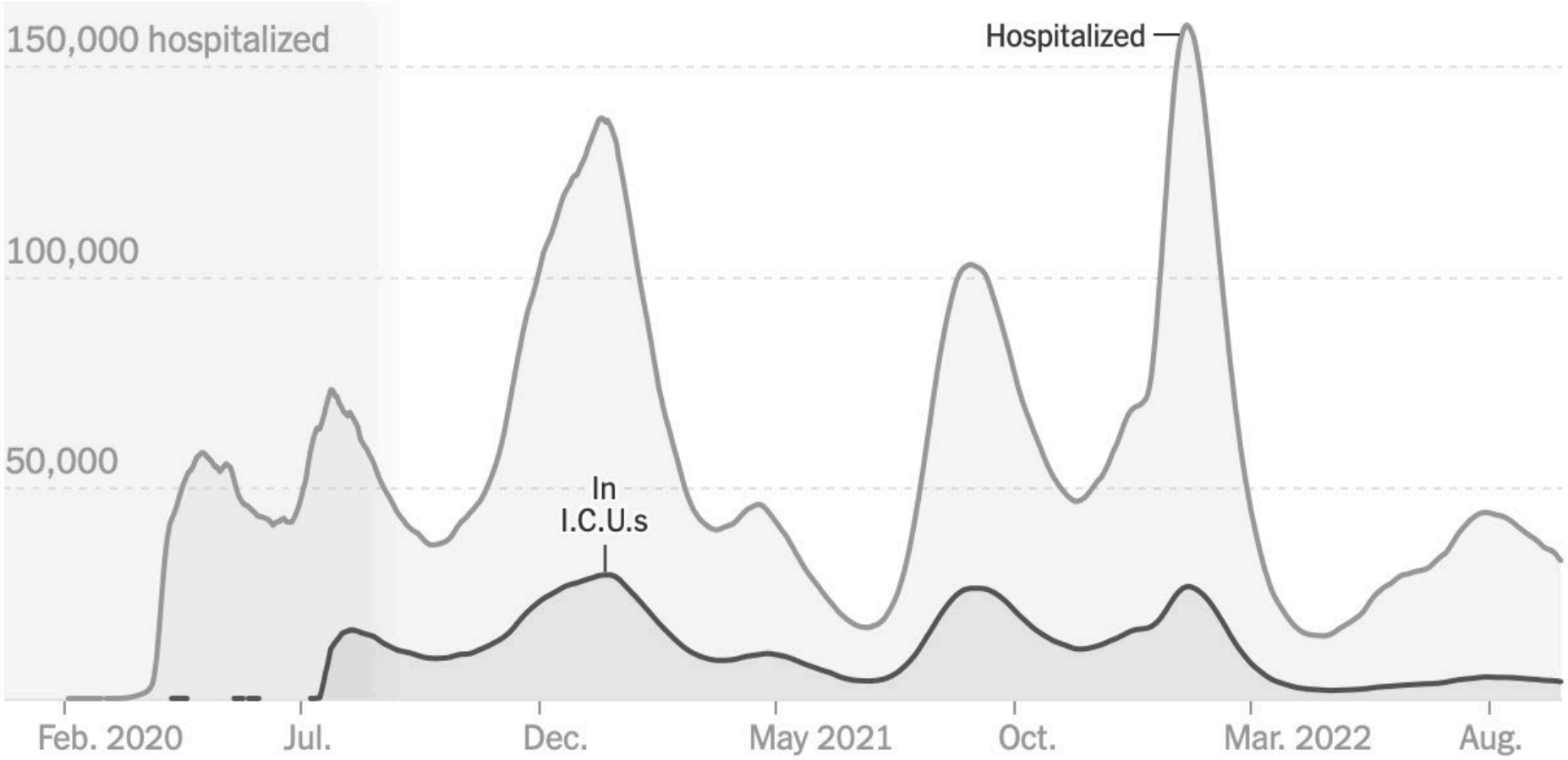
August 14, 2022



August 14, 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



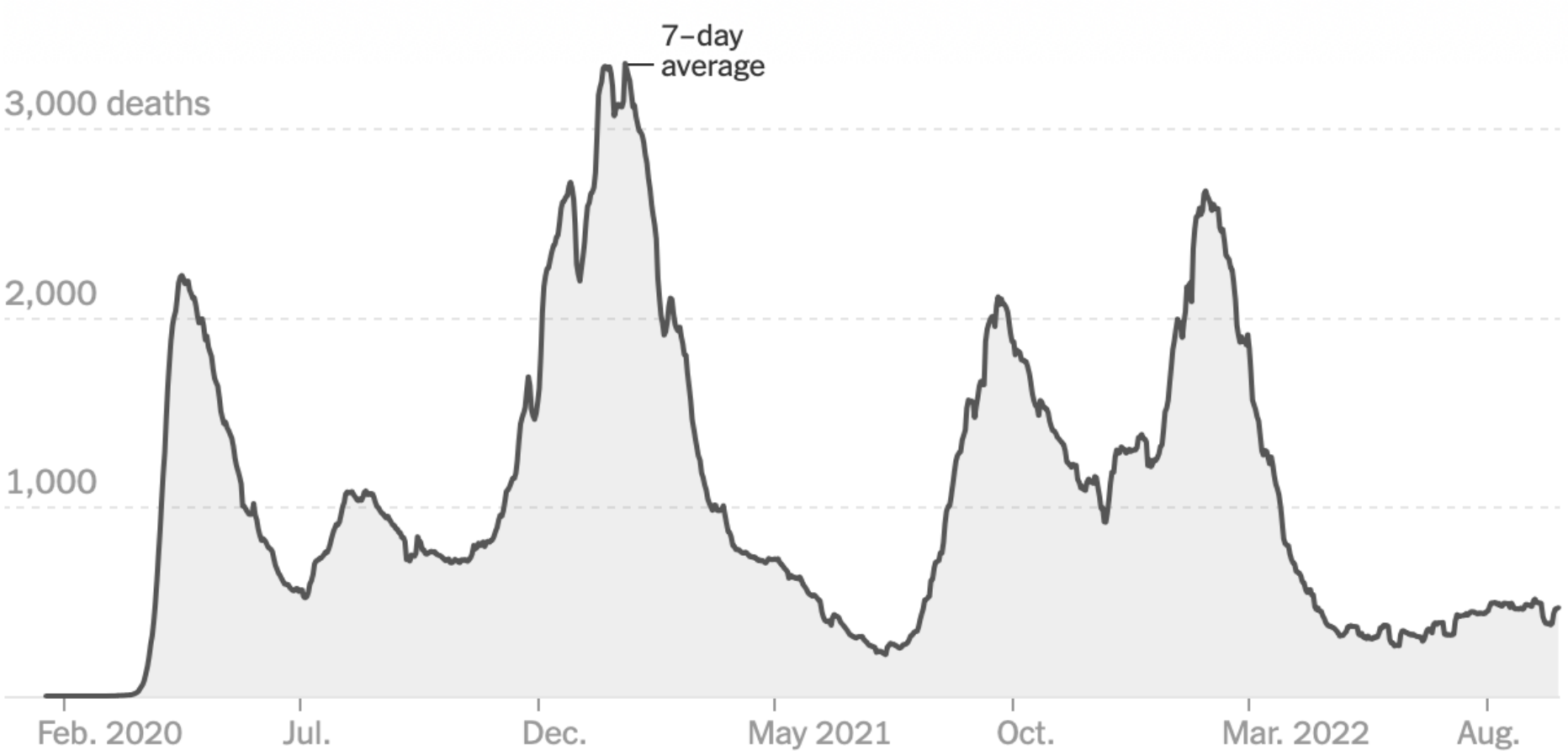
Hospitalizations decreased 12 % from two weeks earlier

ICU hospitalization decreased 10 % from two weeks earlier

Source: New York Times 9-18-22

COVID-19 Deaths in the United States

Cumulative Deaths – 1,049,741



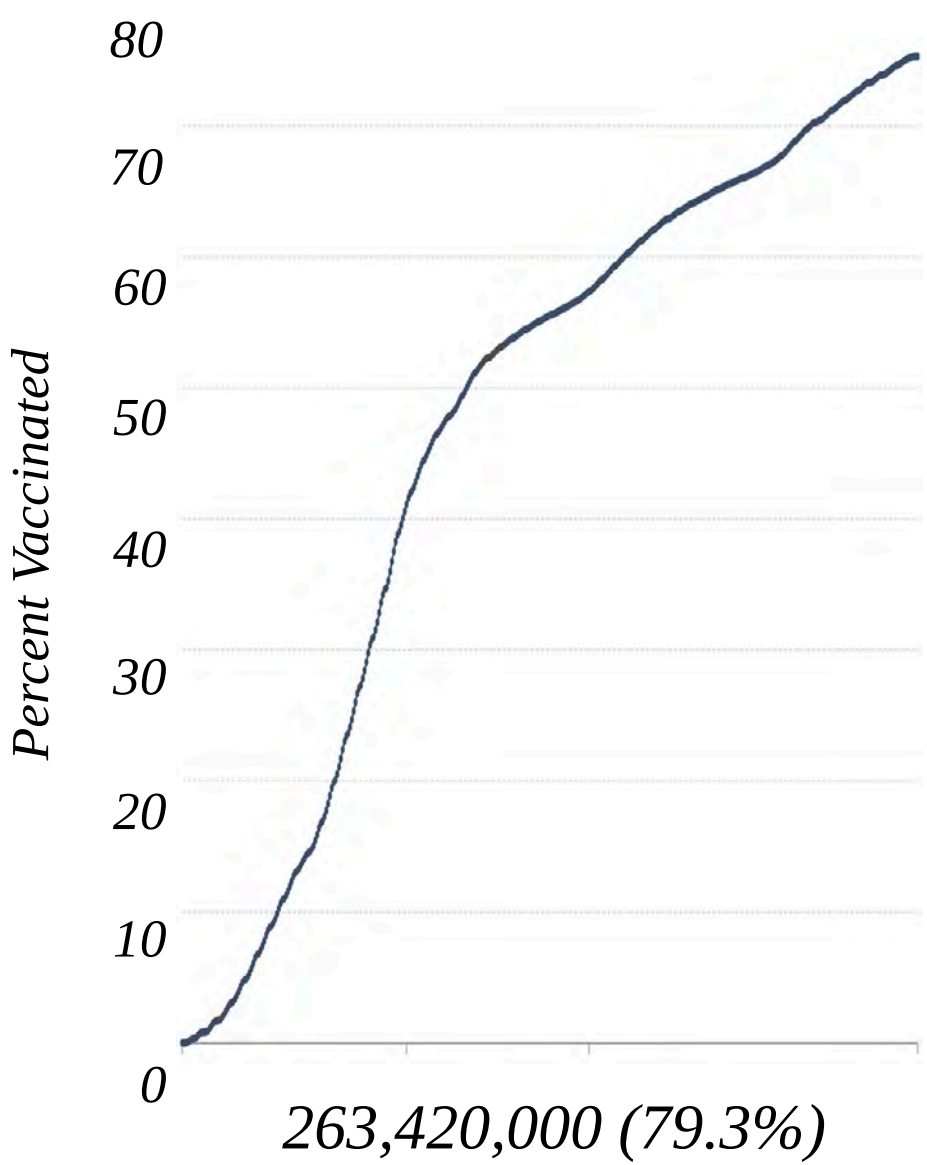
6 % decrease from two weeks earlier

Source: New York Times 9-18-22

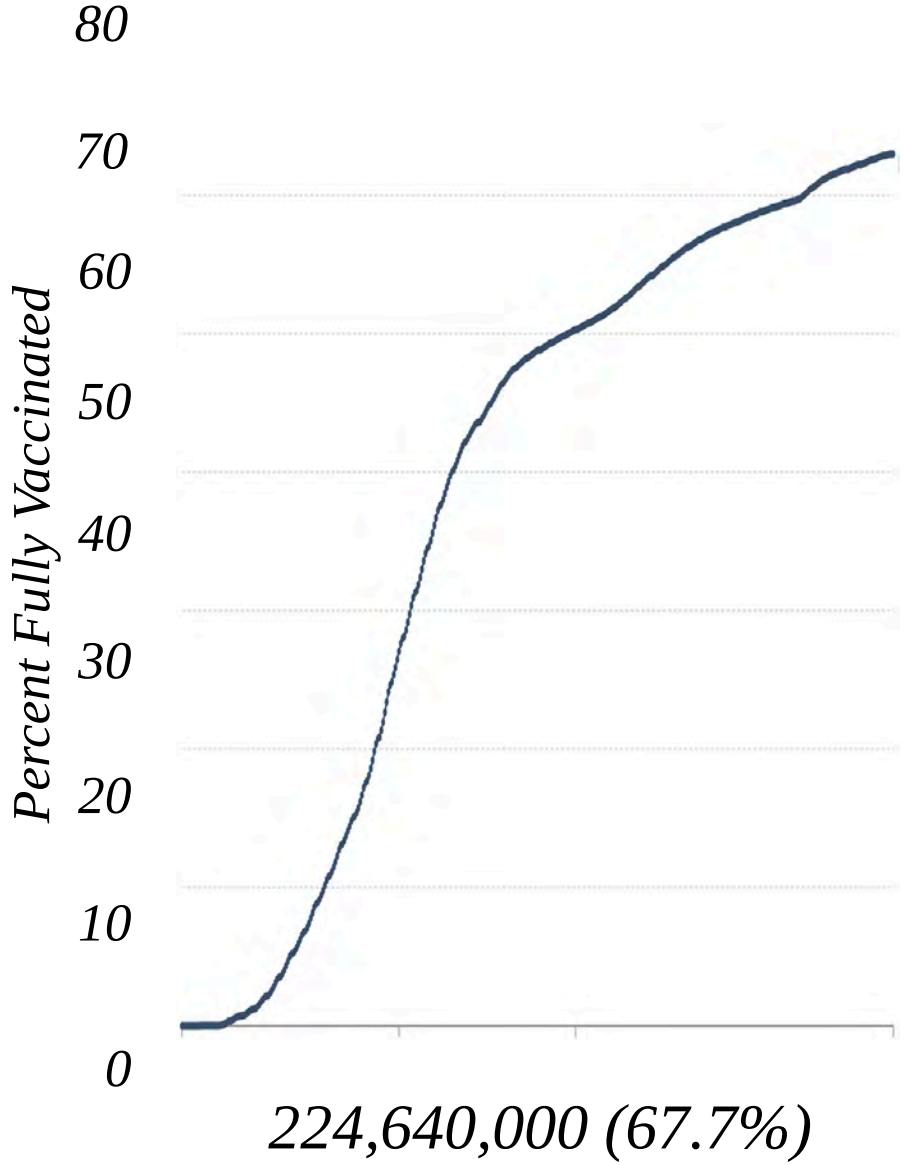
DAILY COVID-19 VACCINATIONS IN THE UNITED STATES

Source: Our World in Data 9-17-22

COVID-19 VACCINATIONS IN THE UNITED STATES



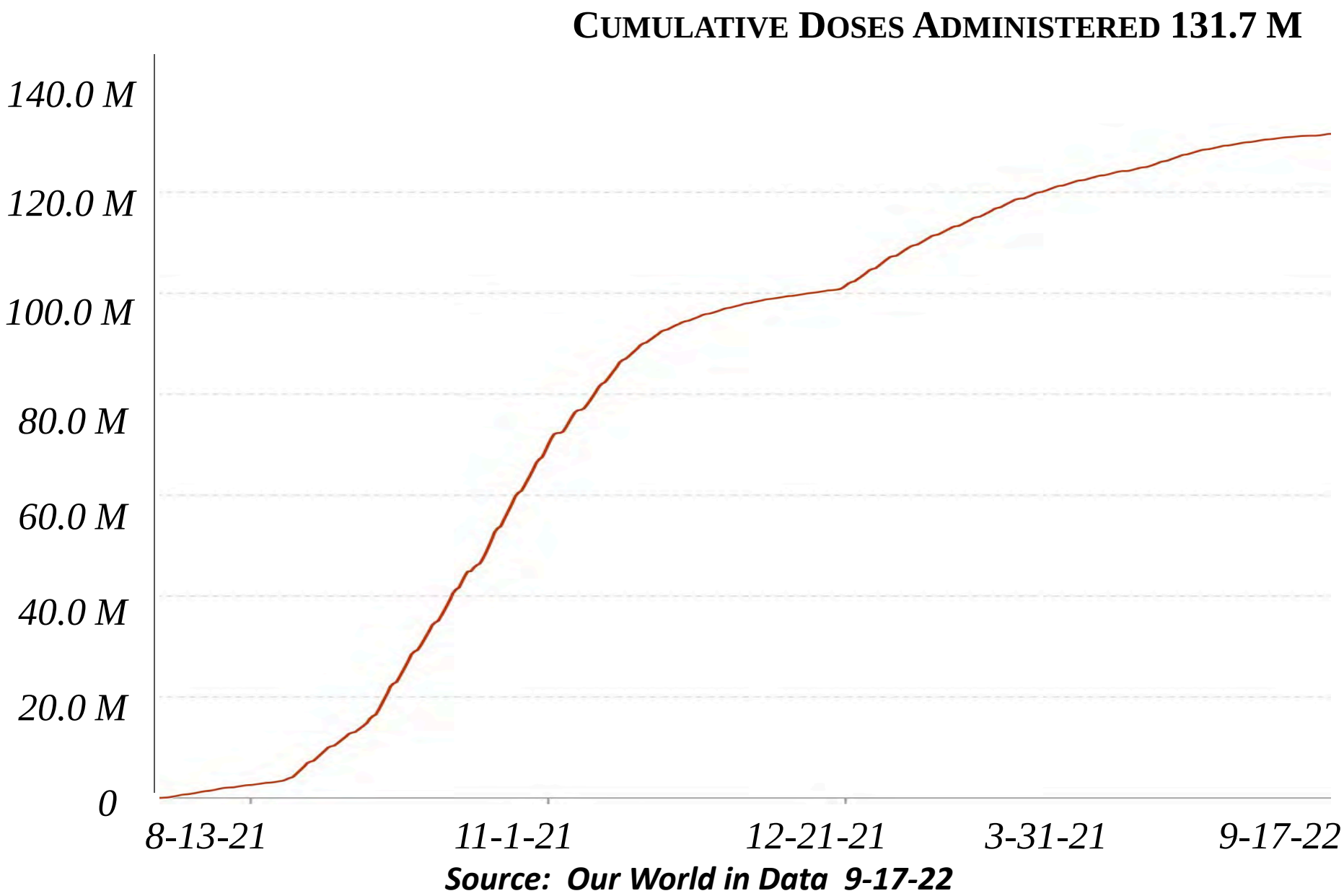
263,420,000 (79.3%)



224,640,000 (67.7%)

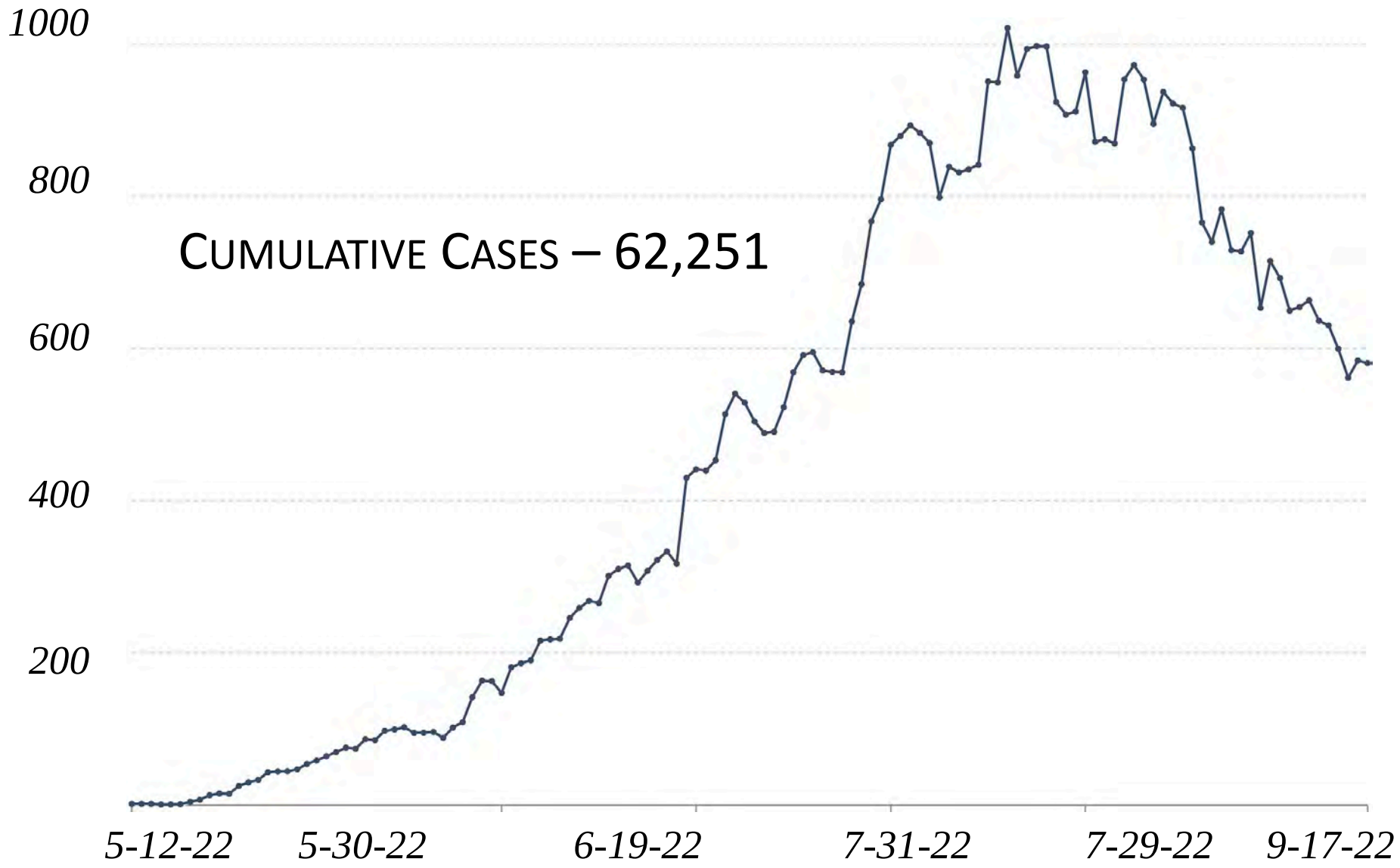
Source: Our World in Data 9-17-22

COVID-19 Booster Doses in the United States



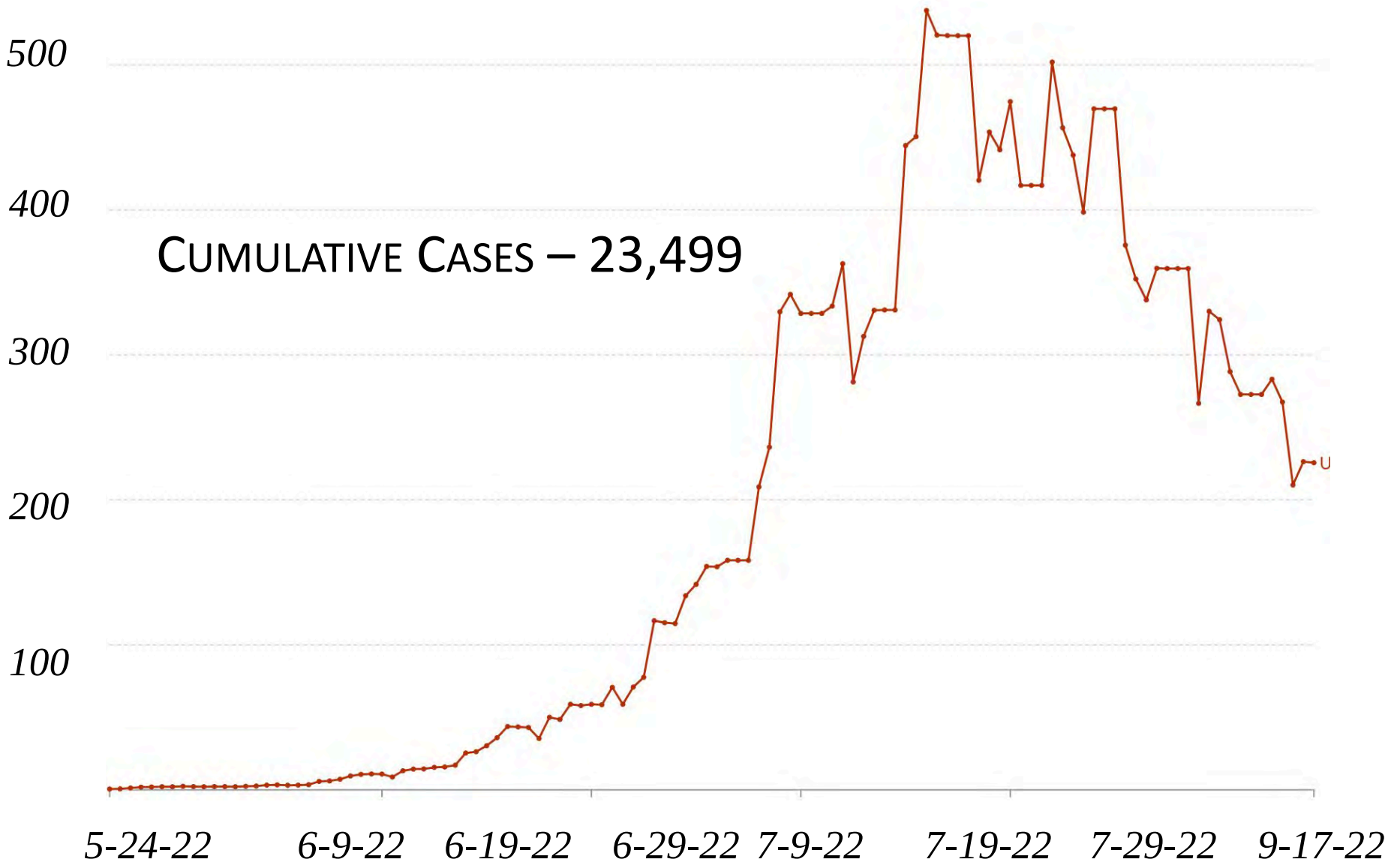
Source: Our World in Data 9-17-22

MONKEYPOX OUTBREAK: DAILY CASES, WORLDWIDE



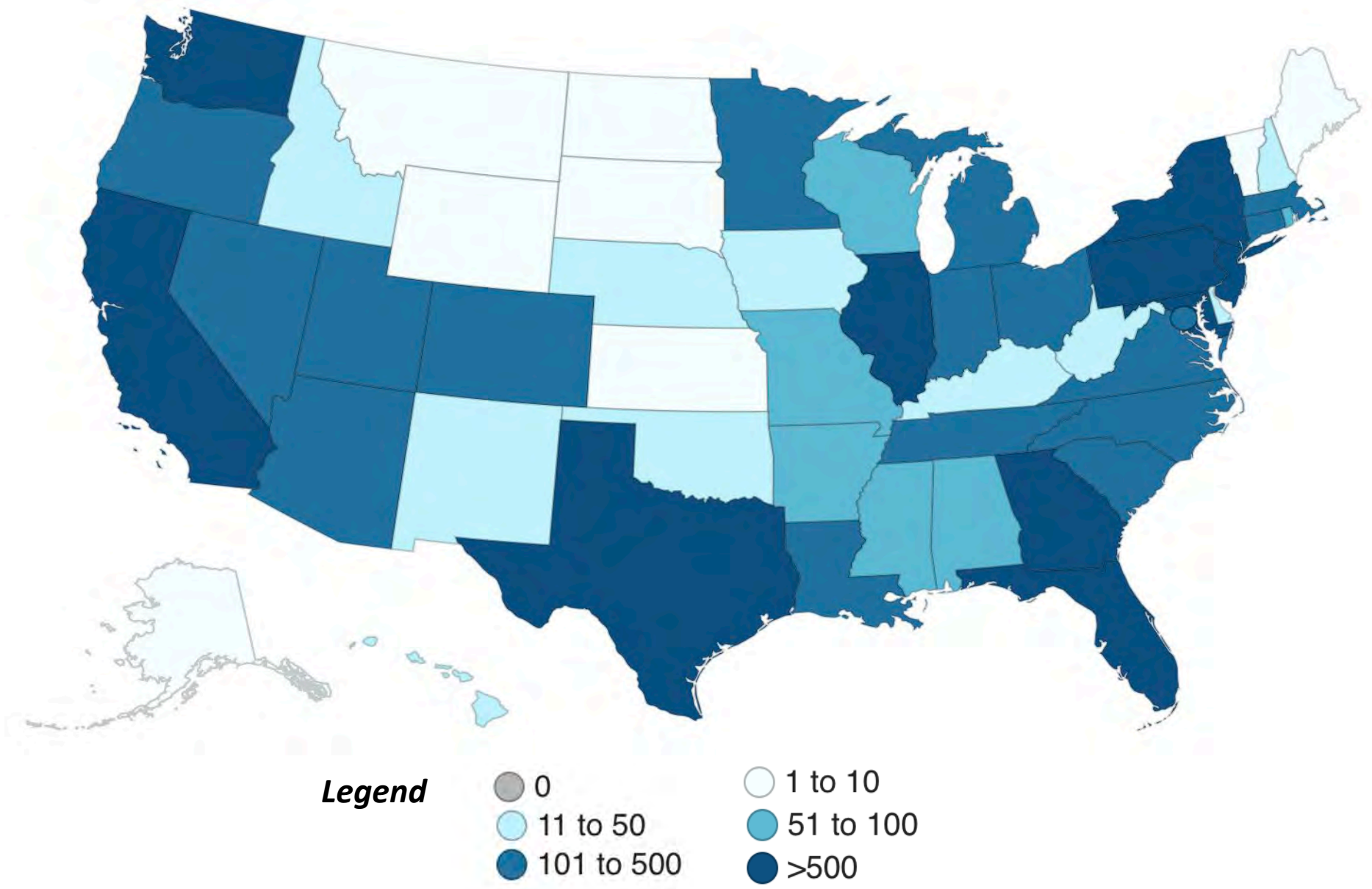
Source: Our World in Data 9-17-22

MONKEYPOX OUTBREAK CURVE: DAILY CASES, UNITED STATES



Source: CDC and Our World in Data 9-17-22

2022 Monkeypox Outbreak, US



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

This Week's COVID Pandemic News

1. ***FDA** provided Emergency Use Authorization and **CDC's Advisory Committee on Immunization Practices** recommended both bivalent COVID vaccines, including omicron-specific components.*
2. *A **Science** paper demonstrated that mosaic receptor-binding domain nanoparticles protect against challenge with diverse sarbecoviruses in animal models .*
3. *A **New England Journal** review discusses immunity, variants, and boosters, with specific reference to SARS-CoV-2 and COVID-19.*
4. *A letter to the **New England Journal** demonstrated the durability of booster mRNA vaccines against SARS-CoV-2 BA.2.12.1, BA.4, and BA.5 subvariants*
5. *A letter to the **New England Journal** demonstrated the relevance of anti-spike mucosal IgA protection against SARS-CoV-2 Omicron infection and argued for a vaccines that induce a combination of mucosal and systemic responses.*
6. *A **JAMA Network Open** paper evaluated of risk factors for post-booster Omicron COVID-19 deaths in England. Older age was found to be the primary risk. .*
7. *A **JAMA Internal Medicine** paper provides a detailed assessment of COVID-19-associated hospitalizations among vaccinated and unvaccinated adults 18 years or older in 13 US States, from January 2021 to April 2022*
8. *A British Medical Journal paper addressed the complexity of categorizing procedures as "aerosol-generating" , illustrates why this problem continues to vex us and advocates for a generally conservative approach to all such procedures .*

References available in the chat

This Week's Monkeypox Epidemic News

1. *A **New England Journal** paper provided a detailed clinical description of the experience with 528 infections diagnosed between April 27 and June 24, 2022, at 43 institutions in 16 countries that was accompanied by an editorial putting these findings into perspective..*
2. *A **New England Journal** opinion piece emphasized the need for controlled clinical trials of Tecovirimat in the treatment of monkeypox.*
3. *In that regard, **CDC** updated CDC updated its Guidance for Tecovirimat Use suggesting that broad use of Tecovirimat could promote resistance and render antiviral drugs ineffective for some patients.*
4. *Another opinion piece in the **New England Journal** discusses the individual and public health benefits of intradermal vaccination for monkeypox..*
5. *A short article in **JAMA** presents what the authors think are what clinicians need to know about monkeypox.*
6. *A brief review in **The Lancet** discusses vaccination as a prevention strategy for monkeypox.*
7. *A news article in **Nature** discusses the state-of-the-art information available currently concerning the mechanisms of transmission of monkeypox . .*
8. *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. Tara Palmore
George Washington University School of Medicine & Health Sciences

Dr. Kristina Bryant
University of Louisville

Dr. David Weber
UNC School of Medicine

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UPDATE: COVID-19 AND M-POX

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

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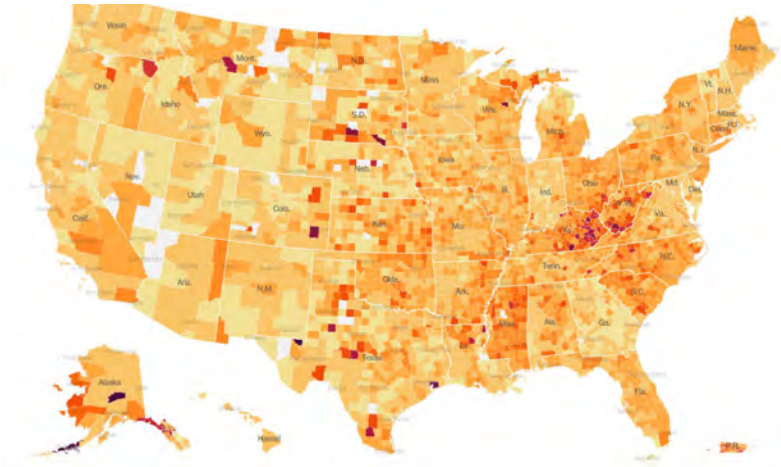
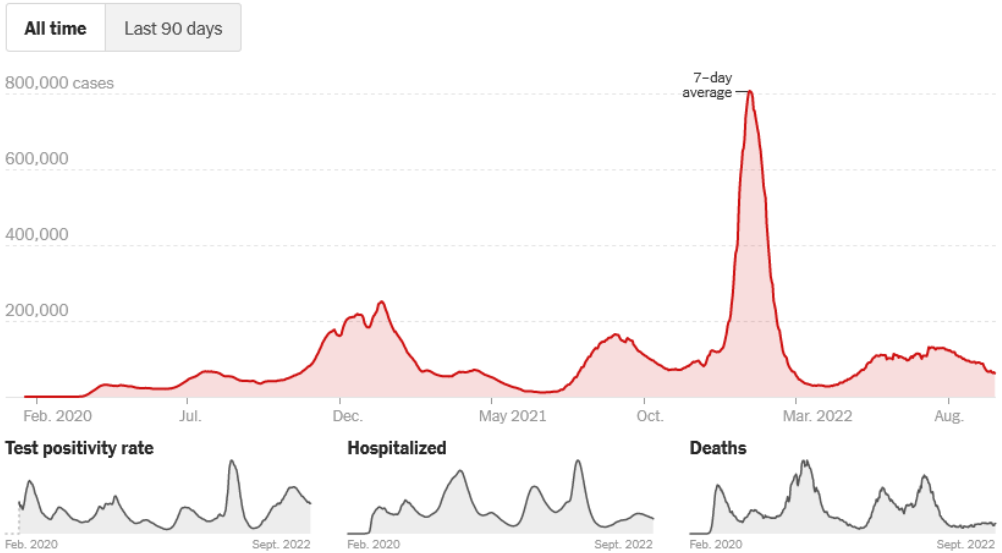
Disclosures: Consultancy; Pfizer, Merck, Sanofi, PDI, Moderna, Germitec, Wellair
All drugs/vaccines issues discussed consistent with FDA approvals or authorizations

COVID-19 UPDATE

- Cases, hospitalizations, deaths falling but remain at a high level
- US ranks below 50th in the world in COVID-19 vaccine coverage
- Novavax vaccine FDA authorized for adults and adolescengs
- Omicron containing bivalent vaccine (BA.4/BA.5) FDA authorized (Pfizer & Moderna) – available ages 12 years and above – dose ≥2 months since primary series or last dose
- "Boosted" persons well protected against serious disease (but less protection against infection)
- BA.4 and BA.5 predominant variants (increased percent with BA.4.6) – reduced prevention by vaccines and monoclonal antibodies (Evusheld ineffective); no effect on antivirals
- No current drug shortages but likely shortages of infusion space
- Pharmacists now allowed to provide Paxlovid





	DAILY AVG. ON SEPT. 16	14-DAY CHANGE	TOTAL REPORTED
Cases	62,156	−29%	95,435,379
Test positivity	12%	—	—
Hospitalized	32,680	−12%	—
In I.C.U.s	3,980	−10%	—
Deaths	467	−6%	1,049,741

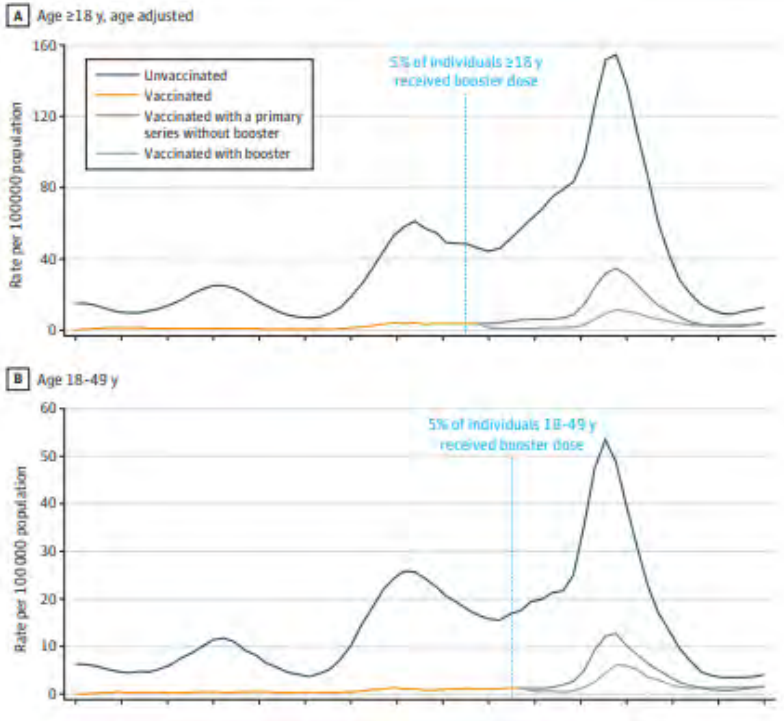
Vaccinations

	FULLY VACCINATED	WITH A BOOSTER
All ages	68%	33%
65 and up	92%	65%

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

COVID hospitalization risk increases with age; but vaccines are protective, boosters even more so!

Figure 2. Three-Week Moving Average Population-Based Rates[a] of COVID-19–Associated Hospitalizations Among Unvaccinated and Vaccinated (With and Without a Booster Dose)[b] Adults 18 Years or Older Admitted January 30, 2021[c] to April 30, 2022, by Week of Admission, COVID-19–Associated Hospitalization Surveillance Network (COVID-NET), 13 States[d]



Data shown for individuals vaccinated with a booster for the following dates: adults 18 years and older (age adjusted), October 30, 2021, to April 30, 2022 (A), age 18 to 49 years, November 27, 2021, to April 30, 2022 (B), age 50 to 64 years, November 6, 2021, to April 30, 2022 (C), and 65 years or older, October 16 to April 30, 2022 (D).[e]

[a] Patients with laboratory-confirmed COVID-19–associated hospitalizations per 100 000 population.

[b] Unvaccinated: persons with a positive SARS-CoV-2 test who had no record of receiving any COVID-19 vaccine. Vaccinated: persons with a positive SARS-CoV-2 test collected 14 days or more after vaccination with a primary series, defined as either the second dose of a 2-dose vaccine series or after 1 dose of a single-dose vaccine. When not otherwise specified, vaccinated persons include those who may have received additional or booster doses. Vaccinated without a booster dose: persons who have received a primary series and who have not received an additional or booster dose. This includes those eligible and not yet eligible for an additional or booster dose. Vaccinated with a booster dose: persons vaccinated with a primary series and an additional or booster dose on or after August 13, 2021, with a positive SARS-CoV-2 test collected 14 days or more after receipt of an additional or booster dose. Because the immune status of all cases is not known, an additional dose (recommended for persons with a weakened immune system) cannot be distinguished from a booster dose.

[c] The week ending January 30, 2021, is the earliest an individual could be considered to have completed a primary series based on the approval of the first COVID-19 vaccines in December 2020.

[d] California, Colorado, Connecticut, Georgia, Maryland (data excluded beginning December 4, 2021), Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah.

[e] Period of data based on when 14 days have passed because at least 5% of the age group-specific population of the COVID-NET surveillance catchment area had received an additional or booster dose.

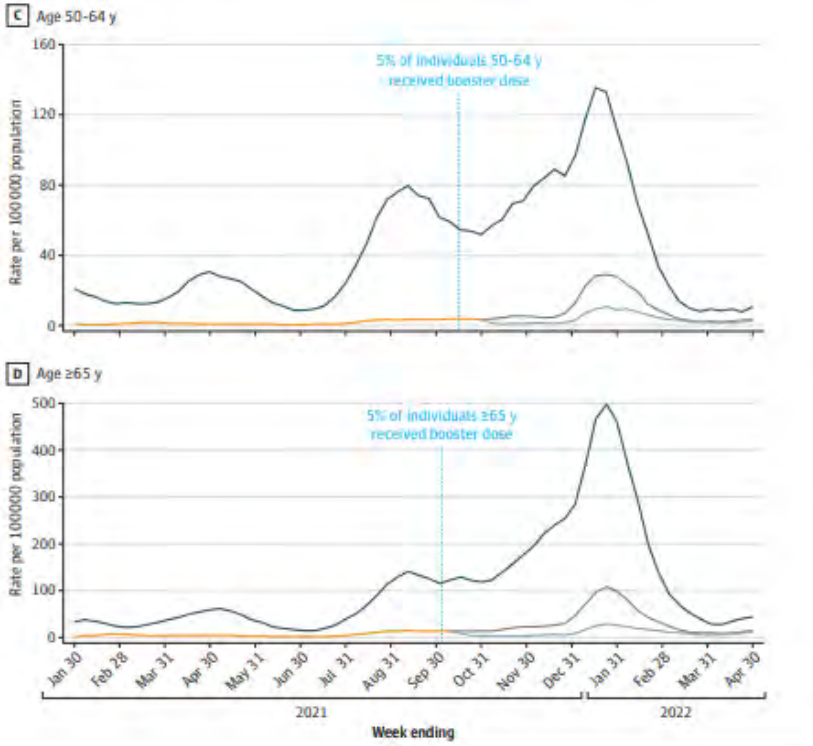
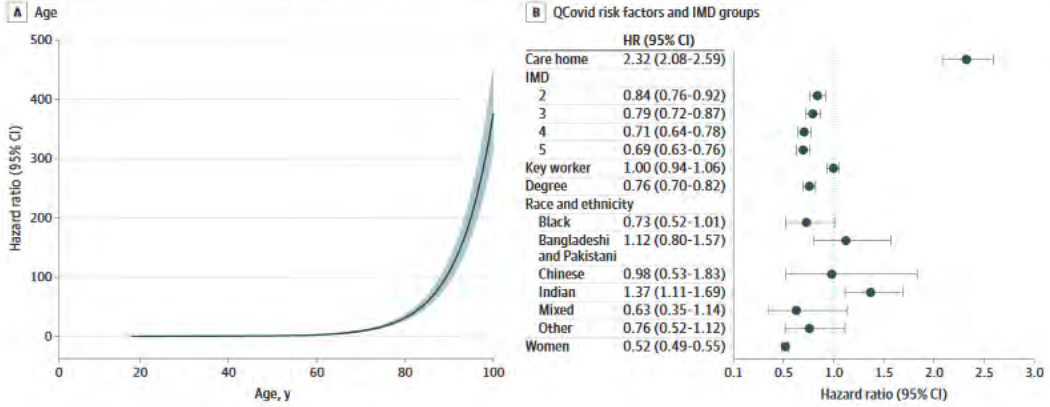
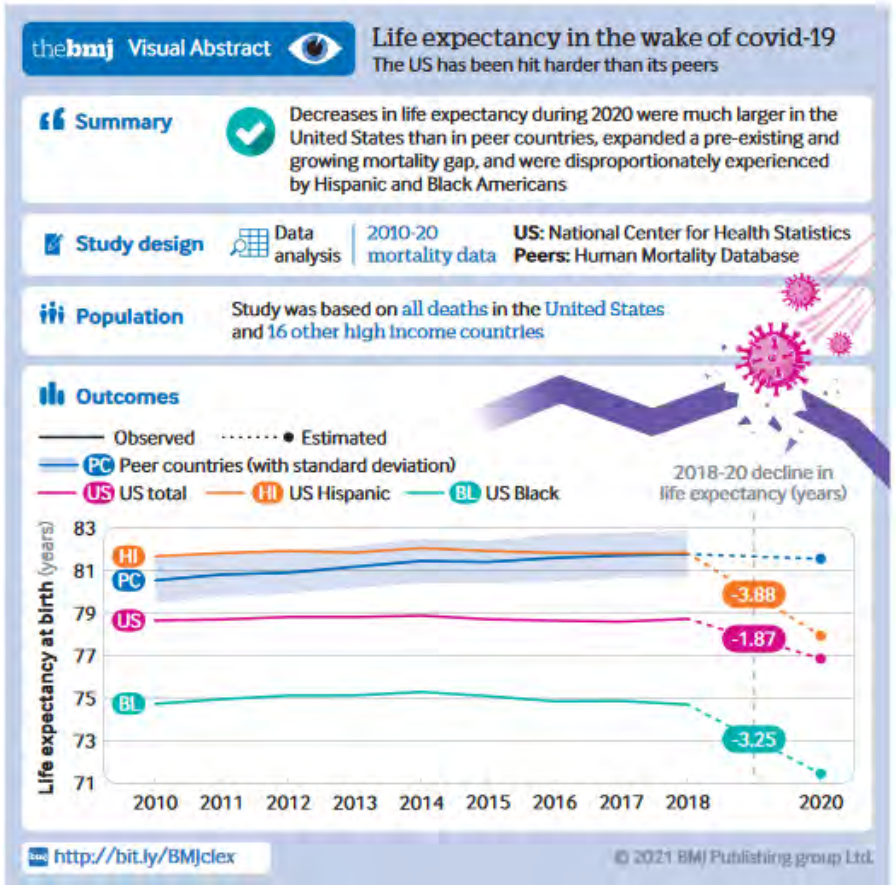


Figure. Risk Factors for Death From COVID-19 After Receiving a Booster



https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2796235
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2796000

Effect of the covid-19 pandemic in 2020 on life expectancy across populations in the USA and other high income countries: simulations of provisional mortality data



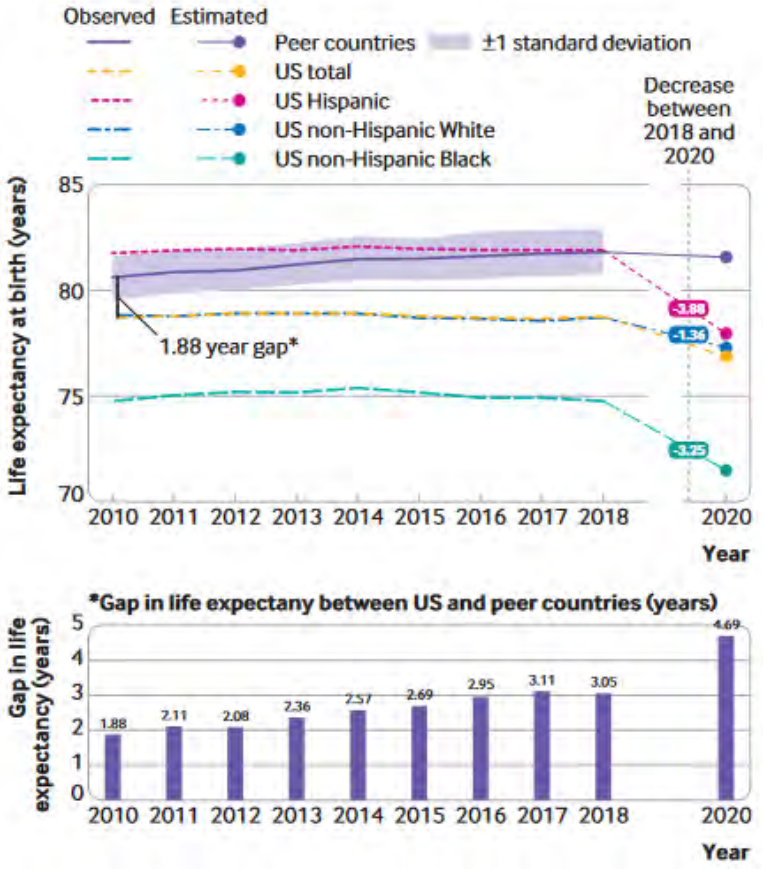


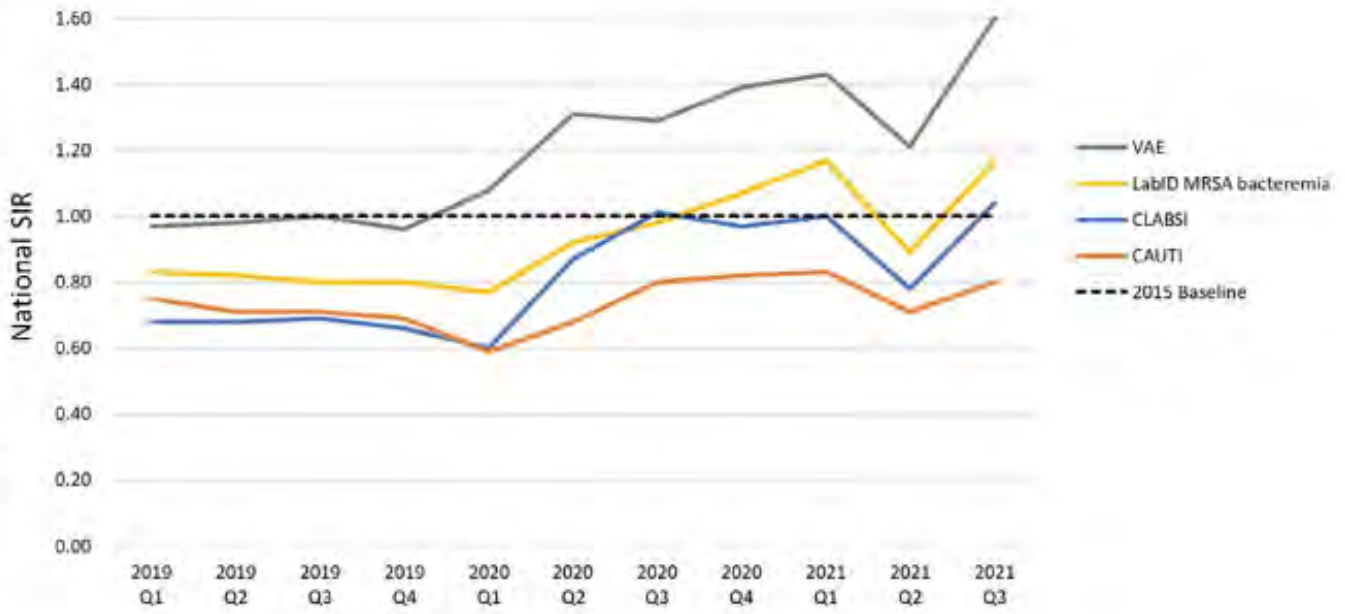
Fig 1 | Life expectancy at birth in the United States, by race and ethnicity, and in peer countries, for years 2010-18 and 2020. Data obtained from the National Center for Health Statistics, US Census Bureau, and Human Mortality Database. Data for 2019 could not be calculated because life table data were unavailable for many peer countries

Woolf SH, et al. BMJ 2021;373”m1343

Continued increases in the incidence of healthcare associated infection (HAI) during the 2nd year of the COVID-19 pandemic

Data from the National Healthcare Safety Network were analyzed to assess the impact of COVID-19 on the incidence of healthcare-associated infections (HAI) during 2021. Standardized infection ratios were significantly higher than those during the prepandemic period, particularly during 2021-Q1 and 2021-Q3. The incidence of HAI was elevated during periods of high COVID-19 hospitalizations.

Fig. 1. Quarterly national SIRs for select HAI types, 2019-Q1 through 2021-Q3. The HAIs shown on this graph have been most affected by the COVID-19 pandemic, as demonstrated by CDC data.[1,2] SIRs for other types of infections are available in Tables 1–3 and in prior reports.[1,2] This graph displays the quarterly SIR point estimates from 2019-Q1 through 2021-Q3 and does not constitute a statistical trend analysis.
Note: SIR, standardized infection ratio; HAI, healthcare-associated infection; VAE, ventilator-associated event; LabID, laboratory–identified; MRSA, methicillin-resistant *Staphylococcus aureus*; CLABSI, central-line–associated bloodstream infection; CAUTI, catheter-associated urinary tract infection.

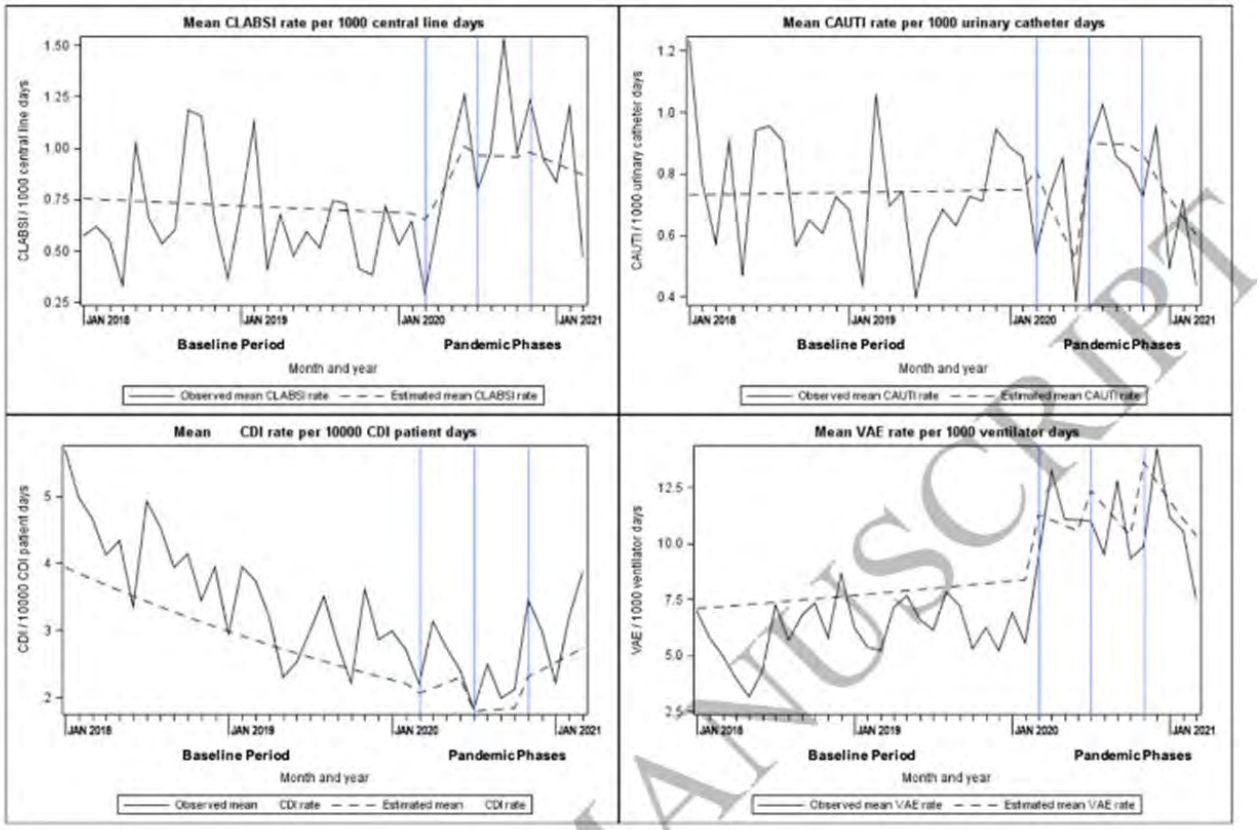


Lastinger LM, et al
ICHE 2022, 1-5

UNC SCHOOL OF MEDICINE

The Disproportionate Impact of COVID-19 Pandemic on Healthcare-Associated Infections in Community Hospitals: Need for Expanding the Infectious Disease Workforce

- Methods: his retrospective longitudinal multi-center cohort study included CLABSIs, CAUTI), CDIs), and VAE3s from 53 hospitals (academic and community) in Southeastern US from 1/1/18 to 3/31/21. Segmented negative binomial regression generalized estimating equations models estimated changes in monthly incidence rates in the baseline (01/2018 – 02/2020) compared to the pandemic period (03/2020 -03/2021, further divided into three pandemic phases).
- Results: CLABSIs and VAEs increased by 24% and 34% respectively during the pandemic period. VAEs increased in all phases of the pandemic, while CLABSIs increased in later phases of the pandemic. CDI trend increased by 4.2% per month in the pandemic period. On stratifying the analysis by hospital characteristics, the impact of the pandemic on healthcare-associated infections was more significant in smaller sized and community hospitals. CAUTIs did not change significantly during the pandemic across all hospital types.



Advanti SD, et al. Clin Infect Dis 2022;23 August (Duke/UNC CDC Epicenter)

COVID-19 Impacts on

18 Antimicrobial-Resistant Bacteria and Fungi

Threat Estimates

The following table summarizes the latest national death and infection estimates for 18 antimicrobial-resistant bacteria and fungi. The pathogens are listed in three categories—urgent, serious, and concerning—based on level of concern to human health identified in 2019.

	Resistant Pathogen	2017 Threat Estimate	2018 Threat Estimate	2019 Threat Estimate	2017-2019 Change	2020 Threat Estimate and 2019-2020 Change
URGENT	Carbapenem-resistant *Acinetobacter*	8,500 cases 700 deaths	6,300 cases 500 deaths	6,000 cases 500 deaths	Stable*	7,500 cases 700 deaths **Overall: 35% Increase*** **Hospital-onset: 78% Increase***
URGENT	Antifungal-resistant *Candida auris*	171 clinical cases†	329 clinical cases	466 clinical cases	Increase	754 cases **Overall: 60% Increase**
URGENT	*Clostridioides difficile*	223,900 infections 12,800 deaths	221,200 infections 12,600 deaths	202,600 infections 11,500 deaths	Decrease	Data delayed due to COVID-19 pandemic
URGENT	Carbapenem-resistant Enterobacterales	13,100 cases 1,100 deaths	10,300 cases 900 deaths	11,900 cases 1,000 deaths	Decrease*	12,700 cases 1,100 deaths Overall: Stable* **Hospital-onset: 35% Increase***
URGENT	Drug-resistant *Neisseria gonorrhoeae*	550,000 infections	804,000 infections	942,000 infections	Increase	Data unavailable due to COVID-19 pandemic
SERIOUS	Drug-resistant *Campylobacter*	448,400 infections 70 deaths	630,810 infections	725,210 infections	Increase	Data delayed due to COVID-19 pandemic‡ 26% of infections were resistant, a 10% decrease
SERIOUS	Antifungal-resistant *Candida*	34,800 cases 1,700 deaths	27,000 cases 1,300 deaths	26,600 cases 1,300 deaths	Decrease*	28,100 cases 1,400 deaths **Overall: 12% Increase*** **Hospital-onset: 26% Increase***
SERIOUS	ESBL-producing Enterobacterales	197,400 cases 9,100 deaths	174,100 cases 8,100 deaths	194,400 cases 9,000 deaths	Increase*	197,500 cases 9,300 deaths **Overall: 10% Increase*** **Hospital-onset: 32% Increase***
SERIOUS	Vancomycin-resistant Enterococcus	54,500 cases 5,400 deaths	46,800 cases 4,700 deaths	47,000 cases 4,700 deaths	Stable*	50,300 cases 5,000 deaths **Overall: 16% Increase*** **Hospital-onset: 14% Increase***

https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf

Association Between Vaccination and Acute Myocardial Infarction and Ischemic Stroke After COVID-19 Infection

- Background: Xie et al showed that, beyond the first 30 d after infection, individuals with COVID-19 are at increased risk of incident cardiovascular disease spanning several categories, including cerebrovascular disorders, dysrhythmias, ischemic and non-ischemic heart disease, pericarditis, myocarditis, heart failure and thromboembolic disease. (Xie Y, et al. Nature Med 2022;28:583)
- Methods: Study was a retrospective cohort study to compare the incidence of AMI and ischemic stroke after COVID-19 infection between patients who were never vaccinated and those who were fully vaccinated (2 doses of mRNA vaccines or viral vector vaccine) against SARS-CoV-2.
- Results: The adjusted risk was significantly lower in the fully vaccinated group (adjusted hazard ratio [aHR], 0.42; 95% CI, 0.29-0.62). The adjusted risk was significantly lower in fully vaccinated patients for both AMI (aHR, 0.48; 95% CI, 0.25-0.94) and ischemic stroke (aHR, 0.40; 95% CI, 0.26-0.63). A lower risk for outcome events in fully vaccinated patients was observed in all subgroups, although some did not reach statistical significance, including those with severe or critical infection (Table 2).

Kim Y-E, et al. JAMA 2022;328:888

Table 2. Risk for Cardiovascular Events by Vaccination Status

	No. of events		Incidence per 1 000 000 person-days			
	Not vaccinated (n = 62 727)	Fully vaccinated (n = 168 310)	Not vaccinated	Fully vaccinated	Adjusted HR (95% CI)	P value
Composite outcome	31	74	6.18	5.49	0.42 (0.29-0.62)	<.001
Acute myocardial infarction	8	24	1.60	1.78	0.48 (0.25-0.94)	.03
Ischemic stroke	23	50	4.59	3.71	0.40 (0.26-0.63)	<.001
Subgroups						
Male	17	48	6.98	7.59	0.41 (0.26-0.66)	<.001
Female	14	26	5.44	3.63	0.42 (0.23-0.76)	.004
Age, y						
40-64	11	22	5.48	3.39	0.38 (0.20-0.74)	.004
≥65	20	51	33.99	12.42	0.41 (0.26-0.66)	<.001
Charlson Comorbidity Index						
<5	25	56	5.22	4.45	0.40 (0.26-0.60)	<.001
≥5	6	18	25.04	19.79	0.54 (0.24-1.22)	.14
Diabetes						
No	23	46	4.89	3.87	0.38 (0.24-0.61)	<.001
Yes	8	28	26.29	17.58	0.47 (0.25-0.91)	.03
Hypertension						
No	20	46	4.41	4.39	0.50 (0.31-0.80)	.004
Yes	11	28	23.11	10.90	0.34 (0.18-0.62)	<.001
Dyslipidemia						
No	27	70	5.58	5.65	0.54 (0.37-0.80)	.002
Yes	4	4	22.50	3.62	0.09 (0.03-0.34)[a]	<.001
Previous history of outcome events						
No	26	67	5.24	5.05	0.44 (0.29-0.65)	<.001
Yes	5	7	97.55	33.26	0.33 (0.10-1.07)	.06
Severe or critical COVID-19						
No	22	65	5.02	5.00	0.37 (0.25-0.55)	<.001
Yes	9	9	14.38	18.51	0.66 (0.20-2.23)	.51

Indirect benefits of COVID-19 vaccines

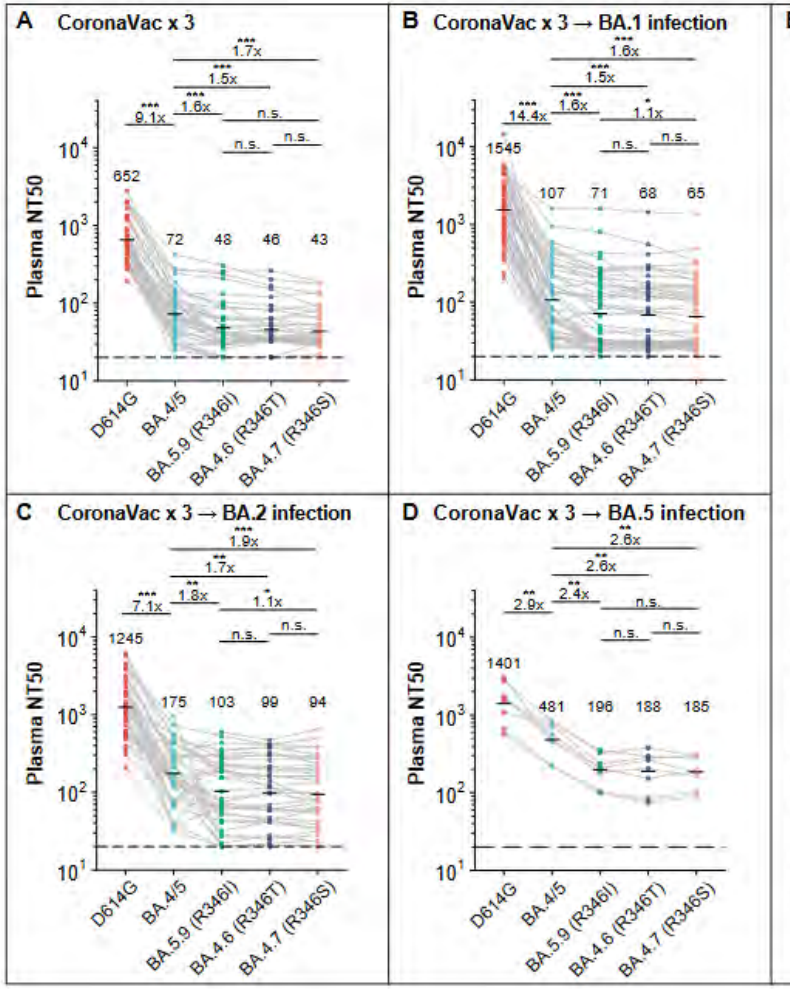
- Reduced risk of long haul syndrome
- ~90% reduced risks of MIS-C (children)
- Reduced risk of infant hospitalizations and death (maternal immunization)
- Reduced risk of late MI and stroke

Further humoral immunity evasion of emerging SARS-CoV-2 BA.4 and BA.5 subvariants

Abstract

Multiple BA.4 and BA.5 subvariants with R346 mutations on the spike glycoprotein have been identified in various countries, such as BA.4.6/BF.7 harboring R346T, BA.4.7 harboring R346S, and BA.5.9 harboring R346I. These subvariants, especially BA.4.6, exhibit substantial growth advantages compared to BA.4/BA.5. In this study, we showed that BA.4.6, BA.4.7, and BA.5.9 displayed higher humoral immunity evasion capability than BA.4/BA.5, causing 1.5 to 1.9-fold decrease in NT50 of the plasma from BA.1 and BA.2 breakthrough-infection convalescents compared to BA.4/BA.5. Importantly, plasma from BA.5 breakthrough-infection convalescents also exhibits significant neutralization activity decrease against BA.4.6, BA.4.7, and BA.5.9 than BA.4/BA.5, showing on average 2.4 to 2.6-fold decrease in NT50. For neutralizing antibody drugs, Bebtelovimab remains potent, while Evusheld is completely escaped by these subvariants.

Results rationalize the prevailing advantages of the R346 mutated BA.4/BA.5 subvariants and urge the close monitoring of these mutants, which could lead to the next wave of the pandemic.



E Therapeutic monoclonal antibodies

Pseudovirus IC50 (ng/mL)	BA.4/5	BA.5.9 (R346I)	BA.4.6 (R346T)	BA.4.7 (R346S)
Etesevimab (LY-CoV016)	*	*	*	*
Bamlanivimab (LY-CoV555)	*	*	*	*
Bebtelovimab (LY-CoV1404)	0.8	1.3	1.0	1.4
Casirivimab (REGN10933)	*	*	*	*
Imdevimab (REGN10987)	520	2701	2195	1362
Tixagevimab (COV2-2196)	*	*	*	*
Cilgavimab (COV2-2130)	23	*	*	*
Amubarvimab (BRII-196)	7124	4023	4356	3395
Romlusevimab (BRII-198)	*	*	*	*
Sotrovimab (S309)	1055	4780	3543	2899
Adintrevimab (ADG-2)	*	*	*	*
Etesevimab+ Bamlanivimab	*	*	*	*
Casirivimab+ Imdevimab	709	3498	4388	2420
Tixagevimab+ Cilgavimab	40	*	*	*
Amubarvimab+ Romlusevimab	*	7695	8307	5209

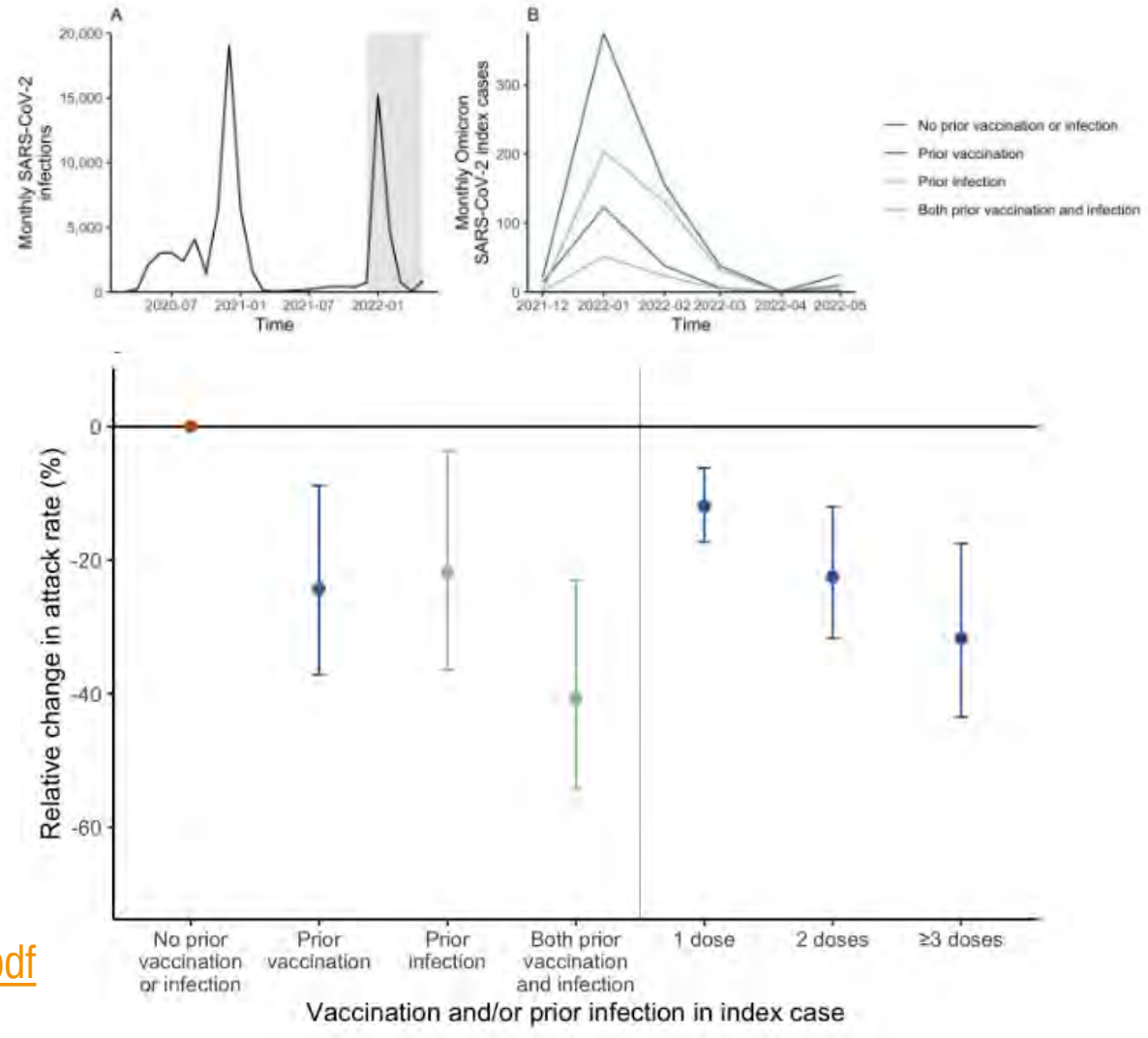
<100 | 100~1,000 | >1,000 | * >10,000

Jian F, et al. https://www.biorxiv.org/content/10.1101/2022.08.09.503384v1.full.pdf

Infectiousness of SARS-CoV-2 breakthrough infections and reinfections during the Omicron wave

- **Abstract**: Breakthrough infections in vaccinated individuals and reinfections among previously infected individuals are increasingly prevalent, especially during the Omicron wave. Here, we analyze data from SARS-CoV-2 surveillance across 35 California prisons to understand the impact of vaccination and prior infection on infectiousness of individuals with SARS-CoV-2 Omicron infections in prison settings. We estimate that vaccination, prior infection, and both vaccination and prior infection reduced an index case's risk of transmitting to close contacts by 24% (9-37%), 21% (4-36%) and 41% (23-54%), respectively. Booster vaccine doses and more recent vaccination further reduced infectiousness. These findings suggest that although vaccinated and/or previously infected individuals remain infectious upon SARS-CoV-2 Omicron infection in this prison setting, their infectiousness is reduced compared to individuals without any history of vaccination or infection.

Tan ST, et al.
https://www.medrxiv.org/content/10.1101/2022.08.08.22278547v1.full.pdf



BIVALENT COVID-19 VACCINE CLINICAL TRIAL DATA

Summary: Clinical Trial Data

- Clinical (human) data from bivalent COVID-19 vaccines in >1700 persons
  - Includes bivalent vaccines with Beta and Omicron variants, both from manufacturers and NIH studies
  - Over 1400 individuals received bivalent vaccine with **Omicron** component specifically
  - While there are subtle differences in mutations between BA.1 and BA.4/BA.5 spike protein sequences, do not anticipate differences in safety or reactogenicity of vaccines based on these limited mutations
  - Overall composition of the vaccine as well as total antigenic load are the same as current booster doses
- Bivalent booster doses of both Moderna & Pfizer-BioNTech COVID-19 vaccines **increase immune response** in those who have completed a primary series and a previous booster
  - Compared with ancestral booster dose
    - Demonstrated superior response to Omicron
    - Demonstrated non-inferior response to ancestral strain
- Similar reactogenicity profile to primary series (and ancestral booster dose)

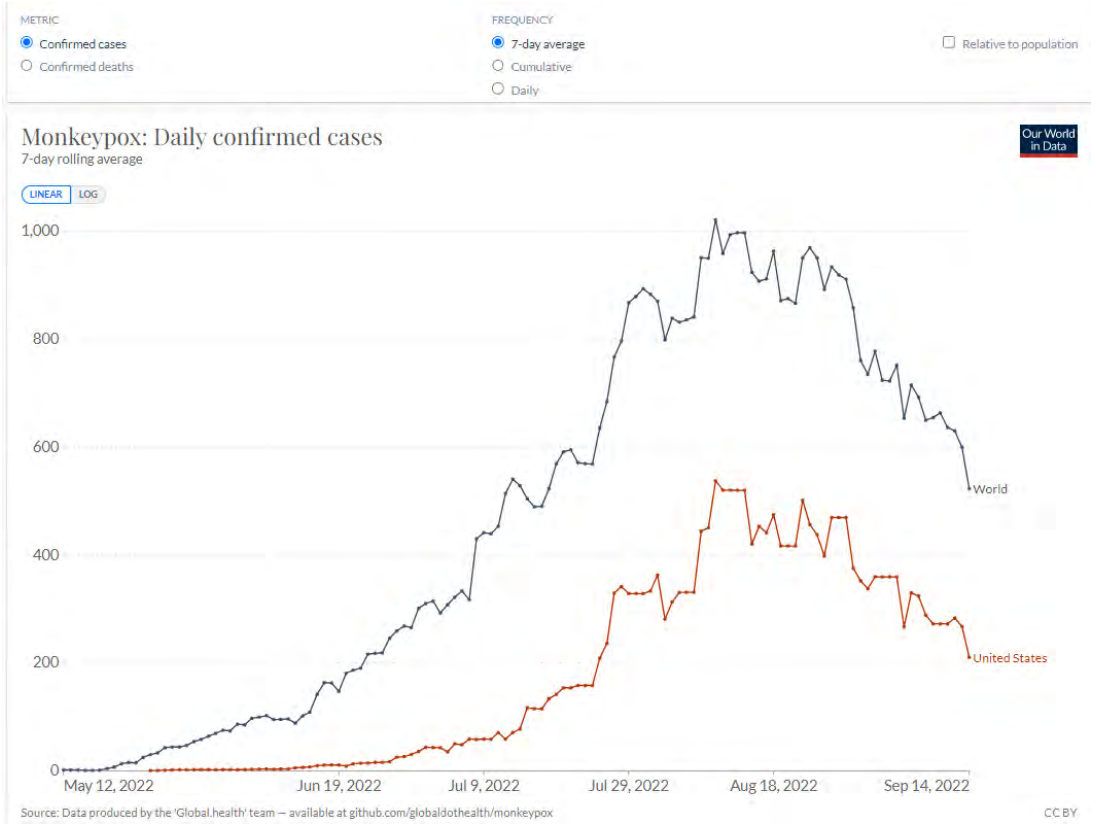
Source, CDC Partner's Call, 6 September 2022

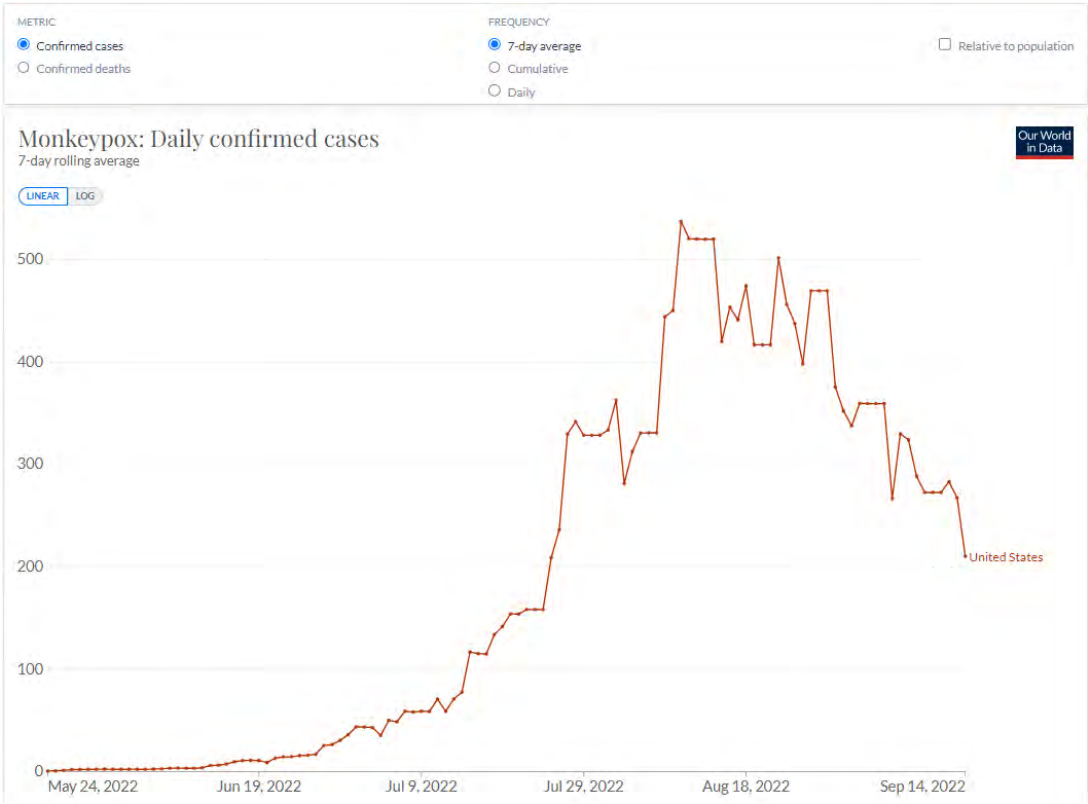
UNC SCHOOL OF MEDICINE

MPX: SUMMARY OF NEW INFORMATION

- Current outbreak largest ever recorded; however, outbreak curve has plateaued/decreased; Outbreak due to a new clade (clade IIb)
- Reproductive number (Ro) = ~1.3 {COVID-19 initial Ro = 2-4; Omicron variants = 8-10}; main transmission mechanism is skin-to -skin contact (others: droplet ; requires prolonged exposure, fomites {shared eating utensils, contaminated bedding/clothes}, transplacental and congenital)
- MPX DNA can be detected in wastewater – may be useful as a monitoring tool (similar to polio and SARS-CoV-2)
- Great majority of cases in men who have sex with men (MSMs); NC ~400 cases, at risk population in NC = 15,700
- Most patients in current outbreak have atypical symptoms compared to classic MPX
- Testing: Available at health departments (free) & many commercial labs (capacity, ~70,000-80,000 tests per week)
- UNC-CH performing “in house” diagnostic tests for UNC Health
- Jynneos vaccine available for pre-exposure (PreP) and post-exposure prophylaxis (PEP)
    - UNC has provided PreP to our microbiologists performing MPX testing
    - 60 first doses provided by Campus Health; similar number in UNC-CH ID clinic
    - FDA has authorized ID administration at 1/5 dose to expand supply (based on limited data; one 2015 paper)
- Tecovirimat (TPOXX) available for treatment: Only case series available regarding effectiveness.

MPX OUTBREAK CURVES: WORLDWIDE & US





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

Case reports of T-POXX
As of 13 August, 25 patients

Reports suggest T-POXX relatively safe and rapidly reduces formation of new lesions

Assessing impact on hospitalizations will require much larger study
Assessing impact on deaths unlikely given rarity of deaths
Need studies with a control group to assess effectiveness

Desai AN, et al
JAMA 2022;22 August

Table. Clinical Characteristics of Patients With Monkeypox Infection Treated With Tecovirimat

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
Smallpox vaccination history	Unk	Unk	No	No	No	No	No	Unk	Unk	Unk	Unk	No	No	No	Unk	No	Unk	Jynneos	Jynneos	No	Jynneos	Remote	No	Jynneos	Unk
HIV,[a] hepatitis B, hepatitis C status	HIV	None	None	None	None	HIV	HIV	HIV	None	HIV	HIV	None	HIV	None	None	HIV	None	None	None	None	None	None	None	None	HIV
Systemic symptoms	None	Fever, backache, fatigue	Nausea, chills, myalgias	Fever	Fatigue	Fever, fatigue	Fever, backache, headache, diarrhea, chills	None	Malaise, fever	Fever	Fever, sore throat, itching, fatigue	Fever, headache	Fever, headache	Headache, shoulder and neck pain	Headache, hoarseness	Fever, fatigue, headache, constipation, sore throat	Fever, headache, nausea, fatigue	Fever, myalgia, headache, sore throat	Fever, chills, urethritis	Fever	Fever, sore throat, back pain	Fever, sore throat	Fever, chills, night sweats	Fever, chills, fatigue, painful bowel movements	Fever
Lymphadenopathy	None	None	None	None	Inguinal	Inguinal and neck	None	None	Neck and inguinal	Cervical	Neck and inguinal	Right inguinal	None	None	Inguinal	Inguinal	None	Inguinal	None	Inguinal	Cervical, inguinal	Cervical	None	Inguinal	None
No. of lesions	10-100	<10	<10	10-100	<10	10-100	10-100	<10	10-100	10-100	10-100	10-100	>100	10-100	<10	<10	10-100	<10	<10	<10	<10	<10	<10	10-100	<10
Genital lesions	Perianal	Perianal	Genital	Genital	Genital	Perianal	Perianal	Genital	Genital	No	Genital	No	Perianal and genital	Genital	Genital	Perianal	Genital	Genital	Perianal	Genital	Perianal and genital	Genital	Genital	Genital	Perianal
Distribution of other lesions	Chest, eyelid, right hand, right knee, shoulder	Face, neck, arms		Scalp, face, forearms, hands, chest, back, legs, buttocks		Face, abdomen, groin, back, legs	Neck, arms, head, legs, abdomen, back		Face, back, arms, hands	Entire body	Throat, chest, arm, abdomen, hand, buttocks	Scalp, face, neck, abdomen, arms, back	Entire body	Arms, scalp		Arm, chest, face	Chest, back	Face, arm, chest	Arm, thigh	Chest	Wrist, chest	Arms, legs	Chest, back, arm, shin	Head, arms, legs, foot	Chest, back, arms, legs
Symptom onset to tecovirimat initiation, d	24	17	6	8	15	6	9	16	10	12	9	14	10	16	7	7	6	12	12	7	19	14	13	10	22
Days of tecovirimat therapy	14	14	14	14	14	14	14	14	21[b]	14	14	14	14[b]	14	14	14	14	14	14	14	14	14	14	14	14
7-Day self-reported outcomes[c]	Rec	Rec	Rec	No new lesions	No new lesions	No new lesions	Rec	No new lesions	New lesions	No new lesions	No new lesions	No new lesions	No new lesions	No new lesions	Rec	No new lesions	Rec	No new lesions	Rec	No new lesions	No new lesions	Rec	No new lesions	Rec	Rec
21-Day self-reported outcomes[c]	Rec	Rec	Rec	Rec	Rec	Rec	Rec	Rec	New lesions	Rec	Rec	Rec	Rec	Rec	Rec	Rec	Rec	Rec	Rec	No new lesions	Rec	Rec	Rec	Rec	Rec
Adverse effects at day 7	Backache, fatigue	None	None	None	Headache, nausea	None	Hand burning, weak nails	None	Fatigue, nausea, itching, headache	Fatigue	Fatigue, itching	None	None	Nausea, headache	None	Fatigue	None	Headache, diarrhea	None	None	Fatigue	Headache	Fatigue, nausea	Dry skin	Diarrhea

Abbreviation: unk, unknown.

[a] Patients with HIV were receiving antiretroviral therapy and confirmed or reported to be virologically suppressed.

[b] Dose increased on day 10 (patient 9) and day 7 (patient 13) due to delayed clinical response and borderline weight-based dosing.

[c] Recovered (rec): all lesions self-reported as crusted or fallen off; new lesions: development of new lesions; no new lesions: no new lesions reported but not yet recovered.

JYNNEOS VACCINE: Q AND A

- If ID administration does NOT raise a bleb or wheal, should another ID dose be administered
  - Yes. If you do not see a “wheal” after the first attempt, repeat dose immediately via intended route (no minimum interval). Repeated dose should be placed at least 2 inches away from the inadvertent site placement. See: https://www.cdc.gov/poxvirus/monkeypox/interim-considerations/errors-deviations.html
- If a patient has a history of keloid formation, should vaccine be provided by SC administration
  - Yes. See Table 2 here: https://www.cdc.gov/poxvirus/monkeypox/interim-considerations/jynneos-vaccine.html#interim
- If a patient has had a SC dose administered, can we administer the 2nd dose ID (we have been saying yes)
  - Yes, a person who received only one dose of the standard regimen before the date of initial Emergency Use Authorization for the alternative regimen (August 9, 2022), may receive one dose with the alternative regimen to complete the series. Also, a person whose 18th birthday occurs between their first and second dose may complete the series with the alternative regimen. See: https://www.cdc.gov/poxvirus/monkeypox/interim-considerations/jynneos-vaccine.html#interchange
- What, if any, local reaction to the 1st dose indicates the 2nd dose should be SC
  - Having local reactions to the first dose is NOT a reason in and of itself to administer the second dose SC. If local reactions to ID placement persist 28 days later, the second dose may be administered ID in the contralateral forearm. See: https://www.cdc.gov/poxvirus/monkeypox/interim-considerations/jynneos-vaccine.html#admin
- If the patient has continued evidence of a cutaneous reaction at the time of the 2nd dose, should the 2nd dose be administered in the other arm
  - Yes correct.
- If an arm is not available for vaccine administration (e.g., extensive burns), can an other body site be used
  - Yes, back beneath the scapula is recommended

Low levels of monkeypox virus neutralizing antibodies after Jynneos vaccination in healthy individuals

ABSTRACT

We measured Jynneos (MVA)-, Vaccinia virus (VACV)-, and M-Pox (MPXV)- reactive binding and neutralizing antibodies with validated in-house assays in cohorts of historically smallpox-vaccinated, MPXV PCR-positive, and recently Jynneos-vaccinated individuals. We show that MPXV neutralizing antibodies were detected across all cohorts in individuals with MPXV exposure as well as those who received historic (VACV) vaccination. However, a primary Jynneos immunization series in non-primed individuals yields relatively low levels of MPXV neutralizing antibodies. As the role of MPXV neutralizing antibodies for protection against disease and transmissibility is currently unclear and no correlate of protection against MPXV infection has been identified yet, this raises the question how well vaccinated individuals are protected. Dose-sparing leads to lower antibody levels, whereas a third Jynneos vaccination further boosts the antibody response.

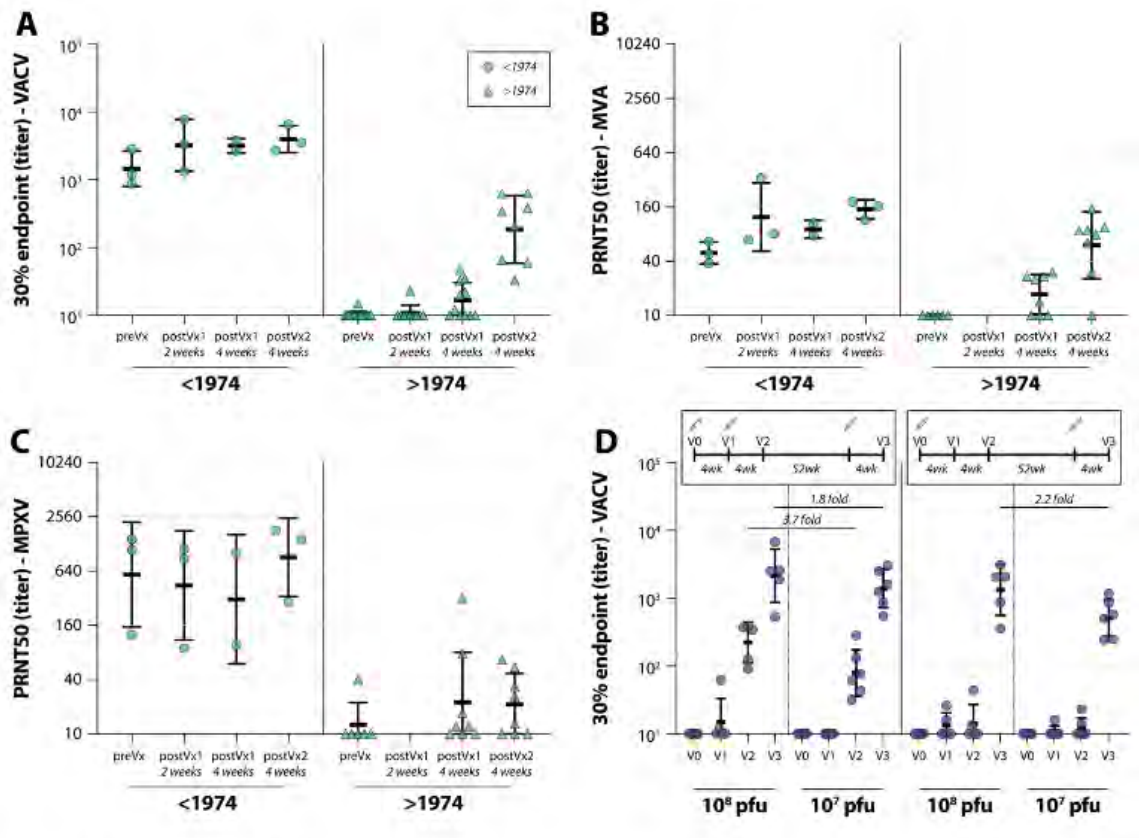


Figure 2. VACV-reactive and MPXV-neutralizing antibodies after Imvanex or MVA-H5 vaccination. (A-C)

Zaeck LM, et al. https://www.medrxiv.org/content/10.1101/2022.08.31.22279414v1.full.pdf