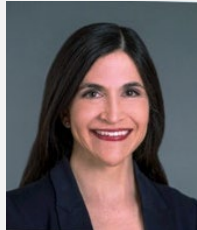




CDC/IDSA Clinician Call

Sept. 24, 2022

Welcome & Introductions



Dana Wollins, DrPH, MGC
Vice President
Clinical Affairs & Guidelines
Infectious Diseases Society of America

- 93rd in a series of calls, initiated in 2020 as a forum for information sharing among frontline clinicians caring for patients with COVID-19.
- The views and opinions expressed here are those of the presenters and do not necessarily reflect the official policy or position of the CDC or IDSA. Involvement of CDC and IDSA should not be viewed as endorsement of any entity or individual involved.
- This webinar is being recorded and can be found online at www.idsociety.org/cliniciancalls.

1. COVID-19: Situation Update, Emerging Variants & Implications for Therapeutics

Update on COVID-19 Epidemiology

Pragna Patel, MD, MPH

Captain, U.S. Public Health Service

Chief Medical Officer (acting)

Coronavirus and Other Respiratory Diseases Division (proposed)

National Center for Immunization and Respiratory Diseases

U.S. Centers for Disease Control & Prevention

COVID-19 Therapeutics Update

Meghan E. Pennini, PhD

Director, Therapeutics

HHS Coordination Operations and Response Element (H-CORE)/

Administration for Strategic Preparedness and Response

U.S. Department of Health and Human Services

2. Monkeypox: Clinical Characteristics and Treatment Options for Severe Disease

Introduction

Agam Rao, MD, MPH

Captain, U.S. Public Health Service

Poxvirus Subject Matter Expert

Multinational Monkeypox Response

U.S. Centers for Disease Control and Prevention

Severe Monkeypox in a Patient With Newly Diagnosed HIV

Robert L. Atmar, MD, FIDSA

Chief, Infectious Diseases, Ben Taub Hospital

Professor, Medicine-Infectious Disease

Baylor College of Medicine

Encephalitis in a Patient With Severe Monkeypox

Matthew J. Copeland, DO

Assist. Professor of Medicine, Georgetown University Medical Center

Attending Physician, Division of Infectious Diseases, Medstar Georgetown University Hospital

Ocular Monkeypox

Vivian Huang, MD, MPH

Assist. Medical Director, Office of Epidemiology and Data Services

Maricopa County Department of Public Health

Nelson Nicolasora, MD

Clinical Assist. Professor, Division of Infectious Disease

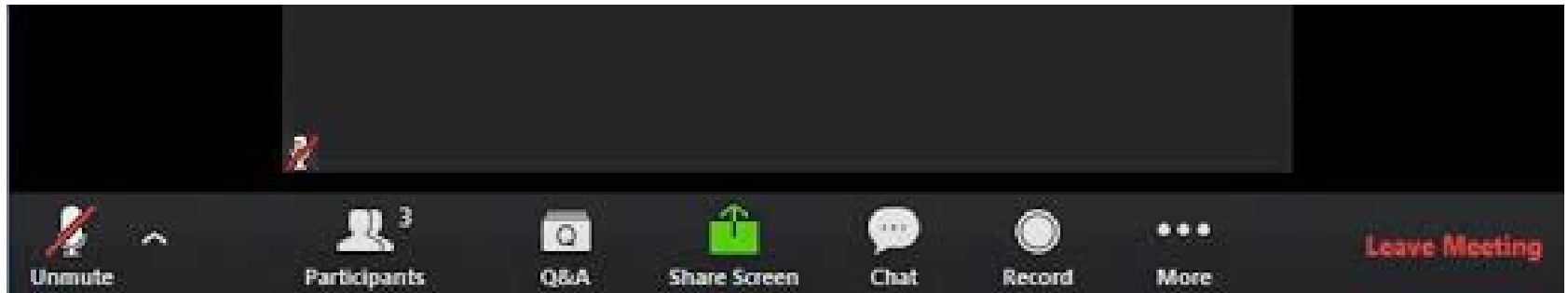
Banner University Medical Center – Phoenix

University of Arizona

Question?
Use the “Q&A” Button



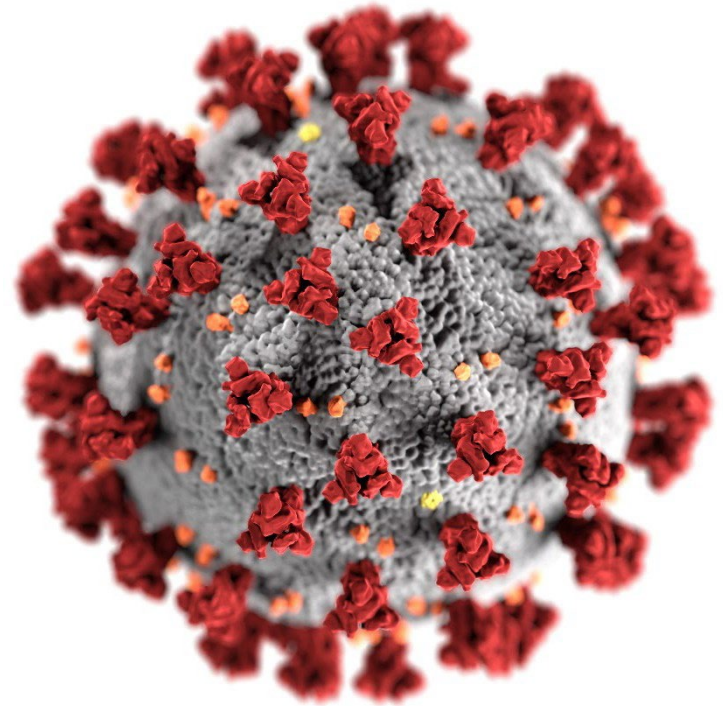
Comment?
Use the “Chat” Button



Update on COVID-19 Epidemiology

Pragna Patel, MD MPH
Acting Chief Medical Officer
Coronavirus and Other Respiratory Viruses Division
(proposed), NCIRD, CDC

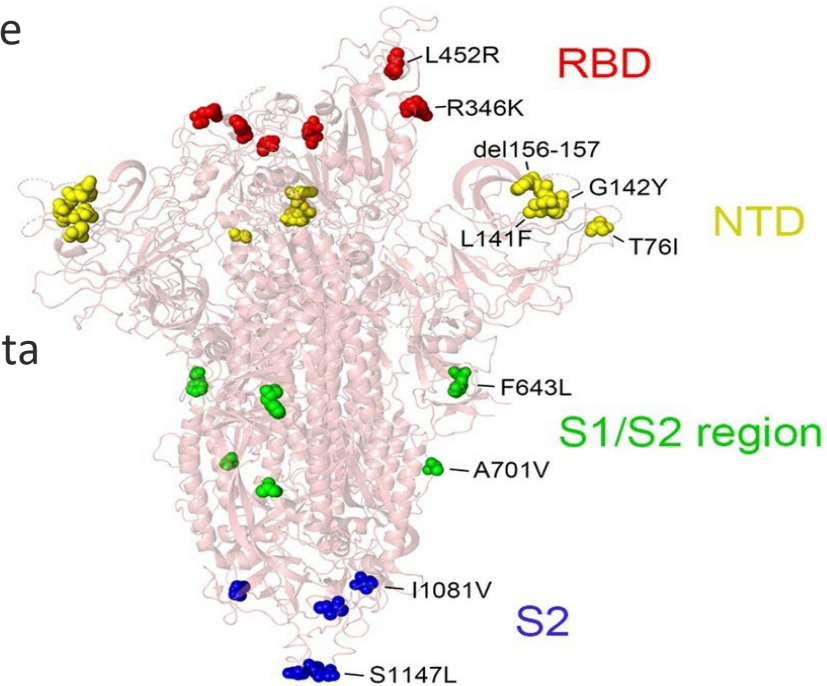
CDC/IDSA Clinician Call
September 24, 2022



cdc.gov/coronavirus

Omicron variant

- Unusually large number of mutations across the SARS-CoV-2 genome
 - **45-52 amino acid changes, deletions, or insertions:**
 - 15 within receptor binding domain**
- More infectious and transmissible than the Delta variant
- Resist neutralization by vaccine- and infection-induced antibodies
- Evade innate immunity
- Resistance to some therapeutics



Daily Change in COVID-19 Cases, United States

January 22, 2020* - September 22, 2022



95,795,378

Total Cases Reported

95,014

New Cases Reported**

53,377

Current 7-Day Average**

Sep 16, 2022 - Sep 22, 2022

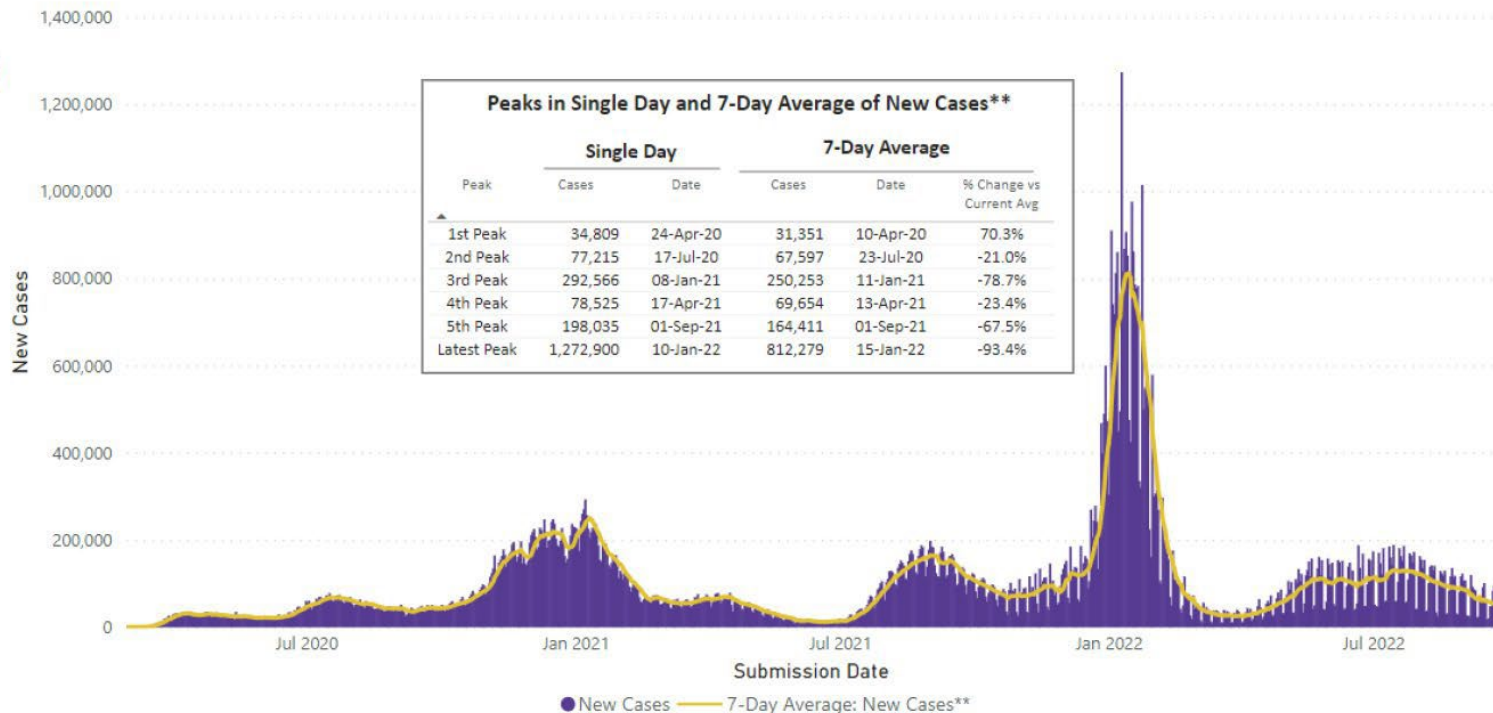
62,578

Prior 7-Day Average**

Sep 09, 2022 - Sep 15, 2022

-14.7%

Change in 7-Day Average



*Graph displays data for Mar 01, 2020, to date. The totals include cases reported since Jan 22, 2020.

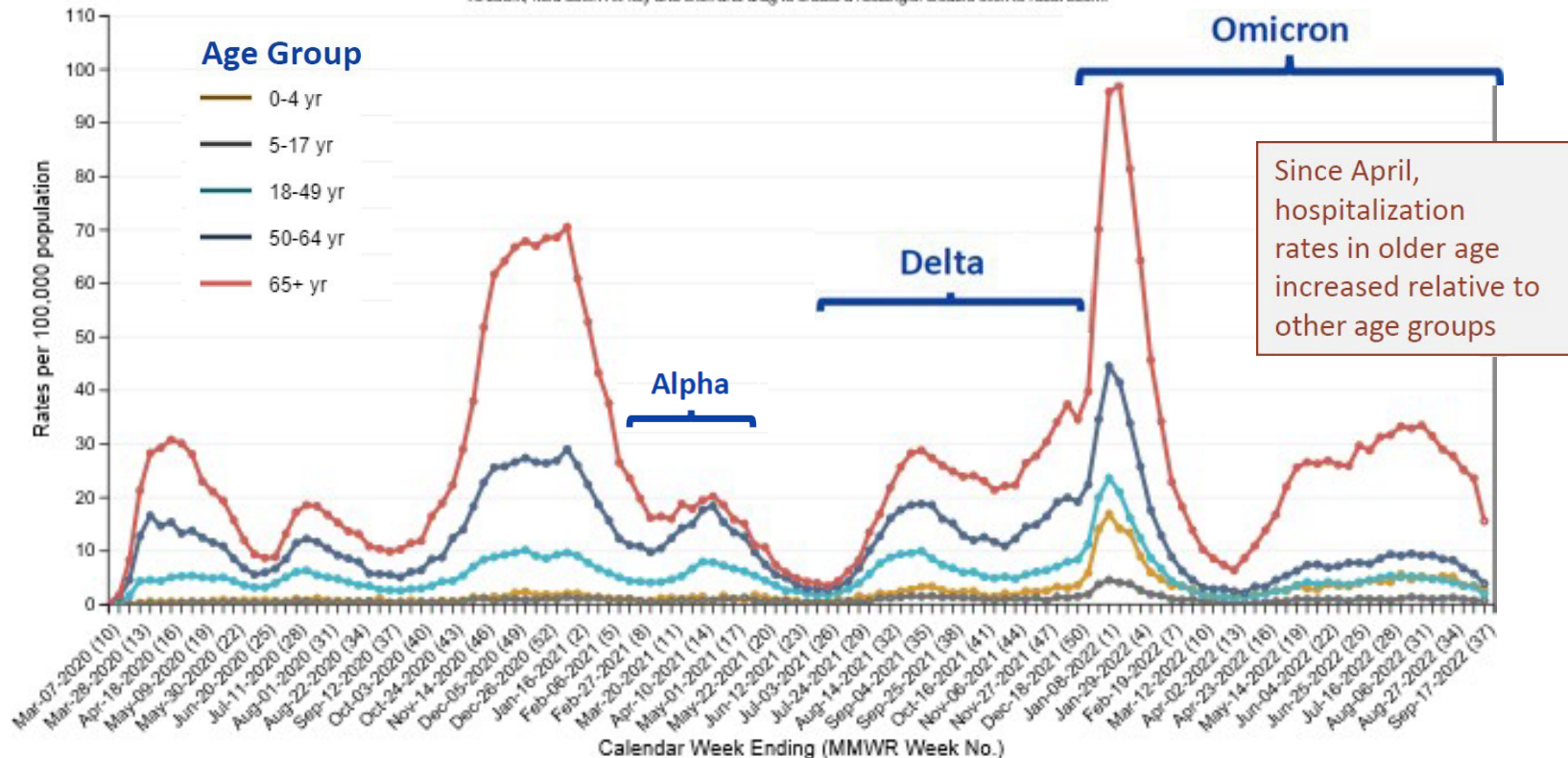
** The histogram, total of new cases in the last 24 hours, and 7-day averages do not include historical cases retroactively that are not yet attributed to the correct date of report.

Of 658,910 historical cases reported retroactively, none were reported on Sep 22, 2022; none in the current week; and 8 in the prior week.

Weekly Trends in COVID-19 Associated Hospitalization Rates by Age group

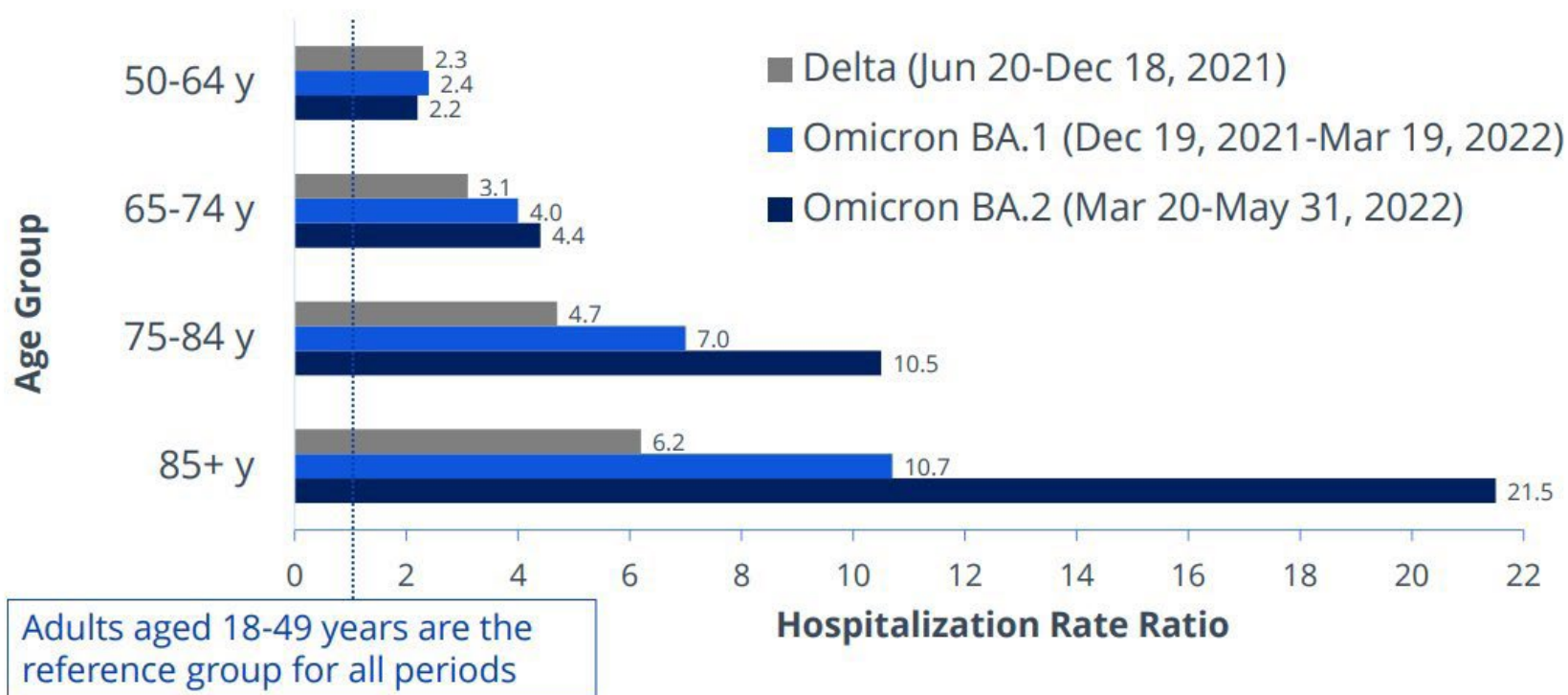
COVID-NET :: Entire Network :: 2020-21 :: Weekly Rate

To zoom, hold down Alt key and click and drag to create a rectangle. Double click to reset zoom.



Hospitalization Rate Ratios by Age Group

COVID-NET, June 2021 – May 31, 2022



Characteristics of hospitalized adults ≥18 years

COVID-NET, June 20, 2021 – May 31, 2022

Characteristic	% of Total Hospitalizations		
	Delta Jun 20, 2021– Dec 18, 2021 (n=5,234)	Omicron BA.1 Dec 19, 2021– Mar 19, 2022 (n=1,804)	Omicron BA.2 Mar 20, 2021– May 31, 2022 (n=1,228)
Age Median (years)	59.9	63.8	70.5
Likely COVID-19-related*	95.5	87.8	85.4
Risk Factors			
Any underlying medical condition	89.3	91.7	95.1
Immunosuppressive condition	11.0	16.0	19.2
Long-term care facility	5.7	9.0	14.2
Outcomes			
Length of stay (days, median)	4.8	3.9	3.3
ICU admission	24.3	17.9	13.2
Mechanical ventilation	13.5	7.6	5.7
In-hospital death	12.4	7.5	5.1

Trends during BA.1 & BA.2

- Median age increased
- Underlying conditions more prevalent
- Clinical outcomes less severe

* COVID-19-related illness as a likely reason for admission is indicated by COVID-19 diagnosis or symptoms consistent with COVID-19 as the chief complaint or reason for admission in the history of present illness. Non-COVID-19 reasons for admission included planned inpatient surgery or procedures, psychiatric admission needing acute medical care, trauma, other, and unknown. Havers et al. MMWR 2022; 71(34):1085–1091. https://www.cdc.gov/mmwr/volumes/71/wr/mm7134a3.htm?s_cid=mm7134a3_w

Factors Associated with Severe Outcomes Among Immunocompromised Adults Hospitalized for COVID-19 — COVID-NET, 10 States, March 2020–February 2022

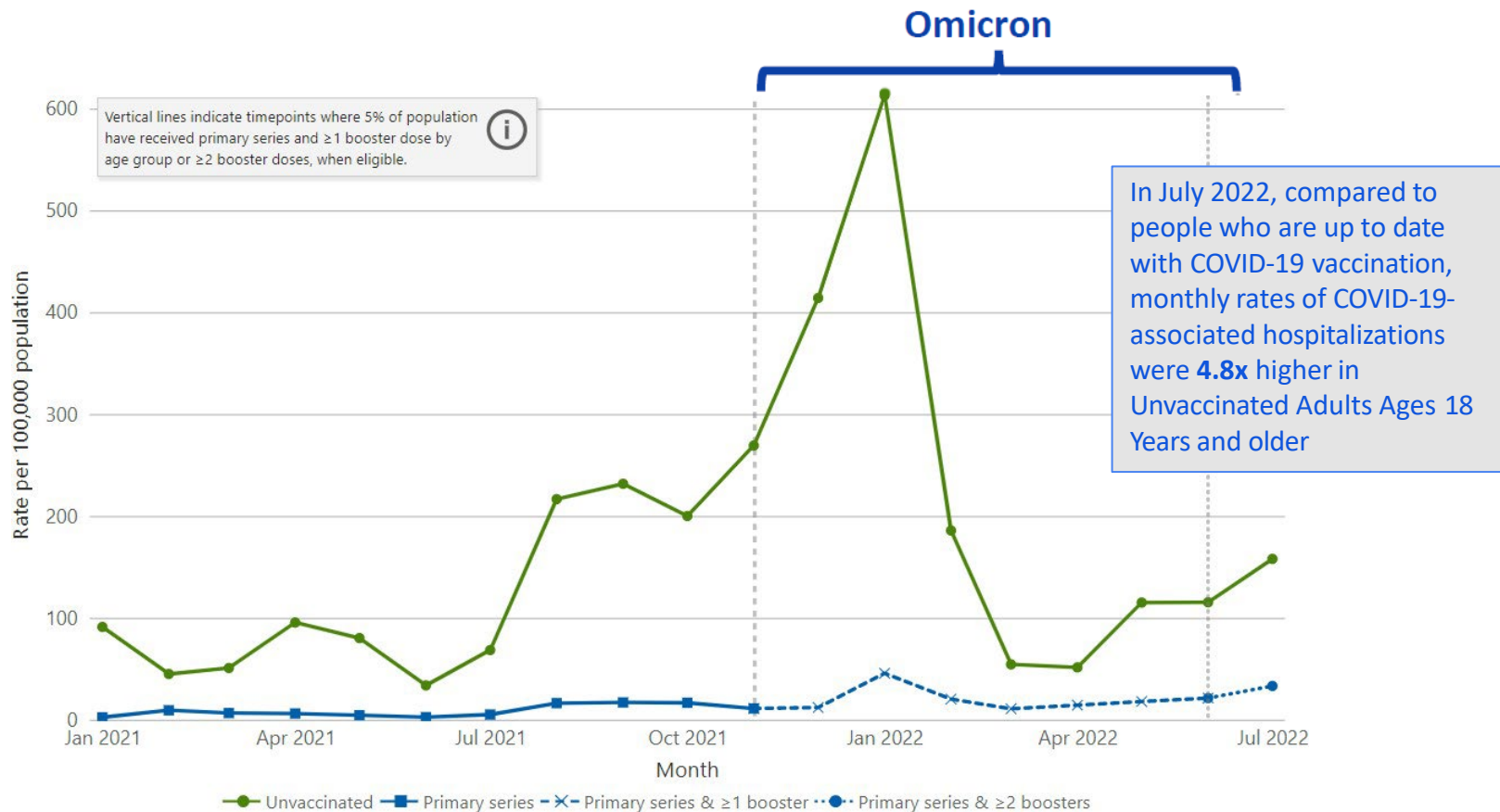
SUPPLEMENTARY TABLE 2. Association of immunocompromise and vaccination status* with in-hospital death among patients hospitalized for COVID-19, by SARS-CoV-2 variant predominant period† — COVID-NET, 10 States, § March 1, 2020–February 28, 2022

Comparison groups	aOR of in-hospital death (95% CI) by SARS-CoV-2 variant predominant period		
	Pre-Delta	Delta	Omicron
Immunocompromised versus nonimmunocompromised			
Unvaccinated [¶]	1.37 (1.02-1.82)**	1.31 (0.74-2.30)	1.04 (0.57-1.91)
Vaccinated*, ^{††}	2.91 (1.69-5.02) ^{§§}	2.51 (1.30-4.83) ^{§§}	0.99 (0.61-1.63)
Vaccinated versus unvaccinated*			
Immunocompromised ^{¶¶}	1.76 (0.82-3.75)	1.23 (0.57-2.64)	1.09 (0.44-2.72)
Nonimmunocompromised***	0.44 (0.23-0.84)**	0.42 (0.28-0.64) ^{§§}	0.84 (0.46-1.57)

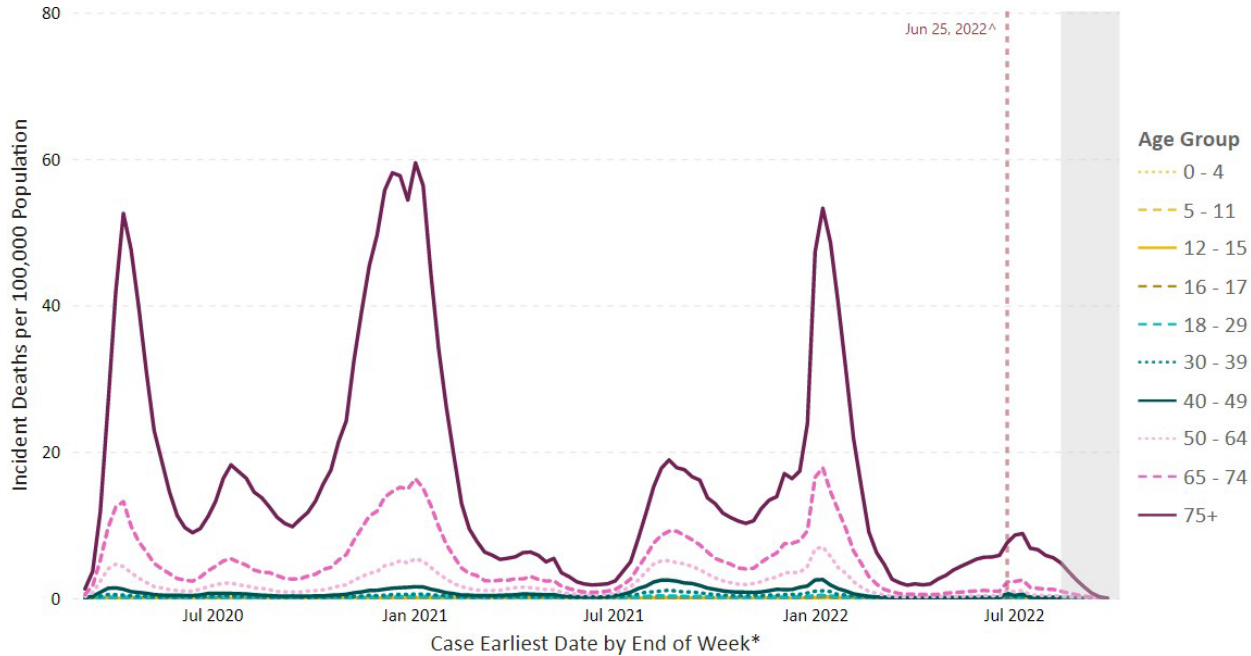
Abbreviations: aOR, adjusted odds ratio; COVID-NET = COVID-19–Associated Hospitalization Surveillance Network.

Pre-Delta period, March 1, 2020–June 26, 2021; Delta period, June 27–December 18, 2021; Omicron period December 19, 2021–February 28, 2022. ** p-value <0.05. Singson et al. MMWR 2022 71 (27) <https://www.cdc.gov/mmwr/volumes/71/wr/pdfs/mm7127a3-H.pdf>

Age-Adjusted Rates of COVID-19 Associated Hospitalizations by Vaccination Status and Receipt of Booster Dose, COVID-NET, January 2021 – July 2022



COVID-19 Weekly Deaths per 100,000 Population

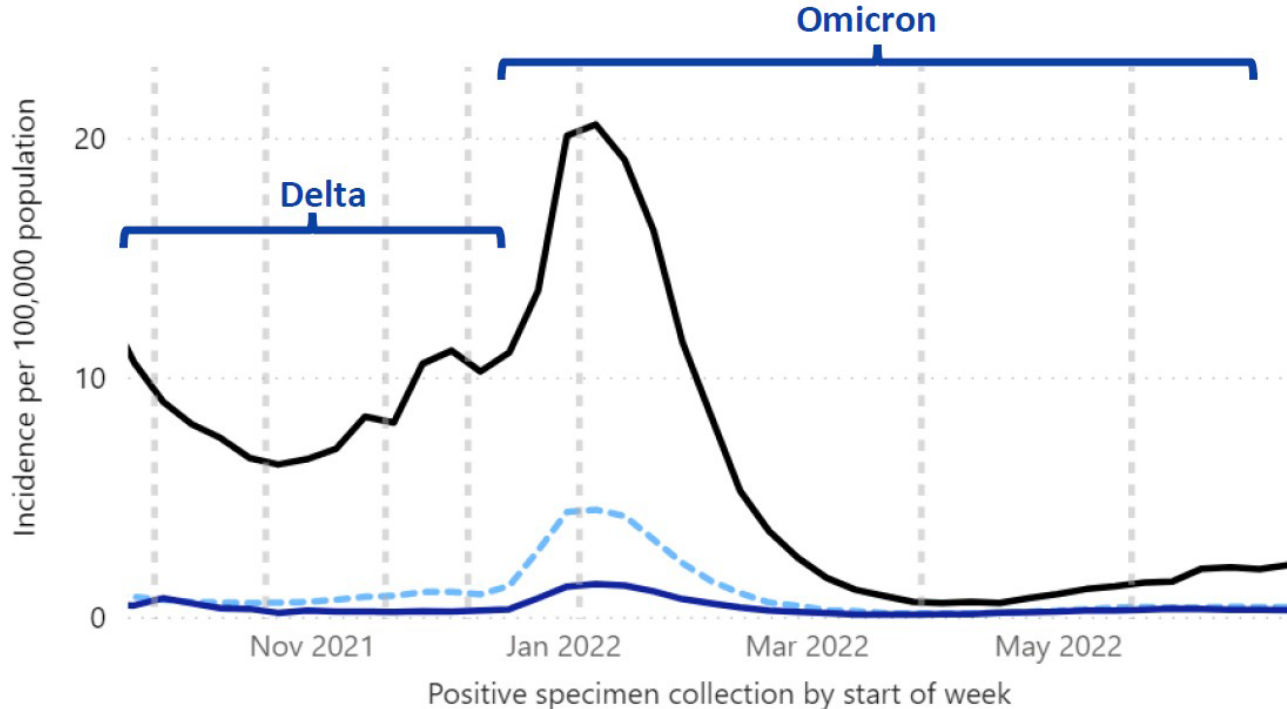


US: The most recent case record was reported during the week ending on Sep 24, 2022. Percentage of deaths among reported cases - 1.03%. Percentage of deaths reporting age by date - 99.91%. US territories are included in case and death counts but not in population counts. Potential six-week delay in case reporting to CDC denoted by gray bars. Weekly data with five or less deaths have been suppressed. *Case Earliest Date is the earliest of the clinical date (related to illness or specimen collection and chosen by a defined hierarchy) and the Date Received by CDC. The date for the current week extends through Saturday. ^The death rate for Texas during the week ending Jun 25, 2022, are reflective of a data reporting artifact.

Source: CDC COVID-19 Case Line-Level Data, 2019 US Census, HHS Protect; Visualization: Data, Analytics & Visualization Task Force and CDC CPR DEO Situational Awareness Public Health Science Team

Age-Adjusted Rates of COVID-19-Associated Deaths by Vaccination Status and Receipt of Booster Dose,* September 19, 2021 – July 2, 2022 (29 U.S. Jurisdictions)

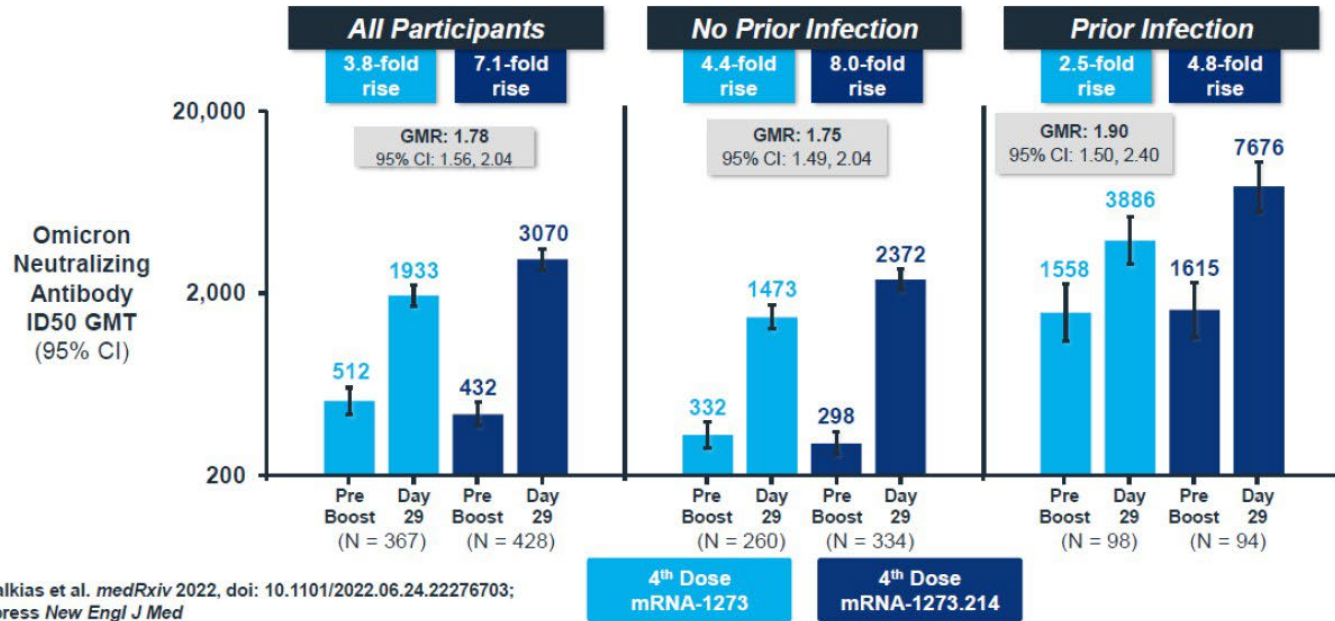
— Unvaccinated — Vaccinated with primary series only — Vaccinated with primary series and 1+ booster dose*



In June 2022, **unvaccinated** people ages ≥ 5 years had **8X higher** COVID-19-associated death rates compared to those with at least **one booster dose**

This was a decrease from **~20X** during January-March 2022

Immunogenicity: Moderna bivalent booster

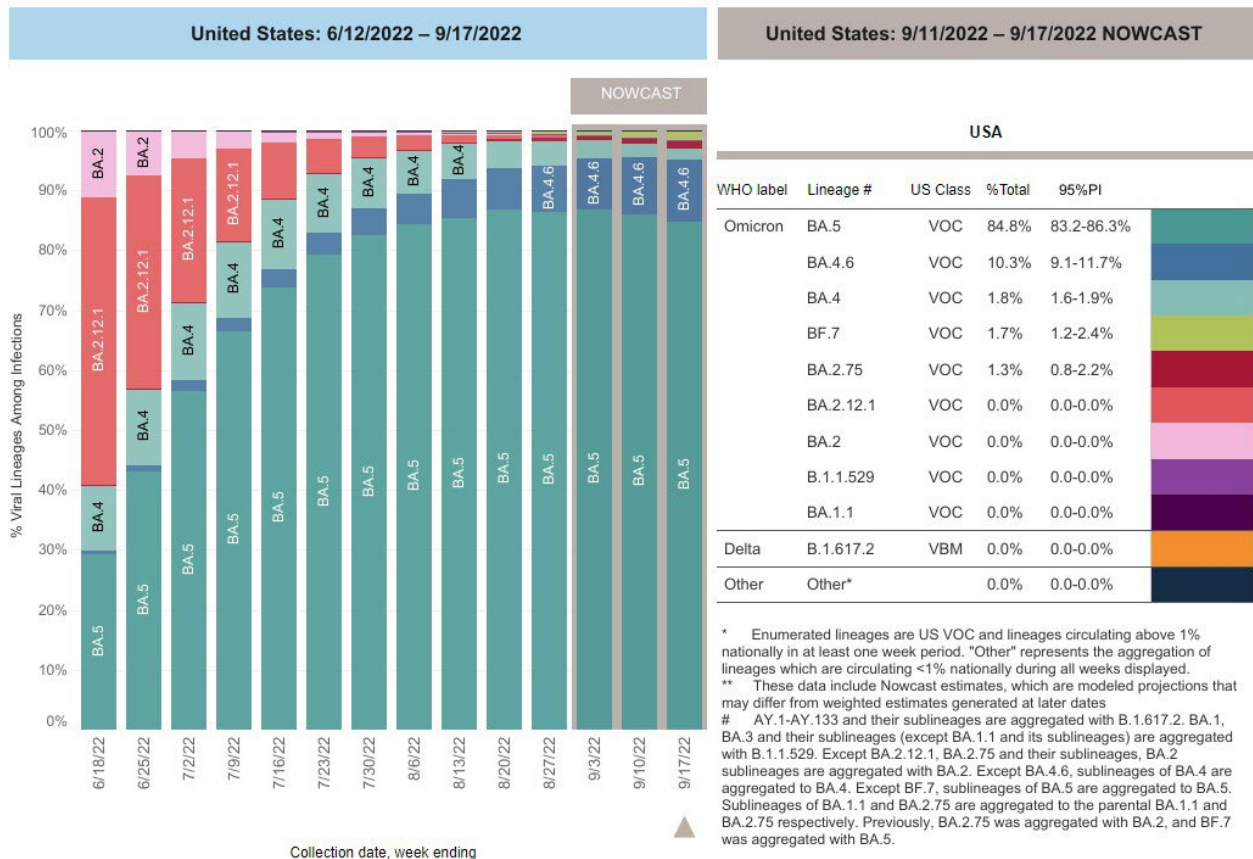


- Met superiority criteria* in participants ≥ 18 years with or without evidence of infection on day 29

*Superiority criterion: the lower bound of the 95% CI for GMR is >1.0

Surveillance for Variants of Concern - NOWCAST

- **BA.5**
 - Predominant in all regions
- **BA.4.6**
 - More prevalent in east and southeast, and HHS Region 7
- **BF.7**
 - Most prevalent in HHS Region 1
- **BA 2.75.2**

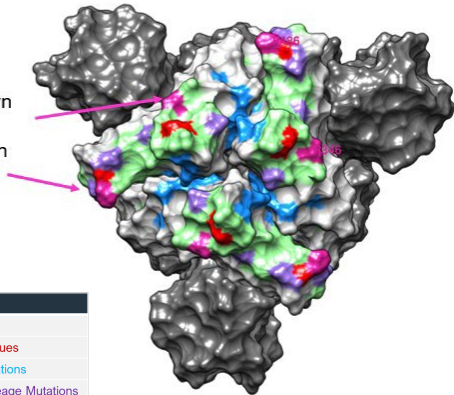


Variants of Concern: Spike Protein R346T Mutation

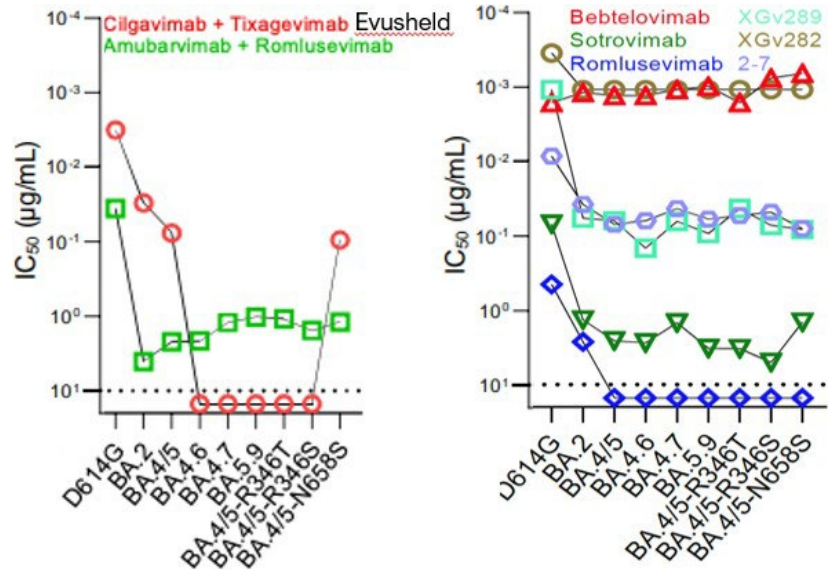
- Evusheld is expected to have reduced potency against lineages with R346T substitutions (BA.4.6, BF.7, BA.2.75.2)
- Bebtelovimab retains potency

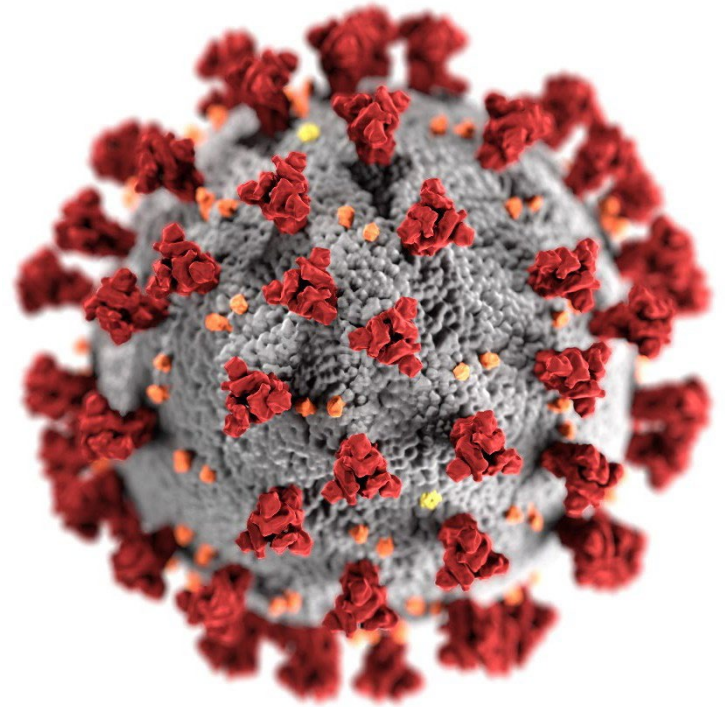
BA.4.6 7 BA.4.6 mutations within binding footprint:
R346T, 440, 452, 477, 478, 484, 486

346, 486: Known resistance and lineage mutation



Key
mAb binding site
mAb Resistance Residues
BA.4/BA.4.6 RBD Mutations
mAb Binding/RBD Lineage Mutations





For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.





COVID-19 Therapeutics Update

Meghan Pennini, PhD
Director, Therapeutics

HHS Coordination Operations and Response Element (H-CORE)/ASPR

September 24, 2022

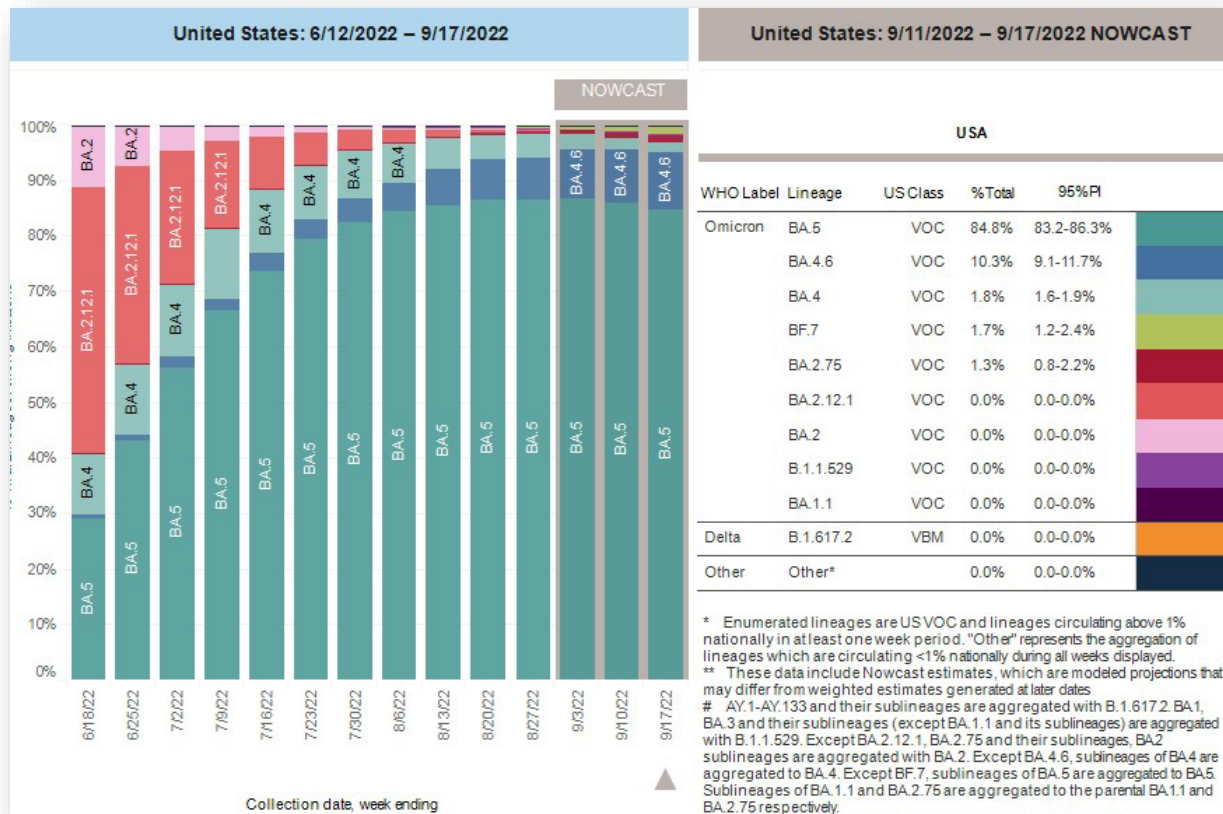
<https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/default.aspx>

Unclassified/For Public Distribution

CDC Nowcast – 9/17/22

CDC NOWCAST for the week ending 17 Sep 22:

- **BA.5 –84.8%**
 - Predominant all regions
- **BA.4.6 – 10.3%**
 - Highest in R7 (17.8%)
 - R346T spike RBD substitution + N658S
- **BF.7 (1.7%) separated from BA.5**
 - R346T
- **BA.2.75 (1.3%) separated from BA.2**
 - Some with R346T (BA.2.75.2)



Efficacy of COVID-19 Therapeutics against Variants

Evusheld (PrEP)

Lineage	Country 1 st Identified	WHO Nomenclature	Key Substitutions Tested	Fold Reduction (Pseudotyped VLPs)	Fold Reduction (Authentic Virus)
BA.1	Botswana	Omicron (BA.1)	G339D+S371L+S373P+S375F+K417N+N440K+G446S+S477N+T478K+E484A+Q493R+G496S+Q489R+N501Y+Y505H	132- to 183-fold [#]	12- to 30-fold
BA.1.1	Multiple country origin	Omicron (BA.1.1) [+R346K]	G339D+R346K+S371L+S373P+S375F+K417N+N440K+G446S+S477N+ T478K +E484A+Q493R +G496S+Q489R+N501Y+ Y505H	424-fold	176-fold
BA.2	Multiple country origin	Omicron (BA.2)	G339D+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+S477N+T478K+E484A+Q493R+Q498R+N501Y+ Y505H	No Change [§]	5.4-fold
BA.2.12.1	United States	Omicron (BA.2.12.1)	G339D+ S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+L452Q+S477N+T478K+E484A+Q493R+Q498R+N501Y+ Y505H	5-fold	ND
BA.3	Multiple country origin	Omicron (BA.3)	G339D+S371F+S373P+S375F+D405N+K417N+N440K+G446S+S477N+T478K+E484A+Q493R+Q498R+N501Y+ Y505H	16-fold	ND
BA.4/5	Multiple country origin	Omicron (BA.4/5)	+G339D+S371F+S373P+S375F+T376A+D405N+R408S+K417N+N440K+L452R+S477N+T478K+E484A+F486V+Q498R+ N501Y+Y505H	33- to 65-fold	ND

<https://www.fda.gov/media/154701/download>

Bebtelovimab (treatment)

Lineage with Spike Protein Substitution	Country First Identified	WHO Nomenclature	Key Substitutions Tested ^a	Fold Reduction in Susceptibility
BA.1.1	South Africa	Omicron [+R346K]	BA.1 + R346K	No change ^b
BA.2	South Africa	Omicron [BA.2]	G339D + S371F + S373P + S375F + T376A + D405N + R408S + K417N + N440K + S477N + T478K + E484A + Q493R + Q498R + N501Y + Y505H	No change ^b
BA.2.12.1	USA	Omicron [BA.2+L452Q]	BA.2 + L452Q	No change ^b
BA.2.75	India	Omicron [BA.2+D339H, G446S, N460K, R493Q (reversion)]	BA.2 + D339H, G446S, N460K, R493Q (reversion)	No change ^b
BA.4/BA.5	South Africa	Omicron [BA.4/BA.5]	G339D + S371F + S373P + S375F + T376A + D405N + R408S + K417N + N440K + L452R + S477N + T478K + E484A + F486V + Q498R + N501Y + Y505H	No change ^b
BA.4.6	USA	Omicron [BA.4+R346T]	BA.4 + R346T	No change ^b

<https://www.fda.gov/media/156152/download>

- Preliminary reports showing retained activity against BA.4/5 for **Veklury**^{1,2} & oral antivirals (**Paxlovid**, **Lagevrio**)²
- Evusheld activity against BA.4.6 is likely diminished

1. <https://www.gilead.com/news-and-press/company-statements/veklury-remdesivir-demonstrates-continued-in-vitro-antiviral-activity-against-omicron-subvariants>
2. <https://www.nejm.org/doi/full/10.1056/NEJM2207519>

Efficacy of COVID-19 Therapeutics against Variants

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

Subvariant	Mean Neutralization Activity of Monoclonal Antibody†							Susceptibility to Antiviral Drug‡			
	Imdevimab	Casirivimab	Tixagevimab	Cilgavimab	Sotrovimab Precursor	Bebtelovimab	Imdevimab+ Casirivimab (Regen-cov)	Tixagevimab+ Cilgavimab (Evusheld)	Remdesivir (Veklury)	Molnupiravir (Lagevrio)	Nirmatrelvir (+rito, Paxlovid)
	ng per milliliter							μmol			
Reference§	7.4	6.1	6.1	7.0	95.1	2.5	3.4	6.3	1.7	2.8	2.7
BA.1	>50,000	>50,000	1552.7	2916.9	40727.1	5.8	>10,000	351.1	1.9	7.5	4.8
BA.1.1	>50,000	>50,000	603.5	>50,000	3769.2	3.9	>10,000	1296.8	2.0	6.0	3.9
BA.2	329.0	>50,000	2756.6	16.9	>50,000	3.3	835.1	34.6	5.9	8.7	6.9
BA.2.12.1	238.1	>50,000	335.2	21.0	>50,000	4.0	452.7	38.1	0.5	3.2	1.8
BA.4	132.6	>50,000	>50,000	53.6	>50,000	2.9	459.1	37.8	1.2	3.3	2.9
BA.5	583.4	>50,000	>50,000	56.8	>50,000	3.3	1093.1	192.5	2.0	4.1	4.4

* The antibodies that were used in this analysis are listed by their commercial names for readability although they were produced in the authors' laboratories in their generic formulations. Omicron subvariants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are listed according to the World Health Organization labels for the Pango lineage.

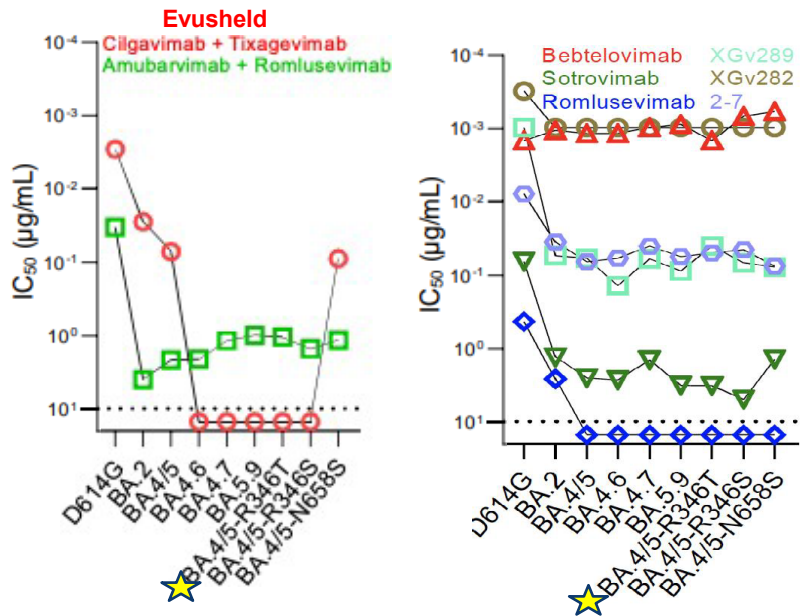
† Individual monoclonal antibodies were tested at a starting concentration of 50,000 ng per milliliter on 50% focus reduction neutralization testing. The monoclonal antibody combinations were tested at a starting concentration of 10,000 ng per milliliter for each antibody.

‡ The susceptibility to antiviral drugs was measured as the 50% inhibitory concentration of the mean micromole value of triplicate reactions. GS-441524 is the main metabolite of remdesivir and EIDD-1931 is the active form of molnupiravir, both of which are RNA-dependent RNA polymerase inhibitors. Nirmatrelvir (PF-07321332) is a protease inhibitor.

§ The reference strain was SARS-CoV-2/UT-NC002-1T/Human/2020/Tokyo.

- Live virus data; <https://www.nejm.org/doi/full/10.1056/NEJMc2207519>
- Data against more recent variants (BA.4.6, BA.2.75.2) pending

Preliminary data: Evusheld Loses Neutralization Potency against BA.4.6 Bebtelovimab Maintains Potency



Pseudovirus Data:

Preprints: [Wang](#) (above);
R346[T/S/I] mutations impact Evusheld activity; ★BF.7

IC ₅₀ (ng/ml)	B.1	BA.5	BA.4.6	BA.2.10.4	BA.2.75.2
S309 (sotrovimab)	119	559	925	560	442
Cilgavimab	12	71	>1000	168	>1000
Tixagevimab	4	>1000	>1000	>1000	>1000
Evusheld	6	120	>1000	816	>1000
LY-CoV1404 (bebtelovimab)	4	1	2	3	2
REGN10933 (casirivimab)	14	>1000	>1000	>1000	>1000
REGN10987 (imdevimab)	10	>1000	>1000	>1000	>1000
LY-CoV016 (etesevimab)	29	>1000	>1000	>1000	>1000
LY-CoV555 (bamlanivimab)	9	>1000	>1000	>1000	>1000
ADG-20	56	>1000	>1000	>1000	>1000
S2E12	4	>1000	>1000	>1000	>1000
S2K146	18	118	78	207	62
A23-58.1	6	>1000	>1000	>1000	>1000

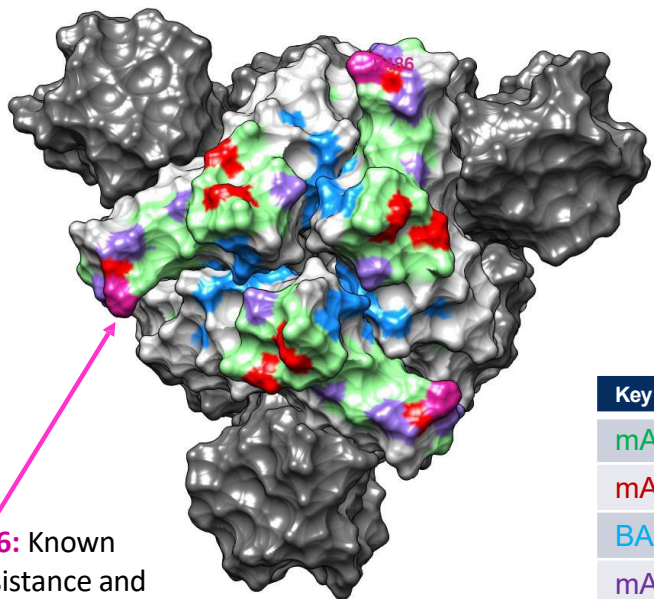
Preprint: [Sheward](#)

BA.4 vs BA.4.6: Example of Impact of R346T to Evusheld

BA.4

6 BA.4 mutations within binding footprint:
440,452,477,478,486,484

***Evusheld neutralizes BA.4

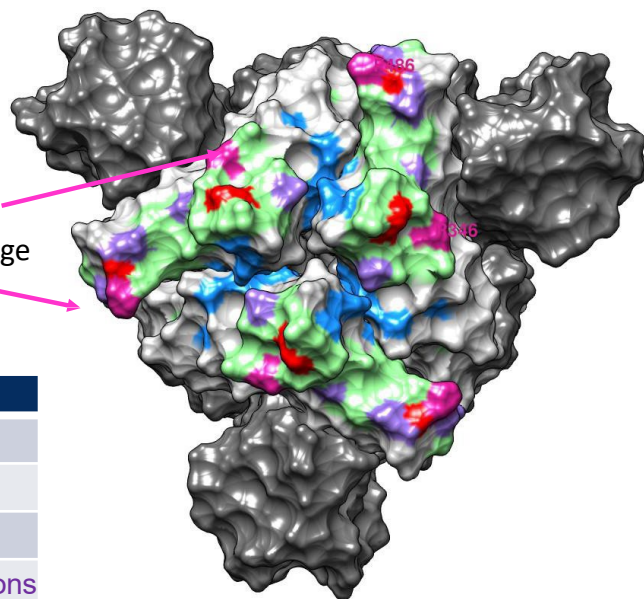


486: Known resistance and lineage mutation

BA.4.6

7 BA.4.6 mutations within binding footprint:
R346T,440,452,477,478,484,486

***Evusheld potency likely significantly reduced



346, 486: Known resistance and lineage mutation

Key

mAb binding site

mAb Resistance Residues

BA.4/BA.4.6 RBD Mutations

mAb Binding/RBD Lineage Mutations

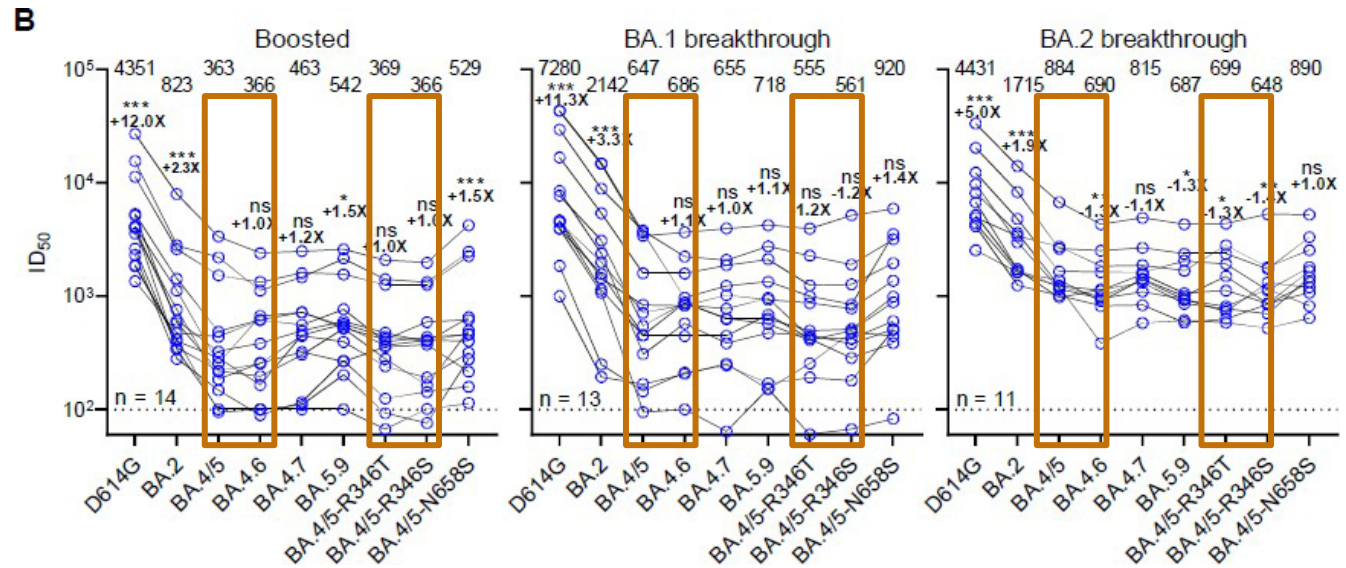
Other Lineages with R346T: BF.7, BA.2.75.2

Unclassified/For Public Distribution

Note: BA.2.75 w/o R346T is likely susceptible to Evusheld

Pseudovirus neutralization of Omicron variants by Vaccine Sera

- Immune evasion: D614G < BA.2 ~ BA.2.75 < BA.4/5 ~ BA.4.6 ~ BA.4.7 ~ BA.5.9

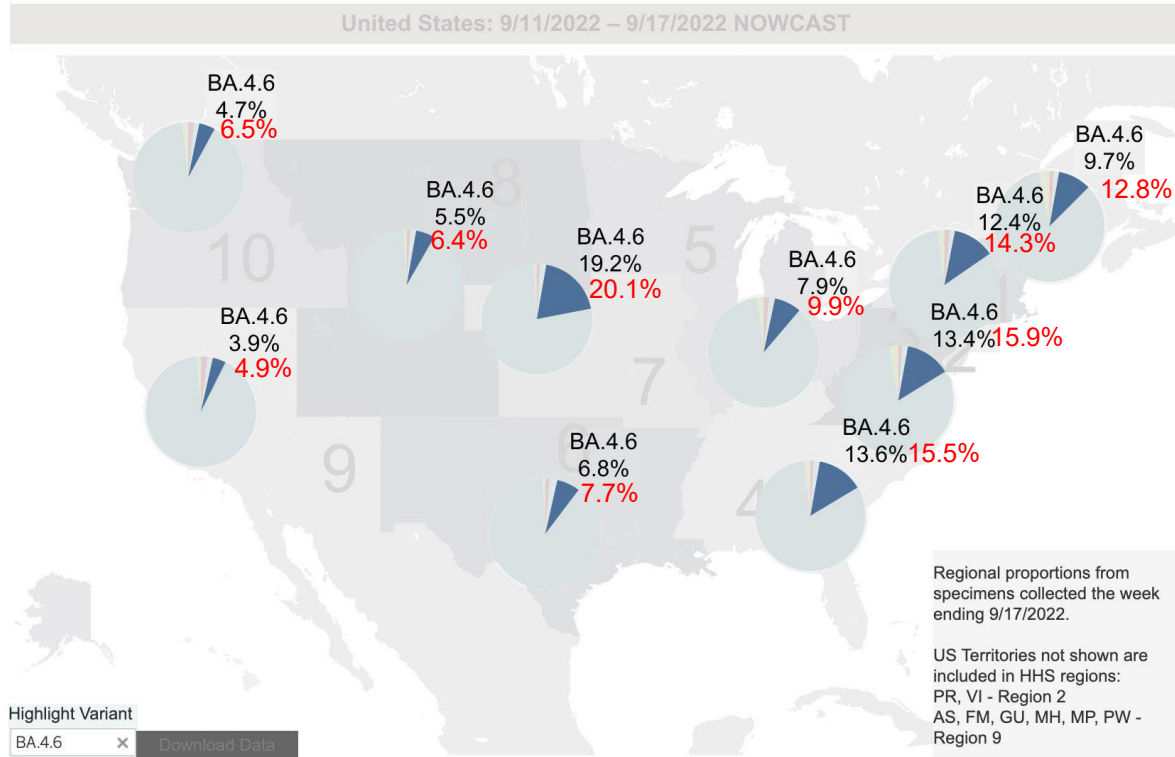


- R346T, R346S, and N658S in the background of BA.4/5 had minimal impact on vaccine sera neutralization

Wang *et al*, bioRxiv 2022.09.05.506628;
<https://doi.org/10.1101/2022.09.05.506628>

BA.4.6 US Regional Epidemiology Data

BA.4.6
BA.4.6+BF.7

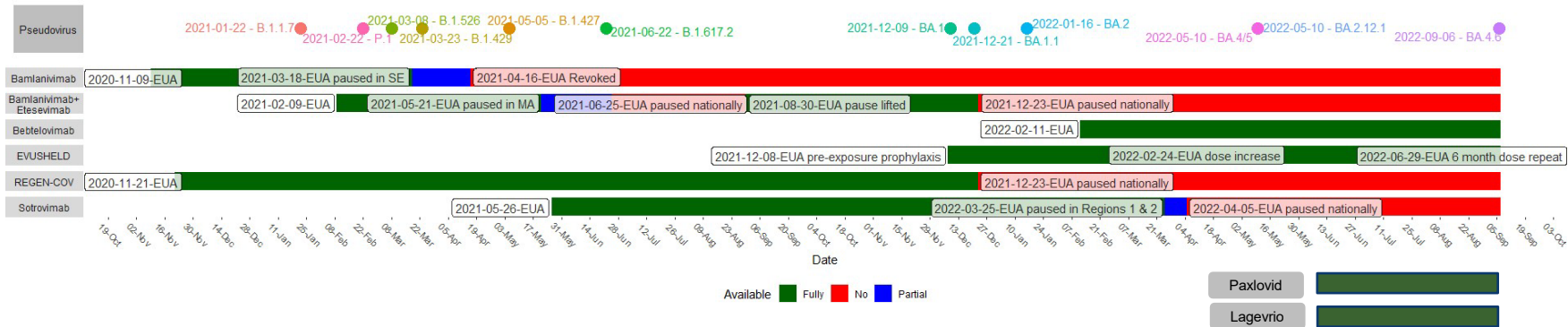
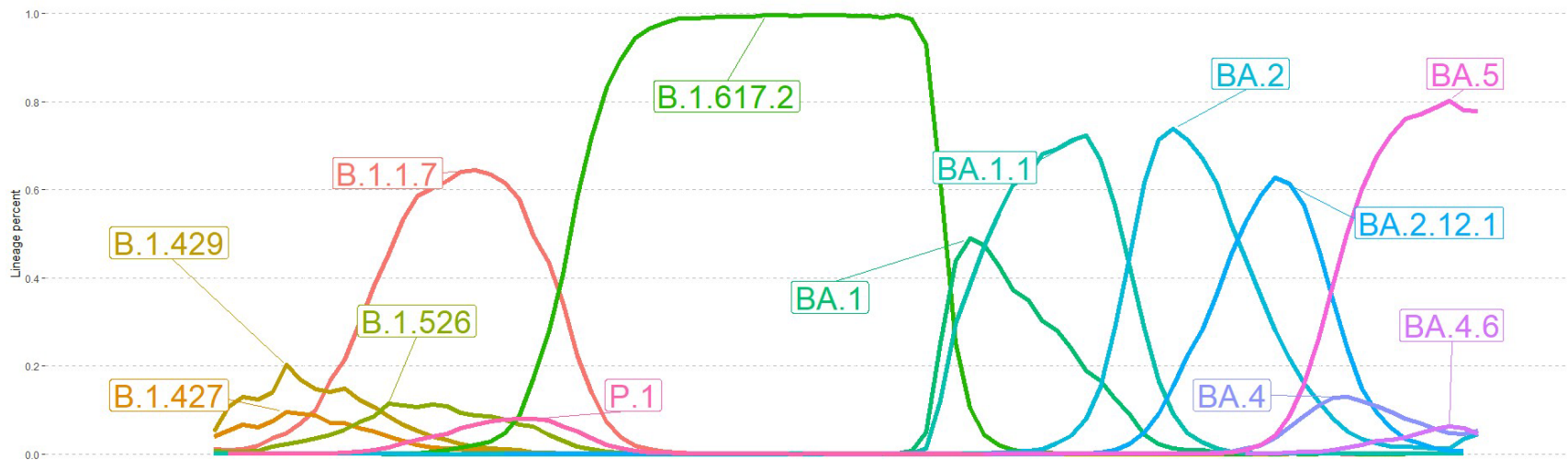


Lineages called using pangolin v4.1.2, pangolin-data v1.14 and usher v0.5.4.

Updated September 16, 2022

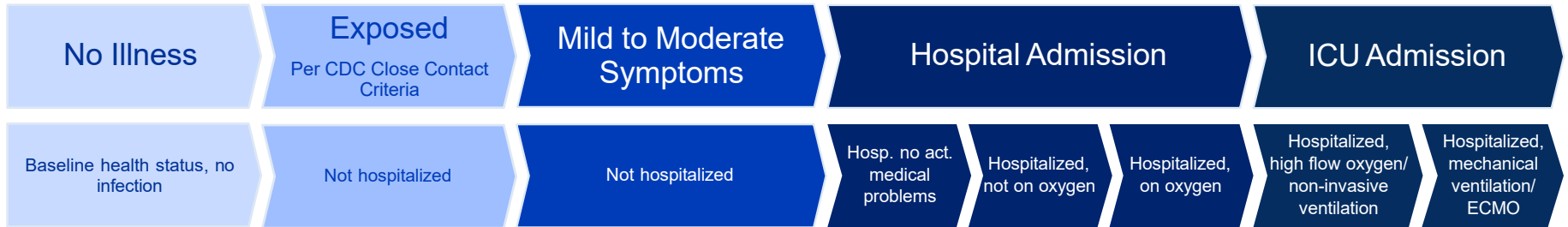
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Predominant PANGO lineages and EUA mAb availability in the USA



Unclassified/For Public Distribution

Summary of COVID-19 Preventative Agents & Treatments



COVID-19 Vaccines

Monoclonal Antibodies for PrEP

- Evusheld (tixagevimab + cilgavimab, AZ)

None currently authorized for use in any US state or territory.

Oral Antivirals

- Paxlovid (nirmatrelvir + ritonavir, Pfizer)
- Lagevrio (molnupiravir, Merck) – **Alternative**

Monoclonal Antibodies

- Bebtelovimab (Lilly) – **Alternative**

Veklury® (remdesivir, Gilead)

Please see [NIH Current Inpatient Therapies](https://www.covid19treatmentguidelines.nih.gov/therapies/) (<https://www.covid19treatmentguidelines.nih.gov/therapies/>)

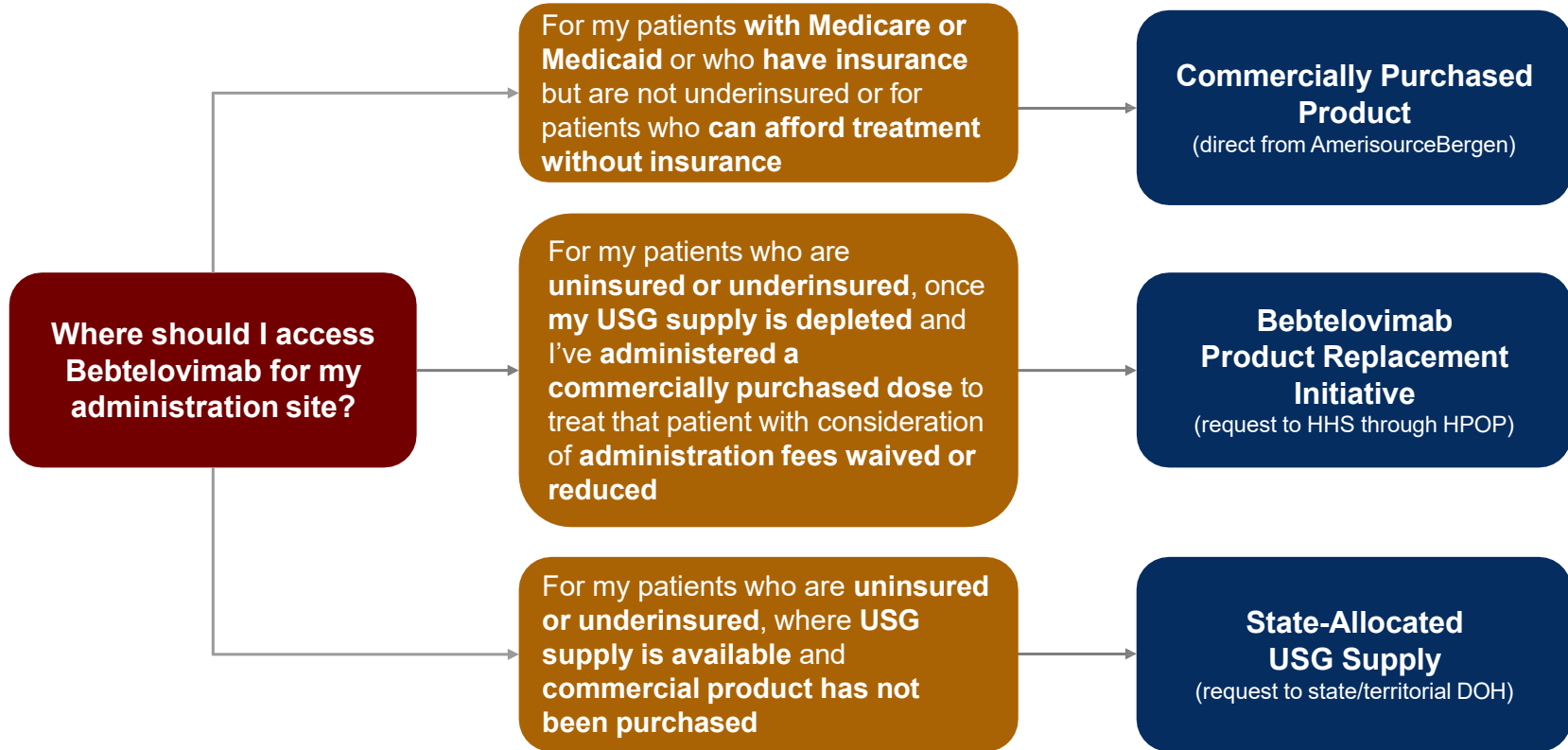
• There is currently **ample supply** of all therapeutics – every eligible patient should have access to these medications

[Therapeutic Management of Nonhospitalized Adults With COVID-19](#)
[Therapeutic Management of Hospitalized Adults With COVID-19](#)

Bebtelovimab Transition to Commercial Market: bebtelovimab product replacement initiative now available

- How it works: A provider who has commercial supply and treats an under or uninsured patient with a purchased dose can request a replacement dose, at no charge, from USG
- Provider site should:
 - Have **used all their USG supply** acquired through the HHS distribution program
 - Have **purchased commercial bebtelovimab** and **attest** to using a purchased dose for an under or uninsured patient
 - **Charge a reasonable administration fee** for bebtelovimab for that patient
 - Consideration to waive or reduce fee to be reasonable for the patient being treated
- Process: Requests made in the Health Partner Ordering Portal (HPOP)
 - Provider attests to verifying the patient who received treatment was uninsured (has no insurance coverage/can't afford treatment) or underinsured (can use guidelines for other federal or local programs)
- How to access: Providers already registered in HPOP have immediate access; others should contact their state or territorial health department to access HPOP
 - Replacement dose must replace a commercially purchased dose
 - Replacement dose shipped to provider is commercially labelled supply and can be used for any patient; payment is allowable for the replacement dose received

Bebtelovimab Supply Options



Related Resources

Helpful Information and Resources

- [HHS Therapeutics Homepage](#)
- [Product Expiration Date Extensions](#)
- [Test to Treat Initiative webpage and Fact Sheet](#)
- [Test to Treat Site Locator](#) and [Digital Tool Kit](#)
- [General Therapeutics Locator](#)
- [HHS Clinical Implementation Guide](#)
- [Outpatient Therapeutics Decision Aid](#)
- [Side-by-Side Overview of Outpatient Therapeutics](#)
- [ASPR Regional Emergency Coordinators](#)
- [CMS reimbursement information for mAbs](#)
- [CMS reimbursement information for oral antivirals](#)

Latest COVID-19 Therapeutics Updates Found at aspr.hhs.gov

MONKEYPOX

Update: Severe manifestations of monkeypox—United States

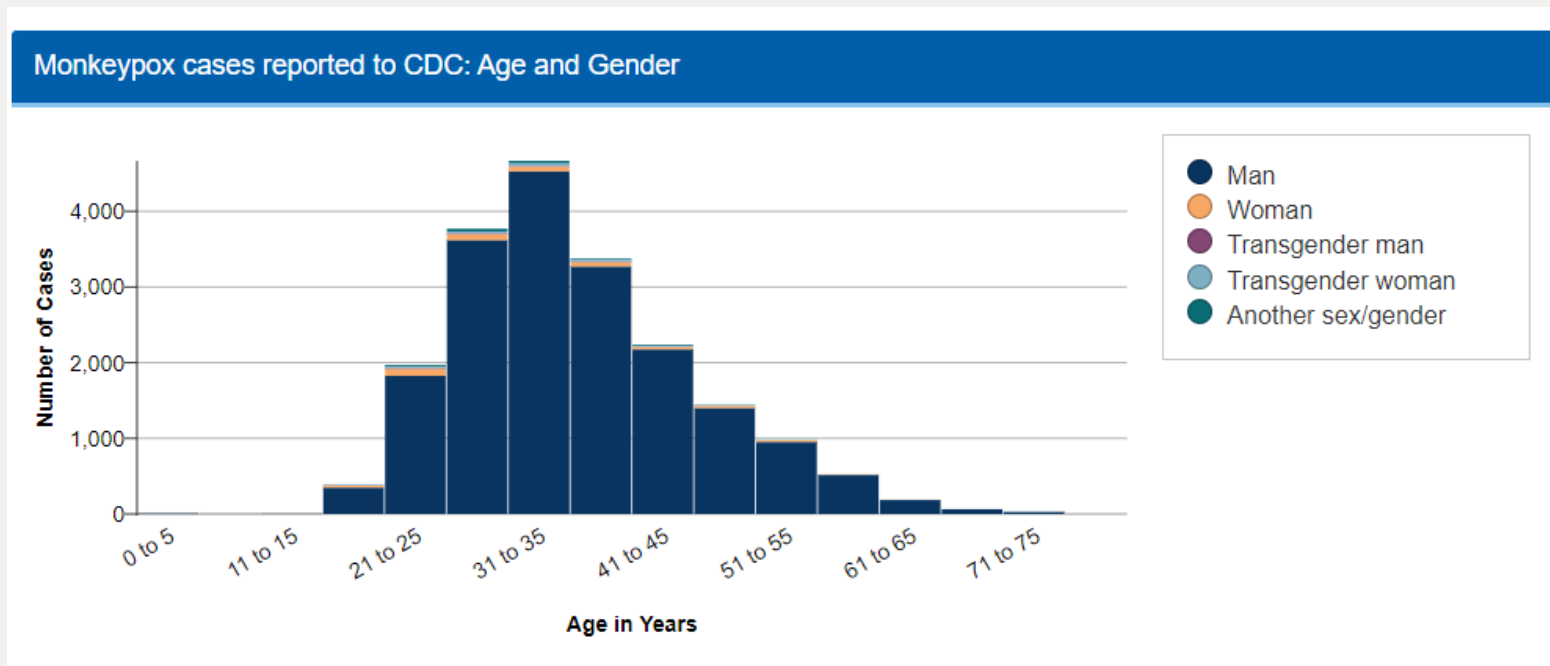
CDC/IDSA Clinician Call
Saturday, Sept 24th, 2022

Agam Rao, MD
CAPT, U.S. Public Health Service
Monkeypox Subject Matter Expert, CDC



Age and Gender (9/21/22)

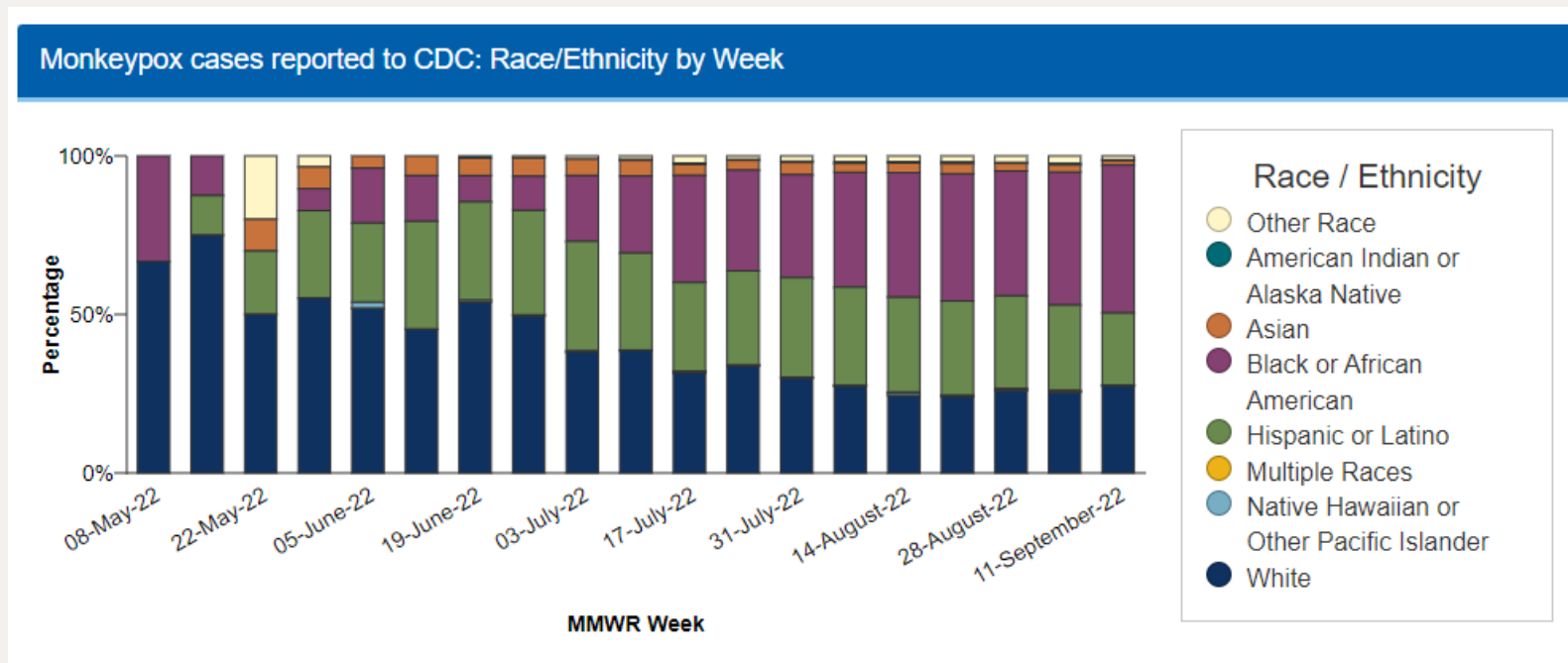
<https://www.cdc.gov/poxvirus/monkeypox/response/2022/demographics.html>



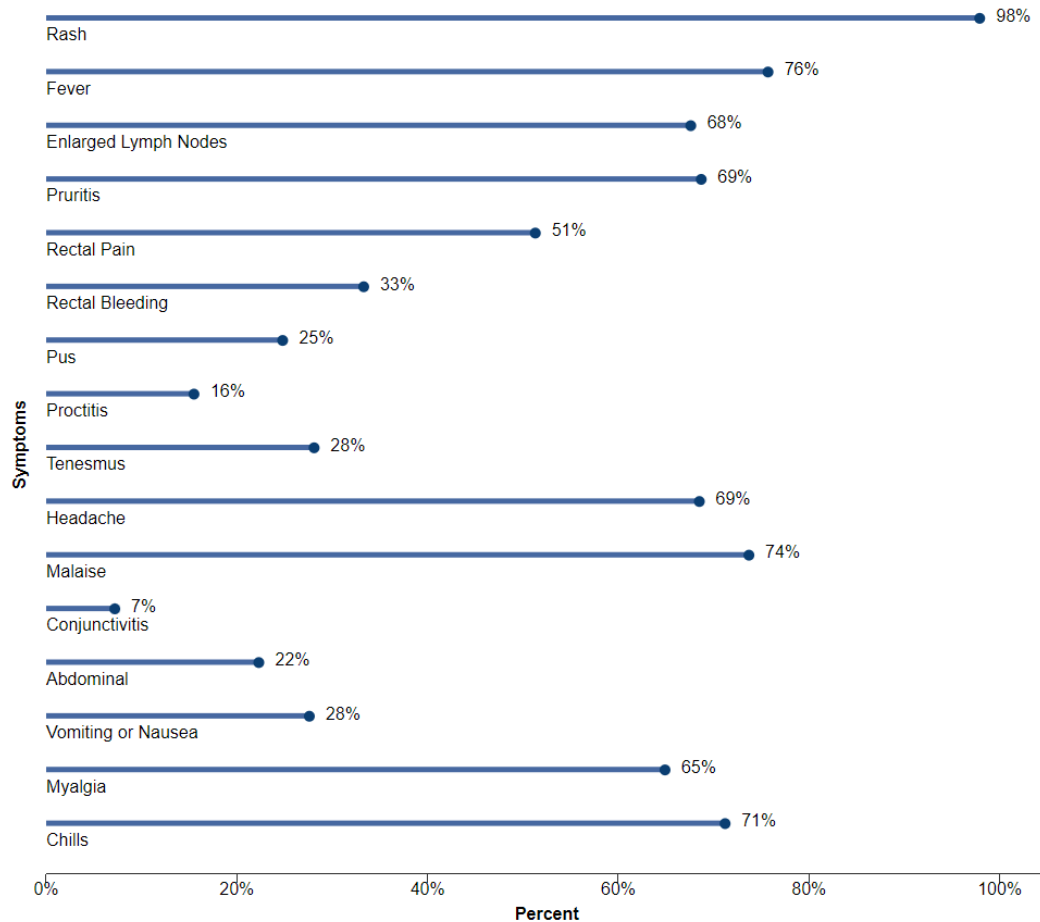
Up to 94% of patients report recent male-to-male sexual contact in the last 3 weeks*

(*[Epidemiologic and Clinical Characteristics of Monkeypox Cases — United States, May 17–July 22, 2022 | MMWR \(cdc.gov\)](#))

Race/Ethnicity (9/21/22)



Signs and symptoms (9/21/22)



Most common:

Rash (98%)

Fever (76%)

Malaise (74%)

Chills (71%)

Enlarged lymph nodes (68%)

Myalgia (65%)

Other:

Rectal Pain (51%)

Tenesmus (28%)

Proctitis (15%)

<https://www.cdc.gov/poxvirus/monkeypox/responses/2022/demographics.html>

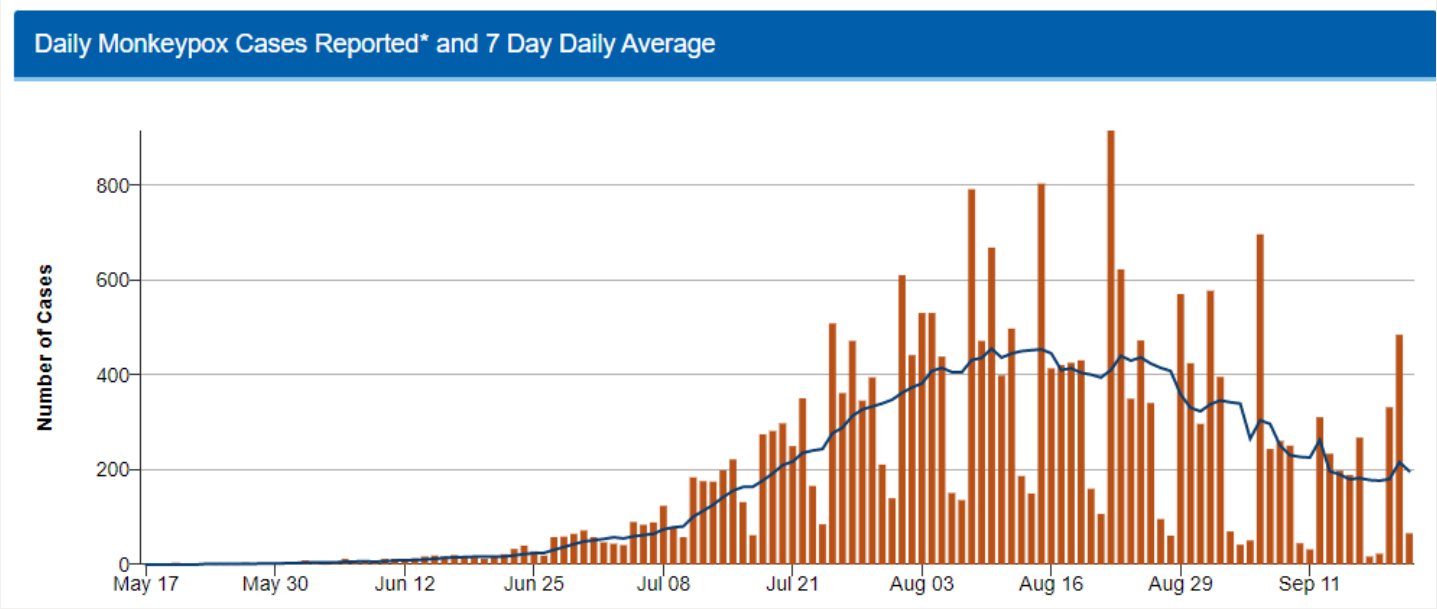
Management of most patients

- Most immunocompetent patients recover with pain management* and other supportive care
- Tecoviromat should be considered for some conditions[†]
 - Severe disease: hemorrhagic disease, large number of lesions, sepsis, encephalitis, ocular or periorbital infections, other conditions requiring hospitalization
 - Lesions involving anatomic areas that could cause severe infection (e.g., pharynx, penile foreskin, vulva, vagina, urethra, anus)
 - Lesions in persons who are at high risk for severe disease
 - ❖ Immunocompromise
 - ❖ Pediatric populations
 - ❖ Pregnant or breastfeeding
 - ❖ Condition affecting skin integrity

*<https://www.cdc.gov/poxvirus/monkeypox/clinicians/pain-management.html>

[†]<https://www.cdc.gov/poxvirus/monkeypox/clinicians/treatment.html>

Cases decreasing—United States, September 21, 2022



Severe infections

- Demographics of affected patients
 - 100% male
 - Ages 21–58 years (median= 32 years)
 - Majority Hispanic or non-Hispanic Black
 - Most immunocompromised due to advanced HIV
 - 2 patients receiving chemotherapy for cancer
- Progressive illness
 - >100 lesions; new lesions despite treatment
 - Coalesced lesions and necrosis
 - Significant lymphadenopathy
 - Hemodynamic instability
 - Sepsis and secondary infections

CDC Clinical Consultations

- Available 24/7 through health departments
- Can facilitate
 - Treatment with stockpiled VIGIV and in the future, brincidofovir
 - Determination of antibody response (i.e., serology)
 - Evaluation of certain biopsy and autopsy specimens for orthopoxviruses
 - Genome sequencing, including to evaluate for tecoviromat resistance
 - Case specific advice based on accumulated clinical knowledge
- Learn together about clinical manifestations so that national guidance about use of stockpiled therapeutics and other countermeasures can be made accordingly
- >175 case specific consultations

Spectrum of questions

- Interpretation of unexpected OPX+ test result
- Use of tecoviromat in patients with renal insufficiency
- Suspicion for recurrent monkeypox
- Myocarditis
- Ocular infections
- Encephalitis
- Severe illness in severely immunocompromised persons

Next steps, CDC

- Continue to answer clinical inquiries and provide clinical consultations, therapeutics, and laboratory testing
- Gather information about patient outcomes, including severely ill patients with monkeypox
- Develop interim guidance about use of stockpiled therapeutics (informed by input from clinical experts)
- Promote assistance provided by CDC for management of severe cases
- **Increase clinician awareness of severe cases**

Acknowledgments

- Clinicians caring for patients with monkeypox
- Health departments investigating cases
- CDC Multinational Monkeypox Outbreak Response
 - Clinical Consultations Team
 - Clinical Guidance Team
 - Vaccine Implementation Team
 - Worker Safety Team
 - Infection Prevention and Control Team
 - Special Case Investigations Team



For more information, contact CDC

1-800-CDC-INFO (232-4636)

TTY: 1-888-232-6348 www.cdc.gov

Or visit the 2022 U.S. Monkeypox Outbreak Response website:

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

Severe Monkeypox in a Patient with Newly Diagnosed HIV

Robert L. Atmar, M.D.

Andrew DiNardo, M.D.

Baylor College of Medicine

Clinical Case - History

- **26 yo man (MSM) presented to outside hospital 12 days PTA with rash on flank and back pain**
 - Smoked hookah with female friend diagnosed with monkeypox
 - Flank lesions swabbed
 - Prescribed Medrol dose-pack for back pain
 - Notified a few days later of orthopox PCR (+) test → isolate at home
- **Day of admission (evening) complained of progressive symptoms**
 - Rash involved all of body with black central eschar in some ulcerated lesion
 - Increased dyspnea on exertion, dry cough, post-tussive emesis
 - Continued back pain; painful neck swelling
 - Last sexual partner – 3 months earlier

Clinical Case – Physical Examination

- VS: T **102.8 F**, P **128**, BP 134/78, RR 20
- Diffuse rash involving face, trunk, extremities; central ulceration/eschar; some necrotic/gangrenous (dry)
- HEENT – facial lesion; oral ulcerations, no eye involvement
- Neck – large tender mass with overlying induration in left neck
- Lungs – Clear
- Cor – Tachycardic
- Abd – no HSmegaly
- Ext – no edema, clubbing
- Neuro – Alert, fully oriented, no focal sensory/motor findings

Clinical Case – Laboratory (initial)

- Na: 126 mM
- BUN/creat: 30.9/1.4 mg/dL
- AST/ALT: 40/19 U/L
- Tot. bili: 1.2 mg/dL
- H/H: 12.7/36.2 (MCV 78)
- WBC: **30.1** (92% PMNs)
- Platelets: 140K
- PT/INR: 16.3/1.3
- U/A: 1+ protein, 1+ ketones, 1+ bilirubin; 0 WBCs, 2 RBC/HPF
- HIV Ag/Ab combo – **POSITIVE**
 - Viral load – 878K
 - CD4: **79**
 - CD4%: **3%**
- Syphilis screen: negative
- Ferritin: **5417** ng/mL
- Troponin I: <0.03
- Blood cultures: 1/4 bottles corynebacteria

Clinical Case – Initial Radiology

- **Admit CXR – no acute abnormality**
- **CT neck – 6.9 x 7.7 x 9.8 cm dense heterogeneous mass in left neck; multiple deep cervical nodes**

Clinical Case – Hospital Course

- **HD#2, next morning – consented to TPOXX**
- **Flexible nasolaryngoscopy – thrush**
- **HD#2, afternoon – increasing somnolence; evaluation by MICU; fully oriented and protecting airway**
 - **Non-contrast CT head: no mass lesion**
- **HD#2, evening/night: progressive confusion/stupor – transfer to MICU with elective intubation for airway protection**
- **HD#3, early morning: 1st dose IV TPOXX administered**
- **HD#3, morning: septic shock requiring pressor support, increasing creatinine (1.7); good ventilation/oxygenation**
- **HD#3, morning: generalized tonic-clonic seizure**

Clinical Case – Hospital Course

- **Problems: Septic shock with organ failure; encephalopathy/encephalitis?**
- **Diff dx: monkeypox vs. AIDS-associated OI vs. both**
- **Empiric treatment for bacterial and OIs; diagnostic studies unrevealing for OI**
- **Consult CDC for consideration of VIGIV**
- **Progressive hypotension increasing pressor requirement**
- **HD#4 – received VIGIV**
- **HD#5 – dilated, unresponsive pupils, no gag**
- **HD#6 – Brain scan without cerebral perfusion**

Case Summary

- **Rapidly progressive illness when presented in patient with previously undiagnosed HIV infection/AIDS**
- **Autopsy pending**
- **Opportunities during management**
 - **Check for evidence of HIV infection in risk groups**
 - **Avoid high dose steroids in treatment of symptoms**
 - **Counsel patient to seek care with progressive symptoms**

MPOX associated encephalomyelitis

Matthew J. Copeland, DO

Assistant Professor of Medicine, Georgetown University Medical Center
Attending Physician, Division of Infectious Diseases, Medstar Georgetown
University Hospital

History of Illness

34-year-old generally healthy man

Day of Illness (DoI) 2: Seen at local emergency room with 2 days of diffuse pustular rash (hands, arms, legs, torso), low grade fever, and myalgias. Discharged home to quarantine while awaiting Orthopox PCR testing. PCR swab for Orthopox returns positive (later confirmed MPOX).

- ~DoI 4: Starts to notice LE weakness, balance trouble, and difficulty with urination
- DoI 5: Presents to local ER, found to have LE flaccid paralysis, decreased rectal tone, and urinary hesitancy
- DoI 6: Develops obtundation requiring intubation and is transferred to our hospital



Denies: Respiratory symptoms, dysuria, rectal pain, ocular complaints, hearing changes, diarrhea, vomiting, dysphagia/odynophagia, facial weakness

Medical History

Past Medical History:

- 1) Early latent syphilis ~6 months prior to illness (treated with single dose IM Penicillin 2.4mil units)
- 2) Chlamydial proctitis ~6 months prior to illness (treated with doxycycline x 7 days)

Surgical history: tooth extraction in his 20's; No prior spinal surgery or injections

Social history:

- Identifies as a gay man, in monogamous relationship with male partner
- Travel to NYC ~1 week prior to onset of rash and Texas ~2 weeks prior to onset of rash; no known MPOX contacts
- No recent vaccinations; previously vaccinated against polio and COVID-19 (3 doses mRNA)
- No prior smallpox vaccination
- No GI illness prior to onset
- No significant animal contact, including bites/scratches

Family history: No known history of neurologic disease or familial disorders

Laboratory studies (serum)

CMP: Cr 0.94, AST 29, ALT 58, Tbili 0.7, protein 8.1, globulin 3.4

CBC: WBC 11.3 (ANC 8K, ALC 2.5K, Mono 700), H/H 14.7/44.2, PLT 327 K

CRP 6 (normal 0-3)

ESR 26

CPK: 238

HIV 4th generation screen and RNA PCR: negative

RPR negative

GC/CT NAAT from urine, pharynx, rectum negative

WNV IgM negative

Lyme IgG negative

ANA negative

C-ANCA 1:20

Anti SM 1:80 and Anti Actin IgG 34

MOG IgG <1:10

AQP 4 Receptor Ab <1.5

ACE level: 24 (normal)

Vitamin B12: 950 (high)

Laboratory studies (CSF)

RBC: 4

WBC: 30 (89% Lymph, 11 % Mono)

Glucose 65

Protein 60

Meningoencephalitis panel negative

HSV/VZV PCR negative

Bacterial culture negative

Fungal/AFB stains negative

VDRL negative

Cryptococcal antigen negative

WNV IgM negative

Lyme IgG negative

Enterovirus PCR negative

Orthopox PCR negative (University of Washington)

Oligoclonal Bands: 3 (abnormal)

ACE level: normal

Aqp 4 Rec Ab negative

MOG Ab negative

NMDA IgG negative

Autoimmune/paraneoplastic panel negative

Imaging



CT Abd/Pelvis: Rectal wall thickening c/w proctitis, enlarged pelvic lymph nodes

CT Chest: segmental and subsegmental PE in R lung vasculature

Imaging



Hospital Course

DoI 7: Noted some loss of tone in UE, **Starts PO Tecovirimat 600mg BID through OG tube, Starts IV methylprednisolone 1000mg**

DoI 9: **Switched to IV Tecovirimat** d/t concerns regarding absorption with tube feeds

DoI 12: Modest improvement in cognition, MRI after 5 days IVMP with unchanged spinal/brainstem disease, **IVIg started**

DoI 15: High, spiking fevers, IVIG stopped, treated for MSSA VAP

DoI 19: MRI Brain with progression of diffusion restriction through cerebellum and brainstem

DoI 20: **Starts plasma exchange**

DoI 22: Extubated

DoI 24: **Completes 14-day course of Tecovirimat**, lesions crusted

(DoI 25): Normal strength UE and improvement in LE weakness; completes 5-day course PLEX

(DoI 26): Receives **rituximab maintenance therapy**

(DoI 31): Able to sit-stand twice from bed

(DoI 38): Able to transfer to bedside commode

(DoI 44): **Ambulates 15 feet with assistance**; lesions healed

(DoI 46): Discharged to acute rehab

(DoI 55): Able to complete most ADLs, ambulates with assistance

Final Presumed Diagnosis

MPOX associated encephalomyelitis

Autoimmune vs. CNS viral invasion

Questions this case presented:

- CNS penetration of Tecovirimat? PO vs. IV?
- Best test to evaluate for CNS involvement of MPOX? (PCR vs. IgM)
- Approach to auto-immune associated encephalomyelitis in the setting of active viral infection?
- Vaccination after immune mediated encephalomyelitis?

THANK YOU!

My ID, Neurology, Radiology, and PCCM colleagues at MGUH
Georgetown University Medical Center
The CDC MPOX Response Task Force

Public Health Perspective: TPOXX Program in Maricopa County, Arizona

Vivian Huang, MD, MPH
Assistant Medical Director, Office of Epidemiology & Data Services
Saturday, 9/24/2022, CDC/IDSA Clinical Call

TPOXX Consultations

7/7/22 – 8/22/22



- 221 total MPXV cases
- Provided 62 clinical consultations
- 41/221 cases treated = 18.6%
 - 18 (44%) HIV+
 - 2 (5%) peri-orbital, 1 (2%) orbital
- 9/221 cases hospitalized = 4.1%
 - (6 treated, 3 not treated)



Key Points:

- Process put in place for providers to obtain TPOXX
 - Providers could call to reach Med Epi to go over cases
- At the same time, staged TPOXX across Maricopa County at hospitals and clinics
- Early eye evaluation is important



THE UNIVERSITY OF ARIZONA
College of Medicine
Phoenix

29 year old male with HIV/AIDS on cART with recently diagnosed MPX and visual loss

Nelson Nicolasora, MD
Clinical Assistant Professor
Division of Infectious Disease
Banner University Medical Center – Phoenix
University of Arizona

Outpatient Timeline

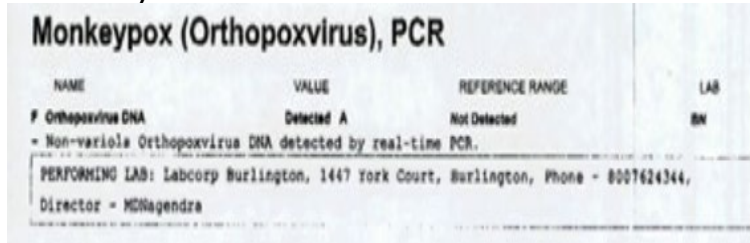
Reported encounter with a partner diagnosed with MPXV.
PCP eval.
Rash in face, trunk, extremities.
MPX PCR negative.

Increasing conjunctival redness and constitutional SSx's.

Rashes - some are scabbed, some fresh.

Doxy, Pred eye gtts to left eye,
Ophtho referral

MPXV PCR of arm lesion (result:D 15)



Initiated
Rx's :
Tecovirimat

----->

Trifluridine

Increasing left eye pain,
irritation, photosensitivity, and
blurriness of vision.

Admitted.
Started on
Trifluridine,
Tecovirimat IV.

Day 0

Day 10

Day 17-19

Day 21

Diagnostics

WBC 5.8 Hgb 13.2 Hct 39.2 platelet 254

Diff. Count.

PMN 74.6%

L 10.7%

M 11.3%

ALC 0.62

CMP normal

Meds:

Azithromycin, 500 mg, Oral, Daily

Biktarvy oral tablet, 1 tab, Oral, Daily

Megestrol 40 mg oral tablet, 200 mg= 5 tab, Oral, Daily

Promethazine 25 mg oral tablet, 25 mg= 1 tab, Oral, PRN

Docusate sodium-S 50 mg-8.6 mg oral tablet, 1 tab, Oral, BID

PMH:

5/2021 : Diagnosed and treated for :

HIV/AIDS - CD4 15 VL 132K, Rx Biktarvy

PJP – Rx Bactrim, changed to Atovaquone for fever, did not comply with Pentamidine

Giardiasis – Rx Metronidazole

1/27/2022 CD4 19 VL 4270

History of OA, degenerative disc disease, anxiety disorder, depression, and ADHD



- Felt cold
- No chills or fever
- No nausea or vomiting
- Moderate global headache
- No neck stiffness
- No chest pain or dyspnea
- No GI/GU symptoms
- Excessive tearing
- Visual loss, left eye
- Significant eye pain
- Significant photophobia, limits evaluation
- Bed-ridden
- Mild pre-auricular LAD

DAY 21 – DATE OF ADMISSION



Facial and periorbital lesions of MPXV





Day 21 – D1 in Hospital



Day 23– D3 in Hospital

Ophthalmological Examination:

	<u>OD</u>	<u>OS</u>
Visual Acuity: sc: cc:	20/20	20/40
Pupils:	Eq & Reactive	Eq & Reactive
EOM's:	Full	Full
Adnexae:	Normal	2 vesicles on forehead
Eyelids:	Normal	Normal
Conjunctiva:	Normal	3+ injected, mostly inferiorly
Cornea:	Normal	superficial 4 mm X 2 mm corneal ulcer 6 o'clock limbus with surrounding conj injection
Ant Chamber:	Deep & Clear	Deep & Clear
Lens:	Clear	Clear
Iris:	Normal	Normal
Fundus:	Normal	Not clearly visible
Vitreous:	Normal	Not clearly visible
Optic Nerves:	Normal	Not clearly visible
IOP:	NTP	NTP

Ophthalmology Management

Ofloxacin (Ocuflox) ophth drops Q-4-h

Trifluridine ophth drops q-2-h Left Eye.

Discussed with Katalina in pharmacy; non-formulary, not available in hospital. I discussed that these drops are generally available in outpatient pharmacies; she will urgently research and get the drops in house to start OS q-2-h

Erythromycin ophth q-6-h

Need to avoid topical steroids

Inpatient Timeline

Increased left eye irritation and pain, photosensitivity, and blurriness of vision.
Right eye 20/20
Left eye 20/40

Admitted.

Started on Trifluridine gtts:
Left eye q 2 H
Right eye q 8 H

Tecovirimat IV

Started on Gancyclovir IV

Ulcer at 6 o'clock limbus has shrunken - down to ~ 1 mm X 2 mm and superficial.
Visual acuity unchanged.

No involvement of right eye.
Remainder of ophthalmological exam unremarkable.

Decrease Trifluridine to q4H L eye, continue R eye TID x 1 week after discharge.

CMV IgG negative – GCV Dc'd

Skin lesions starting to involute.

Improved eye pain and photophobia

Improving constitutional symptoms.

Discharged on:
Trifluridine eye gtts;
Erythromycin ointment;
Tecovirimat po x 14 days.

Biktarvy
Atovaquone PCP
PPx;
FF-up.

Day 21

Day 22

Day 23

Day 25-26

Severe conjunctivitis with corneal ulceration (4-6'oclock limbus), Hospital Day 2



Diagnostics

HIV VL 8190 copies per mL CD4 25 (2.7%), outpatient resistance testing sent

CRAG – negative

Syphilis screen - negative

Toxo IgG – negative

Coccidioides screen - negative

CMV PCR undetectable/ CMV IgG negative

Urine GC/chlamydia - negative

Hep B surface Ab - >1000, immune

Hep B surface Ag -NR

Hep C Ab - NR

Lessons Learned

Thornhill, et. Al. (NEJM 2022)

528 cases, 41% with HIV & 95% with HIV VL < 50 copies per mL.

3/217 nasal and eye (1% of all mucosal **lesions**)

20% incidence of conjunctivitis (Jezek JID 1987; Ogoina CID 2020; Farahat Ann Clin Micro 2022; Hughes IJID 2014).

3.6-7.5% keratitis (Ogoina CID 2020; Jezek WHO Bulletin 1988)

"Conjunctivitis" - tend to have more constitutional SSx (Hughes IJID 2014)

Mazzota et. al. (Journal of Infection 8/2022) - PCR + from
conjunctival swab with replication-competent virus (grew in culture)

Lessons Learned

- False negative test, delay in results.
- Should one empirically treat while waiting for the test? Consider the host and the severity of illness? Consider the delay in getting the medication.
- A complete eye exam is necessary. Severe photophobia, eye pain and excessive tearing can potentially give a lower read on VA exam.
- Early ophthalmological evaluation is important.
- Maintain DDx.
- Hand hygiene to prevent autoinoculation.
- Care coordination and is key.

Q&A/ Discussion

Selected Resources

Update on COVID-19 Epidemiology: Pragna Patel

Ou, J., Lan, W., Wu, X. *et al.* Tracking SARS-CoV-2 Omicron diverse spike gene mutations identifies multiple inter-variant recombination events. *Sig Transduct Target Ther* 7, 138 (2022). <https://doi.org/10.1038/s41392-022-00992-2>

Pre-Delta period, March 1, 2020–June 26, 2021; Delta period, June 27–December 18, 2021; Omicron period December 19, 2021–February 28, 2022. ** p-value <0.05. Singson *et al.* *MMWR* 2022 71 (27) <https://www.cdc.gov/mmwr/volumes/71/wr/pdfs/mm7127a3-H.pdf>

<https://covid.cdc.gov/covid-data-tracker/#demographicsovertime>

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

COVID-19 Therapeutics Update: Meghan Pennini

<https://www.gilead.com/news-and-press/company-statements/veklury-remdesivir-demonstrates-continued-in-vitro-antiviral-activity-against-omicron-subvariants>

<https://www.nejm.org/doi/full/10.1056/NEJMc2207519>

Live virus data; <https://www.nejm.org/doi/full/10.1056/NEJMc2207519>

<https://www.biorxiv.org/content/10.1101/2022.09.16.508299v1.full.pdf>

Wang *et al.*, *bioRxiv* 2022.09.05.506628; <https://doi.org/10.1101/2022.09.05.506628>

<https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults--therapeutic-management/>

<https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults--therapeutic-management/>

Update: Severe Manifestations of Monkeypox: Agam Rao

https://www.cdc.gov/mmwr/volumes/71/wr/mm7132e3.htm?s_cid=mm7132e3_w

<https://www.cdc.gov/poxvirus/monkeypox/response/2022/demographics.html>

<https://www.cdc.gov/poxvirus/monkeypox/response/2022/demographics.html>

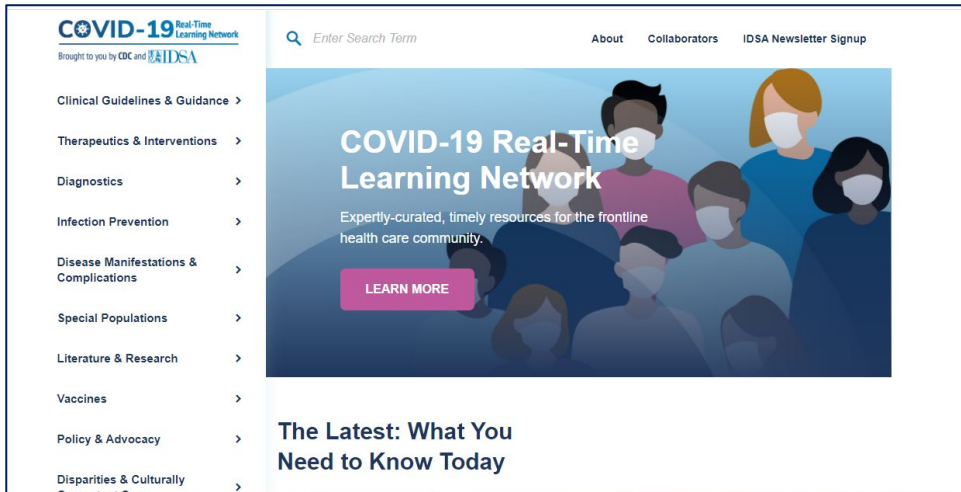
<https://www.cdc.gov/poxvirus/monkeypox/clinicians/pain-management.html>

<https://www.cdc.gov/poxvirus/monkeypox/clinicians/treatment.html>

COVID-19 Real-Time Learning Network

Brought to you by CDC and IDSA

An online community bringing together information and opportunities for discussion on latest research, guidelines, tools and resources from a variety of medical subspecialties around the world.



Specialty Society Collaborators

American Academy of Family Physicians
American Academy of Pediatrics
American College of Emergency Physicians
American College of Obstetricians & Gynecologists
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

www.COVID19LearningNetwork.org

@RealTimeCOVID19

#RealTimeCOVID19

CDC-IDSA Partnership: Clinical Management Call Support

FOR WHOM?

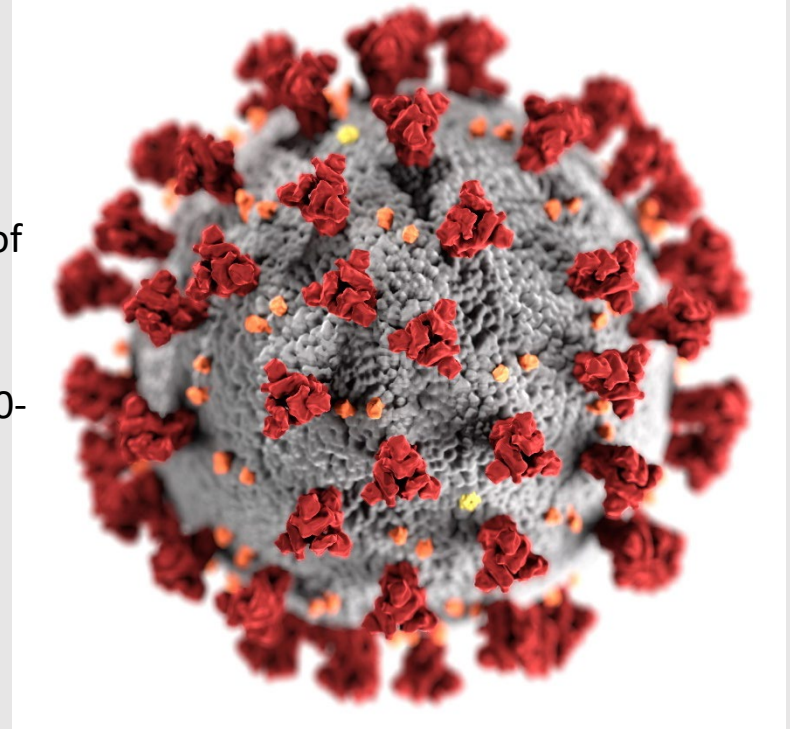
- Clinicians who have questions about the clinical management of COVID-19

WHAT?

- Calls from clinicians will be triaged by CDC to a group of IDSA volunteer clinicians for peer-to-peer support

HOW?

- Clinicians may call the main CDC information line at 800-CDC-INFO (800-232-4636)
- To submit your question in writing, go to www.cdc.gov/cdc-info and click on Contact Form



IDSA
Infectious Diseases Society of America

cdc.gov/coronavirus

THANK YOU

We want to hear from you!

Please complete the post-call survey.

A recording of this call, slides and the answered Q&A will be posted at

www.idsociety.org/cliniciancalls

-- library of all past calls available --

Contact Us:

Dana Wollins (dwillins@idsociety.org)

Deirdre Lewis (dlewis@idsociety.org)