CDC/IDSA COVID-19 Clinician Call

July 31, 2021

Welcome & Introduction

Dana Wollins, DrPH, MGC
Vice President, Clinical Affairs & Guidelines
IDSA

- 71st in a series of weekly calls, initiated by CDC 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.

TODAY'S CALL:

More on the Delta Variant, CDC Masking Recommendations and Updates from ACIP

More on the Delta Variant & CDC Masking Recommendations

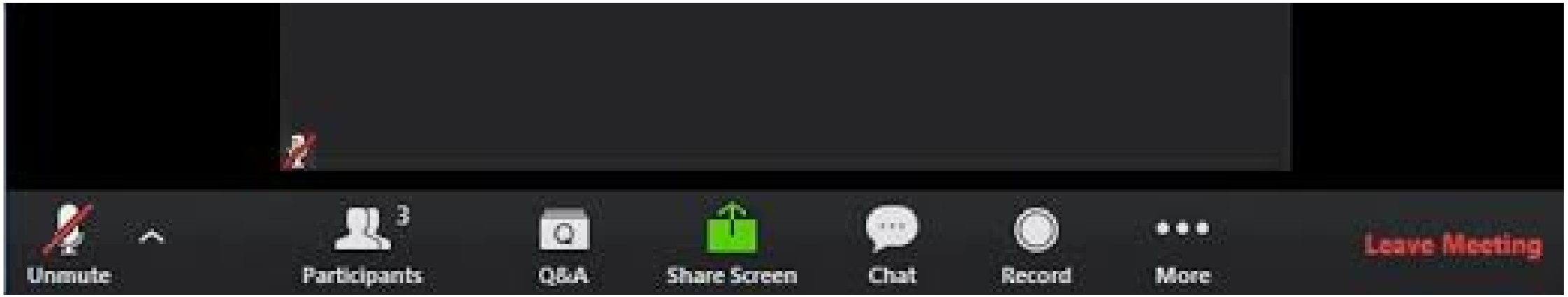
John T. Brooks, MD
Chief Medical Officer
COVID-19 Response
Centers for Disease Control and Prevention

Immunocompromise and COVID-19 Vaccine

Helen "Keipp" Talbot, MD, MPH
Associate Professor of Medicine
Department of Medicine
Division of Infectious Diseases
Vanderbilt University Medical Center

Question?
Use the “Q&A” Button

Comment?
Use the “Chat” Button



CDC/IDSA COVID-19 Clinical Call: Immuncompromise & COVID-19 Vaccine

Keipp Talbot, MD MPH

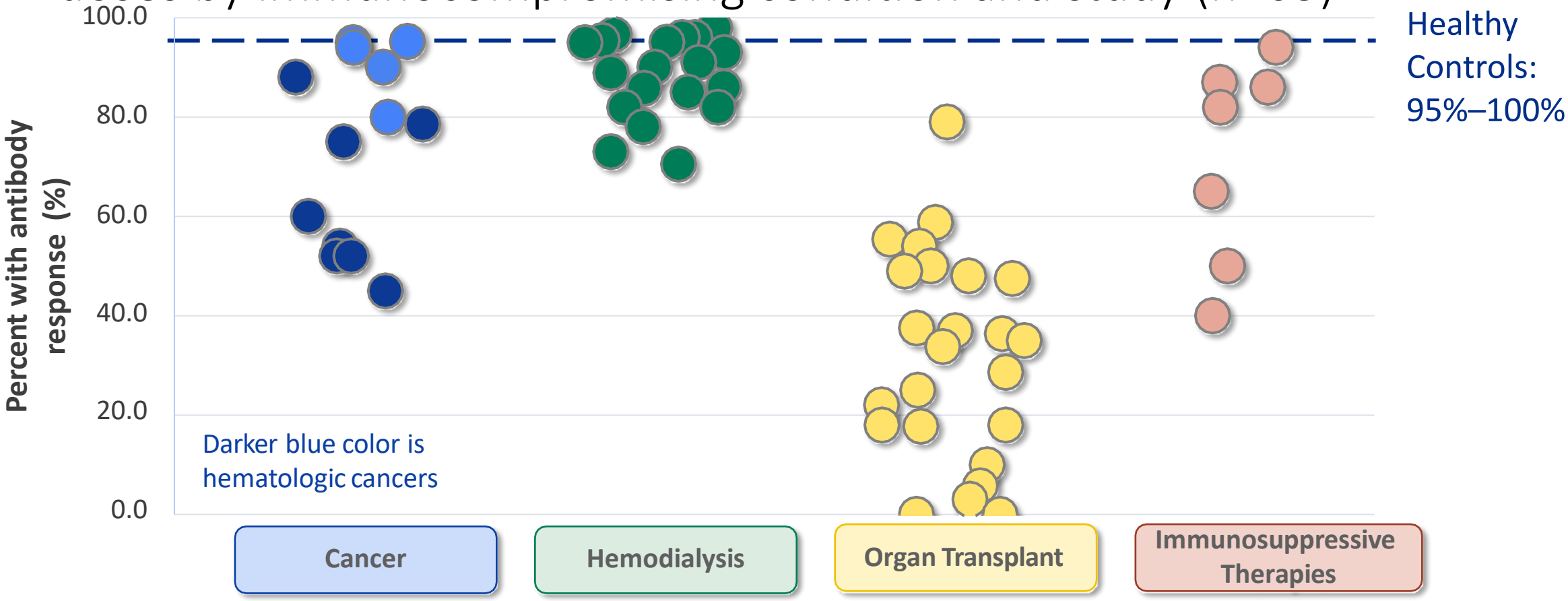
July 31, 2021

Immunocompromised people & SARS-CoV-2 infection

- Immunocompromised people comprise ~2.7% of U.S. adults[1]
- More likely to get severely ill from COVID-19
- Higher risk for:
  - Prolonged SARS-CoV-2 infection and shedding
  - Viral evolution during infection and treatment (hospitalized patients)
  - Low antibody/neutralization titers to SARS-CoV-2 variants
- More likely to transmit SARS-CoV-2 to household contacts
- More likely to have breakthrough infection
- Early VE reports range from 59% to 74%

Adapted from ACIP Data and Clinical Considerations for Additional Doses in Immunocompromised People Sara Oliver ACIP July 22, 2021

Percent of subjects with antibody response after two mRNA vaccine doses by immunocompromising condition and study (n=63)



- Studies that compared response after 1st and 2nd dose demonstrated poor response to dose 1
- Antibody measurement and threshold levels vary by study protocol

Adapted from ACIP Data and Clinical Considerations for Additional Doses in Immunocompromised People
Sara Oliver ACIP July 22, 2021

Comparing evidence 3rd mRNA COVID-19 vaccine dose in immunosuppressed people with seropositive response

Study	Patient Population	2nd Dose			3rd Dose Seronegative after 2nd dose		
		Sample Size	Seronegative N (%)	Seropositive N (%)	Sample Size	Seronegative N (%)	Seropositive N (%)
Kamar et al.	Recipients of solid-organ transplant	99	59 (60)	40 (40)	59	33 (56)	**26 (44)**
Werbel et al.*	Recipients of solid-organ transplant	30	24 (80)	6 (20)	24	16 (67)	**8 (33)**
Longlune et al.	Patients on hemodialysis	82	13 (16)	69 (84)	12	7 (58)	**5 (42)**
Maxime et al.	Patients on hemodialysis	106	66 (62)	40 (38)	12	6 (50)	**6 (50)**

* Recipients received homologous mRNA prime followed by either a single Moderna, Pfizer, or Janssen boost

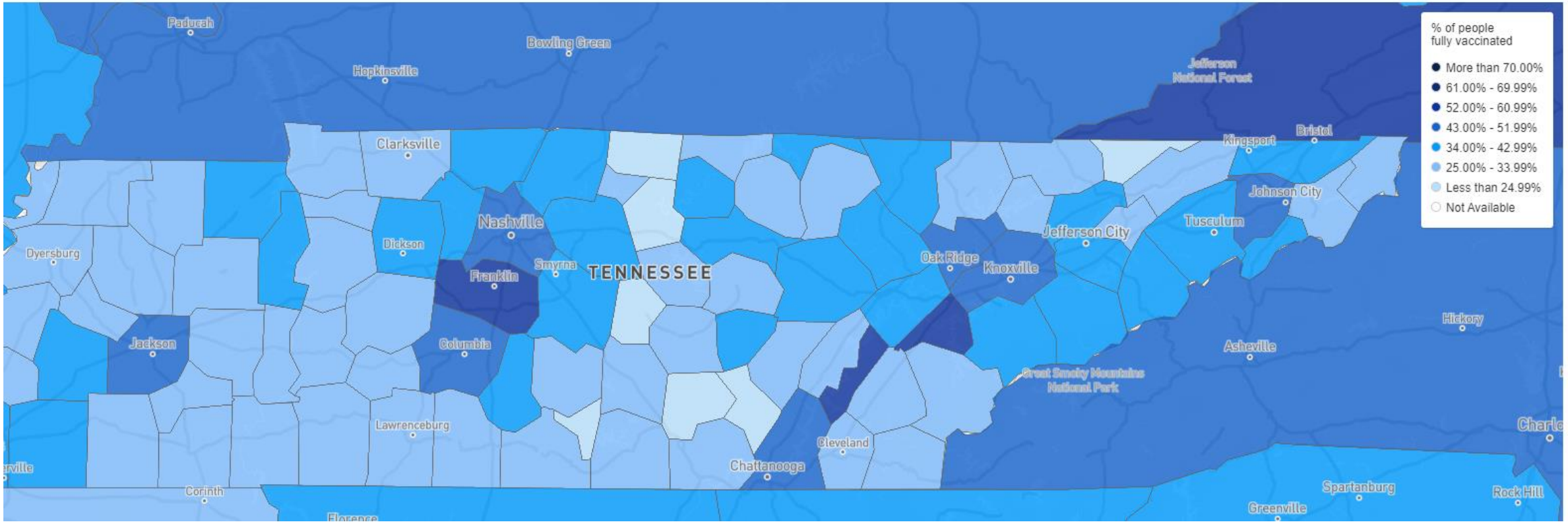
- Among those who had **no detectable antibody** response to an initial mRNA vaccine series,

33-50% developed an antibody response to an additional dose

See references list at end

Adapted from ACIP Data and Clinical Considerations for Additional Doses in Immunocompromised People Sara Oliver ACIP July 22, 2021

TN COVID-19 Vaccination by County



Conclusions

Vaccine breakthrough does occur in those immunocompromised

Studies ongoing to see if a third dose provides better protection

Critically important to vaccinate those who interact with the immuncompromise

Adapted from ACIP Data and Clinical Considerations for Additional Doses in Immunocompromised People Sara Oliver ACIP July 22, 2021

International policies on additional doses for immunocompromised people

- France[1] (Announced April 11, 2021)
  - 3rd dose 4 weeks after the 2nd dose for patients who are “severely immunocompromised”
  - Could be extended at a later date to include a larger immunocompromised population

- United Kingdom[2] (Announced July 1, 2021)
  - Proposal for an additional dose for immunocompromised people ≥16 years (among others), to be implemented between 6 September and 17 December 2021
  - Decision pending

- Israel[3] (Announced July 11, 2021)
  - People living with organ or stem cell transplants, blood cancer, autoimmune disease and treatment with specific immunosuppressive medications
  - People with breast, lung, or colon cancer do not qualify

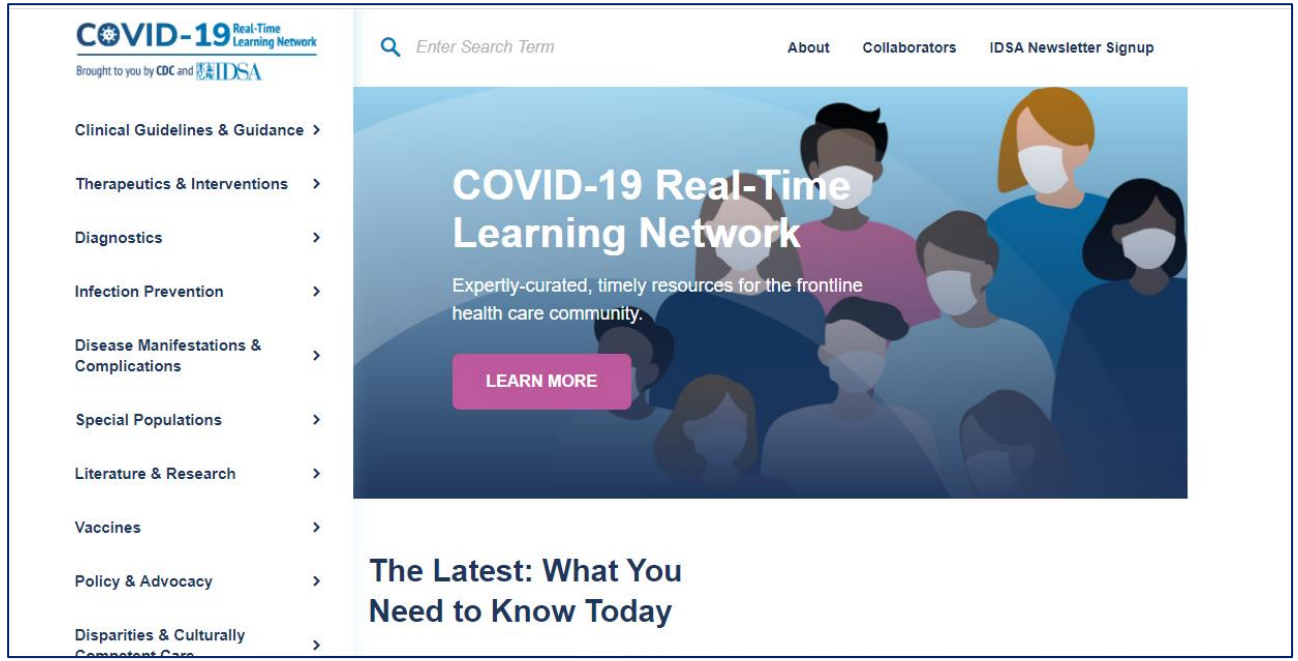
1.dgs_urgent_n43_vaccination_modalites_d_administration_des_rappels.pdf (solidarites-sante.gouv.fr), 2. C1327-covid-19-vaccination-autumn-winter-phadvicease-3-planning.pdf
3.https://govextra.gov.il/media/30095/meeting-summary-15122020.pdf

Q&A and Discussion

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 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?

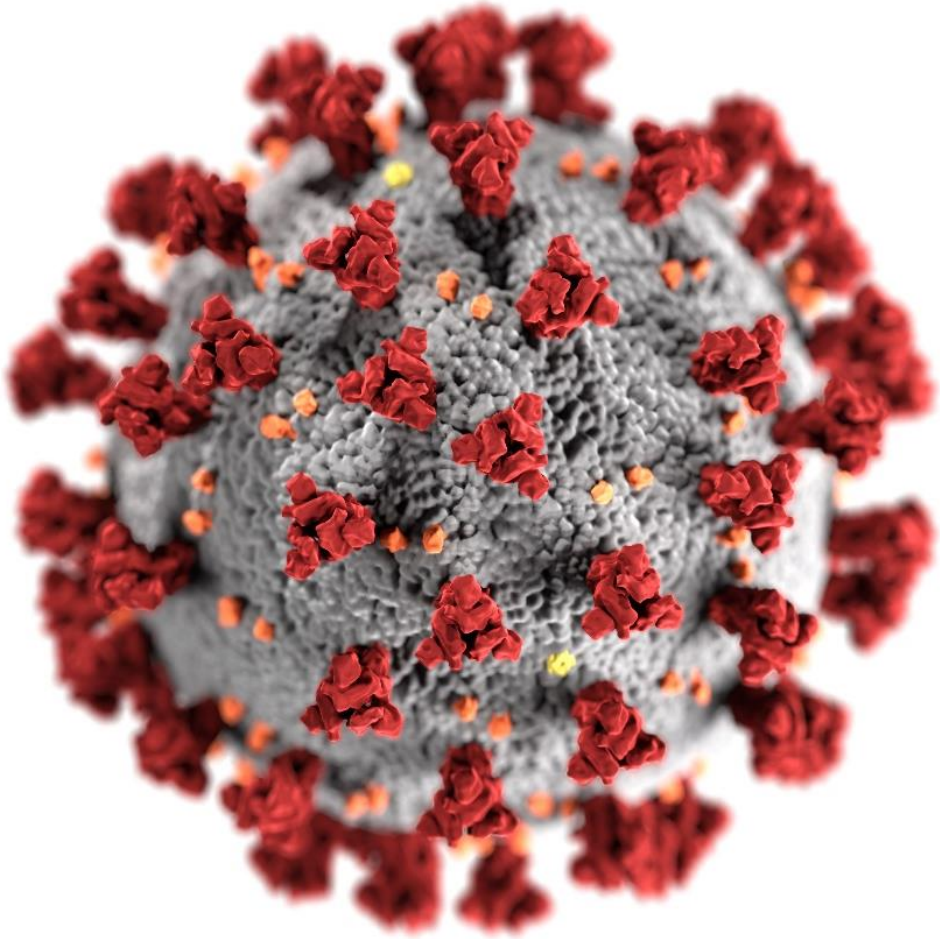
- Clinicians who have questions about the clinical management of COVID-19

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

IDWeek™

idweek.org

Virtual Conference

Save the Date

Sept. 29 – Oct. 3, 2021

Attend, Learn & Collaborate.

Advancing Science, Improving Care

Important Dates:

- Registration is Open
- Abstract Submission Deadline – June 9
- Case Submission Deadline – June 9

Continue the conversation on Twitter

@RealTimeCOVID19
#RealTimeCOVID19

We want to hear from you!

Please complete the post-call survey.

Clinician calls are now twice a month:

Updated Summer Schedule:

August 14

August 28

A recording of this call will be posted Monday at **www.idsociety.org/cliniciancalls**

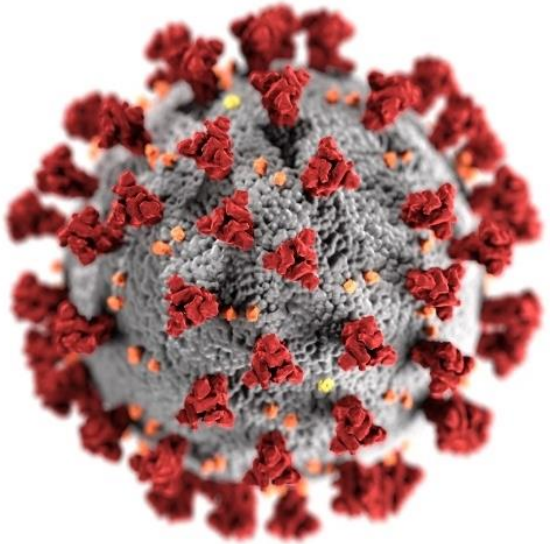
-- library of all past calls available --

Contact Us:

Dana Wollins (dwollins@idsociety.org)
Deirdre Lewis (dlewis@idsociety.org)

Infectiousness of the Delta Variant (B.1.617.2)

John T. Brooks
CDC COVID-19 Emergency Response
IDSA Saturday Call July 31, 2021

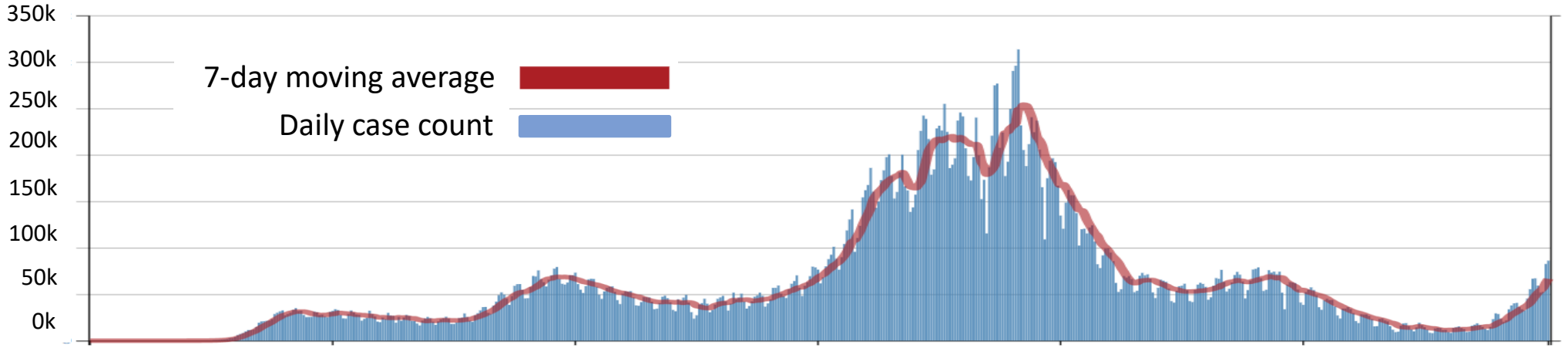


cdc.gov/coronavirus

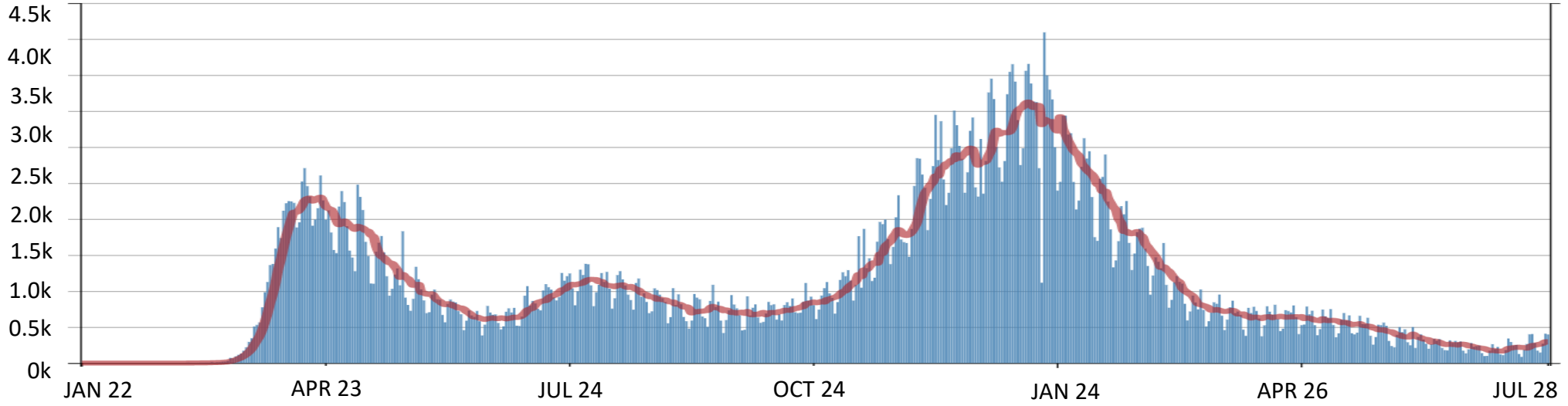
Current Situation

Daily Number of COVID-19 Cases and Deaths: United States Through 28 July 2021 - CDC COVID Data Tracker

Cases



Deaths



https://covid.cdc.gov/covid-data-tracker/#trends_dailytrends

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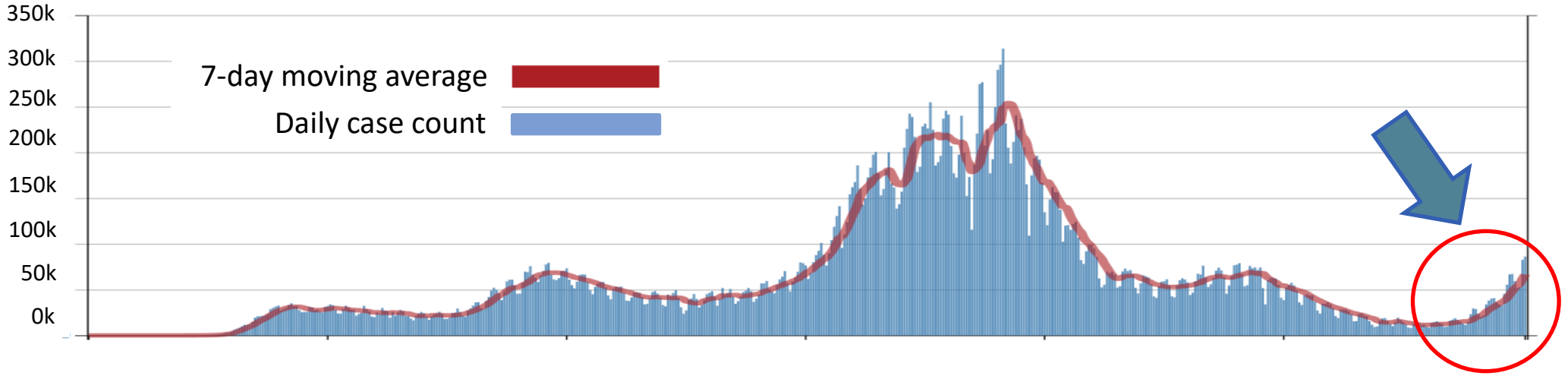

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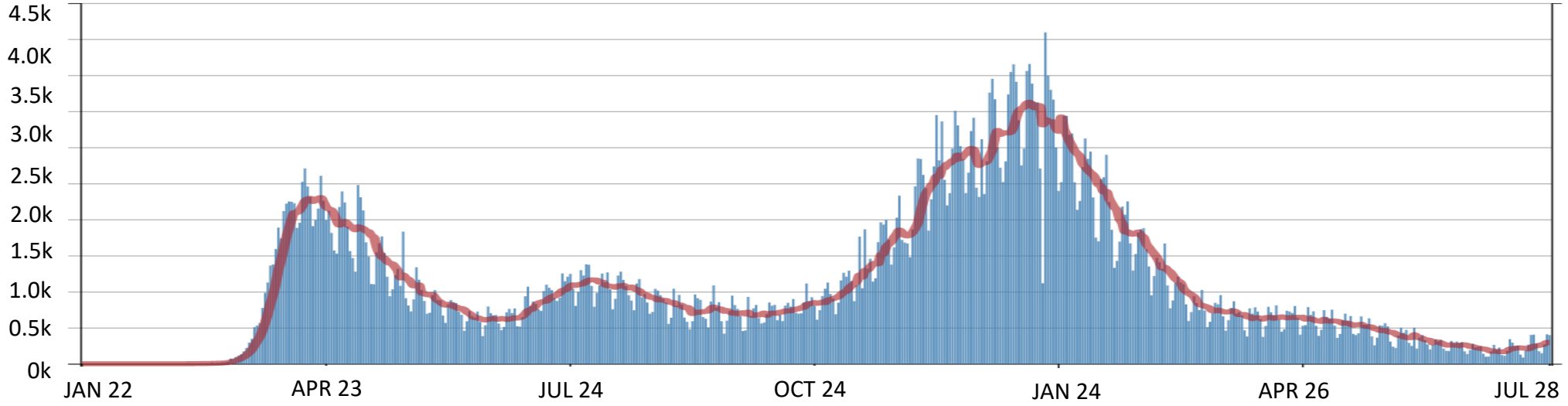

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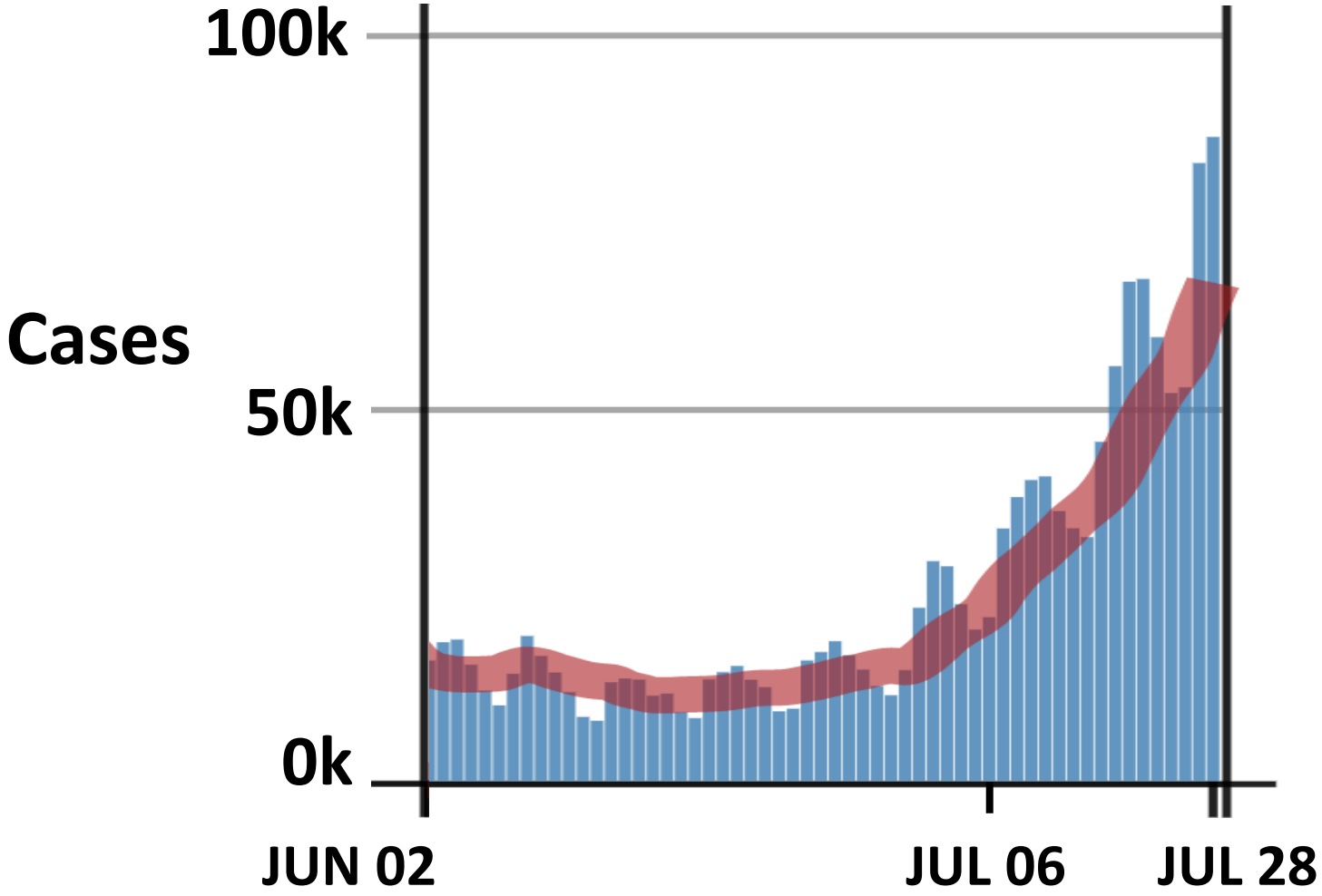
Nationwide Cases are Rising Steeply By Over 400% in Weeks



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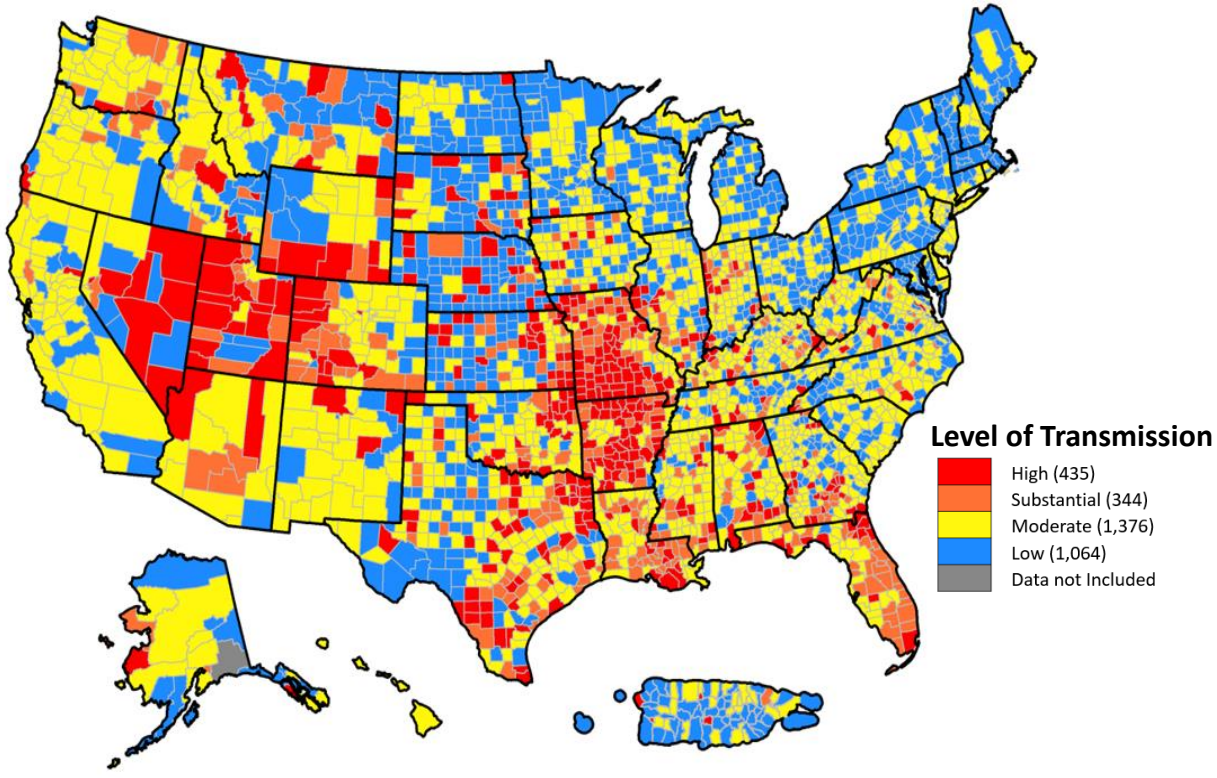
Nationwide Cases are Rising Steeply By Over 400% in Weeks

July 6, 2021

24% of counties

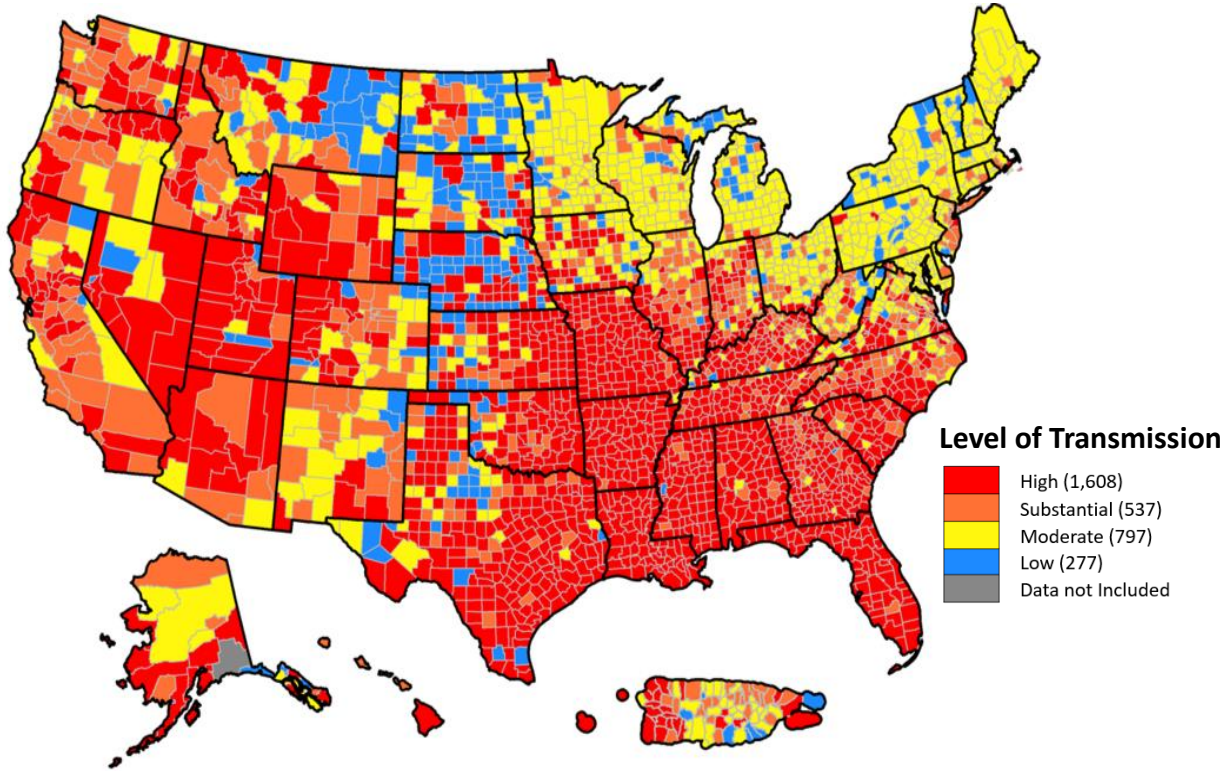
at substantial to high levels of transmission



July 28, 2021

67% of counties

at substantial to high levels of transmission



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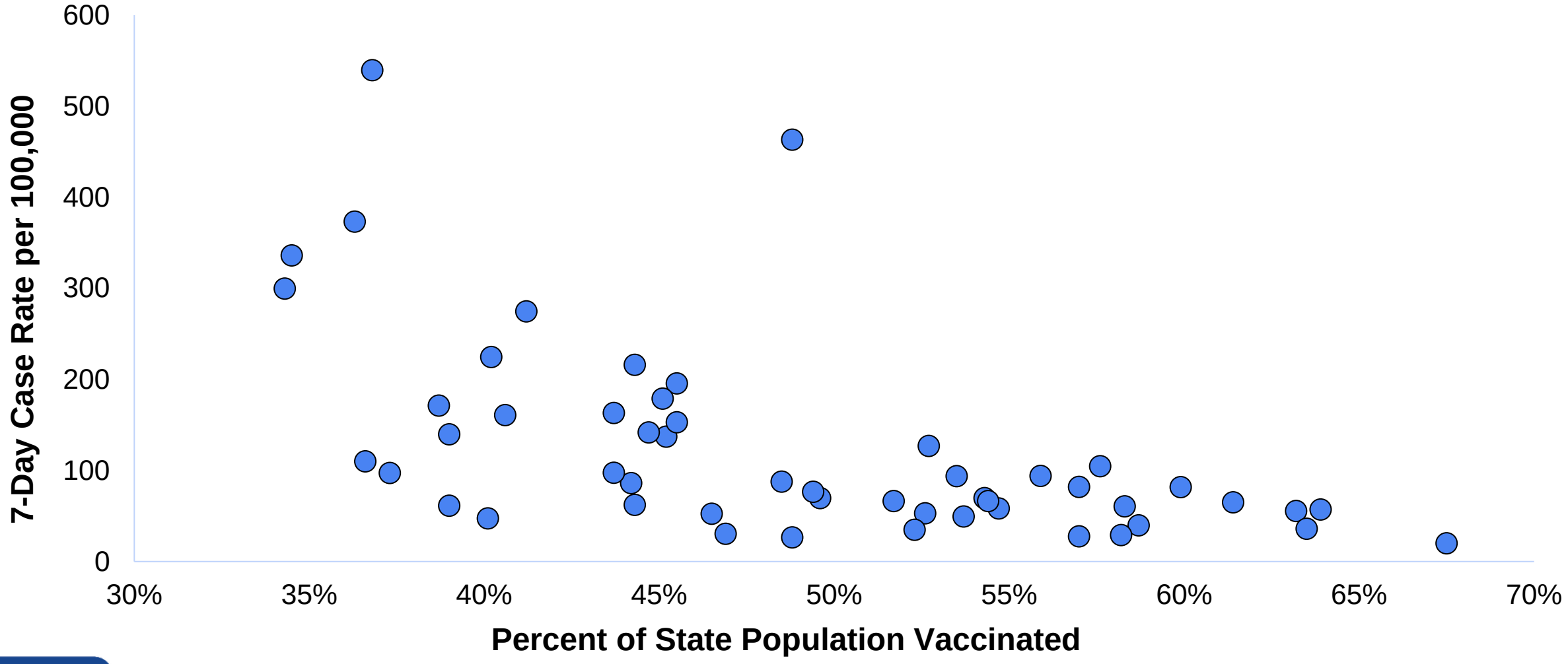
COVID-19 Case Rate (7-day rate per 100,000) By Percent of State Population Fully Vaccinated, July 22-28, 2021



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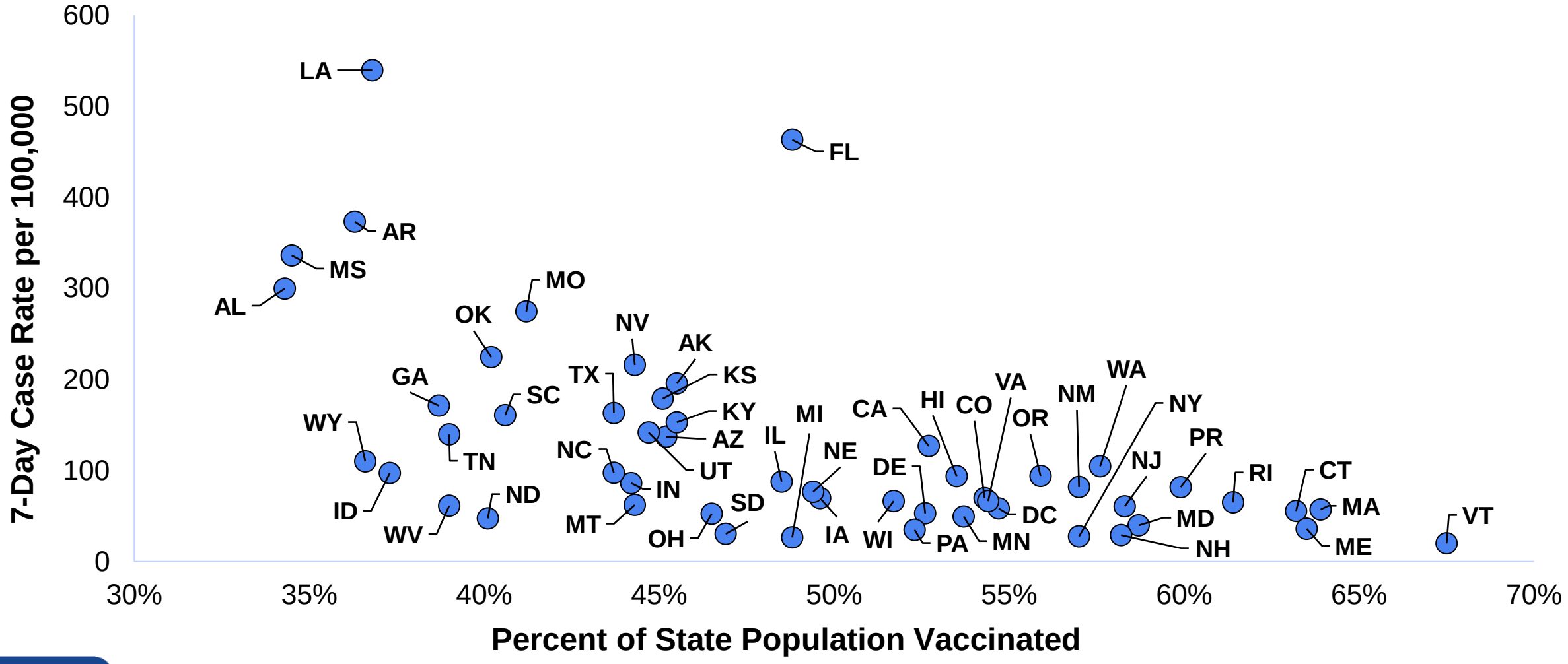

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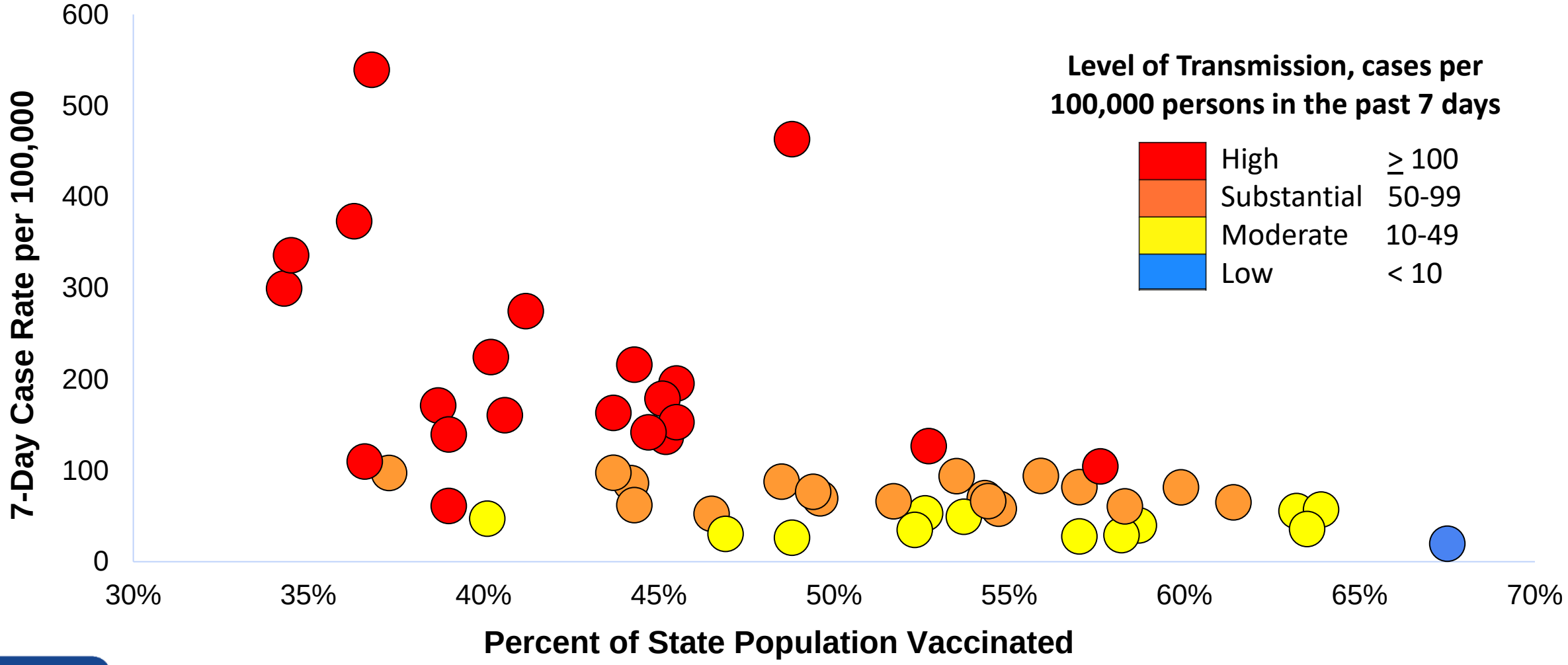

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Daily Number of COVID-19 Cases and Deaths: Louisiana Through 28 July 2021 - CDC COVID Data Tracker

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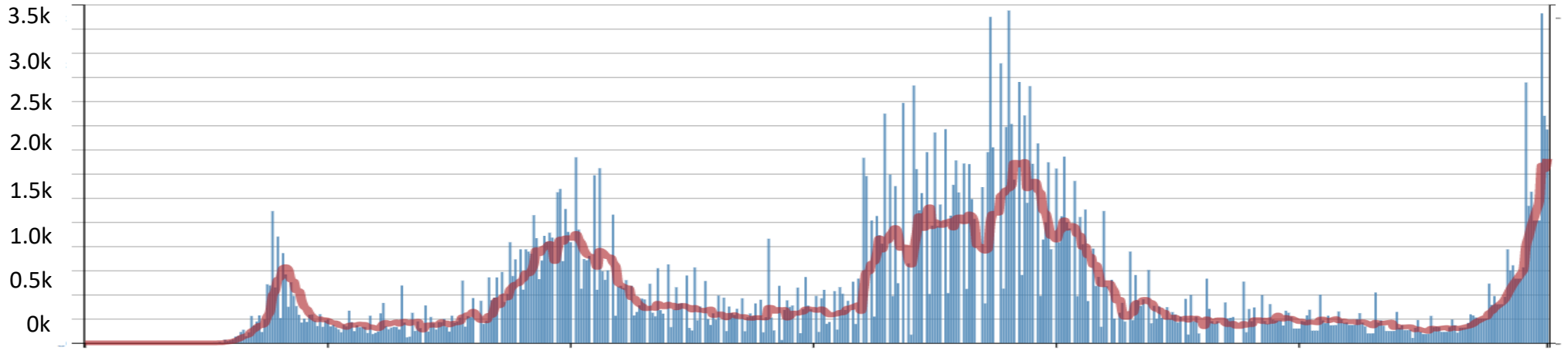

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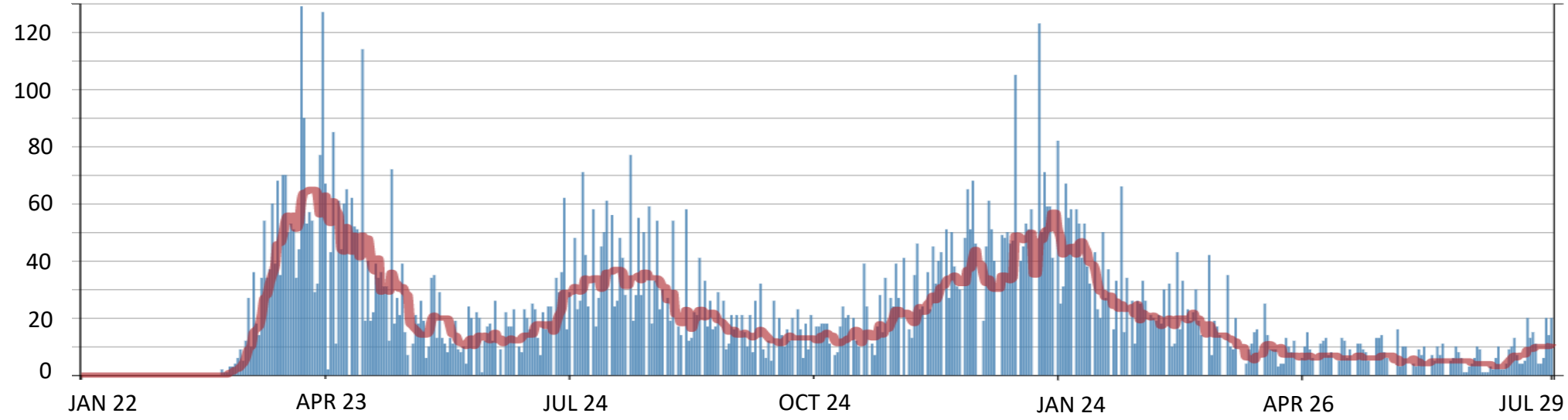

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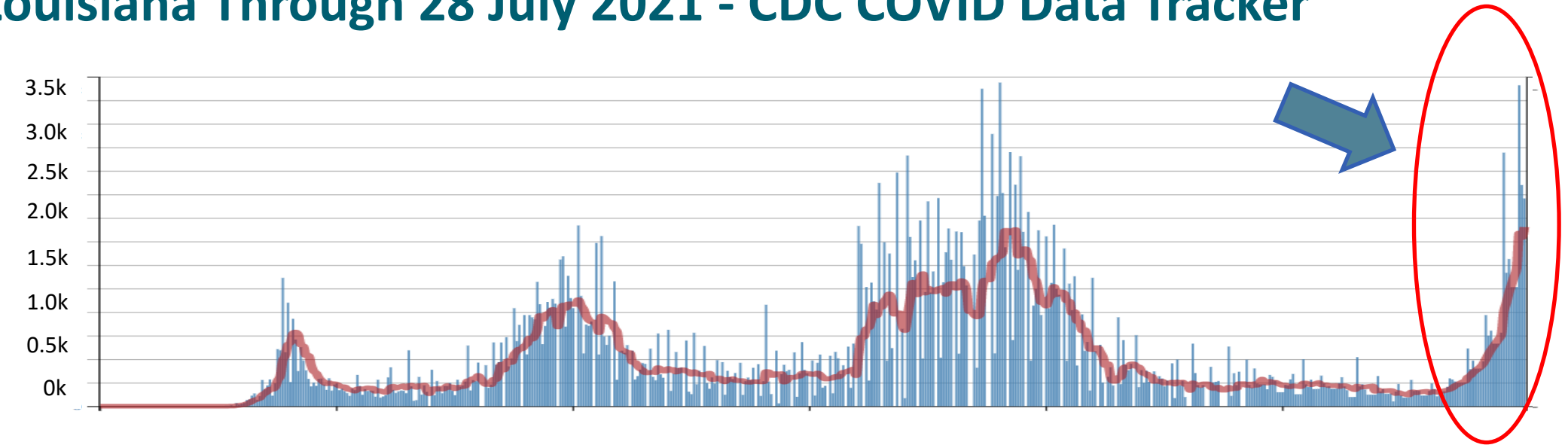

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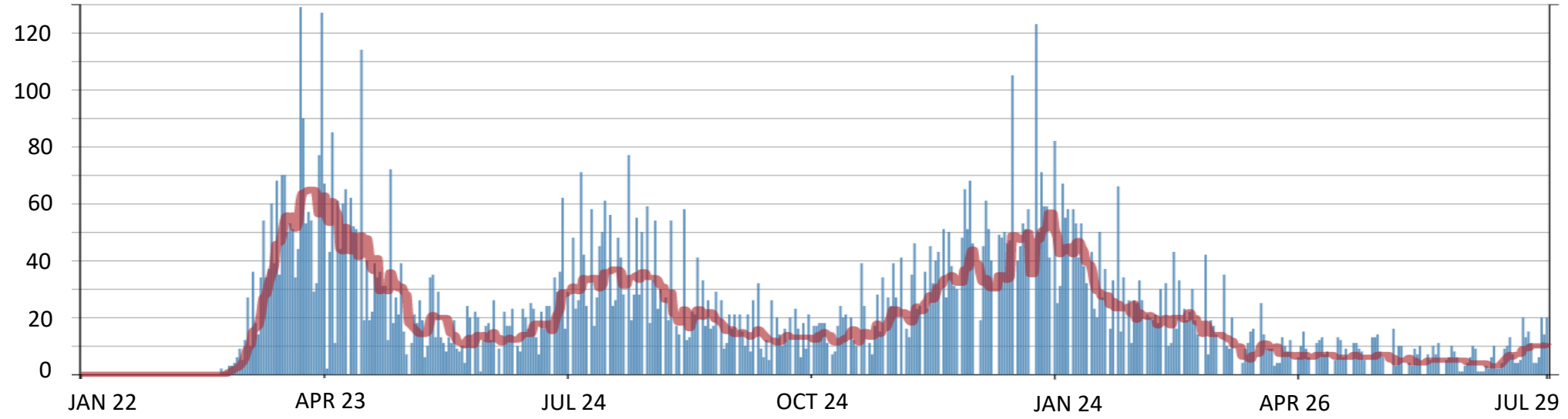
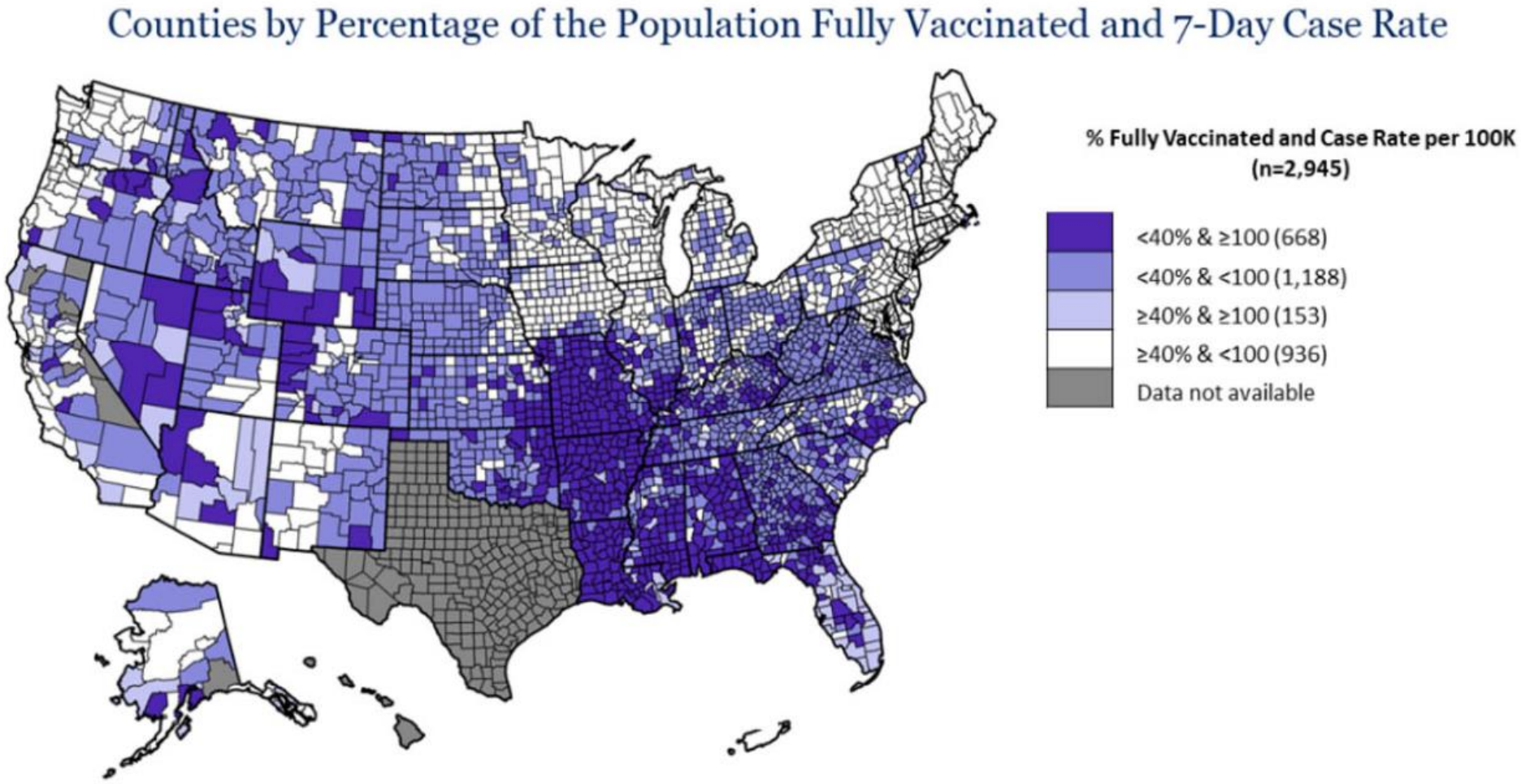


https://covid.cdc.gov/covid-data-tracker/#trends_dailytrends

Vaccination Coverage Remains Low, Especially in High Transmission Areas



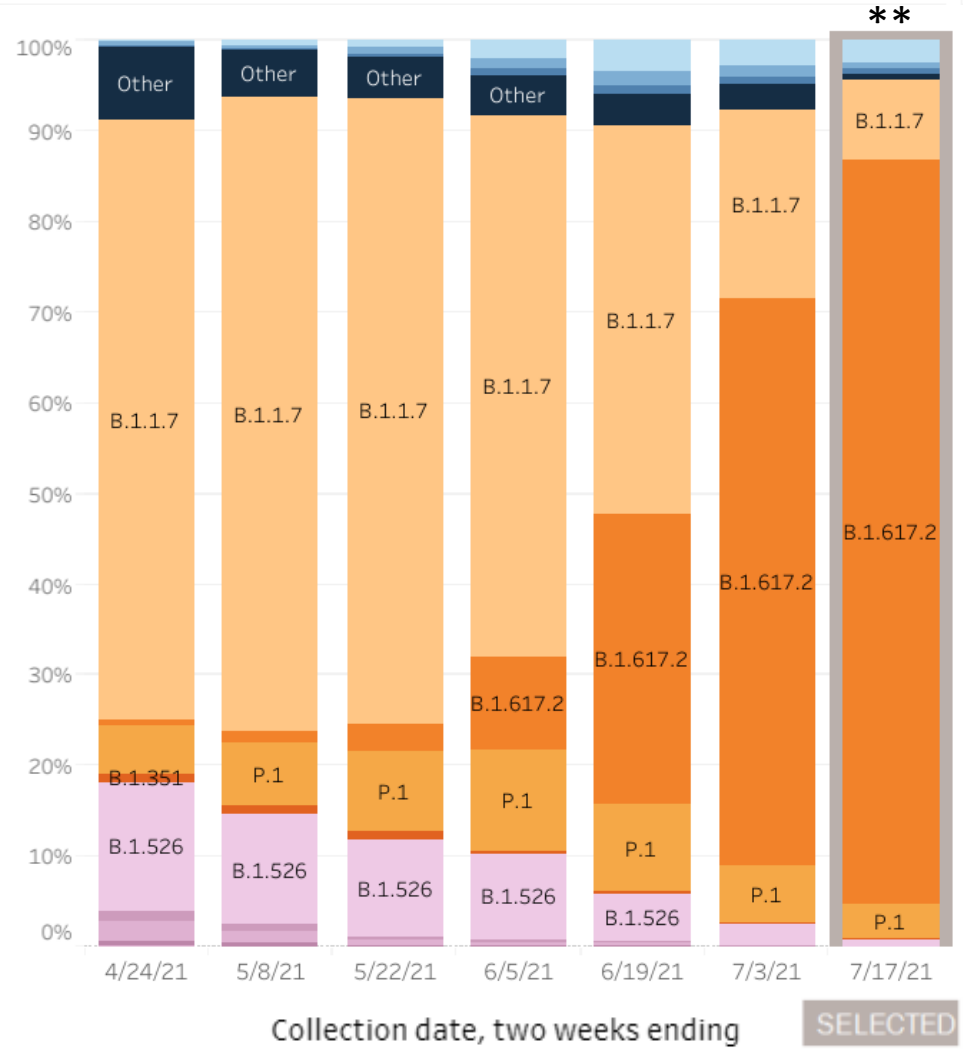
Among U.S. counties that reported information on completed vaccination series (n=2,945): 22.7% (668/2,945) have <40% of the population fully vaccinated and have 7-day case rates ≥100/100,000. Estimates for 50 states, D.C., and Puerto Rico. Time period: Fri Jul 23, 2021. Data source: COVID Data Tracker. Hawaii and Texas are excluded as county-level vaccination information is unavailable. California counties with <20k population, Virginia counties (independent cities) that did not report data, and the Valdez-Cordova Census Area in Alaska also are excluded. County data for Puerto Rico are not displayed. Excluded counties are shaded in gray.

https://emergency.cdc.gov/han/2021/han00447.asp

Vaccine Effectiveness Against Variant Infection

SARS-CoV-2 Variants Circulating in the United States

United States: 4/11/2021 – 7/17/2021



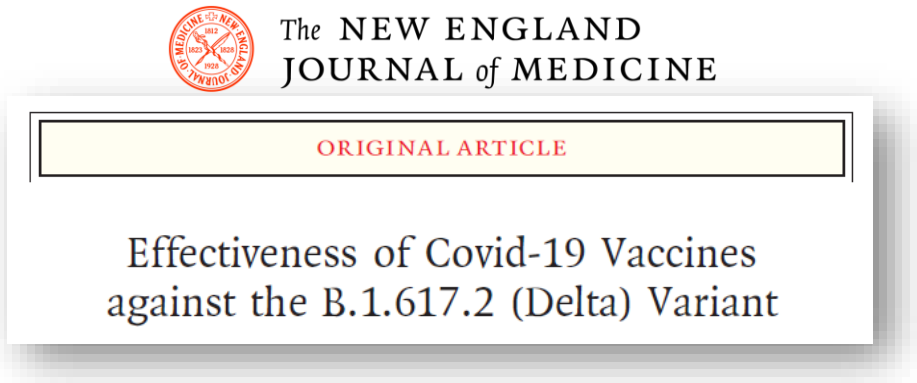
United States: 7/4/2021 – 7/17/2021 NOWCAST

USA

Lineage		Type		%Total	95%PI
B.1.617.2	Delta	VOC	82.2%	78.3-86.0%	
B.1.1.7	Alpha	VOC	9.0%	6.3-12.0%	
P.1	Gamma	VOC	3.8%	2.0-5.8%	
B.1.621			2.4%	1.0-4.0%	
B.1.628			0.8%	0.0-1.8%	
B.1.621.1			0.7%	0.0-1.5%	
B.1.526	Iota	VOI	0.8%	0.0-1.8%	
B.1.351	Beta	VOC	0.1%	0.0-0.5%	
B.1.525	Eta	VOI	0.0%	0.0-0.2%	
B.1.617.3		VOI	0.0%	0.0-0.2%	
B.1.429	Epsilon	VOI	0.0%	0.0-0.2%	
B.1.427	Epsilon	VOI	0.0%	0.0-0.2%	
Other			0.4%	0.0-3.5%	

* Other represents lineages each circulating at <1% of viruses over the last 4 weeks of weighted data.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# Sublineages of P.1 and B.1.351 (P.1.1, P.1.2, B.1.351.2, B.1.351.3) are aggregated with the parent lineage and included in parent lineage's proportion. AY.1, AY.2, and AY.3 are aggregated with B.1.617.2.

Effectiveness of COVID-19 Vaccines Against Variants



Published July 21, 2021

Against symptomatic disease:

- 94% effective for Alpha
- 88% effective for Delta

(For BNT162b2, mRNA)

Effectiveness of COVID-19 vaccines against hospital admission with the Delta (B.1.617.2) variant

Posted June 14, 2021

Against hospitalization:

- 95% effective for Alpha
- 96% effective for Delta

(For BNT162b2, mRNA)

https://www.nejm.org/doi/pdf/10.1056/NEJMoa2108891.
https://khub.net/web/phe-national/public-library/-/document_library/v2WsRK3ZlEig/view/479607266

Risk of Delta Transmission Before Vaccination (Unvaccinated)

Cycle Threshold Values: Unvaccinated Persons

Median cycle threshold values for 2,349 patients among 4,920 for whom variant type was known (includes approximately 6.5% fully vaccinated persons)

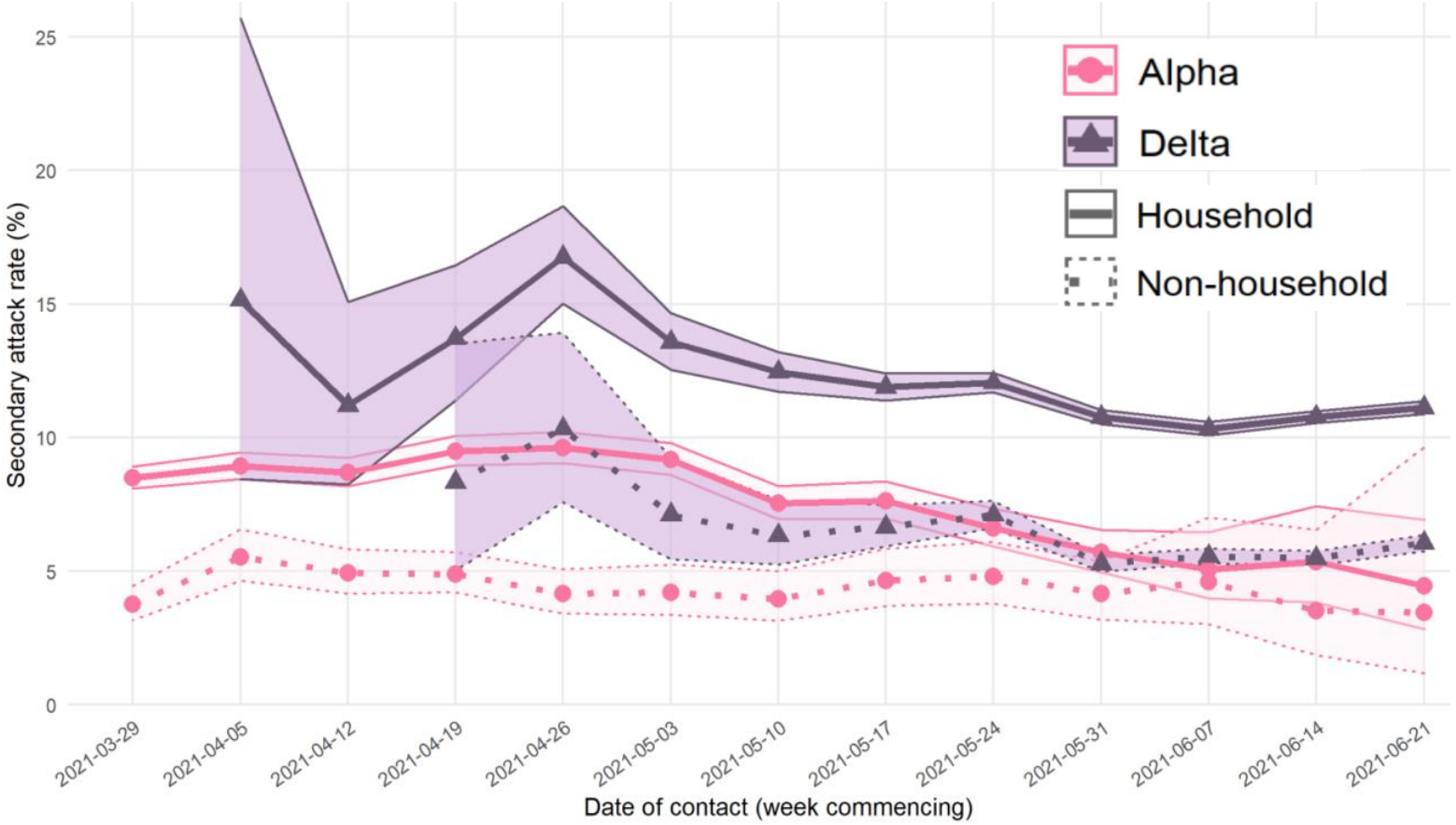
PCR Platform	Delta Variant	Other Variants
Abbott Alinity (n = 1924)	20.67 (n = 326)	24.09 (n = 1598)
Hologic Panther (n = 601)	21.10 (n = 88)	24.50 (n = 513)

In unvaccinated persons, Delta infection achieves lower Ct values than non-Delta variants

Musser et al. 2021, Delta variants of SARS-CoV-2 cause significantly increased vaccine breakthrough COVID-19 cases in Houston, Texas | medRxiv

Secondary Infections

Secondary attack rates amongst household and non-household contacts of non-travel cases of Alpha and Delta, with 95% confidence intervals (29 MAR 2021 to 27 JUN 2021)



In a general population, Delta variant infections about twice as infectious as infections with non-Delta variants

Public Health England: SARS-CoV-2 variants of concern and variants under investigation in England, Technical Briefing 19
Investigation of SARS-CoV-2 variants of concern: technical briefings - GOV.UK (www.gov.uk)

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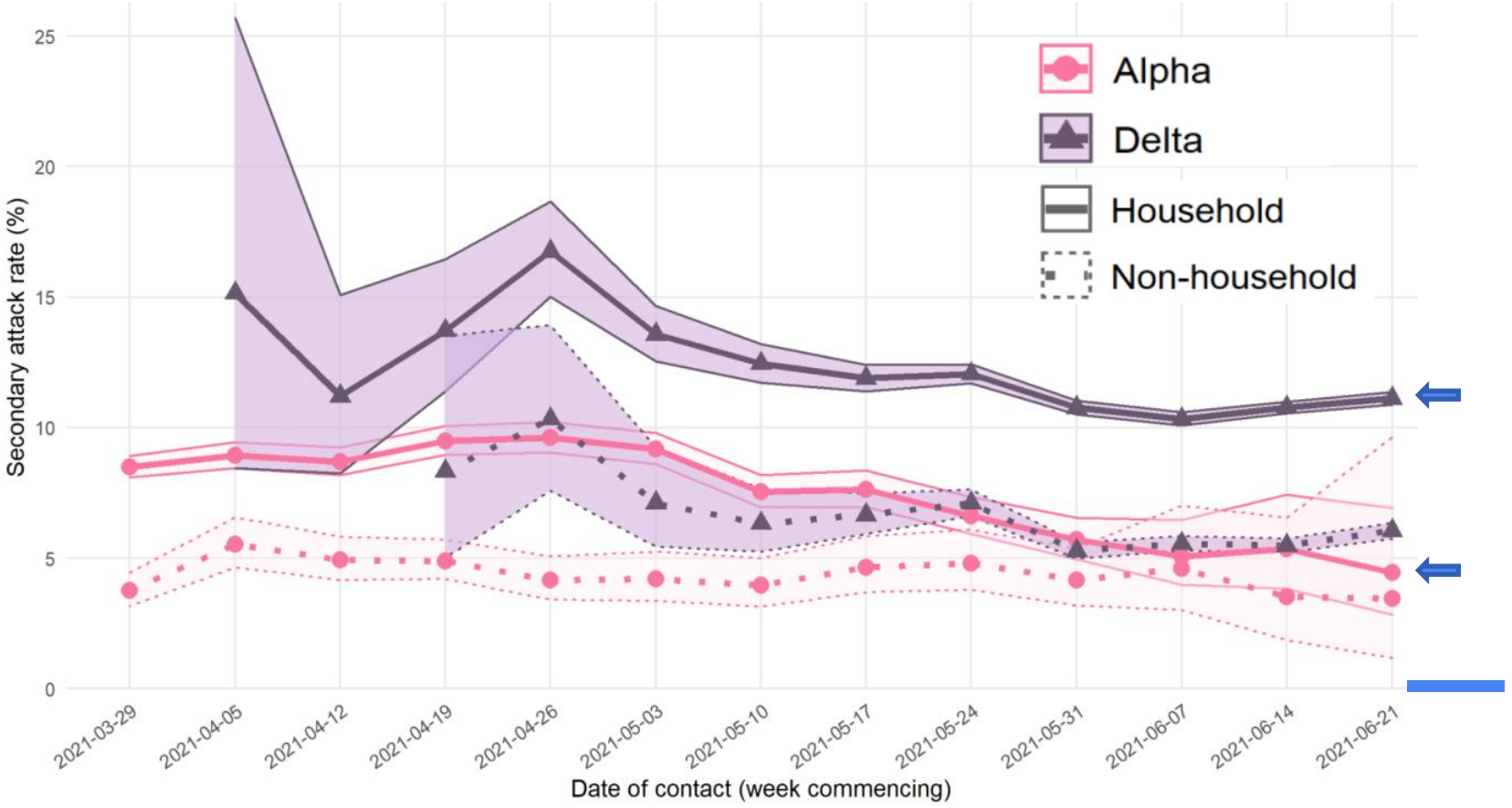

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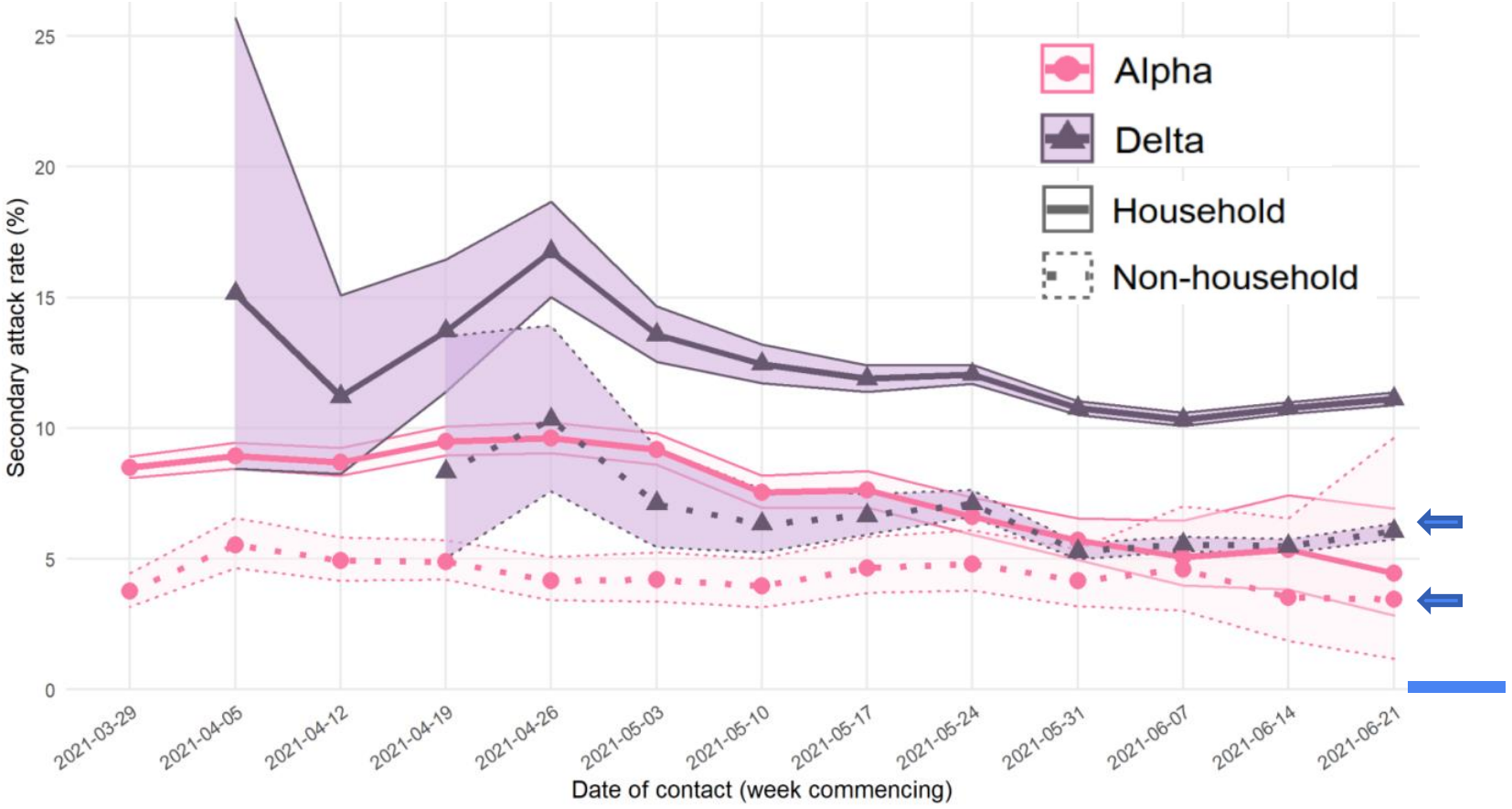

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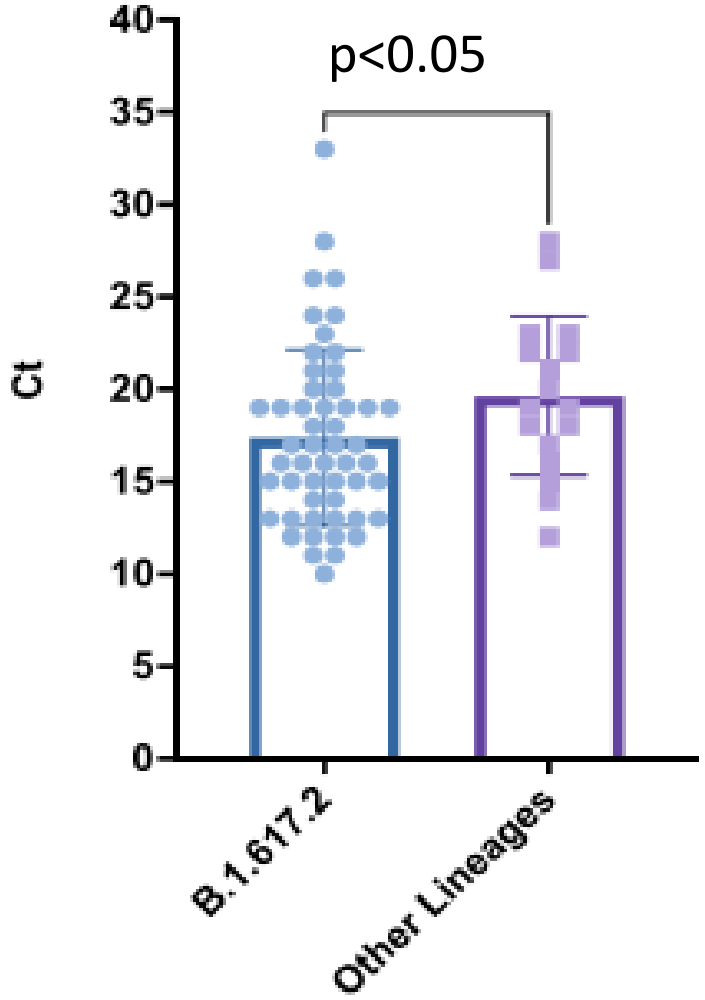
Risk of Delta Transmission After Vaccination (Vaccinated)

Cycle Threshold Values: Vaccinated Persons



Average Ct values*

Delta	16.5
Non-Delta	19.0

In vaccinated persons, Delta infection appears to also achieve lower Ct values than non-Delta variants

* The vaccine used was Covishield (ChAdOx1), which is not available in the U.S.

Mlcochova et al. 2021, SARS-CoV-2 B.1.617.2 Delta variant emergence and vaccine breakthrough | Research Square

Secondary Infections: Vaccinated Persons

Investigators in India assessed secondary infections among HCW associated breakthrough infections

- **Non-Delta variant infections in HCW**
  mean cluster size: 1.1 persons
- **Delta variant infections in HCW**
  mean cluster size: 3.3 persons

No clusters of non-Delta infections comprising >2 individuals, whereas there were ten such clusters for Delta variant.

In vaccinated persons, Delta infections appeared more infectious than non-Delta variants based on secondary infections

Mlcochova et al. 2021, SARS-CoV-2 B.1.617.2 Delta variant emergence and vaccine breakthrough | Research Square

Risk of Delta Transmission
Unvaccinated vs. Vaccinated People Compared

Infections in Unvaccinated vs. Vaccinated Compared

Table 3. Viral RNA Load, Duration of Viral RNA Detection, Frequency of Febrile Symptoms, and Duration of Illness in Vaccinated and Unvaccinated Participants with SARS-CoV-2 Infection.*

Variable	Unvaccinated	Partially or Fully Vaccinated	Difference (95% CI)
Viral RNA load			
No. assessed	155	16	—
Mean — $\log_{10}$ copies/ml†	3.8±1.7	2.3±1.7	40.2 (16.3–57.3)‡
Duration of viral RNA detection			
No. assessed	155	16	—
Mean — days	8.9±10.2	2.7±3.0	6.2 (4.0–8.4)
Detection of viral RNA for >1 week — no./total no. (%)	113/156 (72.4)	4/16 (25.0)	0.34 (0.15–0.81)§
Febrile symptoms — no./total no. (%)¶	94/149 (63.1)	4/16 (25.0)	0.42 (0.18–0.98)‖
Total days of symptoms			
No. assessed	148	16	—
Mean — days	16.7±15.7	10.3±10.3	6.4 (0.4–12.3)
Days spent sick in bed			
No. assessed	147	15	—
Mean — days	3.8±5.9	1.5±2.1	2.3 (0.8–3.7)

HEROES-RECOVER Cohorts

- 3,975 healthcare personnel and other essential and frontline workers
- Provide weekly NP swabs
- SARS-CoV-2 confirmed in 204 persons
- Compared laboratory and clinical illness characteristics in unvaccinated (n=155) and partially (n=11) or fully vaccinated (n=5)

Thompson et al. 2021, N Engl J Med 385:320-9. DOI: 10.1056/NEJMoa2107058

Infections in Unvaccinated vs. Vaccinated Compared

Table 3. Viral RNA Load, Duration of Viral RNA Detection, Frequency of Febrile Symptoms, and Duration of Illness in Vaccinated and Unvaccinated Participants with SARS-CoV-2 Infection.*

Variable	Unvaccinated	Partially or Fully Vaccinated	Difference (95% CI)
Viral RNA load			
No. assessed	155	16	—
Mean — $\log_{10}$ copies/ml†	3.8±1.7	2.3±1.7	40.2 (16.3–57.3)‡
Duration of viral RNA detection			
No. assessed	155	16	—
Mean — days	8.9±10.2	2.7±3.0	6.2 (4.0–8.4)
Detection of viral RNA for >1 week — no./total no. (%)	113/156 (72.4)	4/16 (25.0)	0.34 (0.15–0.81)§
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Mean — days	3.8±5.9	1.5±2.1	2.3 (0.8–3.7)

HEROES-RECOVER Cohorts

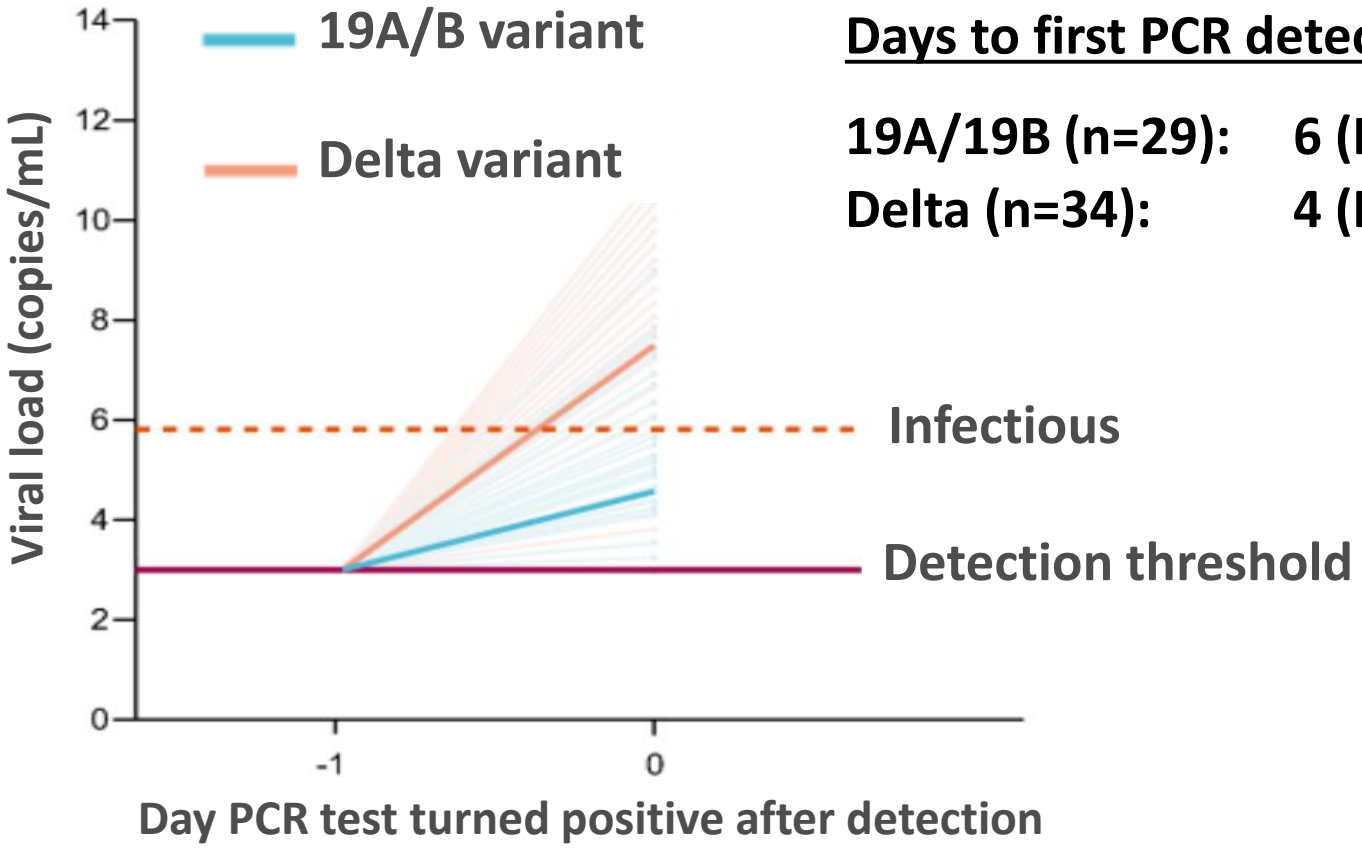
Vaccinated breakthroughs:

- *Lower* viral load
- RNA detection *resolved faster*
- *Less symptomatic*
- *Shorter* illness duration
- *Fewer sick days* in bed

Thompson et al. 2021, N Engl J Med 385:320-9. DOI: 10.1056/NEJMoa2107058

Pace of Infection in Terms of Viral Load

Estimated Viral Load Growth Rate in Unvaccinated Quarantined Patients



Days to first PCR detection

19A/19B (n=29): 6 (IQR 5-8)
Delta (n=34): 4 (IQR 3-5)

With Delta infection:

- **RNA is detected earlier**
- **Ct values peak earlier***

The incubation period of infection may be shorter, **but duration of infectiousness remains unknown**

*for 19A/B 5.61 days, for Delta 3.71 days

Li et al. 2021, Viral infection and Transmission in a large well-traced outbreak caused by the Delta SARS-CoV-2 variant | medRxiv

Delta vs. Other SARS-CoV-2 Variants

- In *unvaccinated* people without prior infection:
  - Delta achieves a higher viral load than other variants
  - Delta is about twice as infectious as other variants
- In *vaccinated* people with breakthrough infections:
  - Delta also achieves a higher viral load than other variants
  - How much more infectious Delta is remains unknown at this time

Public Health England: SARS-CoV-2 variants of concern and variants under investigation in England, Technical Briefing 19Investigation of SARS-CoV-2 variants of concern: technical briefings - GOV.UK (www.gov.uk). Li et al. 2021, medRxiv: Viral infection and transmission in a large, well-traced outbreak caused by the SARS-CoV-2 Delta variant | medRxiv. Musser et al. 2021, medRxiv: Delta variants of SARS-CoV-2 cause significantly increased vaccine breakthrough COVID-19 cases in Houston, Texas | medRxiv. Mlcochova et al. 2021, Research Square SARS-CoV-2 B.1.617.2 Delta variant emergence and vaccine breakthrough

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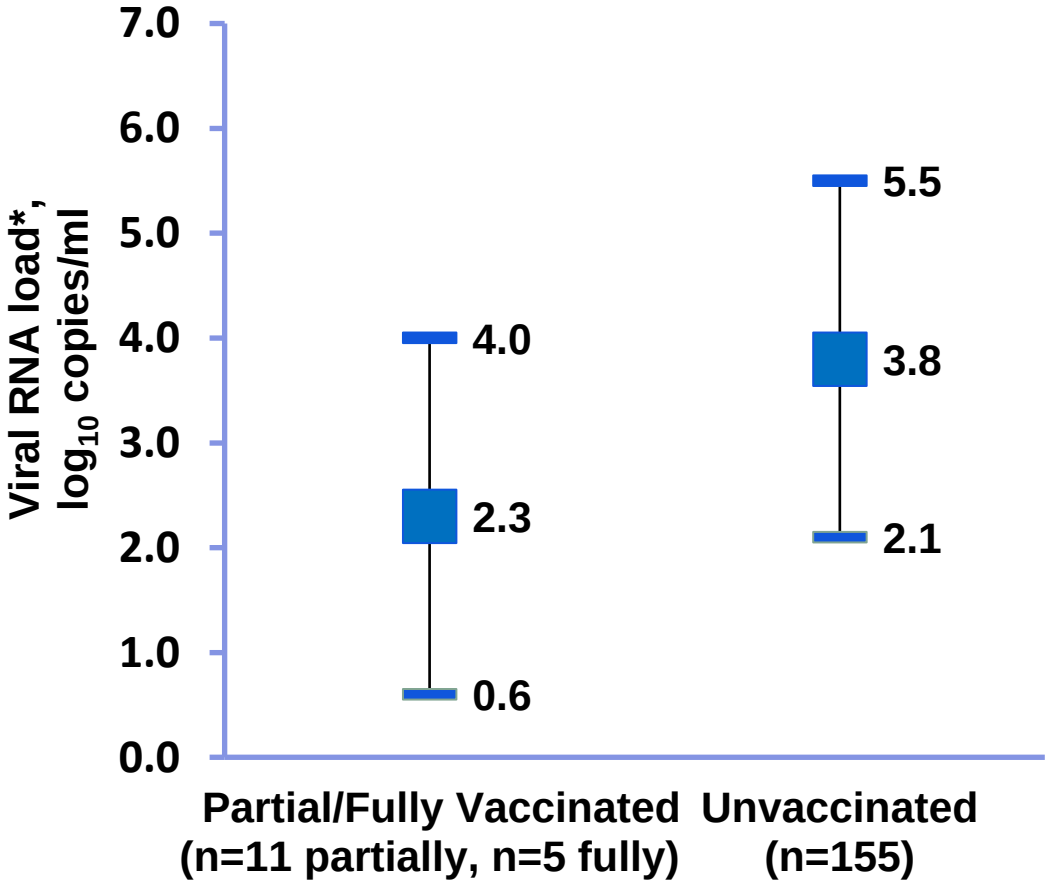
How do the viral loads in unvaccinated and vaccinated people compare if they are infected with the same variants?

Public Health England: SARS-CoV-2 variants of concern and variants under investigation in England, Technical Briefing 19Investigation of SARS-CoV-2 variants of concern: technical briefings - GOV.UK (www.gov.uk). Li et al. 2021, medRxiv: Viral infection and transmission in a large, well-traced outbreak caused by the SARS-CoV-2 Delta variant | medRxiv. Musser et al. 2021, medRxiv: Delta variants of SARS-CoV-2 cause significantly increased vaccine breakthrough COVID-19 cases in Houston, Texas | medRxiv. Mlcochova et al. 2021, Research Square SARS-CoV-2 B.1.617.2 Delta variant emergence and vaccine breakthrough

Infections in Unvaccinated and Vaccinated Compared



Data from CDC Cohorts

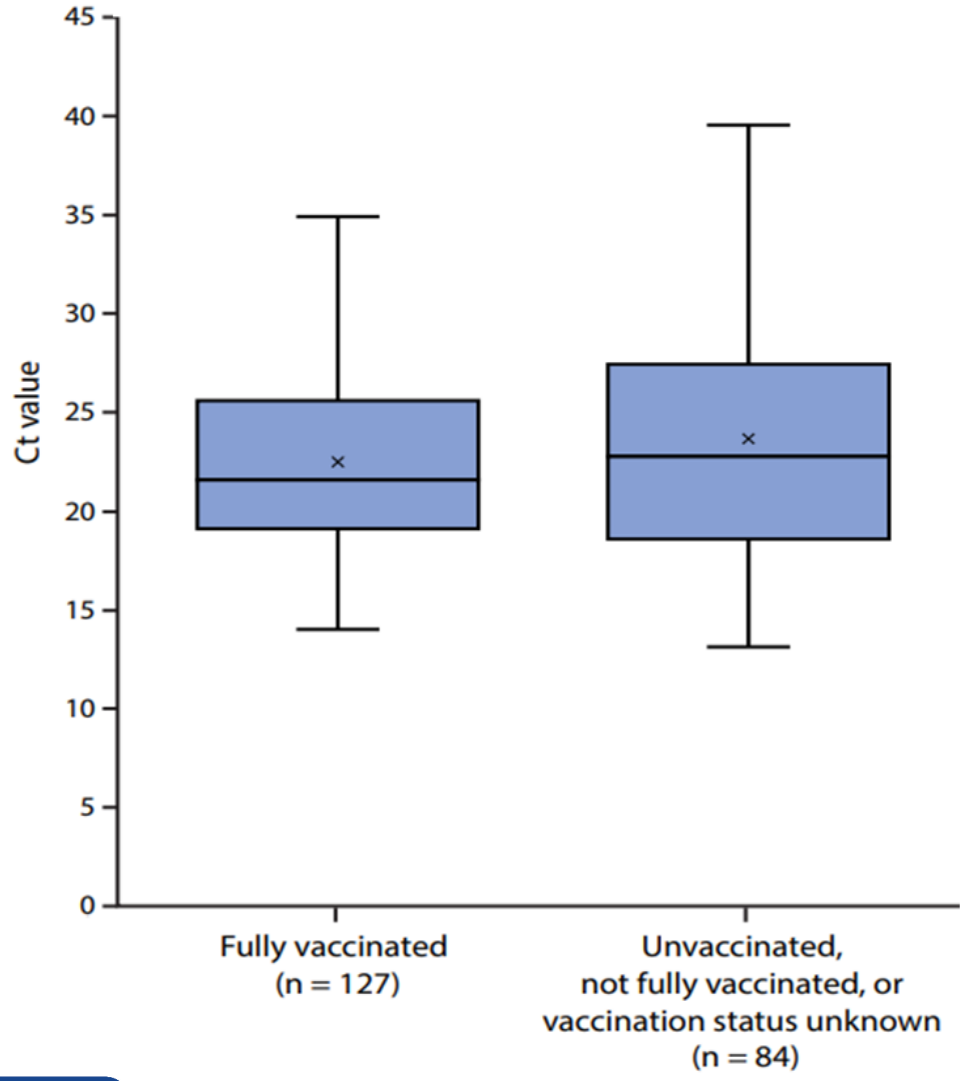
- *No* Delta infections**
- Viral load has been lower in vaccinated people who get infected than in unvaccinated people
- **Vaccinated *less* infectious than unvaccinated**

*mean viral load ± standard deviation

** In unvaccinated persons: 10 variants of concern (VOC): 9 B.1.427/9 and 1 B.1.1.7 (alpha). In vaccinated, 3 VOCs all B.1.429.

Thompson et al. 2021, N Engl J Med 385:320-9. DOI: 10.1056/NEJMoa2107058

Infections in Unvaccinated and Vaccinated Compared



<u>Data from Barnstable, MA Outbreak</u>*

- *All* Delta infections (as of July 25, 2021)
- Viral load** the same in both vaccinated unvaccinated people with infection
- **Vaccinated *equally* infectious as unvaccinated**

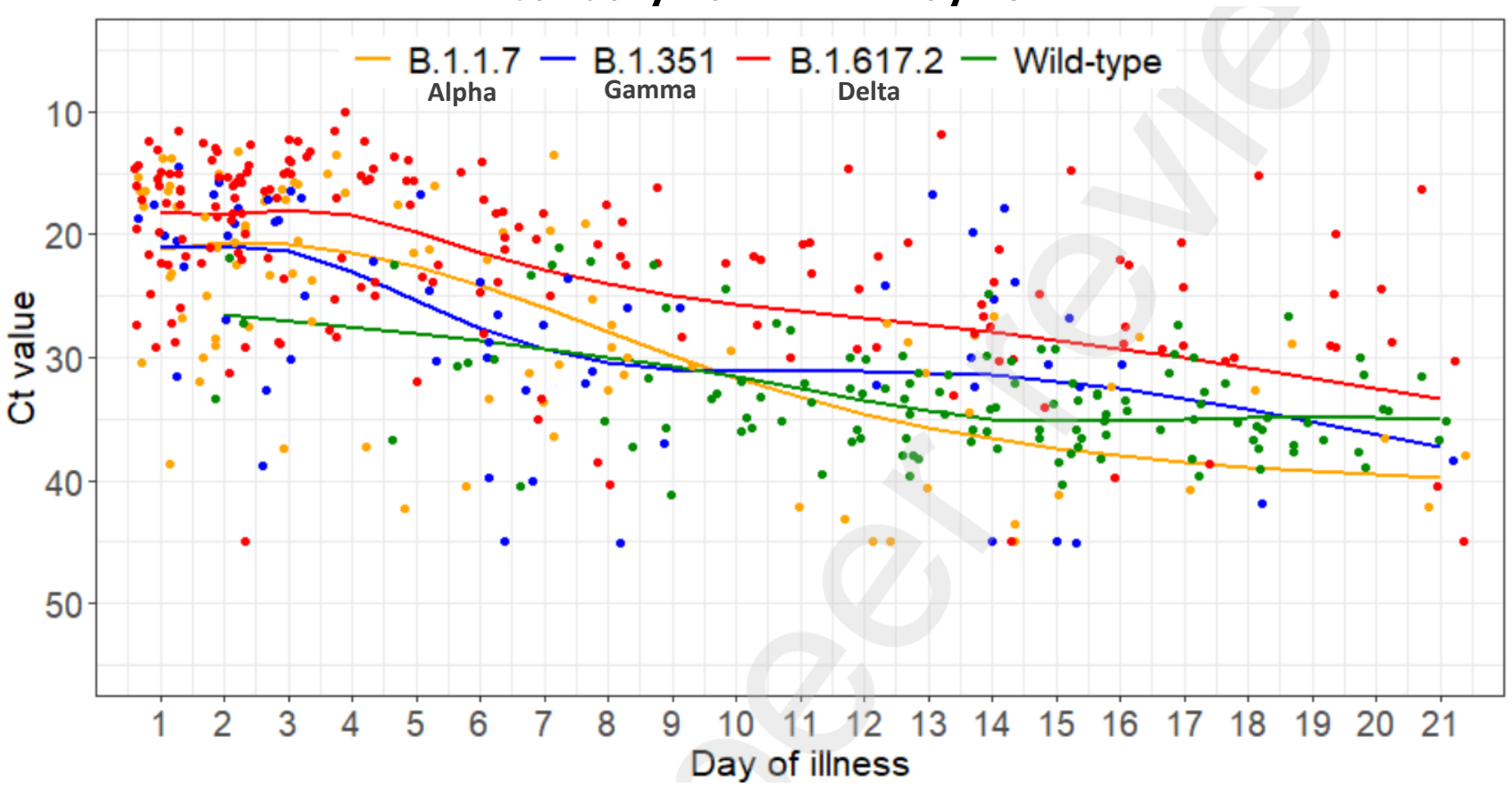
* 469 Massachusetts cases investigated of whom 364 (74%) vaccinated. Four breakthroughs (1.1%) hospitalized (two with underlying medical conditions), no deaths.
** Data presented are Ct values that in aggregate generally correlate with viral burden.

Brown et al. 2021, <u>MMWR:</u> https://www.cdc.gov/mmwr/volumes/70/wr/pdfs/mm7031e2-H.pdf

Delta Variant Infection Produces High Viral Loads Compared with Other Variant Infections

Data from 846 Diagnoses Infection with Variant and Wild Type - Singapore

1 January 2021 – 22 May 2021

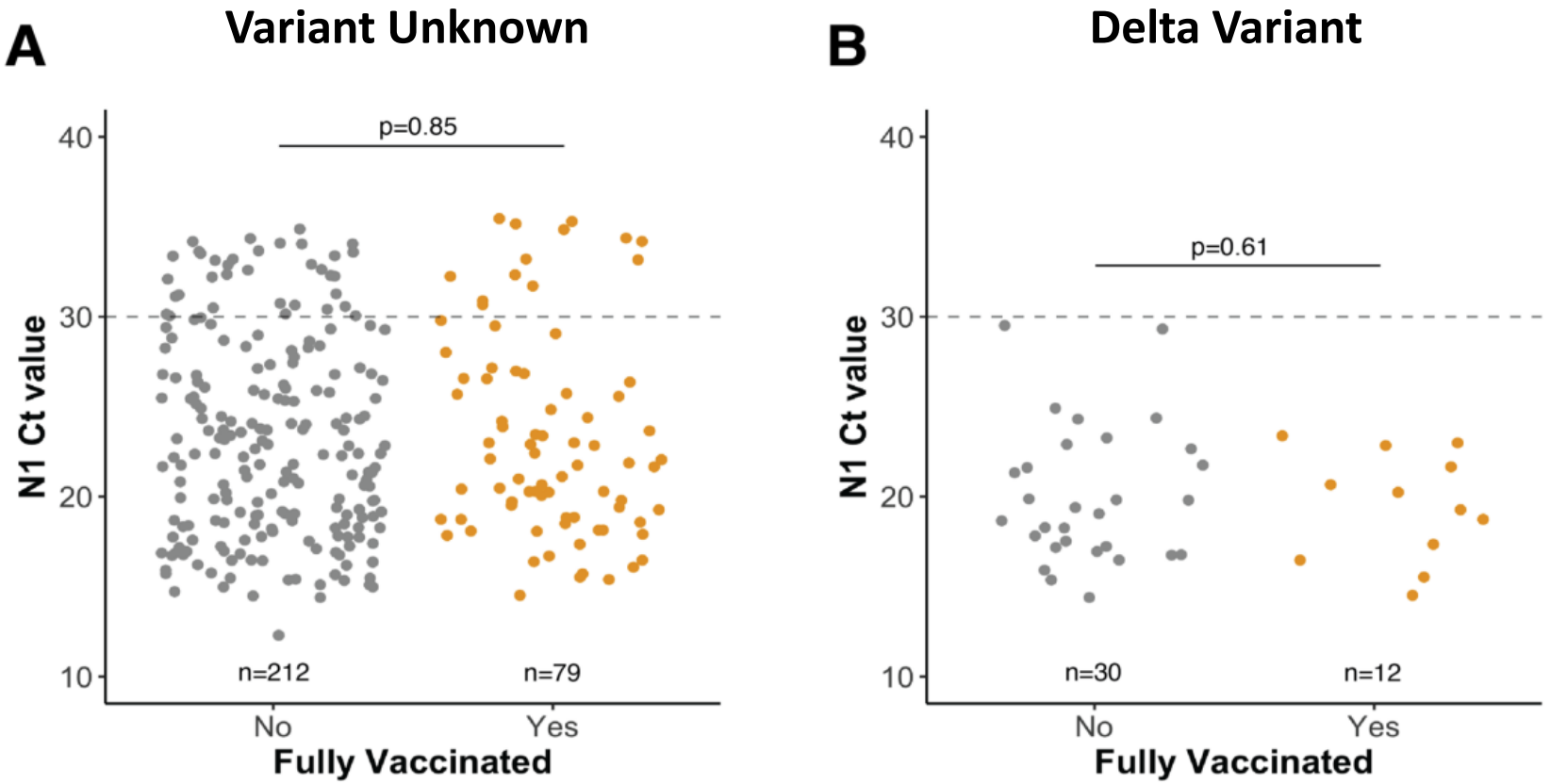


Ong et al. 2021, medRxiv: Retrospective cohort study comparing clinical and virological features B.1.1.7 (Alpha), B.1.315 (Beta) B.1.617.2 (Delta) Singapore

Infections in Unvaccinated and Vaccinated Compared

Data from Dane County WI and Surrounding Counties Served Laboratory

28 June 2021 – 24 July 2021, When Delta Was Predominant Variant

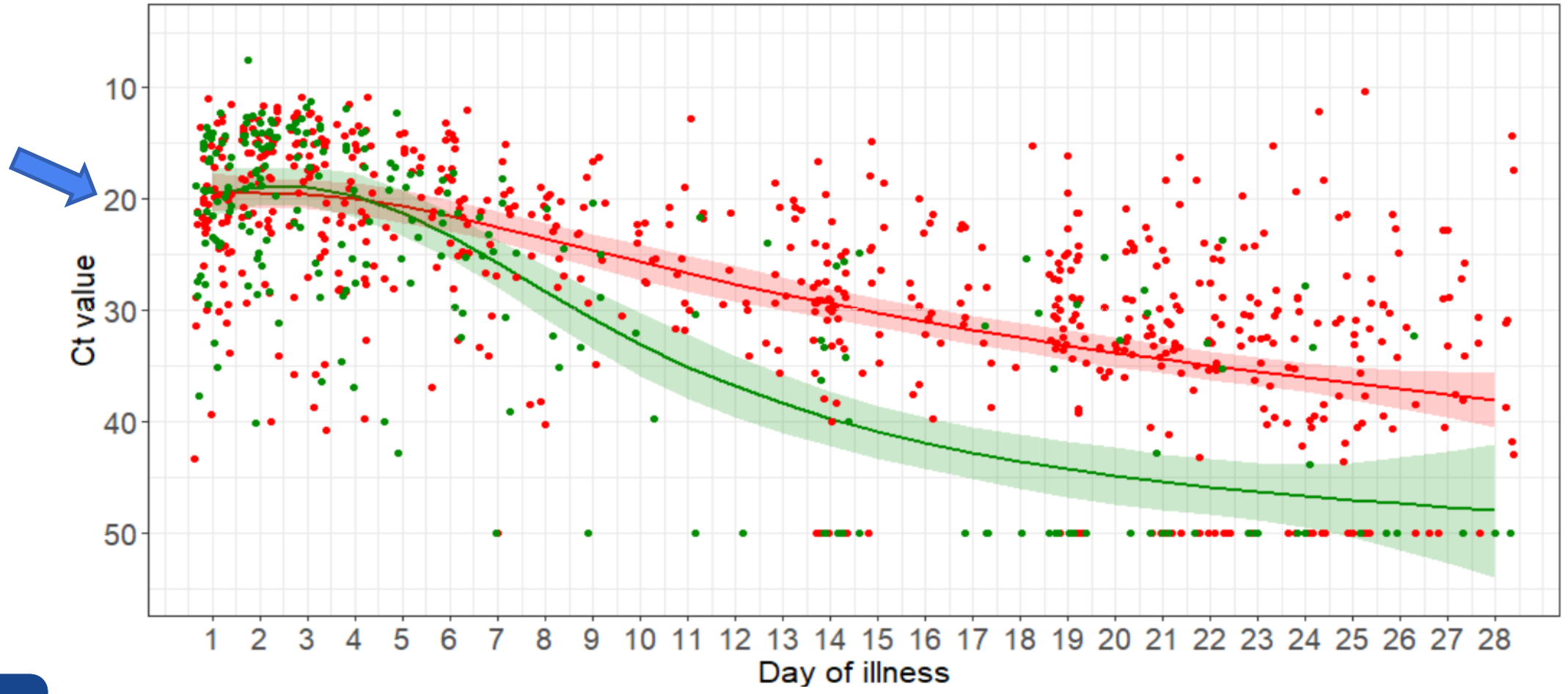


Riemersma et al. 2021, medRxiv: Vaccinated and unvaccinated individuals have similar viral loads in communities with a high prevalence of the SARS-CoV-2 delta variant.

Infections in Unvaccinated and Vaccinated Compared

Data from 218 Patients Admitted with Delta Variant Infections - Singapore

1 April 2021 – 15 June 2021



Chia et al. 2021, medRxiv: Virological and serological kinetics of SARS-CoV-2 Delta variant vaccine-breakthrough infections - medRxiv.pdf

Infections in Unvaccinated and Vaccinated Compared

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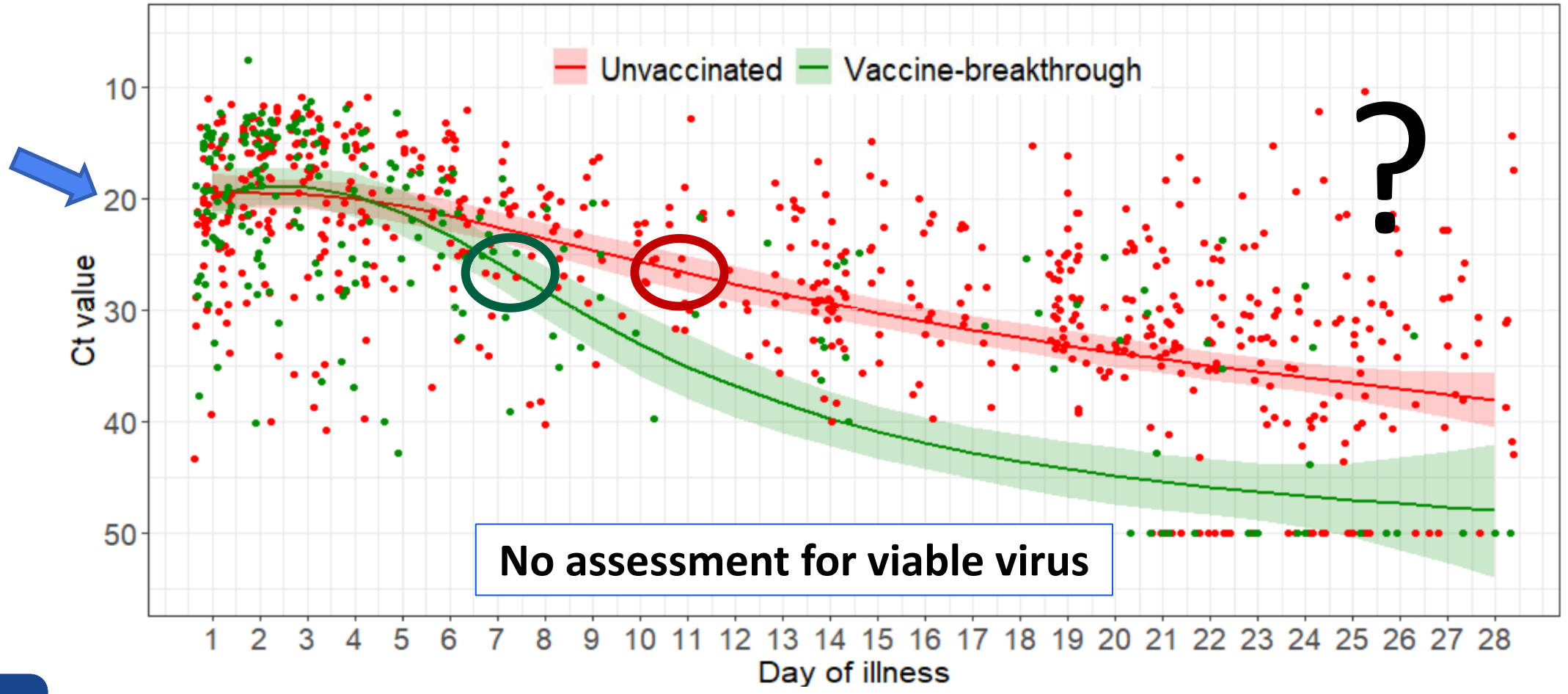

Chia et al. 2021, medRxiv: Virological and serological kinetics of SARS-CoV-2 Delta variant vaccine-breakthrough infections - medRxiv.pdf

Despite Delta, FDA Authorized Vaccines Still Work

- Despite these developments, vaccination continues to save lives
- Vaccine effectiveness (VE) might be decreasing for symptomatic illness
- However, all evidence indicates high levels VE against severe illness or death after full vaccination with Pfizer or Moderna product
  - Data more limited for J&J
- Increasing vaccination coverage remains the number one priority to reduce transmission as well reducing the risk of more emerging variants

Topline Messages

1. **Getting vaccinated** prevents severe illness, hospitalization, and death; it also helps reduce the spread of the virus in communities.
    - Unvaccinated individuals should get vaccinated and continue masking until they are fully vaccinated.
    - With the Delta variant, this is more urgent than ever. The highest spread of cases and severe outcomes is happening in places with low vaccination rates

Topline Messages

2. **Data show Delta is different than past versions of the virus**: it is much more contagious.
    - Some vaccinated people can get Delta in a breakthrough infection and may be contagious.
    - Even so, vaccinated individuals represent a very small amount of transmission occurring around the country.
    - Virtually all hospitalizations and deaths continue to be among the unvaccinated.

Topline Messages

3. In areas with substantial and high transmission, **CDC recommends that everyone (including fully vaccinated individuals) wear a mask in public indoor settings** to help prevent spread of Delta and protect others.

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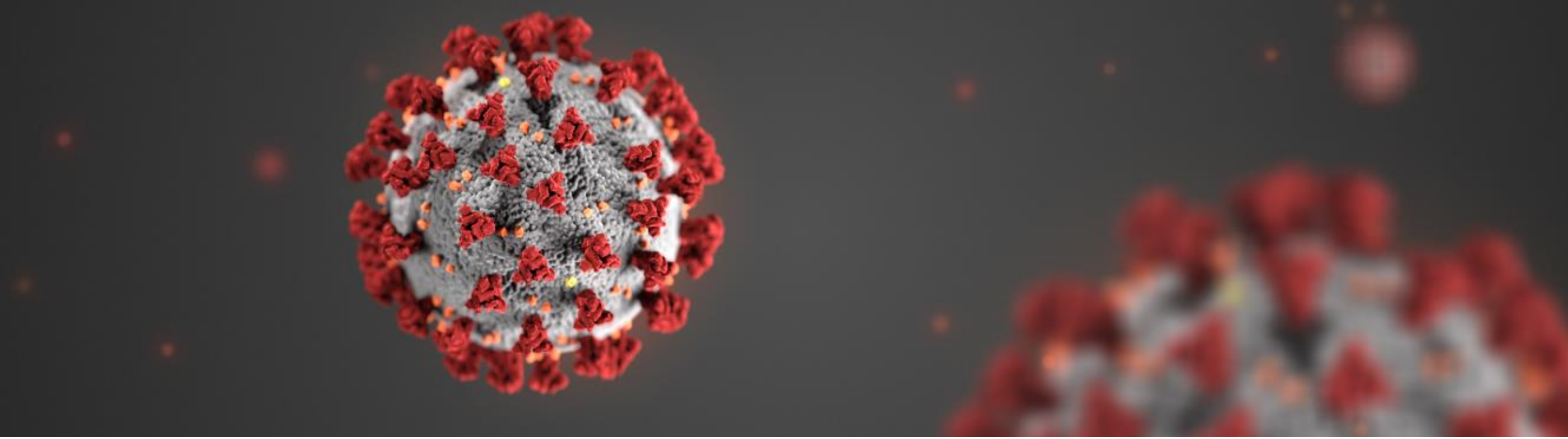
4. **CDC recommends that community leaders encourage vaccination and masking** to prevent further outbreaks in areas of substantial and high transmission.

Topline Messages

3. In areas with substantial and high transmission, **CDC recommends that everyone (including fully vaccinated individuals) wear a mask in public indoor settings** to help prevent spread of Delta and protect others.
4. **CDC recommends that community leaders encourage vaccination and masking** to prevent further outbreaks in areas of substantial and high transmission.
5. **CDC recommends universal indoor masking for all teachers, staff, students, and visitors to K-12 schools, regardless of vaccination status.** Children should return to full-time in-person learning in the fall with layered prevention strategies in place.



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.