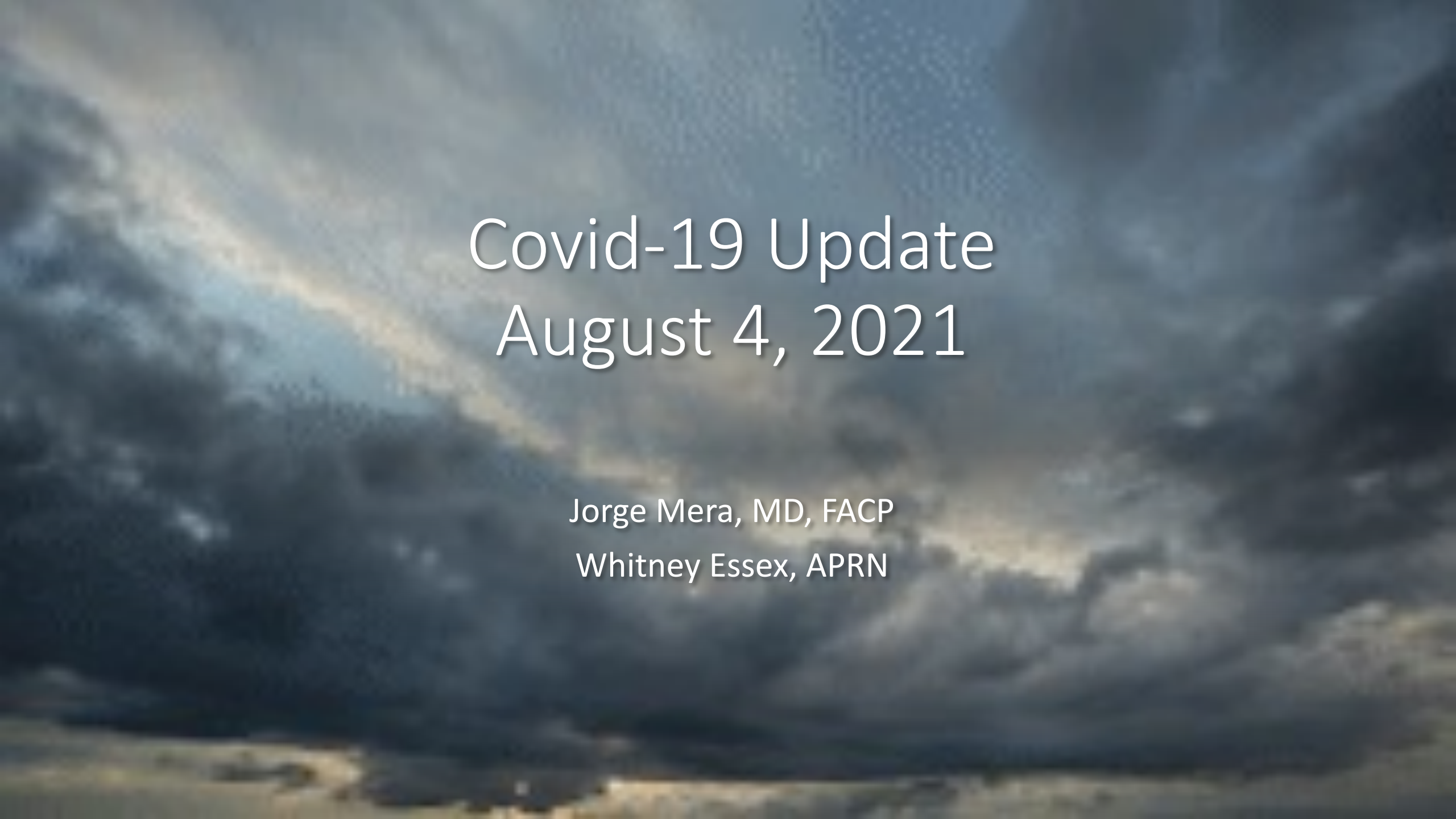
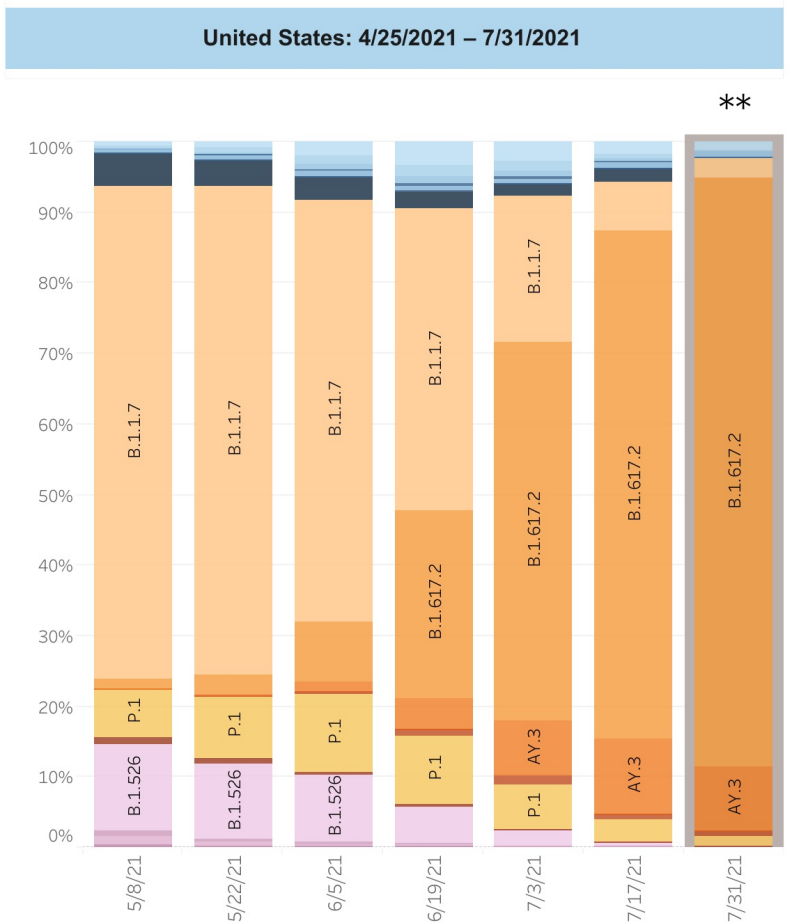
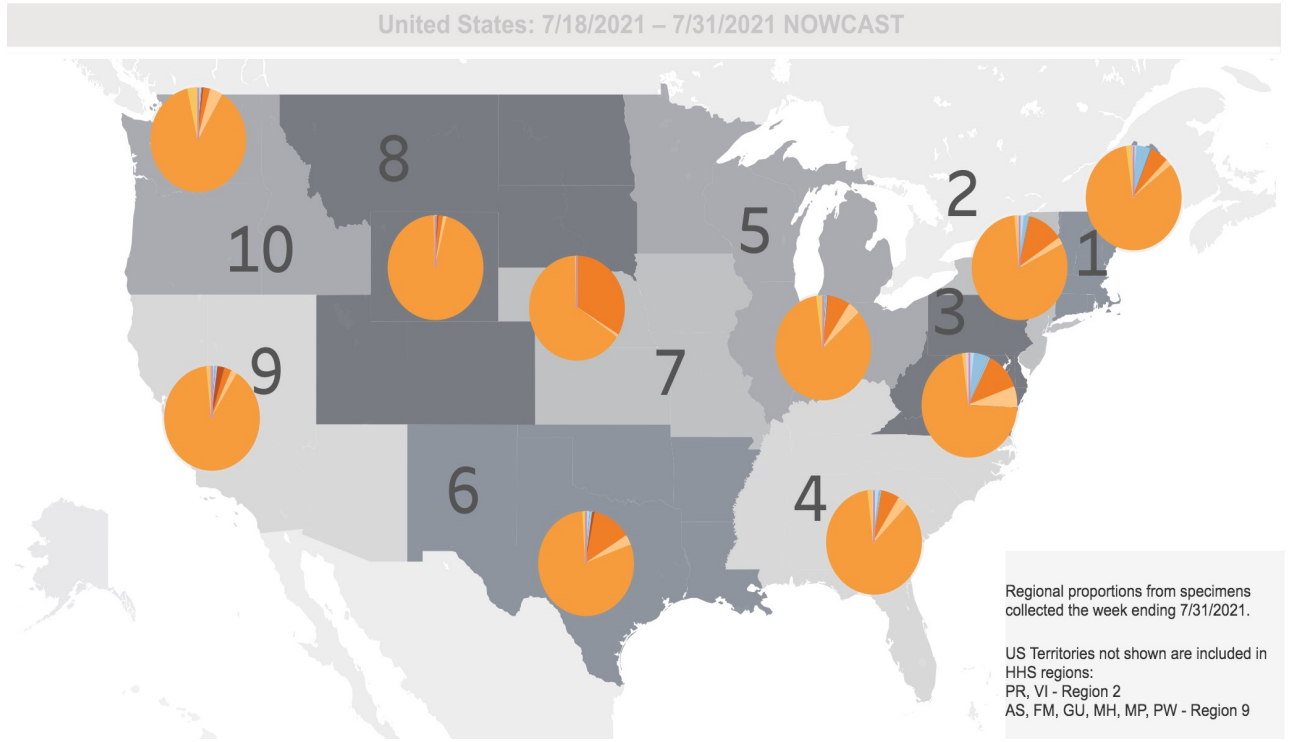


Covid-19 Update
August 4, 2021

Jorge Mera, MD, FACP

Whitney Essex, APRN





Variants of Concern in the USA

Updated Aug 3, 2021

Variant of Concern B.1.617.2 (Delta)

First detected in the United States in March 2021.

- It was initially identified in India in December 2020.

This variant seems to spread more easily and quickly than other variants, which may lead to more cases of COVID-19.

- An increase in the number of cases will put more strain on healthcare resources, lead to more hospitalizations, and potentially more deaths.

So far, studies suggest that the current authorized vaccines work on the circulating variants.

Attributes:

- Increased transmissibility
- Potential reduction in neutralization by some EUA monoclonal antibody treatments
- Potential reduction in neutralization by post-vaccination sera

COVID-19 Weekly Cases per 100,000 Population by Race/Ethnicity, United States

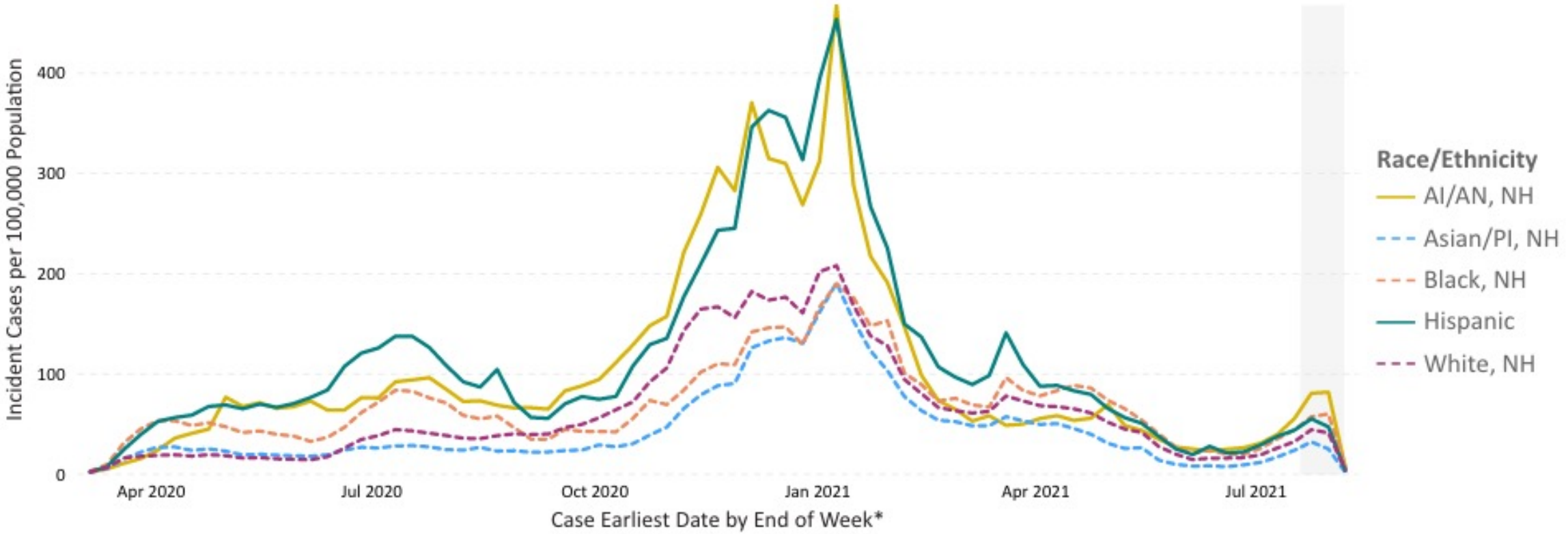
Jurisdiction: US

3/7/2020 – 8/7/2021

March 01, 2020 - August 07, 2021

Cases: Sex | Age | Race/Ethnicity

Deaths: Sex | Age | Race/Ethnicity



US: The most recent line level case record was reported during the week ending on Aug 07, 2021. Percentage of cases reporting race by date - 60.25%

*US territories are included in case and death counts but not in population counts. Potential two-week delay in case reporting to CDC denoted by gray bars. AI = American Indian, AN = Alaska Native, NH = Non-Hispanic, PI = Pacific Islander. Excludes cases with unknown or multiple races. *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.*

Last Updated: Aug 04, 2021

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

COVID-19 Weekly Deaths per 100,000 Population by Race/Ethnicity, United States

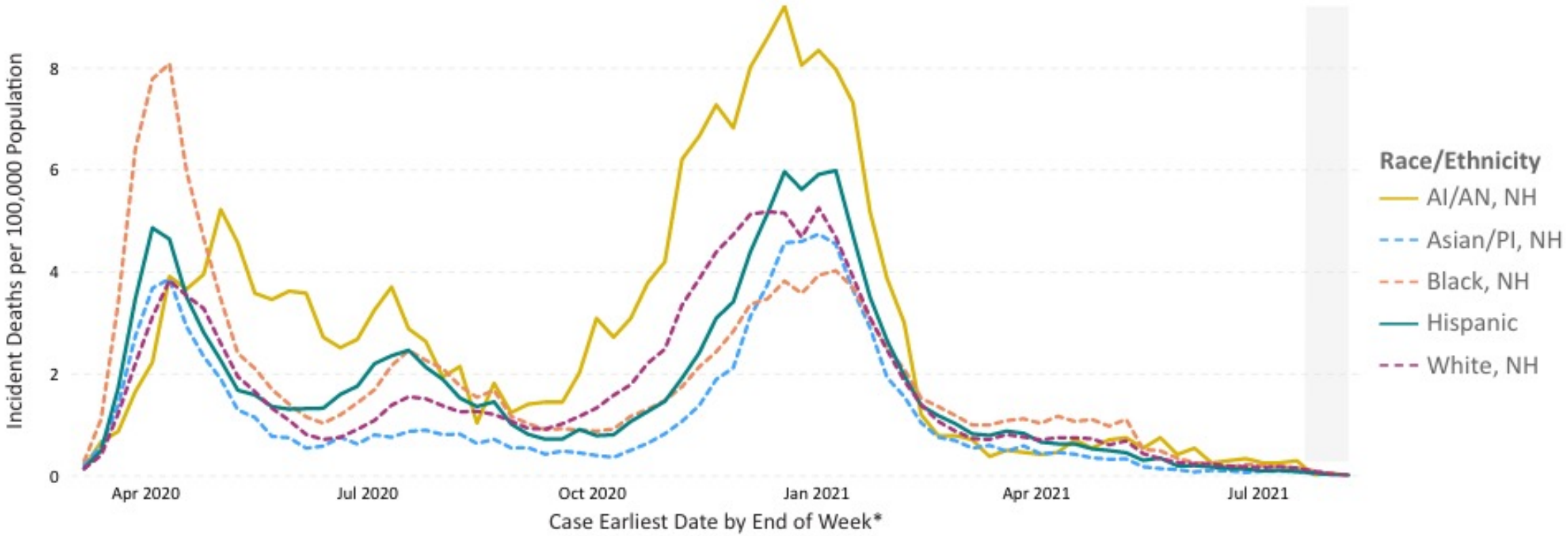
Jurisdiction: US

3/7/2020 – 8/7/2021

March 01, 2020 - August 07, 2021

Cases | Deaths

Sex | Age | Race/Ethnicity



US: The most recent line level case record was reported during the week ending on Aug 07, 2021. Percentage of deaths among reported cases - 1.77%. Percentage of deaths reporting race by date - 80.23%

*US territories are included in case and death counts but not in population counts. Potential two-week delay in case reporting to CDC denoted by gray bars. AI = American Indian, AN = Alaska Native, NH = Non-Hispanic, PI = Pacific Islander. Excludes deaths with unknown or multiple races. *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.*

Last Updated: Aug 04, 2021

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

The “Legal Epidemiology” of Pandemic Control

Scott Burris, J.D., Evan D. Anderson, J.D., Ph.D., and Alexander C. Wagenaar, M.S.W., Ph.D.

NEJM, May 27, 2021

Infrastructure of Three Research Areas that Need To Be Scaled Up

- Study of the mechanisms, effects, side effects, and implementation of laws designed to influence health, such as Covid control measures

- Research on how the legal infrastructure of the U.S. health system, the allocation of powers and duties, as well as limits on authority influences the effectiveness of the system

- How laws that may appear to have no health purposes, such as the tax code, minimum wage, and labor rules shape the social determinants of health.

The “Legal Epidemiology” of Pandemic Control

Law has significant health effects. Failure to study these effects and translate that knowledge into better law reflects problems of culture, not science

COVID-19

Prevention Update

FDA authorizes REGEN-COV monoclonal antibody therapy for post-exposure prophylaxis (prevention) for COVID-19

Prophylaxis with REGEN-COV is not a substitute for vaccination against COVID-19

REGEN-COV should only be used as post-exposure prophylaxis for individuals who are:

- Not fully vaccinated **or** who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, people with immunocompromising conditions, including those taking immunosuppressive medications), **and**
- have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per Centers for Disease Control and Prevention (CDC), **or**
- who are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (for example, nursing homes or prisons)

Clinical trial revealed 62% reduction in RT-PCR confirmed symptomatic COVID-19 cases in the REGEN-COV group compared to placebo at day 29

REGEN-COV (Casirivimab/imdevimab)

COVID-19

Diagnostic Updates

Diagnosis

Nucleic acid amplification tests to detect viral RNA are recommended for diagnosis

- Imperfect sensitivity and prolonged shedding of RNA in the absence of viable virus require careful test interpretation

Antigen tests may improve speed and accessibility of testing

- However, their accuracy is incompletely defined in the published literature

Nasopharyngeal viral shedding peaks before the onset of symptoms and declines thereafter

- Making the timing of sampling relative to symptom onset an important determinant of test performance

Viral load in the lungs or plasma may be more reflective of disease progression

Longitudinal Assessment of Diagnostic Test Performance Over the Course of Acute SARS-CoV-2 Infection

Background:

- Serial screening is critical for restricting spread SARS-CoV-2 by facilitating timely identification of infected individuals to interrupt transmission.
- Variation in sensitivity of different diagnostic tests at different stages of infection has not been well documented.

Methods: Longitudinal study of 43 adults newly infected with SARS-CoV-2

- **All provided daily saliva and nasal swabs for:**
  - Quantitative reverse transcription polymerase chain reaction (RT-qPCR)
  - Quidel SARS Sofia antigen fluorescent immunoassay (FIA)
  - Live virus culture

Smith RL, Gibson LL, Martinez PP et al. *The Journal of Infectious Diseases*, 2021;,jiab337, https://doi.org/10.1093/infdis/jiab337

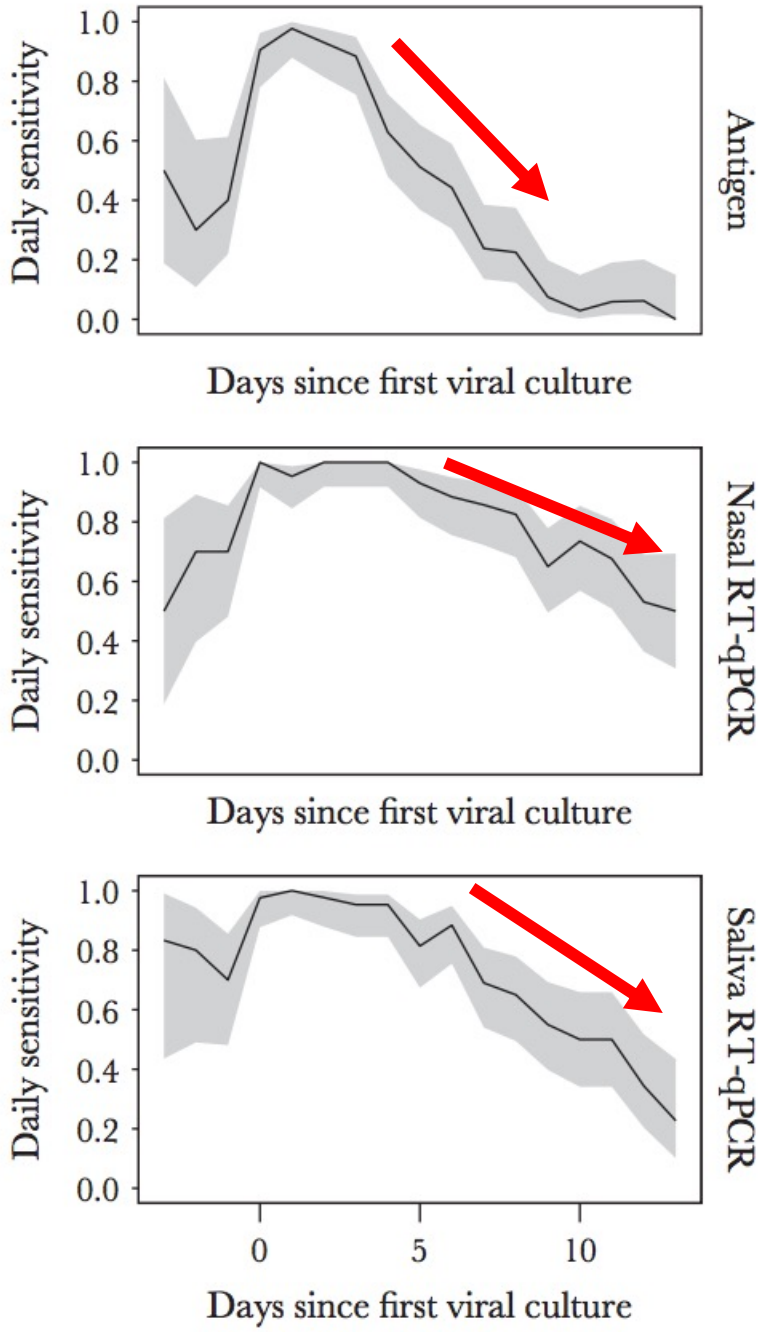
Table 1. Demographic Information on Study Participants

Variable	Data (n = 43)
Age, y, mean (SD)	33.1 (12.8)
Race, No. (%)	
Native American	0 (0.0)
Asian	1 (2.3)
Black	4 (9.3)
Other	4 (9.3)
Pacific Islander	0 (0.0)
White	34 (79.1)
Sex, No. (%)	
Female	20 (46.5)
Male	23 (53.5)
Ethnicity, No. (%)	
Hispanic	8 (18.6)
Non-Hispanic	35 (81.4)

Smith RL, Gibson LL, Martinez PP et al. *The Journal of Infectious Diseases*, 2021;,jiab337, https://doi.org/10.1093/infdis/jiab337

Longitudinal Assessment of Diagnostic Test Performance Over the Course of Acute SARS-CoV-2 Infection

- Participation in this study was limited to faculty, students, and staff of the University of Illinois at Urbana-Champaign
- Participant population included here was primarily young, non-Hispanic white, and skewed slightly towards men.
- All infections were either mild or asymptomatic, and no participants were hospitalized for COVID-19.,

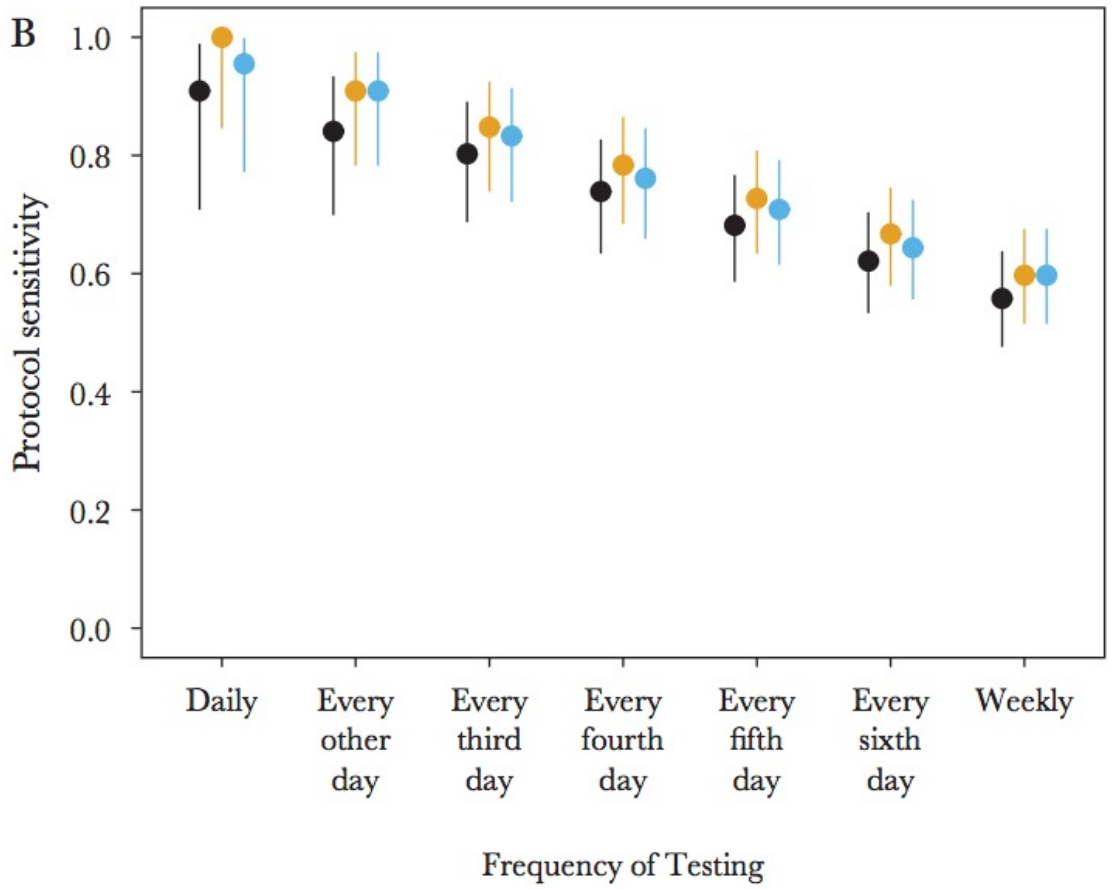


Daily sensitivity of each test platform relative to the day of first positive viral culture result

Shaded areas represent the 95% confidence interval around the observed proportion.

Smith RL, Gibson LL, Martinez PP et al. *The Journal of Infectious Diseases*, 2021;,jiab337, https://doi.org/10.1093/infdis/jiab337

Longitudinal Assessment of Diagnostic Test Performance Over the Course of Acute SARS-CoV-2 Infection



- Protocol sensitivity of each test platform to detect an infected person
- Before or on days where nasal samples were viral culture positive, relative to the frequency of testing.
- Bars indicate 95% confidence interval around the observed proportion. Abbreviation: RT-qPCR, quantitative reverse transcription polymerase chain reaction

Smith RL, Gibson LL, Martinez PP et al. *The Journal of Infectious Diseases*, 2021;,jiab337, https://doi.org/10.1093/infdis/jiab337

Protocol Sensitivity of Each Testing Platform To Detect an Infecting Person During a 14-day Testing Period Relative to the Frequency of Testing

			Nasal Antigen				Saliva RT-qPCR				Nasal RT-qPCR			
			Probability of Detection		No. Positive		Probability of Detection		No. Positive		Probability of Detection		No. Positive	
Testing Frequency	No.	No. Before or While VC+[a]	Any Time[b]	Before or While VC+	Any Time	Before or While VC+	Any Time	Before or While VC+	Any Time	Before or While VC+	Any Time	Before or While VC+	Any Time	Before or While VC+
Daily	43	22	1	0.909	43	20	1	0.955	43	21	1	1	43	22
Every other day	86	44	1	0.841	86	37	0.988	0.909	85	40	1	0.909	86	40
Every third day	129	66	1	0.803	129	53	0.984	0.833	127	55	1	0.848	129	56
Every fourth day	172	88	0.959	0.739	165	65	0.983	0.761	169	67	1	0.784	172	69
Every fifth day	215	110	0.921	0.682	198	75	0.981	0.709	211	78	0.995	0.727	214	80
Every sixth day	258	132	0.864	0.621	223	82	0.965	0.644	249	85	0.992	0.667	256	88
Weekly	301	154	0.797	0.558	240	86	0.963	0.597	290	92	0.987	0.597	297	92

Smith RL, Gibson LL, Martinez PP et al. *The Journal of Infectious Diseases*, 2021;,jiab337, https://doi.org/10.1093/infdis/jiab337

Longitudinal Assessment of Diagnostic Test Performance Over the Course of Acute SARS-CoV-2 Infection

Results:

- Both RT-qPCR and antigen peaked in sensitivity during the period in which live virus was detected in nasal swabs, but sensitivity of RT-qPCR tests rose more rapidly prior to this period.
- Serial testing multiple times per week increases the sensitivity of antigen tests.

Conclusions:

- RT-qPCR tests are more effective than antigen tests at identifying infected individuals prior to or early during the infectious period
- All tests showed >98% sensitivity for identifying infected individuals if used at least every 3 days.
- **Daily screening using antigen tests can achieve approximately 90% sensitivity for identifying infected individuals while they are viral culture positive**

Smith RL, Gibson LL, Martinez PP et al. *The Journal of Infectious Diseases*, 2021;,jiab337, https://doi.org/10.1093/infdis/jiab337

COVID-19

Treatment Update

Remdesivir Versus Standard-of-Care for Severe Coronavirus Disease 2019 Infection: An Analysis of 28-Day Mortality

Olender SA, Walunas TL, Martinez E, Open Forum Infect Dis. 2021 May 26;8(7)

Remdesivir Versus Standard-of-Care for Severe Coronavirus Disease 2019 Infection

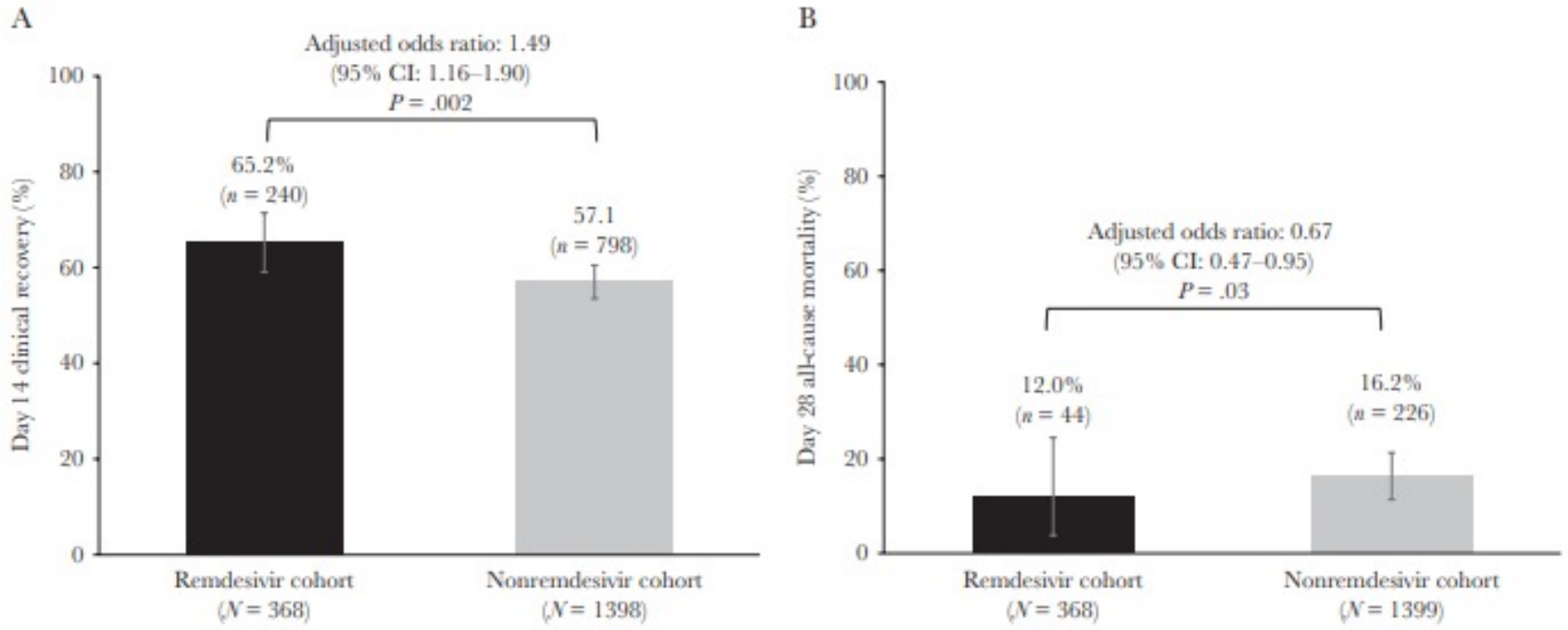
Background:

- Remdesivir is approved by the FDA for the treatment of patients hospitalized with COVID-19 and has been shown to shorten time to recovery and improve clinical outcomes in randomized trials

Methods:

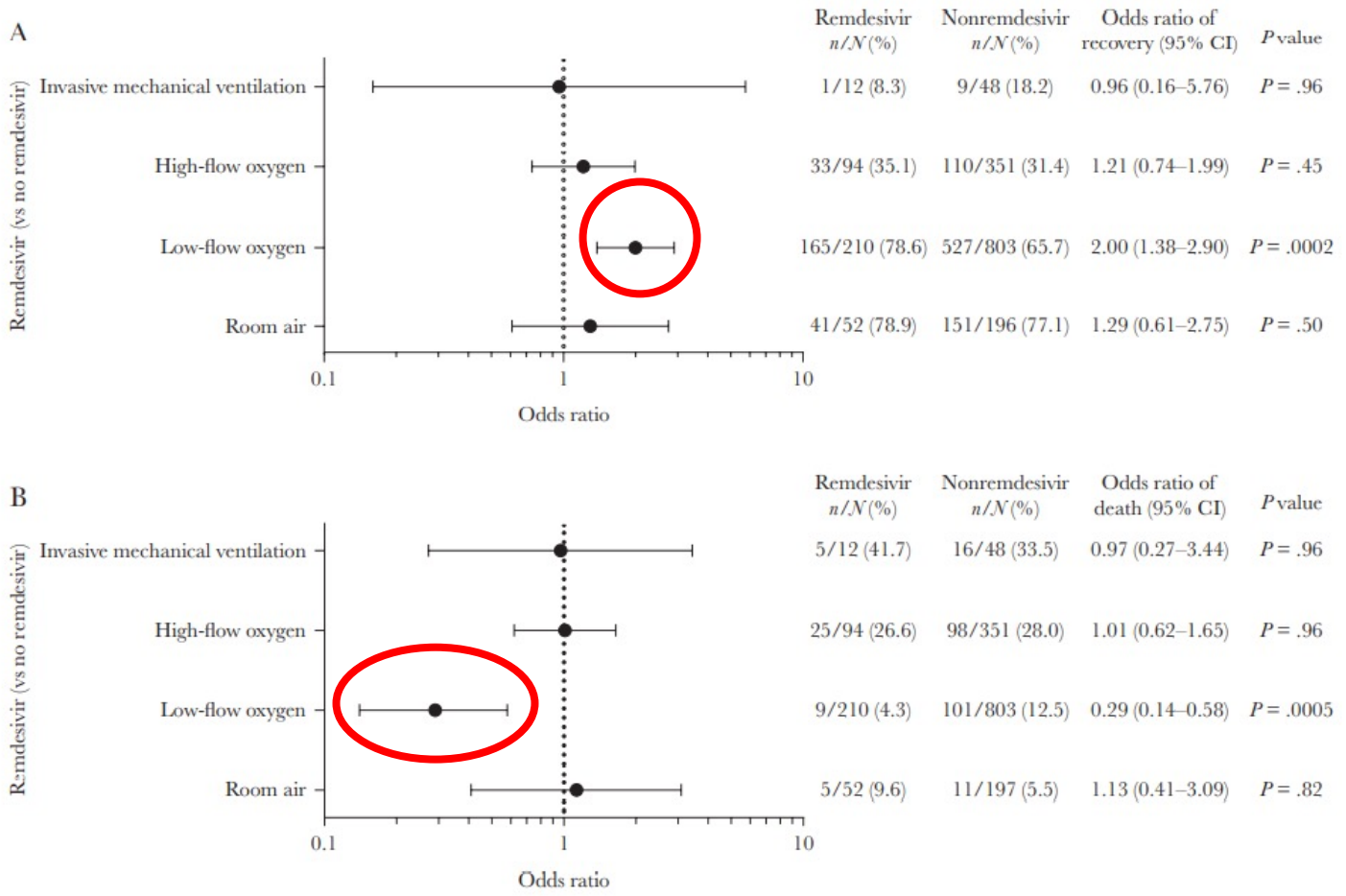
- Day 28 comparative analysis of data from a phase 3, randomized, open-label study comparing 2 remdesivir regimens (5 vs 10 days, combined for this analysis **[remdesivir cohort**]) was compared with a real-world retrospective longitudinal cohort study of patients receiving standard-of-care treatment **(nonremdesivir cohort).**
- **Eligible patients**, aged ≥18 years, had confirmed SARS-CoV-2, oxygen saturation ≤94% on room air or required supplemental oxygen, with pulmonary infiltrates.
- **Propensity score matching** (up to 1:10 ratio) was used to ensure comparable populations.
- **Outcomes measured:**
  - Day 14 clinical recovery (determined using a 7-point ordinal scale)
  - Day 28 all-cause mortality (coprimary endpoints).

Remdesivir Versus Standard-of-Care for Severe Coronavirus Disease 2019 Infection



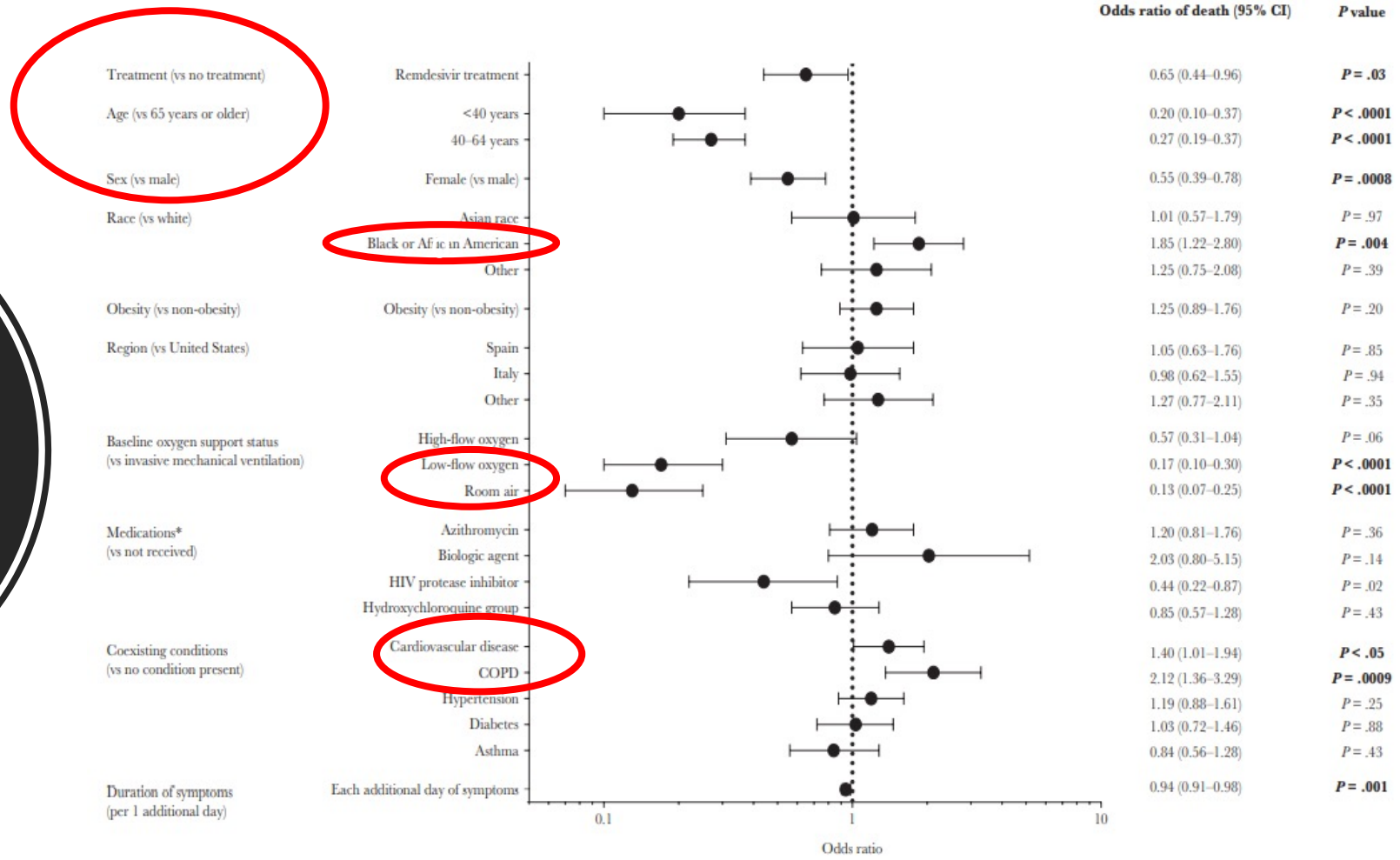
Primary endpoint analyses: (A) odds ratio for day 14 clinical recovery; (B) odds ratio for day 28 all-cause mortality. P value, odds ratio, and 95% confidence interval (CI) were based on the generalized estimating equation logistic regression with propensity-matched sets considered as clusters. Numbers for the nonremdesivir cohort are based on weighted statistics.

Remdesivir Versus Standard-of-Care for Severe Coronavirus Disease 2019 Infection



- Subgroup analysis of patients categorized according to oxygen support status required at baseline (based on propensity score matching) for (A) day 14 recovery and (B) day 28 all-cause mortality. P value, odds ratio, and 95% confidence interval (CI) were based on the generalized estimating equation logistic regression with matched sets considered as clusters. Numbers for the nonremdesivir cohort are based on weighted statistics

Remdesivir Versus Standard-of-Care for Severe Coronavirus Disease 2019 Infection



- **Multivariable analysis of the odds ratio for day 28 all-cause mortality using generalized estimating equation logistic regression model. *Medications potentially active against coronavirus disease 2019. CI, confidence interval; COPD, chronic obstructive pulmonary disease**

Remdesivir Versus Standard-of-Care for Severe Coronavirus Disease 2019 Infection

Results:

- A total of 368 (remdesivir) and 1399 (nonremdesivir) patients were included in the matched analysis.
- The day 14 clinical recovery rate was significantly higher among the remdesivir versus the nonremdesivir cohort (65.2% vs 57.1%; odds ratio [OR], 1.49; 95% confidence interval [CI], 1.16–1.90; P = 0.002).
- **The day 28 mortality rate was significantly lower in the remdesivir cohort** versus the nonremdesivir cohort (12.0% vs 16.2%; OR, 0.67; 95% CI, 0.47–.95; P = .03)

Conclusions:

- Remdesivir was associated with significantly higher rates of day 14 clinical recovery, and lower day 28 mortality, compared with standard-of-care treatment in hospitalized patients with COVID-19.
- These data, taken together, support the use of remdesivir to improve clinical recovery and decrease mortality from SARS-CoV-2 infection

Impact of Bamlanivimab Monoclonal Antibody Treatment on Hospitalization and Mortality Among Nonhospitalized Adults With Severe Acute Respiratory Syndrome Coronavirus 2 Infection

Bariola JR, McCreary EK, Wadas RJ, et al. Open Forum Infect Dis. 2021 May 17;8(7):

Impact of Bamlanivimab Monoclonal Antibody Treatment on Hospitalization and Mortality Among Nonhospitalized Adults With Severe Acute Respiratory Syndrome Coronavirus 2 Infection

Background

- Monoclonal antibody treatment may prevent complications of coronavirus disease COVID-19

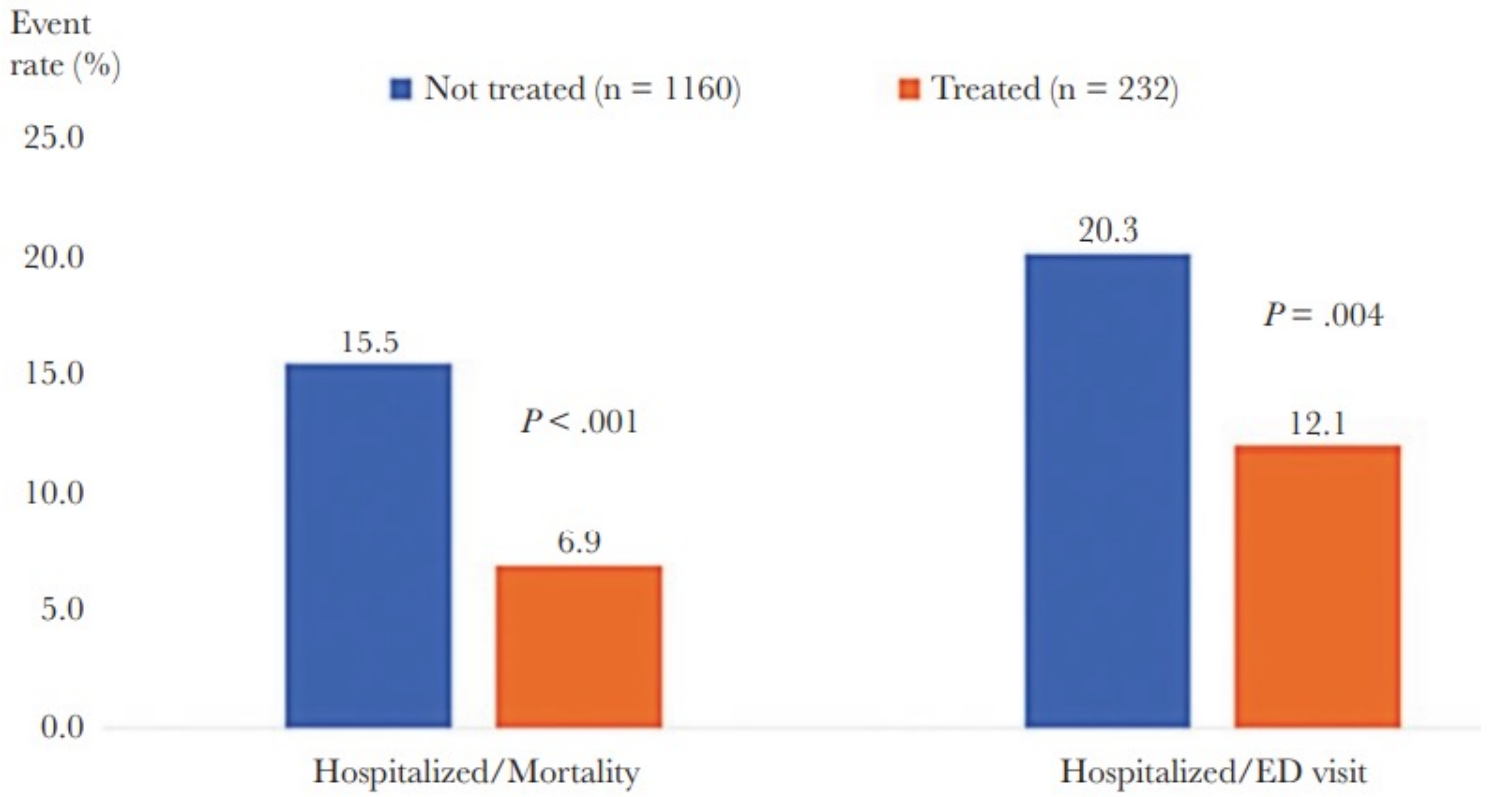
Objective:

- Quantify the impact of bamlanivimab monoclonal antibody monotherapy on hospitalization and mortality among outpatients at high risk of COVID-19 complications.

Methods:

- Observational study comparing outpatients who received bamlanivimab monoclonal antibodies to nontreated patients with a positive PCR or antigen test SARS-CoV-2 during the same period who were eligible for monoclonal antibody.
- **Primary outcomes: 28-day hospitalization or all-cause mortality**
- **Secondary outcome: Hospitalization or emergency department visit without hospitalization.**
- The risk-adjusted odds of outcomes determined using 1:5 propensity matching and multivariable logistic regression

Impact of Bamlanivimab Monoclonal Antibody Treatment on Hospitalization and Mortality Among Nonhospitalized Adults With SARS-CoV-2 Infection

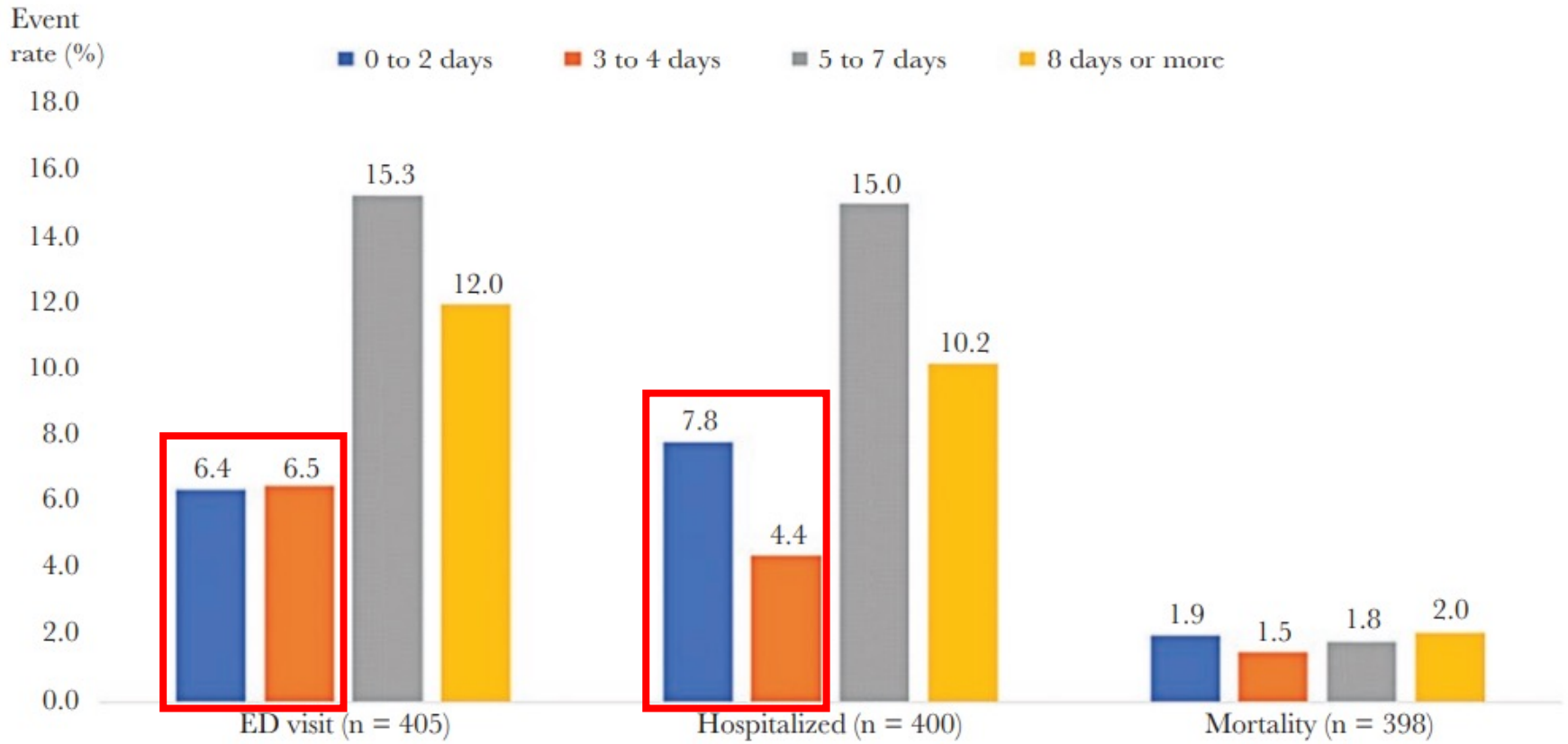


Frequency of 28-day study outcomes among propensity-matched patients receiving and not receiving bamlanivimab monoclonal antibody treatment.

Graph depicts the frequency of 28-day hospitalization or mortality 408 (primary outcome) and hospitalization or emergency department (ED) visit without hospitalization (secondary outcome) among the matched patients receiving bamlanivimab monoclonal antibody treatment (orange bars) versus those not receiving bamlanivimab monoclonal antibody treatment (blue bars).

P values are from the matched cohort logistic regression models.

Frequency of 28-day study outcomes among patients receiving bamlanivimab monoclonal antibody treatment, stratified by timing of treatment.



Impact of Bamlanivimab Monoclonal Antibody Treatment on Hospitalization and Mortality Among Nonhospitalized Adults With Severe Acute Respiratory Syndrome Coronavirus 2 Infection

Results:

- Among 232 patients receiving bamlanivimab matched with 1160 comparator patients, the mean age was 67 years, 56% were female, and 196 (14%) of patients experienced hospitalization or mortality.
- Bamlanivimab treatment was associated with:
  - **A significantly reduced risk-adjusted odds of hospitalization or mortality within 28 days**
  - (odds ratio [OR], 0.40; 95% confidence interval [95% CI], 0.24–0.69; P < 0.001
  - **A significantly lower risk adjusted odds of hospitalization or emergency department visit without hospitalization** (OR, 0.54; 95% CI, 0.35–0.82; P = .004). The results were most strongly associated with patients age 65 years and older

Conclusions:

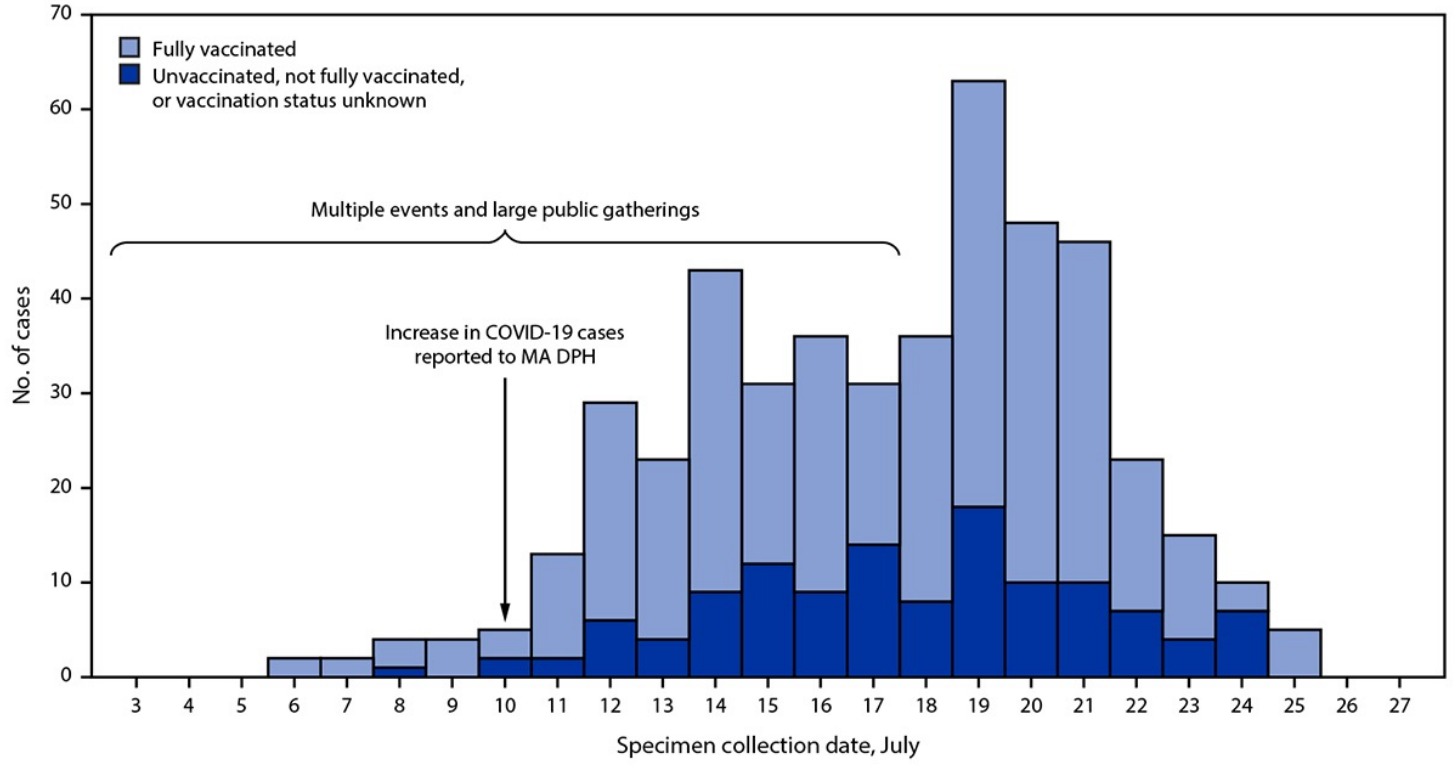
- Bamlanivimab monoclonal antibody monotherapy was associated with reduced hospitalizations and mortality within 28 days among outpatients with mild to moderate COVID-19

Outbreak of SARS-CoV-2 Infections, Including COVID-19 Vaccine Breakthrough Infections, Associated with Large Public Gatherings — Barnstable County, Massachusetts, July 2021

- **What is already known about this topic?**
- Variants of SARS-CoV-2 continue to emerge. The B.1.617.2 (Delta) variant is highly transmissible.
- **What is added by this report?**
- In July 2021, following multiple large public events in a Barnstable County, Massachusetts, town, 469 COVID-19 cases were identified among Massachusetts residents who had traveled to the town during July 3–17; **346** (74%) occurred in fully vaccinated persons.
- Testing identified the Delta variant in 90% of specimens from 133 patients.
- Cycle threshold values were similar among specimens from patients who were fully vaccinated and those who were not.
- **What are the implications for public health practice?**
- Jurisdictions might consider expanded prevention strategies, including universal masking in indoor public settings, particularly for large public gatherings that include travelers from many areas with differing levels of SARS-CoV-2 transmission.

Outbreak of SARS-CoV-2 Infections, Including COVID-19 Vaccine Breakthrough Infections, Associated with Large Public Gatherings — Barnstable County, Massachusetts, July 2021

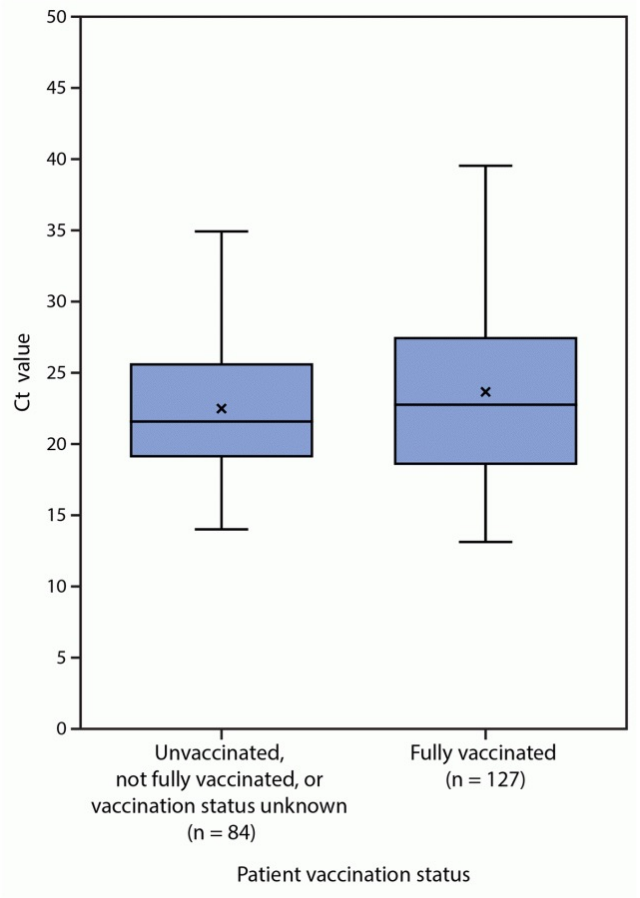
FIGURE 1. SARS–CoV–2 infections (N = 469) associated with large public gatherings, by date of specimen collection and vaccination status* — Barnstable County, Massachusetts, July 2021



Abbreviation: MA DPH = Massachusetts Department of Public Health.

Brown CM, Vostok J, Johnson H, et al. MMWR Morb Mortal Wkly Rep. ePub: 30 July 2021.

SARS-CoV-2 real-time reverse transcription–polymerase chain reaction cycle threshold values* for specimens from patients with infections associated with large public gatherings, by vaccination status† — Barnstable County, Massachusetts, July 2021§



Brown CM, Vostok J, Johnson H, et al. MMWR Morb Mortal Wkly Rep. ePub: 30 July 2021.

Outbreak of SARS-CoV-2 Infections, Including COVID-19 Vaccine Breakthrough Infections, Associated with Large Public Gatherings — Barnstable County, Massachusetts, July 2021

Persons with breakthrough infection, 274 (79%) the most common reported signs or symptoms were:

- Cough, headache, sore throat, myalgia, and fever

Among the fully vaccinated symptomatic persons, the median interval from completion of ≥14 days after the final vaccine dose to symptom onset was 86 days (range = 6–178 days).

Among persons with breakthrough infection, four (1.2%) were hospitalized, and no deaths were reported.

Real-time RT-PCR Ct values in specimens from 127 fully vaccinated patients (median = 22.77) were similar to those among 84 patients who were unvaccinated, not fully vaccinated, or whose vaccination status was unknown (median = 21.54)

Brown CM, Vostok J, Johnson H, et al. MMWR Morb Mortal Wkly Rep. ePub: 30 July 2021.