COVID-19 Update

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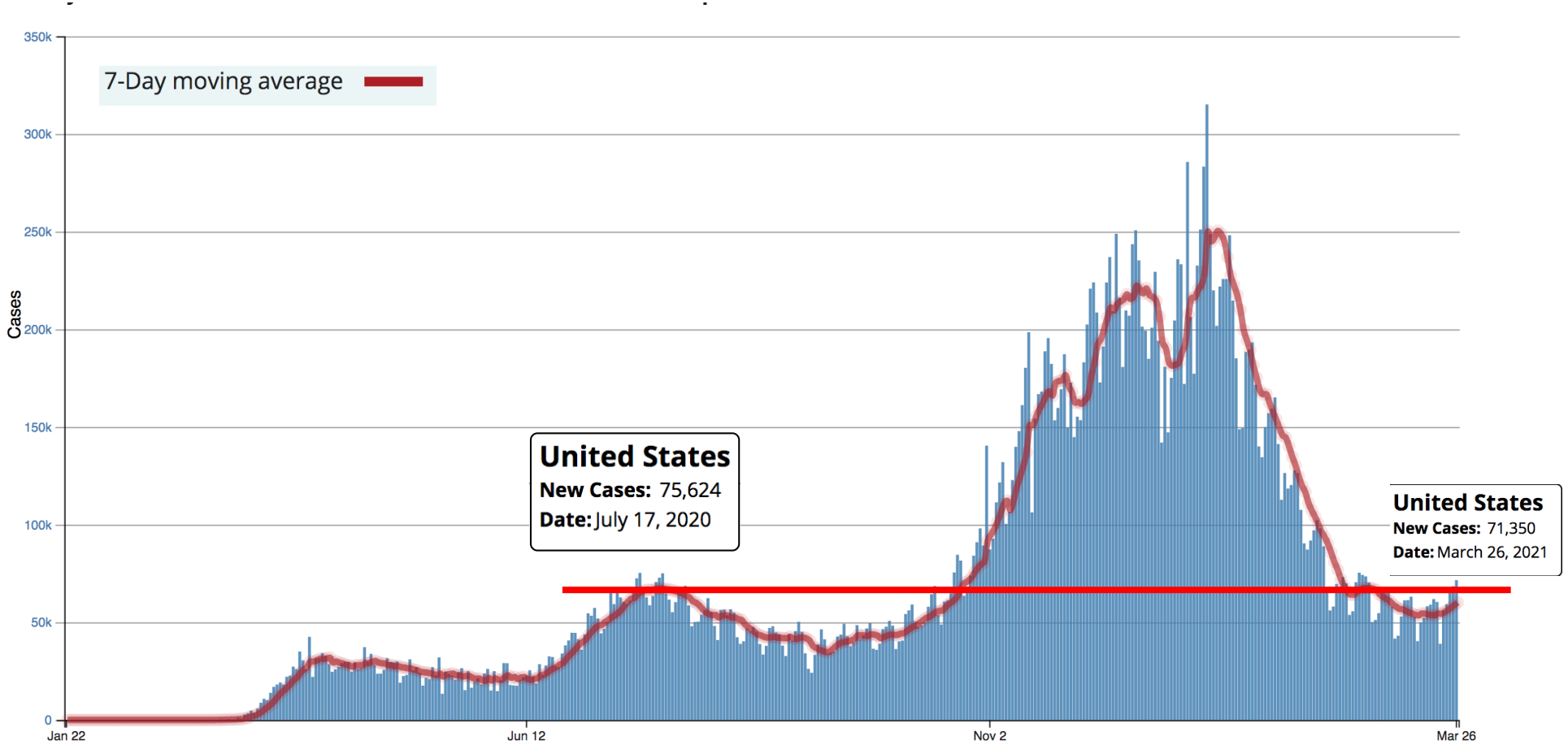
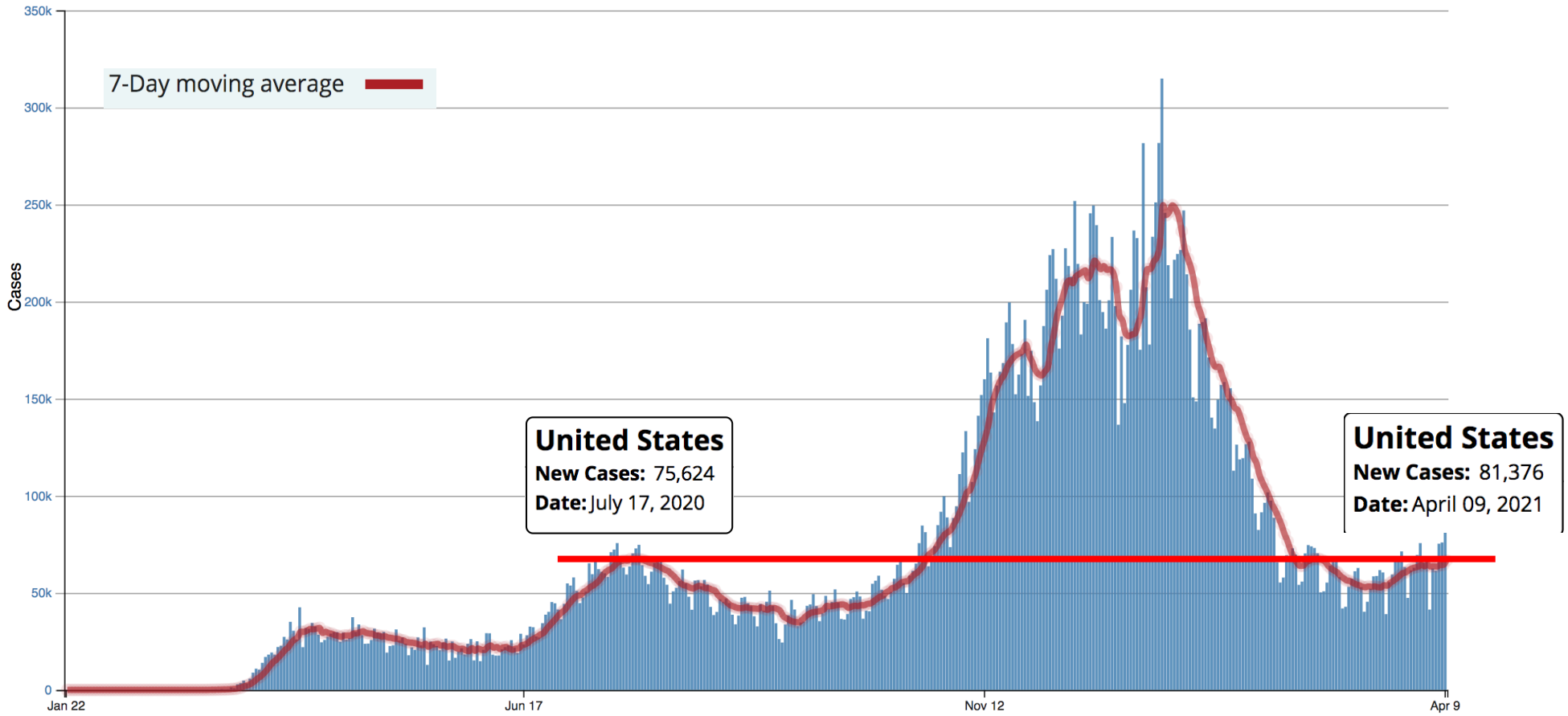
Daily Trends in Number of COVID-19 Cases in the United States Reported to CDC
Updated Until March 26, 2021



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

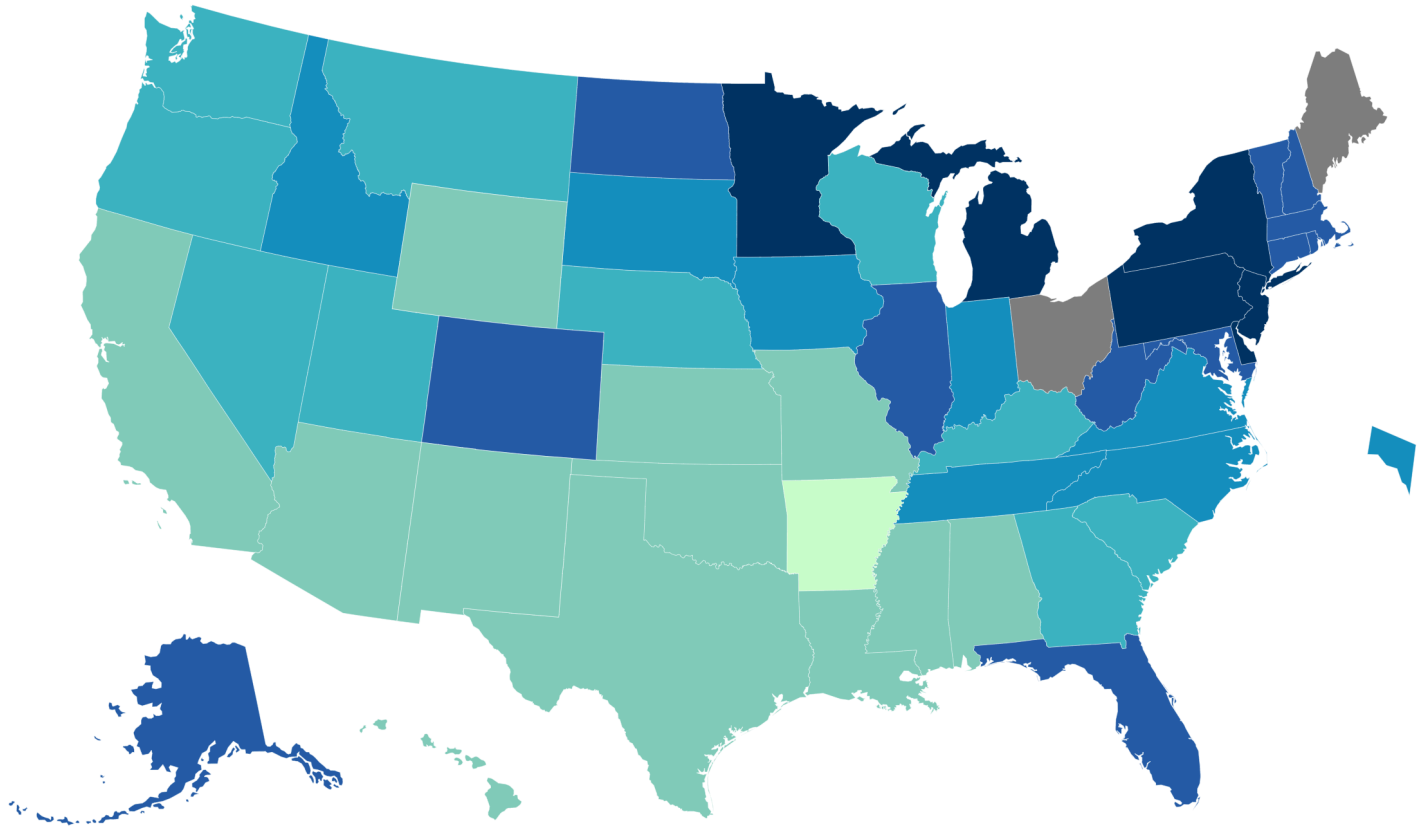
Daily Trends in Number of COVID-19 Cases in the United States Reported to CDC
Updated Until April 9, 2021



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

US COVID-19 7-Day Case Rate per 100,000, by State/Territory

This shows the number of COVID-19 cases for every 100,000 people over the last 7 days, allowing you to compare areas with different population sizes.



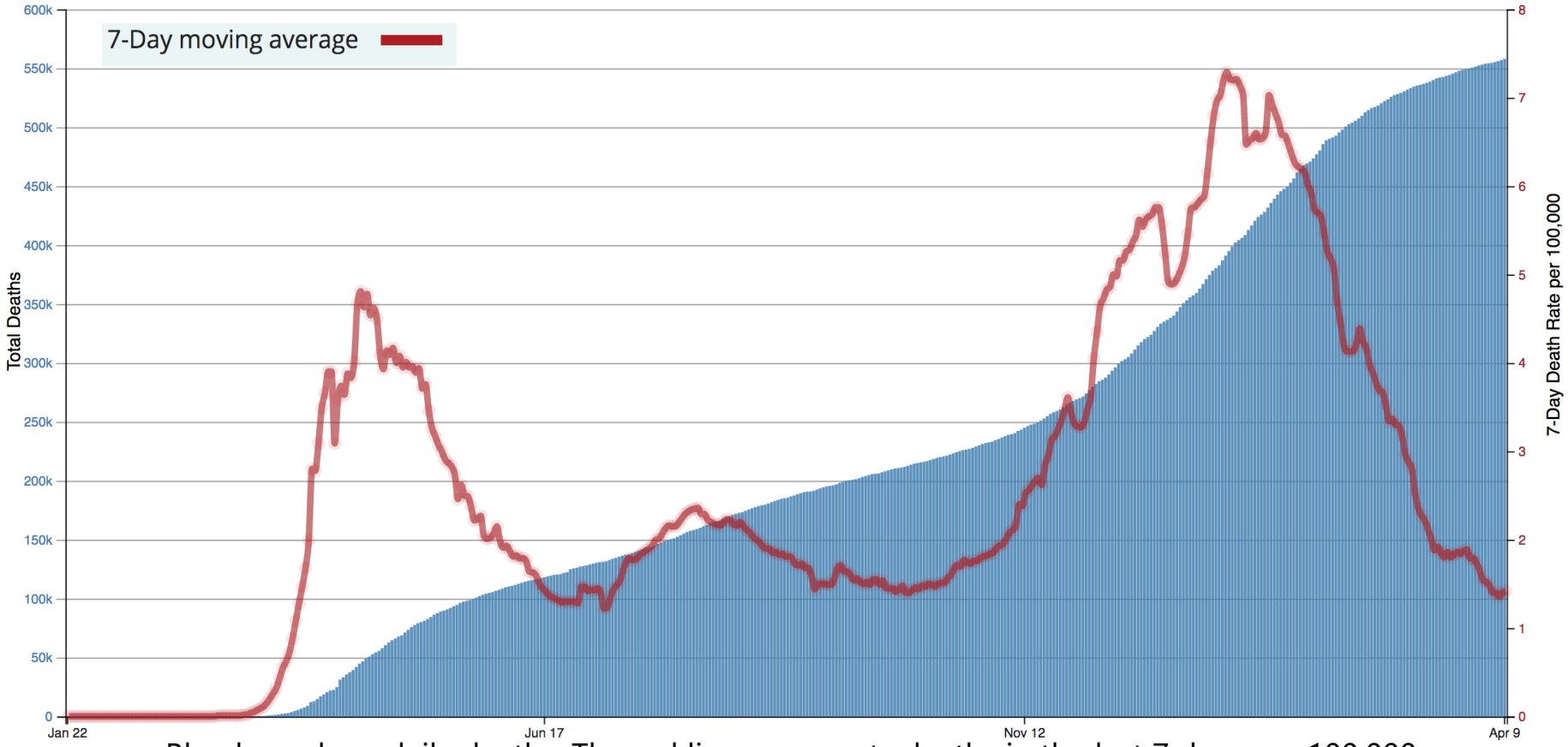
7-Day Case Rate per 100,000

Data not available | 0 - 38.2 | 40.1 - 73.6 | 78.8 - 105.6 | 107.8 - 144.8 | 147.5 - 218.3 | 225.3 - 533.4

Territories

AS	FSM	GU	MP	PR	PW	RMI	VI

Trends in Total and 7-Day Cumulative Incidence Rate of COVID-19 Deaths in the United States Reported to CDC, per 100,000 population until April 9,2021



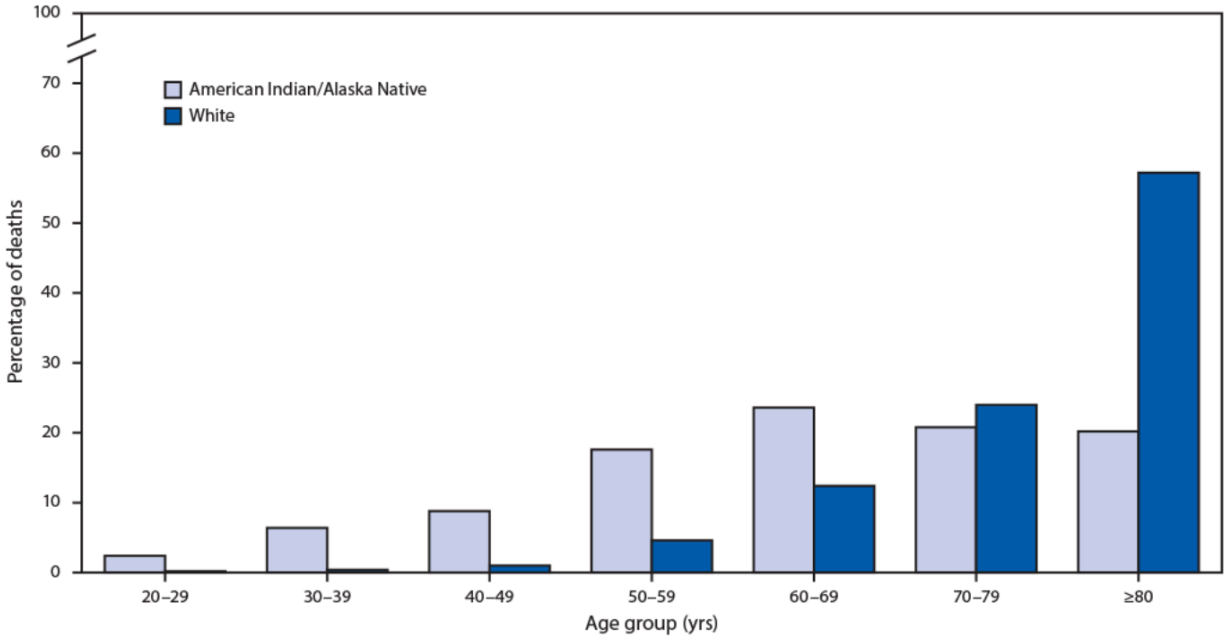
Blue bars show daily deaths. The red line represents deaths in the last 7 days per 100,000, allowing for comparisons between areas with different population sizes.

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

COVID-19 Mortality Among American Indian and Alaska Native Persons — 14 States, January–June 2020

Arrazola J, Masiello MM, Joshi S, et al. COVID-19 Mortality Among American Indian and Alaska Native Persons — 14 States, January–June 2020. MMWR Morb Mortal Wkly Rep 2020;69:1853–1856.

FIGURE. Percentage distribution of COVID-19–associated deaths among American Indian/Alaska Native* and non-Hispanic White persons aged ≥20 years, by age group† — 14 states,§ January 1–June 30, 2020



Abbreviation: COVID-19 = coronavirus disease 2019.

* Includes Hispanic and non-Hispanic ethnicities.

† Percentages by age group are not age-adjusted.

§ Alaska, Arizona, Louisiana, Minnesota, Mississippi, Nebraska, New Mexico, New York, North Dakota, Oklahoma, Oregon, South Dakota, Utah, and Washington.

COVID-19 incidence and mortality rates* among American Indian or Alaska Native (AI/AN) and White persons,†,§ by age group and sex¶ — Montana, March 13–November 30, 2020

Characteristic	AI/AN		White		AI/AN to White rate ratio (95% CI)
	No. (%)	Rate (95% CI)	No. (%)	Rate (95% CI)	
Cumulative incidence					
Total	**7,069 (100)**	**9,064 (8,852–9,275)**	**39,040 (100)**	**4,033 (3,993–4,073)**	**2.2 (2.1–2.5)**
Sex					
Female	3,752 (53)	9,517 (9,212–9,821)	20,498 (52)	4,272 (4,213–4,330)	2.2 (2.1–2.4)
Male	3,242 (46)	8,405 (8,116–8,695)	17,995 (46)	3,687 (2,633–3,741)	2.3 (2.1–2.5)
Age group, yrs					
<65	6,388 (90)	8,947 (8,728–9,167)	31,842 (82)	4,137 (4,091–4,182)	2.2 (2.0–2.4)
≥65	681 (10)	10,321 (9,546–1,097)	7,198 (18)	3,632 (3,549–3,716)	2.8 (2.6–3.1)
Cumulative mortality					
Total	**208 (100)**	**267 (232–306)**	**664 (100)**	**71 (66–77)**	**3.8 (3.2–4.4)**
Sex					
Female	88 (42)	223 (179–275)	306 (46)	66 (59–74)	3.4 (2.7–4.3)
Male	120 (58)	311 (258–372)	358 (54)	76 (68–84)	4.1 (3.3–5.0)
Age group, yrs					
<65	87 (42)	122 (98–150)	72 (11)	10 (8–12)	12.5 (9.1–17.1)
≥65	121 (58)	1,834 (1,522–2,191)	592 (89)	302 (278–328)	6.1 (5.0–7.4)

Abbreviation: CI = confidence interval. * The number of COVID-19 cases or deaths by race and by race and sex/age group per 100,000 in the same race or race and sex/age group. † Includes Hispanic and non-Hispanic persons. § Race data were missing for 13,913 of 63,339 (22%) patients, and ethnicity data were missing for 23,435 of 63,339 (37%) patients; race and ethnicity data were complete for all deaths. ¶ Sex data were missing for 75 (1%) AI/AN patients and for 547 (1%) White patients

Williamson LL, Harwell TS, Koch TM, et al. COVID-19 Incidence and Mortality Among American Indian/Alaska Native and White Persons — Montana, March 13–November 30, 2020. MMWR Morb Mortal Wkly Rep 2021;70:510–513.

COVID-19 Incidence and Mortality Among American Indian/Alaska Native and White Persons Montana, March 13–November 30, 2020

What is already known about this topic?

- Aggregate analyses of data from selected U.S. states indicate that COVID-19 incidence and mortality are higher among American Indian or Alaska Native (AI/AN) persons than they are among White persons.

What is added by this report?

- COVID-19 incidence and mortality rates among AI/AN persons in Montana were 2.2 and 3.8 times, respectively, those among White persons.
- The case-fatality rate among AI/AN persons was 1.7 times that among White persons.

What are the implications for public health practice?

- These findings reinforce importance of using state-level surveillance to develop state and tribal COVID-19 vaccine allocation strategies and to inform local implementation of culturally appropriate public health measures that might help reduce COVID-19 incidence and mortality in AI/AN communities.

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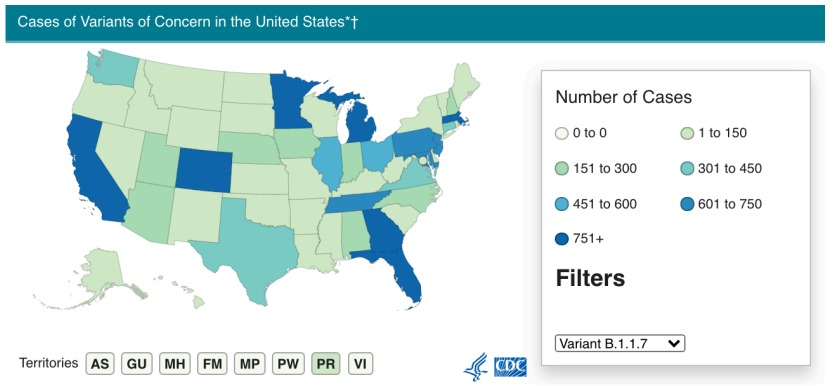
CDC SARS-CoV-2 Variant Classification System

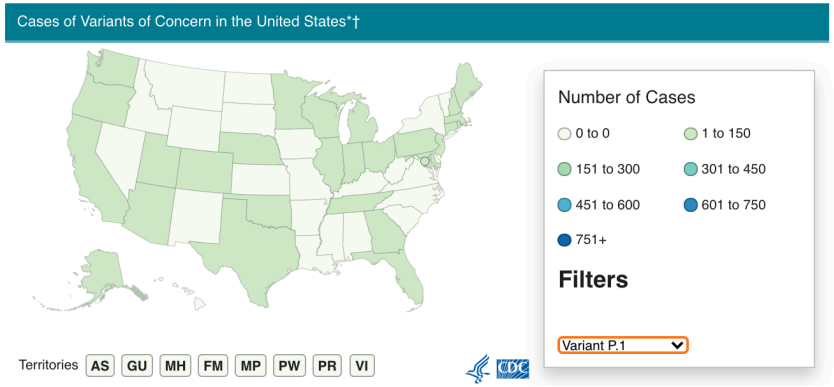
	Variant of Interest	Variant of Concern	Variant of High Consequence*
Predicted to be more contagious	Yes	Yes	Yes
Predicted to be more difficult to detect	Yes	Yes	Yes
Evidence of more cases or unique clusters of outbreaks	Yes	Yes	Yes
Evidence shows this variant might require alternative treatments and vaccines might be less effective	No	Yes	Yes
Evidence shows this variant spreads more easily from person to person	No	Yes	Yes
Evidence shows this variant causes more severe disease	No	Yes	Yes
Requires notification to the World Health Organization and CDC	No	Yes	Yes
Evidence shows significant diagnostic testing failures	No	No	Yes
Evidence shows that vaccines are significantly less effective at preventing severe illness	No	No	Yes
Treatment is significantly less effective	No	No	Yes

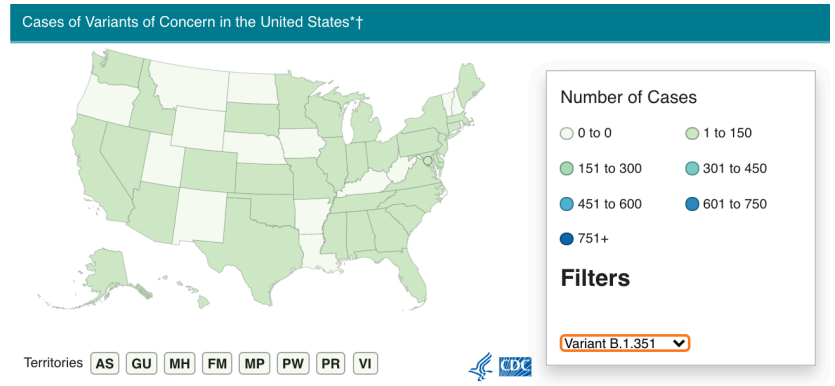
Variants may have one or more of the listed attributes

https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html

US COVID-19 Cases Caused by Variants of Concern



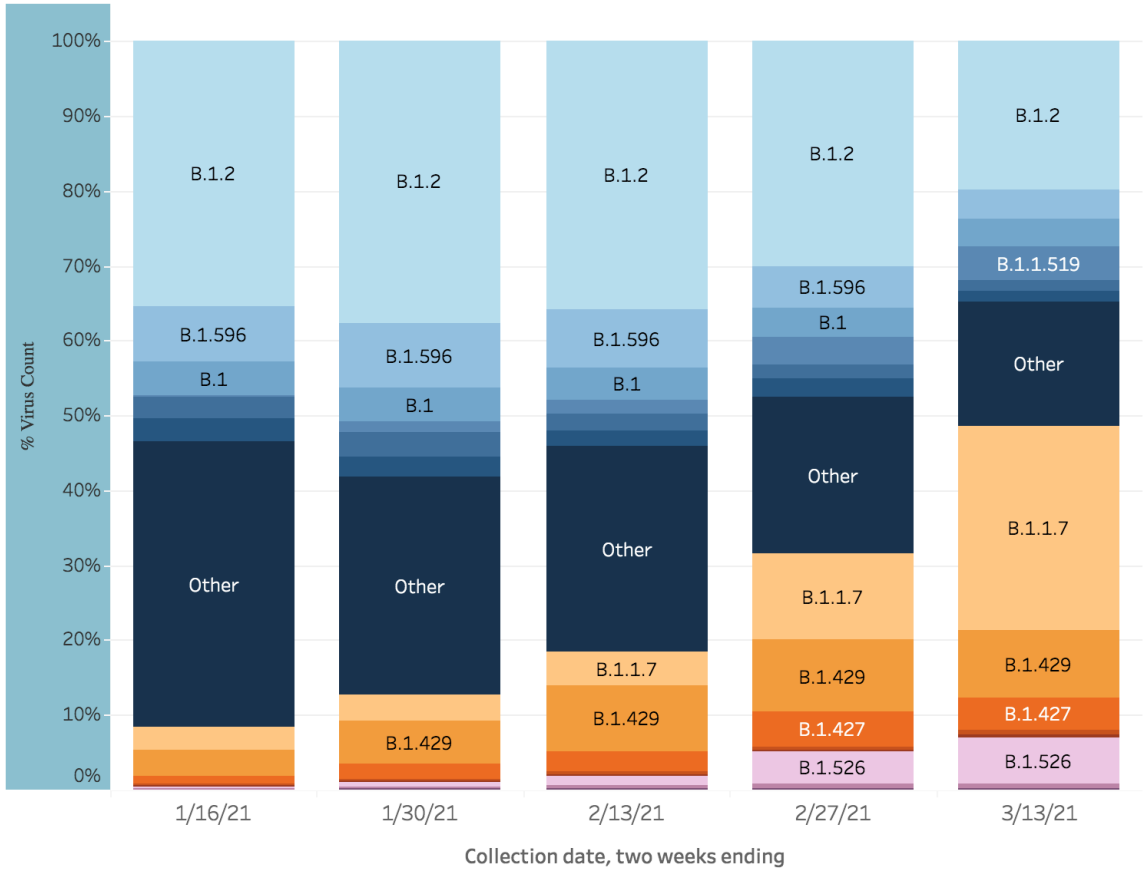




Variant	Reported Cases in US	Number of Jurisdictions Reporting
B.1.1.7	19,554	52
B.1.351	424	36
P.1	434	28

https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html

SARS-CoV-2 Variants Circulating in the United States



	Lineage	% Total	95%CI	Type
Most common lineages	B.1.1.7	27.2%	24.6-29.9%	VOC
	B.1.2	19.8%	17.3-22.6%	
	B.1.429	9.1%	6.8-12.1%	VOC
	B.1.526	6.2%	4.3-8.8%	VOI
	B.1.1.519	4.7%	3.8-5.8%	
	B.1.427	4.3%	3.3-5.6%	VOC
	B.1.596	3.9%	3.2-4.7%	
	B.1	3.7%	2.9-4.6%	
	B.1.234	1.4%	1.0-1.9%	
	B.1.243	1.4%	1.1-1.8%	
Additional VOI/VOC lineages	P.2	0.5%	0.3-0.7%	VOI
	P.1	0.5%	0.3-0.8%	VOC
	B.1.351	0.5%	0.3-0.7%	VOC
	B.1.525	0.3%	0.2-0.4%	VOI
Other*	Other	16.6%	14.4-19.2%	

Summary data that appear in the table include specimen collection dates from February 28 through March 13, 2021.
* Other represents >200 additional lineages, which are each circulating at <2% of viruses

The data above shows the estimated biweekly prevalence of the most common SARS-CoV-2 lineages circulating in the United States, based on >40,000 sequences collected through CDC's national genomic surveillance since Dec 20, 2020 and grouped in 2-week intervals. Data are subject to change over time and will be updated as more data become available. Variant proportions in Figure 1 are adjusted using statistical weighting† to correct for the non-random sampling of sequencing data over time and across states and to provide more representative national estimates.

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

What Can We Do About Variants?

- The best way to slow the emergence of new variants is to slow the spread of COVID-19 by:
  - Wearing a mask that covers your nose and mouth
  - Staying 6 feet away from people who don't live with you
  - Avoiding crowds and poorly ventilated indoor spaces
  - Getting a COVID-19 vaccine as soon as it is available to you

https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html

High-throughput, single-copy sequencing reveals SARS-CoV-2 spike variants coincident with mounting humoral immunity during acute COVID-19

Hypothesis:

- Mutant sequences of SARS-CoV-2 arising during any individual case of COVID-19 could theoretically enable the virus to evade immune responses or antiviral therapies that target the predominant infecting virus sequence.

Methods

- Through novel technology for sequencing large numbers of individual SARS-CoV-2 genomic RNA molecules were sequenced from 7 individuals with COVID-19 as well as SARS-COV-2 obtained from a viral culture

Published in Plos Pathogens: April 8, 2021 https://doi.org/10.1371/journal.ppat.1009431

High-throughput, single-copy sequencing reveals SARS-CoV-2 spike variants coincident with mounting humoral immunity during acute COVID-19

Finding # 1: Diversity

- Extensive genetic diversity in cultured viruses from a clinical isolate of SARS-CoV-2
- Lower diversity in samples from 7 individuals with COVID-19.

Finding # 2: Concurrent analysis of paired serum samples in selected individuals revealed

- Low levels of antibody binding to the SARS-CoV-2 spike protein at the time of initial sequencing.
- As time goes by there was:
  - Increased serum binding to spike protein
  - Multiple SARS-CoV-2 variants bearing independent mutations in a single epitope were detected
  - Transient increase in virus burden.

Published in Plos Pathogens: April 8, 2021 https://doi.org/10.1371/journal.ppat.1009431

High-throughput, single-copy sequencing reveals SARS-CoV-2 spike variants coincident with mounting humoral immunity during acute COVID-19

Conclusions

- These findings suggest that SARS-CoV-2 replication creates sufficient virus genetic diversity to allow immune-mediated selection of variants within the time frame of acute COVID-19.

- Large-scale studies of SARS-CoV-2 variation and specific immune responses will help define the contributions of intra-individual SARS-CoV-2 evolution to COVID-19 clinical outcomes and antiviral drug susceptibility.

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A human coronavirus evolves antigenically to escape antibody immunity

Neutralizing and anti-spike antibodies elicited by natural infection correlate with reduced SARS-CoV-2 infection of humans

- Vaccines that elicit such antibodies protect humans with high efficacy
- However, humans are repeatedly re-infected with the “common-cold” coronaviruses 229E, OC43, HKU1, and NL63

Serological studies suggest that the typical person is infected with 229E every 2–3 years, which has led to concerns that coronavirus immunity is not “durable.”

Antigenic evolution could be the explanation to this phenomenon (Example: Influenza)

- Infection with influenza virus elicits antibodies that generally protect humans against that same viral strain for at least several decades
- Unfortunately, influenza virus undergoes rapid antigenic evolution to escape these antibodies meaning that although immunity to the original viral strain lasts for decades, humans are susceptible to infection by its descendants within about 5 years.

In the 1980s, human-challenge studies found that individuals infected with one strain of 229E were resistant to re-infection with that same strain, but partially susceptible to a different strain

Eguia RT, Crawford KHD, Stevens-Ayers T, et al. (2021) A human coronavirus evolves antigenically to escape antibody immunity. PLoS Pathog 17(4): e1009453.

A human coronavirus evolves antigenically to escape antibody immunity

Question:

- It is unknown if coronaviruses evolve to escape immunity, and if so, how rapidly.

One way of answering the question:

- Characterization of historical evolution of other human coronaviruses, like CoV 229E (the common cold virus)

How:

- By demonstrating that serum obtained from individuals in the 1980's can neutralize CoV 229E isolated in the 80's but not CoV 229E isolated years later

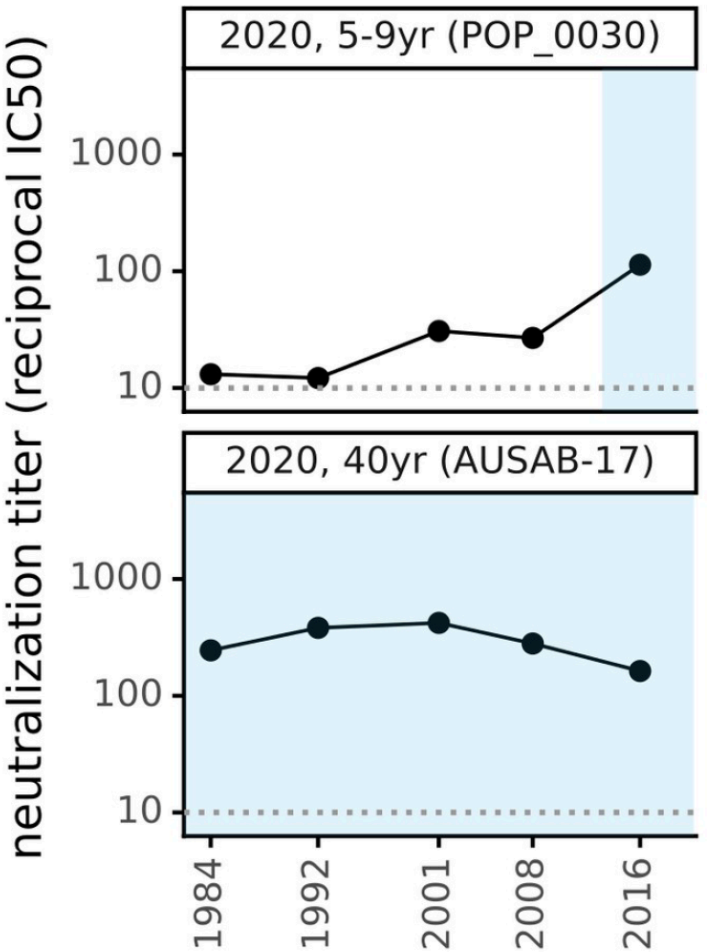
Eguia RT, Crawford KHD, Stevens-Ayers T, et al. (2021) A human coronavirus evolves antigenically to escape antibody immunity. PLoS Pathog 17(4): e1009453.

A human coronavirus evolves antigenically to escape antibody immunity

Neutralizing titers of sera collected in 2020 are higher against historical viruses that circulated during an individual's lifetime than viruses isolated before the individual was born.

Each plot facet is a different serum with the title giving the individual's age and black points indicating the titer against spikes from viruses isolated in the indicated year.

Blue shading represents the portion of the plotted timeframe during which the individual was alive: for adults this is the entire timeframe, but for children the left edge of the blue shading indicates the birth year.



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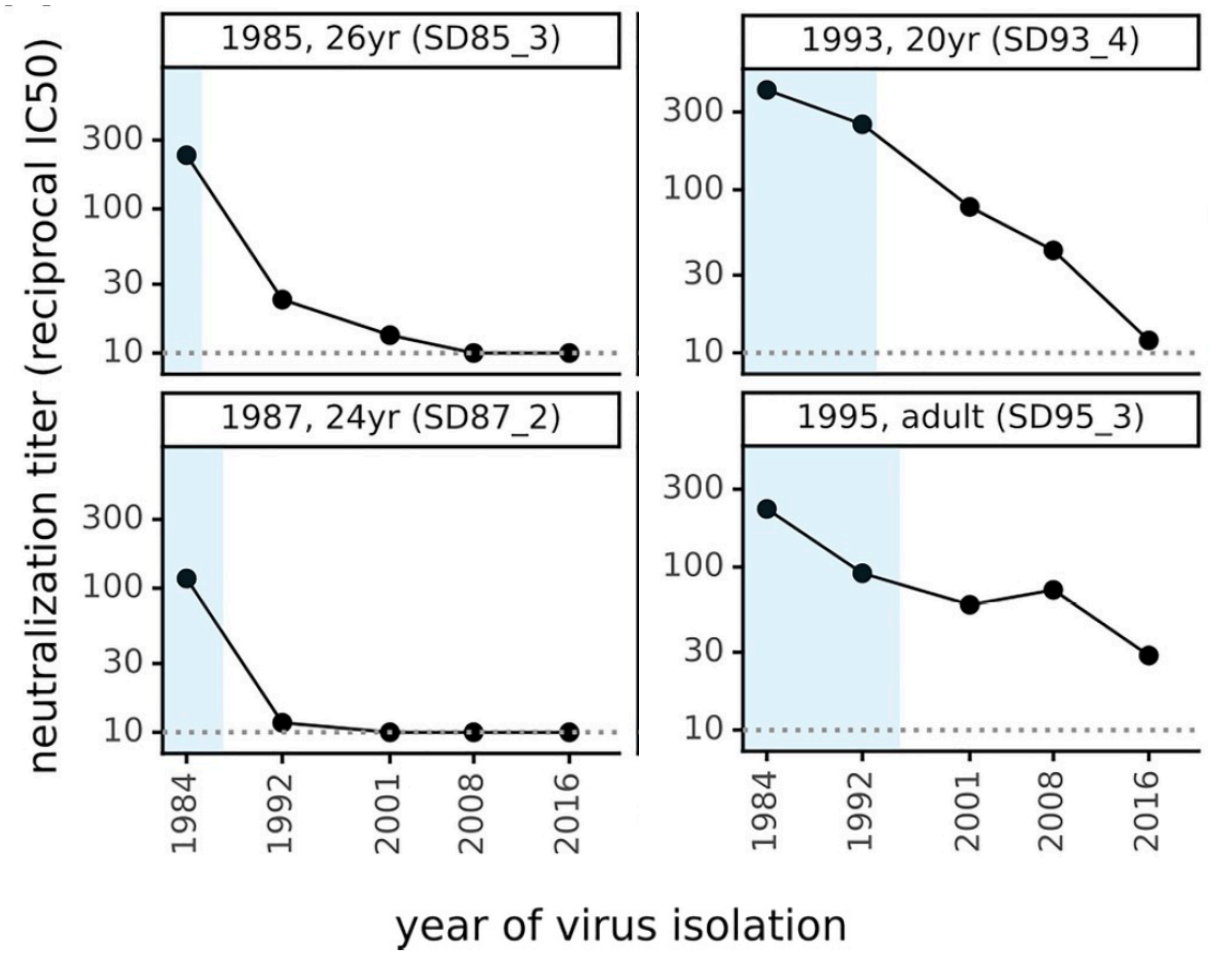

- Each plot facet is a different serum, and black points show its neutralizing titer against viruses from the indicated year.
- Blue shading indicates the portion of plotted timeframe during which the individual could have been infected prior to serum collection.
- The dotted gray horizontal line indicates the limit of detection (titer of 1:10).

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A human coronavirus evolves antigenically to escape antibody immunity

Methods:

- Human sera from the 1980s and 1990s that have neutralizing titers against contemporaneous CoV 229E that are comparable to the anti-SARS-CoV-2 titers induced by SARS-CoV-2 infection or vaccination were characterized

Results:

- Neutralizing titers (from the 80's) are lower against these "future" viruses (90's) and in some cases, serum that neutralized contemporaneous 229E viral strains with titers >1:100 do not detectably neutralize strains isolated 8–17 years later.
- The decreased neutralization of "future" viruses is due to antigenic evolution of the viral spike, especially in the receptor-binding domain.

Conclusions:

- If these results extrapolate to other coronaviruses, then it may be advisable to periodically update SARS-CoV-2 vaccines.

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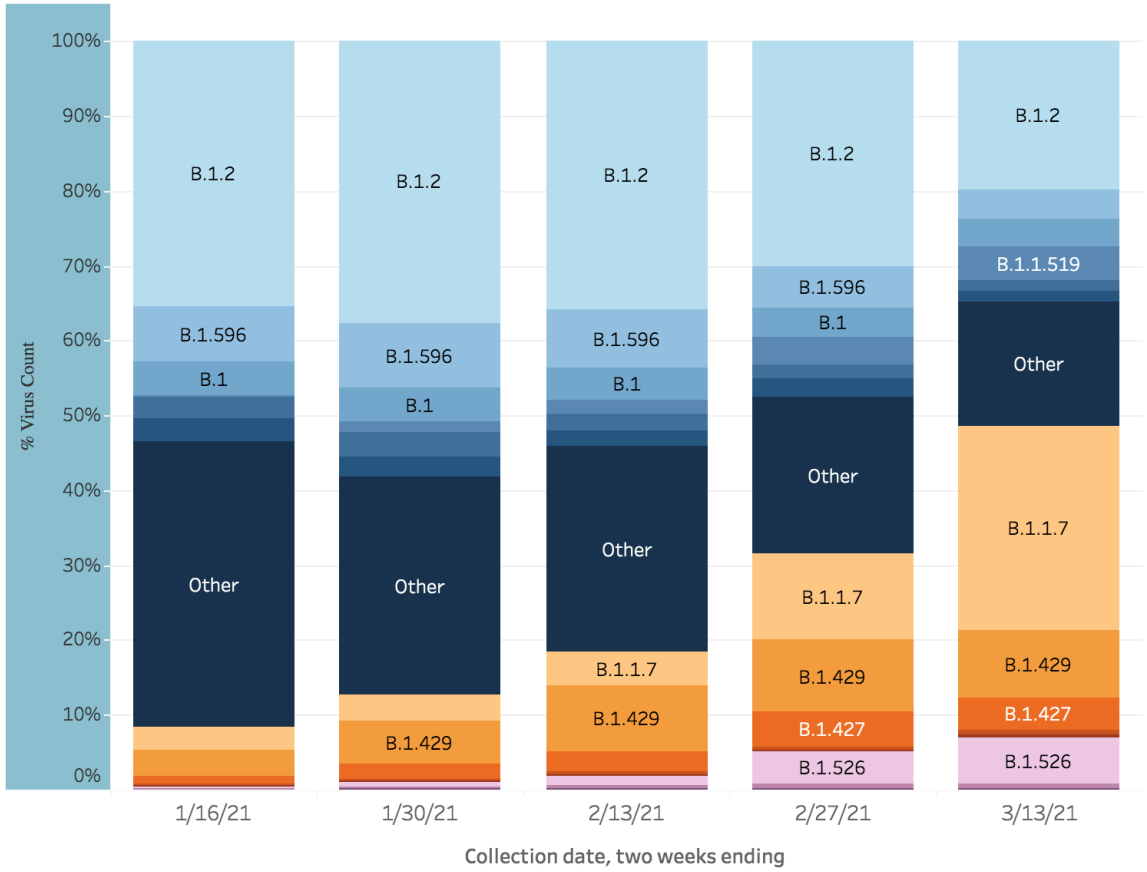
SARS-CoV-2 Variants Circulating in the United States



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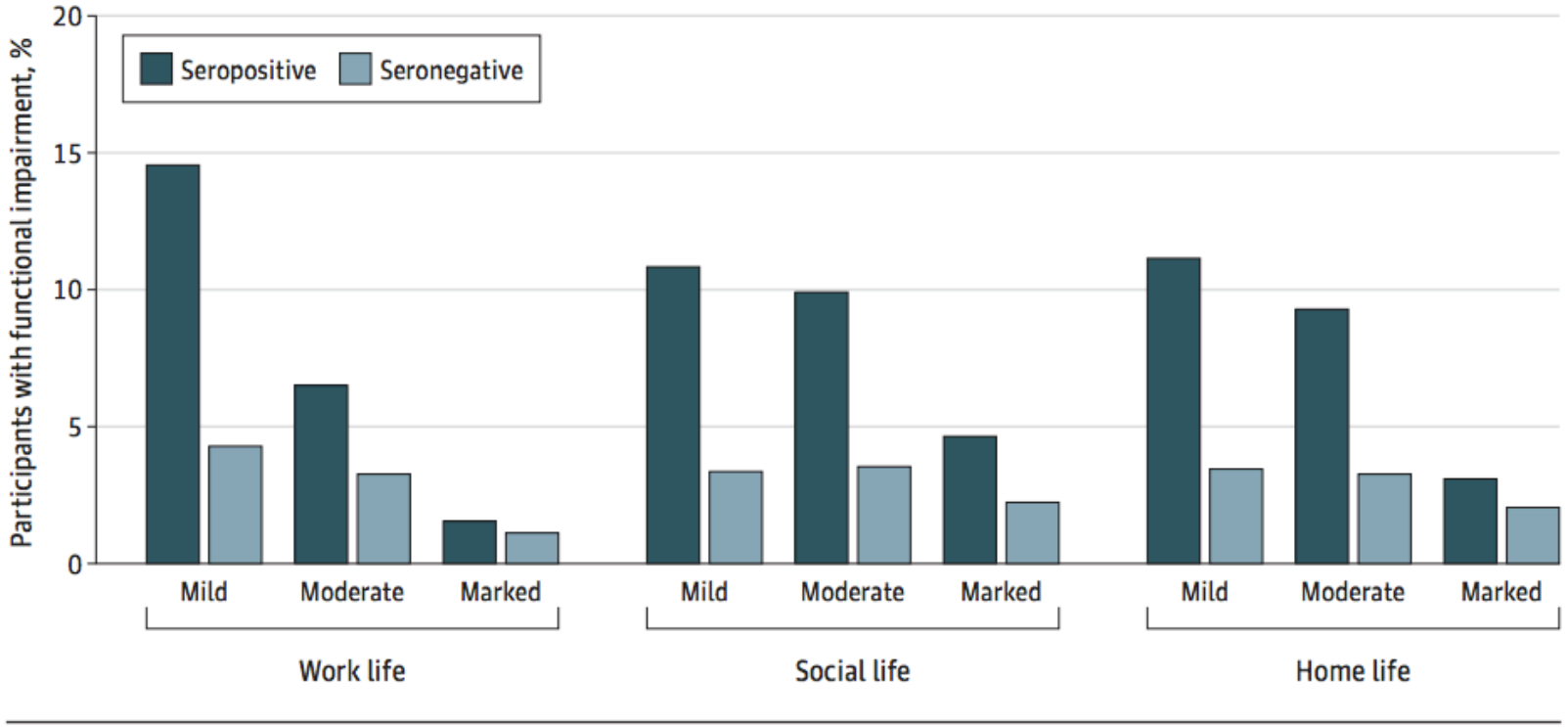
Symptoms and Functional Impairment Assessed 8 Months After Mild COVID-19 Among Health Care Workers

Figure. COVID-19–Related Long-term Functional Impairment



The percentage of seropositive (n = 323) and seronegative (n = 1072) participants reporting symptoms lasting at least 2 months and their related functional impairment in their work, social, and home life using the Sheehan Disability Scale (1-3, mild; 4-6, moderate; and 7-10, marked).

Digital Health Passes in the Age of COVID-19Are "Vaccine Passports" Lawful and Ethical?

Benefits

- Digital health passes offer health and economic benefits until herd immunity is achieved. By allowing a safe return to more normal life, DHPs encourage people to be vaccinated.
- Digital health passes also allow a gradual reopening of the economy in key sectors such as food, retail, entertainment, and travel.
- Consumers are likely to rejoin recreational and commercial activities if they are confident doing so is safe. Digital health passes offer a less restrictive means to relax COVID-19 preventive measures such as quarantines, business closures, and stay-at-home orders.

JAMA. Published online April 7, 2021. doi:10.1001/jama.2021.5283

Scientific and Technical Challenges

Variable effectiveness by

- Vaccine type, effectiveness in preventing(65.5% to 94.6%)
- Transmission
- Durability of immunity
- Emergence of variant strains

The duration of protection afforded by SARS-CoV-2 vaccines is uncertain.

- Digital health passes should include dates of series completion to determine expiration once longevity of vaccine protection is better defined

Authentication of vaccine status.

- The US has no national immunization information system (IIS), a confidential, secure, population-based digital database that records all vaccine doses.
- States administer IISs, with variable quality.
- Vaccination facilities must report vaccine administration to the relevant IIS within 72 hours.
- Preventing falsification of vaccine status is vital to DHP integrity.
- School programs already systematically authenticate and enforce immunization status through standardized forms.
- Companies are also developing technologies to securely validate immunization status.

JAMA. Published online April 7, 2021. doi:10.1001/jama.2021.5283

Are DHPs Lawful?

Governments have power to validate and monitor vaccination status while requiring proof of vaccination for access to certain privileges.

- International law poses few restrictions on DHPs.
- The International Health Regulations, signed by 196 countries, grant wide discretion to exercise evidence-based public health powers.
- Article 31 of these regulations specifically allows governments to require “proof of vaccination or other prophylaxis,” while Annex 7 authorizes yellow fever vaccination certificates for international travel.

In the US, individual states hold primary public health powers.

- States already condition school entry on proof of vaccination.
- States have also required masks and social distancing in certain venues.

The president has broad power to require vaccination for entry to airports and federal buildings and land

- Federal DHP system would likely require congressional action, Government DHPs must navigate constitutional and civil rights constraints.
- While the Supreme Court grants public health agencies wide discretion, it is more protective of First Amendment freedoms, including religion, speech, and assembly.

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Are DHPs Lawful?

The Equal Employment Opportunity Commission (EEOC) issued guidance on SARS-CoV-2 vaccinations, which applies to any vaccine "approved or authorized by the Food and Drug Administration," suggesting that employers could require vaccinations even under an Emergency Use Authorization.

- The EEOC allows employers to require SARS-CoV-2 vaccination to return to the workplace, thus ensuring employees do "not pose a direct threat to health or safety."
- Employers also can use DHPs for proof of vaccination
- Businesses can require employees to "provide proof they have received a COVID-19 vaccination."
- Requiring proof of vaccination, moreover, does not violate the Americans With Disabilities Act or the Genetic Information Nondiscrimination Act.
- However, employers should caution employees "not to provide any medical information as part of the proof."

Digital health passes also would be unlikely to violate privacy laws

- Including the Health Insurance Portability and Accountability Act (HIPAA)
- Employers typically are not "covered entities" under HIPAA.
- Digital health passes could actually be advantageous because they provide proof of vaccination without sharing any other medical information.

Although employers may require proof of vaccination, they must abide by civil rights law.

- Thus, employers, whenever possible, should afford persons with disabilities "reasonable accommodations
- Employers should provide reasonable accommodations to individuals who hold a "sincere religious belief, practice, or observance." Some states are considering prohibiting private-sector use of DHPs, but courts may decide whether they have the legal authority to do so

JAMA. Published online April 7, 2021. doi:10.1001/jama.2021.5283