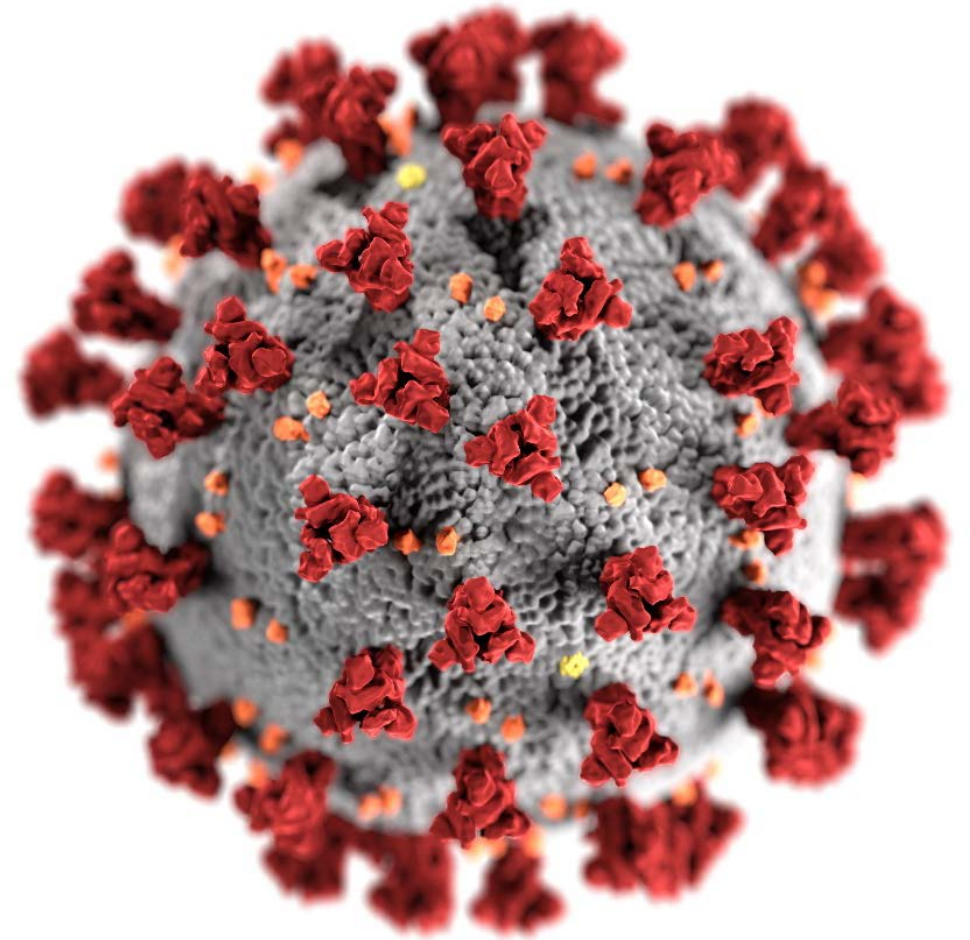


Update on Emerging SARS-CoV-2 Variants and COVID-19 vaccines

Heather Scobie, PhD, MPH
ACIP Meeting
August 13, 2021



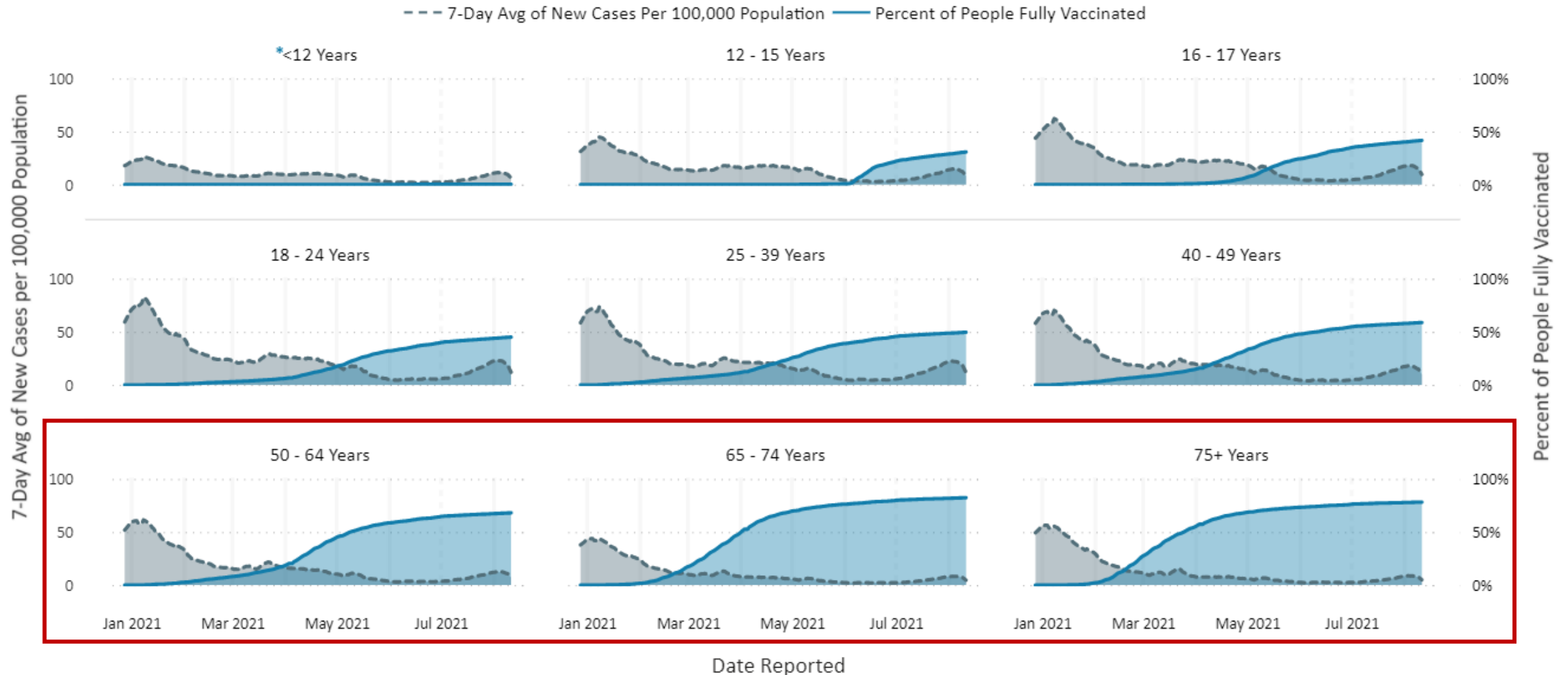
cdc.gov/coronavirus



Impact of COVID-19 Vaccination



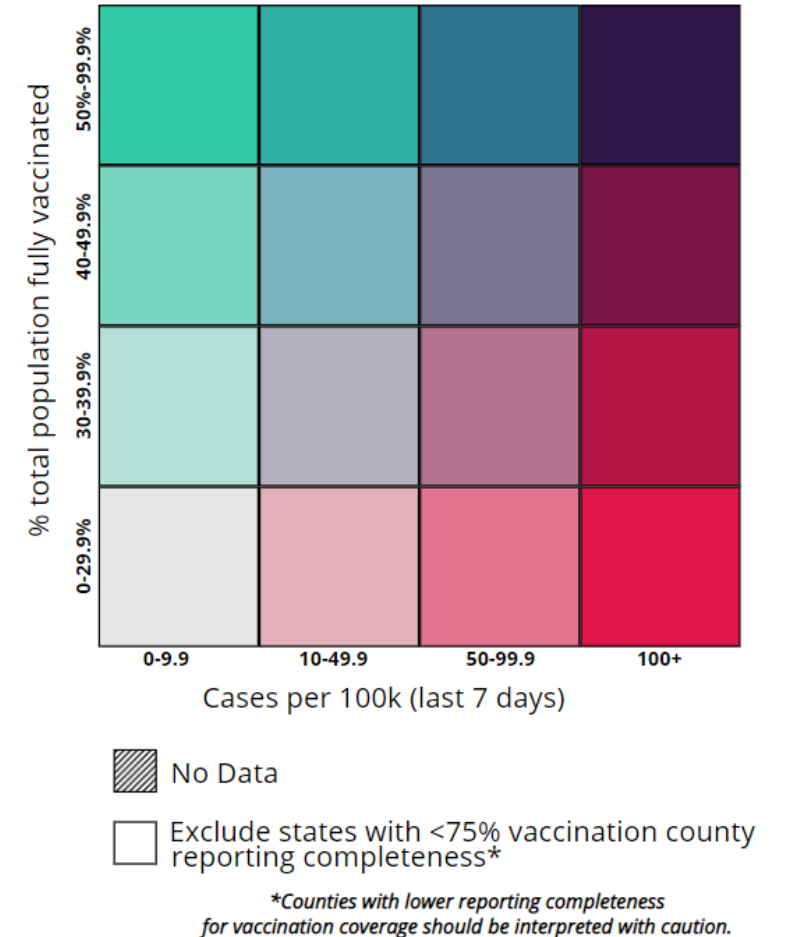
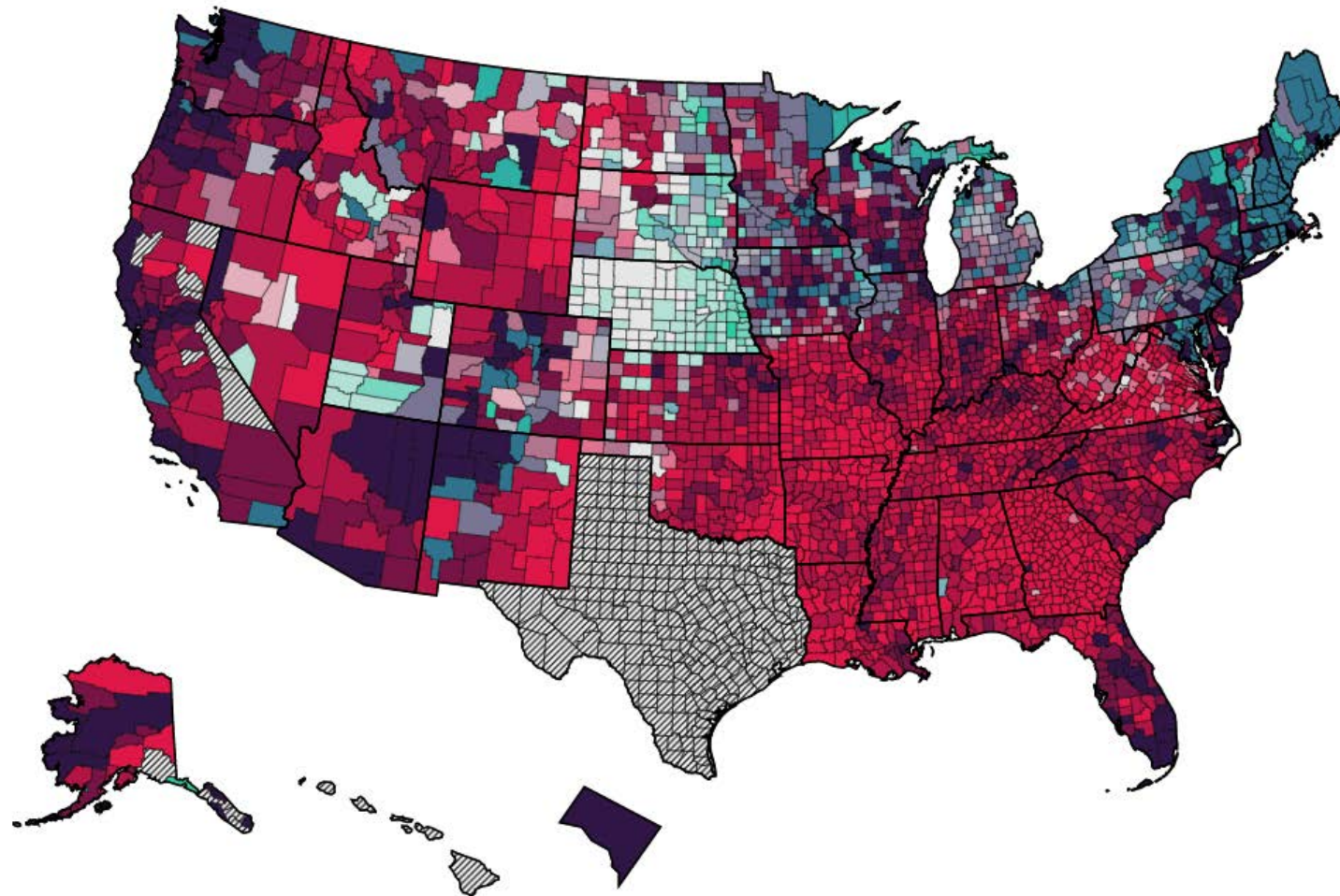
Percent of People Fully Vaccinated and Cases per 100,000 Population by Age, United States (Dec. 28, 2020 – Aug. 11, 2021)



*Currently, persons under age 12 are not eligible to be vaccinated.

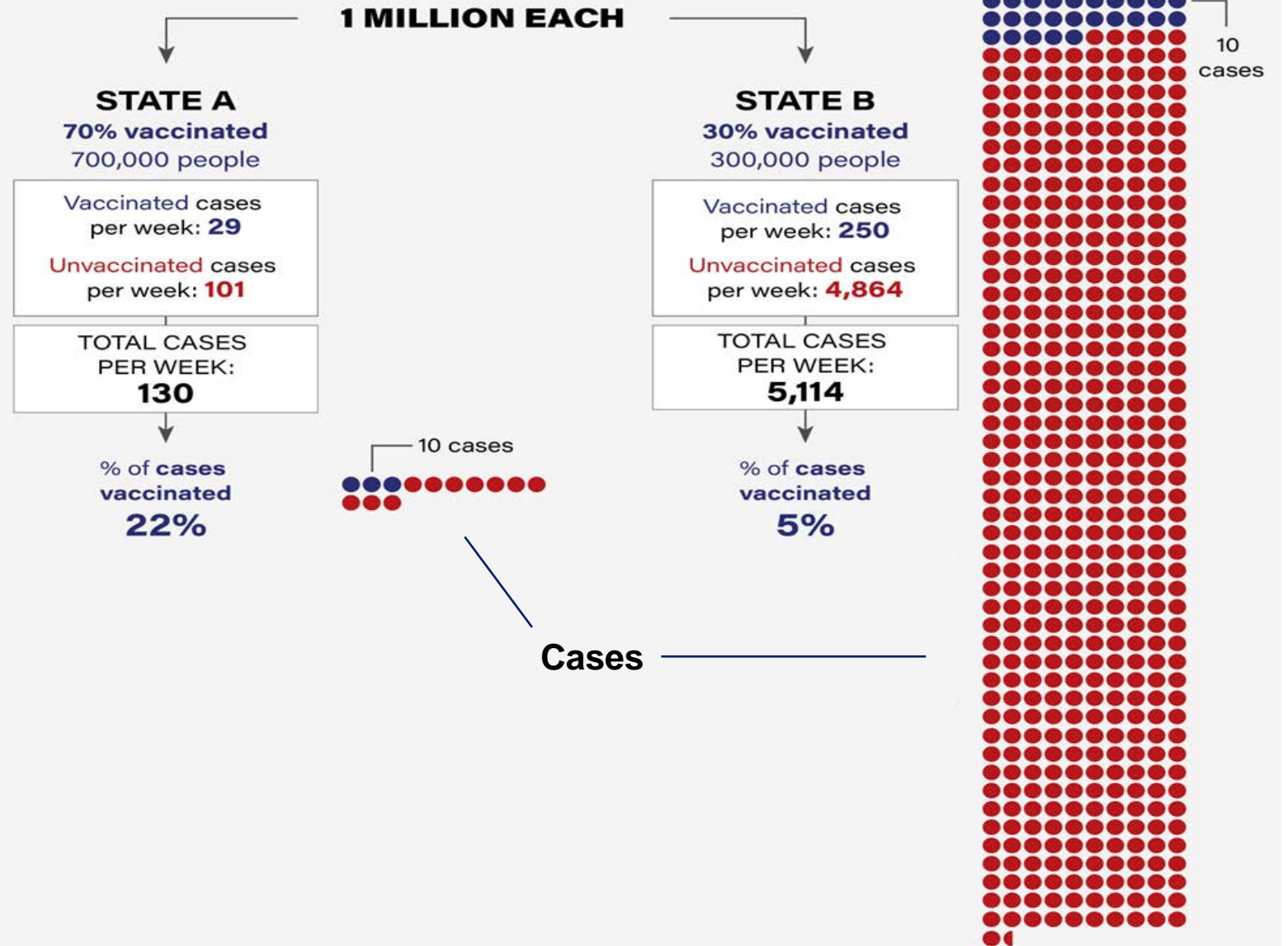
<https://covid.cdc.gov/covid-data-tracker/#vaccinations-cases-trends>

COVID-19 Reported Cases per 100,000 Population (last 7 days) and Percent of Total Population Fully Vaccinated, United States



DELTA CASES

Two example states with 1 million population and different levels of vaccination coverage (70% vs 30%)

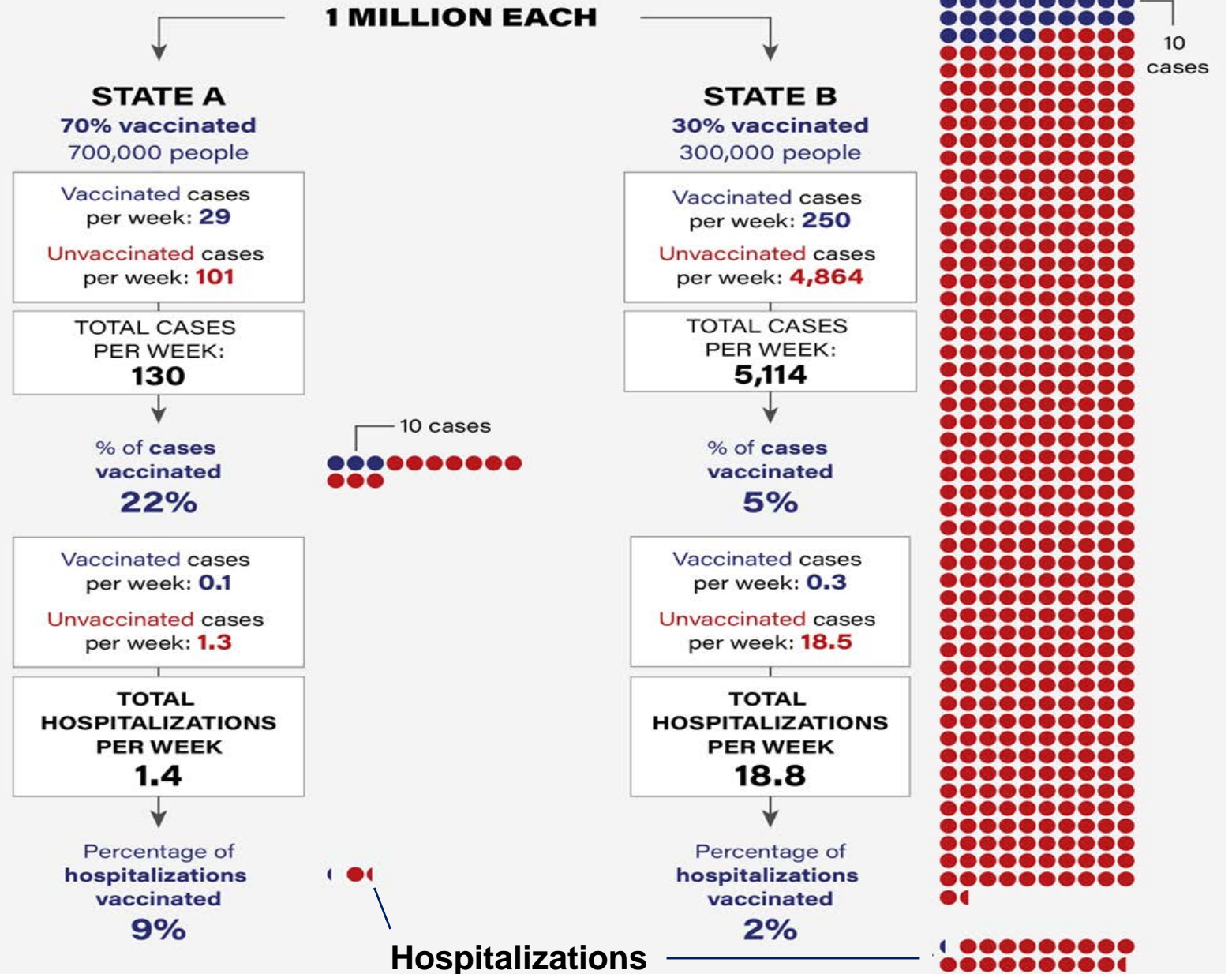


DELTA CASES AND HOSPITALIZATIONS

Two example states with 1 million population and different levels of vaccination coverage (70% vs 30%)

Higher vaccination coverage leads to fewer cases and hospitalizations, but greater % of vaccinated cases and hospitalizations

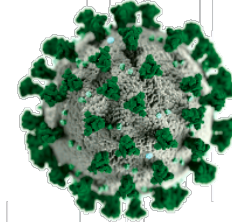
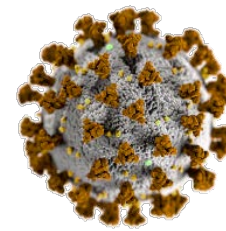
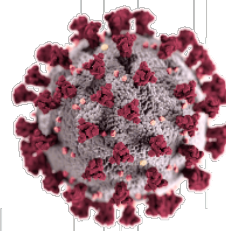
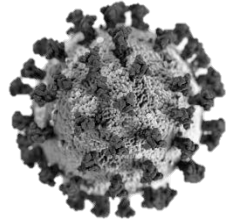
In both scenarios, cases and hospitalizations are greater among unvaccinated than vaccinated persons



Emerging SARS-CoV-2 Variants & Vaccines: What do we know now?



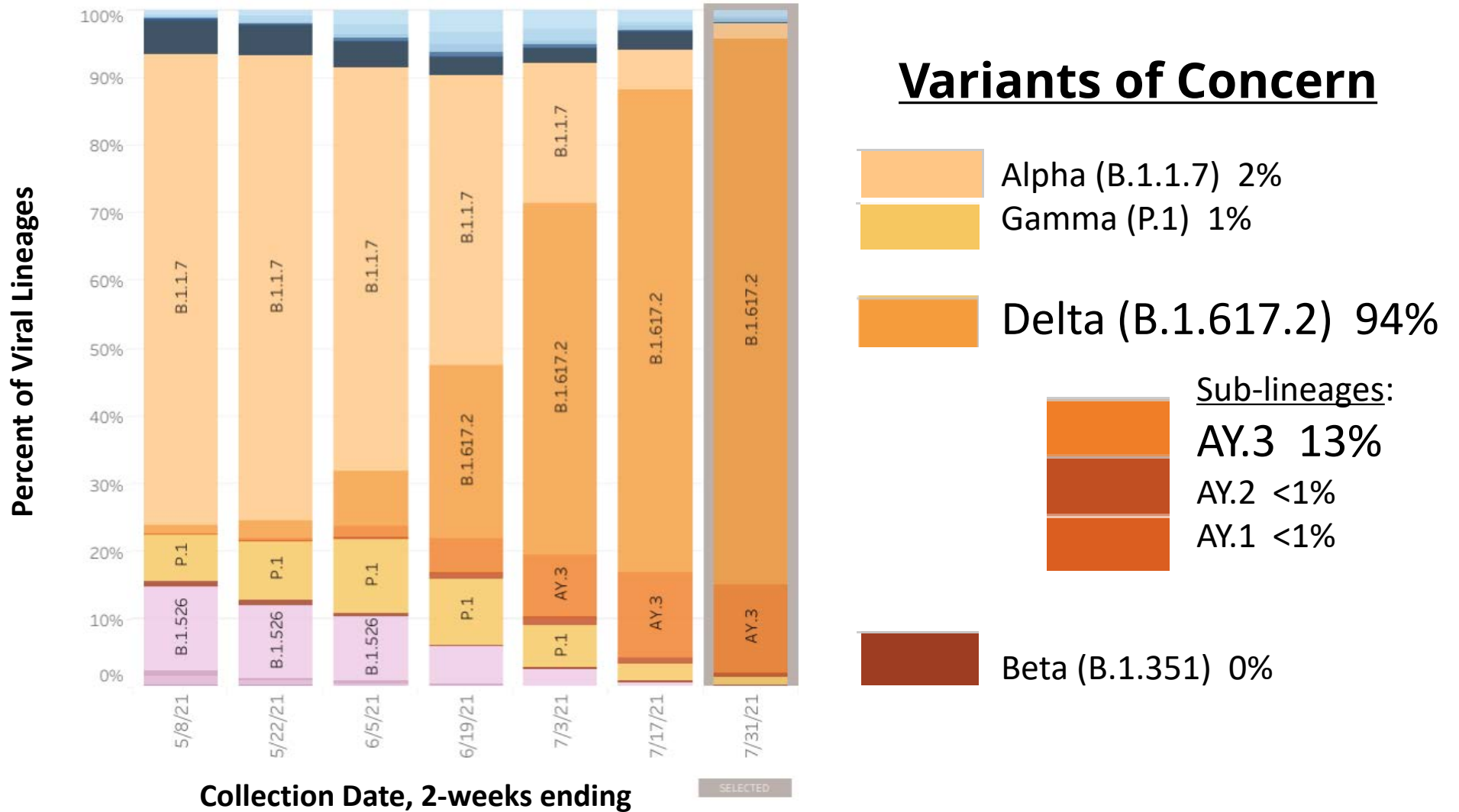
Variants of Concern



WHO label	Alpha	Beta	Gamma	Delta
PANGO Lineage	B.1.1.7	B.1.351	P.1	B.1.617.2
First detected	United Kingdom	South Africa	Japan / Brazil	India
No. of spike mutations	10-13	10	11	11-15
Receptor binding domain mutations	N501Y	K417N E484K N501Y	K417T E484K N501Y	(K417N*) L452R T478K
Attributes	<ul style="list-style-type: none"> • 50% increased transmission • Minimal impact on neutralization by convalescent or vaccine sera • No impact on antibody therapies 	<ul style="list-style-type: none"> • 50% increased transmission • Significantly reduced efficacy of some antibodies • Reduced neutralization by convalescent or vaccine sera 	<ul style="list-style-type: none"> • Significantly reduced efficacy of some antibodies • Reduced neutralization by convalescent or vaccine sera 	<ul style="list-style-type: none"> • Increased transmission • Potential reduced antibody efficacy • Potential reduced neutralization by vaccine sera

Estimated Proportions of SARS-CoV-2 lineages in the US

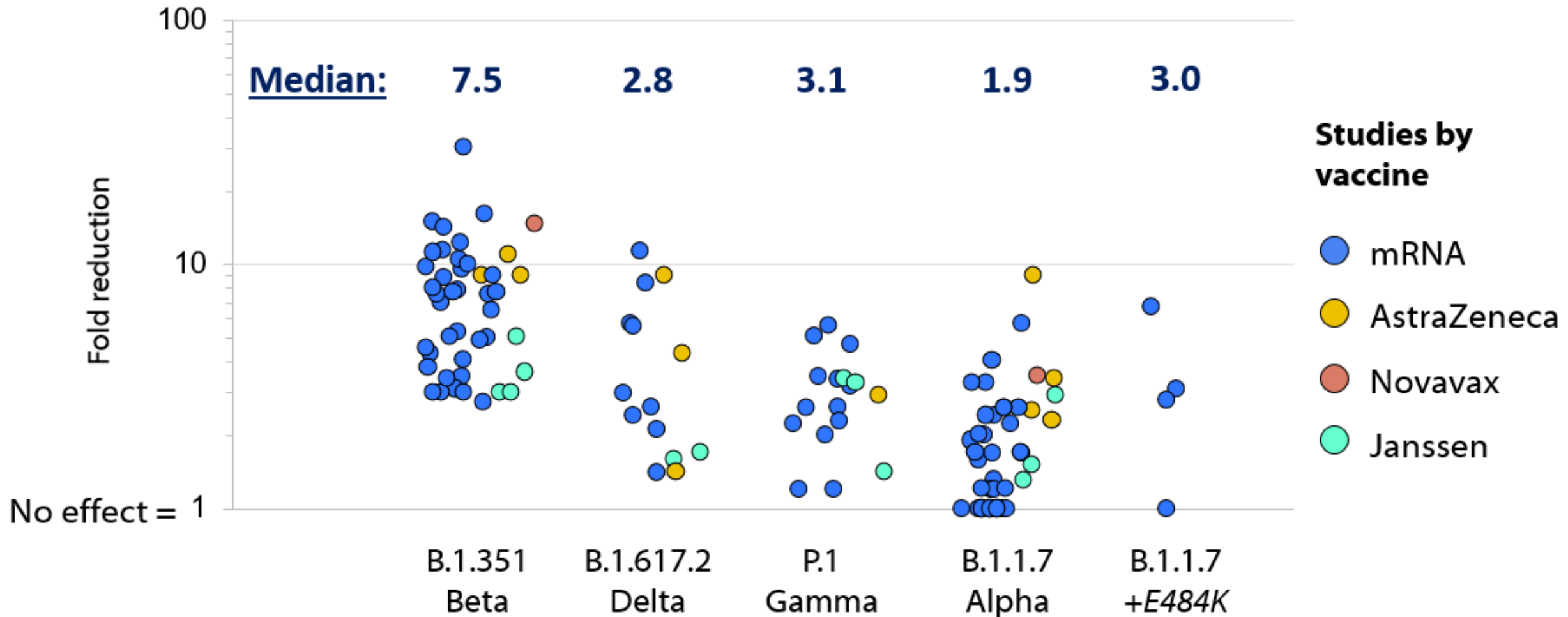
April 25 – July 31, 2021 with NOWCAST



Types of evidence for monitoring vaccine efficacy

- Antibody neutralization — laboratory
 - Correlate of protection not yet established
 - Good correlation of vaccine efficacy with resulting neutralizing antibody levels
 - Likely first evidence we will get on impact of variants on vaccines
- Vaccine efficacy in clinical trials and real-world effectiveness
 - Greater protection against severe disease > symptomatic illness > confirmed infection (including asymptomatic)
 - Protection against severe disease requires lower antibody levels & less affected by differences in vaccine efficacy
- Vaccine breakthrough infection

Reduced antibody neutralization activity of vaccine sera relative to wildtype/dominant strain by study (n=50)



Duration of immunity

- To date, available data demonstrate antibody persistence at least:
 - 8 months after COVID-19 infection
 - 6 months after 2nd mRNA vaccine dose; 8 months after receiving single Janssen dose
- May maintain long-term protection from severe illness by antigenically similar strain, even if become susceptible to mild infection
- Two studies show combined impact of waning immunity and reduced variant neutralization — ~50% protected against ancestral strain have undetectable neutralizing titers against Beta/Gamma at 6 months after Moderna vaccine
 - Small study 8 months post-receipt of Janssen vaccine — minimal decline in neutralizing titers & improved protection against Beta/Gamma/Delta vs. 1-month post-vaccine

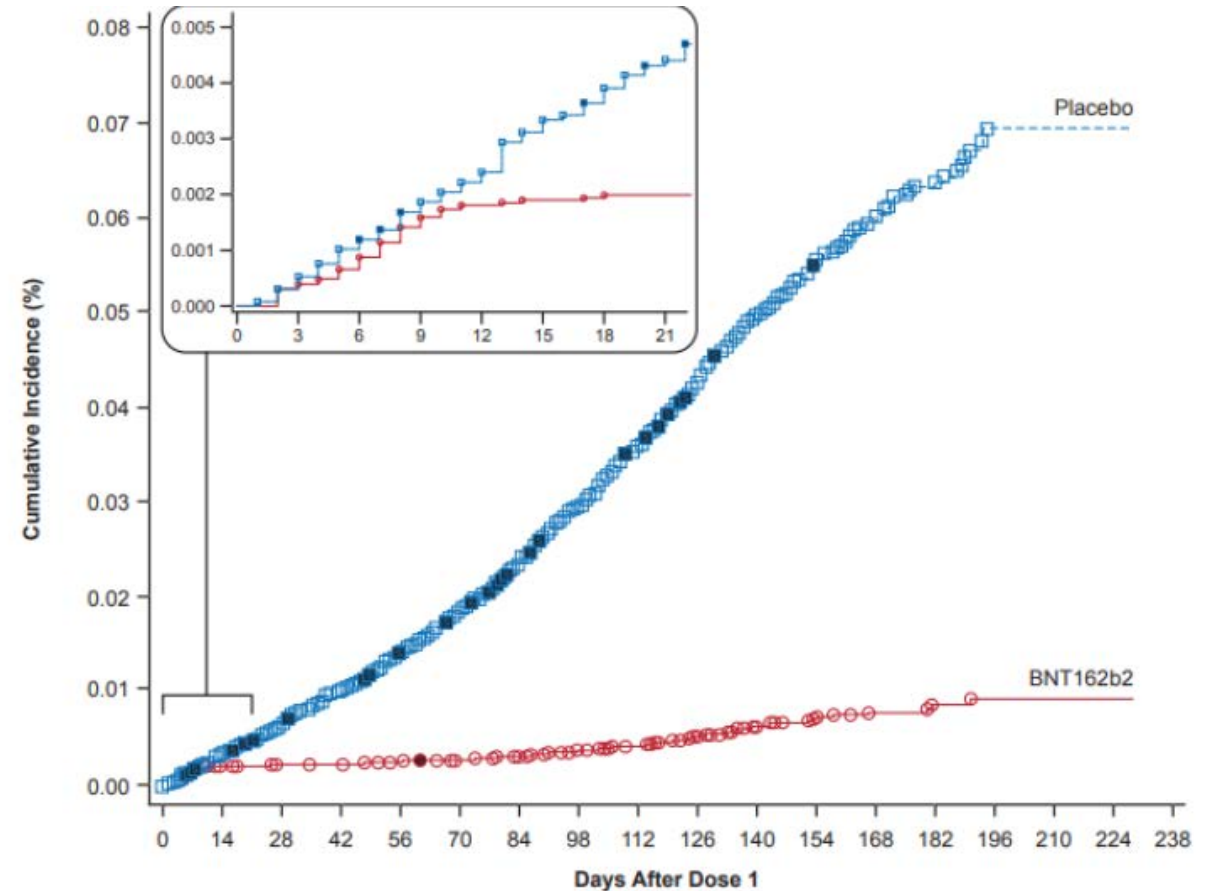
Pfizer vaccine 6-month efficacy

VE against infection: 91% (89, 93)

Period after dose 2	% VE (95% CI)
≥7 days to <2 mos	96 (94, 98)
≥2 mos to <4 mos	90 (87, 93)
≥4 mos to <6 mos	84 (75, 90)

VE against severe illness: 97% (80,100)

Moderna press release:
93% VE against infection at 6 months (unpublished)



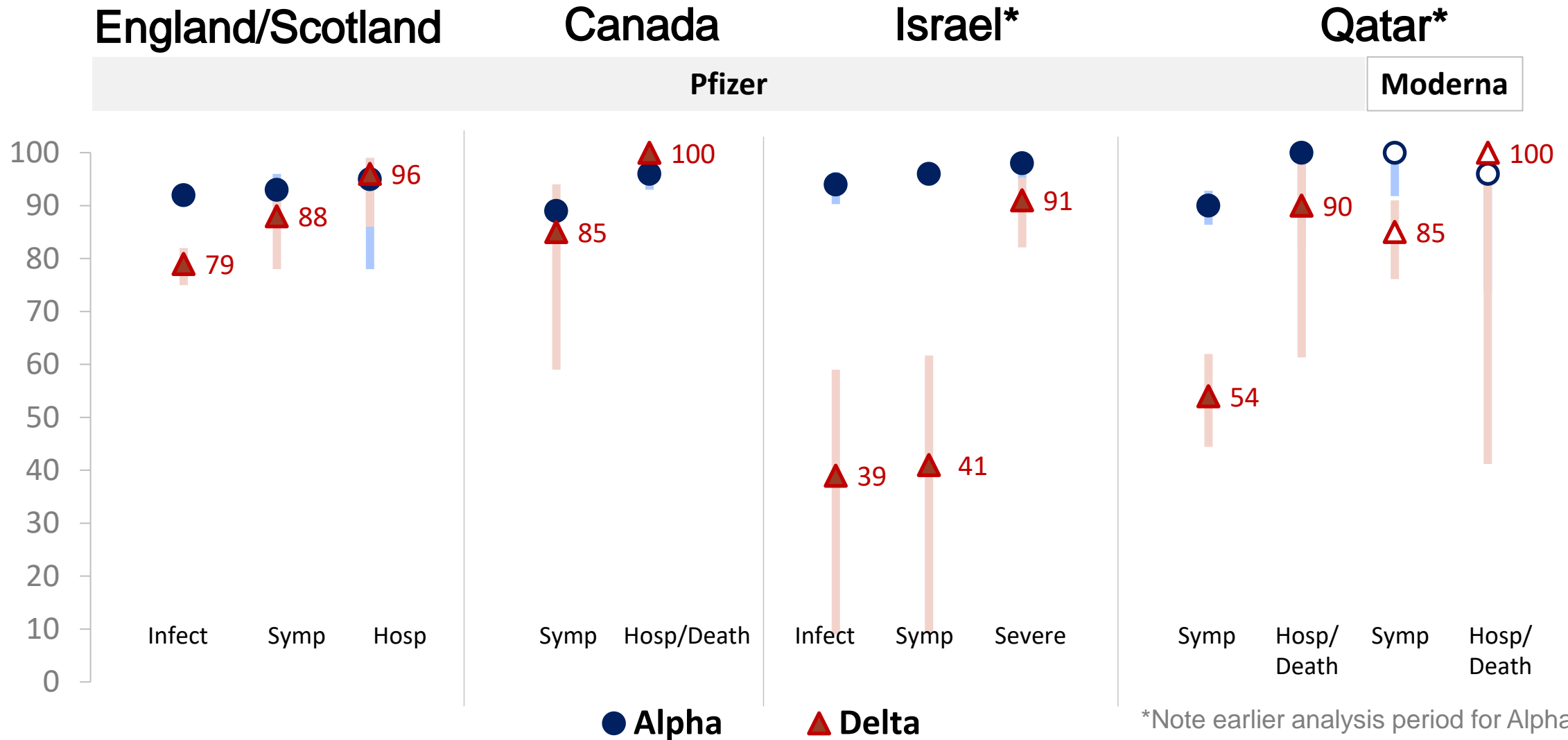
Vaccine efficacy and effectiveness (VE) against variants

- **Alpha (B.1.1.7)** — mRNA vaccines **>85%** real-world VE against confirmed infection in United States and multiple other countries
- **Gamma (P.1)** — mRNA vaccines **84%–88%** real-world VE against symptomatic infection and **79%** against confirmed infection when P.1 in wide circulation in Canada
- **Beta (B.1.351)**
 - Moderna (**96%**) & Pfizer (**75%**) real-world VE against confirmed infection in Qatar
 - Janssen **52%** VE against moderate/severe disease in South Africa (vs. 74% in US)
 - **High VE against severe disease** — **96%–100%** for mRNA vaccines in Qatar, **73%** at ≥ 14 days and **81%** at ≥ 28 days for Janssen in South Africa

Delta variant: What we know

- Nearly twice as contagious as previous variants
- Some evidence of increased illness severity vs. previous strains in unvaccinated persons
- Greatest risk of transmission still among unvaccinated people
- Fully vaccinated people with Delta breakthrough infections can spread virus to others
 - However, vaccinated people with Delta appear to be infectious for a shorter period than unvaccinated persons with Delta

Pfizer & Moderna 2-Dose Effectiveness for Alpha vs. Delta



*Note earlier analysis period for Alpha vs Delta

Sheikh et al. Lancet (2021): [https://doi.org/10.1016/S0140-6736\(21\)01358-1](https://doi.org/10.1016/S0140-6736(21)01358-1); Lopez Bernal et al. medRxiv preprint; <https://doi.org/10.1101/2021.05.22.21257658>; Stowe et al. PHE preprint: https://khub.net/web/phe-national/public-library/-/document_library/v2WsRK3ZIEig/view/479607266; Nasreen et al. medRxiv preprint: <https://doi.org/10.1101/2021.06.28.21259420>; Haas et al Lancet (2021): [https://doi.org/10.1016/S0140-6736\(21\)00947-8](https://doi.org/10.1016/S0140-6736(21)00947-8) ; Israel MOH: https://www.gov.il/BlobFolder/reports/vaccine-efficacy-safety-follow-up-committee/he/files_publications_corona_two-dose-vaccination-data.pdf Abu-Radad and Butt. NEJM (2021); Chemaiteilly et al. Nature Med (2021): [Tang et al medRxiv](https://doi.org/10.1038/s41591-021-1311-1)

Differences in COVID vaccination program by country with potential impact on comparability of VE results

Country	U.S.	Israel	Qatar	U.K.	Canada
Vaccines used [authorized]	Pfizer Moderna Janssen	Pfizer [Moderna]	Pfizer Moderna	Pfizer AstraZeneca [Moderna] [Janssen]	Pfizer Moderna AstraZeneca [Janssen]
Interval	3-4 weeks	3 weeks	3-4 weeks	12 weeks	16 weeks
Note	-	Tight cohort	-	Mix-and-match	

- Extended intervals between doses (12 weeks) shown to improve immunogenicity and VE for Pfizer and AstraZeneca vaccines compared with standard interval, including ages ≥ 80 years
- Pfizer has lower mRNA dosage and accelerated schedule (3 weeks) compared with Moderna (4 weeks)

Declines in VE against infection

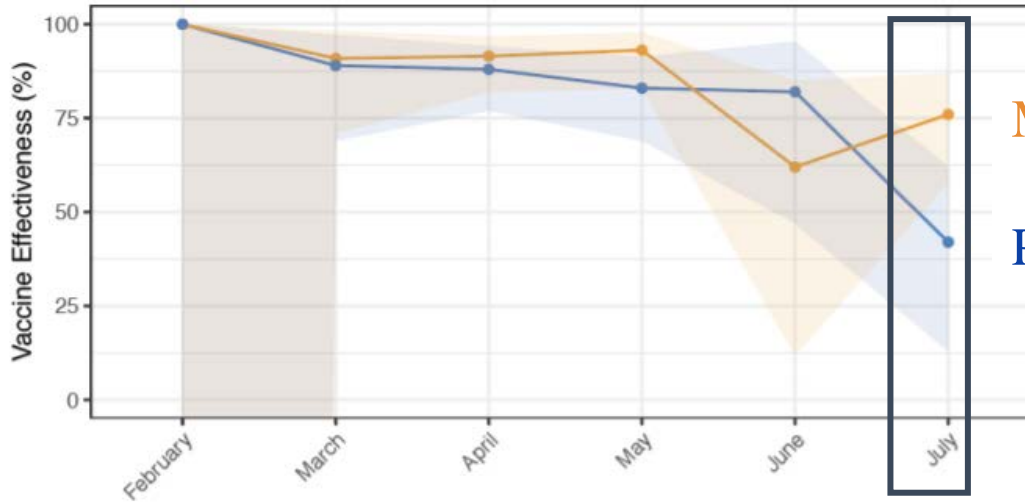
Preprint and unpublished data from Israel

- Ministry of Health analysis — higher breakthrough rates and lower Pfizer VE against infection for persons vaccinated in Jan–Feb 2021 more recent months for persons aged 16–59 and ≥ 60 years
- Two retrospective cohort studies of persons vaccinated with Pfizer in large healthcare systems :
 - 2.3-fold increased risk for breakthrough infection among persons vaccinated with Pfizer in January vs. April 2021 (n=1.35 million)
 - Higher breakthrough infection rate (2.4% v. 1.1%, OR=2.2) among those who received 2nd dose ≥ 5 months ago compared to < 5 months ago (n=33,993)
 - Higher magnitude of difference with increasing age

VE against Infection and Hospitalization July vs. Jan-May

Mayo Clinic Health System, Minnesota, n=25,589

SARS-CoV-2 Infection

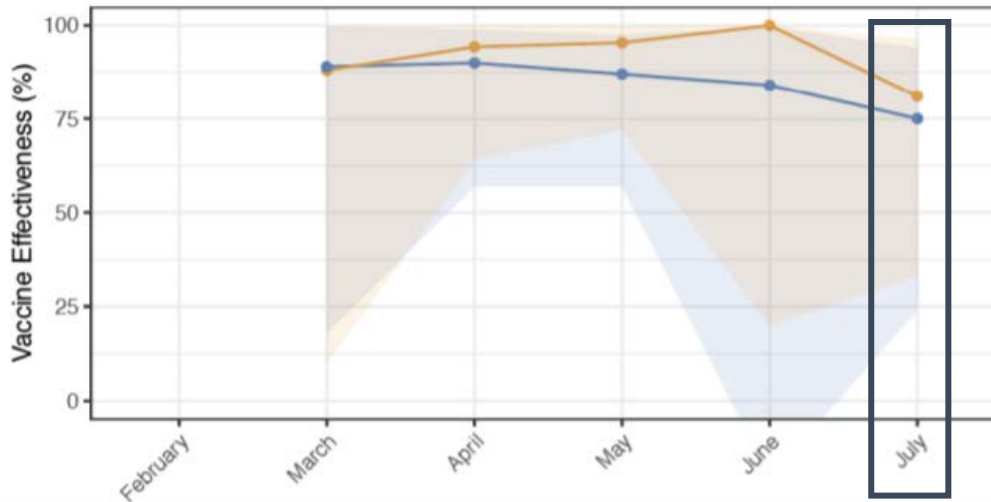


Moderna: 76% (95% CI: 58%-87%)

Pfizer: 42% (95% CI: 13%- 62%)

Delta prevalence increased from 0.7% in May to >70% in July

COVID-19 Hospitalization



Moderna: 81% (95% CI: 33%-96%)

Pfizer: 75% (95% CI: 24%- 94%)

U.S. COVID-19 Vaccine Breakthrough Cases

- Despite high vaccine efficacy, vaccine breakthrough cases* are expected
 - Some will be caused by variants, even if vaccine has similar effectiveness against variants
 - CDC monitors nationwide vaccine breakthrough resulting in hospitalization or death
- As of August 2, among more than 164 million fully vaccinated in U.S., there have been 7,101 hospitalizations & 1,507 deaths with vaccine breakthrough reported to passive surveillance**
 - Among hospitalized or fatal breakthrough cases, 74% among persons aged ≥ 65 years
 - Variants of concern (%) among breakthrough cases similar to national genomic surveillance
- COVID-NET data on COVID-19-associated hospitalizations among aged persons ≥ 18 years
 - $\sim 32\%$ of all vaccinated cases are immunocompromised vs. 11% of unvaccinated cases

* **Vaccine breakthrough case:** Person with SARS-CoV-2 RNA or antigen detected in respiratory specimen collected ≥ 14 days after completing primary series of an FDA-authorized COVID-19 vaccine

** CDC website as of 8/5/21; 1,816 hospitalizations and 316 fatal cases reported as asymptomatic or not related to COVID-19. CDC. MMWR (2021); COVID-NET: <https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covid-net/purpose-methods.html>

Summary of Preliminary Data: Implications of SARS-CoV-2 Variants of Concern on Vaccine Effectiveness

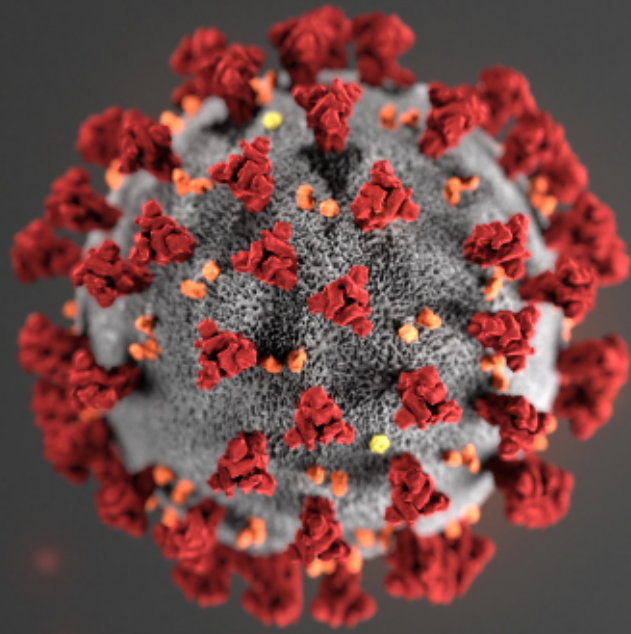
B.1.1.7 (Alpha)	<ul style="list-style-type: none">• Low prevalence in United States• Minimal impact on VE; attention needed for additional substitutions in receptor binding domain (RBD), e.g., E484K
B.1.351 (Beta)	<ul style="list-style-type: none">• Low prevalence in United States• Moderate impact on VE against infection, but appear to protect against severe disease
P.1 (Gamma)	<ul style="list-style-type: none">• Low prevalence in United States• Moderate impact on VE for some vaccines; more data needed
B.1.617.2 (Delta)	<ul style="list-style-type: none">• High prevalence in United States• Moderate impact on VE for infection, but appear to protect against severe disease; more data needed, especially for Janssen

Boosters and Second-Generation Vaccines Against SARS-CoV-2 Variants

- Manufacturers conducting booster studies of current vaccines and/or second-generation vaccines against Beta (B.1.351)
- Moderna — preliminary phase 2 results of single 50 µg booster of authorized (mRNA-1273) and variant-specific vaccine (mRNA-1273.351)
 - Both vaccines — acceptable safety; boosted immunity to wild-type, Beta, Gamma
- Pfizer has also submitted preliminary data on booster of original vaccine to FDA
- No Delta-specific booster vaccine studies shared to date

Summary

- Currently authorized vaccines offer protection against known variants — important to increase vaccine uptake in eligible populations
- CDC is closely monitoring real-world vaccine effectiveness and breakthrough infections using multiple methods, populations, and outcomes
- CDC continues to monitor emerging variants — prevalence and impact on disease incidence, severity, and vaccine breakthrough
- ACIP will review evidence submitted for boosters and any next-generation vaccines
- Changing landscape — CDC will communicate promptly about new evidence



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.

