CDC/IDSA COVID-19 Clinician Call

July 17, 2021

Welcome & Introduction

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

- 70th 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:

Update on Variants & Immunity

CDC Update on SARS-CoV-2 Surveillance

David E. Wentworth, PhD

Lead, Surveillance & Emerging Variants Team, Laboratory and Testing Task Force, CDC COVID-19 Emergency Response
Chief, Virology Surveillance and Diagnosis Branch
Centers for Disease Control and Prevention

Delta Variant Update

Jonathan Z. Li, MD

Associate Professor of Medicine, Division of Infectious Diseases
Brigham and Women's Hospital, Harvard Medical School

The Latest on Vaccines & Immunity

Varun Phadke, MD

Assistant Professor of Medicine, Division of Infectious Diseases
Emory University School of Medicine

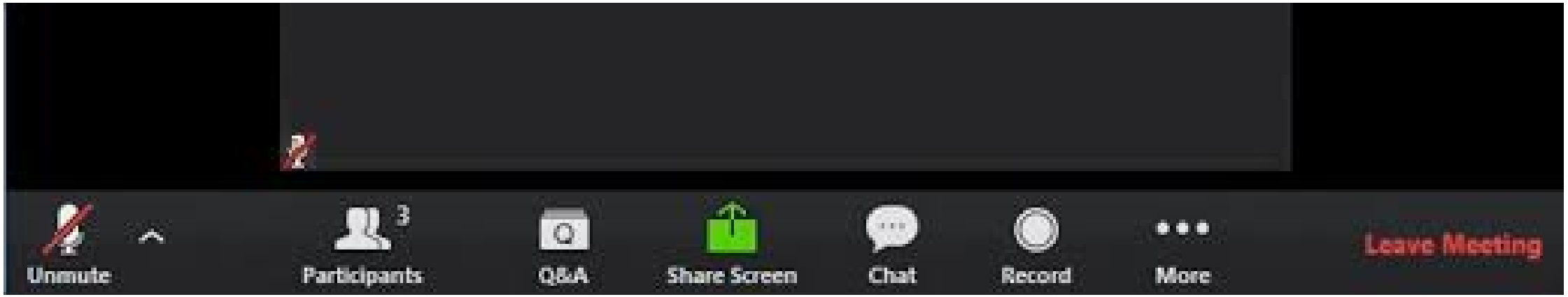
Covid-19 Serology Tests – What Can They Tell about Immunity and Protection

Timothy T. Stenzel, MD, PhD

Director, OHT7: Office of In Vitro Diagnostics and Radiological Health, Office of Product Evaluation and Quality, Center for Devices and Radiological Health
U.S. Food and Drug Administration

Question?
Use the “Q&A” Button

Comment?
Use the “Chat” Button



CDC Update on SARS-CoV-2 Surveillance

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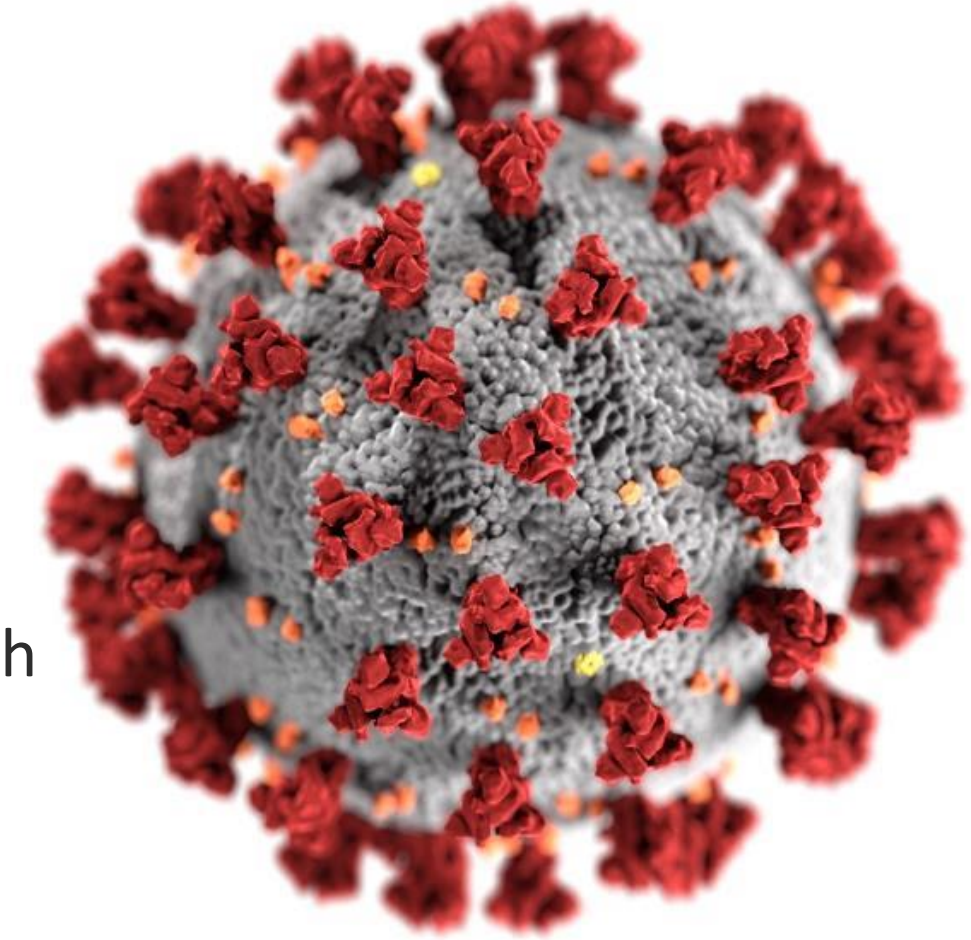
Surveillance and Emerging Variants Team
Laboratory and Testing Task Force
CDC COVID-19 Emergency Response

Chief, Virology Surveillance and Diagnosis Branch
Influenza Division, NCIRD, CDC

CDC/IDSA clinician webinar, July 17, 2021

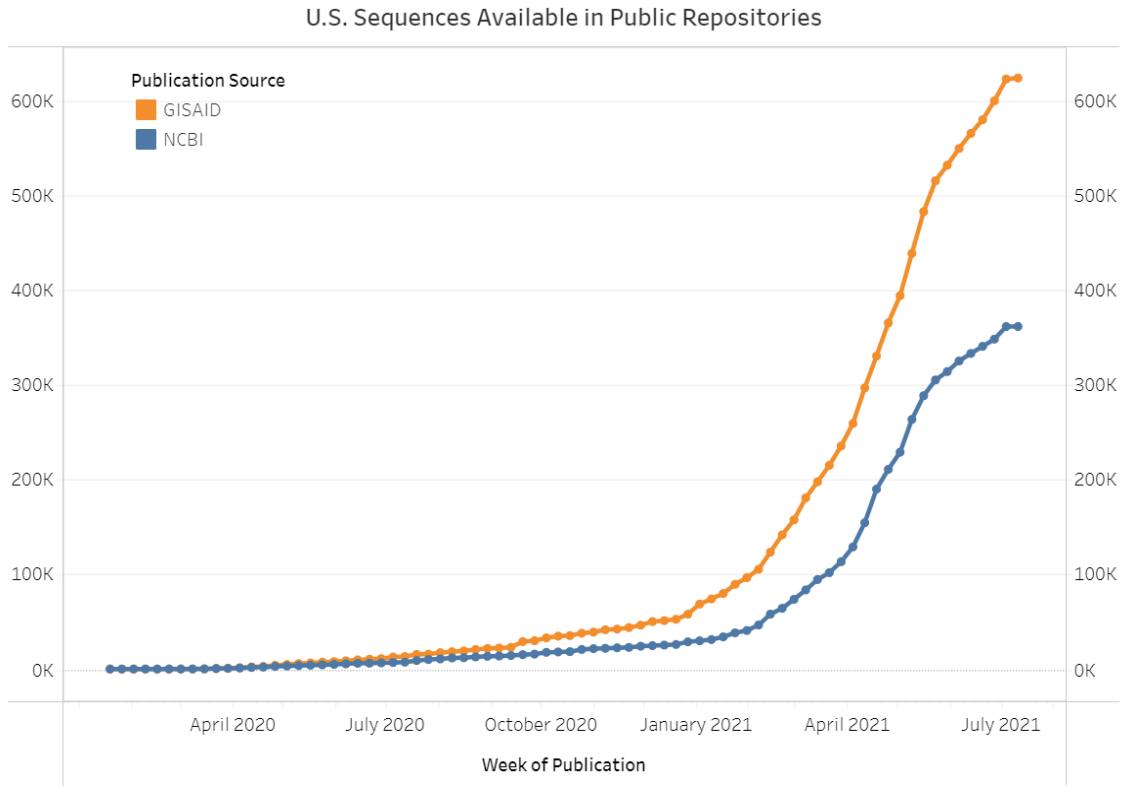


cdc.gov/coronavirus

National SARS-CoV-2 Genomic Surveillance

In the United States, CDC tracks and analyzes emerging SARS-CoV-2 variants through genomic surveillance

- Leading the National SARS-CoV-2 Strain Surveillance (NS3) system
- Partnering with commercial diagnostic laboratories
- Partnering with universities
- Supporting state, territorial, local and tribal health departments
- Leading the SARS-CoV-2 Sequencing for Public Health Emergencies Response, Epidemiology, and Surveillance (SPHERES) Consortium

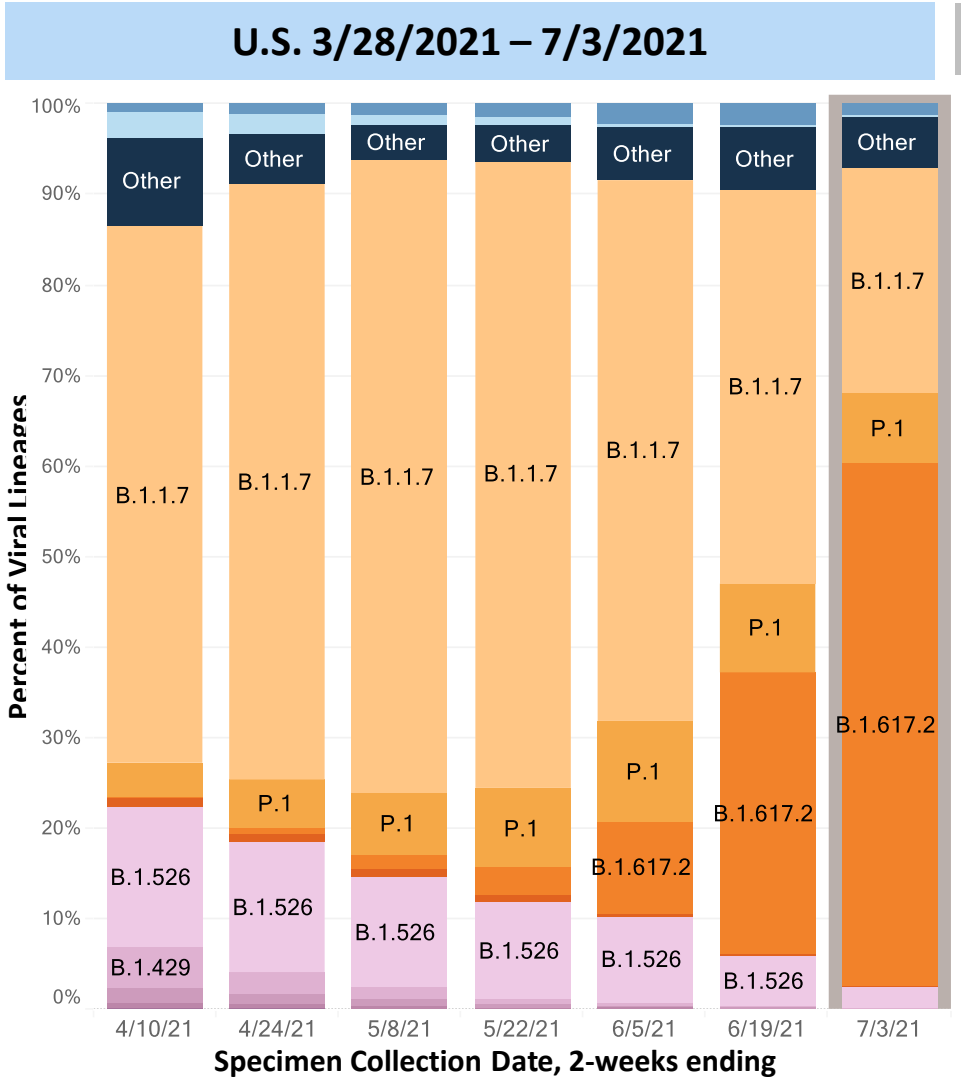


https://www.cdc.gov/coronavirus/2019-ncov/variants/cdc-role-surveillance.html

https://covid.cdc.gov/covid-data-tracker/#published-covid-sequences

National Nowcast Estimates SARS-CoV-2 Lineages

- **B.1.617.2 (Delta)** Prediction increased
  - ~31% (6/19) to 58% (7/3)
- **B.1.1.7 (Alpha)** continues to decline
  - ~43% (6/19) to 25% (7/3)
- **P.1 (Gamma)** decreased
  - 10% (6/19) to 8% (7/3)



NOWCAST U.S. 7/3/2021

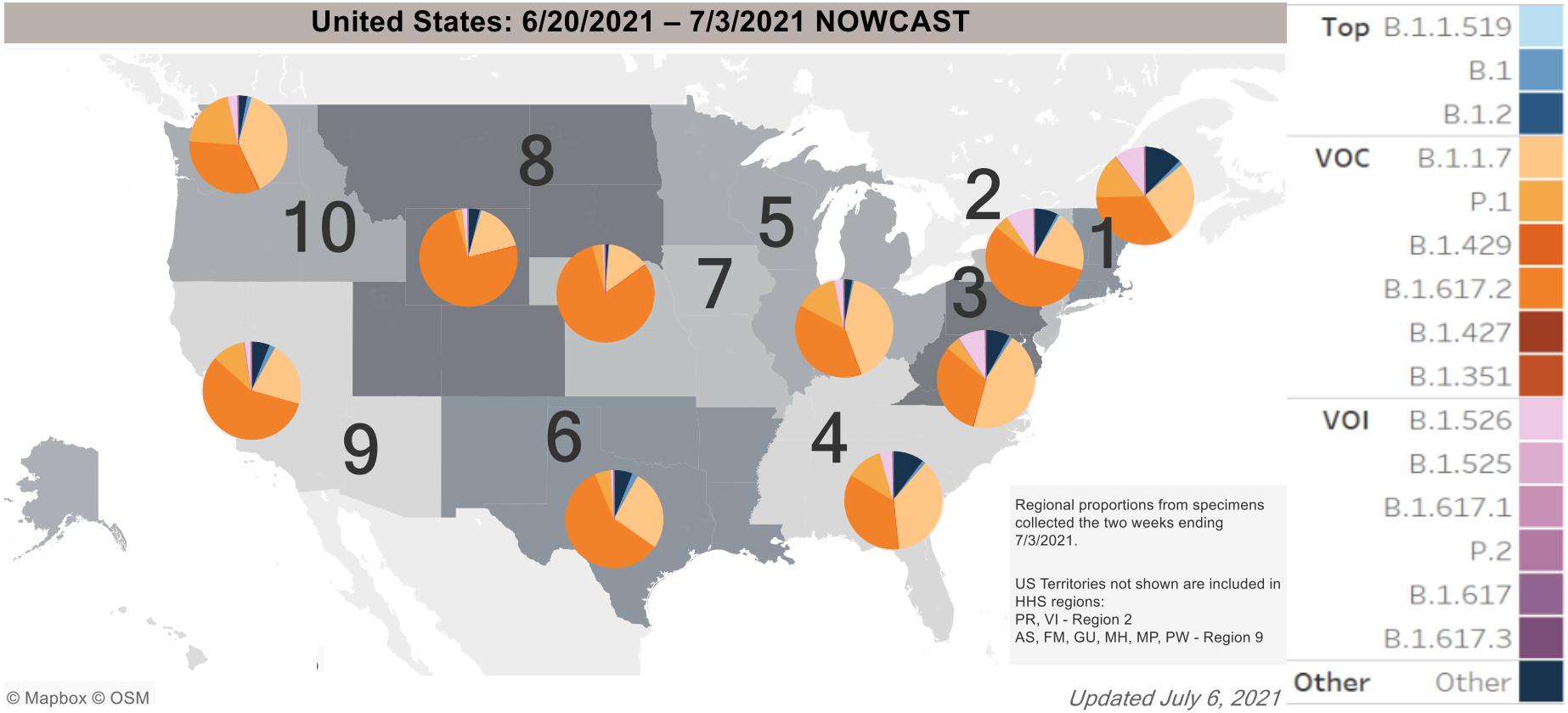
	Lineage	Type	%Total	95%PI	
Most common lineages #	B.1.617.2	Delta	VOC	57.6%	52.7-62.8%
	B.1.1.7	Alpha	VOC	24.9%	20.5-29.4%
	P.1	Gamma	VOC	7.7%	5.1-10.6%
	B.1.526	Iota	VOI	2.4%	1.0-4.1%
	B.1			1.3%	0.3-2.5%
	B.1.1.519			0.1%	0.0-0.3%
Additional VOI/VOC lineages #	B.1.351	Beta	VOC	0.1%	0.0-0.5%
	B.1.525	Eta	VOI	0.0%	0.0-0.3%
	B.1.429	Epsilon	VOI	0.0%	0.0-0.3%
	B.1.427	Epsilon	VOI	0.0%	0.0-0.3%
	B.1.617.1	Kappa	VOI	0.0%	0.0-0.3%
	P.2	Zeta	VOI	0.0%	0.0-0.3%
Other*	Other			5.7%	3.0-8.9%

* Other represents >200 additional lineages, which are each circulating at <1% of total viruses
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# Sublineages of P.1 (P.1.1, P.1.2) and B.1.351 (B.1.351.1, B.1.351.2, B.1.351.3) are aggregated with the parental lineage. AY.1 and AY.2 are aggregated with B.1.617.2

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

Regional Nowcast Prevalence of SARS-CoV-2 Variants

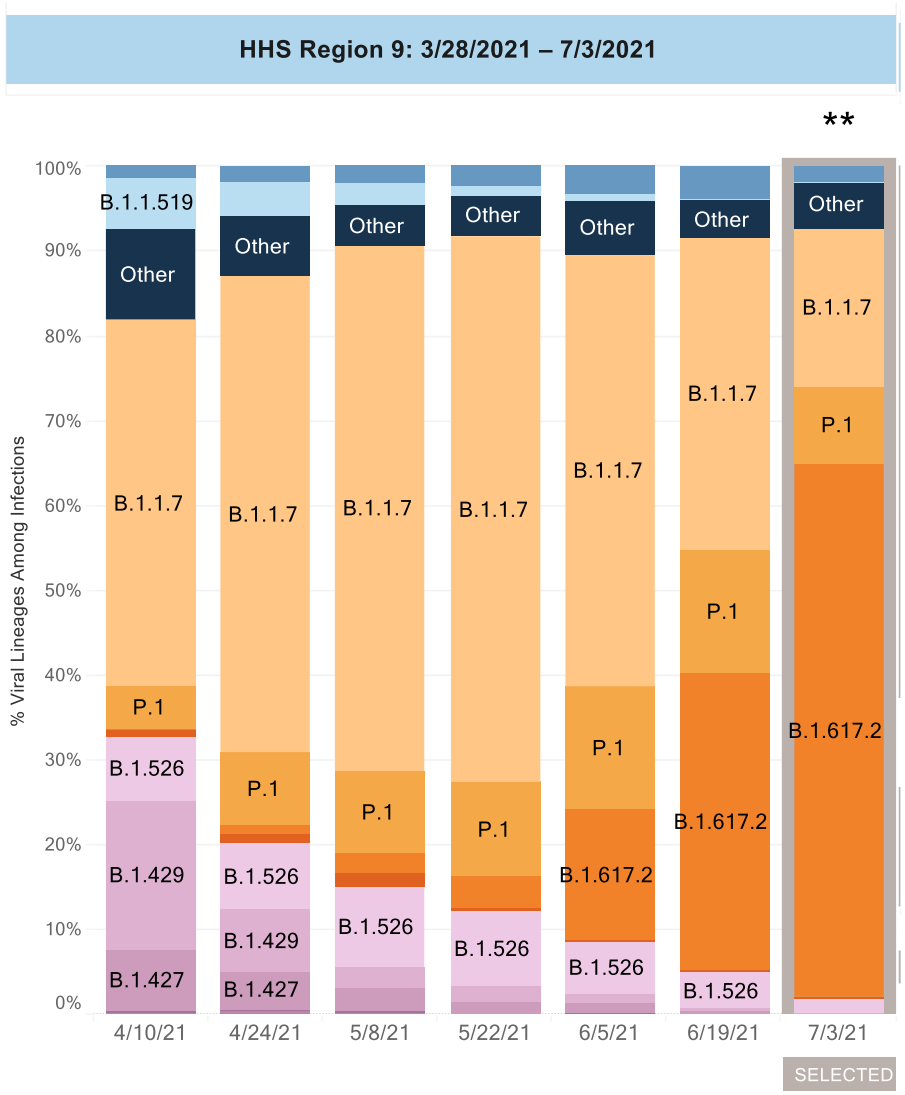
- **B.1.617.2 (Delta)**
  - >38% in all regions
  - >50% in Regions 2, 6-9
  - 87% in Region 7
  - 79% in Region 8
- **B.1.1.7 (Alpha)**
  - <50% in all regions
  - <25% in Regions 2, 6-9



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

HHS Region 9 Nowcast Estimated SARS-CoV-2 Variant Proportions

- **B.1.617.2 (Delta)** Predicted to be higher than national average
  - ~63% (Nat. ~58%)
- **B.1.1.7 (Alpha)** continues to decline and lower than national average
  - ~19% (Nat. ~25 %)
- **P.1 (Gamma)** similar to national average
  - ~9%



HHS Region 9: 6/20/2021 – 7/3/2021 NOWCAST

Region 9 - Arizona, California, Hawaii, Nevada, American Samoa, Commonwealth of the Northern Mariana Islands,..

	Lineage	Type	%Total	95%PI	
Most common lineages #	B.1.617.2	Delta	VOC	62.9%	47.1-79.4%
	B.1.1.7	Alpha	VOC	18.7%	5.9-32.4%
	P.1	Gamma	VOC	9.1%	0.0-20.6%
	B.1			1.8%	0.0-5.9%
	B.1.526	Iota	VOI	1.8%	0.0-5.9%
	B.1.1.519			0.1%	0.0-2.9%
Additional VOI/VOC lineages #	B.1.351	Beta	VOC	0.1%	0.0-2.9%
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	P.2	Zeta	VOI	0.0%	0.0-2.9%
Other*	Other			5.5%	0.0-14.7%

* Other represents >200 additional lineages, which are each circulating at <1% of viruses
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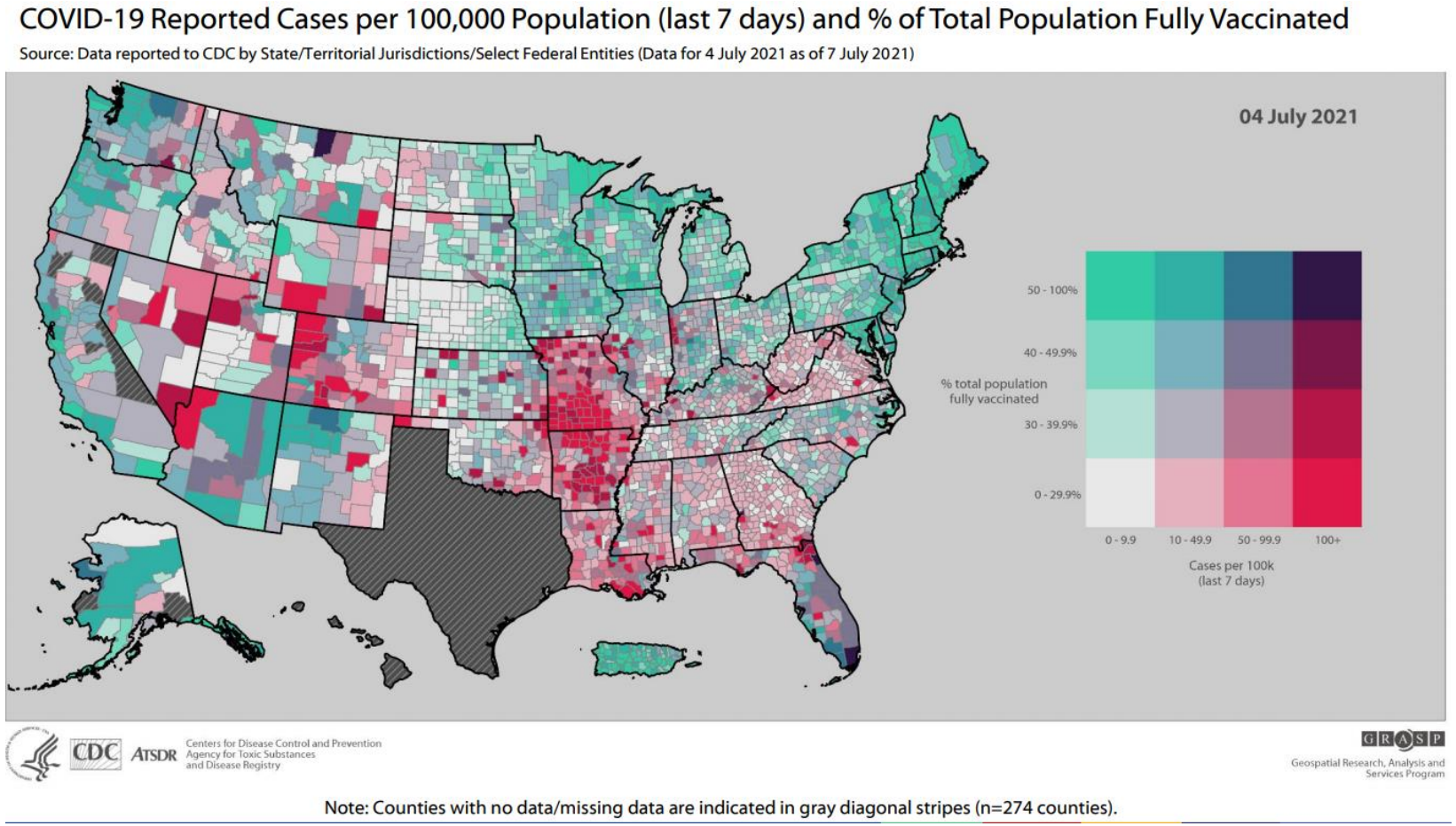
# Sublineages of P.1 and B.1.351 (P.1.1, P.1.2, B.1.351.2, B.1.351.3) are aggregated with the parent linteage and included in parent lineage's proportion. AY.1 and AY.2 are aggregated with B.1.617.2.

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

Summary

- Evolution of SCoV-2 variants is expected
- B.1.617.2 (Delta) is primarily displacing the B.1.1.7 (Alpha) as the dominant variant
- Proportions vary regionally
- Vaccination reduces cases



https://www.cdc.gov/coronavirus/2019-ncov/images/communication/covid-data-tracker/Vaccinations_By_Case_Rate_FINAL_07072021.pdf

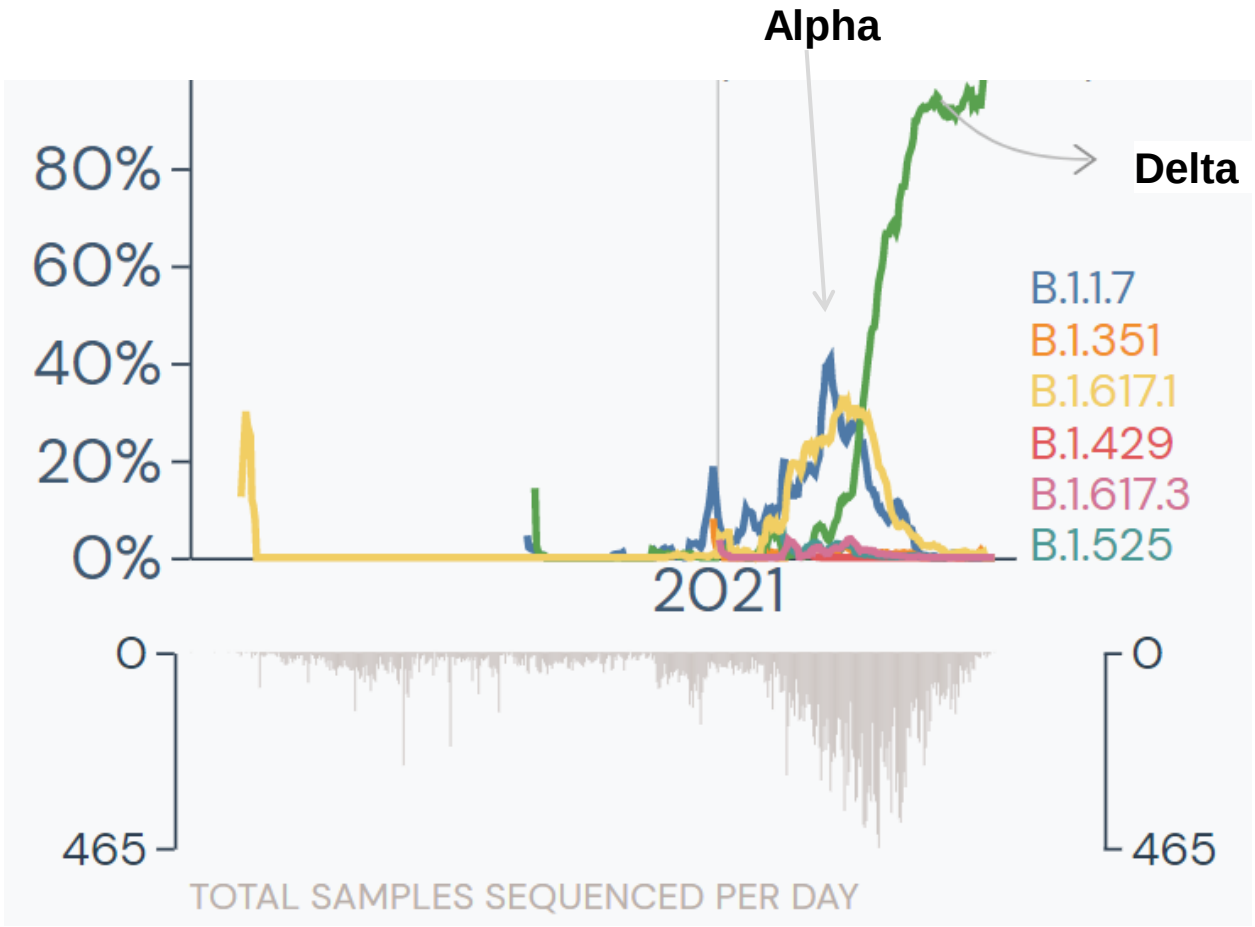
The Delta Variant

Jonathan Li, MD, MMSc
Associate Professor of Medicine
Brigham and Women's Hospital
Harvard Medical School

Overview

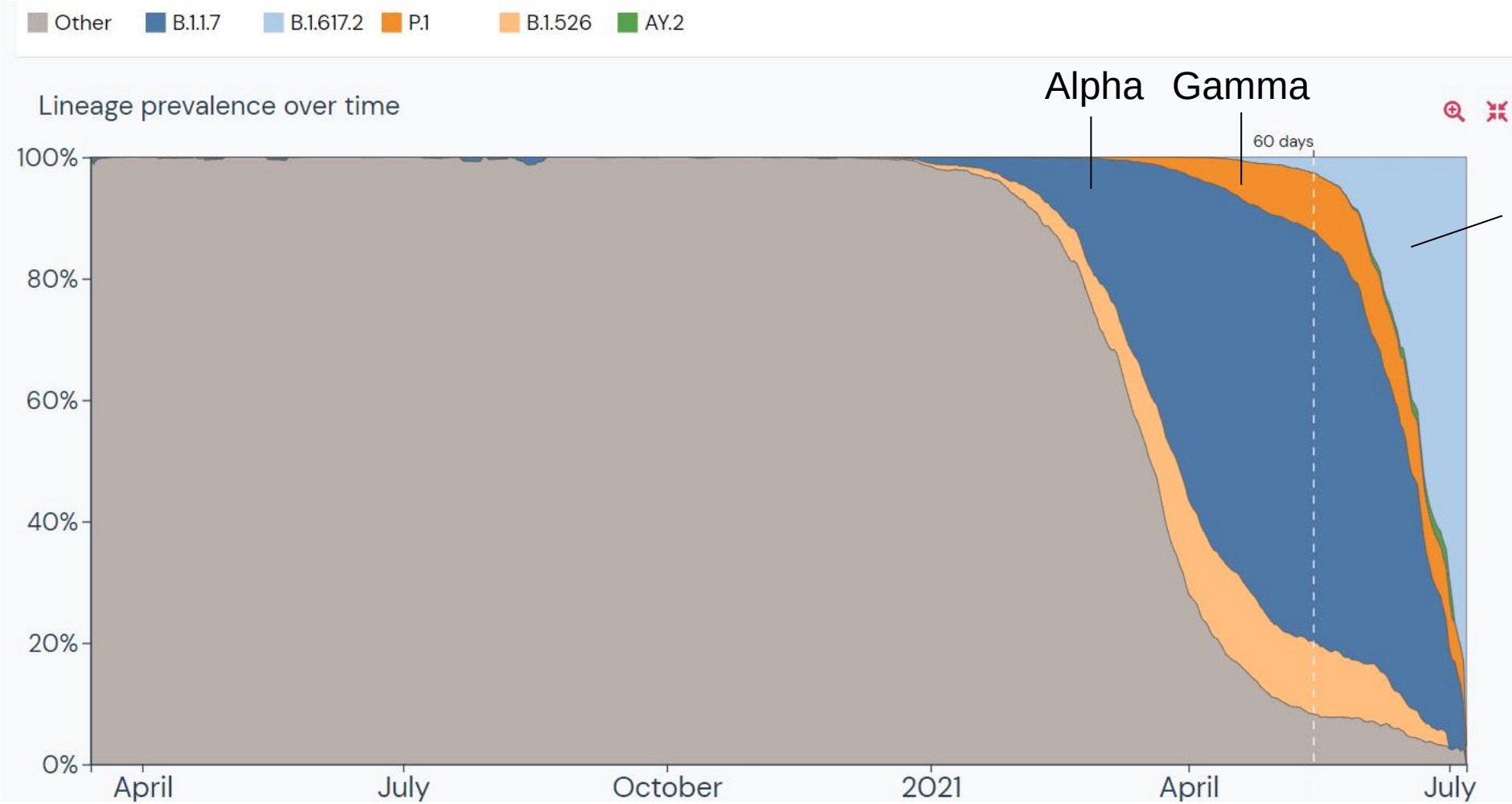
- Mutations in the Delta variant
- Transmissibility of the Delta variant: how much and why?
- Does the Delta variant cause more severe disease?
- Impact of Delta variant on monoclonal antibody treatments
- Impact of Delta variant on vaccine efficacy

Rise of Delta (B.1.617.2) Variant in India



Outbreak.info

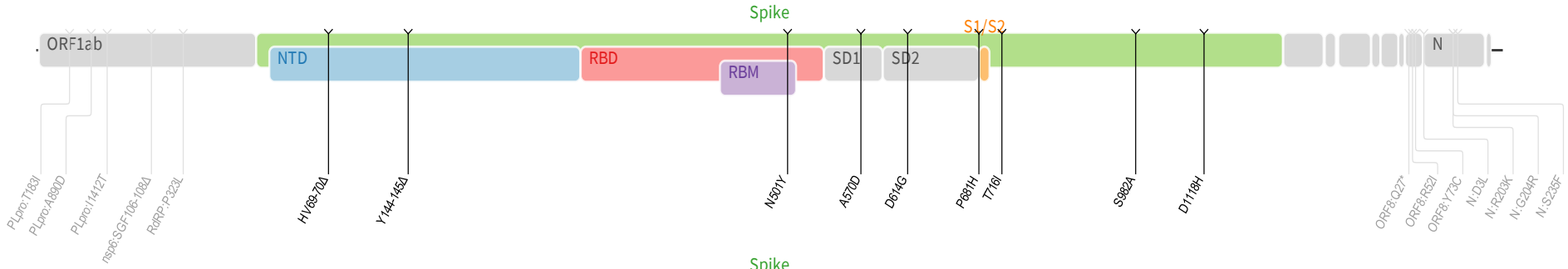
Delta now Dominant in the United States



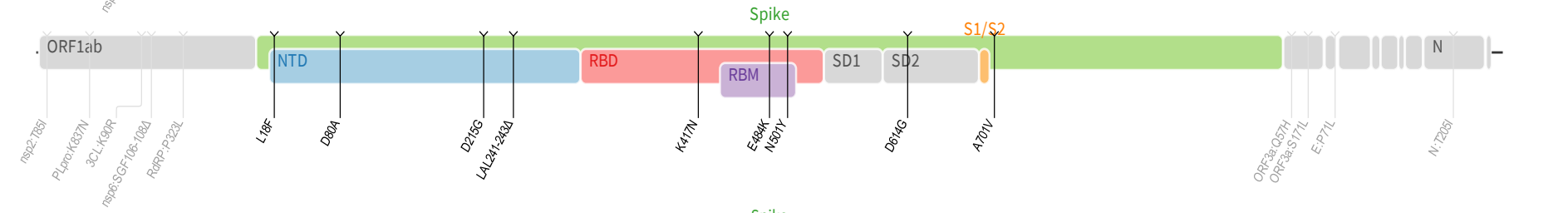
Outbreak.info

Key mutations in variants of concern

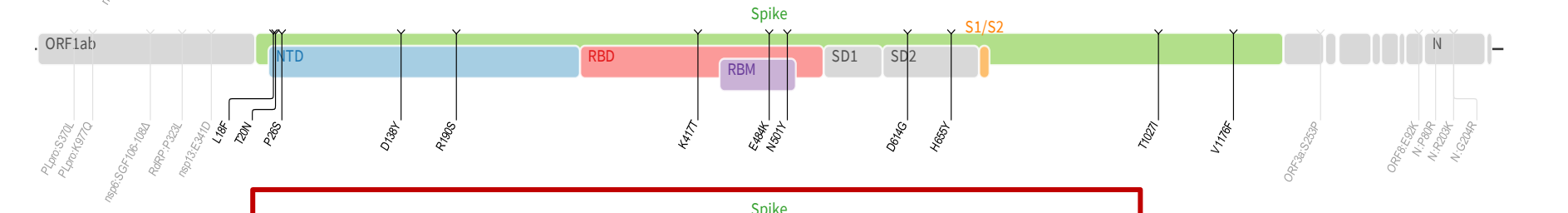
Alpha



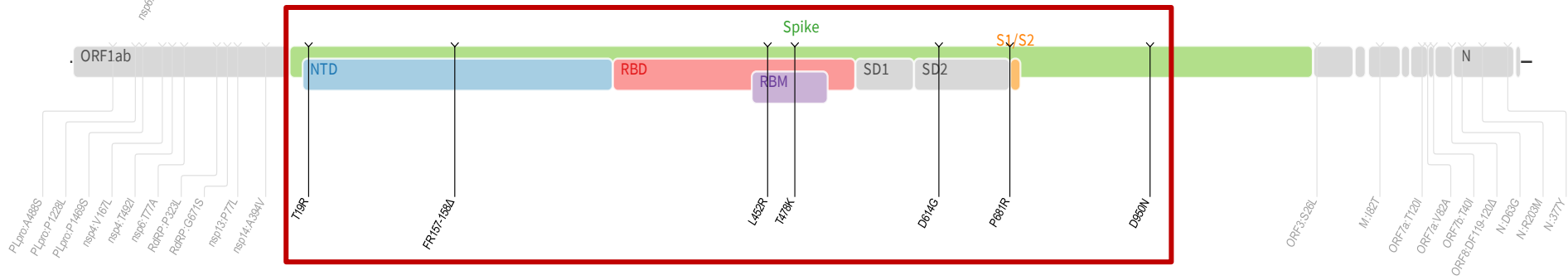
Beta



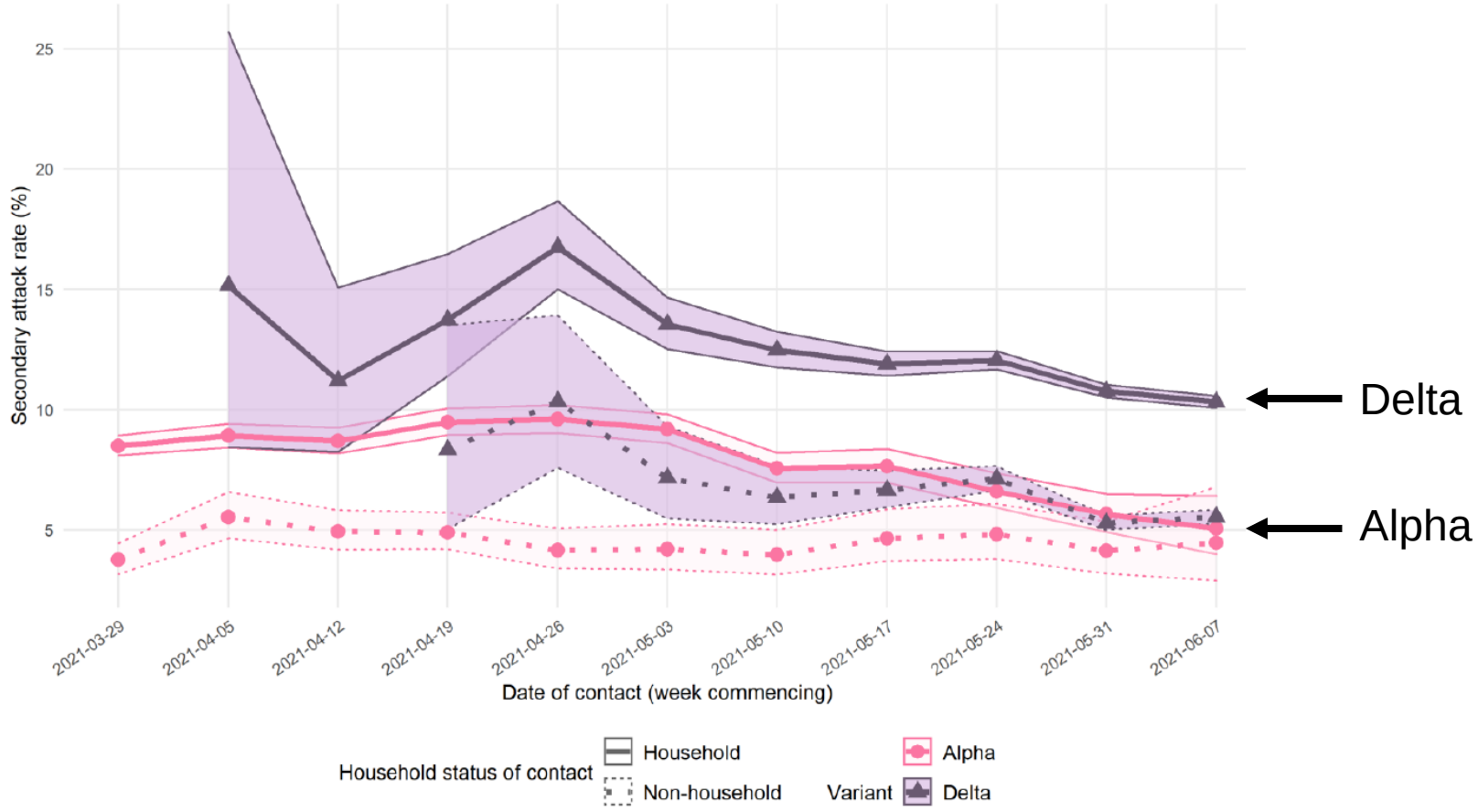
Gamma



Delta

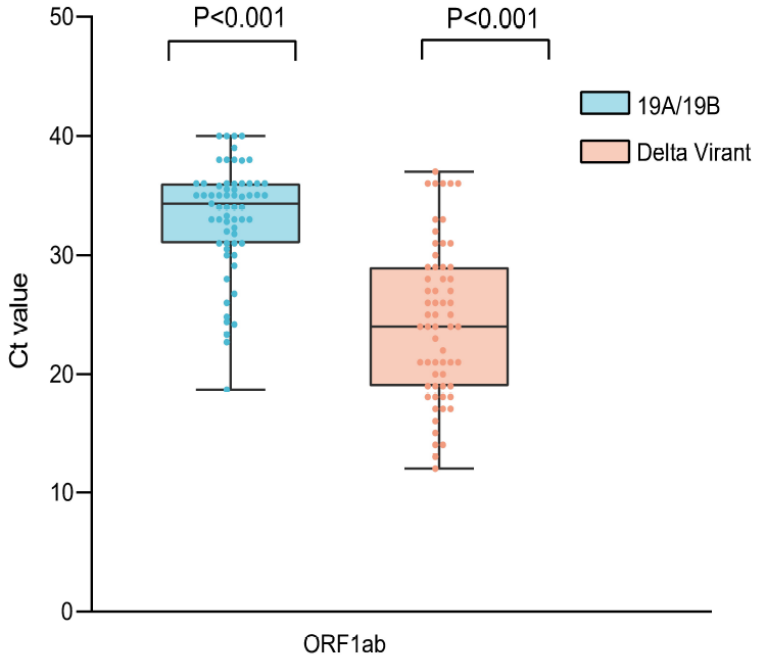


Higher secondary attack rates with Delta vs Alpha variants



Higher viral shedding early in disease course by the Delta variant

Viral infection and transmission in a large well-traced outbreak caused by the Delta SARS-CoV-2 variant



"viral loads in the Delta variant infections…were 1260 times higher than the 19A/19B strains infections…on the day when viruses were first detected"

Li, medRxiv 2021

Does the Delta variant cause more severe disease?

THE LANCET

SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness

On May 19, 2021, the Delta Variant of Concern (VOC), formerly known as the Indian VOC or B 1.617.2, became the dominant strain of SARS-CoV-2 in Scotland. The Alpha VOC (formerly known as the Kent VOC, B.1.1.7, or S gene negative) had been the dominant strain previously, but it has rapidly been replaced (appendix p 1).

Samples were analysed using ThermoFisher's TaqPath RT-PCR, which tests for the presence of three target genes from SARS-CoV-2. S gene-negative samples had a deletion in S gene of B.1.1.7 (Alpha VOC) at position 69–70, with cycle threshold (Ct) values less than 30 for at least one of the *OR* and *N* genes. S gene-positive samples had Ct values less than 30 for the S gene and valid Ct values for the other two genes. In contrast, a weak S gene-positive sample had a Ct of 30 or less for S. Sequencing data from Scotland has found that for April 1 to May 28, 2021, the latest date until which data were available, 97% of S gene positive cases sequenced in Scotland were the Delta variant and that 99% of Delta variants were S gene positive.

COVID-19 hospital admissions in S gene-positive cases. We also employed a test-negative design to estimate vaccine effectiveness against risk of SARS-CoV-2 infection.[5] This analysis was based upon all individuals who have a PCR test for SARS-CoV-2 in the study period, and it compares the proportions positive among individuals vaccinated at the time of the swab test with those unvaccinated when they are tested, adjusting for demographic and temporal covariates.

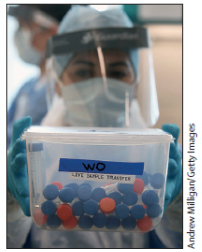
Building on methods that have previously been described in detail, we defined a COVID-19 hospital admission as being within 14 days of testing positive for SARS-CoV-2.[3,5] Individuals who tested positive within 2 days after a hospital admission were also included. Individuals tested during a hospital stay from day 3 onwards were excluded. Hospital-acquired COVID-19 infections were excluded.

Our analysis covered the period from April 1 to June 6, 2021, for the demographic distribution of cases. By April 1, 2021, 44·7% of the population in Scotland had received one dose of the COVID-19 vaccine, and 7·6% had received two doses. Among people aged 65 years or older, the percentages were 91·2% and 15·9%, respectively. By the end of the study period (ie, June 6, 2021), 59·4% had received one dose and 39·4% two doses; the corresponding proportions were 91·7%

inverse deprivation gradient with S gene-positive cases disproportionally seen in the most socioeconomically affluent quintile. Most cases (70%) had no underlying relevant comorbidities. 70% of S gene-positive cases had not had any COVID-19 vaccination doses, compared to 75% of S gene-negative cases.

The Cox regression analysis for time to hospital admission found that S gene-positive cases were associated with an increased risk of COVID-19 hospital admission: hazard ratio (HR) 1·85 (95% CI 1·39–2·47) when compared to S gene-negative cases, after adjusting for age, sex, deprivation, temporal trend, and comorbidities. A greater number of COVID-19 relevant comorbidities increased the risk of COVID-19 hospital admission (appendix p 3).

Overall, a strong vaccine effect did not clearly manifest until at least 28 days after the first vaccine dose (HR 0·32, 95% CI 0·22–0·46; appendix p 3). Among S gene-negative cases, the effect of vaccination (at least 28 days after first or second dose) was to reduce the risk of hospital admission (HR 0·28, 95% CI 0·18–0·43) compared to unvaccinated. The corresponding hazard ratio for risk of hospital admission for S gene-positive cases was 0·38 (95% CI 0·24–0·58), with an interaction test p value of 0·19, suggesting that there was no evidence of a differential vaccine effect on


Andrew Milligan/Getty Images

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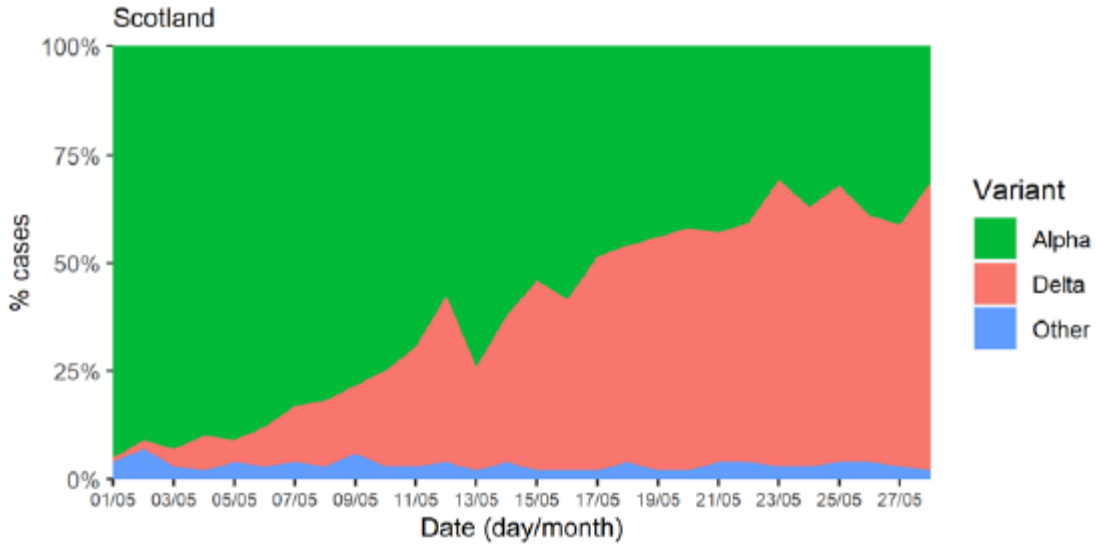
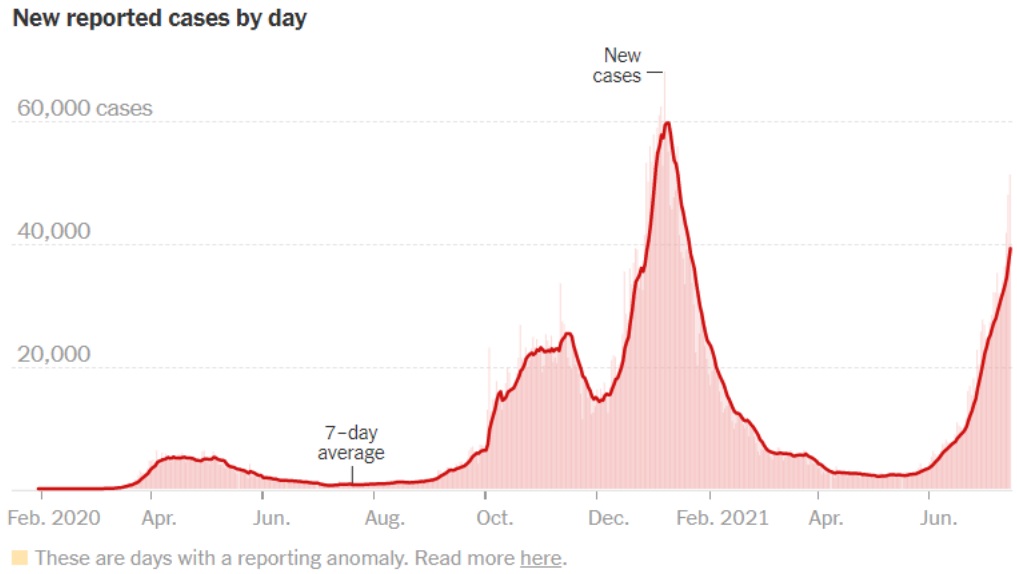
https://doi.org/10.1016/S0140-6736(21)01358-1

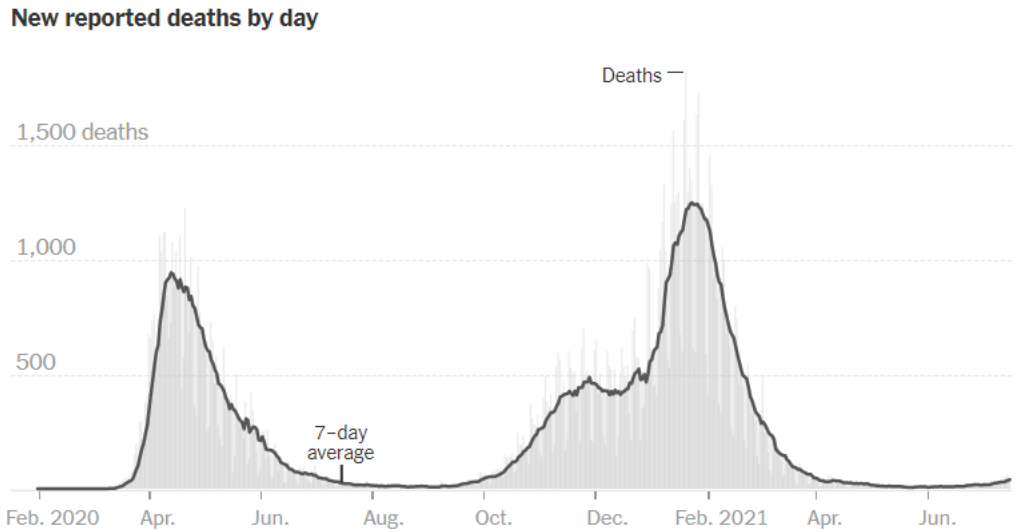
See Online for appendix



Delta "*cases were associated with an increased risk of COVID-19 hospital admission: hazard ratio (HR) 1·85 (95% CI 1·39–2·47)*"

Hospitalization/death rates have remained low in England



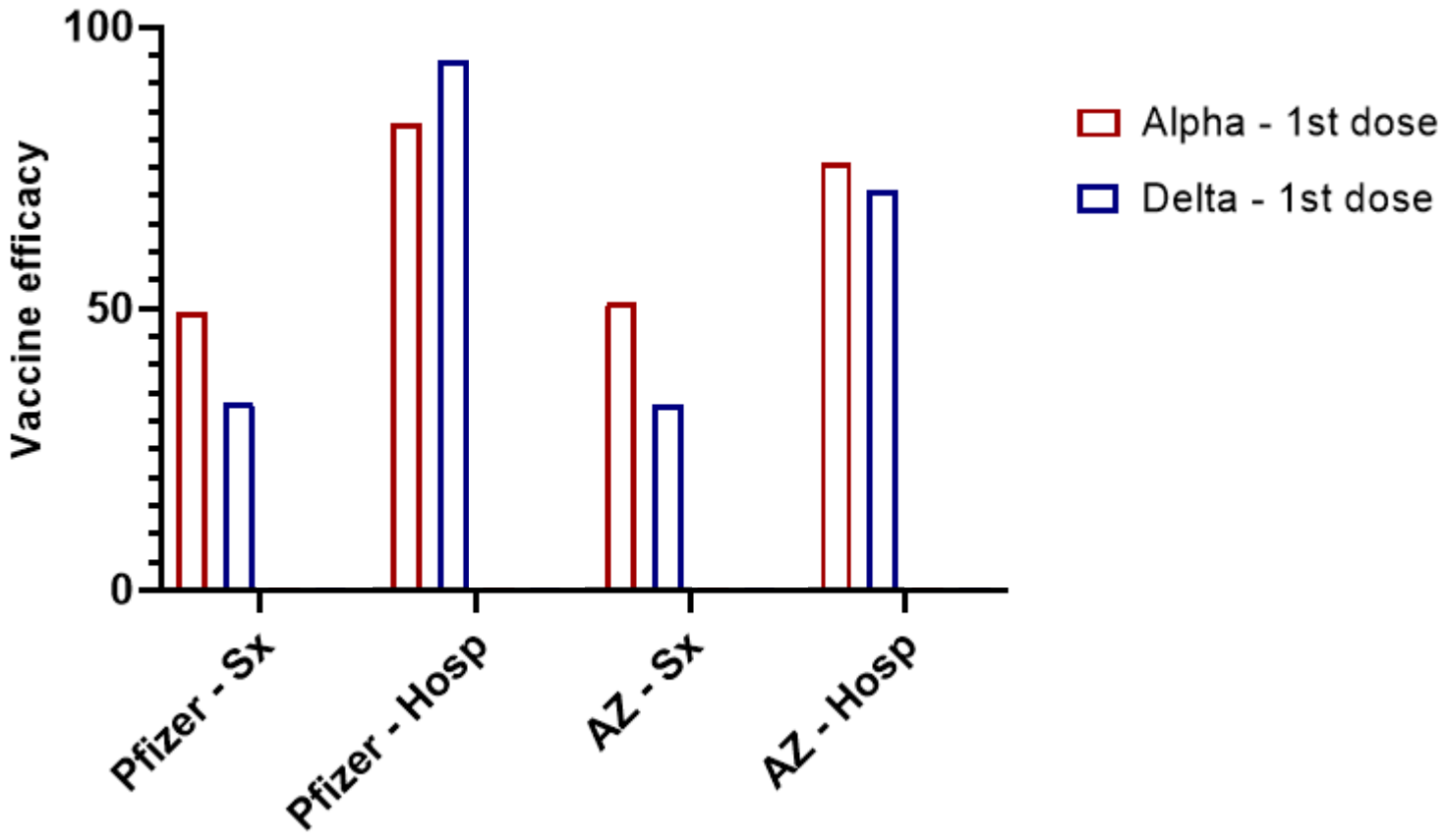


New York Times

Predicted activity of variants vs monoclonal antibodies

	Bamlanivimab/ Etesevimab	Casirivimab/ Imdevimab	Sotrovimab
Alpha (B.1.1.7)	✓	✓	✓
Beta (B.1.351)	✗	✓	✓
Gamma (P.1)	✗	✓	✓
Delta (B.1.617.2)	✓	✓	✓

Vaccines Maintain Robust Protection vs Delta



Public Health England
Bernal, medRxiv 2021; Stowe 2021

The Latest on Vaccines & Immunity to SARS-CoV-2

Varun Phadke, MD
Assistant Professor of Medicine
Division of Infectious Diseases
Emory University School of Medicine

COVID-19 Real-Time Learning Network
Brought to you by CDC and IDSA

EMORY UNIVERSITY SCHOOL OF MEDICINE

Disclosures

- I am Associate Editor of the Vaccines & Immunity section of the IDSA COVID-19 Real-Time Learning Network

Objectives

- Describe evidence for **natural immunity** following SARS-CoV-2 infection

- Discuss available evidence **comparing natural and vaccine-induced** immunity to SARS-CoV-2

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Natural Immunity to SARS-CoV-2

Immune Responses

- Immune responses to SARS-CoV-2 following natural infection can persist for months (maximum follow-up time is ~11 months)[1-3]

- Magnitude/longevity of immune responses correlate with severity of initial SARS-CoV-2 infection[3]

- Neutralizing antibody responses in previously infected individuals against novel VOC vary by disease severity[4]

[1]Science. 2021 Feb 5;371(6529):eabf4063
[2]Nature. 2021 Jul;595(7867):421-425
[3]https://www.medrxiv.org/content/10.1101/2021.04.19.21255739v2
[4]https://www.medrxiv.org/content/10.1101/2021.05.26.21257441v1

Natural Immunity to SARS-CoV-2

Observational Studies

- Prior infection with SARS-CoV-2 (assessed by antibody or PCR test result) associated with a decreased risk of subsequent infection in multiple countries
  - USA
  - UK
  - Denmark
  - Italy
  - France
  - Switzerland
  - Qatar

>80% protective effect across studies

Author/Year	Location	Prior Infection?	Time Period of Prior Infection	Time Period of Follow-Up
Sheehan/2021	USA	PCR	March-August 2020	June 2020-February 2021
Letizia/2021	USA	Antibody	May-November 2020	May-December 2020
Harvey/2021	USA	Antibody	January-August 2020	January-August 2020
Rennert/2021	USA	PCR	August-October 2020	December 2020-May 2021
Lumley/2021	UK	Antibody	April-November 2020	April-November 2020
Hall/2021	UK	Antibody/PCR	June-December 2020	June 2020-January 2021
Lumley/2021	UK	Antibody	April 2020-February 2021	Sept 2020-February 2021
Hansen/2021	Denmark	PCR	March-May 2020	September-December 2020
Vitale/2021	Italy	PCR	February-July 2020	May 2020-February 2021
Manica/2021	Italy	Antibody	May 2020	June 2020-January 2021
Dimeglio/2021	France	Antibody	June-July 2020	November-December 2020
Leidi/2021	Switzerland	Antibody	April-June 2020	April 2020-January 2021
Abu-Raddad/2020	Qatar	PCR	February-August 2020	April-August 2020
Bertollini/2021	Qatar	PCR	Before November 2020	February-April 2021

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Abu-Raddad/2020	Qatar	PCR	February-August 2020	April-August 2020
Bertollini/2021	Qatar	PCR	Before November 2020	February-April 2021

Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study

Christian Holm Hansen, Daniela Michlmayr*, Sophie Madeleine Gubbels, Kåre Mølbak, Steen Ethelberg*

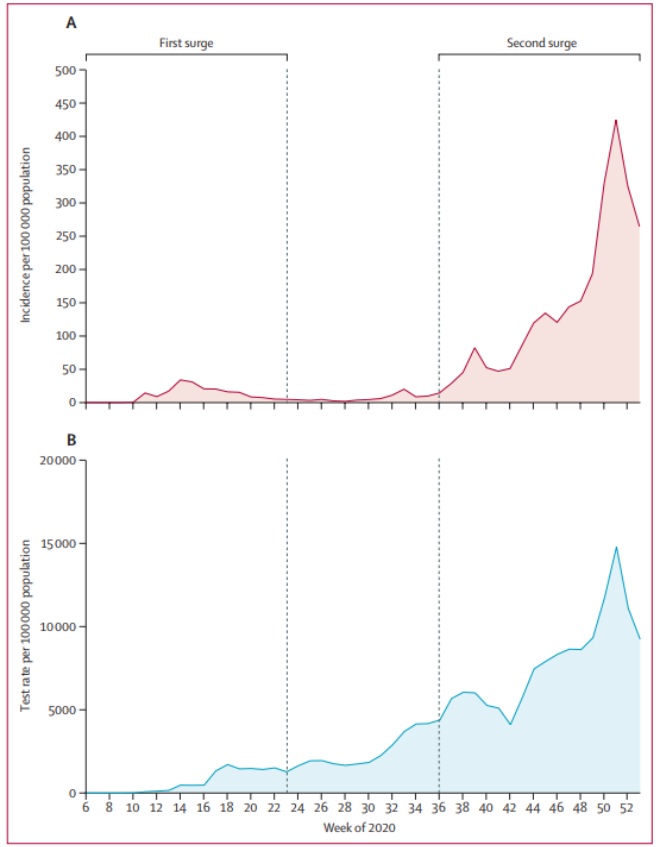

Figure 1: **Weekly incidence of PCR-confirmed SARS-CoV-2 (A) and test rate (B) in Denmark over 2020**
Data are presented per 100 000 population between Feb 3 (week 6) and Dec 31 (week 53), 2020.

	Number of infections during follow-up		Infection rate*		Adjusted rate ratio (95% CI)†	Estimated protection (95% CI)	p value‡
	Exposed individuals	Unexposed individuals	Exposed individuals	Unexposed individuals			
Overall	138	53 991	5·64	30·94	0·212 (0·179–0·251)	78·8% (74·9–82·1)	..
Sex							
Female	78	30 225	5·68	30·87	0·209 (0·167–0·261)	79·1% (73·9–83·3)	0·84
Male	60	23 766	5·59	31·03	0·216 (0·168–0·279)	78·4% (72·1–83·2)	..
Age group, years							
0–34	49	26 829	5·92	38·13	0·173 (0·131–0·229)	82·7% (77·1–86·9)	<0·0001
35–49	32	12 071	5·16	31·92	0·199 (0·141–0·282)	80·1% (71·8–85·9)	..
50–64	26	10 111	4·25	27·42	0·187 (0·127–0·274)	81·3% (72·6–87·3)	..
≥65	31	4980	8·01	16·92	0·529 (0·372–0·753)	47·1% (24·7–62·8)	..
Time in follow-up, months							
3–6	84	37 357	5·57	27·28	0·207 (0·167–0·256)	79·3% (74·4–83·3)	0·67
≥7	54	16 634	2·66	14·48	0·223 (0·171–0·291)	77·7% (70·9–82·9)	..

*Rate of infection per 100 000 person-days of follow-up. †Adjusted for sex, age group, test frequency, and start month of follow-up. ‡p value from likelihood ratio tests comparing models with and without interaction terms to capture evidence of effect heterogeneity across subgroups.

Table 2: **Protection against reinfection with SARS-CoV-2 by sex, age group, and time since first infection, in the alternative cohort analysis**

Lancet. 2021 Mar 27;397(10280):1204-1212

Author/Year	Location	Prior Infection?	Time Period of Prior Infection	Time Period of Follow-Up
Sheehan/2021	USA	PCR	March-August 2020	June 2020-February 2021
Letizia/2021	USA	Antibody	May-November 2020	May-December 2020
Harvey/2021	USA	Antibody	January-August 2020	January-August 2020
Rennert/2021	USA	PCR	August-October 2020	December 2020-May 2021
Lumley/2021	UK	Antibody	April-November 2020	April-November 2020
Hall/2021	UK	Antibody/PCR	June-December 2020	June 2020-January 2021
Lumley/2021	UK	Antibody	April 2020-February 2021	Sept 2020-February 2021
Hansen/2021	Denmark	PCR	March-May 2020	September-December 2020
Vitale/2021	Italy	PCR	February-July 2020	May 2020-February 2021
Manica/2021	Italy	Antibody	May 2020	June 2020-January 2021
Dimeglio/2021	France	Antibody	June-July 2020	November-December 2020
Leidi/2021	Switzerland	Antibody	April-June 2020	April 2020-January 2021
Abu-Raddad/2020	Qatar	PCR	February-August 2020	April-August 2020
Bertollini/2021	Qatar	PCR	Before November 2020	February-April 2021

Author/Year	Location	Prior Infection?	Time Period of Prior Infection	Time Period of Follow-Up
Sheehan/2021	USA	PCR	March-August 2020	June 2020-February 2021
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Rennert/2021	USA	PCR	August-October 2020	December 2020-May 2021
Lumley/2021	UK	Antibody	April-November 2020	April-November 2020
Hall/2021	UK	Antibody/PCR	June-December 2020	June 2020-January 2021
Lumley/2021	UK	Antibody	April 2020-February 2021	Sept 2020-February 2021
Hansen/2021	Denmark	PCR	March-May 2020	September-December 2020
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Leidi/2021	Switzerland	Antibody	April-June 2020	April 2020-January 2021
Abu-Raddad/2020	Qatar	PCR	February-August 2020	April-August 2020
Bertollini/2021	Qatar	PCR	Before November 2020	February-April 2021

Follow-up period in highlighted studies included time when VOC (mostly Alpha/B.1.1.7) had become predominant

Author/Year	Location	Prior Infection?	Time Period of Prior Infection	Time Period of Follow-Up
Sheehan/2021	USA	PCR	March-August 2020	June 2020-February 2021
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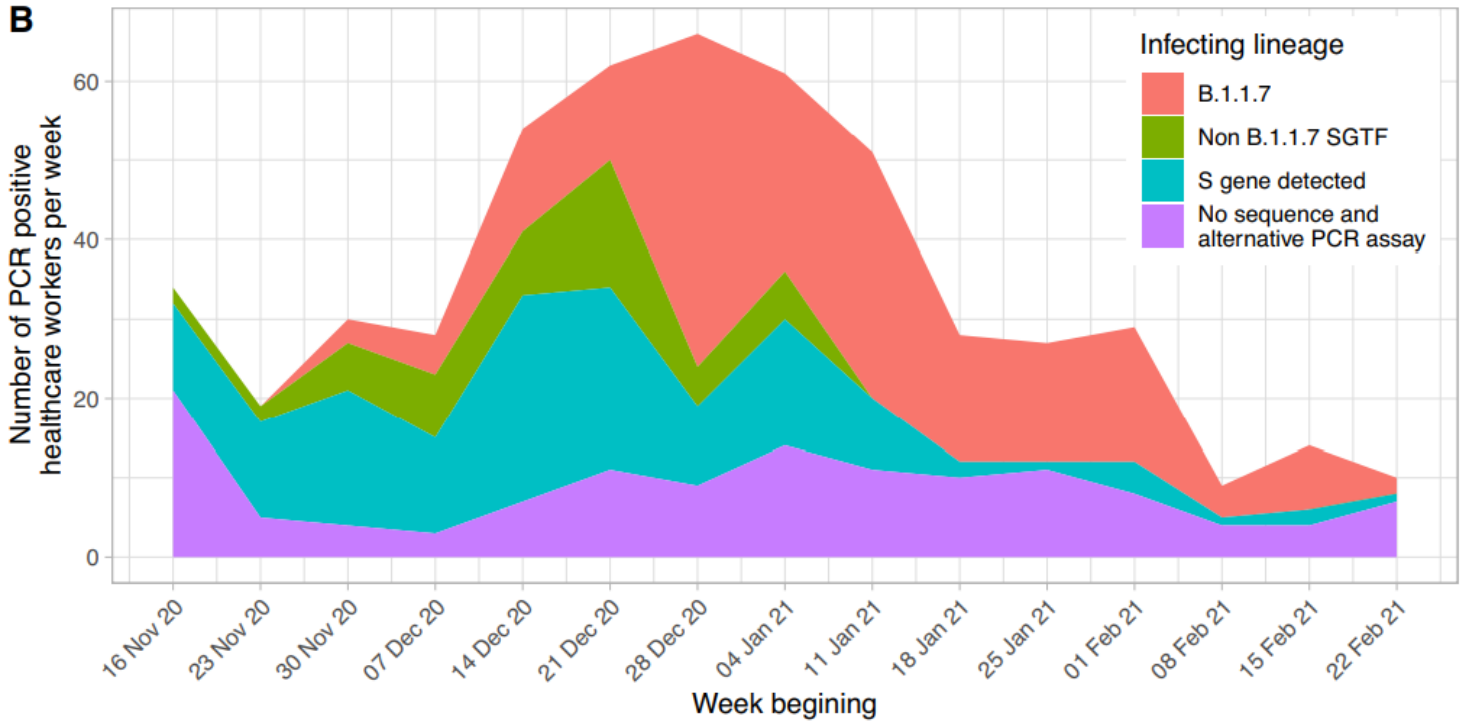
Abu-Raddad/2020	Qatar	PCR	February-August 2020	April-August 2020
Bertollini/2021	Qatar	PCR	Before November 2020	February-April 2021

An observational cohort study on the incidence of SARS-CoV-2 infection and B.1.1.7 variant infection in healthcare workers by antibody and vaccination status

Sheila F Lumley[1,2,3,4], Gillian Rodger[2] , Bede Constantinides[2], Nicholas Sanderson[2,3], Kevin K Chau[2], Teresa L Street[2,3], Denise O'Donnell[2], Alison Howarth[2], Stephanie B Hatch[2], Brian D Marsden[2,5], Stuart Cox[1], Tim James[1], Fiona Warren[1], Liam J Peck[6], Thomas G Ritter[6], Zoe de Toledo[6], Laura Warren[1], David Axten[1], Richard J Cornall[2], E Yvonne Jones[2], David I Stuart[2], Gavin Screaton[2], Daniel Ebner[2,7], Sarah Hoosdally[2,3,4], Meera Chand[8], Oxford University Hospitals Staff Testing Group, Derrick W Crook[2,3,4], Anne-Marie O'Donnell[1,9], Christopher P Conlon[2], Koen B Pouwels[4,9], A Sarah Walker[2,3,4], Tim EA Peto[2,3,4], Susan Hopkins[8], Timothy M Walker[2,10], Nicole E Stoesser[1,2,3,4], Philippa C Matthews[1,2,3,4], Katie Jeffery[1], David W Eyre[3,4,9,11], on behalf of the Oxford University Hospitals Staff Testing Group*



"There was no evidence that B.1.1.7 changed the extent of protection from any PCR positive infection in those who were seropositive"

Clin Infect Dis. 2021 Jul 3:ciab608

Natural Immunity to SARS-CoV-2

Observational Studies

- Prior infection with SARS-CoV-2 (assessed by antibody or PCR test result) associated with a decreased risk of subsequent infection in multiple countries

- Limitations
  - Ecological studies of reinfection have largely not stratified analyses by variables that may impact the magnitude/duration of immunity
  - Protective effect of prior infection against reinfection during periods of increased VOC circulation remains poorly characterized

Objectives

- Describe evidence for **natural immunity** following SARS-CoV-2 infection

- Discuss available evidence **comparing natural and vaccine-induced** immunity to SARS-CoV-2

Natural vs. Vaccine-Induced Immunity

Immune Responses

- mRNA-1273 vaccine-elicited antibodies bind more broadly across SARS-CoV-2 spike receptor binding domain (RBD) than convalescent sera[1]
  - Neutralizing activity less susceptible to single RBD mutations

- Reduced **but preserved** neutralizing antibody titers against Alpha/B.1.1.7 and Beta/B.1.351 in recipients of two doses of BNT162b2[2]
  - 40% of HCWs with a history of mild COVID-19 had no neutralizing antibodies

- Similar neutralizing antibody titers against VOC (Alpha/B.1.1.7, Beta/B.1.351, Gamma/P.1) among BNT162b2 vaccinees and previously hospitalized COVID-19 patients[3]
  - 39% of patients with mild COVID-19 had no neutralizing antibodies against B.1.351

[1]Sci Transl Med. 2021 Jun 30;13(600):eabi9915
[2]Clin Infect Dis. 2021 May 29:ciab492
[3]https://www.medrxiv.org/content/10.1101/2021.05.26.21257441v1

Natural vs. Vaccine-Induced Immunity

Observational Studies

- Few studies have directly compared the incidence of infection in seropositive and vaccinated individuals in the same population over the same follow-up period

- In three studies (2 published, 1 pre-print), the protective effect of prior infection was similar to 2 doses of a COVID-19 vaccine*[1-3]
  - Two studies of **HCWs** (USA and UK), one of **returning air travelers** (Qatar)

*mRNA-1273, BNT162b2, and ChAdOx1

[1]JAMA. 2021 Jul 13;326(2):185-188
[2]Clin Infect Dis. 2021 Jul 3:ciab608
[3]https://www.medrxiv.org/content/10.1101/2021.06.01.21258176v2

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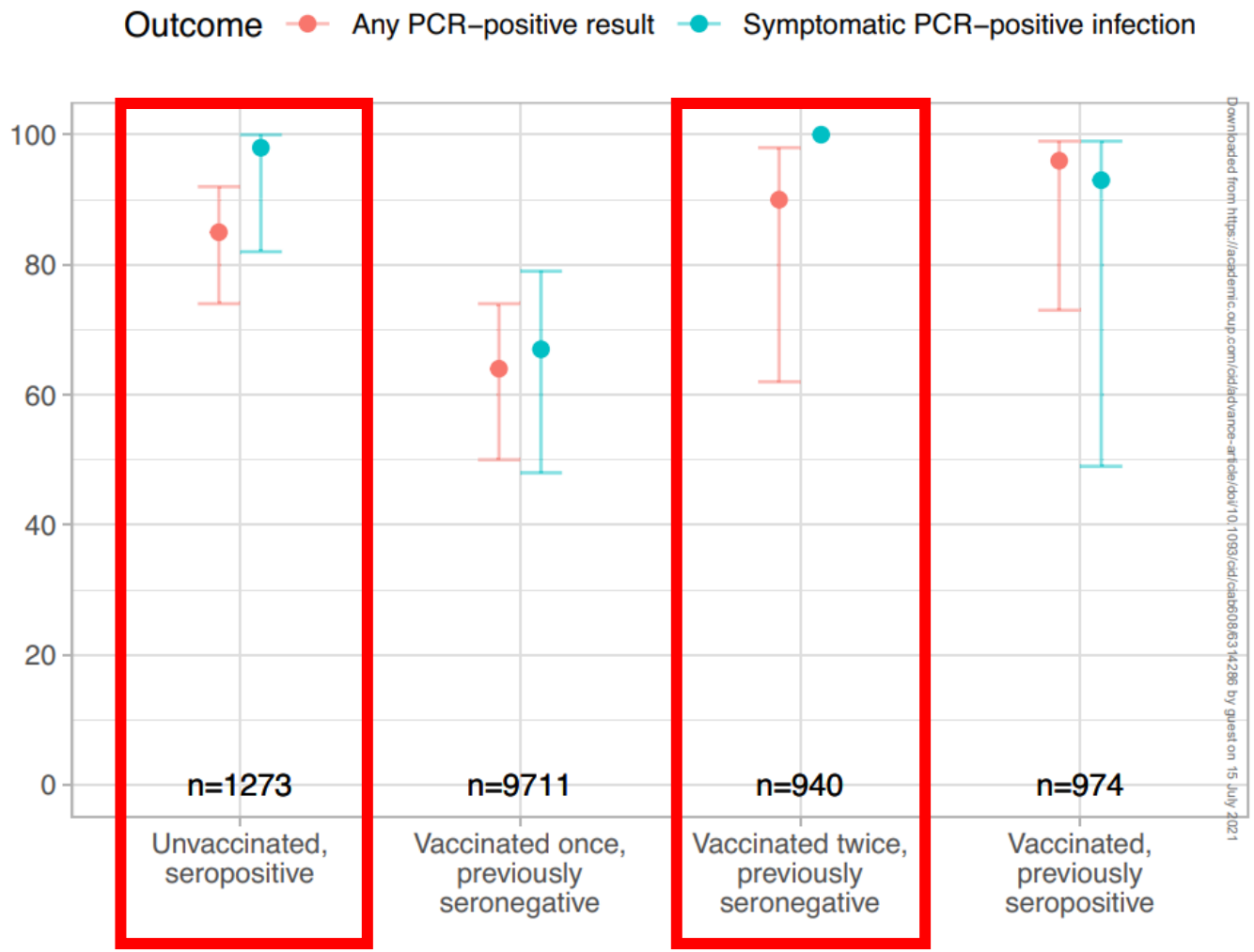
Percent protection from infection

(vs. unvaccinated seronegative individuals)



Clin Infect Dis. 2021 Jul 3:ciab608

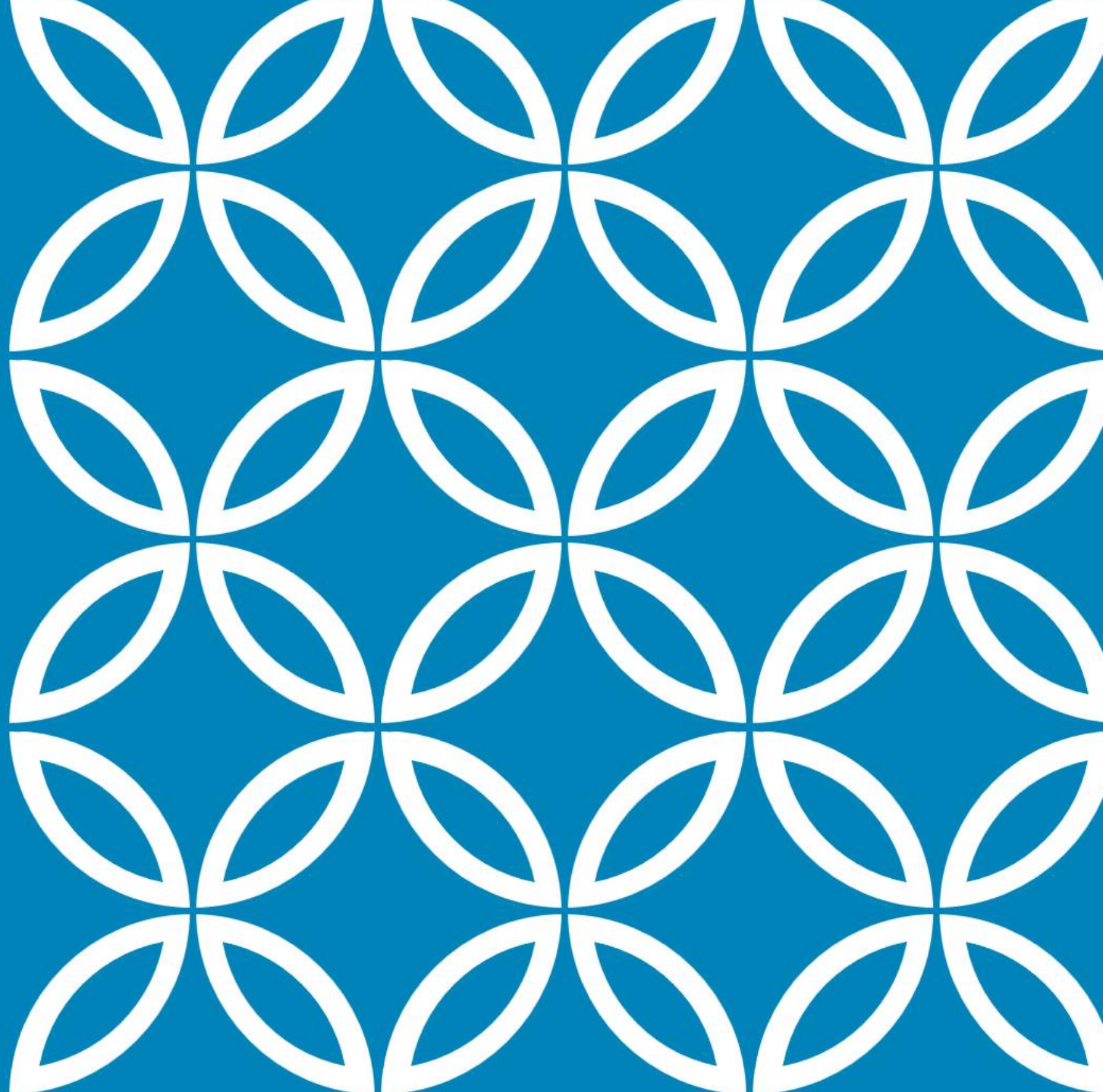
Summary

- Immune responses to SARS-CoV-2 following natural infection can persist for at least 11 months
  - Magnitude/durability of this response may vary by age, disease severity, etc.
- Natural infection (as determined by a prior positive antibody or PCR-test result) can confer protection against SARS-CoV-2 infection
  - Most observational studies have not stratified analyses by key covariates
  - Protective effect of prior infection against VOC remains uncertain
- Comparative protective effect of natural infection and vaccination remains poorly characterized
  - vaccination appears to elicit higher quality antibody response

COVID-19 SEROLOGY TESTS – WHAT CAN THEY TELL ABOUT IMMUNITY AND PROTECTION

July 2021

Tim Stenzel, MD, PhD
Director
Office of In Vitro Diagnostics and Radiological Health
U.S. Food & Drug Administration



EUA LAW AND SEROLOGY INTENDED USE

- Federal Food, Drug, and Cosmetic Act section 564(b)(1)(C):
  - "…the known and potential benefits of the device when used for that purpose outweigh the known and potential risks of the device."
- SARS-CoV-2 serology intended use statements:
  - "an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection."

COVID-19 SEROLOGY TESTS OVERVIEW

85 Serology tests including

- 11 Point-of-care
- 1 Neutralizing antibody test
- 1 Quantitative
- 16 Semi-quantitative

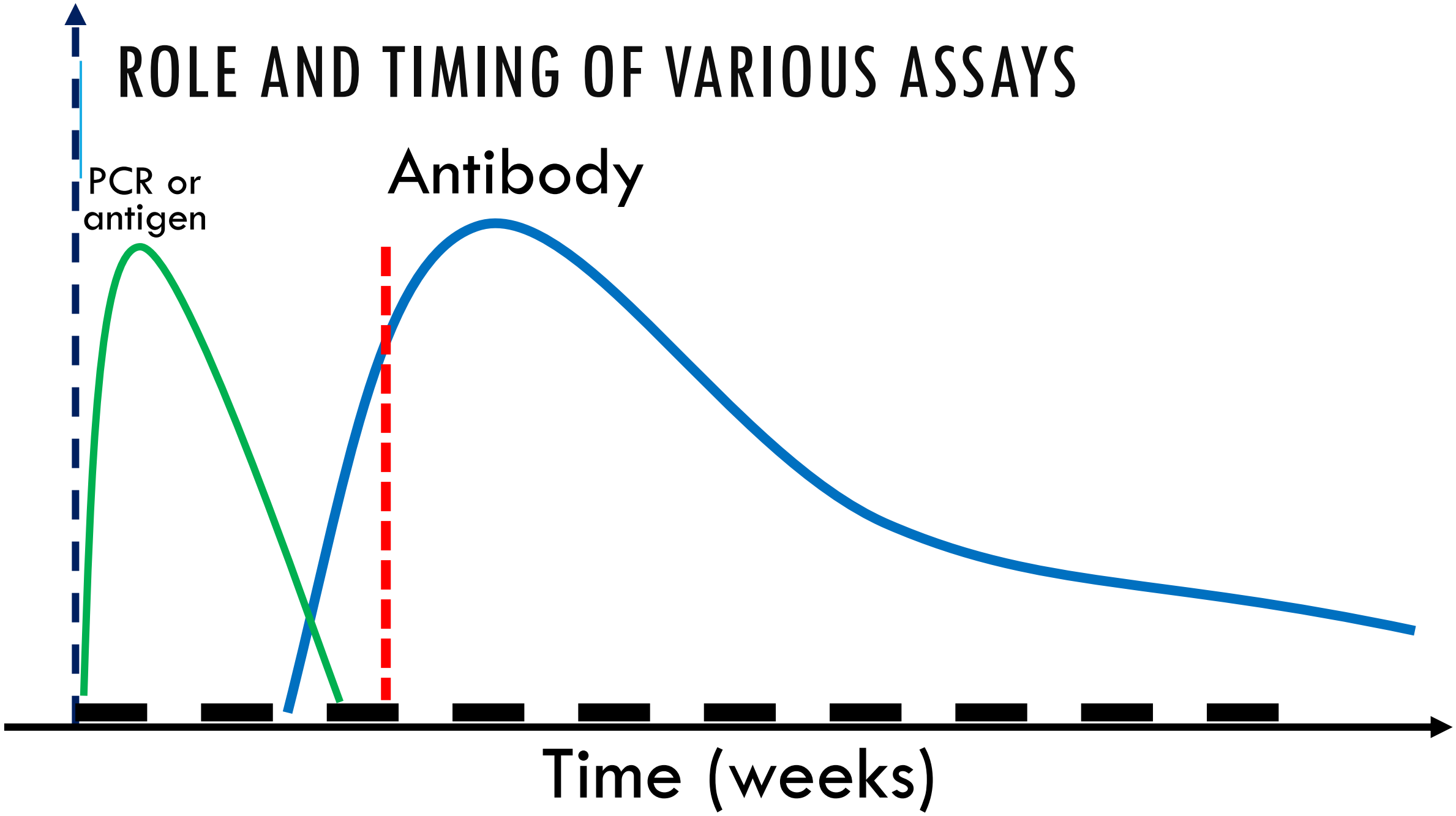
COVID-19 NEUTRALIZING ANTIBODY TESTS

- Currently authorized: cPass SARS-CoV-2 Neutralization Antibody Detection Kit
- Available template: Template for Test Developers of Serology Tests that Detect or Correlate to Neutralizing Antibodies

QUANTITATIVE SEROLOGY TESTS FOR COVID-19

- Currently authorized: One (Ortho-Clinical)
- Available template: not at this time, recommendations communicated upon request
- De novo/510(k): traceability to a national or international certified reference material (CRM)
  - Calibrators
  - Analytical sensitivity
    - Cutoff sensitivity study
    - Recovery Linearity
    - Regression analysis

ROLE AND TIMING OF VARIOUS ASSAYS



ANTIBODY TESTS FOR OTHER VACCINES

WHERE DOES SARS-COV-2 FIT ON THIS SCALE?

HIV

Syphilis

Hepatitis C virus

? Tetanus ?

? Pertussis ?

? Influenza ?

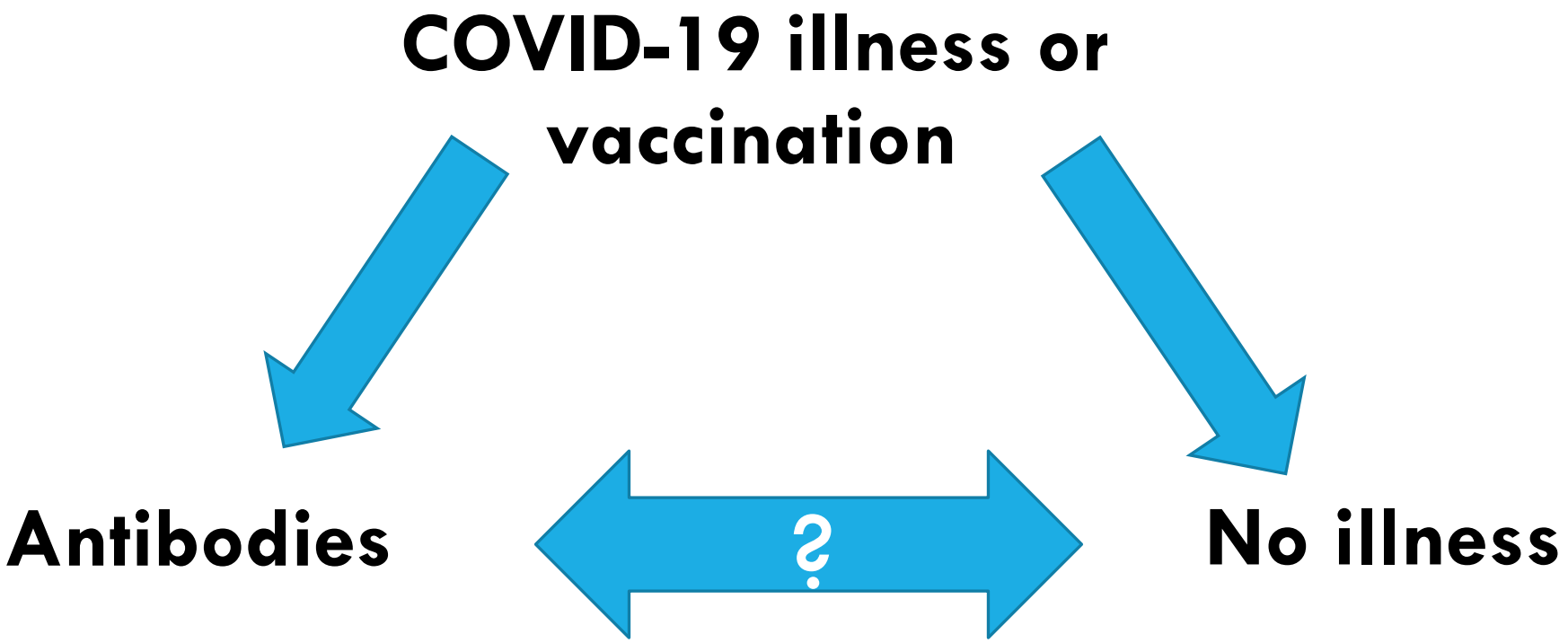
Hepatitis A virus*

Hepatitis B virus*

Rubella*

* FDA has authorized vaccination and/or immunity claims. They are traceable to international standards, and sterilizing levels of antibodies are known in each case.

WHAT WE KNOW



WHAT WE NEED

- Use of antibody tests that are traceable to a standardized reference material – FDA has authorized the first such test
  - Results need to be comparable for different tests
- Is there a correlation of antibodies to protection from infection?
- What is that antibody concentration?
  - Longitudinal patient follow-up studies
- Serology test results may not tell an individual anything about protection from reinfection.

ONGOING STUDIES

- NCT04373148
- NCT04377724
- NCT04494893
- NCT04329546
- NCT04365166
- NCT04385108
- NCT04431414
- NCT04448145
- NCT04620798
- NCT04653844
- NCT04498286
- NCT04528901
- NCT04540484
- NCT04568044
- NCT04573348

FDA RECOMMENDATIONS

Antibody testing is not currently recommended to assess immunity to COVID-19 after a COVID-19 vaccination. Outcome data needed in people who have received a COVID-19 vaccination. While a positive antibody test result can be used to identify antibodies that are part of the body's immune response to SARS-CoV-2 infection, the correlate to a person's level of immunity or protection from COVID-19 have not been established at this time.

Since vaccines induce antibodies to specific viral protein targets, post-vaccination antibody test results will be negative in persons without history of previous natural infection if the test used does not detect the antibodies induced by the vaccine. Currently authorized SARS-CoV-2 antibody test data have not been evaluated to assess the level of protection provided by an immune response to COVID-19 vaccination. Health care providers considering antibody testing in vaccinated patients should follow the Centers for Disease Control and Prevention's guidelines for antibody testing.

FDA RESOURCES

- In Vitro Diagnostics EUAs
  - (templates with validation recommendations and authorized tests)
- Coronavirus Disease 2019 (COVID-19) Emergency Use Authorizations for Medical Devices
- FAQs on Testing for SARS-CoV-2
- Serology/Antibody Tests: FAQs on Testing for SARS-CoV-2

Q&A and Discussion

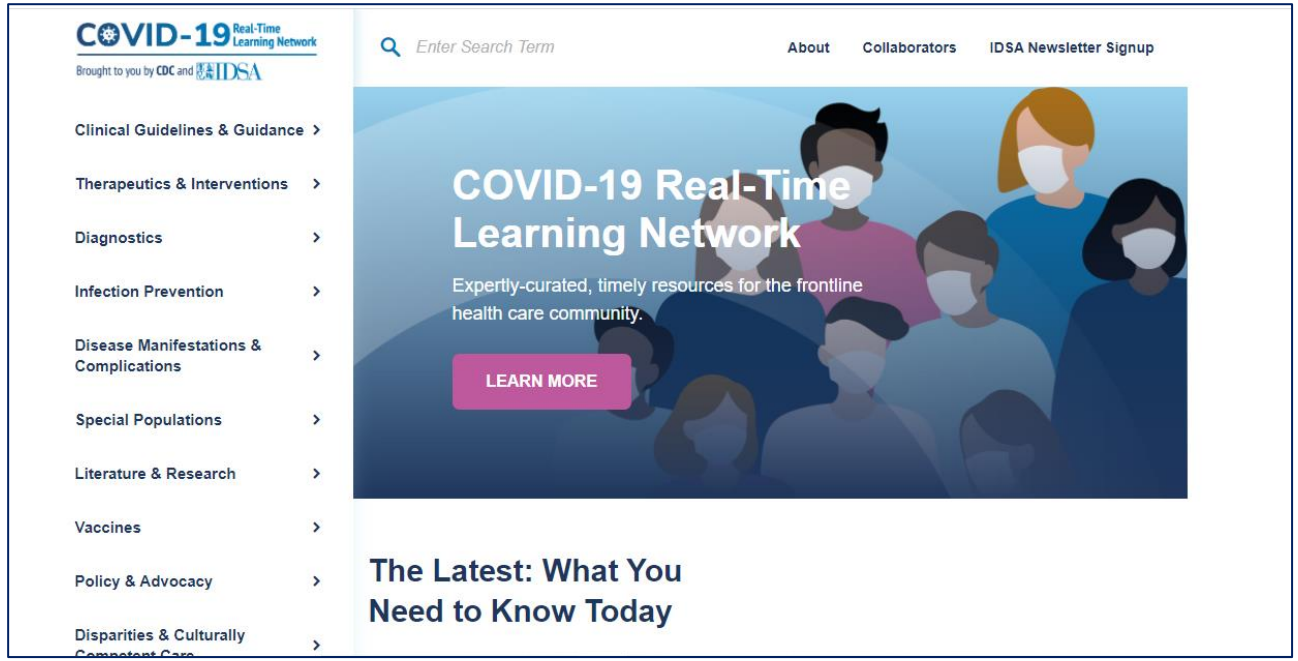
Links and Resources

- Slide 1 - https://www.idsociety.org/cliniciancalls
- Slide 5 - https://www.cdc.gov/coronavirus/2019-ncov/variants/cdc-role-surveillance.html
- Slide 5 - https://covid.cdc.gov/covid-data-tracker/#published-covid-sequences
- Slides 6, 7 & 8 - https://covid.cdc.gov/covid-data-tracker/#variant-proportions
- Slide 9 - https://www.cdc.gov/coronavirus/2019-ncov/images/communication/covid-datatracker/Vaccinations_By_Case_Rate_FINAL_07072021.pdf
- Slide 25 -https://www.medrxiv.org/content/10.1101/2021.04.19.21255739v2
  https://www.medrxiv.org/content/10.1101/2021.05.26.21257441v1
- Slide 36 - https://www.medrxiv.org/content/10.1101/2021.05.26.21257441v1
- Slide 37 - https://www.medrxiv.org/content/10.1101/2021.06.01.21258176v2
- Slide 50 - https://www.fda.gov/medical-devices/safety-communications/antibody-testing-not-currently-recommended-assess-immunity-after-covid-19-vaccination-fda-safety
  https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-serology-and-other-adaptive-immune-response-tests-sars-cov-2
  https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html
- Slide 51 - In Vitro Diagnostics EUA: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas
  Coronavirus Disease 2019 (COVID-19) Emergency Use Authorizations for Medical Devices: https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices
  FAQs on Testing for SARS-CoV-2: https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/faqs-testing-sars-cov-2
  Serology/Antibody Tests: FAQs on Testing for SARS-CoV-2: https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/serologyantibody-tests-faqs-testing-sars-cov-2
- Slide 54 - https://www.idsociety.org/covid-19-real-time-learning-network/
- Slide 55 - https://www.cdc.gov/cdc-info/
- Slide 56 – https://idweek.org/

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?

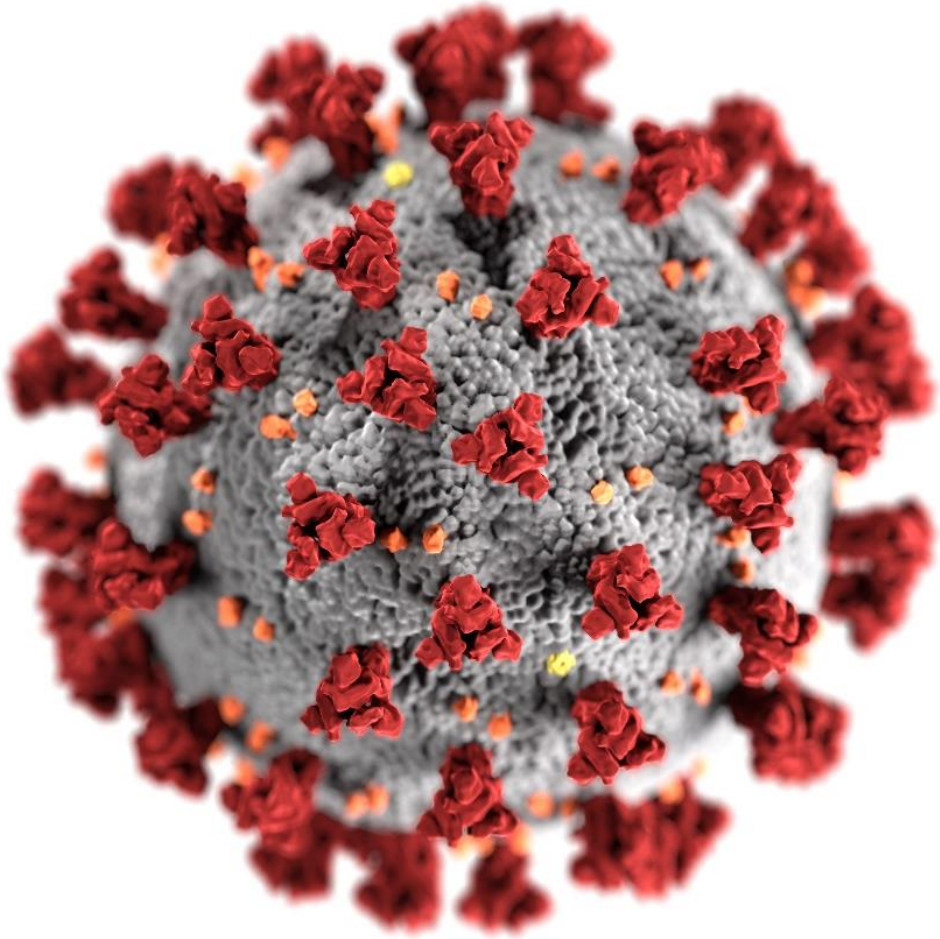
- Clinicians who have questions about the clinical management of COVID-19

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:

July 31

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)