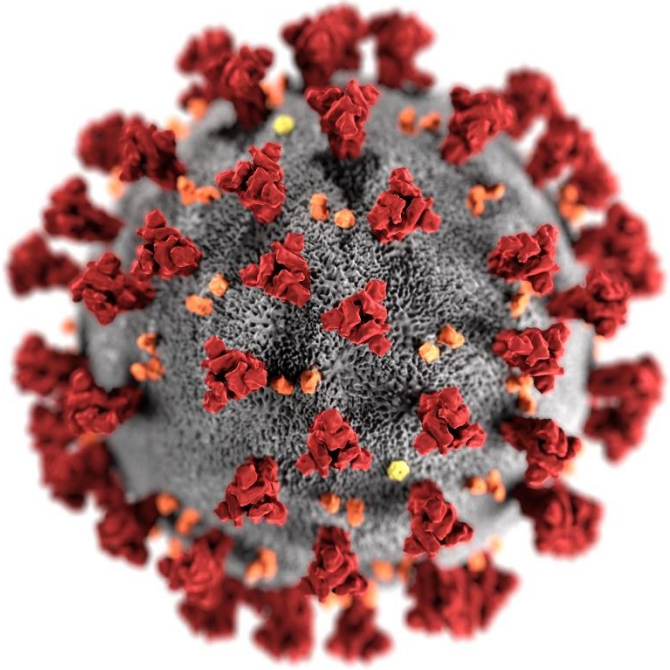
Update on Emerging SARS-CoV-2 Variants and Vaccine Considerations



CDR Heather Scobie PhD, MPH

ACIP Meeting

May 12, 2021

Background


DEPARTMENT OF HEALTH & HUMAN SERVICES • USA
CDC
Centers for Disease Control and Prevention

SARS-CoV-2 Variants

- Multiple SARS-CoV-2 variants circulating globally
  - Viruses constantly change through mutation, so new variants are expected
  - After emerging, some disappear; others persist
- CDC and others are studying these variants to understand whether they:
  - Spread more easily from person to person
  - Cause milder or more severe disease in people
  - Detected by available diagnostic tests
  - Respond to therapeutics currently used to treat people for COVID-19
  - Change effectiveness of COVID-19 vaccines

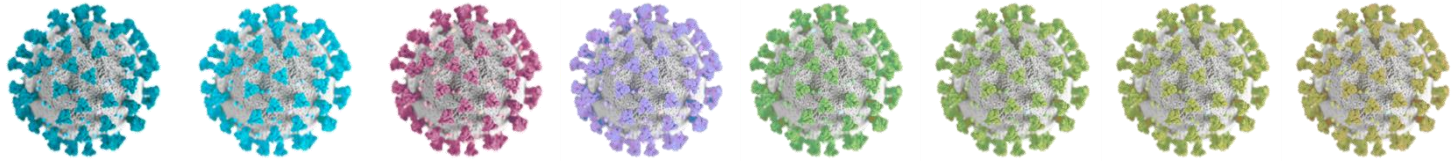
https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant.html

Variant Classifications

- Established in collaboration with the SARS-CoV-2 Interagency Group (SIG)
- **Variant of Interest (VOI):** Genetic markers associated with changes to receptor binding, reduced antibody neutralization, reduced efficacy of treatments, potential diagnostic impact, or predicted increase in transmissibility or disease severity
- **Variant of Concern (VOC)**: Evidence of increased transmissibility, more severe disease, significant reduction in neutralization by antibodies, reduced effectiveness of treatments or vaccines, or diagnostic detection failures
- **Variant of High Consequence (VOHC)**: Clear evidence that prevention measures or medical countermeasures have significantly reduced effectiveness **[None yet]**

SARS-CoV-2 Variants Classifications & Definitions | CDC

Variants of Interest

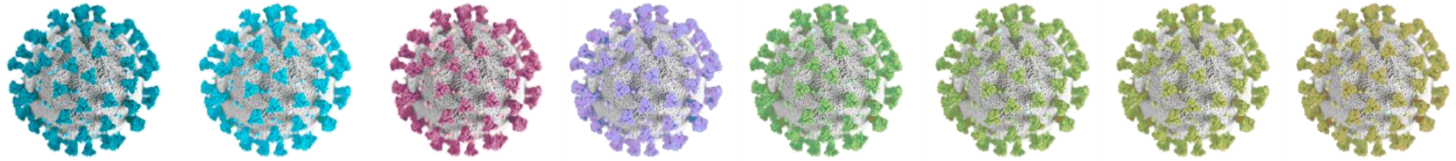


	B.1.526	B.1.526.1	B.1.525	P.2	B.1.617	B.1.617.1	B.1.617.2	B.1.617.3
First detected	New York	New York	UK/Nigeria	Brazil	India	India	India	India
No. of spike mutations	3-7	6-8	8	3-4	3	7-8	9-10	7
Receptor binding domain mutations	(S477N*) (E484K*)	L452R	E484K	E484K	L452R E484Q	L452R E484Q	L452R T478K	L452R E484Q
Attributes	• **Reduced** antibody efficacy • **Reduced** neutralization convalescent or vaccine sera	• Potential reduced antibody efficacy • Potential reduced neutralization by vaccine sera		• Potential reduced antibody efficacy • **Reduced** neutralization by vaccine sera	• Potential reduced antibody efficacy • **Reduced** neutralization by vaccine sera	• Potential reduced antibody efficacy • Potential reduced neutralization by vaccine sera		

SARS-CoV-2 Variants Classifications & Definitions | CDC

(*) = detected in some sequences but not all

Variants of Interest



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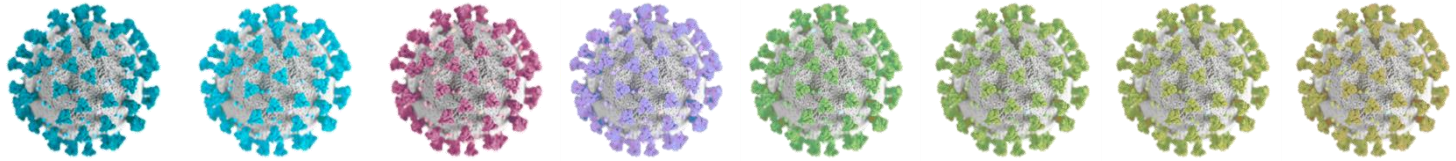

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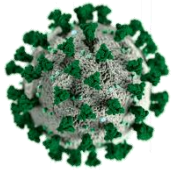
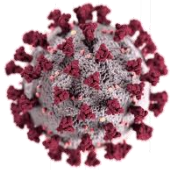
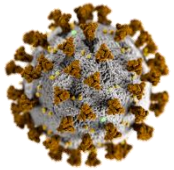
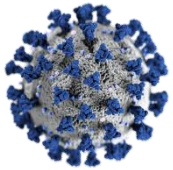
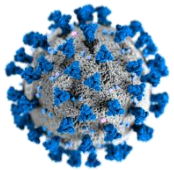
Variants of Concern

	B.1.1.7	B.1.351	P.1	B.1.427	B.1.429
First detected	United Kingdom	South Africa	Japan / Brazil	California	California
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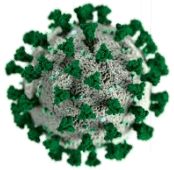
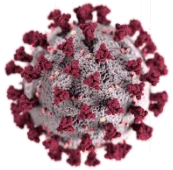
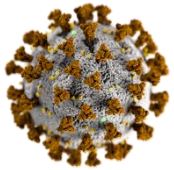
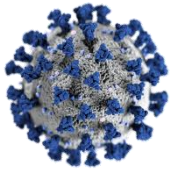
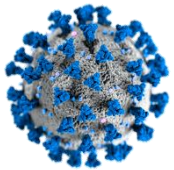
SARS-CoV-2 Variants Classifications & Definitions | CDC

Variants of Concern

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SARS-CoV-2 Variants Classifications & Definitions | CDC

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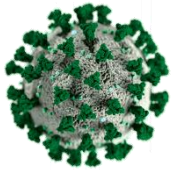
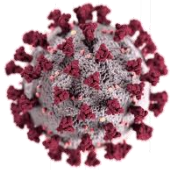
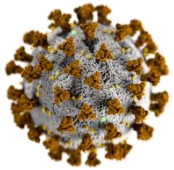
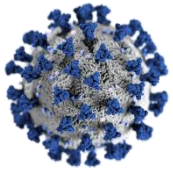
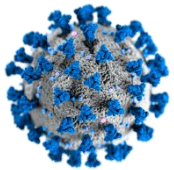

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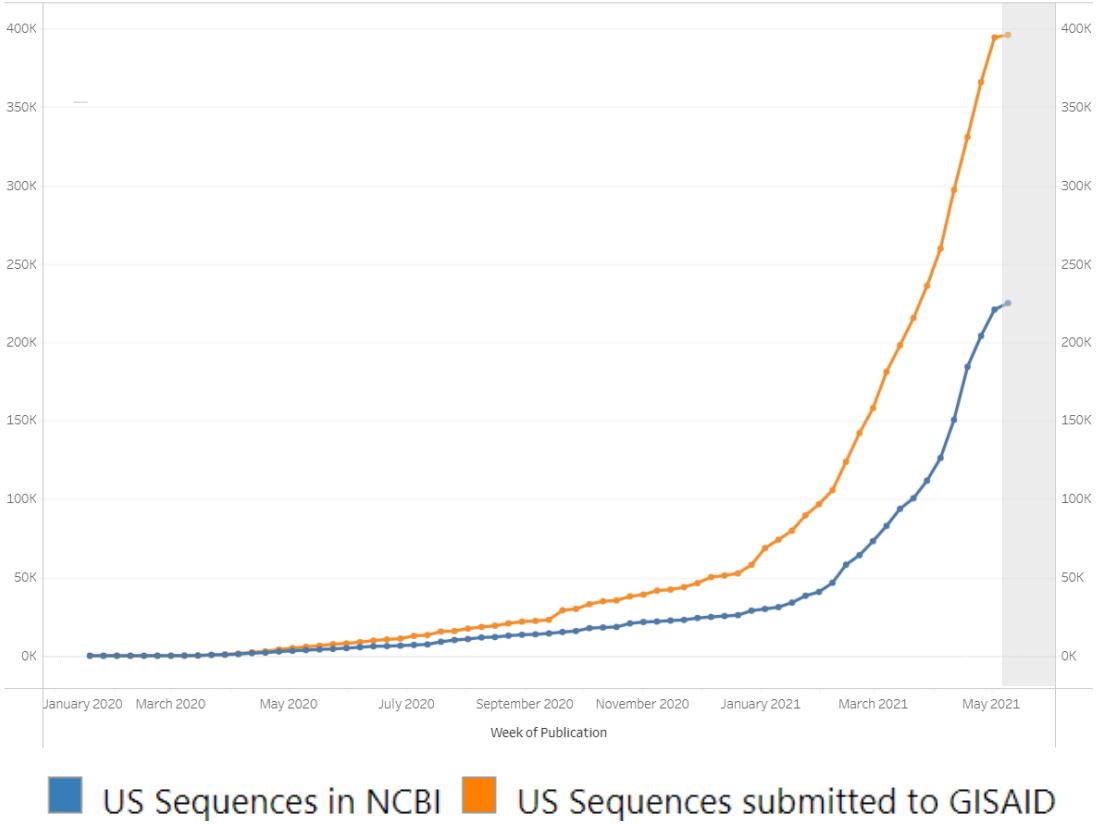
SARS-CoV-2 Variants Classifications & Definitions | CDC

Genomic Surveillance & Epidemiology of SARS-CoV-2 Variants

U.S. Sequences Available in Public Repositories

6%-9% of SARS-CoV-2 positive cases sequenced weekly



Data collection ongoing

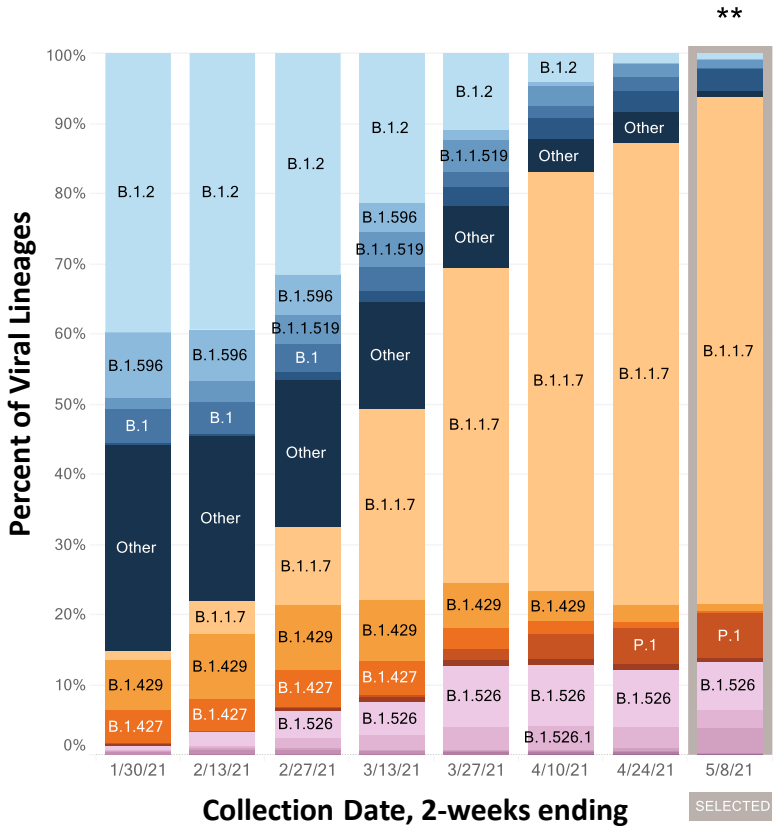
[CDC COVID Data Tracker](#)

As of 5/11/21

NCBI=National Center for Biotechnology Information; GISAID, a global initiative maintaining a repository of viral sequencing data

National SARS-CoV-2 Variant Proportions, United States

January 17 – May 8, 2021 with NOWCAST



VOC / VOI

B.1.1.7 72%

B.1.427/B.1.429 1%

P.1 6%

B.1.351 <1%

B.1.526 7%

B.1.526.1 3%

B.1.617.2 3%

Estimates for April 25-May 8, 2021

	Lineage	Type	%Total	95%PI
Most common lineages	B.1.1.7	VOC	72.4%	67.4-77.1%
	B.1.526	VOI	6.8%	4.2-9.6%
	P.1	VOC	6.2%	3.7-9.1%
	B.1.617.2	VOI	3.3%	1.4-5.7%
	B.1.526.2		3.1%	1.4-5.1%
	B.1.526.1	VOI	2.8%	1.1-4.5%
	B.1.1.519		1.2%	0.3-2.3%
	B.1.2		0.7%	0.0-1.7%
	B.1		0.3%	0.0-1.1%
	B.1.596		0.1%	0.0-0.6%
Additional VOI/VOC lineages	B.1.429	VOC	0.9%	0.0-2.0%
	B.1.351	VOC	0.6%	0.0-1.4%
	B.1.427	VOC	0.4%	0.0-1.1%
	B.1.525	VOI	0.2%	0.0-0.8%
	B.1.617.1	VOI	0.2%	0.0-0.6%
	P.2	VOI	0.0%	0.0-0.3%
	B.1.617.3	VOI	0.0%	0.0-0.3%
Other*	Other		0.8%	0.0-4.0%

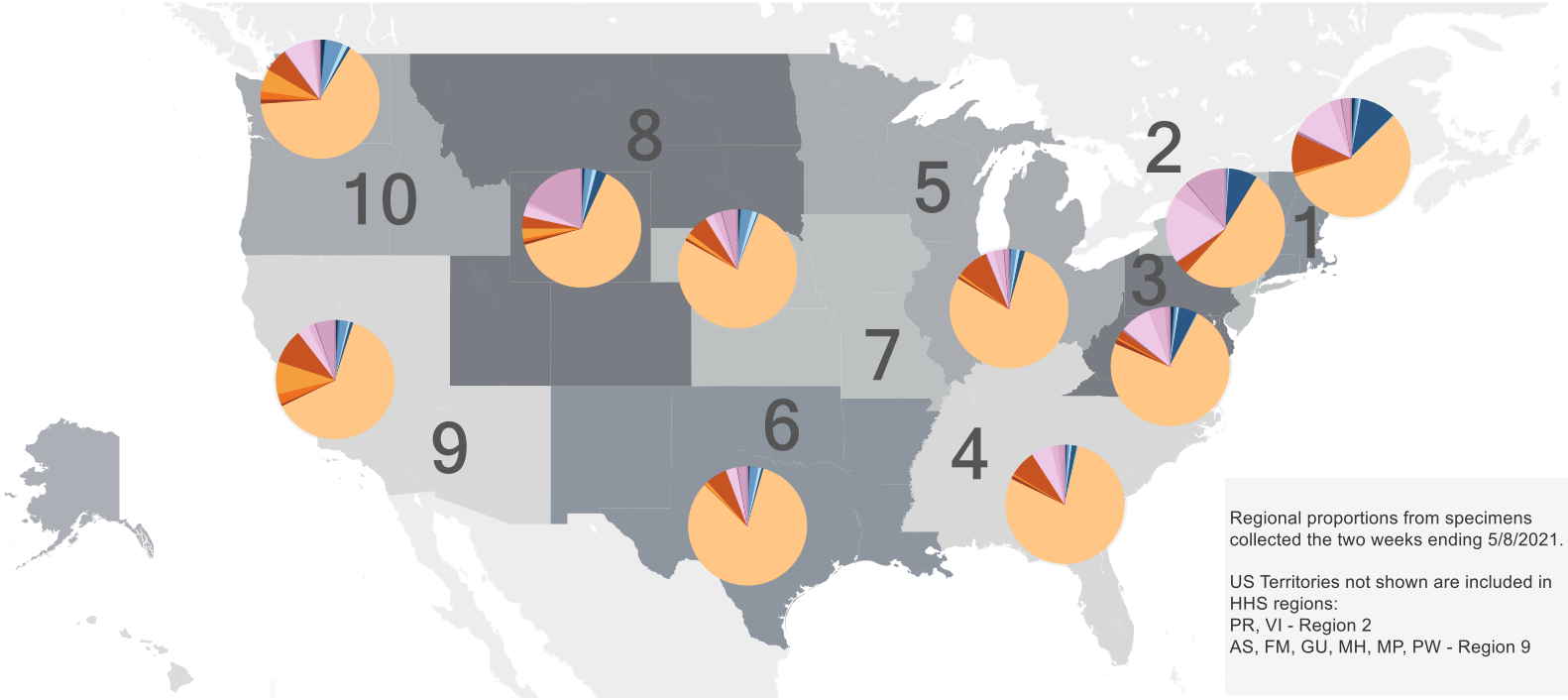
* Other represents >200 additional lineages, which are each circulating a <1% of viruses

** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates

CDC COVID Data Tracker As of 5/11/21; VOC=Variant of Concern; VOI=Variant of Interest

Regional SARS-CoV-2 Variant Proportions

April 25 – May 8, 2021 with NOWCAST



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Vaccine Effectiveness Against SARS-CoV-2 Variants

Vaccine-Induced Antibody Protection and Variants

- Robust correlation between vaccine efficacy (VE) versus:
  - Neutralizing titer (ρ= 0.79)
  - Binding antibody titer (ρ = 0.93)
- **Correlate of protection**, or threshold that protects against SARS-CoV-2, **not yet determined**
- Variants result in reduced protective antibody levels
  - Lower VE and increased breakthrough infection?
  - Shorter duration of immunity?

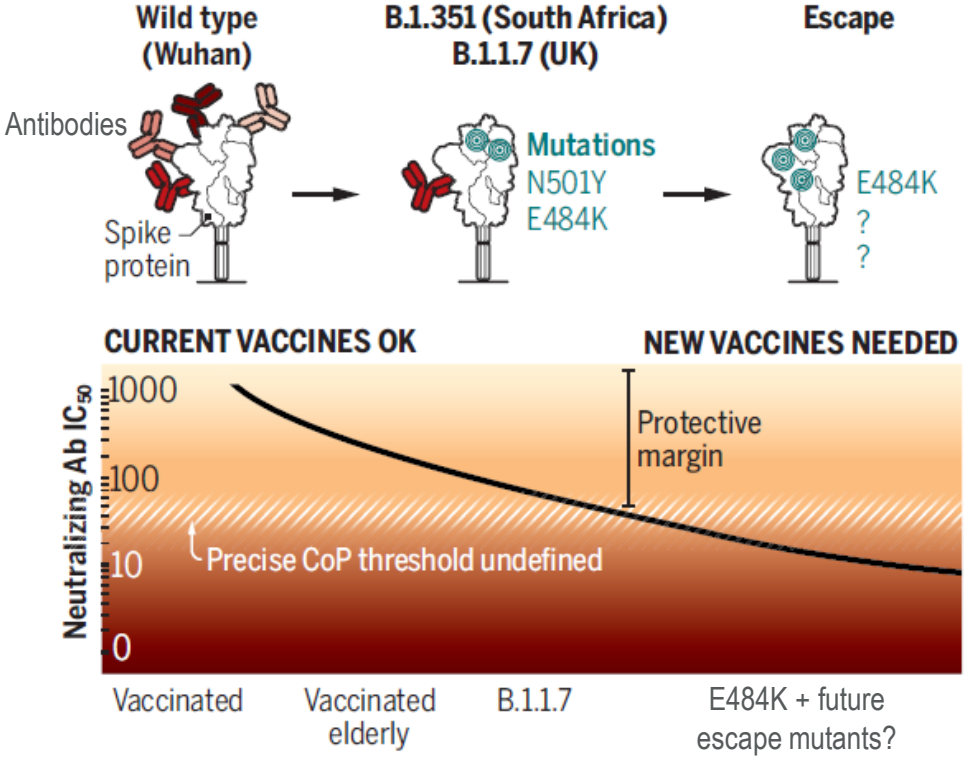

Figure Source: Altman et al (2021): https://science.sciencemag.org/content/371/6534/1103
Earle et al. medRxiv preprint (March 20, 2021): https://doi.org/10.1101/2021.03.17.20200246

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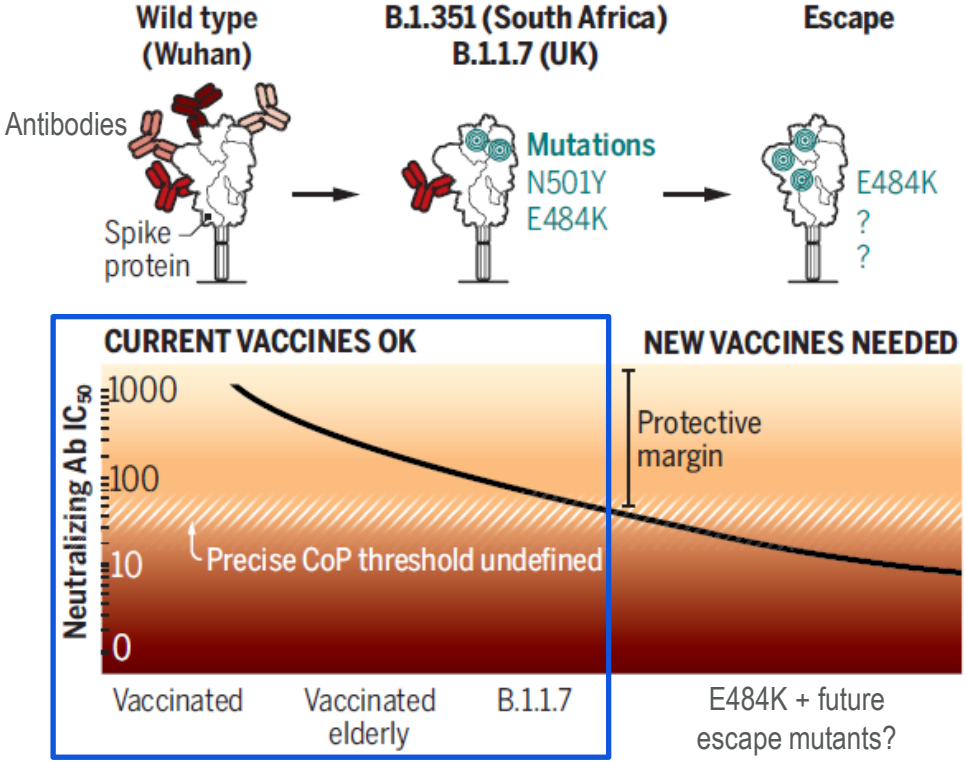

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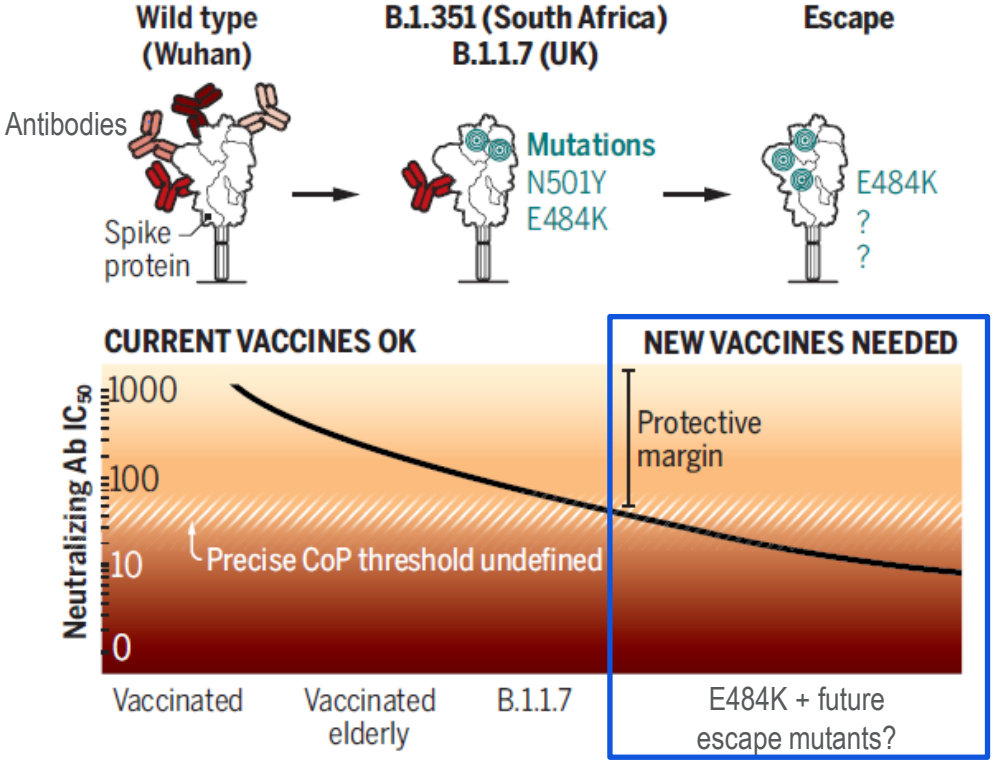

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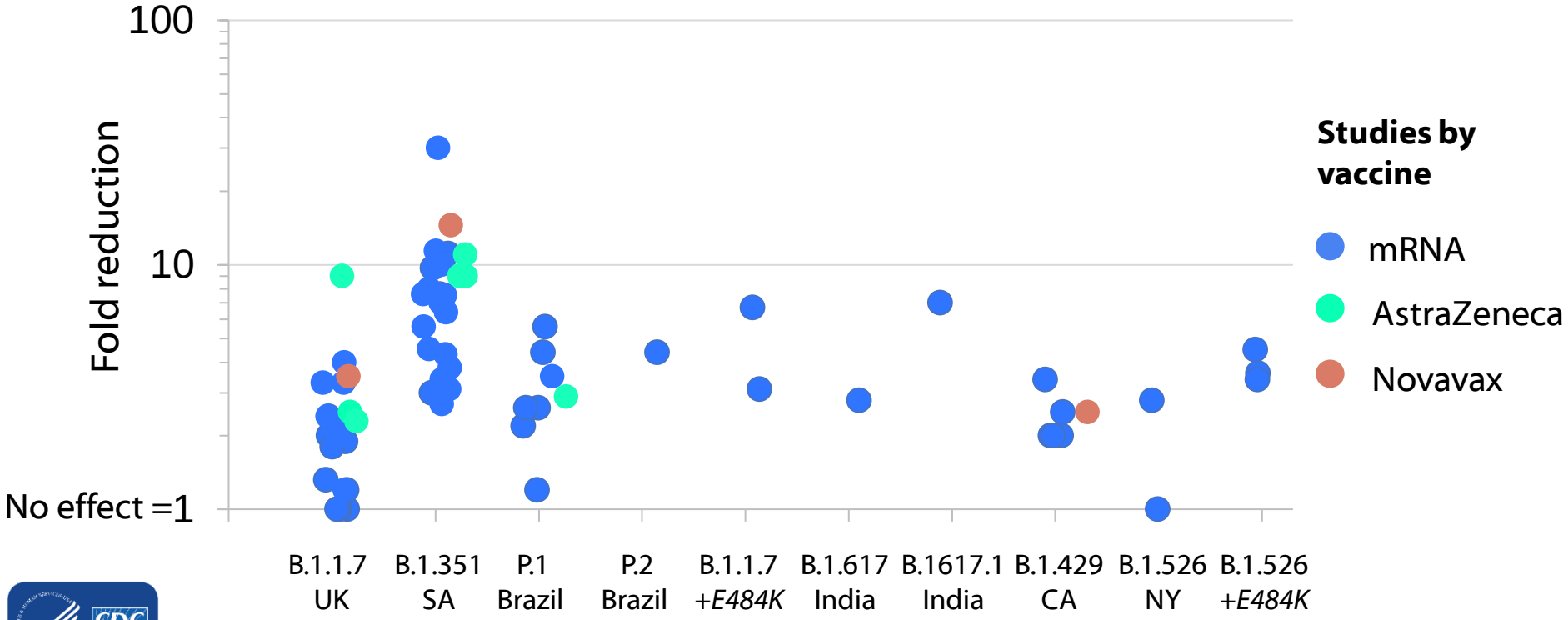
Reduced Neutralization Activity of Vaccine Sera Relative to Wildtype/Dominant Strain, by Study (n=31)



Discussion of Lab Studies

- Largest impacts: **B.1.351** (SA) > **P.1** (Brazil) > **B.1.1.7** (UK), **B.1.427/B.429** (CA)
- Difficult to estimate how results might translate to clinical protection
  - Neutralizing antibodies in sera from mRNA vaccine recipients higher than COVID-19 convalescent sera
- Variation in results may be explained by different experimental conditions
  - Neutralization assays — replicating & nonreplicating pseudovirus vs. SARS-CoV-2
  - Sera — time post-vaccination, or population (e.g., age, COVID-19 history)
  - Use of limited or full sets of spike mutations vs. clinical isolates of variants
- Limitation for all studies — small sample sizes and lack generalizability
  - Almost half of studies are preprints, not yet peer-reviewed

Vaccine Efficacy or Effectiveness (VE) Against Variants

Vaccine	Study type	VE
Pfizer	Post-EUA	• 90% against B.1.1.7 in Qatar* • 75% against B.1.351 in Qatar
Janssen	Pre-EUA	• 74% in U.S. • 66% in Brazil (69% of cases from P.2) • 52% in S. Africa (95% of cases from B.1.351)
Novavax	Pre-EUA Pre-EUA	• 96% against non-B.1.1.7 in UK • 86% against B.1.1.7 in UK • 51% against B.1.351 in S. Africa
AstraZeneca	Pre-EUA Pre-EUA	• 84% against non-B.1.1.7 in UK • 75% against B.1.1.7 in UK • 10% against B.1.351 in South Africa**

* >85% in UK & Israel (predominate B.1.1.7): https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html
Abu-Radad and Butt. Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.1.1.7 and B.1.351 Variants | NEJM
https://www.fda.gov/media/146217/download
Novavax.: https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-demonstrates-893-efficacy-uk-phase-3
Shinde et al. Efficacy of NVX-CoV2373 Covid-19 Vaccine against the B.1.351 Variant | NEJM
Madhi et al. Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant | NEJM
Emary et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7)- The Lancet **mild/moderate illness

Vaccine Efficacy or Effectiveness (VE) Against Variants

Vaccine	Study type	VE	
Pfizer	Post-EUA	• 90% against B.1.1.7 in Qatar* • 75% against B.1.351 in Qatar	100% for severe/ critical disease
Janssen	Pre-EUA	• 74% in U.S. • 66% in Brazil • 52% in S. Africa	73-82% for severe/critical disease in each country
Novavax	Pre-EUA Pre-EUA	• 96% against non-B.1.1.7 in UK • 86% against B.1.1.7 in UK • 51% against B.1.351 in S. Africa	
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Abu-Radad and Butt. Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.1.1.7 and B.1.351 Variants | NEJM

https://www.fda.gov/media/146217/download

Novavax.: https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-demonstrates-893-efficacy-uk-phase-3

Shinde et al. Efficacy of NVX-CoV2373 Covid-19 Vaccine against the B.1.351 Variant | NEJM

Madhi et al. Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant | NEJM

Emary et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7):- The Lancet **mild/moderate illness

Investigating COVID-19 Vaccine Breakthrough Cases

- Despite high vaccine efficacy, vaccine breakthrough cases* expected
  - Some will be caused by variants, even if vaccine has similar effectiveness against variants
- Among 95 million fully vaccinated in U.S., 9,245 breakthrough infections** reported by state & territorial health departments to passive surveillance
  - Case investigation and whole genome sequencing to identify variants
- Starting soon – CDC project with Emerging Infections Program sites on frequency of SARS-CoV-2 variants among vaccinated and unvaccinated people

* **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

** COVID-19 Breakthrough Case Investigations and Reporting | CDC as of 4/26/21

Tehran et al. https://www.cdc.gov/mmwr/volumes/70/wr/mm7017e1.htm

Do SARS-CoV-2 Variants Cause More Breakthrough Cases?

- One preprint study from Israel assessed variants of concern (VOC) in infections of Pfizer-vaccinated cases vs. unvaccinated matched controls
- Context: B.1.1.7 dominant strain; B.1.351 <1% of all specimens
- At least a week after 2nd dose — matched **OR = 8.0** for **B.1.351**
  - Among 149 pairs, 8 vaccinated and 1 unvaccinated persons had B.1.351
- 2 weeks after 1st dose to 1 week after 2nd dose — matched **OR = 2.6** for **B.1.1.7**
  - Among 245 pairs, 221 vaccinated and 205 unvaccinated persons had B.1.1.7
- Conclusion: breakthrough infection more frequent with VOCs
- Limitations: not yet peer-reviewed, small sample sizes (especially B.1.351)

Kustin et al. MedRxiv preprint (16 April 2021): https://www.medrxiv.org/content/10.1101/2021.04.06.21254882v2

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

- **B.1.1.7**
  - Exponential increase in prevalence in United States
  - Minimal impact on VE; attention needed for additional substitutions in receptor binding domain (RBD), such as E484K
- **B.1.351**
  - Currently low prevalence in United States
  - Moderate impact on VE for some vaccines, though may still provide protection against severe disease
- **P.1**
  - Increasing prevalence in United States; same 3 RBD mutations as B.1.351
  - Additional data needed on potential impact on VE

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

- Manufacturers launching booster studies of current vaccines and/or developing second-generation vaccines against B.1.351
- Moderna — preliminary phase 2 results of single 50 µg booster of authorized (mRNA-1273) and variant-specific vaccine (mRNA-1273.351)
  - 6-8 months after primary series (pre-booster), low/undetectable neutralizing antibody titers for B.1.351 and P.1, but titers against wild-type still likely protective
  - Both vaccines — acceptable safety; boosted immunity to all types (wild-type, B.1.351, P.1)
  - mRNA-1273.351 booster more effective than mRNA-1273 at neutralizing B.1.351
  - In progress — bivalent vaccine with 1:1 mix of original & variant vaccine (mRNA-1273.211)

Wu et al. medRxiv preprint (May 6, 2021): https://doi.org/10.1101/2021.05.05.21256716
https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-positive-initial-booster-data-against-sars-cov/
https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-initiate-study-part-broad-development

Updates to Vaccines to Address SARS-CoV-2 Variants

- Periodic update of SARS-CoV-2 vaccines likely needed
- FDA defined data needed to support EUA amendment for a vaccine addressing emerging SARS-CoV-2 variants — immunogenicity studies
- U.S. SIG* developing an evaluation and risk assessment framework
  - Evidence needed to recommend whether modified vaccine needed
- WHO has role in global coordination, developing risk assessment framework

*SARS-CoV-2 Interagency Group (SIG)
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-vaccines-prevent-covid-19

Variants: Implications for Vaccine Policy

- Current prevention measures and authorized vaccines offer protection against SARS-CoV-2 variants
  - Efforts needed to increase uptake
- Continue to monitor evidence:
  - Emergence and spread of SARS-CoV-2 variants
  - Vaccine effectiveness
  - Breakthrough infections in vaccinated or previously infected persons
  - Ability of postvaccination serum to neutralize emerging variant viruses
- ACIP will review evidence submitted for any next generation vaccines

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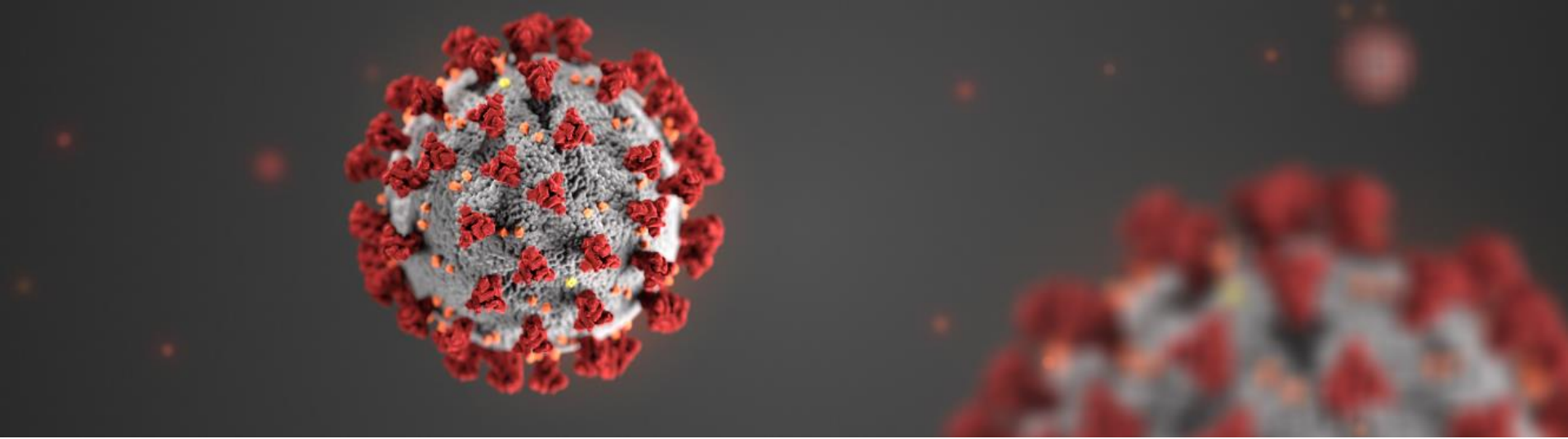

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