Indian Country Infectious Disease ECHO COVID-19 Update

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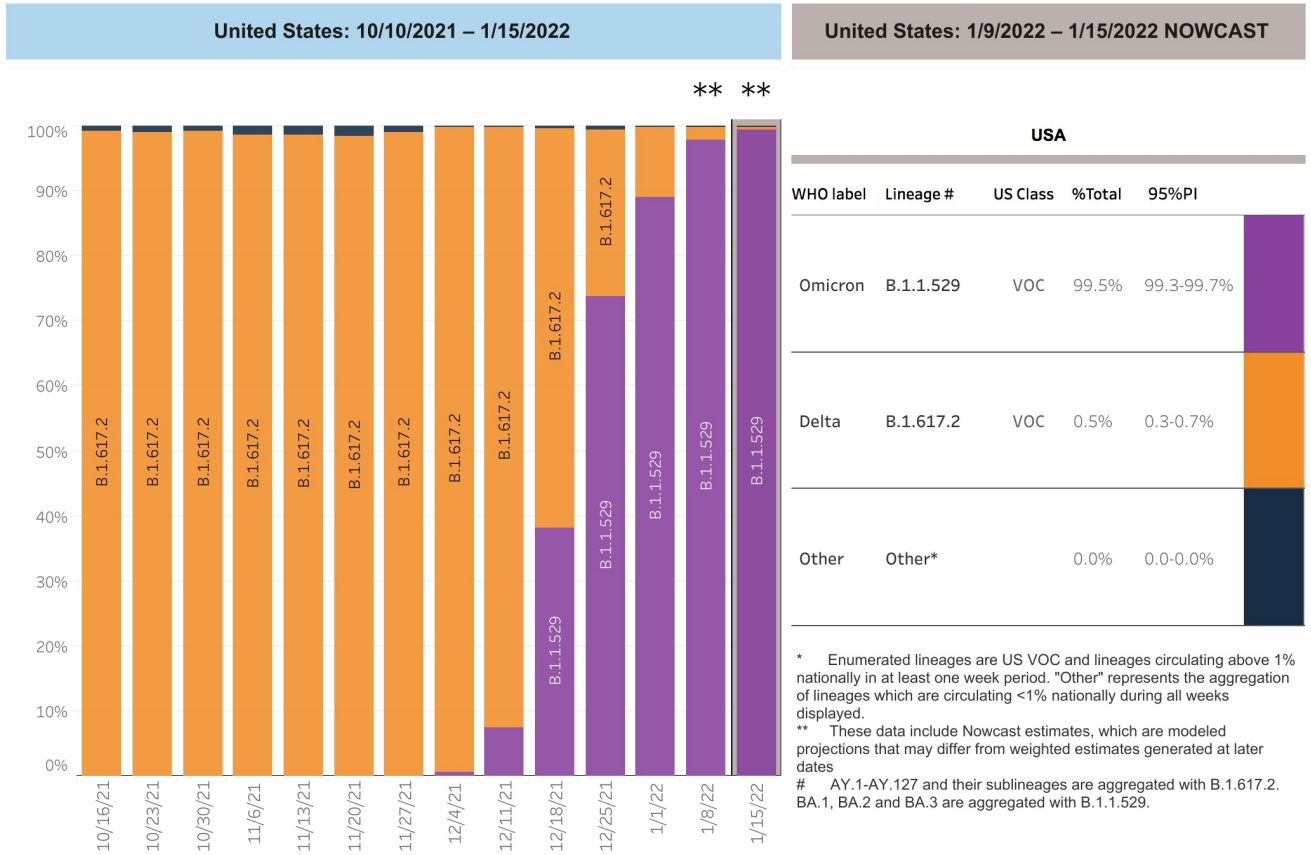
SARS-CVO-2 Virology and Immunology

Omicron Variant

- Makes up 99.5% of USA variants

Compared To Delta

- Probably more transmissible
- Maybe less virulent
- Higher capacity for immune escape



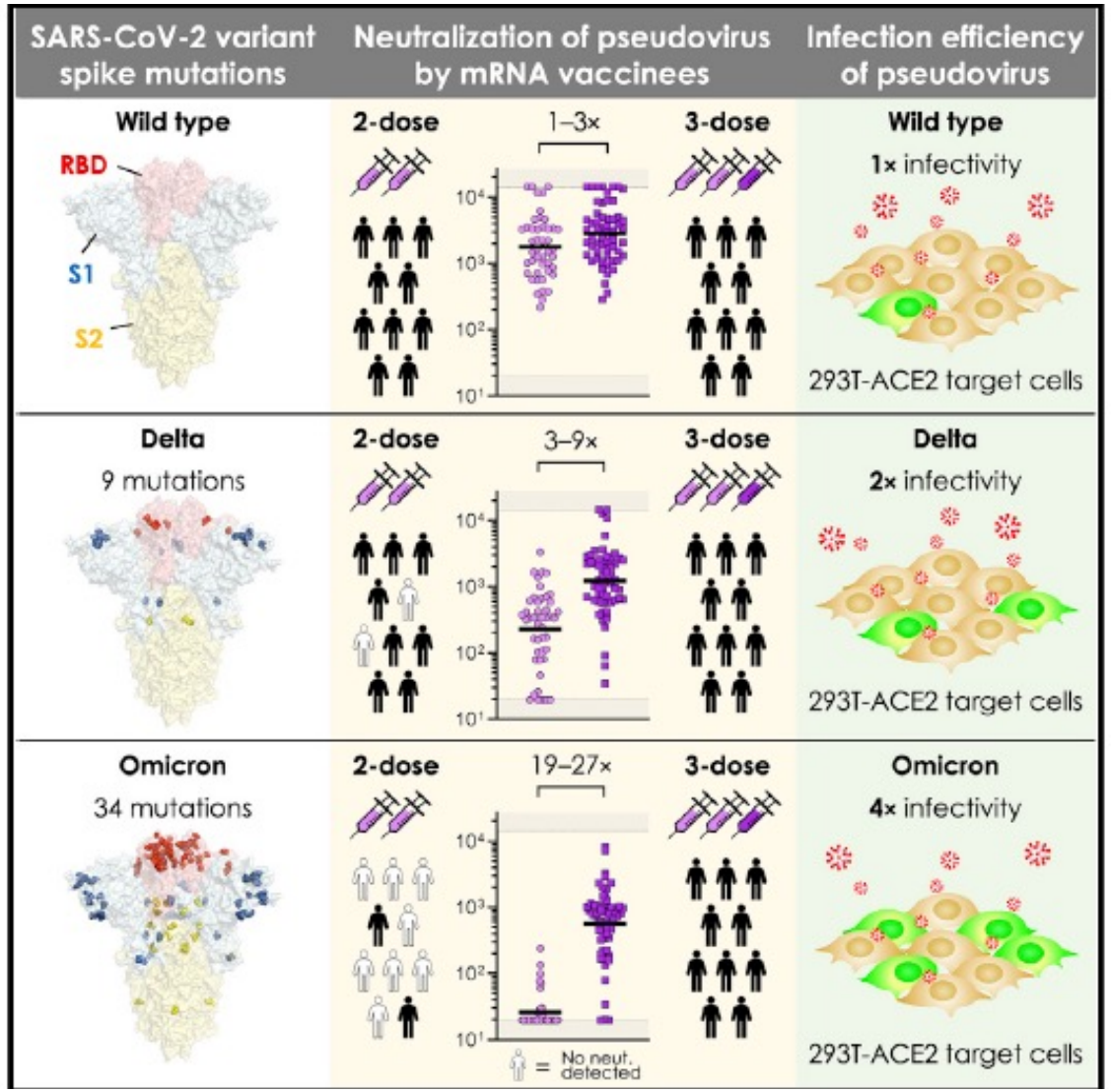
USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	B.1.1.529	VOC	99.5%	99.3-99.7%
Delta	B.1.617.2	VOC	0.5%	0.3-0.7%
Other	Other*		0.0%	0.0-0.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# AY.1-AY.127 and their sublineages are aggregated with B.1.617.2. BA.1, BA.2 and BA.3 are aggregated with B.1.1.529.

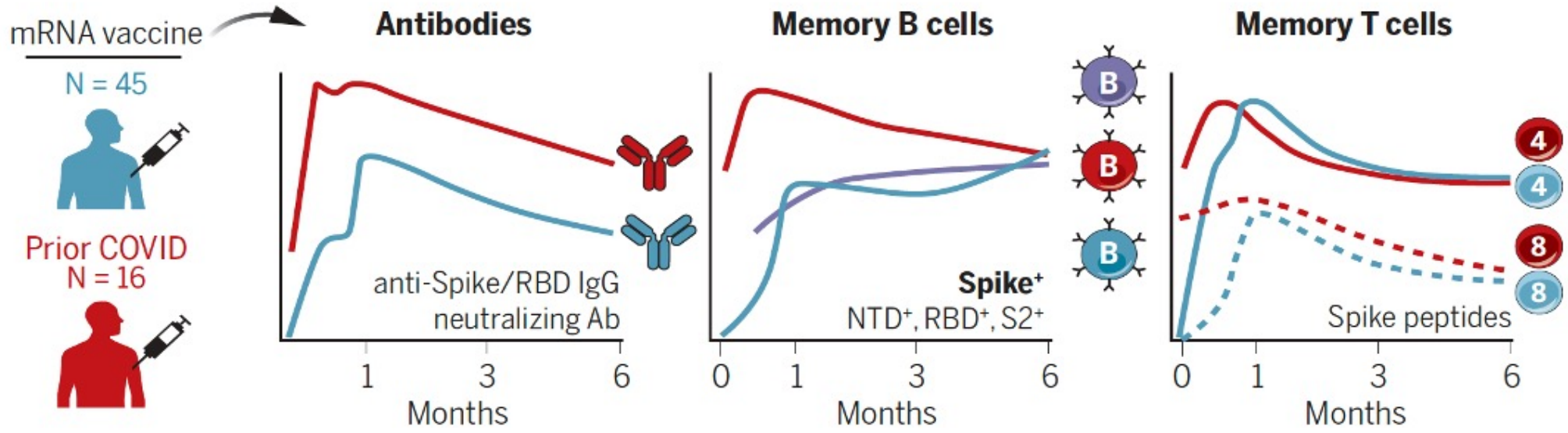
mRNA-based COVID-19 vaccine boosters induce neutralizing immunity against SARS-CoV-2 Omicron variant

- The SARS-CoV-2 Omicron variant harbors 34 mutations in the spike, more than other variants
- Two doses of mRNA-based vaccines elicit poor neutralization of Omicron
- Three mRNA vaccine doses elicit potent variant cross neutralization, including Omicron
- The Omicron pseudovirus infects cells more efficiently than other SARS-CoV-2 variants



Cell 185, 1–10, February 3, 2022

mRNA vaccines induce durable immune memory to SARS-CoV-2 and variants of concern



Immune memory after mRNA vaccination. SARS-CoV-2–specific antibody, memory B, and memory T cell responses were measured at six time points after vaccination, highlighting a coordinated evolution of durable immunological memory. B cell memory was also resilient to VOCs and capable of producing new antibodies upon reactivation. IgG, immunoglobulin G; Ab, antibody; NTD, N-terminal domain; TFH, T follicular helper cell; WT, wild-type.

Goel et al., Science **374**, 1214 (2021) 3 December 2021

Results after Propensity-Score Matching

(Comparison of outcomes from COVID infection in pediatric and adult patients with Omicron and Delta VOC infections)

Adults

- ED visit: **4.55% vs. 15.22%** (risk ratio or RR: 0.30, 95% CI: 0.28-0.33);
- Hospitalization: **1.75% vs. 3.95%** (RR: 0.44, 95% CI: 0.38-0.52]);
- ICU admission: **0.26% vs. 0.78%** (RR: 0.33, 95% CI:0.23-0.48);
- Mechanical ventilation: **0.07% vs. 0.43%** (RR: 0.16, 95% CI: 0.08-0.32).

In children under 5 years old

- ED visits **3.89% vs 21.01%** (RR for ED visit: 0.19, 95% CI: 0.14-0.25)
- Hospitalization **0.96%vs 2.65**; (RR 0.36, 95% CI: 0.19- 0.68).

Similar trends were observed for other pediatric age groups

- (5-11, 12-17 years)
- Adults (18-64 years)
- Older adults (≥ 65 years).

Conclusions

First time SARS-CoV-2 infections occurring at a time when the Omicron variant was rapidly spreading were associated with significantly less severe outcomes than first-time infections when the Delta variant predominated

medRxiv preprint doi: https://doi.org/10.1101/2021.12.30.21268495;

Comparison of outcomes from COVID infection in pediatric and adult patients before and after the emergence of Omicron

Study

- Three-day risks of outcomes in patients who were first infected for the first time during a time period when the Omicron variant was emerging to those in patients who were first infected when the Delta variant was predominant.

Method

- **Retrospective cohort study of electronic health record (EHR) data** of 577,938 first-time SARS-CoV-2 infected patients from a multicenter, nationwide database in the US
  - 14,054 infected during the 12/15/2021–12/24/2021 (“Emergent Omicron cohort”)
  - 563,884 infected during the 9/1/2021–12/15/2021 (“Delta cohort”).
- **After propensity-score matching** the 3- day risks of four outcomes were measured:
  - ED visit, hospitalization, ICU admission, and mechanical ventilation were compared.
  - Risk ratios, and 95% confidence intervals (CI) were calculated.

medRxiv preprint doi: https://doi.org/10.1101/2021.12.30.21268495;

Diagnosis of SARS-COV-2

Rapid RT-PCR or laboratory-based NAAT remain the diagnostic methods of choice

Compared to NAAT Tests, EUA Rapid Antigen testing:

- Have high specificity and low to modest sensitivity
- Sensitivity depends on viral load, symptom presence and time of testing
- Ag tests should be used within seven days of symptom onset

For symptomatic individuals either rapid RT-PCR or laboratory-based NAAT are preferred over rapid Ag tests

- If NAAT is not available or results are expected to be delayed beyond 2 – 3 days, rapid Ag testing could be considered
- If suspicion is high, negative Ag should be confirmed by standard NAAT

Compared to a single standard NAAT:

- **Rapid RT-PCR** tests had a pooled **sensitivity of 97%** (95% CI: 94-99) with **specificity 96%** (95% CI: 94-98)
- **Rapid isothermal NAAT** (primarily Abbott ID NOW) had a **sensitivity of 70%** (95% CI: 56-81) **with specificity 99%** (95% CI, 97-99)

NAAT: Nucleic Acid Amplification Test

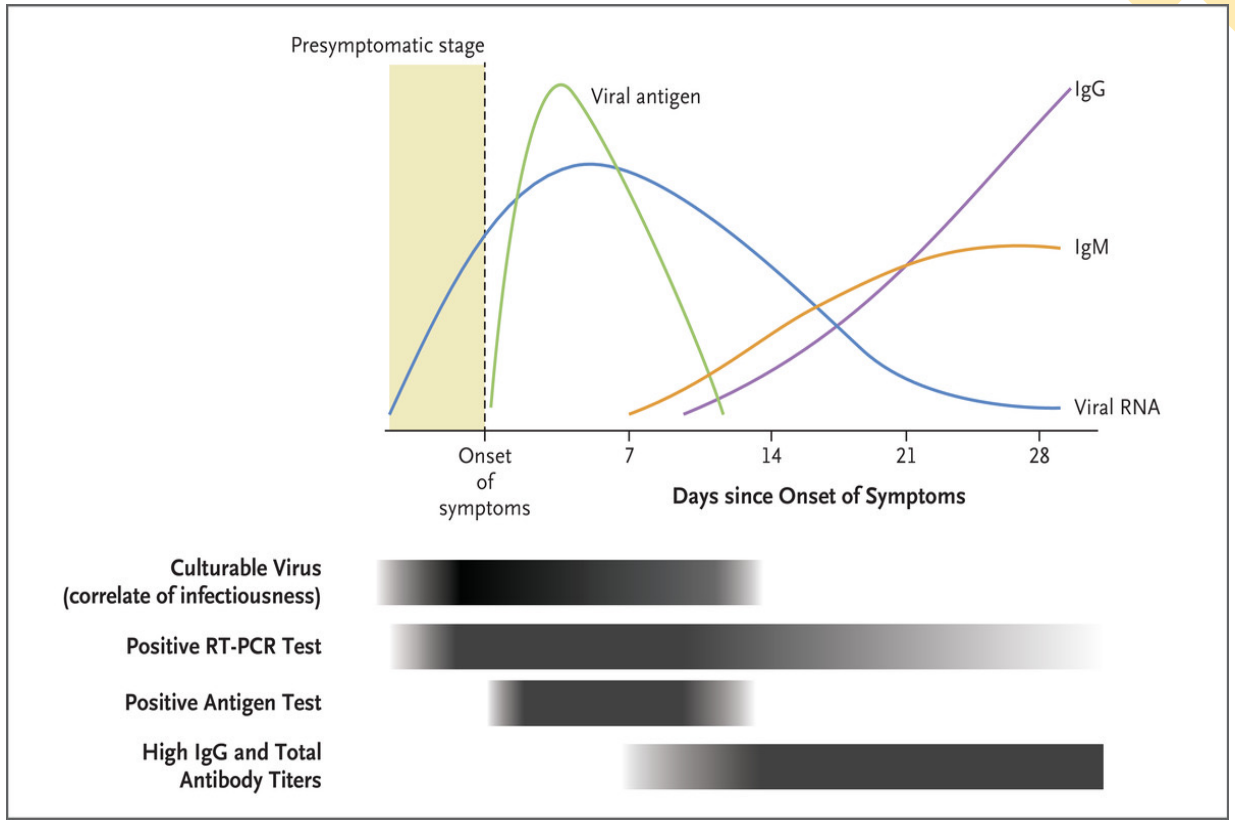


Figure 1. Pathophysiology and Timeline of Viremia, Antigenemia, and Immune Response during Acute SARS-CoV-2 Infection. In some persons, reverse-transcriptase–polymerase-chain-reaction (RT-PCR) tests can remain positive for weeks or months after initial infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), but this positivity rarely indicates replication-competent virus that can result in infection. NEJM

https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/#

NIH Treatment Guidelines Update for Non-Hospitalized Patients

Post Exposure Prophylaxis

- No effective treatment available

Pre-Exposure Prophylaxis

- tixagevimab plus cilgavimab (Evusheld) recommended for specific populations

Symptomatic Patients

- Paxlovid>Sotrovimab >Remdesivir>Molnupiravir

Therapeutic does heparin for For Hospitalized Patients

- For hospitalized, nonpregnant adults who require low-flow oxygen and are not receiving intensive care unit who have a D-dimer above the upper limit of normal (ULN), require low-flow oxygen, and have no increased bleeding risk

•Tier	Risk Group
1	•Immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, **regardless of vaccine status**; *or* •**Unvaccinated individuals** at the highest risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with additional risk factors).
2	•**Unvaccinated individuals** at risk of severe disease not included in Tier 1 (anyone aged ≥65 years or anyone aged <65 years with clinical risk factors)
3	•**Vaccinated individuals** at risk of severe disease (anyone aged ≥65 years or anyone aged <65 with clinical risk factors) **Note:** Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.
4	**Vaccinated individuals** at risk of severe disease (anyone aged ≥65 years or anyone aged <65 with clinical risk factors) **Note:** Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.

Prioritize based on risk for hospitalization or death

COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed [01/02/2021].

SARS-COV-2 Treatment:

Comparison of Treatment Options for High-Risk Nonhospitalized Patients With Mild to Moderate COVID-19

	Nirmatrelvir-ritonavir[1]	Sotrovimab[2]	Remdesivir[3]	Molnupiravir[4]
Efficacy (prevention of hospitalization or death)	• Absolute risk reduction: 6.3%→0.8% • Relative risk reduction: 88% • NNT: 18	• Absolute risk reduction: 7%→1% • Relative risk reduction: 85% • NNT: 17	• Absolute risk reduction: 5.3%→0.7% • Relative risk reduction: 87% • NNT: 22	• Absolute risk reduction: 9.7%→6.8% • Relative risk reduction: 30% • NNT: 35
Advantages	• Highly efficacious • Oral regimen • Ritonavir studied (safe) in pregnancy	• Highly efficacious • Monoclonal antibodies typically safe in pregnancy • Few/no drug interactions	• Highly efficacious • Studied in pregnancy • Few/no drug interactions	• Oral regimen • Not anticipated to have drug interactions
Disadvantages	• Drug-drug interactions	• Requires IV infusion followed by 1-h observation	• Requires IV infusion on 3 consecutive days	• Low efficacy • Concern: mutagenicity • Not recommended in pregnancy/childr en

Abbreviations: IV, intravenous; NNT, number needed to treat.

Gandhi RT, Malani PN, del Rio C . JAMA19 therapeutics for nonhospitalized . doi:10.1001/jama.2022.0335

SARS-COV-2 Vaccines

A third primary dose of the vaccine can be given ≥28 days after the second

- To children 5-11 years old who have undergone solid organ transplantation or have an equivalent level of immune compromise[1,2].

Booster doses of the vaccine are authorized

- For use in children 12-15 years old[3].

Time from completion of primary series to booster immunization

- Reduced from 6 months to 5 months for Pfizer and Moderna vaccine[3,4]

1. FDA News Release. Coronavirus (COVID-19) Update: January 3, 2022
2. FDA Fact sheet for health care providers administering vaccine. EUA for the Pfizer-BionTech COVID-9 vaccine to prevent coronavirus disease 2019 (COVID-19). For 5-11 years of age. January 3, 2022
3. FDA Fact sheet for health care providers administering vaccine. EUA for the Pfizer-BionTech COVID-9 vaccine to prevent coronavirus disease 2019 (COVID-19). For 12 years of age and older. January 3, 2022
4. FDA Fact sheet for health care providers administering vaccine. EUA for the Moderna COVID-9 vaccine to prevent coronavirus disease 2019 (COVID-19). January 7, 2022