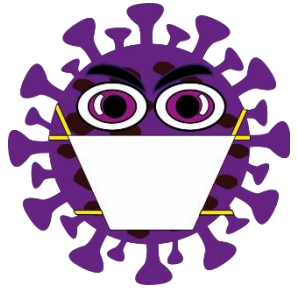


Pediatric COVID: Are we done yet??

AMISHA MALHOTRA, MD

ASSOCIATE PROFESSOR

PEDIATRIC INFECTIOUS DISEASE

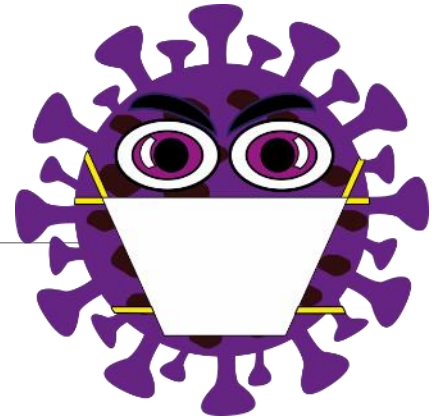
RUTGERS-ROBERT WOOD JOHNSON MEDICAL SCHOOL

NEW BRUNSWICK NJ

Disclosures

I HAVE NO DISCLOSURES

Objectives: Understanding the current state of COVID-19 in children



- Understand the epidemiology of SARS-CoV-2 and its variants
- Describe the clinical presentation and risk profile of COVID in children
- Current management modalities available
- Prevention of COVID-19
  - Vaccine efficacy and safety

OUR PANDEMIC YEAR—A COVID-19 TIMELINE

On March 11, the WHO declared COVID-19 a pandemic. Here is a look back at a year in disruption.

A MYSTERIOUS NEW ILLNESS
Images appear of Wuhan in lockdown, where officials attempt to contain a mysterious virus. Soon after, new cases of and deaths related to (what's later named) COVID-19 surge in Europe.

THE WORLD SHUTS DOWN
Countries seal borders; sports teams cancel seasons; schools close and employees go home. People start wearing masks and "social distancing."

UPTICK IN MENTAL HEALTH ISSUES
People struggle as continued unemployment and/or working from home without childcare/school takes its toll. U.S. break records for daily cases/deaths.

LIGHT AT THE END OF THE TUNNEL?
2021 begins with a race to vaccinate. Cases and deaths begin to fall. But the variants are still a threat, vaccine rollout is uneven, and we are still wearing masks.

THE VIRUS SPREADS, CASES MULTIPLY
The Grand Princess cruise ship, docked outside of San Fran, has passengers with COVID-19; Bay Area is first in the U.S. to announce shelter-in-place orders; hospitals become overwhelmed as cases grow; there is a nationwide shortage of PPE.

FLATTENING THE CURVE—FOR A WHILE
After "flattening the curve," cases begin to skyrocket again as states "reopen" in different phases. Researchers continue to race to identify treatments and make vaccines.

NEW HOPE, NEW MUTATIONS
The FDA authorizes two vaccines. Major variants begin to circulate, some of which might impact the effectiveness of vaccines.

https://www.yalemedicine.org/news/covid-timeline

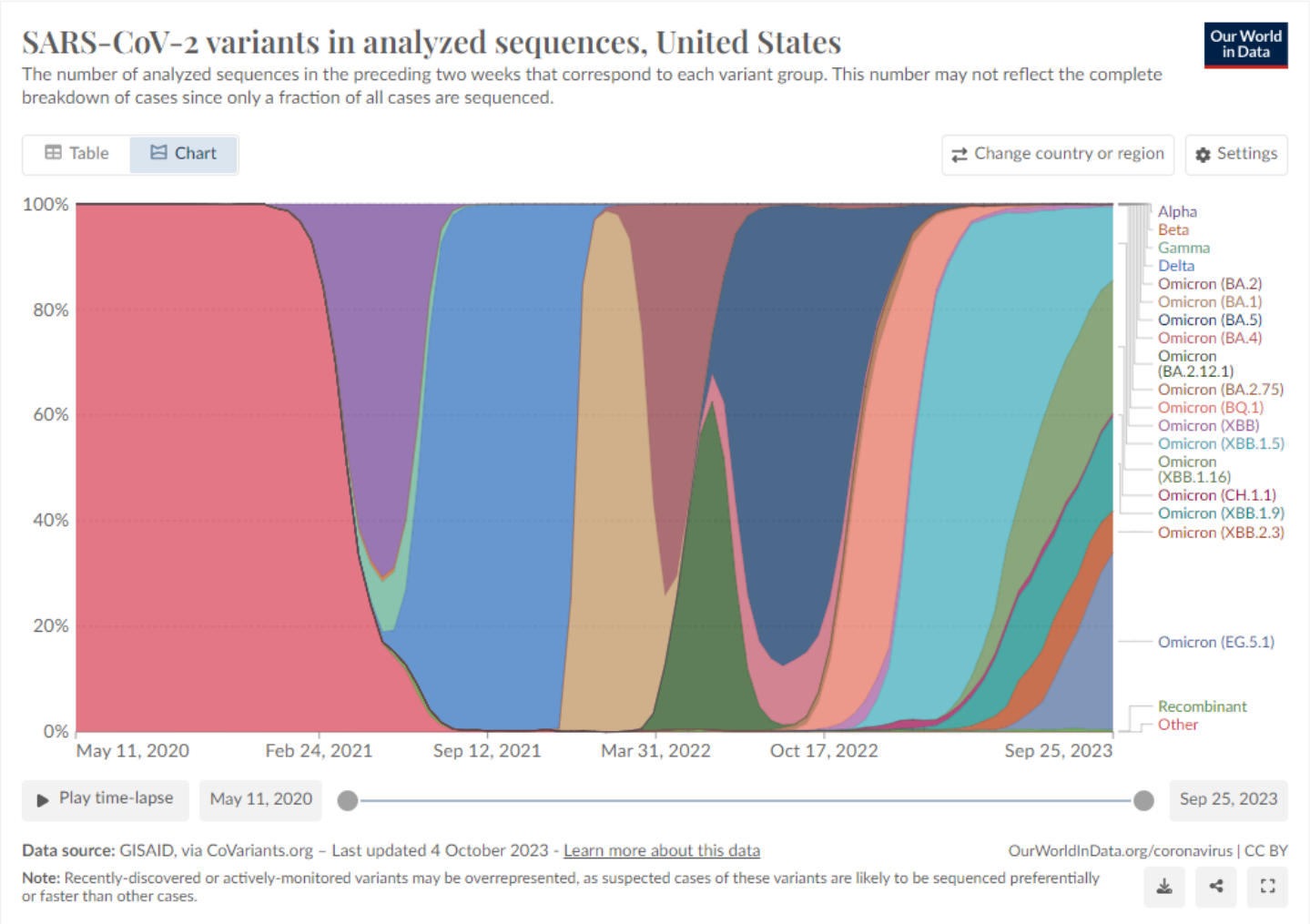
Where did it come from??

- Still uncertainty about the origins of SARS-CoV-2
- Experts believe that SARS (Severe Acute respiratory Syndrome) came from bats and that MERS (Mediterranean Respiratory Syndrome) crossed over to people from camels
- However, for SARS-CoV-2, researchers have not all agreed on any of the many existing theories:
- 1. SARS-CoV-2 might have come directly from bats
  - Scientists discounted that theory, though, as the spike protein on SARS-CoV-2 is very different from that on the coronaviruses present in bats
- 2. It is likely that the virus originated in bats but had an intermediate host between bats and people
  - Unclear what the intermediate animal hosts might be
- Conspiracy theorists: did SARS-CoV-2 escape from a laboratory in Wuhan,
  - The WHO has dismissed this theory as “extremely unlikely.”

Dyer, O. *BMJ* 2021;372:n428. doi: https://doi.org/10.1136/bmj.n428
Wacharapluesadee, *et al.* Evidence for SARS-CoV-2 related coronaviruses circulating in bats and pangolins in Southeast Asia. *Nat Commun* **12**, 972 (2021). https://doi.org/10.1038/s41467-021-21240-1

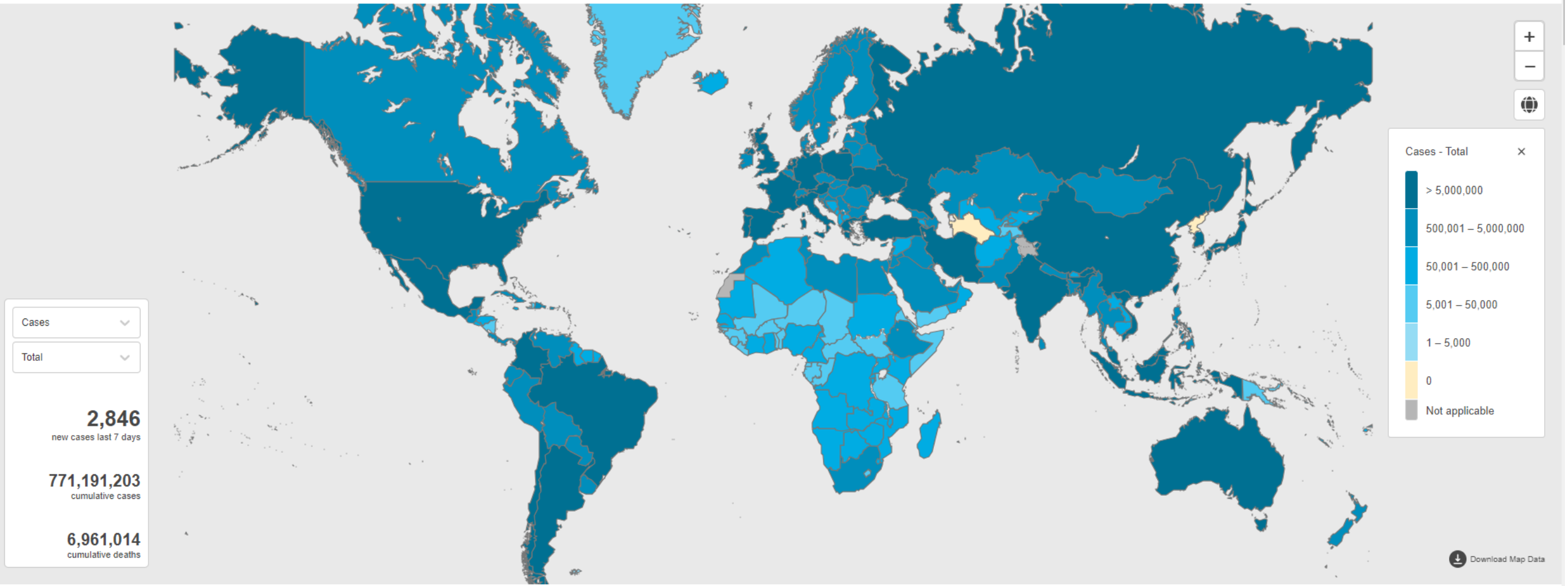
The Rise of Variants

- Variants of concern and their initial identification
  - **Alpha (B.1.1.7):** The U.K., September 2020
  - **Beta (B.1.351):** South Africa, October 2020
  - **Gamma (P.1):** Brazil, December 2020
  - **Delta (B.1.617.2):** India, October 2020
  - **Omicron (B.1.1.529):** Multiple countries, November 2021



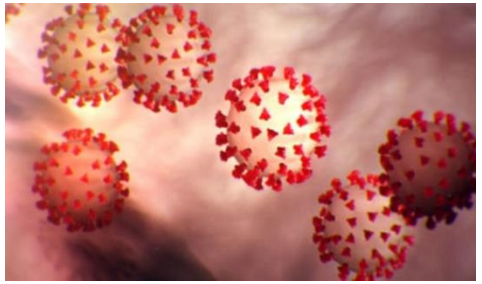
- Currently subvariants of omicron are circulating, including EG.5, XBB.1.5, and XBB.1.16
- One thing we know for sure about SARS-CoV-2 is that it is changing constantly

World Health Organization (WHO) COVID-19 Global Dashboard: 10/17/2023



https://covid19.who.int/
Accessed 10/17/2023

Epidemiology of Pediatric COVID-19



- SARS-CoV-2 infection and severe disease and death due to COVID-19 occur less often in children than in adults
  - Small percentage of children with COVID-19 will require medical attention
  - Percentage of intensive care unit (ICU) admissions among hospitalized children is comparable to that for hospitalized adults with COVID-19
  - Black/African American children were 2 times more likely to be hospitalized and 5 times more likely to be admitted to the ICU than White children
- True burden of pediatric SARS-CoV-2 infection remains unclear
  - Children with mild symptoms are seldom systematically tested
  - Contact tracing and seroprevalence studies are not generally conducted
- Overall incidence of SARS-CoV-2 infection and COVID-19-related hospitalizations among children has increased substantially
  - Emergence of recent variants of concern (VOCs), particularly Omicron
  - By February 2022, approximately 75% of children and adolescents had serologic evidence of prior SARS-CoV-2 infection
  - Spike in pediatric hospitalizations Jan 2023 with BA.5

Marks KJ, Whitaker M, Anglin O, et al. Hospitalizations of children and adolescents with laboratory-confirmed COVID-19—COVID-NET, 14 states, July 2021–January 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71(7):271-278. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35176003
Holmes L, Jr, Wu C, Hinson R, et al. Black-White risk differentials in pediatric COVID-19 hospitalization and intensive care unit admissions in the USA. *J Racial Ethn Health Disparities*. 2022; Available at: https://www.ncbi.nlm.nih.gov/pubmed/35604543
Clarke KEN, Jones JM, Deng Y, et al. Seroprevalence of infection-induced SARS-CoV-2 antibodies—United States, September 2021–February 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71(17):606-608. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35482574
https://www.cdc.gov/coronavirus/2019-ncov/covidnetdashboard/de/powerbi/dashboard.html

Clinical manifestations

- Signs and symptoms of SARS-CoV-2 infection in symptomatic children may be similar to those in adults
  - Fever, cough, sore throat, rhinorrhea, headache, fatigue, shortness of breath, or gastrointestinal symptoms (nausea, vomiting, or diarrhea)
  - Some case studies conducted during high levels of Omicron variant transmission have reported a substantial increase in croup
- Greater proportion of children may be asymptomatic or have only mild illness when compared with adults
- True incidence of asymptomatic SARS-CoV-2 infection is unknown
  - Small study reported that 45% of children who underwent surveillance testing at the time of hospitalization for a non-COVID-19 indication had asymptomatic infection
- Most common signs and symptoms of COVID-19 in hospitalized children are:
  - fever, nausea/vomiting, cough, shortness of breath, and upper respiratory symptoms

Poline J, Gaschignard J, Leblanc C, et al. Systematic severe acute respiratory syndrome coronavirus 2 screening at hospital admission in children: a French prospective multicenter study. *Clin Infect Dis*. 2021;72(12):2215-2217.
Kim L, Whitaker M, O'Halloran A, et al. Hospitalization rates and characteristics of children aged <18 years hospitalized with laboratory-confirmed COVID-19—COVID-NET, 14 states, March 1–July 25, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(32):1081-1088.

Comparison of Symptoms Associated With SARS-CoV-2 Variants Among Children in Canada: 2020-2022

- Omicron and Delta infections were associated with fever and cough
- Delta infection was associated with the reporting of upper respiratory tract symptoms while Omicron infection was associated with lower respiratory tract symptoms and systemic symptoms
- Original-type virus most often presented with abdominal pain, anosmia and myalgias

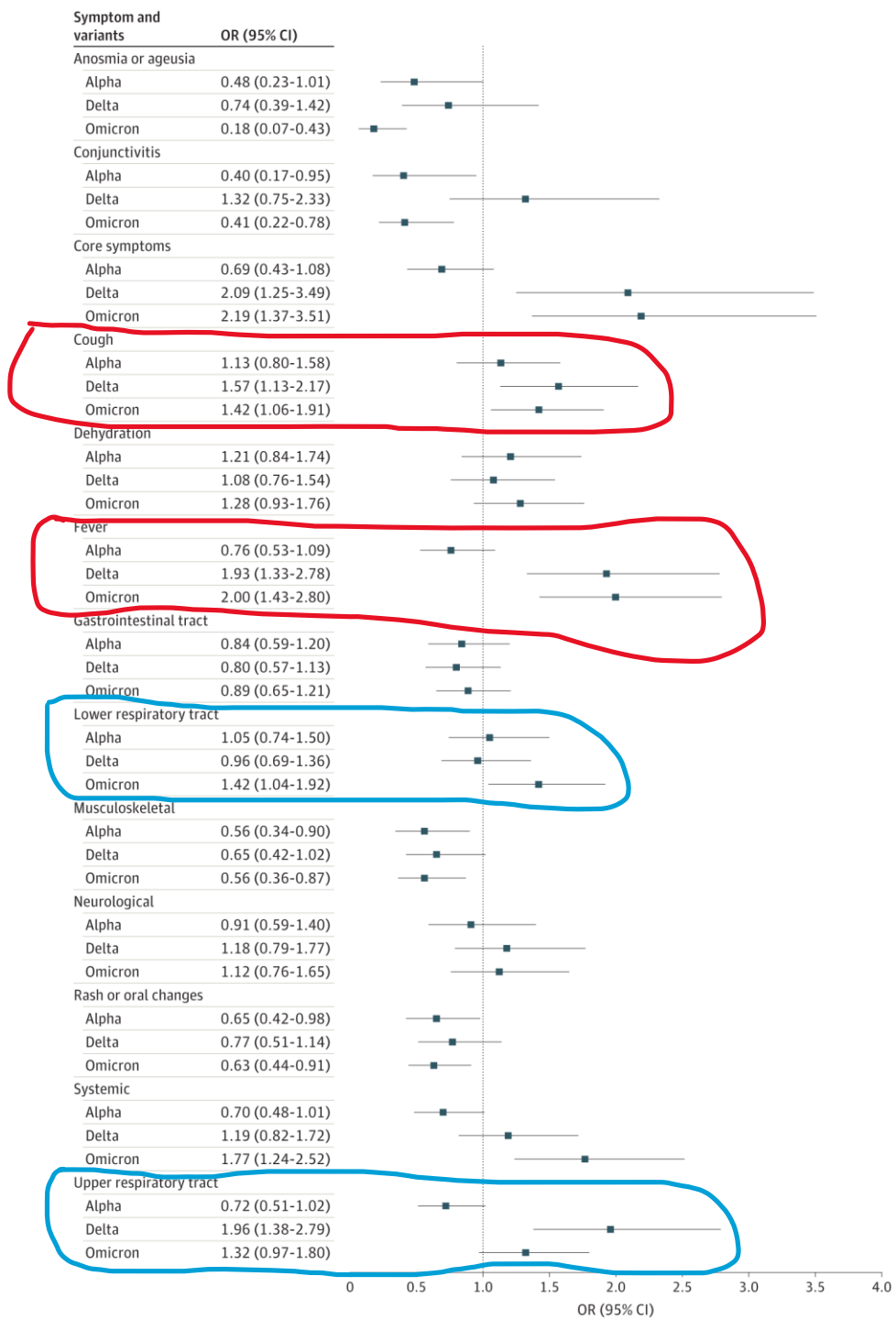


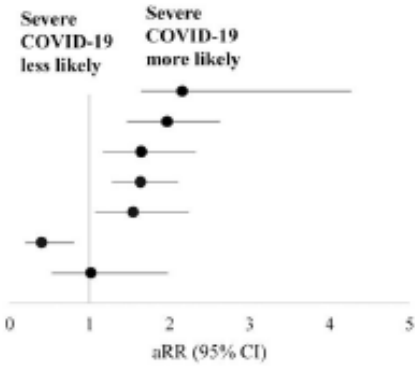
Figure 1: Mixed-Effect Binary Logistic Regression Model Examining the Odds of Experiencing a Given Symptom or Symptom Group by Variant of Concern Original-type SARS-CoV-2 serves as the reference group. N=1440

JAMA Netw Open. 2023;6(3):e232328.
doi:10.1001/jamanetworkopen.2023.2328

Risk factors for severe disease by age

A. Children <2 Years (N=745)

Underlying medical condition	Severe disease n=164 n	(%)	No severe disease n=581 n	(%)	Bivariate models RR	(95% CI)	Multivariable models[a] aRR	(95% CI)
Chronic lung disease	21	(12.8)	17	(2.9)	2.8	(2.0, 3.9)	2.2	(1.1, 4.3)
Neurologic disorder	27	(16.5)	22	(3.8)	2.9	(2.2, 3.8)	2.0	(1.5, 2.6)
Cardiovascular disease	23	(14.0)	34	(5.9)	2.0	(1.5, 2.7)	1.7	(1.2, 2.3)
Prematurity[b]	39	(23.8)	61	(10.5)	2.1	(1.5, 2.9)	1.6	(1.3, 2.1)
Airway abnormality	12	(7.3)	12	(2.1)	2.4	(1.4, 4.1)	1.6	(1.1, 2.2)
Feeding tube dependent	11	(6.7)	22	(3.8)	1.6	(1.0, 2.6)	0.4	(0.2, 0.8)
Other[c]	11	(6.7)	25	(6.7)	1.5	(0.8, 2.7)	1.0	(0.5, 2.0)



B. Children 2–17 Years (N=1,548)

Underlying medical condition	Severe disease n=527 n	(%)	No severe disease n=1,021 n	(%)	Bivariate models RR	(95% CI)	Multivariable models[a] aRR	(95% CI)
Feeding tube dependence	49	(9.3)	32	(3.1)	2.0	(1.7, 2.2)	2.0	(1.5, 2.5)
Diabetes mellitus (type I or 2)	53	(10.1)	35	(3.4)	1.9	(1.6, 2.3)	1.9	(1.6, 2.3)
Obesity[d]	191	(36.2)	287	(28.1)	1.3	(1.1, 1.5)	1.2	(1.0, 1.4)
Chronic lung disease[e]	32	(6.1)	38	(3.7)	1.5	(1.2, 1.8)	1.2	(0.9, 1.5)
Developmental delay	84	(15.9)	104	(10.2)	1.4	(1.3, 1.6)	1.2	(1.0, 1.4)
Immunocompromised condition	37	(7.0)	85	(8.3)	0.9	(0.6, 1.2)	1.1	(0.8, 1.6)
Airway abnormality	18	(3.4)	16	(1.6)	1.6	(1.1, 2.3)	1.0	(0.7, 1.5)
Cardiovascular disease	32	(6.1)	57	(5.6)	1.1	(0.8, 1.4)	1.0	(0.8, 1.3)
Chronic metabolic disease[g]	12	(2.3)	28	(2.7)	0.9	(0.6, 1.4)	0.9	(0.6, 1.3)
Asthma	120	(22.8)	240	(23.5)	1.0	(0.8, 1.2)	0.9	(0.7, 1.2)
Neurologic disorder[e]	34	(6.5)	66	(6.5)	1.0	(0.8, 1.3)	1.9	(0.7, 1.2)
Blood disorder	25	(4.7)	96	(9.4)	0.5	(0.4, 0.7)	0.5	(0.4, 0.7)
Other[f]	17	(3.2)	80	(7.8)	0.5	(0.3, 0.7)	0.4	(0.3, 0.7)

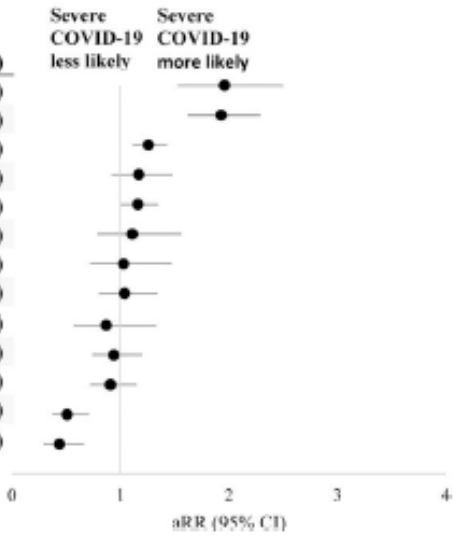


Figure 2. A–B. Underlying conditions associated with severe COVID-19 by age group

Woodruff RC, et.al. COVID-NET surveillance team: Risk factors for severe COVID-19 in children. Pediatrics 149(1) 2022.

Risk factors for severe disease

- **≥1 comorbidities**:
  - Cardiac disease
  - Neurologic disorders
  - Prematurity (in young infants)
  - Diabetes
  - Obesity (particularly severe obesity)
  - Chronic lung disease
  - Asthma
  - Feeding tube dependence
  - Immunocompromised status
  - Complex chronic condition that affected ≥2 body systems
  - Progressive chronic condition or continuous dependence on technology for ≥6 months (e.g., dialysis, tracheostomy with ventilator assistance)
  - Having more severe chronic disease (e.g., active cancer treated within the previous 3 months or asthma with hospitalization within the previous 12 months) when compared with less severe conditions

- **Demographic factors**
  - Age
    - Infants and adolescents have the highest risk of COVID-19-related ICU admission or death (<1 year and 12-17 years)
  - Non-White race/ethnicity

- **Vaccination status**
  - Most children who have been hospitalized for severe COVID-19 have not been fully vaccinated

- **SARS-CoV-2 variant**
  - Omicron vs Delta
    - Hospitalization rates among children and adolescents were higher (children aged <5 years)
    - Proportion of hospitalized children requiring ICU admission was significantly lower

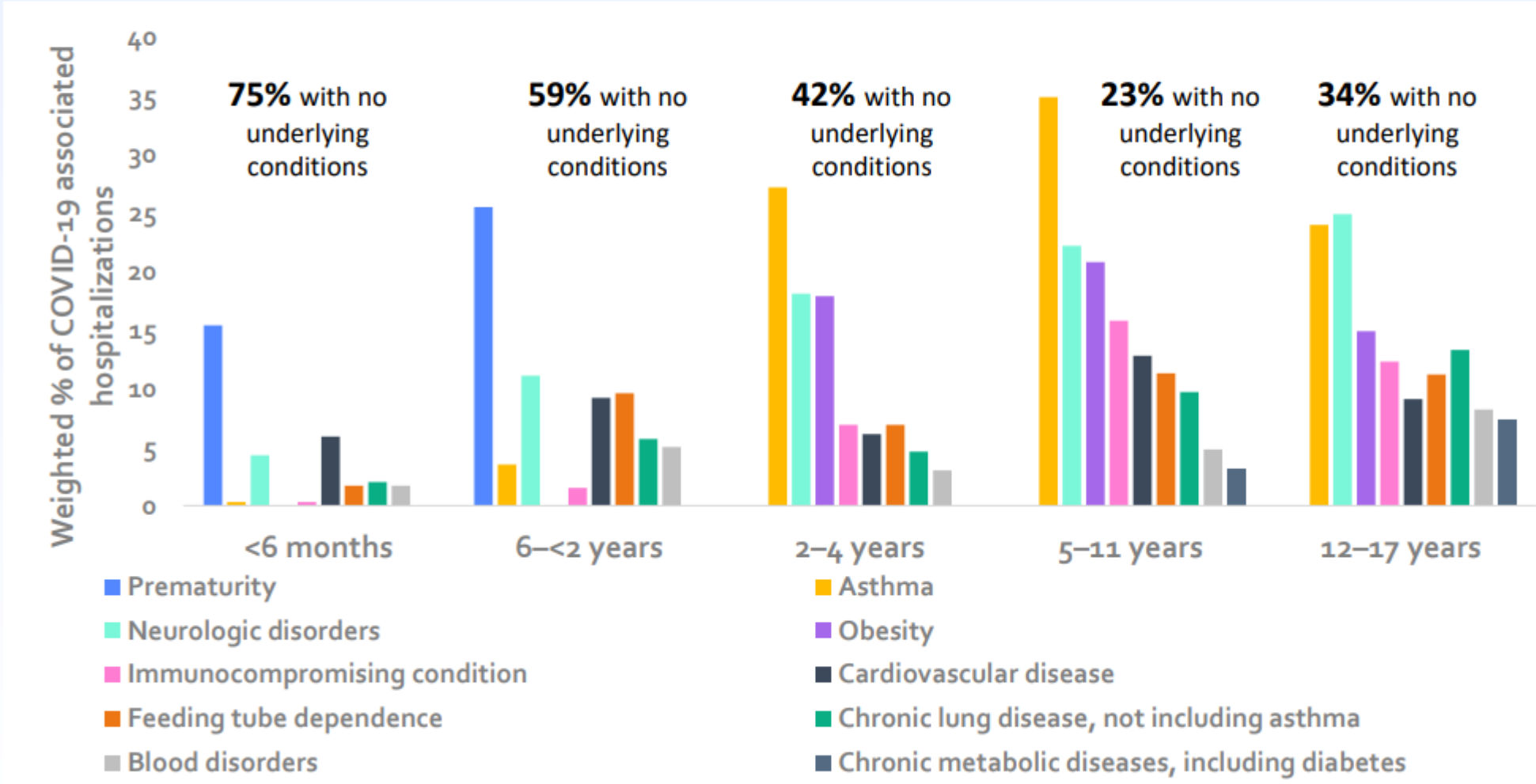
Wanga V, Gerdes ME, Shi DS, et al. Characteristics and clinical outcomes of children and adolescents aged <18 years hospitalized with COVID-19—six hospitals, United States, July–August 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70(5152):1766-1772.
Dorabawila V, Hoefer D, Bauer UE, et al. Risk of infection and hospitalization among vaccinated and unvaccinated children and adolescents in New York after the emergence of the Omicron variant. *JAMA*. 2022;327(22):2242-2244.
Forrest CB, Burrows EK, Mejias A, et al. Severity of acute COVID-19 in children <18 years old March 2020 to December 2021. *Pediatrics*. 2022;149(4):e2021055765

Mortality Risk

- Death from COVID-19 is uncommon in children
- Risk factors for death include having chronic conditions, such as neurologic or cardiac disease, and having multiple comorbidities
- Deaths associated with COVID-19 have been higher for children aged 10 to 20 years
  - young adults aged 18 to 20 years
  - Minorities: Hispanic, Black, or American Indian/Alaskan Native

Bixler D, Miller AD, Mattison CP, et al. SARS-CoV-2-associated deaths among persons aged <21 years—United States, February 12–July 31, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(37):1324-1329

Percent of COVID-19-Associated Hospitalizations with Underlying Medical Conditions among Children and Adolescents Ages 5–17 Years by Age Group — COVID-NET, January–June 2023



- **54%** of hospitalized infants, children, and adolescents ages ≤17 years have **no underlying medical conditions**.
- Hospitalizations children and adolescents **ages ≥5 years** are **more likely to have underlying medical conditions** relative to children and infants ages ≤4 years.

Data are limited to hospitalizations where COVID-19 is a likely primary reason for admission. Figure displays underlying medical conditions present in ≥5% in ≥1 age group.

COVID testing

- Nucleic Acid Amplification Tests (NAATs/PCR)
  - Highly sensitive and highly specific tests
  - Detect one or more viral ribonucleic acid (RNA) genes and indicate a current infection
  - Viral RNA may stay in a person's body for up to 90 days after they test positive
    - NAATs should not be used to test someone who has tested positive in the last 90 days
- Antigen tests
  - Immunoassays that detect the presence of a specific viral antigen
  - Have similar specificity, but are less sensitive than most NAATs
  - Less expensive than NAATs and can provide results in minutes
  - Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions

Treatment of Pediatric COVID-19

- Data evaluating the use of pharmacologic therapy in children with COVID-19 are limited largely to descriptive reports
- Recommendations for the therapeutic management of children are based largely on adult safety and efficacy data from clinical trials

Chiotos K, Hayes M, Kimberlin DW, et al. Multicenter initial guidance on use of antivirals for children with coronavirus disease 2019/severe acute respiratory syndrome coronavirus 2. *J Pediatric Infect Dis Soc*. 2020;9(6):701-715.
Schuster JE, Halasa NB, Nakamura M, et al. A description of COVID-19-directed therapy in children admitted to US intensive care units 2020. *J Pediatric Infect Dis Soc*. 2022;11(5):191-198.

Risk based strategies for treatment of Pediatric COVID-19

Conditions	Risk Level by Vaccination Status		
	Unvaccinated	Primary Series	Up to Date
Strong or Consistent Association With Progression to Severe COVID-19			
• Moderately or severely immunocompromised	High		
• Obesity (BMI ≥95th percentile for age), especially severe obesity (BMI ≥120% of 95th percentile for age) • Medical complexity with dependence on respiratory technology • Severe neurologic, genetic, metabolic, or other disability that results in impaired airway clearance or limitations in self care or activities of daily living • Severe asthma or other severe chronic lung disease requiring ≥2 inhaled or ≥1 systemic medications daily • Severe congenital or acquired cardiac disease • Multiple moderate to severe chronic diseases	High	Intermediate	
Moderate or Inconsistent Association With Progression to Severe COVID-19			
• Aged <1 year • Prematurity in children aged ≤2 years • Sickle cell disease • Diabetes mellitus (poorly controlled) • Nonsevere cardiac, neurologic, or metabolic disease	Intermediate		
Weak or Unknown Association With Progression to Severe COVID-19			
• Mild asthma • Overweight • Diabetes mellitus (well controlled)	Low		

https://www.covid19treatmentguidelines.nih.gov/tables/assessing-risk/

Outpatient treatment management guidelines

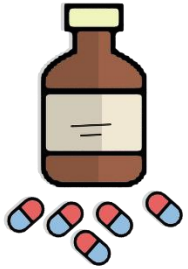
Risk of Severe COVID-19	Panel's Recommendations	
	Aged 12–17 years	Aged <12 years
Symptomatic, Regardless of Risk Factors	• Provide supportive care (AIII).	• Provide supportive care (AIII).
High Risk[a,b]	• Use 1 of the following options (listed in order of preference):[c] ◦ **Ritonavir-boosted nirmatrelvir (Paxlovid)** within 5 days of symptom onset (BIII) ◦ **Remdesivir** within 7 days of symptom onset (CIII)	• Ritonavir-boosted nirmatrelvir is not authorized by the FDA for use in children aged <12 years. • There is insufficient evidence to recommend either for or against routine use of remdesivir. Consider treatment based on age and other risk factors.
Intermediate Risk[b,e]	• There is insufficient evidence to recommend either for or against the use of any antiviral therapy. Consider treatment based on age and other risk factors.	• There is insufficient evidence to recommend either for or against routine use of remdesivir.
Low Risk[b,f]	• Manage with supportive care alone (BIII).	• Manage with supportive care alone (BIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Weak

Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

https://www.covid19treatmentguidelines.nih.gov/tables/therapeutic-management-of-nonhospitalised-children/

Available outpatient treatment options: Antivirals

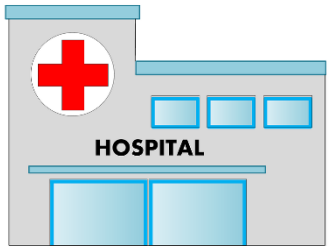


- **Ritonavir-boosted nirmatrelvir (Paxlovid)** (oral)
  - 5 day course
  - protease inhibitor preventing viral replication
  - **Pediatric patients aged ≥12 years and weighing ≥40 kg**
  - Treatment should be initiated as soon as possible and within 5 days of symptom onset
    - Adult Epic trial: enrolled nonhospitalized adults with mild to moderate COVID-19 who were not vaccinated and who were at high risk of progressing to severe disease
      - reduced the risk of hospitalization or death by 89% compared to placebo
- **Remdesivir** (IV)
  - Nucleoside analogue
  - Binds to RNA polymerase and inhibits viral replication by terminating RNA transcription
  - Only antiviral drug that is FDA approved for treatment of COVID-19 in adults and pediatric patients aged ≥28 days and weighing ≥3 kg
  - Mild to moderate COVID-19, remdesivir should be started within 7 days of symptom onset and administered for 3 days
    - Treatment of nonhospitalized adults with mild to moderate COVID-19 who were at high risk of progression to severe disease, resulted in an 87% relative reduction in the risk of hospitalization or death
- **Molnupiravir** (oral)
  - nucleoside analogue
  - works by introducing errors into the SARS-CoV-2 virus' genetic code, which prevents the virus from further replicating
  - **ONLY for adults ≥18 years of age**
    - may affect bone and cartilage growth in <18 years
    - May cause fetal harm when administered to pregnant individuals
  - Outpatient oral medication x 5 days

Hammond J, Leister-Tebbe H, Gardner A, et al. Oral nirmatrelvir for high-risk, nonhospitalized adults with COVID-19. *N Engl J Med*. 2022;386(15):1397-1408. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35172054
Gottlieb RL, Vaca CE, Paredes R, et al. Early remdesivir to prevent progression to severe COVID-19 in outpatients. *N Engl J Med*. 2022;386(4):305-315. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34937145

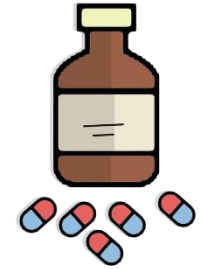
Treatment for children hospitalized for COVID-19

- Need for supplemental O2/ MV/ECMO
  - Remdesivir +/- dexamethasone
  - Biologics: baricitinib (JK inhibitor)
    tocilizumab (IL-6 inhibitor)
- No need for supplemental O2
  - Consider prophylactic anticoagulation ≥12yrs
  - Consider remdesivir in children at high risk of progression to severe disease



https://www.covid19treatmentguidelines.nih.gov/management
Chiotos K, Hayes M, Kimberlin DW, et al. Multicenter initial guidance on use of antivirals for children with coronavirus disease 2019/severe acute respiratory syndrome coronavirus 2. *J Pediatric Infect Dis Soc*. 2020;9(6):701-715.
Dulek DE, Fuhlbrigge RC, Tribble AC, et al. Multidisciplinary guidance regarding the use of immunomodulatory therapies for acute coronavirus disease 2019 in pediatric patients. *J Pediatric Infect Dis Soc*. 2020;9(6):716-737.

Outpatient treatment modalities



Corticosteroids

- Improve clinical outcomes and reduces mortality in hospitalized patients with COVID-19 who require supplemental oxygen
- Corticosteroids are **not indicated for the treatment of COVID-19 in nonhospitalized children**
- Corticosteroids should be used per usual standards of care in children with asthma and croup triggered by SARS-CoV-2 infection
- Patients who are receiving corticosteroids for an underlying condition should continue this therapy as needed

WHO Rapid Evidence Appraisal for COVID-19 Therapies Working Group, Sterne JAC, Murthy S, et al. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. *JAMA.* 2020;324(13):1330-1341. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32876694
Crothers K, DeFaccio R, Tate J, et al. Dexamethasone in hospitalised coronavirus-19 patients not on intensive respiratory support. *Eur Respir J*. 2021;Published online ahead of print. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34824060

Post-COVID conditions (PCC)

Long COVID

post-acute COVID-19

long-haul COVID

chronic COVID

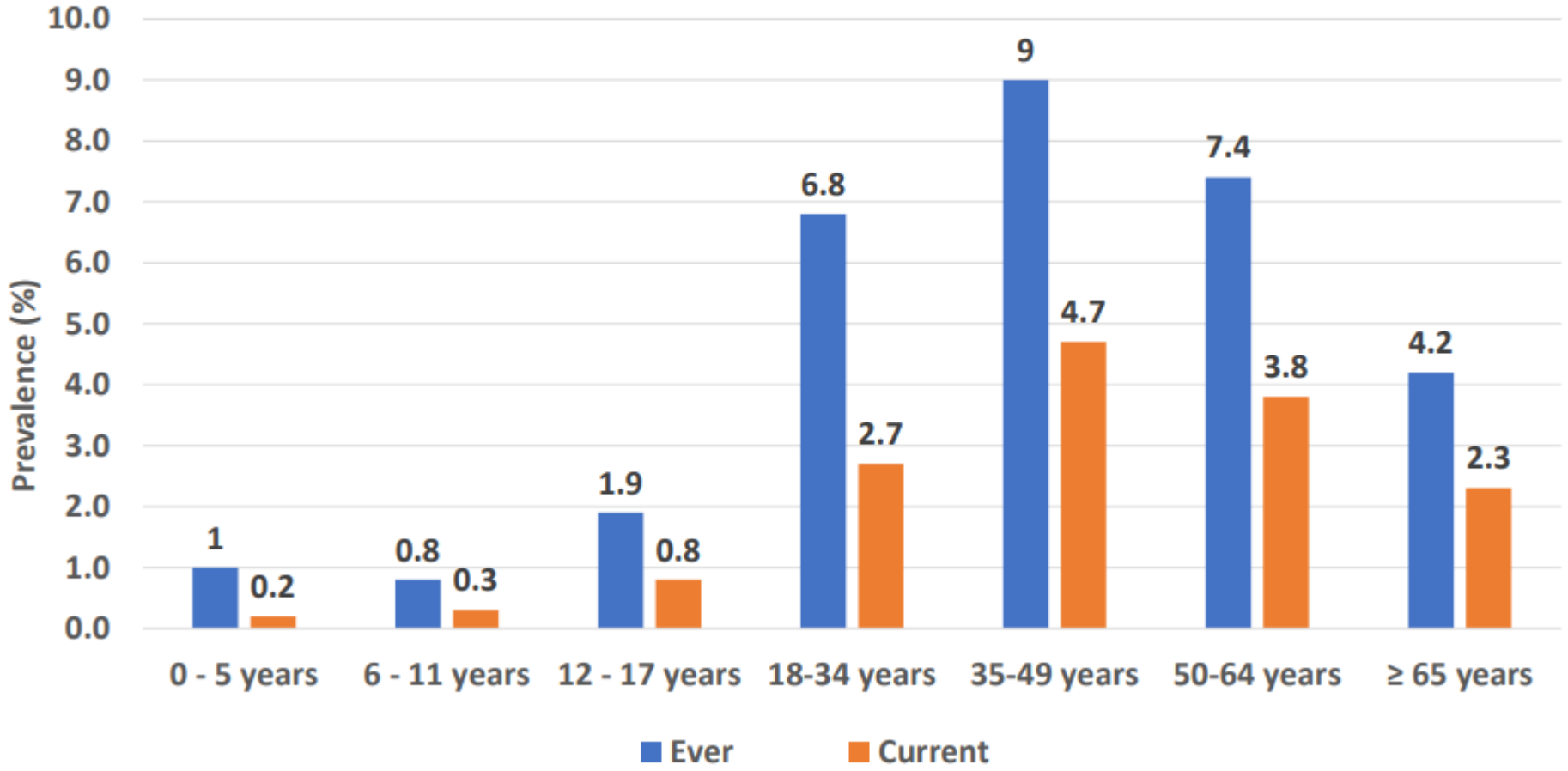
long-term effects of COVID

post-acute sequelae of SARS CoV-2 infection (PASC)

- An umbrella term for the wide range of health consequences that can be present 4 or more weeks after infection with SARS-CoV-2
- Children experience post-COVID conditions, but they appear to be affected less frequently than adults
- Estimates of the proportion of children who experience COVID-19 and later develop post-COVID conditions range widely
  - In 2022, 1.3% of children ever had Long COVID vs 6.9% of adults
  - Girls (1.6%) were more likely than boys (0.9%) to have ever had Long COVID
  - Hispanic children had higher rates than black, white or Asian
- Rates of post-COVID conditions seem to increase with age among children and adolescents
  - Children ages 12–17 years were more likely to get long COVID c/w younger children
- PCCs are found more often in people who had severe acute COVID-19 illness than in people with mild or asymptomatic illness
- Commonly reported signs/symptoms in children can include fatigue, but
  - Common symptoms for children that also occur in adults were changes in taste or smell, a cough, coldlike symptoms, and heart inflammation/myocarditis.
  - Symptoms for children also included hair loss, skin rashes, diarrhea, and abnormal liver enzymes
  - However, children were less likely than adults to have neurological symptoms such as headache, tingling pain, and brain fog or memory loss.
- Some studies of post-COVID conditions in children report that symptoms typically do not persist beyond 12 weeks while others have found that symptoms can linger for longer periods
- Additional research is needed to learn more about symptoms associated with post-COVID conditions in the pediatric population

Rao S, et al. JAMA Pediatr 2022 Oct; 176(10): 1000–1009
Vahratian A, et al. Long COVID in children: United States, 2022. NCHS Data Brief, no 479. Hyattsville, MD: National Center for Health Statistics. 2023. DOI: https://dx.doi.org/10.15620/cdc:132416

Prevalence of on-going symptoms lasting at least 3 months after COVID-19 by age, regardless of COVID status: U.S.

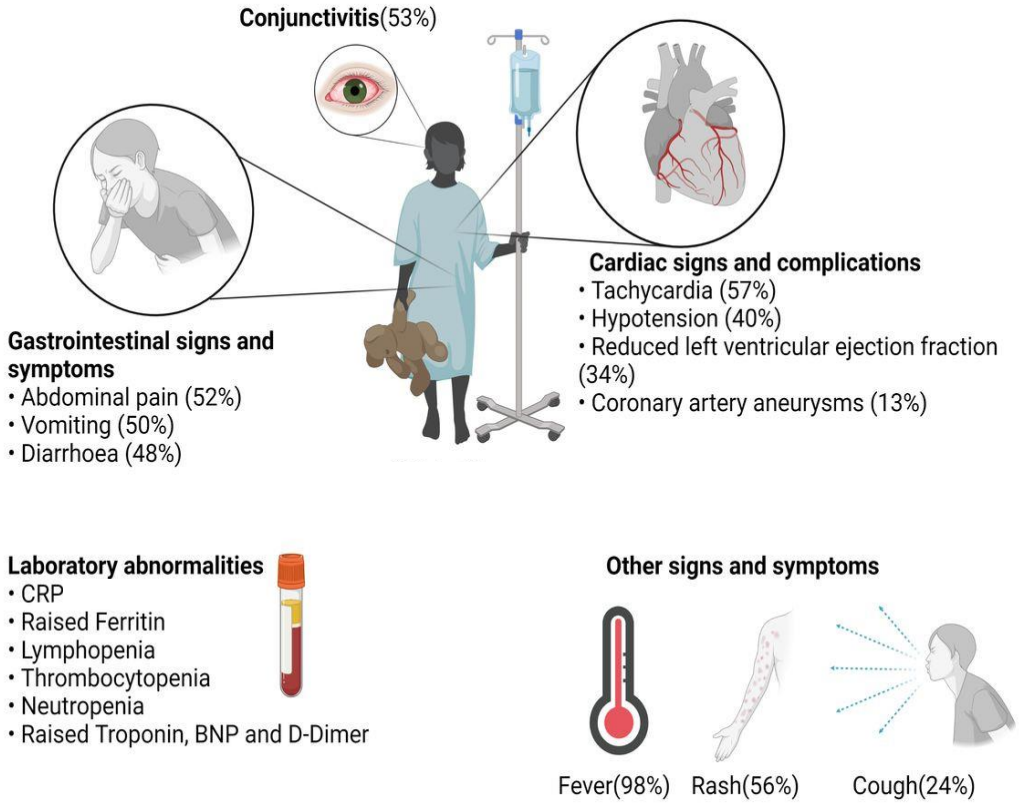


Nationally representative of non-institutional population in the U.S., statistical software was used to account for NHIS's complex sampling design.

UNPUBLISHED CDC DATA – Preliminary estimates from 2022 National Health Interview Survey

Multisystem inflammatory syndrome in children (MISC)

- **What is MISC**: Postinfectious inflammatory syndrome related to SARS-CoV-2
- **Who does it affect**: Small subset of children and young adults with SARS-CoV-2 infection, including those with asymptomatic infection. The majority of children do not have underlying comorbid conditions other than obesity
- **When do we see MISC**: Incidence of MIS-C lags about 4 weeks behind the peak of acute pediatric COVID-19-related hospitalizations
- **What is the current trend**: Studies have reported that early in the COVID-19 pandemic, MIS-C occurred in 1 out of approximately 3,000 to 4,000 children and adolescents
  - MIS-C has become rarer since the start of the pandemic: the number of MIS-C cases reported decreased from 2020 to 2023
  - We do not know how that trend may change in the future and CDC continues to monitor reported cases of MIS-C
- **Why do some children get MISC**: Risk factors for the development of MIS-C have not been established. ICU admission was more likely for patients aged 6 to 12 years, and it was more likely for children who identified as non-Hispanic Black
- **How do we prevent it**: COVID-19 vaccination protects against the development of MIS-C



Abrams JY, Oster ME, Godfred-Cato SE, et al. Factors linked to severe outcomes in multisystem inflammatory syndrome in children (MIS-C) in the USA: a retrospective surveillance study. *Lancet Child Adolesc Health*. 2021;5(5):323-331.
Feldstein LR, Rose EB, Horwitz SM, et al. Multisystem inflammatory syndrome in U.S. children and adolescents. *N Engl J Med*. 2020;383(4):334-346.

Prevention of COVID-19: Vaccination

- **Staying up to date with COVID-19 vaccinations remains the most effective way to prevent severe COVID-19**
- *Who is eligible?* children ≥6 months of age
- *What vaccines are available for children?*
  - **1. mRNA (Pfizer-BioNTech, Moderna)**
  - **2. Recombinant protein S subunit (Novavax)**
    - ≥12 years

- *Current state of vaccination status*
  - Primary series are monovalent vaccines (Omicron XBB.1.5)
  - Children aged 6 months–4 years should get two or three doses of updated COVID-19 vaccine depending on which vaccine they receive
  - Children aged 5 years – 11 years who are unvaccinated or have previously gotten a COVID-19 vaccine before September 12, 2023, should **get 1 updated Pfizer-BioNTech or Moderna COVID-19 vaccine**
- People aged 12 years and older who are unvaccinated should get either:
  - 1 **updated Pfizer-BioNTech** or **updated Moderna COVID-19** vaccine, OR
  - 2 doses of **updated Novavax COVID-19 vaccine**

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html

Safety of COVID-19 vaccines

- Evidence from the hundreds of millions of COVID-19 vaccines already administered in the United States, and the billions of vaccines administered globally, demonstrates that they are safe and effective
- Side effects
  - Mild
  - Usually occur within 7 days of administration
  - Systemic effects (fever, chills, tiredness, headaches) more common after 2nd dose
- Adverse effects
  - Severe allergic reactions to vaccines are rare but can happen
  - Rare risk of myocarditis and pericarditis associated with mRNA COVID-19 vaccination,
    - mostly among males ages 12–39 years
    - rare risk may be further reduced with a longer interval between the first and second dose.
  - Cases of myocarditis and pericarditis have also been reported in people who received Novavax COVID-19 vaccine
  - There was a potential cause-and-effect relationship between the J&J/Janssen COVID-19 vaccine and thrombosis with thrombocytopenia syndrome (TTS)
    - The J&J/Janssen COVID-19 vaccine is no longer available in the U.S.

Source: National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases

VSD incidence rates of verified myocarditis or pericarditis in the 0–7 days after mRNA vaccination in 5–39-year-olds, by product, age groups, sex and dose number*

Product and Patient Group	Dose 1		Dose 2		First Booster	
	Cases/Doses Administered†	Incidence Rate/ Million Doses (95% CI)	Cases/Doses Administered†	Incidence Rate/ Million Doses (95% CI)	Cases/Doses Administered†	Incidence Rate/ Million Doses (95% CI)
Pfizer‡						
Male, *age*						
5–11 y	0/221 975	0.0 (0.0–13.5)	3/207 958	14.4 (3.0–42.2)	0/50 415	0.0 (0.0–59.4)
12–15 y§	2/212 977	9.39 (1.1–33.9)	31/205 955	150.5 (102.3–213.6)	5/81 613	61.3 (19.9–143.0)
16–17 y	1/105 147	9.51 (0.2–53.0)	14/102 091	137.1 (75.0–230.1)	9/47 874	188.0 (86.0–356.9)
18–29 y	4/348 080	11.5 (3.1–29.4)	27/331 889	81.4 (53.6–118.4)	7/166 973	41.9 (16.9–86.4)
30–39 y	1/352 403	2.8 (0.1–15.8)	5/341 527	14.6 (4.8–34.2)	3/197 554	15.2 (3.1–44.4)
Female, *age*						
5–11 y	0/215 986	0.0 (0.0–13.9)	0/202 596	0.0 (0.0–14.8)	0/49 261	0.0 (0.0–60.8)
12–15 y	0/210 741	0.0 (0.0–14.2)	5/204 074	24.5 (8.0–57.2)	0/84 114	0.0 (0.0–35.6)
16–17 y	1/110 066	9.1 (0.2–50.6)	1/107 173	9.3 (0.2–52.0)	2/55 004	36.4 (4.4–131.3)
18–29 y	1/414 730	2.4 (0.1–13.4)	2/400 321	5.0 (0.6–18.0)	1/240 226	4.2 (0.1–23.2)
30–39 y	0/420 934	0.0 (0.0–7.1)	3/410 713	7.3 (1.5–21.3)	1/268 412	3.7 (0.1–20.8)
Moderna‖¶						
Male, *age*						
18–29 y	5/207 073	24.2 (7.8–56.3)	19/195 809	97.0 (58.4–151.5)	7/109 337	64.0 (25.7–131.9)
30–39 y	1/223 064	4.5 (0.1–25.0)	8/216 583	36.9 (15.9–72.8)	1/149 468	6.7 (0.2–37.3)
Female, *age*						
18–29 y	1/253 773	3.9 (0.1–22.0)	0/243 560	0.0 (0.0–12.3)	1/156 707	6.4 (0.2–35.6)
30–39 y	1/265 362	3.8 (0.1–21.0)	1/259 780	3.9 (0.1–21.4)	2/191 765	10.4 (1.3–37.7)

* Data through August 20, 2022

Goddard K, et al. . *Ann Intern Med.* 2022;175:1169-1771.

Summary of Safety Findings after COVID-19 Vaccines in the VSD

Anaphylaxis

- The rate of anaphylaxis was ~ 5 cases/million doses for the mRNA primary series.
  - The rate of anaphylaxis was <5 cases/million doses for mRNA booster doses.

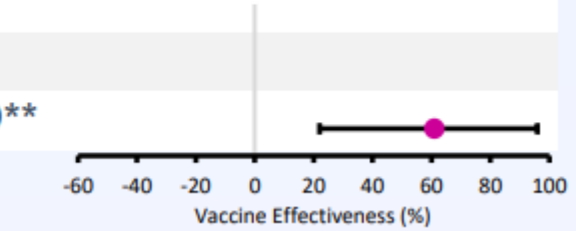
Myocarditis/Pericarditis after mRNA vaccines

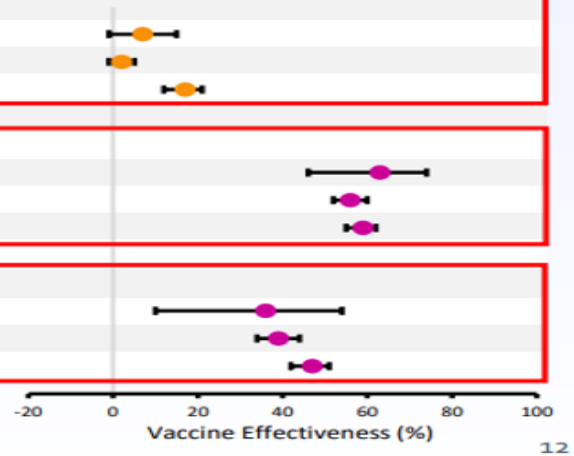
- During days 0-7 post vaccination, both mRNA vaccines were associated with increased risk of myocarditis/pericarditis in 12–39-year-olds.
- Risk estimates of myocarditis/pericarditis in 18–39-year-olds during days 0-7 after 2 doses were modestly higher after Moderna than after Pfizer.
- For persons ages 12–39 years, rates of myocarditis/pericarditis 0–7 days after primary and monovalent boosters were highest among male 12-15 and 16–17-year-olds.
  - Evidence suggests there was an increased risk for myocarditis/pericarditis following monovalent booster dose for some age groups.
  - No current evidence for an increased rate of myocarditis/pericarditis following bivalent boosters. Uptake was low in age groups expected to be at highest risk.

Goddard K, et al. Safety of COVID-19 mRNA Vaccination Among Young Children in the Vaccine Safety Datalink. Pediatrics. 2023 Jul 1;152(1):e2023061894.

Vaccine Efficacy: Bivalent vaccine against ED/UC encounters (2022-2023)

Vaccination status (months since last dose)	Total tests	SARS-CoV-2 positive, N (%)	Median interval since last dose, days (IQR)	Adjusted VE (95% CI)
Regardless of manufacturer, ≥1 bivalent dose (ages 6mo–5 years)				
Unvaccinated	34,582	1,505 (4.3)	NA	Ref
≥1 **bivalent** dose (≥14 days)	458	8 (1.8)	66 (39–103)	**61 (22 to 83)****
***Original monovalent* doses only**				
5-17 years	28,369	1,092 (4)	334 (253-439)	**7 (-1 to 15)**
18-64 years	14,9267	14,270 (10)	441 (334-564)	**2 (-1 to 5)**
≥65 years	69,989	8,538 (12)	383 (266-531)	**17 (12 to 21)**
***Bivalent* booster, 7-59 days earlier**				
5-17 years	1,858	30 (2)	30 (18-44)	**63 (46 to 74)**
18-64 years	9,763	549 (6)	33 (21-46)	**56 (52 to 60)**
≥65 years	1,1826	970 (8)	35 (21-48)	**59 (55 to 62)**
***Bivalent* booster, 60-119 days earlier**				
5-17 years	1,268	37 (3)	89 (74-105)	**36 (10 to 54)**
18-64 years	9,558	682 (7)	86 (72-102)	**39 (34 to 44)**
≥65 years	12,753	1,255 (9)	87 (73-102)	**47(42 to 51)**





VE estimates adjusted for age, sex, race and ethnicity, geographic region, and calendar time. CDC unpublished data

12

- 1 dose of original monovalent Moderna or Pfizer-BioNTech vaccines did not provide significant protection
- 2 doses of either product (and 3 doses of Pfizer-BioNTech) provided protection against ED/UC and hospitalization, though waning was evident (similar to older children and adults)
- A bivalent dose provided protection, though sample size was limited

Link-Gelles R, Ciesla AA, Rowley EA, et al. Effectiveness of Monovalent and Bivalent mRNA Vaccines in Preventing COVID-19–Associated Emergency Department and Urgent Care Encounters Among Children Aged 6 Months–5 Years —VISION Network, United States, July 2022–June 2023. MMWR Morb Mortal Wkly Rep 2023;72:886–892.

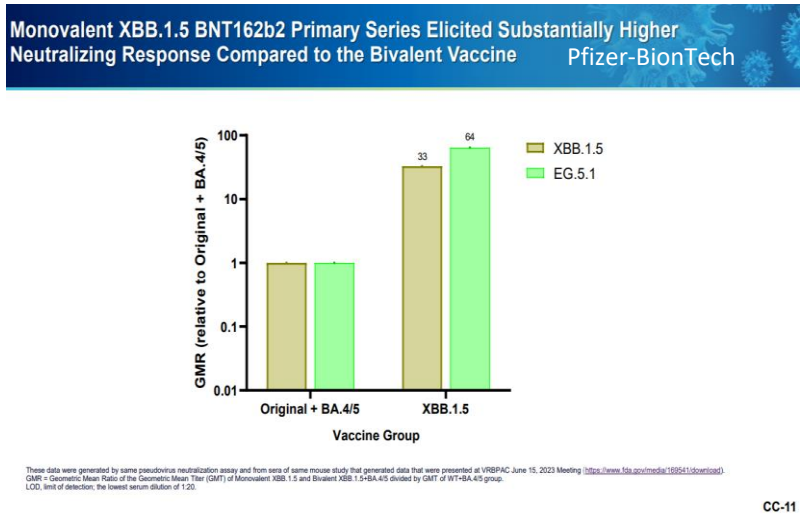
Context for interpreting VE across age groups

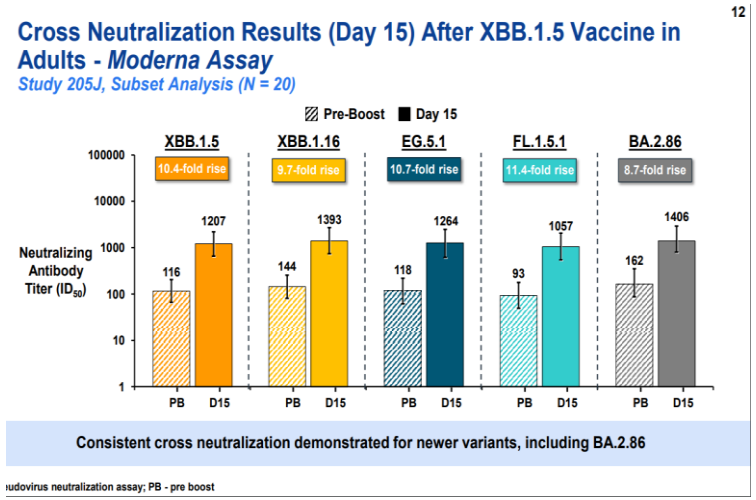
- High rates of infection-induced immunity by July–August 2022.*
- VE findings should be interpreted as the incremental benefit provided by COVID-19 vaccination in a population with a high prevalence of infection-induced immunity.

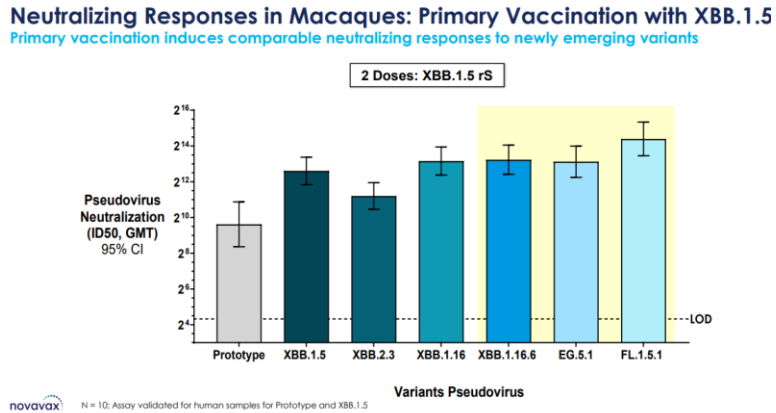
Age group	% with infection-induced immunity
6-11 month	66%
12-23 months	74%
2-4 years	83%
5-11 years	88%
12-17 years	86%
16-29 years	83%
30-49 years	78%
50-64 years	68%
≥65 years	48%

* https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-COVID-Jones-508.pdf; data on children aged 6 months – 17 years is from cross-sectional blood specimens collected by commercial laboratories. Data on persons aged ≥16 years is from a longitudinal, national cohort of >70,000 blood donors.

Neutralizing response of current 2023 monovalent vaccine to SARS-CoV-2 XBB.1.5 variant and others

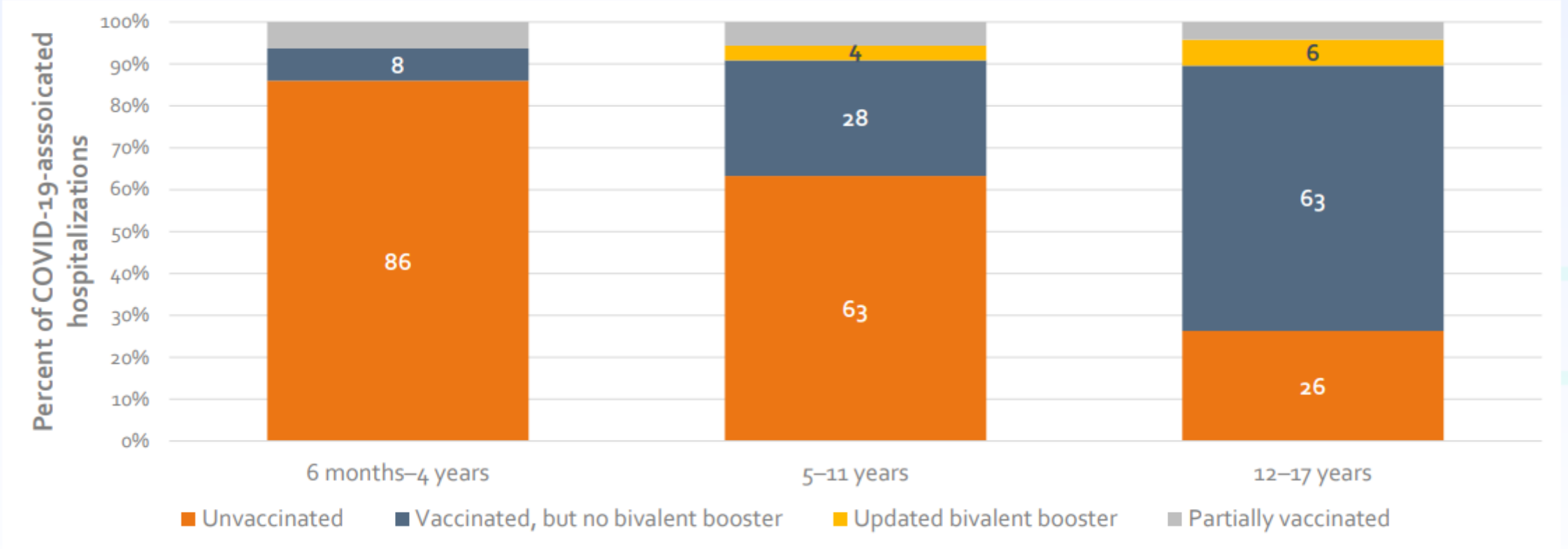






- XBB.1.5 vaccine is anticipated to be effective against current SARS-CoV-2 variants
- No preferential recommendation for the use of any one COVID-19 vaccine over another

Vaccination Status by Age Group among Infants, Children and Adolescents Ages ≤17 Years Hospitalized for COVID-19 — COVID-NET, January–June 2023



Data are limited to hospitalizations where COVID-19 is a likely primary reason for admission. ***Unvaccinated****: No recorded doses of COVID-19 vaccine.* ***Vaccinated, but no bivalent booster****: Completed a primary series with or without ≥1 booster dose but did not receive an updated bivalent booster dose.* ***Updated bivalent booster****: Received updated bivalent booster dose.* ***Partially vaccinated****: Received at least one dose of COVID-19 but was not considered fully vaccinated at the time of a positive SARS-CoV-2 test. Persons with unknown vaccination status are excluded.*

Vaccination status and intent among children, by demographics, United States

Data Collection Period: May 28 - June 30, 2023 (N= 12,183)

Select Age Range

- (●) 6 months-17 years
- ( ) 6 months-4 years
- ( ) 5-17 years
- ( ) 5-11 years
- ( ) 12-17 years

Vaccination Status

- (●) Vaccinated (≥1 dose)
- ( ) Received bivalent booster (among completed series)

Overall 6 months-17 years

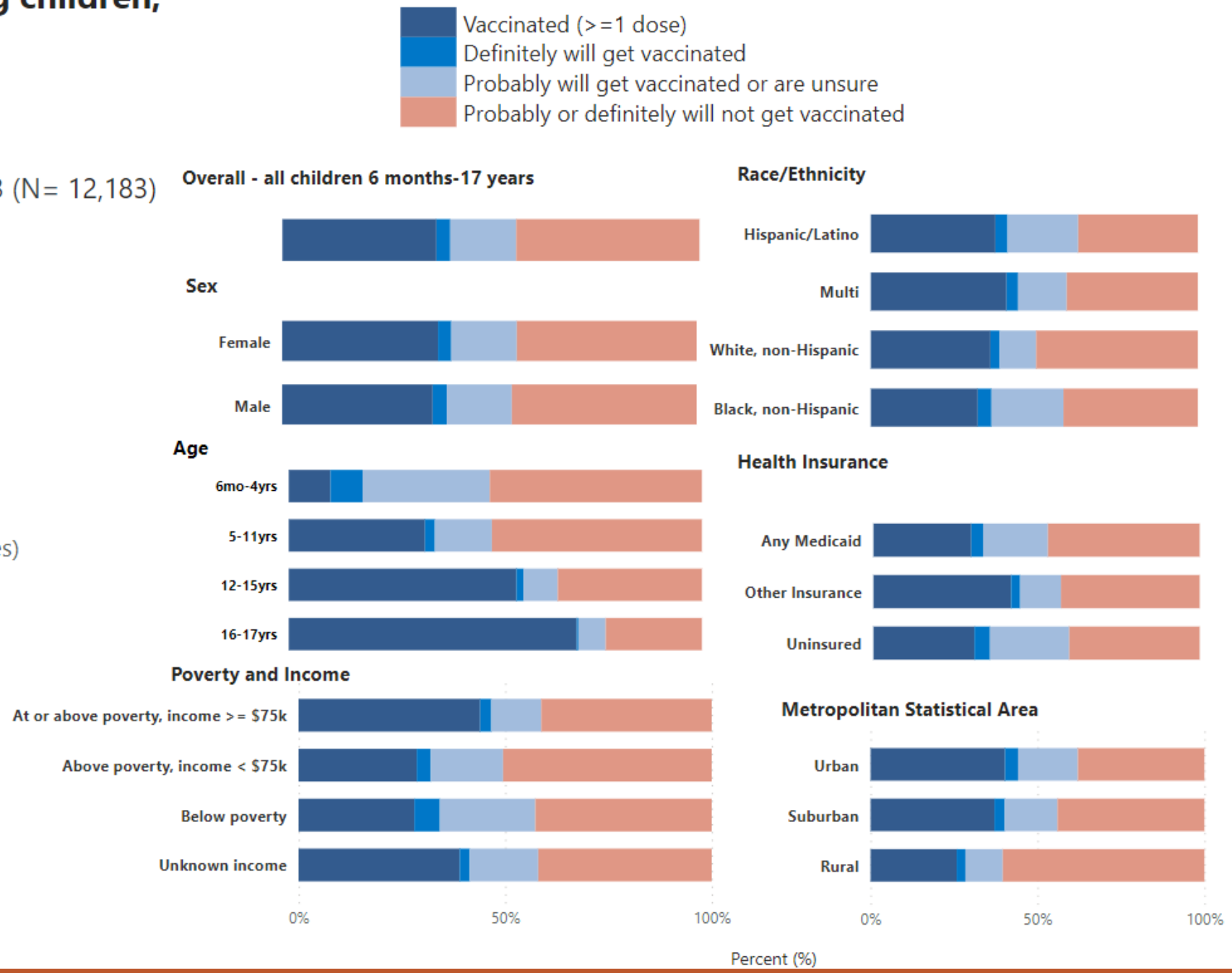
40.2% are **Vaccinated (>=1 dose) (36.9%)**

or

Definitely will get vaccinated (3.3%)

15.8% **Probably will get vaccinated or are unsure**

43.9% **Probably or definitely will not get vaccinated**



https://covid.cdc.gov/covid-data-tracker/#vaccine-confidence

Vaccination status and intent among all adults ages 18+, by demographics, United States

Data Collection Period: June 25 - June 30, 2023 (N= 18,035)

Vaccination status

- (●) Vaccinated (≥1 dose, among all adults)
- ( ) Received bivalent booster (among adults who completed primary series)

National | Jurisdictional

Overall

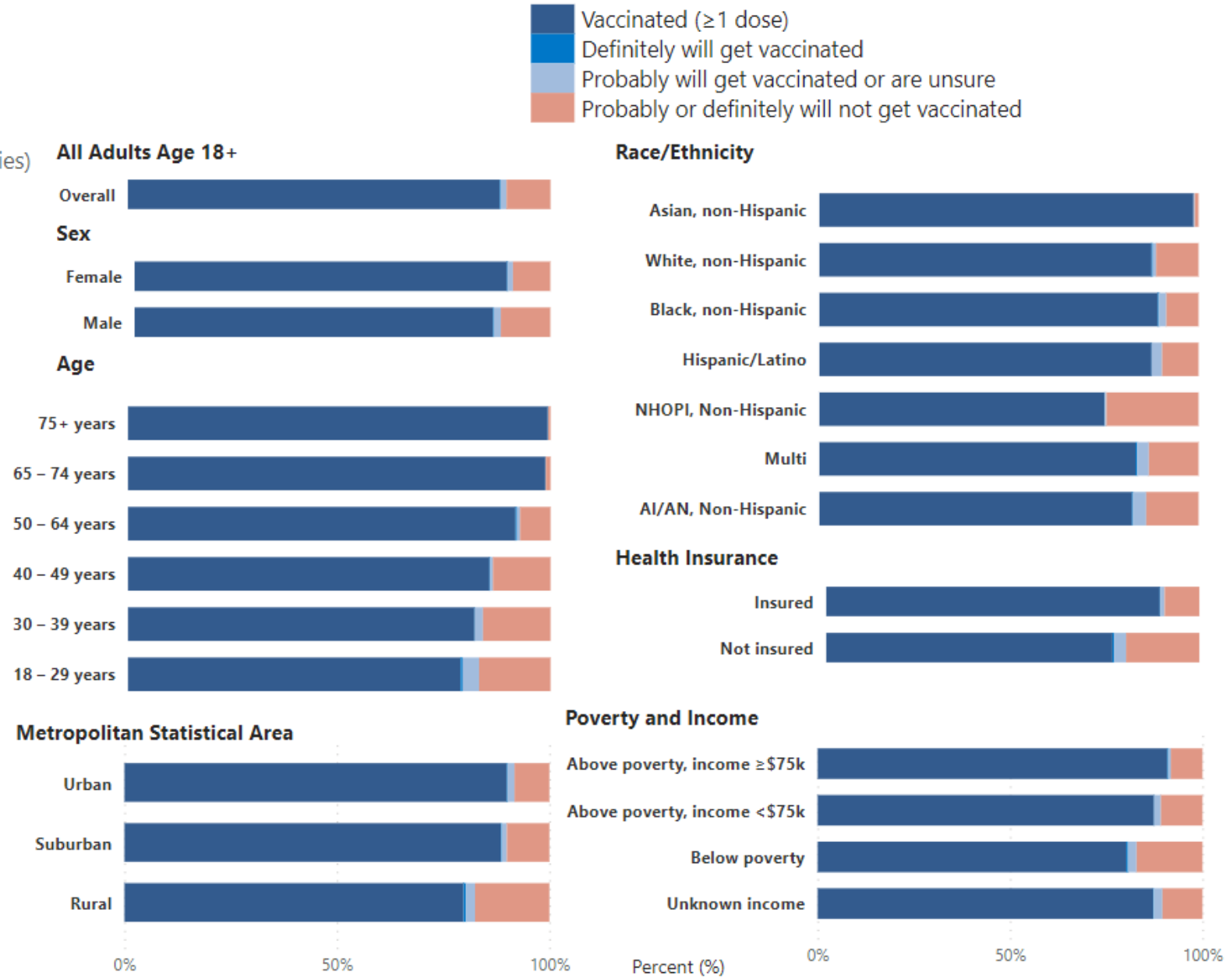
88.2% are **Vaccinated (≥1 dose) (88.0%)**

or

Definitely will get vaccinated (0.2%)

1.4% **Probably will get vaccinated or are unsure**

10.4% **Probably or definitely will not get vaccinated**



https://covid.cdc.gov/covid-data-tracker/#vaccine-confidence

Are we done yet?
Pandemics don’t end…they echo

-Brian Michael Jenkins

‘From a plague in Athens during the Peloponnesian War in 430 BCE…through the Black Death in the Middle Ages and on through the 1918 flu epidemic (which killed between 50 and 100 million people) and this century's deadly SARS outbreak, plagues have been a much more relentless fact of life than many realize….

The legacy of epidemics is not only one of lives lost but of devastated economies and social disorder, all of which have severe political repercussions’

The effect of the COVID-19 pandemic will be felt long after the last rapid test comes back positive…politically, socially, economically, medically…