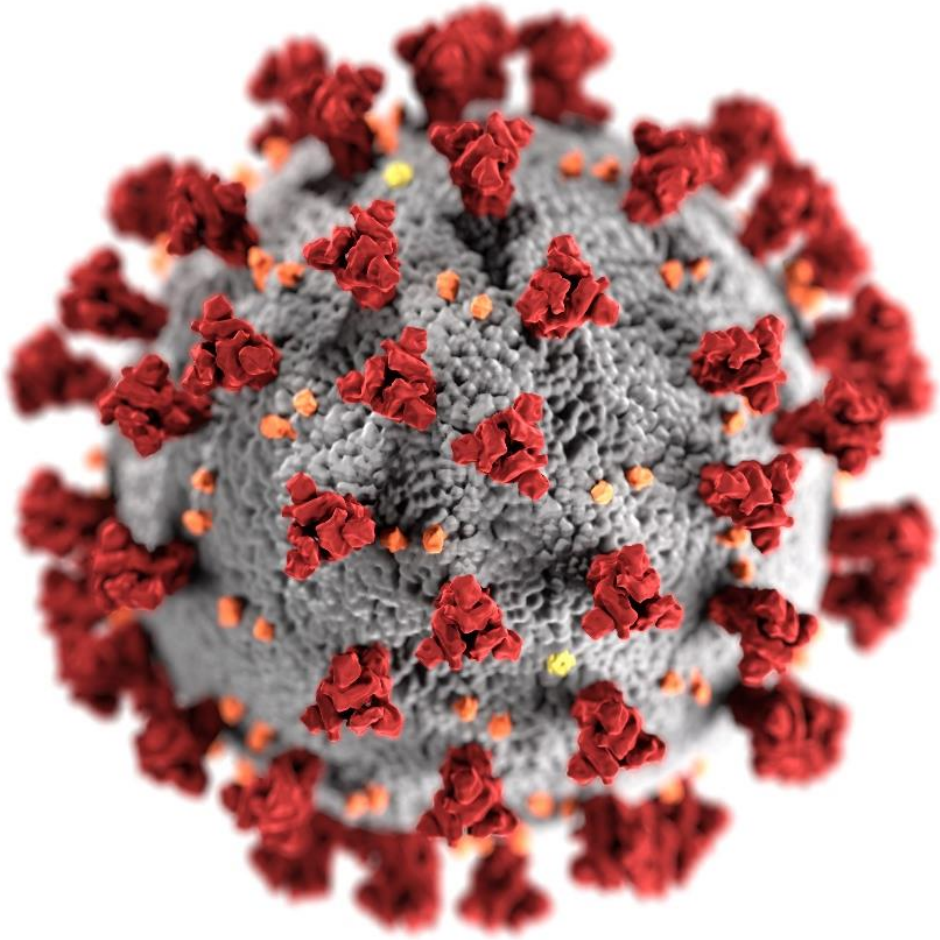
Updates to the Evidence to Recommendation Framework:

Pfizer-BioNTech COVID-19 booster in children aged 5-11 years



Sara Oliver, MD, MSPH

ACIP Meeting

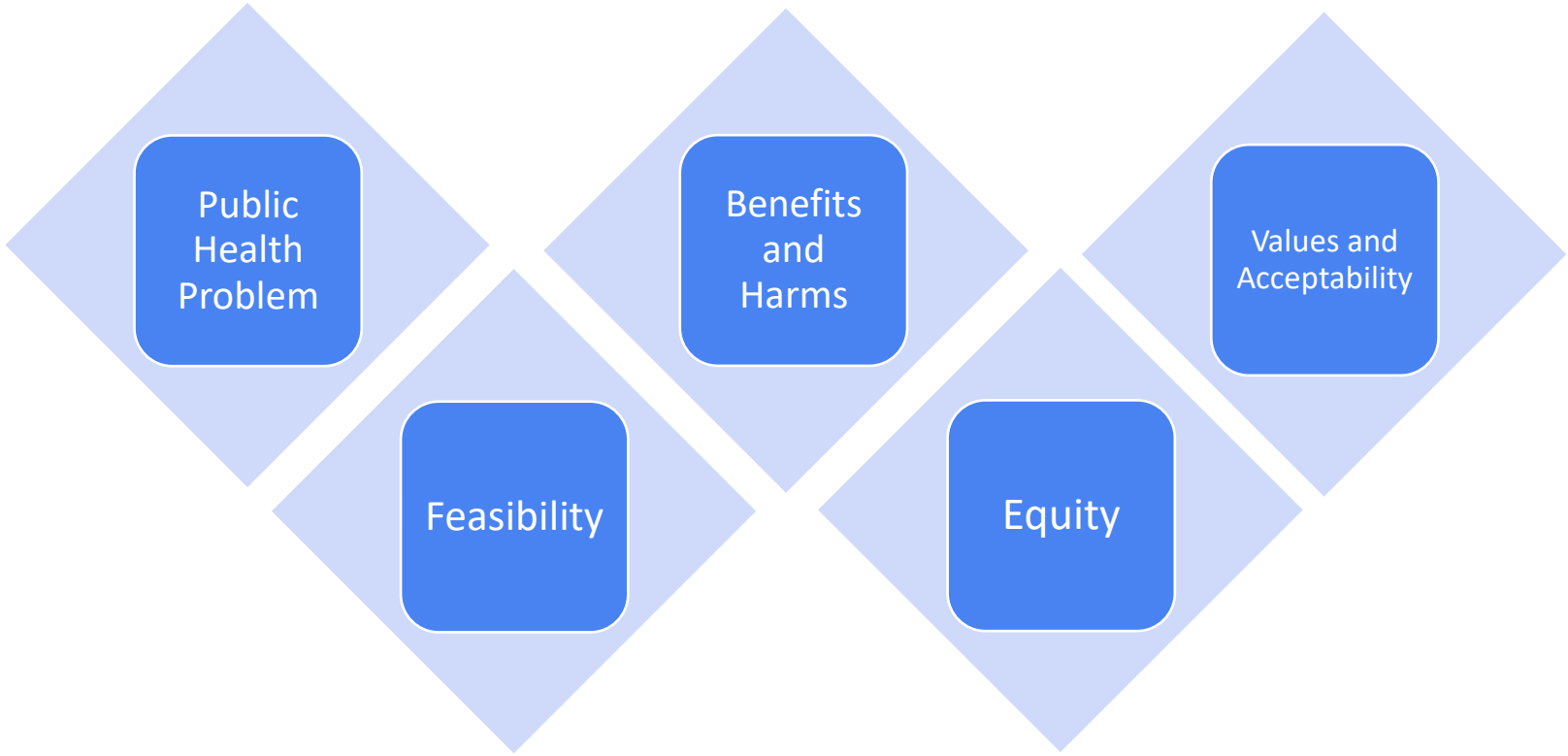
May 19, 2022

cdc.gov/coronavirus

Policy question

- Should individuals **ages 5–11 years** receive a Pfizer-BioNTech COVID-19 vaccine booster dose at least **5 months** after completion of the primary series, based on the balance of benefits and risks?

Evidence to Recommendations (EtR) Framework



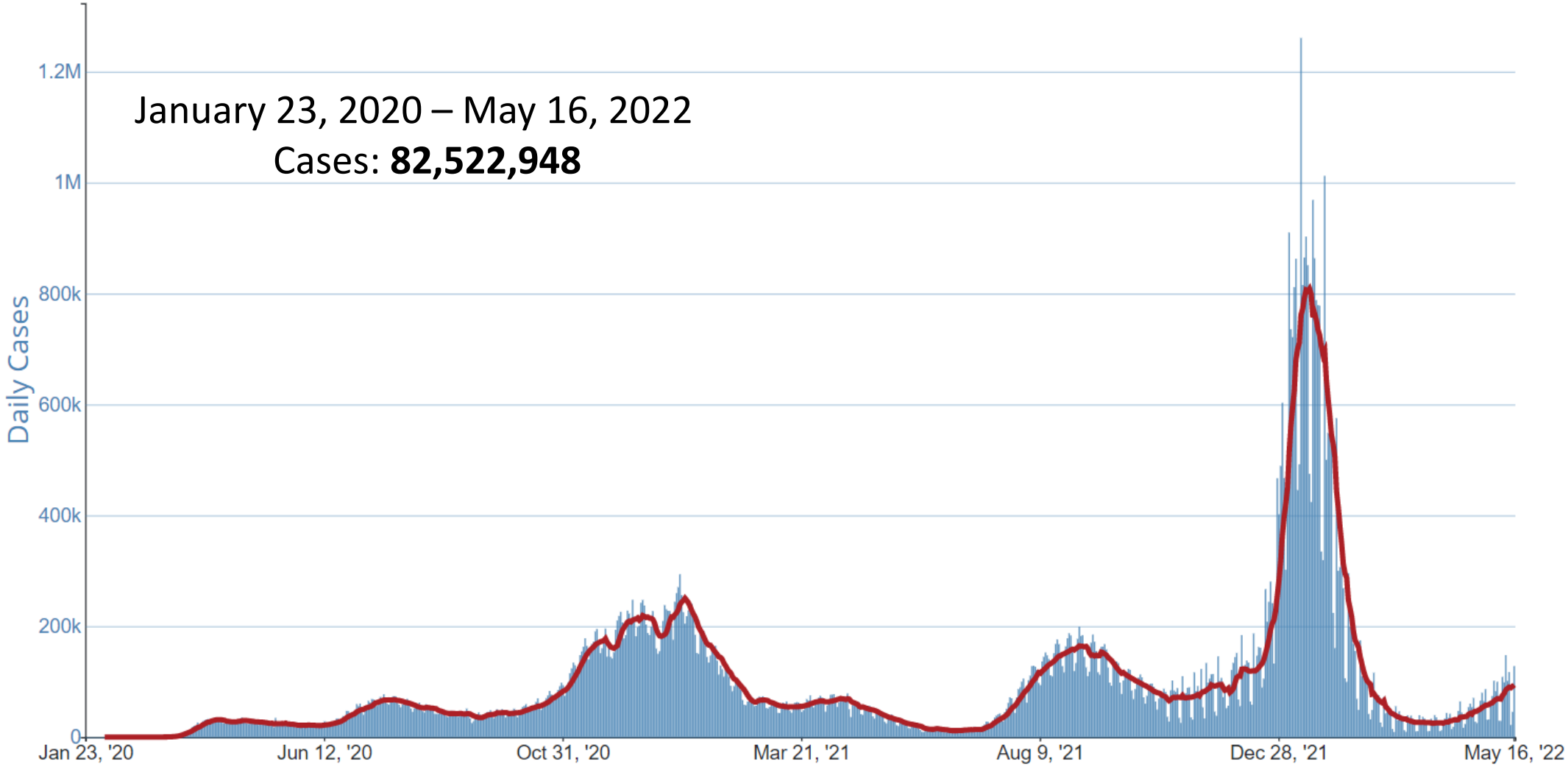
Evidence to Recommendations Framework

Booster doses of COVID-19 vaccines

Public Health Problem:
Review of the available evidence

- COVID-19 incidence and burden estimates
- COVID-19 associated hospitalization rates
- COVID-19 associated mortality
- Multisystem Inflammatory Syndrome in Children (MIS-C)
- Post-COVID conditions
- Missed school
- COVID-19 vaccine doses administered

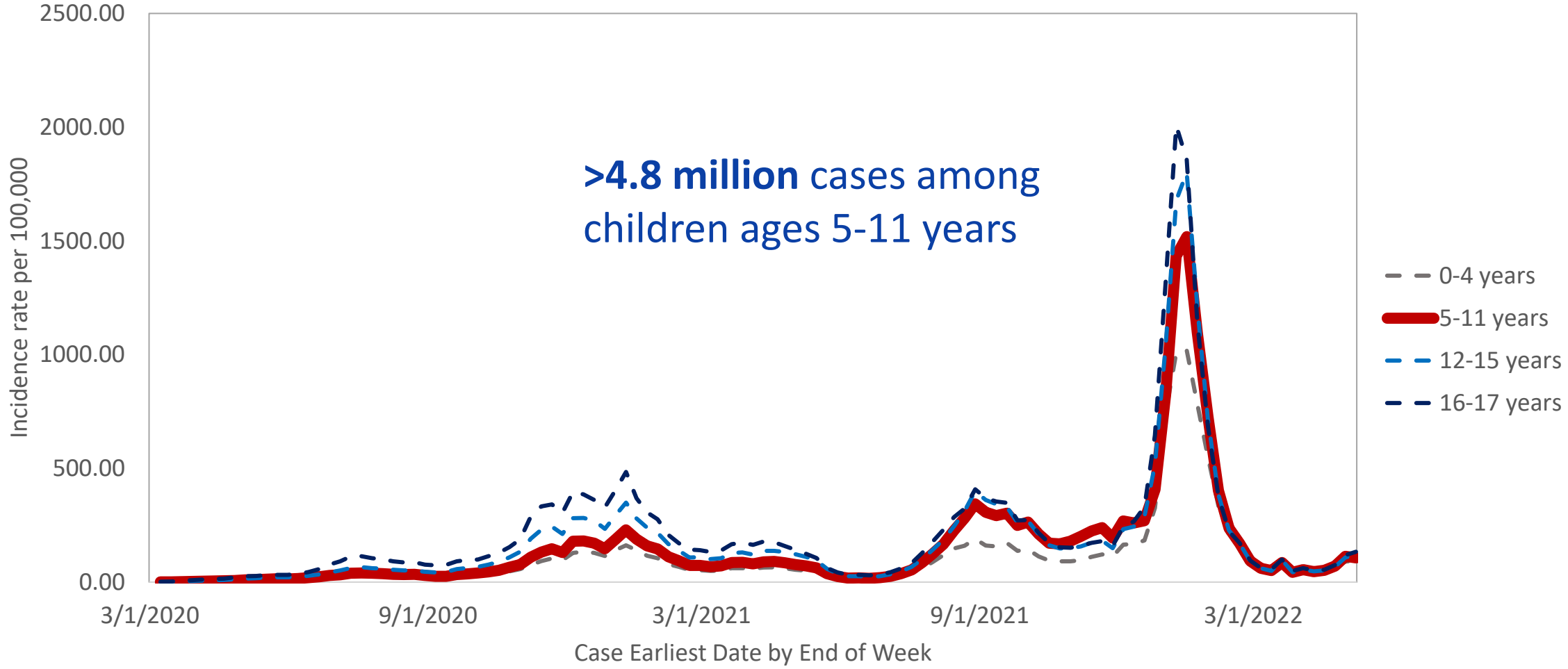
Trends in number of COVID-19 cases in the United States among all persons



Source: COVID Data Tracker, https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases , accessed 5/18/2022

COVID-19 weekly cases per 100,000 among children and adolescents ages 0-17 years, by age group

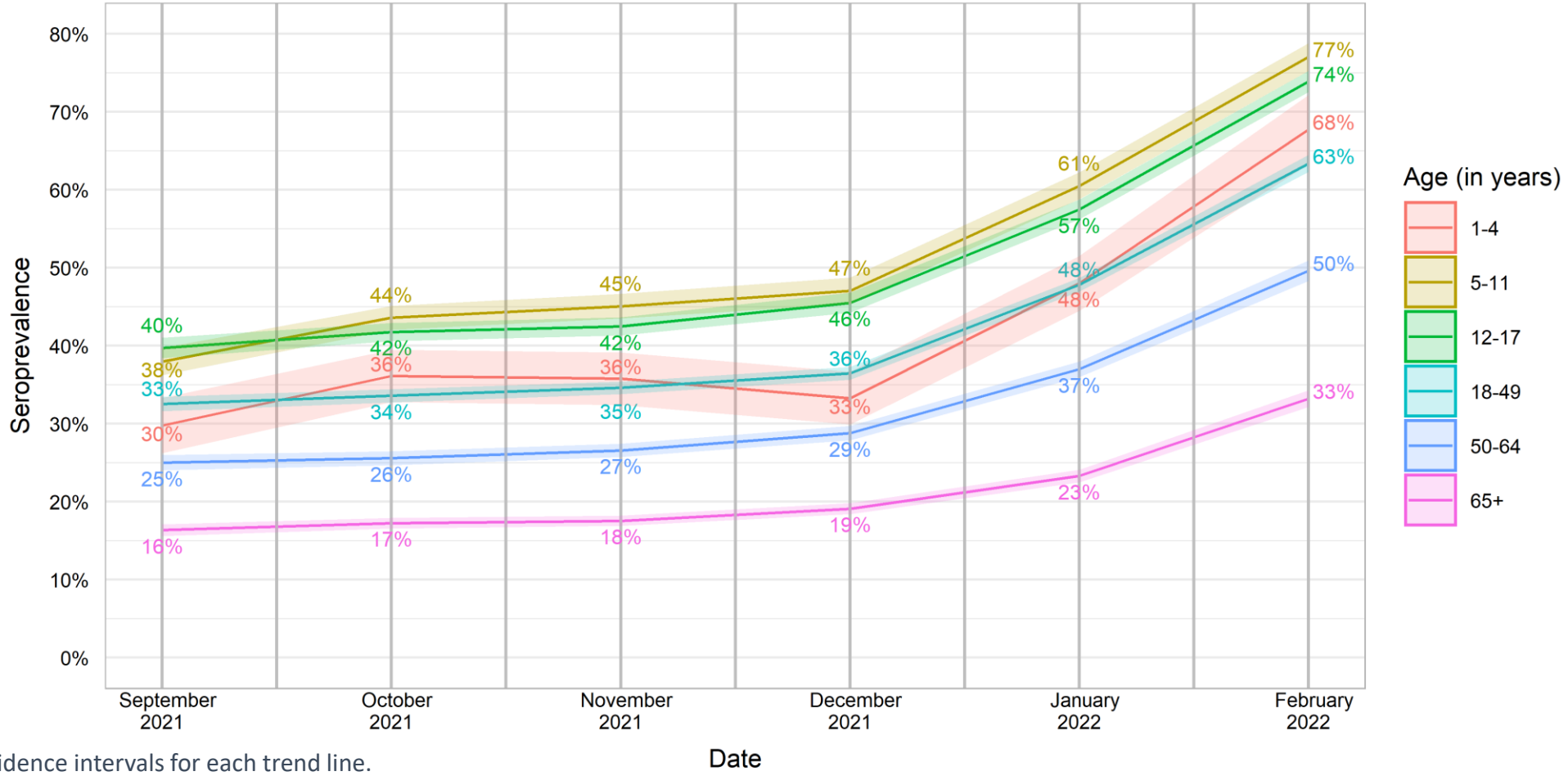
March 1, 2020 – May 8, 2022



Source: COVID Data Tracker, https://covid.cdc.gov/covid-data-tracker/#demographicsovertime, accessed 5/13/22

Seroprevalence of Infection-Induced SARS-CoV-2 Antibodies —National Commercial Lab Seroprevalence Study

September 2021–February 2022

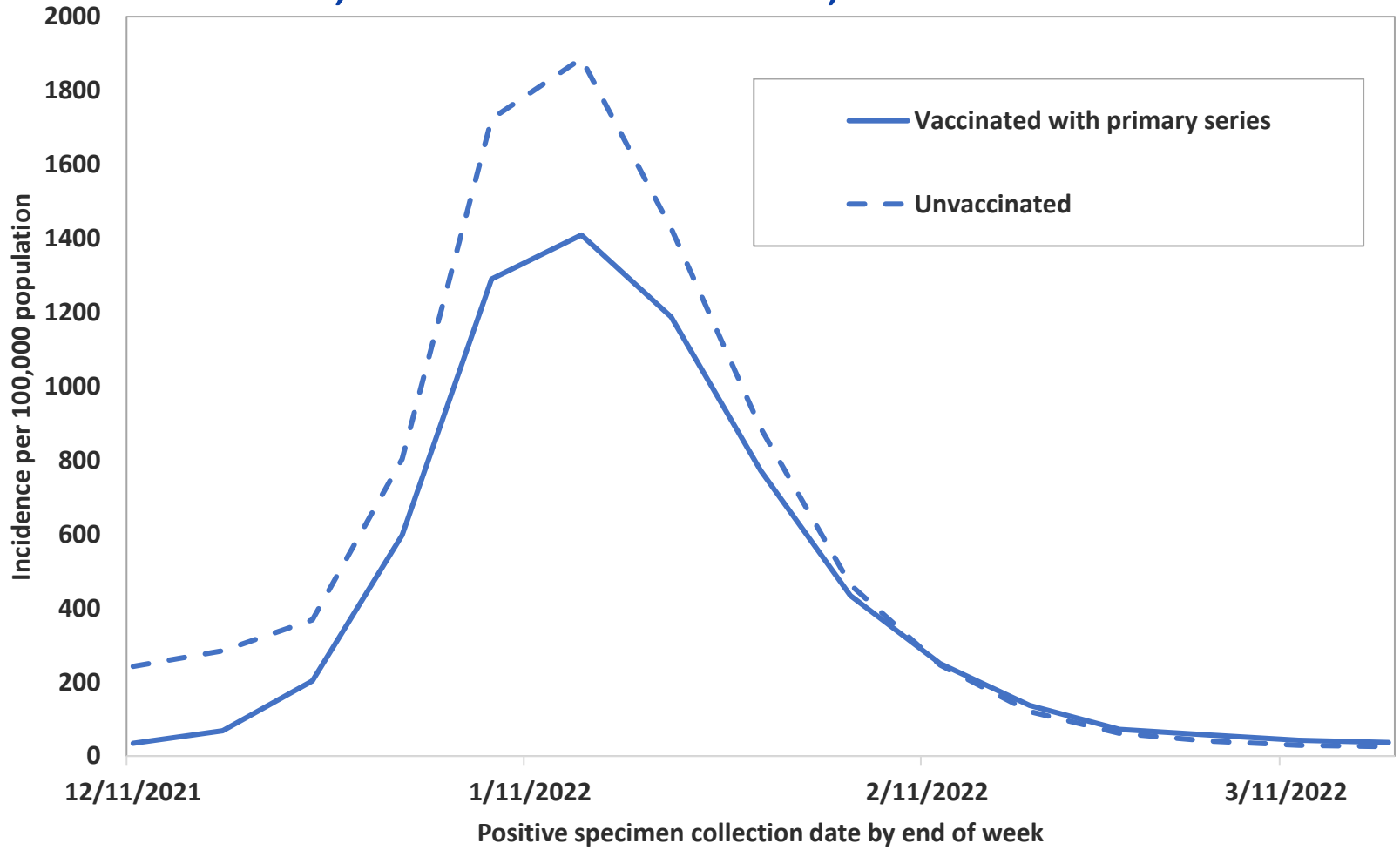


Shading indicates confidence intervals for each trend line.

Preprint: Clarke K, Kim Y, Jones J et al. Pediatric Infection-Induced SARS-CoV-2 Seroprevalence Estimation Using Commercial Laboratory Specimens: How Representative Is It of the General U.S. Pediatric Population? (April 26, 2022). Available at SSRN: https://ssrn.com/abstract=4092074 or http://dx.doi.org/10.2139/ssrn.4092074

Rates of COVID-19 cases by vaccination status among children ages 5-11 years in 27 U.S. jurisdictions

December 11, 2021 – March 19, 2022

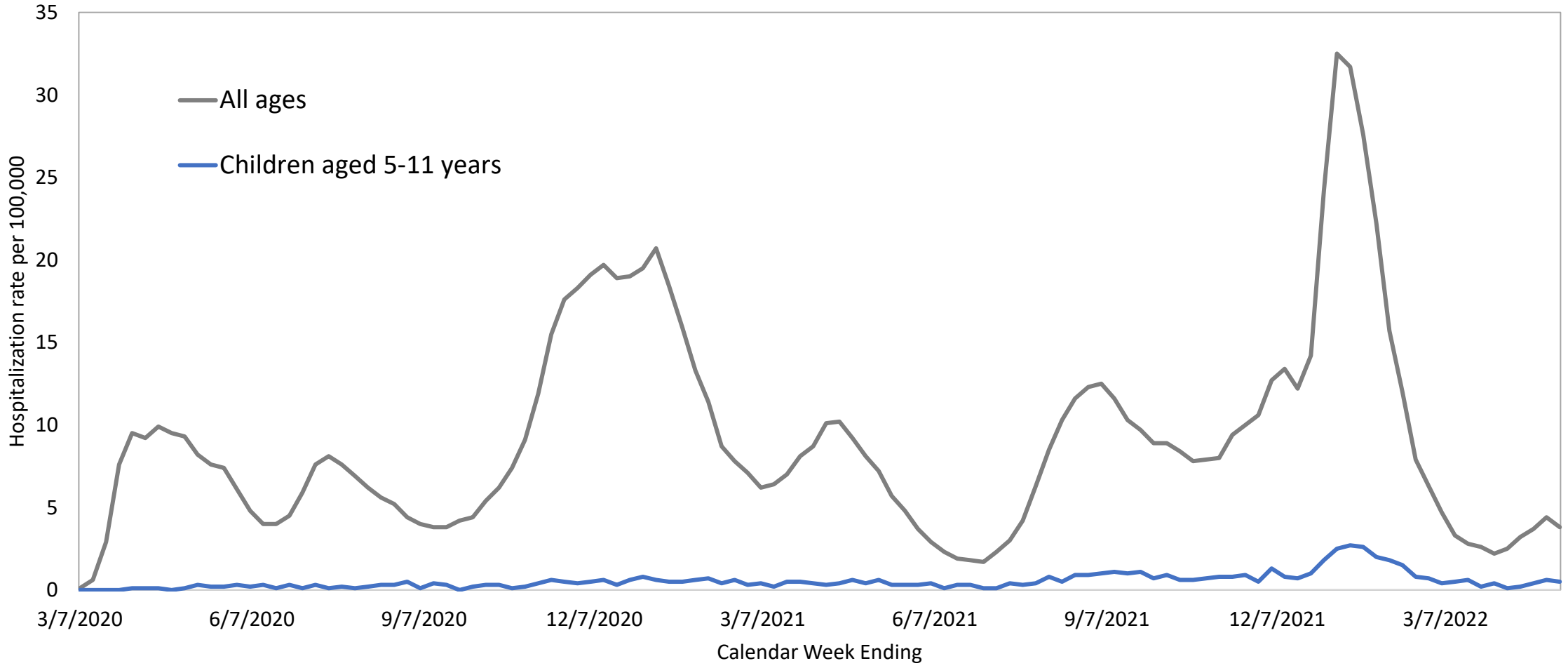


During Omicron predominant period, COVID-19 incidence rates among unvaccinated children ages 5 – 11 years were **1.3X** higher than rates in children vaccinated with a primary series.

Source: COVID Data Tracker, https://covid.cdc.gov/covid-data-tracker/#rates-by-vaccine-status, accessed 4/22/22

COVID-19-associated hospitalization rates, COVID-NET

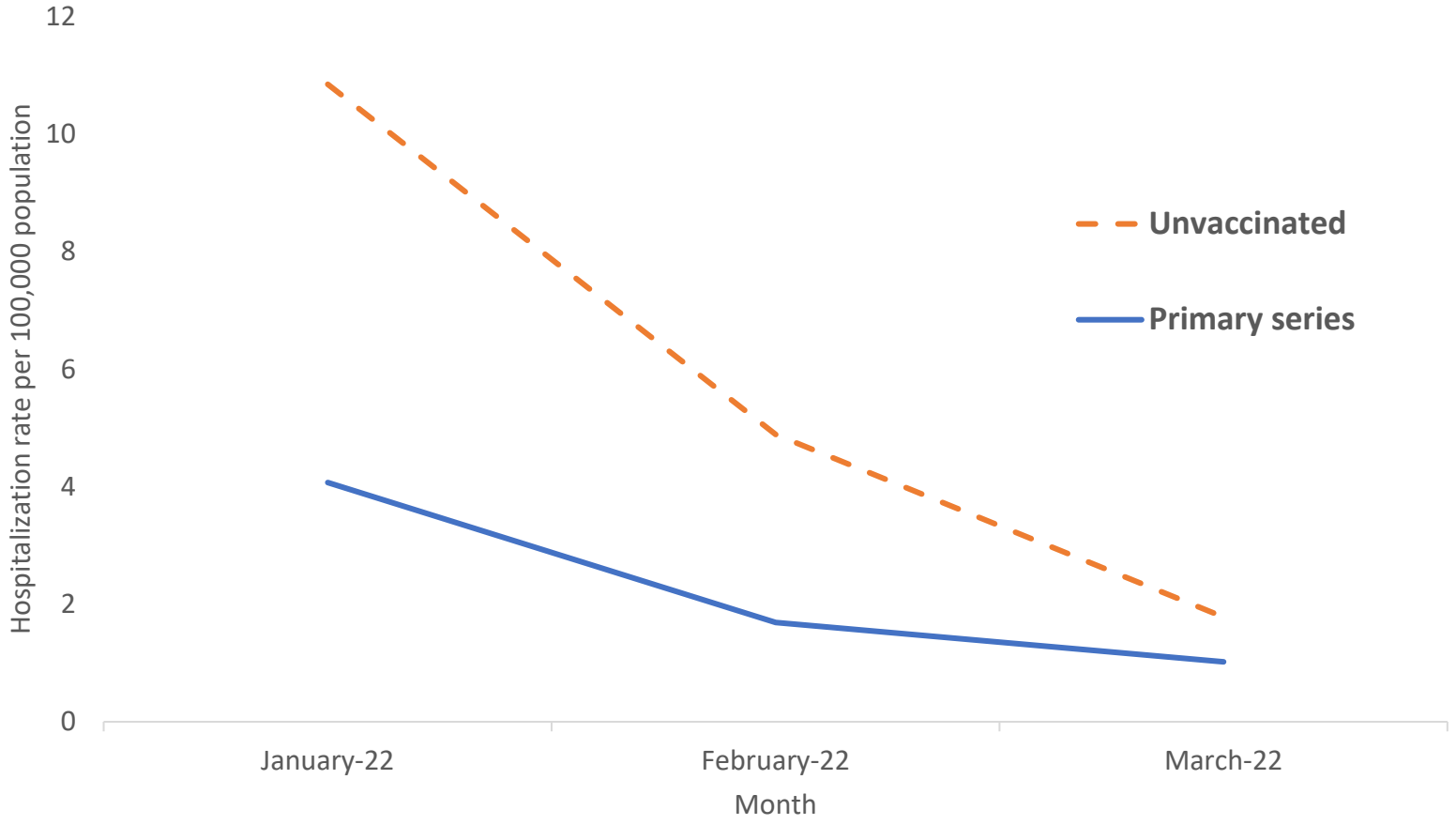
March 7, 2020 – May 7, 2022



Source: COVID-NET, https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html, accessed 5/14/22

Rates of COVID-19-associated hospitalizations by vaccination status in children ages 5-11 years

January 2022 – March 2022



During Omicron predominant period (12/19/21–2/28/22), COVID-19-associated hospitalization rates among unvaccinated children ages 5-11 years were **twice** as high as rates in children vaccinated with a primary series.

CDC COVID Data Tracker: COVID-NET Hospitalizations by Vaccination Status Accessed 5/12/22

Shi DS, Whitaker M, Marks KJ, et al. Hospitalizations of Children Aged 5-11 Years with Laboratory-Confirmed COVID-19 – COVID-NET, 14 States, March 2020-February 2022. MMWR Morb Mortal Wkly Rep 2022;71:574-581. DOI: http://dx.doi.org/10.15585/mmwr.mm7116e1

Characteristics of COVID-19-associated hospitalizations in children ages 5-11 years, COVID-NET

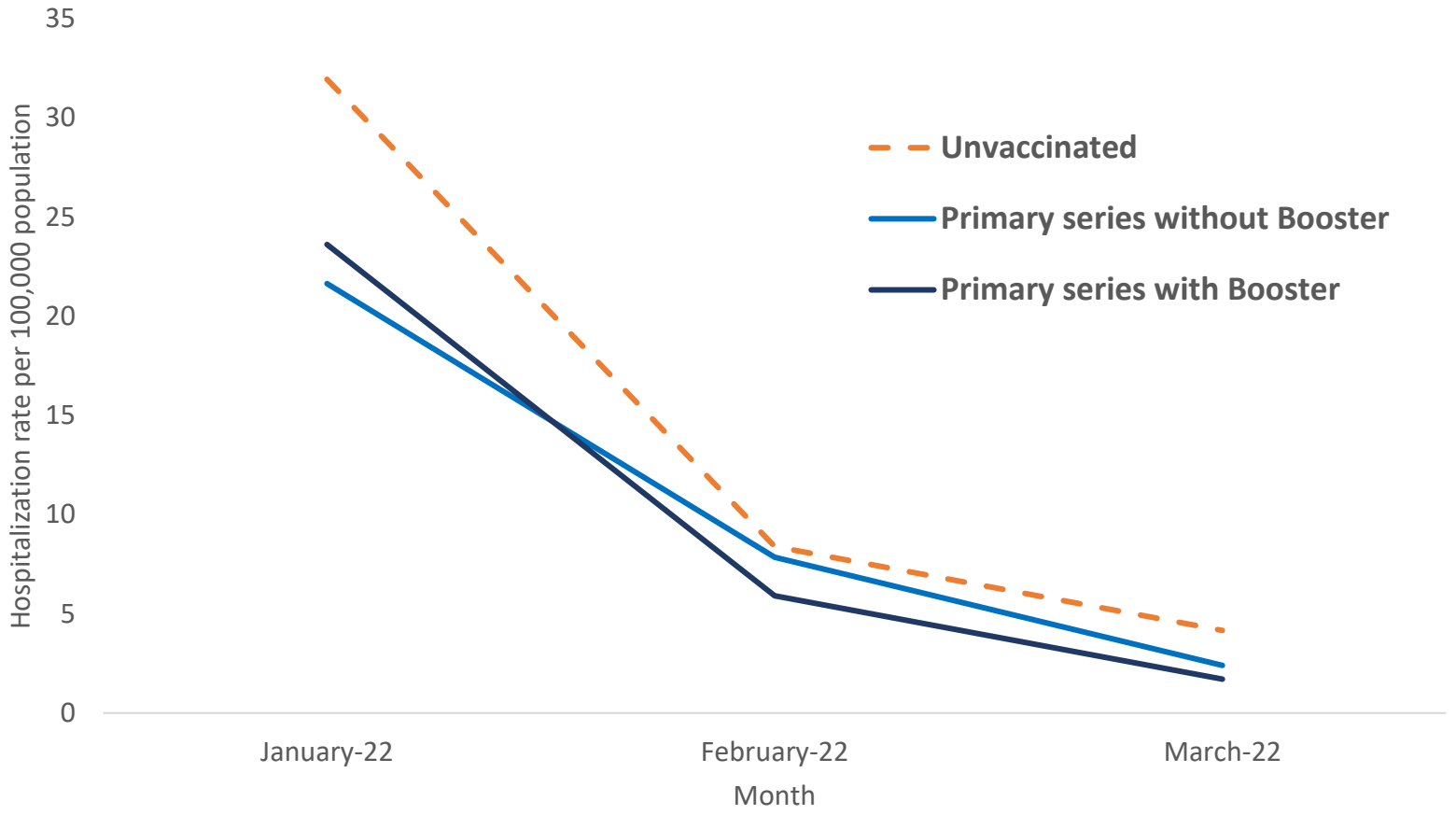
Omicron Predominant Period: December 19, 2021–February 28, 2022

- Most (**87**%) hospitalized children were unvaccinated
  - 53% were Black or Hispanic
- One-third of hospitalized children had no underlying medical conditions
- 27% required ICU admission
- No significant differences were found for severe outcomes by vaccination status (low numbers of vaccinated children)
  - No vaccinated children required higher level O^2 support

Shi DS, Whitaker M, Marks KJ, et al. Hospitalizations of Children Aged 5-11 Years with Laboratory-Confirmed COVID-19 – COVID-NET, 14 States, March 2020-February 2022. MMWR Morb Mortal Wkly Rep 2022;71:574-581. DOI: http://dx.doi.org/10.15585/mmwr.mm7116e1

Rates of COVID-19-associated hospitalizations by vaccination status in adolescents ages 12-17 years

January 2022 – March 2022

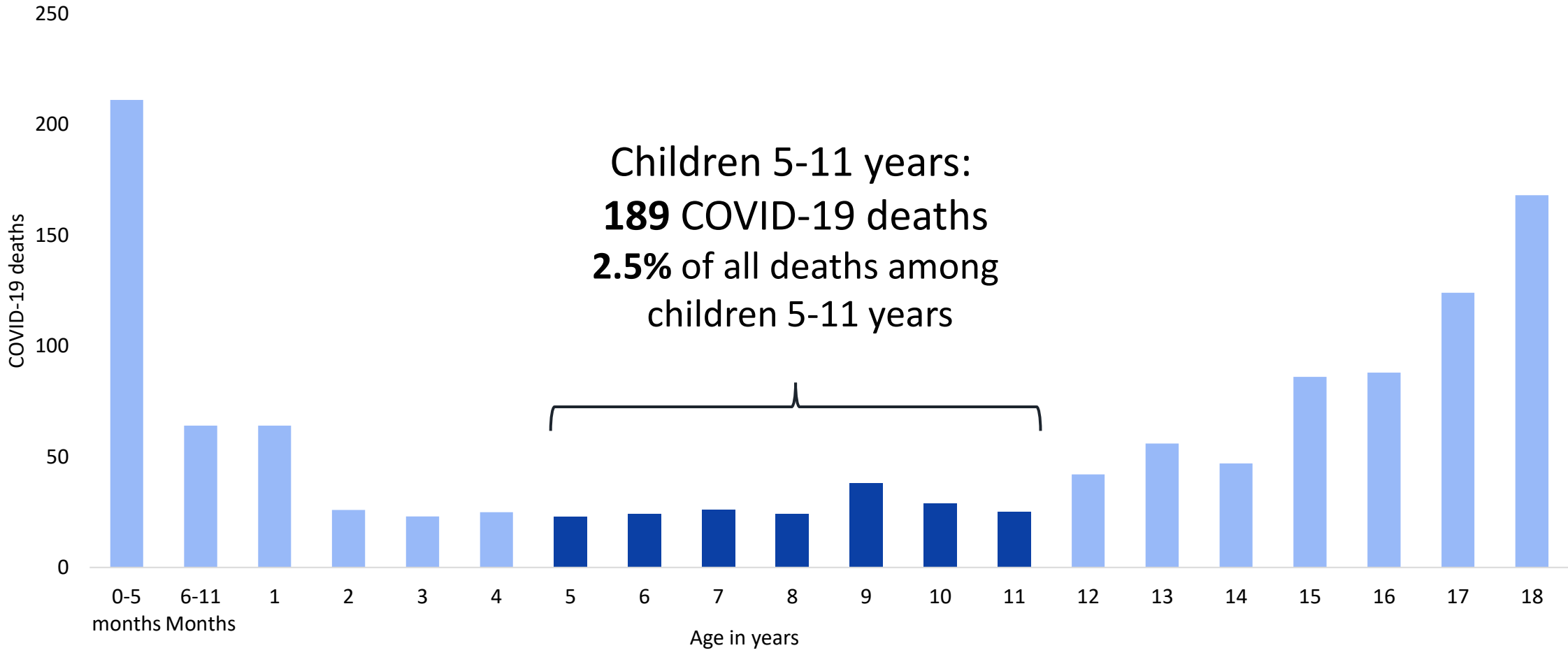


During March, monthly COVID-19-associated hospitalization rates among unvaccinated adolescents ages 12-17 years were **2.5X higher** compared to rates among adolescents vaccinated with primary series plus a booster or additional dose.

CDC COVID Data Tracker: COVID-NET Hospitalizations by Vaccination Status Accessed 5/11/22

COVID-19 deaths in children by age group, NCHS

January 1, 2020–May 7, 2022



https://data.cdc.gov/NCHS/Provisional-COVID-19-Deaths-Counts-by-Age-in-Years/3apk-4u4f/data. Accessed 5/14/22

Leading causes of death in children ages 5-11 Years, NCHS, 2020

Causes of Death	Death (n)	Crude rate per 100,000
Accidents (unintentional injuries)	953	3.4
Malignant neoplasms	532	1.9
Assault (homicide)	249	0.9
Congenital malformations, deformations and chromosomal abnormalities	216	0.8
Chronic lower respiratory diseases	93	0.3
Intentional self-harm (suicide)	87	0.3
Diseases of the heart	84	0.3
Influenza and pneumonia	75	0.3
Cerebrovascular diseases	49	0.2
In situ neoplasms, benign neoplasms and neoplasms of uncertain or unknown behavior	35	0.1
COVID-19	26	0.1

CDC NCHS WONDER Online Database. Accessed at http://wonder.cdc.gov/ucd-icd10.html on April 22, 2022 Total population 5-11 years, 2020: 28,409,706

Multisystem Inflammatory Syndrome in Children (MIS-C)

- Severe hyperinflammatory syndrome occurring 2-6 weeks after acute SARS-CoV-2 infection, resulting in a wide range of manifestations and complications
  - 60-70% of patients are admitted to intensive care, 1-2% die[1,2]

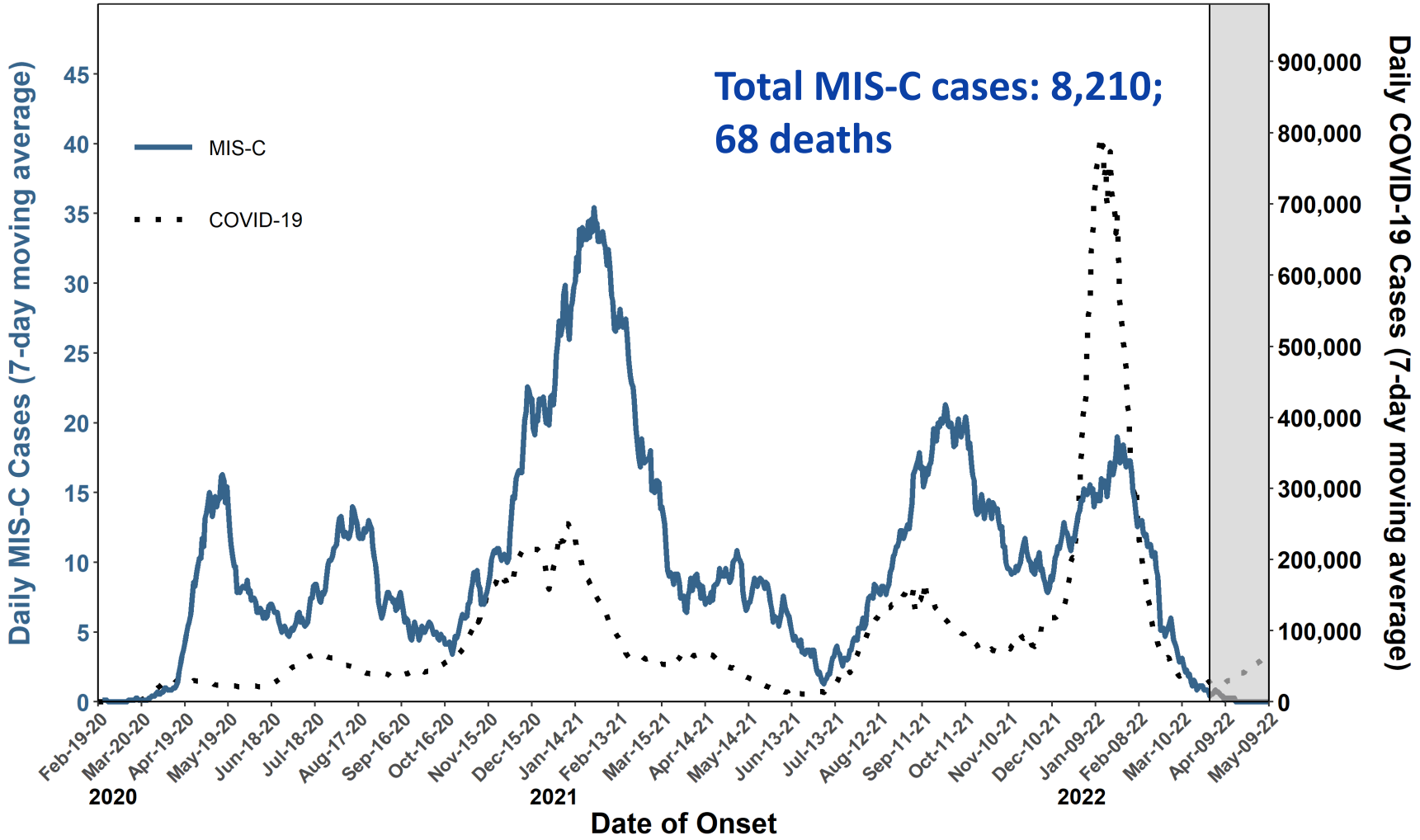
- Incidence early in the COVID-19 pandemic (April – June 2020) was approximately 1 case of MIS-C per 3,000 SARS-CoV-2 infections in persons <21 years[3]
  - Incidence was highest among racial/ethnic minority children and adolescents, including non-Hispanic Black and Hispanic or Latino children and adolescents[3]

1. Feldstein LR, et al. Characteristics and Outcomes of US Children and Adolescents With Multisystem Inflammatory Syndrome in Children (MIS-C) Compared With Severe Acute COVID-19. JAMA. 2021;325(11):1074-1087. doi:10.1001/jama.2021.2091

2. Belay ED, et al. Trends in Geographic and Temporal Distribution of US Children With Multisystem Inflammatory Syndrome During the COVID-19 Pandemic. JAMA Pediatr. 2021;175(8):837-845. doi:10.1001/jamapediatrics.2021.0630

3. Payne AB, et al. Incidence of Multisystem Inflammatory Syndrome in Children Among US Persons Infected With SARS-CoV-2. JAMA Netw Open. 2021 Jun 1;4(6):e2116420. doi: 10.1001/jamanetworkopen.2021.16420.

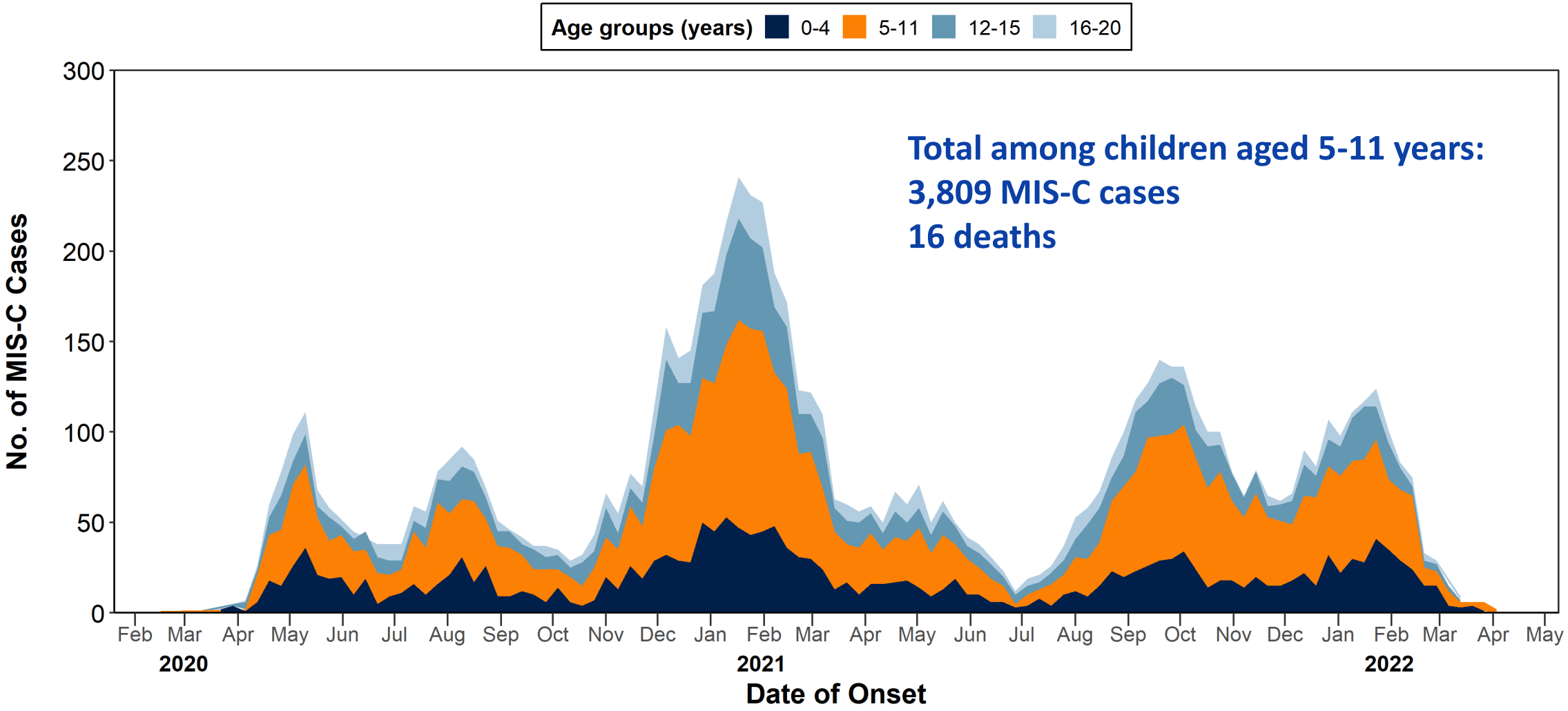
Daily MIS-C and COVID-19 cases reported to CDC (7-day moving average), onset February 19, 2020–May 2, 2022



MIS-C cases are among individuals ages <21 years. COVID-19 cases reflect all cases reported to CDC (among individuals of all ages). The grayed-out area on the right side of the figure represents the most recent 6 weeks of data, for which reporting of MIS-C cases is still incomplete. Date of onset was missing for 1 of the 8,210 cases.

https://covid.cdc.gov/covid-data-tracker/#mis-national-surveillance

Weekly MIS-C Case Counts by Age Group (N=8,210)
February 1, 2020 – May 2, 2022



CDC data

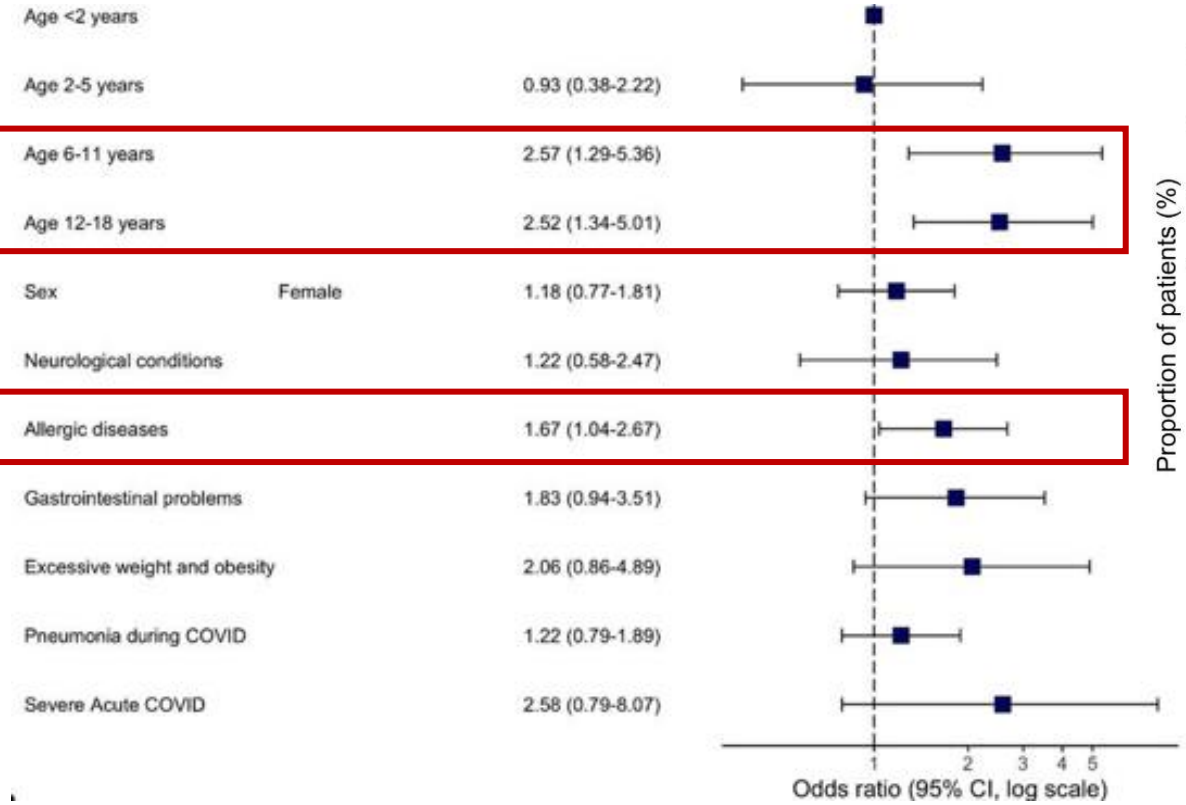
Post-COVID conditions in children

- **Post-COVID conditions in children**
  - Appears to be less common in children than in adults
  - A national survey in the UK found **7-8%** of children with COVID-19 reported continued symptoms >12 weeks[1]
  - Can appear after mild to severe infections, and after MIS-C
- **Most common symptoms:** Similar to adults and include fatigue, headache, insomnia, trouble concentrating, muscle and joint pain, and cough[2,3]
- **Impact on quality of life:** Limitations of physical activity, feeling distressed about symptoms, mental health challenges, decreased school attendance/participation[2]

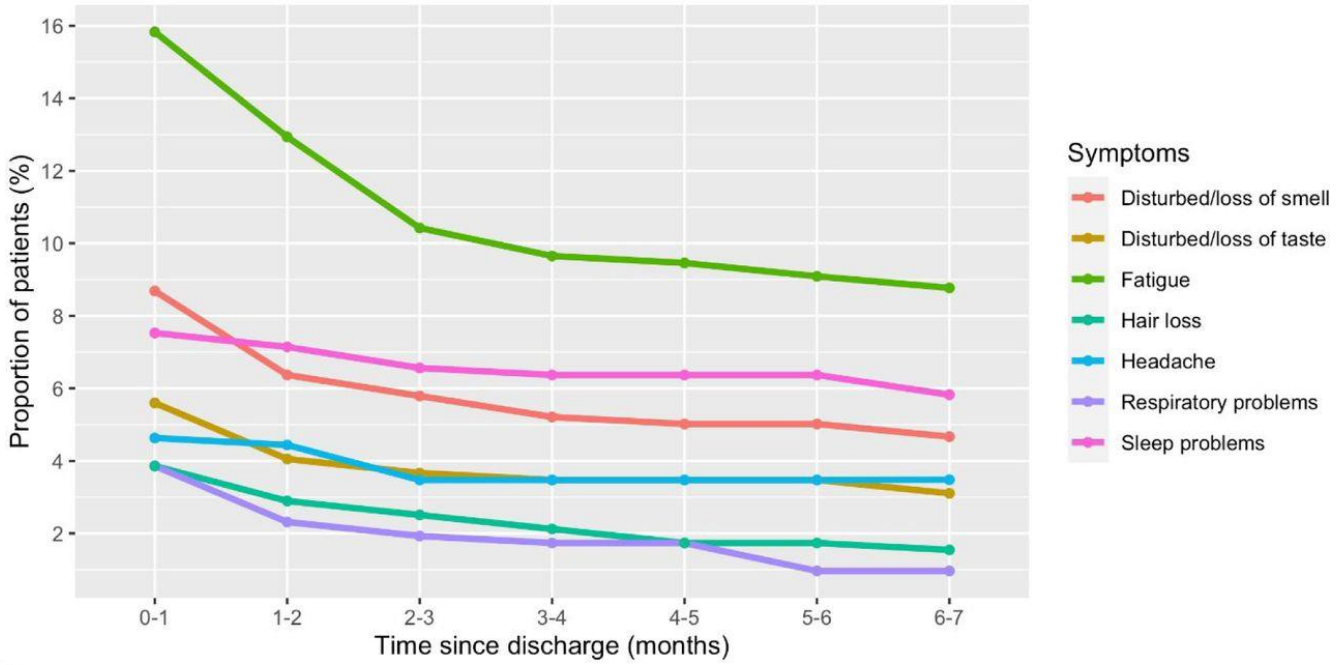
[1]Office for National Statistics United Kingdom. (2021) Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK. Retrieved on September 17, 2021 from Office for National Statistics' website. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/1april2021
[2]Buonsenso D, Munblit D, De Rose C, et al. Preliminary evidence on long COVID in children. *Acta Paediatr*. 2021;110(7):2208-2211. doi:10.1111/apa.15870.
[3]Molteni E, Sudre CH, Canas LS, et al. Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2. Lancet Child Adolesc Health 2021; 5: 708–18. https://www.thelancet.com/action/showPdf?pii=S2352-4642%2821%2900198-X

Post-COVID conditions in children previously hospitalized for COVID-19

- **Risk factors include older age and allergic disease**



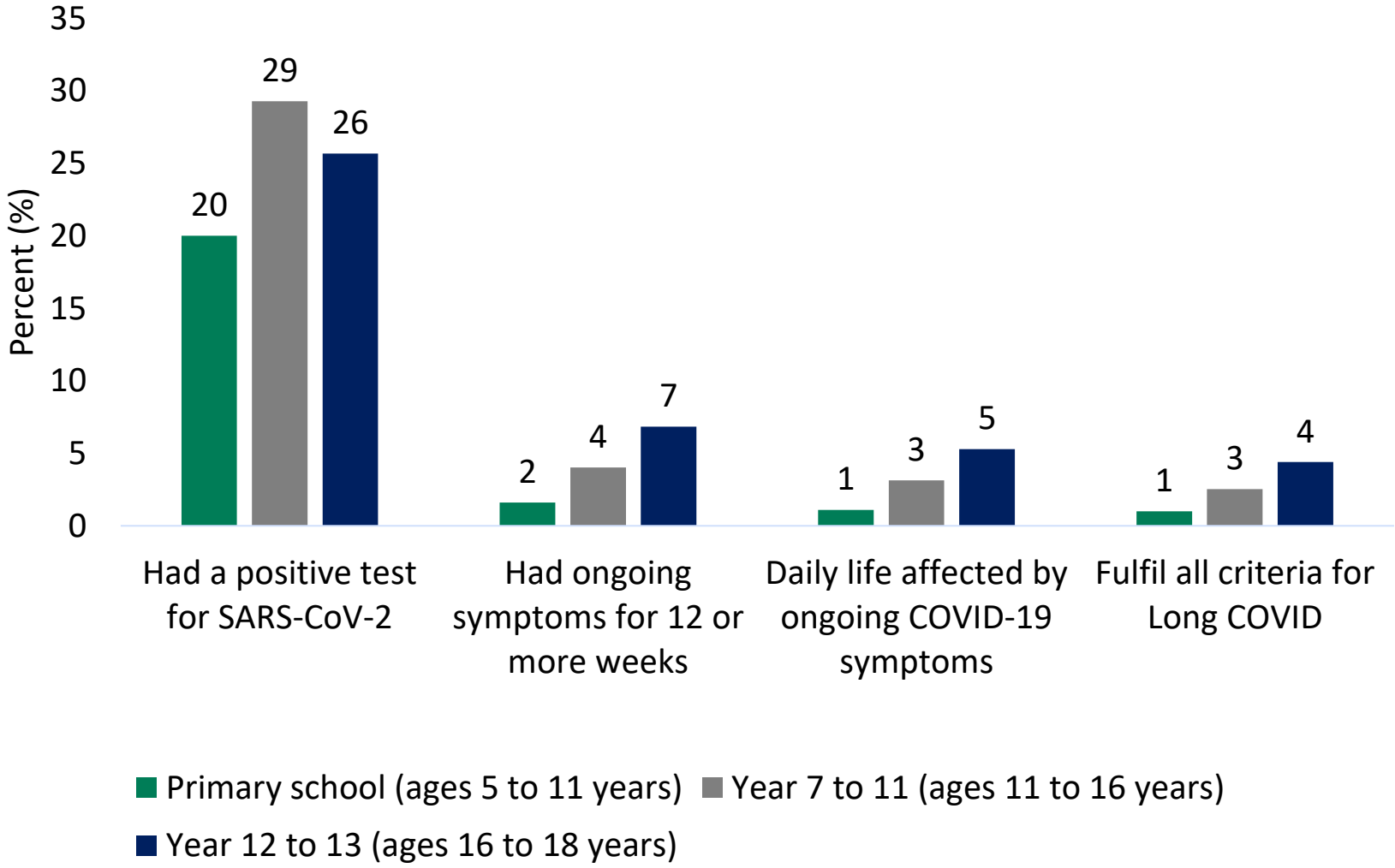
- **Symptoms decrease over time**



Osmanov et al. Risk factors for long COVID in previously hospitalized children. European Respiratory Journal 2021

Non-hospitalized children also experience post-COVID conditions

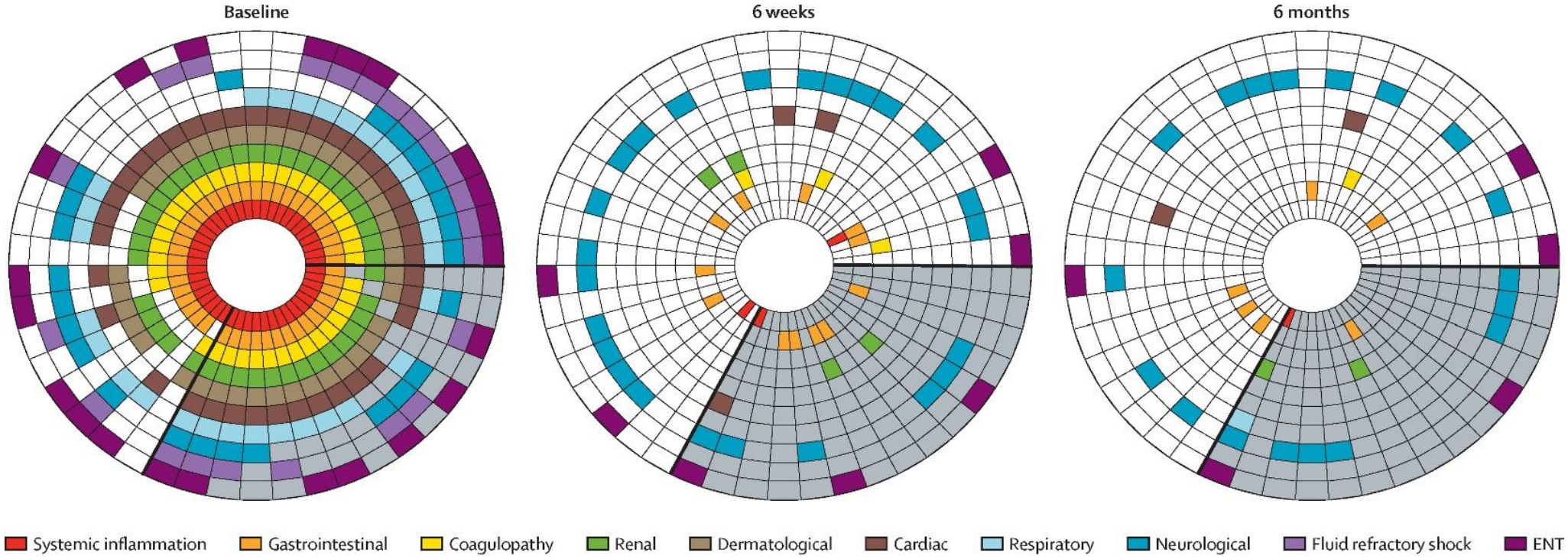
- Survey of school age children and parents in the UK (n = 4,530)
  - Weighted to ages 5 - 18 years, UK population
- Occurrence higher among adolescents



COVID-19 Schools Infection Survey, England: mental health and long COVID November to December 2021 - Office for National Statistics. Accessed March 2022

Children with MIS-C are at risk of ongoing symptoms

- Continued difficulties at 6 months were reported by 35% of children and 21% of parents
- Specific system involvement decreased by 6 months



Penner J. et al. 6 month follow-up MIS-C. Lancet Pediatric 2021

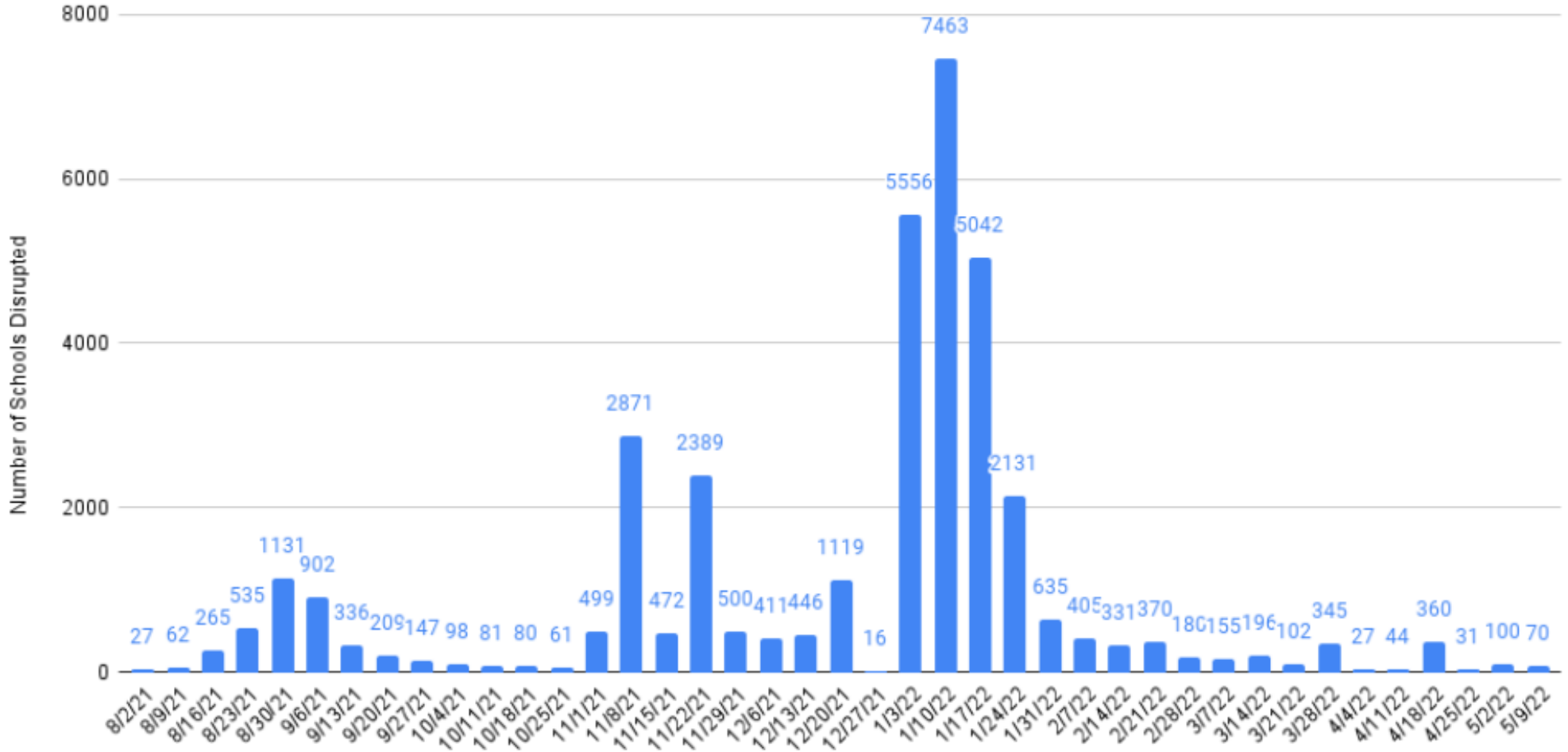
Post-COVID conditions may be less likely to occur after vaccine breakthrough

- While most studies on post-COVID conditions occurring after vaccine breakthrough have focused on adults, two included adolescents [1,2]
  - Persons who were previously vaccinated were less likely to have symptoms between 12 and 20 weeks after infection compared to persons who were unvaccinated (OR 0.22, 95% 0.20, 0.25)[1]
  - Persons who were previously vaccinated had a lower occurrence of post-COVID conditions after infection compared to persons who were unvaccinated [2]

1. Simon et al. Reduced Incidence of Long-COVID Symptoms | medRxiv 2022
2. Tarquet et al. Six-month sequelae of post-vaccination SARS-CoV-2 infection| medRxiv 2022

COVID-19 related K-12 school disruptions by week,

August 2, 2021 – May 9, 2022



Data from burbio: https://cai.burbio.com/school-opening-tracker/. Accessed May 14, 2022.

* A COVID-19 related school disruption is defined as a school moving away from regular in-person instruction caused in some way by the pandemic

Indirect impacts of COVID-19 pandemic on children

- Worsening of mental or emotional health

- Widening of existing education gaps

- Decreased physical activity and increased body mass index (BMI)

- Decreased healthcare utilization

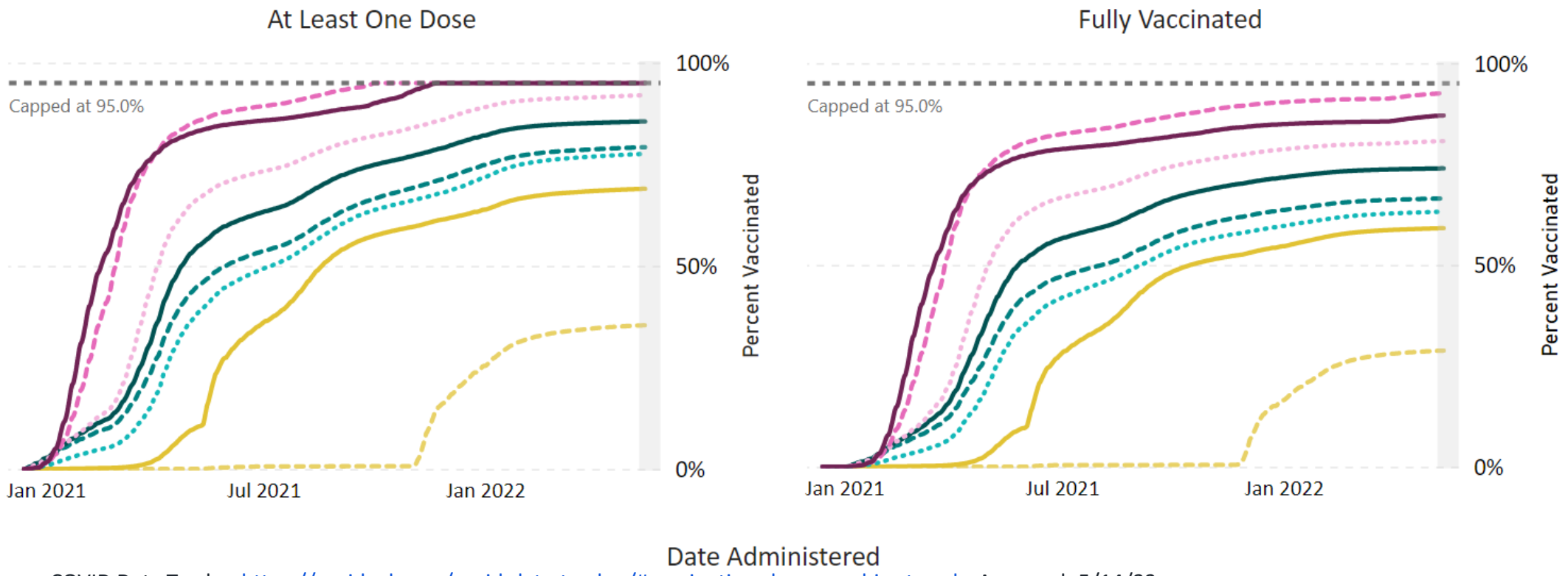
- Decreased routine immunizations

- Increase in Adverse Childhood Experiences (ACEs)

Vaccination coverage by age group, United States

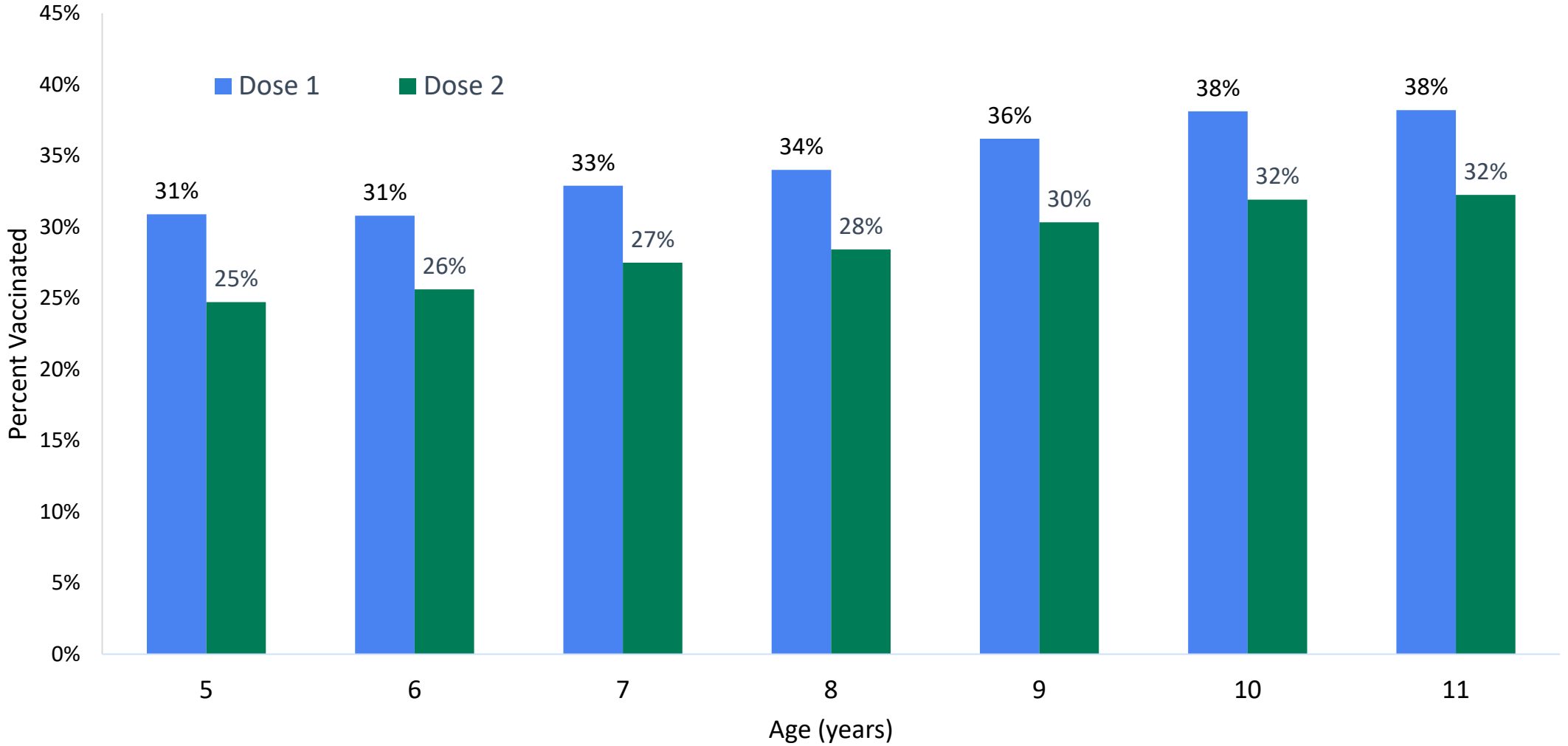
December 14, 2020-May 14, 2022

	5-11 yrs	12-17 yrs	18-24 yrs	25-39 yrs	40-49 yrs	50-64 yrs	65-74 yrs	75+ yrs
At Least One Dose	35.4%	69.0%	77.6%	79.2%	85.5%	92.0%	95.0%	95.0%
Fully Vaccinated	28.8%	59.1%	63.2%	66.5%	73.9%	80.7%	92.6%	87.0%



Source: COVID Data Tracker https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends. Accessed: 5/14/22

Vaccination coverage by age as of May 7, 2022, United States



Notes: Excludes vaccine refusals and vaccines administered by DoS (Department of State). Excludes Texas and Idaho data as these states only report aggregate data and do not report data for individual age years.

Source: CDC's Immunization Data Lake. Accessed May 13, 2022.

Public Health Problem:
Summary of the available evidence

- **Children ages 5-11 years are at risk of severe illness from COVID-19**
  - Over 4.8 million reported cases and >15,000 hospitalizations to date
  - In 2020, COVID-19 was a leading cause of death in children ages 5 – 11 years
- **Children who have received a COVID-19 vaccine primary series have better outcomes than children who are unvaccinated, particularly against severe illness**
- **28.8% of children ages 5-11 years have completed their primary series**

Evidence to Recommendations Framework

Booster doses of COVID-19 vaccines

Benefits and Harms:
Review of the available evidence

- Benefits:
  - Immunogenicity of a third dose
- Harms:
  - Adverse events from clinical trial
  - Reactogenicity from clinical trial
- Other considerations:
  - Seroprevalence
  - Myocarditis
  - Estimates of benefit/risk analysis

Immunogenicity

- Open label continuation of Pfizer phase 2/3 randomized controlled trial (unpublished, data obtained from sponsor)
- Children ages 5 – 11 years in United States
  - 3-Dose set: 67 participants who received 10µg booster dose (dose 3) completed the 1-month post-dose 3 visit, and were SARS-CoV-2 negative at baseline
  - 2-Dose set: 67 participants randomly selected from the previously analyzed dose 2 evaluable immunogenicity population who were SARS-CoV-2 negative at baseline
- Immunogenicity analyses were based on immune responses at each time point with descriptive comparison of immune responses at 1-month post-Dose 3 compared with immune responses at 1-month post-Dose 2.
- All participants who received dose 3 got the booster dose ≥7 months after Dose 2, most commonly between 8 and 9 months post-dose 2 (69.9%).

Immunogenicity Population

Population	Description	N
2-dose set	Independent population from the 3-dose group. Participants with 1 month post dose 2 assay results, without evidence of prior infection	67
3-dose set	Participants in the 3 dose-set that had 1 month post dose 2 assay results, without evidence of prior infection	29
3-dose set	Participants in the 3 dose-set that had 1 month post dose 3 assay results, without evidence of prior infection	67

Summary of Geometric Mean Titers

	3-dose set			2-dose set		Total	
Outcome	Sampling time point	N	GMT[a] (95% CI)	N	GMT[a] (95% CI)	N	GMT[a] (95% CI)
SARS-CoV-2 neutralization assay – NT50 (titer)	Prior to dose 1	79	20.5 (20.5, 20.5)	67	20.5 (20.5, 20.5)	146	20.5 (20.5, 20.5)
	1 month post dose 2	29	1659.4 (1385.1, 1988.0)	67	1110.7 (965.3, 1278.1)	96	1253.9 (1116.0, 1408.9)
	Prior to dose 3	67	271.0 (229.1, 320.6)	-	-	67	271.0 (229.1, 320.6)
	1 month post dose 3	67	2720.9 (2280.1, 3247.0)	-	-	67	2720.9 (2280.1, 3247.0)

Abbreviations: NT50 = 50% neutralizing titer; GMT = geometric mean titer; CI=confidence interval

[a] GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution).

Summary of Geometric Mean Ratio (GMR)

	1 Month Post Dose 3		1 Month Post Dose 2		
Outcome	N	GMT[a] (95% CI)	N	GMT[a] (95% CI)	GMR[b] (95% CI)
SARS-CoV-2 neutralization assay - NT50 (titer)	67	2720.9 (2280.1, 3247.0)	96	1253.9 (1116.0, 1408.9)	2.17 (1.76, 2.68)

Abbreviations: NT50 = 50% neutralizing titer; GMT = geometric mean titer; GMR = geometric mean ratio; CI=confidence interval

[a] GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

[b] GMRs and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titers (1-month post–Dose 3 – 1-month post–Dose 2) and the corresponding CI (based on the 1-sample Student t distribution).

Available data for harms

- Open label continuation of Pfizer phase 2/3 randomized controlled trial (unpublished, data obtained from sponsor)
- Included all participants ages 5 – 11 years who received a 10µg booster dose (dose 3) (N=401)
  - 5.5% were baseline SARS-CoV-2 positive
- Data through March 22, 2022, median follow-up: 1.3 months

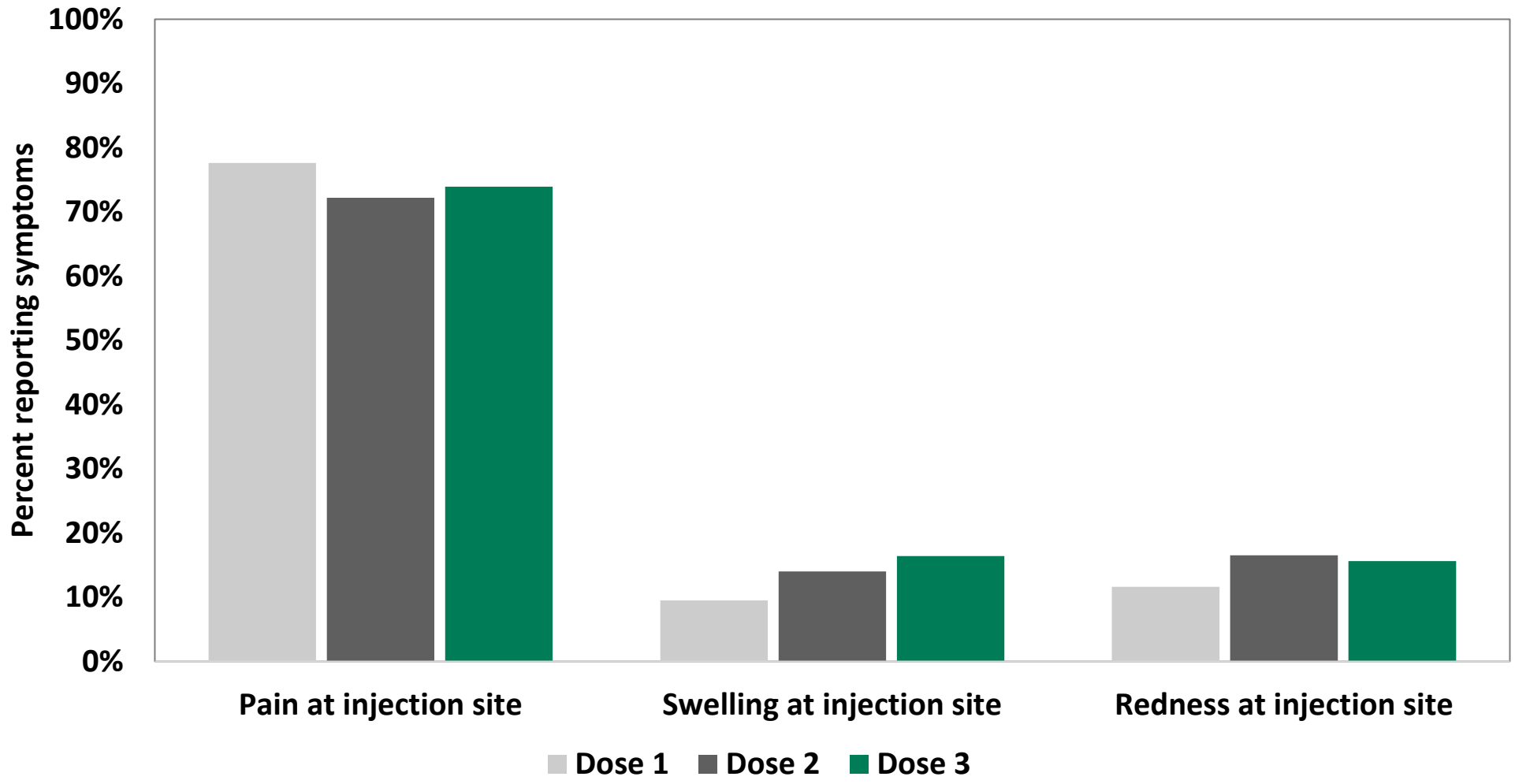
Adverse Events

- No serious adverse events reported among trial participants
- No deaths reported among trial participants
- No cases of anaphylaxis or myocarditis
- Cases of **lymphadenopathy** (including palpable lymph node or axillary mass) were reported by 10 participants (2.5%)
  - This frequency after Dose 3 in children ages 5 to 11 years is higher than previously observed after Dose 2 (0.9%), and less than that observed following Dose 3 in adults ages 18 and older (5.2%)
  - All cases reported after Dose 3 were mild; most occurred in axillary or cervical nodes, had an onset within 2 days of booster vaccination, and were reported as resolved within approximately 1 week after onset

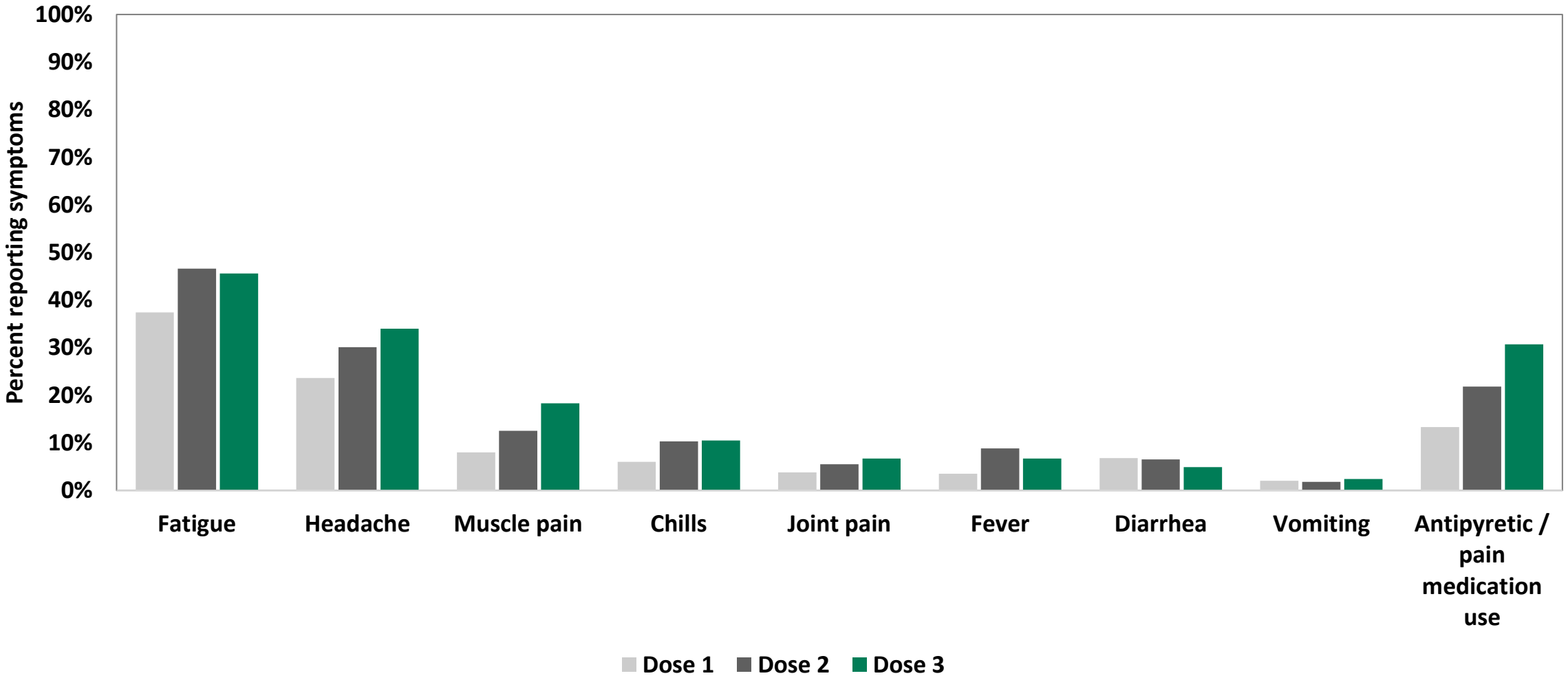
Reactogenicity, Severe (Grade ≥3) Definitions

- Local reactions (redness, swelling, pain at injection site)
  - Grade 3: pain at injection site that prevents daily activity; redness >10 cm; and swelling >10 cm
  - Grade 4: emergency room visit or hospitalization for severe pain at the injection site, necrosis (redness and swelling categories) or exfoliative dermatitis (redness category only).
- Systemic events (fever, nausea/vomiting, headache, fatigue, chills, new or worsened muscle pain, new or worsened joint pain)
  - Grade 3: fever >38.9°C to 40.0°C; vomiting that requires IV hydration; diarrhea of ≥6 loose stools in 24 hours; severe fatigue, severe headache, severe muscle pain, or severe joint pain that prevents daily activity.
  - Grade 4: fever >40.0°C; fatigue, headache, muscle pain, joint pain, diarrhea, or vomiting that require emergency room visit or hospitalization.

Reactogenicity among children ages 5 – 11 years, any grade by local symptom



Reactogenicity among children ages 5 – 11 years, any grade by systemic reaction



Reactogenicity, ≥ Grade 3

- Severe local reactions (i.e., prevents daily routine activity) were reported infrequently after each dose (≤1%); severe events after Dose 3 included injection site pain (n=2 [0.5%]) and redness (n=1 [0.3%])
  - No Grade 4 local reactions were reported after dose 3
- Severe systemic reactions reported after Dose 3 included fatigue (n=7 [1.9%]), headache (n=3 [0.8%]), chills (n=1 [0.3%]), and diarrhea (n=1 [0.3%])
  - No Grade 4 systemic reaction were reported after dose 3

Harms and benefits summary

- **Benefits**
  - No efficacy estimates, only descriptive immunogenicity
  - A third dose elicited robust neutralizing antibody titers
    - GMTs observed 1 month post-Dose 3 (2720.9) were **substantially higher** than GMTs observed prior to Dose 3 vaccination (271.0)
- **Harms**
  - **No** serious adverse events or cases of anaphylaxis or myocarditis
  - Systemic and local reactogenicity post-Dose 3 was overall **similar** to reactogenicity post-Dose 2
  - Limited numbers to evaluate very rare events

COVID-19 vaccines and seropositivity

Clinical Trial Data

- **5.5%** of children in the booster safety populations were baseline SARS-CoV-2 seropositive
- **~9%** of children in the primary series clinical trial were baseline SARS-CoV-2 seropositive

Data from U.S. studies

- Approximately **77**% of children ages 5–11 years have evidence of prior SARS-CoV-2 infection based on seroprevalence estimates
- Seropositivity should not be interpreted as protection from future infection - prior infection can result in protection against infection but not 100% and likely decreases over time

COVID-19 vaccines and seropositivity

- Omicron-wave surges of pediatric COVID-19 hospitalizations occurred even with high seroprevalence, suggesting this alone is not sufficient to provide broad protection
- No concerns in safety surveillance with vaccination of seropositive individuals
- Vaccination remains the **safest** strategy for preventing complications from SARS-CoV-2 infection and offers additional protection against re-infection
- Recent update to Clinical Considerations states that people who recently had SARS-CoV-2 infection may consider delaying their COVID-19 vaccine booster by **3 months** from symptom onset or positive test
  - An increased time between infection and vaccination may result in an improved immune response to vaccination
  - Low risk of reinfection has been observed in the weeks to months following infection

COVID-19 vaccine booster dose safety

- After 93 million 1st mRNA COVID-19 booster vaccinations in the United States in individuals ages 12 years and older:
  - Local and systemic reactogenicity and health impacts appear similar or slightly less for 1st mRNA COVID-19 vaccination compared to dose 2 of primary series
  - For myocarditis, findings are consistent with those observed with primary series, but the risk appears to be lower following the 1st booster dose compared to dose 2 of primary series
    - Risk of myocarditis highest in younger males, with onset clustering within 0-7 days of 1st booster vaccination
    - An increased risk of pericarditis has also been detected after 1st booster dose administration, but is less common, more evenly distributed between males and females, and more evenly distributed across age groups

Rapid Cycle Analysis (RCA) to Monitor the Safety of COVID-19 Vaccines in Near Real-Time within the Vaccine Safety Datalink (cdc.gov)

Vaccine-associated myocarditis

- Identified rates of myocarditis after primary series in children ages 5-11 years are **lower** than what is seen in those ages 12-17 years
- In other age groups, rates of myocarditis are lower after booster dose than after second dose in primary series

Reporting rates of myocarditis (per 1 million doses administered) after Pfizer-BioNTech vaccine, days 0–7 after vaccination

	Males		Females	
Age group	**Dose 1**	**Dose 2**	**Dose 1**	**Dose 2**
5–11 years	<1†	2.2	<1†	<1†
12–15 years (included for reference)	5.3	47.5	<1	4.1
16–17 years (included for reference)	6.9	73.7	No reports	7.2

Predicted hospitalizations prevented vs. myocarditis cases per million 2nd doses among children ages 5-11 years during the Omicron surge

133 hospitalizations prevented

30 ICU admissions prevented

0-1 deaths prevented

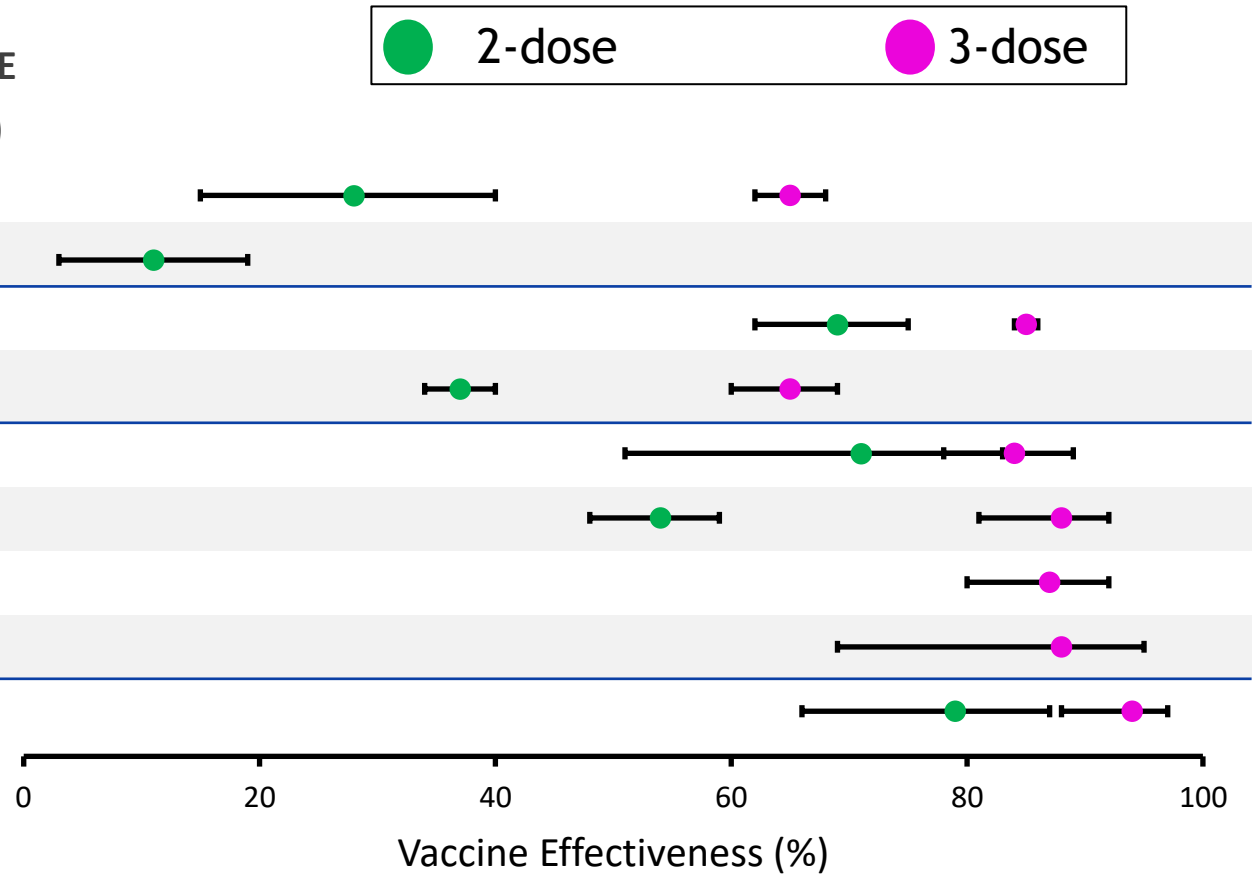
1-2 myocarditis cases

Among the **7.5 million** fully vaccinated children, approximately **1,000 hospitalizations** may have been prevented during the Omicron surge

Based on hospitalization rates during 11/27/2021-2/12/2022, calculated using a 90 day time horizon.

Impact of booster dose for mRNA vaccines during Omicron in adults ≥18 years

		2-dose Adjusted VE % (95% CI)	3-dose Adjusted VE % (95% CI)
Infection	1mo post-last dose, ICATT	28 (15-40)	65 (62-68)
	3mos post-last dose, ICATT	11 (3-19)	--
Emergency department/ urgent care	Last dose <2m ago, VISION	69 (62-75)	85 (84-86)
	Last dose 4-<6m ago, VISION	37 (34-40)	65 (60-69)
Hospitalization	Last dose <2m ago, VISION	71 (51-83)	84 (78-89)*
	Last dose 4-<6m ago, VISION	54 (48-59)	88 (81-92)*
	3rd dose 7-120 days ago, IVY	Not estimated	87 (80-92)*
	3rd dose >120 days ago, IVY	Not estimated	88 (69-95)*
Critical illness/death	2nd dose median 256 days/3rd dose median 60 days ago, IVY	79 (66-87)	94 (88-97)



Booster receipt increases protection across all outcomes.
Booster dose VE remains high among immunocompetent individuals 4-6 months after dose.

*Among immunocompetent individuals ≥65 years of age.

Benefits and Harms:
Summary of the available evidence

- Waning of antibody levels seen after completion of 2-dose primary series; booster doses achieve antibody levels **higher** than after primary series
- Reactogenicity reported after a booster dose similar to what was reported after primary series
- Rates of myocarditis after primary series in children ages 5-11 years considerably **lower** than rates in adolescents; rates after booster doses likely even lower
- Receipt of primary series of COVID-19 vaccines remains important and continues to provide protection against severe COVID-19 outcomes
- Based on information from other age groups, providing booster doses can **increase protection** against both COVID-19 infection and severe disease

Evidence to Recommendations Framework

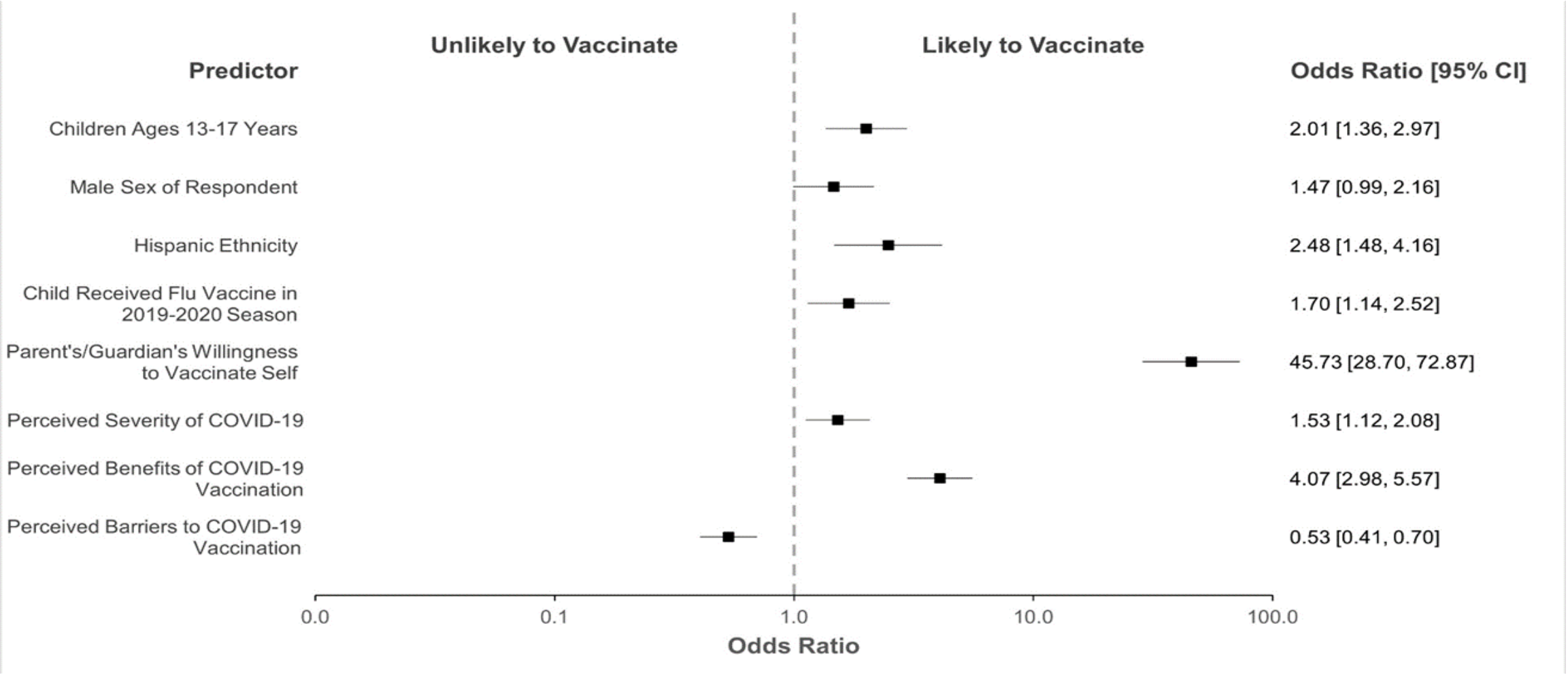
Booster doses of COVID-19 vaccines

Parental COVID-19 vaccine acceptance for children in the United States

- Online cross-sectional nationally representative survey of parents/guardians of children < 18 years in the United States using the Ipsos KnowledgePanel©
  - Samples were selected using the equal probability selection method
  - Weighted against Current Population Survey and American Community Survey
- Survey instrument based on the WHO's Vaccine Hesitancy Scale and informed by the Health Belief Model
- Project Goals and Objectives
  - Assess parental attitudes and beliefs about SARS-CoV-2-related disease and COVID-19 vaccines
  - Gauge parental acceptance of COVID-19 vaccines for children
  - Characterize parents who reported willingness to vaccinate their child against COVID-19
  - Evaluate factors that might influence parental willingness to vaccinate

Source: Hammershaimb, et al., University of Maryland Baltimore (UMB), Children's Hospital Colorado (CU/CHCO), and Ipsos

Wave 1 (February 2021, N=2,265): Predictors of respondents' willingness to have their children receive a COVID-19 vaccine



Source: Hammershaimb, et al., University of Maryland Baltimore (UMB), Children's Hospital Colorado (CU/CHCO), and Ipsos

Conclusions from Wave 1

- Before data on pediatric vaccines were widely available and vaccine rollout to people ages 16 and 17 years began, **66% of parents intended to vaccinate their children**
  - 22.9% early adopters, 49% wanted to “wait and see”
- Those who were **very/somewhat unlikely** to vaccinate their children most frequently reported that **school and travel requirements would make them more likely** to vaccinate
- Those who were **somewhat likely** to vaccinate their children most frequently reported that **healthcare provider recommendation, school requirements, and peer influence** would make them more likely to vaccinate
- **All groups reported that more serious/severe side effects would make them less likely** to vaccinate, even those who were very likely to vaccinate

Source: Hammershaimb, et al., University of Maryland Baltimore (UMB), Children’s Hospital Colorado (CU/CHCO), and Ipsos

Wave 2

- Fielded October 26 – November 30, 2021, N=3,042
  - Ages 0–4 years: not authorized
  - Ages 5–11 years: authorized October 29, 2021
  - Ages 12–15 years: authorized May 10, 2021
- Primary outcome question broken down by age of child
- Questions regarding beliefs about and experiences of SARS-CoV-2 related disease and beliefs about COVID-19 vaccines unchanged
- Questions about influences on COVID-19 vaccine decision-making broken down by age of child

Source: Hammershaimb, et al., University of Maryland Baltimore (UMB), Children's Hospital Colorado (CU/CHCO), and Ipsos

Survey respondent characteristics

Parental Characteristics and Household Composition

- Roughly 60% of parents had more than one child in the household
- The average age of parents in the survey was 40; the modal level of education was ***Bachelor's Degree or higher***
  - 55% of parents in the survey identified as female
- **86%** of parents were **accepting of routine childhood vaccines**
- **71%** were **vaccinated against COVID-19** themselves

Characteristic	N	Weighted %
Age(s) of child(ren) (years)		
0-4	950	36.5
5-11	1,613	53.3
12-17	1,620	50.1
Number of children in household		
1	1,230	40.3
2	1,179	37.8
3	436	15.1
≥ 4	197	6.8

Source: Hammershaimb, et al., University of Maryland Baltimore (UMB), Children's Hospital Colorado (CU/CHCO), and Ipsos

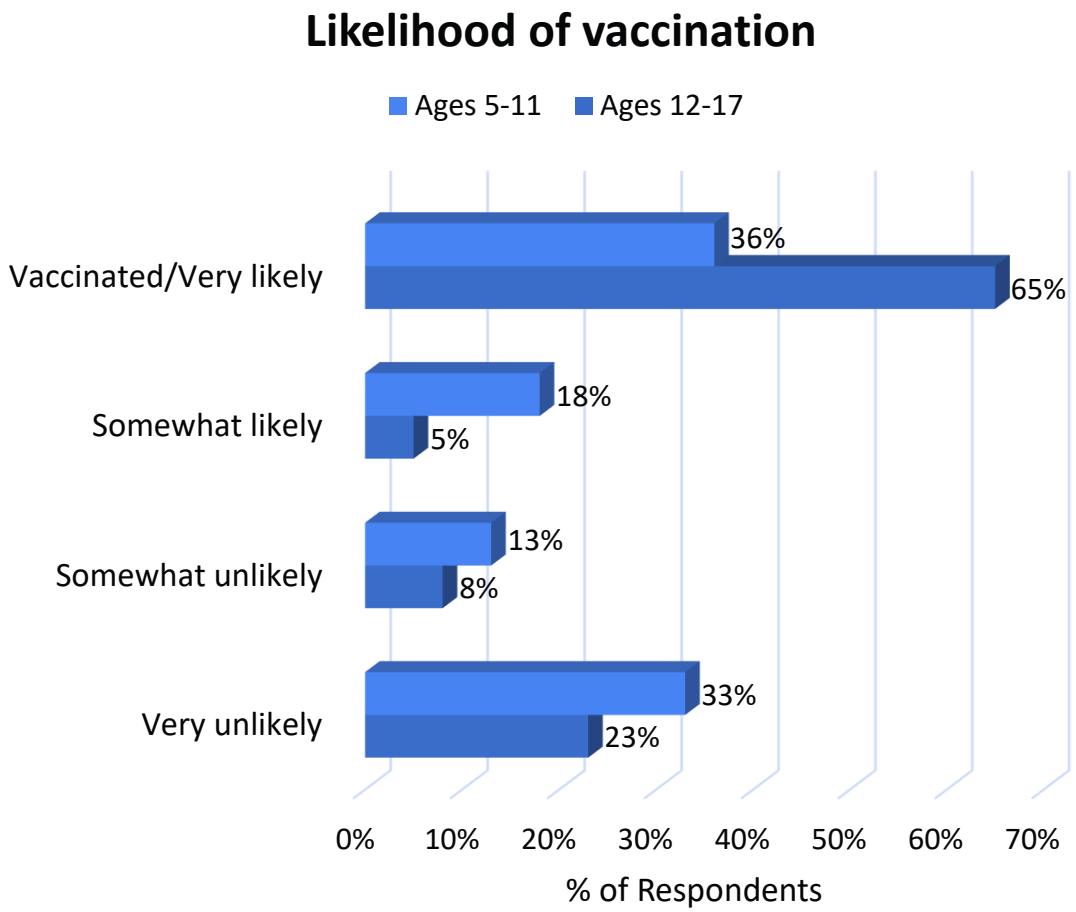
Parental attitudes about COVID-19 vaccines

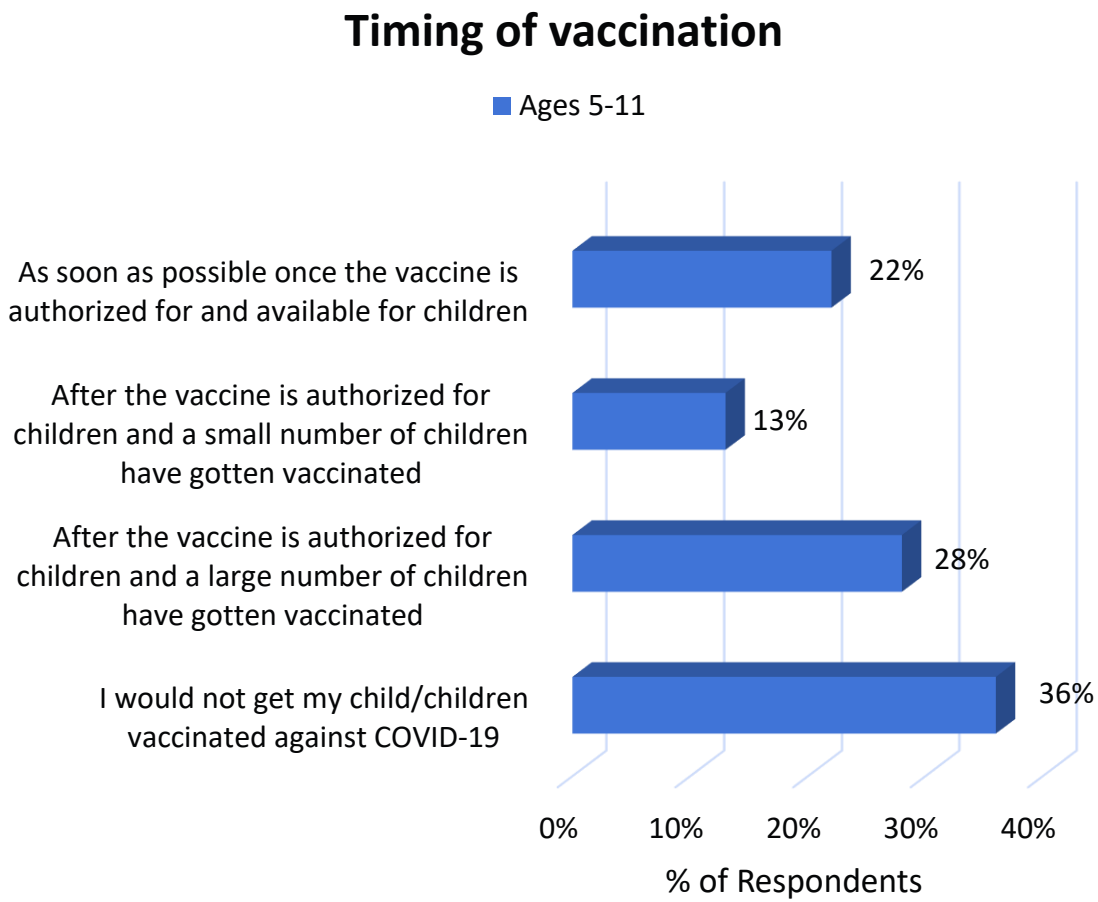
Statement	*Weighted %
Attitudes and Beliefs About COVID-19 Vaccines	
My child/children's healthcare provider is a reliable and trustworthy source of information about COVID-19 vaccines.	58.8
I am concerned about possible serious side effects of COVID-19 vaccines in children.	50.4
Having my child/children vaccinated against COVID-19 would protect the health of others in my community.	49.4
I am concerned about possible rare side effects of COVID-19 vaccines in children.	47.6
Getting a COVID-19 vaccine would protect my child/children from COVID-19.	46.1
Being able to give my child/children a COVID-19 vaccine would make me more comfortable sending them to daycare or school.	42.5
COVID-19 vaccines have been developed too quickly.	40.9
The COVID-19 vaccine may not work to prevent COVID-19 in children.	28.7
Most children do not need a COVID-19 vaccine.	27.4

**Percentage indicates combined percentages (survey weighted) for "Very strongly agree" or "Strongly agree" vs. "Somewhat agree" or "Do not agree."*

Source: Hammershaimb, et al., University of Maryland Baltimore (UMB), Children's Hospital Colorado (CU/CHCO), and Ipsos

Likelihood and expected timing of vaccinating children





Source: Hammershaimb, et al., University of Maryland Baltimore (UMB), Children's Hospital Colorado (CU/CHCO), and Ipsos

Net predictors for vaccine acceptance and factors influencing parents' decision to get their child vaccinated

- Belief in benefits of COVID-19 vaccination and acceptance of routine childhood vaccines were the most important predictors of COVID-19 vaccine acceptance for their children
  - Positive predictors also included:
    - Ages 5-11: perception that pediatric COVID-19-related disease is severe for children
    - Ages 5-11 and 12-17: Hispanic ethnicity and parental COVID-19 vaccination
- The desire to protect their child from COVID-19 and protect their child against new COVID-19 variants were the primary determining factors toward parents' decision to get their child vaccinated

Source: Hammershaimb, et al., University of Maryland Baltimore (UMB), Children's Hospital Colorado (CU/CHCO), and Ipsos

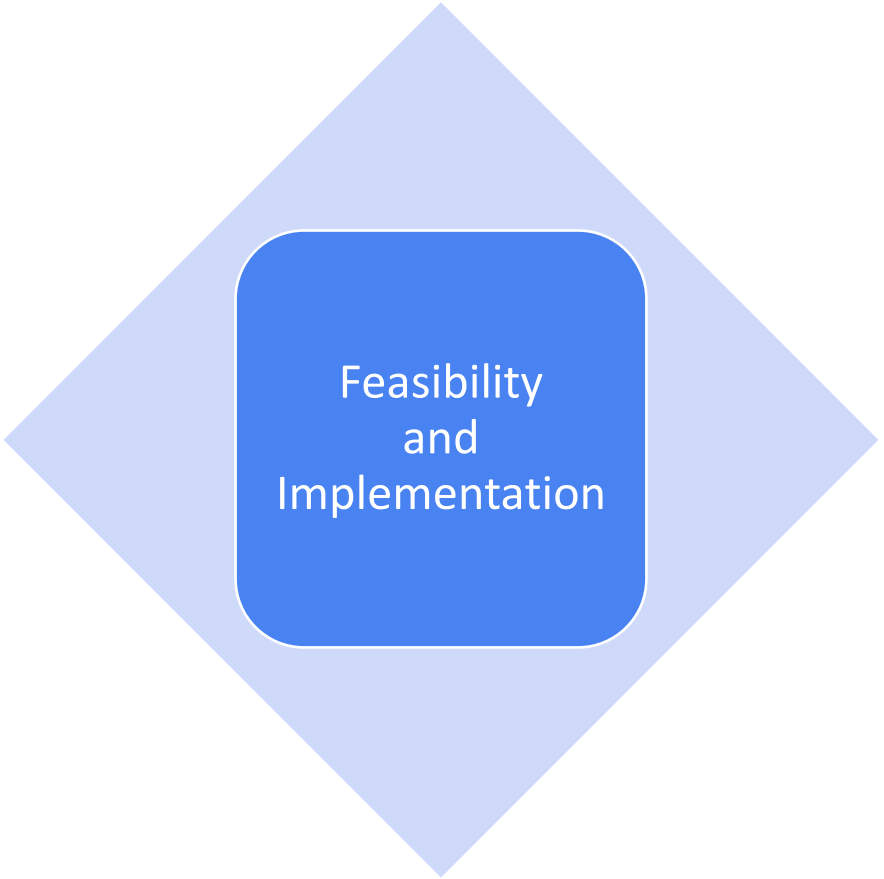
Summary

- About half of parents are worried about **rare** and **serious side effects** of the COVID-19 vaccines, but many are also worried about how **new variants will affect children**
- We can expect to see **slow COVID-19 vaccine uptake** in the 5–11-years age group as about 4 in 10 (41%) parents plan to "wait and see," **but ultimately, 63% of parents of children ages 5-11 years intend to vaccinate their children** at some point
- Most parents **trust their children's healthcare provider** as a source of information about COVID-19 vaccines

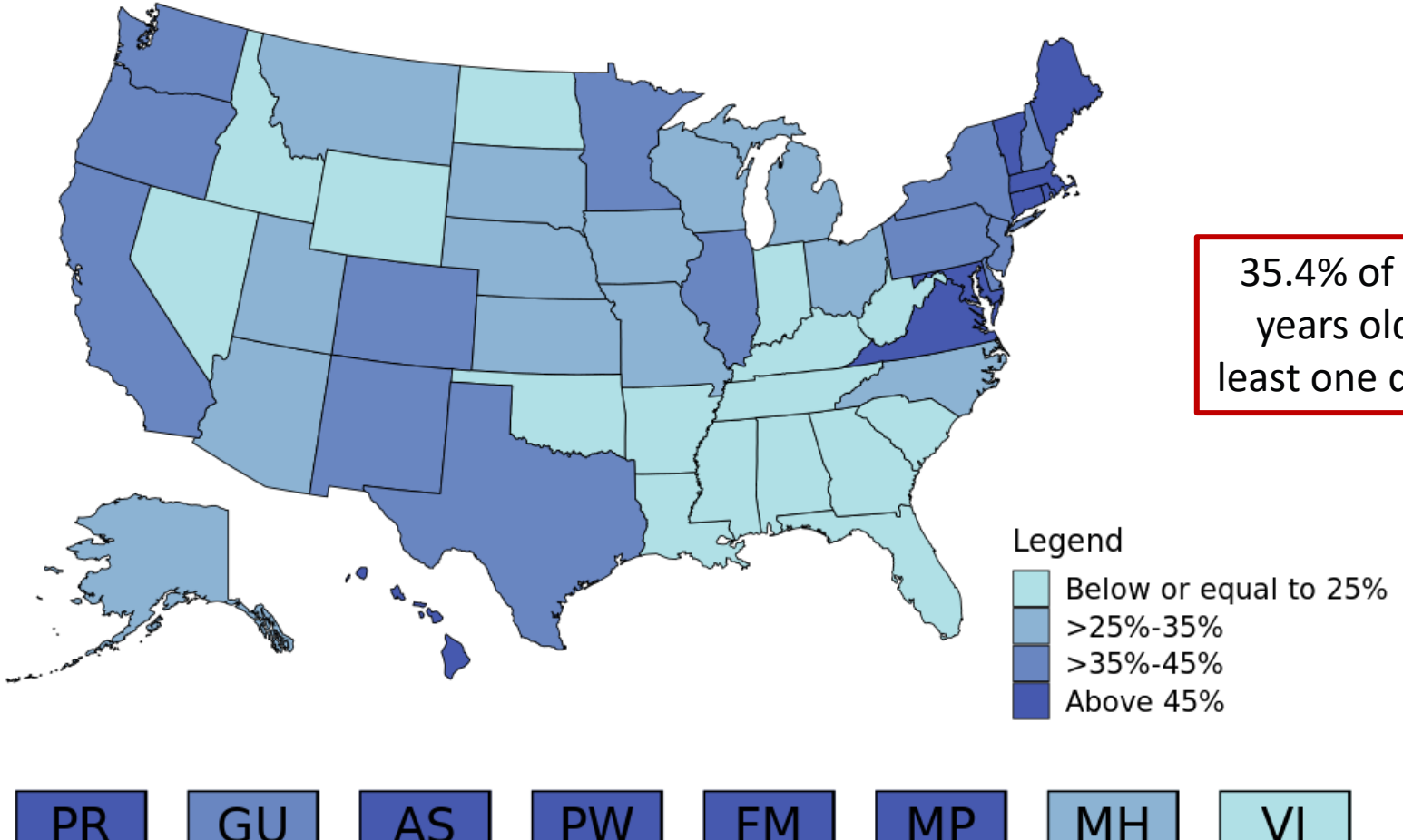
Source: Hammershaimb, et al., University of Maryland Baltimore (UMB), Children's Hospital Colorado (CU/CHCO), and Ipsos

Evidence to Recommendations Framework

Booster doses of COVID-19 vaccines



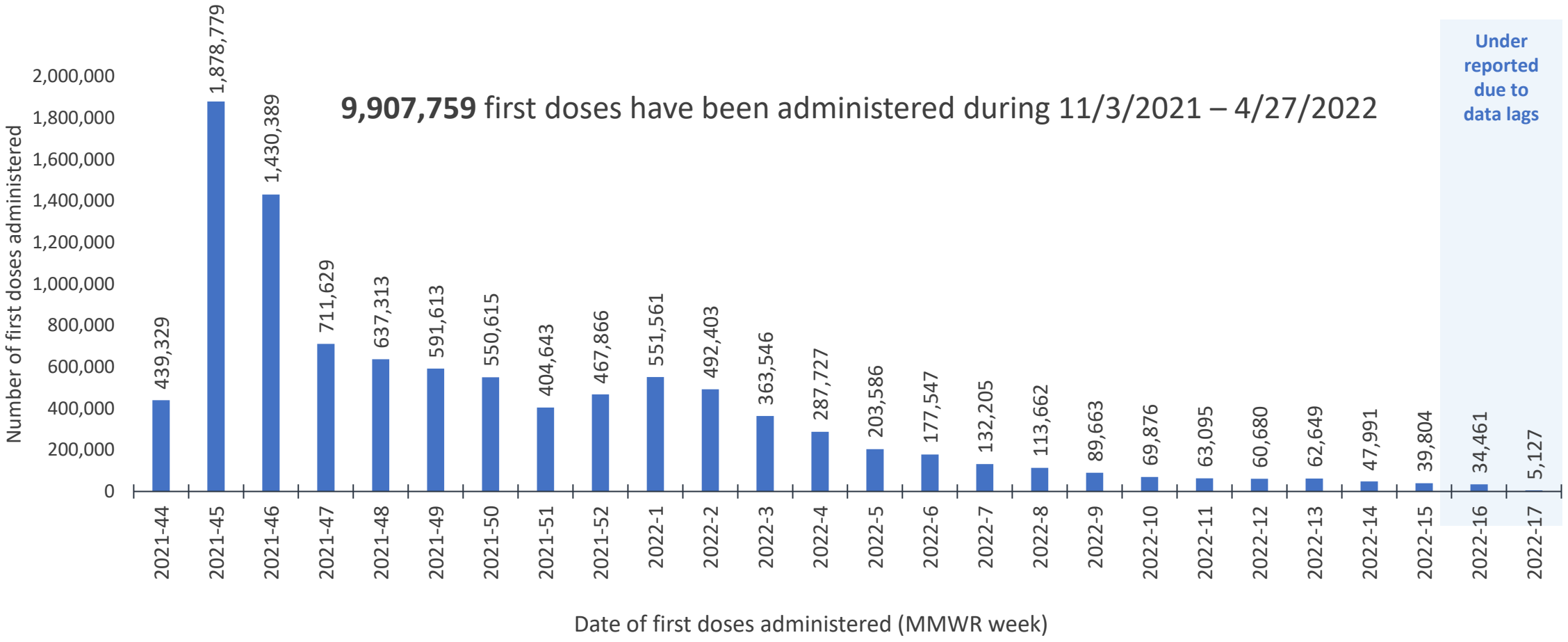
Percent of children ages 5-11 years who received at least one dose of the COVID-19 pediatric vaccine by jurisdiction



35.4% of children 5-11 years old received at least one dose of vaccine

Notes: Children who received at least one dose prior to the Emergency Use Authorization for pediatric vaccination are included in this report. CDC received reports of children who received COVID-19 vaccination when <12 years old, prior to the Emergency Use Authorization for vaccination for children 5-11 years old on November 2, 2021. These reports included **203,019** first doses and **127,737** dose completions. These reports are as a result of: (1) participation in a clinical trial (2) 12-year-old children miscategorized as 11-year-olds due to recoding of incomplete birth dates submitted (e.g., year of birth only) or (3) in rare cases, data reporting issues. First doses and dose completions are mutually exclusive categories.
Children 5-11 years old receiving a first dose are attributed to the jurisdiction in which the child resides. CDC has capped the percent of population coverage metrics at 95%.
Source: Immunization Data Lake. Data as of April 27, 2022, 06:00 hrs.

Weekly number of COVID-19 vaccine first doses administered to children ages 5-11 years, starting November 3, 2021



Notes: Children who received at least one dose prior to the Emergency Use Authorization for pediatric vaccination are included in this report. CDC received reports of children who received COVID-19 vaccination when <12 years old, prior to the Emergency Use Authorization for vaccination for children 5-11 years old on November 2, 2021. These reports included **203,019** first doses and **127,737** dose completions. These reports are as a result of: (1) participation in a clinical trial (2) 12-year-old children miscategorized as 11-year-olds due to recoding of incomplete birth dates submitted (e.g., year of birth only) or (3) in rare cases, data reporting issues. First doses and dose completions are mutually exclusive categories. Of those children receiving at least the first dose and of those completing the series, 94% and 97%, respectively, of those coded as being <12-year-old children are coded as being 11-year-olds.
The most recent five days of reporting may be underreported due to delays in reporting. All reported numbers might change over time as historical data are reported to CDC.
Source: Vaccine administration data from Tiberius. Data as of April 27, 2022, 16:00 hrs.

Parent-reported place of COVID-19 vaccination among children ages 5-11 years, National Immunization Survey-Child COVID-19 Module (NIS-CCM), November – February 2022

	Place of vaccination				
	Medical Place	Pharmacy	School	Mass Vaccination Site	Other Non-Medical Place
Overall	**47%**	**37%**	**9%**	**5%**	**2%**
5-6 (referent)	55%	31%	7%	4%	3%
7-8	*46%	*37%	9%	5%	3%
9-11	*45%	*38%	*10%	5%	2%

* indicates a statistically significant difference compared to the referent group (5-6 years), P<0.05

Notes: The NIS-CCM is an on-going random-digit-dialed telephone survey that began in July 2021 to collect COVID-19 vaccination status and intent for children from adult respondents knowledgeable about the child's vaccination status. All estimates are weighted to represent the non-institutionalized U.S. population of children and mitigate possible bias that can result from an incomplete sample frame or non-response. Survey weights were calibrated to vaccine administration data reported to CDC. For more information about the survey, see https://www.cdc.gov/vaccines/imz-managers/nis/about.html#nis-ccm and https://www.cdc.gov/vaccines/imz-managers/coverage/covidvaxview/index.html.

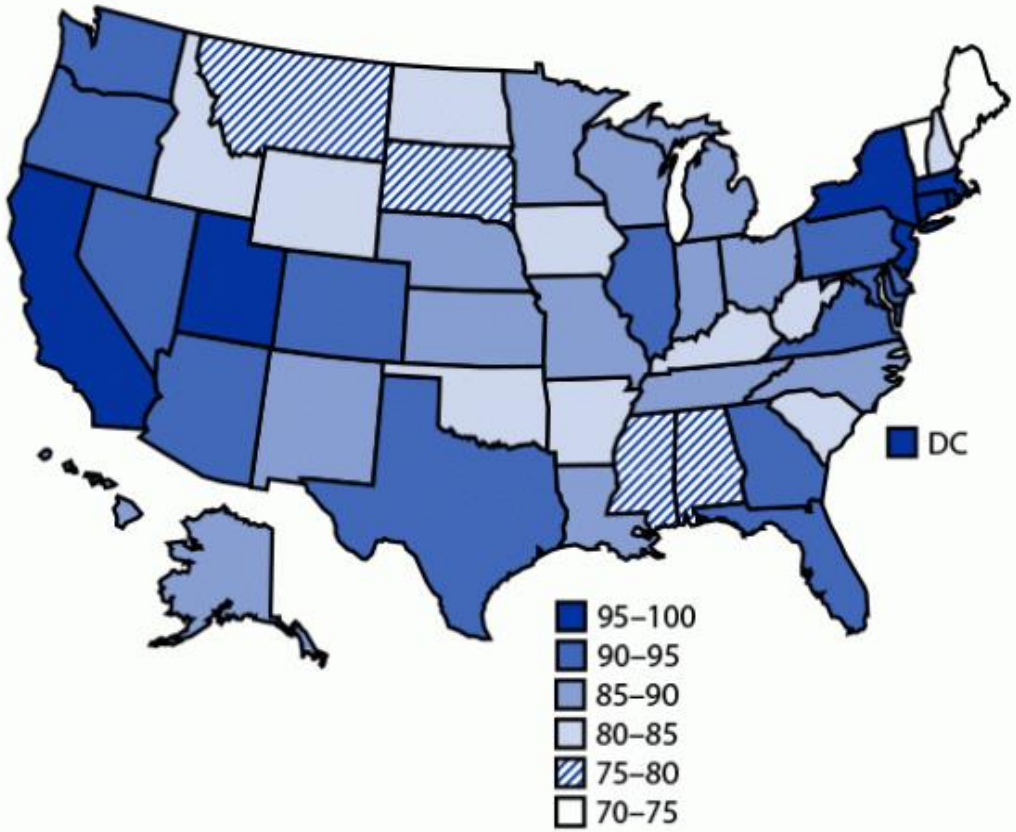
CDC unpublished data

The pediatric COVID-19 vaccine provider network: An assessment of access

Provider network for children ages 5-11 years[1]

- 38,732 total providers
  - 17,064 pharmacies
  - 12,171 **(out of ~38,000)** VFC providers
  - 923 federal entities
  - 8574 other
- 92% of children live ≤ 5 miles of a provider
  - Same when restrict to high SVI counties

Percentage of children 5–11 years living ≤ 5 miles of a provider, by state, 4 weeks after pediatric vaccination program launch[1]



1 - Kim C, Yee R, Bhatkoti R, et al. COVID-19 Vaccine Provider Access and Vaccination Coverage Among Children Aged 5–11 Years — United States, November 2021–January 2022. MMWR Morb Mortal Wkly Rep 2022;71:378–383. DOI: http://dx.doi.org/10.15585/mmwr.mm7110a4

Vaccines for Children (VFC) providers: Barriers to participation

- Among ~38,000 VFC providers
  - ~2/3 are enrolled to administer COVID-19 vaccine
  - ~1/3 have ever-administered COVID-19 vaccine to children ages 5-11 years

- Common barriers to enrollment/participation in the 5–11-year-old program[1]
  - Vaccine available elsewhere in the community
  - Concerns about vaccine wastage (vial/package size)
  - Low demand/parental hesitancy
  - Limited staff resources
  - Limited storage space
  - Reporting burden

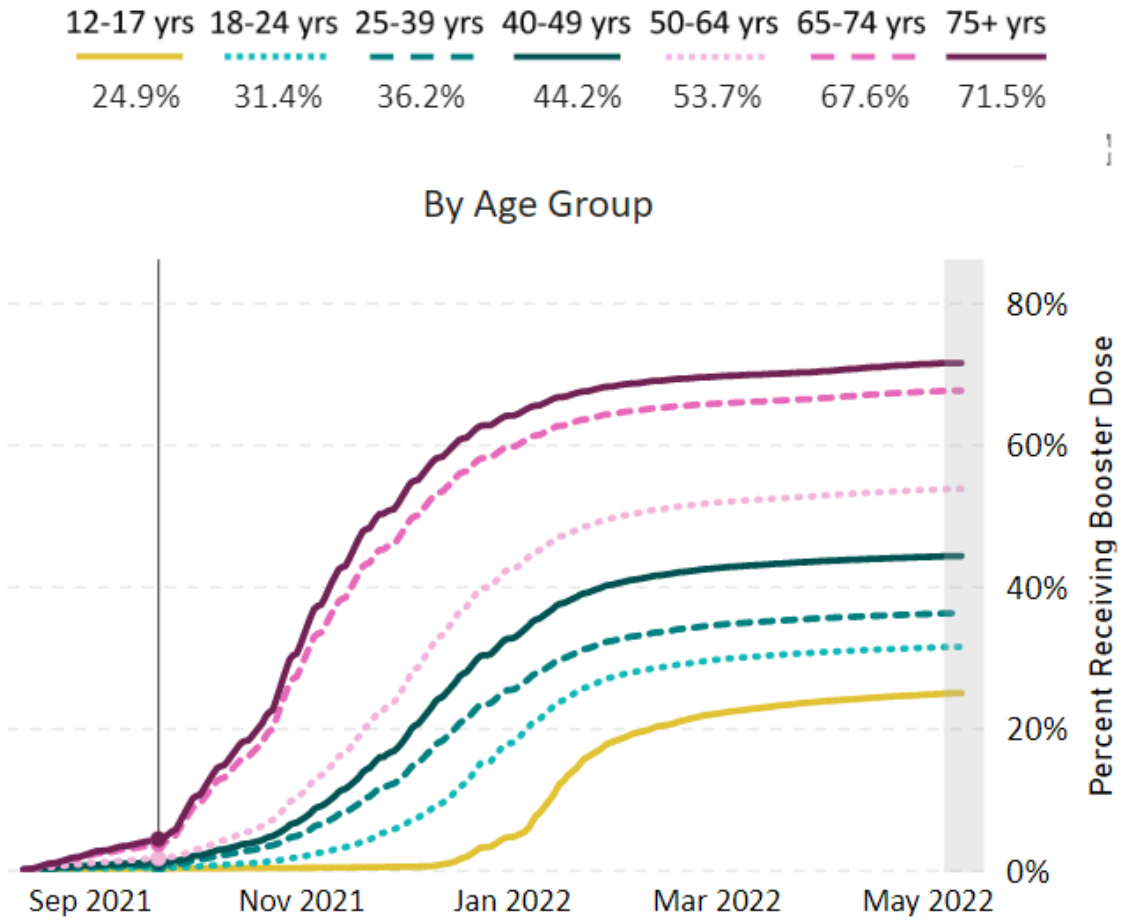
1 – Preliminary results from a VFC provider survey fielded in March 2022, listening sessions with jurisdiction staff

CDC activities to maintain/strengthen the provider network

- Created jurisdiction-specific maps of providers to assist jurisdictions identifying gaps
- Encourage jurisdictions to partner with local AAP/AAFP chapters for support
- Continue to emphasize the importance of VFC provider participation
- Addressed identified enrollment/participation barriers:
  - Waste may be necessary at times
  - Extended inventory reporting requirement from 24 hours to at least weekly
- Continue support of the Federal Retail Pharmacy Program partnership

Percent of fully vaccinated people receiving a first COVID-19 booster dose, by age group, United States

August 13, 2021-May 11, 2022



Source: COVID Data Tracker CDC COVID Data Tracker: Vaccination Demographics Trends. Accessed: 5/11/22

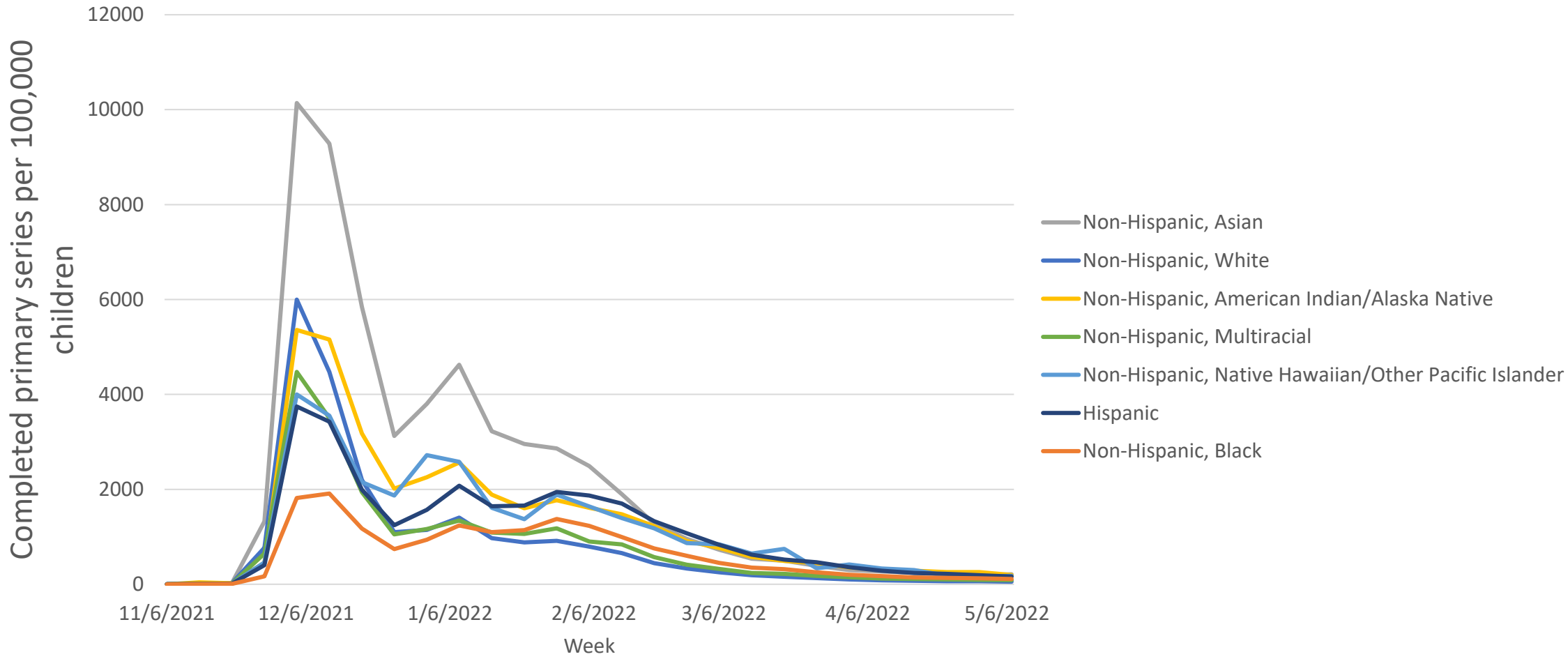
Feasibility and Implementation:
Summary of the available evidence

- **35.4%** of children ages 5-11 years received at least one dose of the COVID-19 pediatric vaccine
  - Nearly 10 million first doses have been administered since November 3, 2021
- Medical facilities and pharmacies were the highest reported place of vaccination among children ages 5-11 years
- Efforts to strengthen the provider network and mitigate barriers to provider participation is crucial to improving pediatric COVID-19 vaccination coverage
- Booster dose coverage lower among adolescent and young adult populations

Evidence to Recommendations Framework

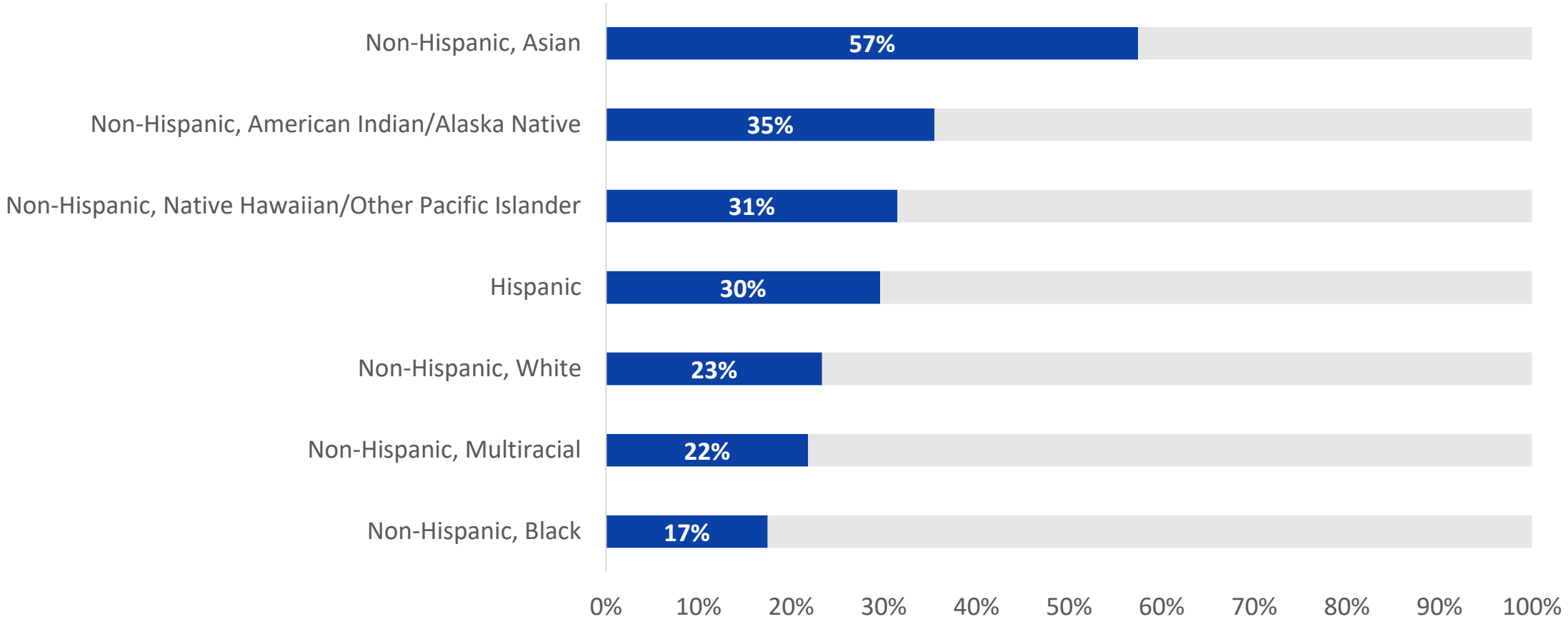
Booster doses of COVID-19 vaccines

Completed primary series per 100,000 children ages 5-11 years by week and race and ethnicity as of May 7, 2022



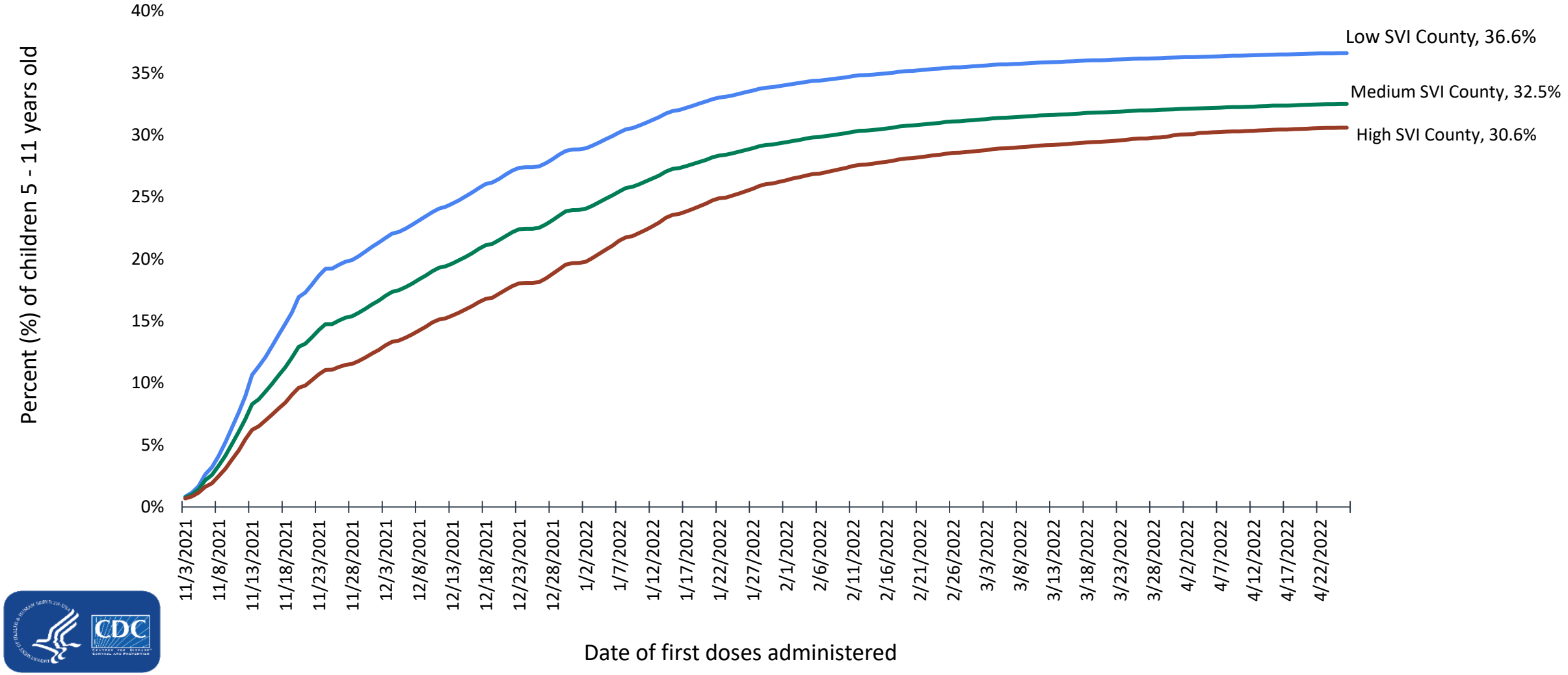
Notes: Excludes vaccine refusals and vaccines administered by DoS (Department of State). Excludes Texas and Idaho data as these states only report aggregate data and do not report data for individual age years.
Source: CDC's Immunization Data Lake. Accessed May 13, 2022.

Percent of children ages 5-11 years with a completed primary series by race and ethnicity as of May 7, 2022

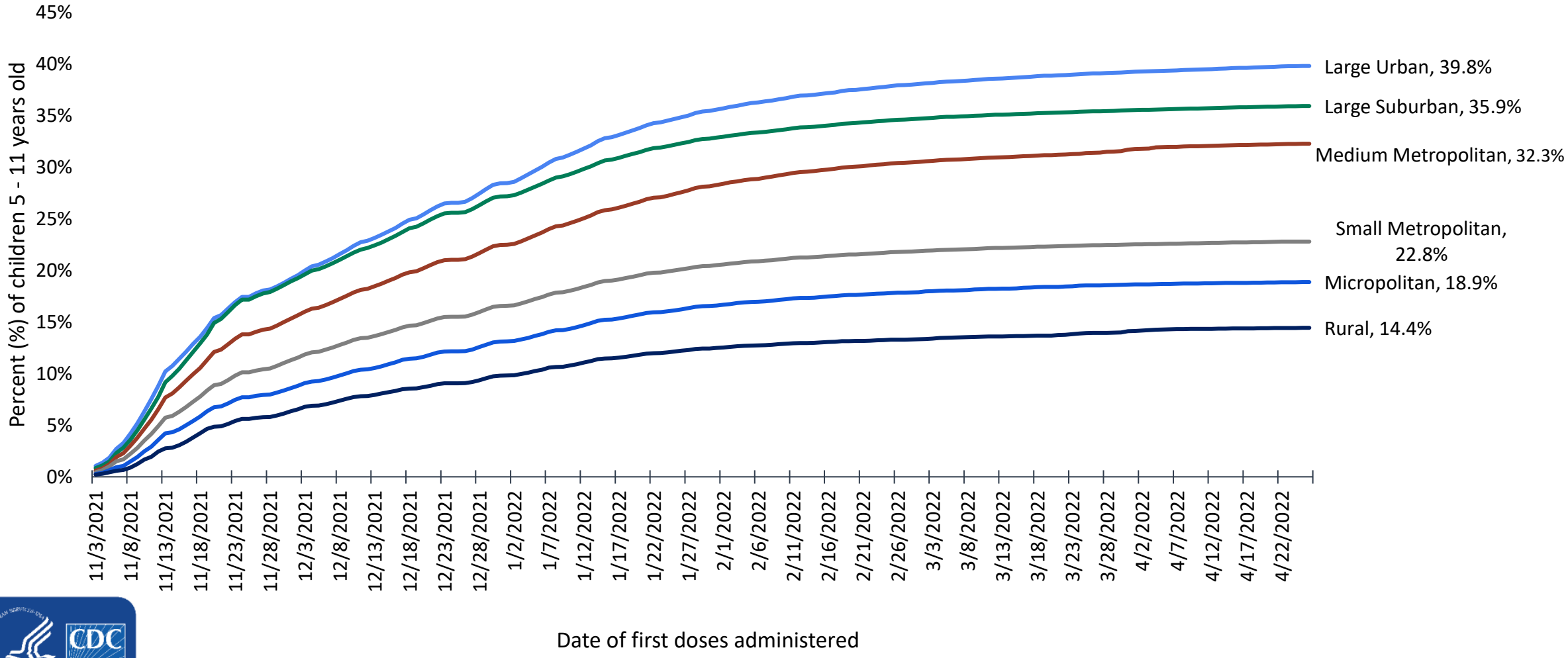


Notes: Excludes vaccine refusals and vaccines administered by DoS (Department of State). Excludes Texas and Idaho data as these states only report aggregate data and do not report data for individual age years.
Source: CDC's Immunization Data Lake. Accessed May 13, 2022.

Percent of children ages 5-11 years with at least one dose of COVID-19 pediatric vaccine, by Social Vulnerability Index (SVI) of the county of residence, from November 3, 2021 – April 27, 2022

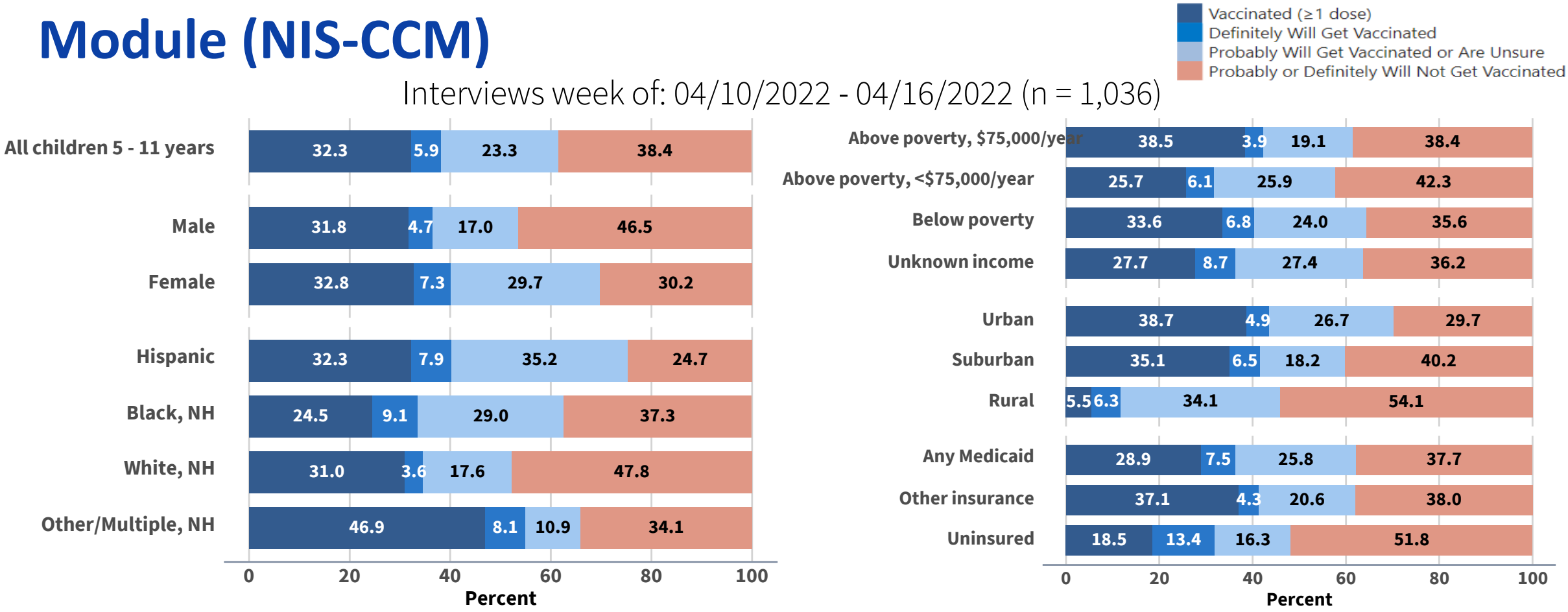


Percent of children ages 5-11 years with at least one dose of COVID-19 pediatric vaccine, by urban/rural status of the county of residence, from November 2, 2021 – April 27, 2022



Vaccination coverage and parental intent for children ages 5-11 years, National Immunization Survey Child COVID Module (NIS-CCM)

Interviews week of: 04/10/2022 - 04/16/2022 (n = 1,036)

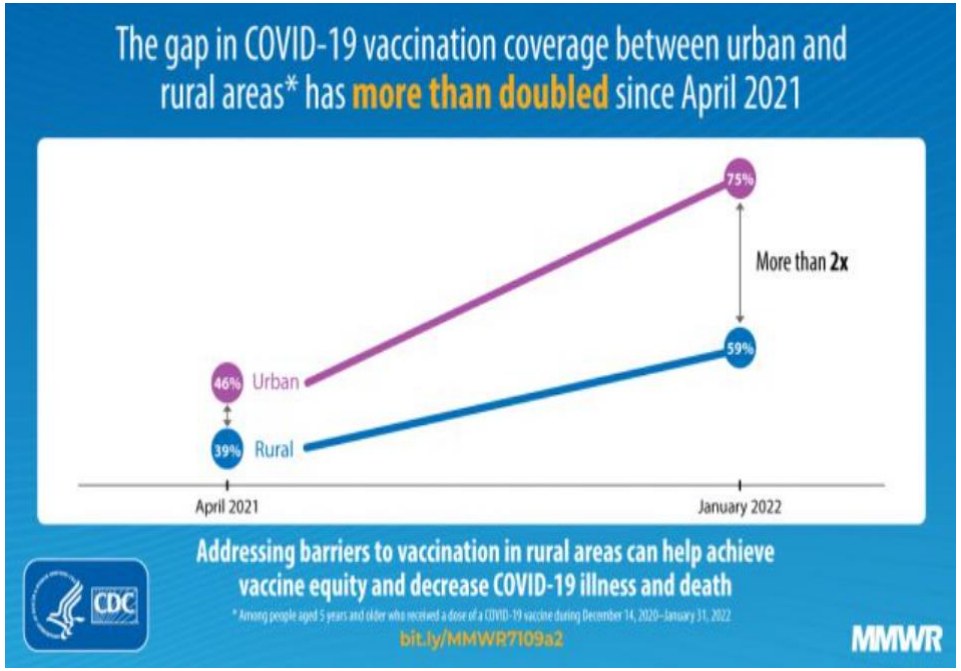


Notes: The NIS-CCM is an on-going random-digit-dialed telephone survey that began in July 2021 to collect COVID-19 vaccination status and intent for children from adult respondents knowledgeable about the child's vaccination status. All estimates are weighted to represent the non-institutionalized U.S. population of children and mitigate possible bias that can result from an incomplete sample frame or non-response. Survey weights were calibrated to vaccine administration data reported to CDC. Vaccination status is parent/guardian reported and not verified with medical records. Estimates of vaccination coverage may differ from vaccine administration data reported at https://covid.cdc.gov/covid-data-tracker/#vaccinations. For more information about the survey, see https://www.cdc.gov/vaccines/imz-managers/nis/about.html#nis-ccm and https://www.cdc.gov/vaccines/imz-managers/coverage/covidvaxview/index.html.

Disparities in COVID-19 vaccination coverage between urban and rural counties – United States

December 14, 2020 – January 31, 2022

- Across the United States, COVID-19 vaccination coverage was lower in rural counties than in urban counties
- Compared with previous estimates, urban-rural disparities among those now eligible for vaccination (ages ≥5 years) have **increased** more than twofold through January 2022, despite increased availability and access to COVID-19 vaccines
- Among all age groups, vaccination coverage with ≥1 dose was lower in rural counties, with the largest differences in pediatric populations



Saelee R, Zell E, Murthy BP, et al. Disparities in COVID-19 Vaccination Coverage Between Urban and Rural Counties — United States, December 14, 2020–January 31, 2022. MMWR Morb Mortal Wkly Rep 2022;71:335–340. DOI: http://dx.doi.org/10.15585/mmwr.mm7109a2

Disparities in COVID-19 vaccination coverage between urban and rural counties – United States

December 14, 2020 – January 31, 2022

- Factors that may have contributed to increasing disparities in pediatric COVID-19 vaccination coverage:
  - Parents in rural communities were approximately twice as likely to state that their child will **"definitely not"** get a COVID-19 vaccine compared with those in urban communities
  - Notably, **76%** of parents in rural areas indicated that their trusted source of vaccination information for their children is their health care provider
    - However, nearly **40%** of rural parents reported that their child's pediatrician did not recommend a COVID-19 vaccine, compared with only **8%** of parents in urban communities
- Vaccine recommendations from a **health care provider** are strong predictors of COVID-19 vaccination

Saelee R, Zell E, Murthy BP, et al. Disparities in COVID-19 Vaccination Coverage Between Urban and Rural Counties — United States, December 14, 2020–January 31, 2022. MMWR Morb Mortal Wkly Rep 2022;71:335–340. DOI: http://dx.doi.org/10.15585/mmwr.mm7109a2

Addressing Vaccine Equity

- **Developing and disseminating** culturally and linguistically appropriate messaging through trusted channels, identified by partners working closely in the communities of interest
- **Implementing** targeted digital, radio, and out of home media buys to reach parents/caregivers representing groups and areas with low **vaccination** coverage among children
- **Promoting** new webpages for clinicians and families focused on children with disabilities and special healthcare needs
- **Supporting** rural vaccine communication and education partnerships
- **Developing** rural addendum to *COVID-19 Vaccination Field Guide: 12 Strategies for Your Community*

Equity:
Summary of the available evidence

- There are noted disparities in vaccination coverage and parental intent for children ages 5-11 years by **race and ethnicity, income** and **geographic location**
- Addressing barriers to vaccination in rural areas is critical to achieving vaccine equity, reducing disparities, and decreasing COVID-19–related illness and death in the United States[1]
- Additional outreach is critical, especially in high SVI areas, to improve vaccine confidence and increase coverage rates among children ages 5–11 years[2]
- Disseminating culturally and linguistically appropriate messaging through trusted channels is pertinent to reaching parents and caregivers who reside in areas with low vaccination coverage among children

1. Saelee R, Zell E, Murthy BP, et al. Disparities in COVID-19 Vaccination Coverage Between Urban and Rural Counties — United States, December 14, 2020–January 31, 2022. MMWR Morb Mortal Wkly Rep 2022;71:335–340. DOI: http://dx.doi.org/10.15585/mmwr.mm7109a2
2. Kim C, Yee R, Bhatkoti R, et al. COVID-19 Vaccine Provider Access and Vaccination Coverage Among Children Aged 5–11 Years — United States, November 2021–January 2022. MMWR Morb Mortal Wkly Rep 2022;71:378–383. DOI: http://dx.doi.org/10.15585/mmwr.mm7110a4

Summary

Summary

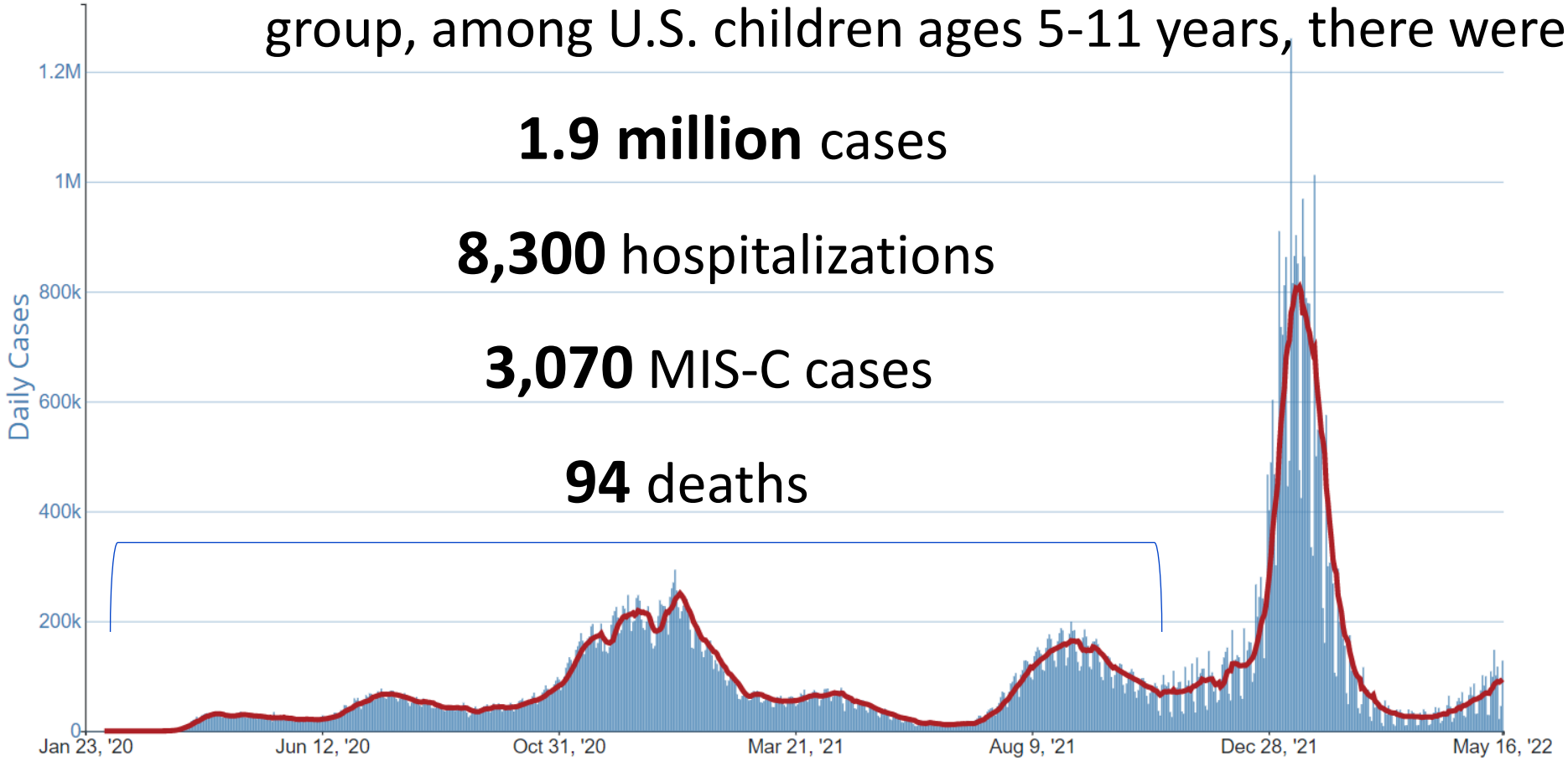
Prior to COVID-19 vaccine authorization for children in this group, among U.S. children ages 5-11 years, there were

1.9 million cases

8,300 hospitalizations

3,070 MIS-C cases

94 deaths



Summary

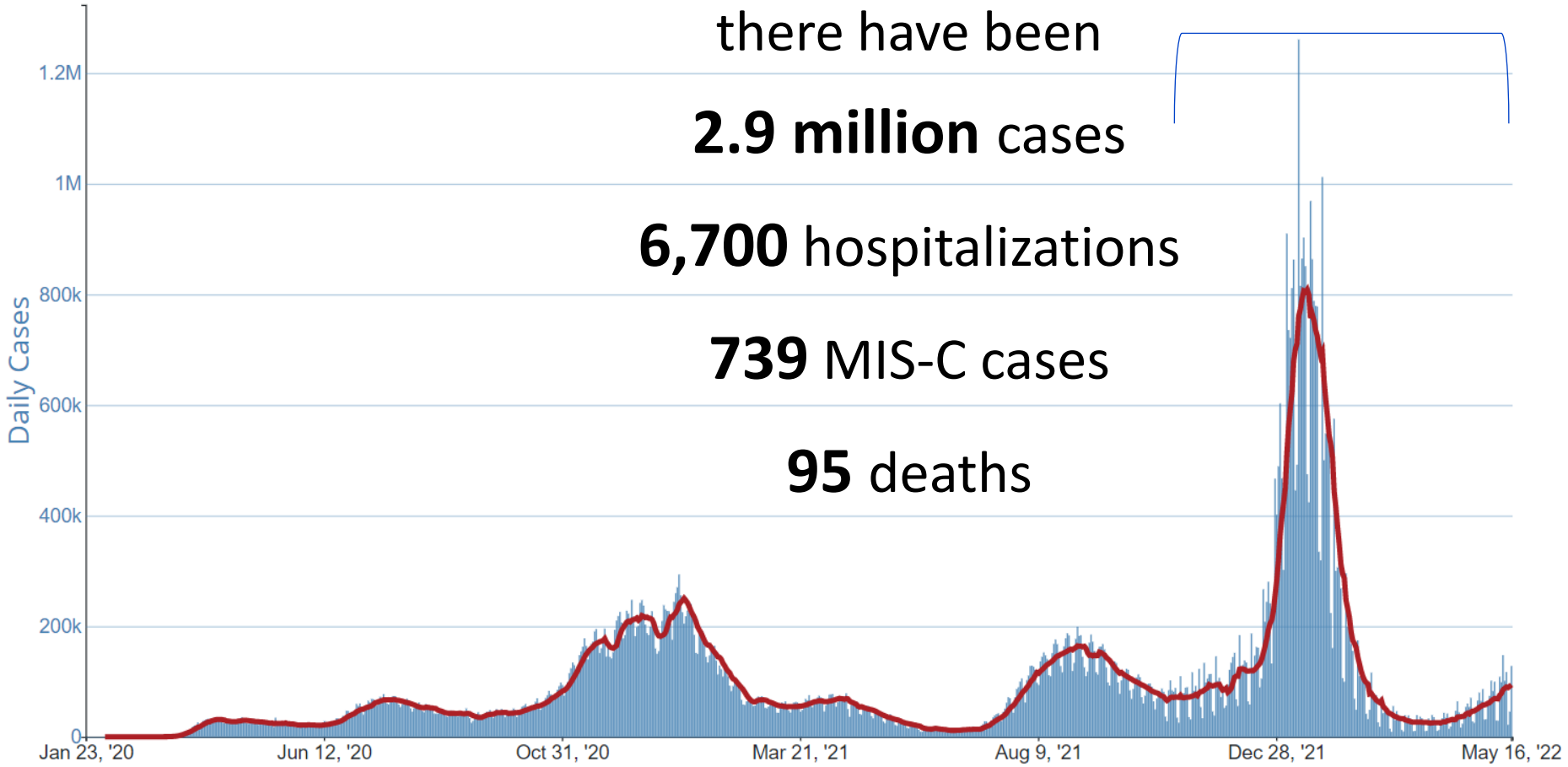
Since authorization of COVID-19 vaccines
for children ages 5-11 years
there have been

2.9 million cases

6,700 hospitalizations

739 MIS-C cases

95 deaths



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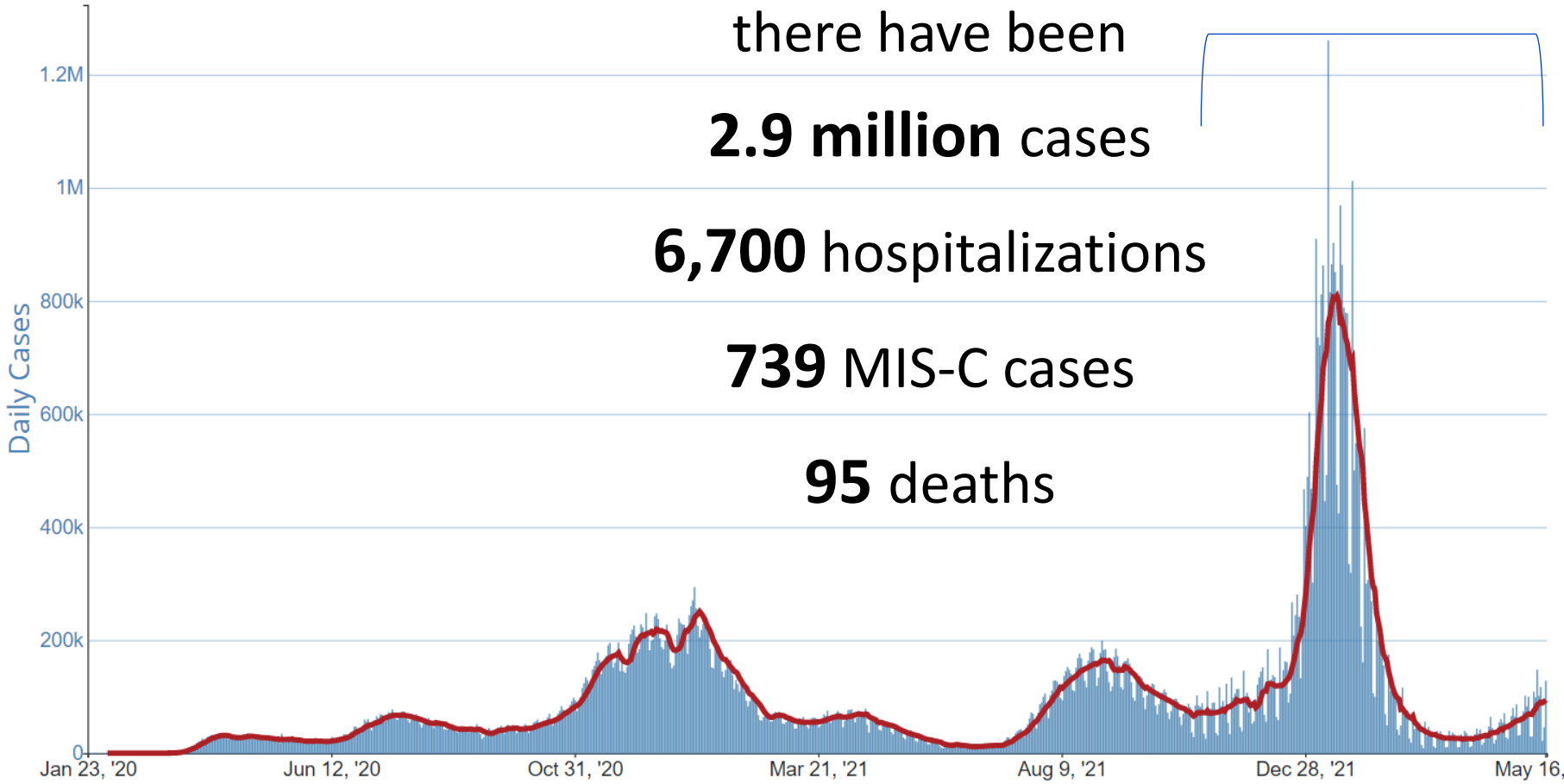


~90% of children hospitalized unvaccinated

93% of MIS-C cases unvaccinated

Work Group Interpretation

- Receipt of a primary series provides protection against COVID-19, especially against **severe disease**
- Myocarditis after COVID-19 vaccines in children ages 5-11 years is **rare**
- Only 29% of children ages 5-11 years are fully vaccinated with a primary series
- Future surges will continue to impact children, with unvaccinated children remaining at higher risk of severe outcomes
- **Benefits** of COVID-19 vaccines continue to outweigh risks

Receipt of **COVID-19 vaccine primary series** continues to be important

Work Group Interpretation

- COVID-19 vaccine booster doses have been shown to **increase protection** against all outcomes in those ages 12 years and over
  - Waning of protection over time after 2 doses noted for ages 12 years and over (limited time to detect waning in children 5-11 years)
- For each age, myocarditis after booster doses of COVID-19 vaccines lower than after 2nd dose in primary series
- Likely that children ages 5-11 years would **benefit** from a COVID-19 vaccine booster dose
- Work Group discussed vaccine policy where children ages 5-11 years ‘may receive’ or ‘should receive’ a COVID-19 vaccine booster dose

Work Group Interpretation

Type of recommendation	PROS	CONS
Standard recommendation **"Should receive"**	• Simple to communicate • Consistent with booster recommendations in other ages groups • Likely that all ages will benefit from 3 doses of mRNA COVID-19 vaccines	• Limited numbers of children ages 5-11 years received booster in clinical trial • Uncertainty around future of fall boosters • Many children recently infected with SARS-CoV-2 during Omicron surge
Recommended for individuals based on assessment of benefits and risks **"May receive"**	• Reflects uncertainty around fall epidemiology and variant booster • Allows access for children who would benefit the most from a booster dose • Flexibility to adjust to a stronger recommendation in the fall	• More complicated to communicate • Not consistent with booster recommendations for other age groups • Likely that all ages will benefit from 3 doses of mRNA COVID-19 vaccines

Current recommendations for COVID-19 vaccine first booster doses

Age	Pfizer-BioNTech COVID-19 vaccine primary series	Moderna COVID-19 vaccine primary series	Janssen COVID-19 vaccine primary series
≥18 years	**Should** receive a booster **5 months** after receipt of primary series dose	**Should** receive a booster **5 months** after receipt of primary series dose	**Should** receive a booster **2 months** after receipt of primary series dose
12–17 years	**Should** receive a booster **5 months** after receipt of primary series dose	Not authorized	Not authorized

Proposed recommendations for COVID-19 vaccine first booster doses: Children ages 5-11 years "should receive"

Age	Pfizer-BioNTech COVID-19 vaccine primary series	Moderna COVID-19 vaccine primary series	Janssen COVID-19 vaccine primary series
≥18 years	**Should** receive a booster **5 months** after receipt of primary series dose	**Should** receive a booster **5 months** after receipt of primary series dose	**Should** receive a booster **2 months** after receipt of primary series dose
5–17 years	**Should** receive a booster **5 months** after receipt of primary series dose	Not authorized	Not authorized

Proposed recommendations for COVID-19 vaccine first booster doses:

Children ages 5-11 years "may receive"

Age	Pfizer-BioNTech COVID-19 vaccine primary series	Moderna COVID-19 vaccine primary series	Janssen COVID-19 vaccine primary series
≥18 years	**Should** receive a booster **5 months** after receipt of primary series dose	**Should** receive a booster **6 months** after receipt of primary series dose	**Should** receive a booster **2 months** after receipt of primary series dose
12–17 years	**Should** receive a booster **5 months** after receipt of primary series dose	Not authorized	Not authorized
5–11 years	**May** receive a booster **5 months** after receipt of primary series dose		

Work Group Interpretation

- Overall, Work Group supported current recommendation that children ages 5-11 years **may receive** a COVID-19 vaccine booster dose
  - Flexibility to adjust to a stronger recommendation in the fall, if epidemiology warrants or if newer vaccines available
  - Not unanimous; both viewpoints represented on the Work Group

Recommendations for COVID-19 vaccines

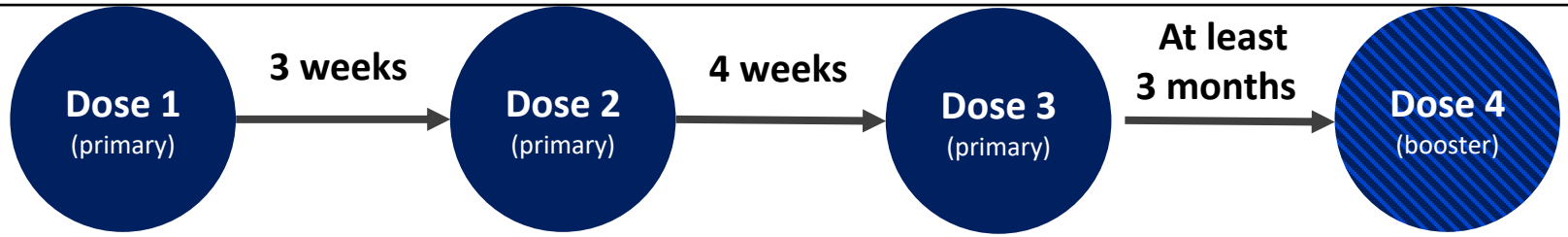
Children ages 5-11 years

Children who are not moderately to severely immunocompromised

Pfizer-BioNTech
(ages 5–11 years)

Children who are moderately to severely immunocompromised

Pfizer-BioNTech
(ages 5–11 years)



Everyone in the age group **SHOULD** receive the dose

Formulation for Ages 5–11 Years (Orange Cap)

Orange cap formulation

Age indications	5 through 11 years
Doses per vial	10
Dilution required	Yes—1.3 mL
Dose	10 mcg
Dose volume	0.2 mL
Storage	• Ultra-cold freezer until expiration date • Refrigerator for up to 10 weeks

https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/pfizer-bioNTech-children-adolescents.html

Policy Question

- Should individuals ages 5-11 years receive a Pfizer-BioNTech COVID-19 vaccine booster dose at least 5 months after completion of the primary series, based on the balance of benefits and risks?

Questions to ACIP

- What does ACIP think about recommendations for booster doses of COVID-19 vaccines in children ages 5-11 years?
  - What are the ACIP thoughts about a “may” recommendation for boosters in this population?
  - What are the ACIP thoughts about a “should” recommendation for boosters in this population?

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- VTF ACIP WG Team
- ACIP COVID-19 Vaccines Work Group
- Vaccine Task Force
- Epi Task Force
- Data Analytics and Visualization Task Force
- Respiratory Viruses Branch