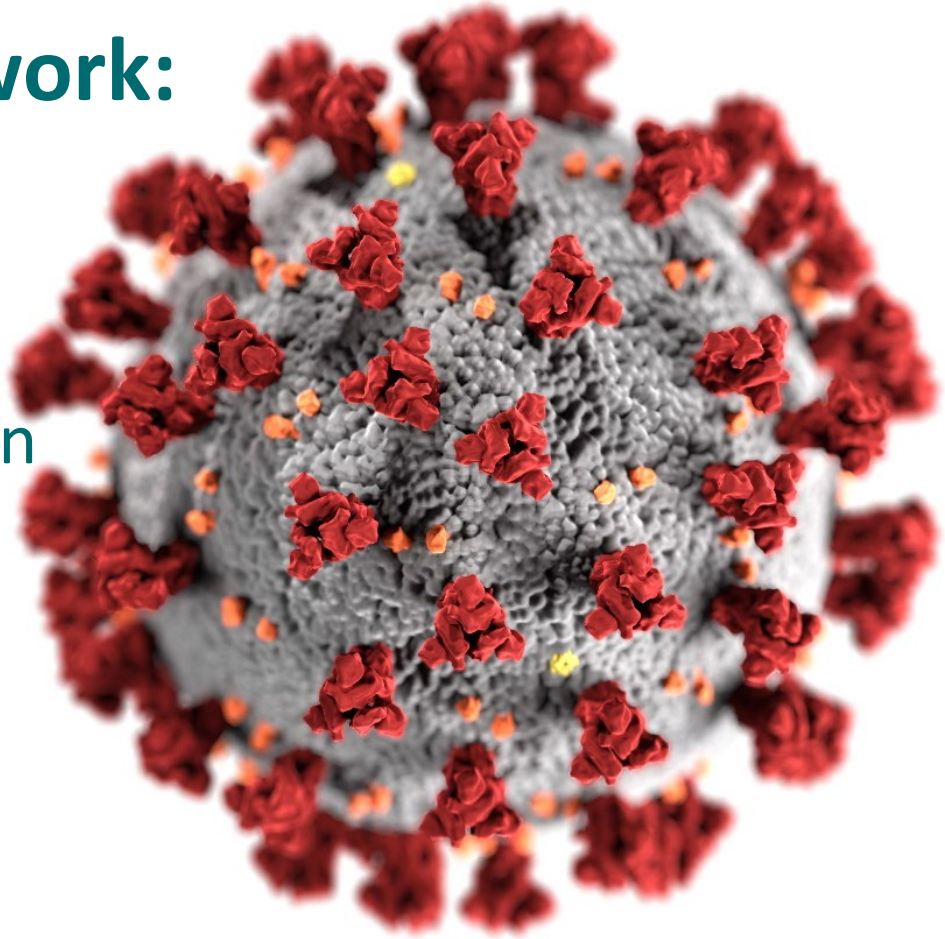
Evidence to Recommendation Framework:

Moderna COVID-19 vaccine in children
ages 6 months – 5 years
&
Pfizer-BioNTech COVID-19 vaccine in children
ages 6 months – 4 years



Sara Oliver, MD, MSPH
ACIP Meeting
June 17, 2022

cdc.gov/coronavirus

Evidence to Recommendations Framework

Evidence to Recommendations (EtR) Framework

- Structure to describe information considered in moving from evidence to ACIP vaccine **recommendations**
- Provide **transparency** around the impact of additional factors on deliberations when considering a recommendation

Evidence to Recommendations (EtR) Framework

Policy Question

- Should vaccination with **Moderna COVID-19 vaccine** (2-doses, 25µg, IM) be recommended for children **6 months–5 years of age**, under an Emergency Use Authorization?

- Should vaccination with **Pfizer-BioNTech COVID-19 vaccine** (3-doses, 3µg, IM) be recommended for children **6 months–4 years of age**, under an Emergency Use Authorization?

Evidence to Recommendations (EtR) Framework:
PICO Question

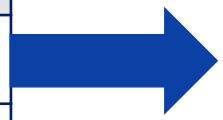
Population	Children ages 6 months – 4 years or 5 years
Intervention	Moderna COVID-19 vaccine (mRNA-1273) 2-doses, 25µg, IM –or– Pfizer-BioNTech COVID-19 vaccine (BNT162b2) 3-doses, 3µg, IM
Comparison	No vaccine
Outcomes	Symptomatic laboratory confirmed COVID-19 Hospitalization due to COVID-19 Multisystem inflammatory syndrome in children (MIS-C) Asymptomatic SARS-CoV-2 infection Serious adverse events Reactogenicity grade ≥3

Evidence to Recommendations (EtR) Framework

EtR Domain	Question(s)
Public Health Problem	• Is the problem of public health importance?
Benefits and Harms	• How substantial are the desirable anticipated effects? • How substantial are the undesirable anticipated effects? • Do the desirable effects outweigh the undesirable effects?
Values	• Does the target population feel the desirable effects are large relative to the undesirable effects? • Is there important variability in how patients value the outcome?
Acceptability	• Is the intervention acceptable to key stakeholders?
Feasibility	• Is the intervention feasible to implement?
Resource Use	• Is the intervention a reasonable and efficient allocation of resources?
Equity	• What would be the impact of the intervention on health equity?

Evidence to Recommendations (EtR) Framework

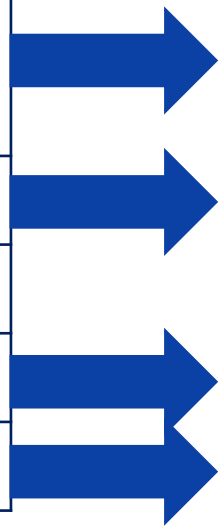
EtR Domain
Public Health Problem
Benefits and Harms
Values
Acceptability
Feasibility
Resource Use
Equity



Data for young children **overall** will be presented

Evidence to Recommendations (EtR) Framework

EtR Domain
Public Health Problem
Benefits and Harms
Values
Acceptability
Feasibility
Resource Use
Equity



Use of mRNA COVID-19 vaccines **broadly** will be presented

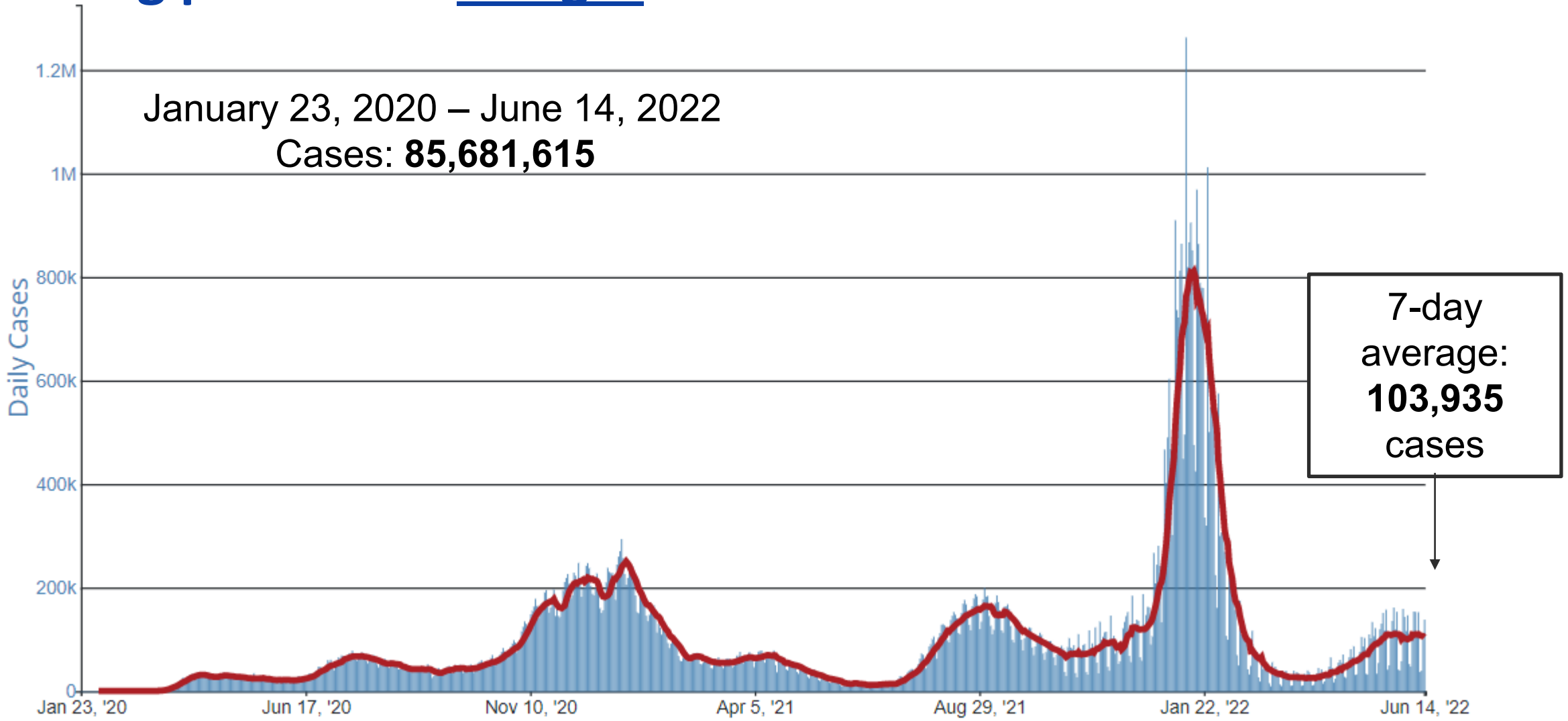
Evidence to Recommendations (EtR) Framework

EtR Domain
Public Health Problem
Benefits and Harms
Values
Acceptability
Feasibility
Resource Use
Equity

Manufacturer-specific
data
will be presented

EtR Domain: Public Health Problem

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

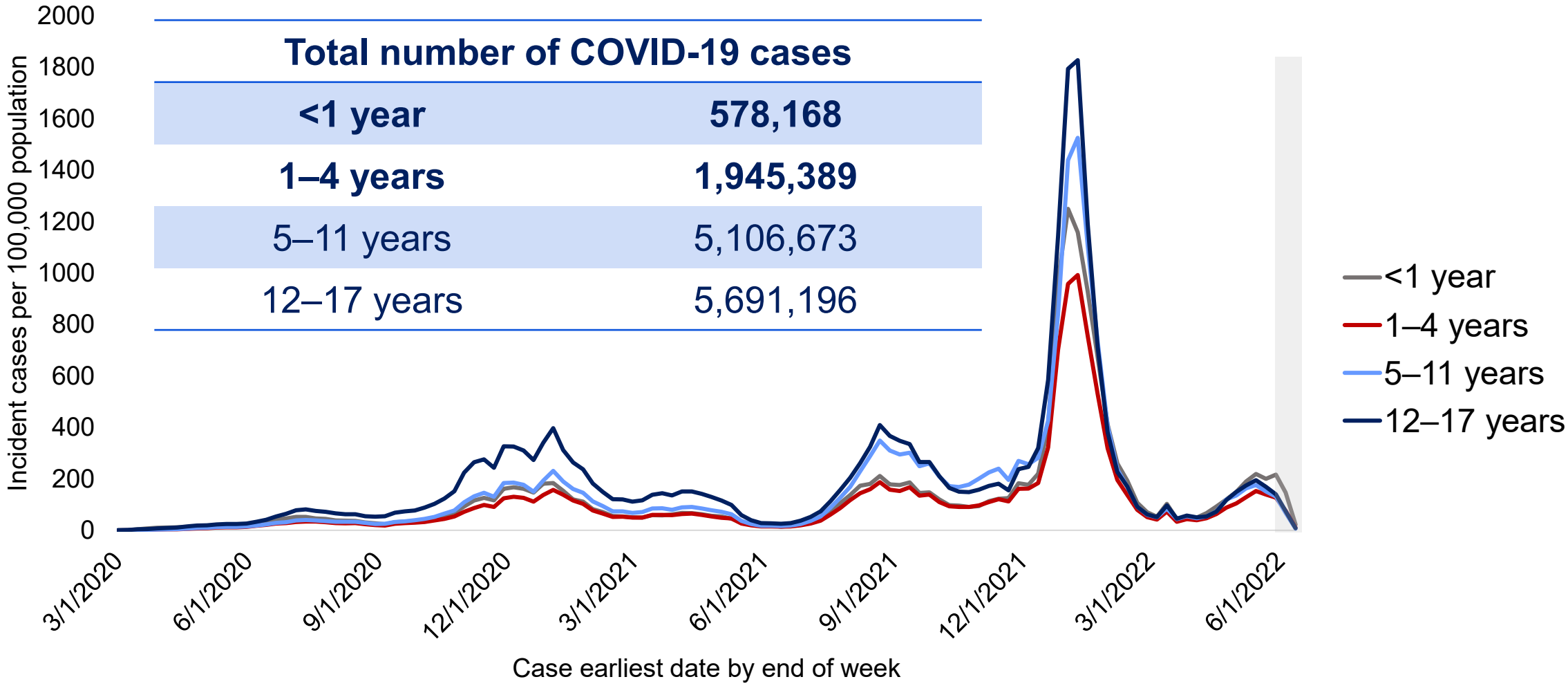


Source: COVID Data Tracker, https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases. Accessed 6/16/2022

COVID-19 weekly cases per 100,000 population among children ages 0 – 17 years by age group – United States

March 1, 2020 – June 14, 2022

Total number of COVID-19 cases	
<1 year	**578,168**
1–4 years	**1,945,389**
5–11 years	5,106,673
12–17 years	5,691,196

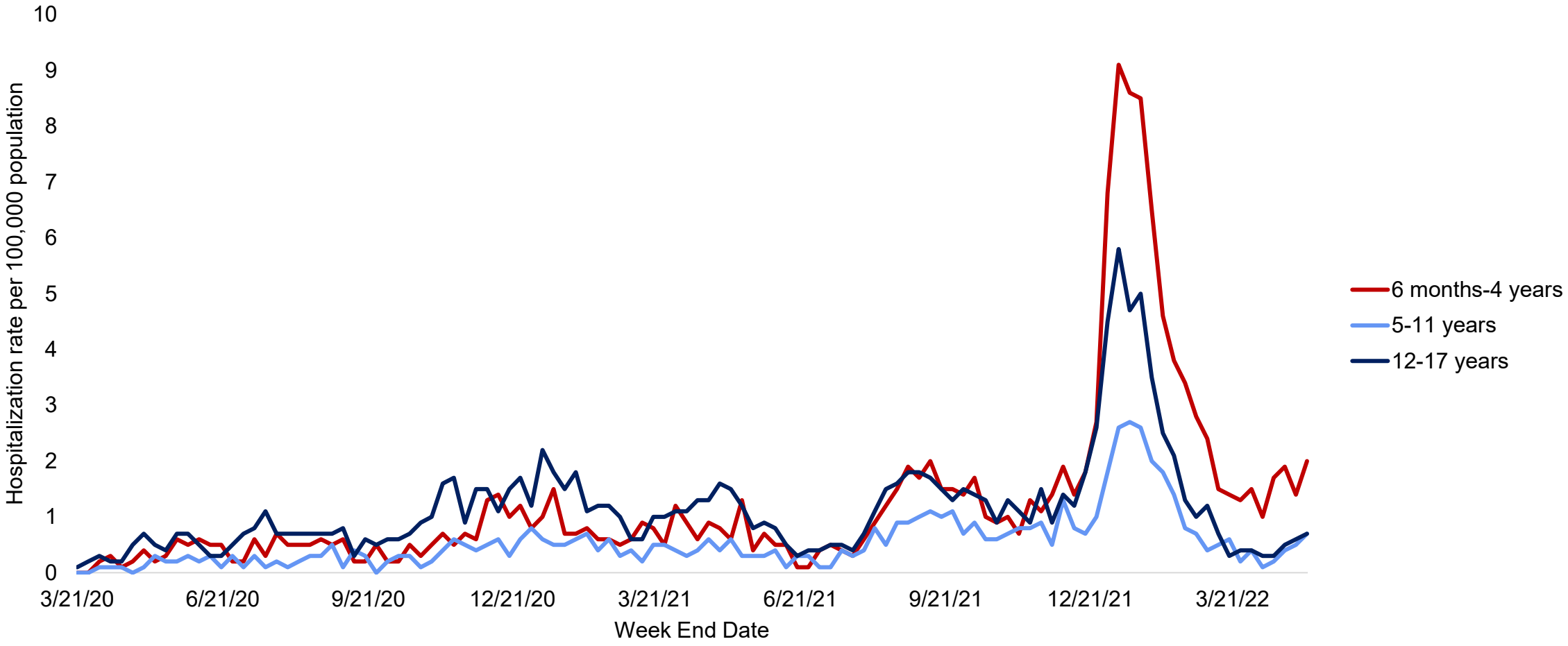


Reporting may be incomplete for the most recent two weeks of data, denoted by the grey box.

Source: COVID Data Tracker, https://covid.cdc.gov/covid-data-tracker/#demographicsovertime. Accessed 6/14/2022

COVID-19-associated hospitalizations among children and adolescents ages 6 months – 17 years, COVID-NET

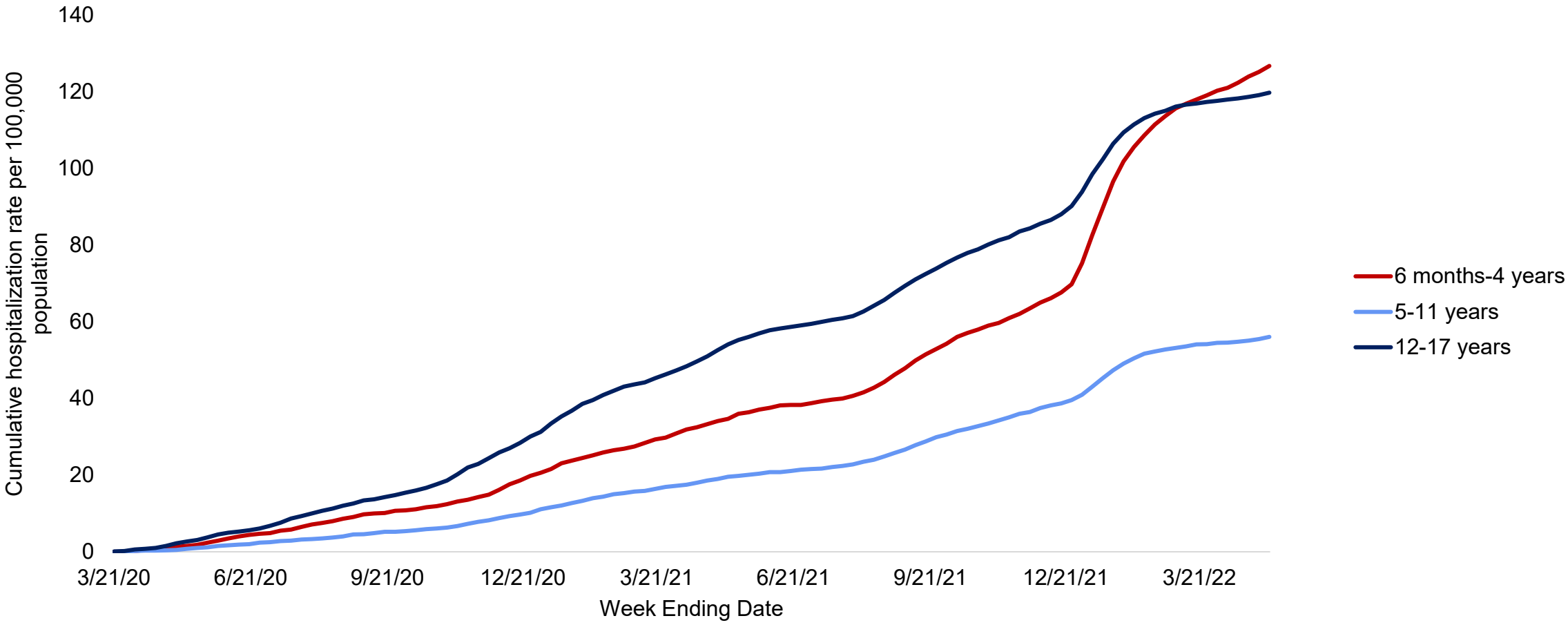
March 21, 2020 – May 7, 2022



Source: COVID-NET, https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html. Accessed 5/21/2022

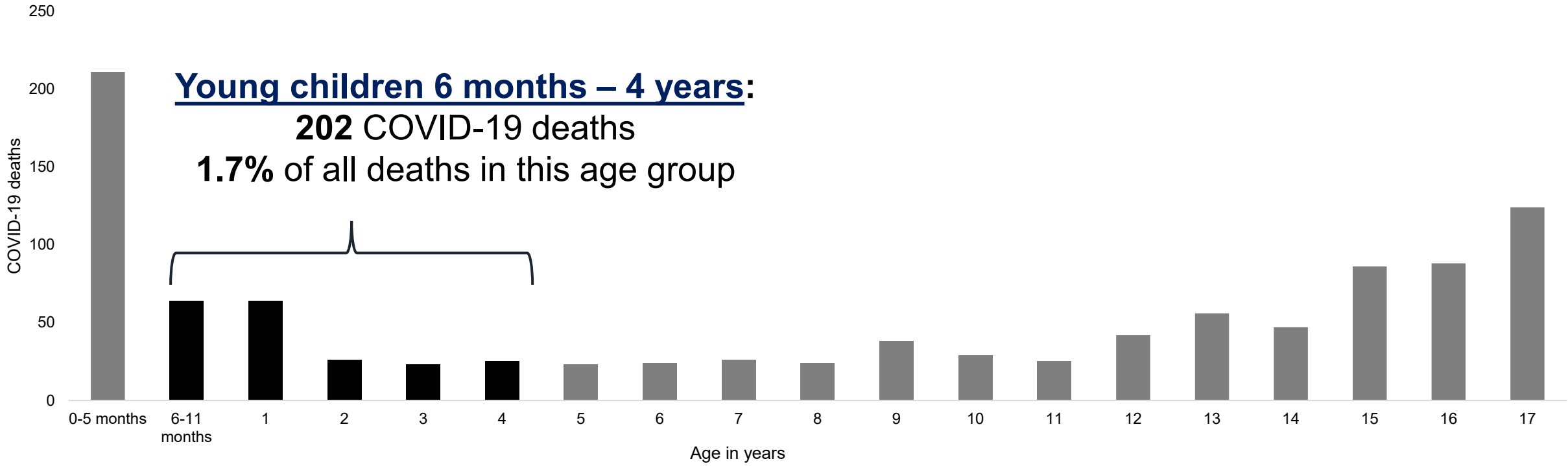
Cumulative COVID-19-associated hospitalizations among children and adolescents ages 6 months – 17 years, COVID-NET

March 21, 2020 – May 7, 2022



Source: COVID-NET, https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html. Accessed 5/21/2022

COVID-19 deaths in children and adolescents by age based on death certificate data, National Center for Health Statistics, January 1, 2020 – May 11, 2022



The provisional counts for COVID-19 deaths are based on a current flow of mortality data in the National Vital Statistics System. National provisional counts include deaths occurring within the 50 states and the District of Columbia that have been received and coded as of the date specified. It can take several weeks for death records to be submitted to National Center for Health Statistics (NCHS), processed, coded, and tabulated. Therefore, the data may be incomplete, and will likely not include all deaths that occurred during a given time period, especially for the more recent time periods.

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

COVID-19 was a leading cause of death among children ages 0 – 4 years

March 1, 2020 – April 30, 2022

Age group	Rank of COVID-19 among causes of death
<1 year	**4**
1 – 4 years	**5**
5 – 9 years	5
10 – 14 years	4
15 – 19 years	4

Based on death certificate data from the National Center for Health Statistics. COVID-19 based on cumulative total incidence of COVID-19 deaths from March 1, 2020-April 30, 2022.

Source: Preprint: Flaxman S, Whittaker C, Semenova E et al. Covid-19 is a leading cause of death in children and young people ages 0-19 years in the United States. medRxiv 2022.05.23.22275458; doi: https://doi.org/10.1101/2022.05.23.22275458

COVID-19 is a leading cause of death among infants age <1 year

March 1, 2020–April 30, 2022

Causes of Death	Crude rate per 100,000	Death (n)
1. Certain conditions originating in the perinatal period	272.1	10294
2. Congenital malformations, deformations and chromosomal abnormalities	113.7	4301
3. Accidents (unintentional injuries)	33.5	1266
4. Covid-19 (cumulative)	**7.2**	**269**
5. Diseases of heart	7.1	268

Based on death certificate data from the National Center for Health Statistics. COVID-19 based on cumulative total incidence of COVID-19 deaths from March 1, 2020-April 30, 2022.

Source: Flaxman S, Whittaker C, Semenova E et al. Covid-19 is a leading cause of death in children and young people ages 0-19 years in the United States. medRxiv 2022.05.23.22275458; doi: https://doi.org/10.1101/2022.05.23.22275458

COVID-19 is a leading cause of death among children ages 1–4 years

March 1, 2020–April 30, 2022

Causes of Death	Crude rate per 100,000	Death (n)
1. Accidents (unintentional injuries)	7.3	1149
2. Congenital malformations, deformations and chromosomal abnormalities	2.6	416
3. Malignant neoplasms	1.8	285
4. Assault (homicide)	1.8	284
5. Covid-19 (cumulative)	**0.9**	**134**

Based on death certificate data from the National Center for Health Statistics. COVID-19 based on cumulative total incidence of COVID-19 deaths from March 1, 2020-April 30, 2022.

Source: Flaxman S, Whittaker C, Semenova E et al. Covid-19 is a leading cause of death in children and young people ages 0-19 years in the United States. medRxiv 2022.05.23.22275458; doi: https://doi.org/10.1101/2022.05.23.22275458

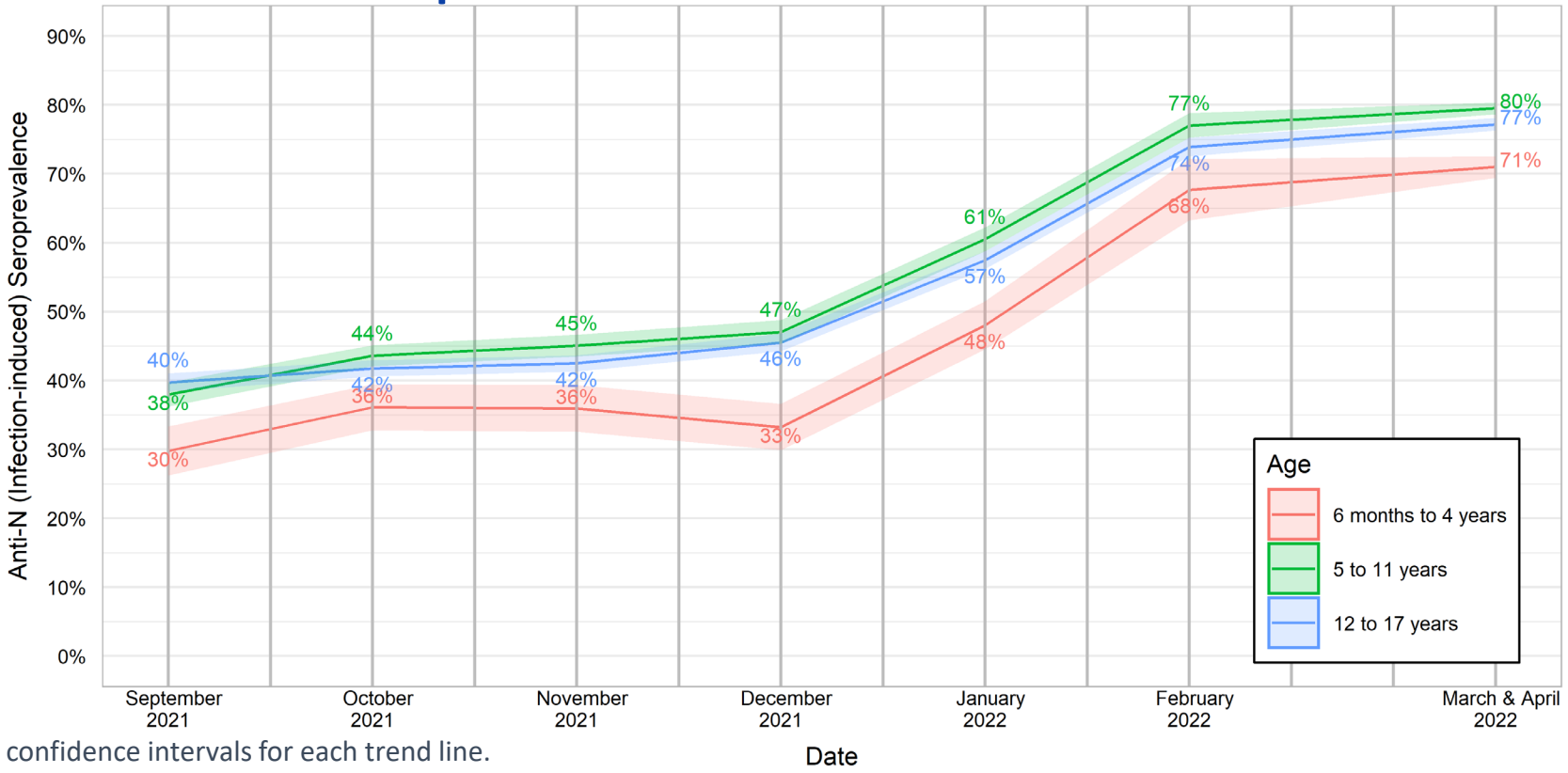
Pediatric vaccine preventable diseases: Deaths per year in the United States prior to recommended vaccines

	Hepatitis A[1]	Meningococcal (ACWY)[2]	Varicella[3]	Rubella[4]	Rotavirus[5]	COVID-19[6]
Age	<20 years	11–18 years	5–9 years	All ages	<5 years	6 months – 4 years
Time period	1990–1995	2000–2004	1990–1994	1966–1968	1985–1991	Jan 2020–May 2022
Average deaths per year	**3**	**8**	**16**	**17**	**20**	**86**

[1]Vogt TM , Wise ME, Bell BP, Finelli L. Declining hepatitis A mortality in the United States during the era of hepatitis A vaccination. J Infect Dis2008; 197:1282–8.
[2]National Notifiable Diseases Surveillance System with additional serogroup and outcome data from Enhanced Meningococcal Disease Surveillance for 2015-2019.
[3]Meyer PA, Seward JF, Jumaan AO, Wharton M. Varicella mortality: trends before vaccine licensure in the United States, 1970-1994. J Infect Dis. 2000;182(2):383-390. doi:10.1086/315714
[4]Roush SW , Murphy TV; Historical comparisons of morbidity and mortality for vaccine-preventable diseases in the United States. JAMA 2007; 298:2155–63.
[5] Glass RI, Kilgore PE, Holman RC, et al. The epidemiology of rotavirus diarrhea in the United States: surveillance and estimates of disease burden. J Infect Dis. 1996 Sep;174 Suppl 1:S5-11.
[6] https://data.cdc.gov/NCHS/Provisional-COVID-19-Deaths-Counts-by-Age-in-Years/3apk-4u4f/data. Accessed 5/14/22

Seroprevalence of infection-induced SARS-CoV-2 antibodies among children ages 6 months–17 years — National Commercial Lab Seroprevalence Study

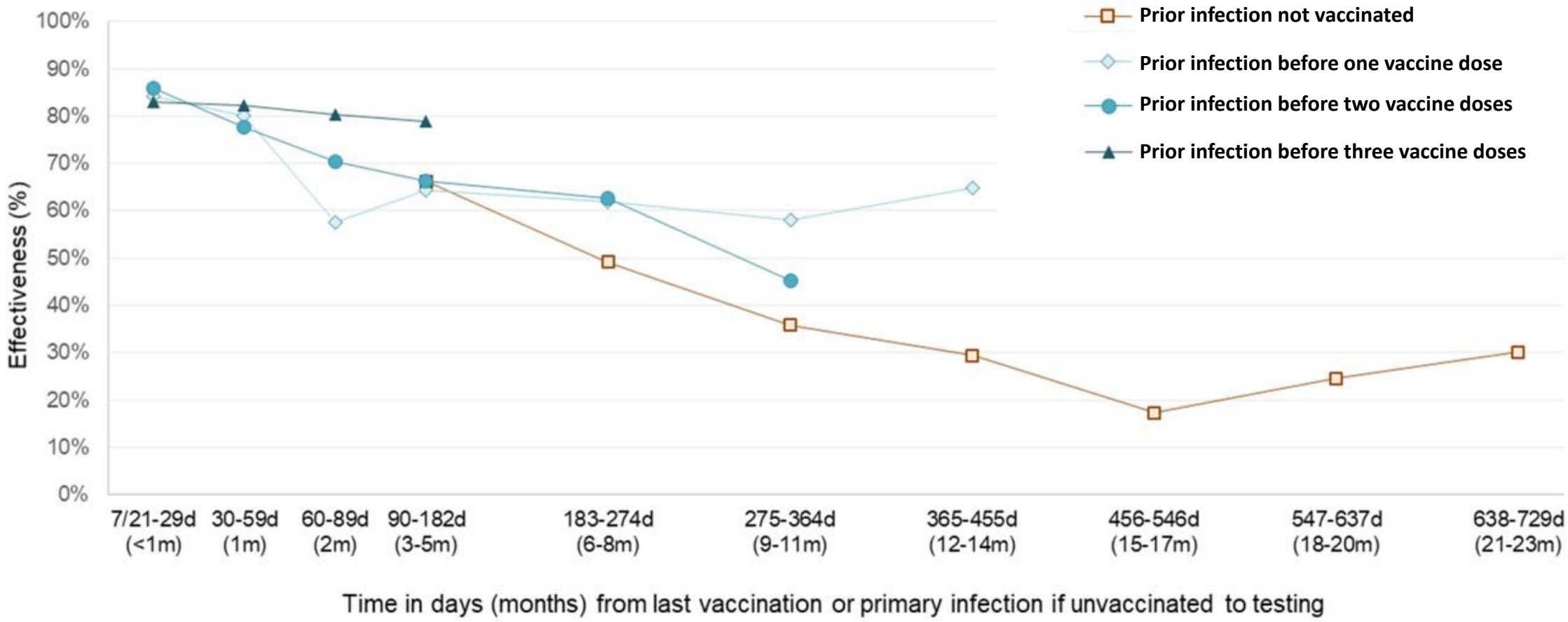
September 2021– April 2022



Shading indicates confidence intervals for each trend line.

Data updated for March/April 2022, based on 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).
SSRN: https://ssrn.com/abstract=4092074 or http://dx.doi.org/10.2139/ssrn.4092074

Reinfection occurs more frequently in those previously infected and not vaccinated compared to infected and vaccinated



Carazo S, Skowronski DM, Brisson M, et al. "Protection against Omicron re-infection conferred by prior heterologous SARS-CoV-2 infection, with and without mRNA vaccination" *medRxiv,* May 2022. Protection against Omicron re-infection conferred by prior heterologous SARS-CoV-2 infection, with and without mRNA vaccination | medRxiv

***Data on hospitalizations**:* Plumb ID, Feldstein LR, Barkley E, et al. Effectiveness of COVID-19 mRNA Vaccination in Preventing COVID-19–Associated Hospitalization Among Adults with Previous SARS-CoV-2 Infection — United States, June 2021–February 2022. MMWR Morb Mortal Wkly Rep 2022;71:549-555. DOI: http://dx.doi.org/10.15585/mmwr.mm7115e2

Improved antibody response after vaccination

- Among children, COVID-19 vaccine induces a **broader neutralizing antibody** response compared with infection induced immunity:
  - From a U.S. multicenter cohort, antibody profiles of unvaccinated pediatric patients hospitalized for COVID-19 were compared to profiles of vaccinated children.
  - In contrast to those with SARS-CoV-2 infection, **children vaccinated with two doses demonstrated higher titers** against Alpha, Beta, Gamma, Delta and Omicron.
  - The findings suggest that antibodies produced by prior SARS-CoV-2 infection (pre-Omicron) may not neutralize the currently circulating Omicron variant.
  - This builds on evidence among adults that previous infection provides poor protection from infection with Omicron.
- Highlights the importance of vaccinating **children with prior infection** to prevent both severe disease and future infections.

Tang J, Novak T, Hecker J, et al. "Cross-reactive immunity against the SARS-CoV-2 Omicron variant is low in pediatrics patients with prior COVID-19 or MIS-C." *Nature Communications*. (2022) 13:2979. https://doi.org/10.1038/s41467-022-30649-1

Summary
U.S. COVID-19 epidemiology in children 6 months–4 years

- COVID-19 has caused **>2 million cases** among children ages 6 months – 4 years
- Children 6 months–4 years of age are **at risk of severe illness** from COVID-19
  - More than half of hospitalized children ages 6 months–4 years had **no underlying conditions**
  - COVID-19 associated hospitalizations among children ages 6 months–4 years have similar or increased severity compared to older children and adolescents
  - Burden of COVID-19 associated death is **similar to** or **exceeds** that of other pediatric vaccine preventable diseases
- Prior infection may not provide broad protection against newer SARS-CoV-2 variants
- COVID-19 pandemic continues to have significant impact on families

Public Health Problem

Work Group Interpretation

Is COVID-19 disease among children ages 6 months – 5 years of public health importance?

○ No	○ Probably no	○ Probably yes	○ Yes	○ Varies	○ Don't know

EtR Domain: Benefits and Harms

Benefits and Harms Summary

- Moderna COVID-19 vaccine
  - GRADE summary
- Pfizer-BioNTech COVID-19 vaccine
  - GRADE summary
- Other considerations
- Number needed to vaccinate assessment

GRADE

Moderna COVID-19 vaccine: Children ages 6 months–5 years

- Moderna phase 2/3 randomized controlled trial in United States
- Randomized **3:1** vaccine to saline placebo
- Analyses performed separately for 6–23 months and 2–5 years, results pooled for a combined estimate for 6 months–5 years
- Data evaluated: all eligible randomized participants who received all vaccinations as randomized within the predefined window and no other important protocol deviations
  - Data cut off: Feb 21, 2022
- Per protocol, the two co-primary endpoints for immunobridging were geometric mean ratios (GMR) & serologic response
  - Efficacy data also provided for symptomatic infection. Relative risks (RR) were calculated from cases in the study population. Vaccine efficacy estimates were defined as 100% x (1-RR)
    - Sensitivity analyses of VE were performed to include COVID-19 cases that were identified using home testing lacking RT-PCR confirmation

Outcome: Symptomatic Lab-confirmed COVID-19

Moderna COVID-19 vaccine: Children ages 6 months–5 years

Population	Events/Vaccine (n/N)	Events/Placebo (n/N)	Vaccine efficacy[a] (95% confidence interval)
Per protocol population			
CDC case definition[b], no evidence of prior infection, ≥14 d post dose 2	170/4105	95/1371	40.3% (23.9% , 53.3%)
CDC case definition[b], *seropositive[c] or seronegative*, ≥14 d post dose 2	181/4791	97/1597	37.8% (20.9%, 51.1%)
CDC case definition[b], sensitivity analysis including home tests, ≥14 d post dose 2	253/4105	133/1371	36.6% (22.4%, 48.1%)
Adult trial case definition[d] ,no evidence of prior infection, ≥14 d post dose 2	108/4105	61/1371	40.9% (19.6%, 56.8%)

[a] Manufacturer vaccine efficacy estimates calculated using incidence rates. For GRADE, vaccine efficacy calculated from the relative risk
[b] Requires at least 1 prespecified clinical symptom and a positive RT-PCR
[c] Approximately 10% of participants were seropositive at baseline
[d] Requires at least 2 prespecified systemic symptoms or at least 1 respiratory symptom and a positive RT-PCR

Outcome: Symptomatic Lab-confirmed COVID-19

Moderna COVID-19 vaccine: Children ages 6 months–5 years

Immunobridging: Summary of Geometric Mean Ratio (GMR)

Outcome	N[b]	GMT (model based) [c] (95% CI)	N[b]	GMT (model based) [c] (95% CI)	GMR (model based) [c] (95% CI)	Met Noninferiority Objective[d]
	6-23 Months		18-25 Years			
Pseudovirus neutralizing antibody level by pseudovirus neutralizing assay (ID50)[a]	230	1780.7 (1606.4, 1973.8)	291	1390.8 (1269.1, 1524.2)	1.28 (1.12, 1.47)	Yes
	2-5 Years		18-25 Years			
Pseudovirus neutralizing antibody level by pseudovirus neutralizing assay (ID50)[a]	264	1410.0 (1273.8, 1560.8)	291	1390.8 (1262.5, 1532.1)	1.01 (0.88, 1.17)	Yes

Abbreviations: ID50 = 50% inhibitory dose; GLSM = geometric least squares mean; GMR = geometric mean ratio; CI=confidence interval

[a]Sampling time point was at 28 days after the second dose (day 57).

[b]Subjects with a negative serology test at baseline and completion of the 2-dose series on schedule.

[c]The log-transformed antibody levels are analyzed using an ANCOVA model with the group variable (children in P204 and young adults in P301) as fixed effect. The resulted LS means, difference of LS means, and 95% CI are back transformed to the original scale for presentation.

[d]Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67.

GRADE: Symptomatic Laboratory-confirmed COVID-19

Moderna COVID-19 vaccine: Children ages 6 months–5 years

Assessed Using Direct Efficacy

- RR 0.62 (0.49, 0.79)
- No serious concerns in certainty assessment
- Evidence type: **High certainty (type 1)**

RR= relative risk

GRADE: Symptomatic Laboratory-confirmed COVID-19

Moderna COVID-19 vaccine: Children ages 6 months–5 years

Assessed Using Immunobridging

- Ages 6–23 months
  - GMR 1.28 (1.12, 1.47); non-inferiority criteria met
- Ages 2–5 years
  - GMR 1.01 (0.88, 1.17); non-inferiority criteria met
- Serious concerns of indirectness because immunogenicity is a surrogate measure of efficacy
- Evidence type: **Moderate certainty (type 2)**

Outcome: Asymptomatic SARS-CoV-2 infection

Moderna COVID-19 vaccine: Children ages 6 months–5 years

- Asymptomatic SAR-CoV-2 infection is identified by absence of symptoms AND at least 1 of following:
  - Binding antibody level against SARS-CoV-2 nucleocapsid protein negative at Day 1 that becomes positive post-baseline. Antibody levels taken only on the immunogenicity subset (n=494)
  - Positive RT-PCR test post-baseline at scheduled or unscheduled visit

Outcome: Asymptomatic SARS-CoV-2 infection

Moderna COVID-19 vaccine: Children ages 6 months–5 years

Study/population	Events/Vaccine (n/N)	Events/Placebo (n/N)	Vaccine Efficacy[a] (95% confidence interval)
bAb level against SARS-Cov 2 nucleocapsid protein negative at Day 1 that becomes positive post-baseline or positive RT-PCR test post-baseline at scheduled or unscheduled/illness visit without symptoms	111/4105	44/1371	16.0% (-18.5%, 40.5%)
bAb level against SARS-Cov 2 nucleocapsid protein negative at Day 1 that becomes positive post-baseline or positive RT-PCR **or home antigen** test post-baseline or where test modality was not identified at scheduled or unscheduled/illness visit without symptoms	135/4105	52/1371	21.1% (4.5%, 34.8%)

[a]Manufacturer vaccine efficacy estimates calculated using incidence rates. For GRADE, vaccine efficacy calculated from the relative risk

GRADE: Asymptomatic SARS-CoV-2 infection

Moderna COVID-19 vaccine: Children ages 6 months–5 years

- RR 0.84 (0.60, 1.19)
- Serious concerns of indirectness because asymptomatic SARS-CoV-2 PCR testing on the full cohort only occurred once and serology was not done on all participants
- Serious concerns of imprecision due to the wide confidence interval
- Evidence type: **Low certainty (type 3)**

RR= relative risk

Outcome: Serious Adverse Events[a,b,c]

Moderna COVID-19 vaccine: Children ages 6 months–5 years

Study/population[d]	Events/Vaccine (n/N)[e]	% SAE Vaccine	Events/Placebo (n/N)[e]	% SAE Placebo	Associated with vaccination
Moderna, unpublished RCT- **6-23 months**	15/1761	0.85%	1/589	0.17%	1[f]
Moderna, unpublished RCT- **2-5 years**	9/3031	0.30%	2/1007	0.20%	0
Moderna, unpublished RCT- **6 months-5 years**	24/4792	0.50%	3/1596	0.19%	1[f]

[a] Serious adverse event (SAE) is defined as death, life-threatening event, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, medically important event, or congenital anomaly/birth defect

[b] No deaths were reported in any trial participants

[c] Follow up through Feb 21, 2022

[d] Included all randomized participants who received at least 1 dose of vaccine

[E] Number of participants experiencing SAEs (participants may experience more than one SAE)

[F] One participant experienced two SAEs of fever and febrile seizure that were considered possibly related to the study intervention by FDA

RCT= randomized controlled trials

GRADE: Serious Adverse Events

Moderna COVID-19 vaccine: Children ages 6 months–5 years

- RR 2.67 (0.80, 8.84)
- Serious concerns of indirectness due to short duration of follow up of 2 months after dose 2
- Very serious concerns of imprecision due to the study size and width of the confidence interval
- Evidence type: **Very low certainty (type 4)**

RR= relative risk

Outcome: Reactogenicity, Severe (Grade ≥3)

Moderna COVID-19 vaccine: Children ages 6 months–5 years

- **Local reactions**
  - Grade 3:
    - 6–23 months: pain at injection site preventing daily activity; injection site redness >5 cm or swelling >5 cm; axillary (underarm or groin) swelling or tenderness ipsilateral to injection side
    - 2–5 years: pain at injection site preventing daily activity; injection site redness >10 cm or swelling >10 cm; axillary (underarm or groin) swelling or tenderness ipsilateral to injection side
  - Grade 4: emergency room visit or hospitalization for axillary (underarm or groin) swelling or severe pain at the injection site, necrosis (redness and swelling categories) or exfoliative dermatitis (redness category only)
- **Systemic events**
  - Grade 3:
    - ≤36 months: fever 39.6°C to 40.0°C, irritability/crying, sleepiness, or loss of appetite that prevents daily activity
    - 37 months–5 years: fever 39°C to 40°C, nausea/vomiting, chills, fatigue, headache, muscle pain, or joint pain that prevents daily activity
  - Grade 4: fever >40.0°C, fatigue, headache, muscle pain, joint pain, or nausea/vomiting that require emergency room visit or hospitalization

Outcome: Reactogenicity, Severe (Grade ≥3)[a]

Moderna COVID-19 vaccine: Children ages 6 months–5 years

Study/population	Events/Vaccine (n/N)	% Vaccine	Events/Placebo (n/N)	% Placebo
Moderna, unpublished (either dose)	366/4774	7.7%	65/1582	4.1%
Any local (either dose)	84/4774	1.8%	6/1582	0.4%
Any systemic (either dose)[b]	288/4774	6.0%	59/1582	3.7%

[a] Reactogenicity outcome includes local and systemic events, grade ≥3 after either dose. Grade 3: prevents daily routine activity. Grade 4: requires emergency room visit or hospitalization.

[B] There were 15 fevers of > 40.0 °C in the vaccine group and 3 in the placebo group

GRADE: Reactogenicity, Severe (Grade ≥3)

Moderna COVID-19 vaccine: Children ages 6 months–5 years

- RR 1.87 (1.44 to 2.42)
- No serious concerns in certainty assessment
- Evidence type: **High certainty (type 1)**

RR= relative risk

Summary of GRADE

Moderna COVID-19 vaccine: Children ages 6 months–5 years

Outcome	Importance	Design (# studies)	Findings	Evidence type
Benefits				
1. Symptomatic lab-confirmed COVID-19	Critical	RCT (1)	Moderna COVID-19 vaccine is effective in preventing symptomatic COVID-19	**1**
1b. Symptomatic lab-confirmed COVID-19 (immunobridging)	Critical	RCT (1)	Moderna COVID-19 vaccine is effective in preventing symptomatic COVID-19	**2**
2. Hospitalization due to COVID-19	Important	No studies	Data not available from any studies	**ND**
3. Multisystem inflammatory syndrome in children (MIS-C)	Important	No studies	Data not available from any studies	**ND**
4. Asymptomatic SARS-CoV-2 infection	Important	RCT (1)	The vaccine did not demonstrate efficacy in prevention of asymptomatic SARS-CoV-2 infection	**3**
Harms				
5. Serious adverse events	Critical	RCT (1)	0.5% of participants with SAEs among vaccinated and 0.2% among unvaccinated; certainty in the estimate was very low. Two SAEs which occurred in one participant were judged by the investigator to be related to vaccination.	**4**
6. Reactogenicity	Important	RCT (1)	Severe reactions were more common in vaccinated; any grade ≥3 reaction was reported by 7.7% of vaccinated vs. 4.1% of placebo group	**1**

Evidence type: 1=high; 2=moderate; 3=low; 4=very low; ND, no data

Conclusions

Moderna COVID-19 vaccine: Children ages 6 months–5 years

- Efficacy seen after two doses of Moderna COVID-19 vaccine in children ages 6 months–5 years of age consistent with real-world vaccine effectiveness in all other ages during Omicron predominance
- Antibody levels after 2 doses in children ages 6 months–5 years produces similar antibody levels after 2 doses in individuals ages 18–25 years
- Reactogenicity post-vaccine consistent with other recommended vaccines in this age group

GRADE

Pfizer-BioNTech COVID-19 vaccine: Children ages 6 months–4 years

- Pfizer-BioNTech phase 2/3 RCT conducted in United States, Finland, Poland, and Spain
- Randomized **2:1** vaccine to saline placebo
- Analyses performed separately for 6-23 months and 2-4 years, results pooled for a combined estimate for 6 months-4 years
- Interval between Dose 1 and Dose 2 of 21 days
- Interval between Dose 2 and Dose 3 varied
  - Ages 6–23 months: Median interval of **16 weeks**
  - Ages 2–4 years: Median interval of **11 weeks**
- Data evaluated: direct efficacy and immunobridging (per protocol co-primary endpoint) on all eligible randomized participants who received all vaccinations as randomized and no other important protocol deviations
  - Data cut-off: April 29, 2022 median follow-up after dose 3: 1.3 months
  - Relative risks (RR) were calculated from cases in the study population. Vaccine efficacy estimates were defined as 100% x (1-RR)

RCT= randomized controlled trial

GRADE

Pfizer-BioNTech COVID-19 vaccine: Children ages 6 months–4 years

Population 6 months–4 years	Vaccine n (%)	Placebo n (%)	Total n (%)
Randomized population	3013 (100%)	1513 (100%)	4526 (100%)
Dose 1	3013 (100%)	1513 (100%)	4526 (100%)
Dose 2	2985 (99.1%)	1503 (99.3%)	4488 (99.2%)
Dose 3	992 (32.9%)	464 (30.7%)	1456 (32.2%)

Outcome: Symptomatic Lab-confirmed COVID-19

Pfizer COVID-19 vaccine: Children ages 6 months–4 years

Population	Events/Vaccine (n/N)	Events/Placebo (n/N)	Vaccine efficacy[a] (95% confidence interval)
Evaluable efficacy[b]			
With or without[c] evidence of prior infection (≥7 d post Dose 3), **ages 6–23 months**	1/386	2/184	76.2 (-161.2, 97.8)
With or without[c] evidence of prior infection (≥7 d post Dose 3), **ages 2–4 years**	2/606	5/280	81.5 (5.3, 96.4)
With or without[c] evidence of prior infection (≥7 d post Dose 3), **ages 6mo–4 years**	3/992	7/464	80.0 (22.8, 94.8)

[a]Manufacturer vaccine efficacy estimates calculated using incidence rates. For GRADE, vaccine efficacy calculated from the relative risk

[b]All eligible randomized participants who received all vaccinations as randomized and had no other important protocol deviations as determined by the investigator

[c]Approximately 30% of participants were seropositive at baseline

Outcome: Symptomatic Lab-confirmed COVID-19

Pfizer COVID-19 vaccine: Children ages 6 months–4 years

Immunobridging: Summary of Geometric Mean Ratio (GMR)

	n[c]	GMT[d] (95% CI)	n[c]	GMT[d] (95% CI)	GMR[e] (95% CI)	Met Noninferiority Objective[f]
	6–23 months (3 doses, 3 µg)		16–25 years (2 doses, 30 µg)			
SARS-CoV-2 neutralization assay – NT50[a,b]	82	1406.5 (1211.3, 1633.1)	170	1180.0 (1066.6, 1305.4)	1.19 (1.00, 1.43)	Yes
	2–4 years (3 doses, 3 µg)		16–25 years (2 doses,30 µg)			
SARS-CoV-2 neutralization assay – NT50[a,b]	143	1535.2 (1388.2, 1697.8)	170	1180.0 (1066.6, 1305.4)	1.30 (1.13, 1.50)	Yes

Abbreviations: NT50 = 50% neutralizing titer; GMT = geometric mean titer; GMR = geometric mean ratio; LLOQ = lower limit of quantitation

[a]Among participants who had no serological or virological evidence (1-month post-Dose 2 [16-25 years] or 1-month post-Dose 3 [6 mo – 4 years]) of past SARS-CoV-2 infection and had negative NAAT at any unscheduled visit up to one month after dose two.

[b]Sampling time point was one month after dose two.

[c]Number of subjects with valid and determinate assay results for the specified assay at the given dose and sampling time point.

[d]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.

[e]GMRs and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titers (Group 1a [6 to 23 months] or Group 1b [2 to 4 years] – Group 2 [16–25 years]) and the corresponding CI (based on the Student t distribution).

[f]Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67.

Outcome: Symptomatic Lab-confirmed COVID-19, dose 2 efficacy

Pfizer COVID-19 vaccine: Children ages 6 months–4 years

Population	Events/Vaccine (n/N)	Events/Placebo (n/N)	Vaccine efficacy[a] (95% confidence interval)
6–23 months			
With or without evidence of prior infection, ≥7 Days after Dose 2 to before Dose 3, **ages 6–23 months**[b]	80/1178	48/598	15.4 (-19.4, 40.0)
2–4 years			
With or without evidence of prior infection, ≥7 Days after Dose 2 to before Dose 3, **ages 2–4 years**[c]	100/1835	74/915	32.6 (10.0, 49.6)

[a]Manufacturer vaccine efficacy estimates calculated using incidence rates. For GRADE, vaccine efficacy calculated from the relative risk

[b]Met non-inferiority criteria for immunobridging to 16–25-year-olds

[c]Did not meet non-inferiority criteria for immunobridging to 16–25-year-olds

GRADE: Symptomatic Laboratory-confirmed COVID-19

Pfizer COVID-19 vaccine: Children ages 6 months–4 years

Assessed Using Direct Efficacy

- RR 0.2 (0.05, 0.77)
- Serious concern for indirectness due to the short duration of follow-up of 1.3 months
- Very serious concerns for imprecision due to study size
- Evidence type: **Very low certainty (type 4)**

RR= relative risk

GRADE: Symptomatic Laboratory-confirmed COVID-19

Pfizer COVID-19 vaccine: Children ages 6 months–4 years

Assessed Using Immunobridging

- Ages 6–23 months
  - GMR 1.19 (1.00, 1.43); non-inferiority criteria met
- Ages 2–4 years
  - GMR 1.30 (1.13, 1.50); non-inferiority criteria met
- Serious concerns of indirectness because immunogenicity is a surrogate measure of efficacy
- Evidence type: **Moderate certainty (type 2)**

Outcome: Serious Adverse Events

Pfizer-BioNTech COVID-19 vaccine: Children ages 6 months–4 years

- Safety population, approximately 1700 ages 6–23 months
  - Included all randomized participants who received at least 1 dose of vaccine*
  - Data from Dose 1 to data cutoff date (April 29, 2022); Median follow-up after dose 3: 1.3 months
- Safety population, approximately 2700 ages 2–4 years
  - Included all randomized participants who received at least 1 dose of vaccine*
  - Data from Dose 1 to data cutoff date (April 29, 2022); Median follow-up after dose 3: 1.4 months

*Six participants in 6-23 months age group and 9 participants in 2 to 4 years age group excluded due to not receiving vaccine or placebo.

Outcome: Serious Adverse Events[a,b]

Pfizer-BioNTech COVID-19 vaccine: Children ages 6 months–4 years

Study/population[c]	Events/Vaccine (n[d]/N)	% SAE Vaccine	Events/Placebo (n[d]/N)	% SAE Placebo	Associated with vaccination
Pfizer/BioNTech RCT **Ages 6 – 23 months**	17/1178[e]	1.4	14/598[f]	2.3	0
Pfizer/BioNTech RCT **Ages 2 – 4 years**	12/1835[g]	0.7	8/915[h]	0.9	1[i]
Pfizer/BioNTech RCT **Ages 6 months – 4 years**	29/3013	1.0	22/1504	1.5	1

[a] Serious adverse event (SAE) is defined as any untoward medical occurrence that, results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, or is a congenital anomaly/birth defect. SAEs after dose 1 or dose 2 or dose 3 are reported.
[b] No deaths were reported in any trial participants
[c] Included all randomized participants who received at least 1 dose of vaccine.
[d] Number of participants experiencing SAEs (participants may experience more than one SAE), data cutoff 29 April 2022.
[e] Twenty-two SAEs were reported in 17 vaccine recipients ages 6 to 23 months.
[f] Eighteen SAEs occurred in 14 placebo recipients ages 6 to 23 months.
[g] Fifteen SAEs were reported in 12 vaccine recipients ages 2 to 4 years.
[h] Eight SAEs occurred in 8 placebo recipients ages 2 to 4 years.
[i] One vaccine recipient had 2 SAEs (fever and pain in extremity requiring hospitalization) considered possibly related by the Investigator. FDA considered the events potentially consistent with symptoms due to unspecified viral infection

GRADE: Serious Adverse Events

Pfizer COVID-19 vaccine: Children ages 6 months–4 years

- RR 0.66 (0.38, 1.15)
- Very serious concern for indirectness due to the short duration of follow-up of 1 month post dose 3 and because only 31% of trial participants received dose 3, limiting the ability to detect serious adverse events that occur at a higher rate after dose 3
- Serious concerns of imprecision due to the study size
- Evidence type: **Very low certainty (type 4)**

RR= relative risk

Outcome: Reactogenicity, Severe (Grade ≥3)

Pfizer-BioNTech COVID-19 vaccine: Children ages 6 months–4 years

- **All ages:** Local reactions (redness, swelling, pain/tenderness at injection site)
  - Grade 3: pain at injection site that prevents daily activity; redness >7 cm; and swelling >7 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)
- **Ages 6–23 months**: Systemic events (fever, decreased appetite, drowsiness, irritability)
  - Grade 3: fever >38.9°C to 40.0°C or events that prevent daily activity
  - Grade 4: fever >40.0°C or events that require emergency room visit or hospitalization
- **Ages 2–4 years**: Systemic events (fever, vomiting, diarrhea, 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

Outcome: Reactogenicity, Severe (Grade ≥3)[a]

Pfizer-BioNTech COVID-19 vaccine: Children ages 6 months–4 years

Study/population	Events/Vaccine (n/N)	% Vaccine	Events/Placebo (n/N)	% Placebo
Pfizer-BioNTech, unpublished (any dose)	129/3010	4.3%	54/1510	3.6%
Any local (any dose)	4/3010	0.1%	3/1510	0.2%
Any systemic (any dose)[b]	125/3010	4.2%	52/1510	3.4%

Note: Grade 3: prevents daily routine activity. Grade 4: requires emergency room visit or hospitalization

[a] Reactogenicity outcome includes local and systemic events, grade ≥3 after either dose.

[b] Six fevers of > 40.0 °C were reported among vaccine recipients and one among placebo recipients

GRADE: Reactogenicity (Grade ≥3)

Pfizer COVID-19 vaccine: Children ages 6 months–4 years

- RR 1.20 (0.88, 1.64)
- Serious concern for indirectness was noted because only 31% of trial participants received dose 3 limiting the ability to detect severe reactogenicity that occurs specifically after dose 3
- Evidence type: **2 (moderate certainty)**

Summary of GRADE

Pfizer COVID-19 vaccine: Children ages 6 months–4 years

Outcome	Importance	Design (# studies)	Findings	Evidence type
Benefits				
1a. Symptomatic lab-confirmed COVID-19 (efficacy)	Critical	RCT (1)	Pfizer-BioNTech COVID-19 vaccine is effective in preventing symptomatic COVID-19; certainty in the estimate was very low	**4**
1b. Symptomatic lab-confirmed COVID-19 (immunobridging)	Critical	RCT (1)	Pfizer-BioNTech COVID-19 vaccine is effective in preventing symptomatic COVID-19	**2**
2. Hospitalization due to COVID-19	Important	No studies	Data not available from any studies	**ND**
3. Multisystem inflammatory syndrome in children (MIS-C)	Important	No studies	Data not available from any studies	**ND**
4. Asymptomatic SARS-CoV-2 infection	Important	No studies	Data not available from any studies	**ND**
Harms				
5. Serious adverse events	Critical	RCT (1)	1.0% of participants with SAEs among vaccinated and 1.5% among unvaccinated; certainty in the estimate was very low. 2 SAEs in 1 participant in the vaccine arm were judged to be related to vaccination.	**4**
6. Reactogenicity	Important	RCT (1)	Severe reactions were slightly more common in vaccinated; any grade ≥3 reaction was reported by 4.3% of vaccinated vs. 3.6% of placebo group	**2**

Evidence type: 1=high; 2=moderate; 3=low; 4=very low; ND, no data

Conclusions

Pfizer-BioNTech COVID-19 vaccine: Children ages 6 months–4 years

- Antibody levels after 3 doses in children ages 6 months–4 years produces similar antibody levels after 2 doses in individuals ages 16–24 years
- Reactogenicity post-vaccine similar after each of the 3 vaccine doses, and similar to reactions seen in placebo recipients
- Efficacy estimates difficult to interpret given small numbers and limited follow-up time
  - Impact of **longer interval** in the trial between dose 2 and dose 3 on efficacy, reactogenicity or safety are unknown

Other considerations for mRNA COVID-19 vaccines in young children

- COVID-19 vaccines and seropositivity
- Myocarditis in young children
- Cardiac complications after SARS-CoV-2 infections
- Vaccine-associated myocarditis in children and adolescents
- Numbers needed to vaccinate analysis

COVID-19 vaccines and seropositivity

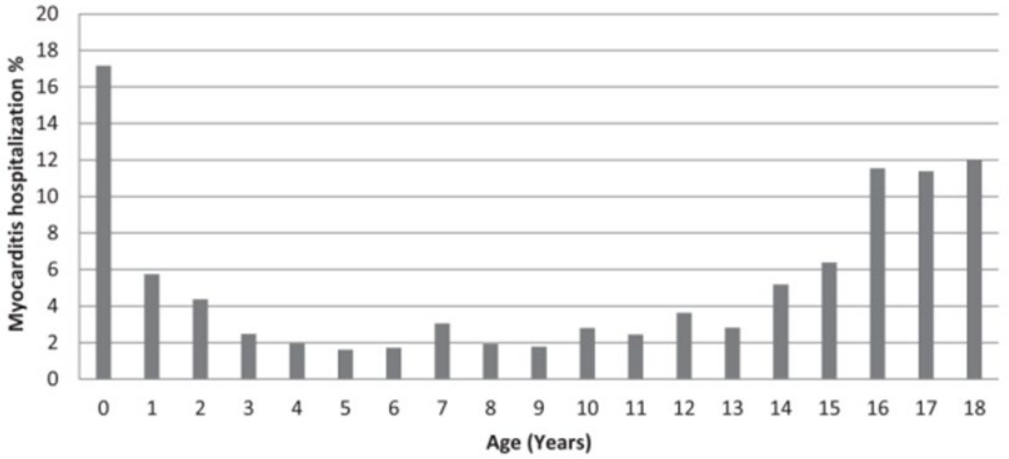
- Omicron-wave surges of pediatric COVID-19 hospitalizations occurred even with high seroprevalence, suggesting this alone is not sufficient to provide broad protection
- **Many** seropositive individuals vaccinated without concerns
- Vaccination remains the **safest** strategy for preventing complications from SARS-CoV-2 infection and offers additional protection against re-infection
  - Prior infection may not provide broad protection against newer SARS-CoV-2 variants
- Clinical Considerations states that people who recently had SARS-CoV-2 infection may consider delaying their COVID-19 vaccine by **3 months** after infection
  - 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

Myocarditis in young children

Background rates

- Before the COVID-19 pandemic, peaks in myocarditis hospitalizations seen in infants and adolescents
  - In adolescents, typically **viral** in etiology
  - In infants, many cases can represent cardiomyopathy with **genetic** component

- Children
  - Annual incidence 0.8 per 100,000
    - In 15-18yo, 1.8 per 100,000 in 2015-2016
  - 66% male
  - Median LOS 6.1 days



Vasudeva et al. *American J Cardiology.* 2021.

LOS = Length of hospital stay

Vasudeva et al. Am J Cardiology 2021 https://www.sciencedirect.com/science/article/pii/S0002914921002617

Previously presented: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/02-COVID-Oster-508.pdf

Cardiac complications due to SARS-CoV-2 in young children

- Cardiac complications in the setting of acute SARS-CoV-2 infection in young children are uncommon
- Most cardiac complications post-SARS-CoV-2 infection in infants related to **MIS-C**
  - 1.8% of MIS-C cases are children ages 6-11 months[1]
  - Infants <1 year of age with MIS-C have severe cardiovascular involvement in ~55-65% of cases[1]

[1] MIS-C National Surveillance Data, provided by Multisystem Inflammatory Syndrome Unit, Epidemiology & Surveillance Task Force, CDC

VAERS reporting rates of myocarditis (per 1 million doses administered) after mRNA COVID-19 vaccination, days 0–7 and 8–21 post-vaccination*,†

		0–7 days			8–21 days			0–7 days			8–21 days		
		Males			Males			Females			Females		
	Age (yrs)	Dose 1	Dose 2	Booster	Dose 1	Dose 2	Booster	Dose 1	Dose 2	Booster	Dose 1	Dose 2	Booster
Pfizer-BioNTech	5–11	0.2	2.6	0.0	0.6	0.0	0.0	0.2	0.7	0.0	0.2	0.0	0.0
Pfizer-BioNTech	12–15	5.3	46.4	15.3	1.2	1.2	0.9	0.7	4.1	0.0	0.4	0.2	0.9
Pfizer-BioNTech	16–17	7.2	75.9	24.1	1.7	3.2	1.3	0.0	7.5	0.0	0.7	0.4	0.0
Pfizer-BioNTech and Moderna	18–24	4.2	38.9	9.9	1.1	2.2	0.4	0.6	4.0	0.6	0.2	0.7	0.0
Pfizer-BioNTech and Moderna	25–29	1.8	15.2	4.8	0.4	1.1	0.5	0.4	3.5	2.0	0.2	0.0	0.8
Pfizer-BioNTech and Moderna	30–39	1.9	7.5	1.8	0.4	0.8	0.2	0.6	0.9	0.6	0.3	0.2	0.0
Pfizer-BioNTech and Moderna	40–49	0.5	3.3	0.4	0.2	0.5	0.0	0.4	1.6	0.6	0.2	0.2	0.0
Pfizer-BioNTech and Moderna	50–64	0.5	0.7	0.4	0.2	0.3	0.1	0.6	0.5	0.1	0.2	0.5	0.1
Pfizer-BioNTech and Moderna	65+	0.2	0.3	0.6	0.3	0.2	0.1	0.1	0.5	0.1	0.1	0.2	0.1

* As of May 26, 2022; reports verified to meet case definition by provider interview or medical record review; primary series and 1st booster doses only

† An estimated 1–10 cases of myocarditis per 100,000 person years occurs among people in the United States, regardless of vaccination status; adjusted for days 0–7 and 8–21 risk intervals, this estimated background is **0.2 to 2.2 per 1 million person-day 0–7 risk interval and 0.4 to 3.8 per 1 million person-day 8–21 risk interval** (peach shaded cells indicate that reporting rate exceeded estimated background incidence for the period)

Vaccine-associated myocarditis in young children

- Risk of myocarditis after mRNA COVID-19 vaccination, if any, in young children is unknown
  - No cases occurred during clinical trials (n=7,804 with at least 7 days of follow-up)
- Based on the epidemiology of classic myocarditis and safety monitoring in children ages 5-11 years, myocarditis after mRNA COVID-19 vaccination in young children is anticipated to be rare
  - Underlying epidemiology of myocarditis fundamentally **different** in infants
  - Dose used in young children **lower** than dose used in older children

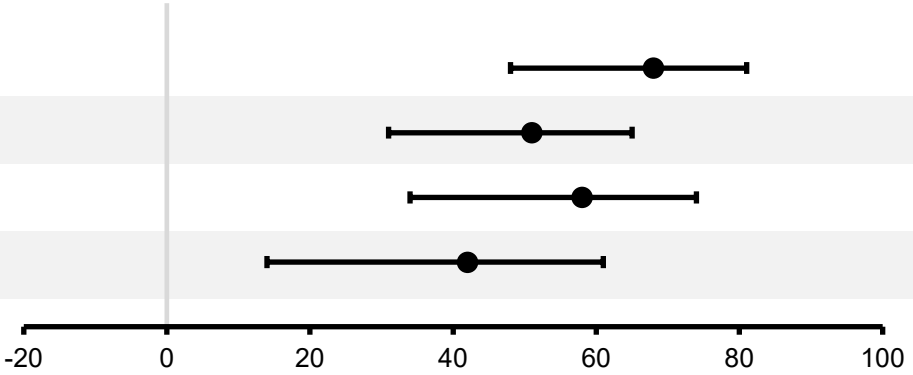
Post-authorization vaccine effectiveness

Overcoming COVID-19 platform

2 doses of Pfizer-BioNTech vaccine against hospitalization, Dec 19, 2021-Apr 27, 2022

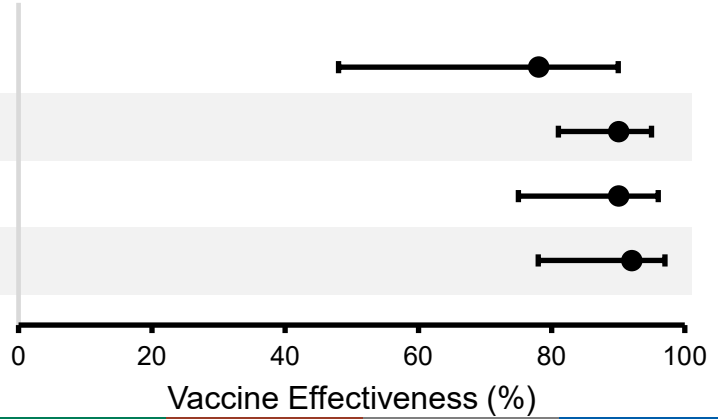
	No. vaccinated COVID-19 patients/Total COVID-19 patients (%)	Adjusted VE % (95% CI)
5–11 years*	25/325 (8)	68 (48-81)
12–18 years	109/286 (38)	51 (31-65)
2–22 weeks since vaccination	42/219 (19)	58 (34-74)
23–45 weeks since vaccination	67/244 (27)	42 (14-61)

*median time from vaccination to hospitalization is 37 days



2 doses of Pfizer-BioNTech vaccine against MIS-C, Jul 1, 2021-Apr 7, 2022

	No. vaccinated MIS-C patients/Total no. MIS-C patients (%)	Median (IQR) days from 2nd dose to MIS-C	Adjusted VE (95% CI)
5–11 years	10/144 (7)	44 (32-56)	78 (48-90)
12–18 years	14/160 (9)	120 (57-169)	90 (81-95)
28-120 days since vaccination	7/153 (5)	60 (42-89)	90 (75-96)
≥121 days since vaccination	7/131 (5)	172 (138-215)	92 (78-97)



Methods for calculation of number needed to vaccinate

Benefits — Calculated per 1 million fully vaccinated with mRNA vaccine

- Age group: 6 months – 4 years
- Pandemic average age-specific incidence rates
  - Hospitalization rates: COVID-NET[1]
  - Case rates: Case based surveillance[2]
- Assumed VE against hospitalization: 42-84%[3]
- Assumed VE against symptomatic infection: 30%-60%[4]
- Time Horizon: 120-day period

VE: Vaccine Effectiveness

[1]https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html

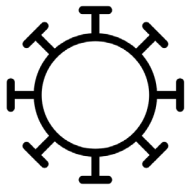
[2] Used rates in children ages 1-4 years because ages in months was not available: https://covid.cdc.gov/covid-data-tracker/#demographicsovertime

[3]Based on the ratio of infection to severe disease seen in 5–11-year-olds applied to the VE against infection seen in 6 months – 4 years

[4]Based on VE seen in pediatric clinical trials

Number of children ages 6 months – 4 years needed to vaccinate to prevent 1 infection or 1 hospitalization over 120 days

Calculated using pandemic average rates



670 – 1,300 vaccinations needed to prevent **1 case**

6,150 -12,300 vaccinations needed to prevent **1 hospitalization**

Assumptions: Benefits accrue over **120 days**; **Data Sources:** COVID-Net https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html.

Number of children ages 6 months – 4 years needed to vaccinate to prevent 1 hospitalization: COVID-19 vs. influenza over 6 months

COVID-19

1,660 - 3,320
vaccinations needed to prevent **1 hospitalization**

Influenza

1,030 - 6,890
vaccinations needed to prevent **1 hospitalization**

Assumptions: Benefits accrue over **6 months**; **Data Sources:** Influenza number needed to vaccinate: Pediatrics. 2007 Sep;120(3):467-72. doi: 10.1542/peds.2007-0167; COVID-Net hospitalization rates from 10/1/2021-4/30/2022: https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html.

Summary

Known and potential benefits

- Clinical trials provide data for protection against **symptomatic infection**
- Clinical trials were not powered to detect efficacy against severe disease in young children, but similar patterns expected to what is seen in everyone ages 5 years and over, with **higher** protection against **severe disease**
- Emerging data in adults suggest that post-COVID conditions may be less likely to occur in vaccinated individuals
- Vaccination in this age group may also provide parents with **increased confidence** to return to pre-pandemic activities, improving social interactions in young children

Summary

Known and potential harms

- Clinical trials provide safety data in nearly **8,000** vaccinated young children
- Post-authorization safety data after almost **600 million doses** of COVID-19 vaccines given in the United States
- Post-authorization safety data for children ages 5-11 years very reassuring: reporting rates of myocarditis in males only slightly elevated compared to background incidence
  - Likely related to both underlying epidemiology of myocarditis and dose de-escalation

Benefits and Harms: Summary of the Available Evidence

- First COVID-19 vaccine clinical trials conducted exclusively during Omicron predominance
  - Post-authorization vaccine effectiveness studies with lower VE in Omicron, compared to previous SARS-CoV-2 variants
- Both mRNA COVID-19 vaccines for young children met non-inferiority criteria for neutralizing antibody levels
  - Differences in certainty of efficacy estimates for each mRNA vaccine; **cannot directly compare** estimates
- Receipt of a primary COVID-19 vaccine series can provide protection against COVID-19 disease and **severe outcomes**
- **Benefits** of COVID-19 vaccines in young children outweigh possible **risks**

Benefits and Harms

How substantial are the desirable anticipated effects?

- How substantial are the anticipated effect for each main outcome for which there is a desirable effect?

○ **Minimal**	○ **Small**	○ **Moderate**	○ **Large**	○ **Varies**	○ **Don’t know**

Benefits and Harms

How substantial are the undesirable anticipated effects?

- How substantial are the anticipated effect for each main outcome for which there is an undesirable effect?

○ Minimal	○ Small	○ Moderate	○ Large	○ Varies	○ Don't know

Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

- What is the balance between the desirable effects relative to the undesirable effects?

- ○ Favors intervention (Moderna COVID-19 vaccine)
- ○ Favors comparison (no vaccine)
- ○ Favors both
- ○ Favors neither
- ○ Unclear

Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

- What is the balance between the desirable effects relative to the undesirable effects?

- ○ Favors intervention (Pfizer-BioNTech COVID-19 vaccine)
- ○ Favors comparison (no vaccine)
- ○ Favors both
- ○ Favors neither
- ○ Unclear

EtR Domain: Values

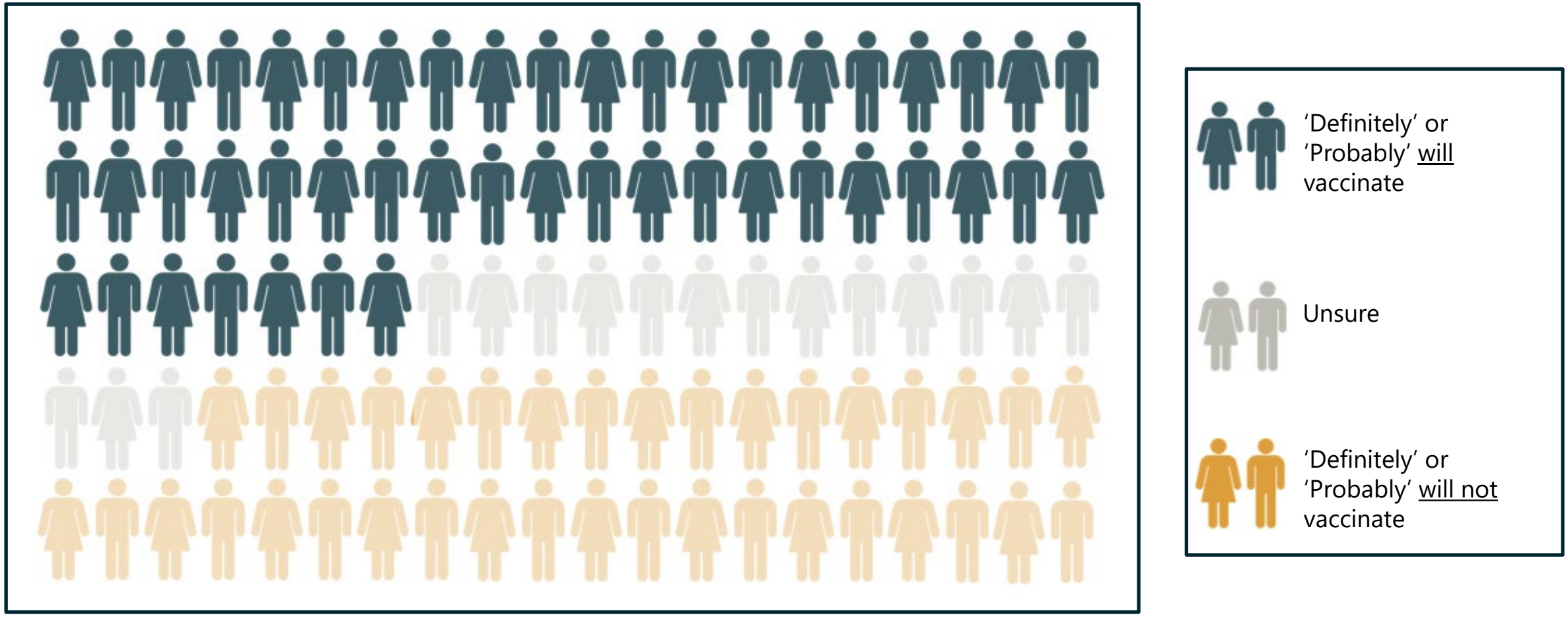
Survey of parental attitudes and intentions toward pediatric COVID-19 and recommended vaccinations

- Survey designed to assess parental beliefs and attitudes toward pediatric COVID-19 vaccinations among children ages 6 months – 4 years
- Data collection period: February 2 – February 10, 2022
- Final sample (N = 2,048)

	CHILD AGE GROUP	GENDER	RACE/ETHNICITY
Targeted percentages	49.9% Child Ages 6 – 23 months 50.2% Child Ages 2 – 4 years	51.1% Female 48.1% Male 0.8% Transgender or Other Gender Identity	34.2% Non-Hispanic White 32.8% Non-Hispanic Black 33.0% Hispanic

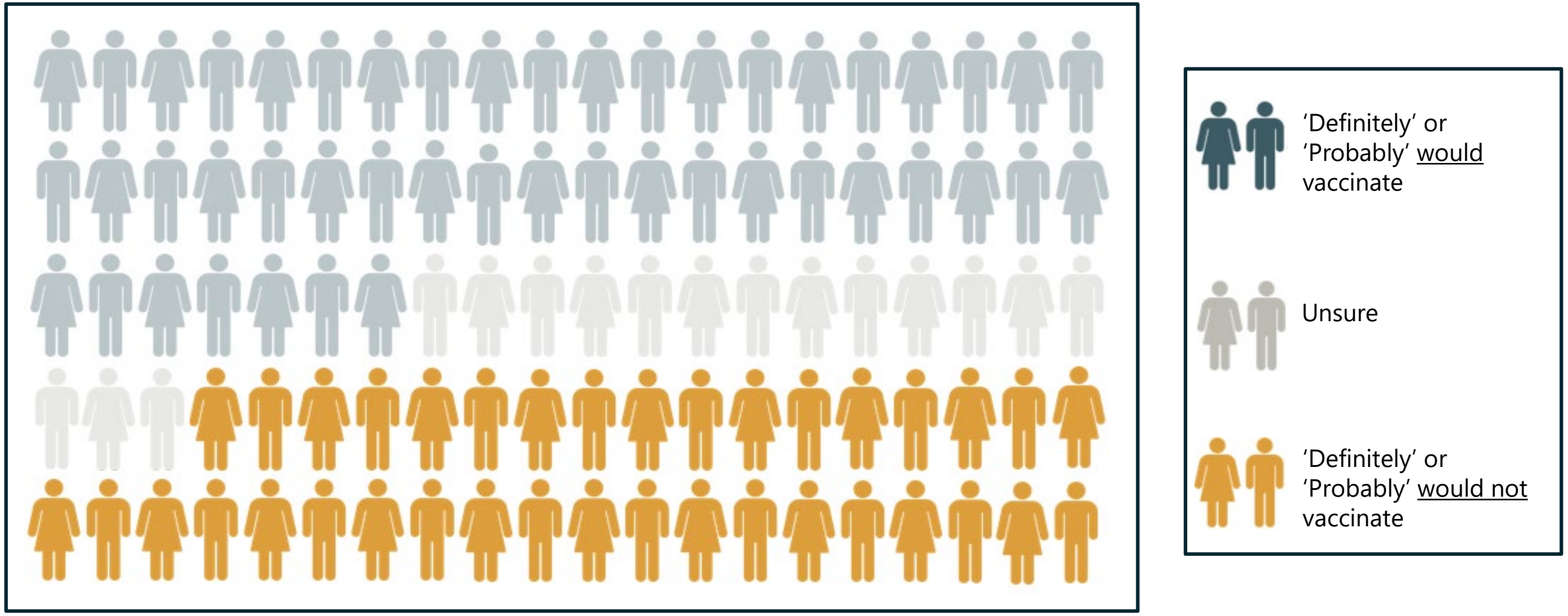
CDC and University of Iowa/RAND survey, unpublished

Half of the parents of children ages 6 months – 4 years said they ‘definitely’ or ‘probably’ would vaccinate their child, once they become eligible



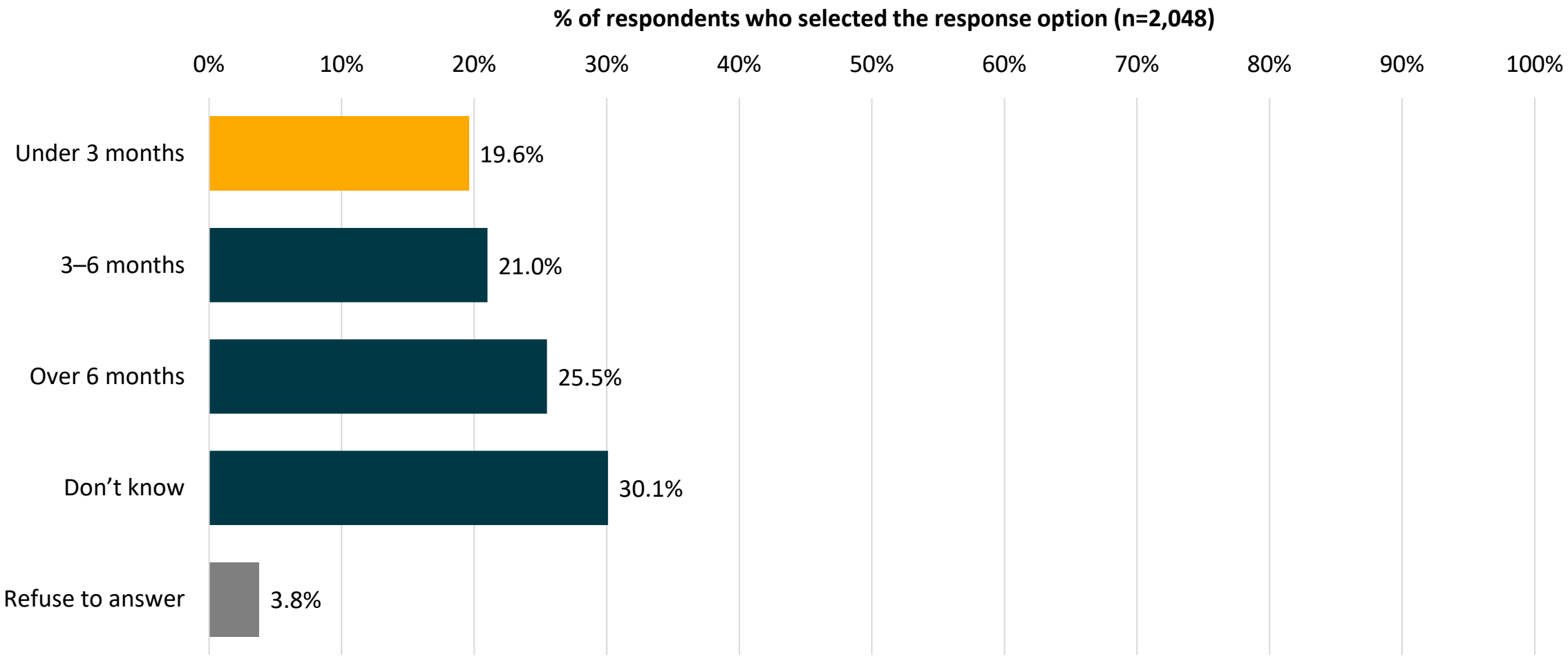
CDC and University of Iowa/RAND survey, unpublished

A third of parents of children ages 6 months – 4 years said they ‘definitely’ or ‘probably’ would not vaccinate their child, once eligible



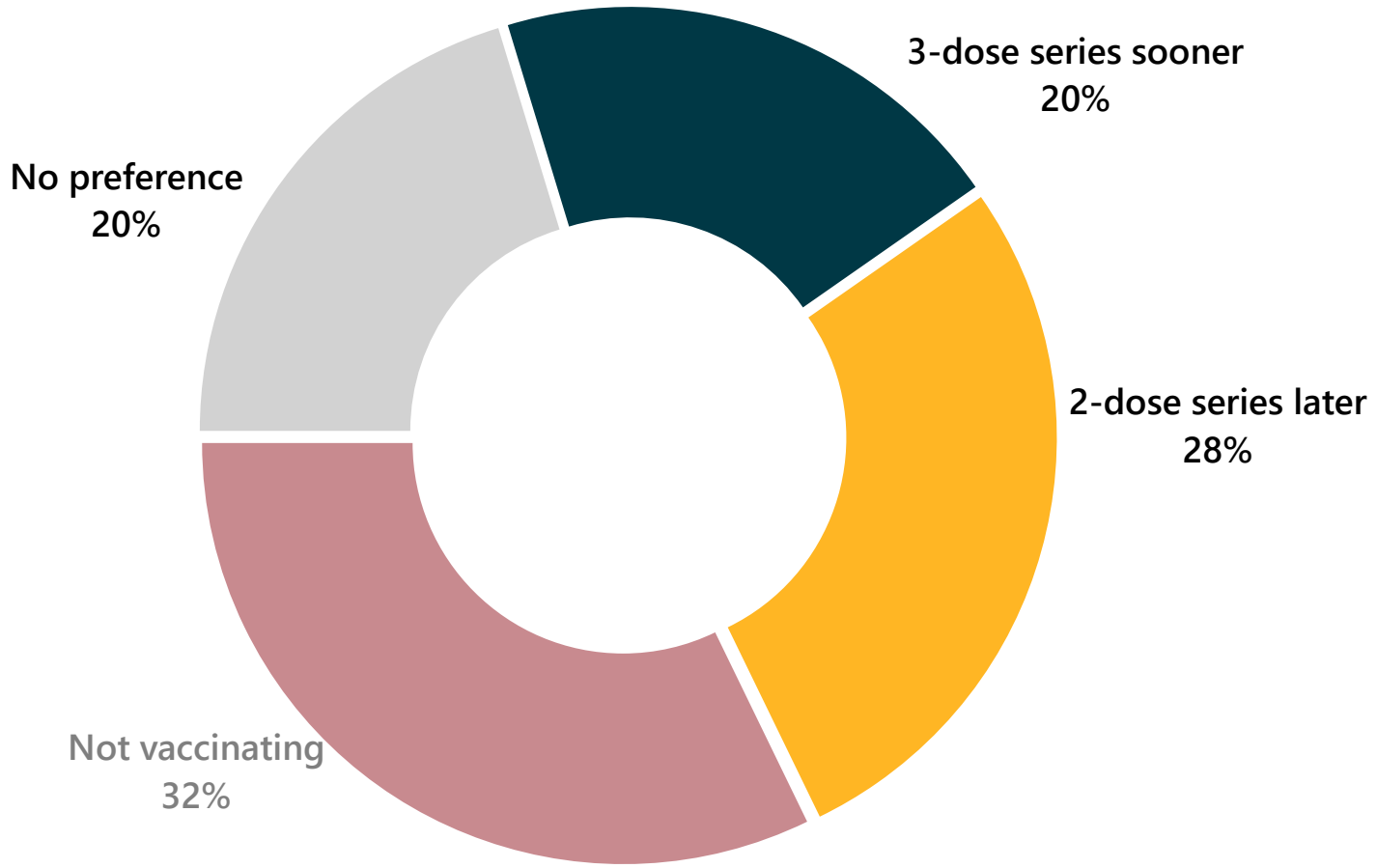
CDC and University of Iowa/RAND survey, unpublished

Only a fifth of all respondents said they would get their child ages 6 months – 4 years vaccinated within 3 months after becoming eligible



CDC and University of Iowa/RAND survey, unpublished

Preference for a 2-dose or 3-dose series



CDC and University of Iowa/RAND survey, unpublished

Impact of demographics on pediatric vaccination intentions

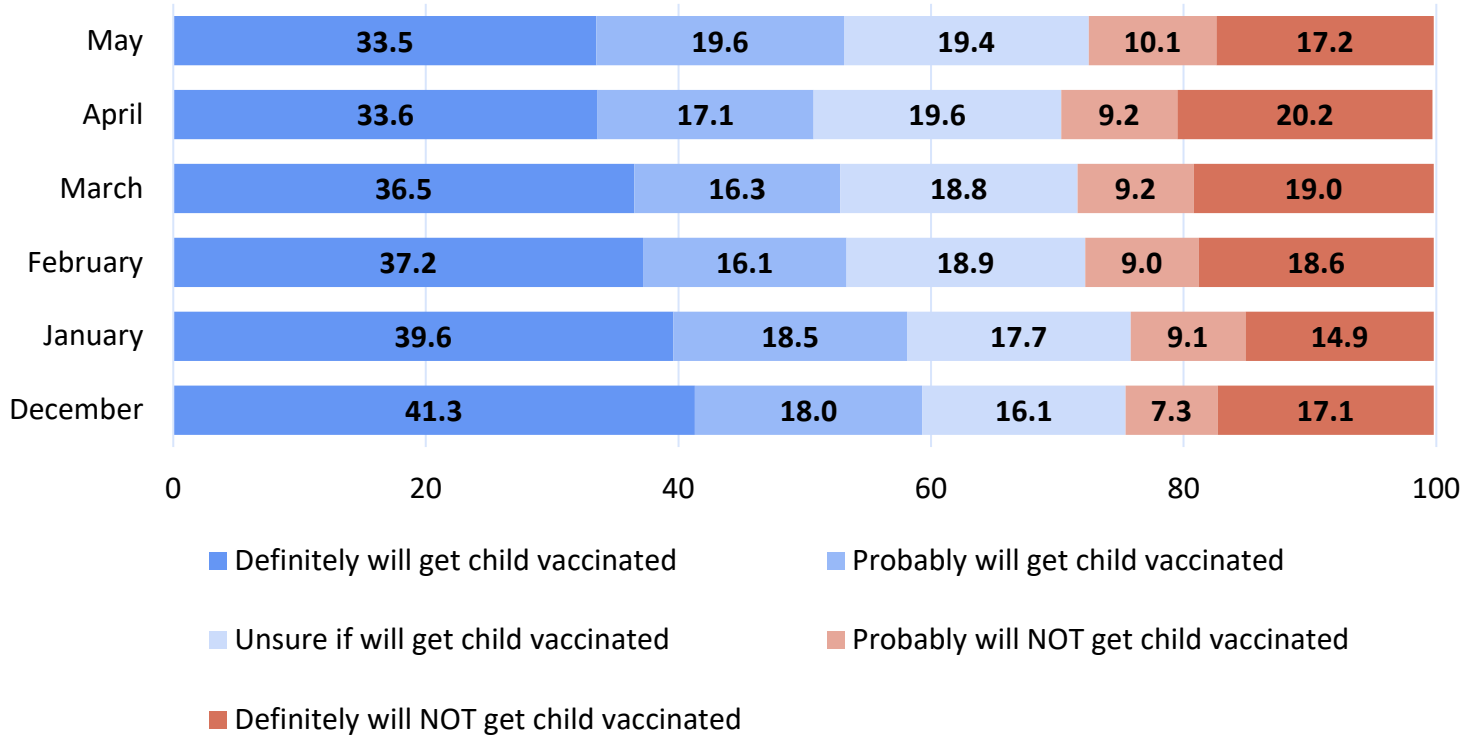
- Percentage of parents of children ages 6 months – 4 years who ‘definitely’ or ‘probably’ will vaccinate their child when eligible significantly varied by:
  - Gender of parent
    - 51% males vs. 44% females
  - Race and Ethnicity
    - 53% Hispanic/Latino vs. 46% NH Black and 43% NH White
  - Education
    - 60% ≥ Bachelor’s degree, 40% Some college/Trade school and 42% ≤ High school degree

CDC and University of Iowa/RAND survey, unpublished

Parental intent for vaccination of children 6 months – 4 years,

National Immunization Survey-Child COVID Module (NIS-CCM), December 2021 – May 2022

- The NIS-CCM is a random-digit-dial cellular telephone survey of households with children that began on July 22, 2021
- In May, one-third (**33.5%**) of parents report they definitely will get their child 6 months–4 years vaccinated
- **17.2%** of parents report they definitely will not get their child vaccinated



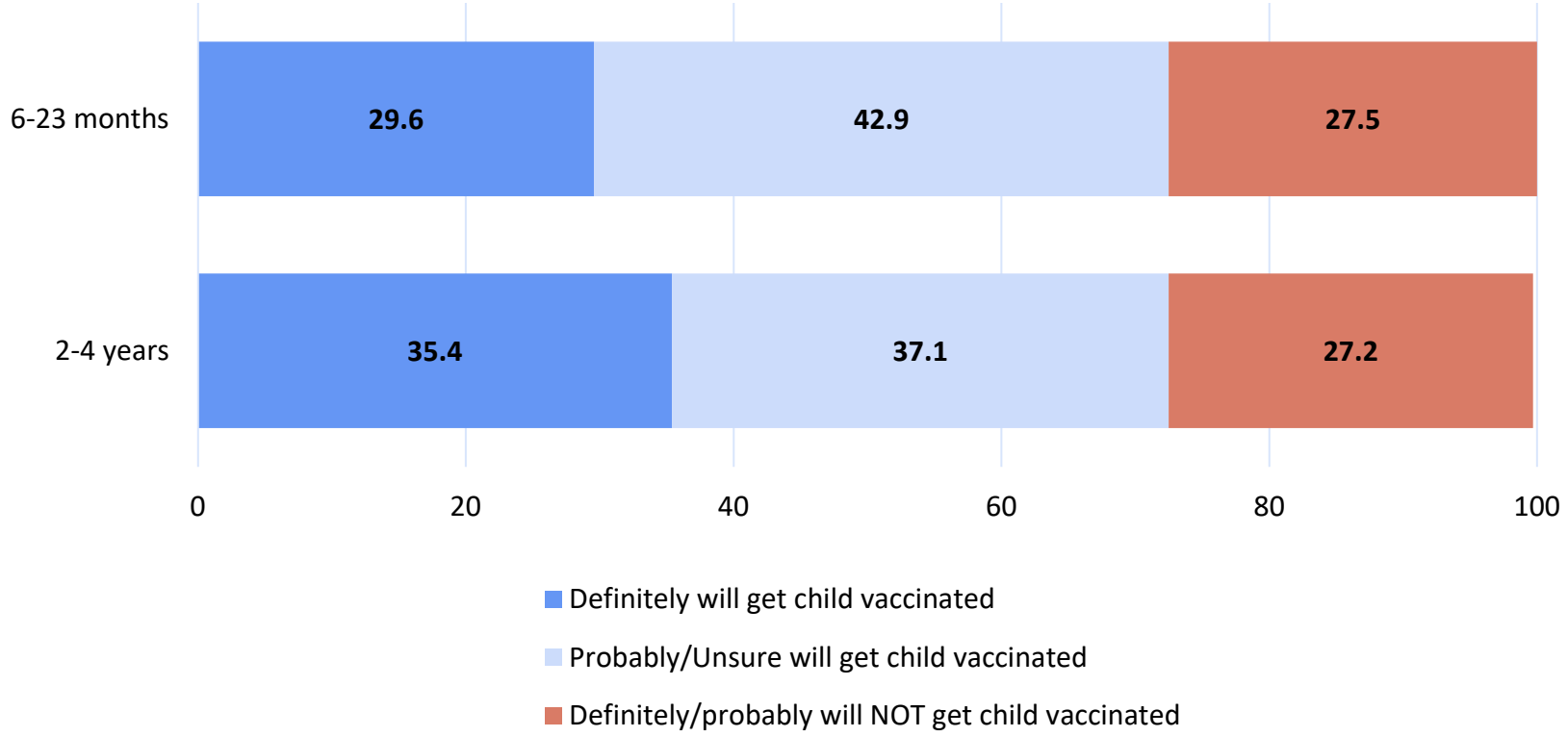
May: Interviews May 1-28, 2022, n=3465; April: Interviews March 27–April 30, 2022, n=4,063; March: Interviews February 27–March 26, 2022, n=3,626 ; February: Interviews January 30–February 26, 2022, n=3,231 ;January: Interviews January 2–29, 2022, n=3,221; December: Interviews November 28 – December 31, 2021, n=1,313

NIS-CCM estimates (5-17 years) available on COVIDVaxView at: https://www.cdc.gov/vaccines/imz-managers/coverage/covidvaxview/interactive.html

Parental intent for vaccination of children 6 months – 4 years,

National Immunization Survey-Child COVID Module (NIS-CCM) , May 2022

- In May, a smaller percentage (**29.6%**) of parents of children 6–23 months reported definite intent to vaccinate their child compared to parents of children 2–4 years (**35.4%**)
- There was no difference in the percentage reporting definite/probably will not get child vaccinated

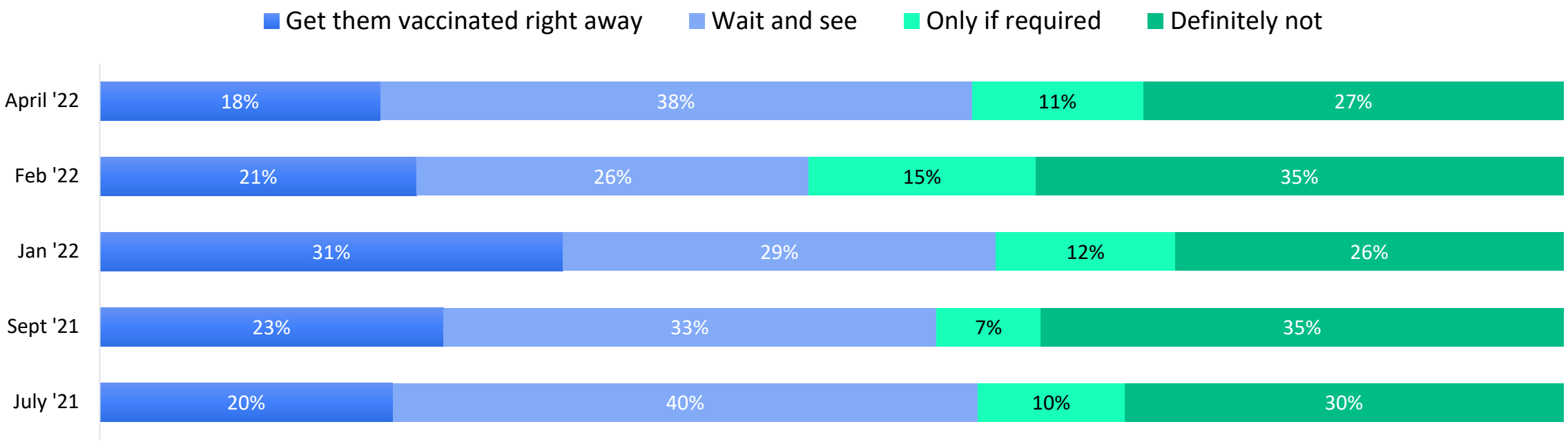


May: Interviews May 1-28, 2022, n=3465

NIS-CCM estimates (5-17 years) available on COVIDVaxView at: https://www.cdc.gov/vaccines/imz-managers/coverage/covidvaxview/interactive.html

One in five parents of children under five will vaccinate their child right away once available, but most remain more cautious

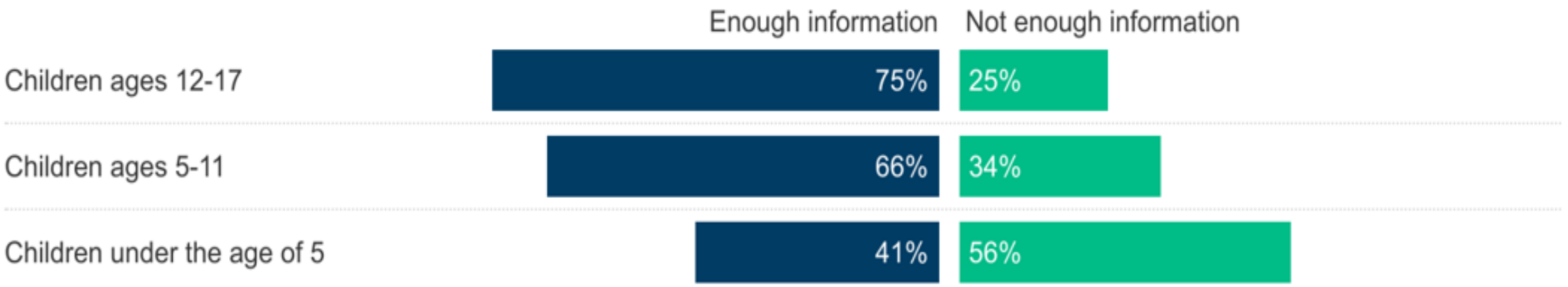
- Survey respondents were asked, “Thinking about your child under the age of 5, once there is a COVID-19 vaccine authorized and available for your child’s age group, do you think you will…?”



KFF COVID-19 Vaccine Monitor. https://www.kff.org/coronavirus-covid-19/dashboard/kff-covid-19-vaccine-monitor-dashboard/#parents Accessed May 25, 2022

Most parents say they don't have enough information about COVID-19 vaccine safety and effectiveness for children under 5

- Survey respondents were asked, "Do you feel you have enough information about the safety and effectiveness of the COVID-19 vaccine for…?



*Survey conducted prior to safety and efficacy information available on COVID-19 vaccines in young children

KFF COVID-19 Vaccine Monitor: April 2022. https://www.kff.org/coronavirus-covid-19/poll-finding/kff-covid-19-vaccine-monitor-april-2022 Accessed May 25, 2022

Values: Summary of the Available Evidence

- Half of parents of children ages 6 months through 4 years definitely or probably would vaccinate their child, once eligible
  - However, nearly a third of parents of children ages 6 months through 4 years definitely or probably would not vaccinate their child, once eligible
- One in five parents of children under 5 (**18%**) are eager to vaccinate their child and plan to do so right away once a COVID-19 vaccine is authorized for their child's age group, but many others remain more cautious
- In a survey conducted prior to available data on COVID-19 vaccines in young children, many parents of children under five say they don't have enough information about the safety and effectiveness of COVID-19 vaccines for children in this age group (**56%**)

Values

Criteria 1:

Does the target population feel that the desirable effects are large relative to undesirable effects?

- How does the target population view the balance of desirable versus undesirable effects?
- Would parents/caregivers feel that the benefits outweigh the harms and burden?
- Does the population appreciate and value the Pfizer-BioNTech & Moderna COVID-19 vaccine?

○ **Minimal**	○ **Small**	○ **Moderate**	○ **Large**	○ **Varies**	○ **Don't know**

Values

Criteria 2:

Is there important uncertainty about, or variability in, how much people value the main outcomes?

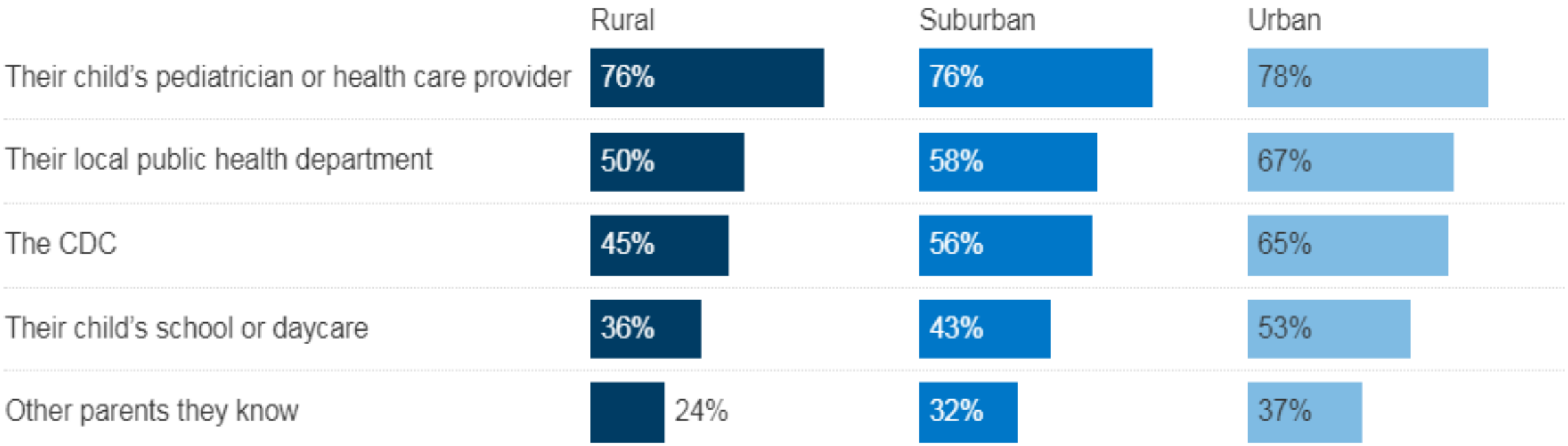
- How much do individuals value each outcome in relation to the other outcomes?
- Is there evidence to support those value judgements?
- Is there evidence that the variability is large enough to lead to different decisions?

- ○ Important uncertainty or variability
- ○ Probably important uncertainty or variability
- ○ Probably not important uncertainty or variability
- ○ No important uncertainty or variability
- ○ No known undesirable outcomes

EtR Domain: Acceptability

Pediatricians are top trusted source of child vaccine information for parents across community types

- Percent of parents who say they trust each of the following a great deal or a fair amount to provide reliable information about the COVID-19 vaccines for children:



KFF COVID-19 Vaccine Monitor: Winter Update on Parents' Views (November 8-23, 2021). https://www.kff.org/coronavirus-covid-19/poll-finding/kff-covid-19-vaccine-monitor-vaccine-attitudes-rural-suburban-urban/ Accessed March 7, 2022

Vaccines for Children (VFC) program and COVID-19

- As of early May 2022, more than two-thirds of Vaccines For Children (VFC) program providers were enrolled as COVID-19 vaccine providers
- For young children, encouraging VFC providers to enroll as COVID-19 vaccine providers and encouraging enrolled providers to administer the COVID-19 vaccine becomes even more critical to ensure access to COVID-19 vaccine as well as all other routine childhood vaccines

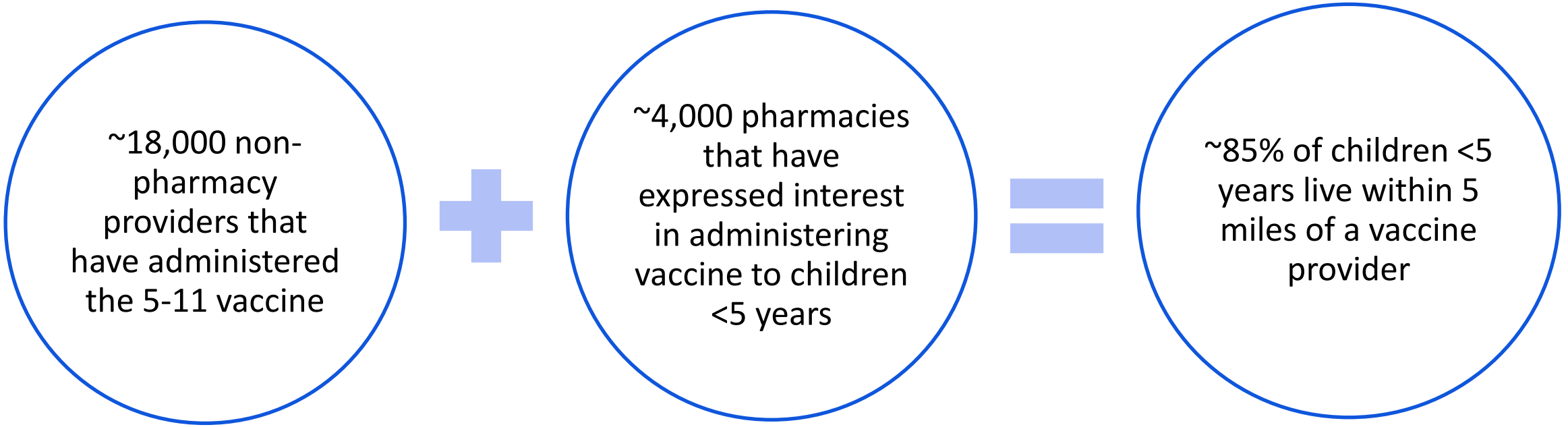
CDC. Updated Pediatric COVID-19 Vaccination Operational Planning Guide – Information for the COVID-19 Vaccine for Children 6 Months through 4 years old and/or COVID-19 Vaccine for Children 6 Months through 5 Years Old. https://www.cdc.gov/vaccines/covid-19/downloads/Pediatric-Planning-Guide.pdf Accessed June 1, 2022

Additional jurisdiction coordination for COVID-19 vaccination among children

- Continued coordination through jurisdictions will be needed for the Indian Health Service (IHS), Tribal and Urban Indian Health Programs, and Health Resources and Services Administration (HRSA) programs
- Similar to the COVID-19 vaccine rollout for 5–11-year-olds, jurisdictions should plan their ordering strategy and identify **priority locations** to vaccinate children ages 6 months – 4 years or 6 months – 5 years
- The goal is an **efficient** rollout resulting in **equitable vaccine access** for young children in the initial weeks when demand is likely to be higher

CDC. Updated Pediatric COVID-19 Vaccination Operational Planning Guide – Information for the COVID-19 Vaccine for Children 6 Months through 4 years old and/or COVID-19 Vaccine for Children 6 Months through 5 Years Old. https://www.cdc.gov/vaccines/covid-19/downloads/Pediatric-Planning-Guide.pdf Accessed June 1, 2022

Possible Network of Providers for Children ages <5 years



Acceptability: Summary of the Available Evidence

- A child's **health care provider** is the **top** trusted source of child vaccine information for parents across community types
- As of early May 2022, more than two-thirds of Vaccines For Children (VFC) program providers were enrolled as COVID-19 vaccine providers
- Continued coordination through jurisdictions and identifying priority locations to vaccinate young children will facilitate efficient rollout resulting in equitable vaccine access for this age group
- Nearly all young children will live within **5 miles** of a vaccine provider for COVID-19 vaccines

Acceptability

Are mRNA COVID-19 vaccines acceptable to key stakeholders?

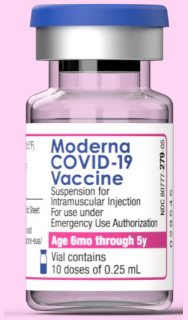
- Are there key stakeholders that would not accept the distribution of benefits and harms?
- Are there key stakeholders that would not accept the undesirable effects in the short term for the desirable effects (benefits) in the future?

○ No	○ Probably no	○ Probably yes	○ Yes	○ Varies	○ Don't know

EtR Domain: Feasibility

Moderna COVID-19 vaccine product for children ages 6 months – 5 years

Moderna COVID-19 Vaccine Products

Age Group	6 months through 5 years (*Primary Series*)	6 years through 11 years (*Primary Series*) *Currently unavailable (Use the vial with dark blue cap and a label with a purple border)*	6 years through 11 years (*Primary Series*)	12 years and older (*Primary Series*)
			18 years and older (*Booster Dose*)	18 years and older (*Booster Dose*)
Vial Cap Color	Dark Blue	Dark Blue	Dark Blue	Red
Vial Label Border Color	MAGENTA	TEAL	PURPLE	LIGHT BLUE
Vial Image				
Primary Dose Volume	0.25 mL	0.5 mL	0.5 mL	0.5 mL
Booster Dose Volume	None	None	0.5 mL	0.25 mL

- The Moderna vaccine for children ages 6 months – 5 years:
  - Ships at -20°C
  - Different color border (magenta)
  - Different concentration than adult primary series (25µg/0.25mL)
  - New national drug code (NDC)
  - Does not require diluent

CDC. Updated Pediatric COVID-19 Vaccination Operational Planning Guide – Information for the COVID-19 Vaccine for Children 6 Months through 4 Years Old and/or COVID-19 Vaccine for Children 6 Months through 5 Years Old. https://www.cdc.gov/vaccines/covid-19/downloads/Pediatric-Planning-Guide.pdf Accessed June 1, 2022

Pfizer-BioNTech COVID-19 vaccine product for children ages 6 months – 4 years

- The Pfizer-BioNTech vaccine for children ages 6 months – 4 years:
  - Ships at -80°C
  - Different color cap (maroon)
  - Different amount of diluent added (2.2mL)
  - New national drug code (NDC)[1]

Pfizer-BioNTech COVID-19 Vaccine Products[2]

	Current Products		Future Product
Age Indications[a]	12 years and older	5 through 11 years	6 mos through 4 years[d]
Vial Cap Color and Label with Color Border	GRAY 	ORANGE 	MAROON 
Preparation	Do Not Dilute	Dilute Before Use	Dilute Before Use
Amount of Diluent Needed per Vial[b]	Do Not Dilute	1.3 mL	2.2 mL
Dose Volume/Dose	0.3 mL/**30 mcg**	0.2 mL/**10 mcg**	0.2 mL/**3 mcg**
Doses per Vial	6 doses per vial	10 doses per vial (after dilution)	10 doses per vial (after dilution)
	Storage Conditions		
ULT Freezer (-90°C to -60°C)[c]	12 months	12 months	12 months
Freezer (-25°C to -15°C)	DO NOT STORE	DO NOT STORE	DO NOT STORE
Refrigerator (2°C to 8°C)	10 weeks	10 weeks	10 weeks
Room Temperature (8°C to 25°C)	12 hours prior to first puncture (including any thaw time)	12 hours prior to first puncture (including any thaw time)	12 hours prior to first puncture (including any thaw time)
After First Puncture (2°C to 25°C)	Discard after 12 hours	Discard after 12 hours	Discard after 12 hours

[a] Use the appropriate product based on the age of the recipient. [b] Use the diluent (Sterile 0.9% Sodium Chloride Injection, USP) included in the ancillary supply kit. Do not use any other normal saline or diluent.
[c] Regardless of storage condition, vaccines should not be used after 12 months from the date of manufacture printed on the vial and cartons.
[d] The vaccine is currently under emergency use authorization review by the Food and Drug Administration (FDA) for children 6 months through 4 years old.

1. CDC. Updated Pediatric COVID-19 Vaccination Operational Planning Guide – Information for the COVID-19 Vaccine for Children 6 Months through 4 Years Old and/or COVID-19 Vaccine for Children 6 Months through 5 Years Old. https://www.cdc.gov/vaccines/covid-19/downloads/Pediatric-Planning-Guide.pdf Accessed June 1, 2022
2. CDC. Pfizer-BioNTech COVID-19 Vaccine Products. https://www.cdc.gov/vaccines/covid-19/downloads/Pfizer-Pediatric-Reference-Planning.pdf Accessed June 16, 2022

Packaging configuration and ancillary supplies for Pfizer-BioNTech and Moderna COVID-19 vaccines for children

- The packaging configuration for both vaccine products is 10-dose vials in cartons of 10 vials each (**100 doses total**) with a minimum order quantity of 100 doses per product
- Ancillary supplies will be provided for both vaccine products, including 1- inch needles and syringes to support 100 doses of vaccine
  - Diluent will be provided with ancillary supplies to support 100 doses per kit for the Pfizer vaccine

CDC. Updated Pediatric COVID-19 Vaccination Operational Planning Guide – Information for the COVID-19 Vaccine for Children 6 Months through 4 Years Old and/or COVID-19 Vaccine for Children 6 Months through 5 Years Old. https://www.cdc.gov/vaccines/covid-19/downloads/Pediatric-Planning-Guide.pdf Accessed June 1, 2022

Feasibility: Summary of the Available Evidence

- Pfizer-BioNTech vaccine for children ages 6 months–4 years
  - Similar product configuration to other Pfizer-BioNTech pediatric products, but with a maroon cap
  - May be more familiar to pediatric healthcare providers
  - Long term storage requires an ultra-low temp (-80^{oF} freezer)
  - Requires diluent
- Moderna vaccine for children ages 6 months–5 years
  - May be less familiar to pediatric healthcare providers
  - Product able to be stored at traditional freezer temperatures
  - Does not require diluent

Feasibility

Is the Moderna COVID-19 vaccine feasible to implement among children ages 6 months – 5 years?

- Is the Moderna COVID-19 vaccine program sustainable?
- Are there barriers that are likely to limit the feasibility of implementing the Moderna COVID-19 vaccine or require considerations when implementing it?
- Is access to Moderna COVID-19 vaccine an important concern?

○ **No**	○ **Probably no**	○ **Probably yes**	○ **Yes**	○ **Varies**	○ **Don't know**

Feasibility

Is the Pfizer-BioNTech COVID-19 vaccine feasible to implement among children ages 6 months – 4 years?

- Is the Pfizer-BioNTech COVID-19 vaccine program sustainable?
- Are there barriers that are likely to limit the feasibility of implementing the Pfizer-BioNTech COVID-19 vaccine or require considerations when implementing it?
- Is access to Pfizer-BioNTech COVID-19 vaccine an important concern?

○ No	○ Probably no	○ Probably yes	○ Yes	○ Varies	○ Don't know

EtR Domain: Resource Use

Resource Use: Review of the available evidence

- No studies were found that evaluated cost-effectiveness of COVID-19 vaccination among children
- Studies in adults have shown COVID-19 related healthcare costs could be **billions** or **trillions** of dollars[1,2]. Given this, COVID-19 vaccines overall are likely cost-saving[3-5].
- In a study conducted by Pfizer, they estimated that Pfizer-BioNTech COVID-19 vaccine use in individuals ages ≥12 years in 2021 averted 9 million symptomatic cases, almost 700,000 hospitalizations and over 110,00 deaths resulting in $30.4 billion direct healthcare cost savings[6]
- At this time, vaccine will be available at no cost to the recipient
- Cost-effectiveness not a primary driver for decision making during a pandemic, but will be reassessed in the future

[1] Bartsch et al https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2020.00426 [2] Cutler and Summers. JAMA https://jamanetwork.com/journals/jama/fullarticle/2771764
[3] Bartsch et al. JID https://academic.oup.com/jid/article/224/6/938/6267841?login=true [4] Kohli et al. Vaccine https://www.sciencedirect.com/science/article/pii/S0264410X2031690X
[5] Li et al. Int JID https://www.sciencedirect.com/science/article/pii/S1201971222001680
[6] Di Fusco et al Full article: Public health impact of the Pfizer-BioNTech COVID-19 vaccine (BNT162b2) in the first year of rollout in the United States (tandfonline.com)

Resource Use

Are mRNA COVID-19 vaccines among children ages 6 months – 5 years a reasonable and efficient allocation of resources?

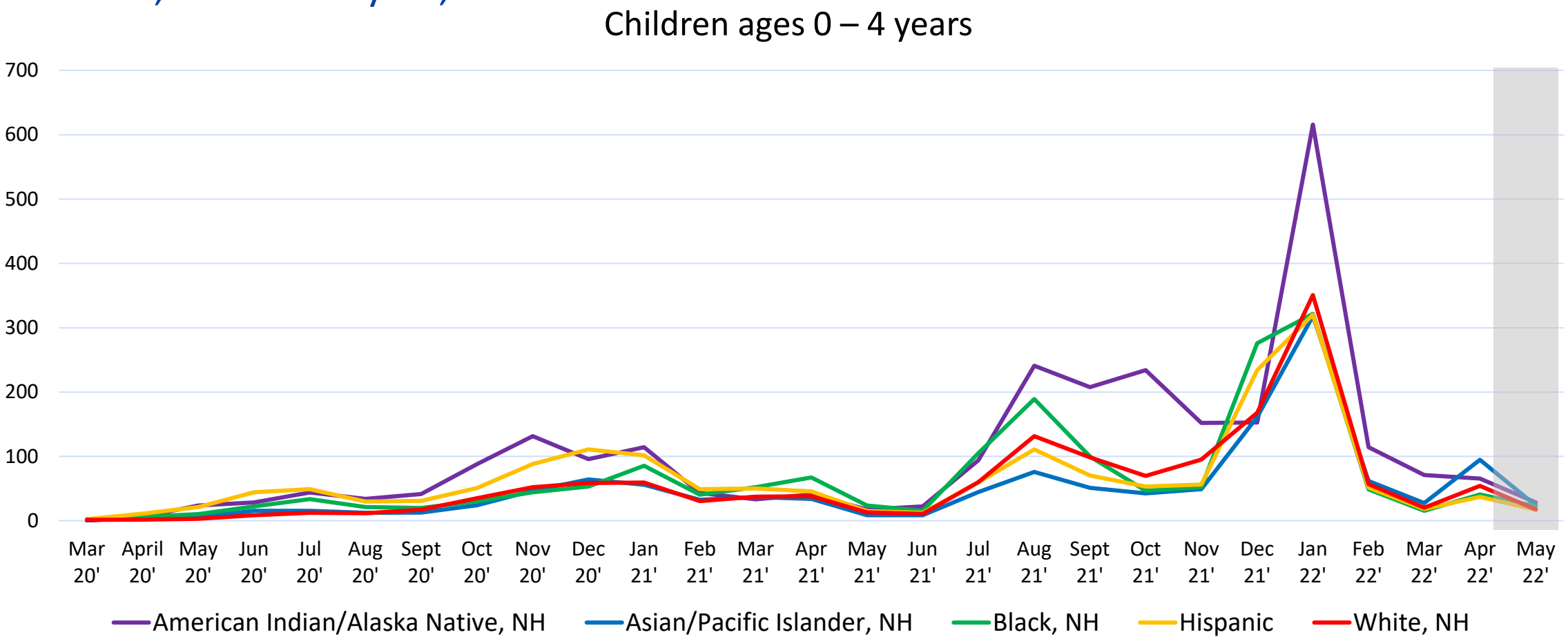
- What is the cost-effectiveness of mRNA COVID-19 vaccines?
- How does the cost-effectiveness of mRNA COVID-19 vaccines change in response to changes in context, assumptions, etc.?

○ **No**	○ **Probably no**	○ **Probably yes**	○ **Yes**	○ **Varies**	○ **Don't know**

EtR Domain: Equity

COVID-19 weekly cases per 100,000 population by race and ethnicity and age group, United States

March 1, 2020 – May 28, 2022

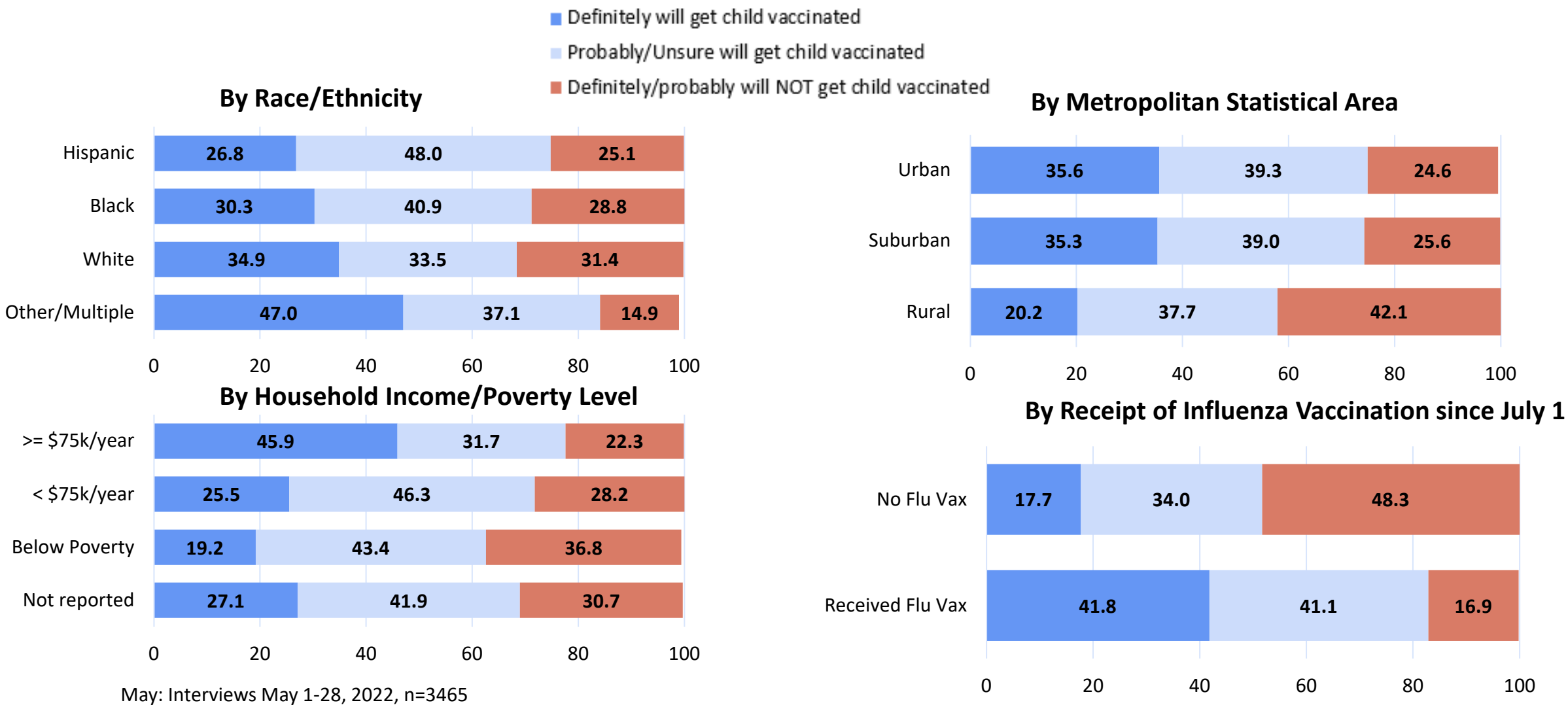


NH = Non-Hispanic

CDC COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#demographicsovertime Accessed May 31, 2022

Parental intent for vaccination of children 6 months – 4 years,

National Immunization Survey-Child COVID Module (NIS-CCM) , May 2022



May: Interviews May 1-28, 2022, n=3465

NIS-CCM estimates (5-17 years) available on COVIDVaxView at: https://www.cdc.gov/vaccines/imz-managers/coverage/covidvaxview/interactive.html

Vaccination intentions of parents of children under 5

HHS/ASPA Focus Groups, COVID-19 Public Education Campaign

- Focus Group Details
  - 18 focus groups with 4-6 participants in each group
  - Varied demographics of parents including Black, Hispanic/Latino, and Overall population
  - Some groups composed of parents ‘Ready to Vaccinate’ others ‘Waiting to Vaccinate’

- Format
  - COVID-19 Context, Attitudes, and Behaviors
    - Participants share thoughts and opinions about the COVID-19 pandemic regarding their child
  - Vaccination intent
    - Participants share thoughts and opinions about getting their child a COVID-19 vaccine when it is authorized and available

Parents of children ages 6 months – under 2 years

Black parents

- Noted that child's pediatrician did not have a strong stance on receiving a COVID-19 vaccine, despite having a strong stance on vaccines in general – making them second guess whether the COVID vaccine is necessary for kids
- Young children can't talk/say what's going on or how they feel, contributing to concerns about vaccinating kids
- The only thing that will make them trust is time

Hispanic/Latino parents

- Want to wait a couple of months perhaps; but want the pediatrician to specifically advise it
- Some parents have talked to their doctor about the options and didn't get a strong recommendation
- If things get worse, that will motivate them to vaccinate their child – like higher cases, worse scenario

Overall population

- Clinical trial data – how many children didn't get COVID after being vaccinated, how many didn't get symptoms
- Complication rate – how many complications per set amount of children
- Lots of mixed information on COVID vaccines for children under 5 – they don't know who to believe

Parents of children ages 2 years – 4 years

Black parents

- COVID is such a new virus, they are still learning about it
- Long term side effects are the big concern –child will be living a long time, want to know that they are safe
- One person admits that they make an intentional choice to NOT pay attention to the news/get information on COVID because it will make them worry too much

Hispanic/Latino parents

- One parent feels like COVID is so new that the information medical professionals have might not be totally right
- One parent would get their young child vaccinated right away based on the experience from themselves and other child – a smaller dose makes them more comfortable
- One parent would rather not get for their child unless they had to – questions need based on case counts

Overall population

- Want to know about the efficacy – to see if it's worth it or not
- Waiting until there is a requirement and mandate
- Parents know the vaccines made them feel bad (short-term side effects) – so they don't want their kids to suffer the same side effects

Major themes of vaccination intentions among parents of children under 5 years

- Parents **personal experience** with COVID (for themselves and for their children) informs how they view the importance of the vaccine
  - If their children already had COVID, and it was mild, they aren't worried about immediately vaccinating
  - If they or their child had severe COVID, they are more amenable to getting vaccinated to avoid that experience from recurring
- Pervasive idea that kids are not at high risk of getting COVID or having severe outcomes from COVID
- **Time** is a major barrier for most parents
  - Time the vaccines have been in production
  - Myth of the vaccines being rushed
  - Others mention wanting time for their children to grow and develop
  - Many parents mention taking time after approval to see how things go for other people before making a final decision

CDC/NCIRD, VTF Research Team, HHS/ASPA COVID-19 Public Education Campaign, Unpublished data

What can be done to improve vaccination intention among parents of children under 5 years

- CDC, doctors are trusted sources for providing information regarding vaccination and COVID-19
  - Some participants have been told **mixed information** by providers about whether to vaccinate their children under 5 years of age
- Parents want to discuss both **pros** and **cons** of vaccination and avoid messages that are overly simplistic or positive
  - Incorporate more information into communications that provide reassurance about possible side effects
- Ads need to include imagery that is **representative** of the specific age group
  - Include **diversity** in racial and ethnic groups, gender, parents (moms and dads should be shown)
- Public health and clinical trial research must be **inclusive** of historically marginalized populations, from before research initiation through completion and dissemination

CDC/NCIRD, VTF Research Team, HHS/ASPA COVID-19 Public Education Campaign, Unpublished data

What communities can do to improve equity in childhood vaccination

- Pediatricians are often the providers who vaccinate children, and many do this through the federally funded Vaccines for Children (VFC) program
  - However, pediatricians are not the only providers who can vaccinate children
- In many areas, pharmacies and community clinics – such as Federally Qualified Health Centers, rural health clinics, and community health centers also administer vaccines for children, and some of these are also VFC providers
- Many schools and school districts partner with health departments, pharmacies, other healthcare providers and trusted community representatives to hold vaccine clinics in schools to vaccinate children who may not otherwise have access
- Community organizations, including faith-based organizations, can serve as vaccination sites or as informational resources to help families find community-based vaccination sites

CDC Vaccines and Immunizations. Equity in Childhood COVID-19 Vaccination. https://www.cdc.gov/vaccines/covid-19/planning/children/equity.html Accessed June 1, 2022

Equity

What would be the impact of mRNA COVID-19 vaccines in young children on health equity?

- Are there groups or settings that might be disadvantaged in relation to COVID-19 disease burden or receipt of mRNA COVID-19 vaccines?
- Are there considerations that should be made when implementing the mRNA COVID-19 vaccine program to ensure that inequities are reduced whenever possible, and that they are not increased?

○ Reduced	○ Probably reduced	○ Probably no impact	
○ Probably increased	○ Increased	○ Varies	○ Don’t know

Summary

EtR Domain	Question	Work Group Judgments
Public Health Problem	Is COVID-19 disease among children ages 6 months – 5 years of public health importance?	Yes
Benefits and Harms	How substantial are the desirable anticipated effects?	Large
	How substantial are the undesirable anticipated effects?	Small
	Do the desirable effects outweigh the undesirable effects (Moderna)?	Favors intervention
	Doe the desirable effects outweigh the undesirable effects (Pfizer)?	Favors intervention
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	Varies
	Is there important variability in how patients value the outcomes?	Probably important uncertainty or variability
Acceptability	Are mRNA vaccines acceptable to key stakeholders?	Yes
Feasibility	Is the Moderna COVID-19 vaccine feasible to implement among children ages 6 months – 5 years?	Yes
	Is the Pfizer-BioNTech COVID-19 vaccine feasible to implement among children ages 6 months – 4 years?	Probably yes
Resource Use	Are mRNA COVID-19 vaccines among children ages 6 months – 5 years a reasonable and efficient allocation of resources?	Yes
Equity	What would be the impact of mRNA COVID-19 vaccines in young children on health equity?	Probably no impact

Work Group Interpretation

- Work Group discussed each mRNA COVID-19 vaccine primary series compared to no vaccine
- **Both** mRNA COVID-19 vaccine primary series in young children met the non-inferiority endpoints, provide **protection** against symptomatic COVID-19 disease, and are expected to provide **higher protection** against **severe disease**
- Two vaccine **options** in this population may allow parents and providers a choice, which may increase uptake and acceptability

Evidence to Recommendations Framework

Summary: Work Group Interpretations (Moderna)

Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences is *closely balanced* or *uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings	There is insufficient evidence to determine the balance of consequences

Two doses of 25µg Moderna COVID-19 vaccine

Evidence to Recommendations Framework

Summary: Work Group Interpretations (Moderna)

Type of recommendation	We do not recommend the intervention	We recommend the intervention for individuals based on shared clinical decision-making	We recommend the intervention

Two doses of 25µg Moderna COVID-19 vaccine

Evidence to Recommendations Framework

Summary: Work Group Interpretations (Pfizer-BioNTech)

Balance of consequences	Undesirable consequences *clearly outweigh* desirable consequences in most settings	Undesirable consequences *probably outweigh* desirable consequences in most settings	The balance between desirable and undesirable consequences is *closely balanced* or *uncertain*	Desirable consequences *probably outweigh* undesirable consequences in most settings	Desirable consequences *clearly outweigh* undesirable consequences in most settings	There is insufficient evidence to determine the balance of consequences

Three doses of 3µg Pfizer-BioNTech COVID-19 vaccine

Evidence to Recommendations Framework

Summary: Work Group Interpretations (Pfizer-BioNTech)

Type of recommendation	We do not recommend the intervention	We recommend the intervention for individuals based on shared clinical decision-making	We recommend the intervention

Three doses of 3µg Pfizer-BioNTech COVID-19 vaccine

Summary

- Since the beginning of the COVID-19 pandemic, among U.S. children ages 6 months – 4 years of age, there have been

  Over **2 million cases**

  Over **20,000 hospitalizations**

  Over **200 deaths**

- COVID-19 can cause severe disease and death among children, including children without underlying medical conditions
- Future surges will continue to impact children, with unvaccinated children remaining at higher risk of severe outcomes

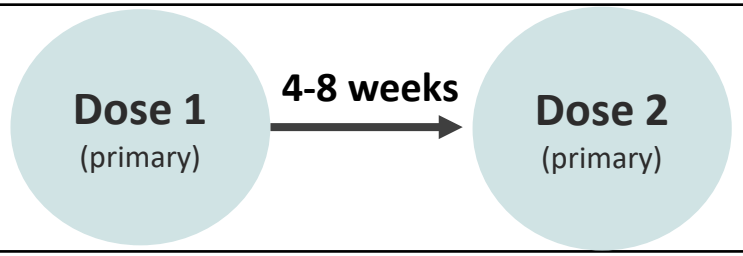
Summary

- As with all other age groups, priority is **vaccination** of **unvaccinated individuals**
- Expansion of vaccine recommendations down to children 6 months of age would allow **18.7 million children** to receive primary COVID-19 vaccine series

Children who are NOT moderately or severely immunocompromised

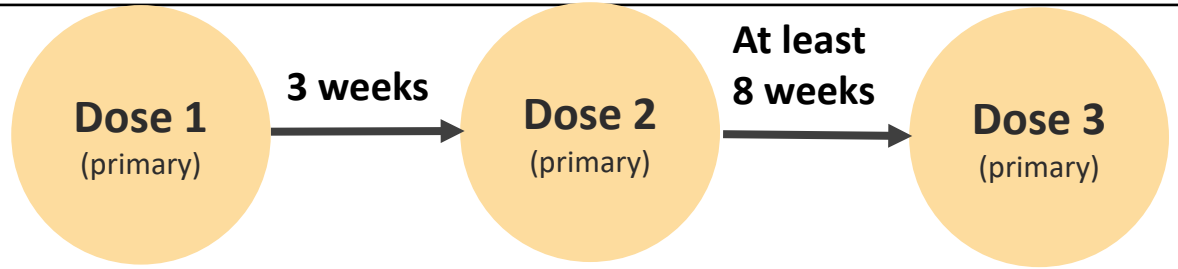
Pfizer-BioNTech
(6 months–4 years)

Moderna
(6 months–5 years)

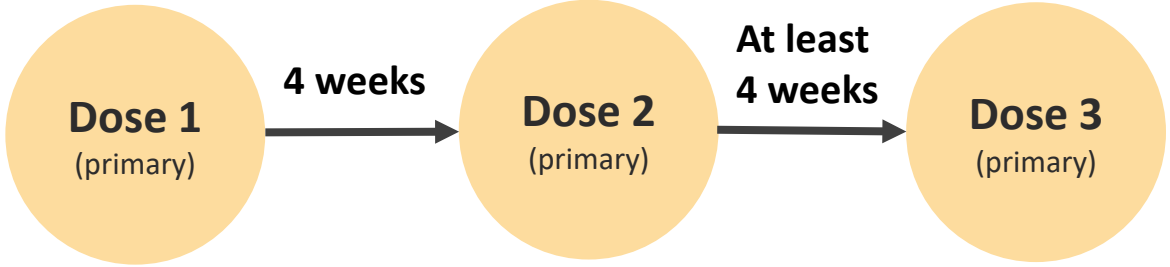


Children who ARE moderately or severely immunocompromised

Pfizer-BioNTech
(6 months–4 years)



Moderna
(6 months–5 years)



Summary

- Current data are for a **2-dose** (Moderna) or **3-dose** (Pfizer-BioNTech) **primary series**
- Post-authorization effectiveness studies can help determine subsequent timing and need of **boosters**
  - Immunocompromised children may also need additional doses for optimal protection

Continued monitoring is critical

- As with all ages, post-authorization **safety** and **effectiveness** monitoring will be critical
- Platforms are in place to monitor vaccine effectiveness; results will be communicated publicly as soon as possible
  - Timing will depend on **vaccine uptake**, as well as **COVID-19 incidence**
- COVID-19 vaccines are being administered under the **most intensive vaccine safety effort** in U.S. history

v-safe

VAERS

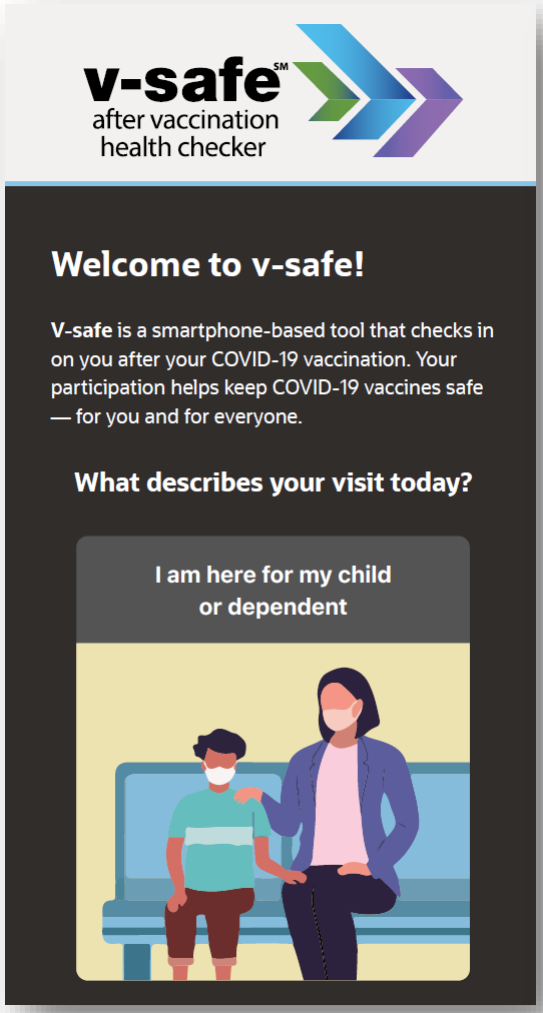
VSD

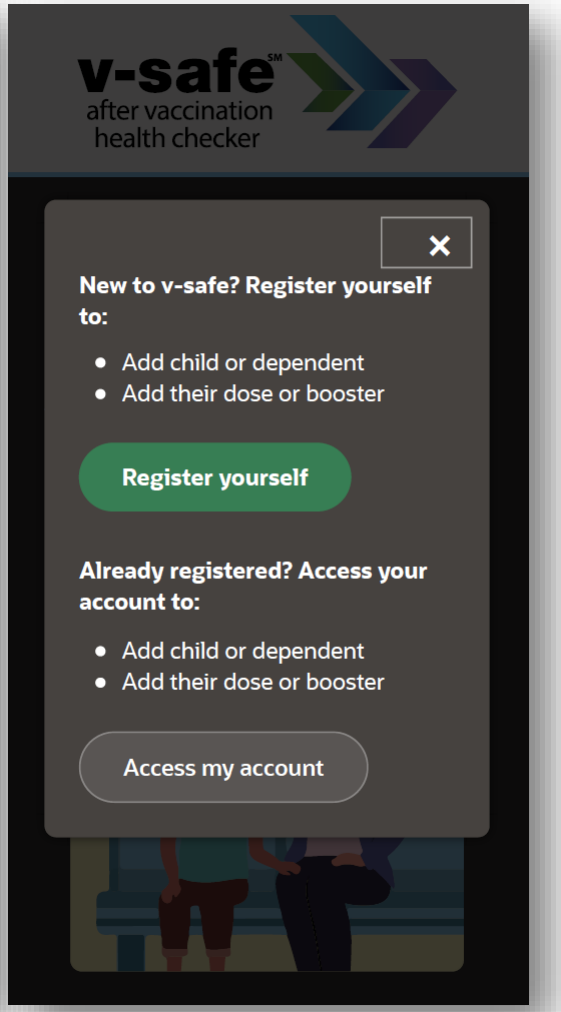
CISA Project

Smartphone-based safety monitoring for COVID-19 vaccines

v-safe is a CDC smartphone-based monitoring program for COVID-19 vaccine safety in the U.S.

- A parent must be registered with v-safe in order to add a child to their account
- If a parent is already registered, they can access their account to add a child
- To register or access your account go to https://vsafe.cdc.gov/en/





v-safe uses text messages and web surveys to check in

- Parents complete surveys on behalf of their child
- Surveys solicit how the child feels after COVID-19 vaccination
  - Local injection site reactions (i.e., pain, redness, swelling)
  - Systemic reactions (i.e., fatigue, headache, joint pain)
  - Health impacts (unable to perform normal daily activities, missed school or work, or received care)
- Surveys have specific questions for young, non-verbal children

Promoting v-safe in practice– we need help!

How:

- Direct patients to https://vsafe.cdc.gov/en/
  - Ideally this should occur before vaccination
- Provide **v-safe** information sheet to patients
- Display posters about **v-safe**

Get vaccinated.
Get your smartphone.
Get started with v-safe.

What is v-safe?

V-safe provides personalized and confidential health check-ins via text messages and web surveys so you can quickly and easily share with CDC how you or your dependent feel after getting a COVID-19 vaccine. It takes just a few minutes to enroll and your participation in **v-safe** helps us monitor the safety of COVID-19 vaccines for everyone.

V-safe features:

- **Enroll your dependents** and complete check-ins on their behalf
- **Enter** and report how you feel after **first, second, additional, and booster doses**

How can I enroll and how does it work?

You can enroll in **v-safe** after any dose of COVID-19 vaccine by using your smartphone and going to vsafe.cdc.gov.

During the first week after each vaccination, **v-safe** will send you a text message each day to ask how you are feeling. After that, you will receive occasional check-ins, which you can opt out of at any time. Depending on your answers, someone from CDC may call to get more information. Your personal information in **v-safe** is protected so it's safe and private*.

How can I enroll my child or dependent?

You can enroll any family member (or friend) who is eligible to be vaccinated in **v-safe.** Children under 16 years old must be enrolled using a parent or guardian's **v-safe** account. You can add a dependent to your existing account or create a new account if you don't have one yet. Creating an account to enroll a dependent does not require that you enter your own vaccination information or complete health check-ins for yourself.

Need step-by-step instructions? Go to: www.cdc.gov/vsafe

v-safe℠
after vaccination health checker

Sign up with your smartphone's browser at vsafe.cdc.gov

OR

Aim your smartphone's camera at this code

Need help with *v-safe*?
Call 800-CDC-INFO (800-232-4636)
TTY 888-232-6348
Open 24 hours, 7 days a week
Visit www.cdc.gov/vsafe

*v-safe uses existing information systems managed by CDC, FDA, and other federal agencies. These systems use strict security measures to keep information confidential. These measures comply, where applicable, with the following federal laws, including the Privacy Act of 1974; standards enacted that are consistent with the Health Insurance Portability and Accountability Act of 1996 (HIPAA); the Federal Information Security Management Act, and the Freedom of Information Act.

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https://www.cdc.gov/coronavirus/2019ncov/vaccines/safety/vsafe/printresources.html

Questions to ACIP

- Should vaccination with **Moderna COVID-19 vaccine** (2-doses, **25µg**, IM) be recommended for persons **6 months – 5 years of age**, under an Emergency Use Authorization?

- Should vaccination with **Pfizer-BioNTech COVID-19 vaccine** (3-doses, 3µg, IM) be recommended for children **6 months – 4 years of age**, under an Emergency Use Authorization?

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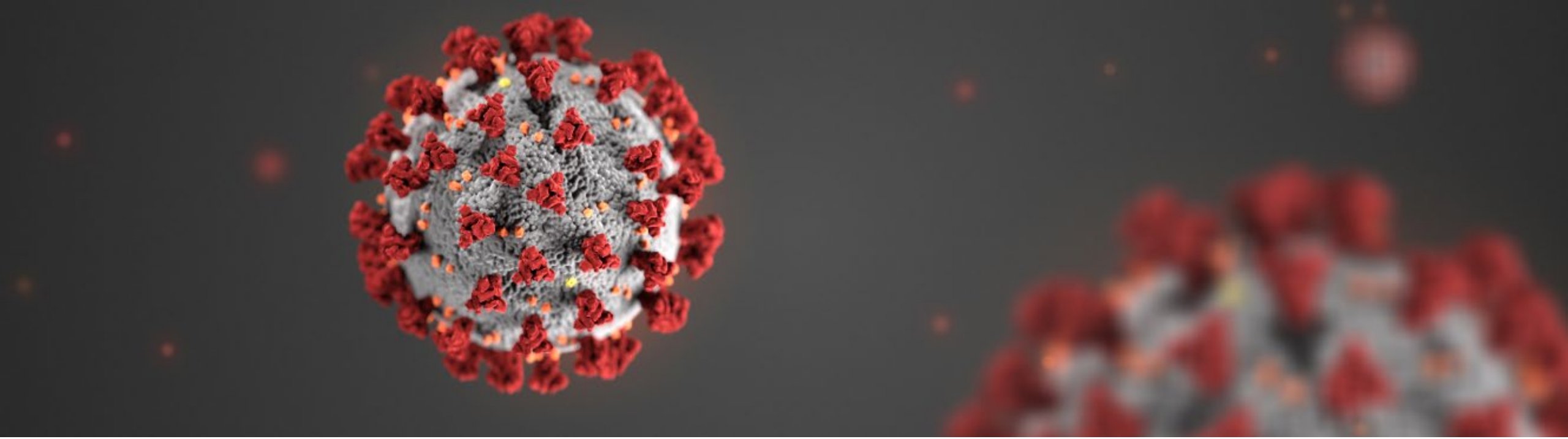
- ACIP COVID-19 Vaccines Work Group
- Vaccine Task Force
- Epi Task Force
- Data Analytics and Visualization Task Force
- Respiratory Viruses Branch
- MIS-C unit
- CICP TF's Monitoring and Evaluation



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.