EtR Framework:

Pfizer-BioNTech COVID-19 vaccine in children aged 5–11 years

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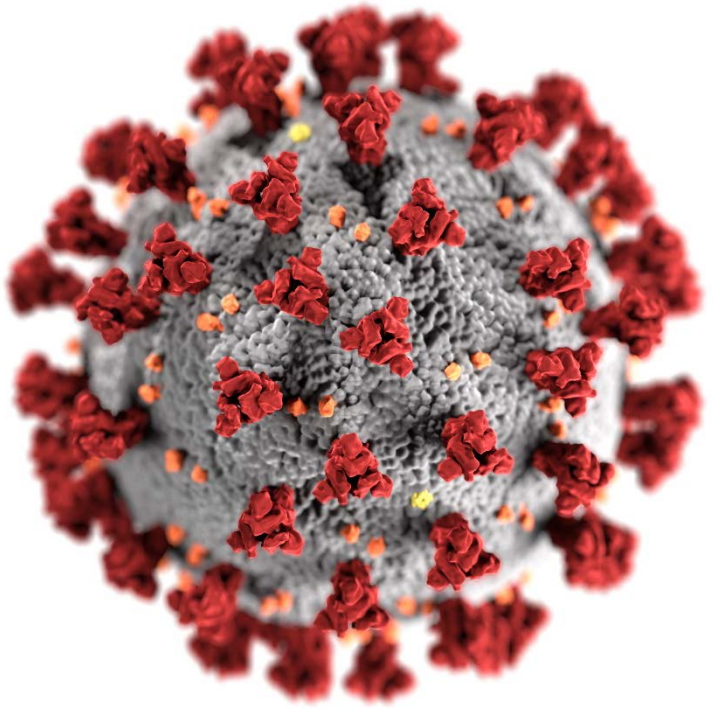
ACIP Meeting

November 2, 2021



cdc.gov/coronavirus

Evidence to Recommendations (EtR) Framework
Policy Question

- Should vaccination with Pfizer-BioNTech COVID-19 vaccine (2-doses, 10µg, IM) be recommended for children 5–11 years of age, under an Emergency Use Authorization?

Evidence to Recommendations (EtR) Framework
PICO Question

Population	Children aged 5–11 years
Intervention	Pfizer-BioNTech COVID-19 vaccine (BNT162b2) (2-doses, 10µg, 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

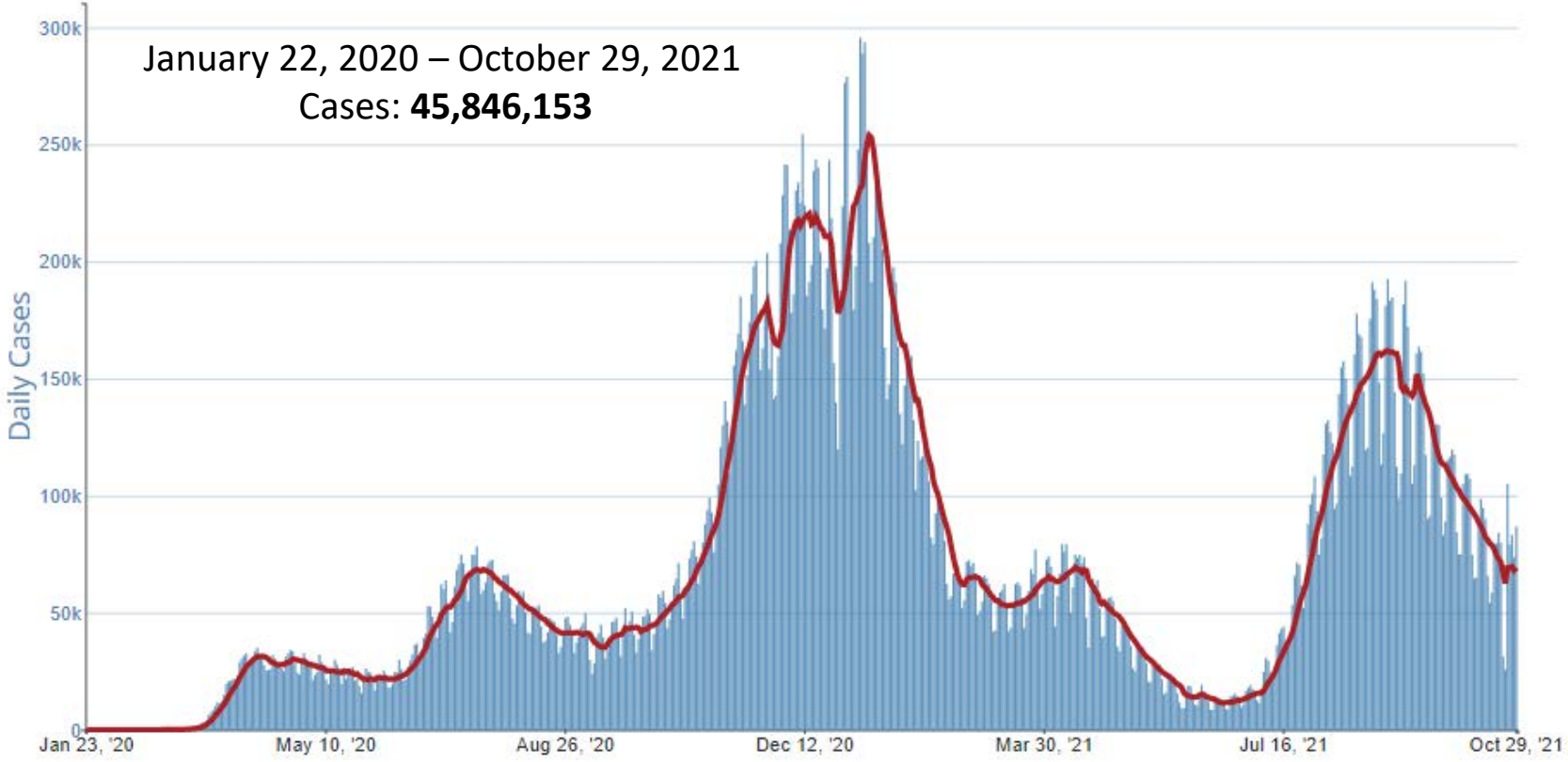
EtR Domain	Question(s)
Public Health Problem	• Is the problem of public health importance?
Benefits and Harms	• How substantial are the desirable anticipated effects? • How substantial are the undesirable anticipated effects? • Do the desirable effects outweigh the undesirable effects?
Values	• Does 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?

"The intervention" = Pfizer-BioNTech COVID-19 vaccine, given to children aged 5–11 years

"The problem" = COVID-19 among children aged 5–11 years

EtR Domain: Public Health Problem

Trends in number of COVID-19 cases in the United States



https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases

Summary

SARS-COV-2 epidemiology in children aged 5–11 years

- **Children are at least as likely to be infected with SARS-CoV-2 as adults**
  - Over 1.9 million reported cases; seroprevalence estimated ~38% among 5–11 years in Sept 2021
  - Infections in children less likely to be reported as cases than infections in adults
- **Children 5-11 years of age are at risk of severe illness from COVID-19**
  - >8,300 COVID-19 related hospitalizations as of mid-October
  - Cumulative hospitalization rate is similar to pre-pandemic influenza seasons
  - Severity comparable among children hospitalized with influenza and COVID-19, with approximately 1/3 of children 5–11 years requiring ICU admission
  - MIS-C most frequent among children 5–11 years
  - Post-COVID conditions have been reported in children
- **Secondary transmission from young school-aged children occurs in household and school settings**

Other pediatric vaccine preventable diseases:

Hospitalizations per year prior to recommended vaccines

	Hepatitis A[1]	Varicella[2] (Chickenpox)	Influenza[3]	COVID-19
Age	5–14 years	<20 years	5–17 years	5–11 years
Time period	2005	1988–1995	2003–2007	Oct 2020–Oct 2021
Hospitalization Burden (per 100,000 population)	**<1**	**4-31**	**30-80**	**25**

[1] https://www.cdc.gov/mmwr/preview/mmwrhtml/ss5603a1.htm

[2] 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

[3] https://www.cdc.gov/flu/weekly/weeklyarchives2007-2008/07-08summary.htm

Other vaccine preventable diseases:

Deaths per year prior to recommended vaccines

	Hepatitis A[1]	Meningococcal (ACWY)[2]	Varicella[3]	Rubella[4]	Rotavirus[5]	COVID-19
Age	<20 years	11–18 years	5–9 years	All ages	<5 years	5–11 years
Time period	1990–1995	2000–2004	1990–1994	1966–1968	1985–1991	Oct 2020–Oct 2021
Average deaths per year	**3**	**8**	**16**	**17**	**20**	**66**

[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. JAMA2007; 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.

Modeling the impact of COVID-19 vaccination in children ages 5–11 years

- Vaccination among 5–11-year-olds is expected to accelerate the decline in cases, reducing cumulative incidence nationally by an expected **8%** (~600,000 cases) from November 2021 to March 2022

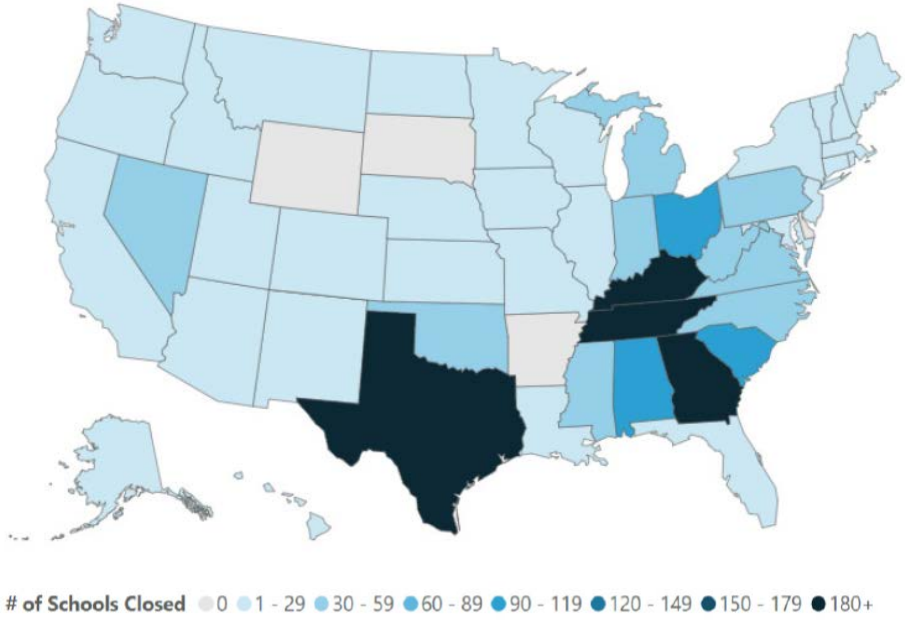
- Vaccination of 5–11-year-olds would dampen, but not eliminate, a new variant emergence

https://covid19scenariomodelinghub.org/

COVID-19 Related K-12 School Closures by State,

August 2, 2021 – October 22, 2021

School districts closed	Total # schools closed*	Estimated # students affected*	Estimated # teachers affected*
313	2,351	**1,217,777**	78,134



Data from the Unplanned School Closure Monitoring Project (DGMQ/CDC), ongoing research that uses systematic daily media searches (methods explained in https://doi.org/10.1371/journal.pone.0248925).

* Number of schools closed in district-wide closures, total number of students, and total number of teachers are estimated by matching the public school district ID or school ID with the district/school data for school year 2019/20 and private school ID with school data for year 2017/18 as obtained from the National Center for Education Statistics (https://nces.ed.gov/ccd/elsi/tableGenerator.aspx, accessed on Apr 20, 2021). Due to missing information in 2019/20 data, the total number of public school teachers in California is estimated using 2018/19 NCES data.

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)

- Loss of caregivers

Public health problem:
Summary of the available evidence

- **Children 5–11 years of age are at risk of severe illness from COVID-19**
  - Over 1.9 million reported cases and >8,300 hospitalizations through mid-October
    - Cumulative hospitalization rate similar to influenza season
    - MIS-C most frequent among children 5–11 years
  - Other post-COVID conditions have been seen in children
- COVID-19 in children leads to missed school for themselves and their communities
- **Wide use of an effective vaccine would reduce public health burden of COVID-19 in children 5–11 years of age**

Public Health Problem

Work Group Interpretation

Is COVID-19 disease among children aged 5–11 years of public health importance?

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

EtR Domain: Benefits and Harms

Benefits and harms assessments

- GRADE
- Potential benefits and harms in seropositive children
- Potential risk of myocarditis

GRADE= Grading of Recommendations, Assessment, Development and Evaluation

PICO question and evidence review

Population	Children aged 5–11 years
Intervention	Pfizer-BioNTech COVID-19 vaccine (BNT162b2) (10 µg, 2 doses IM, 21 days apart)
Comparison	No vaccine
Outcomes	1. Symptomatic lab-confirmed COVID-19 2. Hospitalization due to COVID-19 3. Multisystem inflammatory syndrome in children (MIS-C) 4. Asymptomatic SARS-CoV-2 infection 5. Serious adverse events 6. Reactogenicity

- Evidence review identified 1 clinical trial for inclusion

Outcome #1: Symptomatic lab-confirmed COVID-19

- Pfizer-BioNTech COVID-19 vaccine phase 2/3 randomized controlled trial (RCT)*
- Randomized 2:1 vaccine to placebo (median follow-up time: 3.3 months)
- Vaccine efficacy against symptomatic lab-confirmed COVID-19 was **90.9% (95% CI: 68.3%, 98.3%)**
  - 3 cases in the vaccine arm (N=1461; surveillance time: 369 person-years)
  - 16 cases in the placebo arm (N=714; surveillance time: 179-person-years)
- The geometric mean ratio (GMR) for antibodies in 5–11-year-olds compared with 16–25-year-olds was **1.04** (95% CI:0.93, 1.18), and **met the noninferiority criteria**

*Unpublished, data obtained from sponsor

Evidence table: Outcome #1: Symptomatic lab-confirmed COVID-19

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Comparison	Relative (95% CI)	Absolute (95% CI)		
Vaccine efficacy against symptomatic COVID-19												
1	RCT	Not serious [a]	Not serious	Not serious [b,c]	Not serious	None	3/1461[d] (0.2%)	16/714[e] (2.2%)	**RR 0.10** (0.03 to 0.31)	2,017 fewer per 100,000 (from 2,174 fewer to 1,546 fewer)	Type 1	CRITICAL

[a] Exclusions from evaluable efficacy population occurred in 5.1% of the BNT162b2 group and 2.8% of the placebo group (due to receipt of dose 2 outside of protocol defined window of 19-42 days after dose 1 or other important protocol deviations). This was deemed not serious.

[b] Indirectness was considered because the vaccine efficacy observed at a median 3-month follow-up may differ from that observed over a longer period of time. However, this was deemed not serious.

[c] The RCT excluded children who were immunocompromised or had a prior history of MIS-C. The population included in the RCT may not represent all persons aged 5-11 years. However, this was deemed not serious.

[d] Total surveillance time was 369 person-years

[e] Total surveillance time was 179 person-years

CI: Confidence interval; **RR:** Risk ratio

Outcome #5: Serious adverse events (SAE)

- Pfizer-BioNTech phase 2/3 randomized controlled trial (RCT)*
- None of the SAEs were assessed by the investigator as related to study intervention.
- No deaths were reported in any trial participants

- Initial Enrollment Group (median follow-up time: 3.3 months)

  1 SAEs in 1 participants in the vaccine group (n=1518)
  - Limb fracture

  2 SAEs in 1 in the placebo group (n=750)
  - Pancreatitis
  - Abdominal pain

- Safety Expansion Group (median follow-up time: 2.4 weeks)

  3 SAEs in 3 participants in the vaccine group (n=1591)
  - Infective arthritis (infection of the knee)
  - Foreign body ingestion of a penny
  - Epiphysial fracture

  0 SAEs in the placebo group (n=788)

*Unpublished, data obtained from sponsor; randomized 2:1 vaccine to placebo

Evidence table: Outcome #5: Serious adverse events

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Comparison	Relative (95% CI)	Absolute (95% CI)		
Serious adverse events												
1	RCT	Not serious	Not serious	Serious[a, b]	Very Serious[c]	None	1/1518[d] (0.07%)	1/750[e] (0.1%)	0.49 (0.03,7.89)	68 fewer per 100,000 (from 129 fewer to 919 more)	**Type 4**	CRITICAL

[a]Serious concern of indirectness was noted. The body of evidence does not provide certainty that rare serious adverse events were captured due to the short duration of follow-up (median: 3.3 months).

[b]The effects noted are from an analysis of the initial enrollment group population. A safety expansion group of children aged 5–11 years, 1591 children in the vaccine arm and 788 children in the placebo arm, were not included because of the short duration of follow-up (median: 2.4 weeks). At the time of the data cutoff (October 8, 2021) 3 SAEs (arthritis infective [infection of the knee], foreign body ingestion of a penny, epiphyseal fracture) were reported in 3 children (1 each) in the vaccine group. The pooled relative risks for the initial enrollment group and safety expansion group was 1.98 (95% CI: 0.22, 17.70). All SAEs were assessed by the investigator as not related to the study intervention.

[c]Very serious concern for imprecision was noted based on the 95% confidence interval crossing the line of no effect (1). The width of the confidence interval contains estimates for which different policy decisions might be considered. This outcome may be imprecise due to the small number of events during the observation period.

[d]1 SAE (limb fracture) was reported in a participant in the BNT162b2 group, which was determined by the investigator to be unrelated to the study intervention. All SAEs were assessed by the investigator as not related to the study intervention.

[e]2 SAEs (pancreatitis and abdominal pain) occurred in 1 placebo recipient.

Outcome #6: Reactogenicity, severe (grade ≥3)

- Pfizer phase 2/3 randomized controlled trial (RCT)* solicited events from participants or reported by their parent/legal guardian through electronic diaries for 7 days following each dose

- Local reactions (redness, swelling, pain at the injection site) and systemic reactions (fever, nausea/vomiting, headache, fatigue, chills, new or worsened muscle pain, new or worsened joint pain) were reported for 7 days after each dose
  - **2.7**% of children in the vaccine arm vs **1.1**% in the placebo arm had a local or system grade ≥ 3 reaction after either dose
    - Most reactions were grade 3; 1 child in the vaccine arm with had a grade 4 fever >40.0°C; there were no other grade 4 reactions
  - More common after Dose 2; pain at injection site, fatigue and headache were the most common

*Unpublished, data obtained from sponsor

Evidence table: Outcome #6: Reactogenicity, severe (Grade ≥3)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Comparison	Relative (95% CI)	Absolute (95% CI)		
Reactogenicity, severe (grade ≥3)												
1	RCT	Not serious	Not serious	Not Serious	Serious[a]	None	41/1517 (2.7%)	8/750 (1.1%)	RR 2.53 (1.19 to 5.38)	1,632 more per 100,000 (from 203 more to 4,672 more)	**Type 2**	IMPORTANT

[a] Serious concern for imprecision given the wide 95% confidence interval, which cannot exclude the possibility of no difference between BNT162b2 and placebo.

Conclusion

GRADE: Pfizer-BioNTech COVID-19 vaccine in children aged 5–11 years

- Phase 2/3 RCT conducted among children aged 5–11 years
- **>3,000** children were vaccinated with BNT162b2
- Vaccine efficacy estimate of **90.9%** for prevention of symptomatic laboratory-confirmed COVID-19 (high certainty)
- Serious adverse events were uncommon among vaccine and placebo participants (**0.07%** vs **0.1%**). No SAEs were judged to be related to vaccination and no deaths occurred (very low certainty).
- Grade ≥3 local or systemic reactions were more common among vaccine than placebo recipients and were reported by **2.7%** of vaccine participants (moderate certainty).

Benefits and harms assessments

- GRADE
- Potential benefits and harms in seropositive children
- Potential risk of myocarditis

GRADE= Grading of Recommendations, Assessment, Development and Evaluation

Immune response by serostatus

- Geometric mean titers (GMT) were higher in those with prior infection
- Geometric mean fold rise (GMFR) was less (likely due to higher GMTs initially)

Baseline SARS-CoV-2 status	N (%)	Geometric Mean Titers (GMT)		Geometric Mean Fold Rises (GMFR)
		GMT pre-dose 1 (95% CI)	GMT 1 month post dose 2 (95% CI)	GMFR (95% CI)
Positive	21 (7%)	59.8 (33.5, 106.5)	3270.0 (2032.1, 5261.8)	54.7 (35.3, 84.7)
Negative	273 (93%)	10.1 (9.9, 10.3)	1211.3 (1121.1, 1308.7)	119.6 (110.8, 129.2)

Summary

COVID-19 vaccines and seropositivity

Data from Phase 3 clinical trial

- **~9%** of children in clinical trial were baseline SARS-CoV-2 seropositive
- Post-vaccination antibodies **higher** in children who were baseline seropositive
- Rates of local and systemic reactions, as well as adverse events, were **lower** in children who were baseline seropositive

Data from U.S. studies

- Approximately **38%** of children aged 5–11 years have evidence of prior SARS-CoV-2 infection based on seroprevalence estimates
- Prior infection can result in protection against infection but not 100% and likely decreases over time
- Children have a greater proportion of asymptomatic infection relative to adults[1-4]
  - Asymptomatic infection can result in lower antibody levels than severe disease

1. Viner RM, Ward JL, Hudson LD, et al. [published online ahead of print, 2020 Dec 17]. *Arch Dis Child*. 2020;archdischild-2020-320972
2. Irfan O, Muttalib F, Tang K, Jiang L, Lassi ZS, Bhutta Z. [published online ahead of print, 2021 Feb 16]. *Arch Dis Child*. 2021;106(5):440-448
3. Dawood FS, Porucznik CA, Veguilla V, et al. [published online ahead of print, 2021 Oct 8]. *JAMA Pediatr*. 2021;10.1001/jamapediatrics.2021.4217. doi:10.1001/jamapediatrics.2021.4217
4. Poline J, Gaschignard J, Leblanc C, et al.. *Clin Infect Dis*. 2021;72(12):2215-2217. doi:10.1093/cid/ciaa1044

Balance of benefits and risks by seropositive status

- Delta-wave surges of pediatric COVID-19 hospitalizations occurred even with seroprevalence ~38%, suggesting this alone is not sufficient to provide broad protection
- Limited data on rates of reinfection in children
- Protection against asymptomatic/mild infection important outcome in children
  - MIS-C typically occurs after asymptomatic or mild infection; post-COVID conditions can also occur after mild infection
- No concerns identified in safety surveillance with seropositive adolescents and adults
  - Individuals 12-64 years with seropositivity >30%
- Vaccine recommendations that require serologic testing place unnecessary barriers
- Limited data to estimate impact of vaccination of seropositive children, but risks minimal
- Balance of benefits and risks **favorable** for vaccination of all children

Vaccine-associated myocarditis

- Identified rates of myocarditis are based on data from adolescents and adults receiving 30ug dose of Pfizer-BioNTech COVID-19 vaccine
  - Dose in pediatric (5–11-year-old) age group: 10ug dose
- Rare event, but most common in males 12–29 years of age
- No cases of myocarditis occurred during the clinical trials with 5–11-year-olds
  - N=3,082 with at least 7 days of follow up reported

Benefits and risks of Pfizer-BioNTech COVID-19 vaccine for children 5–11 years of age

Benefits
Pfizer-BioNTech COVID-19 vaccine for children 5–11 years of age

Risks
Pfizer-BioNTech COVID-19 vaccine for children 5–11 years of age

Estimated benefits for every million Pfizer-BioNTech COVID-19 vaccinations in children 5-11 years of age using recent incidence

Females 5-11 years

- **57,301** COVID-19 cases prevented
- **191** hospitalizations prevented
- **130** MIS-C cases prevented
- **60** ICU admissions prevented

Males 5-11 years

- **56,954** COVID-19 cases prevented
- **226** hospitalizations prevented
- **130** MIS-C cases prevented
- **72** ICU admissions prevented

Assumptions: Benefits accrue over **180 days (6 months)**; VE against symptomatic COVID-19: 90%; VE against hospitalization: 95%
Data Sources: COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#vaccination-demographic. COVID Data Tracker https://covid.cdc.gov/covid-data-tracker/#trends_dailycases. COVID-Net https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html. All data are from the week ending on **9/11/2021**.

Estimated benefits for every million Pfizer-BioNTech COVID-19 vaccinations in children 5-11 years of age using pandemic-average incidence

Recent Epidemiology 5-11 years	Pandemic Average 5-11 years
58,204 COVID-19 cases prevented	**18,549** COVID-19 cases prevented
226 hospitalizations prevented	**80** hospitalizations prevented
132 MIS-C cases prevented	**42** MIS-C cases prevented
72 ICU admissions prevented	**26** ICU admissions prevented

Assumptions: Benefits accrue over **180 days (6 months)**; VE against symptomatic COVID-19: 90%; VE against hospitalization: 95%
Data Sources: COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#vaccination-demographic. COVID Data Tracker https://covid.cdc.gov/covid-data-tracker/#trends_dailycases. COVID-Net https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html.
Recent epidemiology data from the week ending on 9/11/2021. Pandemic average data are averaged for the entire pandemic through the week ending on 10/16/2021.

Estimated risks for every million Pfizer-BioNTech COVID-19 vaccinations in children 5-11 years of age

Rates of myocarditis after vaccination in 5–11-year-olds unknown

No cases occurred during clinical trials (n=3,082 with at least 7 days follow-up)

Myocarditis after vaccination in 5–11-year-old population likely **lower** than rates seen in 12–15-year-olds

- Underlying epidemiology of viral myocarditis varies greatly between children aged 5–11 and 12–17 years: substantially **lower** in children 5–11 years of age
- Dose used in 5–11-year-olds (10µg) is a third of dose used in 12–15-year-olds (30µg)

Estimated rates of myocarditis after vaccination in adolescents 12–15 years of age, per million second doses

	Females	Males	Total
VAERS	3.9	39.9	21.5
VSD	12.1	108.5	60.2

VAERS rates as of Oct 6th; VSD rates as of Oct 23rd. Both show risk after second dose, per million doses

Benefits and risks of Pfizer-BioNTech COVID-19 vaccine for children 5–11 years of age

Benefits

Prevention of COVID-19 cases

Likely prevention of hospitalizations, MIS-C and deaths and post-COVID conditions

Possible prevention of transmission

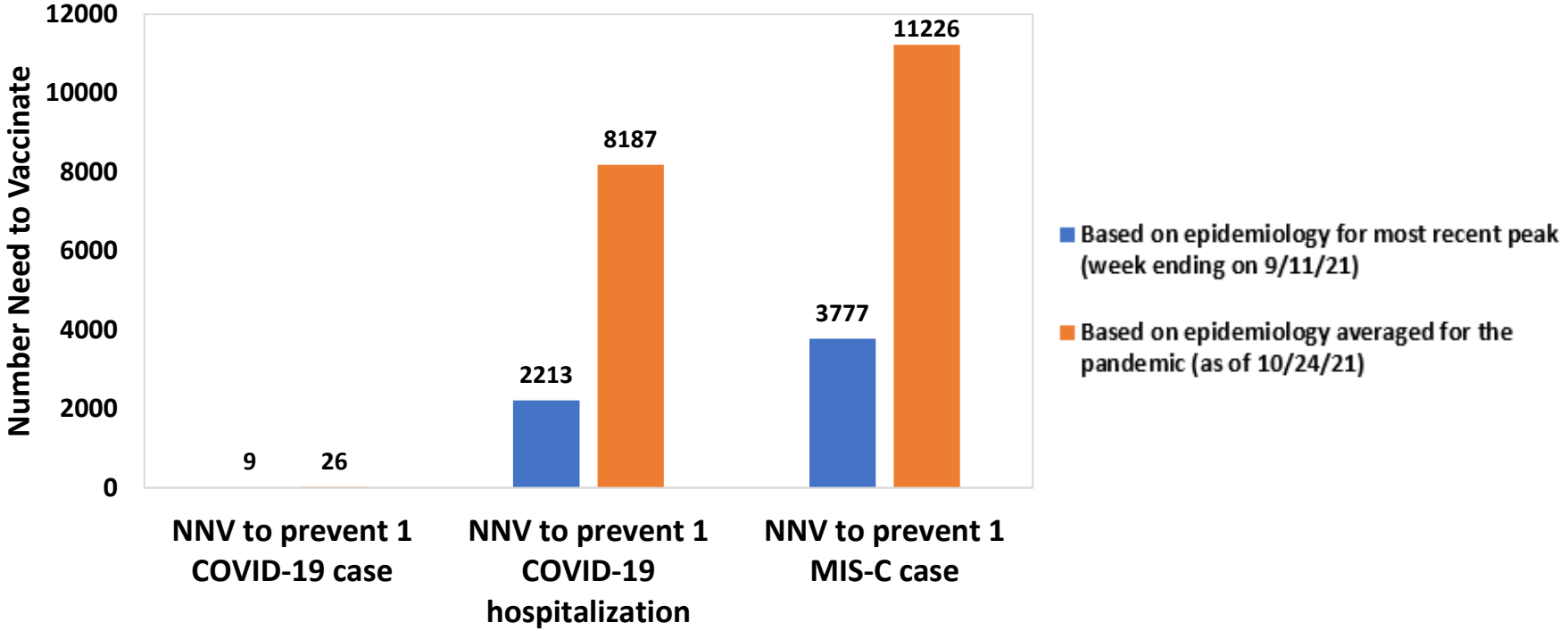
Greater confidence in safer return to school and social interactions

Risks

Myocarditis or other rare events after mRNA vaccines?

Short-term reactogenicity

Number of children aged 5-11 years needed to vaccinate to prevent symptomatic COVID-19, hospitalization, and MIS-C



Assumptions: VE against symptomatic COVID-19: 90%; VE against hospitalization: 95%. Estimated over **180 days (6 months)**;
Data Sources: COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#vaccination-demographic October, 24, 2021; COVID Data Tracker https://covid.cdc.gov/covid-data-tracker/#trends_dailycases. October, 24, 2021; COVID-Net October, 24, 2021, https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html

Benefits and Harms

Summary

- Clinical trial demonstrated Pfizer-BioNTech COVID-19 vaccine is **safe**, **immunogenic** and **efficacious** in children 5–11 years of age
  - Trial not powered to assess rate of rare adverse events; no cases of myocarditis in ~3100 vaccinated children
- Balance of benefits and risks varies by incidence of COVID-19
  - Largest benefits with higher incidence
- Benefit/risk balance **favorable**, regardless of seropositivity rates
  - While many children 5–11 years of age may be seropositive, unknown duration of protection for asymptomatic infection in children
  - Safety data reassuring in seropositive population

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?

O Minimal	O Small	O Moderate	O Large	O Varies	O 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?

O Minimal	O Small	O Moderate	O Large	O Varies	O 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?

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

EtR Domain: Values

Parental surveys

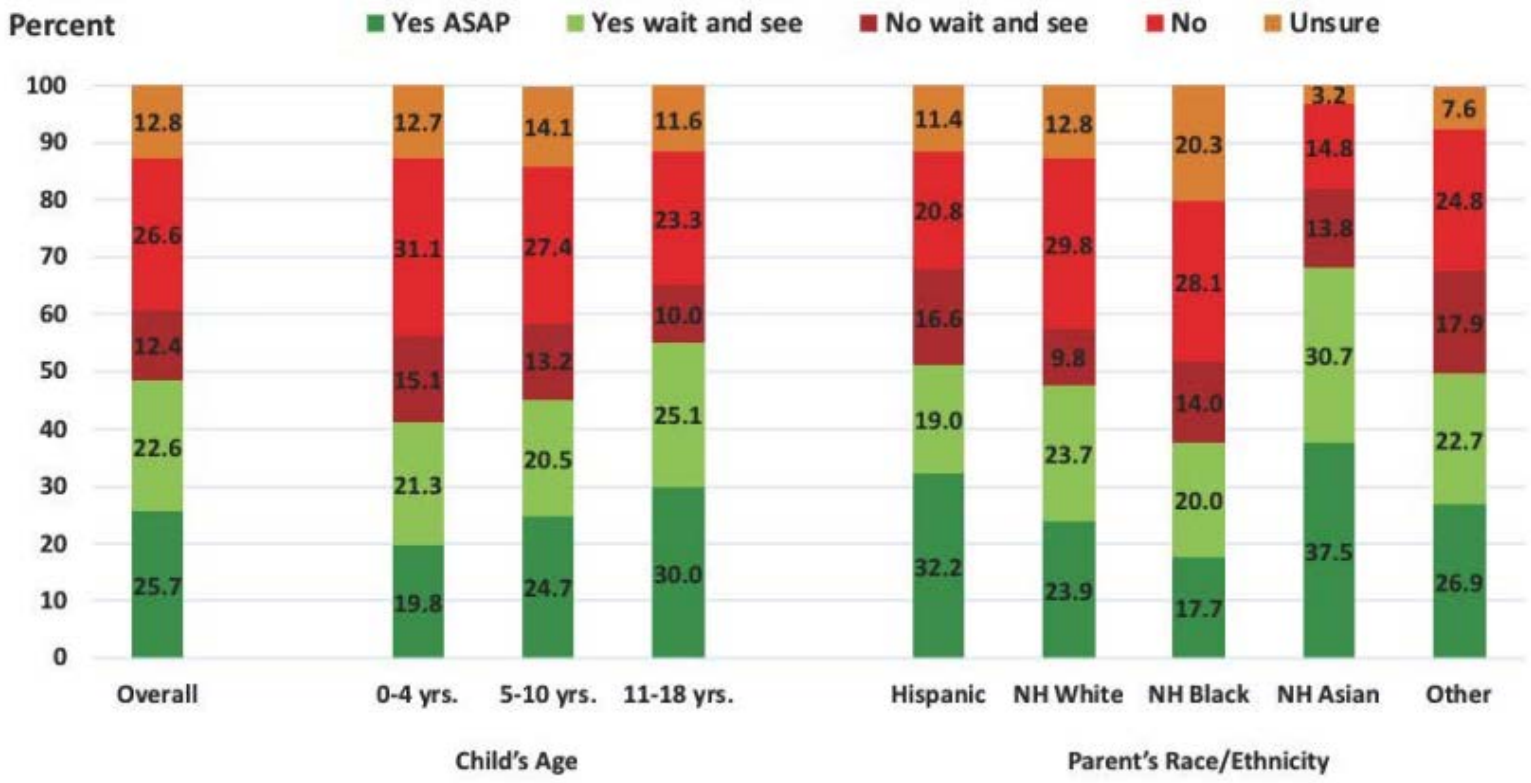
Intent to have children vaccinated

- Among parents surveyed, **34–57**% plan to get their children vaccinated[1-6]
- **90**% of parents ‘very worried’ their child would get COVID-19 reported intent to vaccinate their child, compared to **7**% of parents ‘not worried at all’[5]
- **82**% of fully vaccinated parents reported intent to vaccinate their child, compared to **1**% of parents who are unvaccinated/do not plan to get vaccinated[5]
- Among parents of teens who discussed vaccination with their pediatrician, **three-quarters** of those whose pediatrician recommended vaccination say their child received at least 1 dose[6]

1. Szilagyi PG, et al. Parents' Intentions and Perceptions About COVID-19 Vaccination for Their Children: Results From a National Survey [published online ahead of print, 2021 Aug 3]. Pediatrics. 2021;e2021052335.
2. Ruggiero KM, et al. Parents' Intentions to Vaccinate Their Children Against COVID-19 [published online ahead of print, 2021 Jun 30]. J Pediatr Health Care.
3. Brenan M. In U.S., 55% Would Get COVID-19 Vaccine for Young Child. Gallup. September 28, 2021. Available at: https://news.gallup.com/poll/354998/covid-vaccine-young-child.aspx . Accessed October 1, 2021
4. Unpublished data from the CDC, the University of Iowa, and RAND Corporation Survey of Parents, September 2021
5. Gallup Panel Poll. Available at https://news.gallup.com/poll/354998/covid-vaccine-young-child.aspx. Accessed September 29, 2021.
6. Lopes L, et al. KFF COVID-19 Vaccine Monitor: Available at: https://www.kff.org/coronavirus-covid-19/poll-finding/kff-covid-19-vaccine-monitor-trends-among-children-school/ Accessed: October 1, 2021

Parental surveys

Intent to have child vaccinated varies by age and race/ethnicity

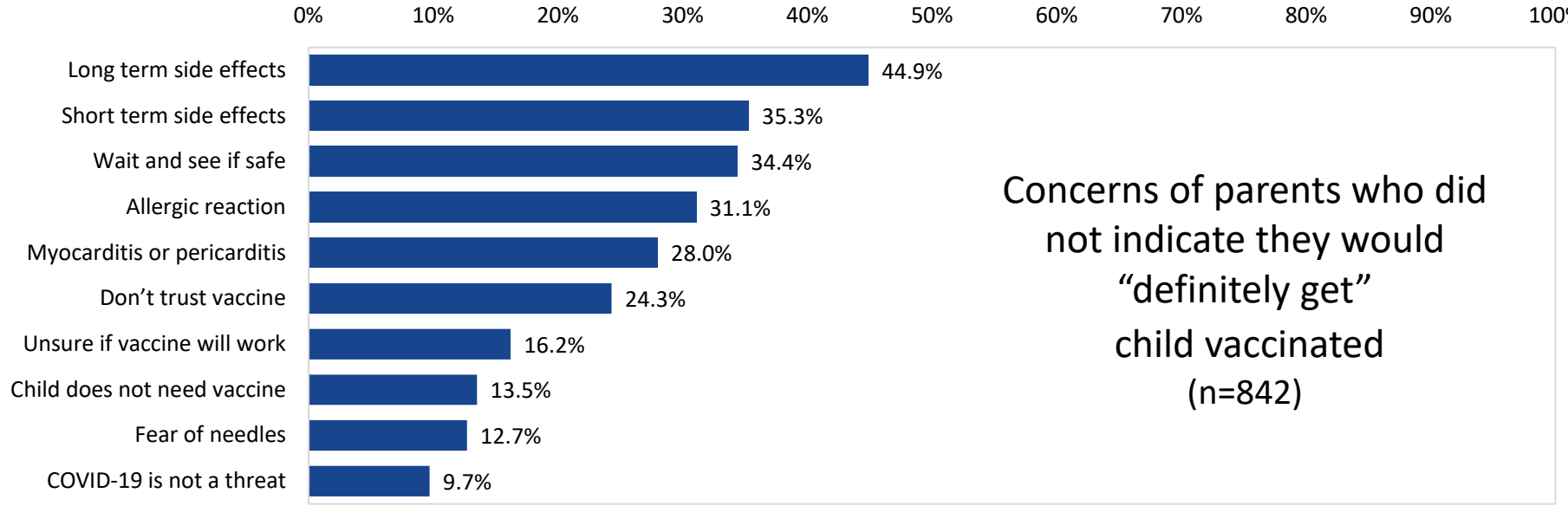


Szilagyi PG, et al. Parents' Intentions and Perceptions About COVID-19 Vaccination for Their Children: Results From a National Survey [published online ahead of print, 2021 Aug 3]. Pediatrics. 2021;e2021052335.

Parental surveys

Survey of 1000 U.S. parents of children aged 5-11, September 2021

57% of parents surveyed stated they would “definitely” (35%) or “probably” (22%) get their child vaccinated

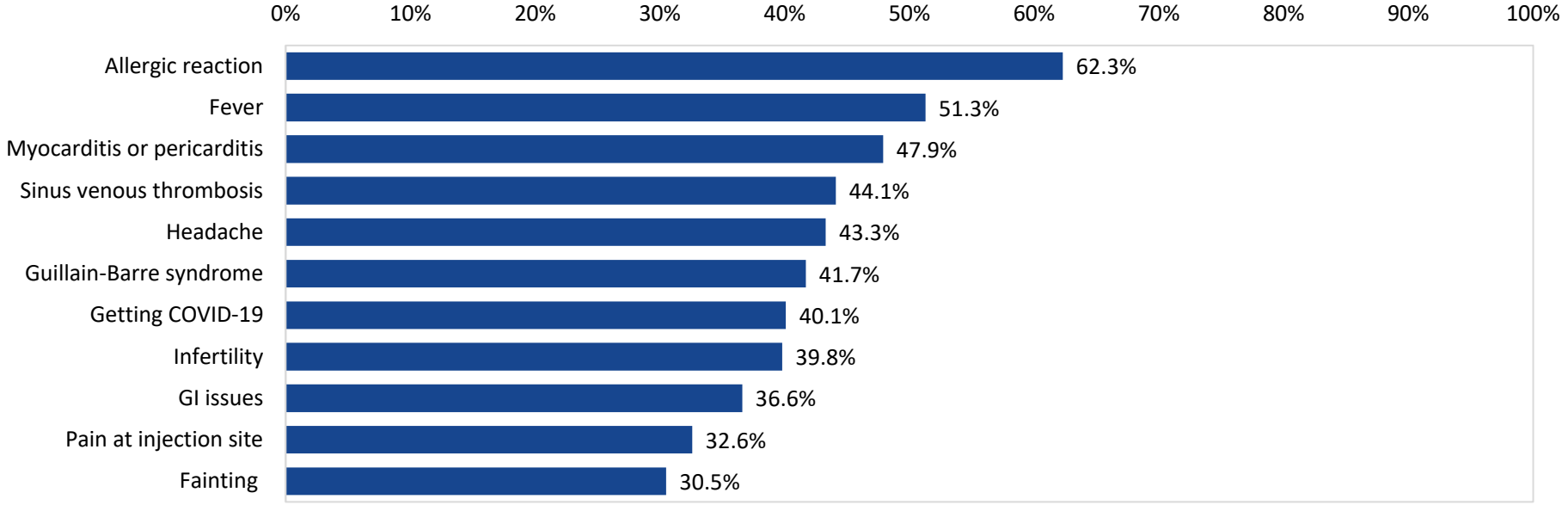


Unpublished data from the CDC, the University of Iowa, and RAND Corporation Survey of Parents, **September 2021**

Parental surveys

Survey of 1000 U.S. parents of children aged 5-11, September 2021

37% of parents reported **side effects** as reason for not wanting COVID-19 vaccine for their child



Unpublished data from the CDC, the University of Iowa, and RAND Corporation Survey of Parents, September 2021

Values
Summary

- Among several polls of U.S. parents, about **half** of parents say they are likely to get their child vaccinated
- Many parents cite concerns for long- or short-term side effects such as fever, anaphylaxis or myocarditis in their decision to vaccinate their child
- Other factors that influence a parents' decision to vaccinate include the parents' vaccination status and provider recommendation

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 patients/caregivers feel that the benefits outweigh the harms and burden?
- Does the population appreciate and value the Pfizer-BioNTech COVID-19 vaccine?

O **Minimal**	O **Small**	O **Moderate**	O **Large**	O **Varies**	O **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?

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

EtR Domain: Acceptability

Acceptability

- As of October 15, **>70%** of Vaccines For Children (VFC) providers were enrolled as COVID-19 providers
  - >70% of VFC providers represent >80% of VFC vaccine that was distributed in 2019 for influenza and MMR

- AAP Pediatrician Life and Career Experience Study (PLACES) survey[1]
  - **75%** of pediatricians in primary care reported that their main work setting is enrolled as a COVID-19 provider with their state
  - **70%** have started giving the vaccine to 12- to 18-year-old patients

1. https://www.aappublications.org/news/2021/10/01/researchupdate100121

AAP= American Academy of Pediatrics

Acceptability

Summary

- Most jurisdictions plan to utilize a variety of implementation strategies to vaccinate children 5–11 years
- Parents report greatest comfort with receiving COVID-19 vaccine at their primary care providers' offices
  - Jurisdictions anticipate most children will be vaccinated at pediatric providers
- >70% of VFC providers are already enrolled as COVID-19 vaccine providers

Acceptability

Is Pfizer-BioNTech COVID-19 vaccine 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?

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

EtR Domain: Feasibility

Pediatric COVID-19 vaccination implementation goals

- Enable access to and availability of vaccine providers where populations are mostly likely to seek vaccination (**reach the most**)
- Ensure programming to ensure access to vaccine for vulnerable and underserved pediatric populations (**hard to reach**)
- **~28.7 million** children 5–11 years of age[1]

[1]U.S. Census Bureau, Population Division, 2020 Demographic Analysis

Feasibility

Pediatric formulation

- Different **vaccine formulation** may lead to administration errors
  - Provider education ongoing

- New formulation can be stored at refrigerator temperature (2–8^{o}C) for up to 10 weeks prior to use

- 100 dose minimum order size

	Formulation for ≥12-year-olds (purple cap)	Formulation for 5–11-year-olds (orange cap)
Age group	12 years and older	5-11 years
Vial cap color		
Dose (mRNA concentration)	30 ug	10 ug
Injection volume	0.3 mL	0.2 mL
Fill Volume (before dilution)	0.45 mL	1.3 mL
Amount of Diluent* Needed per vial	1.8 mL	1.3 mL
Doses per Vial	6 (after dilution)	10 (after dilution)

Source: Jurisdiction data call survey – 09/27/21. n=58.

Feasibility

Is the Pfizer-BioNTech COVID-19 vaccine feasible to implement among children aged 5–11 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?

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

EtR Domain: Resource Use

Resource use

- U.S. Government has purchased enough vaccine to support vaccination of the pediatric population of children 5-11 years[1]
- Vaccine will be available at no cost
- No studies evaluated cost-effectiveness with COVID-19 vaccines and children
- Work Group concluded that cost-effectiveness may not be a primary driver for decision-making during a pandemic and for vaccine used under EUA
  - Will need to be reassessed for future recommendations
- Use of COVID-19 vaccines in as many populations as possible will be important to returning to pre-pandemic activities
  - Return to pre-pandemic activities likely have positive economic impact

[1] https://www.cdc.gov/vaccines/covid-19/downloads/Pediatric-Planning-Guide.pdf

Resource Use

Is the Pfizer-BioNTech COVID-19 vaccine among children aged 5–11 years a reasonable and efficient allocation of resources?

- What is the cost-effectiveness of the Pfizer-BioNTech COVID-19 vaccine?
- How does the cost-effectiveness of the Pfizer-BioNTech COVID-19 vaccine change in response to changes in context, assumptions, etc?

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

EtR Domain: Equity

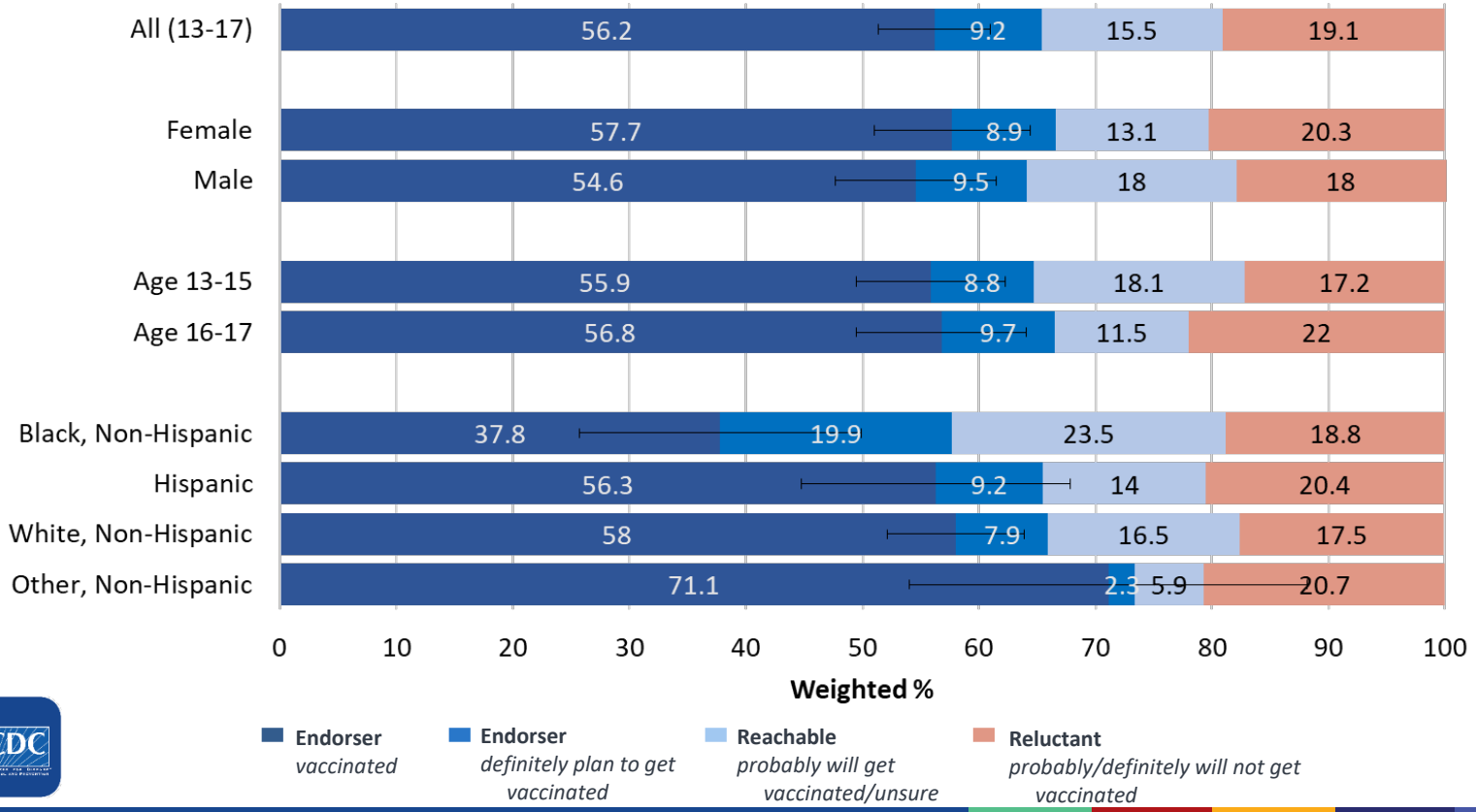
Children that could be disproportionately affected by COVID-19 or in access to healthcare

- **Place of residence**
  - Living in rural/frontier areas
  - Justice-involved (incarcerated persons/families)
  - Living in congregate settings (long-term care facilities, boarding schools)
  - Experiencing homelessness
- **Racial and ethnic minority populations**
  - Black, Hispanic or Latino, and Alaskan Native/American Indian
  - Immigration status
- **Gender/sexual identity**
  - LGBTQ+
- **Socioeconomic status**
  - Families with lower incomes
  - High social vulnerability
- **Personal characteristics associated with discrimination**
  - Children with disabilities
- **Features of relationships**
  - Family instability
  - Not enrolled in school

Disparities in adolescent COVID-19 vaccine coverage

National Immunization Survey – Aug 29 – Sept 25, n=1,445

Adolescents 13–17 years



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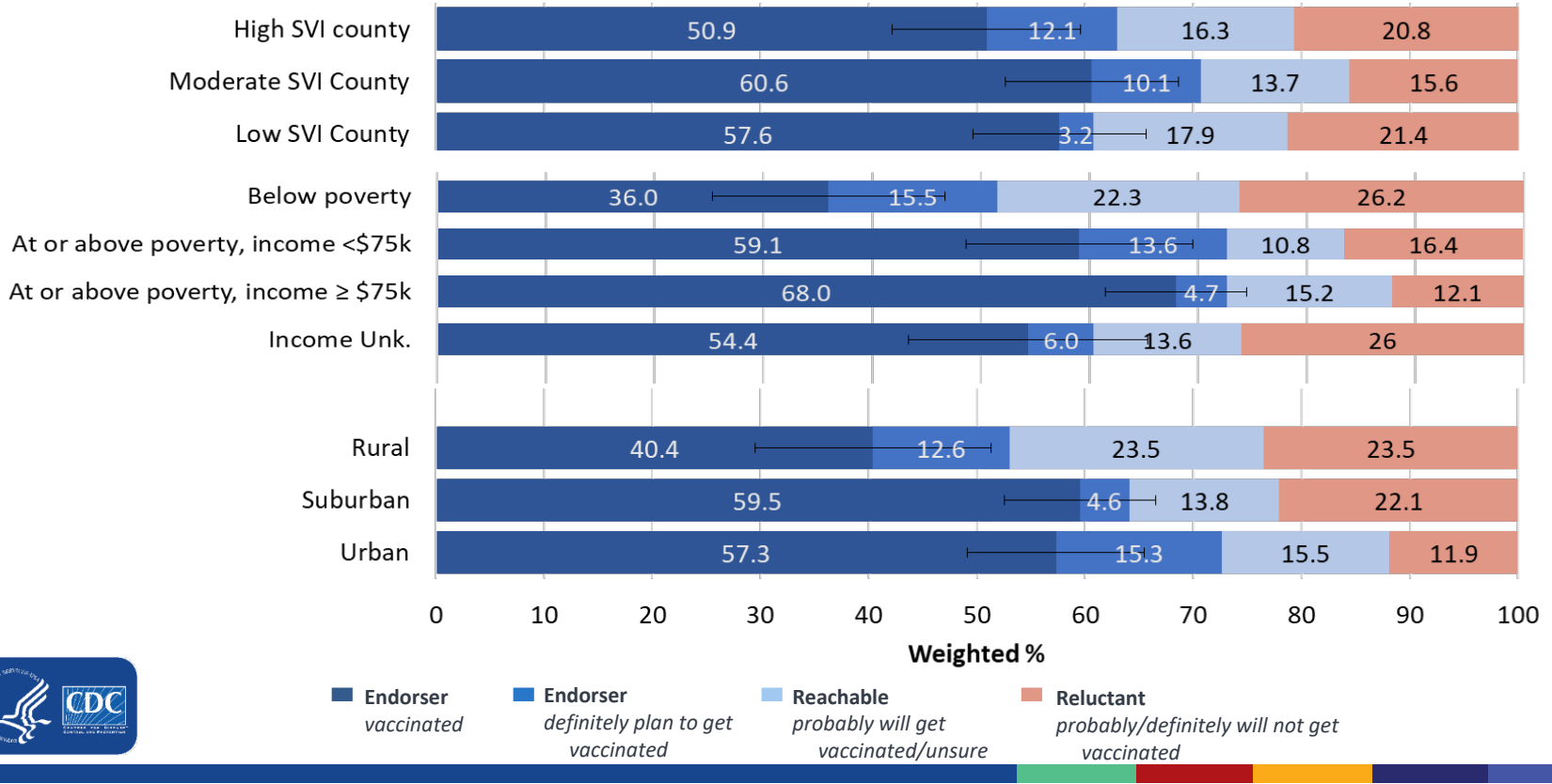


Summary of NIS findings

- Nearly 5 months after adolescent vaccine roll out there remains **unrealized intent** for adolescent COVID-19 vaccinations
  - Largest for adolescents living in poverty and rural areas
- It is critical for CDC and public health partners to redouble efforts for **equitable access** to COVID-19 vaccinations
  - Can include strategies such as **school located** vaccinations

Opportunities to increase equitable access to COVID-19 vaccines

Trusted providers in the **medical home** (primary care providers, FQHCs, rural health clinics, community health centers, children's hospitals)

↑ % VFC providers enrolled
↓ minimum order size
↑ redistribution

Partnerships between schools and pharmacies and local health departments to run **school located vaccination clinics** to improve access for those without a medical home

↑ technical assistance and targeted partnerships

Utilizing the broad reach of **pharmacies**

>60% of adolescents vaccinated received a COVID-19 vaccine through a pharmacy

Equity

What would be the impact of the Pfizer-BioNTech COVID-19 vaccine among children aged 5–11 years on health equity?

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

O Reduced	O Probably reduced	O Probably no impact	
O Probably increased	O Increased	O Varies	O Don't know

Summary

EtR Domain	Question	Work Group Judgments
Public Health Problem	Is COVID-19 disease among children aged 5–11 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?	Favors the intervention
	What is the overall certainty of the evidence for the critical outcomes?	Critical benefits: type 1 Critical harms: type 4
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	Large
	Is there important variability in how patients value the outcomes?	Probably important variability
Acceptability	Is the Pfizer-BioNTech COVID-19 vaccine acceptable to key stakeholders?	Yes
Feasibility	Is the Pfizer-BioNTech COVID-19 vaccine feasible to implement among children aged 5–11 years?	Yes
Resource Use	Is the Pfizer-BioNTech COVID-19 vaccine, given to children aged 5–11 years a reasonable and efficient allocation of resources?	Yes
Equity	What would be the impact of the Pfizer-BioNTech COVID-19 vaccine, given to children aged 5–11 years on health equity?	—

Work Group interpretation

- Vaccine policy decisions made on balance of known benefits and risks to individual
  - Other benefits (prevention of transmission; greater confidence in return to school/social interactions) and risks (extrapolation of myocarditis risk from other ages) part of a broader picture
- Experience with over >400 million doses of mRNA vaccines administered to people 12 years of age and older
- **Benefits** outweigh **risks**
  - Regardless of seropositivity rates, the benefit/risk balance still favorable

Possible impact with vaccination of 5–11-year-old

Prevention of COVID-19 cases

>90%

Likely prevention of COVID-19 related:

Post-COVID conditions

MIS-C

Hospitalization

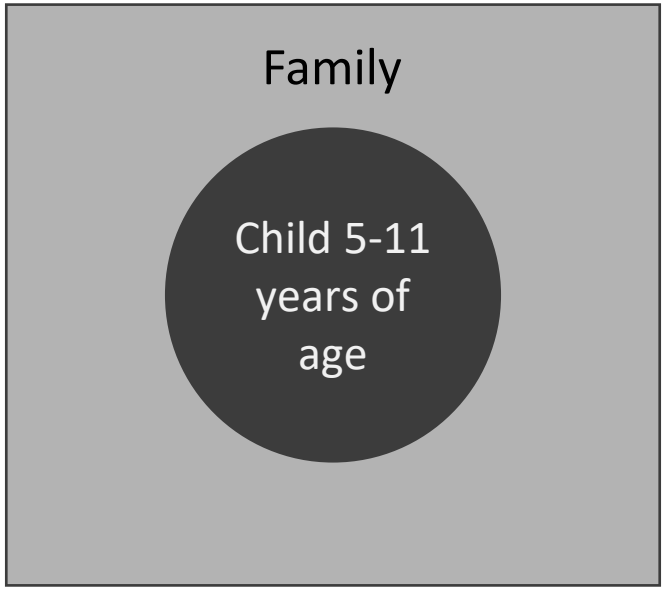
ICU

Death

Possibility for more social interactions and uninterrupted school

Possible impact with vaccination of 5–11-year-old

Possible prevention of transmission to vulnerable family members



Parental participation on work force may be more stable and predicable

Possible impact with vaccination of 5–11-year-old

Could result in **lower transmission** within schools and community

More confident return to in-person learning

Next steps

- As with **all** ages and vaccines, close monitoring of post-authorization safety surveillance is critical and ongoing
- Vaccine recommendations made under EUA are **interim** and will be reviewed at the time of BLA submission
  - At that time, longer follow-up time for children enrolled in clinical trials
  - Can update benefit/risk analysis with additional data from clinical trial, as well as post-authorization safety surveillance
- Continue to evaluate ways to mitigate risks of rare events after vaccination

Plans for post-authorization monitoring of COVID-19 vaccine effectiveness among children 5-11 years of age

	Platform name	Platform details	Outcomes studied: Immunogenicity	Household transmission	Infection	Outpatient	Emergency department/ urgent care	Hospitalization	MIS-C
	PROTECT	Weekly swabbing of 2,000 kids	✓		✓				
	CASCADIA	Weekly swabbing of 715 kids			✓				
	PACC	Weekly swabbing of 400 kids	✓	✓					
	RVTN	Case-ascertained transmission study of 1,500 households		✓	✓				
	ICATT	National pharmacy testing data			✓				
	VISION*	Electronic health records at 458 pediatric hospitals, ED/UCs				✓	✓	✓	
	Overcoming COVID	30-40 pediatric hospitals						✓	✓

First VE estimates may occur as early as 60-90 days after authorization; timelines will depend on vaccine coverage and background rates of disease

PROTECT = Pediatric Research Observing Trends and Exposures in COVID-19 Timelines; ; PACC = Prospective Assessment of COVID-19 in the Community; RVTN = Respiratory Virus Transmission Network; UCSF = University of California, San Francisco; ICATT = Increasing Community Access To Testing partnership

* A cohort design is currently being assembled in a subset of VISION sites.

Summary

Since beginning of the COVID-19 pandemic, among U.S. children 5-11 years of age, there have been

1.9 million cases

8,300 hospitalizations

2,316 MIS-C cases

94 deaths

Summary

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1.9 million cases

8,300 hospitalizations

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94 deaths

COVID-19 is now

vaccine preventable

Evidence to Recommendations Framework

Summary: Work Group Interpretations

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

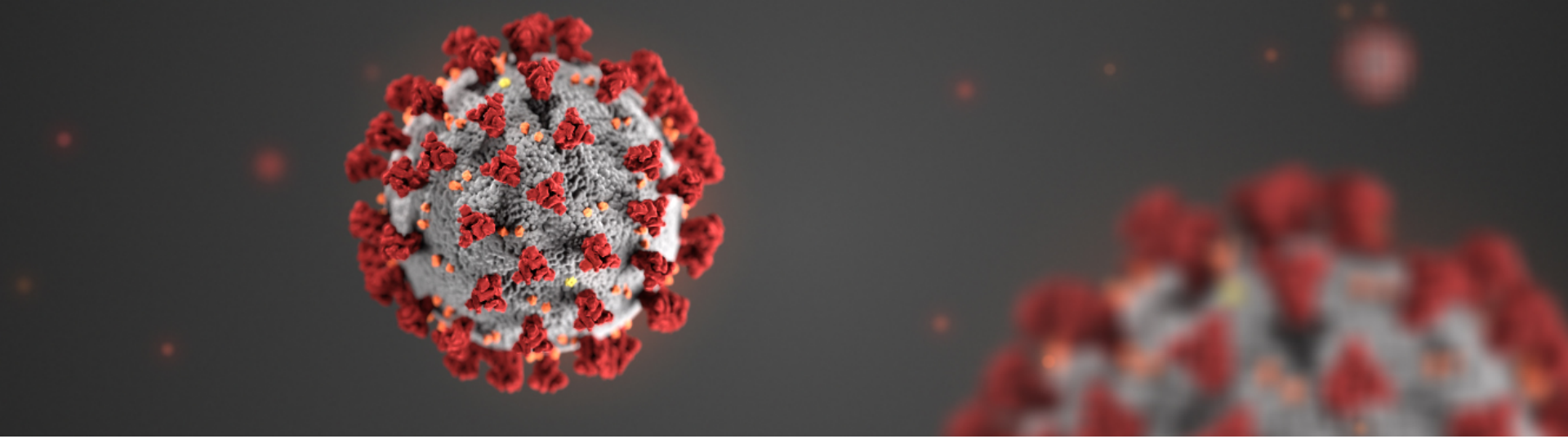
Evidence to Recommendations Framework

Summary: Work Group Interpretations

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

Acknowledgements

- Kate Woodworth
- Danielle Moulia
- Jefferson Jones
- Jennifer Collins
- Steve Hadler
- Jack Gersten
- Eddie Shanley
- Monica Godfrey
- Kathleen Dooling
- Sarah Mbaeyi
- Epi Task Force
  - COVID-NET
  - DVD Enhanced Surveillance
  - Community Surveillance
  - Seroprevalance
- MIS-C unit
- Data, Analytics and Visualization Task Force
- Immunization Services Division
- FluSurv-NET
- Unplanned School Closure Monitoring Project, Division of Global Migration and Quarantine
- Division of Vital Statistics, National Center for Health Statistics



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

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