Pfizer-BioNTech COVID-19 Vaccine in Children aged 5–11 Years

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cdc.gov/coronavirus

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
  - 94 COVID-19 deaths (1.7% of all deaths among U.S. children 5–11 years)
  - 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; 2,316 cases reported among this age group
  - Post-COVID conditions have been reported in children
- Secondary transmission from young school-aged children occurs in household and school settings

COVID-19 Weekly Cases per 100,000 Population by Age — United States, March 1, 2020–October 10, 2021

>1.9 million cases among children 5-11 years of age

Other pediatric vaccine preventable diseases:
Deaths per year prior to recommended vaccines

<table>
<thead>
<tr>
<th>Disease</th>
<th>&lt;20 years</th>
<th>11–18 years</th>
<th>5–9 years</th>
<th>All ages</th>
<th>&lt;5 years</th>
<th>5–11 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A</td>
<td>3</td>
<td>8</td>
<td>16</td>
<td>17</td>
<td>20</td>
<td>66</td>
</tr>
<tr>
<td>Meningococcal (ACWY)</td>
<td>9</td>
<td>20</td>
<td>30</td>
<td>36</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td>Varicella</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>6</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>Rubella</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>COVID-19</td>
<td>2</td>
<td>5</td>
<td>7</td>
<td>9</td>
<td>12</td>
<td>15</td>
</tr>
</tbody>
</table>

Hepatitis A 1, Meningococcal (ACWY) 2, Varicella 3, Rubella 4, Rotavirus 5, COVID-19 6

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

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Unpublished, data obtained from sponsor; randomized 2:1 vaccine to placebo

Data Sources:

Assumptions:

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

<table>
<thead>
<tr>
<th>Recent Epidemiology</th>
<th>Pandemic Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>58,204 COVID-19 cases prevented</td>
<td>18,549 COVID-19 cases prevented</td>
</tr>
<tr>
<td>226 hospitalizations prevented</td>
<td>80 hospitalizations prevented</td>
</tr>
<tr>
<td>132 MIS-C cases prevented</td>
<td>42 MIS-C cases prevented</td>
</tr>
<tr>
<td>72 ICU admissions prevented</td>
<td>26 ICU admissions prevented</td>
</tr>
</tbody>
</table>

Summary
COVID-19 vaccines and seropositivity
Data from Phase 3 clinical trial
- 96% 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
  - Asymptomatic infection can result in lower antibody levels than severe disease

**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

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)
  - 2 SAEs in 2 participants in the vaccine group (n=1518)
  - 2 SAEs in 1 participant in the placebo group (n=750)
- Safety Expansion Group (median follow-up time: 2.4 weeks)
  - 5 SAEs in 3 participants in the vaccine group (n=1591)
  - 2 SAEs in 1 participant in the placebo group (n=788)

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 1.3% in the placebo arm had a local or systemic grade ≥3 reaction after either dose
  - Most reactions were grade 1; 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

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

Vaccine-associated pancreatitis
- 132 participants in 5-11 year old clinical trial were baseline SARS-CoV-2 seropositive
- Incidence of pancreatitis in the seropositive group was 1 case of grade 3 pancreatitis (n=268) and 6 cases of grade 1 pancreatitis (n=268) in the seropositive group

MIS-C cases prevented
- Delta-wave surges of pediatric COVID-19 hospitalizations occurred even with seroprevalence ~38%, suggesting this alone is not sufficient to provide broad protection

Seropositivity
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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-olds 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)

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

Parental surveys

Intent to have children vaccinated
- Among parents surveyed, 34–57% plan to get their children vaccinated
- 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’
- 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
- 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

Formulation and Dosing for Pfizer-BioNTech COVID-19 Vaccines

<table>
<thead>
<tr>
<th>Age group</th>
<th>Formulation for ≥12-year-olds (purple cap)</th>
<th>Formulation for 5-11-year-olds (orange cap)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vial cap color</td>
<td>Purple</td>
<td>Orange</td>
</tr>
<tr>
<td>Dose (mRNA concentration)</td>
<td>30µg</td>
<td>10µg</td>
</tr>
<tr>
<td>Injunct volume</td>
<td>0.3 mL</td>
<td>0.2 mL</td>
</tr>
<tr>
<td>Fill volume (before dilution)</td>
<td>0.45 mL</td>
<td>1.3 mL</td>
</tr>
<tr>
<td>Amount of diluent needed per vial</td>
<td>1.8 mL</td>
<td>1.3 mL</td>
</tr>
<tr>
<td>Doses per Visit</td>
<td>6 (after dilution)</td>
<td>10 (after dilution)</td>
</tr>
</tbody>
</table>

*Diluent: 0.9% sterile Sodium Chloride Injection, USP (non-bacteriostatic; DO NOT USE OTHER DILUENTS)

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</tr>
</thead>
<tbody>
<tr>
<td>Interval</td>
<td>3 weeks (21 days)</td>
<td>3 weeks (21 days)</td>
</tr>
<tr>
<td>Additional primary dose</td>
<td>Moderate and severe immunocompromise</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>
| Booster dose    | Not recommended 12–17 years      | Recommended for certain groups ≥18 years

*Individuals 12 years and older or individuals ages 8 and older with long-term care facilities, long-term care institutional or high-risk settings, have underlying medical conditions, or who work in high-risk settings. (Michalski E, Olthof MC, Coffin L, et al. The Advisory Committee on Immunization Practices’ Interim Recommendations for Additional Primary and Booster Doses of COVID-19 Vaccines—United States, 2021. MMWR Morb Mortal Wkly Rep. ePub: 22 October 2021)
**Vaccine Dosage**

- Children should receive the age-appropriate vaccine formulation regardless of their size or weight.
  - As opposed to many medications, vaccine dosages are based on age and not size or weight.
- The dosage should be based on the child’s age on the day of vaccination.
  - If a child turns from 11 to 12 years of age in between their first and second dose and receives the 5–11 years 10 µg (orange cap) for their second dose, they do not need to repeat the dose and this is not considered an error under the EUA.

**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

COVID-19 is now vaccine preventable

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**ACIP Vote – Interim Recommendation**

The Pfizer-BioNTech COVID-19 vaccine is recommended for children 5–11 years of age in the U.S. population under the FDA’s Emergency Use Authorization.