Use of 20-Valent Pneumococcal Conjugate Vaccine Among U.S. Children: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2023

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Summary

This report compiles and summarizes published recommendations from CDC's Advisory Committee on Immunization Practices (ACIP) for use of pneumococcal vaccines in children and adolescents aged <19 years in the United States. This report also includes new or updated clinical guidance for implementation from CDC.

The 13-valent pneumococcal conjugate vaccine (PCV13 [Prevnar 13, Wyeth Pharmaceuticals, Inc, a subsidiary of Pfizer, Inc]), 15-valent pneumococcal conjugate vaccine (PCV15 [Vaxneuvance, Merck Sharp & Dohme LLC]) and 23-valent pneumococcal polysaccharide vaccine (PPSV23 [Merck Sharp & Dohme LLC]) have been recommended for U.S. children. In April 2023, the Food and Drug Administration (FDA) approved an expanded use for 20-valent pneumococcal conjugate vaccine (PCV20 [Prevnar 20, Wyeth Pharmaceuticals, Inc, a subsidiary of Pfizer, Inc]) to include persons aged 6 weeks–17 years. In addition to serotypes included in PCV15, PCV20 also includes serotypes 8, 10A, 11A, 12F, and 15B conjugated to CRM197 (genetically detoxified diphtheria toxin). On June 22, 2023, CDC's ACIP recommended use of PCV20 as an option to PCV15 for: routine vaccination of all children aged 2–23 months; catch-up vaccination for healthy children aged 24–59 months who have not received age-appropriate doses; and children aged 24–71 months with certain underlying medical conditions at increased risk for pneumococcal disease who have not received age-appropriate doses. In addition, recommendations were updated for children aged 2–18 years with any risk conditions. Indications for risk-based pneumococcal vaccine recommendations were expanded to include children with chronic kidney disease (even if not on maintenance dialysis or nephrotic syndrome), chronic liver disease, and moderate persistent or severe persistent asthma (regardless of high-dose oral corticosteroids use).

Introduction

Despite the success of the pneumococcal vaccine program in the United States, *Streptococcus pneumoniae* continues to be a common bacterial etiology of acute respiratory infections among persons aged <19 years, including pneumonia and acute otitis media (AOM), and invasive diseases such as bacteremia and meningitis. Prior to the COVID-19 pandemic, the 2018–2019 incidence of invasive pneumococcal disease (IPD) in the United States was 7.2 per 100,000 children aged <5 years and 1.5 per 100,000 children aged 5–18 years. PCV13 serotypes accounted for 21% of IPD in children aged <5 years; additional serotypes included in PCV20, but not in PCV13 (PCV20-non-PCV13 serotypes), accounted for 32% of IPD in children aged <5 years. In children aged 5–18 years, IPD caused by PCV13 serotypes and the PCV20 non-PCV13 serotypes accounted for 34% and 29% of IPD, respectively (1). Estimated

incidence in children due to non-invasive pneumococcal disease is higher than invasive disease, with an estimated incidence of pediatric AOM medical visits attributable to PCV20 non-PCV13 (including serotype 15C that may not be distinguished from serotype 15B in some laboratory methods) serotypes of 5.4-7.4 per 1000 person-years (2).

PCV13 was licensed and recommended for use in children in 2010, replacing 7-valent pneumococcal conjugate vaccine (PCV), first introduced in 2000 (3). In 2022, the FDA approved an expanded use of PCV15 for children and ACIP recommended PCV15 as an option to PCV13 for pneumococcal conjugate vaccination. Either PCV13 or PCV15 has been recommended for routine use in children 2 through 59 months of age. These vaccines have also been recommended for children 60 through 71 months with certain underlying medical conditions at increased risk for pneumococcal disease (hereafter, risk conditions*) and children 6 through 18 years with an immunocompromising condition†, cerebrospinal fluid leak, or cochlear implant; PPSV23 has been recommended for children 2 through 18 years with risk conditions. On April 27, 2023, FDA approved an expanded use for PCV20 to include persons aged 6 weeks–17 years, based on studies that compared safety and antibody responses to PCV20 with those to PCV13 (4).

On June 22, 2023, ACIP voted to approve the following recommendations regarding use of PCV20 as an option to PCV15:

- All children aged 2–23 months with no previous PCV vaccination are recommended to receive either PCV15 or PCV20 according to currently recommended PCV dosing and schedules.
- Children aged 24–71 months with an incomplete vaccination status using either PCV13, PCV15, or PCV20 are recommended to receive either PCV15 or PCV20 according to currently recommended PCV dosing and schedules.
    - Healthy children aged 24–59 months with any incomplete PCV vaccination status are recommended to receive a single dose of either PCV15 or PCV20 at least 8 weeks after the last PCV dose.
    - Children aged 24–71 months with any risk condition who have not previously received a PCV or received any incomplete schedule of <3 doses by age 24 months, 2 doses of either PCV15 or PCV20 are recommended at least 8 weeks apart between PCV doses.
    - Children aged 24–71 months with any risk condition who have received 3 doses of PCV, all before 12 months, are recommended to receive one dose of either PCV15 or PCV20 at least 8 weeks after the last PCV dose.
- For children 2–18 years with any risk condition who completed recommended PCV series before age 6 years,
    - if the recommended PCV doses were completed with ≥1 dose of PCV20, no additional doses of any pneumococcal vaccine are indicated. This recommendation may be updated as additional data become available.
    - if the recommended PCV doses were completed using PCV13 or PCV15 (no PCV20), either a dose of PCV20 or ≥1 dose of PPSV23 is recommended to complete the recommended vaccine series.

        - When PPSV23 is used instead of PCV20 for children aged 2–18 years with an immunocompromising condition, either PCV20 or a second PPSV23 dose is recommended ≥5 years after the first PPSV23 dose.
    - For children aged 6–18 years with any risk condition who have not received any dose of PCV13, PCV15 or PCV20, a single dose of PCV15 or PCV20 is recommended ≥8 weeks after the most recent dose of pneumococcal vaccination.
        - When PCV15 is used, it should be followed by a dose of PPSV23 at least 8 weeks after the last PCV dose, if not previously given.
    - Indications for risk-based recommendations were expanded to include: children with chronic kidney disease (even if not on maintenance dialysis or nephrotic syndrome), chronic liver disease, and moderate persistent or severe persistent asthma (regardless of high-dose oral corticosteroids use).

The following is new CDC guidance for implementation:

- If only PCV13 is available when the child is scheduled to receive a PCV, PCV13 may be given as previously recommended.
- If a child started the PCV series with PCV13, the child may complete the series with PCV15 or PCV20 without giving additional doses; the PCV series does not need to be restarted.
- For healthy children aged 24-59 months who completed recommended PCV vaccination series with PCV13 (i.e., 4 doses of PCV13 or another age-appropriate PCV13 schedule), a supplemental dose of PCV15 or PCV20 is not indicated.
- For children aged 6–18 years with a risk condition who have received PCV13 only at or after age 6 years, either a dose of PCV20 or ≥1 dose of PPSV23 is recommended at least 8 weeks after the last PCV13 dose.
    - When PPSV23 is used instead of PCV20 for children aged 6–18 years with an immunocompromising condition, either PCV20 or a second PPSV23 dose is recommended ≥5 years after the first PPSV23 dose.
- Children aged <19 years who are hematopoietic stem cell transplant (HSCT) recipients are recommended to receive 4 doses of PCV20, starting 3–6 months after HSCT. Administer 3 doses of PCV20, 4 weeks apart starting 3–6 months after HSCT. Administer a fourth PCV20 dose ≥6 months after the third dose of PCV20 or ≥12 months after HSCT, whichever is later.
    - If PCV20 is not available, 3 doses of PCV15 4 weeks apart, followed by a single dose of PPSV23 ≥1 year after HSCT, can be administered. For patients with chronic graft versus host disease (GVHD) who are receiving PCV15, a fourth dose of PCV15 can be administered in place of PPSV23 because these children are less likely to respond to PPSV23.
    - A patient's clinical team is best informed to determine the appropriate timing of vaccination.

Methods

During February–June 2023, ACIP reviewed the epidemiology of pneumococcal disease and considerations for use of PCV20 in children. The ACIP Pneumococcal Vaccines Work Group defined

critical outcomes to assess the benefits and harms of PCV20 use in children. After a systematic review of the literature, the Work Group used grading of recommendations, assessment, development, and evaluation (GRADE) to assess certainty of evidence for PCV20 immunogenicity and safety rated on a scale from high certainty to very low certainty. [§] The literature search protocol, including the databases, years searched, and criteria used to select studies are described in the GRADE tables. ACIP employed the Evidence to Recommendation (EtR) Framework[¶] to guide its deliberations regarding use of PCV20 and considered the importance of the public health problem, benefits and harms, the target population's values and preferences, resource use, equity, acceptability, and feasibility of PCV20 use. This report updates previous pneumococcal vaccine recommendations for use in children (3, 5).

Pneumococcal Disease Epidemiology in Persons Aged <19 Years

Invasive Pneumococcal Disease after the COVID-19 Pandemic

Data from CDC's Active Bacterial Core surveillance showed that at the onset of the COVID-19 pandemic, overall IPD incidence in children decreased by >50% in 2020 compared with 2018–2019, consistent with decreased bacterial infections likely due to masking and physical distance measures (6). IPD incidence in children aged <5 years increased in 2021 compared with 2020, although the incidence remained below the pre-pandemic baseline; incidence in children aged 5–18 years in 2021 remained unchanged (1). Preliminary IPD incidence data from 2022 showed that the incidence in November and December exceeded the incidence by ≥50% compared with 2018–2019 in both age groups (7).

Estimated Burden of Acute Respiratory Illness in Children

S. pneumoniae is a common bacterial cause of acute respiratory illness (ARI) in children, such as pneumonia and acute otitis media (AOM) (8, 9). ARIs are the leading cause of outpatient healthcare utilization and antibiotic use among children (10, 11); however, data on the burden preventable by pneumococcal vaccines are limited. Nationally representative surveys and insurance claims data were used to estimate the burden of outpatient pneumonia visits in U.S. children aged <18 years from 2016–2018. Published literature was used to estimate the proportion of pneumonia visits attributable to pneumococcal vaccine serotypes (2). Prior to the COVID-19 pandemic, the estimated incidence of outpatient pneumonia visits attributable to any pneumococcal serotype was 5.5 per 1000 person-years, with rates higher among children aged <2 years compared to children aged 2–4 years (11.5 vs. 0.3 per 1000 person-years, respectively); estimated incidence of pneumonia visits attributable to PCV20 non-PCV13 serotypes (including serotype 15C) was 0.6 to 0.9 per 1000 person-years (2). Data from years post-COVID-19 pandemic are not yet available. While data on serotype distribution of all-cause pneumonia are available, data for non-bacteremic pneumococcal pneumonia in U.S. children are limited due to limitations with diagnostic capacities.

In the above mentioned analysis estimating the burden of outpatient pneumonia visits in U.S. children, AOM was also studied; the estimated incidence of AOM visits attributable to PCV20 non-PCV13 serotypes was 5.4 to 7.4 per 1000 person-years (2). A prospective, longitudinal study evaluating AOM in children aged <3 years in New York during 2015–2019 estimated 24% of clinically diagnosed AOM was attributed to *S. pneumoniae*; among those, 28% were caused by PCV20 non-PCV13 serotypes (including serotype 15C) (8).

Pneumococcal Disease Epidemiology in Children with Risk Conditions

Data on pneumococcal disease among children with risk conditions in the post-PCV13 era are limited. A study using healthcare claims data during 2007–2010 found that children with risk conditions, especially those with an immunocompromising condition or a cochlear implant, had increased rates of pneumococcal disease. Among children aged <5 years in this risk group, IPD rates were 11.2 times higher than among children the same age without risk factors; rates of pneumococcal pneumonia were 6.8 times higher among children with risk conditions compared to children without risk conditions. Among children aged 5–17 years in this same risk category, IPD rates were 40 times higher and rates of pneumococcal pneumonia were 10 times higher compared to children without risk conditions. (12)

Children with certain underlying medical conditions that were not an indication for pneumococcal vaccination under previous recommendations (13) have an increased risk of pneumococcal disease. Children with asthma without oral corticosteroid use had 1.8–2.2 times higher pneumococcal pneumonia rates compared with children without risk conditions (12). A case-control study of Tennessee Medicaid recipients aged 2–49 years reported that asthma is an independent risk factor for IPD (adjusted odds ratio: 2.4; 95% confidence interval [CI]: 1.9–3.1) (14). In a case-control study of children aged 3–59 months, IPD case-patients had 3.6 times the odds of having chronic kidney disease (not on dialysis) compared with age-matched community controls (15). Analyses using healthcare claims data showed that children with chronic liver disease aged <5 years had 18.5 times the risk of IPD and children aged <18 years had 7.0–7.8 times the risk of pneumococcal pneumonia compared with children in the same age group without risk conditions (12). A summary of pneumococcal disease epidemiology of IPD, pneumonia, and AOM in persons aged <19 years of age with and without risk conditions is available in the EtR documents [https://www.cdc.gov/vaccines/acip/recs/grade/PCV20-child-risk-based-etr.html; https://www.cdc.gov/vaccines/acip/recs/grade/PCV20-child-etr.html].

PCV20 immunogenicity

One phase II and one phase III randomized controlled trial (RCT) evaluated the immunogenicity of PCV20 in a 4-dose series compared with PCV13 in healthy children aged <2 years (16, 17). Healthy infants 42–98 days old at time of consent were enrolled and given a dose of PCV20 or PCV13 at age 2, 4, 6, and 12–15 months. Serotype-specific immunoglobulin G (IgG) geometric mean concentrations (GMCs) and opsonophagocytic activity (OPA) titers (in a randomly selected subset of participants as there is no established correlate of protection for OPA antibodies in children) were measured 30 days after dose 3 and 4. The RCTs showed numerically lower antibody responses against the PCV13 serotypes in the PCV20 group compared with PCV13. In the phase II RCT, IgG GMCs in the PCV20 group after dose 3 and 4 were numerically lower compared with the PCV13 group for the 13 shared serotypes and higher for the 7 PCV20 non-PCV13 serotypes (17). In the phase III trial, PCV20 met the non-inferiority criteria**,†† for 8 of 13 PCV13 serotypes (missed for serotypes 1, 3, 4, 9V, and 23F) and 6 of 7 PCV20 non-PCV13 serotypes (missed for serotype 12F) as measured by the percentage of participants with IgG concentrations above predefined concentrations after dose 3; PCV20 met the non-inferiority criteria§§ for all 13 shared serotypes and 7 unique serotypes as measured by IgG GMC ratios after doses 3 and 4. OPA geometric mean titers (GMTs) after dose 3 were numerically similar across the study groups for the 5 shared serotypes (1, 3, 4, 9V and 23F) that failed to meet the post-dose 3 non-inferiority criterion endpoint based on percentage of responders. An OPA antibody response was generated for serotype 12F. After dose 4, OPA GMTs were numerically similar (overlap in 95% confidence intervals) between

the PCV20 and PCV13 group for the 13 shared serotypes, except being lower in the PCV20 group for serotypes 1 and 3 (16).

One single-arm phase III clinical trial of a single PCV20 dose in healthy children aged 15 months through 17 years (all children aged <5 years had documentation of previous receipt of ≥3 doses of PCV13) showed that serotype-specific IgG GMCs were numerically higher 1-month post-PCV20 dose compared with before vaccination for the 13 shared serotypes and 7 unique serotypes (18). Serotype-specific OPA GMTs for the 13 shared serotypes were measured in a randomly selected subset of participants in all groups. For the 7 additional PCV20 non-PCV13 serotypes, OPA GMTs were measured in a random subset of participants in the 15 months to <5 years age groups and all participants in the 5 to 17 years age groups. OPA GMTs were numerically higher for all 20 serotypes across all age groups one month after vaccination with one PCV20 dose compared to before vaccination. No study evaluated PCV20 immunogenicity in children with risk conditions.

PCV20 safety

Safety of PCV20 was assessed in four clinical trials, three in 3,949 healthy children aged <2 years (2,232 who received PCV20 and 1,717 who received PCV13) (16, 17, 19) and one in 831 healthy children aged 15 months through 17 years (18). In the phase III RCT among healthy infants, any prompted local reaction (i.e., injection site redness, swelling and pain) ≤7 days after each dose was reported in 44.8–59.8% and 45.9–56.5% of the PCV20 and PCV13 group, respectively; any prompted systemic reaction (i.e., fever, decreased appetite, irritability, drowsiness/increased sleep) ≤7 days after each dose was reported in 35.1–40.7% and 33.8–41.0% of the PCV20 and PCV13 group, respectively (16, 20). Most adverse reactions were mild to moderate; ≤0.4% and ≤4.5% were severe, local and systemic reactions, respectively. Across three trials assessing safety of 4-dose PCV series in children aged <2 years, serious adverse events (SAEs) ≤6 months after the fourth PCV dose were reported in 101 of 2,232 participants (4.5%) in the PCV20 group and 64 of 1,717 (3.7%) participants in the PCV13 group; there were no notable patterns or imbalances between vaccine groups for specific categories of SAEs that would suggest a causal relationship to PCV20. No deaths due to vaccination were reported (16, 17, 19). The single-arm trial in children 15 months through 18 years reported SAEs in 5 of 831 (0.6%) ≤6 months after PCV20 vaccination; no deaths due to PCV20 vaccination were reported (18). Across all four trials assessing safety in healthy infants or children, febrile seizures were reported in 7 (0.2%) in the PCV20 group and 2 (0.1%) in the PCV13 group. Two febrile seizures were considered to be possibly associated with PCV20 vaccination: one febrile seizure occurred 14 days after the fourth PCV20 dose given with measles, mumps, and rubella and varicella vaccines; another febrile seizure occurred 7 days after the fourth PCV20 dose in a child who was diagnosed with COVID-19; all other febrile seizures occurred >30 days after vaccination.

Cost-effectiveness

Three economic models (Tulane-CDC, Merck, and Pfizer models) assessed the cost-effectiveness of the use of PCV20 (21). In the assessment of the 4-dose series for all children aged <2 years, PCV20 was compared separately to PCV15 and PCV13; base case cost-effectiveness estimates when replacing PCV13 or PCV15 with PCV20 ranged from cost saving [¶¶] to $125,000 for an additional quality adjusted life year (QALY) gained (https://www.cdc.gov/vaccines/acip/recs/grade/PCV20-child-etr.html). In the assessment of PCV20 use among children with risk conditions aged 2 through 18 years, the models varied in their comparisons. The Tulane-CDC and Merck models compared a 4-dose series of PCV20 to 4

doses of either PCV13 or PCV15 followed by 1-2 doses of PPSV23 for children with risk conditions. The Pfizer model compared 1 dose of PCV20 to 1-2 doses of PPSV23 among a cohort of children aged 6 years old with risk conditions who received PCV13. Results from base case across all three models found the use of PCV20 to be cost-saving (https://www.cdc.gov/vaccines/acip/recs/grade/PCV20-child-etr.html).

Rationale for Recommendations

Including PCV20 as an option for pneumococcal vaccination in children is expected to provide protection against additional vaccine serotypes that cause disease and reduce incidence of PCV20-type IPD, pneumonia, and AOM. The RCTs evaluating immunogenicity of PCV20 showed numerically lower antibody responses against the PCV13 serotypes in the PCV20 group compared with PCV13, although clinical implications are unknown. Reported safety in the PCV20 group was comparable with that of PCV13 recipients. There are no studies that have directly compared the safety and immunogenicity of PCV20 with PCV15. Base case cost-effectiveness estimates for PCV20 use only without PPSV23 were cost-saving compared with PCV13 and PCV15 followed by PPSV23 in those with risk conditions; however, uncertainties in the estimates remain since there are no data on PCV20 use in children with risk conditions. Pneumococcal Vaccines Work Group discussions on the use of PCV20 for pneumococcal vaccination in children are summarized in the EtR tables.

Recommendations for Use of PCV

On June 22, 2023, CDC's ACIP voted unanimously on recommendations regarding the use of PCV20 as an option for pneumococcal conjugate vaccination for children; these recommendations are summarized below. Use of either PCV15 or PCV20 is recommended for all children aged 2–23 months according to previously recommended PCV dosing and schedules. Risk-based recommendations for pneumococcal vaccine use in PCV-unvaccinated children with risk conditions were updated.

Children aged 2–23 months with no previous PCV vaccination

Use of either PCV15 or PCV20 is recommended for all children aged 2–23 months according to currently recommended PCV dosing and schedules. (Table 1)

Rationale

A phase III clinical trial evaluated the immunogenicity of PCV20 in a 4-dose series compared with PCV13 in healthy children aged <2 years (16, 17). Healthy infants 42–98 days old at time of consent were enrolled and given a dose of PCV20 or PCV13 at age 2, 4, 6, and 12–15 months. PCV20 effectiveness (against invasive pneumococcal disease due to the 20 vaccine serotypes and otitis media due to serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) in individuals 6 weeks through 15 months of age was demonstrated based on comparisons of serotype-specific antibody responses after PCV20 to the antibody responses after vaccination with PCV13. Safety was evaluated for healthy children aged <2 years in three trials and safety profiles were considered comparable to PCV13. One serious febrile seizure event was considered possibly related to PCV20; no deaths were associated with PCV20 vaccination. Including PCV20 as an option for pneumococcal vaccination in children is expected to provide protection against additional vaccine serotypes that cause disease.

Base-case estimates from economic models assessing PCV20 use as a 4-dose series in children <2 years compared to PCV13 or PCV15 ranged from cost-saving to $125,000 for an additional QALY gained.

Children aged 24–71 months with an incomplete PCV vaccination status

For healthy children aged 24–59 months with an incomplete PCV vaccination status using either PCV13, PCV15, or PCV20, a single dose of either PCV15 or PCV20 is recommended. Routine use of PCV is not recommended for healthy children aged ≥5 years (Table 2).

For children aged 24–71 months with any risk condition (Table 3) who have not previously received a PCV or received any incomplete schedule of <3 doses by age 24 months, 2 doses of either PCV15 or PCV20 are recommended at least 8 weeks apart between PCV doses.

For children aged 24–71 months with any risk condition who have received 3 doses of PCV, all before 12 months, one dose of either PCV15 or PCV20 is recommended at least 8 weeks after the last PCV dose.

Rationale

A single-arm phase III clinical trial in healthy children aged 15 months through 17 years assessed immunogenicity and safety of a single dose of PCV20. All children aged <5 years had documentation of previous receipt of ≥3 doses of PCV13. Serotype-specific IgG GMCs were numerically higher 1-month post-PCV20 dose compared with before vaccination for the 13 shared serotypes and 7 unique serotypes. OPA GMTs, which were the primary endpoint for children 5 to 17 years of age, were numerically higher for all 20 serotypes one month after vaccination with one PCV20 dose compared to before vaccination. SAEs were reported in 5 of 831 (0.6%) participants ≤6 months after PCV20 vaccination; no deaths due to PCV20 vaccination were reported.

In assessing PCV20 use in children with risk conditions, economic models varied in comparisons. However, results from base case across all three models found the use of PCV20 to be cost-saving.

Children 2–18 years with any risk condition who completed recommended PCV series before age 6 years (Table 3)

For children aged 2–18 years with any risk condition who have received all recommended doses of PCV (including ≥1 dose of PCV20) before age 6 years, no additional doses of any pneumococcal vaccine are indicated (Figure 1 and 2). This recommendation may be updated as additional data become available.

For children aged 2–18 years with any risk condition who have received all recommended doses of PCV using PCV13 or PCV15 (no PCV20), either a dose of PCV20 or ≥1 dose of PPSV23 is recommended at least 8 weeks after the last PCV dose to complete the recommended vaccine series (Table 3 and Figure 1). When PPSV23 is used instead of PCV20 for children aged 2–18 years with an immunocompromising condition, either PCV20 or a second PPSV23 dose is recommended ≥5 years after the first PPSV23 dose (Figure 2).

Rationale

There are no PCV20 phase II and phase III trials among children with risk conditions. In a single arm clinical trial that assessed immunogenicity of a single dose of PCV20 in children of 15 months through 17 years, serotype-specific IgG GMCs were numerically higher post-PCV20 compared pre-PCV20 dose. Similarly, OPA GMTs, the primary endpoint for children 5 to 17 years of age, were numerically higher for all 20 serotypes one month after vaccination with one PCV20 dose compared to before vaccination.

Regarding safety, SAEs occurred in 0.6% (5 of 831) ≤6 months after PCV20 vaccination; no deaths related to PCV20 vaccination were reported. Limited PCV13 effectiveness data from observational studies that included children with underlying medical conditions showed that PCV13 confers protection against PCV13-type IPD (22) and PCV13-type pneumonia (23).

Economic models showed base case cost-effectiveness estimates for PCV20 use only without PPSV23 were cost-saving compared with PCV13 or PCV15 followed by PPSV23 among children aged 2–18 years with risk conditions; however, uncertainties in the estimates remain since there are no data on PCV20 use in children with risk conditions.

Children 6–18 years with any risk condition with no previous PCV13, PCV15, or PCV20 vaccination (Table 3)

For children aged 6–18 years with any risk condition who have not received any dose of PCV13, PCV15 or PCV20 a single dose of PCV15 or PCV20 is recommended ≥8 weeks after the most recent dose of pneumococcal vaccination, regardless of whether the child has previously received PPSV23, even if PCV7 was received. When PCV15 is used, it should be followed by a dose of PPSV23 if not previously given. When PCV20 is used, it does not need to be followed by a dose of PPSV23.

Rationale

Previously, children aged 6–18 years with a risk condition who have not received PCV were not recommended to receive PCV unless they had an immunocompromising condition, cerebrospinal fluid leak, or cochlear implant. Instead, they were recommended to receive a single dose of PPSV23 (5). Despite the high PCV coverage in the United States (24), a study using administrative data reported that children aged 5–17 years with non-immunocompromising risk conditions (e.g., asthma, chronic heart disease, chronic liver disease, chronic lung disease, diabetes) had 2–10 times the risk of IPD and 3–7 times the risk of pneumococcal pneumonia compared with children without these conditions (12). While the proportion of children aged 6–18 years with risk conditions who have not received PCV is considered to be small, recommending PCV is expected to provide additional protection for these children at increased risk of pneumococcal disease. In addition, the updated recommendation harmonizes the recommendations across different risk groups as well as with the current pneumococcal vaccine recommendations for adults aged 19–64 years who have indications for risk-based recommendations (25).

TABLE 1. CDC Advisory Committee on Immunization Practices Recommendations for use of PCV in children, June 2023

Age and Risk group	Recommendations
Children aged <24 months	• Use of either PCV15 or PCV20 is recommended for all children aged 2–23 months according to previously recommended PCV dosing and schedules. • If only PCV13 is available when the child is scheduled to receive a PCV, PCV13 may be given as previously recommended. • If a child started the PCV series with PCV13, the child may complete the series with PCV15 or PCV20 without giving additional doses; the PCV series does not need to be restarted. • For children who have received all recommended dosing and schedules with PCV13 or PCV15, a supplemental dose of PCV20 is not indicated.
Healthy children aged 24–59 months with an incomplete PCV vaccination status*	• A single dose of either PCV15 or PCV20 is recommended. • A supplemental dose of PCV15 or PCV20 is not indicated for healthy children who have received 4 doses of PCV13 or who completed another age-appropriate PCV13 schedule.
Children aged 24–71 months with any risk condition†	• Use either PCV15 or PCV20 according to previously recommended PCV dosing and schedules. • If only PCV13 is available when the child is scheduled to receive a PCV, PCV13 may be given as previously recommended.
Children aged 2–18 years with any risk condition who completed a recommended PCV series before age 6 years	Completed series includes ≥1 dose of PCV20: • No additional doses of any pneumococcal vaccine are indicated. • This recommendation may be updated as additional data become available. Completed series using PCV13 or PCV15 (no PCV20): • Either a single dose of PCV20 or PPSV23 using previously recommended dosing and schedules is recommended to complete the recommended vaccine series.
Children aged 6–18 years with any risk condition with no previous PCV13, PCV15, or PCV20 vaccination	• For children aged 6–18 years with any risk condition who have not received any dose of PCV (PCV13, PCV15, or PCV20) a single dose of either PCV15 or PCV20 is recommended. • If the child has previously received PCV7 and/or PPSV23, a single dose of either PCV15 or PCV20 is recommended ≥8 weeks after the most recent dose of pneumococcal vaccination. o PCV15 should be followed by a dose of PPSV23 if not previously given. o PCV20 does not need to be followed by a dose of PPSV23.
Children who have received HSCT	• Children who received HSCT are recommended to receive three doses of PCV20, 4 weeks apart starting 3–6 months after HSCT. • A fourth PCV20 dose is recommended ≥6 months after the third PCV20 dose, or ≥12 months after HSCT, whichever is later. • HSCT recipients who have started their pneumococcal vaccine series with PCV13 or PCV15 may complete their 4-dose pneumococcal vaccine series with PCV20 without giving extra doses. • If PCV20 is not available, three doses of PCV15, 4 weeks apart starting 3–6 months after HSCT, followed by a dose of PPSV23 ≥12 months after HSCT may be given. • For patients with chronic graft-versus-host disease who are receiving PCV15, a fourth dose of PCV15 can be given in place of PPSV23 since these children are less likely to respond to PPSV23. A patient's clinical team is best positioned to determine the appropriate timing of vaccination.

Abbreviations: PCV = pneumococcal conjugate vaccine; PCV13 = 13-valent PCV; PCV15 = 15-valent PCV; PCV20 = 20-valent PCV; PPSV23 = 23-valent pneumococcal polysaccharide vaccine; HSCT = hematopoietic stem cell transplant.

*Routine use of PCV is not recommended for healthy children aged ≥5 years

† Risk conditions include: cerebrospinal fluid leak; chronic heart disease; chronic kidney disease (excluding maintenance dialysis and nephrotic syndrome, which are included in immunocompromising conditions); chronic liver disease; chronic lung disease (including moderate persistent or severe persistent asthma); cochlear implant; diabetes mellitus; immunocompromising conditions (on maintenance dialysis or with nephrotic syndrome; congenital or acquired asplenia or splenic dysfunction; congenital or acquired immunodeficiencies; diseases and conditions treated with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, Hodgkin disease, and solid organ transplant; HIV infection; and sickle cell disease or other hemoglobinopathies). Children with these conditions who received PCV13 or PCV15 are also recommended to receive 23-valent pneumococcal polysaccharide vaccine.

TABLE 2. Recommendations for administering pneumococcal conjugate vaccine* to children, by age at visit, health status, and vaccination history — United States, 2023

Age at visit/Health status	No. of previous PCV13/PCV15/PCV20 doses received	Recommended PCV15/PCV20 regimen*,†	No. of PCV13/PCV15/ PCV20 doses needed to complete series by age 24 mos
All children (healthy and those with risk conditions)			
2–6 mos	0	4 doses: 3 doses, 8 wks apart; last dose at age 12–15 mos	4
	1	3 additional doses: 2 doses, 8 wks apart; last dose at age 12–15 mos	4
	2	2 additional doses: 1 dose 8 wks after most recent dose; last dose ≥8 wks later at age 12–15 mos	4
	3	1 additional dose at age 12–15 mos	4
7–11 mos	0 (at age <7 mos)	3 doses: 2 doses 8 wks apart; last dose at age 12–15 mos	3
	1 or 2 (at age <7 mos)	2 additional doses: 1 dose 8 wks after most recent dose; last dose ≥8 wks later at age 12–15 mos	3 or 4
	3 (at age <7 mos)	1 additional dose at age 12–15 mos	4
	1 (at age ≥7 mos)	2 additional doses: 1 dose 8 wks after most recent dose; last dose ≥8 wks later at age 12–15 mos	3
	2 (at age ≥7 mos)	1 additional dose ≥8 wks later at age 12–15 mos	3
12–23 mos	0 (at age <12 mos)	2 doses: 2 doses 8 wks apart	2
	1 (at age <12 mos)	2 additional doses: 1 dose ≥8 wks after most recent dose; last dose ≥8 wks later	3
	2 or 3 (at age <12 mos)	1 additional dose, ≥8 wks after most recent dose	3 or 4
	1 (at age ≥12 mos)	1 additional dose, ≥8 wks after most recent dose†	2
Healthy children			
24–59 mos	No previous doses or any incomplete schedule by 24 mos	1 additional dose, ≥8 wks after most recent dose	NA
5–18 yrs	No previous doses or any incomplete schedule by 24 mos	No additional dose¶	NA
Children and adolescents with risk conditions§			
24–71 mos**	No previous doses or any incomplete schedule†† and <3 doses by age 24 mos	2 doses: 1 dose ≥8 wks after most recent dose; last dose ≥8 wks later	NA
	3 (all at age <12 mos)	1 additional dose, ≥8 wks after most recent dose	NA
6–18 yrs	No previous doses	1 dose§§††	NA

Abbreviations: NA = not applicable; PCV = pneumococcal conjugate vaccine; PCV15 = 15-valent PCV; PCV20 = 20-valent PCV.

* Either PCV15 or PCV20 may be used to complete the recommended PCV series. If only 13-valent PCV (PCV13) is available when the child is scheduled to receive a PCV, PCV13 may be given as previously recommended.

† Minimum interval between doses is 8 weeks except for children vaccinated at age <1 year, for whom the minimum interval between doses is 4 weeks. The minimum age for administration of first dose is 6 weeks.

§ Risk conditions include: cerebrospinal fluid leak; chronic heart disease; chronic kidney disease (excluding maintenance dialysis and nephrotic syndrome, which are included in immunocompromising conditions); chronic liver disease; chronic lung disease (including moderate persistent or severe persistent asthma); cochlear implant; diabetes mellitus; immunocompromising conditions (on maintenance dialysis or with nephrotic syndrome; congenital or acquired asplenia or splenic dysfunction; congenital or acquired immunodeficiencies; diseases and conditions treated with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, Hodgkin disease, and solid organ transplant; HIV infection; and sickle cell disease or other hemoglobinopathies).

¶ Routine use of PCV is not recommended for healthy children aged ≥5 years

**These children are also recommended to receive either a dose of PCV20 or ≥1 dose of 23-valent pneumococcal polysaccharide vaccine if PCV20 is not given as part of their recommended PCV doses.

††See column "No. of PCV13/PCV15/ PCV20 doses to complete series by age 24 mos" to determine an incomplete schedule of <3 doses by 24 months.

§§When PCV15 is used, it should be followed by a dose of PPSV23 ≥8 weeks after the PCV15 dose if not previously given. When PCV20 is used, it does not need to be followed by a dose of PPSV23.

TABLE 3. Risk-based pneumococcal vaccine recommendations for PCV unvaccinated children and adolescents with risk conditions — United States, 2023

Risk group/Condition	PCV* for children aged <6 yrs	PCV* for persons aged 6–18 yrs	PPSV23 for children aged ≥2 yrs with no previous PCV20 receipt	
	Recommended	Recommended	Recommended	Single revaccination 5 yrs after first dose
Children with chronic medical conditions				
Chronic heart disease[†]	Y	Y	Only if PCV13 or PCV15 used	N
Chronic kidney disease (excluding maintenance dialysis and nephrotic syndrome, which are included in immunocompromising conditions)	Y	Y	Only if PCV13 or PCV15 used	N
Chronic liver disease	Y	Y	Only if PCV13 or PCV15 used	N
Chronic lung disease (including moderate persistent or severe persistent asthma)	Y	Y	Only if PCV13 or PCV15 used	N
Diabetes mellitus	Y	Y	Only if PCV13 or PCV15 used	N
Cerebrospinal fluid leak	Y	Y	Only if PCV13 or PCV15 used	N
Cochlear implant	Y	Y	Only if PCV13 or PCV15 used	N
Children with immunocompromising conditions				
Maintenance dialysis or with nephrotic syndrome	Y	Y	Only if PCV13 or PCV15 used	Only if no previous receipt of PCV20
Congenital or acquired asplenia, or splenic dysfunction	Y	Y	Only if PCV13 or PCV15 used	Only if no previous receipt of PCV20
Congenital or acquired immunodeficiencies[§]	Y	Y	Only if PCV13 or PCV15 used	Only if no previous receipt of PCV20
Diseases and conditions treated with immunosuppressive drugs or radiation therapy[¶]	Y	Y	Only if PCV13 or PCV15 used	Only if no previous receipt of PCV20
HIV infection	Y	Y	Only if PCV13 or PCV15 used	Only if no previous receipt of PCV20
Sickle cell disease or other hemoglobinopathies	Y	Y	Only if PCV13 or PCV15 used	Only if no previous receipt of PCV20
Solid organ transplant	Y	Y	Only if PCV13 or PCV15 used	Only if no previous receipt of PCV20

Abbreviations: N = no; PCV = pneumococcal conjugate vaccine; PCV15 = 15-valent PCV; PCV20 = 20-valent PCV; PPSV23 = 23-valent pneumococcal polysaccharide vaccine; Y = yes.

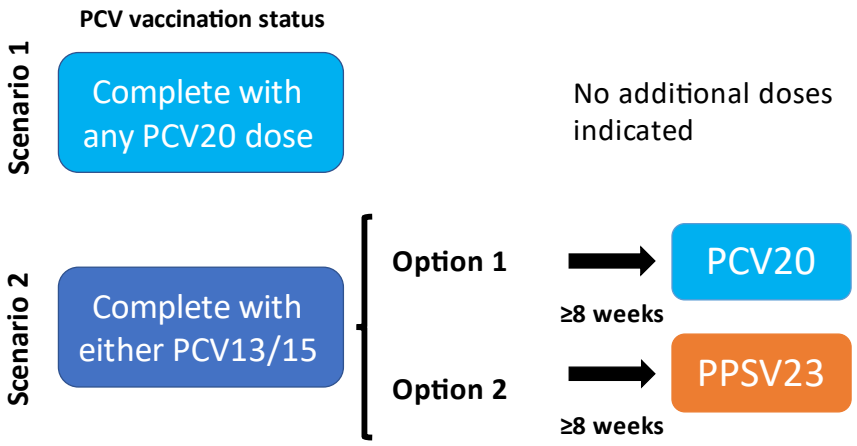
* Either PCV15 or PCV20 can be used.

[†] Recommendations are of particular importance for children with cyanotic congenital heart disease and cardiac failure.

[§] Includes B-(humoral) or T-lymphocyte deficiency; complement deficiencies, particularly C1, C2, C3, and C4 deficiency; and phagocytic disorders (excluding chronic granulomatous disease).

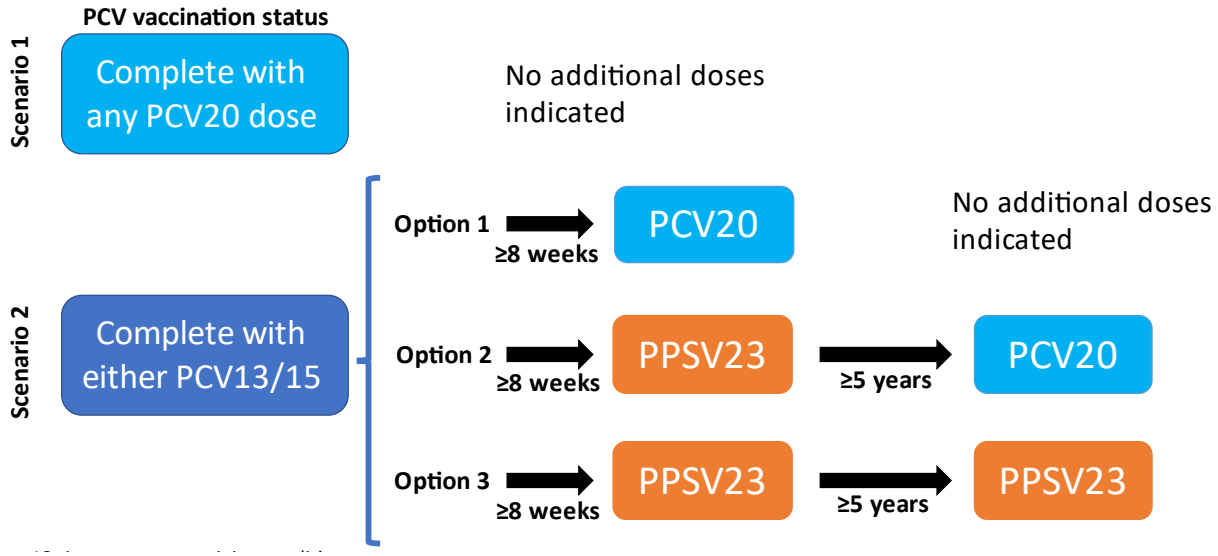
[¶] Including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease.

Figure 1. Pneumococcal vaccine recommendations for children 2–18 years with a chronic medical condition, CSF leak, or cochlear implant who have received all recommended PCV doses before age 6 years



CMC=chronic medical conditions, including chronic kidney disease (excluding maintenance dialysis and nephrotic syndrome, which are included in immunocompromising conditions), chronic heart disease, chronic liver disease, chronic lung disease (including moderate persistent or severe persistent asthma), diabetes mellitus; CSF=cerebrospinal fluid

Figure 2. Pneumococcal vaccine recommendations for children with an immunocompromising condition aged 2–18 years with who have completed all PCV doses before age 6 years



Immunocompromising conditions: On maintenance dialysis or nephrotic syndrome; congenital or acquired asplenia or splenic dysfunction; congenital or acquired immunodeficiencies; diseases and conditions treated with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, Hodgkin disease, and solid organ transplant; HIV infection; and sickle cell disease or other hemoglobinopathies.

CDC Clinical guidance for implementation

Use of PCV13 when neither PCV15 nor PCV20 is available

If only PCV13 is available when the child is scheduled to receive a PCV, PCV13 may be given as previously recommended.

Children who started the PCV series with PCV13

If a child started the PCV series with PCV13, the child may complete the series with PCV15 or PCV20 without giving additional doses; the PCV series does not need to be restarted.

Healthy Children aged 24–59 months who completed recommended PCV vaccination series with PCV13

A supplemental dose of PCV15 or PCV20 is not indicated for healthy children who have received 4 doses of PCV13 or who completed another age-appropriate PCV13 schedule.

Children aged 6–18 years with a risk condition who have received PCV13 only at or after age 6 years

Either a dose of PCV20 or ≥1 dose of PPSV23 is recommended, at least 8 weeks after the last PCV13 dose. When PPSV23 is used instead of PCV20 for children aged 6–18 years with an immunocompromising condition, either PCV20 or a second PPSV23 dose is recommended ≥5 years after the first PPSV23 dose.

Children who have received hematopoietic stem cell transplant (HSCT)

Children who received HSCT are recommended to receive three doses of PCV20, 4 weeks apart starting 3–6 months after HSCT. A fourth PCV20 dose is recommended ≥6 months after the third PCV20 dose, or ≥12 months after HSCT, whichever is later. HSCT recipients who have started their pneumococcal vaccine series with PCV13 or PCV15 may complete their 4-dose pneumococcal vaccine series with PCV20 without giving extra doses.

If PCV20 is not available, three doses of PCV15, followed by a dose of PPSV23 ≥12 months after HSCT may be given. For patients with chronic graft-versus-host disease who are receiving PCV15, a fourth dose of PCV15 can be given in place of PPSV23 since these children are less likely to respond to PPSV23. A patient's clinical team is best informed to determine the appropriate timing of vaccination.

Vaccine administration

PCV15 and PCV20 are available in a single-dose prefilled syringe as a 0.5-mL dose administered intramuscularly. Any PCV can be administered at the same time as other routine childhood vaccinations, including COVID-19 vaccines (26), in separate syringes and using different injection sites. Concurrent PCV20 administration with vaccines containing diphtheria, tetanus, acellular pertussis, inactivated poliovirus, *Haemophilus influenzae* type b, hepatitis B, measles, mumps, rubella, rotavirus, and varicella were studied (16, 17). Immunogenicity of these antigens was similar when administered concurrently with PCV20 or PCV13 (16, 17). Coadministration of PCV20 with meningococcal vaccines has not been studied. The same precautions used for coadministration of PCV13 and meningococcal groups A, C, W, and Y polysaccharide diphtheria toxoid conjugate vaccine (Menactra, Sanofi Pasteur) should be applied when PCV20 is used (27). Of children who received PCV20 concurrently with an influenza vaccine (10-20% of trial participants), no febrile seizures were reported (Pfizer, unpublished data).

Reporting of Adverse Events

Before administering PCV or PPSV23, health care providers should consult relevant package inserts regarding precautions and contraindications (20, 28, 29). Adverse events occurring after administration of any vaccine should be reported to the Vaccine Adverse Event Reporting System (VAERS). More information about VAERS and submitting reports is available at https://vaers.hhs.gov.

Future Research and Monitoring Priorities

CDC and ACIP will continue to assess safety of pneumococcal vaccines and monitor the changes in pneumococcal disease incidence and serotype distribution after implementation of new vaccine recommendations. CDC and ACIP will update pneumococcal vaccination recommendations as more evidence becomes available or FDA makes revisions to current approvals.

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Footnotes

*Risk conditions include: cerebrospinal fluid leak; chronic heart disease; **chronic kidney disease** (excluding maintenance dialysis and nephrotic syndrome, which are included in immunocompromising conditions); **chronic liver disease**; chronic lung disease (**including moderate persistent or severe persistent asthma**); cochlear implant; diabetes mellitus; immunocompromising conditions (on **maintenance dialysis** or with nephrotic syndrome; congenital or acquired asplenia or splenic dysfunction; congenital or acquired immunodeficiencies; diseases and conditions treated with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, Hodgkin disease, and solid organ transplant; HIV infection; and sickle cell disease or other hemoglobinopathies). **Conditions in bold were added to the indications for risk-based recommendations.**

†Immunocompromising conditions: On maintenance dialysis or nephrotic syndrome; congenital or acquired asplenia or splenic dysfunction; congenital or acquired immunodeficiencies; diseases and conditions treated with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, Hodgkin disease, and solid organ transplant; HIV infection; and sickle cell disease or other hemoglobinopathies.

§https://www.cdc.gov/vaccines/acip/recs/grade/PCV20-child-risk-based.html; https://www.cdc.gov/vaccines/acip/recs/grade/PCV20-child.html

¶ https://www.cdc.gov/vaccines/acip/recs/grade/downloads/acip-evidence-recs-framework.pdf

**Noninferiority for a serotype was met if the lower bound of the 2-sided confidence interval for the percentage difference of participants with the predefined IgG concentration (PCV20 minus PCV13) was >-10% for that serotype. The predefined IgG concentration was ≥0.35 µg/mL for all serotypes except for serotypes 5, 6B, 12F, and 19A which were ≥0.23 µg/mL, ≥0.10 µg/mL, ≥0.69 µg/mL, and ≥0.12 µg/mL respectively. For the 7 additional serotypes, the percentage of participants with the predefined IgG concentration to serotype 23F (PCV13 serotype with the lowest percentage, excluding serotype 3) in the PCV13 group was used in the calculation of the percentage difference.

††Measured as the proportion of participants meeting IgG threshold value of ≥0.35 µg/mL except for ≥0.23 µg/ml for serotype 5, ≥0.10 µg/ml for serotype 6B, and ≥0.23 µg/ml for serotype 19A. The direct-binding Luminex® immunoassay (dLIA) that was used to measure the IgG concentration was bridged to the World Health Organization enzyme linked immunosorbent assay to establish dLIA specific threshold values for each vaccine serotype that correspond to the established ≥0.35 µg/mL WHO ELISA threshold value.

§§Noninferiority for a serotype was met if the lower bound of the 2-sided confidence interval of IgG GMC ratio (PCV20/PCV13) was >0.5 for that serotype. For the 7 additional serotypes, the IgG GMC to serotype 19A (PCV13 serotype with the lowest IgG GMC, excluding serotype 3) in the PCV13 group was used in the calculation of the GMC ratio after dose 3. For the 7 additional serotypes, the IgG GMC to serotype 1 (PCV13 serotype with the lowest IgG GMC, excluding serotype 3) in the PCV13 group was used in the calculation of the GMC ratio after dose 4.

¶¶Cost-saving means lower costs and improved health outcomes in the intervention, as compared to the comparator

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