



## POLICY STATEMENT

Immunization for *Streptococcus pneumoniae* Infections  
in High-Risk Children

## abstract

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Routine use of the pneumococcal conjugate vaccines (PCV7 and PCV13), beginning in 2000, has resulted in a dramatic reduction in the incidence of invasive pneumococcal disease (IPD) attributable to serotypes of *Streptococcus pneumoniae* contained in the vaccines. The Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention and the American Academy of Pediatrics recommend the expanded use of PCV13 in children 6 through 18 years of age with certain conditions that place them at elevated risk of IPD. This statement provides recommendations for the use of PCV13 in children 6 through 18 years. A single dose of PCV13 should be administered to certain children in this age group who are at elevated risk of IPD. Recommendations for the use of PCV13 in healthy children and for pneumococcal polysaccharide vaccine (PPSV23) remain unchanged. *Pediatrics* 2014;134:1230–1233

## INTRODUCTION

Invasive disease attributable to *Streptococcus pneumoniae* remains a significant public health problem in children despite widespread use of pneumococcal conjugate vaccines (PCV7 and PCV13; Prevnar; Pfizer, Inc, New York, NY) in US infants 2 through 59 months of age. After the introduction of PCV7 and subsequently PCV13, dramatic decreases in invasive pneumococcal disease (IPD) attributable to vaccine serotypes were noted in young children. However, IPD caused by vaccine serotypes continues to occur in older children with immunodeficiency and certain other high-risk conditions, prompting the need for vaccination recommendations to include these populations.

## BACKGROUND AND RATIONALE

*S pneumoniae* is a leading cause of serious infections, including sepsis and meningitis, and accounts for significant morbidity and mortality in the United States.<sup>1</sup> PCV13 was licensed by the Food and Drug Administration for prevention of IPD and otitis media in infants and young children in February 2010, when it replaced PCV7.<sup>2</sup> PCV13 is recommended for all children 2 through 59 months of age and for children 60 through 71 months of age with chronic medical conditions (eg, heart disease and diabetes); immunocompromising conditions (eg, HIV infection), including functional or anatomic asplenia, including sickle cell disease; cerebrospinal fluid (CSF) leaks; or cochlear implants (Table 1). For children 6 through 18 years with these same high-risk conditions,

## COMMITTEE ON INFECTIOUS DISEASES

## KEY WORDS

pneumococcal vaccine, invasive pneumococcal disease, immunization, PCV13, PPSV23

## ABBREVIATIONS

ACIP—Advisory Committee on Immunization Practices  
CDC—Centers for Disease Control and Prevention  
CI—confidence interval  
CSF—cerebrospinal fluid  
IPD—invasive pneumococcal disease  
PCV—pneumococcal conjugate vaccine  
PPSV—pneumococcal polysaccharide vaccine  
RR—rate ratio

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**TABLE 1** Underlying Medical Conditions That Are Indications for Pneumococcal Immunization Among Children, by Risk Group<sup>a</sup> and Recommended Vaccines

Risk Group	Condition	PCV13		PPSV23	
		Recommended	May Be Considered	1 Dose	Repeat Dose <sup>b</sup>
Immunocompetent children	Chronic heart disease <sup>c</sup>		X	X	
	Chronic lung disease <sup>d</sup>		X	X	
	Diabetes mellitus		X	X	
	CSF leaks	X		X	
	Cochlear implant	X		X	
Children with functional or anatomic asplenia	Sickle cell disease and other hemoglobinopathies	X		X	X
	Congenital or acquired asplenia or splenic dysfunction	X		X	X
Children with immunocompromising conditions	HIV infection	X		X	X
	Chronic renal failure and nephrotic syndrome	X		X	X
	Diseases associated with treatment with immunosuppressive drugs or radiation therapy, including malignant neoplasms, leukemias, lymphomas, and Hodgkin disease; or solid organ transplantation	X		X	X
	Congenital immunodeficiency <sup>e</sup>	X		X	X

<sup>a</sup> Centers for Disease Control and Prevention. Licensure of a 13-valent pneumococcal conjugate vaccine (PCV13) and recommendations for use among children. Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep*. 2010;59(9):258–261.

<sup>b</sup> Repeat PPSV23 doses should be 5 y after the first dose.

<sup>c</sup> Particularly cyanotic congenital heart disease and cardiac failure.

<sup>d</sup> Including asthma, if treated with prolonged high-dose oral corticosteroids.

<sup>e</sup> Includes B- (humoral) or T-lymphocyte deficiency; complement deficiencies, particularly C1, C2, C3, and C4 deficiency; and phagocytic disorders (excluding chronic granulomatous disease).

only PPSV23 has been routinely recommended, although there has been a permissive and off-label recommendation by the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC) for use of PCV13.<sup>2</sup>

In June 2012, the ACIP recommended routine use of PCV13 in addition to PPSV23 for PCV13-naive adults  $\geq 19$  years of age with immunocompromising conditions, including functional or anatomic asplenia, including sickle cell disease; CSF leaks; or cochlear implants.<sup>3</sup> In June 2013, the ACIP recommended routine use of PCV13 for children 6 through 18 years of age with these same conditions who have not previously received PCV13.<sup>4</sup> PCV13 should be administered to these children regardless of whether they received PCV7 or PPSV23 previously. Recommendations for PPSV23 use for children remain unchanged.

## EVIDENCE TO SUPPORT THE RECOMMENDATION

Pneumococcal conjugate vaccines have decreased the rates of IPD directly in

vaccinated children and indirectly (herd protection) in unvaccinated people.<sup>2</sup> From 2007 through 2009, the average annual incidence of IPD among children 6 through 18 years of age was 2.6 cases per 100 000 population, with 57% of IPD caused by serotypes included in PCV13 (CDC, Active Bacterial Core surveillance 2007–2009, unpublished data, 2013). Among immunocompromised children 6 through 18 years of age, 49% of IPD was caused by serotypes included in PCV13, and an additional 23% of IPD was caused by serotypes included in PPSV23. Incidence of IPD caused by serotypes included in PCV13 among children 6 through 18 years of age with hematologic malignancies was estimated at 1282 per 100 000 population. Compared with children without this condition, this is a rate ratio (RR) of 822 (95% confidence interval [CI], 687–983). For children with HIV infection, the incidence was 197 per 100 000 population (RR, 122; CI, 94–161), and for children with sickle cell disease, the incidence was 56 (RR, 27; CI, 9–73) (CDC, Active Bacterial Core surveillance 2007–2009, unpublished data, 2013). Children

with certain chronic diseases (eg, cardiac or lung disease) are also known to have elevated risk of IPD but at levels lower than those among children with HIV infection.<sup>2,5</sup>

## PCV13 Efficacy and Safety Among Immunocompromised People

Studies of pneumococcal conjugate vaccines containing similar but fewer antigens have been conducted among people with immunocompromising conditions. From a randomized controlled trial among HIV-infected children 2 through 45 months of age in South Africa, the efficacy of a 9-valent pneumococcal conjugate vaccine (PCV9) was estimated as 65% (CI, 24%–86%) against IPD and 13% (CI, –7%–29%) against radiologically confirmed pneumonia.<sup>6</sup> Vaccine efficacy of PCV7 against IPD caused by a serotype contained in the vaccine in HIV-infected adults in Malawi was estimated at 74% (CI, 30%–90%).<sup>7</sup> An observational study conducted in the United States among children  $\leq 10$  years of age with sickle cell disease estimated vaccine effectiveness against IPD to be 81% (CI, 19%–96%) among those who

received  $\geq 1$  dose of PCV7.<sup>8</sup> Although vaccine efficacy and effectiveness have been demonstrated, the duration of protection against IPD remains unknown.

In January 2013, the US Food and Drug Administration approved use of PCV13 in healthy children 6 through 17 years of age for the prevention of IPD caused by serotypes included in the vaccine. Current evidence supports the safety of PCV13 in children with immunocompromising conditions.<sup>9,10</sup> An open-label, single-arm study of 158 children 6 through 18 years of age with sickle cell disease who previously received PPSV23 demonstrated that 1 dose of PCV13 was safe.<sup>9</sup> The most common adverse events reported within 7 days of 1 dose included myalgia (74.8%), fatigue (66.1%), and headache (53.6%); less common events included arthralgia (39.8%), fever (26%), vomiting (15.4%), and diarrhea (13.3%). Severe adverse events were reported among 8% of the children and included sickle cell pain crisis (4%), acute chest syndrome (2%), and fever (2%). In a PCV7 efficacy trial among HIV-infected children, the most common adverse events were severe induration, erythema, fever, and restricted leg movement; no serious adverse events were reported.<sup>10</sup>

### **PPSV23 in Immunocompromised Children**

PPSV23 contains 12 of the serotypes included in PCV13, plus 11 additional serotypes, which account for 23% of IPD cases among immunocompromised children 6 through 18 years of age (CDC, Active Bacterial Core surveillance 2007–2009, unpublished data, 2013). PPSV23 currently is recommended for children  $\geq 2$  years of age with elevated risk of IPD.<sup>4</sup> Given the high burden of IPD caused by serotypes included in PPSV23 but not in PCV13, broader protection should be provided through use of both PCV13 and PPSV23.

## **POLICY RECOMMENDATIONS**

**The following recommendation is new and not included in any previous American Academy of Pediatrics (AAP) policy.**

### **Children 6 Through 18 Years of Age With Conditions That Place Them at Highest Risk**

A single dose of PCV 13 should be given to children 6 through 18 years of age who have immunocompromising conditions, including HIV infection and functional or anatomic asplenia, including sickle cell disease; CSF leaks; or cochlear implants and who have not previously received PCV13. PCV13 should be administered to these children regardless of whether they received PCV7 or PPSV23 previously. Children in this group who have not previously been immunized with PPSV23 should receive a dose of PPSV23  $\geq 8$  weeks after their dose of PCV13. For children in this group who have been previously immunized with PPSV23, a single dose of PCV13 should be given  $\geq 8$  weeks after the PPSV23 dose.

**The following recommendation is unchanged from previous AAP policy.**

### **Children 6 Through 18 Years of Age With Conditions That Place Them at Highest Risk**

A second PPSV23 dose is recommended 5 years after the first PPSV23 dose for children with anatomic or functional asplenia, including sickle cell disease, HIV infection, or other immunocompromising conditions. This second dose is not recommended for children with cochlear implants or CSF leaks.

### **Immunocompetent Children 6 Through 18 Years of Age With Conditions That Place Them at Elevated Risk**

Immunocompetent children who have underlying medical conditions that place them at elevated risk for IPD (Table 1)

may also receive PCV13 if they have not previously received PCV13 and regardless of whether they have received PCV7 in the past. If both PCV13 and PPSV23 are used, PCV13 should be administered first, and the administration of PPSV23 should follow at an interval of  $\geq 8$  weeks. A second dose of PPSV23 is not recommended for this group of children.

Recommendations for the use of PCV13 for children younger than 60 months of age and the use of PPSV23 for children of all ages are unchanged. PCV13 is approved for the Vaccines for Children program through 18 years of age, and the vaccine will be covered by the Vaccine Injury Compensation Program. PPSV23 is not covered by the Vaccine Injury Compensation Program.

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