13-valent Pneumococcal Conjugate Vaccine Use in Adults with Immunocompromising Conditions

Kathleen Dooling, MD, MPH
Respiratory Diseases Branch
National Center for Immunization & Respiratory Diseases

Advisory Committee on Immunization Practices
June 20, 2012

Outline

- **PART I: Review: GRADE- PCV13 vs PPSV23**
- **PART II: Pneumococcal vaccination considerations**
  - Vaccination combination
  - Vaccine sequence
  - Interval

GRADE Process

STEP		Feb	June
1	Formulate specific policy question	✓	✓
2	Identify & rank relative importance of outcomes	✓	
3	Summarize all evidence for all outcomes	✓	
4	Assess quality of evidence for each outcome	✓	
5	Summarize quality of evidence across outcomes	✓	✓
6	Review health economic data	✓	✓
7	Assess the balance of risks & benefits	✓	✓
8	Determine the recommendation category	✓	✓

Step 1. Formulate specific policy question

"Should PCV13 be administered routinely to adults with immunocompromising conditions?"

- Population: Adults 19 years of age and older with HIV
- Intervention: Pneumococcal conjugate vaccine (PCV13) administered as a single dose injection
- Control: Pneumococcal polysaccharide vaccine (PPSV23)
- Outcomes: See Step 2

Step 5. Summarize quality of evidence across outcomes

Outcome	Comparison	Study Design	Findings	Quality of Evidence	Overall Quality of Evidence
IPD	PCV7 vs. No vaccination	RCT (1) HIV+	Vaccine Efficacy 74% (95%CI 30-90)	**2/3**	**2/3**
Serious & Systemic adverse events	PCV13 vs. PPSV23	RCT (6) Immuno-competent	No difference; Significantly fewer systemic for PCV13	**2**	
Immunogenicity	PCV13 vs. PPSV23	RCT (2) Immuno-competent	PCV13 non-inferior or superior	**3**	
Immunogenicity	PCV7 vs. PPSV23	RCT (4) HIV+	PCV7 non-inferior or superior	**2**	

Step 6. Review Health Economic Data

- **A cost effectiveness model**
  - HIV/AIDS
  - Hematological Cancer
  - Organ Transplant
  - Dialysis
- **Groups not included in model**
  - Treated with immunosuppressive drugs
  - Congenital immunodeficiency
  - Functional or anatomic asplenia
  - CSF leaks or cochlear implants

Step 7&8. Determine Recommendation Category

Question	Response	
Is the evidence level/quality “Lower“?	**Yes**	Indirectness & lack of evidence for 3 of 4 critical disease outcomes
Is there uncertainty about the balance of benefits versus harms & burdens?	**No**	Very high burden of disease in immunocompromised
Is there variability or uncertainty in what is important?	**No**	WG Consensus on critical outcomes
Is there uncertainty about whether the net benefits are worth the costs?	**Yes**	Uncertainty of costs/benefits of adding PCV13 to current recs

Category B

Conclusions from the Pneumococcal Working Group

- Extremely high burden of disease among immunocompromised adults
- GRADE process led to conclusion that benefits likely outweigh harms for PCV13
- No additional data expected to influence GRADE conclusions for immunocompromised groups
- Indirect effects of PCV13 use in children unlikely to eliminate PCV13 serotypes from immunocompromised adults

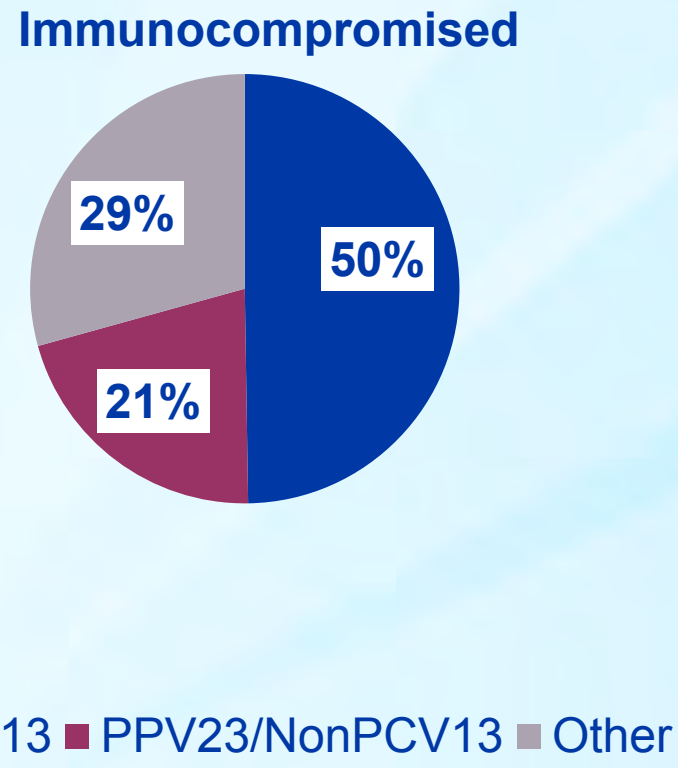
PART II

Pneumococcal vaccination considerations

- Vaccination combination
- Vaccine sequence
- Interval between vaccines

In adults with immunocompromising conditions, should we use PCV13, PPSV23 or Both?

Proportion of IPD by vaccine serotype, 2010



- 21% of disease due to serotypes in PPSV23 not covered by PCV13
- Opportunity for broader serotype protection through use of **BOTH vaccines**

CDC, ABCs, unpublished, 2011

Vaccination Sequence

- **Data for PCV followed by PPSV**
  - 3 studies in HIV+ show that antibodies non-inferior or superior when PCV given prior to PPSV
  - Phase III studies in immunocompetent show that

    PCV13 + PPSV23 > PPSV23 + PCV for 11/12 serotypes

- **Data for PPSV followed by PCV**
  - In 1 study in HIV+ in Uganda, PPSV 5 yrs prior did not affect response to PCV
  - In 1 study in HIV+ in US, there was no difference in immunogenicity between PCV and PPSV given 3-8 years after PPSV

Data support use of PCV13 followed by PPSV23

Interval between vaccines

- **What is the optimal interval between PCV and PPSV?**
  - No studies have been designed to test the optimal interval
  - HIV+ @ 1 & 2 month intervals
  - immunocompetent older adults @ 6 and 12 month intervals

  } All intervals showed significant increases in antibody as well as non-inferior or superior response compared to PPSV alone

- **What is the optimal interval between PPSV and PCV?**
  - No studies have been designed to test the optimal interval
  - Studies in immunocompetent suggest blunting of immune response <5 years after PPSV
  - No evidence of reduced immunogenicity in HIV+ with PCV 5 years after PPSV

Summary: sequence and interval for adults with immunocompromising conditions

- **Pneumococcal vaccine naïve adults**
  - PCV13 followed by PPSV23
  - Interval of at least **8 weeks** between PCV13 and PPSV23
- **PPSV23 previously immunized adults**
  - A dose of PCV13 at least **1 year** after the last PPSV23

Acknowledgements

ACIP members

Nancy Bennett (Chair)

Wendy Keitel

Jeffrey Duchin

Michael Marcy

Ex Officio members

Mark Grabowsky
Kristin Nichol
Lucia Lee

CDC

Tamara Pilishvili
Cynthia Whitney
Matt Moore
Kathleen Dooling
Tom Hennessy
Sandra Steiner
Gina Mootrey
William Atkinson
Jorge Arana
Maria Cano
Erin Kennedy
Carolyn Bridges
Charles LeBaron

Liaison representatives

Lorry Rubin
Rick Zimmerman
William Schaffner
Caroline Quach
Ken Gershman
Daniel Musher
Mary Glode
Jane Zucker
Lisa Jackson
Monica Farley
Kathy Neuzil
Julie Morita
Anthony Brenneman
Sandra Fryhofer