

**Pneumococcal Disease Prevention among Adults:  
Opportunities and Challenges**

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Respiratory Diseases Branch

**Pneumococcal Polysaccharide Vaccine (PPV23)**

- Available since 1983
- Capsular polysaccharide of 23 of the 92 pneumococcal serotypes
- 23 serotypes cause >80% of invasive pneumococcal infections among person in any age group

**Outline**

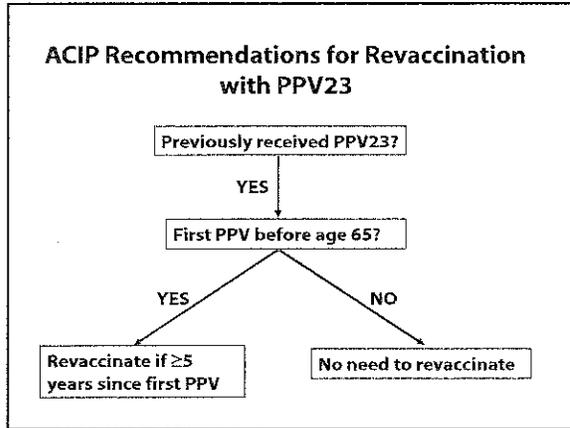
- Current recommendations for pneumococcal polysaccharide vaccine use among adults
- Epidemiology of pneumococcal disease among adults in the U.S.
- Considerations for conjugate vaccine use among adults

**ACIP Recommendations for Pneumococcal Polysaccharide Vaccine**

- All adults 65+ years
- Persons 2-64 years with:
  - chronic cardiovascular or pulmonary disease
  - functional or anatomic asplenia
  - chronic liver disease or alcoholism
  - cerebrospinal fluid leak
  - diabetes mellitus
  - cochlear implant
  - immunocompromising conditions
- Persons 2-64 years old living in high risk settings (long term care)
- Persons 19-64 years who smoke cigarettes } MMWR Policy Update 2010
- Persons 19-64 years with asthma }

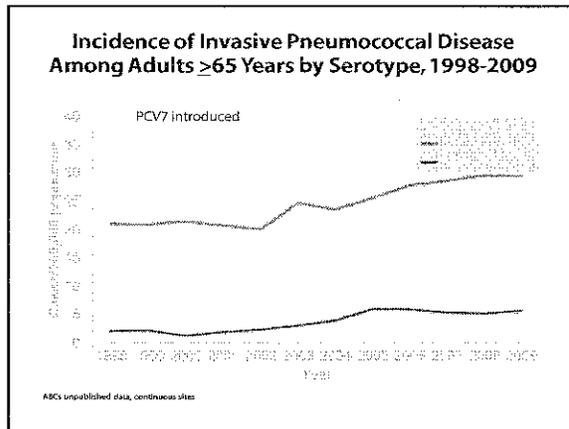
Advisory Committee on Immunization Practices, MMWR 1997;46(RR-8):1-24

**CURRENT RECOMMENDATIONS FOR PNEUMOCOCCAL POLYSACCHARIDE VACCINE USE AMONG ADULTS**

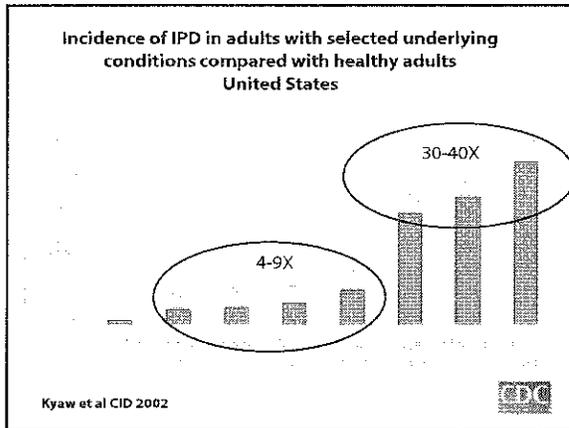
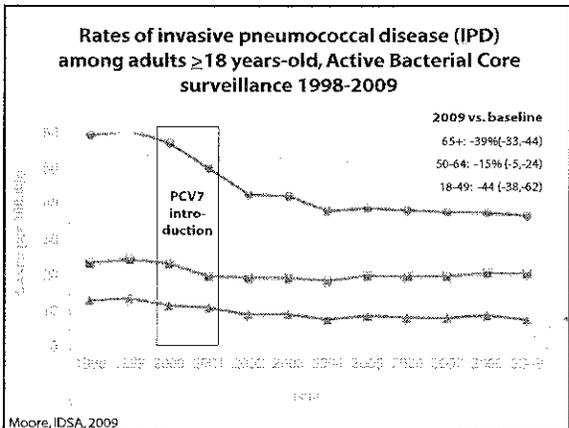
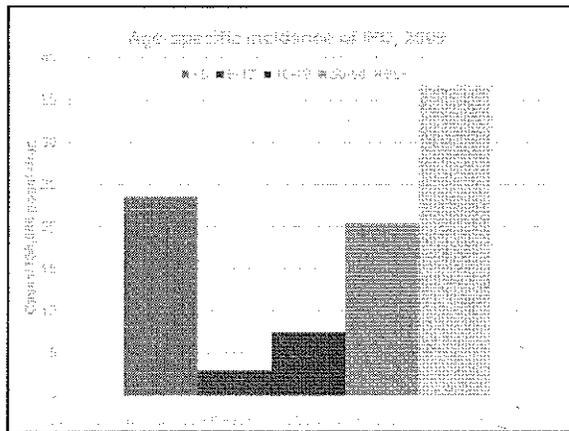


**Limitations of Pneumococcal Polysaccharide Vaccine (PPV23)**

- Limited or no effectiveness against non-bacteraemic pneumonia
- No effectiveness for mucosal infections
- Does not establish immunologic memory (T-cell independent pathways)
- Limited duration of efficacy against IPD
- Effectiveness is further limited in immunocompromised individuals
- Revaccination leads to lower functional immune response compared with the responses after initial immunization



**EPIDEMIOLOGY OF PNEUMOCOCCAL DISEASE AMONG ADULTS IN THE U.S.**



## PNEUMOCOCCAL CONJUGATE VACCINE FOR ADULTS

### PCV vs PPV23 immunogenicity studies in adults

Author	N	Population	PCV vs. PPV23 comparison (ELISA)
Jackson, 2007	219	70-79y PPV23 ≥ 5 yrs	PCV7=PPV23
De Roux, 2008	217	>70y Naive	PCV7>PPV23 for 6/7 serotypes
Scott, 2008	15	20-50y Naive	PCV13=PPV23
Goldblatt, 2009	599	50-80y No PPV23 ≤ 5 yrs	PCV7 > PPV23 for 3/7 serotypes
Ridda, 2009	241	>60y Naive	PCV7=PPV23 (4 serotypes analysed)
Miernyk, 2009	203	55-70y Naive	PCV7=PPV23 (4 serotypes analysed)

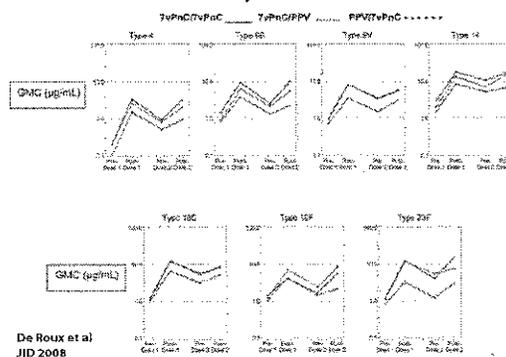
February 2011 ACIP: new immunogenicity studies of PCV13 vs PPV23 in adults 50+ years

### 13-valent Pneumococcal Conjugate Vaccine (PCV13) for adults

- Accelerated approval (applied Dec 2010, expected Oct 2011)
- Proposed Indication
  - Prevention of pneumococcal disease (including pneumonia and invasive disease) in adults 50 years of age and older
  - Prevention of disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F
- Licensure will be based on demonstration of non-inferiority of OPA response to PCV13 compared to PPV23
- Confirmatory trial with pneumonia as the primary endpoint (will be submitted as a post approval supplement)

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### Immune response following PPV23 or PCV7 in adults ≥70 years



### Considerations for PCV13 use among adults

- Immunogenicity non-inferior to PPV23
- Immunologic memory
- No hyporesponsiveness to revaccination
- Duration of antibody persistence
- Efficacy against non-bacteraemic pneumonia
- Efficacy in immunocompromised
- Serotype coverage
- Cost-effectiveness

Journal of the American Medical Association  
ORIGINAL ARTICLE

### Rationale and design of CAPITA: a RCT of 13-valent conjugated pneumococcal vaccine efficacy among older adults

E. Hain<sup>1</sup>, D.E. Grollier<sup>2</sup>, E.A.M. Sanders<sup>3</sup>, T.J.M. Verheij<sup>4</sup>, M. Bollenbaas<sup>5</sup>, S.M. Hooger<sup>6</sup>, W.C. Geurts<sup>7</sup>, S. Tackx<sup>8</sup>, A. McDonough<sup>9</sup>, G. Tsevat<sup>10</sup>, S. Pasternak<sup>11</sup>, A.J. van Alphen<sup>12</sup>, M.J.M. Bonten<sup>13</sup>

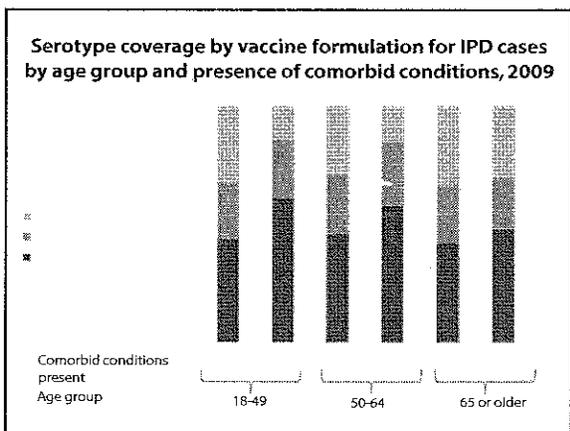
- Randomized placebo-controlled trial (1:1)
- 85,000 community-dwelling, pneumococcal vaccine naïve adults ≥65 years
- Primary objective: efficacy against 1st episode of vaccine serotype community-acquired pneumonia (CAP)
- Secondary objectives: efficacy against non-bacteraemic VT CAP and VT IPD, all pneumococcal CAP; death; safety profile
- Results expected in 2012

### Efficacy of PCV7 and PPV23 in HIV Infected Adults

Vaccine	Endpoint	Vaccine Efficacy (95% CI)
PCV7	Vaccine serotype IPD	74% (30%, 90%)
	All cause pneumonia	25% (-19%, 53%)
PPV23	Vaccine serotype IPD	-100% (-100%, 14%)
	All cause pneumonia	-89% (-100%, -12%)

French N, et al. *N Engl J Med* 2010;362:212-22.  
French N, et al. *Lancet*. 2000;355(9221):2106-2111.

- ### Is there a role for PCV13 use among adults?
- **Pros**
    - Large, potentially preventable burden of adult disease
    - Observations of mucosal immunity in children suggest opportunity for prevention of non-invasive pneumococcal pneumonia among adults
    - Limited acceptability and no evidence of population-level prevention with PPV23
  - **Cons**
    - Increasing vaccine coverage among adult population has been difficult
    - Potential herd effects of PCV13 use among children may limit the utility of PCV13 among adults



- ### Next steps
- Efficacy trial against pneumonia (CAPITA)
  - Evaluate impact of pediatric PCV13 program
  - Advisory Committee on Immunization Practices is in the process of reviewing available data on disease burden, immunogenicity, and cost-effectiveness
  - Revision to recommendations considered as additional data become available

- ### Indirect effects of PCV13 use in children on disease in adults
- #### Will PCV13 use in children reduce disease in adults?
- Carriage and transmission for some serotypes similar to PCV7 serotypes (types 19A, 7F, 6A)
  - Serotype 1 is rarely carried, so unclear if vaccinating children will reduce type 1 disease
  - Efficacy of PCV13 may not be similar to PCV7 for some types (types 1 and 3)

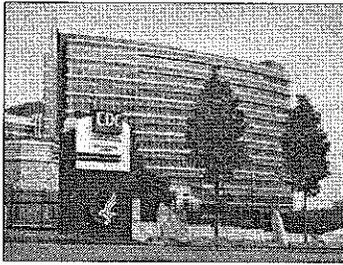
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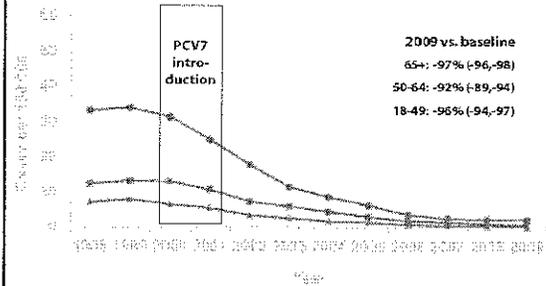
The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

National Center for Immunization and Respiratory Diseases  
Division of Bacterial Diseases



Thank you

**Rates of IPD caused by PCV7 serotypes among adults ≥18 years-old, ABCs 1998-2009**



Moore, IDSA, 2009

**Public Health and Economic Impact of PCV13 in US Adults Aged ≥ 50 Years**

- Assuming use of PCV13 in lieu of PPV23, evaluated outcomes among
  - all persons ≥50 years
  - 58% of persons aged ≥65 years and 32% of moderate- and high-risk persons aged 50-64 years
- Evaluated receipt of PCV13 only at model entry only and at model entry and every 10 years thereafter.
- Use of PCV13 vs PPV23 estimated to reduce over a lifetime
  - 25,000-129,000 IPD cases
  - 456,000-3.3 million non-bacteraemic cases
  - Total costs by \$1.4-\$5.2 billion

Weycker et al IDSA Annual Meeting 2010; Abstract #462

**Prevention of pneumococcal disease among adults: comparison of polysaccharide & conjugate vaccines**

	23-valent polysaccharide (adults)	7-valent conjugate (children)
Coverage against IPD serotypes before PCV7	>80%	>80%
Potential for boosting	-	+
Effectiveness		
Invasive disease	++	++++
All-cause pneumonia	-	++
Mucosal / herd immunity	-	++