Impact of pneumococcal conjugate vaccine: US experience

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San Jose, Costa Rica, August 2007
# Pneumococcal Conjugate Vaccine Introduction in the U.S.

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
</tr>
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<tbody>
<tr>
<td>Feb 2000</td>
<td>7-valent vaccine (Prevnar™) licensed</td>
</tr>
<tr>
<td>Summer &amp; Fall 2000</td>
<td>Recommendations for vaccine use</td>
</tr>
<tr>
<td></td>
<td>Government purchasing</td>
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<tr>
<td></td>
<td>Rapid increase in use</td>
</tr>
<tr>
<td>Aug 2001-Sept 2004</td>
<td>Intermittent shortages</td>
</tr>
<tr>
<td>2005</td>
<td>83% coverage with 3+ doses among children 19-35 months</td>
</tr>
</tbody>
</table>
U.S. Recommendations for Use of Pneumococcal Conjugate Vaccine

- All children <2 years
- Children 2-4 years with
  - Certain chronic illnesses
  - Immunocompromising conditions
- Consider for all children 2-4 with priority to those
  - 24-35 months
  - Alaska Native, American Indian, African American
  - Attending day care

Advisory Committee on Immunization Practices. MMWR 2000
Active Bacterial Core Surveillance (ABCs) Emerging Infections Program Network

Established

Areas
OR (3 counties)
CA (1 county)
MN (7 counties)
GA (20 counties)
MD (6 counties)
CT (entire state)
NY (7 counties)
TN (10 counties)
CO (8 counties)
NM (entire state)
Effect in Target Age Group

Invasive Pneumococcal Disease Rates in Children <5 Years, ABCs, 1998-2005

PCV7

2005 vs baseline
- 77% (<1 yr)
- 82% (1 yr)
- 75% (2 yr)
- 61% (3 yr)
- 26% (4 yr)
## Effectiveness by Serotype and Presence of Underlying Medical Conditions

<table>
<thead>
<tr>
<th>Serotype</th>
<th>Vaccinated (≥1 dose) vs. unvaccinated VE (95%CI)</th>
<th>Underlying medical condition*</th>
<th>No medical condition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>72 (65, 78)</td>
<td>77 (62, 87)</td>
<td>71 (63, 78)</td>
</tr>
<tr>
<td>Vaccine type a</td>
<td>-</td>
<td>81 (57, 92)</td>
<td>96 (93, 98)</td>
</tr>
<tr>
<td>Vaccine related</td>
<td>43 (6, 66)</td>
<td>35 (-151, 83)</td>
<td>44 (5, 67)</td>
</tr>
</tbody>
</table>

N=782 cases and N=2512 controls
*Case/control sets with chronic or immunocompromising medical condition present

\(^a\) p=0.0014

Whitney et al Lancet 2006
# Effectiveness against Vaccine Types by Number and Timing of Doses

<table>
<thead>
<tr>
<th>Schedule, by months of age at time of doses</th>
<th>Effectiveness, %</th>
<th>95% confidence interval, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant schedules</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 dose ≤7 months</td>
<td>73</td>
<td>43, 87</td>
</tr>
<tr>
<td>2 doses ≤7 months</td>
<td>96</td>
<td>88, 99</td>
</tr>
<tr>
<td>3 doses ≤7 months</td>
<td>95</td>
<td>88, 98</td>
</tr>
<tr>
<td>1 dose ≤7 months, 1 dose 7-11 months, 1 dose 12-16 months*</td>
<td>100</td>
<td>88, 100</td>
</tr>
<tr>
<td>2 doses ≤7 months, 1 dose 12-16 months</td>
<td>99</td>
<td>86, 100</td>
</tr>
<tr>
<td>3 doses ≤7 months, 1 dose 12-16 months*</td>
<td>100</td>
<td>94, 100</td>
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</tbody>
</table>

*ACIP recommended schedules

Whitney et al Lancet 2006
Conjugate Vaccine Effect on Carriage
Pneumococcal carriage following introduction of PCV7 by serotype and quarter, 2000-2003

Pelton SI, Pediatr Infect Dis J 2004; 23:101522
Replacement Disease

Are declines in vaccine-type disease associated with increases in non-vaccine type disease?
Relative Magnitude of Changes by Serotype in <2 year olds, ABCs
1998/1999 (Baseline) vs. 2005

<table>
<thead>
<tr>
<th>Type</th>
<th>Cases/100,000 pop</th>
<th>% change</th>
<th>95% CI</th>
<th>Rate Diff.</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>2005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccine</td>
<td>160</td>
<td>2</td>
<td>-99</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-99, -98</td>
<td>-158</td>
</tr>
<tr>
<td>19A</td>
<td>5</td>
<td>15</td>
<td>+180</td>
<td>+10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+95, +303</td>
<td></td>
</tr>
<tr>
<td>Other non-vaccine</td>
<td>13</td>
<td>21</td>
<td>+66</td>
<td>+8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+28, +116</td>
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</table>
Why Serotype 19A?

- Relatively common cause of disease before vaccine use
- Commonly carried
- Vaccine provides no cross protection
- Frequently antibiotic resistant
- Clonal expansion and possible capsular switching (Pai R et al J Infect Dis 2005)
Invasive Disease in Children <2 years by Susceptibility to Penicillin

Incidence (cases per 100,000)

Pen S
Pen NS
Vaccine introduced

Incidence of Pen NS disease
Incidence of Pen S disease

IPD Rates among Alaska Native Children < 2 years old, by Year

Singleton RJ et al.  JAMA 2007;297:1784-1792
What is Herd Immunity?
Susceptible Population
Herd immunity: Partially Vaccinated Population
Evidence of herd immunity reducing disease among children

• Drop in VT disease in children outside vaccinated age group (~50% reduction in infants <2 mos and children 5-17 years)
  Poehling K et al, JAMA 2006

• Observed reduction in VT disease in children <5 yrs (98%) >> expected (77%)
  – Expected reduction = vaccine coverage (83% 3+ doses) X vaccine efficacy (92%)
Transmission from Children to Adults
**Herd Effect in Adults**

Invasive Pneumococcal Disease Rates over Time

ABCs, 1998-2005

Lexau et al. JAMA 2004 and unpublished data
## Herd Effect in Adults 65+ Years

### PCV7 types vs. nonvaccine types

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<tr>
<th>Serotype</th>
<th>Cases/100,000 pop</th>
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<td>Baseline 2005</td>
<td></td>
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<tr>
<td>Vaccine</td>
<td>34</td>
<td>-82</td>
<td>-85, -78</td>
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<tr>
<td>Nonvaccine</td>
<td>26</td>
<td>+26</td>
<td>+14, +39</td>
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ABCs 1998/99 average vs. 2005

Lexau et al. JAMA 2005 and unpublished data
Cost Effectiveness of PCV7 Before and After Incorporating Herd Effects

G. Thomas Ray PIDJ 2006
Big Picture: Impact of PCV7

- Large declines in disease rates in young children
- Shift in circulating serotypes has led to herd benefit in unvaccinated children and adults
- Fewer resistant infections

But....
- Replacement disease reduces benefit (particularly in some highly susceptible groups)
Remaining Questions

• How can we encourage introduction of conjugate vaccines in more places?
• Will results in other settings compare to the U.S.?
• In countries using conjugate vaccine
  – Will replacement disease become a problem?
  – Will pneumococcal resistance increase again?
## Acknowledgements

### ABCs Surveillance

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- LaShondra Shealey
- Dee Jackson

**Emory University**
- Keith Klugman
Decline in pneumonia admissions after PCV7 introduction: Children

- Time series analysis
- Nationwide Inpatient Sample
- Rates of all-cause pneumonia dropped 39% (-506/100,000) by 2004 in children <2 yrs
- Represents ~41,000 fewer pneumonias in 2004
- Pneumococcal pneumonia dropped 65%

Post marketing studies of otitis media

- Diagnostic code studies show decrease in episodes, frequent otitis, and PE tubes
- Studies with isolates not population based, but show decrease in VT and increase in NVT
Decline in pneumonia admissions after PCV7 introduction: Adults

- Time series analysis
- Nationwide Inpatient Sample
- Significant declines in all-cause (-26%) and pneumococcal (-30%) pneumonia in adults 18-39 years
- No significant changes in other adult age groups