Indirect Effects—

Multiplying the benefits of vaccinating children

Cynthia Whitney, MD MPH

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Conflicts of interest: None
Evolution of Thinking on Indirect Effects

• 2000
  – First pneumococcal conjugate vaccine licensed
  – Clinical trials showed protection in children who received vaccine (direct effects)
  – Unclear if vaccination would reduce disease in unvaccinated persons in the community (indirect effects)

• 2013
  – Second generation conjugates in use in many countries
  – Indirect effects recognized as powerful driver of PCV program benefits
Goals

• Explain how indirect effects work
• Review main lessons learned of last decade
  – Children
  – Adults
• Provide background for indirect effects posters/presentations at ISPPD9
What are indirect effects*?

*sometimes called herd effects
Susceptible Population
Indirect Effects: Partially Vaccinated Population
Rates of invasive pneumococcal disease among U.S. children <5 years, 1998-2009

Rapid decrease – was some of this indirect effects?

Moore, IDSA, 2009
Evidence of herd effects reducing disease among children

• Early (2003) observed reduction in VT disease in children <5 yrs (94%) >> expected (64%)
  – Expected reduction = vaccine coverage (68% 3+ doses) X vaccine efficacy (94%)
    CDC MMWR September 16, 2005

• Drop in VT disease in children outside vaccinated age group (~50% reduction in infants <2 mos and children 5-17 years by 2003)
  Poehling K et al, JAMA 2006

• Multiple studies showed drop in carriage of vaccine type strains following routine PCV use
What We’ve Learned
PCV7 Indirect Effects in Children

• VT invasive disease drops quickly in young children following routine PCV introduction
  – Shown in multiple countries
  – Both direct and indirect effects contribute
  – Corresponds with shift in carried serotypes

• Indirect effects provide powerful protection for children
  – Children too young/too old for vaccination
  – Vaccine-eligible children who miss doses
Transmission from Children to Adults
Rates of IPD caused by PCV7 serotypes among adults ≥18 years-old, ABCs 1998-2009

Moore, IDSA, 2009

Slightly slower decrease compared to vaccine-age children

Year

Cases per 100,000

65+ yrs

50-64 yrs

18-49 yrs

PCV7 introduction
Estimated IPD cases prevented among all ages, United States 2001-2009

280,000 cases & 19,000 deaths prevented

Pilishvili JID 2010 & CDC unpublished
Cost Effectiveness of PCV7 Before and After Incorporating Indirect Effects

Later estimate incorporating indirect effects on pneumonia showed program was cost saving.

G. Thomas Ray et al PIDJ
Indirect Effects on Pneumonia: Powerful effect across age groups

- Modeled pneumococcal pneumonia burden prevented by PCV7 use from 2000 to 2006
- Health Care Utilization Project State Inpatient Databases for 1996-2006 from 10 states
- ~789,000 fewer pneumococcal pneumonia hospitalizations
  - 90% age 18+
- ~84,000 fewer deaths
  - 98% age 18+

Many populations have significant indirect effects after PCV introduction

- Multi-country evaluation of PCV effects on rates of IPD
- In adults, effects less consistent than those in children
- Among adults age 65+ years, overall ~58% reduction in vaccine type rates at year 3

13 sites, observed/expected rate ratio: 0.42 (0.35–0.50)

What We’ve Learned
PCV7 Indirect Effects in Adults

• Vaccinating young children reduces vaccine-type disease in adults
• Shown in multiple countries
• Lags a little behind effect in children (~1 year)
• In high-income settings, prevention of disease in adults drives cost-effectiveness of program (deaths mostly in older adults)
Will Indirect Effects Occur in SE Asia?

- **Yes!**
  - New data here at ISPPD9 will show
    - Indirect effects with 2\textsuperscript{nd} generation vaccines (PCV10 and PCV13)
    - Reductions in disease in unvaccinated age groups
    - Effects in a variety of populations – not just high income
  - Therefore, effects should be seen in Asia

- **But…**
  - How quickly depends on vaccination coverage/catch-up
  - Overall benefit from indirect effects will depend on
    - Proportion/rate of disease caused by vaccine serotypes
    - Can be smallish in some older children and adult populations
Role of catch-up campaigns
- Do they speed up indirect effects?
- If so, what kind of campaign works best (<1 yo’s, <2 yo’s, <5 yo’s)?

How much coverage is needed to induce indirect effects?

What schedule is best for indirect effects (does a booster dose help)?
Thank you

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: http://www.cdc.gov

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