Pneumococcal Conjugate Vaccine

Pharmacoeconomic Analyses and the Impact of the Herd Effect
Pneumococcal Conjugate Vaccine

- Review published cost-effectiveness analyses not incorporating indirect effects.
  - Australia, Europe, North America
    - Not incorporating indirect effects
    - Impact of incorporating herd effect
  - Pooled analysis of 72 Global Alliance for Vaccine and Immunizations (GAVI)-eligible countries

- Cost-effectiveness: A way to evaluate the “value” of the vaccine, given its costs
Cost-effectiveness analyses incorporating only direct effects

- 14 published cost-effectiveness studies in high-income countries (through 2006)
  - United States
  - Canada (2)
  - Switzerland
  - Germany
  - United Kingdom (2)
  - Finland
  - Netherlands
  - Spain (2)
  - Australia
  - Italy
  - Norway
Summary of cost-effectiveness analyses incorporating only direct effects

- Conditions prevented by vaccine
  - Otitis media
  - Pneumonia (non-invasive, variously defined)
  - Invasive pneumococcal disease (IPD)
    - Meningitis
    - Bacteremia
  - Long-term sequelae (such as disability/deafness)
  - Ventilatory tube placements
  - Deaths from IPD (all studies)
  - Deaths from pneumonia (5 studies)
Calculating cost effectiveness for PCV

# Doses of vaccine given → Cost of vaccination (doses + admin)

# Episodes of disease prevented
  - Otitis media → - Savings
  - Pneumonia → - Savings
  - Invasive disease → - Savings

# Life years saved = Net cost of vaccine program

Net cost of vaccine program = Cost Per Life-Year Saved

# Life years saved
Calculating cost effectiveness for PCV

- Estimate rates of disease before implementing vaccination program
- Estimate case-fatality rates
- Apply vaccine efficacy
  - Otitis media
  - Pneumonia
  - Invasive pneumococcal disease
- Estimate medical and non-medical cost of each condition
- Estimate cost of vaccine doses and administration
Sample of Main Assumptions Used in Revised U.S. Cost-Effectiveness

Disease incidence (per 100,000 children age 1 to < 2 years)

- IPD: 186
- Pneumonia: 4,415
- Simple Otitis Media: 107,000

Case fatality rates

- Meningitis: 5.1 per 100
- Bacteremia: 0.8 per 100

Vaccine efficacy (% disease prevented, Direct effect)

- IPD: 75%
- Pneumonia (clinically diagnosed): 6%
- Simple Otitis Media: 8%

Costs (medical+non-medical)

- Vaccine dose + administration: $61
- Case of meningitis: $16,424
- Case of bacteremia: $3,136
- Case of pneumonia: $706
- Case of simple otitis media: $246
PCV Cost-effectiveness analyses: Estimated net positive cost of vaccine per child vaccinated (cost of vaccine doses+administration minus savings due to reduced disease (direct effect))

Two studies (Spain and Germany) estimated negative net costs per child vaccinated
Vaccine costs and savings per child vaccinated based on average of 12 cost-effectiveness analyses in Australia, North America and Europe (before incorporating indirect effects)

- Vaccine cost - all doses: $226
- Savings from averted disease:
  - Savings - other cost: $71
  - Savings - medical costs: $81
- Net cost: $226

Average of 12 analyses
PCV Cost-effectiveness analyses: Estimated number of cases averted per 100,000 children vaccinated (direct effect)

Deaths (per 100,000)

= IPD case fatality rate, mean ~3%
* = Also assumed death from pneumonia

Mean = 4.4
Base-Case PCV Cost-effectiveness analyses: Cost per life-year saved, societal perspective (without quality-of-life adjustments or indirect effects)

Country of study: Spain, Ger, Italy, UK, Spain, Can, Neth, USA, Can, Nor, Fin

Cost per life-year saved - societal ($US)

Spain: Cost Saving
Ger: Cost Saving
Italy: Cost Saving
UK: Cost Saving
Spain: Cost Saving
Can: Cost Saving
Neth:Cost Saving
USA: Cost Saving
Can: Cost Saving
Nor: Cost Saving
Fin: Cost Saving
“Indirect” Effect of PCV

- Herd effect
  - Reductions in the incidence of disease in persons who do not receive the vaccine.
Trends in invasive pneumococcal disease after PCV introduction

Introduction of PCV

Cases per 100,000 population

Year

U.S. analysis incorporating herd effects

- Modified prior analysis of direct effects to include herd effects.
  - Estimated cost-effectiveness in U.S. from 2000 to 2004
  - Assumed herd effect was only related to reductions in invasive pneumococcal disease (not pneumonia)
  - Made no assumptions about changes in vaccine efficacy or herd effect in years beyond 2004
Total costs averted per child vaccinated

- Non-vaccinated persons, $40
- Vaccinated persons, $71

IPD cases averted per 1000 children vaccinated

- Non-vaccinated persons, 2.75
- Vaccinated persons, 5.17

Life-years averted per 1000 children vaccinated

- Vaccinated persons, 0.81
- Non-vaccinated persons, 4.96

Relative impact of direct effect versus herd effect ~70% vaccine coverage (2006 U.S. analysis)

Only herd effect on IPD is included here, not pneumonia.
Summary of cost-effectiveness analyses including herd effects - cost per life-year saved ($), base case.

- **UK (1): medical costs**
  - Without herd effect: 7,100
  - With herd effect: 52,000

- **USA: societal**
  - Without herd effect: 7,500
  - With herd effect: 80,000

- **GER: medical costs**
  - Without herd effect: 210
  - With herd effect: 128,814

- **NOR: societal**
  - Without herd effect: 71,000
  - With herd effect: 152,000

- **UK (2): medical costs**
  - Without herd effect: 8,200
  - With herd effect: 176,000
Issues in estimating indirect effect globally

- 3 doses of vaccine versus 4
- *S. pneumoniae* carriage rates
- Population mixing patterns
  - # of persons living in household / how close together people live
  - Daycare
- % of children vaccinated
- Distribution of serotypes and burden of disease by age group.
Global and regional economic analyses of PCV

- Pooled analysis of 72 Global Alliance for Vaccine and Immunizations (GAVI)-eligible countries (Conducted by Anushua Sinha)
List of Global Alliance for Vaccine and Immunization (GAVI) eligible countries

## GAVI - eligible analysis: Assumptions

<table>
<thead>
<tr>
<th>Assumption</th>
<th>Under 5 yrs of age mortality rate (per 1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;150 (N=25)</td>
</tr>
<tr>
<td>Vaccine cost per dose</td>
<td>$5</td>
</tr>
<tr>
<td>Program administration cost per dose</td>
<td>$0.34</td>
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<tr>
<td>Vaccine efficacy against deaths (deaths prevented per 1000)</td>
<td>7.4</td>
</tr>
<tr>
<td>Probability of dying between 3 and 29 months</td>
<td>10.2%</td>
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<tr>
<td>Coverage rate</td>
<td>69%</td>
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<tr>
<td>Cost of fatal disease</td>
<td>$150</td>
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</tbody>
</table>
GAVI-eligible analysis: Results
(Most conservative analysis highlighted)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Lives saved (100k)</th>
<th>Hospitalizations averted (100k)</th>
<th>Disease costs saved ($, mill)</th>
<th>DALYs averted (mill)</th>
<th>International $ per DALY averted</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Deaths</strong> 3 to 29 months</td>
<td>262</td>
<td>262</td>
<td>44</td>
<td>8.3</td>
<td>100</td>
</tr>
<tr>
<td>+ Non-fatal disease 3 to 29 months</td>
<td>262</td>
<td>1,158</td>
<td>218</td>
<td>8.3*</td>
<td>80</td>
</tr>
<tr>
<td>+ Extended protection to 59 months</td>
<td>369</td>
<td>2,458</td>
<td>453</td>
<td>11.7</td>
<td>37</td>
</tr>
</tbody>
</table>
Is pneumococcal conjugate vaccine cost-effective in GAVI-eligible countries?

Under $100 per DALY

Highly cost-effective

Cost-effective

Not cost-effective

World Health Organization criteria
Hold for reserve


References


Comparison and summary of published cost-effectiveness studies

- Compare the number of deaths expected to be prevented for every 100,000 children vaccinated
  - Calculated from studies to facilitate comparisons

- Assumptions that affect these data
  - Incidence of disease, including serotype distribution
  - Case-fatality rates
  - Vaccine efficacy
  - Number of years vaccine is effective
PCV Cost-effectiveness analyses: Estimated number of cases averted per 1000 children vaccinated (direct effect)

Mean = 217
PCV Cost-effectiveness analyses: Estimated number of cases averted per 1000 children vaccinated (direct effect)

Country of study

Cases averted per 1000 children vaccinated

Mean=16
PCV Cost-effectiveness analyses: Estimated number of cases averted per 1000 children vaccinated (direct effect)

- Invasive pneumococcal disease
  - Mean = 1.6
  - ~9%

= IPD case fatality rate, mean ~3%

Mean = 1.6
Estimated percent of total costs averted by type of cost: High income countries (average of all c/e analyses with medical and non-medical costs)
Percent Reduction In Invasive Pneumococcal Disease Among Non-vaccinated Persons in 5 Years After PCV (Baseline=1997-1999)
Vaccine costs and savings per child vaccinated based on U.S. five-year analysis (2000 to 2004) after incorporating indirect effects.
GAVI-eligible analysis: Model

Vaccination

1

- Death (2)
- Hospitalized meningitis* (2)
- Hospitalized pneumonia* (2)
- Outpatient pneumonia* (2)
- No event (2)

No vaccination

* non-fatal events

Go to Node 1

[Diagram showing the flow of events after vaccination and no vaccination, with death, hospitalization, and outpatient pneumonia as outcomes.]