Review of economic evaluation of pneumococcal vaccination in older children and adults

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Road map

• Review of cost-effectiveness analysis
• Economic evaluation of PCV and PPSV23 in adults: International perspective
• Economic evaluation of PCV and PPSV23: Latin America and the Caribbean
• Conclusions

PCV = 13v pneumococcal conjugate vaccine; PPSV23 = 23v pneumococcal polysaccharide vaccine; LAC = Latin America and the Caribbean; US = United States; UK = United Kingdom
Road map

• Review of cost-effectiveness analysis
  – Rationale
  – Components
  – Cost-effectiveness ratio

• Economic evaluation of PCV and PPSV23 in adults: International perspective

• Economic evaluation of PCV and PPSV23: Latin America and the Caribbean

• Conclusions

PCV = 13v pneumococcal conjugate vaccine; PPSV23 = 23v pneumococcal polysaccharide vaccine; LAC = Latin America and the Caribbean; US = United States; UK = United Kingdom
• Ministries of Health and Finance have a finite budget.

• It is necessary to choose and prioritize health interventions.

• Cost-effectiveness, by estimating value for money, informs the best choices of health interventions.

• It aims to maximize health benefit given a finite budget and spend health money more wisely.
Cost-effectiveness analysis: components

Disease burden modeling
- incidence
- case fatality data
- risk factors
- sub-populations/demography

Economic burden modeling
- costs of outpatient disease management
- costs of hospital disease management
- costs to families

Intervention effectiveness
- efficacy
- effectiveness
- coverage

Intervention cost modeling
- target population
- programmatic costs
- vaccine purchase costs

Cost-effectiveness analysis
Cost-effectiveness analysis: cost-effectiveness ratio (CER)

\[
\text{CER} = \frac{\text{Vaccination program Costs} - \text{Disease management costs prevented}}{\text{Health benefits}}
\]

Health benefits
(lives saved, life years gained,
QALYs saved, DALYs averted, etc.)

QALYs = quality-adjusted life years; DALYs = disability adjusted life years
Road map

• Review of cost-effectiveness analysis
• Economic evaluation of pneumococcal vaccines in adults: International perspective
  – US
  – UK
• Economic evaluation of PCV and PPSV23: Latin America and the Caribbean
• Conclusions

PCV = 13v pneumococcal conjugate vaccine; PPSV23 = 23v pneumococcal polysaccharide vaccine; LAC = Latin America and the Caribbean; US = United States; UK = United Kingdom
Cost-effectiveness of Adult Vaccination Strategies Using Pneumococcal Conjugate Vaccine Compared With Pneumococcal Polysaccharide Vaccine

Kenneth J. Smith, MD, MS
Angela R. Wateska, MPH
Mary Patricia Nowalk, PhD, RD
Mahlon Raymund, PhD
J. Pekka Nuorti, MD, DSc
Richard K. Zimmerman, MD, MPH

Context The cost-effectiveness of 13-valent pneumococcal conjugate vaccine (PCV13) compared with 23-valent pneumococcal polysaccharide vaccine (PPSV23) among US adults is unclear.

Objective To estimate the cost-effectiveness of PCV13 vaccination strategies in adults.

Design, Setting, and Participants A Markov state-transition model, lifetime time horizon, societal perspective. Simulations were performed in hypothetical cohorts of US 50-year-olds. Vaccination strategies and effectiveness estimates were developed by a Delphi expert panel; indirect (herd immunity) effects resulting from childhood PCV13 vaccination were extrapolated based on observed PCV7 effects. Data sources for model parameters included Centers for Disease Control and Prevention Active Bacterial Core surveillance, National Hospital Discharge Survey and Nationwide Inpatient Sample data, and the National Health Interview Survey.
US model structure

Adult cohort, entering model at age 50, followed lifetime:

Sub-populations:
Average risk
Immunocompromised
Other comorbid condition

Smith KJ et al. JAMA 2012
US model: pneumococcal disease risk

- Baseline probability of infection (pre childhood PCV13)
- Relative probability of infection (indirect effect, before versus after PCV13)
- Probability of infection with vaccine serotype
- Projected change in probability of vaccine serotype infection (indirect effect)
- Probability of vaccination
- Vaccine effectiveness

Smith KJ et al. JAMA 2012
## US model: vaccine efficacy

<table>
<thead>
<tr>
<th>Vaccine (cost per vaccinated patient)</th>
<th>Healthy 50 yr olds (1, 5, 10, 15 yrs)*</th>
<th>Healthy 65 yr olds (1, 5, 10, 15 yrs)*</th>
<th>Immunocompromise (1, 5, 10, 15 yrs)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPSV23 ($43)</td>
<td>93%, 85%, 20%, 0%</td>
<td>80%, 58%, 0%, 0%</td>
<td>0%, 0%, 0%, 0%</td>
</tr>
<tr>
<td>-- IPD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-- Pneumonia**</td>
<td>0% at all times</td>
<td>0% at all times</td>
<td>0% at all times</td>
</tr>
<tr>
<td>PCV13 ($128)</td>
<td>90%, 70%, 50%, 45%</td>
<td>85%, 70%, 50%, 33%</td>
<td>50%, 35%, 25%, 5%</td>
</tr>
<tr>
<td>-- IPD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-- Pneumonia**</td>
<td>74%, 57%, 41%, 37%</td>
<td>64%, 53%, 38%, 25%</td>
<td>35%, 25%, 18%, 4%</td>
</tr>
</tbody>
</table>

* Expert panel estimates ** Non-bacteremic pneumococcal pneumonia

Smith KJ et al. JAMA 2012
US model: strategies considered

1) No vaccination
2) Current recommendation, PPSV23 at age 65*
3) Substitute PCV13 for PPSV23 in current recommendation at age 65*
4) PCV13 at 50 years; PPSV23 at 65 years
5) PCV13 at 50 years and 65 years
6) PCV13 at 50 and 65 years; PPSV23 at 75 years

* Plus younger persons with high risk conditions

Smith KJ et al. JAMA 2012
## US model: base case results

USD 2006; 3% discount rate

<table>
<thead>
<tr>
<th>Vaccination Scheme</th>
<th>Pneumonia** lifetime incidence per 100,000</th>
<th>IPD lifetime incidence per 100,000</th>
<th>Cost per person</th>
<th>$ per QALY (societal perspective)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No vaccination</td>
<td>9292</td>
<td>858</td>
<td>$1047</td>
<td>--</td>
</tr>
<tr>
<td>PPSV23 at 65 yr*</td>
<td>9292</td>
<td>815</td>
<td>$1059</td>
<td>$34,600</td>
</tr>
<tr>
<td>PCV13 at 65 yr*</td>
<td>9122</td>
<td>822</td>
<td>$1080</td>
<td>$28,900</td>
</tr>
<tr>
<td>PCV13 at 50 yr, PPSV23 at 65 yr</td>
<td>9229</td>
<td>833</td>
<td>$1119</td>
<td>More expensive, less effective</td>
</tr>
<tr>
<td>PCV13 at 50 yr, 65 yr</td>
<td></td>
<td></td>
<td>$1123</td>
<td>$45,100</td>
</tr>
<tr>
<td>PCV13 at 50 yr, 65 yr, PPSV23 at 75 yr</td>
<td>8988</td>
<td>830</td>
<td>$1131</td>
<td>$496,000</td>
</tr>
</tbody>
</table>

* Plus younger persons with high risk conditions  ** Non-bacteremic

Smith KJ et al. JAMA 2012
US model: How do cost-effectiveness results vary as assumptions vary?

<table>
<thead>
<tr>
<th>Scenario</th>
<th>What impact on results?</th>
</tr>
</thead>
<tbody>
<tr>
<td>If PCV13 efficacy against pneumonia is low...</td>
<td>PPSV23 is favored.</td>
</tr>
<tr>
<td>If childhood vaccination prevents more adult disease than modeled ...</td>
<td>Cost–effectiveness ratios increase – value of vaccination somewhat less.</td>
</tr>
<tr>
<td>If childhood vaccination prevents less adult disease than modeled ...</td>
<td>Cost-effectiveness ratios decrease – value of vaccination greater.</td>
</tr>
<tr>
<td>If all parameters set at “worst case”...</td>
<td>“No vaccination” still not favored.</td>
</tr>
<tr>
<td>If PCV13 ~2x base case cost...</td>
<td>PPSV23 favored, depending on willingness-to-pay.</td>
</tr>
</tbody>
</table>
US model: key messages

In the US general population –

• Pneumococcal vaccination saves lives, prevents cases, and is an efficient investment of healthcare dollars.

• When competing vaccine options, efficacy against pneumonia is an important driver of cost-effectiveness, as is herd protection, and vaccine cost.

• Current CDC adult recommendations ➔ PPVS23 except immunocompromised (T Pilishvili presentation 05 March; MMWR Oct 2012).
Vaccination of risk groups in England using the 13 valent pneumococcal conjugate vaccine: economic analysis

Mark H Rozenbaum health economist and infectious disease modeller\textsuperscript{1}, Albert Jan van Hoek health economist and infectious disease modeller\textsuperscript{2}, Douglas Fleming director\textsuperscript{3}, Caroline L Trotter senior research fellow\textsuperscript{4}, Elizabeth Miller consultant epidemiologist\textsuperscript{2}, W John Edmunds professor of infectious disease modelling\textsuperscript{5}

\textsuperscript{1}Unit of PharmacoEpidemiology and PharmacoEconomics, Department of Pharmacy, University of Groningen, Antonius Deusinglaan 1, 9713 AV Groningen, Netherlands; \textsuperscript{2}Immunisation, Hepatitis and Blood Safety Department, Health Protection Agency, London, UK; \textsuperscript{3}Birmingham Research Unit of the Royal College of General Practitioners, Birmingham, UK; \textsuperscript{4}School of Social and Community Medicine, University of Bristol, Bristol, UK; \textsuperscript{5}Centre for the Mathematical Modelling of Infectious Diseases, London School of Hygiene and Tropical Medicine, London, UK
Road map

• Review of cost-effectiveness analysis
• Economic evaluation of PCV and PPSV23 in adults: International perspective
• Economic evaluation of PCV and PPSV23: Latin America and the Caribbean
  – Literature review
  – São Paulo, Brazil
• Conclusions

PCV = 13v pneumococcal conjugate vaccine; PPSV23 = 23v pneumococcal polysaccharide vaccine; LAC = Latin America and the Caribbean; US = United States; UK = United Kingdom
Economic studies of pneumococcal vaccination in adults, LAC region

- 26 country analyses in 16 studies, including two multi-country studies
- 5 peer-reviewed articles/11 abstracts
- 6 disease cost studies/10 cost-effectiveness studies
- Year of publication: 2008 – 2012
- 2 societal/14 health system or public payor perspective

Constenla D and Garcia C, unpublished data
<table>
<thead>
<tr>
<th>Country</th>
<th>Age (yrs)</th>
<th>Pneumonia</th>
<th>Meningitis</th>
<th>Bacteremia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>≥ 18</td>
<td>---</td>
<td>---</td>
<td>Public: $10,996</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Private: $10,677</td>
</tr>
<tr>
<td>Brazil</td>
<td>≥ 60</td>
<td>Public: $1,236*</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Private: $7,044*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mexico</td>
<td>0-10</td>
<td>$6,718**</td>
<td>$23,307</td>
<td>$9,740</td>
</tr>
<tr>
<td>Mexico</td>
<td>≥ 50</td>
<td>$4,270**</td>
<td>$10,921</td>
<td>$7,867</td>
</tr>
<tr>
<td>Multi-Country</td>
<td>≥ 50</td>
<td>Argentina: $34,111, Brazil: $34,111, Brazil: $31,166, Chile: $28,498, Colombia: $25,028, Mexico: $22,237, Venezuela: $23,843</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

* bacteremic pneumonia  ** inpatient pneumonia

Constenla D and Garcia C, unpublished data
Economic burden, disease cost per case

• Cost per single case of meningitis > bacteremia/bacteremic pneumonia > non-bacteremic pneumonia.

• Costs of outpatient pneumonia ~1/20 – 1/10 hospitalized pneumonia → but common → contributes to overall economic burden.

• Costs of meningitis sequelae may be important (19% – 75% of acute management costs in two studies).

Constenla D and Garcia C, unpublished data
Economic studies of pneumococcal vaccination in adults, LAC region

• 26 country analyses in 16 studies, including two multi-country studies

• 5 peer-reviewed articles/11 abstracts

• 6 disease cost studies/10 cost-effectiveness studies

• Year of publication: 2008 – 2012

• An emerging literature with studies in the pipeline

Constenla D and Garcia C, unpublished data
## Cost-effectiveness analyses, LAC region

Two articles, eight abstracts:

<table>
<thead>
<tr>
<th>Vaccine modeled</th>
<th>#</th>
<th>Age group (#)</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCV10 compared to no vaccination</td>
<td>1</td>
<td>0 – 10</td>
<td>Argentina, Brazil, Chile, Colombia, Mexico, and Peru*</td>
</tr>
<tr>
<td>PCV13 compared to PPV23</td>
<td>4</td>
<td>≥ 65 (1)</td>
<td>Brazil, Columbia, Ecuador</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 60 (2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Elderly (1)</td>
<td></td>
</tr>
<tr>
<td>PPV23 compared to no vaccination</td>
<td>5</td>
<td>≥ 60 (4)</td>
<td>Brazil, Columbia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20 – 60 (1)</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* single multi-country study

Constenla D and Garcia C, unpublished data
Cost-effectiveness of the introduction of the pneumococcal polysaccharide vaccine in elderly Colombian population

Carlos Castañeda-Orjuela a,⁎, Nelson Alvis-Guzmán b,1, Ángel José Paternina a,b,1, Fernando De la Hoz-Restrepo a

a Epidemiology and Public Health Evaluation Group, Department of Public Health, Faculty of Medicine, Universidad Nacional de Colombia, Carrera 30 # 45-03, Office 150, Bogotá D.C., Colombia
b Department of Economic and Social Research-DIES, Universidad de Cartagena, Colombia, Calle 70 No. 7-33, Cartagena de Indias, Colombia

Abstract

Background: Streptococcus pneumoniae causes community-acquired pneumonia, otitis media and meningitis, with higher incidences at the extremes of life. PPV-23 vaccine is widely used in prevention of pneumonia and invasive pneumococcal disease in older adults in developed countries. We developed an evaluation of cost-effectiveness of implementing PPV-23 in Colombian population over 60 years.

Methods: The number of cases of pneumonia and meningitis in patients over 60 years and the proportion by S. pneumoniae was estimated based on a revision of literature. A decision tree model with a 5-year horizon was used in order to evaluate the cost-effectiveness of implementing PPV-23 in elderly patients in Colombia.
Cost-effectiveness analysis of pneumococcal polysaccharide vaccination from age 60 in São Paulo State, Brazil

Joao Tonolio Neto,1 Gabriela Tannus Branco de Araujo,1,2,* Anna Gagliardi,1 Amanda Pinho,3 Laure Durand4 and Marcelo Fonseca1,2

1Federal University of Sao Paulo; 2Axia.Bio Consulting; 3sanofi Pasteur; Sao Paulo, Brazil; 4sanofi Pasteur; Lyon, France

Key words: pneumococcal polysaccharide vaccine, cost-effectiveness analysis, Brazil, elderly

Abbreviations: LYG, life year gained; PPV23, 23-valent polysaccharide pneumococcal vaccine; BPP, bacteremic pneumococcal pneumonia; NBPP, non-bacteremic pneumococcal pneumonia; WHO, World Health Organisation; GDP, gross domestic product; QALY, Quality Adjusted Life Year; SUS, Sistema Unico de Saude; CAP, Community-Acquired Pneumonia; IPD, Invasive Pneumococcal Disease; CFR, Case-Fatality Rate
São Paulo model structure

Adult cohort age ≥ 60, followed for five years:

NBPP = non-bacteremic pneumococcal pneumonia
BPP = bacteremic pneumococcal pneumonia

Neto et al Human Vaccines 2011
São Paulo model, probability of pneumococcal disease

• Probabilities of infection (no child PCV)
  – Probability of community-acquired pneumonia
    • Fraction pneumococcal
    • Fraction bacteremic (BPP) versus non-bacteremic (NBPP)
  – International data sources

• Probability of vaccination

• Vaccine efficacy

Neto et al Human Vaccines 2011
### São Paulo model, vaccine efficacy

<table>
<thead>
<tr>
<th></th>
<th>Yr one</th>
<th>Yr two</th>
<th>Yr three</th>
<th>Yr four</th>
<th>Yr five</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-bacteremic pneumonia</td>
<td>21%</td>
<td>19%</td>
<td>17%</td>
<td>15%</td>
<td>14%</td>
</tr>
<tr>
<td>Bacteremic pneumonia</td>
<td>64%</td>
<td>58%</td>
<td>52%</td>
<td>47%</td>
<td>42%</td>
</tr>
</tbody>
</table>

10% annual rate of decline in efficacy, over five time periods
Cost per vaccinated patient = R $27 (= US$ 15 2008)

Neto et al Human Vaccines 2011
São Paulo model: base case results

R$ 2008, 5% discount rate

<table>
<thead>
<tr>
<th></th>
<th>Non-bacteremic pneumonia* cases averted</th>
<th>Bacteremic pneumonia* cases averted</th>
<th>Incremental cost per person (R$)</th>
<th>R$ per life year gained (public payor/public health system perspective)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No vaccination</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>PPSV23 age ≥ 60 yr</td>
<td>12,469</td>
<td>2,967</td>
<td>$12</td>
<td>$10,887/ $8,281</td>
</tr>
</tbody>
</table>

* Pneumococcal, five year cumulative
São Paulo model: How do cost-effectiveness results vary as assumptions vary?

- Effectiveness against NBPP: 21% (0 – 42%)
- Case-fatality rate NBPP: 13% (3.6 – 18%)
- Incidence rate NBPP: 726 (425 – 1099) per 100,000
- Discount rate: 5% (0 – 10%)
- Incidence rate BPP: 54.5 (24 – 85) per 100,000
- Case-fatality rate BPP: 26.6% (11 – 44%)
- Waning rate: 10% (0 – 20%)
- Effectiveness against BPP: 64% (44 – 80%)
- NBPP hospitalization costs
- BPP hospitalization costs
- Hospitalization rate NBPP
- Hospitalization rate BPP

Vaccine dose cost??

Neto et al. Human Vaccines 2011
São Paulo model: key messages

• An early study from LAC, consonant with other studies, showing that PPSV23 is a cost-effective intervention.

• Novel disease cost analysis.

• Some limitations
  – Use of international epidemiological data
  – No consideration of herd protection from childhood vaccination
  – Non-pneumonia invasive pneumococcal disease?
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Conclusions

• Decision makers require disease burden, economic burden, vaccine effectiveness and program costing information. These are all integrated in cost-effectiveness analysis.

• For each of these aspects, further evidence is necessary in the LAC region, ideally using standardized methodological approaches.

• To meet these evidence needs, a literature is emerging from the LAC region but is now primarily in the abstract/ pre-publication stage.

• Contemporary LAC cost-effectiveness models, consonant with work in other regions, suggest pneumococcal vaccination of older adults saves lives and is an efficient use of health dollars.