Full public health impact or cherry-picking?

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Disclosure

• The National Institute for Health and Welfare (THL) has received research funding from GlaxoSmithKline Biologicals SA for the Finnish Invasive Pneumococcal disease vaccine trial (FinIP), a nationwide effectiveness trial of the 10-valent PCV

• No outside support for NVP evaluation

• A Palmu
  – A co-investigator in the FinIP trial
  – Has received honoraria and/or travel support from GSK, Merck and Sanofi-Pasteur
  – No support since 2011
Presentation contents

• **Full public health impact:**
  Vaccine-preventable disease burden (VPDI) in children during the national vaccination programme

• **Cherry-picking:**
  Serotype-specific changes in the elderly after infant NVP introductions

• **Full public health impact:**
  Overall reductions in IPD and pneumonia in the elderly
Streptococcus pneumoniae (Pnc) causes a variety of clinical diseases

- IPD
  - Meningitis
  - Septicemia, bacteremia
  - Bacteremic pneumonia
- Non-bacteremic pneumonia
- Sinusitis
- Otitis media

- >90 serotypes
- Nasopharyngeal carriage important in transmission

Increasing seriousness
Increasing incidence
PCV in the National Vaccination Programme (NVP)

- NVP started in Sep 2010 for children born June 2010 or later
  - 2+1 schedule: 3, 5, 12 mo of age
  - No catch-up, no previous PCV7
  - Since 2009 for high-risk groups under 5 y of age
- Synflorix™ (PCV10) selected based on public tender
- Coverage high based on vaccine consumption
  - National vaccination register being built-up
  - Survey on 1000 children born 2012: coverage 92%
Incidence of invasive pneumococcal disease in children below 2 years of age in Finland
Before-after comparison of PCV10 target cohort 2010 to 2014 with a reference cohort 2004 to 2008

Children 3 to 54 months of age

Vaccination coverage

<2% for PCV
92% for PCV10
Surveillance for impact

- Nation-wide register-based surveillance based on routine diagnostics and treatment
- THL National Infectious Diseases Register
  - Invasive pneumococcal disease (IPD)
- THL Care register (hospital discharge register with in/outpatient hospitalizations and visits)
  - IPD diagnoses
  - Hospital-diagnosed pneumonia
  - Otitis media surgery
- National Insurance Institution (KELA) registers
  - Antimicrobial prescription (open care), surrogate for acute otitis media
  - Otitis media surgery
The disease burden caused by *S. pneumoniae* in infants and the vaccine preventable disease incidences (VPDI)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Incidence, per 10⁵ person-years (py)</th>
<th>Reduction after PCV10 introduction</th>
<th>Proportion of the outcome out of total reduction, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reference cohort</td>
<td>Target cohort</td>
<td>Relative reduction, %</td>
</tr>
<tr>
<td>Laboratory-confirmed IPD</td>
<td>54</td>
<td>11</td>
<td>80 (73-85)</td>
</tr>
<tr>
<td>Non-laboratory-confirmed IPD/sepsis</td>
<td>358</td>
<td>217</td>
<td>39 (35-44)</td>
</tr>
<tr>
<td>Hospital-diagnosed pneumonia</td>
<td>1036</td>
<td>898</td>
<td>13 (10-17)</td>
</tr>
<tr>
<td>Tympanostomy tube placements</td>
<td>5417</td>
<td>4590</td>
<td>15 (14-17)</td>
</tr>
<tr>
<td>Antimicrobial purchases</td>
<td>109084</td>
<td>89550</td>
<td>18 (18-18)</td>
</tr>
<tr>
<td>Any outcome</td>
<td>115949</td>
<td>95226</td>
<td>20683</td>
</tr>
</tbody>
</table>

VE, Vaccine Effectiveness; CI, Confidence Interval; VPDI, Vaccine-Preventable Disease Incidence; IPD, Invasive Pneumococcal Disease; AOM, Acute Otitis Media.
The disease burden caused by *S. pneumoniae* in children and the VPDI during the Finnish NVP. Graphics based on true incidences.
Number needed to vaccinate to prevent one event during two-year follow-up – Finnish NVP

<table>
<thead>
<tr>
<th>Disease</th>
<th>NNV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory-confirmed IPD</td>
<td>1161</td>
</tr>
<tr>
<td>Suspected non-laboratory-confirmed IPD / sepsis</td>
<td>354</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>363</td>
</tr>
<tr>
<td>Tympanostomy tube placement</td>
<td>61</td>
</tr>
<tr>
<td>Antimicrobial purchase</td>
<td>3</td>
</tr>
<tr>
<td>Any of the outcomes above</td>
<td>3</td>
</tr>
</tbody>
</table>

![2+1 doses](image)
Presentation contents 2

• Full public health impact:
Vaccine-preventable disease burden (VPDI) in children during the national vaccination programme

• Cherry-picking:
Serotype-specific changes in the elderly after infant NVP introductions

• Full public health impact:
Overall reduction in IPD and pneumonia in the elderly
Number of 19A IPD cases by calendar year in the elderly (>=65 years) in Finland after infant PCV10 introduction in 2010.
Number of 15A IPD cases (adjusted) by epidemic year in the elderly (>=65 years) in England+Wales after infant PCV7/13 introduction in 2006/2010

![Graph showing the number of 15A IPD cases by epidemic year in England and Wales after PCV7 and PCV13 introduction in infants.](image)


10.11.2017 Arto Palmu / RIVM2017
Incidence of IPD due to 5 most common replacement serotypes in UK by year in the elderly (≥65 years) in England and Wales and in Finland

Incidence of IPD due to 5 most common replacement serotypes in Finland by year in the elderly (>=65 years) in England and Wales and in Finland

Serotypes 19A, 3, 22F, 6A/C, and 11A

Picking serotypes – up to >90 available

• The introduction of 7 or 10 or 13-valent vaccines have the potential to affect the ecology of all the serotypes
  – Adding any serotype in the vaccine, will affect the replacement by the remaining serotypes
• Therefore, all disease needs to be evaluated, not only selected ones

• Public data available at www.thl.fi
  – data on individual serotypes by year and age groups
• Search for "pneumococcal"
• You can pick your own!
Presentation contents 3

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• **Cherry-picking:**
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• **Full public health impact:**
  Overall reductions in IPD and pneumonia in the elderly
Number of all IPD cases and adjusted incidence by epidemic year in the elderly (>=65 years) in England and Wales after infant PCV7/13 introduction in 2006/2010

Incidence of all IPD cases by calendar year in the elderly (>=65 years) in Finland after infant PCV10 introduction in 2010
Reduction in the elderly population or not?

- **Finland**
  - No reduction in pre-post comparison, increase in 2015-2016
  - After adjustment for the baseline trend, 16% (ns.) reduction post PCV10

- **England and Wales**
  - After adjustment for the baseline trend, 19% reduction post PCV7 and further 25% reduction post PCV13 (2013-2014), but back to pre-PCV13 levels in 2015-2016

- **Sweden, both PCV10 and PCV13 used in different counties (N=21)**
  - No reduction in overall IPD observed (pre-PCV7 2005 compared to 2016)
  - However, 10-20% reduction comparing 2007-09 to 2013-16 (Naucler CID2017)
  - No reduction in Sweden/Stockholm with infant PCV13 (Galanis EurRespJ2016)
PCV10 impact on IPD and pneumonia by age group, proportion of number of prevented cases in Finland, with adjusted analyses for the elderly.
Public Health Perspective on the Impact Evaluation

- What’s needed (=public health perspective)
  - All disease syndromes related to the pathogen, not only the severe ones
  - Sensitive case definitions relevant clinically and/or in public health
  - Effects on the total population, including indirect impact
  - Long follow-up times
  - Effectiveness studies and trials
  - Absolute incidences
  - Adjustment for baseline factors and trends where appropriate

- Useful, but not adequate
  - Coverage data, immunology, surrogates like carriage

- What’s not needed (=cherry-picking)
  - Selected specific (microbiological) outcomes (only)
  - Focus on rare outcomes
  - Short per protocol follow-up periods, selected populations
  - Changes in proportions

**ESSENTIAL FOR DECISION-MAKING**

Question: How much disease will reduce due to the intervention?

**LIMITED RELEVANCE FOR PUBLIC HEALTH OR CLINICAL DECISION-MAKING**

Question: Does it work (in optimal conditions)?
Acknowledgements

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  - Heta Nieminen for animations
Nordic Vaccine Meeting 2018 in Helsinki

- 14-15 June 2018, Helsinki, Finland
- Scandic Park Hotel

- https://www.thl.fi/en/web/vaccination/nordic-vaccine-meeting-2018

- WELCOME!