What to do when country specific data are lacking?
Minimum criteria and procedures when developing vaccination recommendations in Finland

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Procedures for the Development of Evidence based Recommendations for Immunization, Berlin 15 September 2011
Disclosures

Holding a position at a governmental research institute THL

Long term research funding and collaboration with sanofi pasteur: PCV11 efficacy study in the Philippines (up to 2005)

Served as a technical expert in vaccines related matters for private sector: GSK, Novartis, Pfeizer / Wyeth, SBL vaccines and public funding bodies ECDC, EU DG Research, SIDA and Finnish Foreign Ministry and WHO, GACVS

@Julia Vuori
NATIONAL INSTITUTE FOR HEALTH AND WELFARE
Martin Friede, WHO

• “Don’t do it, if you cannot measure it!”
Protecting population with vaccination

- Research
- Expert advice
- Policy
- Surveillance Evaluation
- Program implementation
Criteria for introducing new vaccine into NIP

In Finland, since year 2000, the introduction of a new vaccine into NIP is evaluated using a 4-step approach:\(^1\):

The vaccine should have

1. considerable impact on disease burden, and
2. demonstrated safety on individual level, and
3. demonstrated / expected safety when used on large scale, and
4. be reasonably cost-effective to justify the public spending.

\(^1\)Nohynek H. Eur J Publ Health 2008;16:275-80
15 Sept 2011 Nohynek 6

Public health benefit

Vaccine safety on the individual and population level

Cost-effectiveness

Vaccine specific expert group report

CEA of the Vaccination programme

Transmission model

Expert opinion

Expert group recommendation

National Advisory Committee on Vaccination recommendation

National Institute for Health and Welfare recommendation

Decision on a vaccine specific expert group

Surveillance Evaluation

NIP

yes

yes

Decision on universal vaccination programme (MSAH statute)

Decision on the budget

Parliament decision on the budget

MSAH budget proposal

MSAH opinion

Ministry of Social Affairs and Health (MSAH) procedure

Advisory Board on Communicable Diseases comment

Decision on a vaccine specific expert group

yes

no

Transmission model

National Institute for Health and Welfare recommendation

@Heini Salo

MSAH

no

yes

no

yes

Decision on universal vaccination programme (MSAH statute)

Surveillance Evaluation

Decision on a vaccine specific expert group

Expert group recommendation

National Advisory Committee on Vaccination recommendation

National Institute for Health and Welfare recommendation

Advisory Board on Communicable Diseases comment

Ministry of Social Affairs and Health (MSAH) procedure

MSAH opinion

no

yes

yes

no
<table>
<thead>
<tr>
<th>Year</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>NoGo</td>
<td>Pneumococcal conjugate vaccine</td>
</tr>
<tr>
<td>2002</td>
<td></td>
<td>Influenza vaccination for all $\geq$65 years</td>
</tr>
<tr>
<td>2003</td>
<td></td>
<td>DTaP/dtap 6 years fewer IPV boosters</td>
</tr>
<tr>
<td>2005</td>
<td></td>
<td>DTaP-Hib-IPV combination vaccine</td>
</tr>
<tr>
<td>2006</td>
<td></td>
<td>BCG restricted to risk groups only</td>
</tr>
<tr>
<td>2007</td>
<td></td>
<td>Influenza for children 6 to 35 months</td>
</tr>
<tr>
<td>2009</td>
<td></td>
<td>Rotavirus vaccine</td>
</tr>
<tr>
<td>2010</td>
<td></td>
<td>Pneumococcal conjugate vaccine</td>
</tr>
<tr>
<td>2010</td>
<td>NoGo</td>
<td>Varicella</td>
</tr>
<tr>
<td>2011</td>
<td></td>
<td>Human papilloma virus vaccine to girls</td>
</tr>
</tbody>
</table>
Examples of data elements and their use in Finland
Facts about Finland

- Northern European country
- Former colony of Sweden (-1820) and Russia (-1917)
- 5.37 million inhabitants
- 6.8% foreigners or foreign born
- Population density 15.83 / km²
- Birth rate 10.42 / 1000
- GNP /person 35 041 € /y
- Law on Public Health 1974
- Today, 342 communities in charge of public health
In communities, health centers and well baby clinics

- Public health nurses are in charge of maternity care and well baby clinic vaccinations
- Building trust with dialogue in a well educated population
Why influenza vaccine to young children?
Data elements entered into evaluation

* 2 cohort studies in Turku (Heikkinen et al 2004)

Turku University Hospital
Register data 1988-2004

For costs, national registers, special studies, expert panel
Cost-effectiveness of influenza vaccination of healthy children

Heini Salo\textsuperscript{a}, Terhi Kilpi\textsuperscript{a}, Harri Sintonen\textsuperscript{b}, Miika Linna\textsuperscript{c}, Ville Peltola\textsuperscript{d}, Terho Heikkinen\textsuperscript{d,*}

societal perspective. Influenza vaccination resulted in savings in all programs including children $\leq$ 13 years of age from both the health care provider and societal perspective. Investing 1.7 million euros in vaccination of children $<$ 5 years of age yielded savings of 2.7 million euros in health care costs. From the health care provider perspective, the savings per vaccinated child ranged between 5.7 and 12.6 euros in any program including children up to 13 years of age. The vaccination was cost saving in all age groups even with assumed vaccine efficacy of 60%. The results show that influenza vaccination would be cost saving in all children $\leq$ 13 years of age in Finland, which advocates reconsideration of the current influenza vaccine recommendations in all countries.
Criticism from inside and outside

• Why influenza, why not PCV or rota?
• Main driver of cost was AOM;
  AOM is usually of bacterial origin, could have averted by PCV
• Assumptions on VE too high
Why pneumococcal vaccine to children?
Data elements entered into evaluation

- IPD – National Infectious Disease Register
- Pneumonia – Hospital Discharge Register (ICD10-codes: J13, J15.9, J18.1, J18.8 tai J18.9)
- AOM – national outpatient register (all regardless of etiology); FinOM cohort study (proportion Pnc 0,1-0,3)
- Otologic surgery procedures – National Social Insurance register
- Costs – health care (mean care and complication costs), societal (loss of work days)
- VE – published clinical trials
- Doses needed = 3 +1
Pnc disease burden in children <5 years

Finland birth cohort 55 000

70 cases of invasive pneumococcal disease
8 000 cases of pneumonia
250 000 episodes of acute otitis media
15 000 otologic surgery procedures
1 death

Cases per year
### PCV efficacy estimates

<table>
<thead>
<tr>
<th>Disease</th>
<th>%</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive disease</td>
<td>89.1</td>
<td>Black et al. 2000</td>
</tr>
<tr>
<td>Clinically diagnosed pneumonia</td>
<td>17.7</td>
<td>Black et al. 2002</td>
</tr>
<tr>
<td>Clinically diagnosed otitis media</td>
<td>6.0</td>
<td>Eskola et al. 2001</td>
</tr>
<tr>
<td>Tympanostomy tube placement and adenotomy</td>
<td>20.3</td>
<td>Black et al. 2000</td>
</tr>
</tbody>
</table>

Duration of vaccine efficacy 5 years
Pnc disease in children <5 years preventable by universal PCV vaccination

Birth cohort 55 000
Population 5 million

60 cases of invasive pneumococcal disease
1 400 cases of pneumonia
15 000 episodes of acute otitis media
3 000 otologic surgery procedures
0.9 deaths

Cases per year

In 2000, new pneumococcal conjugate vaccine against pneumococcal diseases

- In 2000, cost effectiveness analysis (CEA) of PCV7 introduction was not favorable
- When only direct vaccine impact was considered with 4 doses of PCV, introduction would have costed 6 mi€.
- PCV was not introduced on large scale; a recommendation was made to give it only to medical risk groups

Scandinavian Journal of Infectious Diseases, 2005; 37: 821–832

ORIGINAL ARTICLE

Economic evaluation of pneumococcal conjugate vaccination in Finland

HEINI SALO¹, HARRI SINTONEN², J. PEKKA NUORTI³, MIKA LINNA⁴, HANNA NOHYNEK¹, JOUKO VERHO¹ & TERHI KILPI¹
What is reasonably cost efficacious?

QALY
Criticism from inside and outside

- Finland no longer a model country for NIP development
- Unethical not to introduce PCV
- Too strict in step 4 (CEA) – could have performed sensitivity analysis with preliminary herd impact estimates using carriage reduction as proxy for indirect impact
Incidence of IPD in <5s

Finland: National Infectious Disease Registry - www3.ktl.fi/stat/
USA: ABC surveillance - www.cdc.gov/ncidod/dbmd/abcs/
## Finland in 2007-8
Pneumococcal disease burden without PCV

### Absolute numbers / year

<table>
<thead>
<tr>
<th>Age Group</th>
<th>AOM *</th>
<th>Pneumonia**</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Primary care</td>
<td>Secondary/ Tertiary care</td>
<td>Sepsis</td>
</tr>
<tr>
<td>&lt; 5 y</td>
<td>251 528</td>
<td>1 268</td>
<td>1 698</td>
</tr>
<tr>
<td>5-19 y</td>
<td>2 318</td>
<td>1 326</td>
<td>22</td>
</tr>
<tr>
<td>20-64 y</td>
<td>4 210</td>
<td>5 481</td>
<td>262</td>
</tr>
<tr>
<td>65v +</td>
<td>4 860</td>
<td>13 735</td>
<td>283</td>
</tr>
<tr>
<td>TOTAL</td>
<td>12 656</td>
<td>22 241</td>
<td>665</td>
</tr>
</tbody>
</table>

* Includes all AOM regardless of etiology, proportion of Pnc appr 1/10 – 1/3

**ICD10-codes: J13, J15.9, J18.1, J18.8 tai J18.9

***ICD10-codes: J13, J18.1

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Salo et al 2008

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Recalculation of cost effectiveness of PCV

- In 2008, assumptions made
  - direct impact
  - indirect impact (herd immunity, conservative estimate = half of impact seen in the U.S.)
  - total 3 doses
- Based on the favourable CEA\(^3\), Finland decided to include PCV into its NIP starting from 9/2010 and using the Nordic 2+1 schedule
- After an open tender, PCV10 was selected

Kansanterveyslaitoksen asettaman
lasten pneumokokkirokotustyöryhmän selvitys

www.thl.fi
IPD in infants <2 yrs* before and after introduction of PCV7

*N <1 year in Norway
IPD in the whole population before and after introduction of PCV7

IPD rate per 100,000/year before and after the start of vaccination.
Vaccine vs. medical costs

In 2005 the State of Finland paid appr

- 200 € for vaccines per each Finnish child up to his/her 18 yrs of age
- 95 - 164 € for hyperlipidemia medications (statins) alone / year to each of the 9% of Finns with the diagnostic criteria set
- Need to step out of the immunization box; time to change paradigm and have a more holistic, system approach!
Should HPV be introduced into NIP? Cervical cancer in Finland 1953-2007

/ 100 000 (world standard population)
World statistics

Per 100,000 (world standard population)

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finland</td>
<td>4.3</td>
<td>1.8</td>
</tr>
<tr>
<td>Australia</td>
<td>6.9</td>
<td>1.7</td>
</tr>
<tr>
<td>USA</td>
<td>7.7</td>
<td>3.6</td>
</tr>
<tr>
<td>Estonia</td>
<td>15.5</td>
<td>6.6</td>
</tr>
<tr>
<td>Romania</td>
<td>23.9</td>
<td>18.4</td>
</tr>
<tr>
<td>Ghana</td>
<td>29.3</td>
<td>23.8</td>
</tr>
<tr>
<td>Bolivia</td>
<td>55.0</td>
<td>30.4</td>
</tr>
<tr>
<td>Tansania</td>
<td>68.6</td>
<td>55.6</td>
</tr>
</tbody>
</table>

Globocan 2002
Cervical Cancer in the Nordic Countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iceland</td>
<td>8.3</td>
<td>4.7</td>
</tr>
<tr>
<td>Norway</td>
<td>10.4</td>
<td>3.5</td>
</tr>
<tr>
<td>Finland</td>
<td>4.3</td>
<td>1.8</td>
</tr>
<tr>
<td>Sweden</td>
<td>8.2</td>
<td>3.1</td>
</tr>
<tr>
<td>Denmark</td>
<td>12.6</td>
<td>5.0</td>
</tr>
</tbody>
</table>
Cervical cancer by agegroup in Finland 2001-2007

85% of cases in women >35 yrs

>90% of deaths in women >45 yrs
Finnish approach: Expert group on control of HPV disease

• Assignment
  To give a recommendation on the best measures needed to further reduce cervical cancer and the overall disease burden caused by HPV

• Started in June 2008

• Final report published 30 April 2011
Model structure

- PRIMARY INFECTION
  - TRANSMISSION MODEL
- CANCER DEVELOPMENT
  - NATURAL HISTORY MODEL

INFECTION

INTERVENTIONS
- VACCINATION
- SCREENING TREATMENT

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15 Sept 2011
Nohynek
HPV burden of disease register data sets

Finnish Cancer Registry (1980 – 2008)
- Cancer cases: cervical (C53), vaginal (C52) and vulval (C51)
- Other HPV related cancer cases

The Finnish Care Register, HILMO (1997 – 2008)
- Hospital stays, hospital outpatient visits
- Finnish Cancer Registry id no (C51-53 cancer cases)
- ICD10 and Procedure codes

HUSLAB (1996 – 2008)
- HUS* laboratories
- Pap tests in HUS area (primary and secondary health care)

Mass Screening Registry (1990-2008)
- Organised cervical cancer screening tests
- Referrals for further examinations

Social Insurance Institution, SII (1997-2008)
- Reimbursement register for medical and pharmaceutical expenses
  - Opportunistic screening and procedures (private providers)
  - Medicine expenses of GW (podophyllotoxin, imiquimod)

Finnish Student Health Service Register, FSHS (2000 – 2009)
- Pap tests and procedures

Turku primary health care (2000 – 2009)
- Pap tests and procedures

All data is linked by the personal identification number!

* Hospital District of Helsinki and Uusimaa
Estimated undiscounted and discounted QALYs and life-years gained (LYG) over time following the introduction of HPV vaccination (at year 0)

Cervarix

Gardasil

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Undiscounted costs by HPV vaccination in base case programme over time following the introduction of HPV vaccination (at year 0)

Base case programme (girls aged 12 years, no catch-up programme, 80% vaccine coverage, 100 year time horizon, and 3% discount rate) assuming vaccine protection lasts an average of 20 years.

Cervarix

Gardasil
NACV recommendation

• HPV to girls is very cost-effective, introduce at 12-13 yr school based
• HPV is even cost saving if total cost/person <125 €
• Screening to start at 25 years
  25-34 yrs Papa test
  > 35 yrs HPV test
• Exit test at 65 yrs
• If found HPV+, exit test at 85 yrs
In summary

• Universal introduction only when sufficient data and/or reliable assumptions available

• Build decision making on long term prevention strategy -> use of register based research for programme design and evaluation

• Challenge: how to keep all stakeholders of NIP informed and part of the process
Ownership of National Vaccination Programme

Industry

THL

NACV

Parliament

FIMEA

STM

Kansallinen rokotusasiantuntijaryhmä

Eduskunnan sosiaali- ja terveysvaliokunta

Modified @K.Vuopala