

## E.2. Workshop: Public health economics of infant pneumococcal vaccination strategies

Chairs: Prof Maarten J Postma<sup>1\*</sup>, Dr Göran Henriksson<sup>2</sup>

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### Economic evaluations of pneumococcal conjugate vaccines: what can we learn from the literature?

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We reviewed economic evaluations of pneumococcal conjugate vaccines, published between 2002 and 2008, in terms of methodology, assumptions, results and conclusions. We found a great diversity in assumptions (e.g. vaccine efficacy parameters, incidence rates for both invasive and non-invasive disease) mainly due to local variation in data and opinions. Accordingly, the results varied greatly, from total net savings to over €100 000 per discounted QALY gained. The cost of the vaccination programme as determined by price per dose and schedule (four or three doses, or fewer), and likely herd immunity impacts are highly influential though rarely explored in these published studies. If the net long-term impact (determined by a mixture of effects related to herd immunity, serotype replacement, antibiotic resistance and cross-reactivity) remains beneficial and if a three-dose schedule confers near-equivalent protection to a four-dose schedule, the cost-effectiveness of PCV7 vaccination programmes can be viewed as attractive in developed countries.

### The shifting epidemiology of bacterial infections: the impact on public health and pharmacoeconomic analyses

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*Streptococcus pneumoniae* (pneumococcus) is a major pathogen causing invasive disease (IPD) such as meningitis, sepsis and some forms of pneumonia. The pneumococcus along with non-typeable (unencapsulated) *Haemophilus influenzae* (NTHi), are also the two leading bacterial causes of acute otitis media, a disease which represents a major health and economic burden. A heptavalent vaccine against pneumococcal disease (pneumococcal conjugate vaccine: PCV7) is increasingly used across Europe and new vaccines are in development.

Only recently has attention been paid to dynamic trends in pathogen and serotype distribution, as well as to trying to better understand the true incidence of some of the associated diseases. We shall consider the dynamics of IPD serotype distribution and changes seen in the absence of PCV7 introduction. We shall review the direct clinical impact of vaccination on IPD and AOM, and the indirect herd immunity impact of vaccination. Whether the epidemiological changes are due to vaccine-induced serotype replacement, secular trends, introduction of new clones or antibiotic pressure will be discussed. Furthermore, we consider future vaccine strategies to prevent AOM and IPD that take into account the dynamics of *S. pneumoniae* serotypes as well as NTHi epidemiology.

### Simulation model for comparing the costs and effectiveness of different pneumococcal conjugate vaccines

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#### Background

Economic analyses are increasingly important in the decision to include new vaccines in public health programmes. A 7-valent pneumococcal conjugate vaccine (PCV7) has been licensed and new vaccines with different characteristics are being developed (PHiD-CV, a pneumococcal *Haemophilus influenzae* -protein D conjugate vaccine, and PCV13). The use of PCV7 has been associated with herd protection and bacterial replacement for invasive and non-invasive pneumococcal infections.

#### Methodology

A new static, deterministic, compartmental and steady-state population model was developed for use in a wide variety of epidemiological situations, health care settings and economic contexts. Herd protection and replacement are modelled; outputs include clinical end-points (invasive pneumococcal disease, pneumonia, otitis media and myringotomy with ventilation tube insertion), and economic indices (net costs per case/death prevented, per life-year gained, per quality-adjusted life-year gained and per disability-adjusted life-year gained). Vaccine programme effectiveness values were estimated from post-marketing epidemiological studies in the United States and Canada, where four-dose and three-dose PCV7 programmes have been implemented.

#### Results

Preliminary results show that in children, the target group for vaccination, acute otitis media is the main driver of economic costs. Also variations in the effectiveness of vaccines to prevent otitis and related complications are associated with substantial differences in cost-effectiveness. In the overall population, community-acquired pneumonia, and resulting hospitalization was found to be the major contributor to the pneumococcal disease burden, and to programme benefits in terms of QALYs. Herd protection associated with high vaccine uptake has a major impact on results, whereas replacement could partially offset benefits.

#### Conclusion

Modelling the marginal costs and benefits of different vaccines, programme schedules and coverage is increasingly complex and lessons learnt in North America are extremely important for predicting the impact of new pneumococcal vaccination programmes in Europe.

### Cost-effectiveness of pneumococcal vaccination in the Netherlands; estimations for the 7-valent vaccine and predictions for PCV13

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#### Background

Public health economics has recently strongly underpinned Dutch policy making on introducing the 7-valent pneumococcal conjugate vaccine (PCV7) in the Dutch National Immunization Program. The analyses performed included

both the direct (the vaccinees) as well as the indirect (herd immunity) protective effects of PCV7.

#### Objectives

The aims are: (i) to update cost–effectiveness estimates for PCV7 using recent epidemiological data and new information on resource use to validate and compare previous analyses; and (ii) to forecast cost–effectiveness of potential shifts from PCV7 to pneumococcal vaccines that include additional serotypes, such as the 13-valent vaccine (PCV13).

#### Methodology

We developed a model based on epidemiological information from the bacterial meningitis surveillance system, the national database on hospitalizations and a regional database on GP visits. Specific resource use data were gathered in the University Medical Center Utrecht (The Netherlands), in addition to already existing information from previous research in our group ([http://pcv.healthconomics.nl/cost\\_effectiveness\\_webinterface.html](http://pcv.healthconomics.nl/cost_effectiveness_webinterface.html)). The website provides further information on the general structure of our model. Herd immunity was inserted in the model using an algorithm basically reflecting straightforward proportional calculus.

#### Results

Our current analysis confirms previous findings that cost–effectiveness for infant PCV7 vaccination ranges from €10 000 to 20 000 per QALY gained. Preliminary results now show a potential decrease in the net costs per QALY gained of almost 10% if changing from PCV7 to PCV13, assuming flat pricing of both vaccines. Main drivers of savings were meningitis for direct costs and otitis media for indirect costs. Main driver for QALY gains was again meningitis. If, in sensitivity analysis, herd protection would be excluded, cost–effectiveness even decreases by ~25% if changing from PCV7 to PCV13.

#### Conclusion

We have shown that potentials exist to further improve the cost–effectiveness of the Dutch vaccination strategy against pneumococcal infections by shifting from PCV7 to PCV13. Recent information does suggest serotype replacement taking place negatively affecting herd immunity, further enhancing the importance of increasing the serotype coverage.

### New vaccines against pneumococcal disease and otitis: lessons learnt and what assumptions should we use for future modelling?

Steven Black

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Several pharmacoeconomic models have been developed over the past decade that estimate the epidemiological and economic impact of a 7-valent pneumococcal conjugate vaccine (PCV-7), now licensed and implemented in many countries. Two vaccines in development for the prevention of pediatric *Streptococcus pneumoniae* (*Sp*) infections feature additional serotypes and one also uses a new carrier protein (protein-D from non-typeable *Haemophilus influenzae*, *NTHi*), aiming to expand the prevention of infection from one pathogen *Sp* to two pathogens (*Sp* and *NTHi*).

Previous model development relied on the then-existing clinical and epidemiological data, plus panels of experts to provide guidance on assumptions regarding key vaccine parameters. Over the past several years increased use of the vaccine has not only allowed some of these assumptions to be based more on empirical data, but also permits a reassessment of how 'conservative' previous expert panels were in light of the absence of certain types of data. Based on our experience with previous and current models and the conclusions drawn from these, and keeping in mind the new vaccines in development, we offer our view on what lessons have been learnt and what assumptions might be fairly made in the future when assessing pneumococcal conjugate vaccines. We shall discuss issues that include country-specific epidemiology—serotype distribution and *NTHi*-prevalence; the direct effects of vaccination against invasive diseases, pneumonia, acute otitis media and tympanostomy tube placement; the longevity of direct protection; the indirect effect of vaccination (herd protection of the non-vaccinated population), the impact of dosing schedules, cross-protection against vaccine serotypes and *NTHi*; and bacterial replacement.

## F.2. Workshop: Academic collaborative centres in the Netherlands in action to improve local public health: examples from two centres

Chair: Ien van de Goor\* (The Netherlands)

Organizer: Academic Collaborative Centre for Public Health Tranzo, Tilburg University and Academic Collaborative Centre for Public Health Limburg, Maastricht University, The Netherlands

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Public health is in need of a stronger evidence base. In the Netherlands, the Ministry of Health acknowledges this need to strengthen public health and has installed nine Academic Collaborative Centres for Public Health (ACCs). These centres promote and study the collaboration between actors in the policy, practice and research domain in local public health. Such multi-actor processes are assumed to stimulate more evidence-based policy making and practice in (local) public health.

Objective of the workshop:

to share and discuss our experience and ideas on:

- theoretical perspectives and research on collaboration between policy, practice and research in local public health;
- methods and practical instruments to link scientific findings to policy processes in local public health.

Layout of the workshop:

- Welcome and short introduction by Ien van de Goor, chairperson.
- Presentation one: Maria Jansen: Integration between practice, policy and research in public health: results of a multiple case study.

- Presentation two: Marjan Hoeijmakers: Mapping collaborative relationships between actors in policy, practice and research in local public health.

- Presentation three: Joyce de Goede: Knowledge in process: the use of epidemiological knowledge for local health policy in the Netherlands: results from network analyses.

- Presentation four: Eveline van Eck: Tools for implementation of local epidemiological knowledge into the local health policy-making process: practical experiences.

Questions and discussion: lessons learned.

### Integration between practice, policy and research in public health: results of a multiple case study

Maria Jansen

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