

PRO VAC workshop – September 5th – 8th, 2006
Immunization Unit, PAHO
Washington, D.C. USA

Simplified economic model for the introduction of pneumococcal conjugate vaccine in PAHO member states

Morning session, Friday, September 8th, 2006

Presenters

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1. Agenda for the session (*1 hour 45 minutes*)

Introduction to pneumococcal disease and its surveillance in the Americas – *Lucia Oliveira (PAHO)*

PRO VAC economic model for introduction of pneumococcal conjugate vaccine – *Anushua Sinha (New Jersey Medical School – UMDNJ)*

Practicum for participants: learning to use the PRO VAC PCV model

Practicum facilitators – Carol Levin (PATH), Oscar Mujica (PAHO), Naline Sangrujee (Futures Group), Anushua Sinha (NJMS), Cristiana Toscano (PAHO), Juan Esteban Valencia (CES), Cynthia Whitney (CDC)

2. Materials accompanying the session

User's manual to PRO VAC pneumococcal economic model

USER'S GUIDE TO PRO VAC PNEUMOCOCCAL ECONOMIC MODEL v1.1

1. Overview

Underlying this health economic model is a burden of disease model, in which the effects of vaccination on the following childhood disease syndromes are captured: acute otitis media, pneumonia, and meningitis. While pneumococcal disease has many presentations, these syndromes were chosen as being easily and routinely diagnosed by health care providers across many health care settings and as being of relevance to child health. For the purposes of this workshop, we assume that the majority of bacteremias present in the context of pneumonia or meningitis.

Vaccination's effects are captured by the model in terms of health burden (cases, deaths, life years, disability-adjusted life years) and economic burden (health systems costs, family costs).

The conceptual model is diagrammed in the decision tree shown in Figure 1. This model can be stated as follows: Every child who is born may have a pneumonia, middle ear infection, or meningitis at some point before their fifth birthday. If they have one of these diseases, the disease may be pneumococcal or not. If it is pneumococcal, it may be due to a pneumococcal serotype covered by the conjugated vaccine, or it may be due to a non-vaccine-type pneumococcus. If it is due to a vaccine-type pneumococcus and the child has been vaccinated, then the disease may be averted by vaccination. Not every child will be vaccinated.

Costs will be incurred by vaccination and averted when disease is averted. Health benefits will accumulate as deaths and non-fatal disease cases are averted by immunization. Costs are presented in US\$ 2006, but this could be altered by the analyst.

Costs and health benefits are summarized in incremental cost effectiveness ratios, defined as:

$$\begin{aligned} &\text{Incremental cost-effectiveness ratio} = \\ &\text{Change in costs} / \text{Change in health benefits} = \\ & \frac{(\text{Costs of vaccination} - \text{averted disease-related costs})}{\text{(Health benefits gained, e.g. life-years or DALYs)}} \end{aligned}$$

2. Scenarios

Two scenarios are analyzed: pneumococcal health and economic burden without vaccination and pneumococcal health and economic burden with vaccination program.

Data currently loaded into the model represent a hypothetical analysis for a PAHO member state.

3. Pneumococcal vaccine

The model can be used to analyze the seven-valent conjugate vaccine or any of the pneumococcal conjugate vaccines currently under trial (e.g. 10 or 13-valent products).

Pneumococcal vaccine confers protection directly on immunized children by enhancing actively acquired, specific immunity against pneumococcal bacteria. Pneumococcal vaccine, like other vaccines (e.g. *Haemophilus influenzae* type B), also confers herd immunity on unvaccinated children through indirect means, also reducing their risk of disease. Serotype replacement may occur in a population, with an increase fraction of disease cases then caused by non-vaccine-type pneumococci, resulting in a blunted vaccine effect.

The model currently captures vaccine's direct effects on immunized children, but does not capture indirect effects such as herd immunity or serotype replacement. We will discuss this further during the workshop session.

4. Vaccination program

The vaccination program is assumed to begin in 2007. Planning and planning costs are assumed to begin in 2006 and therefore this is the first year incorporated into the model.

It is assumed that a three dose pneumococcal conjugate vaccine schedule for infants will be used. It is assumed that the pneumococcal vaccine program will not require additional routine health care visits and that pneumococcal vaccine will be co-administered with immunizations currently on national schedules. Vaccination costs are calculated for each cohort of children born from 2006 to 2026 using the VIC tool (see Afternoon session, Thursday September 6th).

Catch-up immunization programs for older children are not modeled. The model is not specifically intended to analyze immunization programs for high-risk populations only, but may be adaptable to this purpose.

5. Perspective of analysis

The analysis can be performed from the health systems perspective, incorporating vaccine, vaccine program, and direct medical treatment costs. It can also be performed from a societal perspective, including family out-of-pocket costs and family productivity losses.

6. Time horizon

It is assumed that the vaccination program is being analyzed for children born from 2007 to 2026 (20 years). Cases of pneumococcal disease occurring up to age five for these birth cohorts are estimated, and health consequences (death, disability) and costs resulting from these cases are collected for each of these cohorts. Calculations of health benefits such as DALYs and life years saved are based on the life expectancy of the child at age 1.

7. Discounting

Both costs and health consequences are discounted by the model. A discount rate of 3 - 6% is suggested. A default value of 3% is input into the model, but this may be modified by the analyst.

8. Using the model

a. Getting started and Data entry/ review

The analyst should open “**PRO VAC pneumococcal economic model v1.1**” from the PC Desktop.

Save a copy of the model to the Desktop under the name “**<Your name here> pneumococcal model.**”

At the bottom of the screen, the analyst will see Tabs containing the titles of each of the worksheets in the workbook. By clicking on these Tabs, the analyst can navigate through the workbook. Alternatively, the **Introduction** sheet functions as a Table of Contents and also allows the analyst to navigate the workbook easily by clicking to each sheet in the table. The **ReadMe** sheet provides contact information for technical support.

There are four sheets for Data Entry into the model: **Demographics, Pneumonia, Meningitis, and Otitis media.**

Start on the **Introduction** sheet. Click on the **Demographics** button to review demographic data loaded into the model. Relevant parameters on the Demographics sheet include:

Annual birth cohort
Life expectancy at age 1
Vaccination coverage rate
Discount rate

Modifiable cells on this sheet (and all other data entry sheets) are highlighted in yellow. Some cells are highlighted in light blue. These cells will be modifiable in future versions of this model but are currently not functional.

Next, click on the sheets titled **Pneumonia, Otitis media, and Meningitis**. Review data pre-loaded into the model for you. Note that vaccine-related costs are imported into the model from the VIC Tool, which is meant to be a companion to this model.

b. Analyzing the model – Base Case or Primary Analysis
In the real world the analyst would compile and enter the data required for the base case, or primary, analysis. This data has been pre-loaded into the model for this workshop session.

After reviewing data on sheets **Demographics, Pneumonia, Otitis media, and Meningitis**, cost-effectiveness results will be available. Click on the sheet **Stream of Events** to view the annual health and economic consequences of introducing pneumococcal conjugate vaccination or not introducing pneumococcal conjugate vaccination.

After reviewing **Stream of Events**, click on the sheet titled **Cost-effectiveness**. Summary cost-effectiveness calculations are presented in the columns numbered 18 to 23 and highlighted in green. However, first review a number of other outputs from the model of use to the analyst.

Column 1: Birth cohort being vaccinated (year of investment into pneumococcal immunization program)

Columns 2 – 3: Discounted and cumulative discounted vaccination program costs

Columns 5 – 6: Discounted and cumulative discounted direct medical costs

Column 9: DALYs averted

Column 12: Life years gained

Column 15: Deaths averted

The cost-effectiveness calculations in columns 18 to 23 are cumulative for the years of investment into the vaccination program. For example, in 2011, one year of program planning costs will have been incurred and the vaccination program will have run for five years. The cost-effectiveness calculations shown in columns 18 to 23 (year of investment 5/ row 13) are based on the cumulative costs and health benefits of vaccination through 2011.

Using the calculations in the **Cost-effectiveness** and **Stream of Events** sheet, please answer the following questions with the help of session facilitators:

1. Over the 20 year duration of the program (through 2020), what are the total vaccine-related costs (discounted) that will be incurred?
2. Over the 20-year duration of the program, what are the total disease-related costs that will be averted?
3. How many deaths will be averted over the 20 years?
4. How many DALYs will be averted over the 20 years?
5. After the full 20-year duration of the vaccination program, what is the cost for each life saved? What is the cost for each DALY averted?
6. Is the pneumococcal vaccination program cost saving?
7. Is the pneumococcal vaccination program cost-effective?
8. Is the pneumococcal vaccination program very cost-effective? For the purposes of this session, assume the hypothetical member state has an annual per capita GNI of \$4,500.

Use the answers to these questions to complete Tables 1 and 2 (see end of document), which could be used in a summary report of analytic results. Summarize your base case analysis in a short paragraph describing key findings and conclusion.

Next the analyst may wish to review the graphs generated from the primary analysis by clicking on the worksheet titled, **Graphs**. These plots include

1: A graph contrasting investment into vaccination and health benefit gained (DALYs averted)

2: A graph summarizing cost-effectiveness by year of investment

3: A graph summarizing the cost impact of vaccination

9. Additional analyses

With the base case, or primary, analysis completed, the analyst will want to perform additional analyses to better understand the investment case for pneumococcal vaccination. These additional analyses are the heart of the cost-effectiveness analysis, as they allow the analyst to understand how robust results are and which parameters most strongly influence the model. What happens to health benefits, costs and cost-effectiveness when key estimates are varied? For example, what if the price of each dose of pneumococcal vaccine is doubled or halved?

These additional analyses are often termed sensitivity analyses and/ or secondary analyses. The following sensitivity/ secondary analyses are recommended.

- a. One way sensitivity analyses: Vary key estimates, using a range around the value used for the base case analysis.
- b. Worst case scenario: Bias all key estimates against the vaccination program.
- c. Best case scenario: Bias all key estimates in favor of the vaccination program.
- d. Threshold analyses/ “break even” analyses: At what point does vaccination become cost saving? For example, how low does vaccine have to be priced before the intervention becomes cost saving?

In the case of pneumococcal vaccination, like certain other vaccines, herd immunity effects have the potential to profoundly influence cost-effectiveness. There is a strong case to include herd immunity in the base case analysis and, at a minimum, it should be considered in secondary analysis.

For this workshop, please perform the following one-way sensitivity analyses:

One way sensitivity analysis of vaccine efficacy against pneumonia:

1. Open workbook “**PRO VAC pneumococcal economic model v1.1**” from PC Desktop.

2. Save the workbook on the Desktop under the name, “<Your name here> pneumococcal model – low estimate PNA VE.”
3. Click on the worksheet **Pneumonia**. Go to cells D99 and D100. Decrease the estimates for vaccine efficacy by 50%.
4. What is the number of deaths averted, DALYs averted, and disease costs averted over the program’s 20 years?
5. Over the 20 years, what is the incremental cost-effectiveness ratio, expressed in cost per DALY averted and including averted disease costs?
6. How does this estimate of cost-effectiveness compare to the base case estimate?
7. Save and close this workbook.
8. Open “**PRO VAC pneumococcal economic model v1.1**” from the Desktop.
9. Save the workbook on the Desktop under the name, “<Your name here> pneumococcal model – high estimate PNA VE.”
10. Click on the worksheet **Pneumonia**. Go to cells D99 and D100. Increase the estimates for vaccine efficacy to 100%.
11. What is the number of deaths averted, DALYs averted, and disease costs averted over the program’s 20 years?
12. Over the 20 years, what is the incremental cost-effectiveness ratio, expressed in cost per DALY averted and including averted disease costs?
13. How does this estimate of cost-effectiveness compare to the base case estimate and the low estimate calculated in steps 1 – 5?
14. Summarize the results of your sensitivity analysis in one or two sentences. Is your conclusion that the analysis is sensitive or insensitive to vaccine efficacy versus vaccine-type pneumococcal pneumonia?
15. Save and close this workbook.

One way sensitivity analysis of vaccine efficacy against otitis media

16. Repeat steps 1 – 15, varying estimates for vaccine efficacy against pneumococcal otitis media from 50% base case estimate to 140% base case estimate.

Save your analyses as “<Your name here> pneumococcal model – low estimate OM VE” and “<Your name here> pneumococcal model – high estimate OM VE.”

Summarize the results of this sensitivity analysis in one or two sentences. Is your conclusion that the analysis more or less sensitive to vaccine efficacy versus vaccine-type pneumococcal otitis media compared to vaccine efficacy against vaccine-type pneumonia?

At your leisure (bonus exercise): Enter the VIC tool and range pneumococcal vaccine cost per dose through the following values: \$0.50, \$1.00, \$5 (~ base case value), \$10, \$50. At what vaccine cost per dose does the vaccination program become cost saving? This is an example of a threshold analysis.

10. Summary: In this workshop, we have explored a simple model analyzing the cost-effectiveness of pneumococcal conjugate vaccination of infants. We have discussed pros and cons of the modeling approach implemented in this model and potential alternative models. We have undertaken a base case analysis, interpreted results, and performed two example sensitivity analyses. As an optional exercise, we have also performed a threshold analysis.

Table 1. Cumulative health benefits and health care utilization with and without pneumococcal vaccination program in hypothetical PAHO member state

	No vaccination	Vaccination	Outcomes prevented by vaccination
Deaths			
Life years			
DALYs			
Hospitalizations			
Ambulatory visits			

Table 2. Cumulative (A) Costs and (B) Cost-effectiveness of pneumococcal vaccination program in hypothetical PAHO member state

(A) Costs

	No vaccination	Vaccination	Costs (Savings) from vaccination
Pneumococcal disease-associated costs (undiscounted)			
- Medical costs			
- Parent work loss and other costs			
Total disease costs (undiscounted)			

(B) Cost-effectiveness

	Vaccination priced at \$2 per dose	Vaccination priced at \$5 per dose	Vaccination priced at \$20 per dose
Health systems perspective			
- US\$ per death averted	--		--
- US\$ per life year saved	--		--
- US\$ per DALY averted	--		--

	Vaccination priced at \$2 per dose	Vaccination priced at \$5 per dose	Vaccination priced at \$20 per dose
Societal perspective			
- US\$ per death averted	--	--	--
- US\$ per life year saved	--	--	--
- US\$ per DALY averted	--	--	--

Figure 1. Diagram of PRO VAC pneumococcal economic model v1.1

