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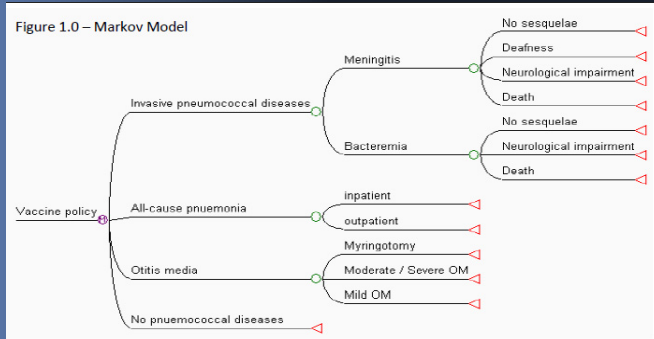
Infectious caused by *Streptococcus pneumoniae* is one of the major causes of death of children under the age of five. There are currently two pneumococcal conjugated vaccines in Malaysia. However, pneumococcal vaccination is not currently part of the national immunization program (NIP). The cost effectiveness and public health impact of NIP using either vaccine has not been previously studied.

Objective

To study the cost-effectiveness of a population-wide, pneumococcal vaccination program in Malaysian children with the 13-valent pneumococcal conjugate vaccine (PCV13) versus the 10-valent pneumococcal conjugate vaccine (PCV10)

Methods

A 10-year Markov model as shown in Figure 1.0, developed by i3 Innovus was used.



- Analysis was conducted based on payer's perspective.
- Cost were calculated based on drug acquisition cost as well as direct medical costs only.
- 3% discount rate was applied to both costs and outcomes.
- Both direct and indirect effects of the vaccines on disease prevention were considered in the analysis
- Deterministic sensitivity analysis was performed by varying the parameters by $\pm 10\%$ from base case

Model input:

- Population size was about 28 million (Year 2011).¹
- Local and regional epidemiology data were used when possible.^{2,3,4,5,6,7,8}
- Outpatient visits for pneumonia were estimated from reported incidence of inpatient pneumonia with an age based coefficient derived from the ratio of outpatient/ inpatient visits in United States (US).^{9, 10, 11}
- Using the ratio of outpatient/ inpatient AOM cases in US as a reference, incidences of outpatient AOM were assumed to be 5 times that of complex AOM.^{9,12}
- PCV 13 and PCV 10 effectiveness was extrapolated from PCV7 data, taking into consideration the local serotype distribution.¹³
- Medical and vaccine costs were obtained from local sources while lifetime medical costs of disability were estimated from US data.⁹
- The additional protection from non-typeable *H. influenzae* with PCV10 was capped at 4% for complex otitis media in children <23 months.¹⁴

Assumptions

- The analysis assumed a 3-dose vaccine series
- 96% vaccine coverage for both PCV13 and PCV 10
- The private market acquisition cost for the vaccines was used
- The model assumed a lower immunogenic response for PCV10 relative to PCV13.^{15,16}
- Based on experience with the 7-valent pneumococcal vaccine, it was assumed that no cross-reactivity occurs for PCV10 with serotypes 6B and 6A as well as 19F and 19A.¹⁷

Conclusion

- Based on the present analysis, PCV13 appears to be a more cost-effective alternative in a NIP

References

1. US Census Bureau, <http://www.census.gov/ipeds/www/ibd/country.php> (assessed on 6th June 2011)
2. Hsieh et al. National survey of invasive pneumococcal diseases in Taiwan under partial PCV7 vaccination in 2007: Emergence of serotype 19A with high invasive potential. *Vaccine*. 2009;27:5513-5518
3. Lim TY et al. Summary of invasive pneumococcal disease burden among children in the Asia-Pacific region. *Vaccine*. 2010;28:7589-7605
4. Lee LH et al. Adult *Streptococcus pneumoniae* meningitis in Southern Taiwan: epidemiological trends and prognostic factor. *Journal of Clinical Neuroscience*. 2005; 12(1):32-35
5. Imran MN et al. Early predictors of mortality in pneumococcal bacteraemia. *Ann Acad Med Singapore* 2005;34:426-431
6. Sirinavin S et al. Pediatric invasive pneumococcal disease in a teaching hospital in Bangkok. *Int J Infectious Diseases*. 2003;7:183-189
7. Song JH et al. Epidemiology and clinical outcomes of community-acquired pneumonia in adult patients in Asian countries: a prospective study by the Asian network for surveillance of resistant pathogens. *International Journal of Antimicrobial Agents*. 2008;31:107-114
8. UNICEF/WHO report: Pneumonia: The forgotten killer of children, 2006.
9. Aljunid et al. Impact of routine PCV7 (Prevenar) vaccination of infants on the clinical and economic burden of pneumococcal disease in Malaysia. *BMC Infectious Disease*. 2011;11:248-257
10. Grijalva CG et al. Decline in pneumonia admissions after routine childhood immunisation with pneumococcal conjugate vaccine in the USA: a time-series analysis. *Lancet* 2007; 369:9568-1179-86.
11. US Dept of Health and Human Services, National Center for Health Statistics. National Ambulatory Medical Care Survey, 2006.
12. Ray GT et al. Cost-effectiveness of pneumococcal conjugate vaccine-evidence from the first 5 years of use in the United States incorporating herd effects. *Pediatr Infect Dis J* 2006;25(6):494-501.
13. Rohani MY et al. Current trend of pneumococcal serotypes distribution and antibiotic susceptibility pattern in Malaysian hospitals. *Vaccine*. 2011;29: 5688-5693.
14. Pyrmula R et al. Pneumococcal capsular polysaccharides conjugated to protein D for prevention of acute otitis media caused by both *Streptococcus pneumoniae* and non-typeable *Haemophilus influenzae*: a randomized double-blind efficacy study. *Lancet* 2006;367:740-48.
15. Vesikari T et al. Immunogenicity of the 10-valent pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine (PHiD-CV) compared to licensed 7vCRM vaccine. *Pediatric Infectious Disease Journal*. 2009;29:566-76
16. Goldblatt D. Establishing the correlate for pneumonia. Presented at the 6th International Symposium on Pneumococci and Pneumococcal Diseases: Reykjavik, Iceland. June 11, 2008.
17. Vakevainen M et al. Cross-Reactivity of antibodies to type 6B and 6A polysaccharides of *Streptococcus pneumoniae*, evoked by pneumococcal conjugate vaccines, in infants. *The Journal of Infectious Diseases* 2001;184:789-93

Results**Efficacy**

- Additional cases of pneumococcal diseases that could be avoided with PCV13 versus PCV10 (over a 10 year period) were as below:
 - IPD: 9,681 cases
 - Hospitalized pneumonia: 400,678 cases
 - Non-hospitalized pneumonia: 1,005,034 cases
- Comparing PCV 13 versus PCV10, cases of hospitalized otitis media (complex otitis media) that could be avoided among children < 5 years old was 82,847 cases.
- Death averted with the implementation of NIP with PCV13 versus PCV10 from IPD was 2,184 cases and also 18,275 cases from hospitalized pneumonia.

Costs

- Due to the higher acquisition cost for PCV13, an additional RM10,056 million is needed for the vaccination program over a 10-year period.
- PCV 13 can potentially lead to RM1,406 million savings in direct medical cost compared to PCV10.
- Majority of the cost savings would occur in children < 5 years old. (Table 1.0)

Economic Results - Total Cost Savings (in millions)					
	IPD	Hospitalized pneumonia	Non-hospitalized pneumonia	Complex AOM	Simple AOM
<12 months	\$12	\$239	\$127	\$12	\$11
12-23 months	\$9	\$224	\$132	\$12	\$11
24-35 months	\$11	\$97	\$36	\$3	\$2
36-47 months	\$11	\$81	\$30	\$3	\$2
48-59 months	\$10	\$66	\$25	\$2	\$2
5-17 years	\$3	\$25	\$45		
18-34 years	\$1	\$18	\$7		
35-49 years	\$1	\$38	\$11		
50-64 years	\$0	\$23	\$6		
65+ years	\$2	\$51	\$6		
TOTAL	\$60	\$862	\$425	\$32	\$28

Table 1.0 - Difference in total cost savings by age group

Cost-effectiveness analysis

- Total life-year saved was 562,180, while total QALYs gained was 514,573
- Cost per life-year saved was at RM15,385 while cost per QALY gained was at RM16,809.

Sensitivity Analysis

- Deterministic sensitivity analysis showed that incidences of non-hospitalized pneumonia was an important factor in determining life-year saved.
- Incidences of hospitalized pneumonia is the most sensitive factor in determining potential cost savings, followed by the medical cost of hospitalized pneumonia. (Figure 2.0)

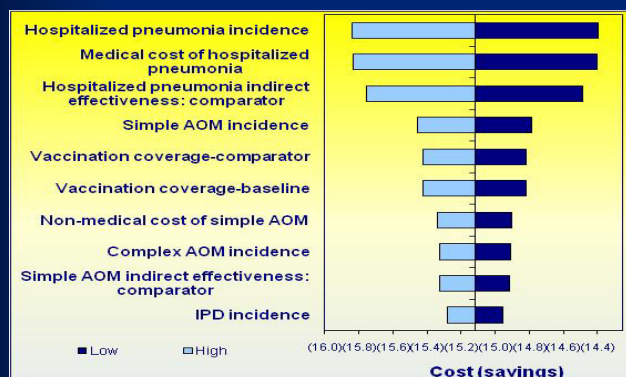


Figure 2.0 – Deterministic sensitivity analysis (cost)