

Economic Evaluation of 7-valent Pneumococcal Conjugate Vaccine (PCV7) in Taiwan: A Cost-Effectiveness Analysis of Universal Infant Vaccination

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Background

- A group of illnesses caused by the bacterium *Streptococcus pneumoniae*, also known as pneumococcus
- Infection with pneumococcal bacteria can result in several different types of diseases such as
 - Pneumococcal meningitis,
 - Pneumococcal bacteraemia,
 - Pneumonia
 - Otitis media
- The first two are known as "IPD" (Invasive Pneumococcal Diseases).

Cost-Effectiveness Analysis of PCV7 in Taiwan

ECONOMIC EVALUATION OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IN TAIWAN: A COST-EFFECTIVENESS ANALYSIS OF UNIVERSAL INFANT VACCINATION

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ABSTRACT

Objectives: This study evaluates the clinical and economic benefits of routine infant vaccination with the 7-valent pneumococcal conjugate vaccine (Pneumovax[®], PCV7) in Taiwan. **Methods:** A decision-analytic model was populated with local age-specific incidence and seroprevalence data obtained from the National Health Insurance Database (NHID) and published literature to simulate the expected health outcomes resulting from universal PCV7 vaccination of an annual birth cohort of ~250,000 children compared to an unvaccinated cohort over a ten-year horizon. Primary analyses were conducted from a payer perspective, with total cost associated with the treatment of pneumococcal disease derived from the NHID database (2001-2006). Vaccine efficacy rates for PCV7 were consistent with results from the Northern California Kaiser Permanente pivotal efficacy trial. The reduction in adult IPD cases and associated cost avoidance due to indirect herd protection was estimated in line with published overseas rates. One-way sensitivity analyses were performed to evaluate the sensitivity of the model findings to plausible variation in specific data inputs. **Results:** In the birth cohort alone, universal PCV7 vaccination was estimated to prevent hundreds of IPD cases over a ten-year horizon, leading to a significant reduction in direct medical costs. Substantial cost savings were further generated when the impact of vaccination on all-cause pneumonia and otitis media was also considered. Indirect protection extended to the unvaccinated population led to a reduction of thousands of adult cases of IPD. From a payer perspective, universal PCV7 vaccination was estimated to have an incremental cost per life year gained of \$2,823.72 (US\$1,182.11) in the base case. Outcomes generated in secondary analyses were equally cost-effective.

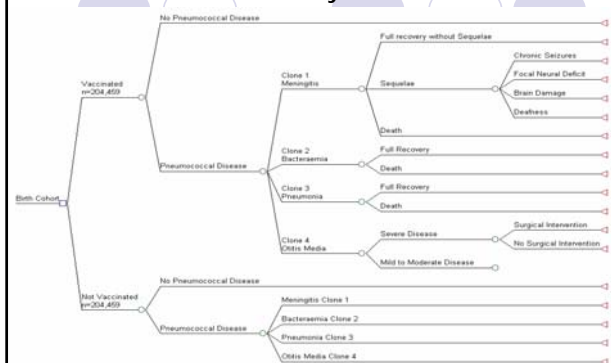
In the primary analysis, the average cost of treatment for each clinical presentation of pneumococcal disease was determined from a payer perspective, and was estimated from two independent sources:
 - National Health Insurance Database (2001-2006)
 - Decision analysis tree constructed by Dr. Yu-Ching Huang
 The cost of introducing universal vaccination program included both PCV7 vaccine acquisition and administration costs. Direct costs associated with the management of pneumococcal disease, including hospitalization, healthcare professional consultation fees, ICU admissions, medications, diagnostic tests and long-term treatment costs for complications were included in the analysis. In the model, where total cost data were unavailable, published UK costs were converted to New Taiwan Dollars (NTD) and inflated to present costs.
 The primary analysis assumed PCV7 vaccinations were administered as a series of 4 doses at 2, 4, 6 and 12 months of age.
 Vaccine efficacy rates observed in the Northern California Kaiser Permanente pivotal efficacy trial were applied, namely a 92.4% reduction in episodes of pneumococcal meningitis and bacteraemia, a 7% reduction in all-cause pneumonia and a 2% reduction in all-cause otitis media. Efficacy rates against pediatric cases of all-cause pneumonia and otitis media were varied in secondary analyses, in line with published overseas effectiveness data, i.e. 50% reduction in all-cause pneumonia and 42.7% reduction in otitis media. The impact of using the vaccine efficacy rate for radiologically confirmed pneumonia, according to the World Health Organization's radiological criteria for pneumonia diagnosis (i.e. 20% IQR CI: 6.5% to 40.7%)² was also considered in an additional analysis.
 Indirect effects (herd protection) of PCV7 on unvaccinated adult populations were also considered by calculating the reduction in adult cases of IPD and associated cost savings, in line with published data from the US experience.³ The indirect effect for the indirect effect was used in the primary analysis, namely 22% (range: 22-41%) for adults aged 20-59 years. The indirect effect for other adult age groups was 10% (range: 11-16%) for adults

BACKGROUND

Model Overview

- A hypothetical cohort (n=204,459) of newly born infants in Taiwan in the year 2006 is followed for a 10-year horizon to simulate the expected health outcomes with or without PCV7 vaccination.
- A Cost-Effectiveness Analysis (CEA).
- A decision-analytic model is used.
- Both direct and indirect effects by the vaccination are included.
 - Direct effect on the vaccinated individual
 - Once a person is vaccinated against a disease, he/she is less likely to develop it
 - Indirect effect, sometimes called "herd effect"¹
 - Once a person is vaccinated against a disease, he/she is less likely both to develop it, as well as pass it on to someone who is not immunized

Decision-Analytic Model



Epidemiological parameters

Model Parameters	Source
Incidence and case fatality rates of pneumococcal disease among pediatric populations	
Age-specific incidence rates for pneumococcal meningitis	Chang Gung Memorial Hospital from 2001-2006
Age-specific incidence rates for pneumococcal bacteraemia	Chang Gung Memorial Hospital from 2001-2006
Age-specific incidence rates for hospitalized pneumonia	Chang Gung Memorial Hospital from 2001-2006
Age-specific incidence rates for all-cause pneumonia	Taiwan Department of health at www.doh.gov.tw
Age-specific incidence rates for otitis media	NHID database
Case fatality rates for pneumococcal meningitis	Death Statistics, Healthy HK, DH, www.health.gov.hk
Case fatality rates for pneumococcal bacteraemia	Death Statistics, Healthy HK, DH, www.health.gov.hk
Case fatality rates for pneumonia	Taiwan statistics on causes of death at www.doh.gov.tw
Annual cases of IPD and associated mortality among adult populations	
Annual cases for pneumococcal meningitis	Taiwan Department of health at www.doh.gov.tw
Annual cases for pneumococcal bacteraemia	Taiwan Department of health at www.doh.gov.tw
Annual cases for pneumococcal pneumonia	Taiwan Department of health at www.doh.gov.tw
Annual deaths for pneumococcal meningitis	Low S et al, 2007, Singapore Med Journal 48(9): 824-9
Annual deaths for pneumococcal bacteraemia	Low S et al, 2007, Singapore Med Journal 48(9): 824-9
Annual deaths for pneumococcal pneumonia	Taiwan Department of health at www.doh.gov.tw

Cost Parameters

Cost Parameter	Values Utilized				Source
Acute Costs (Infants) (NT\$)					
	Pneumococcal bacteraemia	Pneumococcal meningitis	All cause pneumonia	Otitis media	
Direct acute cost per infection - NHI database	54,861	82,912	5,554	1,985	Costs derived from the National Health Insurance Database (2002-2006 data)
Direct acute cost per infection - Expert's opinion	93,905	192,403	93,533	6,704	Average cost per episode derived from Expert's opinion
Indirect costs per infection	11,584	10,376	9,833	6,648	Hong Kong costs converted to Taiwan dollars using September 2007 exchange rate HK\$-NT\$4.2077 from www.xe.com
Acute Costs (Adults) (NT\$)					
Direct acute cost per infection - NHI database	91,040	52,602	30,782	NA	Costs derived from the National Health Insurance Database (2002-2006 data)
Direct acute cost per infection - Expert's opinion	93,905	192,403	93,533	NA	Average cost per episode derived from Expert's opinion

Cost Parameters

Long-term Costs per Disability (NT\$)		Source
	Unit Costs	Proportion of meningitis cases affected
Deafness	4,171,278	15.5%
Brain damage	55,841,663	9.7%
Focal neural deficit	1,038,009	6.0%
Chronic seizures	326,618	7.0%

UK costs modified to Taiwan dollars using GB£1 = NT\$46.1325 and inflated to 2006 values (using adjustment factor 1.04) from www.doh.gov.tw
Incidence of sequelae from Bedford et al. 2001 and PKis et al. 1996 (UK rates)

Model Assumptions

- Primary analysis assumes PCV7 vaccination is provided for infants (<6 months) only and is administered as 3 doses at 2, 4 and 6 months of age with a 4th (booster) dose at 12-15 months.
 - 95% vaccination coverage of the birth cohort was assumed.
 - 3 alternate catch-up vaccination schedules (of infants aged 7-24 months) were also considered in secondary analyses.
- Indirect effects of herd protection are included in the model.

Age groups (years)	Proportion Reduction in IPD due to PCV7 (%)		
	Lower 95% CI*	Mid-point Estimate (Base Case)*	Upper 95% CI**
20 to 39	23	32	41
40 to 64	1	8	20
65 +	11	18	31

* Source: Whitney et al. (2003)
** Source: Whitney CG. (2004)

Model Assumptions

- Vaccine efficacy was consistent with published rates from the Northern California Kaiser Permanente pivotal efficacy trial:
 - IPD: 97.4% reduction
 - All-cause pneumonia: 6% reduction
 - All-cause otitis media: 7% reduction
- Waning vaccine efficacy is assumed: decrease by 1% per year for the first 5 years following vaccination; a 3% annual decrease for the remaining 5 years after initial vaccination was also assumed.
- Life expectancy of infants was assumed to be 75 years.
- A discount rate of 3% was applied to both costs and benefits.
- All costs were converted to Taiwan dollars at 2006 prices.

Model Outcomes

Estimated outcomes: cases and deaths avoided

	Vaccination (a)	No Vaccination (b)	Increment (a-b)
Paediatric group			
<i>Number of cases</i>			
Bacteraemia	60	138	-78
Meningitis	31	79	-48
Hospitalized Pneumonia	256	270	-14
Otitis media	14651	15624	-974
Deaths	6	14	-8
Life years lost	179	422	-243
Adult group			
IPD cases	45225	54025	-8800
Deaths	1182	1492	-310
Life years lost	21093	25559	-4466
Overall life years lost	21272	25981	-4709

- Universal PCV7 vaccination will prevent the loss of 4,709 life-years

Model Outcomes

Estimated costs

Cost estimation scenarios	PCV7 Vaccination (a)	No Vaccination (b)	Increment (a-b)
Cost Estimation by NHI Database			
Birth Cohort			
Vaccination cost	2,214,290,970	0	2,214,290,970
Direct acute cost	21,651,946	32,582,786	-10,930,840
Long-term costs	175,382,120	453,144,734	-277,762,614
Total	2,411,325,036	485,727,520	1,925,597,516
Adults			
Direct acute cost	841,738,864	1,005,526,417	-163,787,552
Total cost	3,253,063,900	1,491,253,937	1,761,809,964
Cost Estimation by Expert Opinion			
Birth Cohort			
Vaccination cost	2,214,290,970	0	2,214,290,970
Direct acute cost	120,190,871	142,621,265	-22,430,394
Long-term costs	175,382,120	453,144,734	-277,762,614
Total	2,509,863,961	595,765,999	1,914,097,962
Adults			
Direct acute cost	4,300,584,982	5,137,396,098	-836,811,116
Total costs	6,810,448,943	5,733,162,097	1,077,286,846

Estimated Incremental Cost-Effectiveness

Cost estimation scenarios	Cost per Life-Year Gained (CLYG) (NT\$)
NHI Database	
With Indirect effects	374,573 (US\$11,925)
No Indirect effects	7,946,161 (US\$252,982)
Expert Opinion	
With Indirect effects	228,846 (US\$7,286)
No Indirect effects	7,892,616 (US\$251,277)

Sensitivity Analysis

Cost Estimation Scenario		NHI Database	Expert Opinion
Parameter varied	Range of values	CLYG (NT\$) (range)	CLYG (NT\$) (range)
Base Case (with indirect effects)	NA	374,573	228,846
Lower 95% bound on indirect effects	23% (20-39yrs), 1% (40-64yrs) and 11% (>65yrs)	390,172	308,545
Upper 95% bound on indirect effects	41% (20-39yrs), 20% (40-64yrs) and 31% (>65yrs)	213,848	189,104
Vaccine serotype coverage	-/+ 5%	369,326 - 379,858	224,002 - 233,723
Vaccine efficacy against IPD	82.7% to 99.9%	372,526 - 386,722	226,948 - 240,105
Vaccine efficacy against all-cause pneumonia	1.5% to 11%	374,519 - 374,655	228,606 - 229,205
Vaccine efficacy against otitis media	4.1% to 9.7%	374,431 - 374,726	228,364 - 229,363
Incidence of pneumococcal meningitis	50% to 200% of base	306,144 - 410,255	163,389 - 262,977
Incidence of pneumococcal bacteraemia	50% to 200% of base	365,274 - 379,386	222,276 - 232,246
Incidence of pneumococcal pneumonia	50% to 200% of base	374,508 - 374,606	228,559 - 228,989
Incidence of otitis media	50% to 200% of base	374,203 - 374,758	227,597 - 229,470

Conclusions

- The indirect benefit extended to unvaccinated individuals following routine infant PCV7 vaccination has been reported in several countries, including the US, where it is estimated that PCV7 has prevented more than twice as many IPD cases through indirect effects than through its direct effect of protecting vaccinated children.
- It is clear from our present study that, by including the adult IPD cases prevented due to the indirect effect, PCV7 becomes highly cost-effective with respect to the WHO's threshold (3 times Taiwan 2005 GDP per capita of NT\$498,326) for cost-effectiveness*.
- The added vaccine savings resulting from the herd protection of adults have made PCV7 a highly cost-effective intervention and a worthwhile investment to ensure the Taiwan population is protected against pneumococcal disease.

* WHO (2007). "Pneumococcal conjugate vaccine for childhood immunization - WHO position paper". *Weekly Epidemiol Record* 82(12): 93-104

A Dynamic Disease Transmission approach

INSTITUTE OF BIOMEDICAL SCIENCES **CHANG GUNG UNIVERSITY**

COST-EFFECTIVENESS ANALYSIS OF 7-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IN TAIWAN: TRANSMISSION DYNAMIC MODEL-BASED EVALUATIONS

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Abstract
To evaluate the long-term economic cost-effectiveness and clinical impact of universal infant vaccination of 7-valent pneumococcal conjugate vaccine (PCV7) in Taiwan by using a dynamic SIR model.
Methods: A dynamic realistic age-structured Susceptible-Infected-Recovered (SIR) model accounting for direct and indirect benefits was used; a payer perspective was adopted. One-way sensitivity analyses were carried out to evaluate model robustness.
Results: PCV7 was estimated to prevent 214 cases of invasive pneumococcal disease (IPD), and 24 deaths in the 10-year birth cohort. PCV7 would have an incremental cost per life-year gained (CLYG) of US\$10,584, when using cost data from the National Health Insurance Database (NHI). CLYG is lowered to US\$9,792 using costs from experts' opinion.

Background
Streptococcus pneumoniae (SP) is one of the major causes of morbidity and mortality worldwide. This is also the case in Taiwan, especially for youths and elders. In 2006, all-cause pneumonia was the 8th most common cause of death. WHO recommends that PCV7 is a priority for inclusion in national childhood immunization programs.¹ With increasing pressures on healthcare cost, an economic cost-effectiveness evaluation of PCV7 should be useful for policy-makers.

Figure 1: Number of the meningitis infection manifested with (green line) and without (red line) vaccination.

Figure 2: Number of the septicaemia infection manifested with (green line) and without (red line) vaccination.

Figure 3: Number of the pneumonia infection manifested with (green line) and without (red line) vaccination.

Table 1: The clinical and economic impacts generated by cohort model and dynamic SIR model.

	cohort model	dynamic SIR model
IPD prevented	143	214
deaths	8	24
CLYG (US\$)	10,584	9,792

Acknowledgement

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Thank you very much for your attention!

