

Clinical and Economic Impact of 13-Valent Pneumococcal Conjugate Vaccination In Singapore and Hong Kong

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BACKGROUND

- Streptococcus pneumoniae* is a major cause of meningitis, bacteremia, pneumonia, and otitis media in infants and children. It is considered a leading cause of vaccine-preventable deaths in children under 5 years-old.¹
- A 7-valent pneumococcal conjugate vaccine (PCV7) was introduced in the United States in 2000 for routine infant immunization.² PCV7 was recently introduced into national immunization programs for Hong Kong and Singapore.
- New pneumococcal conjugate vaccines include 10-valent (PCV10) and 13-valent (PCV13) vaccines.
- Both PCV7 and PCV13 include the CRM197 carrier protein.
- PCV13 offers coverage against six additional serotypes that are not available in PCV7 and three serotypes not available in PCV10. PCV10 offers coverage against three serotypes not available PCV7.
- PCV7 has been shown to reduce nasopharyngeal carriage of vaccine serotypes in vaccinated individuals resulting in indirect or "herd" effects in unvaccinated contacts.^{3,4}
- PCV10 was not found to significantly reduce nasopharyngeal carriage in one study.⁵

OBJECTIVE

- To determine the cost-effectiveness of PCV13 versus PCV7 and versus PCV10 in preventing pneumococcal disease in Singapore and Hong Kong from a payer perspective.

METHODS

- Decision-analytic model estimating the impact of pneumococcal conjugate vaccination on invasive pneumococcal disease (IPD), pneumonia, and otitis media.
- For each vaccination policy, population characteristics, epidemiology, vaccine characteristics, costs, and utilities were used to estimate the costs and outcomes (Figure 1).
- Disease incidence, serotype coverage, percentage of children vaccinated, direct effects and indirect effects were applied to the population to estimate the number of disease cases.
- Direct medical costs were applied to calculate the disease cost.
- Vaccination costs included acquisition and administration costs of the vaccine.
- Disease sequelae reduced an individual's quality of life.
- The model presents results over a 1-year time horizon.
- Age groups of patients (i.e., ages 0-2, 2-4, 5-17, 18-34, 35-49, 50-64, 65+ years-old) enter the model and a vaccination policy is applied.
- The default vaccination policy was based on an infant schedule, and so those in the 0-2 years-old cohort were considered for vaccination.
- Cost and outcomes were discounted at 3%.
- Vaccine costs assumed price parity to the private market unit price for PCV7 and were based on a four dose schedule.
- Specific local data were obtained from regional surveillance and published literature.⁶⁻¹⁸ Where local data were unavailable, proxy data were derived from published US sources.¹⁹⁻²¹

Figure 1. Model Calculations

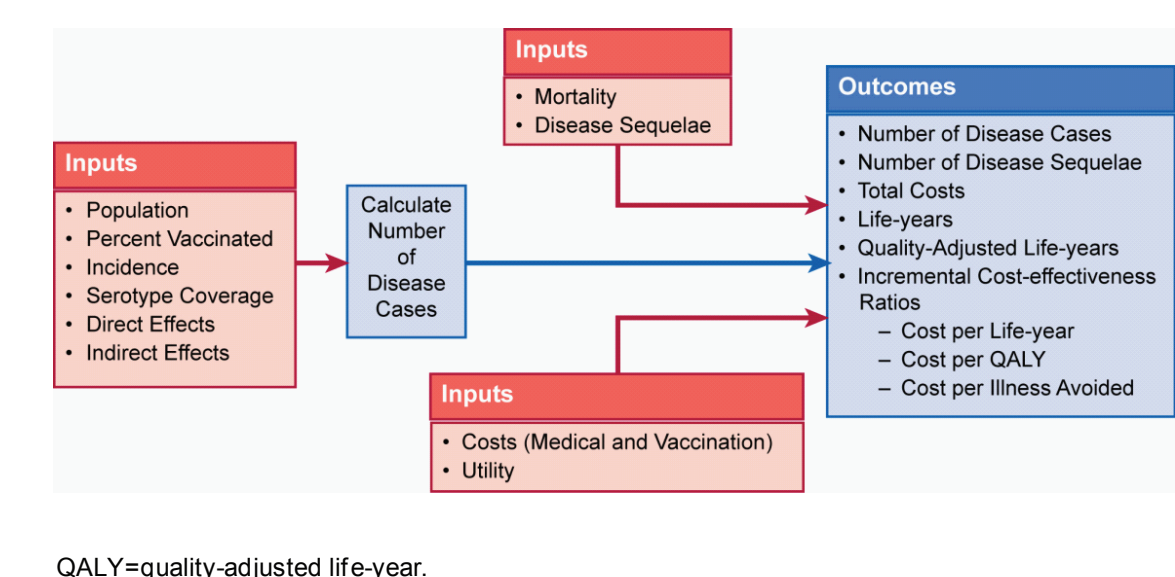


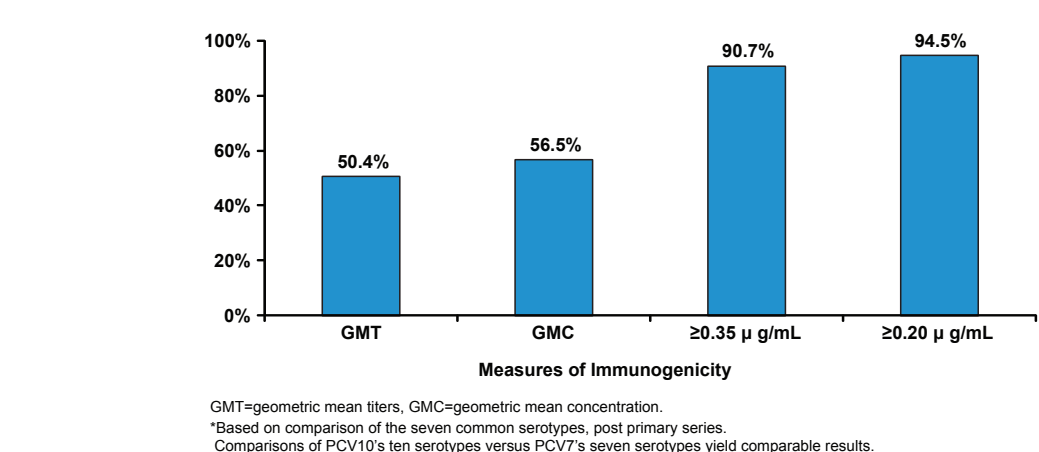
Table 1. Reduced Immunogenicity Adjustments Applied to PCV10 Direct Effect Relative to PCV7

	Pneumococcal Bacteremia	Pneumococcal Meningitis	Pneumonia - Inpatient	Pneumonia - Outpatient	Otitis Media
Adjustment Factor	0.90	0.90	0.85	0.80	0.75

Assumptions

- Vaccination coverage of 95% was applied for each vaccination policy scenario.
- Indirect effects were applied for both PCV7 and PCV13, as PCV7 has demonstrated an indirect effect⁴ and PCV13 shares the same carrier.
- For PCV13, the indirect effects were calculated based on PCV7 indirect effects^{21,25} and PCV13's increased serotype coverage
- The serotype coverage additional to PCV7 was halved to maintain conservative estimates.
- No indirect effects were applied for PCV10 since no publications to date have demonstrated a statistically significant reduction of nasopharyngeal carriage with PCV10.⁵
- Direct effects demonstrated by PCV7 and the increase in serotype coverage that PCV13 and PCV10 have over PCV7 were used to estimate the direct effects of PCV13 and PCV10.^{21,23,26,28}
- Based on immunogenicity data on PCV10 and PCV7,²⁹ a comparative analysis of PCV10 relative to PCV7 demonstrated that PCV10 is less immunogenic than PCV7 (Figure 2).
- PCV10 direct effects were adjusted to reflect a lower immunogenic response compared to PCV7 (Table 1). Pneumonia and otitis media were assumed to have further reduction in direct effects than IPD as attaining seroprotection against mucosal disease is more difficult than against IPD.³⁰
- For PCV10, the model included a 4% relative increased effect on otitis media due to the non-typeable *Haemophilus influenzae*-derived protein carrier.⁵

Figure 2. Lower Immunogenicity of PCV10 Relative to PCV7^{29*}



RESULTS

Table 2. Estimated Percent Reduction in IPD Via Direct Effects

	Hong Kong	Singapore
PCV13	86%	86%
PCV10, including lower immunogenic response adjustment	76%	73%
PCV10, excluding lower immunogenic response adjustment	84%	81%
PCV7	84%	81%

Table 3. Base Case Cost-effectiveness Results, With Indirect Effect for PCV13 and PCV7 and No Indirect Effect for PCV10

Variable	Hong Kong		Singapore	
	PCV13 vs PCV10	PCV13 vs PCV7	PCV13 vs PCV10	PCV13 vs PCV7
Difference in direct costs	-HK\$218,139,650	-HK\$54,345,259	-\$728,099	-\$249,846
Life years gained	13,303	3,868	77	29
Quality-adjusted life years gained	11,976	3,482	71	26
Illnesses avoided	7,444	1,619	672	93
Deaths avoided	1691	492	5	2
Cost per life year gained	PCV13 Dominates PCV10	PCV13 Dominates PCV7	PCV13 Dominates PCV10	PCV13 Dominates PCV7
Cost per quality-adjusted life year	PCV13 Dominates PCV10	PCV13 Dominates PCV7	PCV13 Dominates PCV10	PCV13 Dominates PCV7

Figure 3. Hong Kong Net Cost Per Child Vaccinated For PCV13 Scenarios

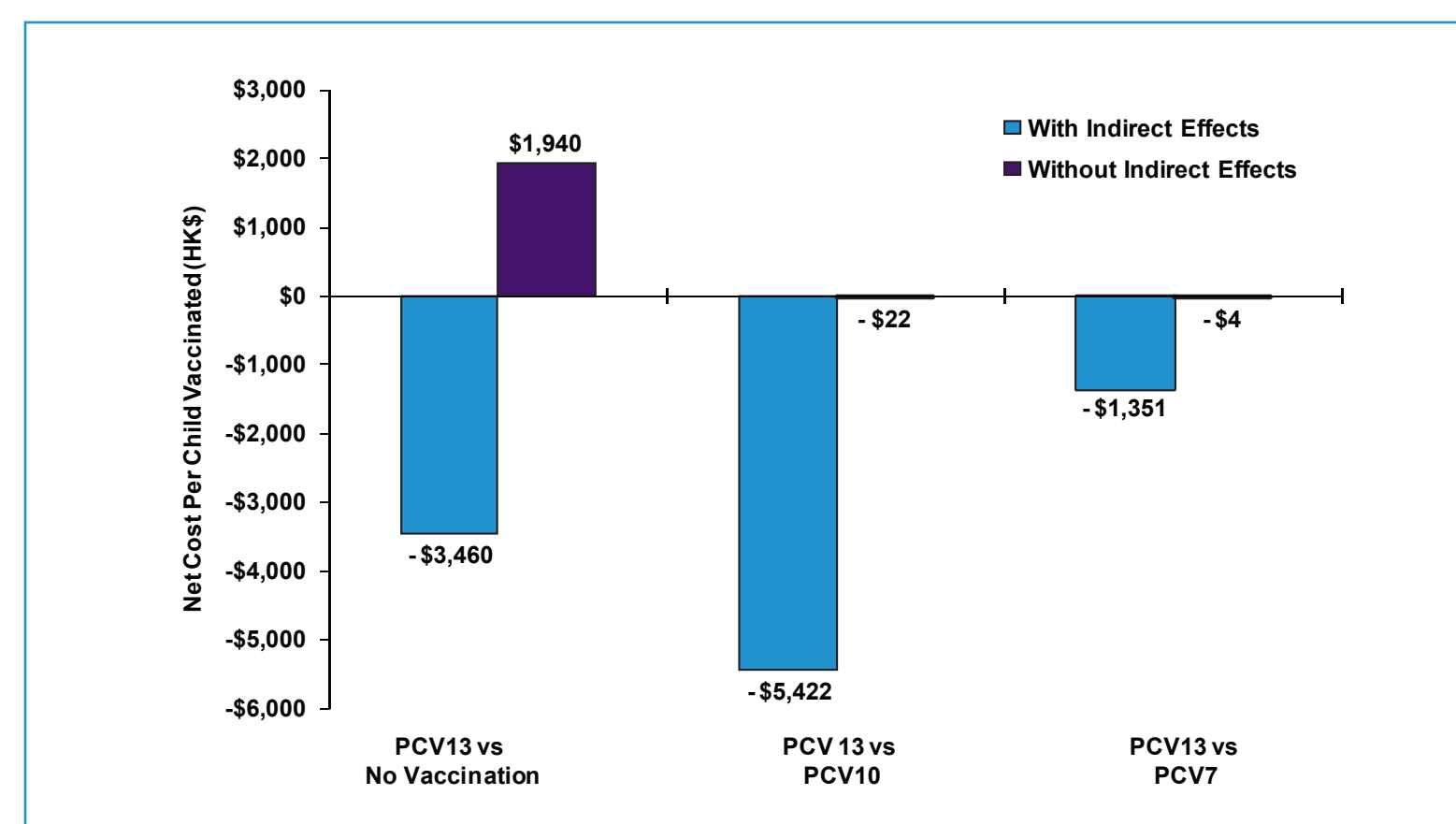


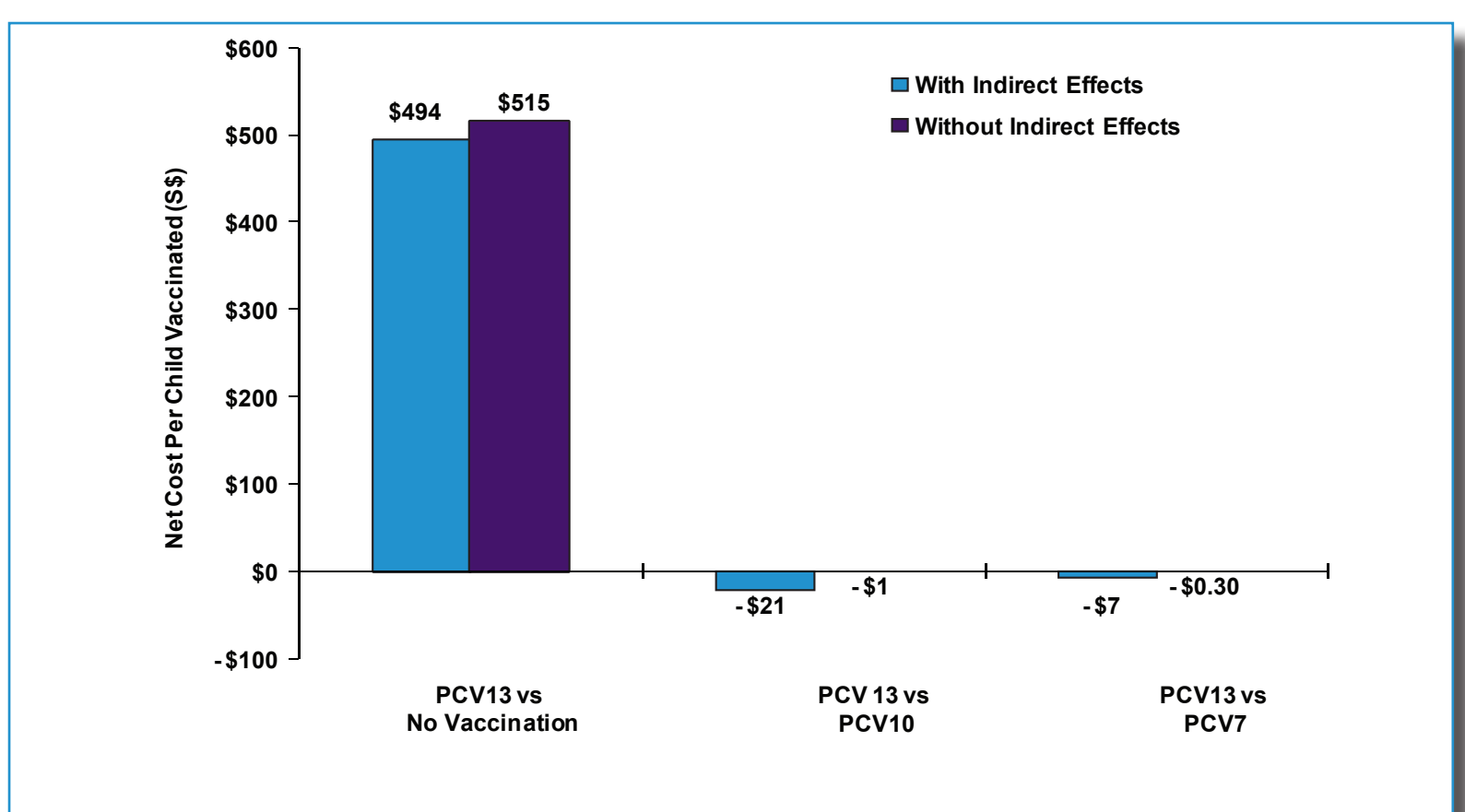
Table 4. Number of Pneumococcal Illnesses Avoided Relative to No Vaccination, With and Without Indirect Effects

Vaccination	Hong Kong		Singapore	
	With Indirect Effects	No Indirect Effects	With Indirect Effects	No Indirect Effects
PCV13	7,816	488	566,261	280,960
PCV10	N/A	373	N/A	201,121
PCV7	6,197	470	446,977	196,080

Table 5. Cost-effectiveness Sensitivity Analysis Results for PCV13 vs. PCV10, Without Reduced Immunogenicity Adjustment for PCV10, Assuming Full Direct Effect and No Indirect Effect for PCV10

Variable	Hong Kong		Singapore	
	With PCV13 Indirect Effects	Without PCV13 Indirect Effects	With PCV13 Indirect Effects	Without PCV13 Indirect Effects
Difference in direct costs	-HK\$217,330,203	-HK\$77,532	-\$692,768	-\$5,596
Net cost per child vaccinated	-HK\$5,401	-HK\$2	-\$20	-\$0.17
Cost per life year gained	PCV13 Dominates PCV10	PCV13 Dominates PCV10	PCV13 Dominates PCV10	PCV13 Dominates PCV10
Cost per quality-adjusted life year	PCV13 Dominates PCV10	PCV13 Dominates PCV10	PCV13 Dominates PCV10	PCV13 Dominates PCV10

Figure 4. Singapore Net Cost Per Child Vaccinated For PCV13 Scenarios



CONCLUSION

- These preliminary results suggest that PCV13 in Singapore and in Hong Kong would decrease pneumococcal illness.
- In addition, the programs are expected to be cost-savings relative to PCV10 and to PCV7.

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Presented at the International Society for Pharmacoeconomic and Outcomes Research Meeting, Atlanta, GA, May 15-19, 2010.

This study was sponsored by Wyeth which was acquired by Pfizer Inc in October 2009