Economic Evaluation of Universal Infant Vaccination with 7vPCV in Hong Kong

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ABSTRACT

Objective: The purpose of this study was to evaluate the clinical and economic benefits of routine infant vaccination with seven-valent pneumococcal conjugate vaccine (7vPCV) in Hong Kong.

Methods: A decision-analytic model was populated with local age-specific incidence data to simulate the expected health outcomes resulting from 7vPCV vaccination of a birth cohort of 37,100 children compared with an unvaccinated cohort over a 10-year horizon. Primary analyses were conducted from a payer perspective, using local inputpatient and outpatient costs associated with the treatment of pneumococcal disease. Vaccine efficacy rates were consistent with results from pivotal clinical trials. The reduction in adult invasive pneumococcal disease (IPD) and associated cost avoidance due to the indirect effect of vaccination were estimated in line with published overseas rates.

Results: Universal 7vPCV vaccination was estimated to prevent 524 cases of IPD and more than 2380 cases of otitis media in the birth cohort over a 10-year period, leading to a reduction of HK$28.7 million (US$3.7 million) in direct medical costs. Additional cost savings from the indirect prevention of 919 adult cases of IPD during this time period also resulted. Overall, 7vPCV vaccination was estimated to have an incremental cost per life-year gained of HK$50,456 (US$6460) from a payer perspective or HK$46,308 (US$5929) when both direct and indirect costs were included.

Conclusion: With reference to the World Health Organization’s threshold for cost-effectiveness, results from this study indicate that routine infant vaccination with 7vPCV is a cost-effective intervention because of the added cost savings resulting from the indirect effect of vaccination on adult disease.

Keywords: cost, herd immunity, pneumococcal disease, vaccine.

Introduction

Pneumococcal disease, caused by the bacterium Streptococcus pneumoniae, is a leading cause of vaccine-preventable death in children less than 5 years of age worldwide [1]. Clinical presentations may be invasive (meningitis, bacteremia, and bacteremic pneumonia, collectively reported as invasive pneumococcal disease [IPD]) or noninvasive (nonbacteremic pneumonia and otitis media) depending on the site of infection. In Hong Kong, pneumococcal disease is a major health-care burden, particularly in young children and the elderly. In 2005, all-cause pneumonia was recorded as the third most common cause of death (11.1% of total deaths) in Hong Kong [2]. Although penicillin remains the drug of choice for patients with pneumococcal disease, the growing incidence of antibiotic-resistant S. pneumoniae is a concern worldwide and has complicated disease management [3]. Furthermore, patients with resistant pneumococcal infections often require greater resource utilization, including longer hospital stays, to manage their condition, highlighting the potential economic consequences of increasing resistance rates of S. pneumoniae [4,5]. Several studies conducted in Hong Kong have indicated rising resistance rates of S. pneumoniae isolates obtained from children, with one study reporting penicillin resistance as high as 58.2% (29.5% intermediate, 26.1% resistant) in children attending day care [6].

Assessments of the cost-effectiveness of public health interventions are assuming increasing influence in assisting decision-making in Hong Kong. With growing pressures on health-care expenditure, an economic evaluation of the cost-effectiveness of universal infant vaccination with 7vPCV will provide a useful decision tool to justify whether vaccine introduction is a worthwhile public health intervention. The present study is the first of its kind in Asia. Against this background, the aim of this study...
was to evaluate the clinical and economic benefits of universal infant vaccination with 7vPCV for both children and adults in Hong Kong.

Methodology

Data Collection

Epidemiological data. Age-specific incidence rates for pediatric cases of pneumococcal meningitis, pneumococcal bacteremia, all-cause pneumonia, and otitis media were obtained from published literature [14–16]. The annual number of adult hospitalizations for confirmed pneumococcal cases of meningitis and bacteremia were estimated from the Hong Kong Hospital Authority (HA) (2005 data), a statutory body that manages all public hospitals in Hong Kong. The burden of pneumococcal pneumonia in adults was also estimated from the HA by including all confirmed pneumococcal cases and assuming that 32% of unspecified cases were due to S. pneumoniae [17]. In the event that an adult had both bacteremia and pneumonia upon admission, a single case of pneumococcal pneumonia was recorded.

Pediatric case fatalities for pneumococcal meningitis, pneumococcal bacteremia, and all-cause pneumonia were derived from 2006 death statistics from the Hong Kong Department of Health [18]. It was assumed that no cases of otitis media resulted in death. Adult deaths were assumed to only occur due to pneumococcal pneumonia, with data obtained from the HA. Vaccine efficacy rates observed in the Northern California Kaiser Permanente pivotal clinical trial were applied [19,20], namely, a 97.4% reduction in episodes of pneumococcal meningitis and bacteremia, a 6% reduction in all-cause pneumonia, and a 7% reduction in all-cause otitis media for pediatric cases. Efficacy rates against pediatric cases of all-cause pneumonia and otitis media were varied in secondary analyses, in line with published overviews of effectiveness data, i.e., 39% reduction in all-cause pneumonia [21] and 42.7% reduction in acute otitis media [22]. The seven serotypes in 7vPCV were estimated to cover 88.6% of IPD cases in children <2 years and 90.6% of IPD cases in children aged 2 to 6 years in line with published local rates [23]. Vaccine serotype coverage in children >6 years of age was assumed to be 42.3% [24]. The waning of vaccine-induced immunity was also considered in the model by assuming that for a period of 5 years after initial vaccination of the birth cohort, vaccine efficacy would decrease by 1% per year and by 3% annually for years 6 to 10 after initial vaccination [25].

Cost Data

The cost of pneumococcal disease was determined from a payer perspective in the primary analysis. Local inpatient cost data were collected from deidentified case records for pediatric patients admitted to the Prince of Wales Hospital or the United Christian Hospital with either IPD (n = 8), pneumonia (n = 22), or otitis media (n = 18) from 2005 to 2006. These costs covered the direct medical resources consumed in the treatment of pneumococcal disease including hospitalization, physician consultation fees, medications, and diagnostic tests. Costs associated with treating adult cases of pneumococcal disease, namely, 7 cases of meningitis, 53 cases of bacteremia, and 5327 cases of pneumonia (all clinically confirmed pneumococcal pneumonia and 32% of all-cause pneumonia cases) in 2005 were obtained from the HA and were used to estimate the weighted average cost for the treatment for adults aged 20 to 34 years, 35 to 64 years, and ≥65 years. All costs were discounted by 5% in the primary analysis.

The cost of pneumococcal disease was also determined from a societal perspective in a secondary analysis to include all of the direct medical expenses of the payer perspective combined with two additional disease-related costs: direct nonmedical costs and indirect costs. Nonmedical costs were included to reflect items, such as transportation costs, incurred for physician visits and hospital stays. Indirect costs reflected the opportunity cost of an individual informally caring for a child with pneumococcal disease and forgoing the use of their time for other economically valuable purposes (e.g., employment). Costs were determined through written surveys sent to 30 local physicians from different regions in Hong Kong who had experience in the treatment of pneumococcal disease. A total of 30 surveys were completed and used for indirect cost estimations. The respondents were requested to estimate the number of sick days that would be required after discharge for each clinical presentation of pneumococcal disease. The number of days a carer would be absent from work was estimated as 50% of the length of hospital stay added to the number of sick days required postdischarge. The median monthly salary (HK$10,000) in 2006, obtained from the Hong Kong Census and Statistics Department, was used to estimate the average total wages lost for each clinical presentation of pneumococcal disease.

The long-term treatment costs for complications experienced by patients with meningitis, such as deafness, brain damage, focal neurological deficit, and chronic seizures, were considered in a secondary analysis. The frequency of each complication was assumed to be 4.3%, 9.7%, 6.0%, and 7.0%, respectively, in line with published rates from the UK, as local estimates were not available [26–28]. Published UK costs [24] for the treatment of each form of sequelae were converted to Hong Kong dollars (HK$) using the May 2008 exchange rate (GBP1 = HK$14.1478) and inflated to present values, in the absence of local costs. The breakdown of the costs included in the model is presented in Table 1.

The cost of introducing a universal vaccination program included both 7vPCV vaccine acquisition (HK$500 per dose) and administration costs (HK$12.07 per injection). Vaccination was assumed to be provided for the birth cohort, i.e., infants less than 6 months of age, as a primary series of three doses at 2, 4, and 6 months of age with a booster (fourth) dose administered in the second year of life at 12 to 15 months of age. A vaccination coverage rate of 95% was assumed for all infants.

Decision Analytic Model

To estimate the long-term outcomes associated with vaccination, a previously developed decision analytic economic model [17,24] was adapted to simulate the expected health outcomes resulting from universal 7vPCV vaccination of a birth cohort of 57,100 infants in Hong Kong compared with no vaccination over a 10-year time horizon (Fig. 1). The cohort was divided into 6-month age bands, and infants less than 6 months of age were further divided into those aged 0 to 2 months and 2 to 6 months. The annual number of pneumococcal infections by clinical presentation in each age band was then calculated, in addition to the reduction in cases that would be afforded with 7vPCV vaccination, and the mortality and cost resulting from these events. Anticipated indirect (herd protection) effects of 7vPCV in unvaccinated adults were estimated by calculating the reduction in adult cases of IPD in line with published rates from the US experience [9,10]. The midpoint estimates for the indirect effects were used in the primary analysis, namely, 32% (range 23–41%) for adults aged 20 to 34 years, 8% (range 1–20%) for adults aged 35 to 64 years, and 18% (range 11–31%) for adults aged ≥65 years.
Cost-Effectiveness Analysis

The cost-effectiveness of a universal 7vPCV vaccination program was calculated in terms of cost per life-year gained (CLYG). Life-years were used to measure deaths avoided, where each death prevented was equated to a certain number of life-years, depending upon the age at which the death was expected to occur and the life expectancy of the individual. Each death avoided
from the birth cohort was equal to the average Hong Kong life expectancy at 5 years of age (approximately 79 years) minus the child’s age at the time of death as determined by the incidence of IPD and its associated mortality. The average life expectancies of adults aged 20 to 34 years (52.9 years), 35 to 64 years (31.7 years), and ≥65 years (8.3 years) were estimated from life tables for 2006 from the Hong Kong Department of Health. The life-years gained from preventing an adult’s death were equal to the relevant life expectancy of the adult at the time the death was avoided. In the primary analysis, life-years gained were discounted at a rate of 5%.

A series of univariate sensitivity analyses were performed to evaluate the sensitivity of the findings to plausible variation in specific data inputs. Parameters varied were: indirect effects (lower and upper 95% confidence bound estimates used), vaccine serotype coverage, vaccine efficacy against IPD, all-cause pneumonia and otitis media, the incidence of each clinical presentation (meningitis, bacteremia, pneumonia, and otitis media), the discount rate, the weighted average cost of treatment for pediatric cases, and the cost per course of 7vPCV.

Results

Outcomes

The incidence of pediatric cases of pneumococcal disease by clinical presentation is summarized in Table 1. Adult cases obtained from the HA and the Hong Kong Department of Health are shown in Table 2. The impact of 7vPCV vaccination with respect to the number of cases of pneumococcal disease and deaths avoided in the birth cohort, and the unvaccinated adult populations is presented in Table 3. In the birth cohort alone, universal 7vPCV vaccination was estimated to prevent 524 cases of IPD (meningitis, bacteremia, and hospitalized cases of pneumonia), approximately 2,580 cases of otitis media, and 2 deaths. With the inclusion of the indirect effect of vaccination, a total of 1081 life-years were gained through the prevention of an additional 919 cases of IPD and 140 deaths in the adult population.

Costs

A summary of treatment costs saved as a result of 7vPCV vaccination is presented in Table 4. All costs presented are discounted at 5%. Overall, universal infant 7vPCV vaccination was estimated to lead to a reduction of at least HK$28.7 million (US$3.7 million) in direct medical costs associated with treatment of the birth cohort over 10 years. By expanding the analysis to include the indirect effects of 7vPCV on the adult population, HK$56.6 million (US$7.3 million) in cost savings were estimated during the time period. With the inclusion of indirect costs, HK$61.1 million (US$7.8 million) in cost savings resulted.

Cost-Effectiveness

The resulting incremental cost-effectiveness ratios for the primary analysis are presented in Table 5. From a payer perspective, universal vaccination with 7vPCV had a discounted CL YG of HK$50,454 (US$6460) when the indirect effects of vaccination on the adult population were taken into account. With the inclusion of both direct and indirect costs, the discounted CL YG decreased to HK$46,318 (US$5929).

Sensitivity Analyses

The results of the various univariate sensitivity analyses previously described are presented in Table 6. All incremental cost-effectiveness ratios are calculated from both a payer and societal perspective, and include both direct and indirect effects of vaccination. The CL YG was most sensitive to variations in assumptions regarding vaccine costs, indirect effects, incidence of all-
cause pneumonia attributable to *S. pneumoniae*, and vaccine efficacy against all-cause pneumonia. Varying the vaccine efficacy rates for pediatric all-cause pneumonia and otitis media in line with effectiveness data from the United States further reduced the incremental cost-effectiveness ratios (Table 7). With the inclusion of overseas long-term treatment costs for sequelae in meningitis survivors (obtained from the UK), the CL YG decreased to HK$44,644 (UK$5718) when only direct costs were included or HK$40,496 (US$5189) when both direct and indirect costs were considered.

**Discussion**

The WHO Choosing Interventions that are Cost-Effective group has developed guidelines on generalized cost-effectiveness analyses for public health interventions and indicates that interventions which cost less than three times the average per capita income per outcome unit are cost-effective [29]. With respect to this threshold, universal 7vPCV vaccination would be considered cost-effective in Hong Kong if the CL YG is below HK$680,007 (US$87,068) per life-year gained, using the 2007 gross domestic product per capita of HK$226,669 [30]. Results from our study indicate that universal 7vPCV vaccination is a cost-effective intervention in Hong Kong with reference to this threshold from both a payer and societal economic perspective.

A conservative incidence rate of bacteremia was employed in the primary analysis, in line with recent hospitalization data [14], namely, 4.2 per 100,000 person-years (in the 0–2 years age group) and 2.1 per 100,000 person-years (in the 3–5 years age group).
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Table 7  Impact of vaccine efficacy against pediatric cases of all-cause pneumonia and otitis media

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Otitis media</th>
<th>All-cause pneumonia</th>
<th>Cost per life year gained (including indirect effect) (HK$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary analysis</td>
<td>7 [19,20]</td>
<td>6 [19,20]</td>
<td>50,456</td>
</tr>
<tr>
<td>Secondary analysis</td>
<td>42.7 [22]</td>
<td>39 [21]</td>
<td>46,308</td>
</tr>
</tbody>
</table>

Impact of vaccination on reducing the burden of all-cause pneumonia in adults was not considered due to limited access to local records on the treatment of pneumonia in the community setting. Another conservative approach adopted was only considering the indirect impact of vaccination on pneumococcal pneumonia deaths in adults. Potential reductions in deaths due to other invasive presentations that may be afforded through herd protection were not included because of lack of available data. Similarly, indirect effects in older children aged 10 to 19 years were not considered in this analysis, as it was assumed that their disease burden would be relatively low.

In Hong Kong, universal infant 7vPCV vaccination is expected to lead to a substantial reduction in the incidence of all clinical presentations of pneumococcal disease in both children and adults. With reference to the WHO’s threshold for cost-effectiveness, results from this study indicate the cost savings from both the direct and indirect effects of vaccination render 7vPCV a cost-effective intervention and a worthwhile investment to ensure that the population of Hong Kong is protected against pneumococcal disease.

Study Limitations

The potential effect of vaccination on other clinical presentations of pneumococcal disease, such as sinusitis and septic arthritis, was not included in the analysis. Furthermore, the indirect effect used in the study could be considered conservative and perhaps could be much higher in reality. With that in mind, routine infant vaccination with 7vPCV may be even more cost-effective than we have estimated.

Conclusion

In Hong Kong, universal infant 7vPCV vaccination is expected to lead to a substantial reduction in the incidence of all clinical presentations of pneumococcal disease in both children and adults. With reference to the WHO’s threshold for cost-effectiveness, results from this study indicate the cost savings from both the direct and indirect effects of vaccination render 7vPCV a cost-effective intervention and a worthwhile investment to ensure that the population of Hong Kong is protected against pneumococcal disease.

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During the study period, Fiona Rinaldi was an employee of Wyeth, which owns and markets the 7-valent pneumococcal conjugate vaccine.

References

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61 Ho PL. Proceedings of the first current topic in infectious diseases: consensus meeting on conjugate vaccines of the Center of Infection, Faculty of Medicine, The University of Hong Kong [Selected Abstracts]. HK J Paediatr 2001;6:127–32.
