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Retrospective cost-effectiveness of the 23-valent pneumococcal polysaccharide vaccination program in Australia

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ABSTRACT

Background: The Australian infant pneumococcal vaccination program was funded in 2005 using the 7-valent pneumococcal conjugate vaccine (PCV7) and the 13-valent conjugate vaccine (PCV13) in 2011. The PCV7 and PCV13 programs resulted in herd immunity effects across all age-groups, including older adults. Coincident with the introduction of the PCV7 program in 2005, 23-valent pneumococcal polysaccharide vaccine (PPV23) was funded for all Australian adults aged over 65 years.
Methods: A multi-cohort Markov model with a cycle length of one year was developed to retrospectively evaluate the cost-effectiveness of the PPV23 immunisation program from 2005 to 2015. The analysis was performed from the healthcare system perspective with costs and quality-adjusted life years discounted at 5% annually. The incremental cost-effectiveness ratio (ICER) for PPV23 doses provided from 2005 to 2015 was calculated separately for each year when compared to no vaccination. Parameter uncertainty was explored using deterministic and probabilistic sensitivity analysis.
Results: It was estimated that PPV23 doses given out over the 11-year period from 2005 to 2015 prevented 771 hospitalisations and 99 deaths from invasive pneumococcal disease (IPD). However, the estimated IPD cases and deaths prevented by PPV23 declined by more than 50% over this period (e.g. from 12.9 deaths for doses given out in 2005 to 6.1 in 2015), likely driven by herd effects from infant PCV programs. The estimated ICER over the period 2005 to 2015 was approximately A$224,000/QALY gained compared to no vaccination. When examined per year, the ICER for each individual year worsened from $140,000/QALY in 2005 to $238,000/QALY in 2011 to $286,000/QALY in 2015.
Conclusion: The cost-effectiveness of the PPV23 program in older Australians was estimated to have worsened over time. It is unlikely to have been cost-effective, unless PPV23 provided protection against non-invasive pneumococcal pneumonia and/or a low vaccine price was negotiated. A key policy priority should be to review of the future use of PPV23 in Australia, which is likely to be more cost-effective in certain high-risk groups.

1. Introduction

Streptococcus pneumoniae, or *pneumococcus*, can cause a wide range of invasive and non-invasive diseases. Infants under two years of age and the elderly are the age-groups at highest risk of invasive pneumococcal disease (IPD). In January 2005, 7-valent pneumococcal conjugate vaccine (PCV7) was funded for infants through the Australian National Immunisation Program (NIP). The infant PCV7 program resulted in substantial herd immunity effects across all age-groups in relation to the 7 targeted types, with these types almost eliminated in the Australian population [1]. As seen in other populations [2], replacement by non-PCV7 strains then occurred (e.g. serotype 19A [3]) [4], prompting the introduction of the 13-valent conjugate vaccine (PCV13) in July 2011 [5].

Coincident with the introduction of the PCV7 program, 23-valent pneumococcal polysaccharide vaccine (PPV23) was funded in January 2005 for all Australians aged over 65 years through the NIP [5]. The impact of this program has been difficult to assess due to the large herd impact of the infant PCV7 program which shares serotypes in common with PPV23 [6]. Also, although funded nationally in 2005 there was already moderate PPV23 coverage established in older adults before this time (e.g. private uptake) [7].

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There is strong evidence that PPV23 provides protection against corresponding vaccine-type IPD [8,9]. However, the available data suggest that the duration of efficacy from PPV23 may be relatively short in older adults [10]. The evidence for PPV23 protection against (non-invasive) pneumococcal community-acquired pneumonia (CAP) remains uncertain with some but no definitive evidence in older adults [11]. The PPV23 program was implemented prior to requirements for a cost-effectiveness evaluation as part of the routine decision making for vaccines in Australia [12]. More recent vaccine funding decisions have been subject to economic evaluations as part of the formal Pharmaceutical Benefits Advisory Committee (PBAC) assessment process in Australia [12].

In June 2016, the use of PCV13 was recommended in older Australians by the PBAC as a replacement for PPV23 [13]. The PBAC meeting notes explicitly point to the lack of cost-effectiveness analysis for PPV23 and suggest that such an analysis in the Australian context would be timely [13]. The level of herd protection effects from the infant pneumococcal program is likely to be important in estimating the cost-effectiveness of the PPV23 vaccination program in older adults and may have evolved since the introduction of PCV7 in 2005 and subsequently PCV13 in 2011 [11,14].

This article evaluates the cost-effectiveness of the PPV23 program in older adults in Australia from 2005 to 2015 with a focus on how the value for money may have changed over time as a result of herd protection effects from infant PCV7 and PCV13 programs.

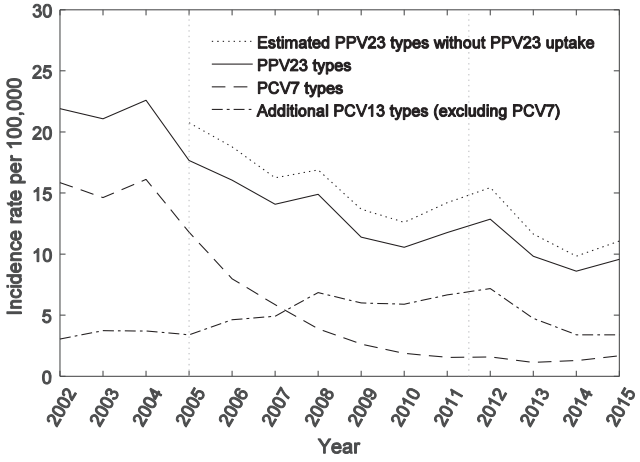

Fig. 1. Historical Australian IPD incidence rate for adults aged 65 years or over in the years of 2002–2015. The different lines represent the incidences caused by different serotype groupings. For example, the additional PCV13 types are those included in PCV13 but not in PCV7. The estimated PPV23 types without PPV23 vaccination corresponds to the hypothetical incidence rate assuming no PPV23 uptake in Australia. The first dotted vertical line corresponds to the timing when the PCV7 infant program and the PPV23 adult program were funded in Australia. The second dotted vertical line corresponds to when PCV13 was funded for Australian infants. The NNDSS public dataset was used from 2009 to 2015 [4]. From 2002 to 2008, when publicly accessible data were not available, requested data provided by the Office of Health Protection, Department of Health, was used (see Acknowledgements). Minor inter-year discrepancies may result from the use of these two sources. Note, we assumed IPD with serotypes listed as untyped and/or not available were distributed proportionally relative to known serotypes.

2. Methods

2.1. Model and study population

A multi-cohort Markov model with a cycle length of one year was used (adapted from a previous study [7]) to evaluate the cost-effectiveness of the retrospective PPV23 immunisation program from 2005 to 2015. The model follows the whole Australian population [15] with a background mortality rate from the Australian Bureau of Statistics (ABS) [16]. Each cohort was followed until protection from PPV23 had fully waned, with the full benefits of prevented pneumococcal related deaths during this period included via a discounted payoff, accumulated over the remaining statistical life span adjusted for age at death. The cohorts were stratified into one-year age bands until the age of 100, with individuals aged above 100 years old being stratified into a single age group. The analysis was performed from the healthcare system perspective with future costs and quality-adjusted life years (QALYs) for the cohorts vaccinated in each year discounted (at 5% annually [17]) from the year of vaccination. The incremental cost-effectiveness ratio (ICER) for PPV23, when compared to no vaccination, was estimated for doses given in each year calculated separately.

In any year t and for each age-group $a < 85$ years, we estimated the PPV23 vaccine-type incidence without PPV (i.e. a hypothetical no vaccination world), $I_{hyp}(a,t)$, using the formula: $I_{hyp}(a,t) = I_{obs}(a,t)/[1 - E(a)C(a,t)W]$ where $I_{obs}(a,t)$ is the observed PPV23 vaccine-type incidence (Figs. 1 and 2), $E(a)$ is the vaccine efficacy (Table 1), and $C(a,t)$ is the cumulative percentage of the cohort aged a who had received PPV23 vaccination during the years from $t-4$ to t, that is, the uptake (Fig. 3). For each age group, the observed coverage is then weighted by the effective waning rate $W = 0.7$ to account for the relative proportions vaccinated 4,3,2,1 and 0 years previously. As the observed time-variation in coverage is relatively small (see Fig. 3a scaled coverage), for the purpose of calculating the impact of waning we assumed constant yearly coverage in time. As PPV23 was assumed to have zero efficacy for the >85 years group [10], incidence rates as estimated in the absence of PPV23 were not inflated for these adults. Please see Appendix 1 for further details.

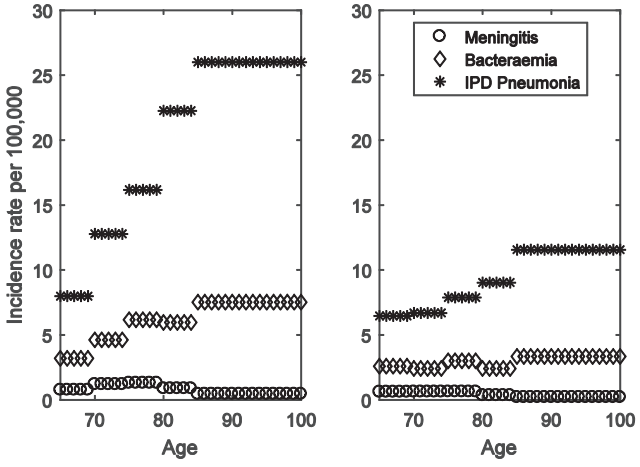

Fig. 2. The average Australian age-dependent IPD incidence for the years 2005 (left) and 2015 (right), for adults aged 65 years or over. The three different plots are different clinic types of IPD. The NNDSS public dataset was used for the year of 2015 [4] and for the year of 2005 requested data provided by the Office of Health Protection, Department of Health, was used (see Acknowledgements).

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.vaccine.2018.08.084.

2.2. Disease parameters

In each year for each five-year age band, IPD incidence rates were computed by dividing notified IPD cases reported to the National Notifiable Diseases Surveillance System (NNDSS) [4] by the corre-