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Short communication

Evolution over time in the cost-effectiveness of pneumococcal conjugate vaccine (PCV13) in older Australians due to herd protection from infant vaccination

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ABSTRACT

In many settings, serotype changes as a result of infant 13-valent pneumococcal conjugate vaccine (PCV13) programs are likely to continue after the introduction of adult PCV13 programs. We applied a multi-cohort model to explore how potential serotype changes may impact on the cost-effectiveness of PCV13 use in Australian adults aged over 65 years. We found assumptions around continued herd protection from infant PCV13 programs to be critical when assessing the cost-effectiveness of adult PCV13 vaccination in Australia. Future cost-effectiveness analyses of adult PCV13 programs need to carefully consider how to predict these future changes in serotypes, with Australian data suggesting that the changes post-PCV13 use in infants may be different than post-PCV7.

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1. Introduction

Streptococcus pneumoniae causes a range of diseases including of invasive pneumococcal disease (IPD) and non-invasive community-acquired pneumonia (CAP). In Australia, 7-valent pneumococcal conjugate vaccine (PCV7) was funded for all infants in January 2005 [1] and was replaced in July 2011 by PCV13, which covers six additional pneumococcal serotypes [2].

In July 2016, the Australian Pharmaceutical Benefits Advisory Committee (PBAC) recommended listing of PCV13 in older adults as a replacement for PPV23 which was funded nationally in 2005 [3]. Although PCV13 covers less serotypes than PPV23, the evidence that it offers better protection against pneumococcal CAP and has a longer overall duration of protection is generally considered more compelling than for PPV23 [4]. However, the herd protection from the infant PCV13 program adds complexity to the evaluation of adult programs, as the herd effects from the infant PCV13 program will evolve over time and may not have stabilised in older adults [5]. The extent and timing of the herd effects after infant pneumococcal vaccine introduction have differed by setting [6–8]. Future potential herd effects are likely to be a major factor

influencing the cost-effectiveness of pneumococcal vaccination in older adults [5].

Many of the existing cost-effectiveness analyses of PCV13 use in adults simulate a single-cohort of older adults [9]. Using this approach, a cohort of 65-year-old adults are vaccinated at a single time point and followed until death. Single-cohort models assume that the cohort followed is representative of future cohorts [10]. In this short report, we apply a multi-cohort model to explore how serotype evolution may impact on the cost-effectiveness of PCV13 use in older Australian adults over time.

2. Methods

A multi-cohort Markov model using a cycle length of one year was used (adapted from [13]) to evaluate the cost-effectiveness of a PCV13 immunisation program in those ≥ 65 years against a comparator of a hypothetical no adult pneumococcal vaccination world. The population was stratified into single age bands. The analysis was conducted from a healthcare system perspective with costs and quality-adjusted life years (QALYs) discounted at 5% per annum [11]. We calculated the incremental cost-effectiveness ratio (ICER) for vaccines administered in each individual year. To illustrate how the childhood PCV13 program can impact on the cost-effectiveness of adult vaccination over time depending on

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the relative timing of each program, we evaluated a hypothetical start to the program from 2012 (the first year PCV13 was funded in Australian infants) to 2021. We also explored the ICER for a PCV13 program over a five-year period from potential introduction in 2017.

Based upon the latest Australian notification data (Fig. 1), there is some evidence that incidence of the additional 6 serotypes (in PCV13) may have stabilised in recent years in those ≥ 65 years, after a rapid decline from 2011 when PCV13 vaccine program was introduced in infants [12]. This differed somewhat from the decline observed after PCV7 introduction in 2005, where vaccine-type incidence in older adults declined over a longer period (approximately 7 years) and stabilised at a lower level. However, as future effects are uncertain we explored **two scenarios**, firstly we assumed a base case scenario of no future serotype changes, only exploring how the past variation in serotypes would have impacted on cost-effectiveness. In the second scenario, the 6 additional types in PCV13 were assumed to continue to decline from 2016 in the same way that PCV7 types declined, with a yearly incidence rate ratio (IRR) of 70.0% for 7 years (until 2019). The IRR was calculated using maximum likelihood estimation. Fig. 1 illustrates the different steady state incidence rates for the additional six serotypes in PCV13 in the two scenarios we model, with substantially lower levels reached when we apply herd declines as observed after PCV7 introduction.

A detailed outline of parameters and the adapted model can be found in [13]. To summarise briefly, we assumed a \$65 price per PCV13 dose and an administration cost of \$10 [14]. Age-specific PCV13 efficacy data against serotype specific IPD and pneumococcal CAP were derived from [15]. We assumed pneumococcal CAP has the same serotype distribution as IPD due to a lack of available data in Australia. The QALY loss per hospitalised case or visiting a general practitioner (for CAP) were assumed to be 0.0709 and 0.0045 respectively [16]. To estimate the cost-effectiveness of

PCV13 vaccination against no adult pneumococcal vaccination, we removed the current PPV23 vaccination by inflating the publicly available [12] age-specific serotype-specific IPD incidence estimates depending on the PPV23 vaccine efficacy and uptake (incidence rates in current world/ $(1 - \text{efficacy} \times \text{uptake})$) [13]. Throughout our model, we apply an age-specific uptake data based on the 2013 uptake data of PPV23 (see Acknowledgements) in the state of New South Wales (NSW) to the PCV13 program in older adults [13,17]. We estimated from this data that 7% of vaccine naïve adults would receive PCV13 vaccination at age 65 years and that the uptake declines at a rate of 15% per year of age (see [13] for further details). All costs in this article are expressed as 2016 Australian dollars.

3. Result

In Fig. 2, ICER results are explored by variation in time. In both scenarios, the adult PCV13 program was most cost-effective in a hypothetical situation of it being introduced in the same year as an infant PCV13 program (i.e. 2012). The cost-effectiveness then worsened over time as the preventable disease burden in adults declined due to the herd effects of the PCV13 infant program. Although we assume the same serotype incidence in both scenarios before 2015, the ICERs estimated for doses given out in these years differ significantly, as those vaccinated between 2012 and 2014 are protected over a number of years into the period where serotype incidence diverges for the two scenarios modelled.

In the base case scenario, assuming no future decline in additional PCV13 serotypes, the ICER over a 5-year program from 2017 to 2021 was estimated to be approximately \$70,000 per QALY gained. For the scenario where the additional six serotypes in PCV13 decline further, the 5-year program from 2017 to 2021 was estimated to be \$164,000 per QALY gained. The results for

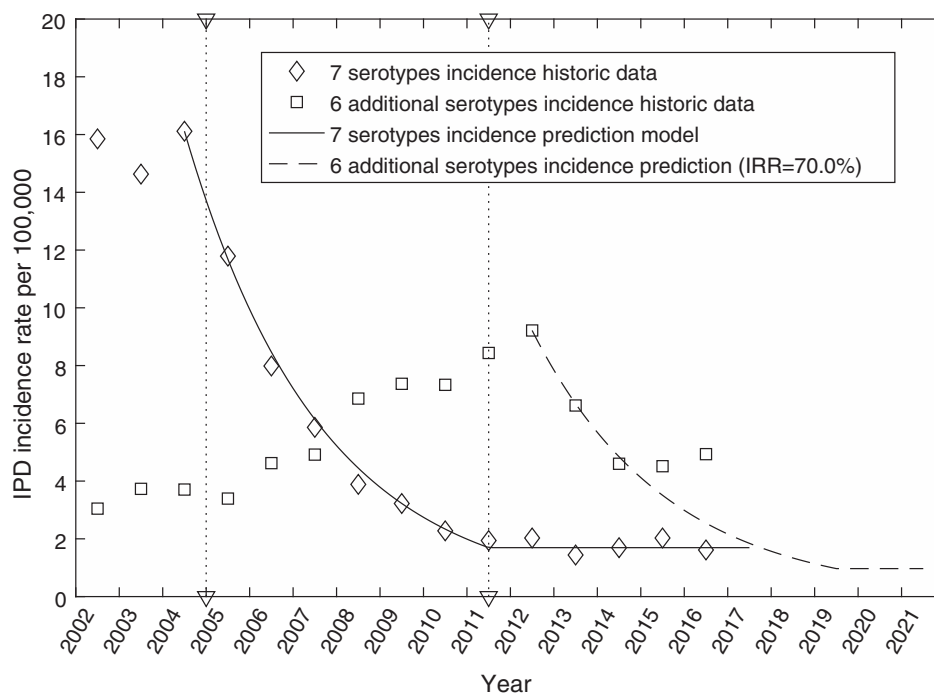


Fig. 1. IPD incidence in Australians ≥ 65 years and model predictions over time. The PCV7 serotypes IPD incidence rate decays exponentially from the introduction of PCV7 vaccine program in infants. A scenario analysis (dashed line) assumes that the 6 additional serotypes will decline exponentially with the same annual rate as the PCV7 serotypes declined ($\text{Incidence}(\text{year}) = \text{Incidence}(2012) \exp[-0.700 \min(\text{year}-2012, 7)]$). The decline was assumed to saturate after 7 years, in 2019. The two dotted vertical lines shows the time when the universal infant PCV7 and PCV13 programs were initiated in January 2005 and July 2011 respectively. NNDSS public dataset was used from 2009 to 2016 [12]. From 2002 to 2008, when publicly accessible data was 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.

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