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The role of timeliness in the cost-effectiveness of older adult vaccination: A case study of pneumococcal conjugate vaccine in Australia

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ABSTRACT

While the impact of the timeliness of vaccine administration has been well-studied for childhood vaccinations, there has been little detailed quantitative analysis on the potential impact of the timeliness of vaccinations in older adults. The aim of this study was to explore the impact of implementing more realistic observed uptake distributions, taking into the account reduced vaccine efficacy but higher pneumococcal disease burden with increasing age beyond 65 years. A multi-cohort Markov model was constructed to evaluate the cost-effectiveness of a pneumococcal (PCV13) immunisation program in Australia, assuming two different uptake modelling approaches. The approach using an estimate of observed uptake was compared with a scenario in which the total cumulative uptake was delivered at the recommended age of vaccination. We found these two approaches produced different results both in terms of cases prevented and cost-effectiveness. The impact of the non-timely uptake in adult programs may sometimes have positive and other times negative effects, depending on several factors including the age-specific disease rates and the duration of vaccine protection. Our study highlights the importance of using realistic assumptions around uptake (including non-timely vaccination) when estimating the impact of vaccination in adults.

1. Introduction

The majority of economic evaluations of adult vaccination programs assume that vaccines are administered at the specific age proposed in the future schedule [1–5]. However, some individuals will receive the vaccine earlier than this recommended age and many more substantially later than this age. For example, while zoster vaccination is recommended in the US for people who are 65 years old, those aged 75 years and above have an uptake of zoster vaccine 2.5 times higher than those between 60 and 75 years [6]. Likewise, Spanish data shows that pneumococcal vaccine uptake in people aged over 75 years is 30% higher than in those aged 65–74 years despite funding being from the age of 65 years [7]. The issues around delays in uptake relative to the initial age of the recommendation are different for vaccines that aim to provide longer-term protection, such as zoster and pneumococcal vaccines, as opposed to influenza where annual vaccination is required.

While the impact of the timeliness of vaccine administration has been well-studied for childhood vaccinations, there has been little detailed quantitative analysis on the impact of the timeliness of adult vaccinations. There are several reasons why accurate assumptions around the age of vaccination are important. For a range of vaccines, immunosenescence in older age results in decreasing vaccine-induced immunity and increasing disease risk with age. For example, it has been shown that pneumococcal vaccines are more efficacious in those aged 65 years when compared to those aged 75 years or older [8,9]. However, those aged over 75 years are more likely to suffer severe pneumococcal related illness [1–4,10] and hence there is often a trade-off between disease burden and vaccine efficacy by age [11,12]. Depending on how these two factors interact (alongside others such as duration of protection), models assuming the (unrealistic) recommended uptake age are likely to either overestimate or underestimate the effectiveness and cost-effectiveness of recommended strategies.

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Using 13-valent pneumococcal conjugate vaccine (PCV13) as an example, this article examines the timeliness of an adult vaccination in Australia and its consequences. In Australia, one dose of PCV13 was recently recommended in Australian adults aged over 65 by the Pharmaceutical Benefits Advisory Committee (PBAC) to replace the existing 23-valent Pneumococcal Polysaccharide Vaccine (PPV23) program [13]. This recommendation at the age of 65 is consistent with most other developed countries. The aim of this study was to explore the impact of using more realistic observed uptake distributions and how this may help develop more effective vaccine policy recommendations.

2. Methods

2.1. Multi-cohort model

A multi-cohort Markov model (adapted from our previous single cohort model [14]) using a cycle length of one year was constructed to evaluate the cost-effectiveness of a PCV13 immunisation program against a comparator of a (hypothetical) world without vaccination. A key reason for use of the multi-cohort model (rather than a single cohort model) was the need to follow adults who are vaccinated at different ages. The cost-effectiveness analysis implements two different modelling approaches to simulating uptake: assuming it matches the observed (PPV23) uptake data by age (*observed uptake*), or assuming all uptake takes place at the initial recommended age (*recommended uptake*), as applied in many other published studies [1–4,10]. The differences in disease and economic outcomes between these two uptake approaches were then compared. The analysis was conducted from a healthcare payer perspective and includes all relevant cost of healthcare utilisation [15]. All costs (reported in 2016 A$) and consequences in the model were discounted at an annual rate of 5%, as suggested by PBAC Guidelines [15].

The multi-cohort model followed a hypothetical Australian population from the start of the program (for ten years) with each cohort being followed until vaccine-induced immunity has fully waned and the full consequences of any death included. The cohorts were stratified into one-year age bands until the age of 100, with individuals aged above 100 years old forming a single age group. The model estimated the demographical changes of the Australian population during this 10 year period from 2017 to 2026 using assumptions made by Australian Bureau of Statistics (ABS) [16]. The model evaluated vaccination of subsequent cohorts over time.

The current invasive pneumococcal disease (IPD) incidence was first inflated to create a (hypothetical) no vaccine world so that we can compare PCV13 vaccination programs with no vaccination scenario (see Appendix 1.1). The inflated incidence rate was applied to individuals with no vaccine protection, either vaccine naïve or waned. The indirect effects of adult pneumococcal vaccination on transmission were not included as there is currently no evidence for this occurring. We did, however, include the herd effects from childhood PCV13 vaccination program via the use of recent incidence data from after the childhood program was put into place (See Appendix 1.2).

For each five-year age band, the current IPD incidence rates were computed by dividing the number of IPD cases observed in 2015 from the National Notifiable Diseases Surveillance System (NNDSS) public data set by the age-specific 2015 Australian population size. The IPD fatality rates were estimated from aggregated age-specific data on the 2002–2013 IPD deaths divided by the notifications over this same period (NNDSS data supplied by the Department of Health; see Acknowledgements and Appendix Table A1).

As the multi-cohort model is used as an illustration of the importance of uptake in cost-effectiveness analysis we have focused on describing in detail the methods and assumptions related to uptake and vaccine efficacy. The other key parameters used in the model are listed in Table 1 and further details are provided in Appendix 1.

2.2. Estimation of vaccine uptake

The pattern of observed future uptake of PCV13 was estimated from a 2013 the New South Wales (NSW) Adult Population Health Survey (8394 participants) of the age-specific prevalence of PPV23 vaccination uptake [17], with data provided by the NSW Ministry of Health. The uptake prevalence rate from this survey by age was used in our model because this was the most recent data available that did not combine the data with revaccination rates. As the NSW data from 2009 was approximately consistent with earlier (2009) national estimates of PPV23 uptake it was considered appropriate for extrapolation [18]. In addition, the NSW data was stratified into finer age bands and collected annually for 14 years. This data time series allowed us to verify that the uptake profile has varied over time but has now stabilised (See Appendix 1.3).

Table 1
Parameters used in the model.[a]

Parameter	Value	Reference
PCV13 vaccine efficacy against vaccine-type IPD[b]	Maximum$(1 - 0.118 \times 1.078^{age-65}, 0)$	[9]
PCV13 vaccine efficacy against vaccine-type CAP[c]	Maximum$(1 - 0.396 \times 1.050^{age-65}, 0)$	[9]
PPV23 vaccine efficacy against vaccine-type IPD	Inflation: 0.58 for 50–74, 0.56 for 75–84 and 0 for 85+	[8] and assumption
PCV13 duration of protection	Five-year full protection and then wane linearly to no protection by the end of year ten	[19] and assumption
PPV23 duration of protection	Two-year full protection and then wane linearly to no protection by the end of year five	[8]
Vaccination cost, PCV13	A$65	[25,26]
Cost of GP[d] visit/s due to CAP	A$126[e]	[29]
QALY[f] loss for IPD inpatients	0.0709	[3,14]
QALY loss for CAP inpatients	0.0709	[3,14]
QALY[e] loss for CAP in GP	0.0045	[3,14]

[a] Please see Appendix Table A1 for other parameters.
[b] IPD = invasive pneumococcal disease.
[c] CAP = community-acquired pneumonia.
[d] GP = general practitioner.
[e] The GP cost from [29] was inflated to 2016 A$ using the Australian Institute of Health Welfare total health price index [30]. We assumed two GP visits for each case.
[f] QALY = quality-adjusted life-years.