Effectiveness of a publicly funded pneumococcal vaccination program against invasive pneumococcal disease among the elderly in Victoria, Australia

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Abstract

Within Australia, Victoria is the only jurisdiction where the 23-valent polysaccharide pneumococcal vaccine (23vPPV) has been publicly funded for the elderly (aged ≥65 years). We compared age-specific rates of invasive pneumococcal disease (IPD) for periods before and after implementation of the program, and data from a comparable Australian population that does not have a funded program. Vaccine effectiveness (VE) was estimated using the screening and indirect cohort methods. Compared to the pre-program period, there was a 36% reduction in the reported rates of IPD among persons aged ≥65 years. Adjusted for under-reporting in the referent rate, the decrease was equivalent to an annual reduction of 112 cases and an estimated 14 deaths among persons ≥65 years. VE was 71% (95% CI 54–82) using the screening method and 79% (95% CI −14 to 96) by the indirect cohort method. Both point estimates were consistent with the VE expected among persons aged ≥65 years, although the small number of isolates meant the indirect cohort method was inconclusive at the lower 95% confidence limit. Consideration should be given to publicly funding pneumococcal vaccine for this age group in other settings.

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1. Introduction

The annual incidence of invasive pneumococcal disease (IPD) in industrialised countries is estimated to be ≥50 cases per 100,000 persons aged ≥65 years [1]. Pneumonia is the most common clinical presentation in this age group where the case fatality rate exceeds 20% [2,3]. An ageing popula-

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Victoria is the only Australian jurisdiction that has a publicly funded 23-vPPV program for the elderly. The program, which commenced in 1998, has resulted in a dramatic increase in estimated vaccine coverage from 7% in 1997 to 51% in 2000 [17]. We assessed the impact against IPD using surveillance data from Victoria for periods before and after implementation of the program, and data from a comparable Australian population that does not have a funded program. We believe our study is the first ecological assessment of the impact of a publicly funded 23-vPPV program against IPD among the elderly.

2. Methods

2.1. Victoria

IPD surveillance data in Victoria were utilised over two time periods (Fig. 1). The first covered the pre-program period (July 1995–June 1998) and contained data collected from participating laboratories by the Victorian Hospital Pathogens Surveillance Scheme (VHPSS) [3]. The second covered the post program period (July 2001–June 2002) and followed the introduction of legislation in May 2001 requiring mandatory reporting by medical practitioners and laboratories of all IPD cases to the Department of Human Services (DHS).

The change from voluntary to mandatory reporting increased case ascertainment through the VHPSS as all laboratories were actively encouraged to forward isolates for serotyping to the Microbiological Diagnostic Unit, Public Health Laboratory, University of Melbourne (coordinators of the VHPSS). We opted to use the DHS rather than the VHPSS data for the post-program period because these data also included information on risk factors, vaccination status and outcome (e.g. length of hospital stay, death) that had been obtained by DHS staff from the treating clinician.

From the post-program data, we classified conditions associated with significantly impaired immunity in accordance with a national protocol that included HIV/AIDS, organ transplantation, haematologic malignancy, asplenia, and chronic immunosuppressant drug therapy [18]. A medical practitioner, hospital or nursing home record of 23-vPPV given between 2 weeks and 5 years prior to illness onset was accepted as a valid record of vaccination.

We estimated the number of cases prevented during the post-program period by multiplying the difference in age-specific disease rates (between the pre- and post-program periods) by the 2001 Australian Bureau of Statistics estimated resident population in Victoria for each age group. The overall rate of disease prevented among the elderly was then calculated as both a crude and age-standardised rate per 100,000 population.

Under-reporting during the pre-program period was estimated at 25% [3]. Although completeness of reporting during the post-program period was unknown, it was likely to have been comparatively higher because reporting had become mandatory. Therefore a true reduction in disease incidence during the post-program period could have been offset by a comparative increase in case ascertainment. In order to assess this, we compared the disease rates for persons aged 40-64 years (not eligible for free vaccine and for whom diagnostic practices were assumed to be similar) over the two time periods. We then adjusted the difference in disease rates by increasing the baseline (pre-program) rate for the elderly by the equivalent increase among persons aged 40-64 years.

From our estimates of cases prevented within each age strata (both unadjusted and adjusted), we applied the case fatality rates from the post-program data for persons aged 65-74 years, 75-84 years and ≥85 years respectively to estimate the number of deaths prevented. This method assumes that cases prevented during the post-program period had the same risk of death as cases that occurred in that time period.

2.2. Urban New South Wales

Data were obtained from active laboratory surveillance in urban New South Wales (NSW) [2], an area of comparable population size and composition but without a publicly funded program. We compared age-specific IPD rates over similar time periods, July 1997–June 1998 versus July 2001–June 2002. Although surveillance conducted in urban NSW (active) differed from that conducted in Victoria (passive), it remained uniform throughout the two time periods. Therefore the relative difference in IPD rates within urban
NSW was unlikely to be affected by changes in case ascertainment and no adjustment was considered necessary.

2.2.1. Vaccine effectiveness

The screening method has been used to monitor vaccine effectiveness (VE) in various settings and is a useful tool for assessing if VE is within the expected range [19–21]. The method compares the proportion of cases vaccinated (PCV) to the proportion of the population vaccinated (PPV) [22]:

\[ VE = 1 - \left( \frac{PCV}{1 - PCV} \right) \left( \frac{1 - PPV}{PPV} \right) \]

We used population coverage of 51% to calculate VE [17], including exact 95% confidence intervals for proportions [23].

We also used the indirect cohort method, which compares the vaccination status of persons with vaccine and non-vaccine serotypes. This method assumes vaccinated persons are at the same risk of non-vaccine type infections as unvaccinated persons [24]. VE = 1 – OR, where OR is the odds ratio of a person with a vaccine serotype being vaccinated compared to that of a person with non-vaccine serotype. Serotypes closely related to those contained in the vaccine and for which cross-protection is expected were considered vaccine serotypes (e.g. 6A, 15C) [16]. We calculated VE and exact 95% confidence intervals using Epi Info version 6.04d [25]. We compared both VE estimates with those of Shapiro et al. [14] and Butler et al. [16].

3. Results

There were 397 IPD notifications in Victoria during the post-program period, including 25 deaths (Table 1). The median time between onset and notification was 8 days. The fatality rate among cases aged ≥65 years was 13% (15/115). During the pre-program period, the case fatality rate among this age group was reported to be 23% (44/190) [3].

Table 2 summarises the deaths that occurred among the elderly during the post-program period:

- Although most deaths were among persons with chronic disease co-morbidities or immunosuppression, most people were living independently (rather than in institutional settings).
- Nine deaths were potentially vaccine preventable–unvaccinated persons infected with vaccine serotypes (7) or indeterminate serotypes (2).
- Five deaths were among vaccinated persons infected with vaccine serotypes (vaccine failures). The youngest had a history of multiple myeloma and was vaccinated less than 2 years prior to death, whereas the others were vaccinated 2–4 years previously and were not severely immunocompromised.
- One deceased person had been vaccinated but the serotype was not determined.
- The median age at death was 81 years for unvaccinated cases and 88 years for vaccinated cases.

The crude notification rate in the post-program period was marginally higher than the annual rate during the pre-program period (8.2 cases versus 8.0 cases per 100,000 population). However, the age-specific rates for the elderly were lower for each age stratum (Fig. 2). IPD rates decreased by 36% for persons aged ≥65 years whilst increasing by 26% among those aged 40–64 years and by 30% for all persons <65 years.

In urban NSW, IPD rates decreased by 10% among the elderly whilst increasing by 14% among persons aged 40–64 years. In comparison to Victoria, the decrease among the elderly was smaller and occurred from age 70 years rather than age 65 years (Fig. 3).

In Victoria, the unadjusted annual rate difference represented 10–18 cases prevented in each age stratum over 65 years (Table 3). The crude rate difference for all persons over 65 years was equivalent to 57 cases and seven deaths prevented (unadjusted), slightly more when the differences were age-standardised (Table 4). When the pre-program rate was increased by 26% to account for under-reporting, the adjusted rate difference was equivalent to a total reduction of 112 cases and 14 deaths (Table 4).

3.1. Vaccine effectiveness

Among the elderly, 27 cases (23%) had been vaccinated compared to 51% in the general population. Using the screening method, VE against IPD was 71% (95% CI 54 to 82) [22]. Exclusion of the 20 persons identified as immunocompromised changed the VE estimate marginally to 73% (95% CI 55 to 84) (assuming population coverage remained the same).

Numbers were too small to draw firm conclusions from the assessment of VE using the indirect cohort method [24]. There were 92 cases with a serotype contained in the 23vPPV, 16 (17%) had been vaccinated. In contrast, only six cases had non-vaccine serotypes with three (50%) being vaccinated. The estimated VE was therefore 79% (95% CI 14 to 96). Exclusion of the immunocompromised cases varied the point estimate slightly but, since the sample size was further reduced, the confidence interval was wider (data not shown).

Seventeen cases were excluded from the indirect cohort analyses because they were not serotyped, eight (47%) of these had been vaccinated. If the distribution of vaccine and non-vaccine types was the same among this group as for those that had been typed, the adjusted VE would be 80% (95% CI 3 to 96).
Table 2


<table>
<thead>
<tr>
<th>Vaccinated (prior to onset)</th>
<th>Age (years)</th>
<th>Institutionalised (nursing Home)</th>
<th>Co-morbidity</th>
<th>LOS prior to death</th>
<th>Serotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (1.9 years)</td>
<td>75</td>
<td>No</td>
<td>Immunocompromised</td>
<td>ND</td>
<td>19F</td>
</tr>
<tr>
<td>Yes (3.9 years)</td>
<td>84</td>
<td>No</td>
<td>Chronic disease</td>
<td>0</td>
<td>ND</td>
</tr>
<tr>
<td>Yes (4.1 years)</td>
<td>88</td>
<td>No</td>
<td>Chronic disease</td>
<td>0</td>
<td>19F</td>
</tr>
<tr>
<td>Yes (2.5 years)</td>
<td>89</td>
<td>No</td>
<td>Chronic disease</td>
<td>41</td>
<td>14</td>
</tr>
<tr>
<td>Yes (3.6 years)</td>
<td>90</td>
<td>Yes</td>
<td>None</td>
<td>12</td>
<td>23F</td>
</tr>
<tr>
<td>Yes (3.7 years)</td>
<td>91</td>
<td>Yes</td>
<td>Chronic disease</td>
<td>ND</td>
<td>19A</td>
</tr>
<tr>
<td>No</td>
<td>65</td>
<td>No</td>
<td>Chronic disease</td>
<td>3</td>
<td>6B</td>
</tr>
<tr>
<td>No</td>
<td>68</td>
<td>No</td>
<td>Unknown</td>
<td>1</td>
<td>ND</td>
</tr>
<tr>
<td>No</td>
<td>71</td>
<td>No</td>
<td>Chronic disease</td>
<td>0</td>
<td>6B</td>
</tr>
<tr>
<td>No</td>
<td>77</td>
<td>No</td>
<td>Chronic disease</td>
<td>45</td>
<td>NS</td>
</tr>
<tr>
<td>No</td>
<td>81</td>
<td>No</td>
<td>Immunocompromised</td>
<td>2</td>
<td>ND</td>
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<tr>
<td>No</td>
<td>82</td>
<td>No</td>
<td>Immunocompromised</td>
<td>0</td>
<td>19F</td>
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<tr>
<td>No</td>
<td>88</td>
<td>No</td>
<td>Chronic disease</td>
<td>23</td>
<td>6B</td>
</tr>
<tr>
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<td>85</td>
<td>No</td>
<td>No</td>
<td>Chronic disease</td>
<td>46</td>
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<tr>
<td>No</td>
<td>90</td>
<td>Yes</td>
<td>Yes</td>
<td>Chronic disease</td>
<td>8</td>
</tr>
</tbody>
</table>

ND: not determined.

*a* Vaccinated 5.2 years prior to onset therefore considered unvaccinated.

*b* Vaccinated 4 years prior but considered unvaccinated since serotype 16 not in 23vPPV.

Fig. 2. Annual age-specific IPD rates per 100,000 population, Victoria, July 1995–June 1998 and July 2001–June 2002.

Fig. 3. Age-specific IPD rates per 100,000 population in urban NSW, July 1997–June 1998 and July 2001–June 2002.
Reduction in the IPD rate between the pre- and post-program period, including cases and deaths prevented in Victoria by age group

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Unadjusted (VHPSS – DHS)</th>
<th>Adjusted ((VHPSS × 1.26) – DHS)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rate diff</td>
<td>Cases prevented</td>
</tr>
<tr>
<td>65–69</td>
<td>6.5</td>
<td>11.3</td>
</tr>
<tr>
<td>70–74</td>
<td>7.7</td>
<td>12.7</td>
</tr>
<tr>
<td>75–79</td>
<td>7.9</td>
<td>10.6</td>
</tr>
<tr>
<td>80–84</td>
<td>14.6</td>
<td>12.3</td>
</tr>
<tr>
<td>&gt;85</td>
<td>25.7</td>
<td>18.0</td>
</tr>
</tbody>
</table>

IPD data: Victorian Hospital Pathogens Surveillance Scheme (VHPSS), July 1995–June 1998, and Department of Human Services (DHS), July 2001–June 2002. Unadjusted: the referent rate is annual age-specific rate/100,000 population from VHPSS data. Adjusted: the referent rate is increased by 26% to account for under-reporting (see Section 2). Rate diff: rate difference (per 100,000 population) between VHPSS and DHS data. Cases and deaths: the estimated reduction in the number of IPD cases and deaths, respectively.

5. Limitations

Although IPD is a highly specific laboratory diagnosis, the clinical criteria for obtaining relevant specimens are open to interpretation and could lead to differences in diagnostic practice. It is unlikely that such differences could be responsible for rates decreasing in Victoria among those aged ≥65 years when the rates had increased among those aged 40–64 years over the same period.

Estimating the degree to which case ascertainment had improved between the pre- and post-program periods is problematic. IPD incidence may vary from year to year in the absence of any intervention. As age-specific rates also increased marginally among younger age groups in urban NSW, at least some of the increase seen in Victoria may be normal variation. Interestingly, the age-specific IPD rates in urban NSW (Fig. 3) were higher than those reported in Victoria over either period, particularly for children and the elderly, more like comparable populations elsewhere [1,26]. Perhaps there is less IPD among all ages in Victoria for some reason related to the epidemiology of the disease, but differential diagnosis or reporting seems more likely with active surveillance being a clear difference in the method of case ascertainment in urban NSW compared to passive surveillance in Victoria.

4. Discussion

The 23vPPV coverage achieved following the introduction of Victoria’s publicly funded program and the availability of data from the period preceding the program provided an ideal opportunity for an ecological study to assess the impact against IPD among the elderly. While ecological studies are methodologically weaker than other observational studies, limitations on biological inference in this instance are not critical because more rigorous studies suggest vaccination is effective against IPD in the healthy elderly [12–16]. A reduction in IPD following the introduction of a public program is not only biologically plausible, it is to be expected if adequate coverage is achieved.

Whilst the true number of cases and deaths prevented is unknown, our study found strong ecological evidence of a reduction in IPD among elderly Victorians between the pre- and post-program periods. Surveillance data showed IPD rates in Victoria decreased for each age stratum ≥65 years at a time when the reported incidence increased for others not eligible for free vaccine. In comparison to urban NSW, the decrease was greater and occurred from the age at which free vaccine became available (rather than age 70 years). Furthermore, the proportion of vaccinated cases in Victoria was consistent with population coverage estimates during the post-program period and the expected VE [14,16]. Differences in vaccination coverage between those infected with vaccine serotypes compared to those infected with non-vaccine serotypes were also consistent with these findings but were not conclusive due to the small number of isolates. We believe increased 23vPPV coverage following the introduction of the publicly funded program is the only plausible reason for these differences.

The case fatality rate in the post-program data was lower than previously reported (13% versus 23%) [3]. However, these data should be interpreted with caution as the reduction may be due to other confounding factors or variations in the surveillance systems. Although the numbers of deaths were small, it was interesting to note that during this period the median age at death was younger for unvaccinated persons (81 years) than vaccinated persons (88 years). There were six deaths among unvaccinated persons aged <84 years compared to one for vaccinated persons.

Estimating the degree to which case ascertainment had improved between the pre- and post-program periods is problematic. IPD incidence may vary from year to year in the absence of any intervention. As age-specific rates also increased marginally among younger age groups in urban NSW, at least some of the increase seen in Victoria may be normal variation. Interestingly, the age-specific IPD rates in urban NSW (Fig. 3) were higher than those reported in Victoria over either period, particularly for children and the elderly, more like comparable populations elsewhere [1,26]. Perhaps there is less IPD among all ages in Victoria for some reason related to the epidemiology of the disease, but differential diagnosis or reporting seems more likely with active surveillance being a clear difference in the method of case ascertainment in urban NSW compared to passive surveillance in Victoria.
Regardless of the cause, differences between Victoria and urban NSW are likely to have been consistent over the study period.

Estimating the number of deaths prevented is also problematic. Our estimates were based on the assumption that cases prevented during the post-program period were at the same risk of death as cases that occurred in that period. We allowed for variations in the risk of death with increasing age (8% CFR for 65–74 years, 10% for 75–84 years and 28% for ≥85 years). We believe this estimate is conservative because, as noted above, it is substantially lower than the previously reported rate for persons aged ≥65 years (13% versus 23%) [3].

We assumed the same case fatality rate when the number of cases prevented was increased to account for under-reporting. If under-reporting is related to the severity of disease then this assumption will not hold as the additional cases may be much less likely to die. One of us (RA) is currently involved in a separate study reviewing hospital admission data to ascertain the level of under-reporting in the post-notification period. These data will enable a review of the assumptions related to the risk of death among unreported cases.

The VE estimate obtained using the screening method is not a precise point estimate and does not account for confounding [22]. The value of the estimate is that the proportion of cases vaccinated was consistent with both the estimated population coverage and the expected VE [14,16]. Errors in the estimated VE will occur if the population vaccination coverage is overestimated or if the proportion of vaccinated cases is underestimated [22]. We used a conservative estimate of population coverage based on medical records of vaccination [17], supported by unpublished data from a contemporaneous cohort of hospitalised elderly persons in Victoria, for which one of us was the principal investigator (RA). It is possible that not all vaccinated cases were identified, but, among the elderly in Victoria, vaccinated persons are more likely to be identified from medical practitioners records than from self report [17]. Even if the proportion of cases vaccinated had increased from 23% (27/115) to 30% (34/115), the revised VE would have been 60% (95% CI 37–73), still consistent with those of Shapiro et al. [14] and Butler et al. [16].

The rationale for the indirect cohort method is that those infected with a vaccine serotype are less likely to be vaccinated than those infected with a non-vaccine serotype. The proportion of vaccinated persons among those infected with a serotype contained in the 23vPPV was lower (17%) than for those infected with a non-vaccine serotype (50%) but the numbers of isolates of a known serotype were too small to confirm that the difference statistically at a α of 0.05.

6. Conclusion

Our study suggests the introduction of the publicly funded 23vPPV program has resulted in a discernible reduction in IPD and associated deaths among elderly Victorians. Consideration should be given to publicly funding pneumococcal vaccine for this age group in other settings.

Acknowledgements

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References


