Annual reports

Invasive pneumococcal disease in Australia 2007 and 2008

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Abstract

Enhanced surveillance for invasive pneumococcal disease (IPD) was conducted in all Australian states and territories in 2007 and 2008 with comprehensive comparative data available since 2002. There were 1,477 cases of IPD notified to the National Notifiable Diseases Surveillance System in Australia in 2007; a notification rate of 7.0 cases per 100,000 population. In 2008 there were 1,628 cases; a notification rate of 7.6 cases per 100,000 population. The overall rate of IPD in Indigenous Australians was almost 6 times the rate in non-Indigenous Australians in 2007 and almost 5 times in 2008. By 2008, the 4th year of a funded universal infant 7-valent pneumococcal conjugate vaccine (7vPCV) program in Australia with a 3+0 schedule, vaccine serotype IPD notification rates in those identified as non-Indigenous decreased in all age groups compared with 2002 levels, most significantly by 96% in children aged less than 5 years. However, rates of disease in non-vaccine serotypes increased by 168% in children aged less than 5 years, including a four-fold increase in the number of cases due to serotype 19A. For the Aboriginal and Torres Strait Islander population, national pre-vaccination data are not available, as the vaccine program was funded for this group from 2001. From 2002 to 2008, the proportion of disease due to 7vPCV serotypes in children aged less than 5 years decreased by 77%, while disease due to non-7vPCV serotypes increased by 76%. In Indigenous adults (≥50 years), rates of 23vPPV serotypes increased by 92%. There were 120 deaths attributed to IPD in 2007 and 113 in 2008, although it should be noted that deaths may be under-reported. The number of invasive pneumococcal isolates with reduced penicillin susceptibility remains low and reduced susceptibility to third-generation cephalosporins is rare. *Commun Dis Intell* 2012;36(2):E151–E165.

Introduction

Streptococcus pneumoniae infection is a major cause of disease worldwide. The organism commonly colonises the nasopharynx, and can spread to the respiratory tract, causing a wide range of diseases ranging from mild, such as otits media and sinusitis, to severe—such as pneumonia, septicaemia and meningitis.[1] The burden of disease is greatest in infants and the elderly. The 23-valent pneumococcal polysaccharide vaccine (23vPPV) was first recommended in Australia in 1994 for certain high risk groups, and a 7-valent pneumococcal conjugate vaccine (7vPCV) program with a 3+0 schedule (i.e. 2, 4 and 6 month schedule without a conjugate vaccine booster) was first funded on the National Immunisation Program (NIP) for Aboriginal and Torres Strait Islander infants in mid-2001 with those in areas of very high incidence also funded for a 23vPPV booster at 18–24 months.[2] The 23vPPV is now funded nationally for all individuals aged 65 years or older and Aboriginal and Torres Strait Islander adults aged 50 years or older and in 2005 the conjugate vaccine was funded for all infants.[2] Enhanced surveillance is carried out for invasive pneumococcal disease (IPD), which has been nationally notifiable in Australia since 2001 with some states and territories having collected data from earlier years. Surveillance reports have been published in *Communicable Diseases Intelligence* for each year from 2002 to 2006.[3–7] This report focuses on the years 2007 and 2008.

Methods and materials

Data collection

IPD has been a nationally notifiable disease in Australia since 2001, with complete data being collected in all states and territories from 2002. To varying degrees across jurisdictions, medical practitioners, laboratories and other health professionals are legally required to report cases of IPD to state and territory health authorities. Information on notified cases is collated by state and territory jurisdictions under jurisdictional public health legislation. The *National Health Security Act 2007* provides the legislative basis for, and authorises the exchange of, health information between jurisdictions and the Commonwealth.[8] The Act provides for the establishment of the National Notifiable Diseases List, which specifies the diseases about which personal information can be provided.[9] IPD is one of the diseases specified in this list. De-identified data on notified cases are reported by jurisdictions electronically to the National Notifiable Diseases Surveillance System (NNDSS), managed by the Australian Government Department of Health and Ageing. National data standards ensure consistency and comparability of data

collected across Australia. Core data are collected for all notified cases such as serotype, sex, age, Indigenous status and vaccination. Enhanced data are collected for notified cases of IPD, including information relating to cases' risk factors, clinical diagnostics and antibiotic susceptibilities. Table 1 outlines the population subgroups for which enhanced data are reported in each jurisdiction.

The Enhanced Invasive Pneumococcal Disease Surveillance Working Group (EIPDSWG), a subcommittee of the Communicable Diseases Network Australia (CDNA), is responsible for finalising IPD data reported to the NNDSS. Data presented in this report were analysed by date of diagnosis. For the purposes of the NNDSS, the date of diagnosis is the onset date or where the onset date was not known, the earliest of the specimen collection date, the notification date, and the notification receive date. Cases presented and analysed in this report had a date of diagnosis between 1 January 2007 and 31 December 2008, inclusive.

Data presented in this report represent a point in time analysis of cases of IPD notified to the NNDSS. Analyses of these cases were finalised in May 2011. Due to the dynamic nature of the NNDSS, data in this report may vary from data reported in other NNDSS reports and reports of IPD notifications at the jurisdictional level. Notification rates were calculated using the mid-year estimated resident populations supplied by the Australian Bureau of Statistics.[10]

Case definition

Cases of IPD were determined to be notified for national notification according to the CDNA case definition of IPD.[11] A confirmed case was defined as the isolation from or detection by nucleic acid test (NAT) in blood, cerebrospinal fluid (CSF) or other sterile site of *S. pneumoniae*.

Indigenous status

Cases of IPD were reported indicating the Indigenous status of the individual. The definition of an Aboriginal or Torres Strait Islander person within the NNDSS aligns with the Commonwealth definition, that is, an Aboriginal or Torres Strait Islander is determined by descent, self-identification and community acceptance.

The small number of cases reported without an Indigenous status were excluded from analyses relating to Indigenous status in this report.

Vaccination

In Australia, pneumococcal vaccination is recommended as part of routine immunisation for children, older Australians and Aboriginal and Torres Strait Islander people. Vaccination with 7vPCV was added to the NIP schedule for Indigenous and medically at-risk children in 2001 and for all children up to 2 years of age from January 2005. A primary series of 7vPCV is given at 2, 4 and 6 months of age, with medically at-risk children requiring a 4th dose of 7vPCV at 12 months of age and a booster dose of 23vPPV at 4 years of age. A 23vPPV booster was also recommended for Indigenous children at 18–24 months in the Northern Territory, Queensland, South Australia and Western Australia. Of note, subsequent to this study period, higher valency vaccines, such as Prevenar13®, have replaced 7vPCV throughout Australia.

Since 1999, the 23vPPV has been funded for Indigenous Australians aged 50 years or older and 15–49 years with risk factors, with non-Indigenous Australians aged 65 years eligible to receive the vaccine under the NIP from January 2005. Recommendations for revaccination with 23vPPV vary by age and Indigenous status, current Australian guidelines can be found on the Immunise Australia web site.[ref: http://www.immunise.health.gov.au] A detailed list of recommendations and funding initiatives for pneumococcal vaccinations in Australia is shown in Table 2.

The definitions of fully vaccinated and vaccination validation for determination of vaccine failure in this report are described in Table 3. These definitions are applied to the vaccination fields reported to the NNDSS and are agreed to by the EIPDSWG.

Vaccine coverage data (7vPCV) were provided by the Australian Childhood Immunisation Register

Table 1: Enhanced invasive pneumococcal disease surveillance data collection performed by states and territories in 2007 and 2008

Age group	Jurisdictions
Under 5 years	Australian Capital Territory, New South Wales, Queensland (South Brisbane Public Health Unit only).
Over 50 years	New South Wales.
All ages	Northern Territory, Queensland (except South Brisbane Public Health Unit), Tasmania, South Australia, Victoria, Western Australia.

Table 2: Recommendations and funding initiatives for pneumococcal vaccinations in Australia

Vaccine	23-valent polysaccharide vaccine	7-valent conjugate vaccine
Pneumococcal serotypes	1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F	4, 6B, 9V, 14, 18C, 19F, 23F
Target populations	All individuals aged 65 years or over to receive a single dose of vaccine with a booster 5 years later* Aboriginal and Torres Strait Islander people aged 50 years or over to receive a single dose of vaccine with a booster 5 years later† Aboriginal and Torres Strait Islander people aged between 15 and 49 years at high risk to receive a single dose of vaccine and appropriate booster(s)‡ Children who have underlying chronic illnesses predisposing to invasive pneumococcal disease (including asplenia and immunocompromised)§ Immunocompetent individuals with chronic illness including chronic cardiac, renal or pulmonary disease, diabetes and alcohol-related problems Individuals with cerebrospinal fluid leaks‖ Tobacco smokers¶ As a booster dose at 18 to 24 months of age following a primary course of 7vPCV in Aboriginal and Torres Strait Islander children in regions of high incidence** As a booster dose at 4 to 5 years of age following a primary course of 7vPCV in children at risk because of predisposing medical conditions**	Children at 2, 4 and 6 months of age†† Children born between 1 January 2003 and 31 December 2004‡‡ Additional booster dose for children in specific high-risk groups**

* Funded in Victoria from 1998. Funded nationally from 2005.

† Targeted funded programs in north Western Australia, Far North Queensland and the Northern Territory from 1995, Funded nationally from 1999.

‡ Funded nationally from 1999. Funded for all children aged 15 years or over in the Northern Territory from 1999.

§ Targeted funded programs for high risk children aged over 2 years in north Western Australia and the Northern Territory from 1986. Recommended nationally for children aged over 2 years (pre-July 2001) and children aged over 5 years from July 2001.

‖ Recommended nationally for children aged over 2 years (pre-July 2001) and children aged over 5 years from July 2001.

¶ Recommended nationally from 2003.

** Funded nationally from July 2001.

†† Funded nationally for Indigenous children from July 2001 and all children from 2005.

‡‡ Funded nationally as a catch-up program in 2005.

Table 3: Definitions of vaccination status and vaccine failure used in this report

Category	Definition
Fully vaccinated	Those that have completed the primary course of the relevant vaccine(s) required for their age, Indigenous status, geographical location and/or other risk factor(s) according to the most recent edition of the *Australian Immunisation Handbook,* at least 2 weeks prior to disease onset with at least 28 days between doses of vaccine. This includes the following; a child that received a vaccine as 'catch up' and therefore does not require a full three dose primary schedule. Providing they have had the number of doses required for the age they were at first dose they should be considered fully vaccinated. NB: A young child who has had all the required doses for their age but is not old enough to have completed the primary course would not be assessed as fully vaccinated.
Vaccination validation	Written confirmation of vaccination through the Australian Childhood Immunisation Register, state or territory immunisation register or health record.
Vaccine failure	A fully vaccinated person (as defined above) with disease due to a serotype found in the corresponding vaccine.

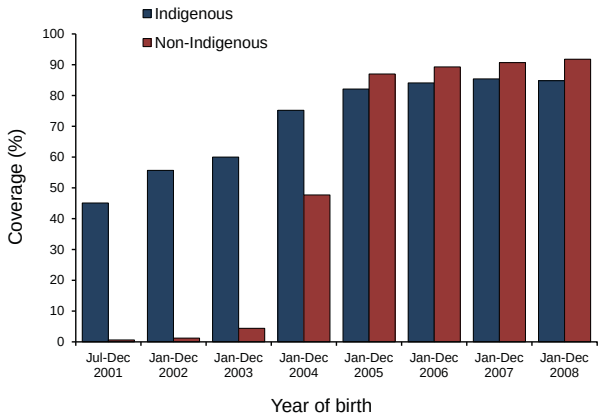
(ACIR). The ACIR records details of vaccinations given to children under the age of 7 years who live in Australia. The ACIR definition of fully vaccinated is a population-based milestone (3 doses by 12 months of age), which differs from the age-appropriate definition used by the EIPDSWG for classification of individuals with IPD.

Results

Vaccination coverage

The proportion of children who are fully vaccinated against pneumococcal disease has increased steadily since 2001 (Figure 1). In 2007, the proportion of children aged 12 months immunised with 3 doses of 7vPCV was 85% in Indigenous children and 91% in non-Indigenous children. In 2008, the proportions were 85% in Indigenous children and 92% in non-Indigenous children.

Figure 1: Proportion of children aged 12 months fully vaccinated with 7vPCV, Australia, 2001 to 2008, by Indigenous status



Source: The Australian Childhood Immunisation Register.

The Australian Childhood Immunisation Register defines fully vaccinated as aged 12 months and immunised with 3 doses of 7vPCV.

Invasive pneumococcal disease notifications

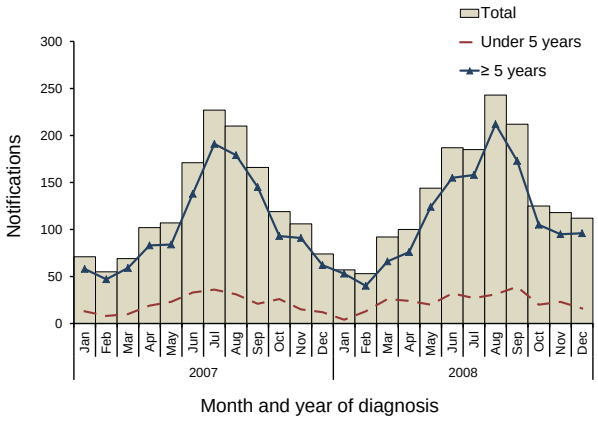
The total number of notifications of IPD in 2007 was 1,477 and in 2008 was 1,628. This represents annual notification rates of 7.0 and 7.6 cases per 100,000 population, respectively.

A summary of the number and rates of notifications by jurisdiction is shown in Table 4. The Northern Territory continued to have the highest notification rate (31.2 per 100,000 population reported in 2007 and 27.3 per 100,000 population in 2008) while the lowest notification rate for 2007 was reported in Victoria (5.4 per 100,000 population) and for 2008 in the Australian Capital Territory (5.5 per 100,000 population).

When notification rates of IPD were examined by geographical distribution, variation within states and territories was apparent (Map).

The number of cases of IPD was greatest in winter months with the peak number of notifications for 2007 reported in July (n=227) and for 2008 in August (n=243). The effect of season was more evident in the distribution of cases aged 5 years or over compared with younger children (Figure 2).

Figure 2: Notifications of invasive pneumococcal disease, Australia, 2007 and 2008, by month of diagnosis and age group

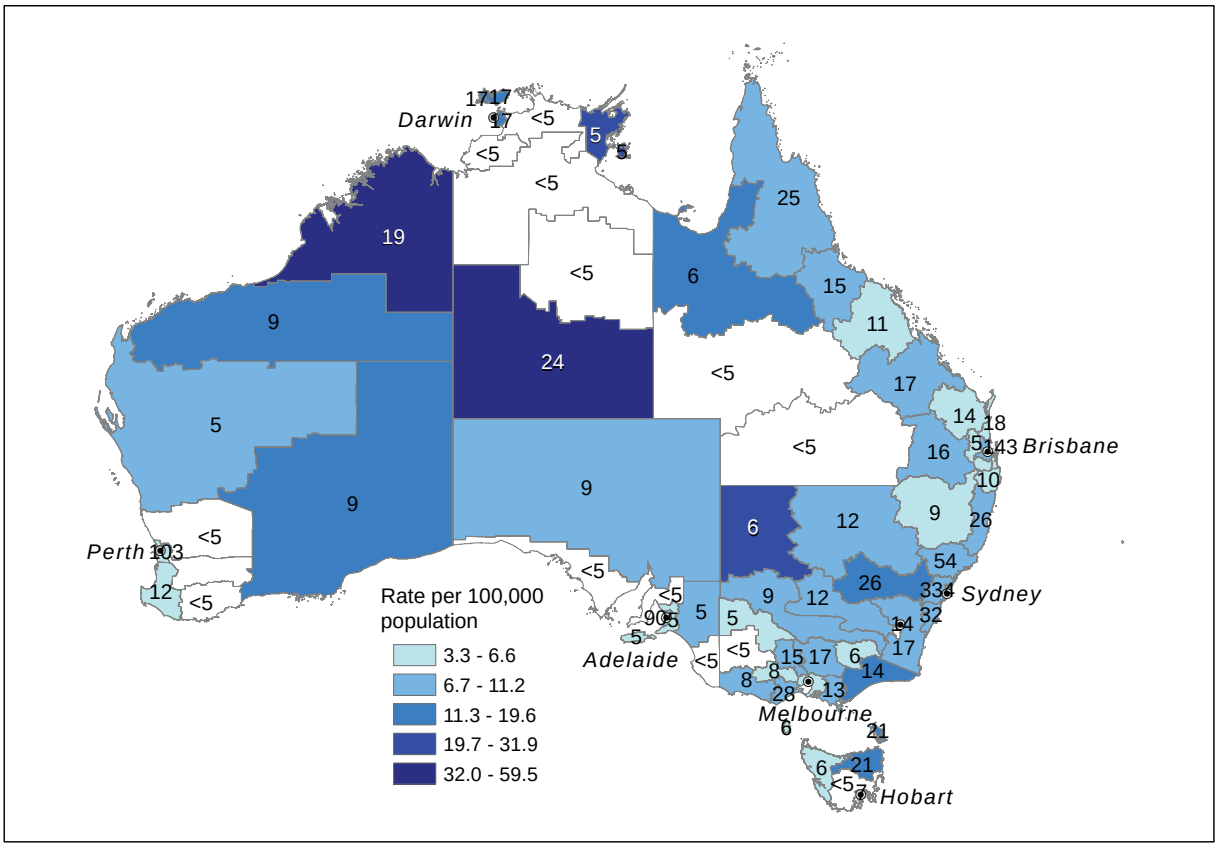


Invasive pneumococcal disease by age and sex

The overall male to female ratio in both 2007 and 2008 was 1.3:1 (Table 4). In almost all age groups there was a greater notification rate of IPD in males than females (Figure 3). The highest rates in 2007 and 2008 combined were among the elderly aged 85 years or over (35.5 per 100,000 population) and in children aged 1 year (32.8 per 100,000 population, Figure 3).

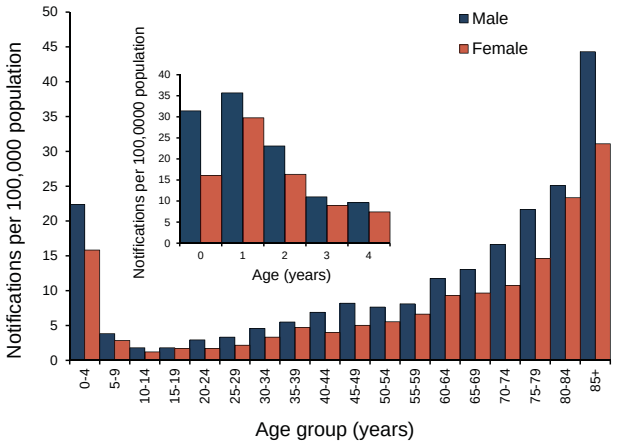
An examination of rates of IPD in different age groups from 2002 to 2008 is shown in Figure 4. There was a small increase in the rate of IPD in children aged under 2 years in 2007 and 2008 (27.5 per 100,000 population and 29.3 per 100,000 population respectively) when compared with 2006 (24.3 per 100,000 population). However, overall the rate maintains the large decrease experienced in this age group as a result of the introduction of the universal 7vPCV immunisation program in 2005. Prior to the vaccination program the notification rate in this age group was close to 100 cases per 100,000 population.

Map: Notification rates for invasive pneumococcal disease, Australia, 2008, by Statistical Division of residence



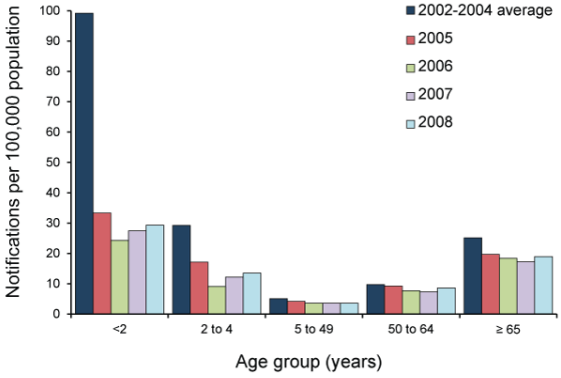
Data point labels represent the number of notifications. Notification rates in geographic areas where estimated residential population and case numbers are small should be interpreted with caution.

Figure 3: Notification rates for invasive pneumococcal disease, Australia, 2007 and 2008, by age group and sex



The rate of IPD in adults aged 65 years or over continued to decline in 2007 (18.4 per 100,000 population) when compared with 2006 (17.2 per 100,000 population), and there was an increase experienced in 2008 (19.0 per 100,000 population).

Figure 4: Notification rate for invasive pneumococcal disease, Australia, 2002 to 2008, by age group



Invasive pneumococcal disease in Aboriginal and Torres Strait Islander people

Indigenous status was reported in 88% of notifications in 2007 (1,301/1,477) and 2008 (1,435/1,628) (Table 4). This level of completeness in reporting Indigenous status was improved in the target popu-

Table 4: Notifications, rates and demographics of invasive pneumococcal disease cases, Australia, 2007 and 2008, by state or territory

	State or territory								
	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Aust
2007									
All cases									
Notifications	35	523	67	318	91	31	280	132	1,477
Rate (notifications per 100,000 population)	10.3	7.6	31.2	7.6	5.7	6.3	5.4	6.2	7.0
Male:female ratio	0.8:1	1.2:1	1.2:1	1.3:1	1.4:1	1.2:1	1.3:1	1.4:1	1.3:1
Indigenous	0	18	56	51	7	0	5	32	169
Non-Indigenous	35	404	11	218	84	26	254	100	1,132
Unknown	0	101	0	49	0	5	21	0	176
Notifications aged <5 years									
Total	9	83	16	49	21	2	38	29	247
Indigenous	0	9	14	8	2	0	1	3	37
Non-Indigenous	9	72	2	34	19	1	35	26	198
Unknown	0	2	0	7	0	1	2	0	12
Notifications aged 5 to 64 years									
Total	10	261	46	172	47	14	133	71	754
Indigenous	0	7	39	37	5	0	4	28	120
Non-Indigenous	10	157	7	110	42	11	115	43	495
Unknown	0	97	0	25	0	3	14	0	139
Notifications ≥ 65 years									
Total	16	179	5	97	23	15	109	32	476
Indigenous	0	2	3	6	0	0	0	1	12
Non-Indigenous	16	175	2	74	23	14	104	31	439
Unknown	0	2	0	17	0	1	5	0	25
2008									
All cases									
Notifications	19	548	60	327	119	39	355	161	1,628
Rate (notifications per 100,000 population)	5.5	7.8	27.3	7.6	7.4	7.8	6.7	7.4	7.6
Male:female ratio	0.9:1	1.2:1	2.2:1	1.1:1	1.3:1	0.8:1	1.4:1	1.7:1	1.3:1
Indigenous	0	14	38	45	6	1	6	42	152
Non-Indigenous	19	429	22	230	112	36	316	119	1,283
Unknown	0	105	0	52	1	2	33	0	193
Notifications aged <5 years									
Total	5	96	15	60	13	10	46	30	275
Indigenous	0	5	12	13	0	0	2	6	38
Non-Indigenous	5	89	3	37	13	10	39	24	220
Unknown	0	2	0	10	0	0	5	0	17
Notifications aged 5 to 64 years									
Total	10	247	43	173	61	15	168	99	816
Indigenous	0	4	25	27	6	1	3	35	101
Non-Indigenous	10	143	18	120	54	12	145	64	566
Unknown	0	100	0	26	1	2	20	0	149
Notifications ≥ 65 years									
Total	4	205	2	94	45	14	141	32	537
Indigenous	0	5	1	5	0	0	1	1	13
Non-Indigenous	4	197	1	73	45	14	132	31	497
Unknown	0	3	0	16	0	0	8	0	27

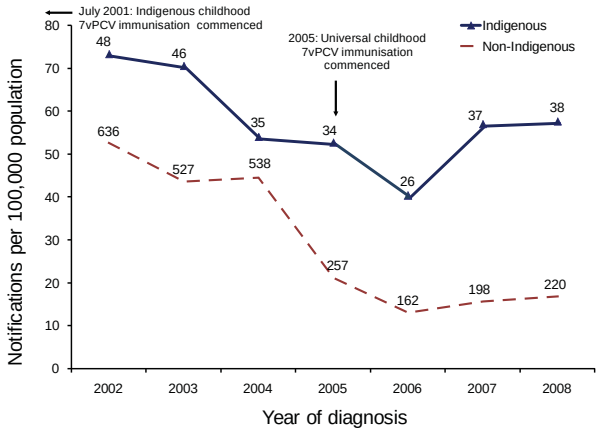
lations of children aged less than 5 years and adults aged 65 years or over, at close to 95% in each of these subgroups in 2007 and 2008.

In 2007, there were 169 cases of IPD reported among Indigenous people (11% of all cases). This represents a rate of 32.0 cases per 100,000 population—a rate almost 6 times that seen in the non-Indigenous population (5.5 per 100,000 population). In 2008, there were 152 cases of IPD reported among Indigenous people (9% of all cases), representing a rate of 28.2 cases per 100,000 population—almost 5 times that seen in the non-Indigenous population (6.1 per 100,000 population). Further analyses of the Indigenous population group are provided throughout this report.

Invasive pneumococcal disease in children

Figure 5 shows the rate of IPD in Indigenous and non-Indigenous children aged less than 5 years since 2002. Rates in Indigenous children in this age group decreased from 73.4 cases per 100,000 population in 2002 (n=48) to 57.6 cases per 100,000 population (n=38) in 2008, a decrease of 21%. In non-Indigenous children aged less than 5 years the rate decreased from 52.5 cases per 100,000 population in 2002 (n=636) to 16.8 cases per 100,000 population (n=220), a decrease of 68%.

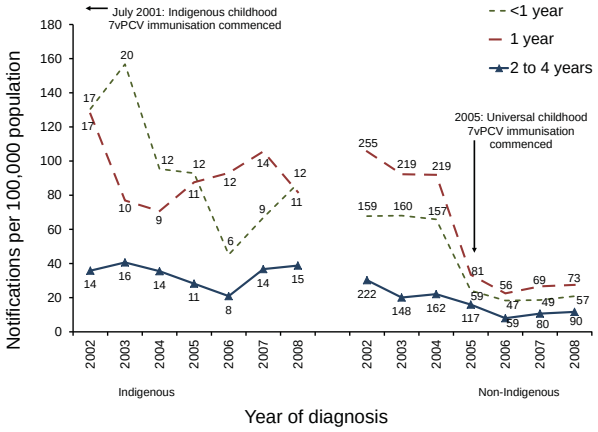
Figure 5: Notification rate for invasive pneumococcal disease in children aged less than 5 years, Australia, 2002 to 2008, by Indigenous status



Data point labels represent the number of notifications.

Figure 6 shows the rates of IPD in children aged less than 5 years by Indigenous status broken down into smaller age groups. The rate of IPD in Indigenous children fluctuated over the period due to the smaller number of notifications from a smaller population. In Indigenous children aged less than 1 year rates decreased from 130.5 cases per 100,000 population (n=17) in 2002 to 86.9 cases per 100,000 population in 2008 (n=12). In Indigenous children aged 1 year, over the same period, the IPD rate decreased from 127.7 cases per 100,000 population (n=17) to 81.8 cases per 100,000 population (n=11), while the 2–<5 years age group increased from 35.8 cases per 100,000 population (n=14) to 38.8 cases per 100,000 population (n=15).

Figure 6: Notification rate for invasive pneumococcal disease in children aged less than 5 years, Australia, 2002 to 2008, by Indigenous status and age group



Data point labels represent the number of notifications.

In non-Indigenous children less variability was seen. A clear and consistent decrease reflected the implementation of the universal 7vPCV immunisation program, introduced in 2005. The IPD rate in non-Indigenous children aged less than 1 year decreased from 67.7 cases per 100,000 population (n=159) in 2002 to 20.8 cases per 100,000 population (n=57) in 2008. In non-Indigenous children aged 1 year, over the same period, the rate decreased from 105.7 cases per 100,000 population (n=255) to 27.5 cases per 100,000 population (n=73), and in children aged 2 to less than 5 years from 30.2 cases per 100,000 population (n=222) to 11.7 cases per 100,000 population (n=90).

Mortality of invasive pneumococcal disease cases

Table 5 shows data on mortality of IPD cases reported in 2007 and 2008. Mortality data were available for 67% (985/1,477) of notifications in 2007 and 72% (1,165/1,628) notifications in 2008. Of these notifications, there were 120 deaths associated with IPD in Australia in 2007 and 113 deaths in 2008.

Overall, case fatality rates in notifications reported as non-Indigenous were higher than in those reported

as Indigenous. In 2007, death associated with IPD was reported in 9 Indigenous cases (CFR=5.3%) and in 106 non-Indigenous cases (CFR=9.4%). In 2008, death was reported overall in 6 Indigenous cases (CFR=3.9%) and in 103 non-Indigenous cases (CFR=8.0%).

In those aged less than 5 years there were 7 deaths associated with IPD in 2007 and 4 deaths in 2008, giving case fatality rates of 2.8% and 1.5%, respectively. One of those deaths was reported in an Indigenous child, occurring in 2008. Further details, including serotype and vaccination history, of the eleven children aged less than 5 years whose deaths were associated with IPD are shown in Table 6.

In the 65 years and older age group there were 63 deaths due to IPD in 2007 and 77 deaths in 2008, giving case fatality rates of 13.2% and 14.3%, respectively. Two of those deaths were reported as Indigenous, both in 2008.

Jurisdictional specific case fatality rates have not been presented in Table 5 for those jurisdictions where completeness of data was less than 50%. Rates shown should be interpreted with caution given the proportion of cases without mortality data reported to the NNDSS, as well as the variability across jurisdictions to report death as primary and secondary causes.

Risk factors for invasive pneumococcal disease

Risk factor data were provided for 60% (1,854/3,105) of cases reported in 2007 and 2008. Of the cases with risk factor data reported, 1,723 cases reported at least 1 risk factor and 131 cases reported that no risk factors were identified. Table 7 shows risk factors in children aged less than 5 years, Indigenous people aged less than 50 years and non-Indigenous people aged greater than 65 years for 2007 and 2008 combined.

In children aged less than 5 years the most frequently reported risk factor in the Indigenous

Table 5: Deaths and case fatality rates* for invasive pneumococcal disease, Australia, 2007 and 2008, by age group, Indigenous status and state or territory

	State or territory								
	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Aust
2007									
Notifications	35	523	67	318	91	31	280	132	1,477
Deaths	0	58	4	6	7	3	19	23	120
Completeness of mortality data (%)	94.3	71.7	100.0	2.5*	75.8	87.1	97.9	100.0	66.7
Deaths in under 5 years	0	0	0	1	1	0	1	4	7
CFR under 5 years	0.0	0.0	0.0	NA	4.8	0.0	2.6	13.8	2.8
Deaths in ≥ 65 years	0	40	1	1	4	1	9	7	63
CRF ≥ 65 years	0.0	22.3	20.0	NA	17.4	6.7	8.3	21.9	13.2
Deaths in Indigenous people	0	0	2	0	1	0	0	6	9
Deaths in non-Indigenous people	0	55	2	6	6	3	17	17	106
2008									
Notifications	19	548	60	327	119	39	355	161	1,628
Deaths	0	48	3	10	14	3	21	14	113
Completeness of mortality data (%)	94.7	77.7	100.0	34.3*	11.8*	69.2	97.7	100.0	71.6
Deaths in under 5 years	0	0	0	1	0	0	1	2	4
CFR under 5 years	0.0	0.0	0.0	NA	NA	0.0	2.2	6.7	1.5
Deaths in ≥ 65 years	0	37	0	7	9	2	16	6	77
CFR ≥ 65 years	0.0	18.0	0.0	NA	NA	14.3	11.3	18.8	14.3
Deaths in Indigenous people	0	0	1	2	0	0	1	2	6
Deaths in non-Indigenous people	0	47	0	8	14	3	19	12	103

* Jurisdictional specific case fatality rates (CFRs) have not been presented for those jurisdictions where completeness of data was less than 50%, denoted as 'NA'. Rates shown should be interpreted with caution given the proportion of cases without mortality data reported to the NNDSS, as well as the variability across jurisdictions to report death as primary and secondary causes.

population was chronic illness, (28% of cases with a risk factor reported), while childcare attendee was the most frequently reported risk factor in the non-Indigenous population (28% of cases with risk factor data reported). Among the adult population groups, Indigenous cases aged greater than 50 years and non-Indigenous cases aged greater than 65 years, chronic disease was the most frequently reported risk factor, with 82% (46/56) and 79% (621/791) reported with this risk factor, respectively.

Pneumococcal serotypes causing invasive disease

Pneumococcal serotypes were identified for 90% (1,336/1,477) of all notified cases in 2007 and for 92% (1,495/1,628) in 2008. Table 8 shows the number and proportion of IPD cases due to serotypes covered by the various pneumococcal vaccines.

Of all the cases reported with a serotype in 2007 and 2008, 24% (678/2,831) were due to serotypes covered by the 7vPCV; this ranged from 10% (2/21) of Indigenous cases aged 5–14 years to 35% (27/78) of non-Indigenous cases in the same age

Table 6: Characteristics of deaths from invasive pneumococcal disease in children aged less than 5 years of age, Australia, 2007 and 2008

Patient	Year of diagnosis	Sex	Age (months)	Indigenous status	Serotype	Doses of 7vPCV	Risk factors
Deaths potentially preventable by 7vPCV							
1	2007	Male	11	non-Indigenous	19F	Unknown	No risk factors
Deaths not preventable by 7vPCV							
2	2007	Female	19	non-Indigenous	11A	3	Premature child care attendee
3	2007	Male	29	non-Indigenous	11A	Unknown	Unknown
4	2007	Male	19	non-Indigenous	15C	3	No risk factors
5	2007	Female	22	non-Indigenous	15C	3	No risk factors
6	2007	Male	5	non-Indigenous	18A	2	No risk factors
7	2007	Male	29	non-Indigenous	19A	3	Child care attendee
8	2008	Female	0	Indigenous	16F	0	Premature
9	2008	Female	0	non-Indigenous	19A	0	Congenital abnormality
10	2008	Female	23	non-Indigenous	35B	3	Premature congenital abnormality
11	2008	Male	5	non-Indigenous	Not typed	1	Unknown

Table 7: Risk factors* for invasive pneumococcal disease population sub-groups, Australia, 2007 and 2008

Risk factor	Children aged less than 5 years		Indigenous aged more than 50 years (n=64)	Non-Indigenous aged more than 65 years (n=936)
	Indigenous (n=75)	Non-Indigenous (n=418)		
Premature birth	10	33	NA	NA
Congenital or chromosomal abnormality	7	20	NA	NA
Anatomic or functional asplenia	1	0	1	13
Immunocompromised	2	8	16	199
Chronic illness	11	26	46	621
Childcare attendee	4	56	NA	NA
Previous episode of IPD	1	0	3	6
Other†	23	17	18	163
No risk factor identified	5	59	0	31
Risk factor data not reported	36	218	8	145
Total cases with risk factor data	39	200	56	791

* Case may be reported with more than one risk factor.

† Other risk factors include but are not limited to exposure to smoke, asthma and previous pneumonia.

NA Not applicable

group. The 3 additional serotypes (1, 5 and 7F) covered by the 10-valent pneumococcal conjugate vaccine (10vPCV) accounted for an additional 7% (195/2,831) of cases in 2007 and 2008; this ranged from 3% (22/868) of non-Indigenous adults aged 65 years or older and non-Indigenous children aged less than 5 years to 38% (8/21) of Indigenous cases aged 5–14 years. The 3 additional serotypes (3, 6A and 19A) covered by the 13-valent pneumococcal conjugate vaccine (13vPCV) in addition to the 10vPCV serotypes accounted for an additional 33% (936/2,831) of cases; this ranged from 0% (0/21) of Indigenous cases aged 5–14 years to 52% (200/381) of non-Indigenous cases aged less than 5 years.

Table 8: Number and proportion of invasive pneumococcal disease cases, Australia, 2007 and 2008, by pneumococcal vaccine serotypes

Age group	Vaccine type	Indigenous			Non-Indigenous		
		Number	%	Cumulative (%)	Number	%	Cumulative (%)
<5 years	7vPCV	7	9.7	9.7	47	12.3	12.3
	10vPCV (non-7vPCV)	6	8.3	18.1	10	2.6	15.0
	13vPCV (non-10vPCV)	13	18.1	36.1	200	52.5	67.5
	Non-conjugate serotypes	46	63.9	100.0	124	32.5	100.0
	Total	72	100.0		381	100.0	
	23vPPV (non-7vPCV)	43	59.7		262	68.8	
5–14 years	7vPCV	2	9.5	9.5	27	34.6	34.6
	10vPCV (non-7vPCV)	8	38.1	47.6	8	10.3	44.9
	13vPCV (non-10vPCV)	0	0.0	47.6	19	24.4	69.2
	Non-conjugate serotypes	11	52.4	100.0	24	30.8	100.0
	Total	21	100.0		78	100.0	
	23vPPV (non-7vPCV)	15	71.4		41	52.6	
15–49 years	7vPCV	16	11.0	11.0	123	29.2	29.2
	10vPCV (non-7vPCV)	27	18.5	29.5	42	10.0	39.2
	13vPCV (non-10vPCV)	30	20.5	50.0	124	29.5	68.6
	Non-conjugate serotypes	73	50.0	100.0	132	31.4	100.0
	Total	146	100.0		421	100.0	
	23vPPV (non-7vPCV)	87	59.6		258	61.3	
50–64 years	7vPCV	5	14.3	14.3	117	24.8	24.8
	10vPCV (non-7vPCV)	5	14.3	28.6	31	6.6	31.4
	13vPCV (non-10vPCV)	8	22.9	51.4	157	33.3	64.8
	Non-conjugate serotypes	17	48.6	100.0	166	35.2	100.0
	Total	35	100.0		471	100.0	
	23vPPV (non-7vPCV)	24	68.6		272	57.7	
>65 years	7vPCV	4	16.7	16.7	240	27.6	27.6
	10vPCV (non-7vPCV)	3	12.5	29.2	22	2.5	30.2
	13vPCV (non-10vPCV)	6	25.0	54.2	271	31.2	61.4
	Non-conjugate serotypes	11	45.8	100.0	335	38.6	100.0
	Total	24	100.0		868	100.0	
	23vPPV (non-7vPCV)	13	54.2		414	47.7	
Total	7vPCV	34	11.4	11.4	554	25.0	25.0
	10vPCV (non-7vPCV)	49	16.4	27.9	113	5.1	30.1
	13vPCV (non-10vPCV)	57	19.1	47.0	771	34.7	64.8
	Non-conjugate serotypes	158	53.0	100.0	781	35.2	100.0
	Total	298	100.0		2,219	100.0	
	23vPPV (non-7vPCV)	182	61.1		1,247	56.2	

Notifications with Indigenous status and/or serotype reported as unknown are excluded.

There are an additional 16 serotypes covered by the 23vPPV, over the 7 covered by the 7vPCV. Of all the cases reported with a serotype in 2007 and 2008, 57% (1618/2831) of all cases were due to these additional 16 serotypes. This ranged from 48% (414/868) of non-Indigenous adults aged 65 years or older to 71% (15/21) of Indigenous cases aged 5–14 years.

The notification rate of IPD due to 7vPCV serotypes fell considerably between 2002 and 2008 in children aged less than 5 years (Figure 7). The rate decreased by 95% in cases aged less than 2 years (70.9 to 3.4 per 100,000 population) and similarly decreased by 95% in cases aged 2–<5 years (27.3 to 1.4 per 100,000 population). The notification rate of IPD in adults aged 65 years or over decreased by 74% from 2002 to 2008 (14.2 to 3.7 per 100,000 population).

Figure 7: Notification rate for invasive pneumococcal disease caused by 7vPCV serotypes, Australia, 2002 to 2008, by age group

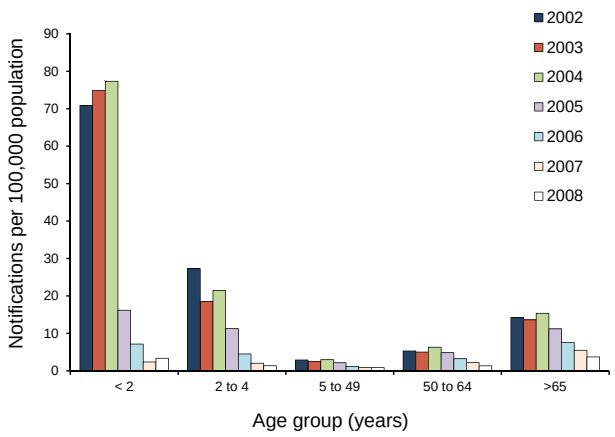
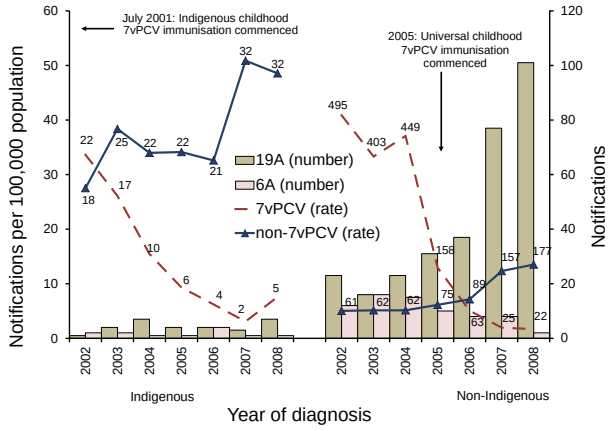


Figure 8 shows rates of IPD caused by 7vPCV serotypes in Indigenous and non-Indigenous children aged less than 5 years since 2002. Disease due to 7vPCV serotypes in Indigenous children has declined from 33.6 cases per 100,000 population in 2002 (n=22) to 7.6 cases per 100,000 population in 2008 (n=5), a decrease of 77%. Similarly in non-Indigenous children over the same period, rates fell from 40.9 (n=495) to 1.7 cases per 100,000 population (n=22), a decrease of 96%.

Rates of disease caused by non-7vPCV serotypes over the same period increased for both Indigenous and non-Indigenous children. In Indigenous children aged less than 5 years the rate increased from 27.5 to 48.5 cases per 100,000 population, an increase of 76%, and in non-Indigenous children from 5.0 to 13.5 cases per 100,000 population, an increase of 168%. The number of cases due to serotype 19A increased over this period in children aged less than 5 years, with 54% (118/221) of disease caused by non-7vPCV types due to this serotype in 2008. The number of cases due to serotype 19A in non-Indigenous children increased from 23 in 2002 to 101 in 2008. The number of cases due to serotype 6A decreased over this period in this age group, with 1% (3/221) of disease caused by non-7vPCV types due to serotype 6A in 2008.

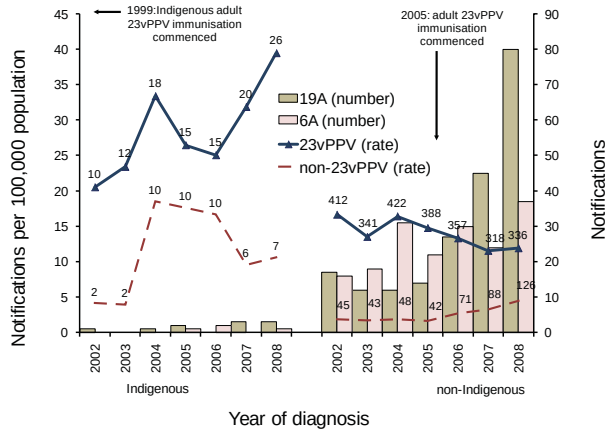
Figure 9 shows rates of IPD caused by 23vPPV serotypes in Indigenous adults aged 50 years or older and non-Indigenous adults aged 65 years or older. In Indigenous adults the rate of disease caused by 23vPPV serotypes increased from 20.5 cases per 100,000 population (n=10) in 2002 to 39.5 cases

Figure 8: Notifications and rates for 7vPCV and non-7vPCV serotypes causing cases of invasive pneumococcal disease in children aged less than 5 years, Australia, 2002 to 2008, by Indigenous status



Data point labels represent the number of notifications.

Figure 9: Notification rates for 23vPPV and non-23vPPV serotypes causing cases of invasive pneumococcal disease in Indigenous adults (aged 50 years or over) and non-Indigenous adults (aged 65 years or over), Australia, 2002 to 2008



Data point labels represent the number of notifications.

per 100,000 population (n=26) in 2008, an increase of 92%. Conversely, in non-Indigenous adults the rate decreased from 16.7 cases per 100,000 population (n=412) to 11.9 cases per 100,000 population (n=336) over the same period, a decrease of 28%. The number of cases due to serotypes 19A in non-Indigenous adults increased over this period, from 17 cases reported in 2002 to 80 cases in 2008. In 2002, serotype 19A represented 4% of all disease due to serotypes covered by the 23vPPV in non-Indigenous adults. This increased to 24% in 2008.

The rate of disease caused by non-23vPPV serotypes increased from 2002 to 2008 for both Indigenous (4.1 to 10.6 cases per 100,000 population respectively) and non-Indigenous adults (1.8 to 4.5 cases per 100,000 population, respectively). The number of cases due to serotype 6A increased over this period in non-Indigenous adults. In 2008, Serotype 6A represented 29% (37/126) of all disease in non-Indigenous adults that was caused by serotypes not covered by 23vPPV.

Vaccine failures

Table 9 shows cases of IPD due to 7vPCV serotypes in children aged less than 5 years who were fully vaccinated with 7vPCV as defined in Table 3. In 2007 and 2008 a total of 25 children who were considered fully vaccinated were notified with disease due to 7vPCV serotypes. Of these cases, 80% (n=20) were reported as non-Indigenous and 12% (n=3) were reported as Indigenous. Serotype 19F was reported in 64% (n=16) of these cases, with 6B the next most frequently reported serotype at 20% (n=5).

Antibiotic resistance

Penicillin and ceftriaxone/cefotaxime susceptibility data were analysed only from jurisdictions that reported susceptibility data for more than 50% of cases. Penicillin susceptibility completeness was suitable for reporting in both 2007 and 2008 for all jurisdictions. However, ceftriaxone/cefotaxime susceptibility completeness was suitable for report-

Table 9: Characteristics of 7vPCV vaccine failures in children aged less than 5 years, Australia, 2007 and 2008

Case	Year of diagnosis	Age (months)	Indigenous status	Serotype	Doses of 7vPCV	Doses of 23vPPV	Clinical category	Risk factors
1	2007	11	non-Indigenous	19F	3	0	Bacteraemia	yes
2	2007	14	non-Indigenous	6B	3	0	Pneumonia	unknown
3	2007	17	non-Indigenous	19F	3	0	Pneumonia	no
4	2007	24	non-Indigenous	19F	3	0	Pneumonia	no
5	2007	28	non-Indigenous	9V	3	0	Pneumonia	yes
6	2007	30	non-Indigenous	6B	3	0	Bacteraemia	no
7	2007	31	non-Indigenous	19F	3	0	Pneumonia	no
8	2007	34	non-Indigenous	19F	3	0	Pneumonia	yes
9	2007	38	non-Indigenous	19F	2	0	Meningitis	no
10	2007	38	non-Indigenous	19F	3	0	Bacteraemia	no
11	2007	58	Indigenous	19F	3	1	Bacteraemia	yes
12	2008	13	non-Indigenous	6B	3	0	Septic arthritis	no
13	2008	16	non-Indigenous	19F	3	0	Bacteraemia	no
14	2008	16	unknown	19F	3	0	Pneumonia	no
15	2008	16	non-Indigenous	4	3	0	Meningitis	no
16	2008	16	Indigenous	19F	3	0	Bacteraemia	unknown
17	2008	20	non-Indigenous	19F	3	0	Bacteraemia	yes
18	2008	22	non-Indigenous	19F	3	0	Pneumonia	no
19	2008	23	unknown	19F	3	0	Pneumonia	no
20	2008	25	non-Indigenous	6B	3	0	Bacteraemia	yes
21	2008	26	Indigenous	23F	3	1	Bacteraemia	yes
22	2008	30	non-Indigenous	19F	3	0	Pneumonia	no
23	2008	42	non-Indigenous	19F	3	0	Bacteraemia	no
24	2008	54	non-Indigenous	18C	3	0	Bacteraemia	yes
25	2008	55	non-Indigenous	6B	2	0	Unknown	yes

ing in both 2007 and 2008 in the Australian Capital Territory, New South Wales, the Northern Territory, Tasmania, Victoria and Western Australia.

In 2007, penicillin susceptibility was reported in 84% (1,246/1477) of all IPD cases (Table 10). Ceftriaxone/cefotaxime susceptibility was reported in 78% (834/1,068) of all analysed cases. A similar level of testing was reported in 2008, with 85% (1,379/1,628) of isolates tested for penicillin and 77% (910/1,182) for ceftriaxone/cefotaxime susceptibility.

In 2007 and 2008, 11% (140/1,246 and 153/1,379 respectively) of isolates with reported penicillin susceptibility had reduced susceptibility to penicillin, which was the same proportion as 2006 (11%, 143/1,351). Of the isolates in 2007 with reduced susceptibility to penicillin, 137 were serotyped with 50% (68/137) of these cases due to a serotype in the 7vPCV and 91% (125/137) of these cases due to a serotype in the 23vPPV. Of the isolates in 2008 with reduced susceptibility to penicillin, 148 were serotyped, with 36% (54/148) of these cases due to a serotype in the 7vPCV and 93% (137/148) due to a serotype in the 23vPPV. Of the isolates with reduced susceptibility to penicillin in 2007, 53 were serotype 19A, 42 were 9V, and 12 were 19F, accounting for 78% (107/137) of isolates with reduced penicillin susceptibility and with a known serotype. Of the isolates with reduced susceptibility to penicillin in 2008, 74 were serotype 19A, 17 were 9V, and 17 were 19F, accounting for 73% (108/148) of isolates with reduced penicillin susceptibility and with a known serotype.

In 2008, 2% (16/910) of isolates with reported ceftriaxone/cefotaxime susceptibility testing had reduced susceptibility to ceftriaxone/cefotaxime, which was lower than in 2007 (3%, 25/834) and in

Table 10: *Streptococcus pneumoniae* susceptibility to penicillin and ceftriaxone/cefotaxime,* for selected states and territories, 2007 and 2008

		9V	19F	All 7vPCV serotypes	19A	All 23vPPV serotypes	Not typed	All Isolates
2007								
Penicillin	Resistant	8	9	21	6	27	0	29
	Intermediate	34	3	47	47	98	3	111
	Sensitive	16	39	243	145	825	62	1106
	Total tested	58	51	311	198	950	65	1246
	Total isolates with reduced susceptibility (%)	42 (72%)	12 (24%)	68 (22%)	53 (27%)	125 (13%)	3 (5%)	140 (11%)
Ceftriaxone	Resistant	2	1	3	0	3	0	3
	Intermediate	10	6	18	4	22	0	22
	Sensitive	28	28	190	136	618	44	809
	Total tested	40	35	211	140	643	44	834
	Total isolates with reduced susceptibility (%)	12 (30%)	7 (20%)	21 (10%)	4 (3%)	25 (4%)	0 (0%)	25 (3%)
2008								
Penicillin	Resistant	3	9	18	9	28	1	31
	Intermediate	14	8	36	65	109	4	122
	Sensitive	15	31	201	213	886	68	1226
	Total tested	32	48	255	287	1023	73	1379
	Total isolates with reduced susceptibility (%)	17 (53%)	17 (35%)	54 (21%)	74 (26%)	137 (13%)	5 (7%)	153 (11%)
Ceftriaxone	Resistant	1	1	4	2	6	0	6
	Intermediate	2	1	4	2	8	0	10
	Sensitive	21	32	163	178	657	43	894
	Total tested	24	34	171	182	671	43	910
	Total isolates with reduced susceptibility (%)	3 (13%)	2 (6%)	8 (5%)	4 (2%)	14 (2%)	0 (0%)	16 (2%)

* Susceptibility data are restricted to jurisdictions with completeness suitable for reporting, that is greater than 50% completeness. Penicillin susceptibility completeness was suitable for reporting in both 2007 and 2008 for all jurisdictions. However, ceftriaxone/cefotaxime susceptibility completeness was suitable for reporting in both 2007 and 2008 in the Australian Capital Territory, New South Wales, the Northern Territory, Tasmania, Victoria and Western Australia.

2006 (3% 30/1046). All of the isolates in 2007 with reduced susceptibility to ceftriaxone/cefotaxime were serotyped with 84% (21/25) due to a serotype in the 7vPCV and 100% (25/25) to a serotype in the 23vPPV. All of the isolates in 2008 with reduced susceptibility to ceftriaxone/cefotaxime were serotyped, with 50% (8/16) due to a serotype in the 7vPCV and 88% (14/16) cases due to a serotype in the 23vPPV.

Discussion

By 2008, the 4th year of a universal funded infant 7vPCV (3+0) vaccination program in Australia, vaccine serotype IPD notification rates in those identified as non-Indigenous decreased in all age groups compared with 2002 levels; most significantly by 96% in children aged less than 5 years. However, rates of disease in non-vaccine serotypes had increased by 168% in this age group, including a 4-fold increase in serotype 19A disease. A similar increase in 19A was also seen in non-Indigenous adults. Combining these two trends, the net change in rates of all-serotype IPD was a 68% decrease in children less than 5 years. Substantial impacts on vaccine-type IPD in vaccinated age groups and herd immunity impacts on adults, as well as moderate levels of serotype replacement, have also been seen in other settings.[12, 13]

For the Aboriginal and Torres Strait Islander population, national pre-vaccination data are not available, as the vaccine was funded for this group from 2001. From 2002 to 2008, in children aged less than 5 years notifications of disease due to 7vPCV serotypes decreased by 77% and non-vaccine serotypes increased by 76%. In Indigenous adults (≥50 years), rates of 23vPPV serotypes increased by 92%. However, the substantial increases in 19A serotype disease seen in non-Indigenous children and adults were not evident in Aboriginal and Torres Strait Islander people. As in the pre-vaccine era, non-7vPCV and non-23vPPV serotypes were a greater proportion of total IPD in Aboriginal and Torres Strait Islanders than for non-Indigenous Australians.[3] Serotype 19A was a greater proportion of IPD in the pre-vaccine era in Aboriginal and Torres Strait Islander people compared with other Australians, and carriage studies have shown 19A to be relatively commonly found in Aboriginal children post-vaccination.[14, 15] Increases in serotype 19A disease in Alaskan Native children resulted in IPD rates almost returning to pre-vaccination levels, while in the Navajo, little serotype replacement was seen.[16, 17] The overall increase in IPD in Aboriginal and Torres Strait Islander adults in recent years is a concern. While coverage data are limited, the latest estimates from 2004–05 of 34% of those aged 50 years or older suggest it has been inadequate to have an impact.[1]

The proportion of IPD cases that had reduced susceptibility to penicillin did not change between 2006 and 2008 (11% in each year), although there was an increase in the proportion of these that were serotype 19A; from 25% to 50%. However, more detailed analysis and interpretation is limited by differences in methods used to assess susceptibility in different laboratories.

These data show a substantial impact in the first 4 years of a publicly-funded 3+0 7-valent conjugate pneumococcal vaccination program (that is without a booster dose). As well as the herd immunity impacts shown here, other Australian studies have shown impacts on non-invasive disease such as hospitalised pneumonia and myringotomy tube insertions.[18, 19] However, the relatively large number of vaccine failures due to serotype 19F should be closely monitored, as well as increases in disease due to serotype 19A.

Post-immunisation surveillance in Australia is essential to monitor trends in IPD, to inform future control strategies, including the targeting of existing and new vaccines and the best options for antibiotic treatment.

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References

1. Chiu C, Dey A, Wang H, Menzies R, Deeks S, Mahajan D, et al. Vaccine Preventable Diseases in Australia, 2005 to 2007. *Commun Dis Intell* 2010;34(Suppl):S1–S172.
2. Australian Technical Advisory Group on Immunisation. *The Australian Immunisation Handbook* 9th edn. Canberra, Australia: National Health and Medical Research Council and the Department of Health and Ageing; 2008.
3. Roche P, Krause V, Andrews R, Carter L, Coleman D, Cook H, et al. Invasive pneumococcal disease in Australia, 2002. *Commun Dis Intell* 2003;27(2):466–477.
4. Roche P, Krause V, Bartlett B, Coleman D, Cook H, Davis C, et al. Invasive pneumococcal disease in Australia, 2004. *Commun Dis Intell* 2006;30(1):80–92.
5. Roche P, Krause V, Bartlett M, Coleman D, Cook H, Counahan M, et al. Invasive pneumococcal disease in Australia, 2003. *Commun Dis Intell* 2004;28(4):441–454.
6. Roche P, Krause V, Cook H. Invasive pneumococcal disease in Australia, 2005. *Commun Dis Intell* 2007;31(1):86–100.
7. Roche P, Krause V, Cook H, Bartlett M, Coleman D, Davis C, et al. Invasive pneumococcal disease in Australia, 2006. *Commun Dis Intell* 2008;32(1):18–30.
8. *National Health Security Act,* No 174. 2007. Accessed on November 2009. Available from: http://www.comlaw.gov.au/ComLaw/Legislation/Act1.nsf/0/A005BA0145A00248CA25736A00126AA5?OpenDocument
9. National Notifiable Diseases List 2008. Accessed on November 2009. Available from: http://www.comlaw.gov.au/ComLaw/legislation/LegislativeInstrument1.nsf/0/7162D634C6DD1BAACA25740B0079D6B8?OpenDocument
10. Australian Bureau of Statistics. Population by age and sex, Australian States and Territories, Estimated Resident Population By Single Year of Age, Australia. Canberra: Australian Bureau of Statistics; 2008. Report No: 3201.0.
11. Communicable Diseases Network Australia. Australian national notifiable diseases case definitions – Pneumococcal disease (invasive) case definition. 2004. Accessed on 27 March 2010. Available from: http://www.health.gov.au/internet/main/publishing.nsf/Content/cda-surveil-nndss-casedefs-cd_pnuemo.htm
12. Miller E, Andrews N, Waight P, Slack M, George R. Herd immunity and serotype replacement 4 years after seven-valent pneumococcal conjugate vaccination in England and Wales: an observational cohort study. Lancet Infect Dis 2011;11(10):760–768.
13. Pilishvili T, Lexau C, Farley M, Hadler J, Harrison L, Bennett N, et al. Sustained reductions in invasive pneumococcal disease in the era of conjugate vaccine. *J Infect Dis* 2010;201(1):32–41.
14. McIntyre P, Chiu C, Jayasinghe S, Menzies R, Krause V, Cook H, et al. Reduction in 19A invasive pneumococcal diseases in Indigenous Australian children receiving conjugate pneumococcal vaccine with polysaccharide booster. In: Pneumococci and Pneumococcal Diseases Symposium. Tel Aviv; 2010.
15. Stubbs E, Hare K, Wilson C, Morris P, Leach A. *Streptococcus pneumoniae* and noncapsular *Haemophilus influenzae* nasal carriage and hand contamination in children: A comparison of two populations at risk of otitis media. *Pediatr Infect Dis J* 2005;24(5):423–428.
16. Singleton R, Hennessey T, Bulkow L, Hammitt L, Zulz T, Hurlburt D, et al. Invasive pneumococcal disease caused by nonvaccine serotypes among Alaska native children with high levels of 7-valent penumococcal conjugate vaccine coverage. *JAMA* 2007;297(16):1784–1792.
17. Weatherholtz R, Millar E, Moulton L, Reid R, Rudolph K, Santosham M, et al. Invasive pneumococcal disease a decade after pneumococcal conjugate vaccine use in an American Indian population at high risk for disease. *Clin Infect Dis* 2010;50(9):1238–1246.
18. Jardine A, Menzies R, McIntyre P. Reduction in hospitalizations for pneumonia associated with the introduction of a pneumococcal conjugate vaccination schedule without a booster dose in Australia. *Pediatr Infect Dis J* 2010;29(7):607–612.
19. Jardine A, Menzies R, Deeks S, Patel M, McIntyre P. The impact of pneumococcal conjugate vaccine on rates of myringotomy with ventilation tube insertion in Australia. *Pediatr Infect Dis J* 2009;28(9):761–765.