Invasive pneumococcal disease in Australia, 2003

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Some minor amendments have been made to this article on 4 May 2005, post-printing. In particular, Tables 15 and 16 have been updated and the Map has been replaced.

Abstract

There were 2,174 cases of invasive pneumococcal disease (IPD) notified to the National Notifiable Diseases Surveillance System (NNDSS) in Australia in 2003; a rate of 10.9 per 100,000 population. The notification rate varied between states and territories and by geographical region with the highest rates in the north of the country. Invasive pneumococcal disease was reported most frequently in children aged less than two years (98.8 cases per 100,000 population). Enhanced surveillance for IPD in 2003 was carried out in all states and territories, providing additional data on 1,842 (85%) of all notified cases. Rates of IPD in Indigenous Australians were three times the rate in non-Indigenous Australians. There were 125 deaths attributed to IPD resulting in an overall case fatality rate of 6.8 per cent. Seventy-one percent of all pneumococcal isolates serotyped were serotypes in the seven-valent conjugate vaccine and 91 per cent were serotypes in the 23-valent polysaccharide pneumococcal vaccine. The clinical presentation and risk factors for IPD varied between Indigenous and non-Indigenous cases and non-vaccine serotypes occurred more frequently among Indigenous children and adults. Data from three years of surveillance indicate an early impact of the 7-valent vaccine in the target population. *Commun Dis Intell* 2004;28:441–454.

Keywords: invasive pneumococcal disease, Streptococcus pneumoniae, *surveillance, vaccination*

Introduction

Infection with *Streptococcus pneumoniae* is a leading cause worldwide of otitis media, pneumonia, bacteraemia, meningitis, responsible for significant morbidity and mortality in infants, the elderly and those with predisposing risk factors. Invasive pneumococcal disease (IPD) is the clinical condition in which *S. pneumoniae* infects a normally sterile site such as blood, cerebrospinal fluid or pleural fluid. IPD presents most commonly as pneumonia in adults and bacteraemia in children. The risk of disease is highest among people who are immunocompromised or have a chronic illness. IPD disease in Australia is generally a disease of the very young and the very old. The incidence of IPD in Indigenous Australians has been much higher than that of non-Indigenous Australians.

The escalating resistance of the pneumococcus to antibiotics has been an important factor for the development and introduction of new pneumococcal vaccines. In Australia the rate of penicillin resistant pneumococci increased from 1 per cent in 1984

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to 25 per cent in 1997.[1] Reduced susceptibilities to other antimicrobials has also emerged in recent years with the rate of reduced susceptibility to third generation cephalosporins in Australia reaching 13 per cent in 1997.[2] Multi-drug resistant pneumococci have been documented around the world and have been associated with outbreaks of meningitis in infants.[3] In 1999, 6.8 percent of invasive and 16.7 per cent of non-invasive pneumococcal isolates in Australia were multi-drug resistant.[4]

Ninety serotypes of *S. pneumoniae* identified by the polysaccharide composition of their capsule have been described. Immunity to pneumococcal infection is thought to be serotype specific. Vaccines containing pneumococcal polysaccharides from a varying number of serotypes have been available for many years, with a 23-valent polysaccharide vaccine (23vPPV) being used in Australia from 1986 (Table 1). Polysaccharide pneumococcal vaccines were shown to be poorly immunogenic in young children.[5] A vaccine in which polysaccharides from seven serotypes coupled to a protein carrier (mutated diphtheria toxoid) was developed to provide an effective pneumococcal vaccine for children and in a trial in the USA in infants aged 2 to 15 months of age demonstrated an efficacy of 93.9 per cent. [6] This conjugate vaccine (7vPCV) was licensed for use in Australia in January 2001 and a nationally funded vaccination program for children at high risk commenced in June 2001 (Table 1).

IPD was made a notifiable disease in all Australian states and territories in 2001 and surveillance data are reported to the National Notifiable Diseases Surveillance System (NNDSS). Additional enhanced surveillance data on IPD has also been collected since 2001 and annual reports have been published.[7,8] In this third report, an analysis of the influence of the 7-valent vaccine on IPD in vaccine eligible children has been performed with respect to overall rates of disease, disease caused by vaccine and non-vaccine serotypes and levels of antimicrobial resistance. Baseline data on IPD in all children and the elderly prior to the introduction of universal child and 65 year and older immunisation programs commencing in January 2005 are presented.

Methods and Materials

Case definition

A case of invasive pneumococcal disease was defined as the isolation from or the detection in blood, cerebrospinal fluid (CSF) or other sterile site of *Streptococcus pneumoniae*.

Data collection

Invasive pneumococcal disease has been a notifiable disease in some Australian states and territories for several years. In 2001, IPD was made notifiable in all states and territories and data are forwarded to the NNDSS. Since this required changes to state and territory public health legislation, the data in 2001 was incomplete in some states and territories, but was complete for all jurisdictions from 2002.

NNDSS data in 2003 comprised core data, which is a set of data collected on all cases of all notifiable diseases as well as data specific for IPD. The list of the data fields collected the IPD enhanced data set is shown in Table 2.

Clinical Presentation

Clinical presentations were coded as pneumonia, meningitis, bacteraemia, other or unknown. Pneumonia was defined as blood culture or nucleic

Table 1. Recommendations for pneumococcal vaccination, Australia, 2003

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
Date implemented	1998	July 2001
Target populations	All individuals aged 65 years and over Individuals with asplenia Immuncompromised patients Aboriginal and Torres Strait Islander people aged 50 years and over Immunocompetent individuals with chronic illness including chronic cardiac, renal or pulmonary disease, diabetes and alcohol-related problems	Tier 1: Indigenous children less than 5 years living in central Australia Tier 2: Indigenous children aged less than 2 years particularly in rural and remote settings Tier 3: Indigenous children under 2 years living in other settings Non-Indigenous children less than 2 years living in Central Australia Non-Indigenous children with conditions predisposing to pneumococcal infection
Data source	*NHMRC Immunisation Handbook* 7th edition, 2000	ATAGI recommendations, 2001

Table 2. Invasive pneumococcal disease surveillance data supplied by states and territories used in this report

Data type	Data fields
Demographic	Date of Birth
	Age
	Indigenous status: (Aboriginal, Torres Strait Islander, Aboriginal and Torres Strait Islander, Other, Unknown)
	Location (optional)
	Postcode
Risk factors	Premature birth (gestation less than 37 weeks)
	Congenital abnormality
	Anatomical or congenital asplenia
	Immunocompromised (e.g. HIV, lymphoma, transplant, multiple myeloma, nephrotic syndrome etc.)
	Chronic illness (e.g. cardiac disease, pulmonary disease, CSF leak, diabetes)
	Other risk factors (variable by State) including chronic suppurative otitis media, failure to thrive, previous IPD or pneumonia, excessive alcohol consumption, smoking or smoke exposure
Clinical data	Clinical presentation (pneumonia, meningitis, bacteraemia, other, unknown)
	Date of onset
	Death due to IPD
Microbiology data	Specimen collection date
	Date laboratory results issued (report date)
	Date notification received
	Specimen type (blood, CSF, pleural fluid, joint fluid, other sterile site)
	Specimen culture positive or *S. pneumoniae* detected by nucleic acid tests
	Antibiotic susceptibility (penicillin, cefotaxime/ceftriaxone)
	Pneumococcal serotype
Vaccination history	Source of vaccination history (validated, not validated, information not collected)
	Pneumococcal vaccination dates, number of doses and type of vaccine
	Vaccination status: fully vaccinated for age, partially vaccinated for age, not vaccinated, unknown

acid test (NAT) positive for *S. pneumoniae* with clinical and/or radiological signs of pneumonia. Meningitis was defined as the detection of *S. pneumoniae* in the cerebrospinal fluid (CSF) and/or blood with supportive clinical findings. Bacteraemia was defined as the detection of *S. pneumoniae* in blood with no localising signs. 'Other' presentations included detection of *S. pneumoniae* in pleural, peritoneal or joint fluid. More than one clinical presentation could be recorded for each case.

Vaccination

The consensus definitions of vaccination status, vaccination confirmation and vaccine failure are shown in Table 3.

Populations under surveillance

There were differences in populations under surveillance between jurisdictions in the collection of enhanced IPD data. The age groups on whom enhanced data was collected in 2003 are shown in Table 4.

NNDSS data for 2003 was analysed by date of disease onset while data in the enhanced data sets was analysed by date of notification.

Data analysis

The notification rates presented in this report were calculated using population data from the Australian Bureau of Statistics (ABS). The Estimated Resident Population (ABS 3201.0) in each state and territory and in Australia as a whole, as at June 30, 2003, was used as the denominator in rate calculations. Estimates of the Indigenous Australia population were based on projections from the 2001 census. The ABS calculated projections based on assump-

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

Category	Definition*
Fully vaccinated (child)	Those that have had the required doses for age of 7vPCV (or 23vPPV if age > 18 months) at least 2 weeks prior to infection. Children aged less than 7 months analysed on an individual basis
Fully vaccinated (adult)	Those that have had the required doses of 23vPPV at least 2 weeks prior to infection
Partially vaccinated (child)	Those that have received at least one dose, but not all the recommended doses of vaccine for age
Partially vaccinated (adult)	Those that have been vaccinated with 23vPPV but the time frame is outside the recommended schedule
Not vaccinated (child or adult)	Those that have never received a pneumococcal vaccine
Vaccination confirmation	Written confirmation through Australian Childhood Immunisation Register, State or Territory Immunisation register or health record
Vaccine failure	A fully vaccinated person (as per the above criteria) with disease due to a serotype found in the corresponding vaccine

* According to the *Australian Immunisation Handbook*, 8th edition 2003.

Table 4. Enhanced Invasive pneumococcal disease surveillance data collection by states and territories in 2003

Age group	Jurisdictions
Under 5 years	Australian Capital Territory (except vaccination status and risk factors)
	Queensland
	Victoria (except risk factor information)
	South Australia (except risk factor information)
	New South Wales (Cases in rural Public Health Units (PHU) and South Western Sydney, Hunter, Illawara, Greater Western Sydney, Wentworth and Southeastern Sydney PHUs)
Over 50 years	Victoria (Indigenous cases and vaccine failures only)
	South Australia (Vaccine failures only)
	New South Wales (Cases in Rural Public Health Units (PHU) and South Western Sydney, Hunter, Illawara, Greater Western Sydney PHUs)
All ages	North Queensland
	Northern Territory
	Western Australia
	Tasmania

tions about future births, deaths and migrations in the Indigenous population and a 'low' and 'high' estimate were reported. The 'low' estimate has been used in this report, consistent with the reporting of other national communicable diseases.

The significance of differences in proportions was calculated using the Chi-square test with Yates correction using Epi-Info 6.

Results

Notifications to NNDSS

There were 2,174 notifications of IPD to the NNDSS in 2003. The numbers of notification and the notification rate per 100,000 population are shown in Table 5.

The rates of IPD disease ranged between 7.7 and 12.4 per 100,000 except in the Northern Territory where the rate was 36.3 per 100,000. When the notification rates of IPD were examined by geographical distribution, variation within states was evident (Map).

The frequency of cases varied by season with 816 (38%) reported in winter months (June to August). The effect of season was more marked in cases aged five years or more than in younger children (Figure 1).

As previously noted, IPD in Australia is largely a disease of the very young and very old. The highest rates of disease were in children aged less than five years and adults aged more than 85 years (Figure 2). Among children aged less than five years, the highest rates were recorded in children aged one year (119 per 100,000 population). There were 488 cases in children aged less than two years of age (98.8 per 100,000) in 2003. In all age groups there were more male than female cases (overall male to female ratio 1.3:1).

Table 5. Notifications and notification rate per 100,000 population, Invasive pneumococcal disease, Australia, 2003*

	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Australia
Notifications	40	784	72	466	176	43	443	150	2,174
Rate per 100,000 population	12.4	11.7	36.3	12.3	11.5	9.0	9.0	7.7	10.9

* By date of disease onset.

Map. Notification rates of invasive pneumococcal disease, Australia, 2003 by statistical division of residence

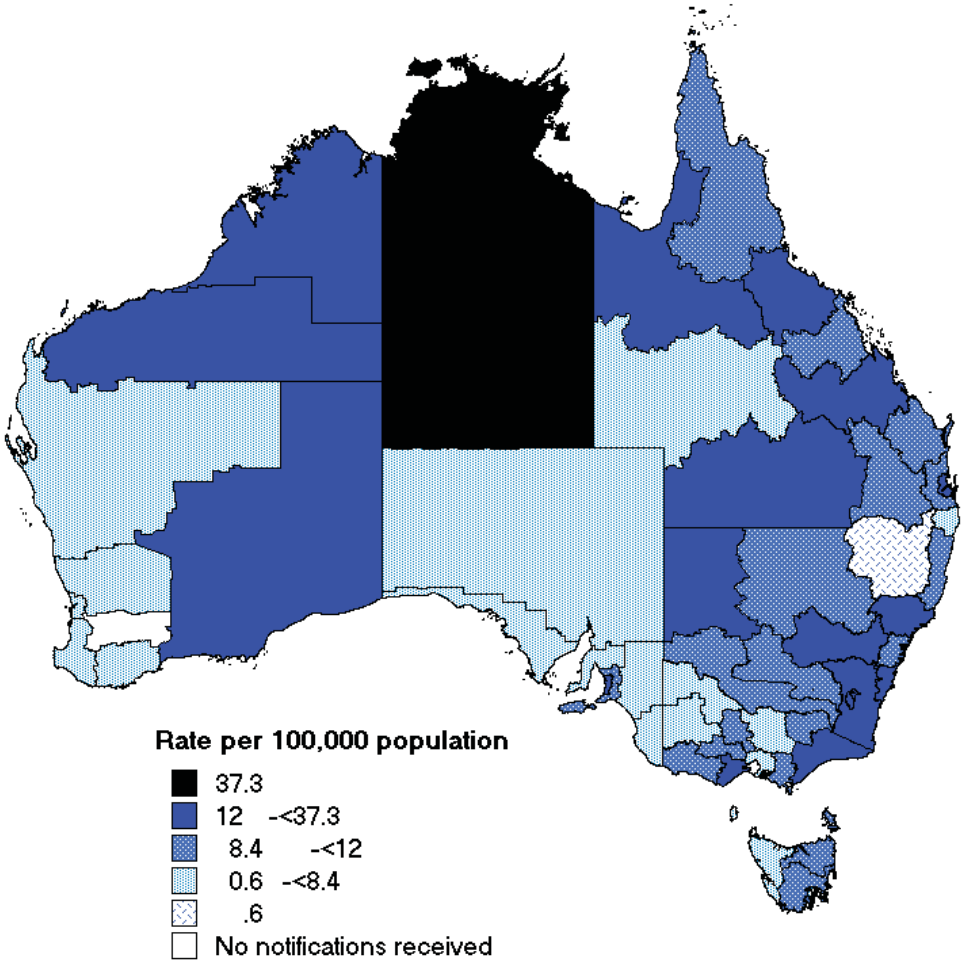


Figure 1. Notifications of invasive pneumococcal disease, by month of report and age group, Australia, 2003

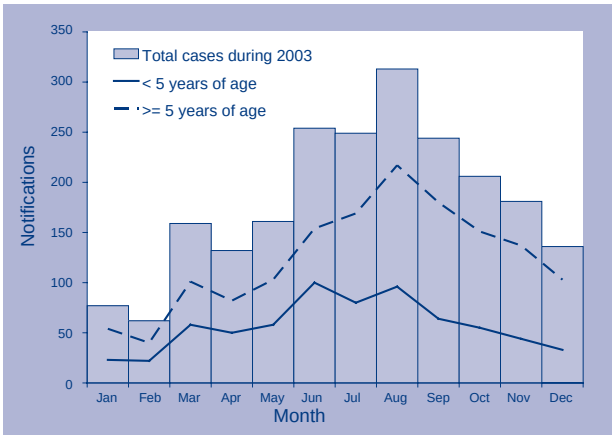
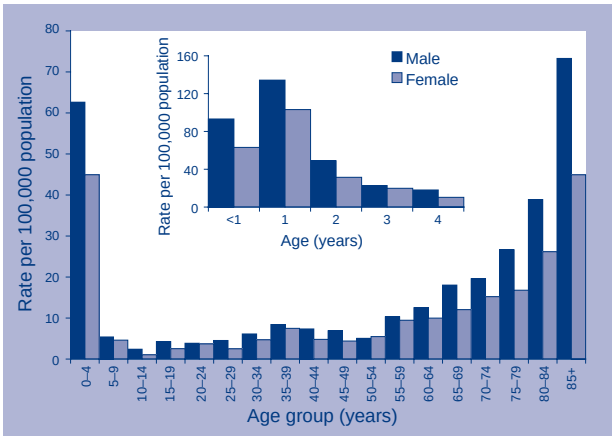


Figure 2. Notification rates of invasive pneumococcal disease, by age and sex, Australia, 2003



Enhanced IPD surveillance data

Enhanced data were available for 1,842 cases or 85 per cent of notified cases—a similar proportion of cases to that reported on in the 2002 annual report.

Demographics

The demographic characteristics of cases on which enhanced data were collected are shown in Table 6.

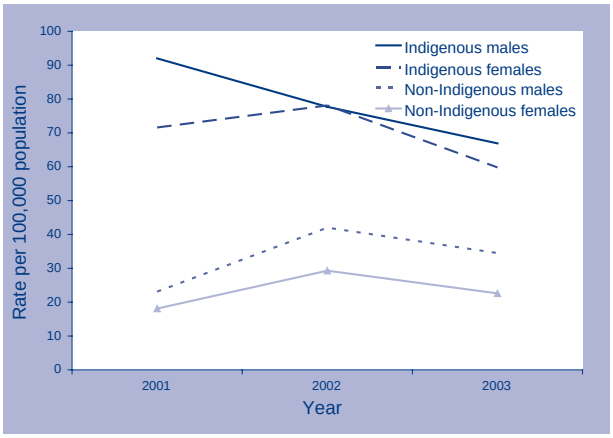
The enhanced data identified 149 cases of IPD among Indigenous people, which represented eight per cent of all cases, a similar proportion to that in 2002. This represented a national rate of 33.5 per 100,000 in Indigenous people compared with the national rate of 10.7 per 100,000. The rates of IPD in Indigenous people were highest in the Northern Territory (87.7 per 100,000) and Queensland (42.6 per 100,000). The national rate of IPD in Indigenous people is likely to be underestimated as incomplete reporting of Indigenous status continues to be a problem in some jurisdictions. Rates in Indigenous children under five years have fallen from 92 to 67 per 100,000 in males and 72 to 60 per 100,000 in females, between 2001 and 2003 respectively, but these represent small declines in total numbers (Figure 3).

Clinical presentation

The clinical presentation was reported in 69.8 per cent (1,286/1,842) of cases with enhanced surveillance information (Table 7).

Pneumonia was the most common clinical presentation (662 cases, 3.3 per 100,000 population) followed by bacteraemia (592 cases, 2.9 per 100,000 population) and meningitis (109 cases, 0.5 per 100,000 population). Other clinical presentations of IPD accounted for 45 cases. These clinical presentation rates were similar to those reported in 2002.

Figure 3. Notification rates of invasive pneumococcal disease, Australia 2001 to 2003 in children under 5 years of age, by Indigenous status



Clinical presentation varied by age with pneumonia being the most common presentation among cases over 65 years (72%) and bacteraemia the most common presentation among cases in children under five years (68%).

The proportion of IPD cases presenting as pneumonia was significantly higher in Indigenous children (37%) compared with non-Indigenous children (22%). There were no significant differences between Indigenous and non-Indigenous children in the proportions of other clinical presentations (Table 8).

Table 6. Demographic profile of Invasive pneumococcal disease cases reported by enhanced surveillance systems, by jurisdiction, Australia, 2003*

Data		ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Total
Number		44	428	72	464	176	43	465	150	1,842
Sex	Male:Female ratio	1.2:1	1.3:1	2:1	1.3:1	1.4:1	1.9:1	1.4:1	1.3:1	1.3:1
Age	<5 years	11	192	20	163	73	4	131	43	637
	5 to 64 years	20	69	49	200	50	27	181	68	664
	≥65 years	13	167	3	101	53	12	153	39	541
Indigenous status	Indigenous	0 (0%)	13 (3%)	51 (71%)	53 (11%)	3 (2%)	0 (0%)	7 (2%)	22 (15%)	149 (8%)
	Non-indigenous	19 (43%)	403 (94%)	21 (29%)	305 (66%)	163 (93%)	39 (91%)	288 (62%)	128 (85%)	1366 (74%)
	Unknown	25 (57%)	12 (3%)	0	106 (23%)	10 (5%)	4 (9%)	170 (36%)	0	327 (18%)

* See Table 4 for details of populations under enhanced surveillance in different jurisdictions in 2003.

Table 7. Clinical presentations of Invasive pneumococcal disease, by jurisdiction, Australia, 2003

Clinical presentation*	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Total
Pneumonia (%)	0	208 (48%)	46 (64%)	78 (17%)	48 (27%)	32 (74%)	146 (31%)	104 (69%)	662 (36%)
Meningitis (%)	1 (2%)	27 (6%)	6 (8%)	19 (4%)	8 (5%)	5 (12%)	32 (7%)	11 (7%)	109 (6%)
Bacteraemia (%)	36 (82%)	180 (42%)	19 (26%)	145 (31%)	87 (49%)	6 (14%)	70 (15%)	49 (32%)	592 (32%)
Other (%)	3 (7%)	8 (2%)	1 (1%)	10 (2%)	5 (3%)	0	5 (1%)	13 (9%)	45 (2%)
Unknown (%)	4 (9%)	5 (1%)	0	252 (54%)	40 (23%)	0	215 (46%)	0	516 (28%)

* Totals may exceed case total and percentages exceed 100 per cent since cases may have had more than one type of clinical presentation in some jurisdictions.

Table 8. Clinical presentations of Invasive pneumococcal disease in Indigenous and non-Indigenous children aged less than 5 years, Australia, 2003

	Number of cases (%)		
	Indigenous n=45	Non-Indigenous n=516	Significance of difference*
Pneumonia	17 (37%)	112 (22%)	p<0.05
Meningitis	8 (17%)	54 (10%)	NS
Bacteraemia	24 (53%)	329 (64%)	NS
Other	0	20 (4%)	–

* Chi-square test with Yates correction.

NS = not significant.

IPD resulted in 125 deaths in Australia in 2003, a case fatality rate of 6.8 per cent (Table 9). The case fatality rate was significantly higher in cases aged more than 65 years (16.6%) compared with children aged less than five years (1.9%, p<0.001). The case fatality rate was not significantly different in Indigenous cases (4.7%) and non-Indigenous cases (6.9%). There were seven deaths in children aged less than two years of age.

Risk factors for pneumococcal disease

The national surveillance working group defined risk factor categories for IPD. Other risk factors were recorded but varied between jurisdictions. More than one risk factor could be recorded for each case. Recognised risk factors for pneumococcal disease were reported in 640 cases. The most common of these was chronic illness, which included chronic respiratory, cardiac and renal disease. Immunocompromising conditions such as long-term immunosuppressant use were common among IPD cases.

The frequency of risk factors for IPD in Indigenous and non-Indigenous people are shown in Table 10. The rates of chronic illness were significantly higher in Indigenous children aged less than five years with IPD compared with non-Indigenous children in the same age group. Among cases aged five years or more, the proportion of immunocompromised cases was significantly higher among non-Indigenous cases than Indigenous cases.

Pneumococcal serotypes causing disease in Australia

Pneumococcal serotypes were identified in 86 per cent (1,583/1,842) of the cases under enhanced surveillance in 2003. Of these, 71 per cent (1,129/1,583) of serotypes contained in the 7-valent conjugate pneumococcal vaccine and 91 per cent (1,444/1,583) were serotypes contained in the 23-valent polysaccharide pneumococcal vaccine (Table 11).

The frequency of vaccine serotypes in the conjugate and polysaccharide was further analysed in the target age groups for these vaccines and

Table 9. Case fatality rates for Invasive pneumococcal disease, by jurisdiction, Australia, 2003

Data	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Total
Cases	44	428	72	464	176	43	465	150	1,842
Deaths	4	63	4	8	9	6	22	9	125
Case fatality rate (%)	9%	14.7%	5.5%	1.7%	5.1%	13.9%	4.7%	6%	6.8%
Deaths in Aged < 5y /total cases aged <5y (%)	1/11 9%	4/192 (2.1%)	2/20 (10%)	1/163 (0.6%)	1/73 (1.4%)	0/4 (0%)	2/131 (1.5%)	1/43 (2.3%)	12/ 637 (1.9%)
Deaths in Aged >65y /total cases aged >65y (%)	2/13 15%	54/167 (32.3%)	0/3 (0%)	5/101 (5%)	6/53 (11.3%)	3/12 (25%)	15/153 (9.8%)	5/39 (12.8%)	90/541 (16.6%)
Deaths in Indigenous people/total Indigenous cases (%)	0/0 (0%)	2/13 (15.4%)	2/51 (3.9%)	2/53 (3.7%)	0/3 (0%)	0/0 (0%)	1/7 (14.3%)	0/22 (0%)	7/149 (4.7%)
Death in non-Indigenous /total non-Indigenous + 'unknown' cases (%)	4/44 (9%)	61/415 (14.7%)	2/21 (9.5%)	6/411 (1.4%)	9/173 (5.2%)	6/43 (13.9%)	21/458 (4.6%)	9/128 (7%)	118/1693 (6.9%)

Table 10. The frequency of risk factors for Invasive pneumococcal disease, by age group and Indigenous status, Australia, 2003

	Cases aged less than 5 years			Cases aged 5 years or over		
	Indigenous (n=19)	Non Indigenous (n=93)	Significance of difference*	Indigenous (n=76)	Non-Indigenous (n=452)	Significance of difference*
Premature birth	2 (11%)	28 (30%)	NS	–	–	–
Congenital abnormality	3 (16%)	11 (12%)	NS	–	–	–
Asplenia	0	1 (1.1%)	–	–	7 (1.5%)	–
Immuno-compromised	2 (11%)	8 (8.6%)	NS	7 (9%)	98 (22%)	p<0.05
Chronic illness	9 (47%)	15 (16%)	p<0.01	53 (70%)	275(61%)	NS

* Chi-square test with Yates correction.

NS = not significant.

Table 11. Proportion of pneumococcal serotypes in cases of Invasive pneumococcal disease, covered by the 7-valent and 23-valent pneumococcal vaccines* by jurisdiction, Australia, 2003

Vaccine	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Total
7v	23/40 58%	256/339 76%	18/69 26%	298/410 73%	118/153 77%	25/35 71%	298/395 75%	93/142 65%	1,129/1,583 71%
23v	36/40 90%	320/339 94%	51/69 74%	374/410 91%	137/153 89%	31/35 88%	371/395 94%	124/142 87%	1,444/1,583 91%

* As a proportion of serotyped isolates.

by Indigenous status (Table 12). The proportion of 7-valent conjugate vaccine serotypes was significantly lower in Indigenous children aged less than two years (34.6%) than in non-Indigenous children (88.3%, p<0.001). Similarly the proportion of 23-valent polysaccharide vaccine serotypes in Indigenous cases aged two years and above was significantly lower (69%) than in non-Indigenous cases (91%, p<0.001).

Trends in the numbers of 7-valent vaccine and non-7-valent vaccine serotypes in Indigenous and non-Indigenous cases aged less than two years between 2001 and 2003 are shown in Figure 4A and 4B.

The decline in IPD due to 7-valent serotypes in Indigenous children under two years was largely seen in the Northern Territory, Queensland and Western Australia (Table 13), the jurisdictions with the largest proportion of Indigenous people.

Table 12. The proportion of pneumococcal serotypes isolated from cases of invasive pneumococcal disease, which were serotypes in the 7-valent and 23-valent pneumococcal vaccine, by age and Indigenous status, Australia, 2003

	Number (%) serotypes in pneumococcal vaccines					
	Cases aged less than 2 years with serotypes in 7-valent conjugate vaccine			Cases aged 2 years or more with serotypes in 23-valent vaccine		
	Indigenous	Non-Indigenous	Significance of difference*	Indigenous	Non-Indigenous	Significance of difference*
ACT	–	3/7 (42%)	–	–	30/33 (90%)	–
NSW	3/3 (100%)	96/107 (89.7%)	NS	5/6 (83%)	203/224 (90.6%)	NS
NT	0/11 (0%)	4/4(100%)	p<0.001	26/38 (68%)	14/16 (87.5%)	NS
Qld	1/7(14%)	91/102 (89%)	p<0.001	32/44 (73%)	235/257 (91.4%)	p<0.005
SA	–	41/44 (93.2%)	–	0/1 (0%)	95/108 (87.9%)	p=0.07
Tas	–	1/1 (100%)	–	–	27/34 (79%)	–
Vic	3/3 (100%)	63/75 (85%)	NS	2/4 (50%)	294/313 (94%)	p<0.005
WA	2/2 (100%)	19/21 (90%)	NS	12/19 (63%)	90/100 (90%)	p<0.01
Australia	9/26 (34.6%)	318/361 (88.3%)	p<0.001	77/112 (69%)	988/1,085 (91.3%)	p<0.001

* Differences tested by Chi square test with Yates correction.

NS = not significant.

Figure 4A. Number of 7-valent vaccine and non-7-valent vaccine serotypes causing cases of invasive pneumococcal disease in Indigenous children aged less than 2 years, Australia 2001 to 2003

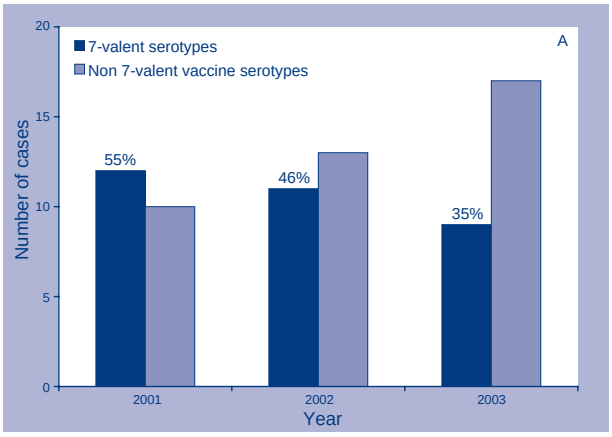


Figure 4B. Number of 7-valent vaccine and non-7-valent vaccine serotypes causing cases of invasive pneumococcal disease in non-Indigenous children aged less than 2 years, Australia 2001 to 2003

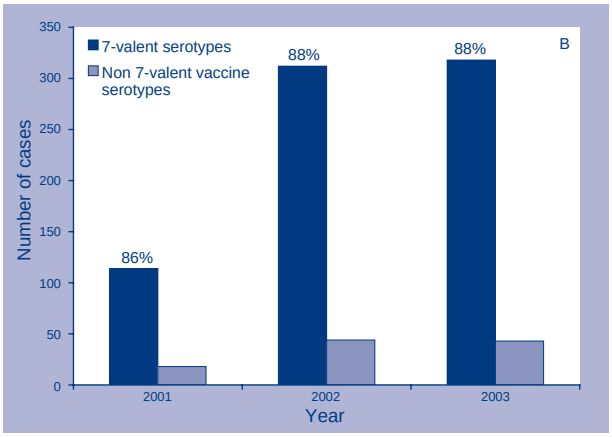


Table 13. Pneumococcal serotypes in Indigenous children aged less than two years, 2001 to 2003, Western Australia, Queensland and Northern Territory

A. 7 valent vaccine serotypes

	Northern Territory	Queensland	Western Australia	Total
2001	8	9	2	19
2002	4	4	1	9
2003	0	1	2	3

B. non-7 valent vaccine serotypes

	Northern Territory	Queensland	Western Australia	Total
2001	4	0	6	10
2002	3	6	4	13
2003	11	8	0	19

Vaccination status of Invasive pneumococcal disease cases

Data on pneumococcal vaccination were available for 58 per cent of the cases in 2003. Of the 1,082 cases with a vaccination history, the majority (758, 70%) was reported as unvaccinated. IPD was reported in 12 cases who had received vaccination with the 7-valent conjugate vaccine and in 161 cases who had received the 23-valent polysaccharide pneumococcal vaccine (Table 14).

Further investigations were made of the 12 cases of IPD presumptively vaccinated with 7-valent conjugate vaccine. Of the six cases in the Northern Territory, five were infected with pneumococcal serotypes not in the 7-valent vaccine and one case had no serotype information. Similarly four cases in Queensland were infected with non-vaccine serotypes and one case had no serotype information. There was no serotype data in the South Australian case. Therefore there was no evidence for any vaccine failure with the 7-valent conjugate pneumococcal vaccine in Australia in 2003 for those fully vaccinated. (Table 15).

The majority of the 161 cases of IPD in recipients of the 23-valent vaccine, occurred in those with predisposing risk factors for IPD. Thirty-six (22%) of the serotypes causing disease in these patients were not in 23-valent vaccine. In total 131 cases were presumptive 23-valent vaccine failures (Table 16).

Antibiotic resistance in pneumococcal cases

The antibiotic susceptibilities of 1,193 isolates to penicillin were tested in six jurisdictions and 719 isolates to ceftriaxone were tested in five jurisdictions (Table 17).

Table 14. Vaccination status of Invasive pneumococcal disease cases (all serotypes), by age group and jurisdiction, Australia, 2003.

A. Invasive pneumococcal disease cases aged less than 2 years

Vaccination status	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Total
Fully vaccinated for age	0	0	6	5	1	0	0	0	12
Partially vaccinated for age	0	0	5	3	50	0	0	1	59
Not vaccinated	0	131	5	14	0	0	79	21	250
Unknown	7	4	0	101	0	1	10	4	127

B. Invasive pneumococcal disease cases aged 2 years or more

Vaccination status	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Total
Fully vaccinated for age	0	53	16	21	20	4	44	3	161
Partially vaccinated for age	0	1	5	6	0	0	3	1	16
Not vaccinated	1	207	34	44	57	30	128	74	575
Unknown	36	32	1	270	46	7	197	46	635

Table 15. Details of the cases of invasive pneumococcal disease that occurred in those fully vaccinated for age with 7-valent conjugate pneumococcal vaccines, by jurisdiction, Australia, 2003

	NSW	NT	Qld	SA	Tas	Vic	WA	Total
Number	0	6	5	1	0	0	0	12
Age range (years)	–	0–1y	0–1y	0–1y	–	–	–	0–1
Indigenous	–	5	4	0	–	–	–	9 (65%)
Risk factors present	–	5/6	1/5	–	–	–	–	6 (43%)
7-valent vaccination confirmed	–	6/6	5/5	0/1	–	–	–	11 (78%)
Serotypes in 7-valent vaccine/ number with known serotype	–	0/5	0/4	0/0	–	–	–	7/12 (58%)
Number of identified vaccine failures	0	0	0	0	0	0	0	0

Table 16. Details of the cases of invasive pneumococcal disease that occurred in those fully vaccinated for age with 23-valent pneumococcal vaccines, by jurisdiction, Australia, 2003

	NSW	NT	Qld	SA	Tas	Vic	WA	Total
Number	53	16	21	20	4	44	3	161
Age range (years)	51–91	21–57	2–80	44–90	21–88	46–90	12–48	2–91
Indigenous	1	16	15	1	0	0	2	35
Risk factors present	51	16	12	11	4	43	1	138
23-valent vaccination confirmed?*	53	16	21	0	0	48	1	135
Serotypes in 23-valent vaccine/ number with known serotype	37/43	8/16	12/21	11/20	4/5	37/43	1/3	110/151
Number of identified vaccine failures	37	8	12	11	4	37	0	109

Table 17. *S. pneumoniae* susceptibility to penicillin and ceftriaxone, New South Wales, Northern Territory, South Australia, Queensland, Tasmania and Western Australia, by jurisdiction

Antibiotic	Susceptibility	NSW	NT	Qld	SA	Tas	WA	Total
Penicillin	Resistant	14	0	18	0	0	1	33
	Intermediate	29	7	45	7	1	20	109
	Susceptible	346	64	384	101	42	114	1,051
	Total tested	389	71	447	108	43	135	1,193
	% reduced susceptibility	11%	9.8%	14.1%	6.4%	2.3%	15.5%	11.9%
Ceftriaxone	Resistant	NT	0	3	0	0	0	3
	Intermediate	NT	0	5	0	0	1	6
	Susceptible	NT	61	439	34	43	133	710
	Total tested	NT	61	447	34	43	134	719
	% reduced susceptibility	–	0%	1.8%	0%	0%	0.7%	1.3%

NT = not tested.

Trends in antibiotic susceptibility were examined in three years combined data from the Northern Territory, South Australia, Tasmania and Western Australia, 2001 to 2003 (Table 18). There were decreases in the number of non-susceptible isolates in the Northern Territory and South Australia, while the proportion of non-susceptible isolates remained almost constant in Tasmania and Western Australia.

There was a decline in penicillin non-susceptible strains in children under five years of age over the three years and a significantly lower proportion of isolates with reduced susceptibility to penicillin compared with isolates from older cases in 2003 (Table 18). In all three years, the rates of penicillin non-susceptible strains were higher in Non-Indigenous cases compared with Indigenous cases, but these differences did not reach statistical significance. There was a small decline in the proportion of penicillin resistant isolates that were in the 7-valent vaccine (92 % in 2001 to 84% in 2003) but the change in proportion was not statistically significant.

Susceptibility to ceftriaxone was less frequently measured. The overall proportion of non-susceptible strains fell from 5.1 per cent to 0.3 per cent over the three years. This decline was seen in non-Indigenous cases and in cases aged five years and older where the changes in proportion of ceftriaxone-non-susceptible strains between 2001 and 2003 were statistically significant. There was

Table 18. Characteristics of patients with non-susceptible pneumococcal isolates, Northern Territory, South Australia, Tasmania and Western Australia combined, 2001 to 2003

Penicillin	**2001**	**2002**	**2003**
Total number of cases with reduced susceptibility	55	41	36
Total cases tested	464	539	357
Percent non-susceptible isolates	11.8%	7.6%	10.1%
Proportion of cases under 5 years with reduced susceptibility	15/182 8.2%	13/191 6.8%	4/108 3.7%
Proportion of cases 5 years and older with reduced susceptibility	40/282 14.2%	28/348 8.0%	32/245 13.1%*
Proportion of Indigenous cases with reduced susceptibility	7/67 10.4%	6/ 82 7.3%	6/69 8.7%
Proportion of non-Indigenous cases with reduced susceptibility	48/362 13.3%	35/457 7.6%	30/284 10.6%
Proportion of cases with serotypes in 7-valent vaccine	49/53 92%	31/35 88%	30/32 94%
Proportion of cases in 23-valent vaccine	53/53 100%	35/35 100%	34/35 97%
Proportion of cases with reduced susceptibility vaccinated	2/55 3.6%	2/41 4.8%	3/36 8%
Ceftriaxone			
Total number of cases with reduced susceptibility	17	9	1
Total cases tested	332	372	272
Percent non-susceptible isolates	5.1%	2.4%	0.3%**
Proportion of cases under 5 years with reduced susceptibility	7/140 5%	4/191 2.1%	0/108 0%
Proportion of cases 5 years and older with reduced susceptibility	10/192 5.2%	5/181 2.8%	1/164† 0.6%
Proportion of Indigenous cases with reduced susceptibility	3/43 7%	2/82 2.4%	0/69 0%
Proportion of non-Indigenous cases with reduced susceptibility	14/289 4.8%	7/290 2.4%	1/203† 0.5%
Proportion of cases with serotypes in 7-valent vaccine	17/17 100%	8/8 100%	0 0%
Proportion of cases in 23-valent vaccine	17/17 100%	8/8 100%	1 100%
Proportion of all cases with reduced susceptibility vaccinated	2/17?	0/9?	0/1?

* Significant difference in proportions, between under 5 and ≥5 years in 2003 p<0.05.

† Significant change in proportions 2001 to 2003: ** p<0.01 † p<0.05.

only a single isolate of ceftriaxone non-susceptible pneumococci in 2003, which was a serogroup 1 from Western Australia in a non-Indigenous case (Table 18).

Discussion

Surveillance data in 2003 suggests a moderate impact of the 7vPCV vaccine on the incidence of IPD since the introduction of the vaccine program in Indigenous children in mid-2001. Evidence for this includes a decrease in the notification rates in Indigenous children under five years, (from 92 to 67 per 100,000 in males and 72 to 60 per 100,000 in females) and a decrease in the rate of disease caused by vaccine serotypes in Indigenous children (from 55% to 34%). A more marked effect on pneumococcal disease will be seen in Australia when a government-funded universal childhood pneumococcal vaccination program commences in January 2005.[9] Continued surveillance to assess whether non 7-valent vaccine serotypes will increase is supported by a suggestion of increase in the northern jurisdiction's Indigenous less than 2 year old populations. Additionally, Whitney *et al* have observed a decreasing incidence of IPD in older adults possibly via herd immunity following universal childhood 7vPCV immunisation in the USA.[10] The impact of the upcoming Australian childhood 7vPCV universal program might also provide herd immunity on other age groups—and therefore enhanced surveillance of all ages is strongly supported.

In 2005, free 23vPPV vaccine will be made available to all Australians aged 65 years and over. Vaccine 'failure' in recipients of the polysaccharide vaccine was noted in this and the two previous IPD surveillance reports.[7,8] There is a need for more data on apparent vaccine failure in the vaccinated elderly to inform re-vaccination schedules. The effectiveness of the polysaccharide vaccine in preventing invasive disease has been estimated at 53 per cent, implying that 20,000 vaccinations are needed to prevent one infection.[11,12] A universal vaccination program for elderly Australians should provide the vaccine coverage required to reduce the incidence of invasive disease in the elderly, which has not declined in the last three years. The need to provide re-vaccination for the elderly at high risk of IPD requires continual evaluation as there is limited data on the precise timing and effectiveness of re-vaccination. The 8th edition of the Australian Immunisation Handbook recommends re-vaccination in non-Indigenous adults aged less than 65 years with risk factors at 65 years or 10 years after the first dose, whichever comes later. Indigenous adults 15 to 49 years with risk factors* should be re-vaccinated five years after the first dose and again at age 50 or 10 years after the first re-vaccination, whichever comes later. Indigenous adults without risk factors should be re-vaccinated five years after initial vaccination.[9]

Ascertainment of IPD cases is necessary for effective surveillance. In Victoria a capture-recapture study in 2004 found, in addition to their 465 notified cases under enhanced surveillance there were 24 non-notified cases of IPD in 2003, largely from hospitals (M. Counahan, personal communication). This failure to notify public health authorities has been observed in the past in Australia [13] and recently in the United Kingdom.[14] Under reporting of cases may also result from changes in surveillance practice and should be taken into account when interpreting the data presented in this report.

Declines in the number of pneumococcal isolates with reduced susceptibility to penicillin and ceftriaxone between 2001 and 2003 in the Northern Territory and among Indigenous cases is important in view of the antibiotic resistance developing during the past 20 years. Reduction of transmission of resistant strains through immunisation of children and lower levels of disease and therefore lower antibiotic use should reduce antibiotic resistance in pneumococcal disease. Continuing high levels of resistance among non-invasive isolates, the lower vaccine efficacy against otitis media and the potential for increased non-vaccine serotype disease make the impact of vaccination on antibiotic resistance uncertain. However it is useful to note the reduction over the past three years in those five years and older with reduced susceptibility for both penicillin and ceftriaxone and the overall proportion of non-Indigenous cases with the reduced susceptibility to ceftriaxone where the majority of these groups are not receiving the 7-valent vaccine. Some of this decrease may relate to other strategies to reduce drug resistance.

As vaccination becomes more widely implemented, concern has been expressed about the incidence of non-vaccine serotype disease increasing. While a trend in this direction may be suggested by 2002–2003 data of the under two year old vaccine eligible Indigenous children it is important that the serotypes continue to be reported in order to ascertain whether this trend will continue reflects the natural fluctuations over time. Therefore, while the overall rates of IPD continue to fall this 'replacement phenomenon' may not pose any threat to disease control, but on-going surveillance and serotyping of all invasive isolates along with anti-microbial resistance patterns is essential.

* The Northern Territory recommend 23vPPV for all Indigenous people 15 and over.

References

1. Collignon PJ, Turnbridge JD. Antibiotic resistance in *Streptococcus pneumoniae. Med J Aust* 2000;173: S58–S64.

2. Turnidge JD, Bell JM, Collignon PJ. Rapidly emerging antimicrobial resistances in *Streptococcus pneumoniae* in Australia*. Med J Aust* 1999;170:152–155.

3. Craig AS, Erwin PC, Schaffner W, Elliott JA, Moore WL, Ussery XT*, et al.* Carriage of multidrug resistant *Streptococcus pneumoniae* and impact of chemoprophylaxis during an outbreak of meningitis at a day care centre*. Clin Infect Dis* 1999;29:1257–1264.

4. Nimmo GR, Bell JM, Collignon PJ. Fifteen years of surveillance by the Australian Group for Antimicrobial Resistance (AGAR)*. Comm Dis Intell* 2003;27 Supplement:S47–S54.

5. Douglas RM, Miles HB. Vaccination against *Streptococcus pneumoniae* in childhood:lack of demonstrable benefit in young Australian children*. J Infect Dis* 1984;149:861–869.

6. Black S, Shinefield H, Fireman B, Lewis E, Ray P, Hansen JR. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children*. Pediatr Infect Dis J* 2000;19:187–195.

7. Roche P, Krause V. Invasive pneumococcal disease in Australia, 2001*. Commun Dis Intell* 2002;26:505–519.

8. Roche P, Krause V, Andrews R, Carter L, Coleman D, Cook H*, et al.* Invasive pneumococcal disease in Australia, 2002*. Comm Dis Intell* 2003;27:466–477.

9. National Health and Medical Research. *The Australian Immunisation Handbook*. 8th edition. Canberra: NH&MRC;2003.

10. Whitney CG, Farley MM, Hadler J, Harrison LH, Bennett NM, Lynfield R*, et al.* Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine*. N Engl J Med* 2003;348:1737–1746.

11. Dear K, Holden J, Andrews R, Tatham D. Vaccines for preventing pneumococcal infections in adults*. The Cochrane Library* 2004;2.

12. Kelly H, Attia J, Andrews R, Heller RF. The number needed to vaccinate (NNV) and population estimates of the NNV:comparison of influenza and pneumococcal vaccine programmes for people aged 65 years and over*. Vaccine* 2004;22:2192–2198.

13. Robinson P. Meningococcal disease and the law: does non-notification really happen? *Commun Dis Intell* 1999;23:97–101.

14. Gjini A, Stuart JM, George RC, Nichols T, Heyderman RS. Capture-recpature analysis and pneumococcal meningitis estimates in England*. Emerg Infec Dis* 2004;10:87–93.