MAJOR ARTICLE

The Changing Epidemiology of Invasive Pneumococcal Disease in Aboriginal and Non-Aboriginal Western Australians from 1997 through 2007 and Emergence of Nonvaccine Serotypes

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Background. In 2001, Australia introduced a unique 7-valent pneumococcal conjugate vaccine (7vPCV) 2-, 4-, and 6-month schedule with a 23-valent pneumococcal polysaccharide vaccine (23vPPV) booster for Aboriginal children, and in 2005, 7vPCV alone in a 2-, 4-, and 6-month schedule for non-Aboriginal children. Aboriginal adults are offered 23vPPV but coverage is poor. We investigated trends in invasive pneumococcal disease (IPD) in Western Australia (WA).

Methods. Enhanced IPD surveillance has been ongoing since 1996. We calculated IPD incidence rates for Aboriginal and non-Aboriginal Australians before and after introduction of 7vPCV.

Results. A total of 1792 cases occurred during the period 1997–2007; the IPD incidence rate was 47 cases per 100,000 population per year among Aboriginal people and 7 cases per 100,000 population per year in non-Aboriginal people. After introduction of 7vPCV, IPD rates among Aboriginal children decreased by 46% for those <2 years of age and by 40% for those 2–4 years of age; rates decreased by 64% and 51% in equivalent age groups for non-Aboriginal children. IPD rates decreased by >30% in non-Aboriginal people ⩾50 years of age but increased among Aboriginal adults (eg, from 59.1 to 109.6 cases per 100,000 population per year among those 30–49 years of age). Although IPD due to 7vPCV serotypes decreased in all age groups, IPD incidence due to non-7vPCV serotypes increased, and it almost doubled among Aboriginal adults 30–49 years of age (from 48.3 to 97.0 cases per 100,000 population per year). Among non-Aboriginal children, 37% of IPD is now due to serotype 19A.

Conclusions. IPD incidence rates have decreased markedly among children and non-Aboriginal adults with a 3-dose infant 7vPCV schedule. However, IPD due to non-7vPCV serotypes has increased and is of particular concern among young Aboriginal adults, for whom an intensive 23vPPV campaign is needed. An immunization register covering all age groups should be established.

Streptococcus pneumoniae is a major cause of pneumonia, meningitis, and septicemia. Invasive pneumococcal disease (IPD, defined as disease associated with identification of pneumococcus in a normally sterile site) is responsible for an estimated 1.6 million deaths annually, the majority of which occur in the developing world [1]. In industrialized countries, indigenous people experience higher rates of IPD than do nonindigenous people and, in contrast to IPD rates among nonindigenous people, IPD rates remain high among young indigenous adults [2–5].

In Australia, a pneumococcal polysaccharide vaccine (23vPPV; Pneumovax [Merck]) covering 23 of the 91 known pneumococcal serotypes that commonly cause disease (serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A,

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11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F) has been available since 1986 for people at increased risk of developing IPD. A funded 23vPPV immunization program commenced in 1999 for Aboriginal Australians aged ⩾50 years or aged 15–49 years with a high risk of IPD [6]. Since January 2005, 23vPPV has been funded for non-Aboriginal Australians aged ⩾65 years [7]. There is no register documenting vaccinations after the age of 7 years. In Western Australia (WA), 23vPPV coverage is estimated to be only 9% among Aboriginal adults aged 18–49 years with known risk factors and 31% for those aged 50–64 years [8].

Heptavalent pneumococcal conjugate vaccine (7vPCV; Prevenar [Wyeth Pharmaceuticals]; serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) is safe and efficacious in young children when given at 2, 4, and 6 months of age with a booster at 12–15 months [9]. Australia has a unique 2-, 4-, and 6-month schedule with no 7vPCV booster in the second year of life. This was based on data available in 2001 from North America and the United Kingdom that indicated adequate protection with 3 doses [9, 10]. The 7vPCV program was funded from July 2001 for Aboriginal and Torres Strait Islander children <2 years of age, non-Aboriginal children <2 years of age living in Central Australia, and for all children <5 years of age with predisposing medical conditions (eg, immune deficiencies, cardiac disease, and chronic lung disease). Aboriginal and Torres Strait Islander children also receive a 23vPPV booster at 18 months of age in view of the broad range of serotypes causing IPD in this population [11]. A catch-up schedule was implemented up to 5 years or 2 years of age for children with or without predisposing medical conditions, respectively. From January 2005, 7vPCV has been funded for all Australian children [7]. In 2005, vaccination coverage of 3 doses of 7vPCV in WA was 75% for Aboriginal children and 88% for non-Aboriginal children [8]. In 2004, 23vPPV coverage among Aboriginal and Torres Strait Islander children in WA was 41% (B. Hull, personal communication).

Post-licensure studies of 7vPCV have shown remarkable decreases in IPD incidence among both indigenous and nonindigenous children [3, 6, 12–15]. Furthermore, 7vPCV programs have led to decreases in IPD rates in unvaccinated infants and adults as a result of herd immunity from reduced nasopharyngeal carriage and transmission of vaccine serotypes [12, 16–18]. However, there have also been reports of increased rates of IPD due to non-7vPCV serotypes [18–23]. Of particular relevance to the Australian Aboriginal population has been the marked increase in IPD due to serotype 19A in the Alaska Native population [23]. Serotype 19A has also recently emerged as the predominant cause of IPD in WA's non-Aboriginal population but, in contrast with elsewhere, in WA it is not an antibiotic-resistant strain [24–27].

Enhanced surveillance of IPD has been ongoing in WA since 1996 through the Vaccine Impact Surveillance Network. We previously reported a reduction between the period 1996–2001 and the period 2002–2005 in both IPD incidence and the disparity between Aboriginal and non-Aboriginal children associated with the introduction of 7vPCV for Aboriginal children. We found no increase in IPD due to nonvaccine serotypes in the first year of universal 7vPCV vaccination [3]. To determine the longer term impact of 7vPCV and 23vPPV immunization programs, we report here the trends in IPD incidence among Aboriginal and non-Aboriginal people of all ages in WA over an extended period (1997–2007).

METHODS

Setting. WA covers an area of ~2.5 million km^2 and has a population of 2.2 million, 3.5% of whom identify as Aboriginal or Torres Strait Islander (hereafter referred to as Aboriginal). In WA, life expectancy is 14 years less for Aboriginal men and 13 years less for Aboriginal women than it is in the corresponding non-Aboriginal population [28].

IPD surveillance. IPD became notifiable in 2001. Methods for surveillance have been described in detail elsewhere [3] and have not changed over time. In brief, IPD cases were identified via an enhanced surveillance system involving all public and private hospitals in WA. Demographic, clinical, vaccination, and risk factor data were collected. Serotypes causing IPD were classified as vaccine serotypes (VTs) if the serotype was included in the vaccine under discussion (7vPCV or 23vPPV), vaccine-related serotypes (VRTs) if the serotype belonged to the same serogroup but a different factor type (eg, 19A related to 19F in 7vPCV), or nonvaccine serotypes (NVT) for unrelated serotypes.

Laboratory methods. Pneumococci were identified using standard laboratory methods [29]. All isolates were serotyped and factor-typed by the Quellung reaction at the Queensland Health Microbiology Reference Laboratory using commercial antisera obtained from the Statens Seruminstitut.

Analysis. Age-specific IPD incidence rates were calculated for the Aboriginal and non-Aboriginal populations. Annual population estimates were derived from the Australian Bureau of Statistics 2006 census data [30]. IPD notifications were grouped into 3 time periods: 1997–2001 to reflect the pre-7vPCV era (coverage was limited in 2001); 2002–2004, the period after 7vPCV introduction for Aboriginal children and with limited availability of 7vPCV for non-Aboriginal children; and 2005–2007, the period of the universal 7vPCV program in Australia. EpiBasic, version 1.0, was used for descriptive analysis. Incidence rate ratios (IRRs) with 95% confidence intervals (CIs) were used to compare groups of interest.

Ethical approval to conduct the study was given by the Princess Margaret Hospital for Children Ethics Committee and the

Table 1. Incidence of Invasive Pneumoccoccal Disease in the Western Australian Aboriginal population, 1997–2007

	Rate, cases per 100,000 population per year (no. of cases)			Incidence rate ratio (95% confidence interval)		
Serotypes, age group	1997–2001	2002–2004	2005–2007	2002–2004 vs 1997–2001	2005–2007 vs 1997–2001	2005–2007 vs 2002–2004
7vPCV serotypes[a]						
<2 Years	118.5 (20)	71.5 (7)	10.8 (1)	0.60 (0.2–1.5)	0.09 (0.0–0.6)	0.15 (0.0–1.2)
2–4 Years	30.2 (8)	26.2 (4)	0 (0)	0.87 (0.2–3.2)	…	…
5–14 Years	7.3 (6)	3.9 (2)	9.6 (5)	0.53 (0.1–3.0)	1.30 (0.3–5.1)	2.47 (0.4–25.9)
15–29 Years	4.7 (4)	7.2 (4)	5.0 (3)	1.53 (0.3–8.2)	1.06 (0.1–6.2)	0.69 (0.1–4.1)
30–49 Years	15.8 (12)	13.5 (7)	7.2 (4)	0.86 (0.3–2.4)	0.46 (0.1–1.5)	0.53 (0.1–2.1)
50–64 Years	18.9 (4)	12.7 (2)	10.8 (2)	0.67 (0.1–4.7)	0.67 (0.1–4.7)	0.85 (0.1–11.7)
⩾65 Years	11.8 (1)	0 (0)	0 (0)	…	…	…
Overall	17.4 (55)	12.6 (26)	6.9 (15)	0.72 (0.4–1.2)	0.40 (0.2–0.7)	0.55 (0.3–1.0)
Non–7vPCV serotypes[a]						
<2 Years	65.2 (11)	51.0 (5)	86.4 (8)	0.78 (0.2–2.4)	1.32 (0.5–3.6)	1.69 (0.5–6.6)
2–4 Years	7.6 (2)	26.2 (4)	27.3 (4)	3.47 (0.5–38.3)	3.62 (0.5–40.0)	1.04 (0.2–5.6)
5–14 Years	13.5 (11)	5.8 (3)	9.6 (5)	0.43 (0.1–1.6)	0.71 (0.2–2.2)	1.64 (0.3–10.6)
15–29 Years	10.6 (9)	16.2 (9)	28.2 (17)	1.53 (0.5–4.4)	2.66 (1.1–6.7)	1.74 (0.7–4.4)
30–49 Years	36.8 (28)	48.3 (25)	97.0 (54)	1.31 (0.7–2.3)	2.64 (1.6–4.3)	2.01 (1.2–3.4)
50–64 Years	42.5 (9)	57.1 (9)	75.5 (14)	1.34 (0.5–3.8)	1.78 (0.7–4.7)	1.32 (0.5–3.5)
⩾65 Years	35.3 (3)	31.6 (2)	12.9 (1)	0.90 (0.1–7.8)	0.37 (0.0–4.6)	0.41 (0.0–7.9)
Overall	23.4 (74)[c]	27.7 (57)	47.3 (103)	1.18 (0.8–1.7)	2.02 (1.5–2.8)	1.71 (1.2–2.4)
All cases[b]						
<2 Years	201.5 (34)	132.7 (13)	107.9 (10)	0.66 (0.3–1.3)	0.54 (0.2–1.1)	0.81 (0.2–1.1)
2–4 Years	45.3 (12)	72.0 (11)	27.3 (4)	1.59 (0.6–3.9)	0.6 (0.1–2.0)	0.38 (0.0–1.2)
5–14 Years	20.8 (17)	11.6 (6)	21.0 (11)	0.56 (0.2–1.5)	1.01 (0.4–2.3)	1.81 (0.6–6.0)
15–29 Years	17.7 (15)	23.4 (13)	33.2 (20)	1.33 (0.6–3.0)	1.88 (0.7–3.1)	1.42 (0.7–3.1)
30–49 Years	59.1 (45)	63.8 (33)	109.6 (61)	1.08 (0.7–1.7)	1.85 (1.2–2.8)	1.72 (1.1–2.7)
50–64 Years	61.4 (13)	76.1 (12)	86.3 (16)	1.24 (0.5–2.9)	1.41 (0.6–3.2)	1.13 (0.5–2.6)
⩾65 Years	47.1 (4)	47.5 (3)	12.9 (1)	1.01 (0.2–6.0)	0.27 (0.0–2.8)	0.27 (0.0–3.4)
Overall	44.6 (141)[c]	44.1 (91)	56.4 (123)	1.00 (0.8–1.3)	1.27 (1.0–1.6)	1.28 (1.0–1.7)

NOTE. 7vPCV, 7-valent pneumococcal conjugate vaccine; 23vPPV, 23-valent pneumococcal polysaccharide vaccine.

[a] Only cases with known serotype.

[b] All cases, including 20 cases due to pneumococci with unknown serotype and 5 cases due to nonserotypeable strains.

[c] Includes 1 case with missing date of birth.

Confidentiality of Health Information Committee of the Health Department of WA.

RESULTS

Incidence of invasive pneumococcal disease. A total of 1792 cases of IPD (male sex, 990 cases; female sex, 795 cases; unknown sex, 7 case) were reported in WA from January 1997 through December 2007, giving an average annual IPD incidence rate of 8.4 cases per 100,000 population. Ethnicity was documented for 99% of cases; the 24 cases with unknown ethnicity were excluded from further analysis. The average annual IPD rate was 6.7 times higher in the Aboriginal population (47 cases per 100,000 population) than it was in the non-Aboriginal population (7 cases per 100,000 population per year) and 20% ($n = 355$) of all IPD cases occurred in Aboriginal people, although they account for only 3.5% of the population.

Age-specific incidence rates were higher among Aboriginal than among non-Aboriginal people <65 years of age (Tables 1 and 2; Figure 1). IPD incidence rates in the non-Aboriginal population were highest among children <2 years of age, children 2–4 years of age, and adults ⩾65 years of age (Table 2; Figure 1). In the Aboriginal population, rates were highest among those <2 years of age and 30–64 years of age. The low incidence among Aboriginal people aged ⩾65 years reflects the low life expectancy in this population and survival bias.

Between the period 1997–2001 and the period 2005–2007, IPD rates decreased by 46% in Aboriginal children <2 years of age and by 40% in those 2–4 years of age. In contrast, rates in those ⩾5 years of age increased in all but 1 age group, the most marked being an 85% increase from 59.1 cases per 100,000 population per year during 1997–2001 to 109.6 cases per 100,000 population per year during 2005–2007 in the 30–49-

Table 2. Incidence of Invasive Pneumoccoccal Disease in the Western Australian Non-Aboriginal population, 1997–2007

	Rate, cases per 100,000 population per year (no. of cases)			Incidence rate ratio (95% confidence interval)		
Serotypes, age group	1997–2001	2002–2004	2005–2007	2002–2004 vs 1997–2001	2005–2007 vs 1997–2001	2005–2007 vs 2002–2004
7vPCV serotypes[a]						
<2 Years	61.2 (142)	55.5 (76)	6.6 (9)	0.91 (0.7–1.2)	0.11 (0.1–0.2)	0.12 (0.1–0.2)
2–4 Years	17.9 (65)	15.5 (33)	4.2 (9)	0.87 (0.6–1.3)	0.24 (0.1–0.5)	0.27 (0.1–0.6)
5–14 Years	2.3 (29)	1.0 (8)	0.5 (4)	0.46 (0.2–1.0)	0.23 (0.1–0.7)	0.50 (0.1–1.9)
15–29 Years	1.6 (31)	2.1 (25)	0.7 (8)	1.33 (0.8–2.3)	0.41 (0.2–0.9)	0.31 (0.1–0.7)
30–49 Years	1.4 (38)	3.2 (55)	1.3 (22)	2.33 (1.5–3.6)	0.91 (0.5–1.5)	0.39 (0.2–0.7)
50–64 Years	3.4 (46)	5.3 (51)	2.8 (30)	1.57 (1.0–2.4)	0.84 (0.5–1.4)	0.54 (0.3–0.9)
⩾65 Years	12.6 (124)	12.7 (84)	6.5 (47)	1.01 (0.8–1.3)	0.52 (0.4–0.7)	0.51 (0.4–0.7)
Overall	5.3 (476)[b]	5.9 (332)	2.2 (129)	1.11 (1.0–1.3)	0.42 (0.3–0.5)	0.38 (0.3–0.5)
Non–7vPCV serotypes[a]						
<2 Years	9.1 (21)	7.3 (10)	13.9 (19)	0.81 (0.3–1.8)	1.54 (0.8–3.0)	1.91 (0.8–4.6)
2–4 Years	2.5 (9)	2.8 (6)	4.2 (9)	1.14 (0.3–3.6)	1.71 (0.6–4.9)	1.5 (0.5–5.1)
5–14 Years	0.5 (6)	0.9 (7)	1.2 (9)	1.93 (0.6–7.0)	2.48 (0.8–8.5)	1.28 (0.4–4.1)
15–29 Years	0.8 (15)	0.5 (6)	0.7 (9)	0.66 (0.2–1.8)	0.96 (0.4–2.4)	1.47 (0.5–5.0)
30–49 Years	1.2 (34)	0.8 (14)	1.3 (23)	0.66 (0.3–1.3)	1.07 (0.6–1.9)	1.61 (0.8–3.4)
50–64 Years	1.0 (14)	2.8 (27)	2.3 (24)	2.72 (1.4–5.6)	2.21 (1.1–4.6)	0.81 (0.5–1.5)
⩾65 Years	5.8 (57)	5.6 (37)	5.8 (42)	0.96 (0.6–1.5)	1.00 (0.7–1.5)	1.04 (0.7–1.7)
Overall	1.7 (156)	1.9 (107)	2.3 (135)	1.08 (0.8–1.4)	1.32 (1.0–1.7)	1.21 (0.9–1.6)
All cases[c]						
<2 Years	73.8 (171)	68.0 (93)	24.2 (33)	0.92 (0.7–1.2)	0.33 (0.2–0.5)	0.36 (0.2–0.5)
2–4 Years	21.2 (77)	20.2 (43)	9.9 (21)	0.09 (0.6–1.4)	0.47 (0.3–0.8)	0.49 (0.3–0.8)
5–14 Years	2.8 (29)	2.3 (18)	1.7 (13)	0.83 (0.4–1.5)	0.60 (0.3–1.2)	0.72 (0.3–1.6)
15–29 Years	2.4 (47)	2.7 (32)	1.5 (18)	1.12 (0.7–1.8)	0.62 (0.3–1.1)	0.55 (0.3–1.6)
30–49 Years	2.8 (78)	4.1 (70)	2.7 (47)	1.44 (1.0–2.0)	0.95 (0.7–1.4)	0.66 (0.4–1.0)
50–64 Years	4.7 (64)	8.3 (80)	5.1 (54)	1.77 (1.3–2.5)	1.09 (0.7–1.6)	0.62 (0.4–0.9)
⩾65 Years	19.9 (196)	19.2 (127)	13.0 (94)	0.96 (0.8–1.2)	0.65 (0.5–0.8)	0.68 (0.5–0.9)
Overall	7.5 (670)[b]	8.2 (463)	4.8 (280)	1.09 (1.0–1.2)	0.64 (0.6–0.7)	0.58 (0.5–0.7)

NOTE. 7vPCV, 7-valent pneumococcal conjugate vaccine; 23vPPV, 23-valent pneumococcal polysaccharide vaccine.

[a] Only cases with known serotype.

[b] Includes 1 case with missing date of birth.

[c] All cases, including 70 cases due to pneumococci with unknown serotype and 8 cases due to nonserotypeable strains.

year-old age group (Table 1). Incidence rates among 30–64-year-old non-Aboriginal adults were higher during 2002–2004 than during 1997–2001. Thereafter, IPD incidence decreased in all age groups (Table 2). From the period 2002–2004 to the period 2005–2007, IPD incidence rates decreased by 64% and 51% in non-Aboriginal children <2 years of age and 2–4 years of age, respectively, and by >30% in those ⩾50 years of age.

The IRR between Aboriginal and non-Aboriginal people increased from 6.0 during 1997–2001 and 5.4 during 2002–2004 to 11.8 during 2005–2007. IRRs between Aboriginal and non-Aboriginal people were highest in 30–49-year-olds during 2005–2007 (IRR, 40.9; 95% CI, 27.5–61.2) and lowest among children <2 years of age during 2002–2004 (IRR, 2.0; 95% CI, 1.0–3.5) and adults aged ⩾65 years during 2005–2007 (IRR, 0.99; 95% CI, 0.02–5.7).

Serotype data. Serotype was known for 1689 IPD cases (94%). An additional 13 isolates (0.7%) were nonserotypeable strains. Before introduction of 7vPCV, the serotypes in this vaccine accounted for 87% of serotypeable pneumococci in non-Aboriginal children <5 years of age and 68% of serotypeable pneumococci in Aboriginal children (Table 3). Equivalent figures in adults ⩾15 years of age were 67% and 30%, respectively (Table 4). After introduction of 7vPCV, rates of IPD due to 7vPCV serotypes decreased for both Aboriginal and non-Aboriginal populations. From the period 1997–2001 to the period 2005–2007, IPD rates due to 7vPCV serotypes decreased by 94% (IRR, 0.06; 95% CI, 0.0–0.4) in Aboriginal children <5 years of age (Table 1) and by 86% (IRR, 0.14; 95% CI, 0.1–0.2) in non-Aboriginal children (Table 2). In people ⩾15 years of age, between the period 2002–2004 and the period 2005–

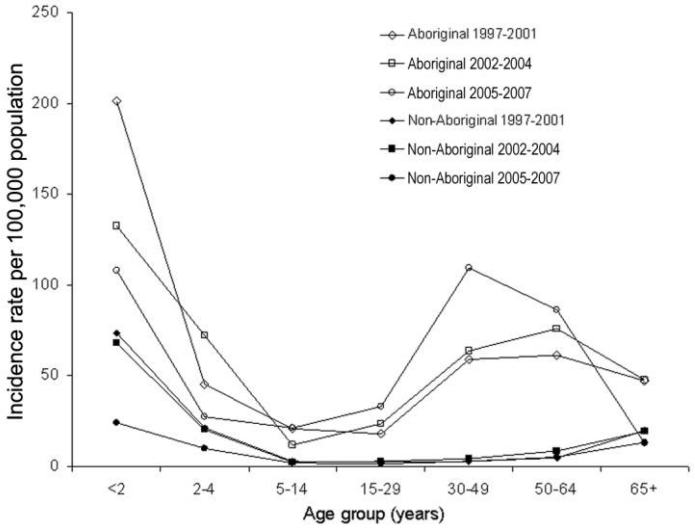

Figure 1. Age-specific incidence rates of all invasive pneumococcal disease in Aboriginal and non-Aboriginal populations during 1997–2001, 2002–2004, and 2005–2007.

2007, rates of IPD due to 7vPCV serotypes decreased by 53% in the non-Aboriginal population (IRR, 0.47; 95% CI, 0.4–0.6) and by 35% in the Aboriginal population (IRR, 0.65; 95% CI, 0.2–1.6).

In contrast, rates of disease due to non-7vPCV serotypes increased during the period 2005–2007 in most age groups (Tables 1 and 2). Between the period 2002–2004 and the period 2005–2007, non-7vPCV IPD rates increased by 40% in Aboriginal children <5 years of age, from 35.9 cases per 100,000 population (95% CI, 16.4–68.1) to 50.2 cases per 100,000 population (95% CI, 25.9–87.7), and by 74% in non-Aboriginal children of the same age, from 4.6 cases per 100,000 population (95% CI, 2.6–7.4) to 8.0 cases per 100,000 population (95% CI, 5.3–11.6). The most marked increase in incidence was among Aboriginal adults 30–49 years of age, for whom non-7vPCV IPD rates doubled between the period 2002–2004 and the period 2005–2007 (from 48.3 [95% CI, 31.3–71.3] to 97.0 [95% CI, 72.9–126.6] cases per 100,000 population; Table 1). No such increase was seen among young non-Aboriginal adults.

In children <5 years of age, serotype 19A accounted for much of the increase in IPD due to non-7vPCV serotypes (Table 3). During 2005–2007, the rate of IPD due to serotype 19A was 12.6 cases per 100,000 (95% CI, 2.6–36.7) in Aboriginal children and 4.9 cases per 100,000 population (95% CI, 2.8–7.8) in non-Aboriginal children, compared with 8.0 cases per 100,000 population (95% CI, 1.0–28.8) in Aboriginal and 0.6 cases per 100,000 population (95% CI, 0.1–2.1) in non-Aboriginal children during the period 2002–2004. In Aboriginal adults ⩾15 years of age, the rate of IPD caused by the non-7vPCV serotypes included in 23vPPV increased by 66%, from 24.5 cases per 100,000 population (95% CI, 16.6–34.8) during 2002–2004 to 40.7 cases per 100,000 population (95% CI, 30.7–53.0) during 2005–2007 (Figure 2), whereas rates of IPD due to serotypes not included in 23vPPV also increased by >200%, from 11.1 (95% CI, 6.1–18.6) to 23.0 (95% CI, 15.6–32.6) cases per 100,000 population over the same period. The increase in IPD in Aboriginal adults was primarily due to increases in disease caused by serotypes 3, 7F, 8, 10F, 18A, and 19A (Table 4). In non-Aboriginal adults ⩾65 years of age, the rate of IPD due to the non-7vPCV serotypes included in 23vPPV remained constant (4.0 cases per 100,000 population during 1997–2001, 3.3 cases per 100,000 population during 2002–2004, and 4.6 cases per 100,000 population during 2005–2007), as did the rate for non-23vPPV serotypes.

Case fatality. Outcome at the time of hospital discharge was known for 1757 (99.4%) of the 1768 patients with IPD with known ethnicity and age. The overall case fatality rate (CFR) was 10.6% (186 deaths among 1757 patients), and there was no difference between Aboriginal and non-Aboriginal people. There were 12 known deaths (2.7%) among non-Aboriginal children <5 years of age and 1 known death among Aboriginal children <5 years of age (1.2%). As the number of IPD cases decreased, the CFR for children aged <5 years increased from 1.1% (3 deaths among 294 children) during 1997–2001 to 1.9% (3 deaths among 160 children) during 2002–2004 and 10.3% (7 deaths among 68 children) during 2005–2007 (χ^2, 19.92, 2df; $P < .001$). One case in 2001, another in 2003, and 6 from 2005 through 2007 were diagnosed postmortem; all these cases occurred among non-Aboriginal children. The CFR in those ⩾5 years of age was 11.7% (31 deaths among 266 patients) for Aboriginal people and 14.7% (142 deaths among 969 patients) for non-Aboriginal people, with no change over time.

Vaccine failures. Three fully vaccinated Aboriginal children (defined as receipt of 3 doses of 7vPCV and 1 dose of 23vPPV)

Table 3. Number (%) of Serotypes from Cases in Children <5 Years of Age, 1997–2007

Serotype	Aboriginal patients			Non-Aboriginal patients		
	1997–2001 (*n* = 41)	2002–2004 (*n* = 20)	2005–2007 (*n* = 13)	1997–2001 (*n* = 237)	2002–2004 (*n* = 125)	2005–2007 (*n* = 46)
7vPCV serotypes						
4	3	1	…	9	6	1
6B	3	2	…	29	22	2
9V	0	1	…	7	10	…
14	8	1	1	95	49	8
18C	9	2	…	22	8	1
19F	2	3	…	36	9	2
23F	3	1	…	9	5	4
Subtotal	28 (68.3)	11 (55.0)	1 (7.7)	207 (87.3)	109 (87.2)	18 (39.1)
7vPCV vaccine related serotypes						
6A	1	1	1	8	5	2
9N	…	…	…	…	1	…
18A	…	1	…	…	…	1
18B	…	…	…	1	…	…
19A	4	2	3	7	2	17
23B	1	…	…	…	…	…
Subtotal	6 (14.6)	4 (20.0)	4 (30.8)	16 (6.8)	8 (6.4)	20 (43.4)
7vPCV nonvaccine serotypes						
1	2	…	1	1	…	…
3	…	…	…	2	1	…
5	2	…	…	1	…	…
7F	1	1	1	1	…	…
8	…	…	…	1	…	1
10A	…	…	2	1	1	1
10F	…	…	2	…	…	…
11A	…	…	…	1	1	2
12F	2	…	…	1	…	…
13	…	…	1	…	…	…
15B	…	1	…	1	…	2
15C	…	…	…	1	…	2
16F	…	…	…	1	…	…
22F	…	1	…	…	2	…
29	…	1	…	…	…	…
33F	…	…	…	1	…	…
35B	…	…	1	…	2	…
38	…	1	…	1	1	…
Subtotal	7 (17.1)	5 (25.0)	8 (61.5)	14 (5.9)	8 (6.4)	8 (17.4)

NOTE. During 1997–2007, 3 cases were due to nonserotypeable pneumococci (1 in an Aboriginal and 2 in non-Aboriginal patients), and serotype was unknown for 37 cases (9 in Aboriginal and 28 in non-Aboriginal patients). 7vPCV, 7-valent pneumococcal conjugate vaccine; 23vPPV, 23-valent pneumococcal polysaccharide vaccine.

developed IPD; 2 cases were due to serotype 19A (patient age, 3 years), and 1 case was due to serotype 8 (patient age, 5 years). Two 6-year-old Aboriginal children developed IPD (due to serotypes 7F and 14) after receipt of the recommended catch-up schedule of 2 doses of 7vPCV and 1 dose of 23vPPV. Two fully vaccinated non-Aboriginal children developed IPD: a 1-year-old child with infection due to serotype 18C, and a 2-year-old child with infection due to serotype 19F. Nine Aboriginal adults (1 each with infection due to serotypes 1, 3, 18C, 10A, and 23F and 2 each with infection due to serotypes 7F and 19F) and 5 non-Aboriginal adults (1 with infection due to serotype 6B and 2 each with infection due to serotypes 9V and 14) developed IPD within 5 years after receiving 1 or more doses of 23vPPV. There were an additional 4 IPD cases that occurred in Aboriginal adults (due to serotypes 8, 17F, 9N, and 19A) and 1 case that occurred in a non-Aboriginal adult (due to serotype

Table 4. Number (%) of Serotypes from Cases in Adults ⩾15 Years of Age, 1997–2007

Serotype	Aboriginal patients			Non-Aboriginal patients		
	1997–2001 (n = 70)	2002–2004 (n = 58)	2005–2007 (n = 95)	1997–2001 (n = 359)	2002–2004 (n = 299)	2005–2007 (n = 205)
Both 7vPCV and 23vPPV serotypes						
4	1	4	6	36	47	16
6B	2	…	…	33	25	25
9V	4	2	…	38	29	12
14	2	…	…	67	66	24
18C	3	6	…	9	6	11
19F	6	…	2	22	16	7
23F	3	1	1	34	26	12
Subtotal	21 (30.0)	13 (22.4)	9 (9.5)	239 (66.6)	215 (71.9)	107 (52.2)
23vPPV serotypes only						
1	9	3	4	13	2	1
2	…	…	…	…	…	…
3	3	4	8	19	16	13
5	2	…	…	3	4	2
7F	3	9	9	…	…	…
8	2	1	8	7	1	3
9N	1	3	3	14	8	6
10A	1	…	2	2	2	1
11A	4	2	1	2	5	7
12F	2	…	4	1	1	1
15B	…	…	…	2	2	2
17F	…	1	2	4	3	5
19A	2	4	6	13	11	23
20	…	…	1	…	…	…
22F	2	1	4	8	7	12
33F	2	3	3	2	…	3
Subtotal	33 (47.1)	31 (53.4)	55 (57.9)	90 (25.1)	62 (20.7)	79 (38.5)
Nonvaccine serotypes						
6A	4	4	2	11	10	11
7C	1	1	2	1	…	…
9A	…	…	1	…	…	…
10F	1	…	6	…	1	…
13	1	…	1	…	1	…
15A	1	…	1	…	…	…
15C	…	…	…	…	2	1
16A	…	…	…	1	…	…
16F	1	…	2	5	3	1
18A	…	3	6	…	…	…
18F	…	…	…	2	…	…
22A	1	1	1	5	1	2
23A	…	1	3	…	…	…
23B	…	…	1	…	…	…
29	1	1	…	…	…	…
31	2	2	…	…	…	…
33B	2	…	…	…	…	1
34	…	…	1	…	3	1
35B	1	1	4	2	…	…
35F	…	…	…	2	…	2
38	…	…	…	1	1	…
Subtotal	16 (22.9)	14 (24.1)	31 (32.6)	30 (8.4)	22 (7.4)	19 (9.3)

NOTE. During 1997–2007, there were 9 cases of invasive pneumoccoccal disease that were nonserotypeable (3 in Aboriginal and 6 in non-Aboriginal patients), and serotype was unknown for 48 cases (10 in Aboriginal and 38 in non-Aboriginal patients). 7vPCV, 7-valent pneumococcal conjugate vaccine; 23vPPV, 23-valent pneumococcal polysaccharide vaccine.

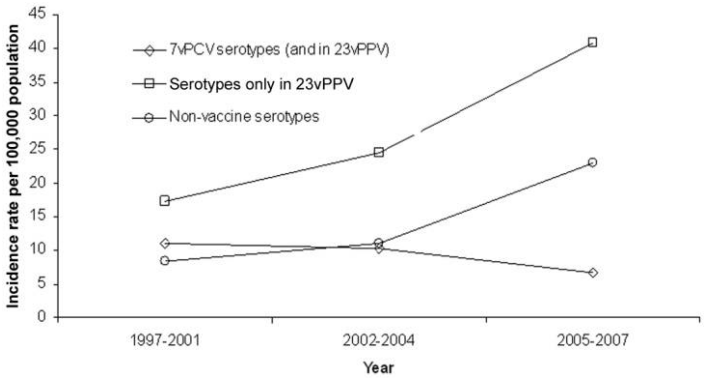

Figure 2. Incidence rate of invasive pneumococcal disease due to pneumococcal serotypes included in both 7-valent pneumococcal conjugate vaccine (7vPCV) and 23-valent pneumococcal polysaccharide vaccine (23vPPV), serotypes included in 23vPPV but not in 7vPCV, and serotypes in neither vaccine among Aboriginal adults >15 years of age.

6B) who received 23vPPV >5 years before onset of disease. All adults who developed IPD after receiving 23vPPV had risk factors that predisposed them to IPD.

DISCUSSION

Following the staggered introduction of 7vPCV to the WA childhood immunization program, we have seen marked decreases in overall IPD rates in Aboriginal and non-Aboriginal children and decreases in non-Aboriginal adults. The decrease in incidence of IPD due to 7vPCV serotypes in Aboriginal and non-Aboriginal adults is evidence of a herd effect following introduction of 7vPCV in children. However, we have also seen an increase in incidence rates of IPD due to non-7vPCV types in non-Aboriginal children and Aboriginal adults, a marked increase in overall IPD incidence in Aboriginal adults, particularly in those 30–49 years of age, and an increasing disparity in recent years between the rates of IPD in Aboriginal and non-Aboriginal populations.

The decrease in IPD rates in children <5 years of age is consistent with findings elsewhere [23, 31–33], although the overall reduction in IPD incidence immediately following introduction of a 7vPCV program was greater in the non-Aboriginal than in the Aboriginal population. This was also the case in Alaska [23] and can be attributed to the broader range of serotypes causing IPD in indigenous populations, compared with non-indigenous populations. Our findings are also consistent with reports from other parts of Australia, where IPD due to 7vPCV serotypes has been virtually eradicated among Aboriginal children [19, 34]. The incidence of IPD due to 7vPCV serotypes in WA Aboriginal children now approximates the rate in non-Aboriginal children.

We found an increase in IPD incidence among non-Aboriginal adults from the period 1997–2001 to the period 2002–2004 (before the universal 7vPCV program). This could be attributable to improved surveillance at nonteaching hospital laboratories after IPD became notifiable in 2001, although this assumes little change in surveillance practices for children over the same time period, because the incidence rate in children remained steady. There was no outbreak of infection due to a particular serotype at the time.

Improved surveillance is unlikely to be the reason for the increasing incidence in IPD seen among young Aboriginal adults in view of the simultaneous sharp decrease in IPD incidence among Aboriginal children. There are several possible reasons for this increase in incidence. First, this could be a result of natural fluctuations of disease incidence or a virulent serotype, such as serotype 8, causing an outbreak [35]. However, we found no evidence of an outbreak of infection due to a particular serotype. Second, serotype replacement is likely to have contributed to the increase in IPD incidence among Aboriginal adults. An increase in IPD incidence after introduction of 7vPCV in children has been reported among Alaska Native adults (although the increase is not as marked as that in WA) [23] and in the general Calgary population [20]. The latter was in part associated with an outbreak of serotype 5 disease among homeless middle-aged illicit drug users, but there was also an increase in disease due to serotypes 8 and 19A [20]. It is interesting that limited serotype replacement has been seen in Aboriginal children in WA despite high carriage rates of non-vaccine serotypes in Aboriginal children [36]. In mid-2008, we began carriage studies in WA Aboriginal communities and found that 85%–90% of carriage isolates in adults and children are now non-7vPCV serotypes (unpublished data). The 23vPPV booster at 18 months may be preventing severe pneumococcal disease due to non-7vPCV serotypes in children 2–4 years of age.

Third, 23vPPV could have a deleterious effect among people who may be immunocompromised because of their multiple risk factors and co-morbidities [37, 38], and repeated doses of 23vPPV may lead to hyporesponsiveness [39]. However, this is

unlikely to be the case among Aboriginal adults in WA, because the incidence of IPD due to both non-23vPPV and non-7vPCV 23vPPV serotypes increased. Furthermore, the estimated 23vPPV coverage is poor in this population.

Finally, high rates of co-morbidities in this population could contribute to the increase in IPD incidence. However, co-morbidity rates have not increased over time (data not shown). Because studies have consistently shown 23vPPV to protect against IPD in healthy young adults [40], a vaccination campaign is urgently needed to vaccinate young Western Australian Aboriginal adults before they experience serious consequences of co-morbidities.

There are some limitations to our study. Despite the same surveillance methods being used throughout the study period, it is possible that surveillance was not optimal during the first few years, and this may have resulted in under-reporting of IPD during the period 1997–2001. Difficulties in obtaining blood cultures before antibiotic therapy is initiated in remote regions (where 42% of Aboriginal people reside [30]) also contribute to likely under-ascertainment of IPD rates in Aboriginal populations. Differentiation between serotype 6A and 6C is currently underway. Finally, when disaggregating data by Aboriginality to compare pre- and post-vaccine IPD rates, case numbers are small, which increases the likelihood of a type II error.

In summary, through enhanced surveillance, we have shown that a 3-dose 7vPCV schedule with no 7vPCV booster reduces IPD incidence in both Aboriginal and non-Aboriginal children and leads to herd immunity. Replacement disease due to serotype 19A has been seen in non-Aboriginal children but may have been limited in Aboriginal children by the 23vPPV booster. Despite encouraging results, disparities between Aboriginal and non-Aboriginal populations continue. IPD rates in Aboriginal adults 30–49 years of age are increasing and are now >40 times those in non-Aboriginal adults of the same age. Higher valency conjugate vaccines are becoming available and will hopefully assist in curbing disease incidence. A 23vPPV campaign in young Aboriginal adults, starting before they experience serious consequences of co-morbidities, is urgently needed. However, poor underlying health may compromise the success of pneumococcal vaccines in many Aboriginal populations [14, 19]. Emergence of nonvaccine serotypes is apparent, and continued enhanced surveillance is warranted. An immunization register covering all age groups is urgently needed to evaluate the effectiveness of adult vaccination programs, including 23vPPV.

VACCINE IMPACT SURVEILLANCE NETWORK

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