Invasive Pneumococcal Disease Among White Mountain Apache Adults, 1991-2005

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Background: Certain Native American populations have high rates of invasive pneumococcal disease (IPD). We aimed to determine the disease spectrum and risk factors of White Mountain Apache adults (age, ≥18 years) with IPD and the use and effectiveness of pneumococcal polysaccharide vaccine (PPV) in this population.

Methods: We conducted active surveillance for IPD between 1991 and 2005. Medical records were reviewed, and isolates were serotyped. Vaccine use was assessed in 2004-2005 among White Mountain Apache adults with an indication for pneumococcal vaccination. The effectiveness of PPV was determined through an indirect cohort method.

Results: Among the 115 IPD cases (in 109 persons), the mean age was 43 years; 62% were male; 91% had risk factors, and alcoholism predominated (73%). Alcoholic patients were younger (mean age, 40.1 years; $P < .001$) and more often male (70%; $P = .001$) compared with nonalcoholic patients. The case fatality rate was 15%; all deaths occurred among those with risk factors. Only age 65 years or older was associated with increased risk of death. Of 447 White Mountain Apache persons at high risk, 76% had received PPV. Vaccination rates were highest among subjects with pulmonary disease (95%) and diabetes (89%) and lowest among those aged 50 to 64 years (40%). Of the 115 IPD cases for which serotypes were available, 77% were due to serotypes contained in PPV. The effectiveness of PPV against serotype-specific IPD, as measured by the indirect cohort analysis of IPD cases, was 68% (95% confidence interval, 3%-90%).

Conclusions: Among White Mountain Apache adults with IPD, alcoholism is common and contributes to the younger age and male predominance of cases. Pneumococcal vaccination rates are high, and there is suggestive evidence of the effectiveness of PPV in this population. Additional preventive strategies, including risk factor modification and vaccination of younger high-risk adults, should be pursued.

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STREPTOCOCCUS PNEUMONIAE IS a leading cause of morbidity and mortality worldwide.[1] Elderly adults and individuals with certain medical conditions, including diabetes, cardiovascular or lung disease, chronic liver disease, asplenia, alcohol abuse, chronic renal disease, and immunosuppression, are at high risk of serious pneumococcal infections.[2,3]

Certain racial and ethnic groups are also at increased risk for pneumococcal disease, such as African Americans[4] and some Native American populations.[5-8] Rates of invasive pneumococcal disease (IPD) are up to 5 times higher among Navajo and Alaska Natives[5-7] compared with the general US population. The IPD rate among White Mountain Apache (WMA) persons during the 1980s was among the highest reported—13 to 25 times the rate reported in other contemporary, nonnative US populations.[8] The reasons for this increased risk are unclear; possibilities include higher rates of predisposing conditions, underuse of pneumococcal polysaccharide vaccine (PPV), environmental factors such as cigarette smoking and multigenerational households, or immune factors, as has been seen with *Haemophilus influenzae*.[9]

The elevated IPD rates underscore the need to identify factors placing certain Native Americans at a higher risk of pneumococcal disease than the general population so that appropriate preventive measures can be implemented. We aimed to study the epidemiology of IPD among WMA adults, to determine the vaccine coverage of the at-risk adult population, and to assess its effectiveness using the indirect cohort method.

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METHODS

The WMA reservation comprises 1.6 million acres in eastern Arizona; there are 15 000 tribal members. Health care for tribal members is provided by the Indian Health Service (IHS) at the Whiteriver Hospital, Whiteriver, Arizona, and the Phoenix Indian Medical Center, Phoenix, Arizona.

We conducted active surveillance for IPD on the WMA reservation between 1991 and 2005. Whiteriver IHS laboratory records were reviewed daily, and regional laboratories were contacted weekly for case identification. Invasive pneumococcal disease was defined as the isolation of *Streptococcus pneumoniae* from a normally sterile site. Cases were included if they occurred among Native Americans 18 years or older, who resided on or near the WMA reservation; tribal status was self-reported at the time of the IHS health visit. Pneumococcal isolates were serotyped by the Arctic Investigations Program (Centers for Disease Control and Prevention, Anchorage, Alaska) using the Quellung reaction with antisera from the Statens Serum Institute, Copenhagen, Denmark. Incidence rate information will be reported separately (unpublished data, 2008).

We reviewed the medical records of cases for demographic and clinical information; medical history was reviewed to identify preexisting medical conditions and vaccination history. When the record indicated that a case patient had received care at another facility, medical records from that facility were also reviewed whenever possible.

For IPD cases, heart disease was defined as a diagnosis of congestive heart failure, coronary artery disease with a history of myocardial infarction or angina, cardiomyopathy, or pulmonary hypertension. Arrythmias and valvular heart disease were not included unless heart failure was also present. Chronic lung disease was defined as chronic obstructive pulmonary disease, interstitial or restrictive lung disease, a history of pneumonectomy, pulmonary fibrosis, or pneumoconiosis. Immunodeficiency included those caused by human immunodeficiency virus (HIV) infection as well as chronic use of immunosuppressive therapy. Alcoholism was defined as a previous clinical diagnosis of alcoholism, a history of complications related to alcohol use, or 1 or more medical visits related to alcohol use.

An individual was considered to have an indication for PPV if he or she was 65 years or older or had an underlying disease as defined by the Advisory Committee on Immunization Practices.[2] Clinical syndromes (eg, pneumonia and sepsis) were defined by clinicians providing care for the subjects. Medical visits (outpatient, inpatient, emergency, and visiting health nurse) were documented through IHS records.

To assess PPV coverage among WMA adults, IHS coding records were used to identify individuals who, in 2004, had heart disease, chronic lung disease, alcoholism, immunosuppression, or malignancy or who were 50 years or older; persons with diabetes were identified through the WMA Diabetes Registry. For each of these conditions, a random subset of at least 30 persons per indication, stratified by age, was generated. People were included in the analysis if they were Native American and the vaccine indication was confirmed through medical record review. Vaccination history was abstracted between April 2004 and June 2005. When the record indicated that a subject had received care at another facility, medical records from that facility were also reviewed whenever possible.

When serotyping information was available, an episode was classified as a 7-valent pneumococcal conjugate vaccine (PCV7) serotype (4, 6B, 9V, 14, 18C, 19F, and 23F) or non-PCV7 serotype and as a PPV serotype (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F) or non-PPV serotype. For individuals vaccinated before 1984, their isolate was classified as PPV-type if it was contained in the 14-valent vaccine (1, 2, 3, 4, 6A, 7F, 8, 9N, 12F, 14, 18C, 19F, 23F, and 25). For those cases in which 2 separate serotypes grew, an episode was considered "vaccine-type" if either serotype was contained in the vaccine. For the indirect cohort analysis,[10-12] among those vaccinated and nonvaccinated before their illness, we estimated the proportion of IPD cases that were PPV-type. An odds ratio (OR) for vaccination was calculated, and vaccine effectiveness was defined as the following:

$$(1 - \mathrm{OR}_{\mathrm{PPV\ vaccination}}) \times 100\%.$$

The χ^2 or Fisher exact tests were used for comparisons of categorical variables. Comparisons between continuous variables were made with unpaired *t* tests. Odds ratios were performed using univariate logistic regression. All statistical analyses were performed using Stata statistical software (version 8.1; StataCorp, College Station, Texas). A 2-sided *P* value of $\leq .05$ was considered statistically significant.

This protocol was approved by the institutional review boards of the Johns Hopkins Bloomberg School of Public Health, the Phoenix Area IHS, and the WMA Tribe.

RESULTS

IPD EPIDEMIOLOGY

There were 120 episodes of IPD occurring among 114 adults; 5 medical records were unavailable for review and were not included in the analysis. Three episodes occurred among Navajo persons and 2 episodes among San Carlos Apache persons living on the WMA reservation; the remainder occurred among WMA tribal members (**Table 1**). The mean age at the time of illness was 43 years (range, 18-79 years). Sixteen episodes (14%) occurred among those 65 years or older; 84 episodes (73%) occurred in individuals younger than 50 years.

There was an underlying risk factor in 91% of persons with IPD (Table 1). Alcoholism, occurring in 73%, predominated and was the only risk factor for 41 persons (38%). The mean age of alcoholic patients with IPD was 40.1 years, compared with 52.6 years for those without alcoholism ($P < .001$). Alcoholic persons were more likely to be male (70%) than nonalcoholic persons (34%) ($P = .001$).

Streptococcus pneumoniae was isolated from blood in all but 1 case, in which it was isolated from peritoneal fluid. The most common clinical syndrome of those with IPD was pneumonia (84%) (Table 1). The diagnosis of primary or concomitant sepsis was seen in more than a quarter of persons with IPD. Among the patients with IPD, 96% were hospitalized, 37% required intensive care, and 20% required intubation.

The case fatality rate for adults with IPD was 15%. All deaths occurred among those with a prior vaccine indication; no deaths occurred among persons with diabetes, heart disease, or renal failure (**Table 2**). Among those with a vaccine indication, in univariate analysis, prior vaccination did not prevent death (OR, 0.89; 95% CI, 0.24-2.93). In univariate analysis, persons 65 years or older and alcoholic persons had the highest risk of death; small sample size limited our ability to perform adjusted analyses.

Table 1. Demographic and Clinical Features and Underlying Medical Conditions of White Mountain Apache Adults With Invasive Pneumococcal Disease

Variable	No. (%)
Sex[a]	
Male	71 (61.7)
Female	44 (38.3)
Age, y[a]	
18-49	84 (73.0)
50-64	15 (13.0)
≥65	16 (13.9)
Ethnicity[a]	
White Mountain Apache	110 (95.7)
Navajo	3 (2.6)
San Carlos Apache	2 (1.7)
Clinical syndrome[b]	
Pneumonia	95 (84.1)
Sepsis	31 (27.4)
Bacteremia without focus	4 (3.5)
Peritonitis	4 (3.5)
Septic arthritis	3 (2.7)
Meningitis	2 (1.8)
Cellulitis	2 (1.8)
Malignant otitis externa	1 (0.9)
Severity measures[c]	
ICU admission rate	36 (36.7)
Intubation rate	20 (20.4)
Death	17 (15.3)
Underlying medical risk factors[d]	
Alcoholism	80 (73.4)
Cirrhosis	27 (24.8)
Diabetes	20 (18.3)
Current smoker	13 (11.9)
Asthma	12 (11.0)
Heart disease	10 (9.2)
Renal failure	10 (9.2)
Nephrotic syndrome	4 (3.7)
Immunosuppression	4 (3.7)
HIV/AIDS	3 (2.8)
Cancer	2 (1.8)
Chronic lung disease	2 (1.8)
Pregnant	2 (1.8)
Any vaccine indication	99 (90.8)
>1 Vaccine indication	49 (45.0)

Abbreviations: HIV, human immunodeficiency virus; ICU, intensive care unit.
[a] Based on all episodes (n = 115).
[b] Information was available for 113 episodes; persons may have been diagnosed as having more than 1 clinical syndrome.
[c] Severity measures were not known for all cases; ICU and intubation rates were known for 98 episodes, mortality outcomes known for 111 episodes.
[d] Based on first episodes only (n = 109).

Table 2. Medical Risk Factors and Risk of Death From Invasive Pneumococcal Disease

Variable	Case Fatality Rate, %	Unadjusted OR (95% CI) for Death[a]
Sex		
Male	17.4	1.43 (0.41-5.66)
Female	11.9	1 [Reference]
Age ≥65 y	33.3	3.50 (0.79-13.63)
Alcohol	17.6	2.57 (0.53-24.64)
Cirrhosis	20.7	1.68 (0.46-5.63)
Asthma	9.1	0.53 (0.01-4.20)
Current smoker	7.1	0.39 (0.01-3.99)
Diabetes	0	0.22 (0.01-1.58)
Chronic renal failure	0	0.49 (0.01-3.93)
Heart disease	0	0.44 (0.01-3.47)
Any vaccine indication	16.8	2.02 (0.25-92.91)
>1 Vaccine indication	19.6	1.84 (0.57-6.21)
Prior vaccination[b]	15.8	0.89 (0.24-2.93)
No prior vaccination[b]	17.5	1 [Reference]

Abbreviations: CI, confidence interval; OR, odds ratio,
[a] Calculated using the 2-sided Fisher exact test. For those analyses in which cells had zero values, 1 was substituted for zero for analysis. The reference category for each univariate analysis was those individuals without the condition (eg, for "Alcohol," the reference category was nonalcoholic persons).
[b] Among those with an Advisory Committee on Immunization Practices vaccine indication only.

SEROTYPE DISTRIBUTION

Pneumococcal serotyping was available for 92 of the 115 IPD episodes (80%); for 6 episodes, 2 different serotypes were identified for a total of 98 serotypes (**Table 3**). Overall, 77% of the known serotypes were PPV serotypes. The proportion of invasive episodes that were 23-valent serotype declined by age range (**Table 4**); those 65 years or older were less likely to have an infection with a 23-valent serotype than those aged 18 to 49 years (OR, 0.36; 95% CI, 0.08-1.66. There were no significant predictors of having a 23-valent serotype in multiple logistic regression modeling (covariates included age, diabetes, cirrhosis, and prior vaccination).

During 1997 to 2000, a randomized controlled trial of PCV7 was conducted among children 2 years or younger on the WMA reservation.[13] In 2000, PCV7 was licensed and introduced in the infant immunization program. There were no differences in the proportion of IPD episodes among adults that were caused by a PCV7 serotype or serogroup during the pretrial, trial, and routine use time periods (Table 4). The proportion of IPD episodes that were PCV7-type declined by age, though these differences were not significant. Only 1 episode (8%) was caused by a PCV7 serotype among those 65 years or older; 15% and 24% of episodes were PCV7 serotype among those aged 50 to 64 years and those younger than 50 years, respectively.

VACCINATION HISTORY AMONG CASES

Of adults with IPD, 91% had a prior indication for pneumococcal vaccination; however, only 35% of these had received PPV before their IPD episode. Those with chronic renal failure (90%), diabetes (75%), and heart disease (70%) were most likely to be vaccinated; alcoholic persons had the lowest vaccination rate (28%). Among those cases with a vaccine indication, vaccination rates improved over the study period; 59% of those who had IPD between 2001 and 2005 had been vaccinated, compared with 18% of those who were ill during 1991 through 1995 (OR, 0.15; 95% CI, 0.04-0.47) and 33% for those ill during 1996 through 2000 (OR, 0.35; 95% CI, 0.11-1.04).

We evaluated missed opportunities for vaccination among the patients with IPD who had not received PPV

Table 3. Serotype Distribution of Invasive Pneumococcal Disease Isolates Among White Mountain Apache Adults

Serotype	No. (%)[a]
12F	14 (14.3)
7F	13 (13.3)
1	8 (8.2)
4	8 (8.2)
14	7 (7.1)
3	6 (6.1)
31	6 (6.1)
16F	5 (5.1)
19A	4 (4.1)
8	3 (3.1)
6A	2 (2.0)
10A	2 (2.0)
17F	2 (2.0)
18C	2 (2.0)
6	1 (1.0)
9V	1 (1.0)
11A	1 (1.0)
13	1 (1.0)
15C	1 (1.0)
16	1 (1.0)
19F	1 (1.0)
21	1 (1.0)
23B	1 (1.0)
37	1 (1.0)
38	1 (1.0)
Nontypeable	5 (5.1)

[a] Serotyping information was available for 92 invasive pneumococcal disease episodes. For 6 episodes, 2 different serotypes were obtained for a total of 98 serotypes.

before becoming ill; 88% had had at least 1 medical visit within the 5 years prior to their disease episode, 81% had at least 5 medical visits, 58% had at least 10 medical visits, and 36% had at least 20 medical visits.

PPV COVERAGE

We assessed the vaccine coverage among 447 WMA persons with recognized risk factors for IPD regardless of whether they had an episode. Of these, 76% had been vaccinated by 2004-2005. Of those who had been vaccinated, 57% were vaccinated within a year of their indication and 23% had received more than 1 PPV dose (**Table 5**). The highest vaccination rates were seen in those with chronic lung disease, those 65 years or older (independent of other risk factors), and those with diabetes. Immunosuppressed persons and individuals aged 50 to 64 years (irrespective of other risk factors) were least likely to be vaccinated. Subjects aged 50 to 64 years were substantially less likely to be vaccinated than those 65 years or older (OR, 0.06; 95% CI, 0.01-0.22).

Considering only those persons with a medical risk factor, older persons were more likely to be vaccinated than younger persons; 95% of adults 65 years or older with a medical risk factor were vaccinated compared with 80% of those aged 50 to 64 years (OR, 0.20; 95% CI, 0.06-0.59) and 72% of those younger than 50 years (OR, 0.13; 95% CI, 0.04-0.34). For each medical risk factor, older persons were more likely to be vaccinated than younger persons, although this was only significant for patients with heart disease.

Among those who were not vaccinated within 12 months of their indication, missed opportunities were cataloged for up to 5 years from the date of their indication (up to 20 visits). There were a mean of 15.1 missed opportunities for vaccination. Of these, 79% were outpatient visits, 0.1% were inpatient visits, 14% were emergency department visits, and 6% were health nurse visits.

PPV EFFECTIVENESS

Using the indirect cohort method (**Table 6**), we determined that PPV was 68% effective (95% CI, 3% to 90%; $P = .02$) in preventing vaccine-type disease. When considering only those vaccinated within 5 years prior to their IPD episode, the vaccine was 64% effective (95% CI, –25% to 89%). When vaccination status was defined as occurring within the past 10 years, the vaccine was 73% effective in preventing vaccine-type invasive disease (95% CI, 15% to 91%). While pneumococcal vaccination was 96% effective among nonalcoholic persons (95% CI, 47% to 100%), we could not demonstrate effectiveness among alcoholic persons (effectiveness, 25%; 95% CI, –241% to 82%).

COMMENT

Invasive pneumococcal disease remains a significant burden among WMA persons and is occurring at a young age; 73% of cases occurred among individuals younger than 50 years. In a US multicenter surveillance program, only 32% to 33% of adult cases occurred among persons younger than 50 years.[4,14] Demographics may contribute to the discrepancy; in the 2000 US Census, the median age among WMA persons was 21.3 years, compared with 35.3 years in the general US population.[15,16] Only 7% of WMA persons were 65 years or older during the study period; in 2000, 12.4% of US persons were 65 years or older.[15]

Predisposing conditions were common among WMA adults with IPD; overall, 91% of adult cases had a predisposing condition, compared with 59% to 64% of adult IPD cases in the United States.[3,4] Certain risk factors are more common among Native Americans. Native American adults experience high rates of diabetes[17-19]; in 2005, 15% were estimated to have diabetes (both diagnosed and undiagnosed), giving an age-adjusted prevalence that was 2.2 times higher than non-Hispanic whites.[18] Among WMA adults in 2004, the prevalence of diagnosed diabetes was 15%, suggesting that the overall relative risk of diabetes (including undiagnosed) may be even higher among WMA.

Alcohol use was a factor in 73% of WMA adults with IPD and contributes to the skewed age distribution, as alcoholic patients were on average 13 years younger than nonalcoholic patients. Heavy alcohol use is associated with a 7- to 11-fold increased risk of IPD.[3,20] Rates of alcoholism and alcohol-related complications vary substantially between Native American tribes[21]; the rate of alcoholism among WMA is unknown. However, for the

Table 4. Percentage of Invasive Pneumococcal Disease (IPD) Episodes for Which Serotypes Were Included in the Licensed and Prelicensure Conjugate and Polysaccharide Vaccines

Vaccine	Overall, %	Age of Subject, y				Time of IPD Episode			
		18-49, % (n=66)	50-64, % (n=13)	≥65, % (n=13)	*P* Value[g]	1991-1995, % (n=20)	1996-2000, % (n=28)	2001-2005, % (n=44)	*P* Value[h]
PCV7 serotype[a]	20.6	24.2	15.4	7.7	.36	30.0	14.3	20.4	.42
PCV7 serogroup[b]	25.0	28.8	15.4	15.4	.41	35.0	21.4	22.7	.50
PCV10 serotype[c]	43.5	51.5	23.1	23.1	.05	70.0	28.6	40.9	.02
PCV10 serogroup[d]	47.8	56.1	23.1	30.8	.04	75.0	35.7	43.2	.02
PCV13 serotype[e]	57.6	63.6	38.5	46.2	.16	85.0	39.3	56.8	.01
PCV13 serogroup[f]	58.7	65.2	38.5	46.2	.12	85.0	42.9	56.8	.01
PPV23 serotype	77.2	81.8	69.2	61.5	.22	85.0	71.4	77.3	.54

Abbreviations: PCV7, 7-valent pneumococcal conjugate vaccine (PCV); PCV10, 10-valent PCV; PCV13, 13-valent PCV; PPV23, 23-valent pneumococcal polysaccharide vaccine.

[a] The PCV7 serotypes include serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F.

[b] In addition to the PCV7 serotypes, serotypes 6, 6A, and 23B were considered to be vaccine related and were included in the vaccine serogroup analysis.

[c] The prelicensure PCV10 includes serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F.

[d] In addition to the PCV10 serotypes, serotypes 6, 6A, and 23B were considered to be vaccine related and were included in the vaccine serogroup analysis.

[e] The prelicensure PCV13 includes serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.

[f] In addition to the PCV13 serotypes, serotypes 6 and 23B were considered to be vaccine related and were included in the vaccine serogroup analysis.

[g] *P* value generated by χ^2 analysis of the vaccine serotype across age strata.

[h] *P* value generated by χ^2 analysis of the vaccine serotype across time of surveillance.

Table 5. Rates of Pneumococcal Vaccination for High-Risk White Mountain Apache Adults in 2004-2005

Indication	No. of Adults	Proportion Vaccinated, %	Vaccinated Within 12 mo, %[d]	Mean No. of Vaccinations[d]	Proportion Who Received >1 Vaccine, %[d]
Diabetes	131	89.3	50.4	1.15	14.5
Alcoholic	51	74.5	31.6	1.18	18.4
Cardiac, narrow definition[a]	69	82.6	87.7	1.49	42.1
Cardiac, broad definition[a]	95	81.1	87.0	1.44	39.0
Pulmonary	44	95.5	78.6	1.38	33.3
Immunosuppression	55	63.6	74.3	1.40	31.4
Age, y[b]					
50-64	65	40.0	15.4	1.15	15.4
≥65	37	91.9	55.9	1.29	29.4
Total[c]	447	76.1	57.4	1.26	23.2

[a] Narrowly defined, cardiac risk factors include congestive heart failure and pulmonary hypertension. Broadly defined, in addition to congestive heart failure and pulmonary hypertension, we included diagnoses such as coronary artery disease, angina, atherosclerotic heart disease, and valvular heart disease.

[b] Individuals within these age categories included those with and without other medical risk factors.

[c] Because of records that were analyzed more than once for separate indications, the total is not a sum of the individual indications.

[d] Among those within each indication who have been vaccinated.

finding of a 74% alcoholism rate among cases not to be a significant risk factor for IPD, 64% of the adult WMA population would have to be alcoholic, which seems implausible.

The majority of IPD cases were caused by 1 of the 23 PPV serotypes, similar to proportions among the Navajo (80%)[5] and the general US population (86%-88%).[4] Only 22% of cases, however, were caused by a PCV7 serotype; there were no significant trends over time in the proportion of adult cases caused by PCV7 serotypes despite its introduction during the study interval. Before the licensing of PCV7 in the United States, elderly adults had a higher proportion of IPD caused by these serotypes than younger adults.[22,23] In contrast, among WMA persons, the elderly had the lowest likelihood of having PCV7-serotype disease, although this was not statistically significant. The low proportion of PCV7 serotypes among adult WMA IPD cases may explain an apparent lack of indirect benefit from pediatric vaccination; higher valency vaccines may have a greater impact.

The Healthy People 2010 program aims for PPV vaccination rates of 90% for persons 65 years or older and 60% for high-risk persons younger than 65 years. Rates of PPV vaccination in the United States have been improving but still fall short of the goal.[24,25] Among WMA persons, pneumococcal vaccination coverage is substantially higher than among the general US population. When those aged between 50 and 64 years without a medical risk factor are excluded, the WMA have achieved the Healthy People 2010 goals. This feat has been assisted by universal access to health care through the IHS, an extensive visiting nurse program to expand access for those who live furthest from the Whiteriver IHS Hospital, a home-based vaccination program for the elderly,

Table 6. Indirect Cohort Estimation of 23-Valent Pneumococcal Polysaccarhide Vaccine (PPV) Effectiveness[a]

	Vaccinated Prior, No.	Not Vaccinated Prior, No.	Total, No.
Vaccine-type IPD	21	50	**71**
Non–vaccine-type IPD	12	9	**21**
Total	**33**	**59**	**92**

Abbreviation: IPD, invasive pneumococcal disease.
[a]Serotyping information was available for 92 IPD episodes. Vaccine effectiveness was calculated as 1 – odds ratio for having a vaccine-type IPD episode according to prior vaccination status.

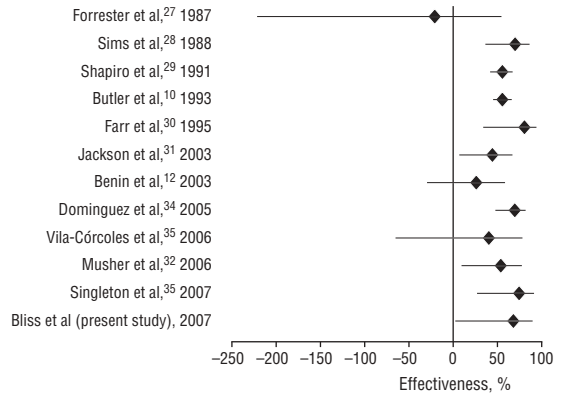

Figure. Clinical effectiveness of pneumococcal polysaccharide vaccine in preventing invasive pneumococcal disease in published studies. Data are given as percentage (95% confidence interval).

and a strong diabetes management program. Efforts to expand immunization to all persons with medical risk factors, particularly those at younger ages, should be pursued further.

In postlicensure studies, estimates of PPV vaccine effectiveness have varied substantially, with reported effectiveness ranging from –21% to 81% (**Figure**).[10,12,26-35] There remains uncertainty about whether the differences in effectiveness are due to dissimilarities between populations or to methodological differences.

We demonstrated the effectiveness of PPV among WMA adults. However, while the vaccine was effective for nonalcoholic persons, we were not able to demonstrate effectiveness for alcoholic persons, who make up the majority of WMA persons with IPD. Alcoholism has been associated with altered immunity, characterized by decreased inflammatory responses, altered cytokine production, impaired cell-mediated immunity, and immune dysregulation.[36,37] Alcoholic persons have been shown to have altered immunological response to PPV in particular.[37] While PPV was not effective for Navajo alcoholic persons (efficacy, –5%; 95% CI, –141% to 54%),[12] the vaccine has been found to be effective among Alaska Native alcoholic persons (efficacy, 80%; 95% CI, 30% to 95%).[35]

Our study has several limitations. First, a small sample size limited detailed analysis; however, we believe that understanding the scope of pneumococcal disease in a high-risk population was nonetheless warranted. Second, in assessing vaccination status, we investigated outside records only if the IHS record indicated that care had been provided elsewhere. This may have led us to underestimate vaccination rates. However, as the IHS provides health care services without charge to WMA persons, and because the large size of the reservation makes access to health care off-reservation less feasible, most tribal members receive their care on the reservation. Furthermore, in our analysis of high-risk WMA persons for vaccine coverage, we relied on coding information to generate lists of persons with medical conditions. If these lists disproportionally captured individuals who have greater health-seeking behaviors, we may have overrepresentated vaccination rates. Finally, as PCV7 was introduced on the reservation in 1997, and as PPV vaccination rates also improved over the study interval, it is possible that some of the apparent PPV effectiveness is due to PCV7 use. However, since there were no substantive changes over time in the proportion of adult disease due to PCV7 serotypes, we believed that this was unlikely.

Pneumococcal disease remains a significant burden among WMA persons. Pneumococcal polysaccharide vaccination is effective in this population, and coverage rates are some of the highest in the United States. However, strategies to improve vaccination, particularly among younger persons with medical risk factors, are still needed. Additional strategies such as alcoholism prevention and treatment programs may help reduce disease burden, and further studies addressing the roles of revaccination of high-risk persons, use of conjugate vaccines, or common antigen formulation vaccines should be pursued. Ongoing surveillance will help to determine if routine use of pneumococcal conjugate vaccine among infants has had an impact on adult disease in this high-risk group.

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