MAJOR ARTICLE

Indirect Effect of 7-Valent Pneumococcal Conjugate Vaccine on Pneumococcal Colonization among Unvaccinated Household Members

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(See the editorial commentary by Azzari and Resti on pages 989–96)

Background. Since the introduction of 7-valent pneumococcal conjugate vaccine (PCV7) in the United States, rates of invasive pneumococcal disease have decreased in both vaccinated and unvaccinated age groups. Reduction of invasive pneumococcal disease in unvaccinated groups has been attributed to reduced transmission of vaccine-type pneumococci in the community. Understanding the impact of PCV7 on carriage among vaccinated and unvaccinated community members is critical to interpreting, predicting, and understanding the impact of PCV7 on disease.

Methods. A group-randomized, phase III efficacy trial of PCV7 was conducted among southwestern American Indian communities. Meningococcal conjugate vaccine against serogroup C was used as the control. After the trial was unblinded, we conducted a carriage study of participating communities to evaluate the impact of PCV7 on colonization among trial participants and their unvaccinated household members.

Results. Adults and unvaccinated children aged <5 years living in households with a PCV7 vaccinee were less likely to be colonized with vaccine-type pneumococci (odds ratio [OR] for adults, 0.57; 95% confidence interval [CI], 0.33–0.99; OR for children, 0.57; 95% CI, 0.26–0.98) than were those living in a household with a control vaccinee. There was no difference for children aged 5–17 years. Decreases in vaccine-type carriage were offset by increases in carriage of nonvaccine types. Among adults living with a trial participant colonized with vaccine-type pneumococcus, those in the households randomized to receive PCV7 were less likely to be colonized with the same serotype than were those in the households randomized to receive the control vaccine (OR, 0.34; 95% CI, 0.11–0.99).

Conclusions. Vaccine-type pneumococcal carriage was lower among adults and unvaccinated children living with a PCV7 vaccinee. This is attributable to reduced exposure and reduced transmission when exposure occurs.

Polysaccharide-protein conjugate vaccines for *Streptococcus pneumoniae* (pneumococcus) are highly effective in the prevention of pneumococcal disease in children. Since the introduction of 7-valent pneumococcal conjugate vaccine (PCV7) (Prevnar; Wyeth Vaccines) in 2000, substantial decreases in US rates of invasive pneumococcal disease (IPD) have been observed among age groups for whom vaccination is recommended [1–4].

IPD rates in the vaccine era have also decreased among unvaccinated older children, adults, and elderly persons [1, 3–5], suggesting that pneumococcal conjugate vaccine has both direct and indirect (i.e., herd immunity) protective effects. Decreases in disease rates among unvaccinated individuals are likely due to reduced exposure and reduced transmission of vaccine-type (VT) pneumococci, because conjugate vaccines prevent nasopharyngeal acquisition of VT organisms among infants and young children [6–8].

Household carriage studies yield valuable information about risk factors, serotype distribution, antibiotic resistance, and patterns of transmission [9–14]. Such studies also permit an evaluation of indirect effects of

Received 15 February 2008; accepted 6 June 2008; electronically published 9 September 2008.

The opinions expressed herein are those of the authors and do not necessarily reflect the views of the Indian Health Service.

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Clinical Infectious Diseases 2008; 47:989–96

1058-4838/2008/4708-0001$15.00
DOI: 10.1086/591966

vaccination on carriage among unvaccinated household members [15]. Observed reductions in VT carriage among unvaccinated individuals may provide the biological basis for decreases in the incidence of IPD among age groups for whom conjugate vaccine is not currently recommended.

The efficacy of PCV7 against IPD was evaluated among American Indian children living in the southwestern United States [16]. The phase III trial used a group-randomized design that permits an evaluation of the combined direct and indirect effects of vaccination [17]. A nested nasopharyngeal carriage study was conducted to assess the impact of vaccine on carriage among vaccinees and their younger and older siblings [8]. After the trial was unblinded, we conducted a follow-up carriage study to evaluate colonization among the trial participants and their unvaccinated household members. From this study, the effect of PCV7 on pneumococcal colonization after vaccination among vaccinees aged 2–4 years has been published [18]. In this article, we describe the indirect effect of vaccination on carriage among unvaccinated adults and children living with children who participated in the trial.

MATERIALS AND METHODS

A group-randomized, controlled efficacy trial of PCV7 was conducted at the Navajo and White Mountain Apache reservations in the southwestern United States from April 1997 to October 2000. Descriptions of the study area, population, and trial design have been published elsewhere [16, 17]. In brief, randomization units at the Navajo and Apache reservations were defined by geography and population size, to allocate communities with significant social interactions of adults and children to the same randomization unit and to allocate communities with minimal social interactions to different randomization units.

Depending on the randomization unit in which the child lived, those who consented to participate in the study received either PCV7 vaccine (serotypes 4, 6B, 9V, 14, 19F, and 23F) or meningococcal conjugate vaccine against *Neisseria meningitidis* serogroup C (MCC) (Meningitec; Wyeth Vaccines) as a control vaccine.

Infants who were enrolled at age 6 weeks to 7 months received 3 doses of vaccine spaced 2 months apart (minimum, 4 weeks apart) and a booster dose at age 12–15 months (primary efficacy group). Infants enrolled at age 7–11 months received 2 doses of the vaccine spaced 4 weeks apart, followed by a booster dose at age 12–15 months. Children aged 12–23 months received 2 doses spaced 4 weeks apart. After the trial was unblinded, we recruited primary efficacy group trial participants and their household members, both children (age, <18 years) and adults (age, ⩾18 years), for a follow-up carriage study from February 2001 through January 2002. PCV7 was introduced into these communities in late October 2001 as part of the routine immunization program of the Indian Health Service. Children with congenital abnormalities of the nasopharynx were excluded from the study.

To evaluate the indirect effect of PCV7 on carriage among unvaccinated individuals, we excluded from final analysis the following groups: (1) efficacy trial participants who received either PCV7 or MCC vaccine, (2) individuals whose specimen information was missing, and (3) entire households (both vaccinees and unvaccinated household members) of vaccinees randomized to receive MCC who had received at least 1 dose of open-label PCV7 before specimen collection.

Trained nurses and field workers collected swab specimens, using an aluminum shaft calcium alginate swab (Fisher Scientific). A single nasopharyngeal swab specimen was collected from children. Both nasopharyngeal and oropharyngeal swab specimens were collected from adults [19]. The swab specimens were inoculated into STGG (containing skim milk, tryptone, glucose, and glycerin) transport media [20], were frozen at −70°C, and were transported to the Centers for Disease Control and Prevention (Atlanta, GA) for culture, isolation, and serotyping. Specimens were streaked onto gentamicin–trypticase soy agar 5% sheep-blood agar plates (Becton Dickinson) and were incubated overnight at 37°C in 5% CO_2.

Phenotypic characteristics (morphological characteristics and α-hemolysis findings) were used for the presumptive identification of pneumococcus. Identification of pneumococci was confirmed by optochin susceptibility and bile solubility assays. A single colony was selected from each plate, and the serotype was determined by the Quellung reaction. If colonies of multiple morphologies were present, each morphological type was serotyped. Both nasopharyngeal and oropharyngeal specimen results were included for adults. Serotypes were categorized into 1 of 3 mutually exclusive categories: VT serotypes (4, 6B, 9V, 14, 18C, 19F, and 23F), vaccine-associated serotypes (serotypes in serogroups 6, 9, 18, 19, or 23 that are not vaccine types), and non–vaccine type/non–vaccine associated (NVT/NVA) serotypes (all others).

An adult household member was interviewed to obtain the following information: number of household members, number of children aged <5 years, presence of a wood- or coal-burning stove, presence of a cigarette smoker, and other potential household-level risk factors for carriage. Individual household members (or parents of children aged <18 years) were interviewed about antibiotic use in the month before specimen collection, day care attendance, and other potential individual-level risk factors for carriage.

Analysis was performed with the SAS software package, version 9.1 (SAS Institute). Frequencies of individual and household characteristics were compared using χ^2 or Fisher's exact test when appropriate. Median values of individual and household characteristics were compared using the Mann-Whitney

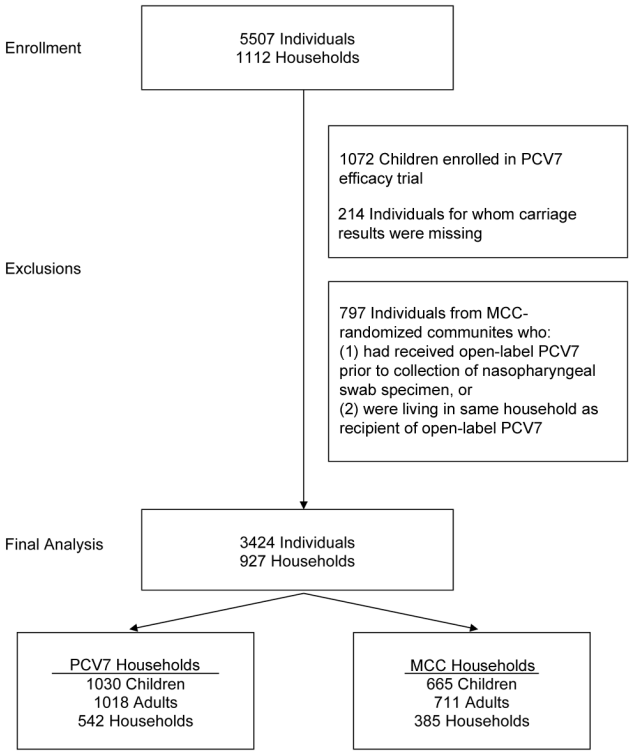

Figure 1. Composition of the population enrolled in the household carriage study. MCC, meningococcal conjugate vaccine against serogroup C; PCV7, 7-valent pneumococcal conjugate vaccine.

U test. Results were considered statistically significant if the 2-tailed *P* value was <.05. We calculated ORs for carriage, using generalized estimating equations to control for clustering within households and within randomization units. To assess the indirect effect of PCV7 vaccination on pneumococcal acquisition and carriage within households, the culture and serotype results for vaccinees and their unvaccinated household members were compared, to identify carriage episodes in which culture and/or serotype results were concordant (i.e., vaccinee and at least 1 unvaccinated household member were colonized with the same serotype). All carriage models included the following potential confounders: age, sex, recent antibiotic use, day care attendance (children only), presence of a wood- or coal-burning stove, presence of a cigarette smoker, and whether ⩾5 persons lived in the household.

The sample size was based on the carriage end point among adult household members. We assumed that 10% of adults living with unimmunized children would be colonized with pneumococcus and that 50% of isolates would be VT. Furthermore, we assumed 50%–80% reduction in VT carriage among adults living in households with PCV7-vaccinated children and that 2 adults per household would be enrolled. To account for the fact that adults living in the same household were not truly independent observations, a design effect of 1.6 was included. With these assumptions, we determined that a sample of 1500 adults from 750 households would give us 80% power to detect a reduction of 70% if the baseline carriage rate was 10%.

The study was approved by the institutional review boards of the Johns Hopkins Bloomberg School of Public Health, the Centers for Disease Control and Prevention, the Navajo Nation, the Phoenix Area Indian Health Service, and the National Indian Health Service. Tribal approval was given by the Navajo Nation and the White Mountain Apache tribe. Parents or guardians provided written informed consent for their children to participate in the study. Adult participants provided written informed consent for their participation.

RESULTS

A total of 5507 individuals from 1112 households were enrolled (figure 1). Of these, 1072 were children enrolled in the efficacy trial; 520 had received PCV7 vaccine, and 552 had received MCC vaccine. Carriage data from these children are included in the concordance analysis only. Culture results from an additional 214 individuals were missing. These records were excluded from the final analysis. Of the remaining 4221 individuals, 797 (from 171 households) in communities randomized to received MCC (hereafter, "MCC-randomized") were excluded because they themselves had received at least 1 dose of

Table 1. Characteristics of the individuals enrolled in the carriage study.

Age group, characteristic	Communities randomized to receive PCV7	Communities randomized to receive MCC	*P*
Adults (age, ⩾18 years)			
No. of subjects	1018	711	
Female	697 (68.6)	499 (70.2)	.23
Navajo	891 (87.5)	592 (83.3)	.003
Age, median years	31.5	32.8	.44
Received antibiotics in the past month	64 (6.3)	34 (4.8)	.36
Smokes cigarettes or cigars	116 (11.4)	64 (9.0)	.25
Chews tobacco/snuff	133 (13.1)	53 (7.5)	<.001
Children (age, <18 years)			
No. of subjects	1030	665	
Female	496 (48.2)	309 (46.5)	.94
Navajo	904 (87.8)	545 (82.0)	<.001
Age, median years	8.3	9.4	<.001
Received antibiotics in the past month	35 (3.4)	18 (2.7)	.54
Attended day care in the past month	85 (8.3)	82 (12.3)	.003

NOTE. Data are no. (%) of individuals, unless otherwise indicated. MCC, meningococcal conjugate vaccine against serogroup C; PCV7, 7-valent pneumococcal conjugate vaccine.

open-label PCV7 before collection of pharyngeal specimens ($n = 200$) or lived in the household with a PCV7-vaccinated child ($n = 597$). The final analysis of unvaccinated household members included 3424 individuals: 1695 unvaccinated children aged <18 years (1030 from communities randomized to receive PCV7 [hereafter, "PCV7-randomized"] and 665 from MCC-randomized communities) and 1729 adults (1018 from PCV7-randomized communities and 711 from MCC-randomized communities) from 927 households (542 from PCV7-randomized communities and 385 from MCC-randomized communities) (table 1).

Children included in the final analysis were older than those who were excluded (data not shown). This was because of the exclusion of efficacy trial participants (median age, 3.3 years) from the analysis. The median number of children aged <6 years in the household was higher among households included in the final analysis than among those that were excluded. The remaining individual and household characteristics did not dif-

Table 2. Characteristics of households enrolled in the carriage study.

Characteristic	Communities randomized to receive PCV7 ($n = 542$)	Communities randomized to receive MCC ($n = 385$)	*P*
Has electricity	502 (92.6)	356 (92.5)	.81
Has plumbing	399 (73.6)	317 (82.3)	<.01
Heating used in the past month	242 (44.6)	191 (49.6)	.25
Wood-burning stove	143/242 (59.1)	97/191 (50.8)	.08
Coal-burning stove	32/242 (13.2)	21/191 (11.0)	.48
Electric heat	19/242 (7.9)	19/191 (9.9)	.44
Gas space heater	9/242 (3.7)	6/191 (3.1)	.74
Open fire	0 (0)	1/191 (0.5)	.26
Smoker lives in household	128 (23.6)	80 (20.8)	.33
No. of bedrooms, median (range)	3 (1–7)	3 (1–8)	.08
Total no. of members, median (range)	6 (2–17)	5 (2–15)	.05
No. of children aged <6 years, median (range)	2 (1–7)	1 (1–5)	<.01

NOTE. Data are no. (%) of households, unless otherwise indicated. MCC, meningococcal conjugate vaccine against serogroup C; PCV7, 7-valent pneumococcal conjugate vaccine.

Table 3. Pneumococcal carriage among unvaccinated adults and children living with a child vaccinated with 7-valent pneumococcal conjugate vaccine (PCV7).

Age group, carriage	Communities randomized to receive PCV7	Communities randomized to receive MCC	OR (95% CI)	*P*
Adults (age, ⩾18 years)				
No. of subjects	1018	711		
Overall	146 (14.3)	95 (13.4)	1.05 (0.78–1.39)	.76
VT	24 (2.4)	29 (4.1)	0.57 (0.33–0.99)	.05
VA	14 (1.4)	8 (1.1)	1.17 (0.47–2.92)	.73
NVT/NVA	108 (10.6)	58 (8.2)	1.25 (0.88–1.78)	.22
Children aged 5–17 years				
No. of subjects	789	566		
Overall	315 (39.9)	207 (36.6)	1.05 (0.79–1.39)	.74
VT	59 (7.5)	45 (8.0)	0.84 (0.56–1.29)	.44
VA	63 (8.0)	44 (7.8)	0.98 (0.62–1.55)	.94
NVT/NVA	193 (24.5)	118 (20.8)	1.15 (0.85–1.56)	.35
Children aged <5 years				
No. of subjects	241	99		
Overall	156 (64.7)	58 (59)	1.27 (0.72–2.23)	.41
VT	29 (12.0)	19 (19)	0.57 (0.26–0.98)	.04
VA	37 (15.4)	18 (18)	0.89 (0.42–1.80)	.71
NVT/NVA	90 (37.3)	21 (21)	2.26 (1.22–4.20)	.01

NOTE. Data are no. (%) of individuals, unless otherwise indicated. MCC, meningococcal conjugate vaccine against serogroup C; NVT/NVA, non–vaccine type/non–vaccine associated serotypes; PCV7, 7-valent pneumococcal conjugate vaccine; VA, vaccine-associated serotypes (serotypes in serogroups 6, 9, 18, 19 or 23 that are not vaccine types); VT, vaccine-type serotypes (4, 6B, 9V, 14, 18C, 19F, or 23F).

fer between those included and those excluded from the final analysis.

The proportion of children attending day care was higher among those living in MCC-randomized communities than among those living in PCV7-randomized communities, whereas the median number of children aged <6 years in a household was higher among PCV7-randomized communities than among MCC-randomized communities. The proportion of adults who used chewing tobacco/snuff was higher among PCV7-randomized communities than among MCC-randomized communities. Household characteristics are presented in table 2. The proportion of households with indoor plumbing was statistically significantly higher among MCC-randomized communities than among PCV7-randomized communities. Households were similar with regard to all other household characteristics.

Adult carriage. The frequencies of overall, VT, vaccine-associated, and NVT/NVA pneumococcal carriage among adults and children are presented in table 3. The odds of overall pneumococcal carriage did not differ between adults living in PCV7-randomized households and those living in MCC-randomized households (OR, 1.05; 95% CI, 0.78–1.39). However, adults living in PCV7-randomized households were less likely to be colonized with VT pneumococci (OR, 0.57; 95% CI, 0.33–0.99). The odds of NVT/NVA carriage did not differ between adults living in PCV7-randomized households and those living in MCC-randomized households (OR, 1.25; 95% CI, 0.88–1.78). Among individuals aged ⩾65 years ($n = 70$), the frequency of overall pneumococcal carriage was 9% (4 of 43) among those in PCV7-randomized communities and 19% (5 of 27) among those in MCC-randomized communities ($P = .26$).

Carriage among children aged 5–17 years. Among unvaccinated children aged 5–17 years, the odds of overall pneumococcal carriage were similar for those in PCV7-randomized households and those in MCC-randomized households (OR, 1.05; 95% CI, 0.79–1.39) (table 3). Among children in this age group, the odds of VT (OR, 0.84; 95% CI, 0.56–1.29) and NVT/NVA (OR, 1.15; 95% CI, 0.85–1.56) carriage did not differ between PCV7-randomized households and MCC-randomized households.

Carriage among children aged <5 years. Among unvaccinated children aged <5 years, the odds of overall pneumococcal carriage did not differ between those in PCV7-randomized households and those in MCC-randomized households (OR, 1.27; 95% CI, 0.72–2.23) (table 3). However, the odds of

Table 4. Most-prevalent carriage serotypes among unvaccinated study individuals, by age and vaccine allocation.

Age group, serotype	Communities randomized to receive PCV7	Communities randomized to receive MCC
Children aged <5 years		
No. of subjects	156	58
6A	27 (17.3)	10 (17)
35B	13 (8.3)	5 (9)
15B	10 (6.4)	3 (5)
6B	9 (5.8)	3 (5)
11A	8 (5.1)	1 (2)
22F	9 (5.8)	1 (2)
23F	7 (4.5)	4 (7)
19F	6 (3.8)	7 (12)
14	5 (3.2)	2 (3)
15A	5 (3.2)	0 (0)
Children aged 5–17 years		
No. of subjects	325	220
3	29 (8.9)	15 (6.8)
35B	28 (8.6)	14 (6.4)
6A	25 (7.7)	14 (6.4)
22F	21 (6.5)	11 (5.0)
23B	18 (5.5)	11 (5.0)
19F	17 (5.2)	19 (8.6)
6B	14 (4.3)	7 (3.2)
16F	12 (3.7)	4 (1.8)
18C	11 (3.4)	8 (3.6)
11A	9 (2.8)	7 (3.2)
Adults aged 18–64 years		
No. of subjects	152	99
35B	15 (9.9)	7 (7)
3	8 (5.3)	4 (4)
NT	8 (5.3)	0 (0)
6B	6 (3.9)	2 (2)
6A	5 (3.3)	3 (3)
11A	4 (2.6)	1 (1)
15A	4 (2.6)	1 (1)
22F	4 (2.6)	2 (2)
8	4 (2.6)	3 (3)
10A	3 (2.0)	0 (0)
Adults aged ⩾65 years		
No. of subjects	4	5
35B	2 (50)	1 (20)
23B	1 (25)	0 (0)
6A	1 (25)	0 (0)
6B	0 (0)	2 (40)
11F	0 (0)	1 (20)
19F	0 (0)	1 (20)

NOTE. Data are no. (%) of individuals. MCC, meningococcal conjugate vaccine against serogroup C; NT, nontypeable; PCV7, 7-valent pneumococcal conjugate vaccine.

VT carriage were lower among children in PCV7-randomized households (OR, 0.57; 95% CI, 0.26–0.98). Children aged <5 years in PCV7-randomized households were also more likely to be colonized with NVT/NVA pneumococci (OR, 2.26; 95% CI, 1.22–4.20).

Indirect effect of PCV7 vaccine on nasopharyngeal acquisition. The risk of carrying VT pneumococci was lower among adults living in PCV7-randomized households in which the vaccinated child was colonized with a VT strain (OR, 0.34; 95% CI, 0.11–0.99). There was no difference between adults in PCV7-randomized households and those in MCC-randomized households with respect to the risk of carrying NVT/NVA pneumococci when the vaccinated child was colonized with an NVT/NVA strain (OR, 1.31; 95% CI, 0.72–2.38).

The risk of carrying VT pneumococci was also lower among unvaccinated children (age, <18 years) living in PCV7-randomized households in which the vaccinated child was colonized with a VT strain (OR, 0.32; 95% CI, 0.09–1.12), although this result did not reach statistical significance. There was no difference between unvaccinated children in PCV7-randomized households and those in MCC-randomized households with respect to the risk of carrying NVT/NVA pneumococci when the vaccinated child was colonized with an NVT/NVA strain (OR, 1.42; 95% CI, 0.79–2.54).

Serotype-specific prevalence. The serotype-specific prevalence of pneumococcal isolates, by age group and vaccine allocation of individuals with carriage, is presented in table 4. The most prevalent serotypes among PCV7-randomized households were 6A, 35B, 3, 22F, 23B, and nontypeable pneumococci. Among MCC-randomized households, the most prevalent serotypes were 6A, 19F, 35B, 23F, 3, 15B, and 6B.

Serotype-specific protection against pneumococcal acquisition. Of the 3424 individuals, 202 (6%) were colonized with VT pneumococci. Among VT pneumococci, serotype-specific reductions in prevalence among PCV7-randomized communities were demonstrated for serotype 19F only (OR, 0.52; 95% CI, 0.31–0.87) (table 5). For vaccine-associated types, there was no difference in the frequency of serotype 6A carriage between PCV7-randomized communities and MCC-randomized communities (2.7% and 2.0%, respectively; OR, 1.26; 95% CI, 0.72–2.21). The frequency of serotype 19A carriage was lower among PCV7-randomized communities than among MCC-randomized communities (0.7% and 1.7%, respectively; OR, 0.34; 95% CI, 0.16–0.75).

DISCUSSION

To our knowledge, this is the first household carriage study to be conducted in the context of a clinical trial of pneumococcal conjugate vaccine. This study demonstrates indirect protection against VT pneumococcal carriage among those living in a household with a PCV7-vaccinated child and provides evidence from a controlled trial that PCV7 reduces transmission of VT pneumococci. This finding confirms a likely biological mechanism for the association of routine use of PCV7 among infants and young children with decreased rates of invasive VT pneumococcal disease among unvaccinated populations.

Table 5. Prevalence of serotype-specific carriage of vaccine-type pneumococci among unvaccinated individuals.

Carriage of serotype	Communities randomized to receive PCV7 (n = 2048)	Communities randomized to receive MCC (n = 1376)	OR (95% CI)	P
4	8 (0.4)	9 (0.7)	0.59 (0.20–1.79)	.36
6B	30 (1.5)	15 (1.1)	1.35 (0.67–2.71)	.40
9V	7 (0.3)	8 (0.6)	0.59 (0.20–1.71)	.33
14	8 (0.4)	4 (0.3)	1.35 (0.37–4.91)	.65
18C	11 (0.5)	13 (0.9)	0.57 (0.22–1.49)	.25
19F	29 (1.4)	37 (2.7)	0.52 (0.31–0.87)	.01
23F	19 (0.9)	11 (0.8)	1.16 (0.55–2.47)	.69

NOTE. Data are no. (%) of individuals, unless otherwise indicated. MCC, meningococcal conjugate vaccine against serogroup C; PCV7, 7-valent pneumococcal conjugate vaccine.

These results are consistent with those of a community-based, observational study of adult carriage conducted by Hammitt et al. [15]. In the prevaccine era, the percentage of adults colonized with VT pneumococci was 28.4%. After the introduction of PCV7 in 8 Alaskan communities, this percentage decreased to 4.5%. Furthermore, the odds of carrying VT pneumococci were lower for adults living in households in which at least 1 child was age-appropriately vaccinated with PCV7 than for adults living in households in which no child was age-appropriately vaccinated.

A number of studies have highlighted the importance of household exposure as a risk factor for carriage, as well as a mechanism for transmission of pneumococcus [9, 11–13]. Carriage rates are highest among children aged <2 years [12, 13], and young children are primarily responsible for introducing new serotypes into a household [11]. In addition, adults with young children in the household have higher rates of carriage than do adults without any children [9, 13]. Given the role of infants and young children in the introduction and dissemination of pneumococcus in the household setting, certain factors—namely, receipt of PCV7—that have a direct impact on carriage in this age group are likely to have an indirect impact on carriage among their household contacts. Our observation that adults (i.e., parents) and children aged <5 years in PCV7-randomized households were less likely to be colonized with VT pneumococci and the lack of reduction apparent in the 5–17-year-old age group suggest that older children may have much less exposure to the youngest children, likely because of their attendance in school and involvement in other activities outside of the household. As a result, the degree of indirect protection may be smaller for this age group.

There are several mechanisms by which PCV7 could reduce transmission of pneumococcus. First, PCV7 reduces acquisition of pneumococcus among vaccinated individuals [7, 8, 21]. Second, it is possible that PCV7 reduces the transmissibility of pneumococcus from individuals who are colonized, because PCV7 has been shown to reduce the density of carriage [8]. PCV7 could also reduce the duration of carriage episodes, although the 2 studies that have attempted to assess this possibility have found no evidence of a reduction in duration of carriage [8, 22].

There are some limitations to this study. It is possible that we missed carriage episodes occurring below the threshold of our pharyngeal sampling procedure [19]. This would bias our results only if PCV7 reduces the density of carriage of VT pneumococci to less than our detection threshold, but this reduced density does not translate to reduced transmission. Because we did not assess the density of carriage, we are unable to examine the relationship between carriage density and the likelihood of nasopharyngeal carriage among household members. Also, because of the cross-sectional design of this study, we could not determine which household member was responsible for the introduction and dissemination of pneumococci within the household. However, other studies suggest that the introduction of pneumococci in households occurs via young children [11, 23]. The frequency of pneumococcal carriage among adults in our study (~15%) was similar to that reported among adults in rural Alaska (median, 18%) [15]. However, carriage frequency among the Alaskan population has increased to 26% since the introduction of PCV7 vaccine, and there have been statistically significant increases in carriage of serotypes 12F, 17F, 19A, 23A, and 34. In our study, the most prevalent nonvaccine types among PCV7-randomized communities were 6A, 35B, 3, 22F, 23B, and nontypeable serotypes.

This study demonstrates the ability of PCV7 to reduce VT pneumococcal acquisition among unvaccinated adults and children living in the same household and/or community as a vaccinee, because of both reduced exposure to a colonized individual and reduced transmission given the colonization of the vaccinee. These indirect effects on pharyngeal carriage may explain the observed reductions in rates of invasive VT pneumococcal disease among age groups for whom the vaccine is not recommended. However, reductions in VT pneumococcal carriage were offset by increased carriage of serotypes not included in the vaccine. The degree to which increased carriage of NVT/NVA serotypes will lead to increased rates of NVT/NVA disease likely varies by population, with drivers of NVT/NVA serotype colonization and disease—in addition to pneumococcal conjugate vaccine—playing a role. In this population, only small changes in the rate of IPD caused by NVT/NVA serotypes have been observed [24]. Continued surveillance of pneumococcal carriage and IPD trends for serotype changes and possible replacement disease is essential for understanding and predicting the impact of routine use of PCV7 in various epidemiological circumstances.

Acknowledgments

We are thankful to the Navajo and White Mountain Apache children and parents for their participation in this study. We also thank the Research Program Assistants, nurses, and staff of the Center for American Indian Health, for the collection of swab specimens and for conducting household interviews; Carolyn Wright and John Walls, for assistance with data management; and Richard Facklam, for serotyping support.

Financial support. Wyeth Vaccines.

Potential conflicts of interest. K.L.O. and M.S. have received consultations, honoraria, or travel grants from Wyeth Vaccines. All other authors: no conflicts.

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