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ORIGINAL CONTRIBUTIONS

Community-Level Predictors of Pneumococcal Carriage and Resistance in Young Children

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Pneumococcal carriage and resistance vary markedly among communities and are not fully explained by individual predictors. Community risk factors may explain this variation. The authors geocoded addresses from a multicommunity sample of 710 Massachusetts children previously swabbed for pneumococcal carriage in 2001. Using regression models, the authors evaluated associations between census tract measures and pneumococcal carriage or resistance. Living in census tracts with an average household size of more than 2.9 predicted carriage (odds ratio = 3.0, 95% confidence interval: 1.7, 5.5), and living in socioeconomically disadvantaged census tracts conferred an additional two- to threefold odds of carriage equal to attending child care. Living in a census tract with a median household income of less than \$35,000 predicted carriage among nonattendees (odds ratio = 2.7, 95% confidence interval: 1.7, 4.3). The predictive value of a low-income census tract was interchangeable with any of several socioeconomic measures, including poverty, unemployment, low educational attainment, and low owner occupancy, in addition to high density of children and limited household plumbing facilities. Furthermore, living in census tracts with low educational attainment significantly predicted resistance (odds ratio = 4.0, 95% confidence interval: 1.3, 12.7) and was interchangeable with a high density of children (odds ratio = 3.5, 95% confidence interval: 1.0, 11.7). The two- to threefold odds of pneumococcal carriage conferred by certain community characteristics suggest that these measures may target communities for interventions to decrease transmission.

census; drug resistance; poverty; risk factors; Streptococcus pneumoniae

Abbreviation: PNSP, penicillin-nonsusceptible Streptococcus pneumoniae.

Streptococcus pneumoniae remains the cause of considerable morbidity and mortality. Prior to the recent release of a conjugate vaccine for children, *S. pneumoniae* caused invasive disease in approximately one of 600 children less than 2 years of age, one of 2,000 adults between the ages of 60 and 79 years, and one of 1,000 adults aged more than 80 years (1). Although the conjugate vaccine has decreased disease due to vaccine-associated serotypes (2, 3), *S. pneumoniae*

remains a significant pathogen, and concerns of serotype replacement persist (4–6).

Methods to prevent morbidity from pneumococcal infection include adult immunization with the polysaccharide pneumococcal vaccine, immunization of young children with the recently introduced heptavalent conjugate pneumococcal vaccine (7–9), and increasing efforts to reduce antibiotic resistance through judicious antibiotic use campaigns (10–13).

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Although many studies have addressed individual characteristics associated with higher risks of pneumococcal carriage, the question of whether community characteristics are predictive of pneumococcal carriage has not been addressed. If predictive, such information, which is publicly available, could be used to direct community-level interventions to improve vaccine penetration or to promote judicious antibiotic use. Community-level characteristics are readily available through US Census data, in comparison with personnel- and timeintensive collection of individual-level data. In addition, the existence of community predictors would emphasize the importance of neighborhood and environmental surroundings as exposures that affect transmission.

The incidence of invasive disease due to *S. pneumoniae* varies widely from community to community (1, 14). Prior US data suggest a greater than twofold range in annual incidence across geographic regions at the city and county level (18–43 per 100,000) (1). This is also true for pneumococcal nasopharyngeal carriage (15, 16), a precursor to invasive disease (17, 18). Carriage has ranged from 14 percent to 52 percent in various cities and communities (15, 16, 19). Although there are clear individual-level risk factors for pneumococcal carriage and disease, these measures, such as young age, child care, young siblings, and recent antibiotics, are not able to fully account for the marked differences seen among communities (10, 14).

Similar regional differences have been observed in the prevalence of antibiotic resistance of *S. pneumoniae* (10, 15, 20, 21). Data from the Centers for Disease Control and Prevention showed that the prevalence of penicillin nonsusceptibility in invasive pneumococcal disease ranged from 15 percent in San Francisco, California, to 33–35 percent in selected counties in Georgia and Tennessee (20).

Numerous studies have evaluated individual-level predictors of pneumococcal carriage (22–26) and resistance (15, 27–29). However, none has determined whether community characteristics can further predict risk of pneumococcal carriage or carriage of a penicillin-nonsusceptible strain. By definition, census tracts are designed to be relatively homogenous with respect to population characteristics, economic status, and living conditions (30). A recent study has confirmed the advantages of using socioeconomic data from census tracts over zip code-based measures in predicting gradients of health outcomes (31).

Although there are no prior studies evaluating censusbased community predictors of pneumococcal carriage, one prior study (32) evaluated the association between invasive pneumococcal disease and geocoded median household income and race. This study found no correlation between median household income and disease until measures of race were included. It reported that lower income areas of predominantly Black race had a higher risk of invasive pneumococcal disease, and higher income areas of predominantly White race had a higher risk of invasive penicillin-nonsusceptible *S. pneumoniae* (PNSP) disease. However, information on community antibiotic use or other area-based measures was not included, and the study did not account for individual-level characteristics.

We hypothesized that community-level characteristics could further predict pneumococcal or PNSP carriage in young children after accounting for individual risk factors. We sought to determine whether community antibioticprescribing rates and census tract measures of demographic and socioeconomic characteristics could reasonably identify geographic areas with high pneumococcal carriage and potentially serve as markers for targeted interventions. We previously reported carriage, susceptibilities, and individuallevel risk factors for pneumococcal carriage and resistance among children less than 7 years of age from 16 Massachusetts communities (16). We now report potential community-level predictors within the same cohort.

MATERIALS AND METHODS

The study population consisted of young children from 16 Massachusetts communities from whom nasopharyngeal swabs were obtained while visiting their medical providers between March and May 2001. Details of our prospective cohort study have been previously described (16). Children were eligible if they were less than 7 years of age, resided in a study community, and presented for either routine well care or a "sick visit" at a participating practice. The study protocol and consenting process were approved by the institutional review board of Harvard Pilgrim Health Care. Massachusetts communities were selected on the basis of community population size, minority fraction, and proportion insured by Medicaid. Surveillance was conducted in all 16 communities for pneumococcal and PNSP carriage. Consenting parents filled out a questionnaire and permitted their children to undergo a nasopharyngeal swab. Swabs were processed for isolation of *S. pneumoniae,* as previously described (16). Individual characteristics predictive of pneumococcal carriage or PNSP carriage were collected by parent questionnaire and medical record review by one of the investigators (S. H.). The four largest pediatric health insurers in Massachusetts provided individual-level data on antibiotic dispensing from April 1, 1999, through March 31, 2000. These data were used to calculate prescribing rates in study communities using previously described methodology $(33-35)$.

Potential community-level predictors were obtained at the census tract level for each individual child. Census tract information was obtained by geocoding street addresses (Tele Atlas North America, Inc., Menlo Park, California), which were obtained from the medical record. We subsequently confirmed a greater than 97 percent accurate assignment of census tracts based upon a 10 percent sample crossreferenced with the US Census Bureau Factfinder (36). We selected, a priori, census tract variables in domains intended to measure population size, population density, age distribution, race, use of child-care facilities, education, hygiene, poverty, and community stability.

Data on census tract characteristics were obtained from the 2000 US Census Bureau website and imported into a SAS (SAS Institute, Inc., Cary, North Carolina) data set. Univariate descriptions of mean, median, and range were obtained for each continuous census tract variable, and linear correlation matrices were obtained using census tract variables and previously described individual-level predictors (16). Variables were dichotomized as a result of our hypothesis that threshold

levels of social and economic disadvantage exist when exerting an effect on pneumococcal carriage and resistance.

We dichotomized each census tract variable according to the threshold most predictive of pneumococcal carriage, in keeping with the exploratory nature of our analysis. This was accomplished through the use of recursive partitioning (37) (Classification and Regression Trees software; Salford Systems, San Diego, California), which determined if a cutpoint existed based upon 10-fold cross-validation. In this process, the data were randomly divided into 10 equal subsets. Nine subsets were used as learning data to determine a cutpoint predictive of carriage with a tenth subset used as a test sample. This process of selecting 10 subsets was repeated 10 times to determine if a valid cutpoint existed based upon statistical measures of error rates. Variables in the domains of education, hygiene, and poverty were dichotomized using the subset of children receiving less than 4 hours of child care per week based upon questionnaire responses. The decision to dichotomize these variables using a subset of children was based upon the finding of an interaction between child care and these domains.

Because previous studies have repeatedly demonstrated a large magnitude of association between individual predictors and pneumococcal carriage and resistance, we anticipated a substantial amount of confounding due to individual-level risk factors. For this reason, we chose to initially evaluate each community-level variable within a base logistic regression model composed of only individual predictors. Using the same individual predictors of carriage of *S. pneumoniae* and PNSP previously found to be significant in this cohort (16), we defined the base logistic regression model composed of only individual predictors. This base model included participation in child care, age (categorized as less than 5 months, from 5 to less than 24 months, 24 to less than 36 months, and greater than or equal to 36 months), siblings less than 6 years of age at home (categorized as none, one, or greater than one), current respiratory tract infection (upper respiratory tract symptoms, otitis media, sinusitis, or cough illness), history of being breastfed for greater than 2 months, and antibiotic exposure within the prior 2 months. Information regarding child care, siblings, and breastfeeding was obtained from questionnaires. Information on respiratory symptoms and antibiotic exposure was obtained from both questionnaires and medical records (16).

Each census tract variable was added one at a time to this base model. Those with cutpoints determined by recursive partitioning were entered as dichotomous variables, and those in which validated cutpoints were not found were entered as continuous variables. Census tract variables predictive of pneumococcal or PNSP carriage at the $\alpha \le 0.15$ level in the base model were then grouped, along with known individual-level predictors, and evaluated with stepwise backwards elimination using generalized estimating equations (38, 39) to account for clustering within census tracts. In this final model, predictors were retained at the $\alpha \leq$ 0.05 level, with the exception of recent antibiotic use, which was locked into the model regardless of the α level. Interactions between child care and measures of education, hygiene, and poverty were further evaluated.

Following the identification of significant census tract predictors, we calculated the excess risk and population attributable risk (etiologic fraction) of pneumococcal carriage associated with census-level versus individual-level variables (40–42). Excess risk was calculated as the risk difference between the risk of carriage in a child with a single predictor of carriage compared with the risk of carriage in a child lacking all evaluated predictors of carriage. Population attributable risk was calculated as the proportion of cases that would have been prevented had that specific risk factor been eliminated from our study population.

RESULTS

Of 742 children with nasopharyngeal cultures and questionnaire data, 710 had available address information that could be localized to 184 US census tracts according to 2000 US Census definitions. The most common reason for lack of census tract assignment was the use of a post office box address. Study population demographics and individual characteristics are shown in table 1 for all study population members with assigned census tracts. Our population consisted predominantly of White children, with half less than 24 months of age. Forty percent of the children had received an antibiotic in the prior 2 months, and half had received at least one dose of the heptavalent conjugate pneumococcal vaccine. Among children aged from 5 months to less than 24 months, 74 percent had received at least two doses of the conjugate vaccine. The number of study population members within any given census tract ranged from one to 19, with a mean of four. Of the 184 children with *S. pneumoniae* isolates, 23 were missing penicillin susceptibility data.

Characteristics of the census tracts in which study population members live are provided in table 2, along with the cutpoints determined by recursive partitioning for carriage of any *S. pneumoniae* strain. A cutpoint could not be found for the three measures of race and two measures of community stability; each of these measures was evaluated in the model as a continuous variable. Community antibiotic rates were based upon 51,574 person-years of insurer enrollment. Each of the four insurers contributed greater than 10,000 person-years of prescribing data.

The value and significance of individual-level characteristics did not vary substantially with the addition of various census variables. When added individually to the base model, 10 census variables had *p* values of 0.15 or less. These variables included living in a census tract with 8,000 persons or more, an average household size of 2.9 persons or more, 700 children or more aged less than 6 years per square mile (2.59 km^2) , 6 percent or more persons less than 6 years of age, 40 percent or more adults with less than a high school education, 0.5 percent or more units lacking plumbing, 20 percent or more persons in poverty, a median household income of less than \$35,000, 6 percent or more unemployment among persons aged more than 16 years who are seeking employment, and less than 45 percent of housing being owner occupied. These ten variables were entered into a backwards stepwise elimination model along with individual predictors.

	No.	$\%$
Age (months)		
$0 - 5$	105	15
$5 - < 24$	258	36
$24 - 36$	99	14
≥36	248	35
Gender distribution		
Female	324	46
Male	386	54
Race		
White	525	77
Black	49	7
Hispanic	52	8
Asian	18	3
Other	29	4
Current respiratory tract infection†	191	27
Current antibiotic use‡	69	10
Antibiotic use within 2 months	285	40
Pneumococcal vaccination (Prevnar§) (doses)		
Ω	389	55
1	108	15
>1	213	30
Child-care participant ($n = 672$)	294	44
Siblings aged <6 years ($n = 674$)		
0	353	52
1	254	38
>1	67	10
Roommates aged <6 years ($n = 650$)	134	21
Smoking in home $(n = 674)$	201	30
Breastfed for >2 months ($n = 652$)	261	40
Prematurity (< 36 weeks) ($n = 729$)	29	4
Nasopharyngeal carriage of Streptococcus pneumoniae	184	26
Nasopharyngeal carriage of penicillin- nonsusceptible S. pneumoniae disease	55	8

TABLE 1. Individual-level characteristics of 710 Massachusetts children, spring 2001*

* Includes all but 32 children from the cohort evaluating individual predictors reported previously by Finkelstein et al. (16). The cohort was restricted to study population members with available address data ($n = 710$ for individual items unless otherwise specified). Numbers vary because of missing data.

† Includes viral upper respiratory tract infection, otitis media, sinusitis, and cough illness.

‡ Reflects the antibiotic status on the day of the swab prior to being seen by the physician.

§ Doses of Prevnar (Wyeth Lederle, Gaithersberg, Maryland) completed 30 days prior to the swab date.

¶ Defined as an affirmative parental response to the survey question, "Does anyone in the child's home smoke cigarettes?"

Figure 1 shows the final model for the outcome of pneumococcal carriage, including significant census tract predictors, individual predictors, and interactions. All evaluated

individual measures were significantly associated with carriage, including recent antibiotic use, which reduced the risk of pneumococcal carriage (odds ratio $= 0.6$). The addition of census tract variables significantly improved the fit of the model in predicting pneumococcal carriage compared with the model with individual predictors alone (chi square = 50.1, df = 3, two-sided $p < 0.0001$). Two census tract measures, living in a census tract with an average household size of 2.9 or more and living in a census tract with a median household income of less than \$35,000, significantly predicted pneumococcal carriage. Furthermore, the predictive value of living in a census tract with a median household income of less than \$35,000 was interchangeable with any of several measures, including living in a census tract with 20 percent or more persons in poverty, 6 percent or more unemployment (of persons over age 16 seeking employment), 40 percent or more adults with less than a high school education, less than 45 percent of housing owner occupied, 0.05 percent or more persons lacking home plumbing facilities, or 700 children or more aged less than 6 years per square mile. The risk of carriage associated with each of these variables when replacing the median household income in the model is provided for children not attending child care (figure 1).

Participation in child care (≥4 hours per week) was inversely correlated with measures of socioeconomic status. In addition, an interaction between child-care attendance and measures of socioeconomic disadvantage was noted. For example, children not attending child care who were living in census tracts with median household incomes of less than \$35,000 had a 2.7-fold increased risk of pneumococcal carriage compared with children not attending child care in census tracts with median household incomes of \$35,000 or more. In census tracts with median household incomes of \$35,000 or more, child care conferred a 2.9-fold increased risk of pneumococcal carriage. However, children attending child care and living in census tracts with median household incomes of less than \$35,000 did not have risks of carriage higher than either predictor alone. This interaction was seen consistently between child care and the other census measures interchangeable with median household income.

In modeling carriage of PNSP, we added census tract variables to a base model of individual predictors including age, child care, respiratory tract infection, and antibiotics within 2 months. In the final model, we found that children living in census tracts with 40 percent or more adults with less than a high school education had a higher risk of PNSP carriage (figure 2). Furthermore, the predictive value of low educational attainment was interchangeable with a high density of children. Although participation in child care and living in census tracts with a lower educational attainment (or a high density of children) appeared to confer additive risks for PNSP carriage, this finding was not statistically significant.

In the final model of pneumococcal carriage, only individual-level antibiotic use, not community-level antibiotic use, was associated with carriage. In the final models of PNSP carriage, neither individual-level nor communitylevel antibiotic use was associated with carriage of PNSP. Other individual-level variables, such as race, frequent otitis media, receipt of the heptavalent pneumococcal vaccine, and

* Cutpoint determined by recursive partitioning with 10-fold cross-validation.

† Number of study population members residing in census tracts meeting that criterion.

‡ Census tract members, expressed as percentage, who relocated their homes between 1996 and 2000.

§ Census tract members, expressed as percentage, who relocated from outside the county between 1996 and 2000.

¶ Antibiotics prescribed per person-year of insurer enrollment for children <6 years of age.

smoking exposure, were similarly not predictive, as previously reported (16).

In calculating the excess risk of total pneumococcal carriage associated with various predictors, we found similar excess risks of carriage associated with child-care attendance and living in low-income census tracts. There was a 9.7 percent excess risk associated with child care and a 9.3 percent excess risk associated with living in a census tract where the median household income was less than \$35,000. There was a 5.4 percent excess risk associated with living in census tracts with an average household size of 2.9 persons or more.

In our study sample, the fraction of pneumococcal carriers attributable to community-level predictors was 2.5 percent for living in a census tract with an average household size of 2.9 persons or more and 3.7 percent for living in a census tract with a median household income of less than \$35,000. In comparison, the population attributable risk for the following individual-level predictors was 4.7 percent for having one or more siblings under 6 years of age, 5.2 percent

FIGURE 1. Individual and census tract predictors of pneumococcal carriage in Massachusetts children less than 7 years of age in 2001. This regression model analysis of pneumococcal carriage includes 672 children with complete data for all model predictors. Individual and census tract variables significantly predictive of pneumococcal carriage are shown with odds ratios and 95% confidence intervals. Census tract measures describe characteristics of the census tracts in which study population members live. Several census tract variables were interchangeable with median household income. The odds ratios associated with replacing median household income with each of these measures are provided for children not attending child care. Metric equivalent for 1 square mile = 2.59 km^2 .

for a concurrent respiratory tract infection, 8.2 percent for child-care attendance, and 16.1 percent for being from 5 to less than 24 months of age.

DISCUSSION

Individual-level risk factors alone have not been able to account for the marked differences in the prevalence of pneumococcal carriage or resistance among various cities or counties (10, 14). One explanation for this is that environmental or community characteristics such as poverty, educational level, or crowding may influence an individual's risk for carriage. This may be particularly relevant to outcomes describing infectious agents, such as *S. pneumoniae*, since transmission to a given child is likely to depend on whether neighboring children or family members have risk factors for organism acquisition. We show that routinely collected, publicly available characteristics of the community surrounding an individual can be predictive of pneumococcal or PNSP carriage in young children.

We found that living in a census tract with an average household size of 2.9 persons or more conferred three times the odds of pneumococcal carriage, possibly due to an increased number of close contacts leading to enhanced pneumococcal transmission. In addition, several measures of socioeconomic disadvantage conferred from 1.7- to 2.7-fold odds of carriage, including measures of household income, home ownership, federal poverty, unemployment, lack of plumbing, and low educational attainment, even after adjusting for individual risk factors such as age, young siblings, history of breastfeeding, respiratory symptoms, recent antibiotics, and child-care attendance. These measures of low socioeconomic status were of similar direction and magnitude, and they were interchangeable within the predicted model, suggesting redundancy. The addition of census tract variables significantly enhanced the fit of the model in predicting pneumococcal carriage. Further investigation is needed to determine whether these variables represent distinct predictors of pneumococcal carriage, or whether they reflect facets of a single predictor.

FIGURE 2. Predictors of penicillin-nonsusceptible Streptococcus pneumoniae carriage in Massachusetts children less than 7 years of age in 2001. This regression model analysis includes 649 children with complete data for all model predictors. Individual and census tract variables significantly predictive of pneumococcal carriage are shown with odds ratios and 95% confidence intervals. Census tract measures describe characteristics of the census tracts in which study population members live. One census tract variable was interchangeable with the percentage of adults with less than a high school (HS) education. The odds ratio for penicillin-nonsusceptible S. pneumoniae carriage associated with this variable is provided for children not attending child care. Metric equivalent for 1 square mile = 2.59 km^2 .

Interestingly, carriage was predicted by a cross-validated cutpoint of poverty where 20 percent or more persons within the census tract live below the US poverty line. This cutpoint coincides with the federal definition of a poverty area (43), supporting our initial hypothesis that a threshold value of community disadvantage may be predictive of pneumococcal carriage. In these poverty areas, 69 percent of persons have individual household incomes above the federal poverty line (43). Although poverty is not an individuallevel risk factor for these individuals, we show that the low average household income in their community confers increased risk of pneumococcal carriage related to external poverty effects. This exemplifies the way an individual's surroundings can affect health outcome beyond individual characteristics.

Much attention has been given to risks of pneumococcal carriage and infection attributed to child-care attendance in young children (44–47), particularly because of concerns that child-care centers may serve as loci of infectious transmission (48–50). In fact, several studies have described methods of intervening in child-care facilities to mitigate this risk (51–53). We found that living in a census tract with a low economic status conferred an excess risk (9–10 percent) of pneumococcal carriage equivalent to that of child-care attendance.

Child-care attendance did not increase the risk of carriage of *S. pneumoniae* for children already living in socioeconomically disadvantaged communities. In contrast, childcare attendance significantly increased the risk of carriage in children from socioeconomically advantaged communities. One explanation for this is that conditions of close contact among numerous young children in child care may enhance pneumococcal transmission similar to conditions of disadvantage, perhaps related to poverty, crowding, or limited opportunities for good hygiene. For example, for both pneumococcal and PNSP carriage, we found that living in a socioeconomially disadvantaged census tract was interchangeable with living in a census tract with a high density of children under 6 years of age. Perhaps transmission within and between densely populated, impoverished neighborhoods partly explains findings that identical antibiotic-resistant pneumococcal clones are found in children from geographically distant child-care centers across multiple years (54, 55).

We also found that low educational attainment was significantly predictive of PNSP carriage and interchangeable with the predictive value of a high density of children. These findings may generally represent a disadvantaged socioeconomic environment. Predictors of PNSP were similar when evaluating pneumococcal carriers alone. We present data from the entire cohort for two reasons. First, carriage status is often unknown. Second, in evaluating antibiotic use, restricting the analysis to carriers introduces bias toward finding an antibiotic effect. This is because the control group (children harboring antibiotic-sensitive strains) is less likely to have received antibiotics since antibiotics enhance organism clearance (56, 57).

We did not find individual- or census tract-level measures of race to be significantly predictive of carriage of *S. pneumoniae* or PNSP. Prior studies have found an association between White race and increased antibiotic use (58–60) but conflicting associations between individual-level race and invasive pneumococcal disease (1, 20). Two studies have shown that invasive pneumococcal disease is more common among Blacks, but invasive disease due to PNSP is more common among Whites (32, 61). It is likely that the high predominance of White race among our study population and the associated census tracts limited our ability to detect a significant association. Nevertheless, perhaps the higher incidence of invasive disease among Blacks is related to an association with low economic status, and perhaps the higher incidence of PNSP among Whites is related to a correlation among White race, higher income, and the ability to afford child care.

Surprisingly, community antibiotic prescribing rates were not associated with either reduced pneumococcal carriage or increased PNSP carriage despite estimates from over 50,000 person-years of prescribing data and a longstanding history of using health plan data in epidemiologic research (62). Although the reason for this is unclear, explanations may include insufficient power due to the limited number of PNSP strains, an inadequate range of community rates to detect a difference, and the choice to account for clustering at the census tract level, rather than at the community level. In support of this, our previous community-cluster analysis of the same cohort demonstrated an association between individual-level antibiotic use and PNSP carriage (16). Finally, it may be necessary to evaluate distinct classes of antibiotics to find an association given the rise in classspecific antibiotic resistance in *S. pneumoniae*.

Although the excess risk of pneumococcal carriage associated with living in a census tract with low socioeconomic position was similar to the excess risk associated with child care, there was a substantially smaller fraction of children who came from socioeconomically disadvantaged census tracts compared with the fraction in child care. Thus, in our study sample, the fraction of cases attributable to community-level predictors was generally smaller for significant census tract variables (3–4 percent) in comparison with the population attributable risk for individual-level predictors, particularly child-care attendance and age (from 5 to less than 24 months of age). It is worth noting that population attributable risks may not be strictly additive in nature (63).

Although individual characteristics are strong predictors of carriage and resistance, attention to the additional risks attributable to the community in which an individual lives may further quantify risks for pneumococcal carriage or resistance. Knowledge of community factors is likely to

have its greatest utility for researchers or public health authorities targeting communities for interventions to increase vaccine penetration, promote hand hygiene, or reduce unnecessary antibiotic prescribing. This is particularly true when individual-level data are not available or easily obtainable. Community factors may also have some utility in better categorizing young pediatric patients as low or high risk, particularly in children not attending child care. Finally, the study of community-level variables such as density, crowding, educational level, and poverty opens important areas of research to help further our understanding of pneumococcal transmission.

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REFERENCES

- 1. Robinson KA, Baughman W, Rothrock G, et al. Epidemiology of invasive *Streptococcus pneumoniae* infections in the United States, 1995–8: opportunities for prevention in the conjugate vaccine era. JAMA 2001;285:1729–35.
- 2. Black S, Shinefield H, Fireman B, et al. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. Pediatr Infect Dis J 2000;19:187–95.
- 3. Black SB, Shinefield HR, Hansen J, et al. Postlicensure evaluation of the effectiveness of seven valent pneumococcal conjugate vaccine. Pediatr Infect Dis J 2001;20:1105–7.
- 4. Sa-Leao R, Tomasz A, Santos Sanches I, et al. Pilot study of the genetic diversity of the pneumococcal nasopharyngeal flora among children attending day care centers. J Clin Microbiol 2002;40:3577–85.
- 5. Veenhoven R, Bogaert D, Uiterwaal C, et al. Effect of conjugate pneumococcal vaccine followed by polysaccharide pneumococcal vaccine on recurrent acute otitis media: a randomised study. Lancet 2003;361:2189–95.
- 6. Obaro SK. Confronting the pneumococcus: a target shift or bullet change? Vaccine 2000;19:1211–17.
- 7. Black SB, Shinefield HR, Ling S, et al. Effectiveness of heptavalent pneumococcal conjugate vaccine in children younger than five years of age for prevention of pneumonia. Pediatr Infect Dis J 2002;21:810–15.
- 8. Fireman B, Black SB, Shinefield HR, et al. Impact of the pneumococcal conjugate vaccine on otitis media. Pediatr Infect Dis J 2003;22:10–16.
- 9. Eskola J, Kilpi T, Palmu A, et al. Efficacy of a pneumococcal conjugate vaccine against acute otitis media. N Engl J Med 2001;344:403–9.
- 10. Belongia EA, Sullivan BJ, Chyou PH, et al. A community intervention trial to promote judicious antibiotic use and reduce penicillin-resistant *Streptococcus pneumoniae* carriage in children. Pediatrics 2001;108:575–83.
- 11. Finkelstein JA, Davis RL, Dowell SF, et al. Reducing antibiotic use in children: a randomized trial in 12 practices. Pediatrics 2001;108:1–7.
- 12. Little P, Gould C, Williamson I, et al. Pragmatic randomised

controlled trial of two prescribing strategies for childhood acute otitis media. BMJ 2001;322:336–42.

- 13. Schaffner W, Ray WA, Federspiel CF, et al. Improving antibiotic prescribing in office practice. A controlled trial of three educational methods. JAMA 1983;250:1728–32.
- 14. Bedos JP, Chevret S, Chastang C, et al. Epidemiological features of and risk factors for infection by *Streptococcus pneumoniae* strains with diminished susceptibility to penicillin: findings of a French survey. Clin Infect Dis 1996;22:63–72.
- 15. Samore MH, Magill MK, Alder SC, et al. High rates of multiple antibiotic resistance in *Streptococcus pneumoniae* from healthy children living in isolated rural communities: association with cephalosporin use and intrafamilial transmission. Pediatrics 2001;108:856–65.
- 16. Finkelstein JA, Huang SS, Daniel J, et al. Antibiotic-resistant *S*. *pneumoniae* in the heptavalent pneumococcal conjugate vaccine era: predictors of carriage in a multi-community sample. Pediatrics 2003;112:862–9.
- 17. Gray B, Dillon HC. Clinical and epidemiological studies of pneumococcal infection in children. Pediatr Infect Dis 1986;5: 201–7.
- 18. Musher DM, Groover JE, Reichler MR, et al. Emergence of antibody to capsular polysaccharides of *Streptococcus pneumoniae* during outbreaks of pneumonia: association with nasopharyngeal colonization. Clin Infect Dis 1997;24:441–6.
- 19. Borres MP, Alestig K, Krantz I, et al. Carriage of penicillinsusceptible and non-susceptible pneumococci in healthy young children in Goteborg, Sweden. J Infect 2000;40:141–4.
- 20. Whitney CG, Farley MM, Hadler J, et al. Increasing prevalence of multidrug-resistant *Streptococcus pneumoniae* in the United States. N Engl J Med 2000;343:1917–24.
- 21. Hyde TB, Gay K, Stephens DS, et al. Macrolide resistance among invasive *Streptococcus pneumoniae* isolates. JAMA 2001;286:1857–62.
- 22. Petrosillo N, Pantosti A, Bordi E, et al. Prevalence, determinants, and molecular epidemiology of *Streptococcus pneumoniae* isolates colonizing the nasopharynx of healthy children in Rome. Eur J Clin Microbiol Infect Dis 2002;21:181–8.
- 23. Marchisio P, Esposito S, Schito GC, et al. Nasopharyngeal carriage of *Streptococcus pneumoniae* in healthy children: implications for the use of heptavalent pneumococcal conjugate vaccine. Emerg Infect Dis 2002;8:479–84.
- 24. Lopez B, Cima MD, Vazquez F, et al. Epidemiological study of *Streptococcus pneumoniae* carriers in healthy primary-school children. Eur J Clin Microbiol Infect Dis 1999;18:771–6.
- 25. Principi N, Marchisio P, Schito GC, et al. Risk factors for carriage of respiratory pathogens in the nasopharynx of healthy children. Ascanius Project Collaborative Group. Pediatr Infect Dis J 1999;18:517–23.
- 26. Ekdahl K, Ahlinder I, Hansson HB, et al. Duration of nasopharyngeal carriage of penicillin-resistant *Streptococcus pneumoniae*: experiences from the South Swedish Pneumococcal Intervention Project. Clin Infect Dis 1997;25:1113–17.
- 27. Borres MP, Alestig K, Krantz I, et al. Carriage of penicillinsusceptible and non-susceptible pneumococci in healthy young children in Goteborg, Sweden. J Infect 2000;40:141–4.
- 28. Guillemot D, Carbon C, Balkau B, et al. Low dosage and long treatment duration of beta-lactam: risk factors for carriage of penicillin-resistant *Streptococcus pneumoniae*. JAMA 1998; 279:365–70.
- 29. Arnold KE, Leggiadro RJ, Breiman RF, et al. Risk factors for carriage of drug-resistant *Streptococcus pneumoniae* among children in Memphis, Tennessee. J Pediatr 1996;128:757–64.
- 30. US Census Bureau. United States Census 2000. Technical documentation, summary file 3 (SF3). Appendix A: geographic terms and concepts. Washington, DC: US Department of Com-

merce, 2003:A11. (http://www.census.gov/prod/cen2000/doc/ sf3.pdf). (Accessed April 9, 2003).

- 31. Krieger N, Chen JT, Waterman PD, et al. Geocoding and monitoring of US socioeconomic inequalities in mortality and cancer incidence: does the choice of area-based measure and geographic level matter? Am J Epidemiol 2002;156:471–82.
- 32. Chen FM, Breiman RF, Farley M, et al. Geocoding and linking data from population-based surveillance and the US Census to evaluate the impact of median household income on the epidemiology of invasive *Streptococcus pneumoniae* infections. Am J Epidemiol 1998;148:1212–18.
- 33. Finkelstein JA, Metlay J, Davis RL, et al. Antimicrobial use in defined populations of infants and young children. Arch Pediatr Adolesc Med 2000;154:395–400.
- 34. Platt R, Davis R, Finkelstein JA, et al. Multicenter epidemiologic and health services research on therapeutics in the HMO Research Network Center for Education and Research on Therapeutics. Pharmacoepidemiol Drug Saf 2001;10:373–7.
- 35. Finkelstein JA, Stille C, Nordin J, et al. Reduction in antibiotic use among US children, 1996–2000. Pediatrics 2003;112:620– 7.
- 36. US Census Bureau. United States Census 2000. Factfinder. Washington, DC: US Department of Commerce, 2003. (http:// factfinder.census.gov). (Accessed April 9, 2003).
- 37. Breiman L, Friedman JH, Olshen RA, et al. Classification and regression trees. The Wadsworth statistics/probability series. Belmont, CA: Wadsworth International Group, 1984.
- 38. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. Biometrics 1986;42:121–30.
- 39. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. Biometrika 1986;73:13–22.
- 40. Cole P, MacMahon B. Attributable risk per cent in case-control studies. Br J Prev Soc Med 1971;25:242–4.
- 41. Miettinen OS. Proportion of disease caused or prevented by a given exposure, trait, or intervention. Am J Epidemiol 1974;99: 325–32.
- 42. Bruzzi P, Green SR, Byar DP, et al. Estimating the population attributable risk for multiple risk factors using case control data. Am J Epidemiol 1985;122:904–14.
- 43. US Census Bureau. Poverty areas. Washington, DC: US Department of Commerce, 2002. (http://www.census.gov/ population/socdemo/statbriefs/povarea.html). (Accessed April 9, 2003).
- 44. Nilsson P, Laurell MH. Carriage of penicillin-resistant *Streptococcus pneumoniae* by children in day-care centers during an intervention program in Malmo, Sweden. Pediatr Infect Dis J 2001;20:1144–9.
- 45. Chiu SS, Ho PL, Chow FK, et al. Nasopharyngeal carriage of antimicrobial-resistant *Streptococcus pneumoniae* among young children attending 79 kindergartens and day care centers in Hong Kong. Antimicrob Agents Chemother 2001;45:2765– 70.
- 46. Kellner JD, Ford-Jones EL. *Streptococcus pneumoniae* carriage in children attending 59 Canadian child care centers. Toronto Child Care Centre Study Group. Arch Pediatr Adolesc Med 1999;153:495–502.
- 47. Loda FA, Collier AM, Glezen WP, et al. Occurrence of *Diplococcus pneumoniae* in the upper respiratory tract of children. J Pediatr 1975;87:1087–93.
- 48. Sa-Leao R, Tomasz A, Santos Sanches I, et al. Pilot study of the genetic diversity of the pneumococcal nasopharyngeal flora among children attending day care centers. J Clin Microbiol 2002;40:3577–85.
- 49. Sa-Leao R, Tomasz A, Sanches IS, et al. Genetic diversity and clonal patterns among antibiotic-susceptible and -resistant *Streptococcus pneumoniae* colonizing children: day care cen-

ters as autonomous epidemiological units. J Clin Microbiol 2000;38:4137–44.

- 50. Givon-Lavi N, Dagan R, Fraser D, et al. Marked differences in pneumococcal carriage and resistance patterns between day care centers located within a small area. Clin Infect Dis 1999; 29:1274–80.
- 51. Dagan R, Givon-Lavi N, Zamir O, et al. Reduction of nasopharyngeal carriage of *Streptococcus pneumoniae* after administration of a 9-valent pneumococcal conjugate vaccine to toddlers attending day care centers. J Infect Dis 2002;185:927–36.
- 52. Ekdahl K, Hansson HB, Molstad S, et al. Limiting the spread of penicillin-resistant *Streptococcus pneumoniae*: experiences from the South Swedish Pneumococcal Intervention Project. Microb Drug Resist 1998;4:99–105.
- 53. Carabin H, Gyorkos TW, Soto JC, et al. Effectiveness of a training program in reducing infections in toddlers attending day care centers. Epidemiology 1999;10:219–27.
- 54. De Lencastre H, Tomasz A. From ecological reservoir to disease: the nasopharynx, day-care centres and drug-resistant clones of *Streptococcus pneumoniae*. J Antimicrob Chemother 2002;50(suppl C):75–82.
- 55. Sa-Leao R, Tomasz A, Sanches IS, et al. Carriage of internationally spread clones of *Streptococcus pneumoniae* with unusual drug resistance patterns in children attending day care centers in Lisbon, Portugal. J Infect Dis 2000;182:1153–60.
- 56. Harris AD, Samore MH, Carmeli Y. Control group selection is an important but neglected issue in studies of antibiotic resistance. (Letter). Ann Intern Med 2000;133:159.
- 57. Harris AD, Samore MH, Lipsitch M, et al. Control-group selection importance in studies of antimicrobial resistance: examples applied to *Pseudomonas aeruginosa*, enterococci, and *Escherichia coli*. Clin Infect Dis 2002;34:1558–63.
- 58. Melnick SL, Sprafka JM, Laitinen DL, et al. Antibiotic use in urban whites and blacks: the Minnesota Heart Survey. Ann Pharmacother 1992;26:1292–5.
- 59. Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. JAMA 1997;278:901–4.
- 60. Halasa NB, Griffin MR, Zhu Y, et al. Decreased number of antibiotic prescriptions in office-based settings from 1993 to 1999 in children less than five years of age. Pediatr Infect Dis J 2002;21:1023–8.
- 61. Hofmann J, Cetron MS, Farley MM, et al. The prevalence of drug-resistant *Streptococcus pneumoniae* in Atlanta. N Engl J Med 1995;333:481–6.
- 62. Selby JV. Linking automated databases for research in managed care settings. Ann Intern Med 2001;127:719–24.
- 63. Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable fractions. Am J Public Health 1998;88:15– 19.