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Risk of invasive pneumococcal disease varies by neighbourhood characteristics: implications for prevention policies

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SUMMARY

This study investigates neighbourhood variation in rates of pneumococcal bacteraemia and community-level factors associated with neighbourhood heterogeneity in disease risk. We analysed data from 1416 adult and paediatric cases of pneumococcal bacteraemia collected during 2005–2008 from a population-based hospital surveillance network in metropolitan Philadelphia. Cases were geocoded using residential address to measure disease incidence by neighbourhood and identify potential neighbourhood-level risk factors. Overall incidence of pneumococcal bacteraemia was 36·8 cases/100 000 population and varied significantly (0–67·8 cases/100 000 population) in 281 neighbourhoods. Increased disease incidence was associated with higher population density [incidence rate ratio (IRR) 1·10/10 000 people per mile^2, 95% confidence interval (CI) 1·0–1·19], higher percent black population (per 10% increase) (IRR 1·07, 95% CI 1·04–1·09), population aged $\leqslant$5 years (IRR 3·49, CI 1·8–5·18) and population aged $\geqslant$65 years (IRR 1·19, CI 1·00–1·38). After adjusting for these characteristics, there was no significant difference in neighbourhood disease rates. This study demonstrates substantial small-area variation in pneumococcal bacteraemia risk that appears to be explained by neighbourhood sociodemographic characteristics. Identifying neighbourhoods with increased disease risk may provide valuable information to optimize implementation of prevention strategies.

Key words: Geographic information systems, neighbourhood risk factors, pneumococcal disease.

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INTRODUCTION

The introduction of the 23-valent polysaccharide vaccine in 1983 and a 7-valent pneumococcal conjugate vaccine for children in 2000 resulted in major epidemiological shifts in pneumococcal disease in both children and adults with marked reductions in disease due to vaccine serotypes [1–5]. However, there has also been an increase in carriage and infections caused by non-vaccine serotypes [6–11]. A new 13-valent conjugate vaccine was recently introduced and recommended for routine administration to infants and young children [12]. Pneumococcal vaccination recommendations are currently based upon our understanding of individual-level factors that influence the risk of pneumococcal disease [13–16]. However, a better understanding of community-level factors such as neighbourhood characteristics or environmental exposures may help elucidate disparities in invasive pneumococcal disease that have persisted despite high vaccination rates [10, 17]. As such, there has been more research focusing upon community-level factors that may influence the risk of pneumococcal carriage and disease [18–21]. This can provide valuable information to inform the implementation of vaccination recommendations and other community-level prevention efforts.

Wide variation in the risk of invasive pneumococcal disease over large geographical areas is well-established. This may be due to differences across geographical areas in seasonal trends for respiratory virus transmission that may encourage pneumococcal infection [22, 23]. Research also suggests that there are community-level characteristics that affect variation in both the incidence of invasive disease and pneumococcal carriage across cities and counties, even after adjusting for individual-level factors [19, 20, 24]. Huang, *et al*. demonstrated that residence in socioeconomically disadvantaged census tracts increased the odds of pneumococcal nasopharyngeal carriage in children [20]. Huang, *et al*. also demonstrated an association between nasal carriage and day-care attendance in socioeconomically advantaged but not disadvantaged communities suggesting that the effect of this individual-level exposure is impacted by neighbourhood characteristics [19].

While previous studies have identified community characteristics associated with increased risk of pneumococcal carriage or disease in individuals, they do not investigate incident pneumococcal disease within neighbourhoods, nor do they directly evaluate the impact of community characteristics on variable rates between communities. The aims of this study were: (1) to investigate whether or not there is small-area variation in the incidence of pneumococcal bacteraemia in both adults and children within neighbourhoods in a large metropolitan region and (2) to determine community-level factors that may explain neighbourhood heterogeneity focusing upon factors known to affect the risk of pneumococcal disease including race, age and population density.

METHODS

Study population

This study was based upon data from a population-based surveillance network for bacteraemic pneumococcal disease in the five-county Philadelphia metropolitan region: Bucks, Chester, Delaware, Montgomery and Philadelphia counties that has been described previously [9, 25]. Based upon U.S. census 2000 data (www.census.gov), 2881132 adults (aged $\geqslant$18 years) and 968515 children reside in these counties. Forty-eight of the 49 paediatric and adult acute-care hospitals that serve this region participate in the network which has been validated for completeness and accounts for $>$97% of all cases of bacteraemic pneumococcal disease in the study region [25]. The single non-participating site is a small hospital closed to external studies. Our study population included all hospitalized adult and paediatric patients with pneumococcal bacteraemia who presented to any of the participating hospitals during 2005–2008 and who resided in one of the five metropolitan Philadelphia counties. The case definition for bacteraemia included at least one positive blood culture drawn at the time of and up to 48 h after admission, initially identified by microbiology personnel at each participating hospital and confirmed in the central laboratory at the University of Pennsylvania. Confirmation criteria included colony morphology, haemolytic activity, Gram stain appearance, catalase reaction, bile solubility and optochin susceptibility [26].

Community-level data

Each subject was geocoded to census tract and neighbourhood using their residential address with Arcview 9·2 (ESRI) and the StreetMaps USA reference database. Residential address was initially obtained from

administrative data associated with each eligible patient's admission and verified through telephone interview (76% of patients). For those without telephone follow-up, the address available in the patient's medical chart was used. Four eligible cases did not provide any address information. We then used minor civil divisions (MCD) to define neighbourhood. MCD is a cluster of one to several census tracts defined as 'the primary governmental or administrative division of a county' [27]. This representation of a neighbourhood division was utilized across all counties, corresponded to a town or township and approximated historically defined communities sharing similar characteristics and resources. All neighbourhood data were extracted from U.S. census 2000 data (www.census.gov). Specific neighbourhood-level factors were chosen based upon previously described individual and community characteristics associated with pneumococcal disease and included population density, percentage of neighbourhood population who were black, percentage of neighbourhood population aged $\leqslant 5$ years and percentage of neighbourhood population aged $\geqslant 65$ years [14, 18, 20, 21].

Statistical analysis

Our goal was to determine whether the rate of pneumococcal bacteraemia varied by neighbourhood. We calculated incidence rates using the number of cases identified through the surveillance network divided by the total population according to U.S. Census 2000. We stratified incidence rate by age group (0–17 years and $\geqslant 18$ years), race (black and white due to the very small proportion of cases from other races) and neighbourhood. Raw neighbourhood incidence rates were illustrated on a map using quartiles.

To determine whether there was variation in incidence rates across neighbourhoods beyond what would be expected from random sampling and whether the variation was related to community characteristics, we utilized a mixed-effects Poisson regression. In the base regression model, the outcome was case count, population was the offset and neighbourhood was the random effect. From this model, we calculated the predicted value of the random effect for each neighbourhood and compared it to the normal distribution to obtain a *P* value, which indicated whether a particular neighbourhood had a significantly higher incidence rate than expected from random sampling. This was illustrated in a *P* value map. We then added neighbourhood characteristics to the base model as fixed effects including neighbourhood population density, proportion of neighbourhood population that is black, proportion of the neighbourhood population aged $\leqslant 5$ years and proportion of the population aged $\geqslant 65$ years. We performed initial regression analyses with each neighbourhood characteristic as a single covariate and then sequentially built two, three, and four variable models, examining the change in the variance of the random effect as a measure of overall neighbourhood-level effect. We report incidence rate ratios (IRRs) for each neighbourhood characteristic.

To determine whether there were other neighbourhood factors that were potentially associated with pneumococcal bacteraemia, we repeated our models using three additional factors: average income, percent below poverty and average household size (as another measure for crowding). We added each of the three factors individually to the base model to examine its association with disease incidence and its impact on the change in the variance of the random effect. We then added the additional factors to the final multivariate model to examine their influence on the estimated effects of the neighbourhood factors. Last, we calculated pairwise Pearson correlations among all the factors to measure for potential collinearity between neighbourhood characteristics.

All analyses were performed using Stata v. 11.0 (StataCorp LP, USA) or SAS v. 9.2 (SAS Institute Inc., USA). A *P* value of 0·05 was used to determine significance for analyses. This study was approved by the Institutional Review Boards at the University of Pennsylvania Perelman School of Medicine and all participating study sites. For a full list of the hospitals, see Appendix.

RESULTS

There were 1422 cases of hospitalized pneumococcal bacteraemia reported during 2005–2008 in a total population of 3849071 adults and children in the Philadelphia five-county metropolitan region. Population characteristics are detailed in Table 1 and individual characteristics of the study population are detailed in Table 2. Four cases did not have a residential address and two cases resided outside of the Philadelphia five-county metropolitan area leaving 1416 cases to include in the analyses. The overall annual incidence of pneumococcal bacteraemia pneumococcal disease was 12·3 cases/100 000 population (3·9 cases/100 000 in children aged 0–17 years and 15

Table 1. *Population characteristics of the metropolitan Philadelphia region, U.S. Census 2000*

County	No. of cases	Total population	Population aged <0–4 years (%)	Population aged ⩾65 years (%)	Population black (%)	Population density*
Bucks	187	563 905	36 137 (6·4)	70 368 (12·5)	18 504 (3·3)	0·97
Montgomery	154	426 936	29 115 (6·8)	50 223 (11·8)	26 244 (6·1)	0·57
Delaware	198	731 251	46 119 (6·3)	109 342 (14·9)	55 737 (7·6)	1·69
Chester	171	546 760	33 958 (6·2)	85 186 (15·6)	76 361 (14·0)	2·97
Philadelphia	683	1516 974	98 141 (6·4)	213 538 (14·1)	655 751 (43·2)	11·99
Other†	23	63 245	3993 (6·3)	2639 (4·2)	5712 (9·0)	0·70
Total	1416	3 849 071	247 463 (6·4)	531 296 (13·8)	838 809 (21·8)	1·78

* Density = 1000 people per mile^2.
† Neighbourhoods in the metropolitan region that did not map to Bucks, Montgomery, Delaware, Chester or Philadelphia counties.

Table 2. *Demographic characteristics of the study population* (*all patients admitted to a surveillance network hospital in metropolitan Philadelphia with pneumococcal bacteraemia, 2005–08*), *N* = *1422**

Characteristics	*N*	%
Gender, male	731	51·4
Age, years		
<18	114	8·0
18–39	157	11·0
40–69	704	49·5
⩾70	446	31·4
Race		
White	824	57·9
Black	487	34·2
Asian	16	1·1
Other†	5	<1
Hispanic ethnicity	73	5·1
Ever smoked	418	30·8
History of asthma	202	14·5
History of pneumococcal vaccination	610	45/0
<5 years old (*n* = 81)	51	63·0
⩾65 years old (*n* = 521)	308	59·0

* Data obtained from telephone interview (76%) or medical chart abstraction (24%.)
† Other = Pacific Islander, Native Hawaiian and Native American.

cases/100 000 in adults aged >18 years). Information regarding race was available for 1329 (93·9%) cases. Of these, 823 cases were in white children and adults and 485 were in black children and adults yielding annual incidence rates of 10·1 cases/100 000 population and 19·3 cases/100 000 population, respectively.

Figure 1 displays the geographical variation in the rate of pneumococcal bacteraemia across the five-county Philadelphia region. Across the 281 neighbourhoods in this region, the annual incidence of disease ranged from 0 cases/100 000 population to 67·8 cases/100 000 population. Forty-six percent of cases resided within Philadelphia County (Fig. 1, inset) compared to 37·7% of the total population residing in Philadelphia County. We next constructed the base mixed-effects model and calculated the predicted random effect for each neighbourhood to identify neighbourhood 'hot-spots' (i.e. areas with statistically higher predicted incidence rates than expected from random sampling.) Figure 2 displays the resulting *P* value map identifying neighbourhoods with higher than expected annual incidence rates for the overall five-county region and for Philadelphia alone (Fig. 2, inset).

Neighbourhood characteristics influencing disease rates

We first measured the overall neighbourhood-level effect on disease rate based upon the variance of the random effect in a mixed-effects model. Without any adjustment for neighbourhood-level covariates, the variance was significant ($P < 0{\cdot}0001$), demonstrating significant differences in the rate of pneumococcal bacteraemia at the neighbourhood level. Table 3 summarizes the impact of the successive addition of neighbourhood-level covariates (neighbourhood population density, percent population black, percent population aged <5 years and percent population aged ⩾65 years) on the variance of the random effect. In the final model, after adjusting for all four characteristics, no significant neighbourhood variation remained ($P = 0{\cdot}0819$). In addition, a *P* value map analogous to Figure 2, based upon predicted values of the random effect from the final model adjusting for all four neighbourhood characteristics revealed no neighbourhoods with significantly higher than expected case counts (data not shown.)

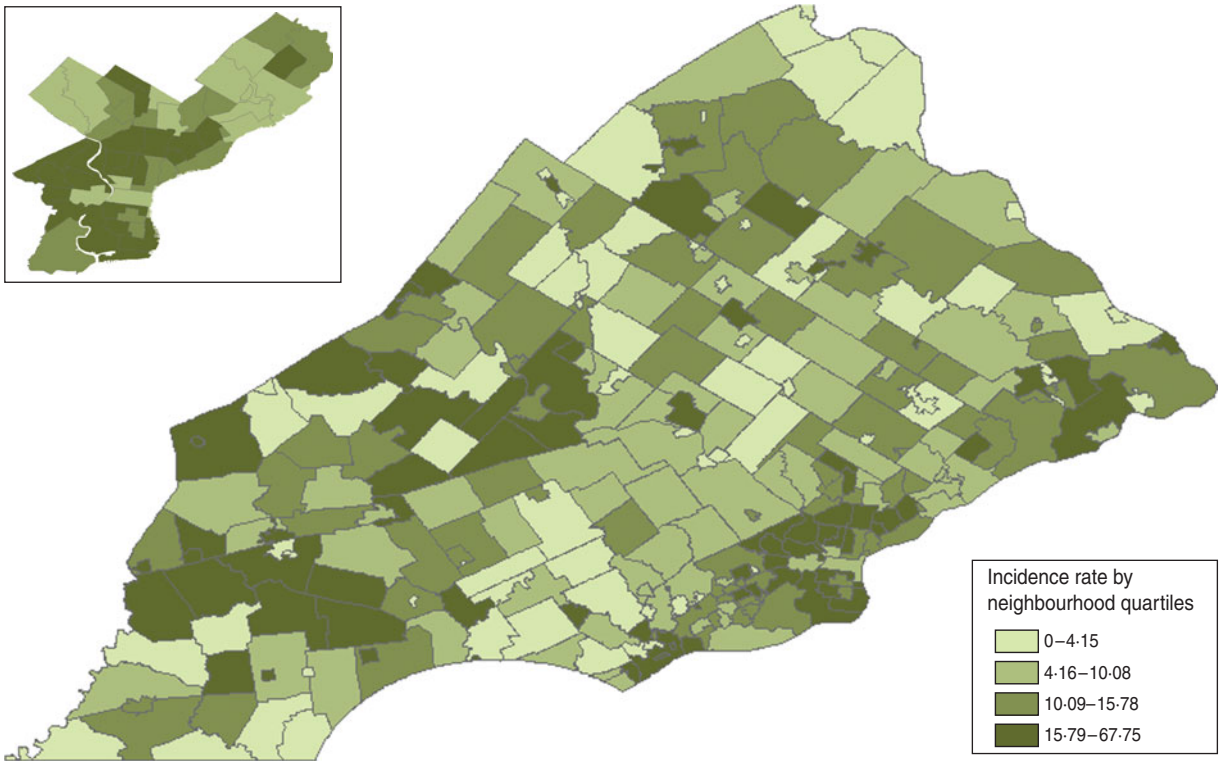

Fig. 1. Raw incidence (per 100 000 population) of invasive pneumococcal infection in the Philadelphia metropolitan area, categorized by quartiles. Inset: Philadelphia County.

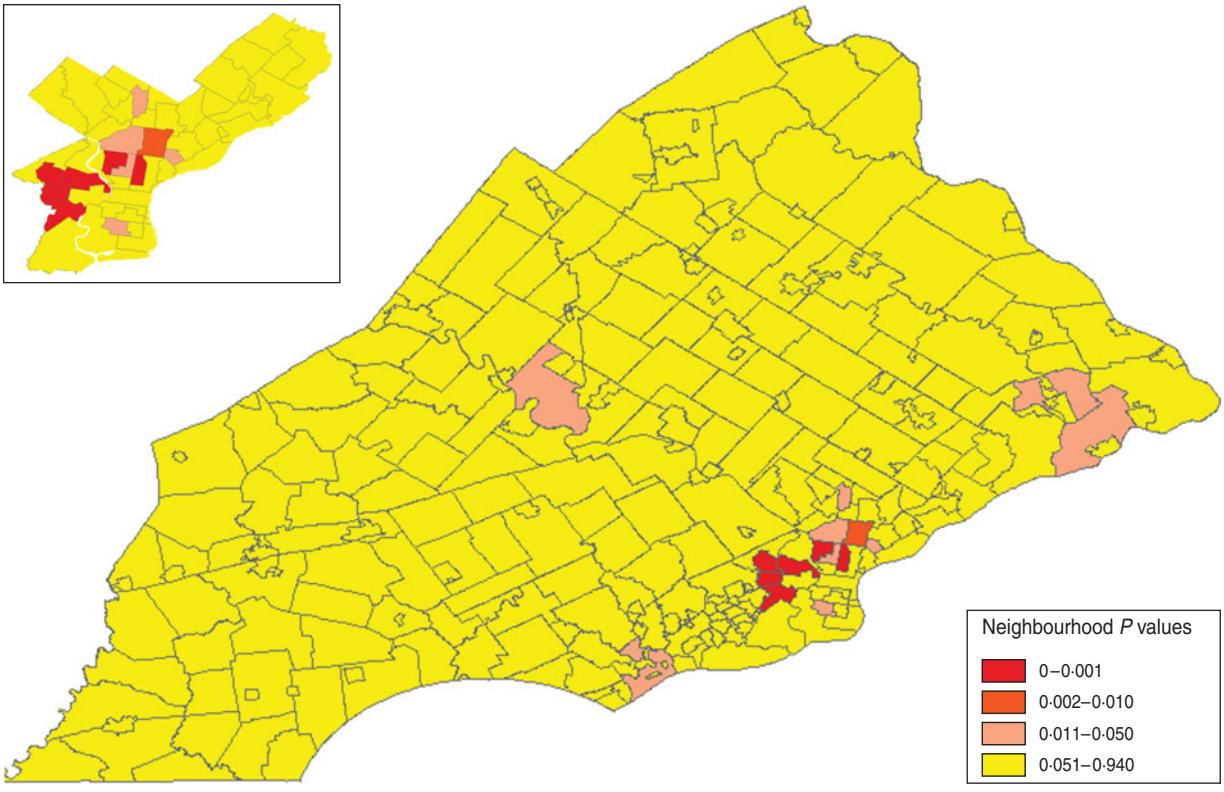

Fig. 2. *P* value map illustrating whether a neighbourhood has a significantly higher incidence rate of invasive pneumococcal disease (comparing predicted *vs.* expected rates). Inset: Philadelphia County.

Table 3. *Mixed-effects Poisson regression to demonstrate effect of neighbourhood characteristics on variance of the random effect, incidence of hospitalized bacteraemic pneumococcal disease in metropolitan Philadelphia, 2005–2008*

Model	Fixed effects in the model	Variance of random effect	*P* value for testing if variance >0
1	Base model	0·1325	<0·0001
2	Neighbourhood density	0·0849	<0·0001
3	% population black	0·0429	<0·0001
4	% population aged <5 years	0·0985	<0·0001
5	% population aged ⩾65 years	0·1304	<0·0001
6	% <5 years, % ⩾65 years	0·0955	<0·0001
7	% black, % ⩾65 years	0·0421	0·0011
8	% black, % <5 years	0·0223	0·0347
9	% black, % <5 years, % ⩾65 years	0·0193	0·0585
10	Density, % black, % <5 years, % ⩾65 years	0·0167	0·0819

Table 4. *Relative rate of bacteraemic pneumococcal disease adjusted for neighbourhood characteristics in metropolitan Philadelphia, 2005–2008*

Effects	Unadjusted RR	95% CI	Adjusted RR	95% CI
Density (100 00 people/mile² increase)	1·29	(1·18–1·41)	1·10	(1·00–1·19)
% population black (10% increase*)	1·08	(1·07–1·11)	1·07	(1·04–1·09)
% population aged <5 years (10% increase*)	3·36	(2·09–5·56)	3·49	(1·80–5·18)
% population aged ⩾65 years (10% increase*)	0·94	(0·79–1·13)	1·19	(1·00–1·38)

RR, Relative rate; CI, confidence interval.
* 10% increase in the percent of the population with each characteristic.

We also estimated IRRs (i.e. relative risks) for each neighbourhood characteristic included in the mixed-effects model (Table 4). In analyses examining single neighbourhood characteristics, higher population density, higher percentage of neighbourhood population that is black, and a higher percentage of the neighbourhood population aged <5 years were all associated with increased incidence of pneumococcal bacteraemia. Percent population aged ⩾65 years was not significantly associated with increased incidence of bacteraemic pneumococcal infection. However, when all four neighbourhood characteristics were included in a multivariable model, they were all significantly associated with increased incidence of disease, (population density: IRR 1·10/10 000 per mile² increase, $P=0·04$; percent population black: IRR 1·07 per 10% increase in proportion, $P<0·0001$; percent population aged <5 years: IRR 3·49 per 10% increase in proportion, $P<0·0001$; percent population aged ⩾65 years: IRR 1·19 per 10% increase in proportion, $P=0·04$).

In the investigation of additional neighbourhood characteristics, both average income and percent population below poverty were significantly associated with incidence of bacteraemic pneumococcal disease – higher average income was associated with lower incidence of disease while a higher proportion of households below poverty was associated with increased disease incidence (data not shown). Average household size was not significantly associated with disease incidence and was therefore not included in the multivariable model. When either income or percent below poverty was added to the multivariable model, density was no longer significant suggesting collinearity. Pairwise Pearson correlation confirmed this conclusion – density and both percent below poverty and average income were highly correlated (correlation coefficients 0·72, $P<0·0001$ and −0·64,

$P<0{\cdot}0001$, respectively.) We therefore only included density, but not poverty or average income in the final multivariable model. Poverty and average income were also highly correlated with percent population black (correlation coefficients 0·73, $P<0{\cdot}0001$ and $-0{\cdot}53$, $P<0{\cdot}0001$, respectively).

DISCUSSION

Our results demonstrate significant neighbourhood variation in the incidence of pneumococcal bacteraemia within a major metropolitan region that appears to be explained by neighbourhood sociodemographic characteristics. In particular, after controlling for neighbourhood population density, percent population black, percent population aged <5 years and percent population aged $\geqslant 65$ years, the neighbourhood effect was no longer significant. This is the first paper to demonstrate this degree of small-area variation in invasive pneumococcal disease rates which may have policy implications for surveillance and resource planning.

The observation that pneumococcal disease rates vary over small areas within an urban region could be explained by at least two mechanisms. First, heterogeneity in the underlying neighbourhood populations may create the appearance of neighbourhood-level variation that is entirely driven by differences in individual-level characteristics. Such an effect likely reflects individual host susceptibility to pneumococcal infection and the development of disease. Epidemiological studies of invasive pneumococcal disease prior to the introduction of PCV7 have identified multiple individual risk factors associated with a higher incidence of infection, including older (>50 years) and younger (<2 years) age and black race [28]. Our results also show a higher rate of infection in black children and adults. Having a higher proportion of individuals residing in a neighbourhood who are at increased risk of infection can contribute to higher neighbourhood rates of disease. The significant racial segregation of neighbourhoods in the Philadelphia region precludes our ability to simultaneously examine individual- and neighbourhood-level effects, particularly in terms of racial composition. We would not have adequate power to investigate both within- and between-neighbourhood variation.

As a second mechanism, there may be true neighbourhood-level effects that influence disease transmission. Other studies have reported small-area variation in pneumococcal carriage and resistance patterns associated with day-care centres suggesting that there may be a role for microenvironments that affect transmission of isolates [19, 24, 29]. Huang *et al.* has also modelled the role that community characteristics may play in risk of pneumococcal carriage in children [20]. Additionally, multiple studies since the introduction of the pneumococcal conjugate vaccine have shown a changing epidemiology of infection, particularly in adults, suggesting that contextual factors associated with transmission are important [1, 6, 7, 25, 30, 31]. For example, carriage of pneumoccoci is highly prevalent in young children [32] and previous research has shown that adults are at increased risk for pneumococcal carriage if they reside with a child aged <5 years or an unvaccinated child [9, 30]. As carriage is a risk factor for the development of invasive disease [33, 34], a population with a higher proportion of young children may have increased rates of invasive pneumococcal disease – this was demonstrated by our results. Information regarding nasopharyngeal carriage and vaccination rates in children within study neighbourhoods may help better explain our findings.

We also found an increased incidence of pneumococcal bacteraemia within neighbourhoods with a higher proportion of residents who are black. Previous research of both pre- and post-conjugate vaccine have demonstrated significantly higher rates of invasive disease in black children and adults compared to white children and adults [10, 21, 28]. The reasons for these differences are not entirely clear and in our results, it is not clear whether race has an effect at the individual or at the community level. For example, black individuals may have a higher prevalence of comorbidities associated with invasive infection. Disparities in the rate of polysaccharide pneumococcal vaccination in adults have been documented [35, 36].

Previous research investigating invasive pneumococcal disease has shown that racial disparities decrease when infection rates are adjusted for socioeconomic indicators such as census tract poverty level [14, 21, 37]. This suggests that race may be a marker of other socioeconomic factors that could affect transmissibility within a neighbourhood such as access to healthcare services, household structure or neighbourhood crowding. We found that average neighbourhood income, percent population living below poverty and neighbourhood population density were all highly correlated with the percent population

that is black, supporting this possibility. However, it is interesting to note that when we included these factors in our multivariable model, percent population black remained significantly associated with incidence of pneumococcal disease. We considered collinearity for the selection of other neighbourhood factors, including neighbourhood density which we included as a measure of crowding. We found that neighbourhood density was highly correlated with neighbourhood income and percent population below poverty and previous studies have suggested that census tract income may be interchangeable with other neighbourhood factors such as crowding [20].

Evaluating both individual and community characteristics can have important implications for infectious diseases epidemiology and public health planning, especially vaccine policies. Despite recommendations for universal childhood vaccination, disparities still persist [38] and our results suggest that there are neighbourhood hot-spots associated with community characteristics that may illustrate these continued disparities. Neighbourhood-level vaccination rates were not available to us at the time of this study; however, National Immunization Survey data from 2005 to 2008 show conjugate vaccine series completion rates of 60·2–81·2% in children aged 19–35 months in Philadelphia County and 73·3–84·4% for the rest of the state [17, 37–41]. This suggests regional differences and also shows that coverage levels had not yet reached the Healthy People 2010 goal of 90%. Understanding the interaction between neighbourhood characteristics and both disease risk and vaccination may best inform effective prevention policies for pneumococcal disease. This is especially important as the epidemiology of pneumococcal disease will probably continue to shift after the introduction of the 13-valent conjugate vaccine.

While our results suggest that community characteristics can explain variation in rates of invasive pneumococcal infection, our work does have limitations. Our study population only includes patients with pneumococcal bacteraemia and therefore may have missed some individuals with invasive pneumococcal disease who only have a positive culture from a different sterile site (i.e. pleural or cerebrospinal fluid). As with any study utilizing geographical data, another limitation is the modifiable areal unit problem. There are no perfect political boundaries to define healthcare patterns and therefore it is possible that alternative definitions for a neighbourhood or community could lead to a more accurate characterization of the community-level factors that are most salient to an individual's disease risk. Moreover, we utilized U.S. 2000 census data and it is possible that census tract boundaries and neighbourhood demographic characteristics shifted by the study period. However, we do not suspect marked changes that would significantly impact our results. We also did not perform spatial analytics and therefore cannot rule out spatial autocorrelation.

Most importantly, we were not able to determine whether our findings are driven by individual factors that are heterogeneously distributed across neighbourhoods or by a true contextual effect of these characteristics. We present data regarding factors associated with neighbourhood rates of infection, not on an individual's risk of developing disease. We were therefore not able to determine the relationship between individual and community characteristics on disease risk, nor could we establish causality between neighbourhood-level characteristics and rates of pneumococcal bacteraemia. Last, we did not measure all neighbourhood-level characteristics that could impact rates of invasive pneumococcal infection.

Despite these limitations, our work presents neighbourhood-level rates of invasive pneumococcal infection from prospective surveillance data among a diverse patient population. We identified neighbourhoods at increased risk of invasive pneumococcal disease which might help inform future public health efforts at prevention, especially vaccination policies after the introduction of a newly approved pneumococcal conjugate vaccine.

APPENDIX

The Delaware Valley Case Control Network includes the following hospitals listed with their respective physician co-investigators and laboratory directors: Abington Memorial Hospital (Robert R. Dee, MD, Herbert Auerbach, DO), Albert Einstein Medical Center (Jerry Zuckerman, MD, Nancy Young, MD), Brandywine Hospital (John H. Bartels, MD, Stephen B. Chasko, MD), Bryn Mawr Hospital (Peter Spitzer, MD), Chester County Hospital (John Roberts MD, Jim Heald, MD), Chestnut Hill Hospital (Lawrence Livornese, MD, Andrew So, MD), Children's Hospital of Philadelphia (Susan E. Coffin, MD, MPH, Karin McGowan, PhD), Crozer-Chester Medical Center, Springfield Hospital and Taylor Hospital (William D. Ravreby, MD, Harvey B.

Spector, MD), Delaware County Memorial Hospital (Jackeline Iaccovella, MD, Lawrence M. Matthews, MD, PhD), Doylestown Hospital (David Loughran, DO, Robert Trotta, MD), Elkins Park Hospital* (Donald Marcus, MD, Xiaoli Chen, MD), Episcopal Hospital* (Peter Axelrod, Allan Truant, PhD), Fox Chase Cancer Center (Peter Axelrod, MD), Aria Health Bucks County, Frankford and Torresdale Campuses (Donald Marcus, MD, Peter Farano, MD), Graduate Hospital* (Milchael Silverman, MD, Fernando Garcia, MD), Grand View Hospital (Abby Huang, MD, Irwin Hollander, MD), Hahnemann University (Mashiul Chowdhury, MD, Christopher Emery, MD), Holy Redeemer Hospital and Medical Center (Robert R. Dee, MD, Pantaleon Fagel, MD), Hospital of the University of Pennsylvania (Joshua P. Metlay, MD, PhD, Paul Edelstein, MD), Jeanes Hospital (Richard Tepper, MD, Irma Palazzo, MD), Jennersville Regional Medical Center (John H. Bartels, MD, James Monihan, MD), Lankenau Hospital (Lawrence Livornese, MD, Olarae Giger, PhD, Albert Keshgegian, MD), Lansdale Hospital (Abby Huang, MD), Lower Bucks Hospital (Donald Marcus, MD, Tatiana Chernova, MD), Mercy Community Hospital*, Mercy Fitzgerald Hospital and Mercy Hospital of Philadelphia (William McNamee, MD, Lorenzo Galindo, MD), Mercy Suburban Hospital (Wayne Miller, DO), Methodist Hospital (Robert Measley, MD, Harvey Bellin, MD), Montgomery Hospital (Hazel Bluestien, MD, Paul H. Belser, MD), Northeastern Hospital (Jerry Zuckerman, MD), Paoli Memorial Hospital (David Trevino, MD), Parkview Hospital* (Jerry Zuckerman, MD), Pennsylvania Hospital (Michael Braffman, MD, John Stern, MD, Julieta Barroeta, MD), Phoenixville Hospital (Raymond Kovalski, MD, Leonas Bekeris, MD), Pottstown Memorial Medical Center (Raymond Kovalski, MD, Dante DiMarzio, DO), Presbyterian Medical Center (Vincent LoRe, MD, MSCE), Riddle Memorial Hospital (Marc Gilbert, MD, Susan Yaron, MD), Roxborough Memorial Hospital (Lawrence Livornese, MD, Pradeep Bhagat, MD), St Agnes Medical Center* (Robert Measley, MD, John McCormick), St Christopher's Hospital for Children (Jane Gould, MD), St Joseph's Hospital (David Loughran, DO, Alberto Millos, MD), St Luke's Quakertown Hospital (Abby Huang, MD, David Anderson, MD), St Mary Medical Center (Donald Marcus, MD, Zenon Gibas, MD), Temple University Hospital (Peter Axelrod, MD, Carmelita Flores), Thomas Jefferson University Hospital (Michael Baram, MD, Stephen Peiper, MD), Veterans Affairs Medical Center (Darren Linkin, MD, MSCE, Laura Chandler, PhD), Warminster Hospital* (David Loughran, DO, Manjula Balasubramanian, MD),

(* Closed during the course of the project)

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DECLARATION OF INTEREST

Dr Lautenbach reports receiving research funding from 3M, AstraZeneca, and Cubist. Dr Feemster reports serving on an advisory board regarding healthcare provider attitudes towards vaccines and vaccine-preventable diseases at Pfizer Inc.

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