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Socioeconomic factors explain racial disparities in invasive community-associated methicillin-resistant *Staphylococcus aureus* disease rates

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Abstract

Introduction—Invasive community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) incidence in the United States is higher among black persons than white persons. We explored the extent to which socioeconomic factors might explain this racial disparity.

Methods—A retrospective cohort was based on CDC's Emerging Infections Program surveillance data for invasive community-associated MRSA cases (isolated from a normally sterile site of an outpatient or on hospital admission day 3 in a patient without specified major

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The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

Conflict of Interest

No relevant conflicts of interest.

healthcare exposures) from 2009–2011 in 33 counties of 9 states. We used generalized estimating equations to determine census tract-level factors associated with differences in MRSA incidence and inverse odds ratio weighted mediation analysis to determine the proportion of racial disparity mediated by socioeconomic factors.

Results—Annual invasive community-associated MRSA incidence was 4.59/100,000 among whites and 7.60/100,000 among blacks (rate ratio: 1.66, 95% CI, 1.52–1.80). In the mediation analysis, after accounting for census tract-level measures of federally-designated medically underserved areas, education, income, housing value, and rural status, 91% of the original racial disparity was explained; no significant association of black race with community-associated MRSA remained (rate ratio: 1.05, 95% CI, 0.92–1.20).

Conclusions—The racial disparity in invasive community-associated MRSA rates was almost entirely mediated by socioeconomic factors. The specific factors that underlie the association between tract-level socioeconomic measures and MRSA incidence, which may include modifiable social (e.g., poverty, crowding) and biological factors (not explored in this analysis), should be elucidated to define strategies for reducing racial disparities in community-associated MRSA rates.

Keywords

methicillin-resistant *Staphylococcus aureus*; antibiotic resistance; racial disparities; social determinants of health

Background

Methicillin-resistant *Staphylococcus aureus* (MRSA) has been recognized for decades as a significant pathogen in healthcare settings and an antibiotic-resistant pathogen of major importance in the United States [1–4]. Currently, guidelines and professional society recommendations provide strategies for preventing MRSA and other drug-resistant organisms in healthcare settings [5–7]; large declines in healthcare-associated MRSA have been documented over the past decade [8,9].

However, in the United States MRSA also emerged in the community in the late 1990s [10,11]. The incidence of invasive infection due to community-associated MRSA has not substantially changed for several years and, owing to declines in health care associated MRSA, now exceeds that of invasive MRSA developing during the course of hospitalization [9,12]. It is estimated that over 15,000 invasive community-associated infections and over 1,000 associated deaths occur annually in the United States [12].

Furthermore, population-based MRSA infection data in North America have consistently documented higher rates in black persons than in white persons [13–16]. Some proposed reasons for the racial disparity have included differences in host factors and differences in patients' underlying medical conditions [10,13,14]. There are no general population-level guidelines or strategies for preventing invasive community-associated MRSA infections or for reducing racial disparities in MRSA infection rates. As potential strategies are developed or considered, the existence of racial disparities raises the question of whether prevention strategies could be developed that would reduce this disparity.

Factors related to lower socioeconomic status, such as prior incarceration, intravenous drug use, and crowding, are known to increase the risk of community-associated MRSA infection [17–19], and lower socioeconomic status in the community has been associated with increased rates of other acute infectious diseases [20]. Furthermore, black persons in the US experience lower socioeconomic status, which has been described to be due to a complex set of historical and current experiences and conditions [21–25]. Socioeconomic factors, therefore, are likely to account for at least some of the observed racial disparities in community-associated MRSA infection rates.

We examined whether area-based socioeconomic factors could explain racial differences in community-associated invasive MRSA infection incidence. In this project, the area-based measures proxy both individual and community level socioeconomic conditions and experiences. Our goal was both to assess which community factors were associated with differences in MRSA infection incidence, and to what extent these factors explained racial differences in MRSA rates. The intention was for results to inform future directions for prevention of invasive community-associated MRSA.

Methods

MRSA surveillance data

The study design was a retrospective cohort using MRSA data obtained from CDC's Emerging Infections Program (EIP) Active Bacterial Core Surveillance for invasive MRSA in 2009–2011. EIP MRSA surveillance is an active, population-based, laboratory-based surveillance program that has been described previously [13]. An invasive community-associated MRSA case was defined as isolation of MRSA from a normally sterile body site (e.g., blood, cerebrospinal fluid, internal body fluid) of a resident of the surveillance catchment area, where the index clinical specimen was obtained either from an outpatient or an inpatient during the first three days of hospitalization, without one of the following healthcare related risk factors: surgery, dialysis, hospitalization, or residence in a long-term care facility within the prior year; or presence of a central venous catheter within two days prior to the culture. During 2009–2011, surveillance was conducted for invasive MRSA in residents of 33 counties in 9 US states, covering a population of 19 million persons. Trained EIP staff in each surveillance site investigated all reports of MRSA from eligible culture sources from laboratories servicing residents of their catchment area. Surveillance data, including demographic (e.g., race) and clinical information, were collected through review of medical records. For this project, EIP site staff geocoded community-associated MRSA case addresses using ArcGIS (ESRI) or Centrus Desktop (Group 1 Software, Inc) and recorded the 2010 census tract. MRSA cases occurring in homeless and incarcerated persons were excluded from geocoding and analysis.

Census tract data

Population denominators were obtained from the 2010 US census. Census tract characteristics came from multiple sources, including the 2010 US census, the 2008–2012 American Community Survey release, and the Health Research and Services Administration (HRSA). Variables were based on those used in the Harvard Public Health Disparities

Geocoding Project [26], encompassing factors related to income (households with low or high income, persons below the poverty level, and income inequality), housing (crowding, expensive homes, rural population), education (low or high education level among adults), and healthcare (health insurance coverage, and whether the census tract is part of a medically underserved area as defined by HRSA [27]). Definitions of each variable including data sources are listed in Table 1. We considered these area-based measures to proxy both individual- and community-level socioeconomic conditions and experiences.

Data analysis

Data analyses were performed using SAS 9.3 (SAS Institute). Patient race was classified as black only, white only, or other (which included persons reported to be of multiple races). As almost all patients with known race were either black only or white only, analyses related to race focused on these two race categories. In addition, Hispanic ethnicity was not examined because a large proportion of our cases (>40%) were reported to have unknown ethnicity. Multiple imputation with 10 imputation data sets was used to account for missing race (14.5% of cases) using the PROC MI procedure, based on the distribution of race and the demographics of the underlying census tract for cases with known race (see Supplemental Methods).

Descriptive analysis of geocoded cases was performed. Case counts were then aggregated by race for each census tract and coordinated with race specific denominators for each tract. Frequency weights were applied so that the counts and denominators appropriately reflected individuals in the analysis. Subsequent analyses used the race-aggregated individual data, nested within census tracts as the unit of level for the analysis. Using a Poisson Generalized Estimating Equations (GEE) model with independent correlation structure at the census tract level, rate ratios (RRs) and corresponding 95% confidence intervals (CIs) for univariate associations between area-based measures of socioeconomic status and invasive community-associated MRSA incidence were calculated. In addition, to evaluate potential interactions between race and socioeconomic status with respect to MRSA incidence, annual invasive community-associated MRSA incidence per 100,000 persons (using the census population to represent the size of the population at risk) was calculated and stratified by race and further stratified by quartiles of census tract-level socioeconomic status. Cochran-Mantel-Haenszel rate ratios for black race stratified by quartiles of tract-level socioeconomic status were calculated.

We hypothesized that race might affect MRSA infection rates through a pathway mediated by socioeconomic factors (indirect effect of race) as well as through a pathway unrelated to socioeconomic factors (direct effect of race). Mediation analysis was used to decompose the total (i.e., observed and unadjusted) effect of race on invasive community-associated MRSA incidence into these direct and indirect effects. Area-based socioeconomic variables were selected as potential mediators based on non-collinearity (assessed through the variance inflation factor) and $P < 0.05$ in a multivariable Poisson GEE model exploring the relationship between race, socioeconomic conditions, and MRSA infection incidence. Direct and indirect effects of race were estimated using the method of inverse odds ratio weighting [28,29]. A further discussion of the method of inverse odds ratio weighting and specific details of our

statistical analysis can be found in the Supplemental Methods. We applied this approach in a Poisson GEE model with clustering at the census tract level and frequency weights to account for the population size of each census tract. The estimated 95% confidence intervals for total, direct, and indirect effects of race were calculated from 1000 bootstrapped runs. The proportion of racial disparity “mediated by” (i.e., explained by) socioeconomic status was calculated as the ratio of coefficients for indirect effect/total effect of black race on invasive community-associated MRSA incidence.

To assess whether results could be influenced by results from individual sites, sensitivity analyses were performed with each EIP site’s data omitted from the model.

Human subjects

The EIP MRSA surveillance program (including geocoding of cases) and this analysis were considered to be nonresearch public health activities at the CDC. EIP sites obtained human subjects and ethics approvals from respective state health department and academic partner institutional review boards.

Results

Geocoding results and description of cases

During 2009–2011, 2722 community-associated MRSA cases were reported, of which 2609 were eligible for analysis (Figure 1). Of these, 2521 (96.6%) of cases’ residential addresses were successfully geocoded to a census tract in the surveillance area.

Among the 2156 cases with reported race, 1382 (64.1%) were reported to be in persons of white race only and 687 (31.9%) in persons of black race only (2069 [96.0%] therefore in either persons of white race only or black race only) (Table 2). Most cases (63.5%) occurred in male patients, and the median age was 52 years (interquartile range: 37–66 years). Diabetes, HIV infection, and intravenous drug use were reported in 27.3%, 8.8%, and 13.3% of cases, respectively. Most (75.3%) cases were associated with a positive blood culture for MRSA.

Unadjusted analyses of socioeconomic status and MRSA rates

Census tract-level factors associated with higher incidence in univariate analysis included low income households (RR: 19.65, 95% CI, 14.78–26.12), persons living under the poverty level (RR: 16.78, 95% CI, 11.92–23.62), income inequality index (RR: 12.99, 95% CI, 6.54–25.82), crowding (RR: 432.72, 95% CI, 173.16–1106.48), low education (RR: 47.65, 95% CI, 33.96–66.86), and being a medically underserved area (RR: 2.40, 95% CI, 2.16–2.68) (Table 3). Conversely, factors associated with lower MRSA infection incidence were high income households (RR: 0.008, 95% CI, 0.003–0.02), expensive homes (RR: 0.46, 95% CI, 0.31–0.68), rural areas (RR: 0.36, 95% CI, 0.25–0.52), high education (RR: 0.11, 95% CI, 0.08–0.14), and health insurance (RR: 0.08, 95% CI, 0.05–0.11).

Crude annual invasive community-associated MRSA incidence was 7.60/100,000 black persons and 4.59/100,000 white persons (RR: 1.66, 95% CI 1.52–1.80). When incidence was stratified by different socioeconomic characteristics (related to income, housing, education,

and health) of the census tracts, for almost all tract-level factors there was narrowing of the gap between incidence in black persons and white persons compared to the crude incidence by race (range of adjusted rate ratios: 1.16–1.37), although in these stratified analyses the aRRs for race remained significant for all variables assessed (Figure 2).

Stratified analysis suggested interaction between race and socioeconomic characteristics in two situations. Increasing RRs for MRSA infection incidence in black persons were seen in census tracts with either greater income inequality (RR: 1.26 in lowest quartile of census tracts vs 1.93 in highest quartile) or larger percentage of expensive homes (RR: 1.44 in lowest quartile versus 2.66 in highest quartile).

Multivariable analyses

In our mediation analyses, the rate ratio for community-associated MRSA capturing the total (i.e., unadjusted) effect of black race compared with white race was 1.68 (95% CI, 1.53–1.84) (Figure 3). Socioeconomic variables determined to be independent and included in our mediation analysis were proportion of expensive homes in a census tract, proportion of persons with high education, proportion of low income households, proportion of persons living in a rural area, and being a medically underserved area.

Illustrative diagrams depicting potential relationships between race, socioeconomic status, and invasive MRSA incidence, as well as results from mediation analysis, are shown in Figure 3. When accounting for all of these census tract-level socioeconomic mediators, 91% of the total effect was explained by census tract-level factors (RR for indirect effect: 1.60, 95% CI, 1.44–1.78). The resultant direct effect of race, representing effect of race on invasive MRSA incidence independent of socioeconomic factors considered, was not significant (RR: 1.05, 95% CI, 0.92–1.20).

Sensitivity analyses

In sensitivity analyses, regardless of which EIP site's data was withheld from mediation analysis, race did not have significant direct effect on MRSA infection incidence when accounting for socioeconomic factors.

Discussion

We found that neighborhoods characterized by lower socioeconomic status and higher urbanicity had higher rates of invasive community-associated MRSA. Furthermore, there was no significant association of black race with MRSA infection rates in the mediation analysis when accounting for socioeconomic factors.

The results of our study suggest that the observed differences in invasive community-associated MRSA rates by race are primarily related to social factors. This is also consistent with findings outside the US that persons living in areas of lower socioeconomic status have higher rates of MRSA [19,31]. These social factors are likely to reflect specific drivers such as availability and affordability of medical care, crowding, and poverty, both at the individual and community levels. There is also biologic plausibility for socioeconomic factors to be the major determinants of invasive community-associated MRSA rates. For

example, poverty has been associated with increased prevalence of MRSA colonization, and there may be less transmission pressure in areas that are more rural [32]. Of note, factors such as differences in surgical procedures and dialysis (both of which have associations with underlying illnesses such as diabetes and predilection to infections) would not explain differences in invasive community-associated MRSA incidence as cases with these major healthcare exposures are excluded from our analysis.

The more proximal causes of racial disparities for invasive MRSA rates could not be directly elucidated by these data, given that we could not examine individual level factors such as medical care, medical conditions, living situation, and socioeconomic status. However, this work provides evidence that disparities in MRSA infection incidence can be explained on the basis of socioeconomic status and thus do not depend on inherited, unchangeable factors. Even though socioeconomic status is difficult to intervene on directly, the drivers for disparities may be modifiable factors. For example, disparities might be the result of behavioral risk factors linked to lower socioeconomic status, such as intravenous drug use, lack of access to treatment for MRSA infections before becoming invasive, or differences in acquired medical conditions resulting from low socioeconomic status. The modifiable factors produced by low socioeconomic status, that are responsible for disparities in MRSA, should be explored further to guide efforts to reduce incidence of community-associated MRSA, particularly since characteristics described in literature to be significantly linked with acquisition of community-associated MRSA (e.g., HIV infection and intravenous drug use [18]) were associated with only a minority of cases in our analysis. These results also suggest that interventions for preventing invasive community-associated MRSA may have greater impact if focused on communities and regions with low socioeconomic status. For example, such interventions could involve targeting educational messages for prevention of community-associated MRSA [33] to communities at highest risk. Alternatively, when designing studies to evaluate potential interventions for preventing invasive community-associated MRSA, conducting them in the communities with highest incidence/burden might have the most impact. In addition, the finding that most of the racial disparity is related to potentially modifiable factors indicates that in principle the disparity can in fact be addressed, which may be an important finding in itself.

Some caution should be exercised when interpreting the meaning, or even absence, of specific area-based measures in our model of MRSA infection incidence for at least two reasons. First, although area-based measures have shown similar effects to individual socioeconomic measures in some studies [34], in this analysis they capture a combination of individual and area socioeconomic status because individual socioeconomic measures are not available. How these serve as a proxy for conditions and experiences that put individuals at risk for acquiring MRSA requires further investigation. Second, some of the area-based measures we considered are highly correlated with each other. For instance, the proportion of persons in an area with health insurance is correlated with other socioeconomic factors, such as income and education levels within that area. Therefore, the absence of “percent insured persons” from the variables considered in our mediation analysis does not necessarily indicate that insurance is unimportant. Instead, lack of health insurance might be accounted for implicitly by other socioeconomic factors in the model.

We relied on race as recorded in the medical record by medical providers and multiply imputed race when missing. Compared to patient self-report (the gold standard for determining patient race), we have evidence that our race data are accurate. First, it has been described in the literature that among patients of white or black race, when documentation of race by administrative hospital data is available, it is highly concordant with patient self-report [35]. Second, our model for imputation of unknown race (affecting <15% of cases) has a high accuracy for predicting race in our surveillance data (see Supplemental Methods).

There are several limitations of this analysis. First, we were not able to explore trends in other races due to sample size constraints, or for Hispanic ethnicity, which might be important as analyses of racial and ethnic disparities in other diseases have found that the role of socioeconomic factors can vary by race and ethnicity [36]. Second, it is possible that the geographic areas where surveillance has been performed are not representative of trends in other areas of the US. For example, some recent studies have suggested associations with swine farming and MRSA infections [37,38], but the geographic regions in our surveillance are not suitable for exploring this risk factor. However, it is a strength in terms of representativeness of the analysis that it includes data from several states throughout the country, and the EIP is therefore a reasonable approximation of the US [39]. Finally, we were unable to directly incorporate some potentially important social or community factors associated with elevated risk of community-associated MRSA, such as prior incarceration, in our analysis. We also did not have individual-level data from control patients or community-level data to account for risk conferred by underlying medical conditions.

In conclusion, racial disparities in invasive community-associated MRSA rates appear to be a result of socioeconomic disparities. Broader understanding of the mechanisms by which socioeconomic status influences MRSA rates could be a major step forward in informing efforts to prevent community-associated MRSA, and focusing prevention efforts on communities with higher risk may worth exploring as a strategy for reducing the public health burden of community-associated MRSA.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key points

In this analysis of methicillin-resistant *Staphylococcus aureus* (MRSA) surveillance data from nine states in the US, socioeconomic factors were found to explain differences in invasive MRSA incidence between white and black persons.

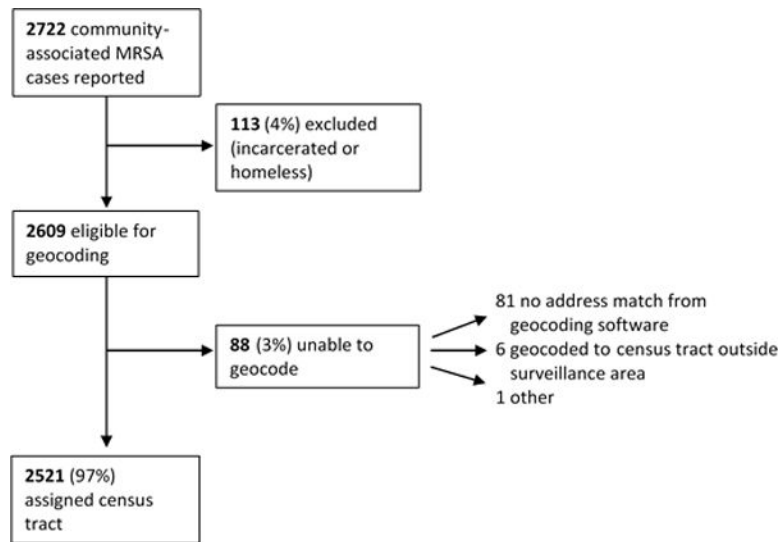


Figure 1. Results of geocoding of community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) cases

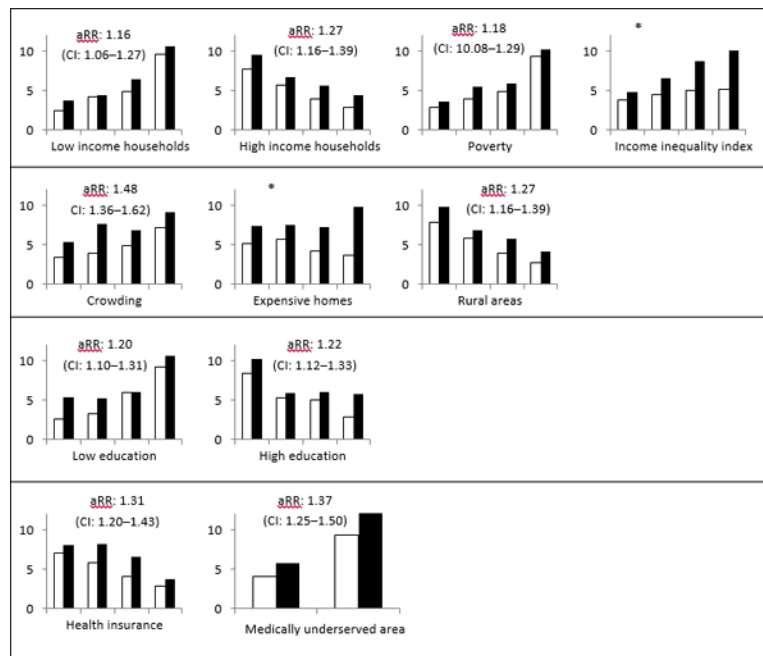


Figure 2. Methicillin-resistant *Staphylococcus aureus* (MRSA) incidence by race, stratified by quartiles of census tracts related to specific (A) income, (B) housing, (C) education, and (D) health variables. Incidences are displayed in increasing quartiles of census tracts, per 100,000 persons for white (no fill) and black (solid fill) persons. The adjusted rate ratio (aRR) and 95% confidence interval (CI) of MRSA in black persons (reference group for aRR: rate in white persons) considering stratification is shown in each graph except when marked by (*) to indicate heterogeneity in rate ratios across quartiles, i.e., interaction between race and the census tract measure. Refer to Table 1 for a description of individual variables.

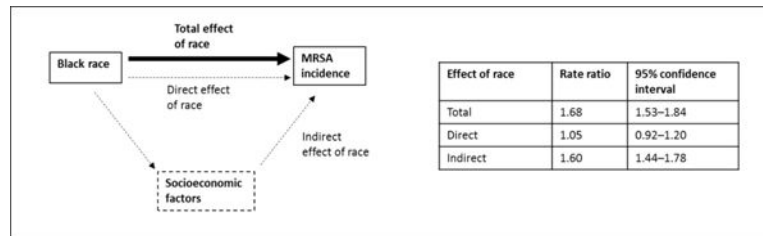


Figure 3.

Results from mediation analysis to estimate the extent to which socioeconomic factors explain racial variation in invasive community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) incidence. Diagram depicts estimated the rate ratio for the total effect of black race on invasive community-associated MRSA incidence (corresponding to unadjusted rate ratio and shown with the thick black arrow) as well as a potential pathway in which race affects invasive community-associated MRSA incidence through socioeconomic factors (indirect effect of race) or independently (direct effect) as shown in dashed lines/arrows. Socioeconomic factors accounted for in the mediation analysis were proportion of expensive homes in a census tract, proportion of persons with high education, proportion of low income households, proportion of persons living in a rural area, and being a medically underserved area.

Table 1

Area-based socioeconomic variables considered for inclusion in the analysis

Variable name	Definition	Data source
Low income households	% households with income <\$25,000, approximates <50% of median US household income.	ACS
High income households	% households with income \$200,000, approximates 400% of median US household income.	ACS
Poverty	% persons below poverty level in past 12 months	ACS
Income inequality index	Gini coefficient ¹	ACS
Crowding	% of occupied households with >1 person/room	ACS
Expensive homes	% of owner-occupied housing units \$750,000 (approximates 400% of median value)	ACS
Rural areas	% population living in rural area.	2010 Census
Low education	% people 25 or older with less than 12th grade education (includes 12th grade, no diploma)	ACS
High education	% people 25 or older with at least bachelor's degree	ACS
Health insurance	% persons with health insurance coverage	ACS
Medically underserved area	Based on percent of population with income below poverty level, percent of population with age over 65 years of age, infant mortality, and availability of primary care providers	HRSA

ACS, 2008–2012 American Community Survey. HRSA, Health Resources and Services Administration.

¹Gini coefficient: ranges from 0 to 1, with extreme values when income is uniformly distributed across all members of population (Gini coefficient=0) or all income belongs to a single person (Gini coefficient=1).

Table 2

Description of community-associated invasive methicillin-resistant *Staphylococcus aureus* (MRSA) cases—
Emerging Infections Program data, 2009–2011

Characteristic	No (%), N=2521
Race	
White	1382 (54.8)
Black	687 (27.3)
Other	87 (3.5)
Unknown	365 (14.5)
Male gender	1601 (63.5)
Age, median (interquartile range)	52 (37–66)
Selected underlying medical conditions	
Diabetes	689 (27.3)
HIV	223 (8.8)
IV drug use	336 (13.3)
MRSA identified from blood culture	1897 (75.3)

Table 3

Univariate rate ratios for association between neighborhood socioeconomic factors and invasive community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) incidence.

Variable	Rate Ratio ^I	95% CI	P
Low income households	19.65	14.78–26.12	<0.0001
High income households	0.008	0.003–0.02	<0.0001
Poverty	16.78	11.92–23.62	<0.0001
Income inequality index	12.99	6.54–25.82	<0.0001
Crowding	437.72	173.16–1106.48	<0.0001
Expensive homes	0.46	0.31–0.68	0.0001
Rural areas	0.36	0.25–0.52	<0.0001
Low education	47.65	33.96–66.86	<0.0001
High education	0.11	0.08–0.14	<0.0001
Health insurance	0.08	0.05–0.11	<0.0001
Medically underserved area	2.40	2.16–2.68	<0.0001

^I Socioeconomic status variables were coded as ranging from 0 (0% of the census tract with this characteristic) to 1 (100% of the census tract with this characteristic). As an example to assist in interpreting the rate ratios, the rate ratio of 19.65 for low income means that for each increase of 10% households in a census tract with low income, we would predict an increase in the MRSA rate (cases/population) of 1.35-fold (the 10th root of 19.65).