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Exploration of individual and area level risk factors for invasive and non-invasive methicillin-resistant *Staphylococcus aureus* infections among children and adults in 8 Georgia counties, 2017

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Gerard Portela

B.A., Rice University, 2016

Thesis Committee Chair: Scott Fridkin, MD

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
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2020

Abstract

Exploration of individual and area level risk factors for invasive and non-invasive methicillin-resistant *Staphylococcus aureus* infections among children and adults in 8 Georgia counties, 2017

By Gerard Portela

Background
Staphylococcus aureus (SA) infection prevention and characterization have primarily focused on hospital- and community-associated methicillin-resistance in adults or children separately, without comparing invasive to non-invasive disease. How place-based factors contribute to risks for staphylococcal-related infections in adults and children are also not well characterized. Our study describes invasive and non-invasive MRSA and MSSA among children and adults by examining individual and area level data.

Methods
We analyzed Emerging Infections Program 2017 surveillance data for SA infections in 8 metro-Atlanta counties. Multivariable logistic regression models with random intercepts were used to compare risk factors of MRSA versus MSSA among invasive and skin/soft tissue infections (SSTIs) in both children and adults. Standardized incidence ratios (SIRs) were calculated using census tracts from georeferenced cases.

Results
After considering patient demographics, children with MRSA SSTIs are more likely to be from areas with crowding (adjusted odds ratio [aOR] 1.44, 95% confidence interval [CI] 1.02-2.04); similar risk is observed in adults (aOR 1.39, 95% CI 1.18-1.65). Children with invasive MRSA are more likely to live in an area with a racial ethnic concentration (aOR 3.10, 95% CI 1.07-8.99), while increased proportions of no health insurance increase adult risk (aOR 4.05, 95% CI 1.09-15.14). MRSA hotspots were found in more densely populated areas with high proportions of black populations.

Conclusions
The risk of MRSA infections in children and adults are defined by unique area level sociodemographic characteristics. Public health interventions to reduce antibiotic resistant disease should focus resources among age groups in areas with risk factors identified in this study.

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Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) presents a challenging infection to treat and prevent due to its resistance to key antibiotics and diverse spread among hospital and community settings. In 2017, an estimated annual 323,700 hospitalized cases of MRSA infections occurred in the United States, with around 10,600 deaths attributed to this infection, leading the Centers for Disease Control and Prevention to classify it as a serious health threat[1].

Hospital-associated MRSA (HA-MRSA) and community-associated MRSA (CA-MRSA) have been well described in previous literature[2, 3]. Overall, MRSA infections are associated with significant health disparities[3]. The rates of invasive HA-MRSA and CA-MRSA infections are highest among extreme age groups, males, black populations, and HIV and hemodialysis patients[4-7]. Patients with HA-MRSA are typically older, have prolonged or intensive-care hospital stays, or have one or more comorbid conditions that may require indwelling catheters[2, 8]. In comparison, CA-MRSA outbreaks have been associated with crowding, poor hygiene, socioeconomic factors, and previous antibiotic use[9]; specific socioeconomic factors include living in households with low income/below poverty level, in a medically underserved area, and in areas of low education[10]. Non-invasive CA-MRSA infections predominantly affect children and young adults, males, and non-white individuals[11]. Skin/soft tissue infections (SSTIs) likely account for at least 90% of non-invasive CA-MRSA and result in more than 14 million ambulatory visits per year[2, 9, 11-16]. However, recent evidence has shown that MSSA is more common than MRSA across all demographic groups[17]. In particular, invasive MSSA accounts for the majority of invasive SA infections, with highest risk among those with less frequent exposure to healthcare settings.

Although risk factors linked with HA- and CA-MRSA have been well described, few studies have explored why children may have different risks compared to adults, factoring in

socioecological or place-based risks. Reasons why children develop non- or invasive forms of MRSA compared to adults also have not been examined. In this study, we sought to (1) characterize both individual and area level risks associated with invasive infections or SSTIs, comparing MRSA to MSSA and (2) highlight differences between children and adults with these infections. This is the first large population study of both adults and children with *S. aureus* infections living in the southeastern US. Furthermore, this is the first study to examine the spatial distribution of MRSA and MSSA and characterize the areas with the highest rates of invasive infections and/or SSTIs among both children and adults in this region. This analysis would allow public health officials and primary care providers to target individual and area level interventions in specific age groups to prevent the spread of resistant forms of invasive and non-invasive *S. aureus.*

Methods

Study design

This is a retrospective study, analyzing data collected as part of a multi-state laboratory-based surveillance on *S. aureus* (SA) conducted by Centers for Disease Control and Prevention's Emerging Infections Program (EIP)[18]. For this study, data was obtained from Georgia's EIP on Georgia Health District 3 (HD3), an 8-county catchment area surveilling a population of approximately 3,951,039, during 2017. Cases were ascertained from 21 reporting laboratories (18 hospital-based and 3 referral) using a standard case report form to collect demographic and clinical data, as previously reported[5].

Case Definition. A case was defined as a resident of the 8-county surveillance area from whom SA had been isolated from any clinical culture; cases were distinguished as MRSA or MSSA based on clinical laboratory testing. Specimen sources were categorized as invasive, non-invasive, or other/uncertain infection. Invasive disease included specimens isolated from a

normally sterile site, as previously described[5]. Non-invasive diseases were sources including urine, lower respiratory, abscess, and sinus. Other positive cultures, whose clinical relevance was unclear, included wound, skin, and unknown specimens. Categorized cultures were then assigned as a 'single infection event' per each unique patient if multiple non-invasive cultures occurred within a 14-day period and if invasive cultures occurred within a 30-day period. Specimen source 'free text' and 'comment' fields in the case report forms were then reviewed by an infectious disease physician (A.W.) to validate the source/clinical relevance of each infection and classify specimens into a standard set of specimen types (invasive blood, invasive other, lower respiratory, upper respiratory, colonization, sinus, skin abscess, superficial skin, urine, unknown). SSTIs included skin abscess and superficial skin infections (wounds, rashes, cellulitis, swabs, and drainage) for which a culture was obtained from the site of infection. Invasive infections included those where the source of positive culture was a normally sterile site, e.g., blood, cerebrospinal fluid, joint/synovial fluid, bone. For this study, we used SSTIs as a proxy for 'non-invasive' infection. See **Figure 1** Enrollment Scheme**.**

Patient Level Data. Demographics (age, race, sex, ethnicity, and home address) were obtained from case report forms to confirm residency status and methicillin-sensitivity of cultured SA.

Geocoding. World Geocoding Service in ArcMap 10.7 software (ArcGIS Desktop, Redlands, CA: Environmental Systems Research Institute) was used by EIP staff to geocode patients' residence to the census tract level. This georeferenced dataset was used for this study.

Missing Data. Among patients with known census tracts, race was unknown in 12.8% of SSTIs ascertained from hospital labs and in 95.5% and 84.4% of SSTIs from two reference labs, respectively. All SSTIs from the two referral labs were removed as we could not assume data were missing at random required for multiple imputation. Ethnicity was unknown for 17.2% of SSTIs collected from hospital labs, while age and sex were missing from 2 hospital lab cases.

Race and ethnicity were unknown in 7.3% and 4.2% of all invasive cases with known census tracts, respectively. Prior to imputation, race was categorized as white, black, and other (Asian, American Indian/Alaska Native, Native Hawaiian or Pacific-Islander), while ethnicity was grouped into Hispanic and non-Hispanic. Age was grouped into clinically relevant categories, including 0-2, >2-5, >5-13, >13-18, 19-25, >25-45, >45-65, and >65 years. Missing demographic data were adjusted through five iterations[19] of multiple imputation based on known population distributions of age category, sex, race, ethnicity, methicillin sensitivity, and county of residence using SAS 9.4 multiple imputation procedure (SAS Institute, Cary, NC, USA). Imputed demographics were used for calculating incidence rates and logistic regression.

Area Level Data. Relevant area variables were abstracted from 2017 US Census Bureau American Community Survey 5-Year Data (ACS-5) based on assigned census tracts. This geographic unit provided population characteristics of 2,500-8,000 residents.

Household Crowding. The US Department of Housing and Urban Development defines household crowding as homes with more than one person per room[20]. The variable was dichotomized by evidence of crowding in the census tract (one or more crowded households) or no evidence.

Racial Ethnic Groups. Based on proportions of non-Hispanic, non-white individuals in each census tract, ‘concentrated' areas of this racial ethnic group was determined using the overall percentage of non-Hispanic, non-white for the state as a reference and adding 10%[21]. For example, the percentage of non-Hispanic, non-white individuals in Georgia was 37.8%, so any census tract >47.8% was defined as a ‘concentrated’ area of non-Hispanic, non-white.

Poverty. Concentrated poverty describes areas where over 40% of the population falls below the national poverty line[22]. Census tracts that met this definition were defined as concentrated poverty areas.

Distance Variables. Euclidean distance was calculated between each patient's assigned census tract and the nearest K-12 school, daycare center, and hospital. For each census tract, the pole of inaccessibility was calculated using QGIS 3.12 (QGIS Information System). This algorithm calculates the most distant internal point from the boundary of a polygon, resulting in a raster dataset with pixel values representing the distance in feet from the pixel center to each feature (daycare, K-12 school, or hospital). The data were aggregated to the census tract level by computing the mean pixel value per census tract for each feature using the Zonal Statistics algorithm. These mean values were added to the census tract points in three separate attribute columns using the Point Sampling plugin. (Daycare was selected as a place-based 'marker' because of its association with CA-MRSA infections in children. Hospitals are also a place-based 'marker' because of their associations with HA-MRSA infections in both adults and children. K-12 public schools were selected to serve as a place-based 'control' marker.)

Other area level variables. The index of income inequality uses the Gini index to represent wealth dispersal across each census tract, where 0 indicates perfect equality and 1 indicates perfect inequality. Proportions for no health insurance, <18 years old, and foreign born were calculated in each census tract. Percent of individuals with no high school diploma was calculated among those >25 years old.

Statistical Analyses

Overview. The basic unit of observation was a unique SA event. Differences in demographic and area level data for SSTI v. invasive and pediatric v. adult cases were examined using the χ^2 test for categorical variables and two-sample t-test for continuous variables. US Census Bureau population estimates in the 8-county area for 2017 were used as denominator values for incidence calculations. Incidence (per 10,000 HD3 population) of SSTIs and invasive infections

were calculated by age group, race, and ethnicity. Statistical analysis was performed using SAS 9.4 (SAS Institute, Carey, NC).

Statistical Models. Bivariate analyses were performed to test associations of variables with MRSA compared to MSSA. Individual patient and census tract level demographic variables, specified above, based on risks or proxies for risks in children and adults reported in the literature[10, 23], were selected for inclusion. Three types of logistic regression models were created for multivariable regression analyses: individual factors only, area level factors only, and individual and area level factors in a multilevel model. To identify independent risk factors, multilevel logistic regression using random intercepts for census tract was used; area level variables with a p-value < 0.15 in multivariable models were included. The three model types were applied to SSTIs and invasive infections among both children and adults. Odds ratios (OR) were used as estimates of relative risks, indicating the magnitude of associations, along with corresponding 95% confidence intervals (95% CI). The Wald test was used to determine the significance of associations; all tests were two-tailed and a p-value of <0.05 was considered significant.

Estimates for race and ethnicity were calculated based on imputation iteration and all iteration estimates were pooled to calculate an average parameter estimate using 'proc minianalyze.' No variance existed between imputation iterations for sex, age, or area level variables, thus a single iteration was used to estimate OR. Adjusted odds ratios (aOR) were measured at the individual and census tract level; estimates were calculated by pooling the imputation iteration results, similar to the crude estimates mentioned above**.**

Spatial Analyses. Georeferencing of all data was previously conducted by EIP[18] and the dataset used for this study included patients' residential census tract. Mapping was projected in 'Georgia West State Plane' and included census tract and 8 county boundaries within the Atlanta

metropolitan area. We linked census tract data with patient culture information and calculated incidence for age groups and infection sources per census tract using the US Census population totals, as described above. Standardized incidence ratios (SIRs) were calculated by using the overall incidence of SSTIs and invasive infections in the surveillance region as reference. Observations of zero events in a census tract were adjusted by adding an arbitrarily small value (0.5) to the observed and expected events as risk of infection in a given area was unlikely to be zero. Ratios were mapped by infection source and age group. Using Getis-Ord Gi* statistic, a hotspot analysis was performed on calculated incidence rates and non-aggregated data. Optimized hotspot analysis is a tool used to evaluate statistically significant spatial clustering. Hotspots were based on SIRs of MRSA among age groups in each census tract. For each observed spatial cluster of high or low value, the 99%, 95%, and 90% confidence was determined and aggregated into categories of 'hot' or 'cold' spots, respectively.

Results

During 2017, 25,335 unique SA events were reported for HD3, including 11,331 (44.7%) SSTIs and 2,258 (8.9%) invasive infections (**Figure 1**). After removing patients with missing location (n=2,517) and demographic data (n=1,234), there were 2,915 (45.8%) adults with MRSA and 3,454 (54.2%) MSSA SSTIs, while pediatric SSTIs included 525 (36.7%) MRSA and 906 (63.3%) MSSA events. Adults with invasive infections included 722 (38.0%) MRSA and 1,178 (62.0%) MSSA events. Pediatric invasive infections included 32 (23.2%) MRSA and 106 (76.8%) MSSA events.

Population Characteristics. Individual demographics and specific determinants of health risks are shown, stratified by clinical condition (SSTI v. invasive, **Table 1a**) and patient age group (pediatric v. adult, **Table 1b**). See **Supplemental Table 1** for imputed demographics by imputation iteration. Although we found no difference overall in racial/ethnic groups, blacks had

significantly higher proportion of all SA and MRSA SSTIs compared to others with SSTIs ($p<0.0001$) and higher proportion of all SA and MRSA invasive infections ($p<0.0001$) (**Table 1a**). A significantly higher proportion of MRSA, compared to MSSA, SSTIs and invasive infections were located within one mile of a daycare center (p-values < 0.05).

Black children had the highest proportion of all SA (56.8%) and MRSA (64.6%), while black adults had the highest proportion of MRSA (50.7%) only. Overall, a higher proportion of black children had any SA compared to black adults ($p < 0.0001$) (**Table 1b.**). At the census tract level, a higher proportion of children with MRSA lived in crowded neighborhoods (87.3%) compared to those with MSSA (82.3%) ($p = 0.0105$). A similar pattern was seen among adults ($p < 0.0001$). There was a significantly lower average percent foreign born population in residential areas of children with MRSA compared to MSSA ($p = 0.0151$), an observation unique to children. No difference existed in the inequality index of residential areas with pediatric compared to adult SA. A higher proportion of all SA occurred in children than adults within one mile of a school ($p = 0.0204$).

The overall incidence of SSTIs in HD3 was 19.74/10,000, compared to 5.16/10,000 for invasive infections. Adults experienced the highest incidences of SSTIs (22.33/10,000) and invasive infections (6.66/10,000). Among children, incidence rates of SSTIs and invasive infections were 13.02/10,000 and 1.26/10,000, respectively. Further, incidence of MRSA SSTIs among adults (10.22/10000) was more than 2 times that of pediatric cases (4.78/10000) and incidence of invasive MRSA (2.53/10000) was almost 9 times that of children (0.29/10000). Likewise, incidence of MSSA SSTIs among adults (12.11/10000) was almost 1.5 times that of children (8.24/10000), while incidence of invasive MSSA (4.13/10000) was over 4 times higher than pediatric cases (0.96/10000). **Figure 2** shows differences in incidence rates stratified by age group, race, and ethnicity.

Risk factors among children and adults. The results from the bivariate and multivariable models for SSTIs (**Table 2a**) and invasive infections (**Table 2b**) comparing children to adults are shown. Risks for MRSA SSTIs were similar for children and adults: blacks were more likely to have MRSA SSTIs compared to whites (children (OR 1.43, 95% CI 1.16-1.76); adults (OR 1.24, 95% CI 1.08-1.42)) and patients were less likely to be Hispanic compared to non-Hispanic (children (OR 0.76, 95% CI 0.65-0.89); adults (OR 0.88, 95% CI 0.78-1.00)) (**Table 2a**). Children who were in the youngest group (<2 years) had the highest risk for MRSA SSTIs compared to adults with MRSA SSTIs who were in the oldest age group (>65 years). Among those with invasive MRSA, no particular sex, ethnicity, or age group among pediatric or adult cases were at increased or decreased risk of infection. However, after adjusting for all individual demographics, there was some evidence that children and adults with invasive MRSA were more likely to be black than white (children (aOR 2.05, 95% CI 0.95-4.45); adults (aOR 1.69, 95% CI 1.25-2.29)) (**Table 2b**). Children and adults with MRSA SSTIs were more likely to live in crowded census tracts (children (OR 1.41, 95% CI 1.04-1.90); adults (OR 1.34, 95% CI 1.17-1.53)) (**Table 2a**). After adjusting for crowding and percent foreign born, children with MRSA SSTIs were more likely to live in areas designated high racial ethnic concentration (aOR 1.31, 95% CI 1.03-1.65), a determinant not seen for adults. Rates of no health insurance was highly correlated with no high school diploma and was therefore dropped from the adult SSTI adjusted model. Percent foreign born was included due to previous evidence of association[24]. After adjusting for crowding, foreign born, and distance variables, proximity to a daycare center (aOR 1.28, 95% CI 1.04-1.58) and higher proportions with no high school degree (aOR 2.57, 95% CI 1.34-4.94) increased adult risk for MRSA SSTIs (**Table 2a**). Adults with MRSA invasive infections were more likely to reside in an area within one mile of a school (OR 1.17, 95% CI 1.05-1.29), day care center (OR 1.50, 95% CI 1.26-1.78), or hospital (OR 2.01, 95% CI 1.35-

2.99) (**Table 2b**). However, these factors were not significant after adjusting for poverty concentration and percent with no health insurance. Children with invasive MRSA were more likely to be from areas with a racial ethnic concentration (OR 4.66, 95% CI 1.85-11.71) and an area within one mile of a school (OR 1.85, 95% CI 1.03-3.30) (**Table 2b**). No adjusted model for children with invasive infections was valid.

Multilevel model analysis of SSTIs revealed that black race was no longer a significant determinant of MRSA infection among children or adults (**Table 3a**). Only crowding remained a significant area level risk for pediatric MRSA SSTIs (aOR 1.44, 95% CI 1.02-2.04), while crowding (aOR 1.39, 95% CI 1.18-1.65), percent with no high school degree (aOR 3.21, 95% CI 1.45-7.09), and distance to the nearest daycare center (aOR 1.38, 95% CI 1.10-1.72) remained significant area predictors of adult MRSA SSTIs. Multilevel models for invasive infections showed black adults were at significantly higher risk of MRSA (aOR 1.52, 95% 1.20-1.92) (**Table 3b**). Racial ethnic concentration remained significantly associated with pediatric risk. After adjusting for individual level variables, poverty concentration, and distance to nearest daycare center and hospital, an increase in percent with no health insurance in the census tract increased the risk for invasive MRSA in adults (aOR 4.05, 95% CI 1.09-15.14).

Spatial densities of skin/soft tissue and invasive MRSA and MSSA infections. Overall, invasive SA was distributed across fewer of the 8-county census tracts than skin/soft tissue SA infections (**Figure 3**). Although there were many census tracts with higher SIRs for both SSTIs and invasive infections, particularly in the southeastern region, highest invasive SIRs were aggregated in smaller spatial areas. Highest SIRs for SSTIs were primarily in 'peripheral' census tracts in all but the northern half of Fulton county. A greater number of census tracts had an SIR >2.0 for MRSA SSTIs and invasive infections, while more areas had a ratio of 1.2-2.0 for MSSA. See **Supplemental Figure 1.** MSSA was higher in the northwest region of metro-Atlanta

(Douglas and Cobb counties). In contrast, MRSA was greater in south-central Atlanta around Fulton, DeKalb, and Clayton counties, three of the four counties with highest population densities in the region. The distribution of SA for adults compared to children was similar, except in Douglas county where there were high SIRs of adult SA but low for pediatric SA (**Figure 4**). Additionally, several more census tracts had an SIR >2.0 for children with SSTIs and invasive infections, while adult SSTIs and invasive infections cover a greater proportion of the region. (See **Supplemental Figure 2.**) Census tracts with high ratios of MRSA also tended to show high ratios of pediatric infections.

Most hotspots had ≥40% black populations, while cold spots were predominantly white populations (**Figure 5**). The distribution of 'hot' and 'cold' spots was similar between adults and children with MRSA. In general, this appears to directly correspond to population density of an area; Cobb and Douglas counties did not follow this observation given these areas are not as populated and are predominantly white. We found evidence that the highly black, densely populated regions of south-central Fulton-Dekalb counties were areas with significant MRSA hotspots. In comparison, there were less significant MRSA hotspots in the less dense areas of east and south Dekalb county. Within the city of Atlanta, we saw no significant 'hot' or 'cold' spots spanning from northwest to southeast.

Discussion

Although children and adults are at risk for developing invasive and non-invasive *S. aureus* infections, the risks for these two populations differ. A number of studies have reported on the racial/ethnic disparities associated with MRSA-related infections[3, 10, 23]. In our analysis, we found the rate of MRSA infections increased among black adults and children, regardless of infection source (SSTI v. invasive). However, this racial disparity was no longer

significant among either adults or children with SSTIs when we controlled for spatial clustering of cases, along with crowding, foreign born, and other apparent age-specific factors. By controlling for crowding, we may have diminished the racial differences considering many of the most densely populated census tracts are black concentrated. Population crowding has been previously cited as a risk for MRSA, regardless of age, sex, or race factors; this risk has been found at both the household and population level[23, 25]. Intuitively, this makes sense given that *S. aureus* is a commensal organism found commonly among the general population. Moreover, spread of *S. aureus*, like many infectious pathogens, follows the 'spatial diffusion' model of transmission. In contrast, the mechanism and risks for invasive MRSA infections differ from those for SSTIs, thus racial disparity persists in the adjusted multilevel model for invasive MRSA disease. (For invasive MRSA, crowding was not a significantly associated risk.)

We observed the 'Hispanic paradox' in identified risk for MRSA infections in both adults and children in our study. This 'protective effect' against MRSA infections compared to those identified as non-Hispanic has been reported by others for both age groups[26, 27]. Reasons for this may be consistent with similar factors seen in other conditions where Hispanics have better health outcomes (e.g., overall, Latinos living in the US tend to be a younger population and have better overall diets and lower smoking rates, though they are twice as likely to be living below poverty and more likely to have no health insurance[28]). The cultural practices that come from living in communities with others of similar ethnicity may contribute to a lower risk of developing MRSA-related infections. For example, lack of health insurance may lead to a decreased exposure to or utilization frequency of antimicrobials or hospitals and therefore, indirectly decrease the risk for development of MRSA. Further research into the specific cultural influences that might explain this phenomenon are needed.

Regardless of age group, SSTIs occurred at higher frequency than invasive disease. Among children, the incidence of MRSA-related SSTIs was more than ten times that of invasive MRSA, a difference not as dramatic in adults. This is likely attributed to the fact that SSTIs commonly involve conditions related to the breakdown of skin integrity, whereas invasive infections occur due to complex clinical situations involving SA seeding into the bloodstream. As our results indicate, children of extremely young ages (0-2) are at increased risk for MRSA SSTIs. Infants have been shown to be colonized with SA in rates of up to 60%[29]. Pediatric conditions that lead to the breakdown of skin (e.g., eczema, diaper dermatitis) occur fairly commonly in this age group and far outweigh other causes of systemic or invasive MRSA infections, especially in the context of community-associated SA.

When considering the neighborhood context, the importance of individual drivers minimizes, indicating the strong influence environmental characteristics have on risk for methicillin-resistant forms of non- and invasive SA infections. Our spatial analyses suggest place-based factors may collectively contribute to risk for MRSA infection, related to the aggregated effect of various determinants of health located in the same geographic area. For example, living in neighborhoods with high concentrated black populations, crowding, and nearby daycare centers or schools concurrently increase a person's risk for MRSA SSTIs.

Areas of concentrated poverty did not appear to be a risk factor for skin/soft tissue MRSA at the community level. However, the transmission dynamics of SSTIs are directly related to spatial proximity of individuals, as previously mentioned. Results from the multilevel models show that crowding appears to propagate the spread of antibiotic resistant SSTIs among both children and adults, consistent with previous findings[23, 25]. About 85% of children and adults with MRSA lived in areas with evidence of crowding. Our hotspot analyses demonstrated a 'band' inside the city of Atlanta, where 'no significant' hot- or cold-spot was found. This area,

which ran northwest to southeast through the city, mapped to a predominantly industrial section where there is little crowding. In comparison, other areas have socioenvironmental conditions of increased opportunities for person-to-person transmission (e.g., settings densely inhabited by children and adults alike, such as neighborhoods with concentrated multi-unit housing, schools, retail, or daycare centers).

This study also revealed that higher proportions of foreign born populations may be protective against MRSA SSTIs in both children and adults. This may be due to the fact that foreign born patients may not access healthcare providers or facilities as frequently and thus, are less likely to receive antibiotics. Jenks et al. reported that foreign born individuals were at higher risk for MSSA than MRSA infections in their analyses of patients presenting with SSTIs in New York[24]. Limited access to medications protects children and adults from the spread of antibiotic-resistant disease. Future studies should examine neighborhood proportions of birthplace origin in conjunction with individual antibiotic use to confirm reduced risk among higher proportions of foreign born populations is mediated by decreased antibiotic usage.

After adjusting for foreign born population and crowding, areas ‘concentrated’ with non-Hispanic, non-white populations may increase the risk for MRSA SSTIs among children, a predictor not significant in adults. This represents the disparities in MRSA risk between racial groups, which may be driven directly by other factors as significance diminished in the multilevel model. However, this racial ethnic concentration remained a risk factor for invasive MRSA similar to persistent racial disparities in black adults with invasive MRSA, in which controlling for other factors does not reduce the effects of mechanisms for invasive disease, as previously described. Alternatively, increasing proportions of individuals without a high school diploma described an increased risk of MRSA SSTIs in adults, as seen in prior studies[30]. Low educational achievement among adults at the census tract level may indicate a lack of awareness

of the risks for MRSA, leading to fewer protective measures against antibiotic-resistant disease. Racial disparities seem to have an impact on children in a manner that increases their risk for MRSA SSTIs, not seen in adults; modifiable factors, such as education, may explain risk for MRSA STTIs in adults.

Close proximity to schools, daycare centers, and hospitals may be independent risk factors for MRSA SSTIs and invasive infections, particularly among adults, but are not strongly associated after considering other area level factors. After adjusting for individual and other area level variables, adults within one mile of daycare centers remain at increased risk for MRSA SSTIs. More than 10 times the number of adults with MRSA, and patients with MRSA SSTIs, lived within one mile of a daycare center than lived more than one mile away. Since attendance to daycare is a known risk for CA-MRSA among children[31], it is possible that children attending daycare throughout HD3 are transmitting infections to adults living nearby.

There were several limitations to this analysis, primarily due to incomplete data for skin/soft tissue infections and for cultures processed in two reference laboratories. The exclusion of all SSTIs from the reference labs, along with those events that were not geocoded to a census tract, may impact the generalizability of these results. Similarly, many of the estimates rely on the accuracy and pooling of multiple imputation for the remaining demographics that were missing. Children as a whole experienced far fewer invasive infections, particularly antibiotic-resistant forms, limiting the reliability of associated risk estimates. Second, a large proportion of cultures were from unknown sources due to limitations in the use of case report forms by participating laboratories. Additionally, the calculation of distance variables assumes the reference point used for each census tract reflects the experience of all individuals within that area, though a larger variability in proximity to the institutions exists. Finally, the surveillance conducted in metro-Atlanta may not be representative of other areas in the United States.

However, the major strength of this study is the use of a large geocoded dataset of laboratory confirmed MRSA or MSSA to identify individual and neighborhood sociodemographic risk factors for infection. The data are representative of all SA in a diverse geographic catchment area and are not limited to single health systems or communities. By using information on census tracts, we have captured smaller clusters of sociodemographic and environmental characteristics for individuals with confirmed infections. Furthermore, we were able to create maps and compute covariates using reliable population estimates based on US Census Bureau data.

This population-based analysis of skin/soft tissue and invasive MRSA compared to MSSA in metro-Atlanta revealed the importance of and contrast between risk factors among children and adults. Targeted interventions among age groups in areas with risk factors for specific clinical presentations of MRSA will help to achieve further declines in overall rates of SA infections.

Funding

This project was supported by funds from the Centers for Disease Control and Prevention (CDC), for surveillance of invasive SA, and through an agreement between Pfizer, Inc. and Emory University for surveillance of non-invasive SA [grant number CDC U50CK000485 Emerging Infections Program; Pfizer CP154653]. Supported in part by the National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number UL1TR002378 and National Library of Medicine, Award Number G08LM013190-01. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Acknowledgements

The authors would like to acknowledge the following individuals from CDC, EIP: Susan Ray for leading the invasive SA infection surveillance; Minerva Mendez and Amber Britton for the

collection of non-invasive SA data; Shanita Shack for her work on geocoding all patients; Amy Tunali, Rahsaan Overton, and Stepy Thomas for their assistance with study design and data collection for invasive SA. We would also like to thank Andrew Webster (A.W.), Emory School of Medicine, for his efforts on data cleaning; Tony Giarrusso, Center for Spatial Planning and Visualization, Georgia Institute of Technology, for his assistance with map visualizations; and Rena Geng, Morehouse School of Medicine, for her assistance in creating visualizations.

Ethics

This research has been approved by the Institutional Review Boards at the Atlanta VA Medical center (data collection) and Emory University (data analysis).

The authors have reported no competing interests to disclose.

Disclaimer

The findings and conclusions of this work are those of the authors and do not necessarily represent the official positions of the Centers for Disease Control and Prevention.

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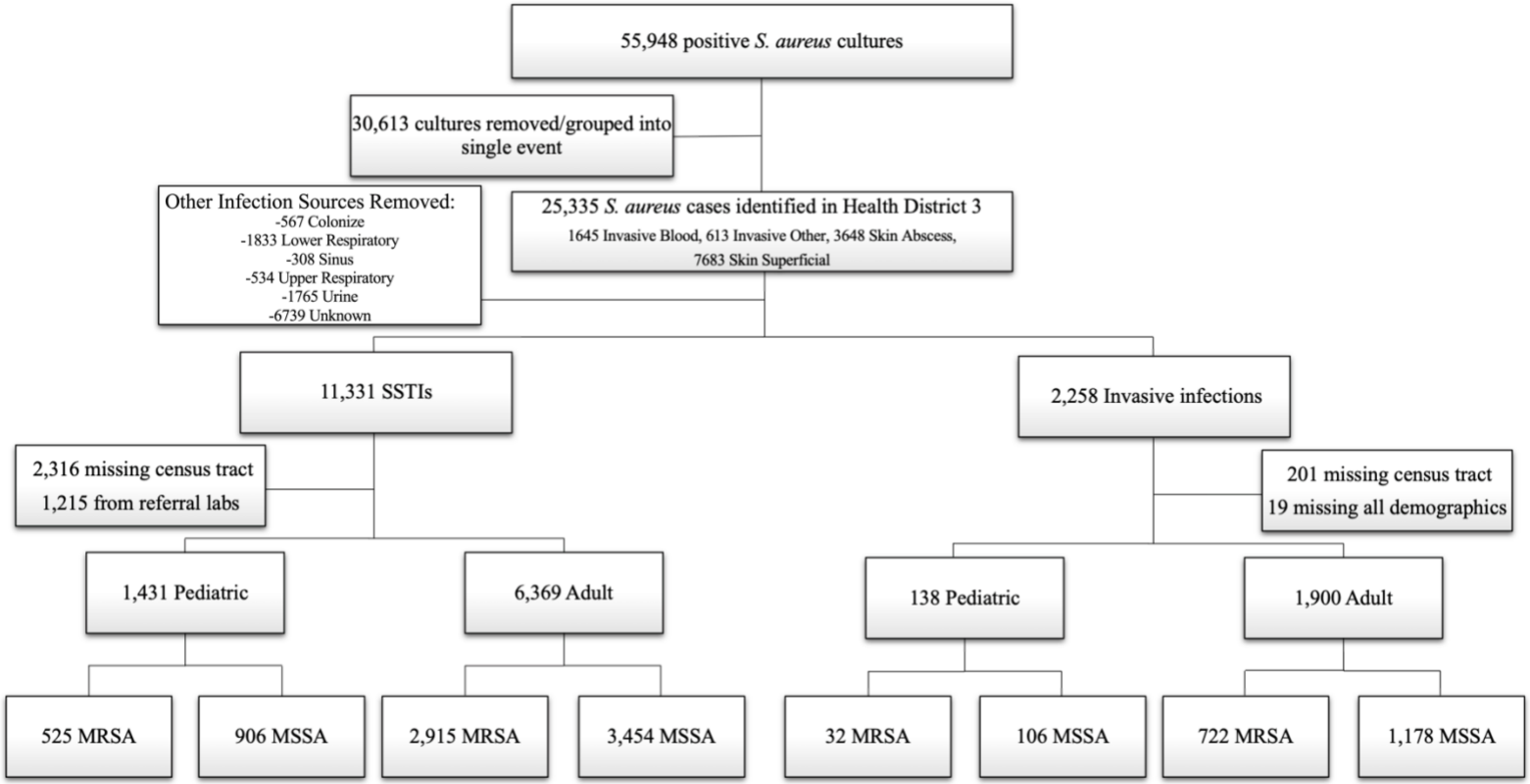


Figure 1. Enrollment scheme illustrating case ascertainment, exclusion criteria, and inclusion of SSTI and invasive infection events

Table 1a. Demographics of incident SSTIs from hospital labs and invasive infections from all labs by methicillin sensitivity status in 2017 EIP surveillance of *S. aureus* based on multiple imputation

	SSTIs				Invasive Infections				
	All (n=7,800)	MRSA (n=3,440)	MSSA (n=4,360)	p-value	All (n=2,038)	MRSA (n=754)	MSSA (n=1,284)	p-value	All p-value
Individual Level, n (%)									
County				<0.0001				0.0013	<0.0001
Clayton	644 (8.3)	311 (9.0)	333 (7.6)		167 (8.2)	77 (10.2)	90 (7.0)		
Cobb	1,884 (24.2)	823 (23.9)	1,061 (24.3)		388 (19.0)	122 (16.2)	266 (20.7)		
DeKalb	1,336 (17.1)	565 (16.4)	771 (17.7)		436 (21.4)	151 (20.0)	285 (22.2)		
Douglas	482 (6.2)	265 (7.7)	217 (5.0)		101 (5.0)	33 (4.4)	68 (5.3)		
Fulton	1,488 (19.1)	667 (19.4)	821 (18.8)		530 (26.0)	228 (30.2)	302 (23.5)		
Gwinnett	1,490 (19.1)	629 (18.3)	861 (19.7)		311 (15.3)	104 (13.8)	207 (16.1)		
Newton	258 (3.3)	87 (2.5)	171 (3.9)		57 (2.8)	19 (2.5)	38 (3.0)		
Rockdale	218 (2.8)	93 (2.7)	125 (2.9)		48 (2.4)	20 (2.7)	28 (2.2)		
Race				<0.0001				<0.0001	0.0920
White	3,759 (48.2)	1,606 (46.7)	2,153 (49.4)		943 (46.3)	303 (40.2)	640 (49.8)		
Black	3,825 (49.0)	1,762 (51.2)	2,063 (47.3)		1,049 (51.5)	442 (58.6)	607 (47.3)		
Other	216 (2.8)	72 (2.1)	144 (3.3)		46 (2.3)	9 (1.2)	37 (2.9)		
Ethnicity				<0.0001				0.0025	0.1940
Non-Hispanic	7,238 (92.8)	3,246 (94.4)	3,992 (91.6)		1,908 (93.6)	722 (95.8)	1,186 (92.4)		
Hispanic	562 (7.2)	194 (5.6)	368 (8.4)		130 (6.4)	32 (4.2)	98 (7.6)		
Sex				0.6506				0.0877	<0.0001
Female	3,542 (45.4)	1,572 (45.7)	1,970 (45.2)		821 (40.3)	322 (42.7)	499 (38.9)		
Male	4,258 (54.6)	1,868 (54.3)	2,390 (54.8)		1,217 (59.7)	432 (57.3)	785 (61.1)		
Area Level, Mean (SD)									
Inequality Index	0.41 (0.05)	0.41 (0.05)	0.41 (0.05)	0.4377	0.42 (0.06)	0.42 (0.06)	0.42 (0.06)	0.0478	<0.0001
Crowding, n (%)				<0.0001				0.4899	0.3610
No	1,345 (17.2)	514 (14.9)	831 (19.1)		334 (16.4)	118 (15.7)	216 (16.8)		
Yes	6,455 (82.8)	2,926 (85.1)	3,529 (80.9)		1,704 (83.6)	636 (84.4)	1,068 (83.2)		
Racial Minority Concentration, n (%)				0.0445				0.2419	0.0002
≤ 47.8%	3,916 (50.2)	1,683 (48.9)	2,233 (51.2)		929 (45.6)	331 (43.9)	598 (46.6)		
> 47.8%	3,884 (49.8)	1,757 (51.1)	2,127 (48.8)		1,109 (54.4)	423 (56.1)	686 (53.4)		
Percent No High School Diploma	0.12 (0.09)	0.13 (0.09)	0.12 (0.09)	0.0010	0.12 (0.08)	0.13 (0.09)	0.12 (0.08)	0.1940	0.4826
Poverty Concentration, n (%)				0.5094				0.0367	0.0003
≤ 40%	7,553 (96.8)	3,326 (96.7)	4,227 (97.0)		1,940 (95.2)	708 (93.9)	1,232 (96.0)		
> 40%	247 (3.2)	114 (3.3)	133 (3.1)		98 (4.8)	46 (6.1)	52 (4.1)		
Percent No Health Insurance	0.17 (0.09)	0.17 (0.09)	0.16 (0.09)	0.4577	0.16 (0.09)	0.17 (0.09)	0.16 (0.09)	0.0823	0.0571

Table 1a., Cont.

Area Level									
Percent Under 18 years-old	0.25 (0.06)	0.25 (0.06)	0.25 (0.06)	0.4359	0.25 (0.06)	0.24 (0.07)	0.25 (0.06)	0.1779	<0.0001
Percent Foreign Born	0.15 (0.11)	0.15 (0.11)	0.16 (0.11)	0.0943	0.14 (0.11)	0.13 (0.11)	0.14 (0.11)	0.1468	<0.0001
Distance to School, n (%)				0.0526				0.1887	0.0115
> 1 mile	1,739 (23.0)	755 (22.0)	1,038 (23.8)		415 (20.4)	142 (18.8)	273 (21.3)		
≤ 1 mile	6,007 (77.0)	2,685 (78.0)	3,322 (76.2)		1,623 (79.6)	612 (81.2)	1,011 (78.7)		
Distance to Daycare Center, n (%)				0.0264				0.0435	0.0923
> 1 mile	615 (7.9)	245 (7.1)	370 (8.5)		138 (6.8)	40 (5.3)	98 (7.6)		
≤ 1 mile	7,185 (92.1)	3,195 (92.9)	3,990 (91.5)		1,900 (93.2)	714 (94.7)	1,186 (92.4)		
Distance to Hospital, n (%)				0.1916				0.0938	<0.0001
> 1 mile	7,789 (99.9)	3,433 (99.8)	4,356 (99.9)		2,018 (99.0)	743 (98.5)	1,275 (99.3)		
≤ 1 mile	11 (0.1)	7 (0.2)	4 (0.1)		20 (1.0)	11 (1.5)	9 (0.7)		

Table 1b. Demographics of incident pediatric and adult *S. aureus* events by methicillin sensitivity status in 2017 EIP surveillance of *S. aureus* based on multiple imputation

	Pediatric				Adult				
	All (n=1,569)	MRSA (n=557)	MSSA (n=1,012)	p-value	All (n=8,269)	MRSA (n=3,637)	MSSA (n=4,632)	p-value	All p-value
Individual Level, n (%)									
County				0.0475				<0.0001	<0.0001
Clayton	147 (9.4)	62 (11.1)	85 (8.4)		664 (8.0)	326 (9.0)	338 (7.3)		
Cobb	408 (26.0)	135 (24.2)	273 (27.0)		1,864 (22.5)	810 (22.3)	1,054 (22.8)		
DeKalb	332 (21.2)	113 (20.3)	219 (21.6)		1,440 (17.4)	603 (16.6)	837 (18.1)		
Douglas	63 (4.0)	31 (5.6)	32 (3.2)		520 (6.3)	267 (7.3)	253 (5.5)		
Fulton	266 (17.0)	101 (18.1)	165 (16.3)		1,752 (21.2)	794 (21.8)	958 (20.7)		
Gwinnett	291 (18.5)	91 (16.3)	200 (19.8)		1,510 (18.3)	642 (17.7)	868 (18.7)		
Newton	37 (2.4)	12 (2.2)	25 (2.5)		278 (3.4)	94 (2.6)	184 (4.0)		
Rockdale	25 (1.6)	12 (2.2)	13 (1.3)		241 (2.9)	101 (2.8)	140 (3.0)		
Race				<0.0001				<0.0001	<0.0001
White	595 (37.9)	176 (31.6)	419 (41.4)		4,107 (49.7)	1,733 (47.6)	2,374 (51.3)		
Black	891 (56.8)	360 (64.6)	531 (52.5)		3,983 (48.2)	1,844 (50.7)	2,139 (46.2)		
Other	83 (5.3)	21 (3.8)	62 (6.1)		179 (2.2)	60 (1.6)	119 (2.6)		
Ethnicity				0.0001				0.0027	<0.0001
Non-Hispanic	1,319 (84.1)	495 (88.9)	824 (81.4)		7,827 (94.7)	3,473 (95.5)	4,354 (94.0)		
Hispanic	250 (15.9)	62 (11.1)	188 (18.6)		442 (5.3)	164 (4.5)	278 (6.0)		
Sex				0.1805				0.2420	0.0015
Female	753 (48.0)	280 (50.3)	473 (46.6)		3,610 (43.7)	1,614 (44.4)	1,996 (43.1)		
Male	816 (52.0)	277 (49.7)	539 (53.3)		4,659 (56.3)	2,023 (55.6)	2,636 (56.9)		
Area Level, Mean (SD)									
Inequality Index	0.41 (0.05)	0.41 (0.06)	0.41 (0.05)	0.6821	0.41 (0.05)	0.42 (0.05)	0.41 (0.05)	0.3199	0.3530
Crowding, n (%)				0.0105				<0.0001	0.1933
No	250 (15.9)	71 (12.8)	179 (17.7)		1,429 (17.3)	561 (15.4)	868 (18.7)		
Yes	1,319 (84.1)	486 (87.3)	833 (82.3)		6,840 (82.7)	3,076 (84.6)	3,764 (81.3)		
Racial Minority Concentration, n (%)				<0.0001				0.6357	0.8557
≤ 47.8%	776 (49.5)	235 (42.2)	541 (53.5)		4,069 (49.2)	1,779 (48.9)	2,290 (49.4)		
> 47.8%	793 (50.5)	322 (57.8)	471 (46.5)		4,200 (50.8)	1,858 (51.1)	2,342 (50.6)		
Percent No High School Diploma	0.13 (0.10)	0.14 (0.09)	0.13 (0.10)	0.2321	0.12 (0.09)	0.13 (0.09)	0.12 (0.09)	0.0606	<0.0001
Poverty Concentration, n (%)				0.1169				0.3530	0.4561
≤ 40%	1,509 (96.2)	530 (95.2)	979 (96.7)		7,984 (96.6)	3,504 (96.3)	4,480 (96.7)		
> 40%	60 (3.8)	27 (4.9)	33 (3.3)		285 (3.5)	133 (3.7)	152 (3.3)		
Percent No Health Insurance	0.18 (0.10)	0.18 (0.10)	0.18 (0.10)	0.1037	0.16 (0.09)	0.17 (0.09)	0.16 (0.09)	0.0864	<0.0001

Table 1b., Cont.

Area Level									
Percent Under 18 years-old	0.26 (0.05)	0.26 (0.05)	0.26 (0.05)	0.2403	0.25 (0.06)	0.25 (0.06)	0.25 (0.06)	0.8475	<0.0001
Percent Foreign Born	0.17 (0.12)	0.15 (0.12)	0.17 (0.13)	0.0151	0.15 (0.11)	0.15 (0.11)	0.15 (0.11)	0.8229	<0.0001
Distance to School, n (%)				0.6422				0.0211	0.0204
> 1 mile	317 (20.2)	109 (19.6)	208 (20.6)		1,891 (22.9)	788 (21.7)	1,103 (23.8)		
≤ 1 mile	1,252 (79.8)	448 (80.4)	804 (79.5)		6,378 (77.1)	2,849 (78.3)	3,529 (76.2)		
Distance to Daycare Center, n (%)				0.8853				0.0027	0.2506
> 1 mile	109 (7.0)	38 (6.8)	71 (7.0)		644 (7.8)	247 (6.8)	397 (8.6)		
≤ 1 mile	1,460 (93.1)	619 (93.2)	941 (93.0)		7,625 (92.2)	3,390 (93.2)	4,235 (91.4)		
Distance to Hospital, n (%)				0.6682				0.1117	0.1480
> 1 mile	1,567 (99.9)	556 (99.8)	1,011 (99.9)		8,240 (99.7)	3,620 (99.5)	4,620 (99.7)		
≤ 1 mile	2 (0.1)	1 (0.2)	1 (0.1)		29 (0.4)	17 (0.5)	12 (0.3)		

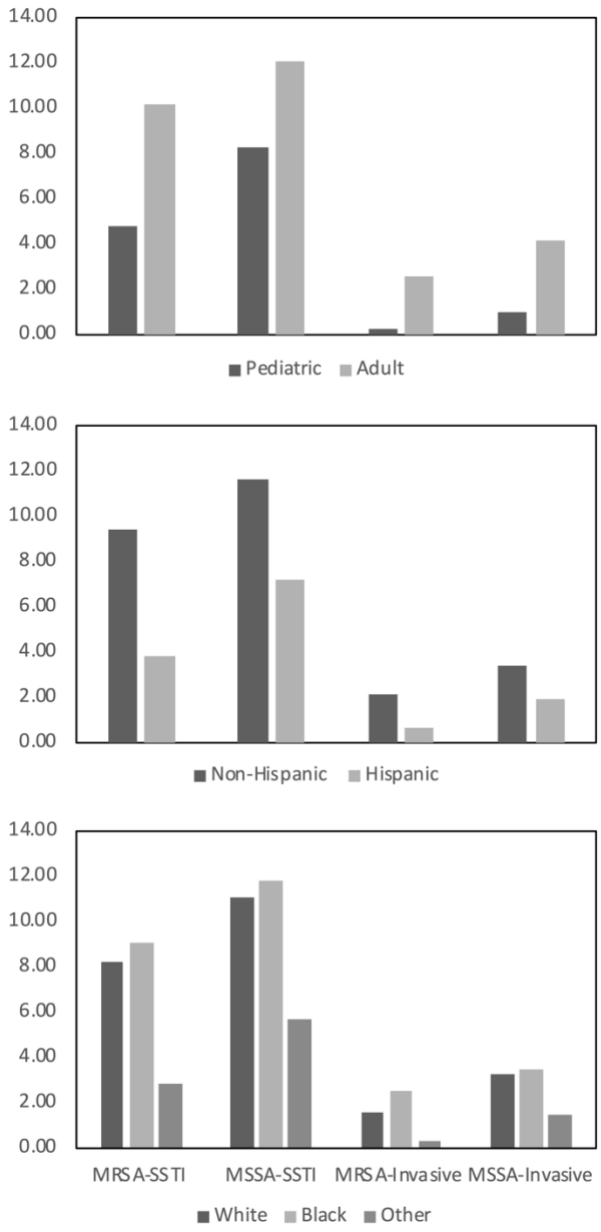


Figure 2. MRSA and MSSA skin/soft tissue and invasive infection incidences per 10,000 HD3 population by age group, race, and ethnicity

Table 2a. Individual and area level factors of SSTI MRSA compared to MSSA infections by pediatric and adult events for bivariate and multivariable crude and adjusted odds ratios

	Pediatric				Adult			
Individual Level	**Crude OR (95% CI)**	**p-value**	**Adjusted OR (95% CI)**	**p-value**	**Crude OR (95% CI)**	**p-value**	**Adjusted OR (95% CI)**	**p-value**
Age[a]								
Level 1	Referent	-	Referent	-	Referent	-	Referent	-
Level 2	1.05 (0.75, 1.48)	0.7838	1.01 (0.71, 1.42)	0.9699	1.21 (0.98, 1.49)	0.0791	1.21 (0.98, 1.50)	0.0772
Level 3	0.55 (0.41, 0.73)	<0.0001	0.55 (0.41, 0.74)	<0.0001	0.98 (0.79, 1.20)	0.8078	0.98 (0.79,1.20)	0.8249
Level 4	0.63 (0.47, 0.85)	0.0022	0.64 (0.47, 0.87)	0.0037	1.25 (1.00, 1.55)	0.0473	1.27 (1.02, 1.58)	0.0352
Sex								
Female	Referent	-	Referent	-	Referent	-	Referent	-
Male	0.87 (0.70, 1.08)	0.2074	0.96 (0.86, 1.07)	0.4546	1.00 (0.90, 1.10)	0.9139	1.01 (0.96, 1.06)	0.6830
Race								
White	Referent	-	Referent	-	Referent	-	Referent	-
Black	1.43 (1.16, 1.76)	0.0009	1.35 (1.09, 1.67)	0.0069	1.24 (1.08, 1.42)	0.0025	1.24 (1.08, 1.43)	0.0020
Other	0.72 (0.48, 1.06)	0.0947	0.69 (0.46, 1.02)	0.0641	0.74 (0.58, 0.95)	0.0173	0.73 (0.57, 0.94)	0.0156
Ethnicity								
Non-Hispanic	Referent	-	Referent	-	Referent	-	Referent	-
Hispanic	0.76 (0.65, 0.89)	0.0009	0.80 (0.67, 0.95)	0.0130	0.88 (0.78, 1.00)	0.0415	0.90 (0.80, 1.02)	0.0856
Area Level								
Inequality Index	1.40 (0.19, 10.57)	0.7425			1.35 (0.53, 3.44)	0.5310		
Crowding								
No	Referent	-	Referent	-	Referent	-	Referent	-
Yes	1.41 (1.04, 1.90)	0.0284	1.40 (1.01, 1.93)	0.0428	1.34 (1.17, 1.53)	<0.0001	1.32 (1.15, 1.52)	0.0001
Racial Ethnic Concentration								
≤ 47.8%	Referent	-	Referent	-	Referent	-		
> 47.8%	1.47 (1.19, 1.83)	0.0004	1.31 (1.03, 1.65)	0.0255	1.03 (0.94, 1.14)	0.5197		
Percent No High School Diploma	1.94 (0.65, 5.75)	0.2329			2.60 (1.49, 4.54)	0.0008	2.57 (1.34, 4.94)	0.0045
Poverty Concentration								
≤ 40%	Referent	-			Referent	-		
> 40%	1.40 (0.81, 2.42)	0.2299			1.04 (0.78, 1.38)	0.8066		
Percent No Health Insurance	2.30 (0.78, 6.84)	0.1331			2.43 (1.42, 4.17)	0.0012		
Percent Under 18 years old	0.29 (0.04, 2.15)	0.2230			1.06 (0.44, 2.52)	0.9009		
Percent Foreign Born	0.31 (0.13, 0.76)	0.0102	0.35 (0.13, 0.90)	0.0303	0.95 (0.61, 1.49)	0.8247	0.48 (0.29, 0.81)	0.0059
Distance to School								
> 1 mile	Referent	-			Referent	-		
≤ 1 mile	1.06 (0.94, 1.19)	0.3724			1.13 (1.08, 1.20)	<0.0001	1.07 (0.93, 1.22)	0.3461

Table 2a., Cont.

Area Level						
Distance to Daycare Center						
> 1 mile	Referent	-	Referent	-		
≤ 1 mile	1.04 (0.86, 1.25)	0.7095	1.26 (1.16, 1.36)	<0.0001	1.28 (1.04, 1.58)	0.0185
Distance to Hospital						
> 1 mile	Referent	-	Referent	-		
≤ 1 mile	1.73 (0.50, 5.97)	0.3879	2.37 (1.28, 4.41	0.0063	2.87 (0.71, 11.52)	0.1373

[a] Pediatric: Level 1= 0-2, Level 2 = >2-5, Level 3 = >5-13, Level 4 = >13-18 (inclusive); Adult: Level 1 = 19-25 (inclusive), Level 2 = >25-45, Level 3 = >45-65, Level 4 = 65+ (non-inclusive)

Table 2b. Individual and area level factors of invasive MRSA compared to MSSA infections by pediatric and adult events for bivariate and multivariable crude and adjusted odds ratios

	Pediatric				Adult			
Individual Level	**Crude OR (95% CI)**	**p-value**	**Adjusted OR (95% CI)**	**p-value**	**Crude OR (95% CI)**	**p-value**	**Adjusted OR (95% CI)**	**p-value**
Age[a]								
Level 1	Referent	-	Referent	-	Referent	-	Referent	-
Level 2	2.21 (0.58, 8.51)	0.2470	2.64 (0.61, 11.40)	0.1946	0.70 (0.39, 1.26)	0.2309	0.68 (0.37,1.22)	0.1968
Level 3	1.19 (0.46, 3.13)	0.7207	2.25 (0.76, 6.69)	0.1434	0.63 (0.36, 1.11)	0.1073	0.64 (0.36, 1.13)	0.1252
Level 4	1.41 (0.40, 5.02)	0.5965	2.11 (0.64, 12.03)	0.1711	1.03 (0.58, 1.81)	0.9289	1.09 (0.61, 1.94)	0.7657
Sex								
Female	Referent	-	Referent	-	Referent	-	Referent	-
Male	0.90 (0.41, 2.00)	0.8005	1.05 (0.68, 1.62)	0.8170	0.84 (0.70, 1.02)	0.0731	0.94 (0.86,1.04)	0.2406
Race								
White	Referent	-	Referent	-	Referent	-	Referent	-
Black	1.85 (0.91, 3.77)	0.0882	2.05 (0.95, 4.45)	0.0681	1.63 (1.21, 2.19)	0.0013	1.69 (1.25, 2.29)	0.0007
Other	1.21 (0.40, 3.69)	0.7330	1.58 (0.48, 5.13)	0.4509	0.55 (0.31, 0.97)	0.0393	0.54 (0.30, 0.96)	0.0363
Ethnicity								
Non-Hispanic	Referent	-	Referent	-	Referent	-	Referent	-
Hispanic	0.76 (0.42, 1.35)	0.3426	1.21 (0.61, 2.42)	0.5799	0.77 (0.62, 0.97)	0.0243	0.89 (0.70, 1.12)	0.3060
Area Level								
Inequality Index	2.65 (0.00, 999.99)	0.8077			4.34 (0.86, 21.98)	0.0760		
Crowding								
No	Referent	-			Referent	-		
Yes	6.34 (0.81, 49.49)	0.0781			1.05 (0.81, 1.34)	0.7324		
Racial Ethnic Concentration								
≤ 47.8%	Referent	-			Referent	-		
> 47.8%	4.66 (1.85, 11.71)	0.0011			1.03 (0.86, 1.24)	0.7355		
Percent No High School Diploma	3.79 (0.07, 214.15)	0.5177			2.24 (0.74, 6.73)	0.1514		
Poverty Concentration								
≤ 40%	Referent	-			Referent	-	Referent	-
> 40%	3.55 (0.68, 18.54)	0.1328			1.46 (0.96, 2.22)	0.0782	1.40 (0.92, 2.15)	0.1201
Percent No Health Insurance	11.60 (0.32, 425.26)	0.1822			2.68 (0.93, 7.75)	0.0689	2.35 (0.79, 7.01)	0.1257
Percent Under 18 years old	0.45 (0.00, 999.99)	0.8405			0.43 (0.10, 1.80)	0.2506		
Percent Foreign Born	0.20 (0.01, 5.04)	0.3303			0.67 (0.27, 1.65)	0.3806		

Table 2b., Cont.

Area Level						
Distance to School						
> 1 mile	Referent	-	Referent	-	Referent	-
≤ 1 mile	1.85 (1.03, 3.30)	0.0382	1.17 (1.05, 1.29)	0.0039	1.01 (0.78, 1.31)	0.9337
Distance to Daycare Center						
> 1 mile	Referent	-	Referent	-	Referent	-
≤ 1 mile	1.53 (0.58, 4.07)	0.3908	1.50 (1.26, 1.78)	<0.0001	1.44 (0.94, 2.12)	0.0926
Distance to Hospital						
> 1 mile			Referent	-	Referent	-
≤ 1 mile			2.01 (1.35, 2.99)	0.0006	2.16 (0.88, 5.29)	0.0911

[a] Pediatric: Level 1= 0-2, Level 2 = >2-5, Level 3 = >5-13, Level 4 = >13-18 (inclusive); Adult: Level 1 = 19-25 (inclusive), Level 2 = >25-45, Level 3 = >45-65, Level 4 = 65+ (non-inclusive)

Table 3a. Multilevel model for SSTI MRSA compared to MSSA by pediatric and adult events for adjusted odds ratios

	Pediatric		**Adult**	
Variable	**Adjusted OR (95% CI)**	**p-value**	**Adjusted OR (95% CI)**	**p-value**
Age[a]				
Level 1	Referent	-	Referent	-
Level 2	1.00 (0.69, 1.45)	0.9849	1.24 (0.97, 1.59)	0.0872
Level 3	0.53 (0.39, 0.73)	0.0001	0.96 (0.75, 1.23)	0.7388
Level 4	0.63 (0.45, 0.87)	0.0053	1.32 (1.02, 1.71)	0.0375
Sex				
Female	Referent	-	Referent	-
Male	0.93 (0.73, 1.17)	0.5311	1.03 (0.92, 1.16)	0.6186
Race				
White	Referent	-	Referent	-
Black	1.09 (0.77, 1.54)	0.6215	1.06 (0.93, 1.21)	0.3877
Other	0.61 (0.30, 1.23)	0.1647	0.61 (0.39, 0.95)	0.0302
Ethnicity				
Non-Hispanic	Referent	-	Referent	-
Hispanic	0.63 (0.43, 0.94)	0.0227	0.74 (0.56, 0.99)	0.0445
Crowding				
No	Referent	-	Referent	-
Yes	1.44 (1.02, 2.04)	0.0403	1.39 (1.18, 1.65)	0.0001
Racial Ethnic Concentration				
≤ 47.8%	Referent	-		
> 47.8%	1.19 (0.90, 1.58)	0.2211		
Percent No High School Diploma			3.21 (1.45, 7.09)	0.0039
Percent Foreign Born	0.55 (0.18, 1.63)	0.2771	0.52 (0.27, 0.98)	0.0438
Distance to Daycare Center				
> 1 mile			Referent	-
≤ 1 mile			1.38 (1.10, 1.72)	0.0047
Distance to Hospital				
> 1 mile			Referent	-
≤ 1 mile			3.36 (0.68, 16.69)	0.1385

[a] Pediatric: Level 1= 0-2, Level 2 = >2-5, Level 3 = >5-13, Level 4 = >13-18 (inclusive); Adult: Level 1 = 19-25 (inclusive), Level 2 = >25-45, Level 3 = >45-65, Level 4 = 65+ (non-inclusive)

Table 3b. Multilevel model for invasive MRSA compared to MSSA by pediatric and adult events for adjusted odds ratios

	Pediatric		Adult	
Variable	**Adjusted OR (95% CI)**	**p-value**	**Adjusted OR (95% CI)**	**p-value**
Age[a]				
Level 1			Referent	-
Level 2			0.66 (0.34, 1.30)	0.2345
Level 3			0.63 (0.33, 1.21)	0.1662
Level 4			1.17 (0.61, 2.25)	0.6323
Race				
White	Referent	-	Referent	-
Black	2.09 (0.62, 7.01)	0.2339	1.52 (1.20, 1.92)	0.0005
Other	1.85 (0.28, 12.13)	0.5234	0.43 (0.16, 1.13)	0.0855
Ethnicity				
Non-Hispanic			Referent	-
Hispanic			0.63 (0.37, 1.09)	0.0978
Crowding				
No	Referent	-		
Yes	4.91 (0.60, 40.29)	0.1383		
Racial Ethnic Concentration				
≤ 47.8%	Referent	-		
> 47.8%	3.10 (1.07, 8.99)	0.0368		
Poverty Concentration				
≤ 40%			Referent	-
> 40%			1.23 (0.75, 2.03)	0.3941
Percent No Health Insurance			4.05 (1.09, 15.14)	0.0370
Distance to Daycare Center				
> 1 mile			Referent	-
≤ 1 mile			1.41 (0.91, 2.19)	0.1247
Distance to Hospital				
> 1 mile			Referent	-
≤ 1 mile			2.39 (0.86, 6.63)	0.0953

[a] Pediatric: Level 1= 0-2, Level 2 = >2-5, Level 3 = >5-13, Level 4 = >13-18 (inclusive); Adult: Level 1 = 19-25 (inclusive), Level 2 = >25-45, Level 3 = >45-65, Level 4 = 65+ (non-inclusive)

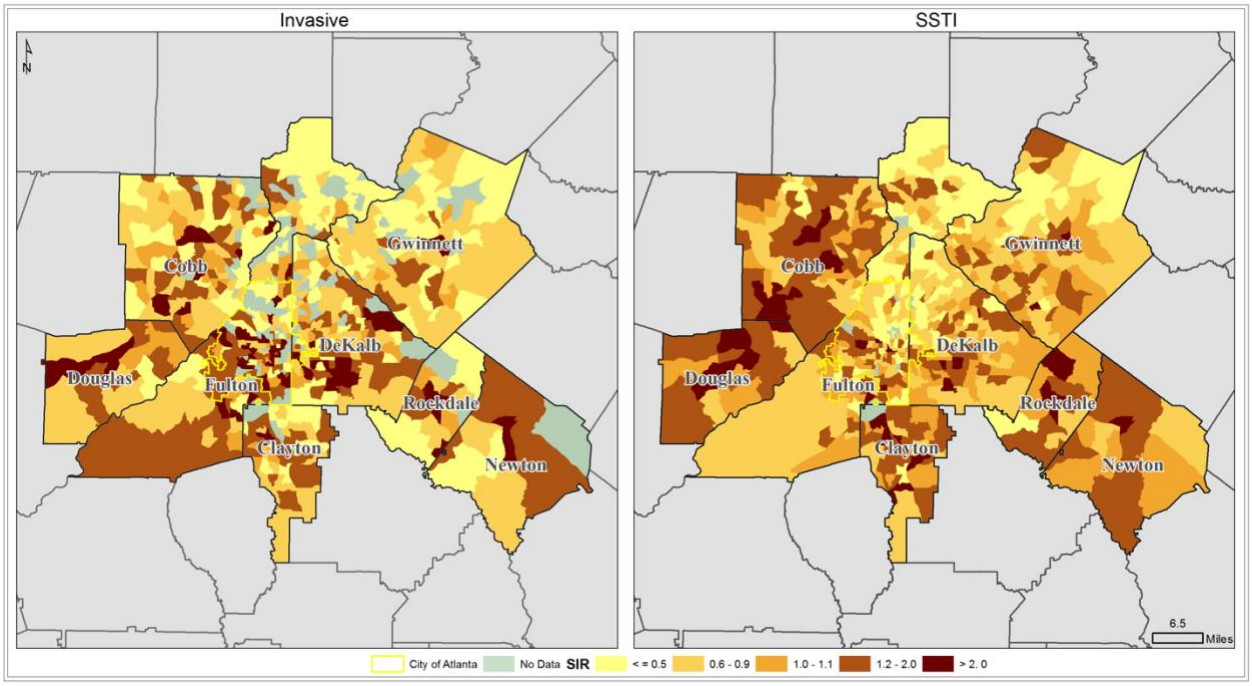


Figure 3. SIRs of invasive and skin/soft tissue infections in metro-Atlanta/HD3 census tracts and counties in 2017, with reference to incidence of corresponding infection source

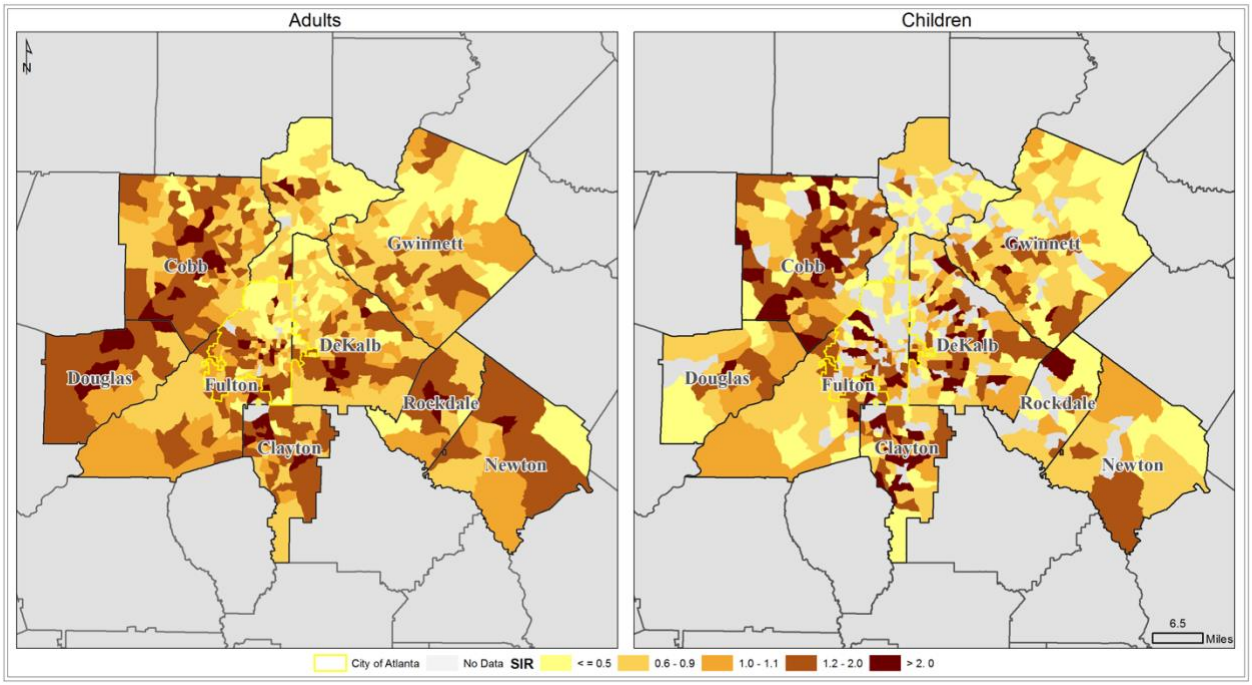


Figure 4. SIRs of pediatric and adult skin/soft tissue and invasive infections in metro-Atlanta/HD3 census tracts and counties in 2017, with reference to incidence of corresponding age group rates

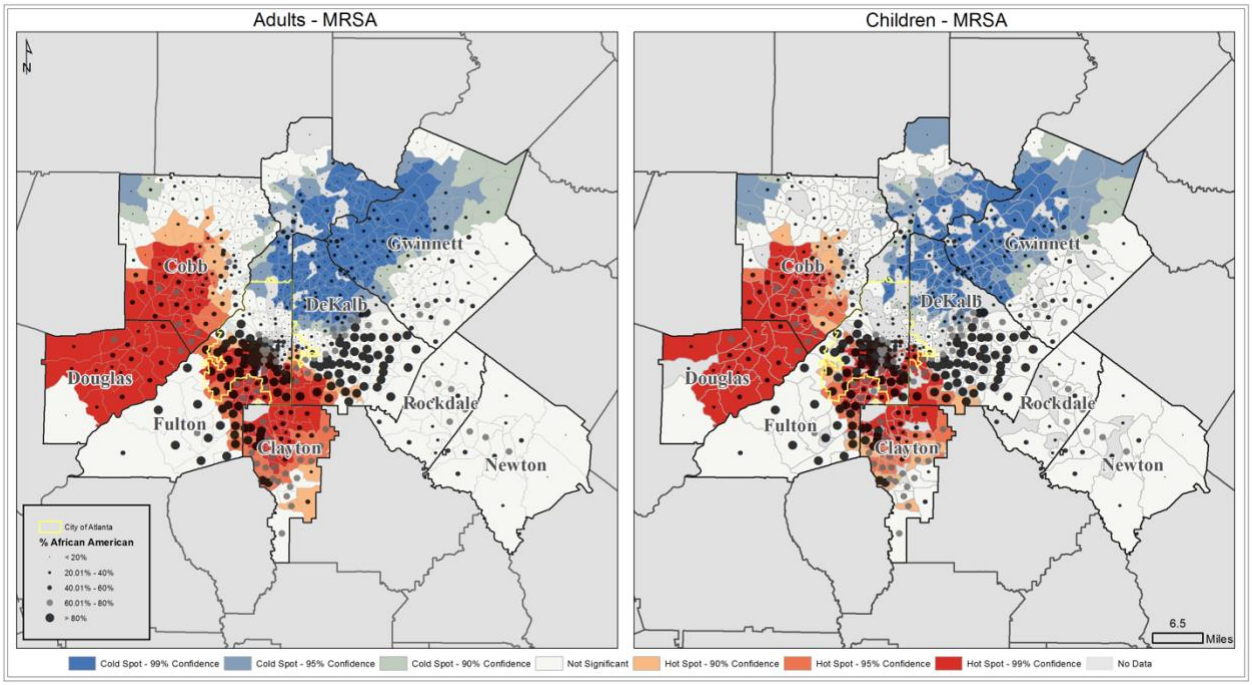
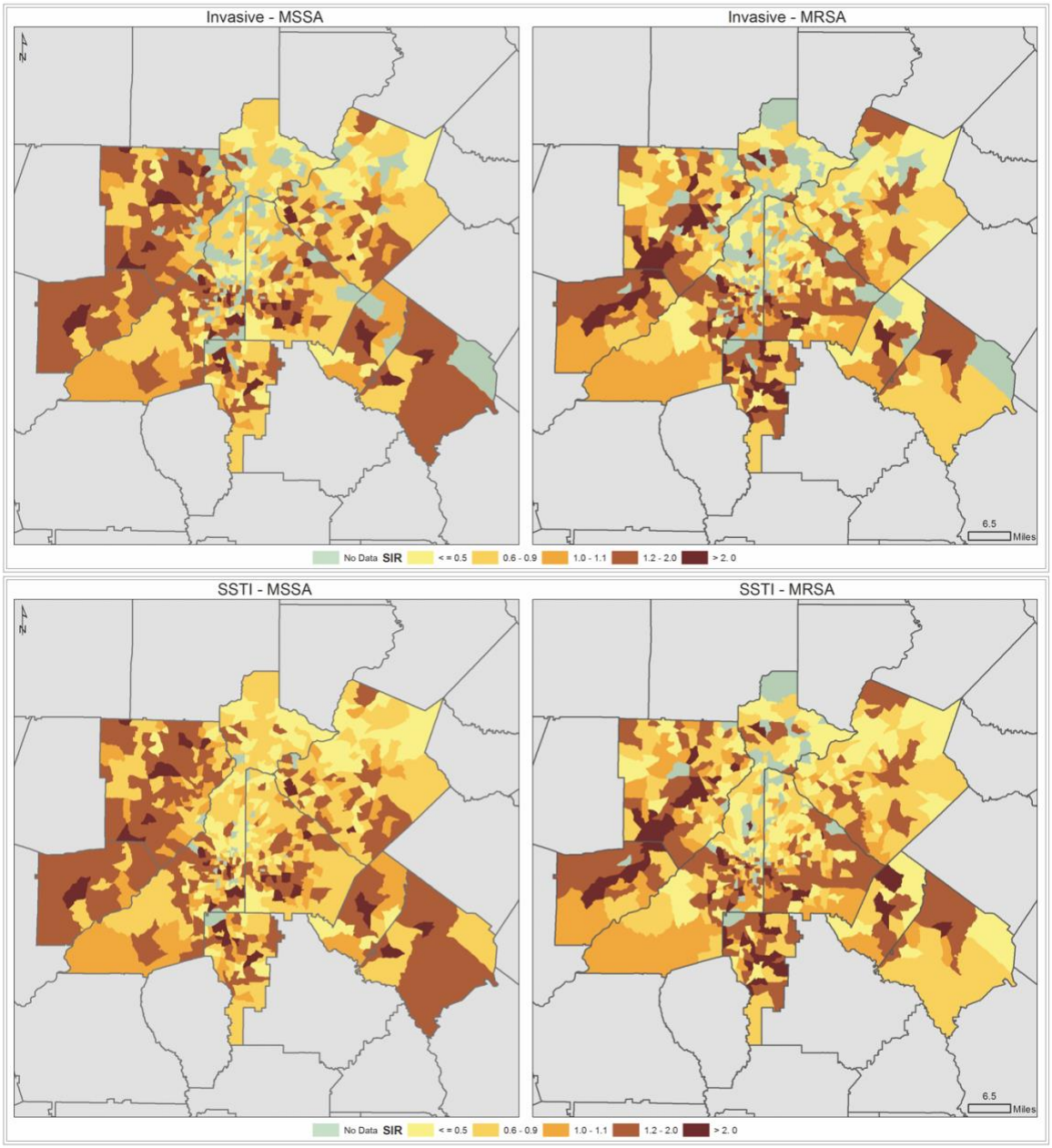


Figure 5. Hotspot analysis of pediatric and adult MRSA skin/soft tissue and invasive infections based on incidence rates and non-aggregated data in metro-Atlanta/HD3 census tracts and counties, 2017

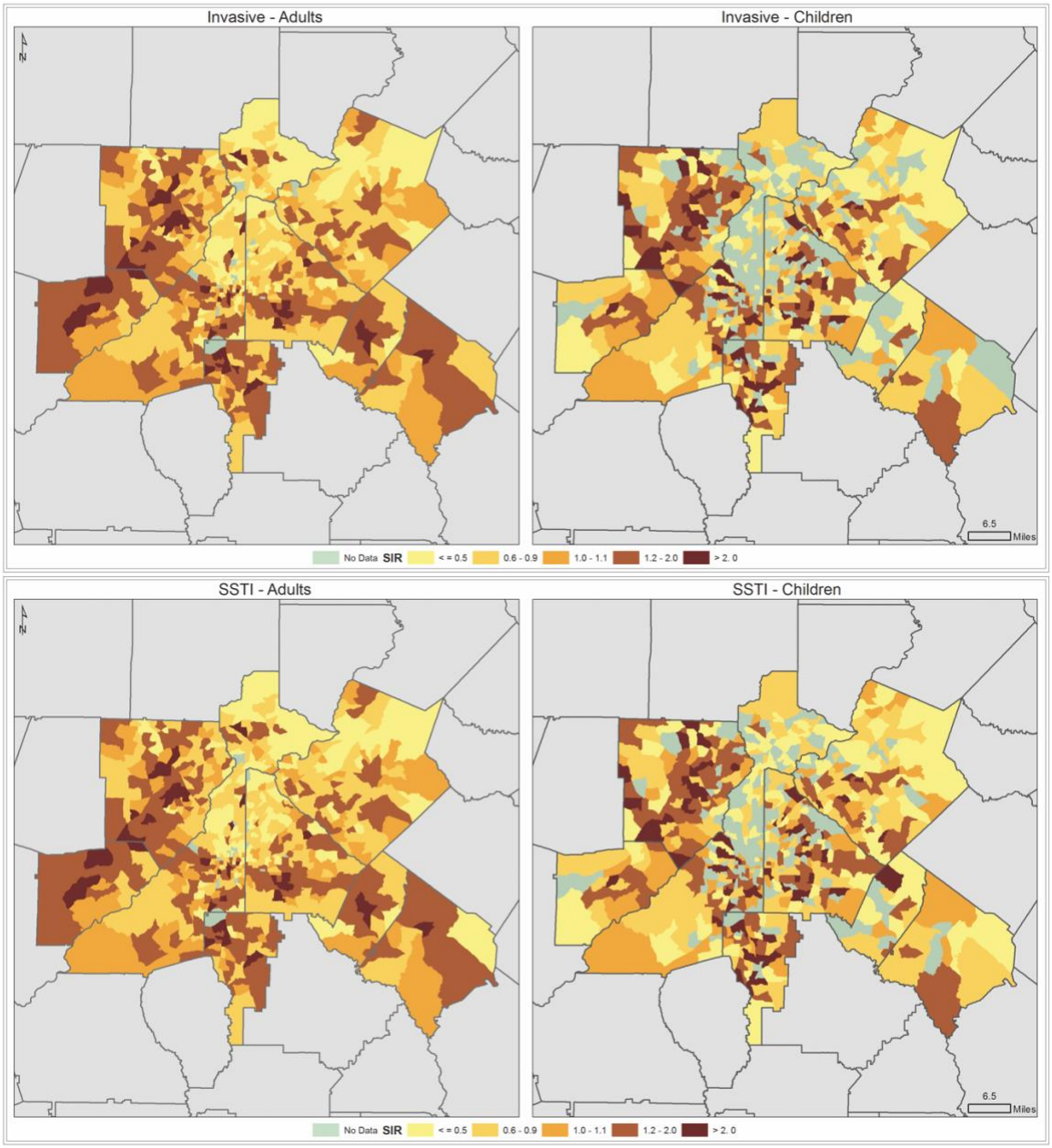
Appendix A. Supplemental Materials

Supplemental Table 1. Demographics of incident *S. aureus* skin/soft tissue infection cultures collected from hospital labs and invasive infection cultures collected from all labs in Health District 3 for cases with known census tract (n=9,838) in 2017 EIP surveillance data by covariate imputation

	All Case Analysis		Multiple Imputation 1		Multiple Imputation 2		Multiple Imputation 3		Multiple Imputation 4		Multiple Imputation 5	
	SSTI (n=7,800)	**Invasive** (n=2,038)	**SSTI** (n=7,800)	**Invasive** (n=2,038)	**SSTI** (n=7,800)	**Invasive** (n=2,038)	**SSTI** (n=7,800)	**Invasive** (n=2,038)	**SSTI** (n=7,800)	**Invasive** (n=2,038)	**SSTI** (n=7,800)	**Invasive** (n=2,038)
Race												
American Indian/Alaska Native	21	4										
Asian	158	32										
Black	3,446	1,012	3,864	1,045	3,838	1,057	3,825	1,049	3,882	1,054	3,862	1,054
Native Hawaiian or Pacific-Islander	13	8										
White	3,162	845	3,715	943	3,744	936	3,759	943	3,702	937	3,727	937
Unknown	1,000	137										
Other	-	-	221	50	218	45	216	46	216	47	211	47
Ethnicity												
Hispanic	488	124	577	130	573	128	562	130	567	127	565	129
Non-Hispanic	5,966	1,846	7,223	1,908	7,227	1,910	7,238	1,908	7,233	1,911	7,235	1,909
Unknown	1,346	68										
Sex												
Male	4,257	821	4,259	821	4,258	821	4,258	821	4,259	821	4,259	821
Female	3,541	1,217	3,541	1,217	3,542	1,217	3,542	1,217	3,541	1,217	3,541	1,217
Unknown	2	0										
Age Category												
0-2	344	78	344	78	344	78	344	78	344	78	344	78
>2-5	216	11	216	11	216	11	216	11	216	11	216	11
>5-13	468	34	468	34	468	34	468	34	468	34	468	34
>13-18	403	15	403	15	403	15	403	15	403	15	403	15
19-25	425	52	425	52	425	52	425	52	425	52	425	52
>25-45	1,941	362	1,942	362	1,942	362	1,942	362	1,942	362	1,941	362
>45-65	2,493	833	2,493	833	2,493	833	2,494	833	2,494	833	2,494	833
>65	1,508	653	1,509	653	1,509	653	1,508	653	1,508	653	1,509	653
Unknown	2	0										



Supplemental Figure 1. SIRs of MRSA and MSSA skin/soft tissue and invasive infections in HD3 counties/census tracts in 2017, with reference to incidence in corresponding infection source



Supplemental Figure 2. SIRs of pediatric and adult skin/soft tissue and invasive infections in HD3 counties/census tracts in 2017, with reference to incidence of corresponding infection source