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Public Health Importance of Invasive Methicillin-sensitive *Staphylococcus aureus* Infections: Surveillance in 8 US Counties, 2016

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Abstract

Background.—Public health and infection control prevention and surveillance efforts in the United States have primarily focused on methicillin-resistant *Staphylococcus aureus* (MRSA). We describe the public health importance of methicillin-susceptible *S. aureus* (MSSA) in selected communities.

Methods.—We analyzed Emerging Infections Program surveillance data for invasive *S. aureus* (SA) infections (isolated from a normally sterile body site) in 8 counties in 5 states during 2016. Cases were considered healthcare-associated if culture was obtained >3 days after hospital admission; if associated with dialysis, hospitalization, surgery, or long-term care facility (LTCF) residence within 1 year prior; or if a central venous catheter was present ≤2 days prior. Incidence per 100 000 census population was calculated, and a multivariate logistic regression model with random intercepts was used to compare MSSA risk factors with those of MRSA.

Results.—Invasive MSSA incidence (31.3/100 000) was 1.8 times higher than MRSA (17.5/100 000). Persons with MSSA were more likely than those with MRSA to have no underlying medical conditions (adjusted odds ratio [aOR], 2.06; 95% confidence interval [CI], 1.26–3.39) and less likely to have prior hospitalization (aOR, 0.70; 95% CI, 0.60–0.82) or LTCF residence (aOR, 0.37; 95% CI, 0.29–0.47). MSSA accounted for 59.7% of healthcare-associated cases and 60.1% of deaths.

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Conclusions.—Although MRSA tended to be more closely associated with healthcare exposures, invasive MSSA is a substantial public health problem in the areas studied. Public health and infection control prevention efforts should consider MSSA prevention in addition to MRSA.

Keywords

methicillin-sensitive *Staphylococcus aureus*; MSSA; MSSA burden

Methicillin-resistant *Staphylococcus aureus* (MRSA) in the United States was estimated to cause 72 444 invasive infections and 9194 deaths in 2014 [1] and has been a focus of attention for more than 3 decades by the clinical and public health communities [2–5]. This emphasis is evident in the development of clinical guidelines for the treatment of MRSA by the Infectious Diseases Society of America [6]; development of guidelines to prevent transmission of MRSA in acute-care hospitals by the healthcare epidemiology community [7]; and inclusion of MRSA as a priority pathogen for national prevention efforts promulgated by the US Centers for Disease Control and Prevention (CDC) [8], the US Health and Human Services [9, 10], the Centers for Medicare & Medicaid Services [11], and the Institute for Healthcare Improvement [12].

MRSA epidemiology has changed over the past decade. From 2005 through 2014, the estimated national rate of invasive MRSA in the United States decreased 39.5%, with the largest declines among hospitalized patients (65.3%) [1, 13]. Much of this decrease is likely attributable to reductions in the traditionally healthcare-associated USA100 strains. Bloodstream infection incidence from USA100 strains decreased >60% from 2005 to 2013 within selected areas of the United States, including a decline of >80% in hospital-onset bloodstream infection incidence [14]. These recent changes in MRSA epidemiology lead to questions regarding the current status of *S. aureus* (SA) epidemiology. Specifically, what is the current contribution of MRSA vs methicillin-susceptible *S. aureus* (MSSA) to the overall SA burden and how do these infections differ?

The literature includes few reports describing MSSA infections in the United States, and those reports primarily coincide with time periods when the above-described changes in MRSA epidemiology were occurring [15–20]. There is a lack of reported information about MSSA epidemiology; prior studies do not describe the incidence of MSSA, are limited to specific subsets of patients (eg, infants/pediatric patients, community-associated cases), or are limited in geographic scope (eg, a single hospital or area). Similarly, studies that describe MSSA mortality have typically been conducted outside the United States (where strain types, demographics, and therefore disease outcomes may differ) and primarily report older data [21–25].

Here, we describe the epidemiology of invasive MSSA infections in a diverse US population using recent data. Our primary objective is to describe the current public health importance of MSSA and MRSA in the United States.

METHODS

The Healthcare-associated Infections–Community Interface component of the Emerging Infections Program (EIP) of the CDC includes ongoing, active laboratory- and population-based surveillance for invasive SA infections. During 2016, 5 EIP sites conducted surveillance for invasive SA infections (ie, including both MRSA and MSSA) in 8 counties (Table 1). Surveillance personnel from each site investigate all laboratory reports of sterile site SA cultures from clinical laboratories that routinely serve the surveillance area and complete a standard case report form that includes demographic and clinical data, as previously described [2]. The total estimated population under surveillance during 2016 was 7 809 686, or 2.4% of the total US population.

A case is defined as isolation of SA from a normally sterile site (eg, blood, cerebrospinal fluid, bone) in a resident of the surveillance area; cases are classified as MRSA or MSSA based on results from local clinical microbiology laboratory testing. Cases are further categorized into the following 3 mutually exclusive epidemiologic classes: hospital-onset (HO) if the culture is obtained after the third calendar day of hospitalization; healthcare-associated community-onset (HACO) if the culture is obtained before the fourth calendar day of hospitalization from a patient with 1 or more of the following risk factors: a history of hospitalization, surgery, dialysis, or residence in a long-term care facility (LTCF) in the previous year or the presence of a central venous catheter within 2 days prior to culture; or community-associated (CA) if none of the previously mentioned criteria are met. The term “healthcare-associated (HA)” refers to both HO and HACO cases. The term “community onset (CO)” refers to both CA and HACO cases. In 2016, 2 of the sites (California and Georgia) collected full case report form data for a random sample of 12%–18% of HO MRSA cases and limited epidemiologic data for the remainder of HO cases (nonsampled cases). Nonsampled cases contributed to case counts and are included in analyses of some demographic variables (sex and age) but were otherwise excluded from analyses unless noted. For cases that were not HO, full case report form data collection was required. The other sites (Minnesota, New York, and Tennessee) did not sample any cases. Race was unknown for all nonsampled cases and in 9.9% of cases with full chart abstraction. Cases for which race was unknown were assigned a race based on the known population distributions of race by sex, age, and receipt of chronic dialysis in each surveillance area, as previously described [5]. Imputed race was used for both incidence calculations and logistic regression.

Three analyses of the surveillance data were conducted. First, we used US Census Bureau bridged-race vintage post-census population estimates for 2016, provided by the National Center for Health Statistics, for surveillance area denominator values used in incidence calculations [26]. We calculated incidence (per 100 000 census population) by site, epidemiologic classification, sex, race, and age group. To calculate incidence, case counts from 1 site that performed surveillance only for 10 months during 2016 (Tennessee) were multiplied by 1.2. Second, we examined differences in the demographics, epidemiologic risk factors, and clinical characteristics of MSSA and MRSA cases using the Wilcoxon rank-sum test for continuous variables and the χ^2 test for categorical variables. Third, to identify independent risk factors for MSSA compared to MRSA, a logistic regression model with random intercepts for EIP site was fitted using backward elimination with a stay criterion of

$P < .05$. We included demographic and epidemiologic risk factors for MSSA infection that had P values ≤ .25 in bivariate analysis and categorized age into the following groups: <18, 18–64, and ≥65 years. Nonindependent risk factors were collapsed into single variables; for example, the 3 variables "hospitalized in past year," "hospitalized ≥4 days at time of initial culture," and "hospital inpatient 4 days prior to culture" were recoded to 1 of 3 hospital-related categories: hospitalized ≥4 days at time of initial culture, hospitalized in past year but not ≥4 days prior to initial culture, and not hospitalized in past year. For all analyses, differences were considered significant if the P value was <.05.

Case reporting and epidemiologic analyses were determined to be routine surveillance activities at the CDC. Additionally, each participating site evaluated the protocol and either deemed it a nonresearch surveillance activity or obtained institutional review board approval with a waiver of informed consent.

RESULTS

During 2016, 3787 cases of invasive SA infection were reported to the surveillance catchment area, including 2004 (52.9%) classified as HACO, 1254 (33.1%) as CA, and 470 (12.4%) as HO. Medical records were not available for 59 (1.6%) cases, resulting in unknown epidemiologic classification. Almost two-thirds (63.8%) of cases were MSSA, though this proportion varied by site (range, 42.3%–69.2%). A higher proportion of MSSA cases were CA (37.2% of MSSA vs 25.9% of MRSA; $P < .01$); a lower proportion of MSSA cases were classified as HACO (49.7% of MSSA vs 58.5% of MRSA; $P < .01$) or HO (11.4% of MSSA vs 14.2% of MRSA; $P = .02$) compared to MRSA cases.

The overall incidence of invasive SA infection was 48.8/100 000, with MSSA incidence (31.3/100 000) 1.8 times higher than MRSA incidence (17.5/100 000). Incidence rates varied by site, epidemiologic classification, race, and age group (Figure 1). The greatest incidence disparity by epidemiologic class was among CA cases, where MSSA incidence (11.7/100 000) was 2.6 times that of MRSA (4.5/100 000). Among racial groups, blacks had the highest SA incidence for both MSSA and MRSA. MSSA incidence was 3.0 times higher than MRSA incidence among Asian/Pacific Islanders and 1.9 times higher among whites. Invasive MSSA incidence was greater than MRSA incidence in each age group, with the MSSA incidence highest in newborns and infants aged <1 year and those aged ≥50 years. Males had higher SA incidence compared to females for both MSSA (41/100 000 vs 22/100 000) and MRSA (21.9/100 000 vs 13.3/100 000).

The bivariate analysis provided in Table 2 indicates unadjusted associations between each variable and methicillin resistance. There were differences in demographics, underlying conditions, and location prior to culture. MSSA patients were less likely than MRSA cases to be hospitalized (odds ratio [OR], 0.59; 95% confidence interval [CI], 0.45–0.78), and those with CO MSSA were hospitalized for a shorter period of time ($P < .01$) than those with CO MRSA. There was no difference in total length of hospital stay between MSSA and MRSA for HO disease. Among all cases, MSSA patients were less likely than MRSA patients to be admitted to the intensive care unit (OR, 0.82; 95% CI, 0.70–0.95) or die during hospitalization (OR, 0.77; 95% CI, 0.63–0.95). Overall, 832 (34.4%) MSSA patients

and 470 (37.0%) MRSA patients had 1 or more of the following: a history of surgery or dialysis in the previous year or the presence of a central venous catheter within 2 days prior to culture.

The results of the multivariate logistic regression model, including adjusted ORs, are shown in Table 3. When adjusting for the other predictor variables included in the model, patients with invasive MSSA were more likely than those with invasive MRSA to be aged 0–17 years (adjusted OR [aOR], 2.06; 95% CI, 1.26–3.39 compared to patients aged 18–64 years), to be Asian/Pacific Islander (aOR, 1.39; 95% CI, 1.05–1.85 compared to whites), and to have no underlying medical conditions (aOR, 1.36; 95% CI, 1.03–1.81). Invasive MSSA patients were less likely to be in a LTCF prior to culture (aOR, 0.37; 95% CI, 0.29–0.47 for the fourth day before culture; aOR, 0.60; 95% CI, 0.43–0.83 for the past year but not the fourth day before culture) compared to patients with MRSA when adjusting for the other predictor variables included in the model. Invasive CO SA cases were less likely to be MSSA if there was a hospitalization in the prior year compared to CO cases without hospitalization (aOR, 0.70; 95% CI, 0.60–0.82). In addition, the state of residence was a significant covariate.

The bivariate analysis provided in Table 4 shows associations between methicillin resistance and infection type, for which patients could have more than 1. Infection type was determined using the diagnoses documented in the medical record. MSSA patients more frequently had a diagnosis of bursitis ($P < .01$), septic arthritis ($P < .01$), catheter site infection ($P = .02$), arteriovenous fistula/graft infection ($P = .01$), or internal surgical site infection ($P = .04$) compared to MRSA patients; pneumonia did not occur more frequently among MSSA patients than MRSA patients ($P = .05$). Conversely, even though we did not detect a difference in frequency of endocarditis ($P = .32$), MRSA patients more frequently had diagnoses of septic emboli ($P = .03$) and skin abscesses ($P = .02$). Similar percentages of MSSA and MRSA patients had bacteremia, cellulitis, and osteomyelitis.

DISCUSSION

Invasive MSSA infections cause substantial morbidity and mortality. For example, invasive MSSA incidence exceeded that of MRSA in all demographic groups and epidemiologic classes. In addition, invasive MSSA infections accounted for the majority of cases, hospitalizations, and deaths associated with invasive SA infections, indicating that invasive MSSA infections contribute significant public health burden in the United States.

There are important similarities between MRSA and MSSA infection in all settings. The incidence of both is greater in blacks compared to whites and males compared to females, and is higher at the extremes of age [2, 3, 27]. However, invasive MSSA infection is more likely in persons with less frequent healthcare exposure, such as those who are younger or have no underlying conditions. Although MSSA was more common than MRSA in most demographic groups, this was particularly apparent for invasive SA infections in persons aged <18 years, with the incidence of MSSA in persons aged <1 year exceeding that of MRSA in age groups <50 years.

Most invasive MSSA infections were HA, and more than one-third of infections overall were associated with prior central venous catheter use, surgery, or dialysis, indicating that continued, consistent implementation of recommended interventions aimed at preventing device- and procedure-associated infections that are commonly caused by SA will continue to be very important [28, 29]. Some strategies that have been primarily targeted at MRSA prevention, such as universal decolonization of patients in intensive care units, are also likely to have an impact on HA invasive MSSA. In addition, persons with invasive MRSA were even more likely than those with invasive MSSA to have had prior exposure to inpatient healthcare, such as hospitalization in the past year or prior LTCF residence. This may indicate that MRSA is more likely than MSSA to have been acquired in healthcare settings. The CDC supports ongoing efforts to promote innovation for strategies to prevent transmission in nonhospital healthcare settings. In addition, although the question is debated in the field [30], the CDC continues to support the use of contact precautions for patients with MRSA colonization or infection as a means of interrupting transmission of MRSA in hospitals [31].

Eight percent of invasive MSSA and 10% of invasive MRSA infections occurred in people who inject drugs. Strategies to prevent invasive SA in this population include primary prevention of opioid misuse through guideline-concordant prescribing; treatment of opioid use disorder with medication-assisted therapies; community-based comprehensive syringe programs that provide access to sterile equipment used to inject drugs and to safe disposal methods; and education on safer injection practices, wound care, and early warning signs of serious infections associated with injection drug use.

Aside from prevention strategies in people who inject drugs, current prevention strategies for CA invasive SA are limited to outbreak containment and general handwashing guidance; prevention programs have primarily targeted MRSA. Further research is needed to either determine if existing CA MRSA interventions also effectively prevent invasive CA MSSA or if new interventions are needed for CA SA. Unfortunately, programs focused on reducing CA invasive SA infections have been hampered by lack of understanding of risk factors and which interventions are effective and feasible. Potential areas that might prove effective in the future include targeted use of skin antiseptics or other means of reducing microbial bioburden, maintaining skin health, and, eventually, development of vaccines against SA. It is clear that given the large burden of invasive CA MSSA, additional research to develop effective interventions to prevent CA disease would have a large public health benefit.

After controlling for demographic characteristics, underlying comorbidities, and prior healthcare exposures, state of residence was significantly associated with the likelihood of MSSA compared to MRSA invasive infections. MSSA incidence also varied up to nearly 2-fold by geographic site; this might be related to differential risk of transmission in different localities or to other community characteristics that were not accounted for in our analysis, such as antibiotic use and socioeconomic status [32].

The most frequently reported infection types (bacteremia, osteomyelitis, and cellulitis) did not vary by methicillin-resistant status except for the association of MSSA with septic arthritis, a finding reported previously [19]. Although smaller studies have reported more

frequent bacteremia, pneumonia, endocarditis, or sepsis among MRSA patients [19, 33], strategies to prevent these common clinical infection syndromes should consider overall invasive SA prevention.

There were several limitations to this analysis. Because of the data collection scheme for HO MRSA cases, epidemiologic data for many HO MRSA cases from 2 sites were incomplete and therefore had to be excluded from some analyses including multivariate modeling. This may impact the generalizability of these results. Additionally, data were collected through medical record review and were subject to the limitations of those data sources. Third, outcomes were only ascertained during the hospitalization period, which likely underestimated mortality. Fourth, the geographic areas in which surveillance was conducted may not be representative of other areas of the United States, with the 3-county San Francisco Bay Area accounting for 46% of the surveillance population. However, a major strength of the analysis is that the data represent invasive SA infections that occur in diverse geographic catchment areas and are not limited to single medical centers, sociodemographic groups, or settings, thus, filling gaps noted in previous studies. Moreover, the principal finding that MSSA is the most prevalent cause of serious SA infections is consistent with the CDC's National Healthcare Safety Network's finding that <50% of HA (mostly HO) SA infections reported nationally are due to MRSA [34]. Although MSSA isolates were not collected in 2016, strain diversity and antimicrobial resistance were described for strains collected from 3 EIP counties from 2014 through 2015. MSSA isolates were more genetically diverse and more susceptible to antimicrobial drug classes (except tetracycline) than MRSA; one-third were susceptible to penicillin [19, 35]. Finally, this analysis did not include socioeconomic data or other community characteristics, which may be useful in describing possible reasons for the wide geographic variation in incidence.

In this population-based analysis of invasive MSSA in the United States, we found that invasive MSSA continues to be an important public health problem, accounting for most invasive SA infections and associated deaths in most of the metropolitan areas evaluated. The historic declines seen for MRSA provide hope that achieving decreases in MSSA infection incidence may be possible as well. However, including prevention of all invasive SA infections, regardless of methicillin-resistance status, in public health practice and research will be critical for success.

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References

1. Centers for Disease Control and Prevention. Active bacterial core surveillance report, Emerging Infections Program Network, methicillin-resistant Staphylococcus aureus. 2014 Available at: https://www.cdc.gov/abcs/reports-findings/survreports/mrsa14.html. Accessed 14 November 2018.
2. Klevens RM, Morrison MA, Nadle J, et al.; Active Bacterial Core Surveillance (ABCs) MRSA Investigators. Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. JAMA 2007; 298:1763–71. [PubMed: 17940231]
3. Iwamoto M, Mu Y, Lynfield R, et al. Trends in invasive methicillin-resistant *Staphylococcus aureus* infections. Pediatrics 2013; 132:e817–24. [PubMed: 24062373]
4. Nguyen D, Lessa F, Bellflower R, et al. Invasive methicillin-resistant *Staphylococcus aureus* infections among patients on chronic dialysis in the United States, 2005–2011. Clin Infect Dis 2013; 57:1393–400. [PubMed: 23964088]
5. Dantes R, Mu Y, Aragon D, et al. National burden of invasive methicillin-resistant *Staphylococcus aureus* infections, United States, 2011. JAMA Intern Med 2013;173:1970–8. [PubMed: 24043270]
6. Liu C, Bayer A, Cosgrove SE, et al.; Infectious Diseases Society of America. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. Clin Infect Dis 2011; 52:e18–55. [PubMed: 21208910]
7. Calfee DP, Salgado CD, Classen D, et al. Strategies to prevent transmission of methicillin-resistant *Staphylococcus aureus* in acute care hospitals. Infect Control Hosp Epidemiol 2008; 29(Suppl 1):S62–80. [PubMed: 18840090]
8. Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2013. CDC: Atlanta, GA; 2013.
9. US Department of Health and Human Services. National action plan to prevent health care-associated infections: road map to elimination. Available at: https://health.gov/hcq/prevent-hai-action-plan.asp. Accessed 24 July 2017.
10. Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria. Initial assessments of the national action plan for combating antibiotic-resistant bacteria. Available at: https://www.hhs.gov/sites/default/files/paccarb-final-report-03312016.pdf. Accessed 24 July 2017.
11. Centers for Medicare & Medicaid Services. Hospital-acquired condition (HAC) reduction program. Available at: https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/Value-Based-Programs/HAC/Hospital-Acquired-Conditions.html. Accessed 8 November 2018.
12. McCannon CJ, Hackbarth AD, Griffin FA. Miles to go: an introduction to the 5 Million Lives campaign. Jt Comm J Qual Patient Saf 2007; 33:477–84. [PubMed: 17724944]
13. Centers for Disease Control and Prevention. Active bacterial core surveillance report, Emerging Infections Program Network, methicillin-resistant *Staphylococcus aureus*. 2005 Available at: https://www.cdc.gov/abcs/reports-findings/urvreports/mrsa05.html. Accessed 14 November 2018.
14. See I, Albrecht V, Mu Y, et al. Changes in incidence and strains of methicillin-resistant *Staphylococcus aureus* bloodstream infections, 2005–2013. New Orleans, LA: IDWeek, 2016.
15. Miller LG, Perdreau-Remington F, Bayer AS, et al. Clinical and epidemiologic characteristics cannot distinguish community-associated methicillin-resistant *Staphylococcus aureus* infection from methicillin-susceptible *S. aureus* infection: a prospective investigation. Clin Infect Dis 2007; 44:471–82. [PubMed: 17243048]
16. Como-Sabetti KJ, Harriman KH, Fridkin SK, Jawahir SL, Lynfield R. Risk factors for community-associated *Staphylococcus aureus* infections: results from parallel studies including methicillin-resistant and methicillin-sensitive *S. aureus* compared to uninfected controls. Epidemiol Infect 2011; 139:419–29. [PubMed: 20513251]
17. Hsiang MS, Shiau R, Nadle J, et al. Epidemiologic similarities in pediatric community-associated methicillin-resistant and methicillin-sensitive *Staphylococcus aureus* in the San Francisco Bay Area. J Pediatric Infect Dis Soc 2012; 1:200–11. [PubMed: 23687577]
18. Sattler CA, Mason EO Jr, Kaplan SL. Prospective comparison of risk factors and demographic and clinical characteristics of community-acquired, methicillin-resistant versus methicillin-susceptible

Staphylococcus aureus infection in children. Pediatr Infect Dis J 2002; 21:910–7. [PubMed: 12394811]

19. Koeck M, Como-Sabetti K, Boxrud D, et al. Burdens of invasive methicillin-susceptible and methicillin-resistant *Staphylococcus aureus* disease, Minnesota, USA. Emerg Infect Dis 2019; 25:171–4. [PubMed: 30561319]
20. Spaulding A, Turm C, Courter J, et al. Epidemiology of *Staphylococcus aureus* infections in patients admitted to freestanding pediatric hospitals, 2009–2016. Infect Control Hosp Epidemiol 2018; 39:1487–90. [PubMed: 30370879]
21. Wang JL, Chen SY, Wang JT, et al. Comparison of both clinical features and mortality risk associated with bacteremia due to community-acquired methicillin-resistant *Staphylococcus aureus* and methicillin-susceptible *S. aureus*. Clin Infect Dis 2008; 46:799–806. [PubMed: 18266610]
22. Wyllie DH, Crook DW, Peto TEA. Mortality after *Staphylococcus aureus* bacteremia in two hospitals in Oxfordshire, 1997–2003: cohort study. BMJ 2006; 333:281–6. [PubMed: 16798756]
23. Shane AL, Hansen NI, Stoll BJ, et al.; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Methicillin-resistant and susceptible *Staphylococcus aureus* bacteremia and meningitis in preterm infants. Pediatrics 2012; 129:e914–22. [PubMed: 22412036]
24. Laupland K, Ross T, Gregson DB. *Staphylococcus aureus* bloodstream infections: risk factors, outcomes, and the influence of methicillin resistance in Calgary, Canada, 2000–2006. JID 2008; 198: 336–43. [PubMed: 18522502]
25. Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteremia: a meta-analysis. Clin Infect Dis 2003; 36:53–9. [PubMed: 12491202]
26. National Center for Health Statistics. Vintage 2016 postcensal estimates of the resident population of the United States (April 1, 2010, July 1 2010–July 1, 2016), by year, county, single-year of age (0, 1, 2, …, 85 years and over), bridge race, Hispanic origin, and sex. Available at: https://www.cdc.gov/nchs/nvss/bridged_race.htm. Accessed 8 August 2017.
27. Morin C, Hadler J. Population-based incidence and characteristics of community-onset *Staphylococcus aureus* infections with bacteremia in 4 metropolitan Connecticut areas, 1998. J Infect Dis 2001; 184: 1029–34. [PubMed: 11574918]
28. Weiner LM, Webb AK, Limbago B, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2011–2014. Infect Control Hosp Epidemiol 2016; 37:1288–301. [PubMed: 27573805]
29. Huang SS, Singh R, McKinnell JA, et al.; Project CLEAR Trial. Decolonization to reduce postdischarge infection risk among MRSA carriers. N Engl J Med 2019; 380:638–50. [PubMed: 30763195]
30. Morgan DJ, Wenzel RP, Bearman G. Contact precautions for endemic MRSA and VRE: time to retire legal mandates. JAMA 2017; 318:329–30. [PubMed: 28654976]
31. Centers for Disease Control and Prevention. Methicillin-resistant *Staphylococcus aureus* (MRSA): preventing infections in healthcare. Available at: https://www.cdc.gov/mrsa/healthcare/inpatient.html. Accessed 28 March 2019.
32. See I, Wesson P, Gualandi N, et al. Socioeconomic factors explain racial disparities in invasive community-associated methicillin-resistant *Staphylococcus aureus* disease rates. Clin Infect Dis 2017; 64:597–604. [PubMed: 28362911]
33. David MZ, Boyle-Vavra S, Zychowski DL, Daum RS. Methicillin-susceptible *Staphylococcus aureus* as a predominantly healthcare-associated pathogen: a possible reversal of roles? PLoS One 2011; 6:e18217. [PubMed: 21533238]
34. Centers for Disease Control and Prevention. Antibiotic resistance patient safety atlas [Internet]. Available at: http://gis.cdc.gov/grasp/PSA. Accessed 29 August 2017.
35. Jackson KA, Albrecht V, Koeck M, Dumyati G, Lynfield R, See I. Epidemiologic and microbiologic characteristics of methicillin-sensitive *Staphylococcus aureus* from surveillance in three US counties, 2014–2015. New Orleans, LA: ASM Microbe, 2017.

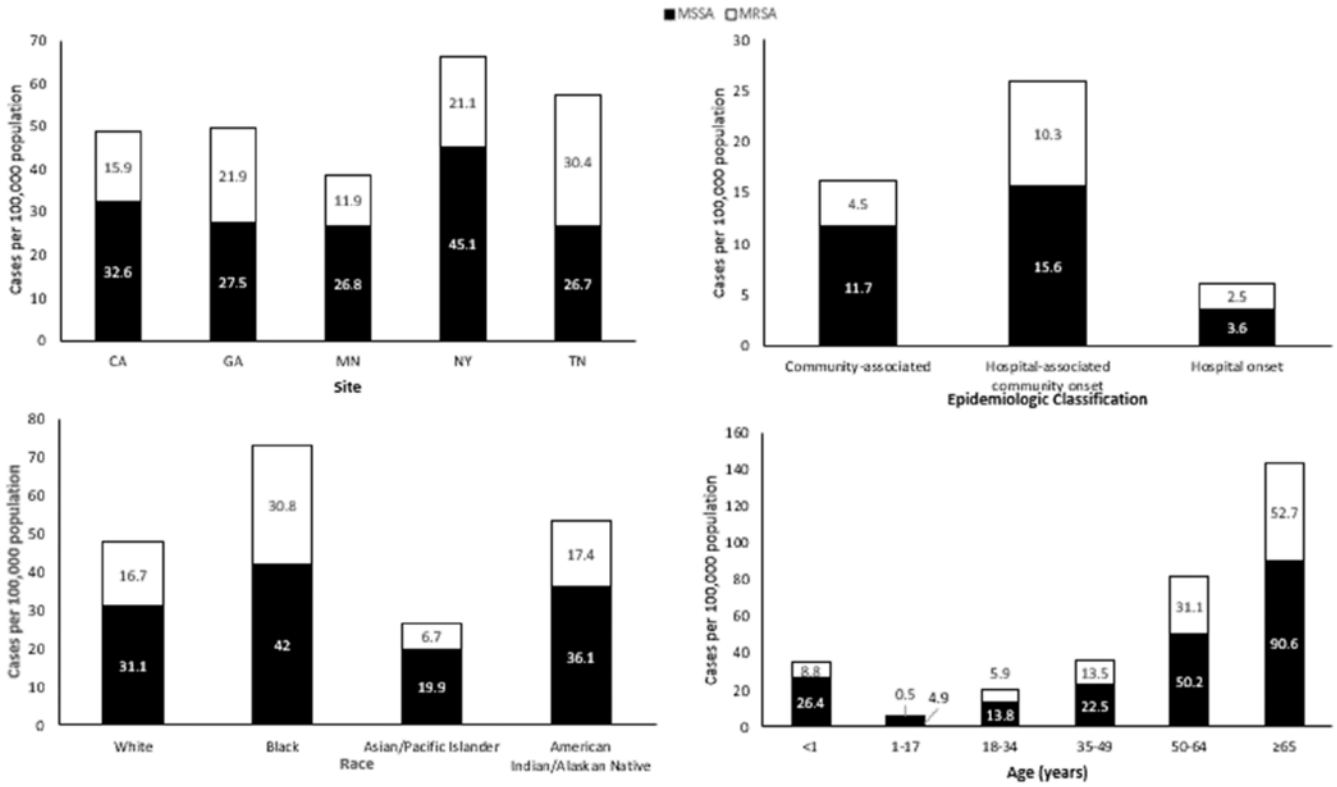

Figure 1.

Invasive MSSA and MRSA incidence per 100 000 population by site, epidemiologic classification, race, and age, 2016. Abbreviations: CA, California; GA, Georgia; MN, Minnesota; MRSA, methicillin-resistant *Staphylococcus aureus;* MSSA, methicillin-susceptible *Staphylococcus aureus;* NY, New York; TN, Tennessee.

Table 1.

Emerging Infections Program's Invasive *Staphylococcus aureus* Surveillance Areas and Estimated Population, 2016

State	Surveillance Area	Estimated Population
California	3 San Francisco Bay Area counties	3 617 982
Georgia	1 Atlanta county	1 007 803
Minnesota	2 metropolitan Minneapolis and Saint Paul counties	1 756 530
New York	1 Rochester county	749 048
Tennessee	1 Nashville county	678 323
Total		7 809 686

Table 2.

Demographic and Epidemiologic Characteristics of Invasive Methicillin-susceptible *Staphylococcus aureus* and Methicillin-resistant *S. aureus* Patients, 8 US Counties, 2016

Characteristic	MSSA, No. (%) (n = 2416)	MRSA,[a] No. (%) (n = 1272)	Odds Ratio for MSSA	95% Confidence Interval	*P* Value
Male sex[b]	1551 (64.2)	841 (61.4)	1.13	0.98–1.29	.09
Median age (range),[b] y	59 (0–103)	61 (0–100)	…	…	<.01
Hispanic ethnicity[c]	219 (10.1)	101 (9.0)	1.14	0.89–1.46	.32
Race[d]					
White	1370 (63.9)	708 (60.8)	1.14	0.98–1.32	.08
Black	512 (23.9)	377 (32.4)	0.66	0.56–0.77	<.01
Asian/Pacific Islander	238 (11.1)	66 (5.7)	2.08	1.57–2.76	<.01
American Indian/Alaska Native	24 (1.1)	14 (1.2)	0.93	0.48–1.81	.83
Location 4 days before culture[b,e]					
Private residence	1861 (776)	866 (63.6)	1.98	1.71–2.29	<.01
LTCF	151 (6.3)	205 (15.1)	0.38	0.30–0.47	<.01
Long-term acute-care hospital	5 (0.2)	7 (0.5)	0.40	0.13–1.28	.11
Homeless	70 (2.9)	61 (4.5)	0.64	0.45–0.91	.01
Incarcerated	2 (0.1)	15 (1.1)	0.07	0.02–0.33	<.01
Hospital inpatient	309 (12.9)	207 (15.2)	0.82	0.68–1.00	.05
Hospitalized ≥4 days at time of initial culture[b,e]	276 (11.4)	194 (14.2)	0.78	0.64–0.95	.01
Hospitalized in past year	1056 (44.2)	735 (58.1)	0.57	0.50–0.66	<.01
Surgery in past year	507 (21.2)	287 (22.7)	0.92	0.78–1.08	.30
Dialysis in past year	322 (13.5)	186 (14.7)	0.90	0.74–1.10	.31
LTCF resident in past year	251 (10.5)	282 (22.3)	0.41	0.34–0.49	<.01
Presence of central venous catheter within 2 days of initial culture	245 (10.2)	156 (12.3)	0.81	0.66–1.01	.06
Underlying medical condition[f]					
None	347 (14.5)	86 (6.8)	2.33	1.82–2.98	<.01

Characteristic	MSSA, No. (%) (n = 2416)	MRSA,[a] No. (%) (n = 1272)	Odds Ratio for MSSA	95% Confidence Interval	*P* Value
Chronic kidney disease	626 (26.2)	384 (30.3)	0.81	0.70–0.95	<.01
Chronic liver disease	213 (8.9)	124 (9.8)	0.90	0.71–1.14	.38
Chronic skin breakdown	236 (9.9)	125 (9.9)	1.00	0.80–1.26	.99
Cognitive deficit, chronic	38 (1.6)	25 (2.0)	0.80	0.48–1.33	.39
Congestive heart failure	392 (16.4)	249 (19.7)	0.80	0.67–0.95	.01
Connective tissue disease	75 (3.1)	35 (2.8)	1.14	0.76–1.71	.53
Current smoker	447 (18.7)	309 (24.4)	0.71	0.60–0.84	<.01
Cerebral vascular accident/stroke	184 (77)	144 (11.4)	0.65	0.52–0.82	<.01
Decubitus/pressure ulcer	102 (4.3)	120 (9.5)	0.43	0.32–0.56	<.01
Dementia	128 (5.4)	92 (7.3)	0.72	0.55–0.95	.02
Diabetes	835 (34.9)	483 (38.2)	0.87	0.75–1.00	.05
Hematologic malignancy	67 (2.8)	34 (2.7)	1.04	0.69–1.59	.84
Hemiplegia/paraplegia	46 (1.9)	54 (4.3)	0.44	0.30–0.66	<.01
Human immunodeficiency virus/AIDS	68 (2.8)	56 (4.4)	0.63	0.44–0.91	.01
Influenza within 10 days of culture[g]	8 (0.3)	6 (0.5)	0.70	0.24–2.04	.52
Intravenous drug user	183 (77)	122 (9.6)	0.78	0.61–0.99	.04
Metastatic solid tumor	108 (4.5)	59 (4.7)	0.97	0.70–1.34	.84
Myocardial infarct	128 (5.4)	55 (4.3)	1.24	0.90–1.72	.18
Obesity	380 (15.9)	176 (13.9)	1.17	0.96–1.42	.11
Peptic ulcer disease	19 (0.8)	5 (0.4)	2.02	0.75–5.42	.15
Peripheral vascular disease	152 (6.4)	115 (9.1)	0.68	0.53–0.87	<.01
Premature birth (cases <12 months)	19 (0.8)	2 (0.2)	5.06	1.18–21.76	.02
Pulmonary disease, chronic	394 (16.5)	282 (22.3)	0.69	0.58–0.82	<.01
Recurrent abscess/boil	22 (0.9)	21 (1.7)	0.55	0.30–1.00	.05
Solid tumor (nonmetastatic)	136 (5.7)	77 (6.1)	0.93	0.70–1.24	.63
Outcome					
Hospitalized[b,h]	2201 (91.3)	1293 (94.7)	0.59	0.45–0.78	<.01
Median length of hospital stay (range), days					

Characteristic	MSSA, No. (%) (n = 2416)	MRSA,[a] No. (%) (n = 1272)	Odds Ratio for MSSA	95% Confidence Interval	*P* Value
Hospital-onset[i]	19 (3–478)	22 (3–289)	…	…	.23
Community-onset[j]	8 (0–217)	9 (0–314)	…	…	<.01
Admitted to intensive care unit[k]	708 (32.7)	436 (373)	0.82	0.70–0.95	<.01
Died during hospitalization[l]	252 (10.5)	167 (13.2)	0.77	0.63–0.95	.01
Discharged to LTCF (among survivors)	644 (30.0)	423 (38.5)	0.68	0.59–0.80	<.01

Abbreviations: HO, hospital-onset; LTCF, long-term care facility; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus.*

[a] Excludes nonsampled HO MRSA cases unless otherwise noted.

[b] Includes an additional 98 HO MRSA cases that were not sampled.

[c] Ethnicity was unknown for 237 MSSA and 144 MRSA patients.

[d] Race was unknown for 264 MSSA and 104 MRSA patients. Eleven who were listed as more than 1 race (8 MSSA and 3 MRSA) were also excluded.

[e] Location 4 days prior to culture was unknown for 17 MSSA and 9 MRSA patients. HO cases, regardless of sampling status, were considered to be hospital inpatient on that date.

[f] Underlying medical condition(s) was unknown for 24 MSSA and 6 MRSA patients.

[g] Based on either a clinical or laboratory diagnosis.

[h] Hospitalization was unknown for 6 MSSA and 4 MRSA patients.

[i] Length of stay was unknown for 13 MSSA and 11 MRSA patients.

[j] Length of stay was unknown for 60 MSSA and 40 MRSA patients.

[k] Admitted to intensive care unit was unknown for 252 MSSA and 103 MRSA.

[l] Outcome was unknown for 13 MSSA and 11 MRSA patients.

Table 3.

Multivariate Analysis of Demographic and Epidemiologic Characteristics of Invasive *Staphylococcus aureus* Cases by Methicillin-resistance Status, 8 US Counties, 2016

Characteristic[a]	Adjusted Odds Ratio for Methicillin-susceptible *Staphylococcus aureus*[a]	95% Confidence Interval	*P* Value
Age Group, y			
0–17	2.06	1.26–3.39	<.01
18–64	Referent		
65+	1.07	0.91–1.26	.41
Race			
American Indian or Alaska Native	1.06	0.54–2.08	.86
Asian/Pacific Islander	1.39	1.05–1.85	.02
Black	0.86	0.72–1.02	.08
Other	1.60	0.49–5.20	.43
White	Referent		
Location 4 days prior to culture: incarcerated	0.10	0.02–0.45	<.01
Location 4 days prior to culture: homeless	0.59	0.41–0.86	<.01
Hospitalization			
Hospitalized ≥4 days at time of initial culture (ie, HO)	1.19	0.90–1.55	.22
Hospitalized in past year but not ≥4 days prior to initial culture (ie, not HO)	0.70	0.60–0.82	<.01
Not hospitalized in past year	Referent		
Long-term care facility			
On fourth day prior to initial culture	0.37	0.29–0.47	<.01
Residence in past year but not on fourth day prior to initial culture	0.60	0.43–0.83	<.01
No stay in past year	Referent		
Underlying condition			
None	1.36	1.03–1.81	<.01
Current smoker	0.78	0.65–0.94	<.01
Decubitus ulcer/pressure ulcer	0.58	0.44–0.78	<.01
Abscess/boil (recurrent)	0.47	0.25–0.87	.02

Characteristic[a]	Adjusted Odds Ratio for Methicillin-susceptible *Staphylococcus aureus*[a]	95% Confidence Interval	*P* Value
Chronic pulmonary disease	0.78	0.65–0.94	<.01

Abbreviation: HO, hospital-onset.

[a]Not depicted: random intercepts for the state of residence of the patient were included in the regression model and were also significant.

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Table 4.

Type(s) of Infection Associated With Cases by Methicillin-resistance Status, 8 US Counties, 2016

Type(s) of Infection[a]	Methicillin-susceptible *Staphylococcus aureus*, No. (%) (N = 2417)[b]	Methicillin-resistant *Staphylococcus aureus*, No. (%) (N = 1272)[b,c]	*P* Value
Abscess (not skin)	213 (8.8)	123 (9.0)	.86
Arteriovenous fistula/graft infection	51 (2.1)	13 (1.0)	.01
Bacteremia	1897 (78.6)	1094 (80.0)	.31
Bursitis	163 (6.8)	34 (2.5)	<.01
Catheter site infection	87 (3.6)	30 (2.2)	.02
Cellulitis	313 (13.0)	175 (12.8)	.88
Chronic ulcer/wound (nondecubitus) infection	53 (2.2)	38 (2.8)	.26
Decubitus/pressure ulcer infection	25 (1.0)	19 (1.4)	.33
Empyema	31 (1.3)	25 (1.8)	.18
Endocarditis	131 (5.4)	85 (6.2)	.32
Meningitis	48 (2.0)	27 (2.0)	.98
Peritonitis	44 (1.8)	20 (1.5)	.41
Pneumonia	194 (8.0)	135 (9.9)	.05
Osteomyelitis	296 (12.3)	180 (13.2)	.42
Septic arthritis	402 (16.7)	143 (10.5)	<.01
Septic emboli	56 (2.3)	48 (3.5)	.03
Septic shock	201 (8.3)	138 (10.1)	.07
Skin abscess	51 (2.1)	46 (3.4)	.02
Surgical incision infection	26 (1.1)	12 (0.9)	.55
Surgical site (internal)[d]	69 (2.9)	24 (1.8)	.04
Traumatic wound infection	14 (0.6)	8 (0.6)	.99
Urinary tract infection[e]	107 (4.4)	71 (5.2)	.29

[a] All patients had a concurrent sterile site culture meeting the case definition.

[b] Patients could have more than 1 type of infection. Type of infection was unknown for 2 methicillin-susceptible *Staphylococcus aureus* and 1 methicillin-resistant *Staphylococcus aureus* (MRSA) patients.

[c] Excludes 98 sampled hospital-onset MRSA cases for which type of infection was not documented.

[d] Refers to infection of a deep tissue or organ space from a closed surgical wound, including hardware and ventriculoperitoneal shunt infections.

[e] Defined as documentation of urinary tract infection, kidney infection (pyelonephritis), obstructive pyelonephritis, and urosepsis in the medical record.