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Racial Disparities in Invasive Methicillin-resistant *Staphylococcus aureus* Infections, 2005–2014

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Abstract

Background.—Despite substantial attention to the individual topics, little is known about the relationship between racial disparities and antimicrobial-resistant and/or healthcare-associated infection trends, such as for methicillin-resistant *Staphylococcus aureus* (MRSA).

Methods.—We analyzed Emerging Infections Program 2005–2014 surveillance data (9 US states) to determine whether reductions in invasive MRSA incidence (isolated from normally sterile body sites) affected racial disparities in rates. Case classification included hospital-onset (HO, culture >3 days after admission), healthcare-associated community onset (HACO, culture <3 days after admission and dialysis, hospitalization, surgery, or long-term care residence within 1 year prior), or community-associated (CA, all others). Negative binomial regression models were

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Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Potential conflicts of interest. L. H. H. has served on a GSK scientific advisory board on meningococcal vaccines. W. S. is a member of the data safety monitoring board at Merck and Pfizer and is a consultant for Dynavax, Shionogi, SutroVax, and Seqirus. All remaining authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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used to evaluate the adjusted rate ratio (aRR) of MRSA in black patients (vs in white patients) controlling for age, sex, and temporal trends.

Results.—During 2005–2014, invasive HO and HACO (but not CA) MRSA rates decreased. Despite this, blacks had higher rates for HO (aRR, 3.20; 95% confidence interval [CI], 2.35–4.35), HACO (aRR, 3.84; 95% CI, 2.94–5.01), and CA (aRR, 2.78; 95% CI, 2.30–3.37) MRSA. Limiting the analysis to chronic dialysis patients reduced, but did not eliminate, the higher HACO MRSA rates among blacks (aRR, 1.83; 95% CI, 1.72–1.96), even though invasive MRSA rates among dialysis patients decreased during 2005–2014. These racial differences did not change over time.

Conclusions.—Previous reductions in healthcare-associated MRSA infections have not affected racial disparities in MRSA rates. Improved understanding of the underlying causes of these differences is needed to develop effective prevention interventions that reduce racial disparities in MRSA infections.

Keywords

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

Racial disparities in healthcare have been a focus for policy makers as far back as 1985 [1]. In 2002, the Institute of Medicine's *Unequal Treatment* called for increasing attention to racial disparities in healthcare and strategies to eliminate them [2]. Since then, several federal initiatives have been established to achieve health equity [3–6]. However, despite a collection of literature detailing racial disparities in healthcare [7–9], little is known about racial disparities in healthcare-associated infections (HAIs) even though HAIs have become established as a major area of public health concern.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most common healthcare-associated pathogens [10, 11] and an important cause of invasive infections in the community [12–14]. Previous research has consistently documented higher rates of MRSA infections among blacks compared to whites across age groups [12, 13], yet questions persist as to why this is the case and how to address these differences. In particular, racial disparities for healthcare-associated MRSA infections have not been well described. For instance, the Centers for Disease Control and Prevention (CDC) estimates indicate the national burden of invasive MRSA infections decreased by 35% from 2005 through 2014, including a 63% decrease in infections with onset during hospitalization [14] However, it is not known whether the success in MRSA prevention has translated to reductions in racial disparities in MRSA rates.

Here, we describe temporal trends in invasive MRSA rates by race, including infections in both community and healthcare settings, and determine whether racial differences in MRSA incidence have changed over time.

METHODS

Surveillance Methodology and Definitions

The Emerging Infections Program (EIP) is a collaboration of the CDC, state health departments, and academic partners. Surveillance for invasive MRSA infections through EIP

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began in July 2004. Nine US states (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, and Tennessee) performed data collection for invasive MRSA in selected metropolitan areas.

Surveillance methods have been described previously [12–14]. Case finding is active, laboratory-based, and population-based. Surveillance officers at participating sites routinely contact clinical laboratories that process sterile site specimens from residents of any age within the surveillance catchment area, including laboratories both within and outside the catchment area, and investigate all reports of laboratory-confirmed invasive MRSA. A case of invasive MRSA is defined as a positive culture of a normally sterile site from a resident of the surveillance catchment area, collected at least 30 days after the last index invasive MRSA culture (if applicable). A standardized case report form was used by surveillance officers at EIP sites to abstract information retrospectively from medical records on demographics, including race as documented in the medical record (case report form standardized race categories are white, black or African American, American Indian or Alaska native, Asian, native Hawaiian or other Pacific Islander, or unknown), source (ie, body site) of invasive MRSA culture, healthcare exposures and risk factors, outcomes, and types of infection associated with the culture. Ethnicity is collected as Hispanic/not Hispanic/unknown.

Study Population

For this project, surveillance data from 1 January 2005 through 31 December 2014 were analyzed. For analyses of 2005–2014 data, only those counties under continuous surveillance for the entire time period (n = 27) were included in the analysis. For analyses of data from 2011 through 2014, data from 33 counties that reported during this time period were used. In 2014, these counties had a population of 20.1 million persons.

Case Definitions

Cases are assigned to 1 of 3 epidemiologic classes reflecting the nature of healthcare exposure prior to culture. The first is hospital-onset (HO), in which the invasive MRSA culture was collected after the third day of admission to an acute care hospital. The second is healthcare-associated community onset (HACO), in which the invasive MRSA culture was obtained in an outpatient setting or before the fourth day of hospitalization in a patient with major healthcare risk factors (dialysis, hospitalization, surgery, or long-term care residence within 1 year prior to collection of the positive MRSA culture; or presence of central venous catheter within 2 days prior). The third is community-associated (CA), in which the invasive MRSA culture was obtained in an outpatient setting or before the fourth day of hospitalization in a patient without the previously listed major healthcare risk factors.

Statistical Analyses

Data were analyzed using SAS version 9.3 (SAS Institute). Analyses were limited to black and white race, as these 2 races comprised the majority (95%) of MRSA cases in our surveillance with known race. Missing race (11% of cases) was imputed based on distribution of known race by age, sex, and state. Cases with multiple races reported were bridged according to standard methodology [15]. Analyses did not take into account

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Hispanic ethnicity, as a large proportion of our cases (>40%) were reported to have unknown ethnicity. In 2014, some participating sites collected limited data from most HO cases, with full case report form data (including race) collected only for a random sample of 10%–20% of HO cases. Therefore, because race was not collected in 2014 for many HO cases, analyses described below requiring data for HO cases were only conducted for 2005–2013.

Unadjusted annual invasive MRSA incidence rates (per 100 000 persons) were calculated as (number of cases/population) × 100 000 and stratified by race and epidemiologic classification. Population denominator values were obtained from US Census Bureau bridged-race vintage post-census population data [15]. Unadjusted rate ratios were calculated as (unadjusted rate in black persons) ÷ (unadjusted rate in white persons) to represent the magnitude of racial differences in MRSA rates. Negative binomial regression models were used to evaluate the adjusted rate ratio (aRR) and 95% confidence intervals (CIs) of invasive MRSA incidence in black patients (vs in white patients) controlling for age, sex, and year. Specific age groups (<2, 2–4, 5–17, 18–49, 50–64, 65+ years) were selected to align with available annual US census denominator data. In addition, the modeled yearly change in overall MRSA incidence (ie, not limited to a single racial group) over the time period was obtained from the same negative binomial regression model. An interaction term between race and year was tested in each model to determine if racial differences in MRSA rates significantly changed over time.

Three additional analyses explored potential reasons for observed trends. First, because of discordant findings between racial trends in the unadjusted vs adjusted analyses, CA MRSA rates were stratified by age categories indicated previously, with adult (≥18 years) and pediatric (<18 years), and trends displayed separately. Second, dialysis patient data were used to partially control for frequency of healthcare access utilization and differences in baseline health. Incidence rates (per 1000 dialysis patients) by race and unadjusted and adjusted black/white rate ratios of HACO MRSA among chronic dialysis patients (which account for >25% of HACO MRSA cases) were calculated using US Renal Data System data for denominator values [16]. Restricting to dialysis patients may largely control for differences in underlying patient illness and access to care/frequency of healthcare encounters (because of the comprehensive nature of Medicare's specific coverage for end-stage renal disease patients). Finally, Charlson comorbidity index scores were calculated for cases that occurred since 2011 (when relevant epidemiologic data were collected) [17]. Mean and median Charlson comorbidity index scores and ranges were stratified by epidemiologic class and race to describe underlying medical comorbidities by race among cases. Significance of differences in Charlson score by race was tested with a Wilcoxon rank-sum test. Statistical significance was set at a P value of <.05.

Human Subjects Considerations

This analysis was performed in accordance with the core objectives of the EIP MRS A surveillance project, which has been determined to be a nonresearch public health surveillance activity by CDC human subjects advisors. In addition, the 9 participating sites obtained local approvals for the surveillance protocol.

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RESULTS

Case Characteristics

The EIP sites reported 45 550 cases of invasive MRSA infections from 1 January 2005 through 31 December 2014, including 17 225 (38%) in patients of black race and 25 977 (57%) in patients of white race. The epidemiologic classifications of these 45 550 cases were 9591 (21%) HO, 27 041 (59%) HACO, and 8256 (18%) CA.

All Epidemiologic Classes Combined

In 2005, incidence rates for all invasive MRSA cases (including all epidemiologic classes) per 100 000 population were 31.23 for whites and 79.11 for blacks. In 2013, rates decreased to 19.78 for whites and 39.93 for blacks; the unadjusted rate ratios for black race in 2005 and 2013 were 2.53 and 2.02, respectively (Figure 1A).

When adjusting for age, sex, and year, the aRR for black race was 3.57 (95% CI, 2.79–4.56; Table 1). Despite a modeled decrease in overall rates of 6% per year, the aRR for black race did not significantly change over time ($P = .60$ for interaction term between race and year).

Hospital-onset Cases

Incidence rates for the 9019 HO cases decreased by more than 65% for both races from 2005 through 2013, from 8.46 to 2.94 per 100 000 white persons and from 18.16 to 6.21 per 100 000 black persons. The unadjusted rate ratios for black race in 2005 and 2013 were 2.15 and 2.11, respectively (Figure 1B).

When adjusting for age, sex, and year, the aRR for black race was 3.20 (95% CI, 2.35–4.35; Table 1). Despite a modeled decrease in overall rates of 12% per year, the aRR for black race did not significantly change over time ($P = .91$ for interaction term between race and year).

Healthcare-associated Community Onset Cases

Incidence rates for the 27 041 HACO cases decreased in white persons from 17.44 to 11.37 (35%) and in black persons from 45.63 to 22.87 (50%). The unadjusted rate ratio for black race decreased from 2.61 in 2005 to 2.01 in 2014 (Figure 1C).

When adjusting for age, sex, and year, the aRR for black race was 3.84 (95% CI, 2.94–5.01; Table 1). Despite a modeled decrease in overall rates of 6% per year, the aRR for black race did not significantly change over time ($P = .51$ for interaction term between race and year).

Community-associated Cases

From 2005 to 2014 CA MRSA rates overall were 6.16 in 2005 vs 5.12 in 2014. Unadjusted incidence rates for black cases decreased from 12.66 in 2005 to 6.02 in 2014. During the same time period, rates for white cases remained stable (4.92 vs 4.85). As a result of the difference in incidence rates, the unadjusted rate ratio of black to white CA cases decreased from 2.57 in 2005 to 1.24 in 2014 (Figure 1D).

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When adjusting for age, sex, and year, the aRR for black race was 2.78 (95% CI, 2.30–3.37), and there was no significant modeled decline in overall rates between 2005 and 2014 (aRR for year, 1.00; 95% CI, 0.96–1.03; Table 1). Unlike what was seen in the unadjusted analysis, the aRR for black race did not significantly change over time ($P = .76$ for interaction term between race and year).

To investigate the difference between racial trends in the unadjusted vs adjusted analyses, the CA MRSA rates were stratified by age. No changes over time were seen for cases of white race when stratified by age (see Supplementary Figure 1). Figure 2A shows the rate of CA MRSA among black adults for 3 age groups; there were decreases for all groups. In contrast, rates increased among black children aged ≤2 years (Figure 2B).

Race and Healthcare Utilization

From 2005 to 2014, the unadjusted rate ratio of black to white cases among chronic dialysis patients in the HACO MRSA epidemiologic class was lower than that for overall HACO cases but remained stable around 1.60 (Figure 3). When adjusting for age, sex, and year, the aRR for race was 1.83 (95% CI, 1.72–1.96), and there was no significant change in the aRR for black race over time ($P = .51$ for interaction term between race and year) despite a modeled decrease in overall rates of 9% per year (Table 1).

Charlson Comorbidity Index

The Charlson comorbidity index scores for the HO epidemiologic class were significantly higher for blacks (mean, 2.7; median, 2; range, 0–13) vs whites (mean, 2.4; median, 2; range, 0–12; $P = .007$). Median scores for the HACO class were 2 for whites (mean, 2.6; range, 0–13) and 3 for blacks (mean, 3.4; range, 0–16; $P < .0001$). CA cases showed no significant difference in Charlson comorbidity index scores (median, 1; range, 0–12 for both blacks and whites; mean, 1.4 and 1.2 for blacks and whites, respectively; $P = .10$).

DISCUSSION

This analysis represents the first description of trends for racial disparities in healthcare-associated infections using data from an entire population area. The analysis also includes previously unreported racial trends for CA MRSA cases. We found that despite substantial decreases in invasive MRSA incidence during 2005–2014 (all epidemiologic classes combined), in adjusted analyses the magnitude of racial disparities in MRSA rates did not significantly decline. The lack of decrease in disparities becomes more apparent when looking at specific epidemiologic classes. For HO cases, incidence rates decreased by more than 70% for both races, without a significant change in the aRR for blacks over time. HACO cases also displayed no significant change in the aRR over time for black race. In summary, blacks continue to have a 2–3 times higher incidence rate of healthcare-associated invasive MRSA despite significant decreases in overall disease rates from 2005 through 2014.

Rates for invasive CA MRSA displayed a different trend. In contrast to healthcare-associated (ie, HO and HACO) MRSA cases, unadjusted rates for CA MRSA overall remained stable, as did rates in white persons. However, the unadjusted rate ratio for black race decreased,

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whereas the aRR did not significantly change over time. The reason for this difference appears to be that invasive MRSA rates among black children aged ≤2 years increased, while rates among older black persons decreased. One retrospective hospital cohort study identified African American race and younger age as risk factors for USA300 MRSA nasal colonization, the most prevalent strain type of CA MRSA [18]. A recent analysis suggests that racial differences in invasive CA MRSA rates are due to socioeconomic factors, which may include decreased availability and affordability of medical care, increased crowding, and higher poverty rates [19]. However, it is not clear from our analysis what factors are responsible for different changes in invasive CA MRSA rates among younger vs older black patients.

We observed greater disparities in healthcare-associated MRSA than in CA MRSA, a finding that has not been previously reported. Observed racial disparities might result from underlying patient-level disparities, such as differences in underlying health, access to medical care, health-seeking behavior, and environmental factors [20, 21]. For example, our data showed that blacks with invasive MRSA associated with healthcare exposure (HO and HACO cases) had more documented chronic medical comorbidities than whites. We also found that compared to all HACO cases, restricting the analysis to dialysis patients decreased, but did not eliminate, racial differences in MRSA rates (aRR from all HACO cases, 3.13 vs aRR for dialysis patients only, 1.34). If the findings for dialysis patients can be generalized to other healthcare-associated MRSA infections, racial disparities in healthcare-associated MRSA may be largely related to differences in underlying health and access to care.

Alternatively, previous publications have posited that racial disparities in healthcare outcomes could be a result of disparities related to the healthcare system itself, such as differences in care provided within hospitals, between hospitals, or both [2]. For example, utilization of cardiac and surgical outcomes, as well as inpatient discharge data, have shown quality-of-care disparities for minority populations increasingly associated with differences in the hospitals serving these populations, rather than differences in care provided within a hospital to different population groups [22–25]. Black hemodialysis patients are less likely than whites to utilize dialysis facilities rated as high quality by federal quality reporting programs, even though they live a significantly shorter distance from these facilities [26].

A critical next step for reducing these disparities is elucidating the contribution of patient-level factors, difference in care across hospitals, or differences in care within hospitals (particularly for HO MRSA). For example, it is possible that observed disparities for HO MRSA might be primarily due to differences in infection control practices (eg, prevention transmission within the hospital or practices to prevent specific healthcare-associated infection syndromes) at hospitals primarily caring for certain patient populations. If this were the case, then efforts to improve infection control practices at those hospitals would likely significantly reduce disparities.

In contrast to our findings, a recent study supported by the Agency for Healthcare Research and Quality (AHRQ) utilizing the Medicare Patient Safety Monitoring System reported no significant difference between rates of healthcare-acquired infections among black patients

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admitted to the hospital compared to whites [27]. The difference in findings may be explained by several differences between our data and data from the AHRQ study. For one, the AHRQ study included only a small number of hospital-acquired MRSA infections from sterile sites (N = 51). In addition, data from the AHRQ study were limited to patients admitted to the hospital for acute cardiovascular disease, pneumonia, or major surgery and might not represent the same trends as for all hospitalized patients. The AHRQ study also excluded a large number of patients with missing race and ethnicity data, which could result in underrepresentation of racial differences.

There are several limitations of our analysis. First, there are some caveats in interpreting differences in Charlson comorbidity index score distribution among cases. While significantly higher Charlson comorbidity index scores were seen for blacks in some epidemiologic classes in this analysis, this may not be the case in the underlying population. We would need to know the distribution of comorbidities in the underlying population to definitively attribute differences in rates by race to differences in medical comorbidity. Second, we did not have data on socioeconomic status to explore this as an explanation for racial disparities seen. Third, despite inclusion of data from multiple states in different regions of the United States, these results may not represent nationwide trends. Fourth, healthcare utilization denominators by race are unavailable for our surveillance area residents. Fifth, the analysis was limited to black and white race, without inclusion of ethnicity or other races. We were not able to explore trends in other races or trends for Hispanic ethnicity due to sample size constraints and unavailability of reliable ethnicity data. The lack of ethnicity data is a persistent challenge in public health surveillance systems, and future work will require the consistent collection of race and ethnicity data [28]. Last, we did not have information on infection prevention practices in healthcare facilities in the surveillance catchment area. Such practices are an important determinant of healthcare-associated MRSA infection risk, and determining how those practices might vary across facilities or whether they may even vary by patient population was beyond the scope of this project.

Our analysis demonstrated persistent racial differences in invasive MRSA among blacks compared to whites, despite observed overall decreases in rates of invasive MRSA during 2005–2014. Eliminating racial disparities will require improved understanding of the determinants that underlie these disparities, as well as prevention strategies to address those determinants. Addressing racial disparities may be an important way to improve patient safety and achieve health equity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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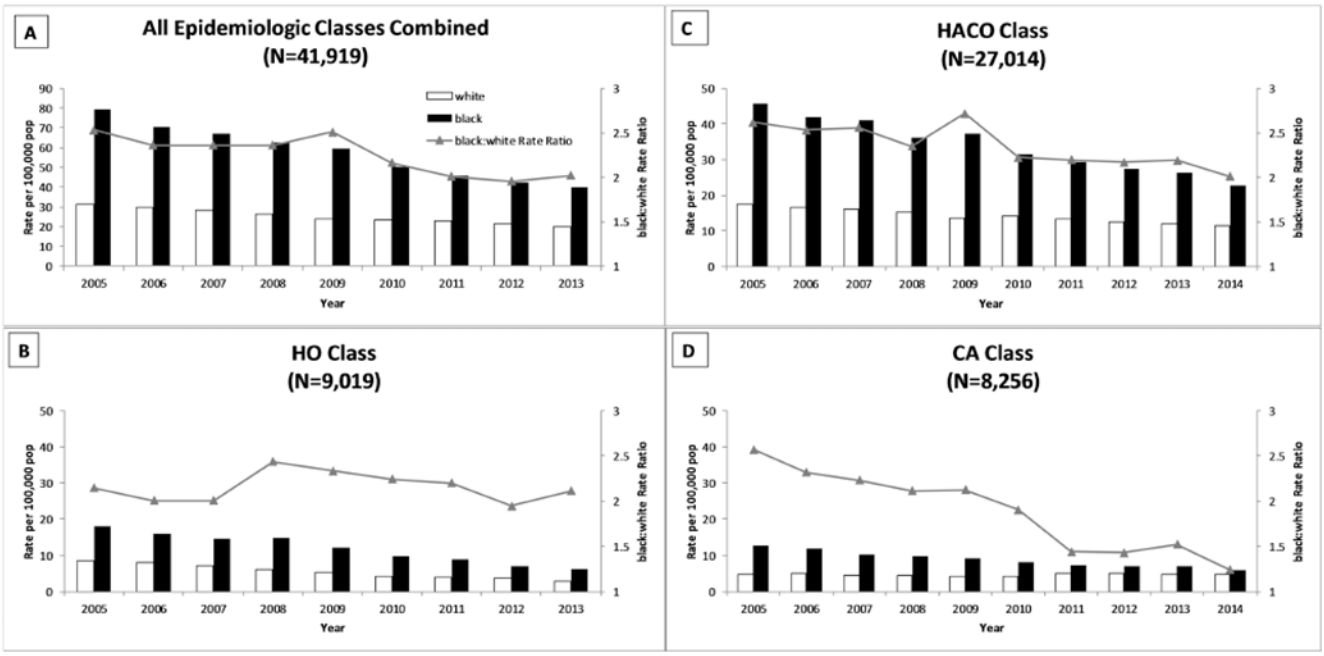

Figure 1.

Unadjusted invasive methicillin-resistant *Staphylococcus aureus* rates by race, 2005–2014. Each panel shows rates for a specific epidemiologic class. (*A*) All epidemiologic classes combined; (*B*) hospital-onset cases; (*C*) healthcare-associated community onset cases; (*D*) community-associated cases. Data for all epidemiologic classes and HO cases do not include 2014 because of sampling methodology. Abbreviations: CA, community associated; HACO, healthcare associated community onset; HO, hospital onset.

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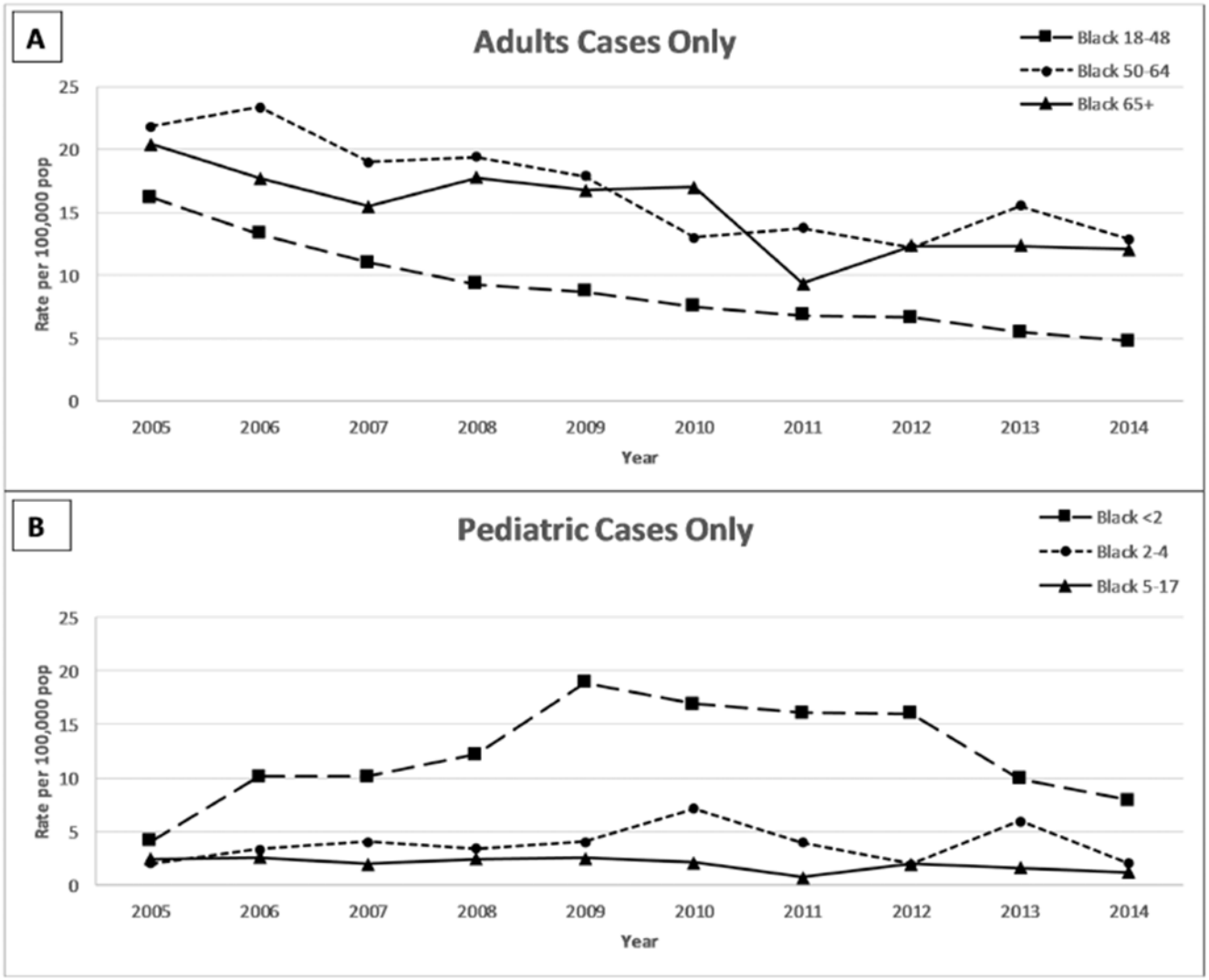

Figure 2.

Invasive community-associated methicillin-resistant *Staphylococcus aureus* rates by age categories and black persons, 2005–2014. *A*, adult cases only (>18 years). *B*, pediatric cases only (<18 years).

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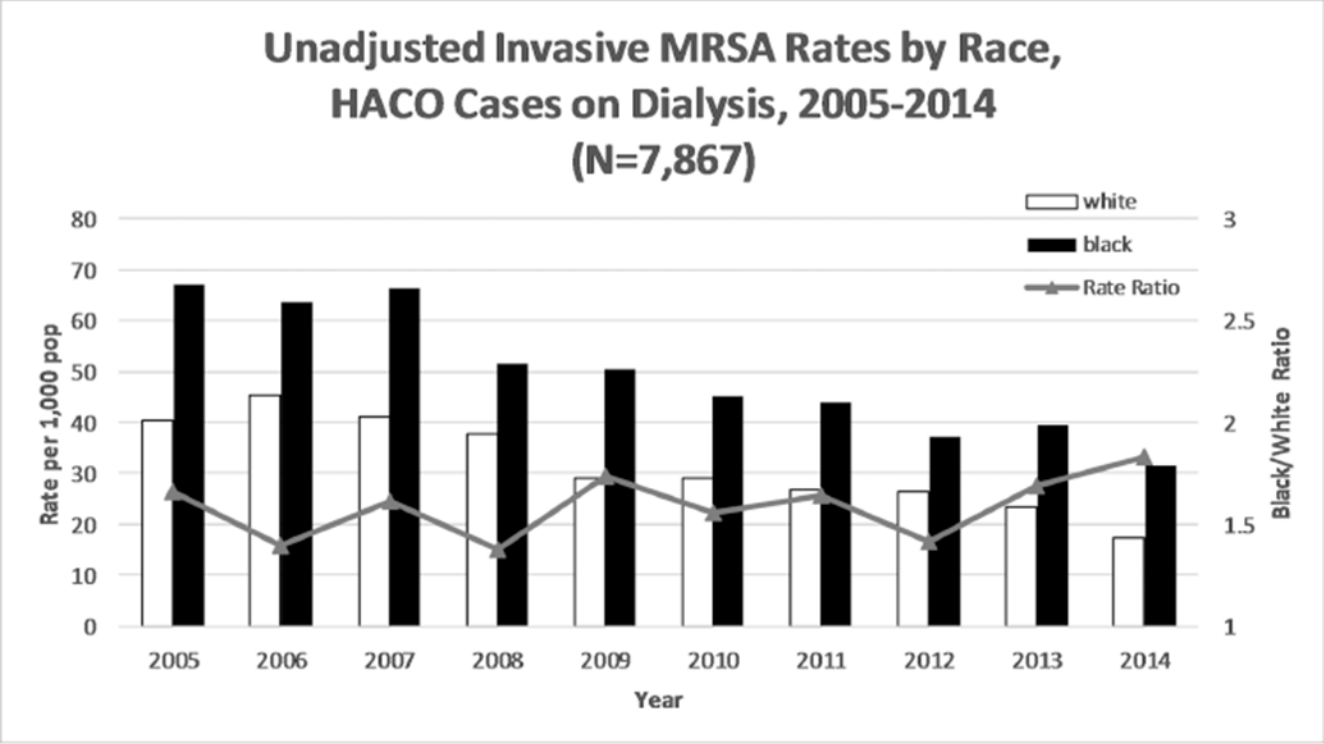

Figure 3.

Unadjusted invasive methicillin-resistant *Staphylococcus aureus* rates by race for healthcare-associated community onset cases among dialysis patients, 2005–2014. Abbreviations: HACO, healthcare-associated community onset; MRSA, methicillin-resistant *Staphylococcus aureus*.

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Table 1.

Adjusted Rate Ratios for Invasive Methicillin-resistant *Staphylococcus aureus* by Epidemiologic Class, 2005–2014

Variable	Adjusted Rate Ratio	95% Confidence Interval	*P* Value
All epidemiologic classes combined			
Black race[a]	3.57	2.79–4.56	<.0001
Year[b]	0.94	0.90–0.98	.01
Age category[c]	1.66	1.57–1.77	<.0001
Female sex	0.69	0.54–0.88	.01
Hospital-onset cases			
Black race[a]	3.20	2.35–4.35	<.0001
Year[b]	0.88	0.84–0.93	<.0001
Age category[c]	1.40	1.30–1.51	<.0001
Female sex	0.71	0.53–0.97	.03
Healthcare-associated community onset cases			
Black race[a]	3.84	2.94–5.01	<.0001
Year	0.94	0.90–0.99	.01
Age category[c]	2.32	2.15–2.50	<.0001
Female sex	0.63	0.48–0.82	.0006
Community-associated cases			
Black race[a]	2.78	2.30–3.37	<.0001
Year	1.00	0.96–1.03	.76
Age category[c]	1.38	1.31–1.46	<.0001
Female sex	0.56	0.46–0.67	<.0001
Healthcare-associated community onset (chronic dialysis cases only)			
Black race[a]	1.83	1.72–1.96	<.0001
Year	0.91	0.90–0.92	<.0001
Age category[c]	0.96	0.92–1.00	.04
Female sex	0.93	0.87–0.99	.03

[a]The interaction term between race and year was not significant for any epidemiologic class and therefore was omitted from final models.

[b]Data for all epidemiologic classes and hospital-onset cases do not include 2014 because of sampling methodology.

[c]Age category includes <2, 2–4, 5–17, 18–49, 50–64, and >65 years and is treated as an ordinal variable.