

Trends and Characteristics of Culture-Confirmed *Staphylococcus aureus* Infections in a Large U.S. Integrated Health Care Organization

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Infections due to *Staphylococcus aureus* present a significant health problem in the United States. Between 1990 and 2005, there was a dramatic increase in community-associated methicillin-resistant *S. aureus* (MRSA), but recent reports suggest that MRSA may be declining. We retrospectively identified *S. aureus* isolates ($n = 133,450$) that were obtained from patients in a large integrated health plan between 1 January 1998 and 31 December 2009. Trends over time in MRSA were analyzed, and demographic risk factors for MRSA versus methicillin-susceptible *S. aureus* (MSSA) were identified. The percentage of *S. aureus* isolates that were MRSA increased from 9% to 20% between 1998 and 2001 and from 25% to 49% between 2002 and 2005 and decreased from 49% to 43% between 2006 and 2009. The increase in MRSA was seen in blood and in other bacteriological specimens and occurred in all age and race/ethnicity groups, though it was most pronounced in persons aged 18 to <50 years and African-Americans. Hospital onset infections were the most likely to be MRSA (odds ratio [OR], 1.58; confidence interval [CI], 1.46 to 1.70, compared to community-associated cases), but the largest increase in MRSA was in community-associated infections. Isolates from African-Americans (OR, 1.73; CI, 1.64 to 1.82) and Hispanics (OR, 1.11; CI, 1.06 to 1.16) were more likely to be MRSA than those from whites. After substantial increases between 1998 and 2005 in the proportion of *S. aureus* isolates that were MRSA, the proportion decreased between 2006 and 2009. Hospital onset *S. aureus* infections are disproportionately MRSA, as are those among African-Americans.

Infections due to *Staphylococcus aureus* present a substantial health problem in the United States (20, 23). *S. aureus* is a major cause of hospital-acquired pneumonia and lower respiratory tract infections (37) and the primary cause of surgical-site infections (36) and skin and soft tissue infections (SSTIs) (29) and is now likely the leading cause of invasive bacterial disease (20, 23). Throughout the 1990s, *S. aureus* infections in hospitalized patients were increasingly caused by methicillin-resistant *S. aureus* (MRSA), making treatment of these infections more difficult (20, 21, 23, 40). Moreover, between 1990 and 2005, there was an even more dramatic increase in community-associated MRSA (CA-MRSA) infections (1, 5, 10, 11, 19, 27, 32). However, there are indications that MRSA may be on the decline. A recent U.S. study found that the incidence of health care-associated invasive MRSA declined from 2005 to 2008 (18), and an analysis of *S. aureus* isolates from outpatient pediatric patients with SSTIs found the percentage of isolates that were MRSA was lower in 2008 and 2009 than in 2005 to 2007 (9).

In general, surveillance activity for MRSA has been limited to bloodstream or invasive infections and to health care-associated and hospital onset disease, and there have been few population-based studies. As the epidemiology of *S. aureus* disease changes, inclusion of community-associated, community onset, and non-invasive disease is important for assessing the magnitude of the burden of disease in the population, for setting priorities for prevention and control, and for creating guidelines for empirical antibiotic treatment.

In this retrospective study covering 12 years, we describe laboratory-confirmed *S. aureus* infections in a large cohort of persons of all ages, using isolates from sterile and nonsterile sites in both ambulatory and inpatient settings. We describe trends in methicillin resistance of laboratory-confirmed *S. aureus* isolates and trends in the

incidence of *S. aureus* bloodstream infections and explore the relationship of patient demographics and infection onset type to the likelihood of *S. aureus* infections being methicillin resistant.

MATERIALS AND METHODS

Setting. Kaiser Permanente of Northern California (KPNC) is a non-profit, integrated health care delivery system providing care to over 3 million members. The member population reflects the general population in the Northern California region, although as an insured population, it underrepresents persons with annual incomes less than \$25,000 (9% of the KPNC member population 25 to 79 years of age versus 21% of the general Northern California population 25 to 79 years of age) and overrepresents persons with annual incomes greater than \$100,000 (30% versus 26%). Although racially diverse, the KPNC population also somewhat underrepresents Latinos/Hispanics (19% versus 22%) and overrepresents African-Americans (8% versus 5.5%) (15). KPNC provides services in more than 15 counties and operates more than 40 outpatient clinics and 18 hospitals throughout Northern California. Laboratory results and diagnostic data from hospital discharges and ambulatory settings, including emergency departments, are archived in databases. KPNC databases contain individual patient records and are readily linked using the patient's unique medical record number, which remains with the patient for life. The study was approved by the KPNC Institutional Review Board. In this retrospective, observational study, clinical decisions regarding diagnosing and testing reflect the usual care by KPNC providers.

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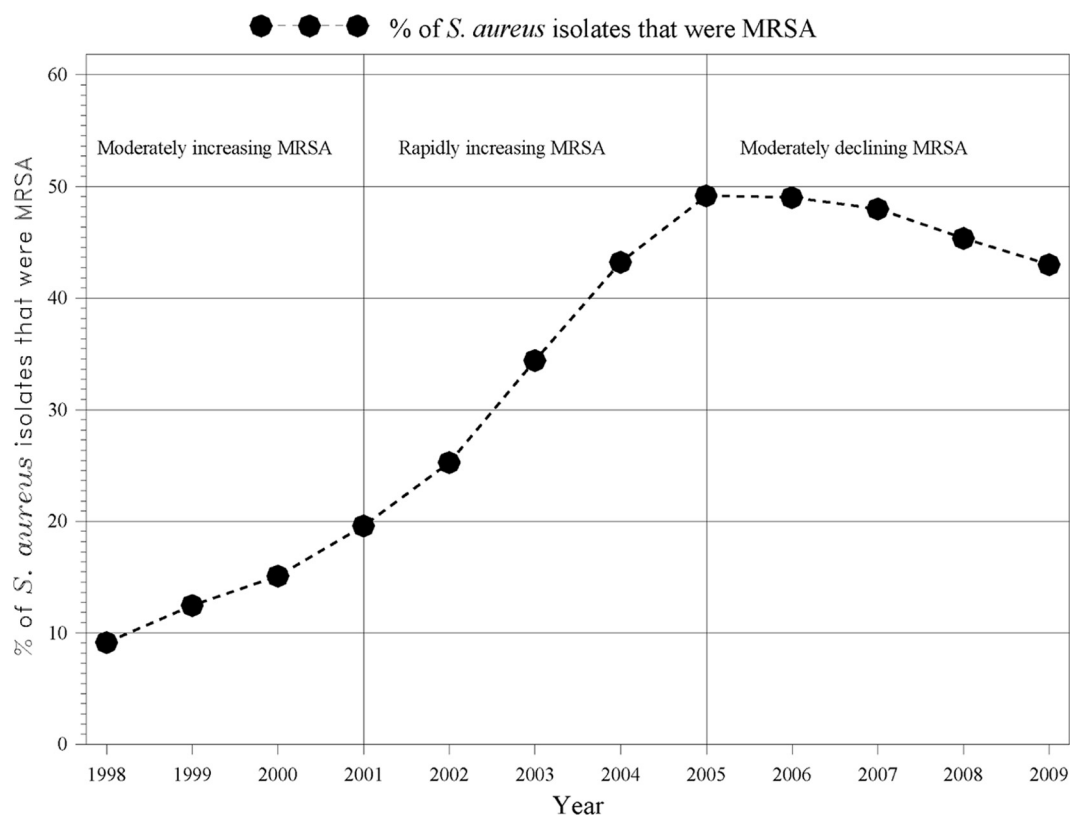


FIG 1 Percentage of *S. aureus* isolates that were MRSA, 1998 to 2009.

Identification of *S. aureus* infections. Using KPNC's Laboratory Utilization and Reporting System, which maintains an account of all laboratory tests performed by KPNC's regional laboratory, we identified all microbiological specimens testing positive for *S. aureus* that were obtained between 1 January 1997 and 31 December 2009. Virtually all microbiology tests ordered by KPNC providers for KPNC members are performed by the KPNC regional laboratory in Berkeley, CA. Because patients may be tested repeatedly, we adapted the Clinical and Laboratory Standards Institute guideline (originally designed for studies of antibiotic resistance) and recommendations in the literature and included only the first isolate per person per 365-day period (not calendar year) (25, 39). (A sensitivity analysis was performed in which we included only the first isolate per person per 30-day period.) In cases where the same individual had more than one isolate from different sources on the same day (about 2.2% of infections), our selection priority was as follows: blood, cerebrospinal fluid (CSF), bone, body fluid, other miscellaneous bacterial cultures, tissue, respiratory, and urine. The first isolate per person per 365-day period was the "index isolate," and the date of the index isolate was the "index date" for that case. In order to identify isolates likely to be related to clinically relevant infections, we restricted our analyses to isolates from blood, bone, CSF, body fluid, urine, tissue, respiratory, and other miscellaneous bacterial specimens (such as those taken from abscesses, pustules, boils, wounds, etc.). Screening tests (nares) and genital, stool, catheter tip, and throat cultures were excluded. In addition, we required patients to have been diagnosed with a potentially *S. aureus*-related clinical syndrome from 7 days before to 7 days after the index date. Clinical syndromes were identified using electronic databases that capture all diagnoses (International Classification of Diseases, 9th Revision, Clinical Modification [ICD9]) received by KPNC patients. The patients could have been diagnosed with more than one clinical syndrome during the applicable period. Only patients who were KPNC members on the index date were included. For analyses restricted to bloodstream infections, the index isolate was the

first isolate from a blood specimen per person per 365-day period meeting the above criteria.

Suspect *Staphylococcus* colonies (catalase-positive, Gram-positive cocci in clusters) were identified by clumping factor and/or protein A or by coagulation of coagulase plasma. Using an 18- to 24-h culture from nonselective medium, isolated *S. aureus* colonies were selected for antimicrobial susceptibility testing using commercial systems (MicroScan [Siemens Healthcare Diagnostics Inc., Sacramento, CA] or Vitek 2 [bioMérieux, Hazelwood, MO] for urine isolates).

Isolates displaying an oxacillin MIC of ≥ 4 $\mu\text{g/ml}$ were subjected to additional confirmatory testing for MRSA. A suspension of the suspect isolate was prepared and used to inoculate a BBL Oxacillin Screen agar plate (Becton, Dickinson and Company, Sparks, MD), which was incubated in an ambient-air incubator at 33 to 35°C for 24 h. Isolates were characterized as MRSA if the isolates both grew on the Oxacillin Screen agar plate and displayed oxacillin MIC values of ≥ 4 $\mu\text{g/ml}$. This method was used throughout the study period.

Definitions of health care- and community-associated infections. Using definitions and terminology adapted from the literature on bacterial infections (10, 22, 23, 33) so as to be applicable to the clinical data available to us, we classified infections into one of three mutually exclusive groups: (i) health care associated, hospital onset (HCA-HO); (ii) health care associated, community onset (HCA-CO); and (iii) community associated (CA). HCA-HO infections were those for which the index specimen was obtained during a hospital stay but more than 48 h after admission. HCA-CO infections were those for which the index specimen did not meet the criteria for HCA-HO but did meet one or more of the following criteria: (i) ordered within 365 days of a hospital stay, outpatient surgery, or dialysis; (ii) ordered within 365 days of a known stay at a skilled nursing facility or nursing home. CA infections were those that were neither HCA-HO nor HCA-CO.

TABLE 1 Characteristics of *S. aureus* infections, Kaiser Permanente of Northern California^a

Characteristic	Value ^b			
	Moderately increasing MRSA (1998–2001)	Rapidly increasing MRSA (2002–2005)	Moderately declining MRSA (2006–2009)	All (1998–2009)
Total no. of infections	21,242 (100)	37,875 (100)	74,333 (100)	133,450 (100)
Isolate type				
MRSA	3,016 (14)	15,449 (41)	34,436 (46)	52,901 (40)
MSSA	18,226 (86)	22,426 (59)	39,897 (54)	80,549 (60)
Sex				
Female	9,301 (44)	17,046 (45)	34,870 (47)	61,217 (46)
Male	11,941 (56)	20,829 (55)	39,463 (53)	72,233 (54)
Age (yr)				
Under 5	1,251 (6)	2,014 (5)	5,461 (7)	8,726 (7)
5 to <18	2,108 (10)	4,088 (11)	10,980 (15)	17,176 (13)
18 to <50	6,584 (31)	13,406 (35)	28,526 (38)	48,516 (36)
50 to <65	4,824 (23)	7,958 (21)	14,847 (20)	27,629 (21)
65+	6,475 (30)	10,409 (27)	14,519 (20)	31,403 (24)
Mean age (SD) (yr)	49 (25)	47 (25)	42 (25)	45 (25)
Race/ethnicity ^c				
Asian	1,645 (8)	2,982 (8)	6,204 (8)	10,831 (8)
African-American	1,852 (9)	3,639 (10)	7,210 (10)	12,701 (10)
Hispanic	2,602 (12)	5,137 (14)	11,912 (16)	19,651 (15)
Other or unknown race	2,803 (13)	5,799 (15)	12,268 (17)	20,870 (16)
White	12,340 (58)	20,318 (54)	36,739 (49)	69,397 (52)
Onset type				
Health care associated, hospital onset	2,152 (10)	3,469 (9)	3,159 (4)	8,780 (7)
Health care associated, community onset	7,395 (35)	11,098 (29)	16,312 (22)	34,805 (26)
Community associated	11,695 (55)	23,308 (62)	54,862 (74)	89,865 (67)
Specimen type of index isolate ^d				
Blood	1,837 (9)	2,207 (6)	2,267 (3)	6,311 (5)
Other	19,405 (91)	35,668 (94)	72,066 (97)	127,139 (95)

^a Infections were defined as the first positive *S. aureus* isolate per patient per 365-day period and patients who were diagnosed with a potentially *S. aureus*-related clinical syndrome from 7 days before to 7 days after the index date. Only isolates from blood, bone, CSF, body fluid, urine, tissue, respiratory, and other miscellaneous bacterial specimens (such as those taken from abscesses, pustules, boils, and wounds) were included.

^b Data are number (%) of *S. aureus* infections unless otherwise indicated.

^c Race was not systematically collected for all patients. Electronic medical records, membership databases, and other administrative databases were searched for indications of race. Persons with high utilization have more chances to have race captured in the electronic systems. Patients were classified as Hispanic if their ethnicity was identified as Hispanic in any of these sources.

^d Specimen type of the first positive *S. aureus* isolate per person per 365-day period. If an isolate from a nonblood specimen preceded an isolate from a blood specimen (within 365 days), only the nonblood isolate was included in the table.

Patient characteristics. Patient age and sex were extracted from KPNC membership databases. Although race/ethnicity is not systematically captured for all members, the race/ethnicity of a majority of patients (about 85%) was identified via a search of electronic medical records, membership databases, and other administrative databases. Patients were classified as Hispanic if their ethnicity was identified as Hispanic in any of these sources. Patient addresses were extracted from membership databases and used to determine the patient's census block group. Using year 2000 U.S. census data, we determined the median census block group income for each patient and classified their index isolate based on the quintile of the median income. Persons whose address information did not map to a valid census block were classified as "unknown."

Risk factors for MRSA versus methicillin-susceptible *S. aureus* (MSSA). We examined the relationship between demographic characteristics and onset type and the risk of MRSA for infections occurring

in the years 2006 through 2009. The analytical data set had a record for each *S. aureus* infection occurring in these 4 years. Odds ratios (OR) were estimated using a multivariate logistic regression where the dependent variable was whether or not the isolate was methicillin resistant and the independent variables were sex, age (treated as a categorical variable with five levels: less than 5, 5 to <18, 18 to <50, 50 to <65, and 65+ years of age), race/ethnicity, quintile of census block income, and onset type. Because some patients had more than one infection between 2006 and 2009 (3.7% of episodes were "repeat" infections), we used a generalized estimating equation approach with an exchangeable covariance structure to account for correlation among records for the same person. The resulting odds ratios represent the odds of testing positive for MRSA given an *S. aureus* infection compared to that of the reference group.

Calculation of *S. aureus* bloodstream infection incidence rates. We calculated incidence rates for the subset of laboratory-confirmed *S. aureus*

TABLE 2 *S. aureus* infections by time period, clinical syndrome, demographics, and onset type, Kaiser Permanente of Northern California^a

Characteristics	Value					
	Moderately increasing MRSA (1998–2001)		Rapidly increasing MRSA (2002–2005)		Moderately decreasing MRSA (2006–2009)	
	No. of infections	% MRSA	No. of infections	% MRSA	No. of infections	% MRSA
Clinical syndromes^b						
Necrotizing fasciitis/toxic shock	37	27	78	37	103	49
Deep organ abscess	317	28	607	51	796	48
Skin and soft tissue infection	15,718	13	30,775	42	66,382	48
Pneumonia or lung related	2,023	33	3,169	51	3,003	50
Joint or bone infection	1,947	14	2,668	30	3,496	34
Urinary tract infection	2,548	30	4,094	49	4,561	48
Ear, nose, throat infections	1,695	5	1,929	18	2,884	25
Shock	307	34	794	51	982	50
Fever	749	18	1,252	34	1,332	35
Other selected syndromes ^c	446	27	626	45	687	42
Age (yr)						
Under 5	1,251	5	2,014	32	5,461	46
5 to <18	2,108	5	4,088	34	10,980	41
18 to <50	6,584	8	13,406	44	28,526	50
50 to <65	4,824	13	7,958	37	14,847	44
65+	6,475	26	10,409	44	14,519	45
Race/ethnicity						
Asian	1,645	10	2,982	29	6,204	35
African-American	1,852	19	3,639	54	7,210	60
Hispanic	2,602	12	5,137	41	11,912	48
Other or unknown race	2,803	10	5,799	43	12,268	48
White	12,340	15	20,318	40	36,739	45
Onset type						
Health care associated, hospital onset	2,152	41	3,469	58	3,159	56
Health care associated, community onset	7,395	20	11,098	40	16,312	45
Community associated	11,695	6	23,308	39	54,862	46

^a Infections were defined as the first positive *S. aureus* isolate per patient per 365-day period and patients who were diagnosed with a potentially *S. aureus*-related clinical syndrome from 7 days before to 7 days after the index date. Only isolates from blood, bone, CSF, body fluid, urine, tissue, respiratory, and other miscellaneous bacterial specimens (such as those taken from abscesses, pustules, boils, and wounds) were included.

^b Clinical syndromes were based on ICD9 codes received by the patient from 7 days before to 7 days after the *S. aureus* specimen was obtained. Patients could have more than one clinical syndrome, and thus, the numbers add up to more than the total number of infections.

^c Includes meningitis, intracranial abscess, tracheostomy infection, esophagostomy infection, gastrostomy infection, nonhealing surgical wounds, acute pericarditis, acute endocarditis, acute myocarditis, other diseases of the pericardium, arterial embolism, and thrombosis.

infections that were identified from blood specimens. These infections tend to represent especially severe cases, and we expected the propensity for microbiological testing of these infections to be stable over time. The denominator used for calculating incidence rates of *S. aureus* bloodstream infections was KPNC member years. We identified all persons who were members of KPNC at any time between 1 January 1998 and 31 December 2009. KPNC membership systems track membership on a monthly basis, and people could enter and leave the health plan throughout this time. We summarized *S. aureus* bloodstream infections and member months for each calendar year and calculated annual incidence rates by dividing the number of cases by member years. To examine trends, we standardized all annual incidence rates to the 2009 KPNC age and sex population using direct adjustment.

RESULTS

We identified 133,450 culture-confirmed *S. aureus* infections during the period 1998 to 2009. Based on visual analysis of the trend in the percentage of isolates positive for MRSA, we defined three

distinct time periods: (i) moderately increasing MRSA period (1998 to 2001), where the percentages of infections that were MRSA were 9, 12, 15, and 20 in each year, respectively; (ii) rapidly increasing MRSA period (2002 to 2005), where the percentages with MRSA were 25, 34, 43, and 49 in each year, respectively; and (iii) moderately declining MRSA period (2006 to 2009), where the percentages with MRSA were 49, 48, 45, and 43 in each year, respectively (Fig. 1). The trend in the percentage of *S. aureus* isolates that were MRSA was statistically significantly different in each of the three periods, with an average increase of 3.4% per year (confidence interval [CI], 2.7% to 4.1%) from 1998 to 2001, 8.1% (CI, 7.3% to 8.8%) from 2002 to 2005, and -2.1% (CI, -2.8% to -1.3%) from 2006 to 2009.

Table 1 describes the *S. aureus* infections by time period. The percentages of isolates that were MRSA were 14% in 1998 to 2001, 41% in 2002 to 2005, and 46% in 2006 to 2009. As a share of all

laboratory-confirmed *S. aureus* infections, those that were health care associated declined over time (10% to 4% for hospital onset and 35% to 22% for community onset), while the share that were community associated increased substantially (55% to 74%). The share of infections where the index isolate was from a blood specimen declined from 9% to 3%. When analyzing the first relevant isolate per person per 30-day period (rather than per 365-day period as described above), the percentages of isolates that were MRSA were 14%, 38%, and 44% in the periods 1998 to 2001, 2002 to 2005, and 2006 to 2009, respectively.

Skin and soft tissue infections were by far the most common clinical syndrome (Table 2). The pattern of increasing and then stabilizing (or declining) MRSA was seen in nearly all clinical syndromes. The same pattern was seen in all age groups, with the largest increase in the 18 to <50 year olds, and in all race/ethnicity groups, with the largest increase in African-Americans. The precipitous increase in the percentage of staphylococcal infections that were MRSA was largely related to community-associated infections, where the percentage increased from about 6% from 1998 to 2001 to 46% from 2006 to 2009. However, consistent with the overall trend seen in Fig. 1, between 2006 and 2009 the percentage of isolates that were MRSA declined modestly for every age (except 0 to 5 year olds) and race/ethnicity group and onset type (not shown).

Multivariate logistic regression indicated that, among *S. aureus* infections, isolates in persons 65 years of age and older and persons 18 to <50 years of age were more likely to be MRSA than those from persons in other age groups (Table 3). Isolates from African-Americans (OR, 1.73; CI, 1.64 to 1.82) and Hispanics (OR, 1.11; CI, 1.06 to 1.16) were more likely to be MRSA than those from whites, while isolates from Asians were less likely to be MRSA than those from whites (OR, 0.69; CI, 0.65 to 0.73). Isolates from persons living in less affluent census blocks were more likely to be MRSA than those from persons living in more affluent census blocks, and hospital onset isolates were more likely to be MRSA than community-associated isolates (OR, 1.58; CI, 1.46 to 1.70). Restricting the analysis to bloodstream infections, the percentage of MRSA isolates increased from about 17% to 44% between 1998 and 2005, after which it stabilized at around 40% (Fig. 2). Although the percentage of *S. aureus* bloodstream infections that were MRSA increased over time, the incidence rate of *S. aureus* bloodstream infections (both MRSA and MSSA) remained nearly constant at around 27 infections per 100,000 person years. When analyzing the first relevant blood isolate per person per 30-day period, the incidence rate of *S. aureus* bloodstream infections (all onset types) was very similar to the rate when using the first isolate per person per 365-day period (25.7 infections per 100,000 in 2009 using the 30-day rule versus 23.4 per 100,000 using the 365-day rule).

In analyses restricted to MRSA bloodstream infections, we found that the incidence rates of community onset and community-associated bloodstream MRSA infections increased between 1998 and about 2007 (Fig. 3). In contrast, the incidence of hospital onset bloodstream MRSA infections peaked in 2002 and declined thereafter.

DISCUSSION

During the 12-year study period from 1998 to 2009, we identified over 133,000 culture-confirmed *S. aureus* infections and documented a 5-fold increase in the percentage of index isolates that

TABLE 3 Risk factors for methicillin-resistant *S. aureus* among isolates positive for *S. aureus*, Kaiser Permanente of Northern California, 2006–2009

Patient characteristic	OR (CI) of MRSA vs. MSSA among <i>S. aureus</i> isolates (n = 74,333) ^a
Sex	
Female	1.05 (1.02, 1.08)
Male	Reference
Age (yr)	
Under 5	1.02 (0.96, 1.09)
5 to <18	0.84 (0.79, 0.88)
18 to <50	1.20 (1.15, 1.26)
50 to <65	0.97 (0.92, 1.02)
65+	Reference
Race/ethnicity	
Asian	0.69 (0.65, 0.73)
African-American	1.73 (1.64, 1.82)
Hispanic	1.11 (1.06, 1.16)
Other/unknown	1.10 (1.05, 1.15)
White	Reference
Census block income quintile	
Unknown	1.38 (1.29, 1.47)
1st (lowest income)	1.54 (1.46, 1.62)
2nd	1.39 (1.32, 1.46)
3rd	1.25 (1.19, 1.31)
4th	1.14 (1.09, 1.20)
5th (highest income)	Reference
Onset type	
Health care associated, hospital onset	1.58 (1.46, 1.70)
Health care associated, community onset	0.96 (0.92, 1.00)
Community associated	Reference

^a Odds ratios were estimated using a multivariate logistic regression. The analytic data set had a record for each *S. aureus* isolate. The dependent variable was whether or not the isolate was methicillin resistant, and the independent variables were gender, age, race/ethnicity, income quintile based on census block, and onset type. Reference, reference group for other odds ratios within a characteristic.

were MRSA. This increase in MRSA occurred most rapidly between 2002 and 2005, after which the percentage of isolates that were MRSA modestly declined. The increase in the percentage of MRSA isolates was seen in blood and, to a greater extent, in other bacteriological specimens and occurred in all ages and race/ethnicity groups, though it was most pronounced in persons aged 18 to <50 years and in African-Americans. Although hospital onset infections were the most likely to be MRSA, the largest increase in MRSA was among community-associated infections.

Although the percentage of *S. aureus* infections that were MRSA increased significantly between 1998 and 2009 among both bloodstream and nonbloodstream infections, the incidence of bloodstream infections remained fairly constant. Thus, among bloodstream infections, MRSA appears to have merely replaced, to some extent, MSSA. This finding is similar to that of a Canadian study that reported a fairly constant incidence of *S. aureus* bloodstream infections in Calgary from 2000 to 2006 (about 2 cases per 10,000 person years) while also noting that a higher proportion was due to MRSA (24). We focused our incidence rate analysis on bloodstream infections because they are usually the most serious

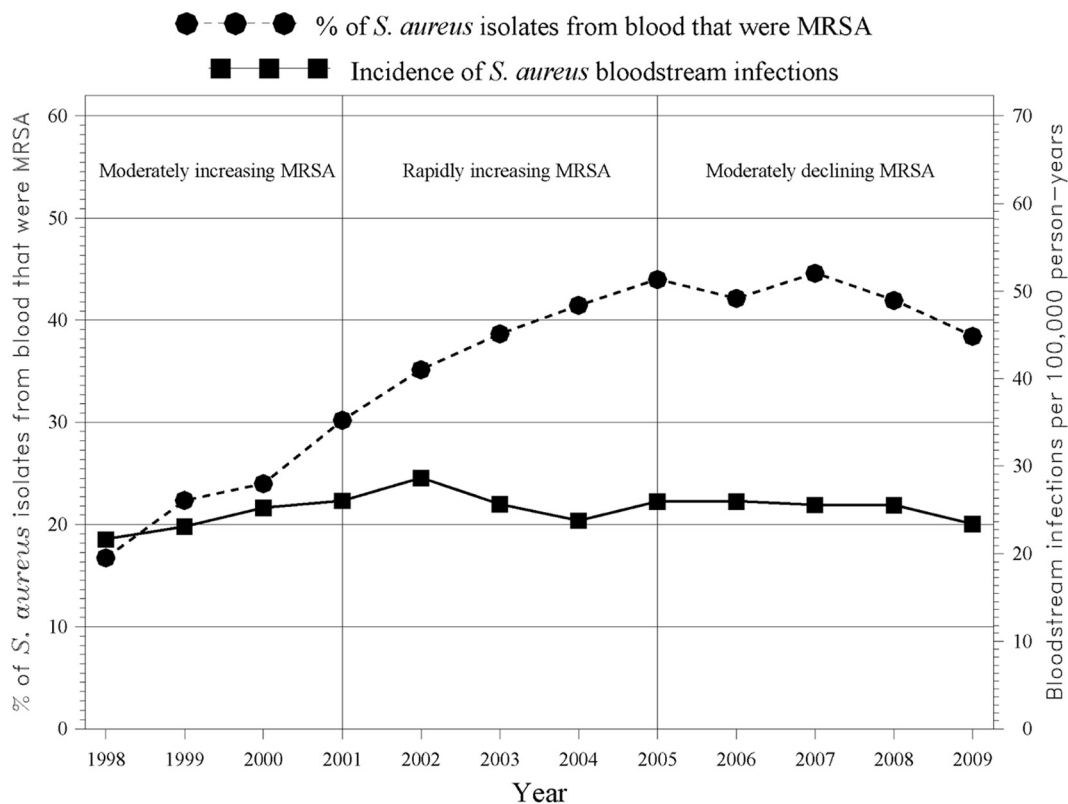


FIG 2 *S. aureus* bloodstream infections: percent MRSA and incidence rate.

infections and because bloodstream infection rates are less likely to be affected by changes in the practice of obtaining cultures.

There are surprisingly few published studies that present data on all types of *S. aureus* infections in a general population in the last decade. Most *S. aureus* epidemiology studies have focused exclusively on MRSA isolates, have been restricted to invasive disease and isolates from hospitalized patients, and/or have been in special populations. (3, 5, 7, 8, 10, 14, 16, 16–18, 20, 23, 25, 26). Nevertheless, numerous studies reported that in the United States by the mid-2000s, MRSA accounted for 40 to 70% of *S. aureus* infections (13, 16, 20, 28, 30, 31, 41).

As far as we know, ours is the first study showing that in a very large and diverse population, the percentage of *S. aureus* isolates that were MRSA began to decrease after 2006. This was true for nearly all ages and races we examined, for blood and nonblood isolates, and for both health care-associated and community-associated infections. These results are consistent with recent national data showing that the incidence of health care-associated invasive MRSA infections appears to have declined after 2005 (18).

Numerous studies have reported that African-American race and low income are risk factors for MRSA infection (14, 18, 23, 25, 38). Our results support these findings. Even in the most current period of stable or declining MRSA, we found that, among persons with an *S. aureus* infection, African-Americans and persons living in lower-income census blocks were at increased risk of MRSA infection after adjusting for other demographic factors and infection onset type. In addition, our findings indicate that Hispanics have a higher risk of MRSA infection and that Asians have a lower risk of MRSA infection than whites.

Limitations. Although the rates of MRSA bloodstream infections in our population were about one-third higher than those reported for the Calgary, Canada, population (24), they were substantially lower than those reported by Kallen et al. (18) for a U.S. population and may not be representative of national rates of MRSA bloodstream infections. In part, the difference is methodological, in that we used a more conservative 365-day isolate deduplication algorithm (compared to 30 days) and required patients to have received an *S. aureus*-related diagnosis. In addition, although KPNC enrolls persons covered by Medicaid and other dues subsidy programs, enrollment is generally through employment, and therefore, the KPNC population likely underrepresents certain populations thought to be at increased risk of MRSA (e.g., incarcerated persons, intravenous drug users, military personnel, the very poor, and the uninsured) (4, 6, 27). Nevertheless, our study population of over 3 million is more representative of the general population than are studies of those special populations. Although we used standard algorithms to classify infections as health care associated and community acquired, we could not establish with certainty the setting in which the *S. aureus* strains originated. In addition, we had limited information on nursing home status, which was used in the algorithm to define health care-associated infection. Members were assumed to be in nursing homes if their home address matched the known address of a licensed nursing home.

Conclusions. It has been suggested that, if the emergence of MRSA follows the same trend as beta-lactamase-positive *S. aureus*, the percentage of community-associated *S. aureus* infections caused by MRSA strains may approach 100% (6). However, this study, along with several other recent studies (9, 18), indicates a

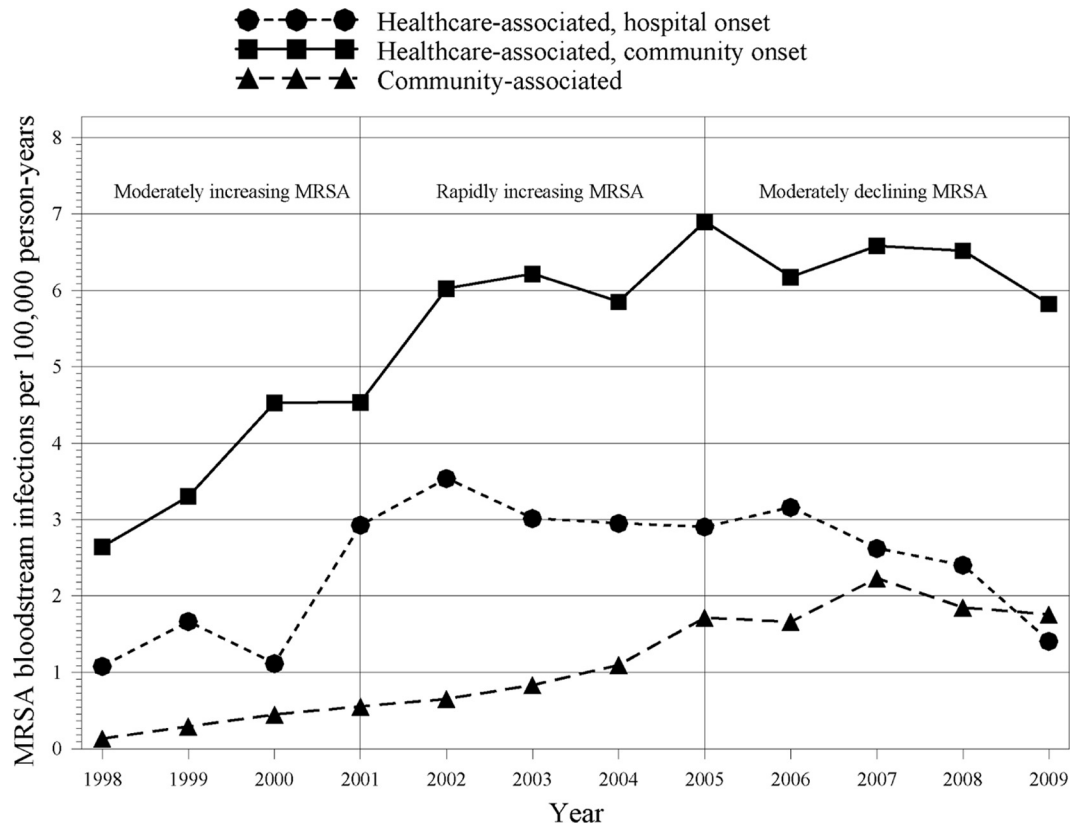


FIG 3 Incidence of bloodstream MRSA infections by onset type.

possible interruption in that trend. Culture and susceptibility testing remain important, because in general, beta-lactam antibiotics are still considered the first line in staphylococcal infections that are susceptible, and knowledge of local resistance patterns of *S. aureus* can help guide empirical therapy. As for future trends in *S. aureus*, it remains to be seen whether a stabilization or reduction in the proportion of *S. aureus* isolates that are MRSA will correspond to an absolute decrease in *S. aureus* infections. The emergence and rapid spread of CA-MRSA may have been related to the emergence of strains possessing certain fitness characteristics, such as carrying Panton-Valentine leukocidin genes (2, 12, 34), rather than to methicillin resistance. There is some evidence that these characteristics are becoming associated with MSSA, making those strains more competitive against MRSA strains (35). Thus, continued surveillance of *S. aureus* epidemiology is important.

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