

Prevalence of *Staphylococcus aureus* Nasal Colonization in the United States, 2001–2002

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(See the editorial commentary by Creech et al., on pages 169–71.)

Background. *Staphylococcus aureus* is a common cause of disease, particularly in colonized persons. Although methicillin-resistant *S. aureus* (MRSA) infection has become increasingly reported, population-based *S. aureus* and MRSA colonization estimates are lacking.

Methods. Nasal samples for *S. aureus* culture and sociodemographic data were obtained from 9622 persons ≥ 1 year old as part of the National Health and Nutrition Examination Survey, 2001–2002. After screening for oxacillin susceptibility, MRSA and selected methicillin-susceptible *S. aureus* isolates were tested for antimicrobial susceptibility, pulsed-field gel electrophoresis clonal type, toxin genes (e.g., for Panton-Valentine leukocidin [PVL]), and staphylococcal cassette chromosome *mec* (SCC*mec*) type I–IV genes.

Results. For 2001–2002, national *S. aureus* and MRSA colonization prevalence estimates were 32.4% (95% confidence interval [CI], 30.7%–34.1%) and 0.8% (95% CI, 0.4%–1.4%), respectively, and population estimates were 89.4 million persons (95% CI, 84.8–94.1 million persons) and 2.3 million persons (95% CI, 1.2–3.8 million persons), respectively. *S. aureus* colonization prevalence was highest in participants 6–11 years old. MRSA colonization was associated with age ≥ 60 years and being female but not with recent health-care exposure. In unweighted analyses, the SCC*mec* type IV gene was more frequent in isolates from participants of younger age and of non-Hispanic black race/ethnicity; the PVL gene was present in 9 (2.4%) of 372 of isolates tested.

Conclusions. Many persons in the United States are colonized with *S. aureus*; prevalence rates differ demographically. MRSA colonization prevalence, although low nationally in 2001–2002, may vary with demographic and organism characteristics.

Staphylococcus aureus is an important cause of human disease. Although staphylococcal disease is most often associated with skin and soft tissue infections, its manifestations are myriad and include syndromes with low morbidity and mortality, such as folliculitis and food poisoning, and fatal systemic illnesses, such as endocarditis and toxic shock syndrome [1].

S. aureus infections, often fatal in the preantibiotic era, now typically respond to a variety of antimicrobial agents [2]. However, the spread of multidrug-resistant strains of *S. aureus* in the health-care setting, particularly methicillin-resistant *S. aureus* (MRSA), have made these infections more difficult to treat [3]. Certain MRSA strains appear to be spreading in the community setting [4, 5].

Most *S. aureus* infections occur in persons who are colonized with the organism; *S. aureus* carriage has long been known to be one of the most strongly associated risk factors for subsequent infection [6, 7]. Elegantly designed studies performed during the early 20th century identified the anterior nares as the most consistent site of staphylococcal colonization [8, 9]. Presence of *S. aureus* nasal colonization can provide an indication of a higher risk for subsequent infection, including with MRSA [10, 11]. However, no population-based prevalence study has been conducted to measure *S. aureus* carriage, and reliable national population estimates are

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lacking. To obtain these data, we measured the prevalence of *S. aureus* colonization in a sample of the US population.

PARTICIPANTS, MATERIALS, AND METHODS

Survey design and collection of data. The National Health and Nutrition Examination Survey (NHANES) is a nationally representative sample of the civilian, noninstitutionalized US population that includes persons selected on the basis of a stratified, multistage, probability cluster design. The stages of sample selection are as follows: (1) selection of primary sampling units (PSUs), which are counties or small groups of contiguous counties; (2) selection of segments within each PSU (a block or group of blocks containing a cluster of households); (3) selection of households within each segment; and (4) selection of 1 or more participants within each household. NHANES has been conducted continuously since 1999 and was conducted periodically before then; data are collected through household interviews, standardized physical exams, and collection of biological samples at mobile examination centers and are released in 2-year cycles [12]. NHANES is reviewed and approved annually by an institutional review board.

Testing for *S. aureus* carriage was completed for all participants ≥ 1 year old in the years 2001 and 2002. To allow for sufficient sample size, age was grouped as follows: 1–5, 6–11, 12–19, 20–29, 30–39, 40–49, 50–59, 60–69, and ≥ 70 years for analysis of *S. aureus* and 1–19, 20–59, and ≥ 60 years for analysis of MRSA. Health-care exposure was defined as an overnight stay in either an acute-care or a long-term health-care facility during the 12 months before participation. Other cofactors examined for their association with carriage included poverty-index ratio, education, military history, diabetes, and dermatologic condition. Dermatologic condition was available only for participants 20–59 years old. Education and military history were analyzed only for participants ≥ 20 years old.

Prevalence estimates were weighted to represent the US population. The current NHANES oversamples low-income persons, pregnant women, adolescents 12–19 years old, persons ≥ 60 years old, non-Hispanic black persons, and Mexican Americans. Weights were calculated for the NHANES sample to account for these unequal probabilities of selection, to adjust for nonresponse to the survey interview or examination, and to poststratify on the basis of the Census Bureau estimates of the US population. The weights were ratio adjusted by age, sex, and race/ethnicity to the US population estimates from the current population survey, which contained an adjustment for undercounts.

SEs were calculated using the Taylor series linearization method with SUDAAN software, to account for the complex sample design [13]. Prevalence estimates were age adjusted by the direct method, using the 2000 standard US population. For MRSA prevalence, 95% confidence intervals (CIs) were calculated using the arcsine transformation method for calculating exact CIs [14].

A backward stepwise logistic modeling procedure in SUDAAN was used to determine cofactors that were independently associated with the prevalence of either *S. aureus* or MRSA. Cofactors with $P < .05$ from a Satterthwaite-adjusted F statistic were considered to be significant. Interactions between age, sex, and race/ethnicity were examined. Odds ratios (ORs) and their 95% CIs are reported for all significant cofactors.

Statistical examination of organism characteristics, as determined by laboratory testing, were performed using SAS (version 8.02; SAS Institute) and were unweighted. Analyses were performed unweighted because the number of participants with MRSA carriage was small, and very small sample sizes were obtained when MRSA isolates were categorized by organism and demographic (e.g., age, sex, and race/ethnicity) characteristics. In small subgroups, individual weights can be highly variable and highly influential. Because NHANES oversamples certain age and racial/ethnic groups (e.g., Mexican Americans and non-Hispanic black persons), the findings of unweighted analyses should not be generalized to the US civilian, noninstitutionalized population and should be interpreted as being descriptive of the sample only.

Laboratory methods. Nasal samples were collected from both anterior nares by use of a culturette swab (BBL Microbiology Systems, Becton Dickinson). Culturettes were plated on mannitol salt agar (MSA; BBL Microbiology Systems, Becton Dickinson). Each distinctive morphotype of mannitol-fermenting colonies was selected from an MSA plate and subcultured on a trypticase soy agar plus 5% sheep blood agar plate (BAP; BBL Microbiology Systems, Becton Dickinson); incubation was at 37°C. Cultures on the BAP were screened using Staphaurex (Remel).

S. aureus isolates were screened for oxacillin resistance using the Clinical Laboratory Standards Institute (CLSI; formerly known as the NCCLS) disk diffusion method [15]. Overnight cultures from the BAP were suspended in Mueller-Hinton broth to the turbidity of a 0.5 McFarland standard and plated on Mueller-Hinton agar, and a 1- μg oxacillin disk was placed within the inoculum. Zone diameters were measured and recorded after a 24-h incubation at 35°C (susceptible, ≥ 13 mm; intermediate, 11–12 mm; and resistant, ≤ 10 mm).

Isolates determined to be resistant to oxacillin (i.e., MRSA) and a random sample of approximately every tenth isolate determined to be susceptible to oxacillin (i.e., methicillin-susceptible *S. aureus* [MSSA]) by disk diffusion were selected and saved for additional testing. Testing included the determinations of MICs by broth microdilution, induction of clindamycin resistance using the CLSI reference methods [16], and polymerase chain reaction (PCR) assays for detection of enterotoxin A, B, C, D, E, and H; toxic shock syndrome toxin-1 (TSST-1); Pantone-Valentine leukocidin (PVL); and staphylococcal cassette chromosome *mec* (SCC*mec*) type I–IV genes [17, 18]. Strain typing

Table 1. Prevalence of *Staphylococcus aureus* and methicillin-resistant *S. aureus* (MRSA) nasal colonization, by demographic characteristics—National Health and Nutrition Examination Survey, 2001–2002.

Category, characteristic	Tested, no.	<i>S. aureus</i>		MRSA	
		Colonization prevalence, % (95% CI)	Colonized persons, estimated no. in millions (95% CI)	Colonization prevalence, % (95% CI)	Colonized persons, estimated no. in millions (95% CI)
All participants (≥1 year old)	9622	32.4 (30.7–34.1)	89.4 (84.8–94.1)	0.8 (0.4–1.4)	2.3 (1.2–3.8)
Sex					
Male	4685	37.0 (34.0–40.1)	49.8 (45.7–53.9)	0.5 (0.2–0.9) ^a	0.7 (0.3–1.2)
Female	4937	28.0 (26.2–29.8)	39.7 (37.1–42.2)	1.2 (0.6–1.9)	1.6 (0.9–2.7)
Race/ethnicity ^b					
Non-Hispanic white	3990	33.0 (31.2–34.9)	61.7 (58.3–65.1)	0.9 (0.5–1.5)	1.7 (0.9–2.7)
Non-Hispanic black	2395	26.9 (24.5–29.2)	9.0 (8.2–9.8)	1.1 (0.6–1.9)	0.4 (0.2–0.6)
Mexican American	2417	30.3 (27.9–32.6)	7.2 (6.7–7.8)	0.3 (0.1–0.6) ^c	0.07 (0.03–0.15)
Age					
1–19 years	4772	36.9 (34.6–39.2)	28.2 (26.5–30.0)	0.6 (0.1–1.4) ^d	0.4 (0.08–1.0)
20–59 years	3290	31.4 (29.3–33.5)	48.7 (45.4–51.9)	0.6 (0.3–1.1) ^a	1.0 (0.4–1.7)
≥60 years	1560	27.7 (24.7–30.7)	12.4 (11.1–13.7)	2.2 (1.2–3.6)	1.0 (0.5–1.6)

NOTE. CI, confidence interval.

^a Estimate unstable (relative SE, 33%).

^b Total includes all racial/ethnic groups, including the other racial/ethnic group, which is not shown as a stratified subgroup.

^c Estimate unstable (relative SE, 39%; based on 10 positive samples).

^d Estimate unstable (relative SE, 55%).

was performed using pulsed-field gel electrophoresis (PFGE) with *Sma*I. The PFGE patterns were analyzed using BioNumerics (Applied Maths), and isolates were grouped into PFGE clonal types using Dice coefficients and 80% relatedness [19].

RESULTS

Of the 10,470 persons ≥1 year old selected and interviewed for NHANES in 2001–2002, 9929 were examined. Of these, cultures were performed for 9622, and 2964 were found to be carrying *S. aureus*. We estimate the weighted *S. aureus* colonization prevalence to be 32.4% (95% CI, 30.7%–34.1%), or 89.4 million persons (95% CI, 84.8–94.1 million persons) in the US population (table 1). *S. aureus* colonization prevalence was highest among participants 6–11 years old (figure 1).

Multivariate analyses were performed to determine the adjusted effects of age, sex, and race/ethnicity on *S. aureus* carriage. Risk of *S. aureus* colonization was highest among participants 6–11 years old (OR, 2.7 [95% CI, 2.0–3.6]; reference group, participants 1–5 years old; $P < .001$). Although males and non-Hispanic white persons also had a higher risk of *S. aureus* colonization, a significant interaction between sex and race/ethnicity was found. To describe the interaction between sex and race/ethnicity, racial/ethnic differences were adjusted for age and stratified by sex, whereas sex differences were adjusted for age and stratified by race/ethnicity (table 2). In summary, the interaction between sex and race/ethnicity was as follows. Racial/ethnic differences were greater among males than among females. Sex differences were statistically significant only among non-Hispanic

white persons and Mexican Americans (they were not significant among non-Hispanic black persons).

Of the 2964 participants with *S. aureus* carriage, 75 had MRSA carriage. The weighted prevalence of MRSA colonization was 0.8% (95% CI, 0.4%–1.4%), or 2.3 million persons (95% CI, 1.2–3.8 million persons) in the US population. In a multivariate model, MRSA colonization was associated with age ≥60 years (OR, 4.3 [95% CI, 1.2–14.8]; reference age, 1–19 years) and being female (OR, 2.0 [95% CI, 1.2–3.4]; reference, males). Non-Hispanic black persons had a higher risk of MRSA colonization, compared with Mexican Americans (OR, 3.1 [95% CI, 1.2–8.3]); comparisons between non-Hispanic white persons and the 2 other racial/ethnic groups were not significant. No statistically significant associations between either *S. aureus* or MRSA colonization and other epidemiologic factors, such as poverty, education, birth outside the United States, military service, health-care exposure, or presence of diabetes or dermatologic condition, were found.

The following analyses did not incorporate the survey weights. Therefore, the data cannot be generalized to the US civilian, noninstitutionalized population, especially the results associated with age or race/ethnicity, which are 2 of the characteristics that define subgroups oversampled in NHANES. There were 297 MSSA and 75 MRSA isolates selected for study. Of the 297 MSSA isolates, 229 (77.1%) were susceptible to all non-β-lactam agents tested, compared with 15 (20.0%) of the 75 MRSA isolates (table 3). Thirty-seven (12.5%) of the 297 MSSA isolates were susceptible to penicillin. The majority of MSSA and MRSA

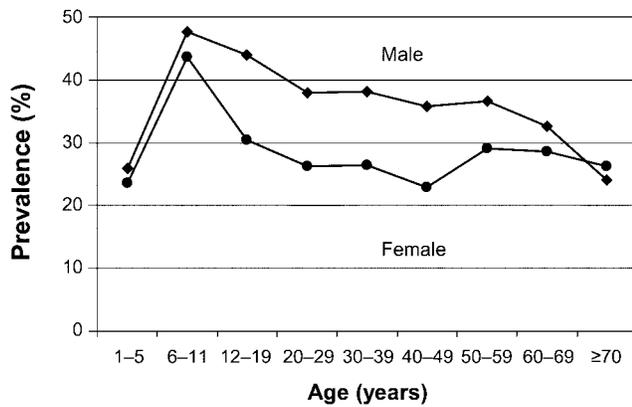


Figure 1. Prevalence of *Staphylococcus aureus* nasal colonization, by age and sex—National Health and Nutrition Examination Survey, 2001–2002.

isolates were susceptible to tetracycline, clindamycin, gentamicin, and rifampin. Seventy-six (71.7%) of the 106 erythromycin-resistant, clindamycin-susceptible isolates showed inducible clindamycin resistance; of these, 23 (59.0%) of 39 were MRSA. No resistance to trimethoprim-sulfamethoxazole (TMP/SMX) or vancomycin was detected.

Enterotoxin A, C, and H genes and the TSST-1 gene were more common in MSSA isolates than in MRSA isolates; the PVL gene and enterotoxin B and D genes were more common in MRSA isolates than in MSSA isolates (table 4). Of the 297 MSSA isolates, 153 (51.5%) had toxin genes detectable; that for TSST-1 was the most common. Of the 75 MRSA isolates, 57 (76.0%) carried at least 1 toxin gene; that for enterotoxin D was the most common.

All MRSA isolates had either the SCCmec type II (38 [50.7%]) or the IV gene (37 [49.3%]). The proportion of isolates with SCCmec type IV gene carriage, compared with those with SCCmec type II gene carriage, appeared to differ by age group (SCCmec type IV gene carriage, 22/26 [84.6%] for age 1–19 years; 11/16 [68.8%] for age 20–59 years; and 4/33 [12.1%] for age ≥60 years) and by race/ethnicity (SCCmec type IV gene carriage, 20/25 [80.0%] for non-Hispanic black persons; 4/10 [40.0%] for Mexican Americans; and 12/36 [33.3%] for non-Hispanic white persons). Thirty (93.8%) of 32 isolates resistant to 0–1 antimicrobial agents had the SCCmec type IV gene, whereas only 7 (16.3%) of 43 isolates resistant to >1 antimicrobial agent had the SCCmec type IV gene. All isolates with the PVL gene and 6 (85.7%) of 7 isolates with the enterotoxin B gene had the SCCmec type IV gene, whereas 11 (25.6%) of 43 isolates with the enterotoxin D gene had the SCCmec type IV gene.

Of the 296 MSSA isolates available for typing analysis, 146 (49.3%) had unique PFGE patterns. These patterns had a minimum of 45.7% relatedness, including 235 isolates clustered into 12 major clonal groups (figure 2). The remaining 61 MSSA

isolates fell outside recognized clonal groups. The most common group, USA200, contained 85 (28.7%) of the 296 isolates. Of the 75 MRSA isolates, 42 (56.0%) had unique PFGE patterns; these patterns had a minimum of 46.4% relatedness and were clustered into 9 major clonal groups and 2 previously undefined PFGE clonal types. The most common group, USA100, contained 34 MRSA isolates (45.3%). Of note, USA300 accounted for only 6 isolates (8.0%).

DISCUSSION

NHANES has provided the first nationally representative sample used to estimate the prevalence of *S. aureus* nasal carriage in the US population. Our data suggest that, although *S. aureus* colonization is common, MRSA colonization in the general population is unusual. Recent concerns about increases in the incidence of MRSA infections in community settings have given surveillance of *S. aureus* greater importance. Older studies have shown an association between carriage of *S. aureus* and subsequent infection among patients in both health-care and community settings, and molecular techniques now have confirmed that infection most often is preceded by colonization caused by the same strain [6, 20]. Therefore, measurement of colonization prevalence provides a useful estimate of the potential for development of staphylococcal disease in the US population.

Soon after the development of the coagulase test for discriminating *S. aureus* from other species of staphylococci, the anterior nares were identified as the most common site of col-

Table 2. Odds ratios (ORs) and age-adjusted prevalences for *Staphylococcus aureus* nasal colonization in the United States, by sex and race/ethnicity—National Health and Nutrition Examination Survey, 2001–2002.

Stratified variable, primary variable	OR (95% CI)	P	Age-adjusted prevalence, % (95% CI)
Males			
Non-Hispanic white	1.7 (1.4–2.0)	.001	37.7 (34.6–40.7)
Mexican American	1.2 (1.1–1.4)	.003	31.4 (28.2–34.5)
Non-Hispanic black	Reference		26.9 (23.8–30.0)
Females			
Non-Hispanic white	1.2 (1.0–1.4)	.070	28.8 (26.6–31.0)
Mexican American	1.1 (0.9–1.3)	.577	27.2 (24.3–30.1)
Non-Hispanic black	Reference		25.6 (22.2–29.0)
Non-Hispanic white			
Males	1.5 (1.3–1.8)	.001	37.7 (34.6–40.7)
Females	Reference		28.8 (26.6–31.0)
Mexican American			
Males	1.3 (1.1–1.6)	.008	31.4 (28.2–34.5)
Females	Reference		27.2 (24.3–30.1)
Non-Hispanic black			
Males	1.1 (0.9–1.3)	.310	26.9 (23.8–30.0)
Females	Reference		25.6 (22.2–29.0)

NOTE. CI, confidence interval.

Table 3. Antimicrobial susceptibility for methicillin-resistant *Staphylococcus aureus* (MRSA) and randomly selected methicillin-susceptible *S. aureus* (MSSA) isolates (unweighted proportions)—National Health and Nutrition Examination Survey, 2001–2002.

Antimicrobial	Isolates susceptible, no. (%)	
	MSSA (n = 297)	MRSA (n = 75)
Penicillin	37 (12.5)	0 (0)
All non- β -lactam agents	229 (77.1)	15 (20.0)
Levofloxacin	296 (99.7)	34 (45.3)
Clindamycin	297 (100)	51 (68.0)
Erythromycin	236 (79.5)	19 (25.3)
Tetracycline	287 (96.6)	69 (92.0)
Vancomycin	297 (100)	75 (100)
Gentamicin	296 (99.7)	75 (100)
Rifampin	297 (100)	74 (98.7)
TMP/SMX	297 (100)	75 (100)

NOTE. Unweighted results are not generalizable to the US population. TMP/SMX, trimethoprim-sulfamethoxazole.

onization, and prevalence rates were measured [8, 21]. Carriage rates of 30%–40% have been estimated on the basis of limited samples, although some early studies suggested rates well over 40% in healthy persons outside the hospital setting; more-recent studies have suggested lower rates [10, 20, 22]. Comparisons between the findings of these limited studies may be confounded by the quality of sampling, culture techniques, and the populations studied.

On the basis of the NHANES sample, we estimated that nearly a third of the 2001–2002 US population had *S. aureus* colonization; however, important differences were found with regard to age, sex, and race/ethnicity. Peak prevalence was found in participants 6–11 years old. The higher prevalence found among non-Hispanic white persons, compared with that among non-Hispanic black persons, was much greater among males, but no such statistically significant racial/ethnic difference was found among females. The higher prevalence among males overall was most pronounced among non-Hispanic white persons and Mexican Americans but did not reach statistical significance among non-Hispanic black persons. Differences with respect to age, sex, and race/ethnicity, including higher *S. aureus* carriage rates among males, white persons, and children, have been reported over the past 50 years, although interactions between these factors have not been previously published [10, 20, 23–25]. Some of these associations may be due to differences in the persistence of certain strains among demographic groups, particularly the high prevalence rates seen in school-age children [25, 26].

Our data suggest that carriage of MRSA is unusual in healthy persons and is associated with age ≥ 60 years and being female.

Limited studies from the same period report a similar low prevalence of MRSA colonization in children without established risk factors [27, 28]. We did not find that health-care exposure was significantly associated with MRSA carriage, a finding that has been widely reported in the literature [29, 30]; however, due to small sample sizes and large SEs, power may have been insufficient to identify the association.

In contrast to MRSA overall, younger persons and non-Hispanic black persons more frequently carried SCCmec type IV-associated MRSA strains. The SCCmec IV gene was also more frequent in isolates with the PVL gene and in isolates with relatively little antimicrobial resistance, a profile associated with many community-associated MRSA infections. However, these results did not take into account the sample weights or the complex sample design, and they cannot be generalized to the US population. Higher rates of community-associated MRSA infections previously have been associated with strains characterized by susceptibility to non- β -lactam agents (with the exception of erythromycin), presence of enterotoxin H and PVL genes, and predilection of infection of persons of certain non-white races/ethnicities, particularly Native Americans and Pacific Islanders [31, 32].

Although the presence of the SCCmec type IV gene showed a specific association with the presence of the PVL gene, the overall proportion of PVL gene-containing isolates in the present sample was low. We also found that MRSA strains with PFGE clonal types associated with virulent community-asso-

Table 4. Presence of enterotoxin A, B, C, D, E, and H; Panton-Valentine leukocidin (PVL); and toxic shock syndrome toxin-1 (TSST-1) genes in methicillin-resistant *Staphylococcus aureus* (MRSA) and randomly selected methicillin-susceptible *S. aureus* (MSSA) isolates (unweighted proportions)—National Health and Nutrition Examination Survey, 2001–2002.

Toxin	Isolates with gene, no. (%)	
	MSSA (n = 297)	MRSA (n = 75)
Any toxin	153 (51.5)	57 (76.0)
Enterotoxin		
A	64 (21.5)	6 (8.0)
B	16 (5.4)	7 (9.3)
C	17 (5.7)	2 (2.7)
D	15 (5.1)	43 (57.3)
E	0 (0)	0 (0)
H	16 (5.4)	1 (1.3)
PVL	3 (1.0)	6 (8.0)
TSST-1	90 (30.3)	5 (6.7)

NOTE. Unweighted results are not generalizable to the US population.

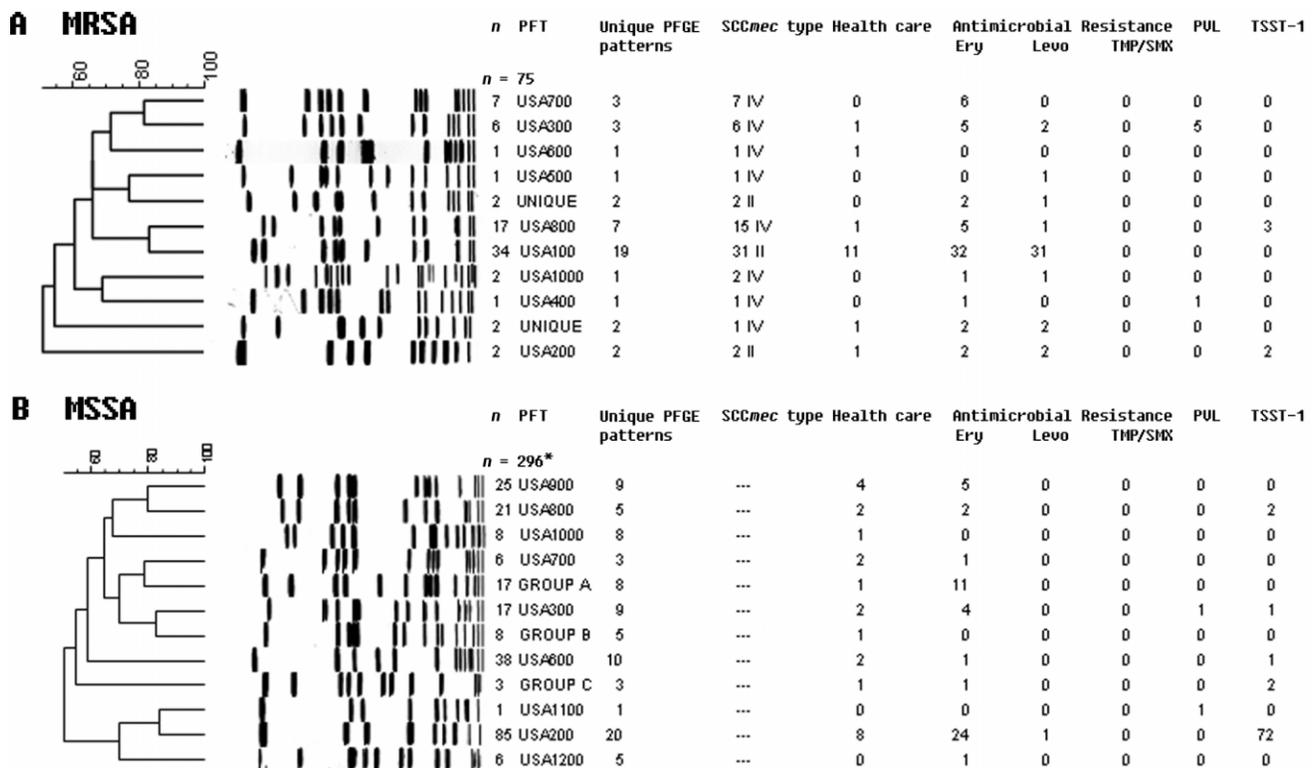


Figure 2. Relationships among pulsed-field gel electrophoresis (PFGE) clonal type (PFT), staphylococcal cassette chromosome *mec* (SCC*mec*) type, health-care exposure, antimicrobial resistance pattern, Pantan-Valentine leukocidin (PVL) gene, and toxic shock syndrome toxin-1 (TSST-1) gene profiles in methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) isolates—National Health and Nutrition Examination Survey, 2001–2002. Each clonal pattern contains a group of closely related PFGE types; the pattern shown is the one that is most representative but may not be identical to all patterns represented in each branch of the relationship tree. Ery, erythromycin; Levo, levofloxacin; TMP/SMX, trimethoprim-sulfamethoxazole. *A total of 235 of the 296 isolates are listed; the remainder fall outside the listed clonal groups.

ciated infections (e.g., among Native Americans and children) and outbreaks (e.g., among sports teams and in prisons) were uncommon colonizers (figure 2) [5, 33, 34]. More than 40 years ago, carriage studies were performed in response to concerns about the emergence of penicillin-resistant *S. aureus*; in a summary of multiple studies, 6 phage types (including type 80/81) were responsible for 43% of all *S. aureus*-associated sepsis but made up only 16% of nasal-carrier strains [20]. A critical question is whether more-virulent strains are more likely to cause disease than are less-virulent strains of those that colonize persons [35]. Recent studies in children have suggested an increasing prevalence in localized pediatric populations; this could reflect an increase in the prevalence of specific (e.g., PVL gene-containing) strain types, which may or may not be observed uniformly in a national sample [26, 36, 37].

NHANES data may be useful for monitoring antimicrobial susceptibility. Although penicillin resistance now is widely prevalent, it is notable that, in unweighted analyses, a sizable minority of MSSA isolates in the present sample were susceptible to penicillin. No staphylococcal isolates were resistant to TMP/SMX or vancomycin, and resistance to rifampin and gentamicin

was unusual. Among MRSA isolates, no tetracycline resistance was noted in isolates with the SCC*mec* type II gene, and no clindamycin resistance was noted in isolates with the SCC*mec* type IV gene (data not shown). Similar differences in antimicrobial profiles between community- and health-care-associated MRSA isolates have been noted previously [29].

Rapid identification of nasal carriers harboring virulent strain types may indicate those at the highest risk for the development of disease, thus allowing targeted implementation of currently available and future interventions, including decolonization and vaccination. Although population-based strategies are unlikely to be effective, selective intervention may be considered if it can be limited to strains associated with increased virulence and an increased risk of infection, which may less commonly colonize [38, 39].

There are at least 5 main limitations to our analysis. First, we measured carriage prevalence in a cross-sectional design; thus, incidence was not measured, and participants were not serially cultured. It is likely that some participants were transiently colonized and, thus, had variable potential to develop infection [10]. At least one study has suggested that certain

strains have a predilection to cause either persistent, transient, or intermittent carriage [25]. It is possible that certain organism characteristics are associated with persistence or lack of carriage, skewing certain associations. Second, a cohort effect that would result in differences between demographic (e.g., age) groups is possible. Third, multiple effects on colonization, such as previous antimicrobial exposure, occupation, or certain underlying conditions (e.g., device use), were not analyzed, and these may have been confounding variables for MRSA colonization. Persons incarcerated, hospitalized, or institutionalized in long-term health-care facilities at the time of the survey were excluded. Fourth, these data were collected in 2001–2002, and colonization rates may have changed in the population since that time. Finally, because of relatively small sample sizes, associations may not have been detected, particularly for MRSA isolates. Because sample sizes were very small when MRSA colonization was examined, estimated SEs were unstable in many of the subgroups analyzed. Results of analyses in which weights were not used and adjustment was not made for the complex sample design (such as the organism-characteristic analyses) should not be considered generalizable to the US population.

In summary, *S. aureus* colonization is common in the US population but varies markedly with demographic characteristics, with the highest prevalence among young school-age children. MRSA carriage is relatively uncommon and is associated with age ≥ 60 years and being female. In unweighted analysis, the SCC_{mec} type IV gene appeared to be more prevalent in isolates with specific characteristics (e.g., PVL gene presence and decreased antimicrobial resistance) and were associated with isolate carriage in specific age and racial/ethnic groups. Continued national surveillance of *S. aureus* carriage will help to determine future trends in the characteristics of carriage and the potential effectiveness of targeted population-based intervention.

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References

- Lowy FD. *Staphylococcus aureus* infections. N Engl J Med **1998**;339:520–32.
- Skinner D, Keefer CS. Significance of bacteremia caused by *Staphylococcus aureus*. Arch Intern Med **1941**;68:851–75.
- Cosgrove SE, Sakoulas G, Perencevich EN, et al. Comparison of mortality associated with methicillin-resistant *Staphylococcus aureus* bacteremia: a meta-analysis. Clin Infect Dis **2003**;36:53–9.
- Herold B, Immergluck LC, Maranan MC, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* in children with no identified predisposing risk. JAMA **1998**;279:593–8.
- Centers for Disease Control and Prevention. Four pediatric deaths from community-acquired methicillin-resistant *Staphylococcus aureus*—Minnesota and North Dakota, 1997–1999. JAMA **1999**;282:1123–5.
- von Eiff C, Becker K, Machka K, et al. Nasal carriage as a source of *Staphylococcus aureus* bacteremia. N Engl J Med **2001**;344:11–16.
- Miles AA, Williams REO, Clayton-Cooper B. The carriage of *S. aureus* in man and its relation to wound infection. J Pathol Bacteriol **1944**;56:513–24.
- Williams REO. Skin and nose carriage of bacteriophage types of *Staph. aureus*. J Pathol Bacteriol **1946**;58:259–68.
- Gillespie EH, Devenish EA, Cowan ST. Pathogenic staphylococci: their incidence in the nose and on the skin. Lancet **1939**;2:870–3.
- Kluytmans J, Van Belkum A, Verbrugh H. Nasal carriage of *Staphylococcus aureus*: epidemiology, underlying mechanisms, and associated risks. Clin Micro Rev **1997**;10:505–20.
- Yu VL, Goetz A, Wagener M, et al. *Staphylococcus aureus* carriage and infection in patients on hemodialysis. N Engl J Med **1986**;315:91–6.
- Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey (NHANES) 1999–2002. Available at: <http://www.cdc.gov/nchs/about/major/nhanes/datalink.htm>. Accessed 25 November 2005.
- Shah BV, Barnwell BG, Bieler GS, La Vange LM. SUDAAN Software for the Statistical Analysis of Correlated Data: User's Manual, Release 7.0. Research Triangle Park, NC: Research Triangle Institute, **1996**.
- Zar JH. The arcsine transformation. In: Biostatistical analysis. Englewood Cliffs, NJ: Prentice-Hall, **1984**:239–41.
- NCCLS. Methods for disk diffusion: approved standard M2-A8: performance standards for antimicrobial disk susceptibility tests. Wayne, PA: NCCLS, **2003**.
- NCCLS. Approved standard M7-A4: methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. Wayne, PA: NCCLS, **1997**.
- Okuma K, Iwakawa K, Turnidge JD, et al. Dissemination of new methicillin-resistant *Staphylococcus aureus* clones in the community. J Clin Microbiol **2002**;40:4289–94.
- Ito T, Okuma K, Ma XX, Yuzawa H, Hiramatsu K. Insights on antibiotic resistance of *Staphylococcus aureus* from its whole genome: genomic island SCC. Drug Resist Updat **2003**;6:41–52.
- McDougal LK, Steward CD, Killgore GE, et al. Pulsed-field gel electrophoresis typing of oxacillin-resistant *Staphylococcus aureus* isolates from the United States: establishing a national database. J Clin Microbiol **2003**;41:5113–20.
- Williams REO. Healthy carriage of *Staphylococcus aureus*. Bacteriol Rev **1963**;27:56–71.
- Chapman HH, Berens C, Peters A, Curcio L. Coagulase and hemolysin tests as measures of the pathogenicity of staphylococci. J Bacteriol **1934**;28:343–63.
- Leman R, Alvarado-Ramy F, Pocock S, et al. Nasal carriage of methicillin-resistant *Staphylococcus aureus* in an American Indian population. Infect Control Hosp Epidemiol **2004**;25:121–5.
- Armstrong-Esther CA. Carriage patterns of *Staphylococcus aureus* in a healthy non-hospital population of adults and children. Ann Hum Biol **1976**;3:221–7.
- Millian SJ, Baldwin JN, Rheins MS, Weiser HH. Studies on the incidence of coagulase positive staphylococci in a normal unconfined population. Am J Pub Health **1960**;50:791–8.
- Eriksen NH. Carriage of *S. aureus* among healthy persons. Epidemiol Infect **1995**;115:51–60.
- Creech CB, Kernodle DS, Alsentzer A, Wilson C, Edwards KM. Increasing rates of nasal carriage of methicillin-resistant *Staphylococcus aureus* in healthy children. Pediatr Infect Dis J **2005**;24:617–21.
- Suggs AH, Maranan MC, Boyle-Vavra S, Duam RS. Methicillin-resistant and borderline methicillin-resistant asymptomatic *Staphylococcus aureus* colonization in children without identifiable risk factors. Pediatr Infect Dis J **1999**;18:410–4.
- Hussain FM, Boyle-Vavra S, Daum RS. Community-acquired methi-

- illin-resistant *Staphylococcus aureus* colonization in healthy children attending an outpatient pediatric clinic. *Pediatr Infect Dis J* **2001**; 20: 763–7.
29. Layton MC, Hierholzer WJ, Patterson JE. The evolving of methicillin-resistant *Staphylococcus aureus* at a university hospital. *Infect Control Hosp Epidemiol* **1995**; 16:12–7.
 30. Steinberg JP, Clark CC, Hackman BO. Nosocomial and community-acquired *Staphylococcus aureus* bacteremias from 1980 to 1993: impact of methicillin resistance. *Clin Infect Dis* **1996**; 23:255–9.
 31. Naimi TS, LeDell KH, Como-Sabetti K, et al. Comparison of community- and healthcare-associated methicillin-resistant *Staphylococcus aureus* infection. *JAMA* **2003**; 290:2976–84.
 32. Centers for Disease Control and Prevention. Community-associated methicillin-resistant *Staphylococcus aureus* infections in Pacific Islanders, 2001–2003. *MMWR Morb Mortal Wkly Rep* **2004**; 53:767–70.
 33. Centers for Disease Control and Prevention. Methicillin-resistant *Staphylococcus aureus* infections in correctional facilities—Georgia, California, and Texas, 2001–2003. *MMWR Morb Mortal Wkly Rep* **2003**; 52:992–6.
 34. Centers for Disease Control and Prevention. Methicillin-resistant *Staphylococcus aureus* infections among competitive sports participants—Colorado, Indiana, Pennsylvania, and Los Angeles County, 2000–2003. *MMWR Morb Mortal Wkly Rep* **2003**; 52:793–5.
 35. Fridkin SK, Hageman JC, Morrison M, et al. Methicillin-resistant *Staphylococcus aureus* disease in three communities. *N Engl J Med* **2005**; 352:1436–44.
 36. Kazakova SV, Hageman JC, Matava M, et al. A clone of methicillin-resistant *Staphylococcus aureus* among professional football players. *N Engl J Med* **2005**; 352:468–75.
 37. Pan ES, Diep BA, Charlebois ED, et al. Population dynamics of nasal strains of methicillin-resistant *Staphylococcus aureus*—and their relation to community-associated disease activity. *J Infect Dis* **2005**; 192: 811–8.
 38. Chambers HF 3rd, Winston LG. Mupirocin prophylaxis misses by a nose. *Ann Int Med* **2004**; 140:484–5.
 39. Ellis MW, Hospenthal DR, Dooley DP, Gray PJ, Murray CK. Natural history of community-acquired methicillin-resistant *Staphylococcus aureus* colonization and infection in soldiers. *Clin Infect Dis* **2004**; 39: 971–9.