Community-Acquired Methicillin-Resistant Staphylococcus aureus: A Meta-Analysis of Prevalence and Risk Factors

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Reports suggest that carriage of methicillin-resistant *Staphylococcus aureus* (MRSA) among persons without health care—associated risks has increased. A meta-analysis of studies reporting the prevalence of community-acquired MRSA (CA-MRSA) among MRSA isolates from hospitalized patients or the prevalence of MRSA colonization among community members was conducted. The CA-MRSA prevalence among hospital MRSA was 30.2% in 27 retrospective studies and 37.3% in 5 prospective studies; 85% of all patients with CA-MRSA had ≥1 health care—associated risk. The pooled MRSA colonization rate among community members was 1.3% (95% confidence interval [CI], 1.04%–1.53%), but there was significant heterogeneity among study populations. Community members from whom samples were obtained in health care facilities were more likely to be carrying MRSA than were community members from whom samples were obtained outside of the health care setting (relative risk, 2.35; 95% CI, 1.56–3.53). Among studies that excluded persons with health care contacts, the MRSA prevalence was 0.2%. Moreover, most persons with CA-MRSA had ≥1 health care—associated risk, which suggests that the prevalence of MRSA among persons without risks remains low (≤0.24%). Effective control of dissemination of MRSA throughout the community likely will require effective control of nosocomial MRSA transmission.

An infection in a hospitalized patient is usually categorized as either nosocomial or community acquired. "Nosocomial infection" has been defined as an infection that develops in the hospital and was not incubating at the time of admission [1]. A "community-acquired infection" is an infection that was present or incubating at the time of admission and was not caused by an organism acquired during previous health care.

Methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as an important pathogen among hospitalized patients. According to recent estimates from the

National Nosocomial Infection Surveillance System of the Centers for Disease Control and Prevention (CDC), the rate of methicillin resistance among *S. aureus* strains causing nosocomial infections in intensive care unit patients has approached 50% in US health care facilities [2]. A number of factors have been found to be associated with a higher risk for nosocomial acquisition of MRSA: prolonged hospitalization, care in an intensive care unit, prolonged antimicrobial therapy, surgical procedures, and close proximity to a patient in the hospital who is infected or colonized with MRSA [3, 4].

Recently, multiple studies have reported that the frequency with which MRSA are acquired in the community is increasing [5–11] and that this is occurring predominantly among persons without typical health care—associated risk factors for MRSA acquisition [5, 8–10]. The goals of the present meta-analysis were to document the prevalence of health care—associated risk factors among community members with MRSA in

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published reports and to document the prevalence of MRSA colonization in community settings among healthy persons who do not have health care—associated risk factors for acquisition. Studies reporting the rates of community-acquired MRSA (CA-MRSA) were reviewed to determine what definitions were used to classify isolates as CA-MRSA, what proportion of patients classified as having CA-MRSA had health care—associated risk factors for acquisition, and the prevalence of MRSA colonization in the community.

METHODS

Data acquisition. A literature search of the English-language MEDLINE database was conducted, and epidemiological studies were identified for the time period spanning January 1966 to February 2002. Keywords (and combinations thereof) used for searches of medical subject headings were "Staphylococcus aureus," "infection," "colonization," "methicillin resistance," "community-acquired," "community-onset," "prevalence," "frequency," and "risk factors." All citations were tracked until no new studies were identified, and the reference lists of relevant articles were reviewed, which also identified studies for inclusion. Finally, a search of abstracts from recent (1996-2001) scientific meetings was conducted, during which additional relevant studies for analysis were identified. Studies considered for inclusion in the meta-analysis were evaluated independently by 2 study investigators (C.D.S. and D.P.C.). Case reports were excluded.

Studies selected for inclusion were divided into 2 groups. The first group included studies that reported the prevalence of CA-MRSA among hospital patients who were colonized or infected with MRSA. The second group consisted of studies that reported the prevalence of MRSA colonization in the community.

Data extraction. Among studies that reported the prevalence of CA-MRSA among hospital patients with MRSA, the extracted data included the definition of CA-MRSA used in the study, the sample size, the number and type of risk factors assessed, and the number of patients with ≥ 1 health careassociated risk factor. Among studies that reported the prevalence of MRSA colonization in the community, the extracted data included sample size, the number and type of risk factors assessed, the number of patients with ≥ 1 risk factor, and the strain type (if reported).

Data pooling and statistical analysis. Because methodological differences can preclude combining some studies with others of the same topic, studies that reported the prevalence of CA-MRSA among hospital patients with MRSA were grouped according to epidemiological type (retrospective vs. prospective). The pooled prevalence of CA-MRSA was calculated for each group by adding up the number of isolates from patients classified as having CA-MRSA and dividing the num-

ber of patients classified as having CA-MRSA by the total number of patients with MRSA. Because no study of the prevalence of CA-MRSA among hospitalized patients provided the total number of patients for whom culture results were reported, the calculated prevalence of CA-MRSA was limited to the prevalence among patients with MRSA. The proportion of patients classified as having CA-MRSA who had ≥1 reported health care—associated risk factor was also calculated.

Studies reporting the prevalence of MRSA colonization in the community were grouped according to the community population being surveyed (e.g., a random community sample, a healthy clinic population, or contacts of individuals known to be colonized with MRSA). The pooled prevalence of MRSA colonization was calculated for each study population by dividing the number of MRSA-colonized subjects by the total number of subjects for whom culture results were reported. The proportion of persons in each community population with ≥1 reported risk factor was calculated, and for studies in which strain typing was performed, the proportion of CA-MRSA strains found to be typical nosocomial strains was also determined. χ^2 Analysis was used to compare proportions and to determine heterogeneity among studies to assess the appropriateness of pooling data (Epi Info 2000; CDC). $P \le .05$ was considered to be significant.

RESULTS

The initial MEDLINE search identified 104 studies. Forty-seven studies were excluded because they were case reports or did not report data on the prevalence of CA-MRSA among hospital patients with MRSA or the prevalence of MRSA colonization among healthy community members. Fifty-seven studies (54.8%) were included in the meta-analysis.

CA-MRSA among hospital patients with MRSA. two publications reported the prevalence of CA-MRSA among hospital patients with MRSA [5, 10, 12-41]. Community acquisition was determined using routine clinical specimens (rather than surveillance cultures done at the time of hospital admission). Twenty-seven of the studies were retrospective [5, 10, 17-41], and 6 different definitions of CA-MRSA were seen in 21 of these [5, 10, 17, 19-22, 24-32, 34, 37, 38, 40, 41]. Six retrospective studies did not report the definition used [18, 23, 33, 35, 36, 39]. Five publications were prospective studies, and 3 different definitions of CA-MRSA were used in this group [12–16]. Seven publications that focused on CA-MRSA among hospital patients with MRSA differed from the other 32 studies because they sought to identify risk factors among hospital patients who had already been classified as having CA-MRSA [8, 42-47]. Four different definitions of CA-MRSA were used in 5 of these studies [8, 42, 45-47], and 2 did not report the definition used [43, 44]. The more common definitions were

based on the timing of the isolation of MRSA in relation to the time of admission, with or without assessment of health care—associated risk factors (table 1).

Assessment of risk factors for MRSA acquisition included ≥1 of the following factors: recent hospitalization (range, 1–24 months before identification of MRSA infection or colonization), recent outpatient visit (usually within 12 months), recent nursing home admission (usually within 12 months), recent antibiotic exposure (range, 1–12 months), chronic illness (e.g., end-stage renal disease, diabetes, or malignancy), injection drug use, and close contact with a person with risk factor(s) for MRSA acquisition.

The pooled CA-MRSA prevalence among 5932 patients from 27 retrospective studies was 30.2% (range, 1.9%-96%). Seventeen of these studies investigated the presence of health care–associated risk factors among 4121 patients [5, 10, 17–19, 21, 22, 24, 25, 28, 30, 31, 34-37, 39]. Recent hospitalization and chronic illness requiring health care visits were the most common risk factors assessed among the patients included in these studies. The median number of risk factors studied was 2 (range, 1-6), and 86.1% of these patients had ≥ 1 health care-associated risk factor. The pooled CA-MRSA prevalence among 636 patients from the 5 prospective studies was 37.3% (range, 18.2%-51.2%). All of these studies investigated the presence of health care-associated risk factors [12-16]. The median number of risk factors studied was 4 (range, 2-4), and 86.9% of these patients had ≥1 health care-associated risk factor. Seven other studies sought to identify risk factors among hospital patients who had already been classified as having CA-MRSA; 84.7% of 515 patients had ≥1 risk factor for health care-related acquisition [8, 42-47].

MRSA in the community. Ten studies used surveillance cultures to report the prevalence of MRSA colonization among members of a community [9, 48-56] (table 2, figure 1). The pooled MRSA colonization prevalence among 8350 people was 1.3% (95% CI, 1.04%-1.53%; range, 0.2%-7.4%). Significant heterogeneity existed among the studies, which suggests that simple pooling of the data may not have been appropriate. Because of the heterogeneity among study populations, subgroup analyses were performed after stratification on the basis of methodological differences. In 9 of these studies, culture samples were obtained before assessment of risk factors [9, 48-55]. The pooled MRSA colonization prevalence among 4825 people was 2.1%. The median number of health care-associated risk factors evaluated was 5 (range, 1-10). At least 47.5% of those with MRSA had ≥1 health care-associated risk factor. The remaining study of 3525 people included only persons without prior health care contact and reported an MRSA colonization prevalence of 0.20% (table 2) [56]. Compared with the subjects in the other 9 studies, which did not exclude those

Table 1. Reported definitions of community-acquisition of methicillin-resistant *Staphylococcus aureus* (MRSA).

Definition	No. of studies using definition, reference(s)				
Isolated within 24 h of admission	1 [46]				
Isolated within 24 h of admission, with other exclusions	1 [10]				
Present at or within 48 h of admission	6 [19, 22, 24, 28, 30, 40]				
Isolated within 48 h of admission, with other exclusions	9 [8, 12, 14, 20, 21, 26, 27, 29, 38]				
Isolated within 48-72 h of admission	1 [47]				
Isolated within 72 h of admission	4 [5, 16, 32, 37]				
Isolated within 72 h of admission, with other exclusions	6 [17, 25, 34, 41, 42, 45]				
Patient from a community clinic/facility	3 [13, 15, 31]				
No definition reported	8 [18, 23, 33, 35, 36, 39, 43, 44]				

NOTE. Most common definitions reported were patient isolates identified within 48 h of hospital admission, with or without other exclusions, which often included recent admission to hospital or long-term care facility or previous history of MRSA colonization.

with a health care contact, these patients were 90% less likely to have MRSA (RR, 0.10; 95% CI, 0.05–0.21).

Seven of these 10 community studies obtained samples for surveillance cultures at the time of a hospital admission, an outpatient clinic visit, or an emergency department visit [9, 50-55]; samples were obtained from 3898 persons altogether. The pooled prevalence of MRSA colonization was 1.8%. Three studies that included 4452 people total were done outside of health care facilities (schools, day care centers, homeless shelters, and military bases) [48, 49, 56]. The pooled MRSA colonization prevalence was 0.76%. Patients from whom samples were obtained in health care facilities were 2.35 times more likely to carry MRSA than were community members from whom samples were obtained outside of the health care setting (95% CI, 1.56-3.53). One study included members of a semiclosed community and found a prevalence of MRSA colonization of 7.4% [49]. Compared with individuals who were not in a semiclosed community [48, 56], these persons were 36 times more likely to carry MRSA (95% CI, 13.7-94.7). Among the 70 MRSA isolates from people without identified health care-associated risk factors, 32 underwent strain typing, and 29 (91%) of those 32 were reported to be similar to strains found in local hospitals.

Four studies evaluated the colonization status of 191 household contacts of 93 patients discharged from the hospital with nosocomial MRSA colonization (figure 1) [57–60]. Of these contacts, 17.8% were found to be colonized with a strain of MRSA with the same antibiogram as the index case. Household contacts of MRSA-colonized patients [57–60] were 14 times more likely to be colonized than were general community mem-

Table 2. Studies reporting methicillin-resistant Staphylococcus aureus (MRSA) colonization in the community.

Study, reference	Year	Location	Sample size (study population)	No. (%) of subjects with <i>S. aureus</i>	No. (%) of subjects with MRSA	Proportion of MRSA-colonized subjects with risk factor, %					
						Recent hospitalization	Recent outpatient visit	Chronic illness	Recent antibiotic use	Injection drug use	Contact
Charlebois et al. [48]	2002	San Francisco	833 Adults (homeless and marginally housed)	190 (22.8)	23 (2.8) ^{a,b}	48	NA	NA	65	91	NA
Abudu et al. [50]	2001	Birmingham, UK	274 Adults (from general practice clinics list)	63 (23.0)	4 (1.5)	50	NA	NA	0	NA	NA
Hussain et al. [16]	2000	Chicago	500 Children (outpatient clinic attendees)	122 (24.4)	3 (0.6)	33 ^e	0	0	0	0	0
Shopsin et al. [52]	2000	New York	275 Children and 225 guardians (pediatric clinic attendees)	96 children (34.9) and 63 adults (28)	1 child (0.4) and 0 adults ^c	100	NA	NA	100	NA	NA
Eicher et al. [49]	2000	Minneapolis	94 Children (students)	34 (36.2)	7 (7.4)	NA	NA	NA	86	NA	NA
Muto et al. [54]	1999	Charlottesville, VA	816 Individuals (hospital admissions)	NA	8 (0.98)	67	NA	100	NA	NA	NA
Suggs et al. [51]	1999	Chicago	500 Children (emergency department attendees)	132 (26.4)	11 (2.2)	0	0	36	27	0	0
Kim et al. [53]	1998	Seoul, Korea	420 Children and 501 adults (outpatient clinic attendees)	190 children (45.2) and 98 adults (19.6)	28 children (6.7) and 4 adults (0.8) ^d	25 adults	0	NA	NA	NA	NA
Troillet et al. [55]	1998	Boston	387 Individuals (hospital admissions)	96 (24.8)	10 (2.6)	≥70	≥60	100	100	NA	NA
Sá-Leão et al. [56]	2001	Oeiras, Portugal	2111 Children and 1414 adults (day care atten- dees, Air Force person- nel, and students)	1001 (28.4)	7 (0.20) ^a						

NOTE. NA, not assessed.

 ^a Excluded subjects with previous hospital contact.
^b Two subjects with MRSA (0.24% of all subjects) had no identifiable risk factors.

^c Total, 1 subject (0.20%).

d Total, 32 subjects (3.5%).

^e A 2-week-old infant who was born in the hospital.

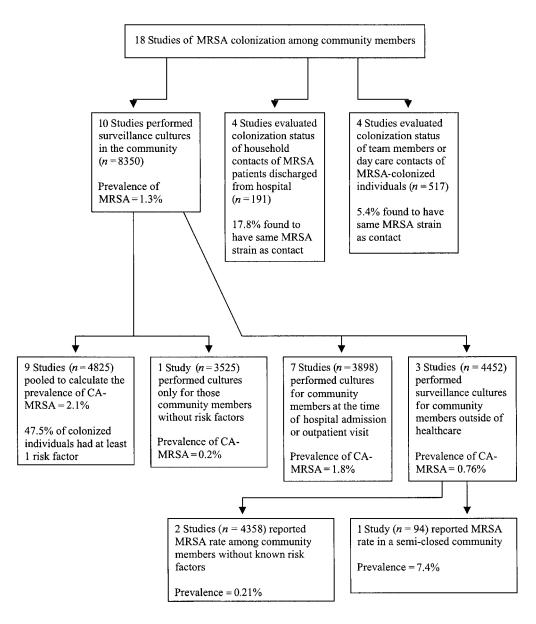


Figure 1. Studies of methicillin-resistant Staphylococcus aureus (MRSA) colonization in communities. CA, community acquired.

bers without a known MRSA contact (95% CI, 9.8–20.1) [9, 48–56]. Four additional studies evaluated the colonization status of 517 sports team members or day care contacts of persons known to be colonized with MRSA (figure 1) and found that 5.4% developed MRSA colonization with the same strain (either identified by antibiogram or pulsed-field gel electrophoresis) as the index case [61–64].

DISCUSSION

The 1999 report of 4 pediatric deaths resulting from CA-MRSA infection [65] resulted in greatly increased interest in this organism among health care providers and raised important questions about the prevalence and origin of CA-MRSA. The pur-

pose of this review was to summarize available data to help describe the epidemiology of MRSA in the community. Epidemiological investigations typically begin with the development of a case definition for the outcome of interest; however, a standard definition has not been created for CA-MRSA. In fact, this review revealed that at least 8 different definitions have been used to classify MRSA infections as community acquired. This could have contributed to heterogeneity among studies and limited the ability to simply pool data.

A majority of studies of CA-MRSA have assessed patients presenting for hospital admission for any reason, and relatively few studies having been conducted among randomly selected healthy members of the community. Most studies of hospitalized patients have used a time-based approach to distinguish

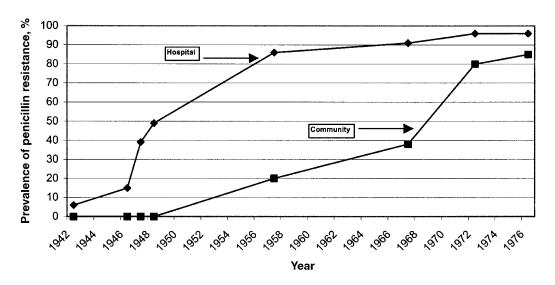


Figure 2. Prevalence of penicillin resistance among *Staphylococcus aureus* in hospitals and in communities, 1940–1974. The prevalence of hospital *S. aureus* strains resistant to penicillin rose dramatically from 1946 to 1958. Penicillin-resistant community-acquired strains of *S. aureus* were not reported until 1949, when the rate of penicillin resistance in hospitals approached 50%. The prevalence of penicillin-resistant *S. aureus* in communities continued to increase throughout the ensuing 20 years, finally approaching the resistance rates seen among hospital strains. Adapted from [68].

between community-acquired and nosocomial infections (e.g., infections present on admission or diagnosed within 48-72 h of admission were considered to be community acquired). This approach has limited utility, however, in the evaluation of staphylococcal infections. MRSA colonization can persist for months to years [3, 66], and 1 study reported an estimated half-life of MRSA colonization of 40 months among patients known to be colonized with MRSA who were admitted to a university hospital [66]. The majority of colonized patients remain completely asymptomatic. Therefore, acquisition of MRSA, whether it occurs in the hospital or in the community, frequently goes unrecognized unless clinical infection develops. Given the duration for which colonization with MRSA can persist, an infection may develop in a setting different from that in which the organism was initially acquired. Thus, in the absence of more epidemiological data, such as the results of surveillance cultures documenting time of acquisition, the true site of acquisition of MRSA is rarely known with certainty. The commonly used term "CA-MRSA" implies that it is known that the organism was acquired in the community. It appears, however, that this term is often used to refer to the detection of colonization or infection in the community, rather than to actual acquisition of MRSA in the community.

These considerations make an assessment of the presence of risk factors known to be associated with the acquisition of MRSA important before classification of an MRSA isolate as community acquired. The present analysis found that, when even minimal risk factor assessment was done, at least 85% of hospital patients who met the time-based definition for CAMRSA and 47.5% of healthy community members found to

be colonized with MRSA had ≥1 health care-associated risk factor for acquisition. This suggests that the prevalence of MRSA among persons without typical risk factors remains relatively low (i.e., ≤0.24%) and that most MRSA colonization and infection develops among those who have health care-associated risk factors or contact with other persons who have such risks. When patients known to be colonized with nosocomial MRSA are discharged from the hospital or nursing home into the community, spread to family members or other close contacts can occur [59]. The much larger population of colonized patients with nosocomial acquisition who were never recognized as such while in the hospital or nursing home likely contributes to the spread of MRSA in this manner. Therefore, the best way to control MRSA within the community may be, paradoxically, to control MRSA within all aspects of the health care setting.

The evolving epidemiology of MRSA could be compared with what has been described for penicillin-resistant *S. aureus*. Penicillin was introduced in 1941, and resistant *S. aureus* strains appeared in 1944 [67]. Initially, these resistant strains were associated with nosocomial infections, but dissemination into the community subsequently followed, seemingly at a time when the rate of penicillin resistance among hospital patients with staphylococcal infections approached 50% (figure 2) [68]. Because the current rate of methicillin resistance among intensive care unit patients with staphylococcal infections appears to be approaching 50% [2], better control of MRSA within the health care setting may be necessary to prevent dissemination of MRSA throughout the community.

This is not meant to imply that development of methicillin

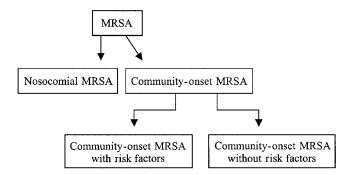


Figure 3. Proposed schematic to classify methicillin-resistant *Staphylococcus aureus* (MRSA) isolates as nosocomial or community-onset strains among individuals with and individuals without health careassociated risk factors.

resistance among staphylococci by acquisition of the mecA gene does not occur in the community, even though molecular epidemiological studies have suggested that this occurs only very rarely in any setting [69, 70]. In fact, it is likely that the majority of such genetic events have always occurred in this setting, rather than among hospitalized patients, simply because of the relative sizes of the groups. Approximately one-third of the general population is colonized with S. aureus, but only ~35 million (12%) of the 281 million people living in the United States are admitted to the hospital each year. Thus, only a small minority of the total population, and presumably of the staphylococci-colonized population, are hospitalized at any given time. The estimated annual number of person-days of S. aureus colonization is, therefore, 733-fold larger in the community than in the hospital (36.9 billion vs. 50.4 million, respectively). Simple probability, therefore, would suggest that most staphylococcal strains that acquire the mecA gene have probably done so in the community. Nevertheless, the high prevalence of antibiotic therapy in the health care environment offers selective pressure for survival, proliferation, and spread of resistant strains, which results in amplification of any MRSA strain that arrives there, regardless of its place of origin.

There also have been several reports of MRSA colonization rates as high as 42% among members of "closed populations," such as Canadian and Australian aboriginal communities and Pacific Islanders [71–73]. Extensive risk factor analysis has not been done among these populations; however, these higher rates of CA-MRSA may be associated with risk factors for spread in the community, such as overcrowding, high rates of skin infections, and frequent use of broad-spectrum antibiotics [74]. One recent study reported an increase in CA-MRSA in Minnesota, mostly involving Native Americans [38]. The study was not population based, so a prevalence could not be reported, but the patients were generally described as young and healthy, without hospitalization, surgery, dialysis, or residence in a long-term care

facility in the previous year. Antibiotic therapy and health care use in outpatient clinics were not investigated as risk factors, but the vast majority of isolates were clonal, which suggests that spread was through transmission, rather than frequent de novo development of methicillin resistance.

This review and meta-analysis has identified several limitations of the current data on CA-MRSA. Well-designed community-based studies that include adequate risk factor analysis would be helpful to further elucidate the epidemiology of MRSA as it occurs in the community. Selection of clinic attendees or patients admitted to the hospital for study appears to result in overestimation of the true MRSA colonization rate among healthy community members. Use of consistent terminology will be important in future investigations. The term "community-onset" MRSA (CO-MRSA), which simply describes the patient's location at the time of identification of MRSA, would be more technically correct than the currently used "CA-MRSA," which implies that the site of MRSA acquisition is known. When a patient with nosocomially acquired MRSA spreads the organism to multiple members of the patient's household or community, this should not be called "community acquisition." Subsequent evaluation of common risk factors could be done to further classify isolates as "CO-MRSA in a patient with risk factors" or "CO-MRSA in a patient without risk factors" (figure 3). Major risk factors for CO-MRSA appear to be those already identified as risk factors for nosocomial MRSA, which suggests that the increase in CO-MRSA among non-hospitalized patients is, in large part, due to the introduction of health care-associated strains into the community.

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