Duration of Colonization and Determinants of Earlier Clearance of Colonization With Methicillin-Resistant *Staphylococcus aureus*

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(See the Editorial Commentary by Calderwood on pages 1497–9.)

Background. The duration of colonization and factors associated with clearance of methicillin-resistant *Staphylococcus aureus* (MRSA) after community-onset MRSA skin and soft-tissue infection (SSTI) remain unclear.

Methods. We conducted a prospective cohort study of patients with acute MRSA SSTI presenting to 5 adult and pediatric academic hospitals from 1 January 2010 through 31 December 2012. Index patients and household members performed self-sampling for MRSA colonization every 2 weeks for 6 months. Clearance of colonization was defined as negative MRSA surveillance cultures during 2 consecutive sampling periods. A Cox proportional hazards regression model was developed to identify determinants of clearance of colonization.

Results. Two hundred forty-three index patients were included. The median duration of MRSA colonization after SSTI diagnosis was 21 days (95% confidence interval [CI], 19–24), and 19.8% never cleared colonization. Treatment of the SSTI with clindamycin was associated with earlier clearance (hazard ratio [HR], 1.72; 95% CI, 1.28–2.30; $P < .001$). Older age (HR, 0.99; 95% CI, .98–1.00; $P = .01$) was associated with longer duration of colonization. There was a borderline significant association between increased number of household members colonized with MRSA and later clearance of colonization in the index patient (HR, 0.85; 95% CI, .71–1.01; $P = .06$).

Conclusions. With a systematic, regular sampling protocol, duration of MRSA colonization was noted to be shorter than previously reported, although 19.8% of patients remained colonized at 6 months. The association between clindamycin and shorter duration of colonization after MRSA SSTI suggests a possible role for the antibiotic selected for treatment of MRSA infection.

Keywords. methicillin-resistant *Staphylococcus aureus* (MRSA); MRSA colonization; MRSA skin and soft-tissue infection; MRSA decolonization.

Staphylococcus aureus is one of the most common causes of infection in community and healthcare settings [1]. Historically, infection with methicillin-resistant *S. aureus* (MRSA) has been restricted almost exclusively to hospitalized and chronically ill patients [2]. However, recently, MRSA infections have been increasingly reported in the community [3].

The prevalence of MRSA colonization in the community is estimated at between 0.2% and 7.4% [3], but rates as high as 67% have been reported in household members of patients with recent MRSA infection [4, 5]. Household interactions may influence the duration of MRSA colonization, presumably in relation to the frequency and duration of exposure [6]. Failure to identify and interrupt colonization within the household may serve as a barrier to preventing persistent colonization or repeated infections [7, 8].

Prior studies have estimated that duration of MRSA colonization in the community ranges from 6 to 9 months [9, 10]. However, the populations studied were not representative of the typical community-dwelling patient with MRSA skin and soft-tissue infection (SSTI) in the United States. In addition, factors associated with clearance of MRSA colonization in the community remain unclear. Therefore, we sought to determine the duration of MRSA colonization and determinants of clearance of colonization in ambulatory patients presenting with an acute MRSA SSTI.

METHODS

Study Design and Study Subjects

We conducted a prospective cohort study between 1 January 2010 and 31 December 2012 at 5 academic medical centers: The Hospital of the University of Pennsylvania, a 782-bed urban adult acute care hospital; Penn Presbyterian Medical Center, a 300-bed urban adult acute care hospital; Pennsylvania Hospital, a 500-bed urban adult community hospital; Children's Hospital of Philadelphia, a 535-bed urban children's hospital; and Penn State Milton S. Hershey Medical Center, a 551-bed urban adult and pediatric hospital. Adults and children presenting to the emergency departments and primary care settings at any of the study sites with an acute SSTI for which a sample was sent for microbiologic culture were approached for entry. Hospitalized patients were approached if an acute SSTI was identified and a lesion swab sample was sent for culture within 48 hours of admission. Eligible subjects were those whose culture subsequently revealed MRSA. To be enrolled, a study subject (ie, index patient) and all members of his or her household were required to agree to participate. Informed consent or assent was obtained from all index patients and household members. This study was approved by the institutional review boards of all participating institutions.

Longitudinal Follow-up and Data Collection

Index patients and household members performed self-sampling for MRSA from 3 anatomic sites (nares, axillae, and groin) every 2 weeks for 6 months from enrollment to assess for MRSA colonization, for a total of 14 potential sampling periods. Self-collection of swabs has proved highly sensitive compared with those collected by research staff [11]. Multiple anatomic sites were chosen to maximize the sensitivity of detection of MRSA colonization [11–13]. Previous studies have shown that the throat [14] and rectum [15] are also sites of MRSA colonization, but self-sampling of these sites was considered infeasible. The ESwab System (Copan Diagnostics) was used for sample collections. Subjects obtained specimens by placing a single swab in both nares and then placing a second swab in both axillae followed by the groin. If the initial skin lesion was present, that site was sampled with a third swab. Subjects then mailed swabs to the study laboratory. At the initial household visit, research staff demonstrated the sampling method. Parents or guardians were instructed to perform the sampling for children, if necessary

Demographic data, medical history, including comorbid conditions and medications, number of persons in the household, and antibiotic use were collected via self-report at the initial home interview and updates requested at each sampling period. These data were confirmed or expanded with medical record review, including prescription records.

Laboratory Testing

Swab samples were plated on BBL ChromAgar MRSA (BD) medium and processed according to manufacturer's instructions [16]. Testing for in vitro susceptibility of *S. aureus* to oxacillin, penicillin, erythromycin, clindamycin, levofloxacin, chloramphenicol, gentamicin, trimethoprim-sulfamethoxazole, rifampin, and vancomycin was performed using the Vitek 2 automated identification and susceptibility testing system with the Advanced Expert System (bioMerieux) and interpreted according to established criteria [17]. Isolates that were erythromycin resistant but clindamycin susceptible were tested for inducible macrolide-lincosamide-streptogramin resistance by the disk diffusion method (D-test) [17].

Data Analysis

Only index patients who returned samples for at least the first 2 consecutive sampling periods were included in analyses. Subjects were assumed to be colonized at the time of infection [18]. Index patients were censored at clearance of MRSA colonization or at the end of follow-up, whichever came first. Clearance of colonization was defined as 2 consecutive sampling periods with no positive MRSA surveillance cultures; the clearance date was identified as the midpoint between the date of the last positive surveillance culture and that of the first negative culture. The median duration of colonization was determined using a Kaplan–Meier estimate. In a second, exploratory analysis, we included only those index patients with ≥1 positive swab sample during the initial 2 visits.
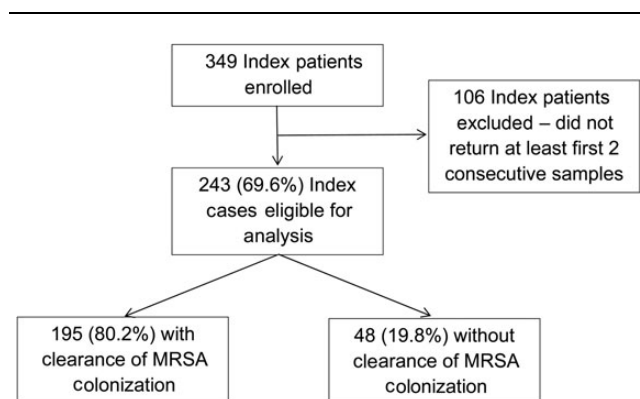
Antibiotic exposure in the index patient was assessed in 4 time periods: the year before diagnosis of SSTI (pretreatment), the 14 days after diagnosis (treatment), and day 15 after

enrollment through the end of follow-up (posttreatment). Antibiotic use in the 14 days before diagnosis was not included because this was assumed to be empiric treatment for the SSTI. The presence of colonization in household members was analyzed in 2 ways: colonization at baseline (ie, first sampling period) and colonization status at each sampling period (treated as a time-varying covariate). Three measures of household member MRSA colonization were defined: ≥1 household member positive, number of household members positive, and proportion of household members positive. Bivariable and multivariable analyses were performed using Cox proportional hazards regression analysis. Multivariable models were developed to determine the association between factors and clearance of MRSA colonization in index patients. Variables were included in the model if they were associated with time to clearance at bivariable analysis (*P* value ≤.20) [19], and they were maintained in the final model if they remained significantly associated with the outcome when manual backward deletion was used. Age and number of household members with MRSA colonization at each sampling period (time-varying covariate) were identified a priori as potential important factors and so were maintained in the model. A hazard ratio (HR) and 95% confidence interval (CI) were calculated to evaluate the strength of associations.

For all calculations, differences were considered significant at *P* < .05 (2 tailed). Statistical calculations were performed using commercially available software (SAS 9.3; SAS Institute).

RESULTS

A total of 349 households provided informed consent. Of these, 243 index patients (69.6%) returned samples for the first 2 sampling periods (permitting a calculation of duration of colonization) and were included in the analysis (Figure 1). The only significant difference between included and excluded subjects was the proportion of white subjects (42.8% of included subjects
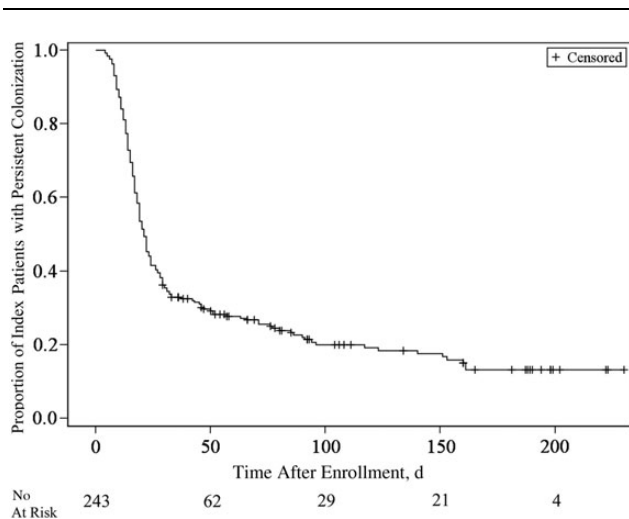
vs 26.4% of excluded subjects; *P* = .004). The 243 households included 803 household members. The median duration of follow-up for index patients and household members was 156 days (interquartile range [IQR], 70–193 days) and 171 days (103–193 days), respectively. Household sampling was completed for a median of 10 episodes (IQR 5–14).

The median age of index patients was 18.9 years (IQR, 3.9–44.4 years), and 152 (62.6%) were female. The median age of household members was 21.9 years (IQR, 8.7–36.5 years), and included 451 (56.2%) females. Fifty-three (29.1%) of the index patients reported a history of prior MRSA infection; however, 61 (25.1%) did not respond to this question.

Antibiotic treatment for the SSTI was prescribed to 223 index patients (91.8%) , most commonly clindamycin (110 subjects; 45.3%) and trimethoprim-sulfamethoxazole (105 subjects; 43.2%). Complete antibiotic susceptibility data were available for 190 patients (85.2%), revealing that 176 (92.6%) received an antibiotic to which the organism was susceptible. Approximately 20% of subjects received a prescription at initial presentation for an intervention to eradicate colonization: 53 (21.8%) were prescribed topical nasal mupirocin, and 47 (19.3%) were prescribed bleach baths/body wipes or chlorhexidine. Prescription of mupirocin and chlorhexidine/bleach baths did not differ significantly between those who reported prior MRSA infection and those who did not (*P* = .97 and *P* = .57, respectively).

Figure 2 shows the Kaplan–Meier curve of MRSA colonization over time. The median duration of colonization was 21 days (95% CI, 19–24 days). Forty-eight (19.8%) of the index patients remained colonized at the end of the study. If only index patients with MRSA colonization confirmed at the first sampling period were analyzed (89 patients; 36.6%), the duration

Figure 1. Flow chart for study subjects. Abbreviation: MRSA, methicillin-resistant *Staphylococcus aureus*.

Figure 2. Kaplan–Meier curve of duration of colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) after diagnosis and treatment of MRSA skin and soft-tissue infection.
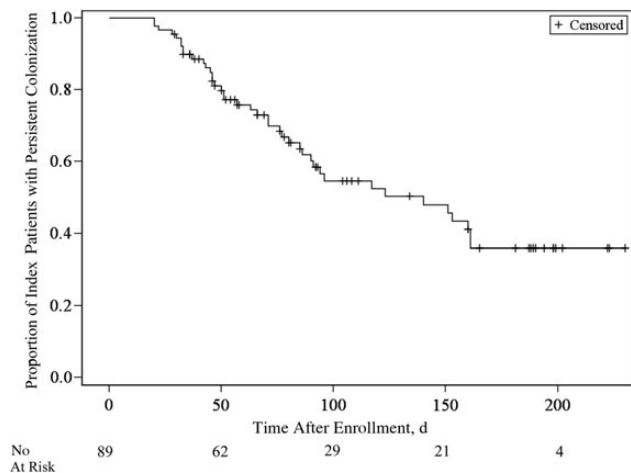
Figure 3. Kaplan–Meier curve of duration of colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) after confirmation of MRSA carriage.

of MRSA colonization was longer, with a median of 140 days (95% CI, 86–161 days) (Figure 3).

In bivariable analyses (Table 1), subjects with later clearance of MRSA colonization were more likely to be older, be white, have a higher proportion of household members <18 years old, or have a diagnosis of diabetes mellitus, cancer, or prior MRSA infection. Table 2 shows the unadjusted associations between duration of MRSA colonization and drug prescriptions in 3 discrete time periods. Prescription of clindamycin in the 14 days after diagnosis was associated with earlier clearance of colonization. Clindamycin was more commonly prescribed in index patients <18 years old ($P < .001$). Exposure to any antibiotics from day 15 after enrollment to the end of follow-up was associated with later clearance of colonization. Receipt of mupirocin or chlorhexidine/bleach baths or wipes after SSTI diagnosis had no association with the duration of MRSA colonization.

In multivariable analyses (Table 3), treatment with clindamycin in the 14 days after diagnosis was associated with earlier clearance of MRSA colonization in the index patient (HR, 1.7; 95% CI, 1.27–1.30; $P < .001$). Conversely, age (HR, 0.99; 95% CI, .98–1.00; $P = .004$) was associated with longer duration of colonization. Given that index patients <18 years old were more likely to receive clindamycin, we looked for effect modification of treatment with clindamycin by age and found no significant interaction ($P = .79$). Although white race was significantly associated with longer duration of colonization, we found that it had significant correlation with cancer (Pearson's correlation coefficient, 0.252; $P < .001$). Based on biologic plausibility, cancer was maintained in the final model. The point estimate for increased number of household members colonized with MRSA reflects a borderline association with later clearance

Table 1. Unadjusted Hazard Ratios for Clearance of MRSA Colonization by Baseline Characteristics

Characteristic	Index Patients, No (%)[a]	HR (95% CI)	P Value
Age, mean (SD), y	25.9 (23.3)	0.99 (.98–.99)	<.001
Age group, y			
<18	119 (49.0)	1.00 (Reference)	Reference
18–44	65 (26.8)	0.68 (.49–.96)	.03
45–65	42 (17.3)	0.53 (.35–.80)	.002
>65	17 (7.0)	0.68 (.20–.70)	.002
Proportion of household members aged <18 y	. . .	1.01 (1.00–1.01)	.02
Female sex	152 (62.6)	1.26 (.94–1.69)	.12
Race			
White	104 (42.8)	0.61 (.46–.83)	.001
Nonwhite	139 (57.2)	1.00 (Reference)	Reference
Black/African American	123 (50.6)	. . .	. . .
Hispanic	3 (1.2)	. . .	. . .
Asian	3 (1.2)	. . .	. . .
Mixed/other	5 (2.1)	. . .	. . .
Refused to answer	5 (2.1)	. . .	. . .
Enrollment site			
HUP	64 (26.3)	1.00 (Reference)	Reference
CHOP	105 (43.2)	1.95 (1.37–2.79)	<.001
HMC	38 (15.6)	1.08 (.68–1.71)	.75
PPMC	34 (12.5)	1.19 (.73–1.93)	.49
PAH	5 (2.1)	0.86 (.27–2.76)	.80
Medical setting			
Emergency department	167 (68.7)	1.00 (Reference)	Reference
Primary care	61 (25.1)	0.92 (.66–1.26)	.59
Inpatient	15 (6.2)	0.76 (.42–1.37)	.36
Comorbid condition[b]			
Hepatic dysfunction	12 (5.0)	0.76 (.39–1.49)	.42
Renal dysfunction	6 (2.5)	0.28 (.07–1.13)	.07
Diabetes mellitus	24 (9.9)	0.52 (.30–.88)	.01
Cancer	18 (6.2)	0.35 (.17–.72)	.004
Organ transplant	4 (1.7)	0.43 (.11–1.73)	.23
Prior MRSA infection[c]	53 (29.1)	0.58 (.40–.83)	.003
Household size, No. of persons			
1	23 (9.5)	1.00 (Reference)	Reference
2	32 (13.2)	0.72 (.38–1.37)	.32
3	41 (16.9)	1.15 (.65–2.05)	.63
4	51 (21.0)	1.42 (.82–2.45)	.21
5	38 (15.6)	1.02 (.57–1.84)	.95
>5	58 (23.9)	1.40 (.82–2.40)	.22

Abbreviations: CHOP, Children's Hospital of Philadelphia; CI, confidence interval; HMC, Penn State Milton S. Hershey Medical Center; HR, hazard ratio; HUP, Hospital of the University of Pennsylvania; MRSA, methicillin-resistant *Staphylococcus aureus*; PAH, Pennsylvania Hospital; PPMC, Penn Presbyterian Medical Center; SD, standard deviation.

[a] Data represent No. (%) unless otherwise specified.

[b] Proportion calculated using available data (available for 242 index patients).

[c] Proportion calculated using available data (available for 182 index patients).

Table 2. Unadjusted Hazard Ratios for Clearance of MRSA Colonization by Drug Treatment

Treatment by Period[a]	Index Cases, No. (%)	HR (95% CI)	P Value
Pretreatment period			
Any antibiotic	39 (16.1)	0.79 (.53–.17)	.23
Amoxicillin	12 (4.9)	1.11 (.59–2.10)	.74
Amoxicillin-clavulanate	7 (2.9)	0.73 (.30–1.78)	.49
Azithromycin	5 (2.1)	0.33 (008–1.34)	.12
Cephalexin	3 (1.2)	4.24 (1.34–13.44)	.01
Clindamycin	9 (3.7)	1.36 (.70–2.65)	.37
Doxycycline	2 (0.8)	0.78 (.19–3.16)	.73
Trimethoprim-sulfamethoxazole	10 (4.1)	1.06 (.52–2.14)	.880
Mupirocin	3 (1.2)	0.19 (.03–1.34)	.10
Bleach bath/chlorhexidine	1 (0.4)	0.00 (0–∞)	.98
Treatment period			
Any antibiotic	223 (91.8)	1.01 (.99–1.03)	.34
Amoxicillin-clavulanate	11 (4.5)	0.94 (.48–1.84)	.86
Cephalexin	15 (6.2)	0.87 (.47 1.60)	.65
Clindamycin	110 (45.3)	1.95 (1.46–2.59)	<.001
Doxycycline	13 (5.4)	0.67 (.36–1.28)	.23
Levofloxacin	4 (1.7)	0.48 (.15–1.50)	.21
Trimethoprim-sulfamethoxazole	105 (43.2)	0.84 (.63–1.12)	.24
Mupirocin	53 (21.8)	0.93 (.65–1.32)	.68
Bleach bath/chlorhexidine	47 (19.3)	0.81 (.56–1.18)	.28
Nasal steroid	12 (4.9)	0.85 (.44–1.66)	.64
Posttreatment period			
Any antibiotic	42 (17.3)	0.53 (.36–.80)	.002
Clindamycin	9 (3.7)	0.89 (.44–1.81)	.75
Doxycycline	6 (2.5)	0.57 (.23–1.39)	.21
Levofloxacin	4 (1.7)	0.26 (.06–1.06)	.06
Trimethoprim-sulfamethoxazole	16 (6.6)	0.53 (.28–1.01)	.05
Mupirocin	8 (3.3)	0.41 (.15–1.09)	.07
Bleach bath/chlorhexidine	6 (2.5)	0.17 (.02–1.23)	.08
Nasal steroid	13 (5.4)	0.76 (.39–1.48)	.42

Abbreviations: CI, confidence interval; HR, hazard ratio; MRSA, methicillin-resistant *Staphylococcus aureus*.

[a] The pretreatment period was defined as the year before study enrollment, not including the 14 days prior diagnosis of skin and soft-tissue infection (SSTI); the treatment period, the 14 days after diagnosis of MRSA SSTI; and the posttreatment period, from 15 days after diagnosis of MRSA SSTI until the end of follow-up.

Table 3. Multivariable Cox Proportional Hazards Regression Model of Variables Associated With Clearance of MRSA Colonization

Variable	HR (95% CI)	P Value
Treatment with clindamycin	1.72 (1.28–2.30)	<.001
Age[a]	0.99 (.98–1.00)	.010
Cancer	0.54 (.26–1.15)	.112
No. of household members colonized with MRSA[a]	0.85 (.71–1.01)	.064

Abbreviations: CI, confidence interval; HR, hazard ratio; MRSA, methicillin-resistant *Staphylococcus aureus*.

[a] HRs for these variables represent hazards for each unit increase.

patient using the various measures of colonization status (Table 4).

DISCUSSION

We found that the median duration of MRSA colonization after diagnosis of SSTI was 21 days, but a significant proportion of subjects (19.8%) remained colonized at the end of the study. Treatment with clindamycin was the only factor associated with earlier clearance of colonization, whereas increased age was associated with longer duration of colonization. Presence of household members colonized with MRSA, household size, or use of mupirocin or chlorhexidine were not associated with duration of colonization.

The median duration of MRSA colonization is shorter than reported in prior studies [20–23]. However, most prior studies calculated duration of colonization according to colonization status at hospital readmission [20, 21, 23] rather than via systematic, longitudinal sampling, which precludes the precise measurement of duration of colonization. Moreover, studies conducted in the community setting included only subjects with confirmed MRSA carriage at study onset, whereas ours examined duration after diagnosis and treatment of MRSA SSTI. Two studies have followed up subjects longitudinally with regular sampling to determine MRSA colonization. Eveillard and colleagues [22] followed up healthcare workers colonized with MRSA, determining colonization status every 3 weeks until clearance or for 6 months, and they found a median duration of MRSA colonization of 83 days. Lucet et al [9] followed up subjects colonized with MRSA discharged from the hospital, checked for MRSA colonization every 3 months, and found a median duration of colonization of 282 days. A third study conducted by Larsson and colleagues [10] in Sweden, where MRSA infections are publicly reported and serial sampling for MRSA colonization is performed until clearance, revealed that the median duration of MRSA colonization was 179 days; however, these authors noted substantial variability, and 43% of subjects were colonized for <2 months.

(HR, 0.85; 95% CI, .71–1.01; P = .06). Exclusion of subjects who received an antibiotic regimen to which their infection was not susceptible did not change the findings (data not shown). The presence of colonization in household members, at baseline and at each sampling period, after adjustment for age, cancer, and treatment with clindamycin, was not significantly associated with time to clearance of MRSA colonization in the index

Table 4. Unadjusted and Adjusted HRs for Clearance of MRSA Colonization in Household Members at Baseline and at Each Sampling Period

Variable	No. (%) or Mean (SD)	Duration of Colonization, Median (IQR), d	HR (95% CI)	P Value (Unadjusted)	aHR (95% CI)	P Value (Adjusted)
Baseline findings						
Patients with no household members colonized, No. (%)	154 (63.4)	20.5 (18–23)	1.00 (Reference)	Reference	1.00 (Reference)	Reference
Patients with ≥1 household member colonized, No. (%)	89 (36.6)	22 (18–30)	0.89 (.67–1.20)	.452	0.81 (.60–1.09)	.16
Proportion of household members colonized, mean (SD), %[a]	15.1 (25.5)	...	0.99 (.99–1.00)	.044	1.00 (.99–1.00)	.09
Household members colonized, mean (SD), No.[b]	0.54 (0.89)	...	0.88 (.74–1.04)	.123	0.84 (.71–1.00)	.06
Findings at each sampling period[c]						
≥1 household member colonized	...	...	0.87 (.65–1.17)	.355	0.78 (.58–1.05)	.10
Proportion of household members colonized[a]	...	...	0.99 (.99–1.00)	.056	1.00 (.99–1.00)	.09
No. of household members colonized[b,d]	...	...	0.89 (.75–1.05)	.167	0.85 (.71–1.01)	.06

Abbreviations: aHR, adjusted hazard ratio (adjusted for age, cancer, and treatment with clindamycin); CI, confidence interval; HR, hazard ratio; IQR, interquartile range; MRSA, methicillin-resistant *Staphylococcus aureus*; SD, standard deviation.

[a] HRs represent hazards of clearance for each 1% increase in household members colonized.

[b] HRs represent hazards of clearance for each 1-unit increase in household members colonized.

[c] Treated as time-varying covariates.

[d] Primary measure used in analysis.

These variable findings demonstrate the important effects of different study methods and populations. Indeed, when we included only subjects with confirmed MRSA colonization at the first sampling period after SSTI treatment, we found a median duration of colonization of 140 days. Our findings reveal the potential effect of treatment for MRSA SSTI on the duration of colonization, which more accurately reflects the clinical situation ambulatory providers typically encounter. In our study, 19.8% of subjects remained colonized at the end of sampling. This finding is similar to those seen in hospitalized patients, where 21%–40% of subjects had persistent colonization [20, 21]. Future studies should attempt to better identify this subset of subjects with persistent colonization to better target decolonization efforts.

Prescription of clindamycin in the 14 days after SSTI diagnosis was associated with earlier MRSA clearance. The vast majority of subjects received antibiotics to which the MRSA isolate was susceptible. Clindamycin was not associated with duration of colonization in the other time periods, but the proportion of index patients who were prescribed clindamycin during these time periods was small (3.7%), limiting the ability to demonstrate a significant association. A previous study showed that treatment of SSTI with antibiotics was associated with shorter duration of MRSA colonization [10].

To our knowledge, ours is the first study to identify the role of specific antibiotics on duration of colonization. Clindamycin has been used as a component of MRSA decolonization bundles owing to its activity against MRSA, with eradication rates of up to 90% [24, 25]. Doxycycline [25, 26] and trimethoprim-sulfamethoxazole [25] have also been studied as part of combination antibiotic treatment for MRSA colonization eradication. These antibiotics were not associated with earlier clearance of colonization in our study, however. The association between clindamycin and more rapid clearance remains unclear. No studies show higher concentrations of clindamycin in specific anatomic sites; in fact, both clindamycin and trimethoprim-sulfamethoxazole both achieve excellent tissue penetration in treatment of MRSA SSTI [27]. It is possible that clindamycin has a differential effect on the skin microbiome. Further studies to explain the association between clindamycin and more rapid clearance of colonization and a randomized controlled trial of clindamycin as part of a decolonization protocol may be warranted. Interestingly, receipt of agents used for decolonization (ie, topical mupirocin, bleach baths, or chlorhexidine) was not associated with duration of colonization in our study. Compliance with these measures was not determined, however, and prescription of these drugs may have been given to patients with a perceived higher risk of recurrence.

Increased age was associated with later clearance of MRSA colonization, with a 1% increase in hazards for each year of age. Several studies have found conflicting results in regard to

the association between age and acquisition and duration of MRSA colonization. Lucet et al [9] determined that older age was a risk factor for both acquisition and transmission of MRSA, whereas Larsson and colleagues [10] found that younger community-dwelling subjects had longer duration of MRSA colonization. The association between age and MRSA colonization needs to be further studied in large populations of community-dwelling adults and children.

There was a borderline significant association between increased numbers of household members with MRSA colonization and longer duration of colonization. The optimal way to measure colonization in household members is unknown. We used several measures and found that increased numbers of colonized household members (at baseline or at each sampling period) yielded the strongest associations with longer duration of colonization, suggesting that an association probably does exist. Interestingly, household size was not associated with prolonged duration of MRSA colonization. It is possible that the more important factor is presence of a colonized household member rather than the "crowding" factor. Prior studies have shown that increased "colonization pressure" (ie, the proportion of patients colonized in a given time period) in hospital units increased the rate of MRSA transmission among hospitalized patients [28, 29]. More recently, Fritz et al [4] and Rodriguez et al [30] showed that this was also true in households of pediatric patients, and Larsson et al [10] demonstrated similar findings in adults in Sweden. Our study contributes to this knowledge by demonstrating this in subjects of all ages in the United States. Colonization with MRSA leads to subsequent infection in up to 38% of subjects [31–33]. It has been noted that up to two-thirds of household contacts of subjects with MRSA SSTI are subsequently colonized with MRSA [4, 5]. Disruption of colonization in household members may play a role in decreasing the burden associated with MRSA SSTI, as shown by Fritz and colleagues [34] in households of pediatric patients. Further studies are needed to determine whether decolonization of households decreases the rate of MRSA colonization and subsequent infection in adults as well as children.

This study has several limitations. Although onset of colonization with MRSA in the index patients was designated as the date of presentation with the SSTI, the onset was likely earlier. However, previous studies report a short time (ie, median 1–2 weeks) between new colonization with MRSA and subsequent MRSA infection [35, 36], so we suspect that our findings approximate the true duration of colonization. Furthermore, index patients may have truly been colonized but with false-negative sampling. However, swabbing of multiple anatomic sites and defining clearance of colonization as all samples negative for 2 consecutive sampling periods decreased the possibility of missing true clearance. Selection bias might have also occurred, but the 107 households that were excluded did not differ substantively from included subjects. Recall bias from survey data may have affected the ascertainment of important variables including antibiotic use and use of decolonization methods; this bias is probably nondifferential given that index patients were unaware of their colonization status. In addition, compliance with antibiotics and decolonization agents was not assessed. Finally, rates and patterns of antibiotic resistance may vary across regions, which may reflect differences in the distribution of risk factors. Nevertheless, this study was conducted at multiple sites comprising a geographically and racially diverse population of both adults and children, which should improve the generalizability of these findings.

In conclusion, we found that median duration of colonization was 21 days, and 19.8% of index patients remained colonized at the end of the 6-month study period. Increased age was associated with longer duration of MRSA colonization in index patients. Clindamycin treatment of MRSA SSTI, on the other hand, was associated with earlier clearance of colonization. There was also a borderline significant association between increased numbers of household members colonized with MRSA and longer duration of colonization. Future studies should examine the predictors of persistent colonization, the impact of prolonged duration of colonization on development of MRSA reinfection, and the potential role of total household decolonization in adults and children. In addition, the unique role of clindamycin in treatment of MRSA infections should be further elucidated.

Notes

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