MAJOR ARTICLE

Staphylococcus aureus Skin Infection Recurrences Among Household Members: An Examination of Host, Behavioral, and Pathogen-Level Predictors

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Background. Many patients suffer from recurrent *Staphylococcus aureus* infections, but there are few data examining recurrence predictors.

Methods. We followed adults and children after treatment for *S. aureus* skin infections and their household contacts in Los Angeles and Chicago. We surveyed subjects for *S. aureus* body colonization, household fomite contamination, and behavioral and clinical factors at baseline and 3 and 6 months later. Using repeated measures modeling, we examined host, pathogen, behavioral, and clinical factors associated with recurrence.

Results. Among 330 index subjects, 182 (55%) were infected with an isolate of the USA300 methicillin-resistant *S. aureus* (MRSA) genetic background. Recurrences occurred in 39% by month 3 and 51% by month 6. Among 588 household contacts, 10% reported a skin infection by month 3 and 13% by month 6. Among index subjects, recurrence was associated with ($P < .05$) Los Angeles site, diabetes, recent hospitalization, recent skin infection, recent cephalexin use, and household *S. aureus* or MRSA fomite contamination; recurrence was inversely associated with recent contact sports participation. In the multivariate model, independent predictors of recurrence in index patients were recent hospitalization, household MRSA fomite contamination, and lack of recent contact sports participation. Among household contacts, independent predictors of subsequent skin infection were Chicago site, antibiotic use in the prior year, and skin infection in the prior 3 months.

Conclusions. In our longitudinal study, patients with a *S. aureus* skin infection were more likely to suffer a recurrence if household fomites were MRSA contaminated. Interventions to prevent recurrence may be enhanced by decontamination of household fomites.

Keywords. *Staphylococcus aureus*; skin infection; predictors; outcomes; molecular typing.

Staphylococcus aureus is a common cause of infections in community-dwelling persons, especially among those who have contact with the healthcare system and hospitalized patients [1, 2]. Recurrent infections are commonly reported after initial *S. aureus* skin infection [3–5]. In the United States, the predominant community-associated methicillin-resistant *S. aureus* (MRSA) clone, USA300 MRSA, has been associated with an upswing in community-associated skin infections and recurrent infections [1, 6]. Recurrence rates have exceeded 50% in some populations [3, 7]. Additionally, community-associated MRSA infections have high attack rates among household contacts of affected persons [8–10].

The reasons for recurrent infection are poorly understood. Nasal *S. aureus* colonization has been associated with subsequent infections in some populations, especially hospitalized patients [2, 11]. However, the relationship in community-dwelling patients is not strong. Many patients with community-associated *S. aureus* infection lack

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antecedent colonization, suggesting that transmission from other persons may predate infection [6]. Acquisition of *S. aureus* from household fomites is another plausible mechanism that can explain recurrent infections, as it is known that *S. aureus* contamination of fomites can be found in many households [12–14] and that *S. aureus* can persist on fomites for months under experimental conditions [15]. In outbreak situations, poor hygienic practices such as sharing towels or inadequate bathing have been associated with a higher risk of *S. aureus* infection [16, 17]. However, the role of hygiene in recurrent infections is poorly understood. Finally, there are data suggesting that the arginine catabolic mobile element (ACME), which is usually carried by USA300 MRSA, is important in spread and virulence [18]. Transcription and translation of genes located on this element could facilitate recurrent infection.

Because data on predictors of recurrent *S. aureus* infections are limited to certain populations such as those with human immunodeficiency virus (HIV) infection [5], we examined predictors of recurrent *S. aureus* infection among patients with skin infections and their household members in 2 large US cities.

METHODS

We performed a prospective longitudinal cross-sectional investigation of children and adults with *S. aureus* skin infection and their household members. Patients were enrolled from Harbor-UCLA Medical Center in Torrance, California and the University of Chicago Medical Center in Chicago, Illinois from August 2008 to June 2010. At each center, the clinical microbiology laboratory was screened daily for new skin cultures growing *S. aureus*. Inpatients and outpatients were eligible for participation. *Staphylococcus aureus* was identified by standard techniques (Vitek 2, bioMérieux, Durham, North Carolina). Patients were eligible for participation if they (1) had the culture taken from a skin infection; (2) were willing to provide infored consent; (3) had ≥1 other household member who would participate; and (4) resided within 25 miles of the site's medical center. Infected patients were designated as index patients. Further details of this investigation's enrollment scheme have been reported [19]. This study was approved by both sites' institutional review boards.

Home Visit

Consenting patients agreed to have a home visit within 21 days of enrollment during which all participating household members or their parent or guardian provided informed consent. Research personnel administered a standardized questionnaire on MRSA risk factors, based on established previously developed surveys of MRSA risk factors [2, 20–32].

To assess *S. aureus* colonization, research personnel obtained separate cultures from the nares and the oropharynx from subjects using a dry rayon tip applicator (CultureSwab, BD Diagnostic Systems, Franklin Lakes, New Jersey). At the same visit, an inguinal skin culture was obtained by the subject or their parent/guardian in private after being provided detailed instructions.

A standard list of fomites was swabbed for contamination: bathroom door handle, bathroom sink handle, toilet seat in the bathroom used most frequently by the index patient, the index patient's hair brush, kitchen countertop, kitchen sink handle, landline telephone, refrigerator door handle, television remote, and the favorite nonplush toy of any consenting child. A separate culture from each fomite was obtained using a premoistened sponge stick (Sponge-Stick, 3M, St Paul, Minnesota). After collection, the Sponge-Sticks were transported promptly to the site's research laboratory and placed in a Stomacher (Seward, Worthing, United Kingdom) to homogenize samples. The sample was then incubated in trypticase soy broth with 7% sodium chloride overnight at 37°C. The culture broth was plated onto BBL CHROMagar *S. aureus* medium (BD) and incubated for 24 hours at 37°C. Isolates were confirmed as *S. aureus* by positive catalase and StaphAureux tests (Remel, Lenexa, Kansas).

At baseline, we provided all subjects with verbal and written information about skin infection and *S. aureus*/MRSA early infection recognition and prevention. Repeat visits as described above were performed 3 and 6 months after enrollment, although fomites were not sampled at the final visit.

Colonization Cultures, Molecular Characterization of Isolates, and Definition of Isolate Relatedness

Cultures were performed using standard techniques described [19]. All isolates identified as *S. aureus* by culture were banked at −80°C for molecular characterization.

Confirmation of *S. aureus* speciation was accomplished by a polymerase chain reaction (PCR) assay specific for *spa* (encoding protein A). *Staphylococcus aureus* isolates were characterized by multilocus sequence typing (MLST) [33], and, for MRSA isolates, typing of the SCC*mec* element, the mobile genetic element that carries *mec*A [34], was performed by PCR as described previously [35], with type assignments using published guidelines [34]. Detection of genes encoding Panton-Valentine leukocidin (PVL) was performed as described elsewhere [36].

Staphylococcus aureus isolates were considered indistinguishable if they shared the same MLST and SCC*mec* type and were concordant with respect to the presence or absence of the PVL genetic determinants. Based on a previous investigation demonstrating that ST8/PVL$^+$/SCC*mec* IV is highly concordant with USA300 MRSA genetic background as assessed by pulsed-field gel electrophoresis [37], isolates with these characteristics were categorized as USA300 MRSA.

Chart Abstraction and Criteria for Community-Associated *S. aureus*

Medical records of index patients were reviewed using a standardized chart abstraction instrument that quantified recent hospitalizations, prior *S. aureus* infections, and comorbidities using a standard index [38]. The Centers for Disease Control and Prevention's (CDC) Active Bacterial Core surveillance case definition was used to classify each infection as community- or healthcare-associated [39], as previously described [19].

Primary Outcome and Statistical Analyses

Our primary outcome was self-reported skin infection at the 3- or 6-month follow-up household visit. Outcome data were obtained via in-person interview by study personnel using a standardized script. Index subjects were asked if their skin infection recurred at the same site or at a different body site. Household contacts were asked similar questions about new skin infections, and parent/guardians were interviewed about children.

Data were analyzed using SAS version 9.1.3 (SAS Institute, Cary, North Carolina). Logistic regression modeling procedures [40] were performed to predict infection of the index patient using general estimating equations and an autoregressive correlation matrix to account for the time-varying responses for each subject. Bivariate analyses were performed to determine odds ratios (ORs), 95% confidence intervals (CIs), and associated *P* values. All variables with a *P* value $\leq .20$ in the bivariate analysis were included in a multivariable analysis. The USA300 genetic background was believed to be an important predictor of subsequent infection; therefore, we controlled for it in our multivariable models. Manual backward elimination was performed using the score test to find the best model of risk factors associated with infection of the index subject. Models were examined for goodness of fit using the Hosmer–Lemeshow statistic. All variables were considered significant at the $\alpha = .05$ level. Similar procedures accounting for clustering of household members were used to identify risk factors for infection in household members.

RESULTS

Among the 350 index subjects enrolled, 330 (94%) completed ≥1 household follow-up visit (at 3 and/or 6 months); 119 (36%) index subjects had methicillin-susceptible *S. aureus* (MSSA), and 211 (64%) had MRSA as their infecting isolate. One hundred ninety-two (58%) were categorized as community-associated infection and 138 (42%) as healthcare-associated infection. Among this group, 172 (53%) were female, 140 (43%) were children, 162 (49%) were African American, and 119 (36%) were Hispanic. Among the index subject's infecting isolates, 182 (55%) were USA300 MRSA. One or more body sites were *S. aureus* colonized in 124 of 300 (38%), 60 (18%) contacts were MRSA colonized at ≥1 body site, and 66 (20%) were colonized at ≥1 body site with an isolate indistinguishable from their infection isolate. Further details on the cohort and behavioral/epidemiologic exposures are summarized in Table 1.

We enrolled 588 household contacts of the 330 index patients. Of these, 208 (35%) were children, and 368 (63%) were female. Two hundred eighty-two (48%) had a *S. aureus* isolate from ≥1 body site, 125 (21%) contacts were MRSA colonized at ≥1 body site, and 95 (16%) were colonized at ≥1 body site with an isolate indistinguishable from the index subject's infection isolate. Other demographic, clinical, behavioral/epidemiologic, and colonization factors are described in Table 2.

Recurrent Infections and Associated Factors Among Index Patients

Among index subjects, 130 of 330 (39%) reported a skin infection between the baseline and the 3-month visit. Of those who completed the 6-month follow-up, 95 of 287 (33%) reported a skin infection between month 3 and month 6. Overall, 167 of 330 (51%) subjects reported ≥1 skin infection during the 6-month follow-up period (Table 3).

In our longitudinal bivariate analysis, factors associated with subsequent skin infection were residence at the Los Angeles site, diabetes, hospitalization in the prior 3 months, skin infection in the 12 months prior to enrollment, use of cephalexin in the 12 months prior to enrollment, household fomite contamination with *S. aureus*, and household fomite contamination with MRSA. Participation in contact sports was inversely associated with subsequent skin infection (Table 4). Notable factors lacking association with subsequent infection included recent surgery, housing density, showering frequency, colonization (nasal, inguinal, or oropharyngeal), CDC community- vs healthcare-associated categorization, methicillin resistance in the index isolate, USA300 genetic background in the index patient's isolate, and body colonization or household fomite contamination with the index subject's infecting isolate (Table 4).

In multivariate analysis, independent predictors of subsequent infection among the index subjects were hospitalization in the previous 3 months (OR, 1.53 [95% CI, 1.09–2.15]) and/or fomite contamination with MRSA (OR, 1.61 [95% CI, 1.05–2.47]). Participation in contact sports was inversely associated (OR, 0.61 [95% CI, .38–.99]) with skin infection in the follow-up periods (Table 5).

Recurrent Infections and Associated Factors Among Household Contacts

Among household contacts, 58 of 588 (10%) reported a skin infection at the 3-month follow-up visit, and of those who completed the 6-month follow-up, 34 of 510 (7%) reported a skin infection between months 3 and 6. Overall, 80 of 640 (13%)

Table 1. Characteristics of Index Subjects at Enrollment

Variable	Index Subjects	
	Total Index Subjects, No. (%) (n = 330)	6 mo, No. (%) (n = 287)
Demographics		
Los Angeles site	170 (52)	149 (52)
Female sex	171 (53)	146 (51)
Age		
Younger child (<5 y)	91 (28)	81 (28)
Child (5–18 y)	49 (15)	42 (15)
Adult (19–65 y)	175 (53)	152 (53)
Older adult (>65 y)	15 (5)	12 (4)
Ethnicity		
African American	162 (49)	139 (48)
White	25 (8)	23 (8)
Hispanic	119 (36)	105 (37)
Other/mixed/unknown	24 (7)	20 (7)
Clinical factors		
Comorbidities		
Charlson comorbidity score		
Mean ± SD	1.4 ± 2.4	1.4 ± 2.4
Median (range)	0 (0–14)	0 (0–14)
Diabetes	56 (17)	50 (17)
HIV infection	14 (5)	12 (5)
In the past 3 mo		
Underwent major surgery	86 (26)	17 (6)
Received dialysis	8 (3)	2 (1)
Hospitalized	172 (52)	38 (13)
In the past 12 mo		
Skin infection prior to enrollment	210 (63)	186 (65)
Any antibiotic exposure	229 (69)	201 (70)
Use of clindamycin	33 (10)	21 (11)
Use of TMP-SMX	36 (11)	32 (11)
Use of cephalexin	17 (5)	17 (6)
Use of immunosuppressant medications	67 (3)	60 (2)
Spent time living in a skilled nursing facility, rehabilitation center, or other type of group facility	8 (3)	6 (2)
Epidemiologic factors		
Household density (persons/bedroom)		
Mean ± SD	2.0 ± 1.1	2.0 ± 1.1
Median (range)	1.7 (0.4–9.0)	1.7 (0.4–9.0)
Homelessness in the past 12 mo	13 (4)	8 (3)
In the past 3 mo		
Illicit drug use	30 (9)	10 (6)
Showered at least once a day	227 (69)	190 (76)
Shared makeup with others	18 (6)	11 (5)
Shared clothes with others with washing	17 (5)	6 (2)
Shared any towels with others	152 (46)	74 (30)
Wore clothes more than once without washing	156 (49)	106 (43)
Hand-washing frequency after using the bathroom		
Mean ± SD	2.6 ± 0.77	2.8 ± 0.59
Median (range)	3 (0–3)	3 (0–3)

Table 1 continued.

Variable	Index Subjects	
	Total Index Subjects, No. (%) (n = 330)	6 mo, No. (%) (n = 287)
Household cleaning scale[a]		
Mean ± SD	1.85 ± 0.91	2.33 ± 0.55
Median (range)	2.0 (0–3.9)	2.33 (0–3.0)
Used a gym	25 (9)	14 (7)
Participated in contact sports	77 (23)	45 (20)
Went to daycare	13 (18)	18 (21)
Colonization		
Any colonization with *S. aureus*	124 (38)	137 (51)
Any colonization with MRSA	60 (18)	72 (27)
Any colonization with index subject's infection isolate	66 (20)	61 (23)
Nasal colonization with index subject's infection isolate	37 (11)	27 (10)
Oropharyngeal colonization with index subject's infection isolate	25 (8)	25 (10)
Inguinal colonization with index subject's infection isolate	39 (12)	35 (13)
Household fomite contamination		
Any contamination with *S. aureus*	160 (49)	132 (49)
Any contamination with MRSA	75 (23)	63 (24)
Any contamination with index subject's infection isolate	69 (21)	60 (22)
Index subject's infection isolate		
MRSA	211 (64)	182 (63)
Community associated[b]	192 (58)	171 (60)
USA300-MRSA genetic background	182 (55)	157 (55)

Abbreviations: HIV, human immunodeficiency virus; MRSA, methicillin-resistant *Staphylococcus aureus*; *S. aureus*, *Staphylococcus aureus*; SD, standard deviation; TMP-SMX, trimethoprim-sulfamethoxazole.

[a] Household cleaning is a measure of the frequency of cleaning for common household items, with higher values representing more frequent cleaning.

[b] Community associated according to definition by the Centers for Disease Control and Prevention.

household contact subjects reported ≥1 skin infection during the 6-month follow-up.

In our longitudinal bivariate analysis, factors associated with subsequent skin infection among household contacts were Chicago site, hospitalization in the prior 3 months, female sex, skin infection in the 3 months prior to the surveillance period, antibiotic use in the 12 months prior to enrollment, MRSA colonization, colonization with the index subject's infection isolate, nasal colonization with the index subject's infection isolate, fomite contamination with MRSA, fomite contamination with the index subject's infection isolate, a USA300-MRSA genetic background for the index subject's infection isolate, and use of any of the following in the 12 months prior to enrollment: clindamycin, trimethoprim-sulfamethoxazole, or cephalexin (Table 4).

In multivariate analysis, independent predictors of subsequent infection among household contacts were Chicago site (OR, 1.72 [95% CI, 1.07–2.77]), antibiotic exposure in the 12 months prior to enrollment (OR, 1.87 [95% CI, 1.18–2.96]), and skin infection in the 3 months prior to the subsequent surveillance period (OR, 7.31 [95% CI, 4.28–12.5]) (Table 5).

DISCUSSION

In our 2-center, longitudinal study of predictors of recurrent *S. aureus* infection, we found that 51% of 330 index patients and 13% of household contacts suffered a recurrent infection in the 6 months after treatment of the index patient for a *S. aureus* skin infection. This infection rate is concerning but consistent with other cohorts in which recurrent infection after community-associated MRSA or community-associated *S. aureus* infection exceeded 50% [3, 7]. Recurrent infections were not associated with an initial infection caused by MRSA, MSSA, or USA300 MRSA, or with having a community-associated *S. aureus* infection [1, 2].

We examined factors predictive of recurrent infection. Previous data suggested that behavioral, host, and pathogen factors each might be important. Understanding predictors of recurrence is of great clinical importance, especially factors that are amenable to change, such as behavior, colonization, and environmental contamination. Remarkably, a subsequent infection was not associated with asymptomatic colonization in an

Table 2. Characteristics of Household Contacts at Enrollment (Non–Index Subjects)

Variable	3 mo, No. (%) (n = 588)	6 mo, No. (%) (n = 510)
Demographics		
Los Angeles site	303 (52)	245 (48)
Female sex	368 (63)	334 (66)
Age		
Younger child (<5 y)	79 (13)	56 (11)
Child (5–18 y)	129 (22)	104 (20)
Adult (19–65 y)	353 (60)	324 (64)
Older adult (>65 y)	27 (5)	26 (5)
Ethnicity		
African American	282 (48)	261 (51)
White	35 (6)	34 (7)
Hispanic	232 (40)	186 (37)
Other/mixed/unknown	39 (7)	29 (6)
Clinical factors		
Comorbidities		
Charlson comorbidity score		
Mean ± SD	0.4 ± 0.9	0.4 ± 0.9
Median (range)	0 (0–7)	0 (0–7)
Diabetes	56 (10)	48 (10)
HIV infection	4 (1)	4 (1)
In the past 3 mo		
Underwent major surgery	39 (7)	10 (2)
Received dialysis	1 (0)	2 (0)
Hospitalized	66 (11)	14 (3)
Skin infection	57 (10)	40 (9)
In the past 12 mo		
Any antibiotic exposure	181 (32)	158 (32)
Use of clindamycin	7 (1)	9 (2)
Use of TMP-SMX	8 (1)	9 (2)
Use of cephalexin	14 (2)	12 (2)
Use of immunosuppressant medications	57 (10)	58 (12)
Spent time living in a skilled nursing facility, rehabilitation center, or other type of group facility	18 (3)	15 (3)
Epidemiologic factors		
Homelessness in the past 12 mo	30 (5)	24 (5)
In the past 3 mo		
Illicit drug use	34 (8)	20 (6)
Showered at least once a day	432 (74)	338 (75)
Shared makeup with others	63 (12)	40 (10)
Shared clothes with others with washing	29 (5)	17 (4)
Shared any towels with others	297 (51)	149 (34)
Wore clothes more than once without washing	283 (49)	209 (47)
Hand-washing frequency after using the bathroom		
Mean ± SD	2.7 ± 0.61	2.8 ± 0.56
Median (range)	3 (0–3)	3 (0–3)
Participated in contact sports	147 (25)	94 (21)
Went to daycare	10 (11)	13 (14)
Colonization		
Any colonization with *S. aureus*	282 (48)	207 (42)
Any colonization with MRSA	125 (21)	85 (17)
Any colonization with index subject's infection isolate	95 (16)	62 (13)
Nasal colonization with index subject's infection isolate	41 (7)	32 (7)
Oropharyngeal colonization with index subject's infection isolate	44 (7)	28 (6)
Inguinal colonization with index subject's infection isolate	47 (8)	26 (5)

Table 2 continued.

Abbreviations: HIV, human immunodeficiency virus; MRSA, methicillin-resistant *Staphylococcus aureus*; *S. aureus*, *Staphylococcus aureus*; SD, standard deviation; TMP-SMX, trimethoprim-sulfamethoxazole.

individual index patient nor in a household contact, which was contrary to our expectations; this calls into question the priority given to body decolonization as a preventive measure. Also, we did not find that pathogen-level factors were associated with recurrence.

However, we did find an independent association between environmental contamination of sampled fomites with MRSA and subsequent skin infection among index subjects. Although there are ample data that *S. aureus* contamination in households is common [12–14] and that *S. aureus* can persist on fomites for months [15], the relationship between the contamination of fomites and infection risk has been unclear. Our data suggest that contaminated household fomites play an important role in causing recurrences among index subjects. Alternately, it is possible that infected index subjects contaminated household fomites, making the directionality of this fomites–infection relationship unclear. We also found another independent predictor of subsequent infections in index patients: hospitalization

Table 3. Reported Recurrent, Relapsed, or New Skin Infections Among All Subjects During Follow-up

Follow-up Period	Index Subjects, No. (%)	Household Contacts (Non–Index Subjects), No. (%)
3 mo	130/330 (39)	58/588 (10)
6 mo	95/287 (33)	34/510 (7)
Overall[a]	167/330 (51)	80/640 (13)

[a] Overall number of subjects who reported a recurrent, relapsed, or new skin infection over the follow-up period.

Table 4. Longitudinal Bivariate Analysis Among Index Subjects With Recurrent, Relapsed, or New Skin Infections Versus Those Who Did Not Have Another Skin Infection During Follow-up

	Index Subjects			Household Contacts		
Variable	Odds Ratio	95% CI	*P* Value	Odds Ratio	95% CI	*P* Value
Demographics						
Los Angeles site	**1.45**	**1.01–2.13**	**.04**	**0.61**	**.37–.98**	**.04**
Female sex	1.05	.73–1.52	.77	**1.73**	**1.02–2.92**	**.04**
Age						
Younger child (<5 y)	0.92	.60–1.42	.71	0.64	.28–1.47	.29
Child (5–18 y)	0.70	.39–1.25	.22	0.62	.32–1.21	.17
Adult (19–65 y)	Ref.			Ref.		
Older adult (>65 y)	2.07	.93–4.57	.07	0.94	.31–2.83	.92
Ethnicity						
African American	0.88	.45–1.72	.72	0.98	.39–2.45	.97
White	Ref.			Ref.		
Hispanic	1.48	.75–2.93	.27	0.68	.26–1.78	.44
Other/mixed/unknown	2.03	.84–4.93	.12	0.26	.05–1.30	.10
Clinical factors						
Comorbidities						
Charlson comorbidity score	1.03	.96–1.11	.37	0.97	.74–1.27	.82
Diabetes	**1.70**	**1.07–2.72**	**.03**	1.44	.73–2.84	.29
HIV infection	1.03	.41–2.59	.96	1.78	.19–16.4	.61
In the past 3 mo						
Underwent major surgery	1.45	.94–2.24	.09	1.94	.84–4.48	.12
Received dialysis	1.42	.49–4.16	.51	3.76	.39–36.3	.25
Hospitalized	**1.60**	**1.16–2.19**	**.004**	**2.12**	**1.08–4.15**	**.03**
In the past 12 mo						
Previous skin infection prior to enrollment	**1.50**	**1.01–2.21**	**.04**	**9.9**	**6.02–16.4**	**<.001**
Household member had previous skin infection prior to enrollment	1.45	.88–2.40	.14	[a]	[a]	[a]
Any antibiotic exposure	1.12	.76–1.66	.56	**2.65**	**1.64–4.30**	**<.001**
Use of clindamycin	0.91	.47–1.80	.79	**8.71**	**2.9–26.08**	**.001**
Use of TMP-SMX	1.74	.96–3.16	.07	**3.65**	**1.28–10.39**	**.02**
Use of cephalexin	**2.70**	**1.14–6.38**	**.02**	**2.70**	**1.12–6.51**	**.03**
Use of immunosuppressant medications	0.79	.49–1.27	.34	1.05	.48–2.32	.91
Spent time living in a skilled nursing facility, rehabilitation center, or other type of group facility	1.34	.36–5.00	.67	2.16	.82–5.71	.12
Epidemiologic factors						
Household density	1.05	.90–1.22	.55	1.06	.82–1.36	.67
Homelessness in the past 12 mo	0.98	.30–3.28	.98	2.08	.88–4.89	.10
In the past 3 mo						
Illicit drug use	1.12	.57–2.22	.74	1.64	.72–3.76	.24
Showered at least once a day	0.75	.50–1.12	.16	0.71	.45–1.11	.14
Shared makeup with others	1.06	.54–2.08	.87	0.93	.42–2.06	.86
Shared clothes with others with washing	1.19	.51–2.78	.69	0.80	.21–3.06	.74
Shared any towels with others	1.27	.91–1.77	.15	1.08	.70–1.70	.71
Wore clothes more than once without washing	0.94	.66–1.32	.72	1.0	.65–1.53	.99
Hand-washing frequency after using the bathroom	0.98	.76–1.25	.86	0.86	.64–1.15	.31
Household cleaning scale[b]	0.93	.75–1.15	.49	0.90	.69–1.18	.45
Used a gym	0.92	.47–1.81	.81	0.53	.19–1.43	.21
Participated in contact sports	**0.57**	**.35–.92**	**.02**	0.85	.49–1.47	.56
Went to daycare	1.18	.48–2.87	.72	2.00	.55–7.36	.29

Table 4 continued.

Variable	Index Subjects			Household Contacts		
	Odds Ratio	95% CI	*P* Value	Odds Ratio	95% CI	*P* Value
Colonization						
Any colonization with *S. aureus*	0.80	.58–1.10	.17	1.47	.93–2.31	.10
Any colonization with MRSA	1.03	.69–1.53	.90	**1.84**	**1.16–2.94**	**.01**
Any colonization with index subject's infection isolate	0.91	.60–1.39	.67	**2.11**	**1.27–3.50**	**.004**
Nasal colonization with index subject's infection isolate	0.61	.34–1.09	.10	**3.10**	**1.68–5.69**	**.003**
Oropharyngeal colonization with index subject's infection isolate	1.02	.56–1.85	.95	1.77	.89–3.51	.10
Inguinal colonization with index subject's infection isolate	1.30	.77–2.18	.33	**2.55**	**1.34–4.85**	**.004**
Household fomite contamination						
Any contamination with *S. aureus*	**1.39**	**1.003–1.93**	**.048**	1.45	.95–2.21	
Any contamination with MRSA	**1.60**	**1.07–2.40**	**.02**	**1.67**	**1.04–2.67**	**.03**
Any contamination with index subject's infection isolate	1.51	1.00–2.29	.051	**1.88**	**1.13–3.15**	**.02**
Index subject's infection isolate						
MRSA	1.12	.77–1.64	.55	1.63	.95–2.79	.08
Community associated[c]	1.06	.73–1.53	.77	1.38	.86–2.21	.18
USA300-MRSA genetic background	1.07	.75–1.54	.71	**1.92**	**1.15–3.21**	**.01**

Statistically significant relationships are indicated in bold text.

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; MRSA, methicillin-resistant *Staphylococcus aureus*; Ref., reference group; *S. aureus*, *Staphylococcus aureus*; TMP-SMX, trimethoprim-sulfamethoxazole.

[a] Not calculated as all household members had been exposed to a skin infection prior to enrollment.

[b] Household cleaning is a measure of the frequency of cleaning for common household items with higher values representing more frequent cleaning.

[c] Community associated according to epidemiologic definitions.

in the 3-month period prior to enrollment. This relationship is not surprising, as patients with healthcare system contact have long been known to be at increased risk for *S. aureus* infection.

The inverse association with participation in contact sports, which suggests that contact sports participation may be "protective" against subsequent infection, was surprising. Clearly, community-associated MRSA infections have been linked to contact sport participation, although many of these reports were prepared during the early years of the community-associated MRSA epidemic [41–43] and subsequent educational interventions for contact sports participants on MRSA prevention have been widely used [44, 45]. Perhaps the "protective" effect of this exposure in our population is due to increased awareness of community-associated MRSA infection among contemporary sports participants and reflects increased attention to hygiene.

We identified many factors that unexpectedly lacked association with subsequent infection among index patients and their household contacts. We hypothesized that infection with USA300 background would be predictive of subsequent skin infection given this strain's repeated associations with recurrences and community "outbreaks" [1]. Molecular characteristics of USA300, such as carriage of ACME and upregulation of master virulence gene regulator systems such as *agr* and *sae*, may facilitate transmission and infection [6, 18, 46]. The lack of observed association in our study suggests that either no relationship exists or that our study was too small to elucidate a relatively modest association of recurrence with this MRSA strain type.

In contrast to expectations, nares, oropharynx, and inguinal *S. aureus* colonization was not associated with subsequent skin infection. Although colonization is well established as a risk factor for subsequent *S. aureus* infection in hospitalized patients, its role as a predisposing factor for community-associated infection is far less clear [6]. This lack of association is even more surprising given that body decolonization of patients with recurrent *S. aureus* infection decreases the risk of subsequent infection [3, 47]. However, the effectiveness of body decolonization at preventing *S. aureus* recurrence in community-dwelling persons has been modest in many investigations, and often patients continue to experience recurrences after a decolonization regimen [3, 48].

In terms of behavioral predictors, we found no association between worse hygiene practices and recurrent skin infections. Although relationships to suboptimal hygiene and *S. aureus* infections have been reported from a variety of settings [1, 16, 22], these associations are typically found in closed populations such as jails or sports teams. The strength of associations in these other settings may not be applicable to community-dwelling persons.

Finally, among the household contacts, the independent relationship that we identified between prior antibiotic exposure and subsequent infection was expected. Prior antibiotic use

Table 5. Independent Predictors of Subsequent Skin and Soft Tissue Infection in Index Patients and Household Contacts (Multivariate Model)

Variable	OR	95% CI
Index subjects		
Hospitalization in prior 3 mo	1.53	1.09–2.15
Household fomite *Staphylococcus aureus* contamination	1.39	1.003–1.93
Participation in contact sports	0.61	.38–.99
Household contacts		
Chicago site	1.72	1.07–2.77
Antibiotic exposure in the 12 mo prior to enrollment	1.87	1.18–2.96
SSTI in the 3 mo prior to the subsequent surveillance period	7.31	4.28–12.5

Abbreviations: CI, confidence interval; OR, odds ratio; SSTI, skin and soft tissue infection.

likely is correlated with exposure to the healthcare system, comorbidities, and prior infections, suggesting that the household contacts were at higher risk for infection in general. We also identified a strong, independent association between previous skin infection and subsequent infection (OR, 7.31 [95% CI, 4.28–12.5]). This further demonstrates the frequent phenomenon of recurrent skin infection in our studied population.

There are strengths to our investigation. First, our study was longitudinal, allowing use of repeated measures modeling. Repeated measures modeling has the advantage of incorporating time-dependent predictors of outcomes that may vary over the course of the study (eg, antibiotic use, recent surgery, showering/bathing frequency). Because exposures predate clinical outcomes, predictors of subsequent infection are more likely to be causal than mere associations [49]. Second, we enrolled a large cohort of subjects. Third, our retention rates were high (94% at 3 months and 87% at 6 months), enhancing our validity. Fourth, we performed a holistic investigation of recurrent infection, examining clinical, behavioral/epidemiologic, colonization, and bacterial factors, including genotyping of all infecting, colonizing, and fomite isolates. Previous investigations on this topic tended to focus only on 1 or 2 of these factors [24, 32, 50, 51].

Our investigation has limitations. First, skin infection outcomes were obtained via interview; thus, the results are subject to recall bias or subjects' failure to comprehend the definition of a skin infection. However, study staff underwent detailed training in recognizing skin infections and used standardized scripts for quantifying these outcomes, and the incidence of skin infection among index subjects was similar to that of other investigations (28%–72%) [3, 4, 7]. Additionally, self-reported and physician-documented skin infection rates correlate well [3]. Second, we studied urban US populations from 2 large, albeit heterogeneous, urban areas. The applicability of our findings to other populations is uncertain. Nevertheless, our population was mostly racial/ethnic minorities, the population in the United States most disproportionally affected by community-associated MRSA infections [52]. Third, study subjects were both MSSA and MRSA infected and included patients with both community-associated- and healthcare-associated *S. aureus* infections. By combining these groups, we may not have been able to detect associations with recurrence distinctive to one subpopulation or another. Finally, our index patient study population had documented *S. aureus* infections, and risk factors among patients with skin infections that were not cultured may differ.

In summary, we found that recurrent *S. aureus* infections in community-dwelling persons were associated with household MRSA fomite contamination. Our findings suggest that environmental decontamination, and perhaps not body decolonization, may be a key component of future successful *S. aureus* and MRSA prevention efforts. Given the high rate of recurrent skin infections in our population, prospective trials of household environmental decontamination should be undertaken to improve our ability to prevent these extremely common and potentially life-threatening infections.

Notes

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