



Interplay of personal, pet, and environmental colonization in households affected by community-associated methicillin-resistant *Staphylococcus aureus*

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SUMMARY

Objective: We sought to determine the prevalence, molecular epidemiology, and factors associated with *Staphylococcus aureus* environmental surface and pet colonization in households of children with community-associated methicillin-resistant *S. aureus* (CA-MRSA) infection.

Methods: Between 2012 and 2015, 150 children with CA-MRSA infections and their household contacts and pets were enrolled in this cross-sectional study in metropolitan Saint Louis, MO. Cultures to detect *S. aureus* were collected from 3 anatomic sites of household members, 2 dog/cat sites, and 21 environmental surfaces in each household. Molecular epidemiology of *S. aureus* isolates was determined via repetitive-sequence PCR. Generalized linear models were developed to identify factors associated with *S. aureus*/MRSA household contamination.

Results: MRSA was recovered from environmental surfaces in 69 (46%) households (median 2 surfaces [range 1–18]). The enrollment infecting strain type was the most common strain recovered from the environment in most (64%) households. In generalized linear models, factors associated with a higher proportion of MRSA-contaminated environmental surfaces were household member MRSA colonization burden, MRSA as the dominant *S. aureus* strain colonizing household members, more strain types per household member, index case African-American race, and renting (vs. owning) the home. Of 132 pets, 14% were colonized with MRSA. Pets whose primary caretaker was MRSA-colonized were more likely to be MRSA-colonized than pets whose primary caretaker was not MRSA-colonized (50% vs. 4%, $p < 0.001$).

Conclusions: Household environments and pet dogs and cats serve as reservoirs of MRSA. Household member MRSA colonization burden predicts environmental MRSA contamination. Longitudinal studies will inform the directionality of household transmission.

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Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is an important cause of skin and soft tissue infection (SSTI) in children.¹ Incomplete understanding of the epidemiology of carriage and transmission of these strains has contributed to their widespread dissemination in communities and, recently,

into hospitals, where healthcare-associated (HA)-MRSA strains once predominated.^{2,3} While preventive measures in hospitalized patients have curtailed the incidence of HA-MRSA infections,^{4,5} similar strides have not been achieved in the community setting. Indeed, after performing decolonization, up to 50% of SSTI patients develop recurrent infections over the ensuing year.⁶

CA-MRSA is a disease of households, facilitated by complex transmission dynamics yet to be fully understood.^{2,7} Dogma holds that *S. aureus* colonization poses risk for recurrent SSTI and spread

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among household contacts.⁸ Instances of discordance between infecting *S. aureus* strains and those colonizing index cases and their household contacts,^{9,10} and varied effectiveness of decolonization trials,^{6,11} indicate that exclusive focus on human colonization may be inadequate. The household environment is increasingly recognized as a community reservoir of *S. aureus*. Indeed, household MRSA environmental contamination is significantly more prevalent in homes of MRSA-infected patients than in control households.^{12,13} Additionally, household companion animals can carry *S. aureus* and may contribute to *S. aureus* household transmission.^{7,14} Studies to date^{9,12,13,15,16} have been limited by examining only a subset of household members, discounting socioeconomic status, sampling a small number of surfaces, or disregarding pet colonization.

Understanding these complex community MRSA reservoirs is imperative to mitigate transmission. The objectives of this study were to determine the prevalence, molecular epidemiology, and factors associated with *S. aureus*, and specifically MRSA, environmental surface contamination and pet carriage in households of children with CA-MRSA infection.

Methods

Participants

Between January 2012 and October 2015, 377 children with SSTI were screened for the HOME: Household Observation of MRSA in the Environment study. Screening took place at St. Louis Children's Hospital (SLCH), Cardinal Glennon Children's Hospital, and community pediatric practices affiliated with the Washington University Pediatric and Adolescent Ambulatory Research Consortium. Children with HA-MRSA infections¹⁷ (e.g., recent hospitalization, invasive medical device, residing in long-term care facility) were excluded from screening. One hundred thirty subjects did not meet eligibility criteria (e.g., SSTI not verified as MRSA, time interval from infection to screening, distance from medical center). Of 247 eligible patients with CA-MRSA infection, 150 index cases (149 with SSTI, 1 invasive infection) were enrolled, along with their household contacts (individuals sleeping in the home ≥ 4 nights per week) and indoor pet dogs and cats. The Washington University Institutional Review Board and Institutional Animal Care and Use Committee approved study procedures. Written, informed consent/assent was obtained for all household members (by participant and/or guardian) and pets (by primary caretaker).

Data collection

An enrollment visit was conducted in the index case's primary home. Participants were queried about demographics, socioeconomic surrogates (e.g., insurance status, home ownership, household crowding), prior *S. aureus* infections, personal hygiene practices, activities, pet characteristics, and household layout and cleaning practices. To control for potential bias introduced by participants misrepresenting their cleaning habits, the research team assigned each household an objective 'home cleanliness score' from 1 (above average) to 4 (very dirty), which considered odor, clutter, and grime, modified from the Environmental Cleanliness and Clutter Scale.¹⁸

Index case infecting isolates were obtained from the clinical microbiology laboratory when available. At enrollment, colonization cultures were collected by trained study personnel from the anterior nares, axillae, and inguinal folds of each household member (Eswab, Becton Dickinson [BD], Franklin Lakes, NJ) and from the nares (minitip Eswab, BD) and dorsal fur (Eswab) of indoor pet dogs and cats. Twenty-one environmental surfaces¹⁹ were sampled (Table 1); standardized environmental sampling employed the

Baird Parker Agar contact plate (Hardy, Santa Maria, CA) and the Eswab.^{19,20}

Laboratory procedures

From Eswabs, *S. aureus* was recovered using broth-enrichment. From the contact plate, colonies were selected based on morphology. *S. aureus* identification and antibiotic susceptibility testing were performed in accordance with established techniques²¹ (Supplementary Methods). Molecular typing was performed on all recovered *S. aureus* isolates by repetitive-sequence PCR (repPCR).^{22,23} Isolates with unusual repPCR patterns and all isolates recovered from pets were confirmed as *S. aureus* by matrix-assisted laser desorption ionization time-of-flight mass spectrometry (VITEK MS v2.0).²⁴

Statistical analysis

Household member *S. aureus* (MRSA) colonization pressure was calculated as:

$$\frac{\text{(number of } S. \text{ aureus (MRSA) anatomical sites colonized)}}{\text{(number of sampled household members)} * \text{(number of sampled anatomic sites)}}$$

To compare the proportion of household environmental surfaces contaminated with *S. aureus* or MRSA, as well as the number of unique strains (by repPCR) recovered from households, across various attributes, nonparametric Mann-Whitney U and Kruskal-Wallis tests were performed. The relationship between environmental surface contamination prevalence and household colonization pressure was determined by linear regression. Pearson's χ^2 tests compared pet carriage with primary caretaker colonization and various pet factors. Data analyses were performed with SPSS 23 for Windows (IBM SPSS, Chicago, IL).

Generalized linear Poisson models were developed (in R language²⁵; Supplementary Methods) in a Bayesian framework to define the impact of household member colonization pressure and individual and household-level cleanliness variables on the proportion of household environmental surfaces contaminated with *S. aureus* or MRSA. The 'Personal Colonization and Pet Carriage' model considered how colonization status and strain distribution of household members and pets and socioeconomic factors influence household contamination. The 'Household Practices and Personal Behaviors' model examined how hygiene and epidemiological factors influence household contamination. See Supplementary Tables 1 and 2 for primary and secondary covariates included.

Results

Study population and *S. aureus* colonization prevalence

The 150 index cases (53% female) had 546 household contacts, of which 521 (52% female) enrolled (96% participation). The median age of index cases and household contacts was 3 years (range 0.1–18) and 27 years (range 0.1–82), respectively. Index cases were primarily Caucasian (68%) or African-American (25%); 6% were of Hispanic/Latino ethnicity. The majority of participants lived in houses (81%, vs. apartments/townhomes) that they owned (66%, vs. rented) in urbanized areas (87%, vs. urban clusters or rural areas).^{26,27} Median household size was 4 (range 2–13). Enrollment visits were conducted a median of 20 days (range 3–95) following MRSA infection. The study area encompassed 4,035 miles² (household distance from SLCH: median 17 miles, range 1–76). Fifty-seven (38%) index cases and 218 (43%) household contacts were colonized with *S. aureus* at enrollment (30% and 23% with MRSA, respectively). Sixty-two (41%) index cases and 87 (17%) household contacts had a history of confirmed *S. aureus* infection (excluding

Table 1
Prevalence of *S. aureus* on household environmental surfaces and pets.

Household surface ^a or pet ^b	<i>S. aureus</i> at site, N (%)	MRSA at site, N (%)	MSSA at site, N (%)
Any environmental surface	95 (63)	69 (46)	56 (37)
Living room	49 (33)	32 (21)	22 (15)
TV remote control (<i>n</i> = 148)	33 (22)	22 (15)	11 (7)
Computer keyboard and mouse ^c (<i>n</i> = 129)	22 (17)	15 (12)	8 (6)
Videogame controller (<i>n</i> = 109)	17 (16)	9 (8)	8 (7)
Telephone ^d (<i>n</i> = 148)	16 (11)	11 (7)	5 (3)
Bathroom	72 (48)	50 (33)	38 (25)
Countertop (<i>n</i> = 148)	30 (20)	17 (11)	13 (9)
Toilet seat (<i>n</i> = 150)	22 (15)	11 (7)	11 (7)
Bathtub (<i>n</i> = 150)	22 (15)	11 (7)	11 (7)
Sink (<i>n</i> = 150)	21 (14)	14 (9)	7 (5)
Sink faucet handle (<i>n</i> = 150)	18 (12)	12 (8)	6 (4)
Light switch (<i>n</i> = 150)	18 (12)	10 (7)	8 (5)
Soap bar and dish (<i>n</i> = 81)	10 (12)	8 (10)	2 (2)
Hand towel (<i>n</i> = 98)	11 (11)	9 (9)	2 (2)
Index case bath towel (<i>n</i> = 86)	8 (9)	3 (3)	5 (6)
Toilet handle (<i>n</i> = 150)	14 (9)	10 (7)	4 (3)
Door handle (<i>n</i> = 150)	13 (9)	7 (5)	6 (4)
Kitchen	51 (34)	34 (23)	20 (13)
Refrigerator door handle (<i>n</i> = 149)	28 (19)	16 (11)	12 (8)
Table top (<i>n</i> = 145)	20 (14)	17 (12)	3 (2)
Hand towel (<i>n</i> = 102)	11 (11)	7 (7)	4 (4)
Sponge or cloth (<i>n</i> = 136)	13 (10)	10 (7)	3 (2)
Sink faucet handle (<i>n</i> = 150)	10 (7)	8 (5)	2 (1)
Bedroom	33 (22)	22 (15)	12 (8)
Index case bed linens ^c (<i>n</i> = 149)	33 (22)	22 (15)	12 (8)
Any dog or cat cultured in household^b (<i>n</i> = 71)	22 (31)	15 (21)	9 (13)
Dog (<i>n</i> = 100)	24 (24)	16 (16)	10 (10)
Nares	19 (19)	12 (12)	7 (7)
Dorsal fur	9 (9)	6 (6)	3 (3)
Cat (<i>n</i> = 32)	4 (13)	3 (9)	1 (3)
Nares	4 (13)	3 (9)	1 (3)
Dorsal fur	0 (0)	0 (0)	0 (0)

Abbreviations. MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*

Note. Culturing technique used for each surface: Eswab (Living room - TV remote control, computer keyboard and mouse, videogame controller, telephone; Bathroom - sink faucet handle, light switch, hand towel, index case bath towel, toilet handle, door handle; Kitchen - hand towel, sponge or cloth, sink faucet handle; Bedroom - index case bed linens) or Baird Parker Agar contact plate (Bathroom - countertop, toilet seat, bathtub, sink, soap bar and dish; Kitchen - refrigerator door handle, table top).

^a All objects and surfaces were not present in all homes; if present, the object/surface was sampled. *n* represents the number of households in which this surface was present.

^b A dog or cat was present in 81 (54%) households; 132 dogs and cats were cultured in 71 (47%) households.

^c Both MRSA and MSSA were recovered from 1 computer keyboard/mouse and 1 index case bed linens.

^d If a landline was not present, the mobile phone of the index case or his/her mother was cultured.

the infection prompting study enrollment); 59% and 27%, respectively, reported an SSTI (of any etiology) in the year prior to enrollment.

Prevalence of *S. aureus* environmental contamination and pet carriage

S. aureus was recovered from ≥ 1 environmental surface in 95 (63%) of 150 households (median 3 surfaces [range 1–18]); MRSA was recovered from surfaces in 69 (46%) households (median 2 surfaces [range 1–18]) (Table 1). Of households with *S. aureus* contamination, 39 (41%) were contaminated exclusively with MRSA, 26 (27%) exclusively with methicillin-susceptible *S. aureus* (MSSA), and 30 (32%) with both.

The most common sites of environmental MRSA contamination were the index case's bed linens (15%), television remote control (15%), kitchen table (12%), computer keyboard/mouse (12%), bathroom countertop (11%), and refrigerator door handle (11%) (Table 1). Surfaces that were less frequently MRSA-contaminated overall (index case bath towel, kitchen sink faucet handle or hand towel, and bathtub soap bar/dish) were more likely to be contaminated in households with a higher proportion of MRSA-contaminated environmental surfaces (Fig. 1).

Pet dogs or cats were present in 81 (54%) households (median 2 [range 1–9] pets per household). Overall, 100 dogs and 32 cats from 71 households were swabbed; 16 (16%) dogs and 3 (9%) cats

carried MRSA (Table 1). While 50% of pets whose primary caretaker (i.e., the human primarily responsible for their feeding, exercising, and waste clean-up) was MRSA-colonized also carried MRSA, just 4% of pets whose primary caretaker was not MRSA-colonized carried MRSA ($p < 0.001$); for 3 of the 4 pets who carried MRSA without an MRSA-colonized caretaker, an alternate household member was colonized. Pets with MRSA carriage lived in households with higher household member MRSA colonization pressure (median 0.50, interquartile range [IQR] 0.25–0.75) than pets without carriage (median 0.08, IQR 0.00–0.27; $p < 0.001$). No relationship was observed between pet MRSA carriage and pet daycare/boarding attendance, sleeping with colonized household members, overall health, or infection history.

Factors associated with environmental contamination

In univariate analyses, a higher proportion of MRSA-contaminated environmental surfaces was associated with the index case being African-American or multiracial (vs. Caucasian, $p = 0.01$), renting the home (vs. owning, $p = 0.001$), index case MRSA colonization ($p < 0.001$), and any household member MRSA colonization ($p < 0.001$) (Supplementary Table 3). In addition to the covariates significantly associated with a higher proportion of MRSA-contaminated environmental surfaces, a higher proportion of *S. aureus*-contaminated environmental surfaces was associated with Medicaid or no health insurance (vs. private or Tricare,

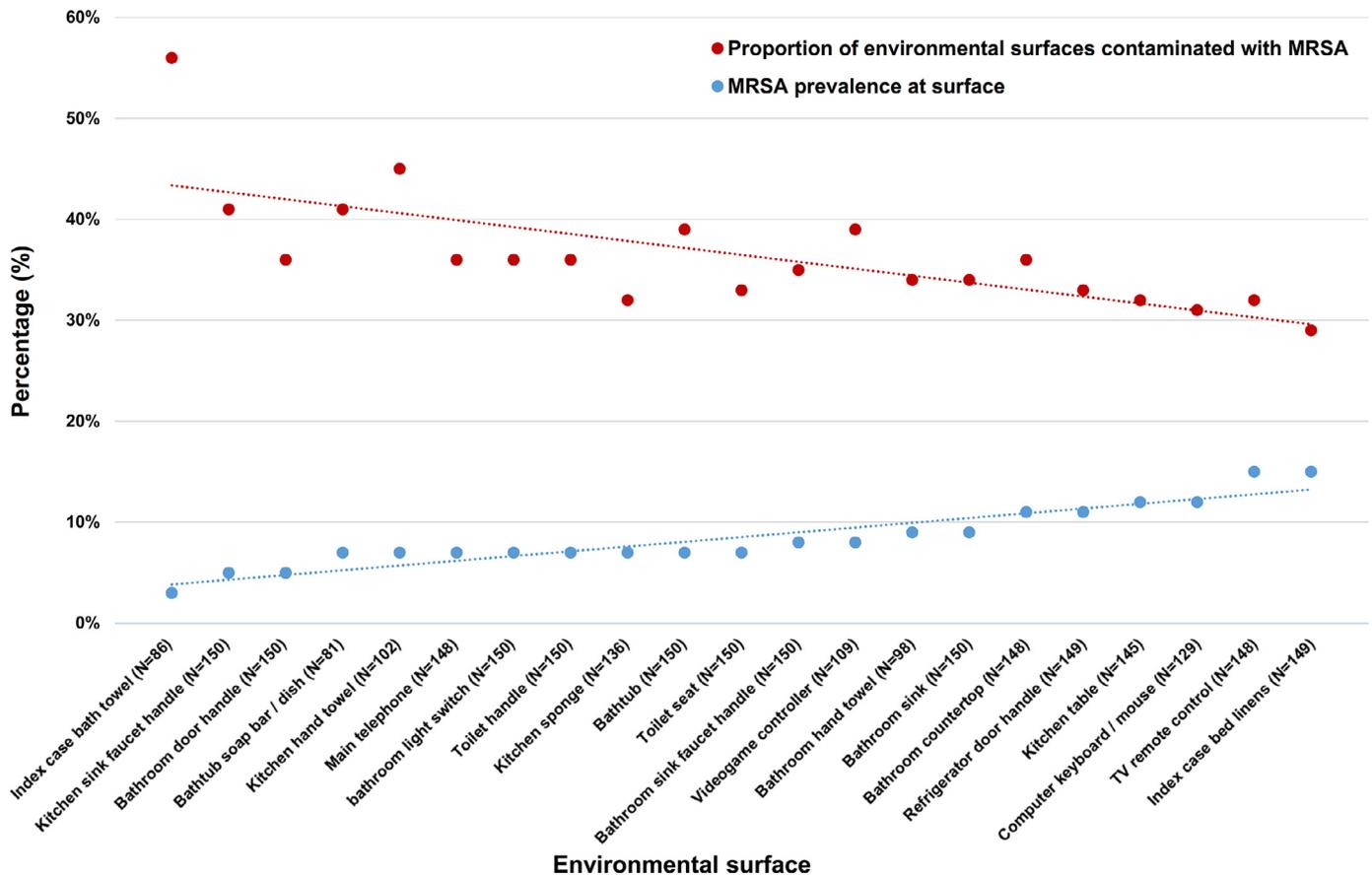


Fig. 1. Prevalence of MRSA contamination at specific surfaces (blue dots/bottom trendline) is inversely related to the proportion of environmental surfaces contaminated with MRSA in households when given surface is contaminated with MRSA (red dots/top trendline). Environmental surfaces are listed from left to right in order of increasing MRSA prevalence. When infrequently colonized surfaces (e.g., the index case bathroom towel) are contaminated with MRSA, the proportion of environmental surfaces contaminated with MRSA is high, suggesting these surfaces require a high burden of MRSA in the household prior to becoming colonized. Conversely, the most frequently contaminated surfaces (e.g., the index case bed linens) are contaminated in the context of a low proportion of environmental surfaces contaminated with MRSA, suggesting these surfaces are the first fomites to be colonized (inverse relationship between colonization prevalence and the proportion of environmental surfaces contaminated with MRSA demonstrated via linear regression analysis; $\beta = -0.696$, $p < 0.001$).

$p = 0.03$) and presence of more unique *S. aureus* strains in the household ($p < 0.001$). Neither prior *S. aureus* infections nor past-year SSTIs in household members were associated with *S. aureus* or MRSA surface contamination.

Predicting environmental contamination: multivariable models

Personal colonization and pet carriage model

Covariates significantly predictive of a higher proportion of MRSA-contaminated environmental surfaces included increased household member MRSA colonization pressure, MRSA as the dominant *S. aureus* strain colonizing household members, increased number of unique *S. aureus* strains (by repPCR) per household member, and renting (vs. owning) the home (Table 2).

Household practices and personal behaviors model

Given the strong influence of personal colonization on environmental contamination in the 'Personal Colonization and Pet Carriage' model, we developed models that excluded human colonization and pet carriage to discern the influence of personal behaviors on household environmental contamination. Renting (vs. owning) the home and index case African-American (or multiracial) race (vs. Caucasian) were predictive of a higher proportion of MRSA-contaminated environmental surfaces (Table 2, Supplementary Figure 1).

Molecular epidemiology of *S. aureus* strains in households

Overall (including index cases, household contacts, environmental surfaces, and pets), up to 7 (median 2) unique strains (by repPCR) were recovered from a single household. Up to 4 strains (median 1) were recovered from the environmental surfaces of a single household. Crowded households (> 2 people per bedroom) harbored more strains overall (median 2, interquartile range [IQR] 2–4) than non-crowded households (median 2, IQR 1–2; $p = 0.004$). Households assigned a home cleanliness score of below average or very dirty harbored more strains (median 2, IQR 1–3) than average or above average households (median 1, IQR 1–2; $p = 0.01$). Households with more strains also had a higher proportion of *S. aureus*-contaminated environmental surfaces ($p = 0.001$, Supplementary Table 3, Supplementary Figure 1).

The MRSA isolate from the enrollment infection was available for 91 (61%) index cases, and a concordant strain was recovered from an environmental surface in 44 (48%) of these households. The enrollment infecting strain was the most common strain recovered in 37 (64%) of 58 MRSA-contaminated household environments. An environmental surface was contaminated with a *S. aureus* strain concordant with an index case colonizing or infecting strain in 60 (52%) of 116 households with an available index case strain (Supplementary Figure 2A); an environmental surface was contaminated with a household contact-concordant strain in 68

Table 2
Factors associated with proportion of environmental surfaces contaminated with *S. aureus* and MRSA, multivariable model.

Factor	<i>S. aureus</i>		MRSA	
	Rate Ratio (95% CrI)	pMCMC	Rate Ratio (95% CrI)	pMCMC
Personal Colonization and Pet Carriage Model				
Household member <i>S. aureus</i> colonization pressure ^a	14.8 (5.2–41.2)	<0.001	–	–
Household member MRSA colonization pressure ^a	–	–	21.6 (5.3–102.8)	<0.001
MRSA dominant <i>S. aureus</i> colonizing household members (vs. MSSA)	1.4 (1.1–1.7)	0.002	2.6 (1.8–3.6)	<0.001
Number of unique strains (by repPCR) per household member	3.4 (1.5–7.4)	0.002	5.2 (2.1–12.8)	<0.001
Renting (vs. owning) home	1.5 (1.01–2.4)	0.05	1.9 (1.2–3.1)	0.009
Proportion of household members reporting SSTI in prior year ^b	–	–	0.4 (0.1–0.9)	0.03
Individuals per square foot of home	1.12 (0.99–1.3)	0.06	–	–
Household Practices and Personal Behaviors Model^c				
Renting (vs. owning) home	2.5 (1.5–4.2)	<0.001	3.1 (1.5–7.0)	0.003
African–American or multiracial ^d (vs. Caucasian) race of index case	1.7 (1.0–2.9)	0.05	2.7 (1.2–6.5)	0.02
Public (vs. private) insurance status of index case	–	–	0.4 (0.2–1.1)	0.06
Proportion of household members reporting SSTI in prior year ^b	0.6 (0.3–1.6)	0.33	0.5 (0.1–1.9)	0.30
Proportion of household members reporting bathing once daily or more	–	–	1.03 (0.4–2.8)	0.96
Proportion of household members reporting washing bed linens once weekly or more	–	–	0.8 (0.3–2.0)	0.63

Note. Poisson generalized linear mixed models constructed in the R library 'MCMCglmm'. See **Supplementary Methods** for runtime parameters and **Supplementary Tables 1 and 2** for primary and secondary covariates used in model selection. “–” denotes variable not included in applicable model.

Abbreviations: MRSA, methicillin-resistant *S. aureus*; CrI, credible interval; SSTI, skin and soft tissue infection.

^a Colonization pressure calculated as (number of *S. aureus* [MRSA] colonized anatomic sites) / [(number of sampled household members)*(number of sampled anatomic sites)].

^b This does not include the infection that prompted enrollment into the study.

^c Excludes personal colonization and pet carriage information.

^d Multiracial participants include African–American/Caucasian ($N=9$), Caucasian/American Indian ($N=1$), and African–American/Caucasian/American Indian ($N=1$).

(45%) of 150 households. Strains discordant with index case strains were recovered from the environment in 18 (23%) of 78 households with both an available index case strain and environmental contamination (Supplementary Figure 2B); only 4 (5%) of these 78 household environments yielded a strain not recovered from a human household member. Among household contacts, siblings of index cases were the most likely to be colonized with a strain recovered from an environmental surface (31%), while adults other than the index case's parents were least likely to be colonized with environmental strains (11%, $p=0.03$).

Overall, the index case's bed linens, TV remote control, and refrigerator door handle were most often colonized with a *S. aureus* strain concordant with an index case strain (Supplementary Figure 2A), reflective of environmental sites with high colonization prevalence (Table 1). Focusing on contaminated surfaces, in households with an available index case strain, the bathroom soap bar/dish, bathroom hand towel, and bathroom door handle were most often colonized with a strain concordant with an index case strain (Supplementary Figure 2B). Certain high-touch surfaces shared by all household members, such as the toilet handle, kitchen hand towel, and videogame controller were more often colonized with a household contact strain than an index case strain (Supplementary Figure 2B).

Of 130 swabbed pets with a swabbed primary caretaker, 104 (80%) did not carry *S. aureus*. Sixteen (12%) pets carried a *S. aureus* strain concordant with a primary caretaker strain, while 4 (3%) pets carried a strain discordant from primary caretaker strains; the primary caretaker was not colonized for 6 (5%) pets carrying *S. aureus* (Fig. 2). Overall, 6 (5%) of 132 swabbed pets carried a distinct strain not recovered from a human household member. Likelihood of strain concordance did not differ between dogs and cats nor between pets who did and did not sleep with a household member. In 14 households with both environmental contamination and pet carriage, 13 (93%) displayed strain concordance between these sites.

Discussion

In the present study characterizing households of children with MRSA SSTI, nearly half of homes were found to harbor environ-

mental MRSA contamination. In addition to the index case's bed linens, commonly touched and shared surfaces (TV remote control, computer keyboard/mouse, and kitchen table) were the fomites most likely to be MRSA-contaminated. In most households, the index case infecting strain was the predominant environmental strain. Moreover, while >20% of households with pets had dogs and/or cats with MRSA carriage, such carriage rarely occurred in the absence of a MRSA-colonized household member. While the cross-sectional nature of our study precludes defining directionality of transmission, our data support the premise that infected/colonized household members contaminate their home environment and subsequently, environmental reservoirs perpetuate the cycle of reacquisition and transmission.

The prevalence of household environmental MRSA contamination (46%) was higher in the present study compared to two prior US studies in homes of patients with MRSA SSTI. Studies conducted in Chicago/Los Angeles and New York recovered MRSA from environmental surfaces in 27% and 30% of homes, respectively.^{12,28} Our higher measured prevalence of environmental contamination may reflect inclusion of more surfaces (21 vs. ~8–11) and solely pediatric index cases (vs. households without children), who may be in closer contact with their environment; indeed, strains recovered from children had the highest concordance with environmental strains. While several surfaces with high MRSA prevalence (e.g., TV remote control, refrigerator door handle, computer, index case bed linens) were sampled across all studies, the present study identified other frequently contaminated sites (e.g., kitchen table, bathroom countertop) that represent potential targets for intervention.

It has been demonstrated that occupants leave an identifiable bacterial signature on household surfaces. Lax and colleagues monitored household microbial communities before and after a physical move; bacterial communities of participants' new homes promptly converged on the communities of their original homes, implicating household members as the vector.²⁹ Collectively, our predictive models indicate that household member colonization pressure is the most significant predictor of the burden of MRSA environmental contamination. In the majority of households in our study, the index case infecting strain was the predominant environmental strain; in prior studies, environmental contamination

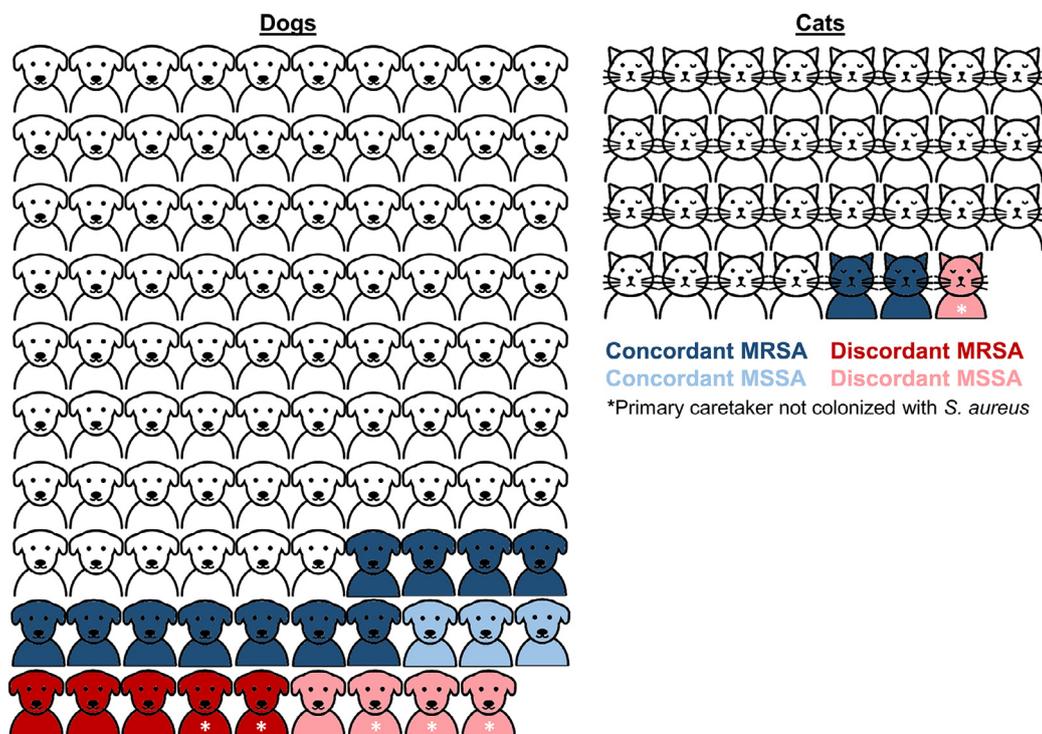


Fig. 2. Molecular epidemiology of *S. aureus* strains recovered from pet dogs ($N=99$) and cats ($N=31$) and their primary caretakers (i.e., the human who is primarily responsible for their feeding, exercising, and waste clean-up). Pets carrying strains concordant or discordant with their primary caretaker are shaded in blue and red, respectively; pets shaded in white did not carry *S. aureus*. Darker and lighter shades represent MRSA and MSSA pet carriage, respectively. Asterisk (*) denotes that the pet carried *S. aureus* while the primary caretaker was not colonized with *S. aureus* (and thus, colonization status was discordant). Figure excludes one cat and one dog who each carried *S. aureus* but whose primary caretakers were not sampled. Artwork created by Llisole from Noun Project (<https://thenounproject.com>).

with clinical *S. aureus* strains has been associated with household transmission, reacquisition, and recurrent infection.^{12,28,30} In total, the available data indicate that household contamination with *S. aureus* is a marker of household member colonization, which itself is driven by complex influences of epidemiological, behavioral, and genetic factors. When household member MRSA colonization (the strongest influence on environmental contamination) was removed in our models, home renting (vs. ownership) was the most informative covariate in predicting environmental MRSA contamination. This relationship may be influenced by crowding and lower home cleanliness, possible surrogates of lower socioeconomic status in our study.³¹

The present study of household MRSA contamination is strengthened by the sampling of companion animals. While *S. aureus* has been recovered from pets, such carriage can resolve without antimicrobial treatment, suggesting that pets are not a natural *S. aureus* reservoir.⁷ A study in the United Kingdom sequenced genomes of 46 isolates from MRSA-infected pets, all of which clustered with human colonizing strains from unrelated patients, representing the circulating epidemic clade.³² These data suggest *S. aureus* transmission from human to pet, though the study did not include colonizing isolates of human household contacts. In the present study of households of children with MRSA SSTI, more than 20% of sampled companion animals carried *S. aureus* (14% carried MRSA). Importantly, pets were more likely to carry MRSA if their primary caretaker was MRSA-colonized and if household member MRSA colonization pressure was higher. Additionally, pets almost exclusively carried strains concordant with both the index case infecting strain and strains found on environmental surfaces. Collectively, these studies indicate that while pets may participate in household *S. aureus* transmission, humans represent the primary source of *S. aureus* in pets.

Compared to other recent studies,^{9,12} the present work systematically sampled a much higher proportion of household members and more environmental surfaces, and included companion animals, to provide the most comprehensive available picture of household *S. aureus* dynamics. Our conclusions are based on substantial epidemiologic data and advanced statistical modeling techniques. We quantified the proportion of contaminated surfaces rather than recording only presence or absence of environmental *S. aureus*, though we did not measure the density of *S. aureus* at each surface. As the primary objective of this study was to identify household reservoirs of MRSA to inform interventions to interrupt MRSA transmission and prevent recurrent infections, we only sampled households of children with MRSA SSTI. Strain concordance between the MRSA enrollment infection isolate and other recovered isolates could only be evaluated in the 91 households where it was available. A further limitation of the study is that due to its cross-sectional nature, directionality of transmission among humans, pets, and the environment were not definitively established. Finally, while whole-genome sequencing would provide the highest strain resolution, repPCR has been shown to be highly discriminatory, especially in the household context.²³

In this comprehensive investigation of households affected by CA-MRSA, we have demonstrated that household member colonization pressure is the most significant predictor of household environmental contamination. These findings suggest that environmental reservoirs, particularly those shown here to harbor a high burden of MRSA, may perpetuate the cycle of reacquisition and transmission. Thus, in addition to personal decolonization, integrating environmental hygiene measures (which have been effective in healthcare settings³³) may prove beneficial in household infection prevention efforts. Longitudinal studies are needed to fur-

ther elucidate *S. aureus* household transmission dynamics, prevalence and factors associated with persistent colonization, and how these phenomena relate to recurrent infection, ultimately informing the design of interventions to disrupt transmission and prevent infection.

Conflicts of interest

All authors declare no conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2018.11.006.

References

- Kaplan SL. Community-acquired methicillin-resistant *Staphylococcus aureus* infections in children. *Semin Pediatr Infect Dis* 2006;**17**:113–19.
- Miller LG, Diep BA. Clinical practice: colonization, fomites, and virulence: rethinking the pathogenesis of community-associated methicillin-resistant *Staphylococcus aureus* infection. *Clin Infect Dis* 2008;**46**:752–60.
- Diekema DJ, Richter SS, Heilmann KP, Dohrn CL, Riahi F, Tendolkar S, et al. Continued emergence of USA300 methicillin-resistant *Staphylococcus aureus* in the United States: results from a nationwide surveillance study. *Infect Control Hosp Epidemiol* 2014;**35**:285–92.
- Kallen AJ, Mu Y, Bulens S, Reingold A, Petit S, Gershman K, et al. Health care-associated invasive MRSA infections, 2005–2008. *JAMA* 2010;**304**:641–8.
- Huang SS, Septimus E, Kleinman K, Moody J, Hickok J, Avery TR, et al. Targeted versus universal decolonization to prevent ICU infection. *N Engl J Med* 2013;**368**:2255–65.
- Fritz SA, Hogan PG, Hayek G, Eisenstein KA, Rodriguez M, Epplin EK, et al. Household versus individual approaches to eradication of community-associated *Staphylococcus aureus* in children: a randomized trial. *Clin Infect Dis* 2012;**54**:743–51.
- Davis MF, Iverson SA, Baron P, Vasse A, Silbergeld EK, Lautenbach E, et al. Household transmission of methicillin-resistant *Staphylococcus aureus* and other staphylococci. *Lancet Infect Dis* 2012;**12**:703–16.
- Fritz SA, Epplin EK, Garbutt J, Storch GA. Skin infection in children colonized with community-associated methicillin-resistant *Staphylococcus aureus*. *J Infect* 2009;**59**:394–401.
- Miller LG, Eells SJ, Taylor AR, David MZ, Ortiz N, Zychowski D, et al. *Staphylococcus aureus* colonization among household contacts of patients with skin infections: risk factors, strain discordance, and complex ecology. *Clin Infect Dis* 2012;**54**:1523–1535.
- Rodriguez M, Hogan PG, Burnham CA, Fritz SA. Molecular epidemiology of *Staphylococcus aureus* in households of children with community-associated *S. aureus* skin and soft tissue infections. *J Pediatr* 2014;**164**:105–11.
- Kaplan SL, Forbes A, Hammerman WA, Lamberth L, Hulten KG, Minard CG, et al. Randomized trial of “bleach baths” plus routine hygienic measures vs. routine hygienic measures alone for prevention of recurrent infections. *Clin Infect Dis* 2014;**58**:679–82.
- Knox J, Uhlemann AC, Miller M, Hafer C, Vasquez G, Vavagiakis P, et al. Environmental contamination as a risk factor for intra-household *Staphylococcus aureus* transmission. *PLoS ONE* 2012;**7**:e49900.
- Uhlemann AC, Knox J, Miller M, Hafer C, Vasquez G, Ryan M, et al. The environment as an unrecognized reservoir for community-associated methicillin resistant *Staphylococcus aureus* USA300: a case-control study. *PLoS ONE* 2011;**6**:e22407.
- Morris DO, Loeffler A, Davis MF, Guardabassi L, Weese JS. Recommendations for approaches to methicillin-resistant staphylococcal infections of small animals: diagnosis, therapeutic considerations and preventative measures. Clinical Consensus Guidelines of the World Association for Veterinary Dermatology. *Vet Dermatol* 2017;**28**:304–e69.
- Shahbazian JH, Hahn PD, Ludwig S, Ferguson J, Baron P, Christ A, et al. Multidrug and mupirocin resistance in environmental methicillin-resistant *Staphylococcus aureus* (MRSA) collected from the homes of people diagnosed with a community-onset (CO-) MRSA infection. *Appl Environ Microbiol* 2017;**83**:e01369–17.
- Ng W, Faheem A, McGeer A, Simor AE, Gelosia A, Willey BM, et al. Community- and healthcare-associated methicillin-resistant *Staphylococcus aureus* strains: an investigation into household transmission, risk factors, and environmental contamination. *Infect Control Hosp Epidemiol* 2017;**38**:61–7.
- Klevens RM, Morrison MA, Fridkin SK, Reingold A, Petit S, Gershman K, et al. Community-associated methicillin-resistant *Staphylococcus aureus* and healthcare risk factors. *Emerg Infect Dis* 2006;**12**:1991–3.
- Halliday G, Snowdon J. The environmental cleanliness and clutter scale (ECCS). *Int Psychogeriatr* 2009;**21**:1041–50.
- Fritz SA, Hogan PG, Singh LN, Thompson RM, Wallace MA, Whitney K, et al. Contamination of environmental surfaces with *Staphylococcus aureus* in households with children infected with methicillin-resistant *S. aureus*. *JAMA Pediatr* 2014;**168**:1030–8.
- Hogan PG, Burnham CA, Singh LN, Patrick CE, Lucas JC, Wang JW, et al. Evaluation of environmental sampling methods for detection of *Staphylococcus aureus* on fomites. *Ann Public Health Res* 2015;**2**:1013.
- Cockerill F. *Performance standards for antimicrobial susceptibility testing: twenty-third informational supplement; M100-S23*. Wayne, PA: Clinical and Laboratory Standards Institute; 2013.
- Del Vecchio VG, Petroziello JM, Gress MJ, McCleskey FK, Melcher GP, Crouch HK, et al. Molecular genotyping of methicillin-resistant *Staphylococcus aureus* via fluorophore-enhanced repetitive-sequence PCR. *J Clin Microbiol* 1995;**33**:2141–4.
- Rodriguez M, Hogan PG, Satola SW, Crispell E, Wylie T, Gao H, et al. Discriminatory indices of typing methods for epidemiologic analysis of contemporary *Staphylococcus aureus* strains. *Medicine* 2015;**94**:e1534.
- Rychert J, Burnham CA, Bythrow M, Garner OB, Ginocchio CC, Jennemann R, et al. Multicenter evaluation of the Vitek MS matrix-assisted laser desorption ionization-time of flight mass spectrometry system for identification of Gram-positive aerobic bacteria. *J Clin Microbiol* 2013;**51**:2225–31.
- R Core Team. *R: A language and environment for statistical computing*, Vienna, Austria: R Foundation for Statistical Computing; 2016. Available from: <https://www.R-project.org/>.
- National Archives and Records Administration, Department of Commerce, Bureau of the Census Qualifying Urban Areas for the 2010 Census. *Federal Register* 2012;**77**:18651–69.
- U.S. Department of Commerce USCB. *Tiger/Line Shapefiles* Available from: <ftp://ftp2.census.gov/geo/tiger/TIGER2012/UAC/>.
- Eells SJ, David MZ, Taylor A, Ortiz N, Kumar N, Sieth J, et al. Persistent environmental contamination with USA300 methicillin-resistant *Staphylococcus aureus* and other pathogenic strain types in households with *S. aureus* skin infections. *Infect Control Hosp Epidemiol* 2014;**35**:1373–82.

29. Lax S, Smith DP, Hampton-Marcell J, Owens SM, Handley KM, Scott NM, et al. Longitudinal analysis of microbial interaction between humans and the indoor environment. *Science* 2014;**345**:1048–52.
30. Miller LG, Eells SJ, David MZ, Ortiz N, Taylor AR, Kumar N, et al. *Staphylococcus aureus* skin infection recurrences among household members: an examination of host, behavioral, and pathogen-level predictors. *Clin Infect Dis* 2015;**60**:753–63.
31. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Smith GD. Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006;**60**:7–12.
32. Harrison EM, Weinert LA, Holden MT, Welch JJ, Wilson K, Morgan FJ, et al. A shared population of epidemic methicillin-resistant *Staphylococcus aureus* 15 circulates in humans and companion animals. *mBio* 2014;**5**:e00985–13.
33. Datta R, Platt R, Yokoe DS, Huang SS. Environmental cleaning intervention and risk of acquiring multidrug-resistant organisms from prior room occupants. *Arch Intern Med* 2011;**171**:491–4.