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Longitudinal, Strain Specific *Staphylococcus aureus* Introduction and Transmission Events in a Prospective Cohort Study of Households with Community-Associated Methicillin-Resistant *S. aureus* Skin and Soft Tissue Infection

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Abstract

Background—We comprehensively defined household longitudinal, strain-level *Staphylococcus aureus* transmission dynamics in households of children with community-associated methicillin-resistant *S. aureus* (CA-MRSA) skin and soft tissue infection (SSTI).

Methods—Between 2012–2015, 150 children, their household contacts, and pets were enrolled in a prospective cohort study in metropolitan Saint Louis, MO. Serial cultures to detect *S. aureus* were collected from three anatomic sites of household members, two dog/cat sites, and 21

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Contributors

RLM, PGH, SJG, CDB, and SAF contributed to the study concept and design. PGH, CEM, MGB, RMT, JJM, JS, RCO, and SAF contributed to acquisition of clinical data. PGH, CEM, MLS, JJM, CDB, and SAF contributed to acquisition of laboratory data. RLM, PGH, AR, and SAF contributed to statistical analysis. RLM, PGH, SJG, JBW, CDB, and SAF contributed to data interpretation. RLM, PGH, and SAF contributed to initial manuscript drafting. RLM, PGH, CEM, MGB, RMT, MLS, JJM, JS, RCO, SJG, JBW, CDB, AR, and SAF contributed to revisions for intellectual content. SAF, AR, and JBW obtained funding. RMT provided technical support. All authors approved the final version and agreed to be accountable for all aspects of the manuscript.

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Declaration of interests

We declare that we have no conflicts of interest.

environmental surfaces five times over 12 months. Molecular epidemiology of *S. aureus* isolates was determined via repetitive-sequence PCR. Longitudinal, multivariable generalized mixed-effects logistic regression models identified factors associated with *S. aureus* acquisition.

Findings—Household MRSA acquisitions (N=1267) were driven equally by introduction of novel strains into households (N=510) and transmissions within households (N=602; between household members, environmental surfaces, and pets), each associated with distinct factors. Participants demonstrating frequent handwashing practices were less likely to introduce novel strains into the household (odds ratio [OR] 0.86, credible interval [CrI] 0.74–1.01). Transmission recipients were less likely to own their homes (OR 0.77, CrI 0.63–0.94) and were more likely to share bedrooms with strain-colonized individuals (OR 1.33, CrI 1.12–1.58), live in homes with higher environmental *S. aureus* contamination burden (OR 3.97, CrI 1.96–8.20), and report interval SSTI (OR 1.32, CrI 1.07–1.64). Transmission sources were more likely to share bath towels (OR 1.25, CrI 1.01–1.57). Pets were often transmission recipients, but rarely the sole transmission source.

Interpretation—The household environment plays a key role in transmission, a factor associated with SSTI. Future interventions should inclusively target household members and the environment, focusing on straightforward changes in hand hygiene and sharing behaviors.

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Introduction

Staphylococcus aureus causes a spectrum of infections, from asymptomatic colonization to invasive, life-threatening disease. Contemporary skin and soft tissue infections (SSTIs) are most commonly attributed to the emergence in the late 1990s of epidemic strains of community-associated methicillin-resistant *S. aureus* (CA-MRSA).^{1,2} Up to 70% of patients with CA-MRSA SSTI experience recurrent infections within one year.^{3,4} Thus, devising comprehensive control strategies to prevent transmission and recurrent infection is of high priority.

MRSA colonization prevalence in household contacts of patients with CA-MRSA infection is high, frequently with a strain concordant with the index patient's infecting strain, while the prevalence is much lower among household contacts of individuals colonized, but not infected, with MRSA.^{5–9} We previously investigated a household approach to decolonization, comprising topical antimicrobials and improved hygiene measures targeted at index patients and all household contacts. While this household approach significantly reduced subsequent SSTI incidence compared to decolonization of the index patient alone, it did not sufficiently eliminate the problem.³ Thus, although *S. aureus* transmission has traditionally been attributed to person-to-person contact, other vectors, including environmental sources and companion animals, also warrant evaluation. Environmental surfaces and fomites can harbor MRSA for prolonged periods.^{10,11} While numerous studies have illuminated transmission within hospitals,^{12,13} our understanding of the impact of

environmental contamination and pet carriage on MRSA transmission dynamics within the household is limited.

Devising effective, targeted preventive approaches requires an understanding of the dynamics of both introduction of MRSA into the household and its subsequent intra-household transmission. While MRSA colonization among household members has been evaluated, prior studies, including a pilot study by our group, have been limited by assessing only a single time point, collecting limited epidemiologic data, discounting the household environment, excluding companion animals, or performing low-resolution strain typing.^{6,14–16} The objective of this study was to comprehensively define household longitudinal, strain-level *S. aureus* dynamics, including the introduction of novel strains and the transmission of established strains among household members, environmental surfaces, and pets, in households of children experiencing CA-MRSA infections. These dynamics were assessed in the context of extensive demographic, hygiene, health, and activity characteristics to inform household-level interventions to interrupt MRSA transmission and prevent recurrent infections.

Methods

Participants and data collection

Participants—From 2012–2015, otherwise healthy pediatric patients with culture-confirmed, community-onset MRSA infections were recruited for the “HOME: Household Observation of MRSA in the Environment” prospective cohort study from hospitals and community practices in metropolitan St. Louis. Children with healthcare-related risk factors were excluded, as determined by evidence of recent hospitalization, invasive medical device, or residence in a long-term care facility.¹⁷

Within a median of 20 days (range, 3–95 days) after infection, a baseline visit was conducted in the index patient’s primary home. Household contacts (individuals sleeping in the home 4 nights per week) and indoor dogs and cats were also enrolled. The baseline visit included a detailed epidemiologic interview and sampling of people, pets, and environmental surfaces for recovery of *S. aureus*. Four quarterly visits consisted of follow-up interviews and repeat sampling of people, pets, and environmental surfaces (Supplementary Table 1). The Washington University Institutional Review Board and Institutional Animal Care and Use Committee approved study procedures. Informed consent/assent was obtained for all participating household members and pets.

Data collection—Prior *S. aureus* infections, hygiene practices, activities, pet characteristics, household attributes, and cleaning practices were surveyed at baseline. To ensure a bias-free assessment of household cleanliness, the research team assigned a four-point “household cleanliness score.”¹⁸

Longitudinal surveys measured interval SSTIs, healthcare exposure, and use of systemic and topical antimicrobials. At each visit, colonization cultures were collected from the anterior nares, axillae, and inguinal folds of all household members (Eswab, Becton Dickinson [BD], Franklin Lakes, NJ) and from the nares (minitip Eswab, BD) and dorsal fur (Eswab) of

indoor dogs and cats. Up to 21 environmental surfaces were also sampled (Eswab and Baird Parker Agar contact plate [Hardy, Santa Maria, CA]): electronics (television remote control, main telephone, computer keyboard/mouse, videogame controller), kitchen (refrigerator door handle, table, sink faucet handle, sponge/cloth, hand towel), bathroom (sink, bathtub, toilet seat, countertop, soap bar/dish, toilet handle, light switch, door handle, index patient bath towel, sink faucet handle, hand towel), and bedroom (index patient bed sheets/pillowcases).¹⁹

Microbiological methods—Available MRSA isolates (n=91) and antibiotic susceptibility profiles from the enrollment SSTI were obtained from clinical microbiology laboratories. *S. aureus* was recovered from swabs using broth enrichment and from contact plates based on colony morphology (Supplementary Methods). *S. aureus* was identified and antibiotic susceptibility profiles were determined according to the Clinical and Laboratory Standards Institute.²⁰ Molecular typing was performed by repetitive-sequence PCR (repPCR), using a 95% similarity cutoff to define distinct *S. aureus* strains within each household.^{21,22}

Definitions

Strain type: composite of repPCR designation and methicillin resistance profile for each recovered *S. aureus* isolate; unique to each household.

Acquisition: strain type recovered from an individual, environmental surface, or pet not colonized with the given strain at the prior sampling. An acquisition could occur via a strain introduction or transmission.

Strain introduction: strain type first appeared within a household at a sampling beyond baseline. The number of introductions at a time point is the number of individuals or pets colonized by the novel strain at its first appearance (i.e., “personal introductions”), and one additional if the strain appears on 1 environmental surface (i.e., “environmental introduction”); e.g., a strain newly recovered from two individuals, one pet, and two environmental surfaces would constitute four household introductions.

Transmission: person became colonized for the first time (i.e., “transmission recipient”) with a strain recovered at the preceding time point from 1 person, pet, or environmental site (i.e., “potential transmission source”). The number of transmissions at a time point is equal to the number of transmission recipients. Since multiple individuals, pets, and environmental sites may be colonized with a given strain at prior sampling, the number of “potential transmission paths” is the number of transmission sources multiplied by the number of transmission recipients for a given strain.

Personal colonization pressure: the number of anatomic sites (three per person: axillae, nares, and groin) colonized with *S. aureus*, MRSA, or a given strain, divided by the number of sites sampled (personal *S. aureus*, MRSA, or strain colonization pressure, respectively).

Environmental contamination pressure: the number of contaminated environmental sites divided by the number of sites sampled.

Statistical analysis

Univariate analyses were conducted in R²³ or Python version 2.7.15 using the scipy package (version 1.1.0).²⁴ Fisher's exact test was employed for all 2×2 contingency table tests. Kruskal-Wallis nonparametric one-way analysis of variance was used for pairwise comparisons between sets of continuous observations. Spearman's nonparametric rank correlation was used when calculating correlation between two covariates. See the Supplementary Methods for more detail regarding statistical tests.

The *strain introduction*, *transmission recipient*, and *transmission source* models (Supplementary Methods) are longitudinal, multivariable generalized mixed-effects logistic regression models fitted using the R library "MCMCglmm,"²⁵ with random effects for individual and household included to control for repeated sampling. For model inclusion, each observation in each model was required to be complete (i.e., no missing values allowed). See Supplementary Tables 2–4 for primary and secondary covariates included in each model.

Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

Results

Study population, environment, and colonization status

From 2012–2015, 150 children (median age 3 years, range 1 month–18.6 years) presenting with CA-MRSA infections (149 SSTIs, 1 invasive) and their household contacts (n=521; median age 25 years, range 1 month–82.3 years) were enrolled at baseline; 21 participants who joined the household during the 12-month longitudinal study were also enrolled. Median household size was 4 (range 2–13). Of the 150 households enrolled, 135 (90%) completed the 12-month study visit. Supplementary Table 1 provides details of demographics and individual, environmental, and pet sampling completion over five study visits.

Over 12 months, 513 (74%) individuals were colonized at least once with *S. aureus*, 319 (46%) with MRSA (Supplementary Table 1). Of the 671 individuals participating in 1 follow-up visit, 173 (26%) reported an interval SSTI (including 75 of 144 [52%] index patients). Of 154 pets sampled, 68 (44%) were colonized with *S. aureus* at least once, 44 (29%) with MRSA. Across 12 months, 1 environmental site was contaminated with *S. aureus* in 136 (91%) homes, 104 (69%) with MRSA.

Incidence of acquisitions (strain introductions or transmissions) in household members

Among 650 household members sampled at least twice consecutively in 144 households, we observed 703 total acquisitions. Of these, 308 (44%) were introductions and 297 (42%) were transmissions (Figure 1). The remaining 98 (14%) indeterminate acquisitions involved strains present in the household previously but not at the immediately preceding sampling; it

is unclear whether these represented transmissions or re-introductions. Of these 650 participants, 246 (38%) experienced 1 introduction, 205 (32%) were transmission recipients and 265 (41%) were potential transmission sources (Table 1). Exemplar household acquisitions are illustrated in Figure 2 and Supplementary Figure 1. Significantly more introductions were associated with MSSA (n=209) than MRSA strain types (n=99, $p<0.0001$), while transmissions occurred equally between MSSA (n=150) and MRSA (n=147, $p=0.87$).

Strain introductions

Introduction incidence

The incidence of *S. aureus* introduction was 0.52 introductions per person sampling year (i.e., ~2 individuals would need to be followed for one year to observe one *S. aureus* introduction event). Specifically, an MSSA strain was introduced twice as often as an MRSA strain (0.35 vs. 0.17 introductions per person sampling year, Table 1). Among 341 introduction events, the novel strain was found on 1 household member in 237 (70%) of these events, and in 1 environmental site in 180 (53%) (Table 2). In 94 (28%) introductions, the strain appeared exclusively in the environment (Supplementary Figure 2A). When an introduction event occurred, a median of 1 (range 0–4) household member(s) became colonized (Supplementary Figure 2B) and 1 (range 0–10) environmental site(s) became contaminated (Supplementary Figure 2C) with the novel strain.

Factors associated with strain introductions

We sought to specify demographic, health, hygiene, and activity factors that were associated with strain introductions. In univariate analyses (Supplementary Table 5), individuals who reported washing hands at least “sometimes” after preparing food or “always” after using the bathroom were less likely to experience an introduction. Introductions were more likely to occur in children and daycare attendees, individuals spending fewer nights in the household, and those in households with a lower personal *S. aureus* colonization pressure.

In the longitudinal, multivariable generalized mixed-effects logistic regression model (Supplementary Table 2), introductions were more common in colder months (Table 3). Frequent handwashing remained in the final model, and though not statistically significant ($p=0.06$), reflects a clinically significant factor in reducing strain introductions. Healthcare exposure and visiting public locations (e.g., hair salons, locker rooms, and pools) did not persist in the final introductions model.

Transmissions

Transmission incidence

The incidence of *S. aureus* transmission was 0.50 transmissions per person sampling year (i.e., 2 individuals would need to be followed for one year to observe one *S. aureus* transmission event). MSSA and MRSA strains were equally likely to be transmitted (0.25 transmissions per person sampling year for both, Table 1). Across 205 recipients who became colonized upon 297 transmissions (some were transmission recipients at multiple

samplings), there were 545 potential transmission paths from household members as potential sources (Table 1, Figure 1). Of 297 transmissions, 138 (46%) were associated with a sole transmission source. Environmental sites served as potential sources in 178 transmission paths, and as the sole source in 62 (35%) (Table 2). Transmissions were most common between siblings (112, 21%) and from offspring to parent (101, 19%). Cohabiting parents rarely transmitted strains to each other (25, 5%). Environmental surfaces frequently served as sources of transmitted strains, and varied across recipient age and gender (see Supplementary Figure 3 for normalized transmission risk).

Factors associated with transmissions

At the household level, significantly more transmissions occurred in homes with lower cleanliness scores, rented homes, and those with a higher number of individuals per square foot (Supplementary Table 6). Across samplings, households with higher personal *S. aureus* colonization pressure, higher environmental *S. aureus* contamination pressure, and a higher number of strain types across the environment and household members experienced significantly more transmissions.

Source-recipient pairs were significantly more likely to share a bedroom and/or bed, towel (hand, face, or bath), and hygiene items (e.g., razor, hairbrush) compared to all pairs of household members (Supplementary Table 6). We performed separate analyses for transmission recipients and sources, to determine distinct factors that influence colonized sources in transmitting their strains and eligible recipients in becoming colonized with transmitted strains.

Transmission recipients—In univariate analyses, hygiene practices such as showering (vs. bathing), brushing teeth at least twice daily, and using antibacterial hand soap were significantly associated with reduced transmission reception (Supplementary Table 6). Transmission recipients were more likely to be children, share a bath towel or cosmetics, report an SSTI during the same interval as the transmission, and live in households with higher personal *S. aureus* colonization pressure than non-recipients.

In the multivariable model (Supplementary Table 3), transmission reception was associated with increasing environmental contamination pressure of the transmitted strain, sharing a bedroom with an individual colonized with the transmitted strain, and reporting an SSTI since the prior sampling (Table 3). Conversely, the likelihood of transmission reception of a given strain type was significantly reduced by increasing environmental contamination pressure of all other strain types in the household, showering primarily (vs. taking a bath), and home ownership (vs. renting).

Transmission sources—In univariate analyses, colonized individuals sharing a bedroom or bath towel or using bar soap for handwashing were significantly more likely to be potential transmission sources (Supplementary Table 6). However, colonized individuals using antibacterial hand soap were significantly less likely to be potential transmission sources.

In the multivariable transmission source model (Supplementary Table 4), although we examined many hygiene and sharing behaviors, sharing a bath towel was the only behavior significantly associated with increased likelihood of being a potential transmission source. A higher number of individuals per bathroom was significantly associated with an increased occurrence of transmissions to others in a household (Table 3).

Incidence and factors associated with pet strain introductions and transmissions

A total of 154 pets in 75 households were sampled. Nineteen pets (16 dogs and 3 cats) were associated with 22 introductions, 10 of which appeared exclusively in pets (Supplementary Figure 4, Supplementary Table 7). Thirty-five pets (33%) were transmission recipients. The pet's primary caretaker was a potential source in 13 of 67 transmission paths from household members to pets. Fifteen pets served as potential transmission sources across 26 transmission paths to people; in 3 of these 26 paths, the pet was the exclusive source. While more dogs than cats played a role in household transmissions ($p=0.07$ for both transmission recipient and potential source), no other pet characteristics (age, sharing a bed with a household member, health, history of SSTI) influenced their likelihood of experiencing an introduction or transmission event (Supplementary Table 8).

Discussion

Targeting *S. aureus* household transmission requires understanding the sources of acquisition of novel strains. Previous studies addressing household *S. aureus* have not distinguished whether a strain originates from within the household or the greater community.^{6,7,11,14,15} In contrast, the design of the present study affords the ability to truly discern household acquisition dynamics: 96% of household members were enrolled, colonization samples were obtained five times longitudinally over one year from people, environmental surfaces, and pets, and molecular typing with high discriminatory power²² was performed on all recovered *S. aureus* isolates ($n=3819$). We demonstrate that household MRSA acquisition is driven equally by introduction of novel strains into the household and by transmissions within the household, and that household environmental contamination serves as a key reservoir for transmission. Future interventions must therefore inclusively target household members and their environments.

The present study demonstrates that MRSA acquisition occurs through household introductions and transmissions. Ng et al. reported that in 40% of 68 households with MRSA-infected index patients and non-MRSA-colonized household contacts at initial screening, 1 household contact acquired colonization within 3 months.⁷ Our study suggests that these observed acquisitions were equally likely to be introductions or transmissions; further, MRSA acquisition in households is driven not by one strain type, but likely multiple strain types acquired from sources exogenous to the household. We found that poor handwashing practices and daycare attendance were associated exclusively with introductions in univariate analysis, while strain specific environmental contamination pressure and sharing fomites with colonized individuals were associated with transmission risk assessed via the multivariable model. While these factors have previously been correlated with overall *S. aureus* colonization,^{5,11,26–28} we now demonstrate that

introductions from sources outside the household and transmissions within households are distinct epidemiologic events, each with specific risk factors.

We queried a number of factors and activities exogenous to the household to identify mechanisms of *S. aureus* introduction into households. We found that *S. aureus* introductions significantly occurred in children; moreover, the only activity external to the household that was associated with acquisition in children was daycare attendance in univariate analysis. While contact sports have been associated with MRSA colonization²⁹ and MRSA has been recovered from exercise equipment at fitness centers,³⁰ sports participation and gym attendance were not significantly associated with introductions in our study. Likewise, employment sites linked to high colonization risk, such as schools³¹ or healthcare facilities,³² were not significantly associated with introductions. However, strain types from such locations may already have been established in households before study initiation. Importantly, hand hygiene was shown to be particularly protective against introductions; optimal hand hygiene practices may protect individuals from acquisitions in daily life even when exposure to *S. aureus* is high. Interestingly, one quarter of all household introductions were exclusively on environmental surfaces. Potential mechanisms for these introductions include intermittently colonized household members who had spontaneously resolved their personal colonization prior to the time of sampling, household visitors, or contaminated (and unsampled) fomites brought into the home (e.g., shoes or clothing).

To identify targets for intervention, we also sought to discern strain-level household transmission dynamics. Transmission recipients often shared personal hygiene items or towels with strain-colonized sources. While sharing a bedroom and/or towels was previously associated with increased individual colonization risk,²⁶ the longitudinal and strain-level detail provided by the present study specifies these items as reservoirs of transmission. Additionally, the burden of a given *S. aureus* strain in the household environment was highly predictive of its transmission. This demonstrates that, in addition to personal contact and a high burden of colonization among household members,^{8,33} environmental contamination plays a substantial role in transmission. Lastly, transmission recipients experienced significantly higher incidence of SSTI. While our sampling interval of three months precludes distinguishing cause from effect, acquisition of a novel strain via a transmission event may have often led to SSTI development.

Although concordant colonization with MRSA in pets and their owners or veterinary personnel has been described, the directionality of transmission remains unclear.³⁴ Shahbazian et al. associated the presence of pets with increased risk of household environmental MRSA contamination.³⁵ In the present study, dogs and cats participated in overall household *S. aureus* transmission dynamics. One third of pets were transmission recipients over 12 months; approximately one third of these transmission paths to pets were associated with the primary caretaker or someone sharing a bed with the pet. In contrast, pets were rarely the presumptive source of transmission; only three transmission events occurred in which the pet was the sole putative source. Concordantly, in a study by Davis et al., pets of recently MRSA-infected individuals were not implicated as transmission sources to humans, as discerned by whole-genome sequencing.³⁶ These findings support the prevailing view that humans more commonly transmit *S. aureus* to pets, who may not

represent natural hosts for *S. aureus*, but may serve as reservoirs for transmission or reacquisition.^{37,38} Future research will illuminate the effect of decolonization of people and decontamination of the household environment on pet carriage.

A principal focus of this study was to identify targets to prevent MRSA introduction into homes, interrupt transmission, and prevent recurrent SSTIs. As *S. aureus* transmission was associated with interval SSTI, measures to reduce transmission among household members, including providing separate towels and hygiene items for each family member, might also reduce subsequent SSTI. Likewise, improved handwashing may reduce *S. aureus* acquisition, as community-based trials providing hand hygiene education materials and alcohol-based hand sanitizers have decreased the incidence of gastrointestinal and respiratory illnesses.^{39,40} While the importance of hand hygiene may seem trite, compliance, even in high-stakes, controlled settings (such as hospitals), remains sub-optimal, despite education and ready access to hand hygiene products.⁴¹ Individuals in the community face additional barriers, including limited resources. Potentially straightforward public health programs to implement simple and effective hand hygiene in households and community settings could have far-reaching benefits to prevent a spectrum of infections.⁴² Lastly, *S. aureus* household environmental contamination significantly predicted transmission. As enhanced environmental disinfection in healthcare settings has reduced pathogen transmission and acquisition,⁴³ priority should be given to studies directly testing the effectiveness of targeted surface decontamination in households to reduce *S. aureus* transmission and SSTI.

Longitudinal sampling of household members, their environment, and pets, combined with comprehensive molecular typing and personal and household epidemiologic data, have allowed for the novel delineation of acquisition via strain introduction versus transmission, and features associated with these acquisition modalities. This study does have several limitations. The isolate from interval SSTIs was often unavailable, precluding definite association of these incident SSTIs with individual acquisition events. While repPCR allows for a high degree of strain discrimination,²² it is not as comprehensive as whole genome sequencing (WGS), preventing the analysis of specific genomic signatures associated with transmission. The findings of this study may not be generalizable to geographic locales with lower MRSA colonization prevalence and SSTI incidence. Finally, as all index patients were children, strain acquisition dynamics may not be generalizable to adult-only households.

In this comprehensive investigation of households, we determined that individuals acquire MRSA via both introductions from exogenous sources and within-household transmissions; these routes of acquisition exhibit distinct hygiene and behavioral etiologies, and transmission is significantly associated with SSTI. Introductions and transmission may be mitigated through straightforward changes in household practices, including frequent handwashing and modified sharing behaviors. Prospective studies of high-risk populations should test targeted decolonization regimens for sources as well as protective hygiene practices for their cognate recipients, combined with targeted environmental surface decontamination.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Research in Context

Evidence before this study

We searched PubMed for articles published through November 1, 2018, to identify studies of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) in household settings, particularly acquisition and transmission, using the search terms (“*Staphylococcus aureus*”) AND (“household” OR “home”) AND (“transmission” OR “acquisition” OR “environment” OR “contamination” OR “pet”), which returned 381 results. We screened these articles for relevance as well as those listed in the ‘Similar articles’ tab; references cited within relevant articles were also screened. The household environment and companion animals have both been implicated as potential reservoirs for *S. aureus* in households of children with SSTI. Previously, factors associated with human colonization and environmental contamination have been described and *S. aureus* transmission in the hospital setting has been documented. However, the existing literature regarding *S. aureus* acquisition and transmission in the community setting, and the specific role the household environment and pets play in those dynamics, have been limited by an inadequate definition of transmission, in which studies have assessed a single time point, collected limited epidemiologic data or lacked participation by household contacts, overlooked the household environmental reservoir, omitted companion animals, or employed low-resolution strain typing methodology. Devising targeted, effective preventive approaches requires probing beyond detecting *S. aureus* within the household to determine how it is introduced, and once there, its transmission dynamics.

Added value of this study

This comprehensive, year-long investigation of 150 households affected by CA-MRSA, including sampling of nearly all household members, pet dogs and cats, and an exhaustive list of household surfaces for the detection of *S. aureus*, combined with comprehensive molecular typing, personal and household epidemiologic data, and sophisticated statistical modeling revealed that acquisition of MRSA occurs via both introductions from sources external to the household and transmissions within. Hygiene and behavioral factors associated with introductions and transmissions are distinct, and may be alleviated through modest changes in household practices, such as frequent handwashing and modified sharing behaviors (e.g., designated personal bath towels), respectively. Transmission recipients are at increased risk of reporting interval SSTIs, further implicating the household in the proliferation of CA-MRSA disease.

Implications of all the available evidence

To interrupt *S. aureus* transmission and ultimately prevent SSTI, evidence-based strategies are needed. Future longitudinal studies must investigate targeted decolonization regimens for transmission sources, test protective hygiene practices for potential household recipients, and assess targeted environmental surface decontamination.

Figure 1. Flow diagram of *S. aureus* strain acquisitions.

Across household members, pets, and environmental surfaces, a total of 1267 strain acquisition events were observed. Of these, 510 were novel strain introduction events, 602 were transmission events, and 155 were indeterminate events (present in the household previously but not at the immediately preceding sampling; it is unclear whether these represented transmissions or re-introductions). For these 602 transmission events, there were 749 paths from potential transmission sources to household members. Each individual or pet who became colonized with a strain not present at the prior sampling counted for one acquisition, while one acquisition for the environment was counted when a strain not found anywhere in the environment at the prior sampling appeared on 1 environmental sites.

Icon key
Anterior nares		Toilet seat
Axillae		Toilet handle
Inguinal folds		Light switch
Dog dorsal fur		Sink
Television remote control		Bathtub
Main telephone		Countertop
Computer keyboard & mouse		Soap bar and dish in bath or shower
Videogame controller		Door handle
Index patient bed linens		Index patient bath towel
Hand towel		Refrigerator door handle
Sink faucet handle		Table
Strain from index patient enrollment SSTI	X	SSTI reported
		A	Antibiotics taken
Infection strain	D	Decolonization performed

Figure 2. Longitudinal strain dynamics in exemplar households.

“X” denotes a reported interval SSTI, “A” denotes interval oral or IV antibiotics, and “D” represents interval decolonization (nasal mupirocin, bleach baths, or chlorhexidine body washes). For households A and B, the index patient’s enrollment infection isolate, MRSA_1, is indicated with red hash marks; the red box around this cell signifies an infection (with MRSA_1) prior to the infection prompting enrollment.

Household A. The Index patient experienced an SSTI 3 months prior to the infection that prompted enrollment. Between the 3-month and 6-month follow-up visits, the Index patient experienced a recurrent SSTI caused by MRSA_1 (the enrollment infection strain), denoted by a red box around the cell; for this infection, the Index patient received systemic antibiotics and subsequently performed decolonization. Example introduction events occurred at the 3-month follow-up visit: novel strain MSSA_7 appeared on Half-sister 3, Dog 1, and electronic and bathroom environmental surfaces; novel strain MSSA_6 appeared

on electronic, bathroom, and kitchen environmental surfaces. Example transmission events occurred between the enrollment and 3-month follow-up visits in which strain MSSA_2 was transmitted from potential sources Half-sister 2 or bathroom environmental surfaces to recipients Dad, Mom, Half-sister 1, and the kitchen.

Household B. The Index patient experienced an SSTI one year prior to the infection that prompted enrollment. Example introduction events occurred at the 3-month follow-up visit: novel strain MSSA_1 appeared on Index patient and Half-sister 2; novel strain MSSA_3 appeared on Half-sister 1; novel strain MSSA_5 appeared on kitchen environmental surfaces. Example transmission events occurred between the enrollment and 3-month follow-up visits in which strain MRSA_2 was transmitted from potential sources Half-sister 3 or electronic or bathroom environmental surfaces to the kitchen. Subsequently, between the 3-month and 6-month visits, this strain was transmitted from the potential source kitchen to recipients Index patient, Dad, Mom, and electronics.

Table 1.

Observed longitudinal strain introductions and transmissions

Strain introductions	Unique individuals experiencing 1 introduction, N (row %)	Rate of introductions, per person sampling year ^a
People, N=650	246 (37.8)	0.52
MRSA, N=650	87 (13.4)	0.17
MSSA, N=650	176 (27.1)	0.35
Child, N=351	152 (43.3)	0.58
Index patient, N=144	66 (45.8)	0.62
Non-index child, N=207	86 (41.5)	0.53
Infant, ^b N=30	15 (50.0)	0.72
Adult, N=299	94 (31.4)	0.45
Mother, N=138	45 (32.6)	0.42
Father, N=103	37 (35.9)	0.48
Non-parent, N=58	12 (20.7)	0.46
Strain introductions	Households experiencing 1 introduction, N (row %)	Rate of introductions, per person sampling year ^a
Present 1 environmental site, N=108	87 (80.6)	1.53
Exclusively present in environment, N=108	58 (53.7)	0.80
Strain transmissions	Unique transmission recipients, N (row %)	Rate of transmissions, per person sampling year ^a
People, N=650	205 (31.5)	0.50
MRSA, N=650	98 (15.1)	0.25
MSSA, N=650	107 (16.5)	0.25
Sibling→Sibling, N=304	67 (22.0)	0.40
Offspring→Parent, N=247	56 (22.7)	0.43
Infant→Father, N=20	3 (15.0)	0.23
Infant→Mother, N=29	7 (24.1)	0.29
Parent→Offspring, N=338	58 (17.2)	0.25
Father→Infant, N=21	4 (19.0)	0.15
Mother→Infant, N=30	6 (20.0)	0.37
Cohabiting parents, ^c N=210	25 (11.9)	0.13
Environmental source, N=650	147 (22.6)	0.36
Transmitted strain exclusively present in environment, N=650	57 (8.8)	0.13

ABBREVIATIONS: MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S.aureus* NOTE: analysis included individuals with 2 observations over year of longitudinal samplings; N=650

^aRate is calculated as (#of introductions or transmissions) / (# of total person-samplings conducted / 4per year)

^bInfant refers to a child<1year of age; not exclusive of other child categories

^cCohabiting parents refers to two parents who share the same bed

Table 2.

Strain introductions and transmissions by environmental site

Environmental site	Sampling method ^a	Colonized at sampling, N	Colonized by introduction, N (row %)	Colonized, potential transmission source, N (row %)
<i>Electronics</i>				
Television remote control	Eswab	64	16 (25.0)	40 (62.5)
Main telephone or index cell phone	Eswab	62	18 (29.0)	23 (37.1)
Computer keyboard and mouse	Eswab	49	22 (44.9)	26 (53.1)
Videogame controller	Eswab	46	13 (28.3)	25 (54.3)
<i>Kitchen</i>				
Refrigerator door handle	Contact plate	93	24 (25.8)	58 (62.4)
Table	Contact plate	72	26 (36.1)	33 (45.8)
Sink faucet handle	Eswab	41	10 (24.4)	18 (43.9)
Sponge or cloth	Eswab	38	19 (50.0)	15 (39.5)
Hand towel	Eswab	26	8 (30.8)	16 (61.5)
<i>Bathroom</i>				
Sink	Contact plate	81	18 (22.2)	36 (44.4)
Bathtub	Contact plate	77	21 (27.3)	40 (51.9)
Toilet seat	Contact plate	74	16 (21.6)	39 (52.7)
Countertop	Contact plate	65	22 (33.8)	43 (66.2)
Soap bar and dish in bath or shower	Contact plate	16	5 (31.3)	13 (81.3)
Toilet handle	Eswab	54	14 (25.9)	27 (50.0)
Light switch	Eswab	47	12 (25.5)	28 (59.6)
Door handle	Eswab	46	10 (21.7)	22 (47.8)
Index patient bath towel	Eswab	41	14 (34.1)	12 (29.3)
Sink faucet handle	Eswab	65	16 (24.6)	27 (41.5)
Hand towel	Eswab	25	11 (44.0)	11 (44.0)
<i>Bedroom</i>				
Index patient bed sheets and pillowcases	Eswab	121	37 (30.6)	61 (50.4)

^aEswab (Becton Dickinson [BD], Franklin Lakes, NJ) and Baird Parker Agar contact plate (Hardy, Santa Maria, CA)

Table 3.

Factors remaining in final multivariable models: strain introduction, transmission recipient, and transmission source

Covariate	OR (95% CrI)	pMCMC
<i>Strain introduction^a</i>		
Average monthly low temperature (°F) at time of sampling	0.91 (0.85–0.98)	0.011
Frequent handwashing score ^b	0.86 (0.74–1.01)	0.064
Pet in household	0.89 (0.75–1.05)	0.190
<i>Transmission recipient^c</i>		
Strain environmental contamination pressure at prior sampling ^d	3.97 (1.96–8.20)	0.0004
Shares bedroom with individual colonized with transmitted strain at prior sampling	1.33 (1.12–1.58)	0.0008
Environmental contamination pressure of other household strains at prior sampling ^e	0.44 (0.23–0.77)	0.003
Home ownership	0.77 (0.63–0.94)	0.009
Interval SSTI	1.32 (1.07–1.64)	0.010
Showers primarily (vs. takes bath)	0.81 (0.69–0.96)	0.010
Sex (male)	1.16 (1.00–1.35)	0.051
Shares towel (hand, face, or bath) with individual colonized with transmitted strain at prior sampling	1.16 (0.98–1.35)	0.081
Nights per week spent in household	1.07 (0.96–1.18)	0.214
<i>Transmission source^f</i>		
People per bathroom	1.10 (1.02–1.19)	0.016
Shares bath towel	1.25 (1.01–1.57)	0.047
Household cleanliness score (clean) ^g	0.95 (0.71–1.27)	0.750

ABBREVIATIONS: OR, odds ratio; CrI, credible interval; pMCMC, Markov chain Monte Carlo *p*-value; SSTI, skin and soft tissue infection

NOTE: For all observations across models, all values are present for all covariates (i.e. complete observations with no missing values)

^aEligible individuals were those sampled at two consecutive visits who completed the enrollment interview, totaling 2363 observations of 640 individuals in 143 households across samplings

^bAggregate variable defined as washing hands “always” after using bathroom, “always” before preparing food, at least “frequently” before eating, and at least “frequently” after changing a diaper (when applicable)

^cEligible individuals were those who had completed the enrollment interview, had been sampled at the prior and current sampling, had their environment sampled at the prior sampling, and lived in households with 1 *S. aureus* strain present at the prior sampling, providing 2952 observations among 603 household members in 134 households across samplings

^dThe number of environmental sites contaminated with the transmitted strain divided by the number of environmental sites sampled in the household at prior sampling

^eThe number of environmental sites contaminated with all other strains in the household (other than the transmitted strain) divided by the number of environmental sites sampled in the household at prior sampling

^fEligible individuals were those who completed the enrollment interview, were colonized with 1 *S. aureus* strain at the prior sampling, and lived in households with other individuals not colonized with this strain, yielding 1125 observations of 477 individuals in 139 households across samplings

^gWhether the research team rated the overall dwelling clean (above average/average) vs. dirty (below average/very dirty), considering odor, clutter, and grime per standardized protocol