Longitudinal, strain-specific *Staphylococcus aureus* introduction and transmission events in households of children with community-associated meticillin-resistant *S aureus* skin and soft tissue infection: a prospective cohort study

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Summary

Background Devising effective, targeted approaches to prevent recurrent meticillin-resistant *Staphylococcus aureus* (MRSA) skin and soft tissue infection requires an understanding of factors driving MRSA acquisition. We comprehensively defined household longitudinal, strain-level *S aureus* transmission dynamics in households of children with community-associated MRSA skin and soft tissue infection.

Methods From 2012–15, otherwise healthy paediatric patients with culture-confirmed, community-onset MRSA infections were recruited for the Household Observation of MRSA in the Environment (HOME) prospective cohort study from hospitals and community practices in metropolitan St Louis (MO, USA). Children with health-care-related risk factors were excluded, as determined by evidence of recent hospital admission, an invasive medical device, or residence in a long-term care facility. Household contacts (individuals sleeping in the home ≥four nights per week) and indoor dogs and cats were also enrolled. A baseline visit took place at the index patient's primary home, followed by four quarterly visits over 12 months. At each visit, interviews were done and serial cultures were collected, to detect *S aureus* from three anatomic sites of household members, two anatomic sites on dogs and cats, and 21 environmental surfaces. Molecular typing was done by repetitive-sequence PCR to define distinct *S aureus* strains within each household. Longitudinal, multivariable generalised mixed-effects logistic regression models identified factors associated with *S aureus* acquisition.

Findings Across household members, pets, and environmental surfaces, 1267 strain acquisition events were observed. Acquisitions were driven equally by 510 introductions of novel strains into households and 602 transmissions within households, each associated with distinct factors. Frequent handwashing decreased the likelihood of novel strain introduction 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-colonised 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 skin and soft tissue infection (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 skin and soft tissue infection. Future interventions should inclusively target household members and the environment, focusing on straightforward changes in hand hygiene and household sharing behaviours.

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Introduction

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

Prevalence of MRSA colonisation in household contacts of patients with community-associated MRSA

Research in context

Evidence before this study

We searched PubMed for articles published until Nov 1, 2018, to identify studies of community-associated meticillin-resistant *Staphylococcus aureus* 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. Our search did not have any language restrictions. We screened these articles for relevance as well as those listed in the similar articles tab on PubMed; references cited within relevant articles were also screened. Companion animals and the household environment have both been implicated as potential reservoirs for *S aureus* in households of children with skin and soft tissue infection. Factors associated with human colonisation and environmental contamination have been previously described and *S aureus* transmission in the hospital setting has been documented. However, existing literature regarding *S aureus* acquisition and transmission in the community setting, and the specific role of the household environment and pets is scarce and has been limited by an inadequate definition of transmission. For instance, studies have assessed a single time-point, collected limited epidemiological 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 establish how it is introduced and its transmission dynamics.

Added value of this study

Paediatric patients with culture-confirmed, community-onset MRSA infections were recruited for the Household Observation of MRSA in the Environment (HOME) prospective cohort study from hospitals and community practices in metropolitan St Louis (MO, USA). Over the next 12 months, nearly all household members and pet dogs and cats of the 150 households affected by community-associated MRSA were enrolled in the study. After the baseline visit, quarterly visits consisted of follow-up interviews and repeat sampling of people, pets, and an exhaustive list of environmental surfaces for the detection of *S aureus*. Using comprehensive molecular typing of *S aureus*, personal and household epidemiological data, and sophisticated statistical modelling we found that acquisition of MRSA occurs both via introductions from sources external to the household and via transmissions within. Hygiene and behavioural factors associated with introductions and transmissions are distinct, and could be alleviated through modest changes in household practices, such as frequent handwashing and modified sharing behaviours (eg, designated personal bath towels). Transmission recipients are at increased risk of reporting interval skin and soft tissue infections, further implicating the household in the proliferation of community-associated MRSA.

Implications of all the available evidence

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

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 colonised, but not infected with MRSA.[5–9] We previously investigated a household approach to decolonisation, comprising topical antimicrobials and improved hygiene measures targeted at index patients and all household contacts. Although this household approach significantly reduced subsequent skin and soft tissue infection incidence compared with decolonisation 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 harbour MRSA for prolonged periods;[10,11] and although numerous studies have illuminated transmission within hospitals,[12,13] our understanding of the effect 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. MRSA colonisation among household members has been evaluated in previous studies, including a pilot study by our group, but they have been limited by assessing only a single time-point, collecting limited epidemiological data, discounting the household environment, excluding companion animals, and 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 transmission of established strains among household members, environmental surfaces, and pets, in households of children with community-associated 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.

Panel: Definitions

Strain type
A composite of repetitive-sequence PCR designation and meticillin resistance profile for each recovered *Staphylococcus aureus* isolate, unique to each household.

Acquisition
This occurs when a *S aureus* strain type is recovered from an individual, environmental surface, or pet not colonised with the given strain at the previous sampling. An acquisition could occur via a strain introduction or transmission.

Strain introduction
This occurs when a *S aureus* strain type first appears within a household at a sampling beyond baseline. The number of introductions at a time-point is the number of individuals or pets colonised by the novel strain at its first appearance (ie, personal introductions), and one additional introduction if the strain appears on at least one environmental surface (ie, environmental introduction). For instance, a strain newly recovered from two individuals, one pet, and two environmental surfaces would constitute four household introductions.

Transmission
This occurs when a person becomes colonised for the first time (ie, transmission recipient) with a strain recovered at the previous time-point from at least one person, pet, or environmental site (ie, 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 colonised with a given strain at previous 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 colonisation pressure
The number of anatomic sites (three per person: axillae, nares, and groin) colonised with *S aureus*, MRSA, or a given strain, divided by the number of sites sampled (personal *S aureus*, MRSA, or strain colonisation pressure).

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

Methods

Study design and participants

From 2012–15, otherwise healthy paediatric patients with culture-confirmed, community-onset MRSA infections were recruited for the Household Observation of MRSA in the Environment (HOME) prospective cohort study from hospitals and community practices in metropolitan St Louis (MO, USA). Children with health care-related risk factors were excluded, as determined by evidence of recent hospital admission, an invasive medical device, or residence in a long-term care facility.[17] A baseline visit took place at the index patient's primary home at the earliest feasible date after the infection prompting study enrolment. Household contacts (individuals sleeping in the home ≥four nights per week) and indoor dogs and cats were also enrolled. The baseline visit included a detailed epidemiological 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 (appendix p 9). See the panel for definitions of terms used throughout this study.

The Washington University Institutional Review Board and Institutional Animal Care and Use Committee approved the study procedures. Informed consent and assent was obtained for all participants (parents or caregivers provided consent for children and pets).

Procedures

Previous *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 skin and soft tissue infections, health care exposure, and use of systemic and topical antimicrobials. At each visit, colonisation cultures were collected from the anterior nares, axillae, and inguinal folds of all household members (ESwab, Becton Dickinson, Franklin Lakes, NJ, USA) and from the nares (Minitip ESwab, Becton Dickinson) 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 Diagnostics, Santa Maria, CA, USA]): electronics (television remote control, main telephone, computer keyboard and mouse, videogame controller), kitchen (refrigerator door handle, table, sink tap handle, sponge, cloth, hand towel), bathroom (sink, bathtub, toilet seat, countertop, soap bar and dish, toilet handle, light switch, door handle, index patient bath towel, sink tap handle, hand towel), and bedroom (index patient bed sheets and pillowcases).[19]

Available MRSA isolates and antibiotic susceptibility profiles from the enrolment skin and soft tissue infection were obtained from clinical microbiology laboratories. *S aureus* was recovered from swabs using broth enrichment and from contact plates on the basis of colony morphology (appendix p 2). *S aureus* was identified and antibiotic susceptibility profiles were established according to the Clinical and Laboratory Standards Institute.[20] Molecular typing was done by repetitive-sequence PCR, using a 95% similarity cutoff to define distinct *S aureus* strains within each household.[21,22]

Statistical analysis

Univariate analyses were done in R (version 3.5.3) or in Python (version 2.7.15) with the SciPy package (version 1.1.0). Fisher's exact test was employed for all

See Online for appendix

For the **SciPy package** see https://www.scipy.org/

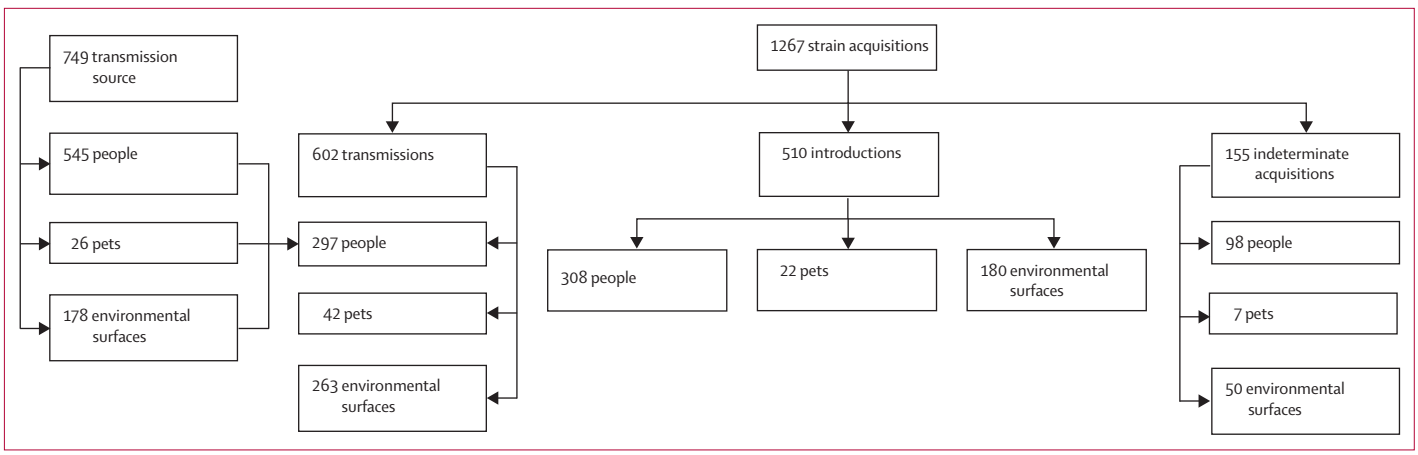


Figure 1: **Flow diagram of *Staphylococcus aureus* strain acquisitions**
Across household members, pets, and environmental surfaces, 1267 strain acquisition events were observed. Of these, 510 were novel strain introduction events, 602 were transmission events, and 155 were indeterminate events (present 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 colonised with a strain not present at the previous 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 at least one environmental site.

2×2 contingency table tests. Kruskal-Wallis non-parametric one-way analysis of variance was used for pairwise comparisons between sets of continuous observations. Spearman's non-parametric rank correlation was used when calculating correlation between two covariates. See the appendix (p 3) for more detail regarding statistical tests. The strain introduction, transmission recipient, and transmission source models (appendix pp 3–4) are longitudinal, multivariable generalised mixed-effects logistic regression models which were fitted using the R package MCMCglmm,[23] 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 (ie, no missing values allowed). See appendix (pp 10–15) for primary and secondary covariates included in each model.

Role of the funding source

The funders of the study 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 the data in the study and had final responsibility for the decision to submit for publication.

Results

From 2012–15, 150 children with a median age of 3 years (range 1 month–18·6 years) presenting with community-associated MRSA infections (149 skin and soft tissue infections, one invasive; 91 isolates from these infections were available for molecular typing) were enrolled. The baseline visit took place a median of 20 days (IQR 13–29) after the infection prompting study enrolment. Additionally, 521 household contacts (median age 25 years [1 month–82·3 years]) were enrolled at baseline, and 21 participants who joined the household during the 12-month longitudinal study were also enrolled. Median household size was four individuals (range 2–13). Of the 150 households enrolled, 135 (90%) completed the 12-month study visit. 3819 *S aureus* isolates were recovered and analysed. The appendix (p 9) provides details of demographics and individual, environmental, and pet sampling completion over the five study visits.

	Unique individuals or households experiencing ≥1 introduction	Rate of introductions per person sampling year
Individuals		
All household members	246/650 (38%)	0·52
MRSA	87/650 (13%)	0·17
MSSA	176/650 (27%)	0·35
Children	152/351 (43%)	0·58
Index patients	66/144 (46%)	0·62
Non-index children	86/207 (42%)	0·53
Infants*	15/30 (50%)	0·72
Adults	94/299 (31%)	0·45
Mothers	45/138 (33%)	0·42
Fathers	37/103 (36%)	0·48
Non-parents	12/58 (21%)	0·46
Households		
Strain present ≥1 environmental site	87/108 (81%)	1·53
Strain exclusively present in environment	58/108 (54%)	0·80

Analyses included individuals with at least two observations over the year of longitudinal samplings. MRSA=meticillin-resistant *Staphylococcus aureus*. MSSA=meticillin-susceptible *S aureus*. Rate of introductions per person sampling year was calculated as: number of introductions/(total number of person samplings conducted/4 per year). *Infant refers to a child below 1 year of age and is not exclusive of other child categories.

Table 1: **Observed longitudinal strain introductions**

	Unique transmission recipients	Rate of transmissions per person sampling year
All household members	205/650 (32%)	0·50
MRSA	98/650 (15%)	0·25
MSSA	107/650 (17%)	0·25
Sibling to sibling	67/304 (22%)	0·40
Offspring to parent	56/247 (23%)	0·43
Infant* to father	3/20 (15%)	0·23
Infant* to mother	7/29 (24%)	0·29
Parent to offspring	58/338 (17%)	0·25
Father to infant	4/21 (19%)	0·15
Mother to infant	6/30 (20%)	0·37
Cohabiting† parents	25/210 (12%)	0·13
Environmental source	147/650 (23%)	0·36
Strain exclusively present in environment	57/650 (9%)	0·13

Analyses included individuals with at least two observations over the year of longitudinal samplings. MRSA=meticillin-resistant *Staphylococcus aureus*. MSSA=meticillin-susceptible *S aureus*. Rate of transmissions per person sampling year was calculated as: number of transmissions/(total number of person samplings conducted/4 per year). *Infant refers to a child below 1 year of age and is not exclusive of other child categories. †Cohabiting parents refers to two parents who share the same bed.

Table 2: **Observed longitudinal strain transmissions**

Over 12 months, 513 (74%) individuals were colonised at least once with *S aureus* and 319 (46%) with MRSA (appendix p 9). Of the 671 individuals participating in at least one follow-up visit, 173 (26%) reported an interval skin and soft tissue infection, including 75 (52%) of 144 index patients. Of 154 pets sampled, 68 (44%) were colonised with *S aureus* at least once, 44 (29%) with MRSA. Across 12 months, at least one environmental site was contaminated with *S aureus* in 136 (91%) homes, 104 (69%) with MRSA.

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%) were indeterminate acquisitions that 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 650 household members, 246 (38%) experienced at least one introduction, 205 (32%) were transmission recipients and 265 (41%) were potential transmission sources (table 1; table 2). Exemplar household acquisitions are illustrated in figure 2 and the appendix (pp 31–36). Significantly more introductions were associated with meticillin-susceptible *S aureus* (MSSA; n=209) than with MRSA strain types (n=99; p<0·0001), while transmissions occurred equally between MSSA (n=150) and MRSA (n=147; p=0·87).

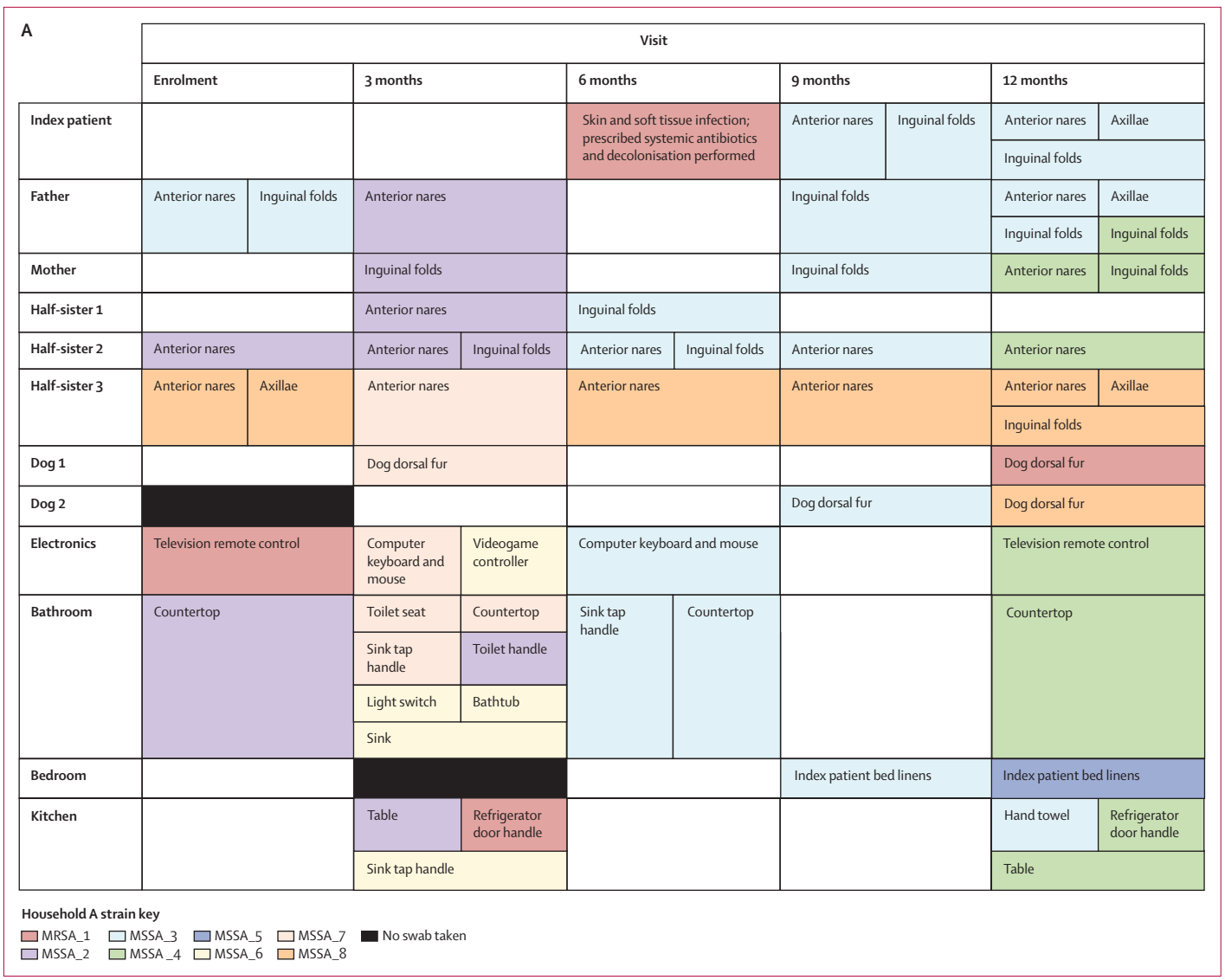
The incidence of *S aureus* introduction was 0·52 introductions per person sampling year (ie, at least two individuals would need to be followed for 1 year to observe one *S aureus* introduction event). Specifically, an MSSA strain was introduced twice as often as an MRSA strain (0·35 MSSA strain introductions per person sampling year compared with 0·17 MRSA strain introductions per person sampling year; table 1). Among 341 introduction events, the novel strain was found on at least one household member in 237 (70%) of these events, and in at least one environmental site in 180 (53%; table 3). In 94 (28%) introductions, the strain appeared exclusively in the environment (appendix p 37). When an introduction event occurred, a median of one household members (range zero to four) became colonised (appendix p 37) and one environmental sites (range zero to ten) became contaminated (appendix p 37) with the novel strain.

We sought to specify demographic, health, hygiene, and activity factors that were associated with strain introductions. In univariate analyses (appendix pp 16–20), 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 individuals in households with a lower personal *S aureus* colonisation pressure.

In the longitudinal, multivariable generalised mixed-effects logistic regression model (appendix pp 10–11), introductions were significantly more common in colder months (table 4). Frequent handwashing remained in the model as a clinically significant, but not statistically significant, factor in reducing strain introductions (p=0·06). Health care exposure and visiting public locations (eg, hair salons, locker rooms, and pools) did not persist in the introductions model.

The incidence of *S aureus* transmission was 0·50 transmissions per person sampling year (ie, two individuals would need to be followed for 1 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 2). Across 205 individuals who became colonised upon 297 transmissions (some were transmission recipients at multiple samplings), there were 545 transmission paths from household members as potential sources (table 2; 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 3). Transmissions were most common between siblings (112 transmissions [21%]) and from offspring to parent (101 transmissions [19%]). Cohabiting parents rarely transmitted strains to each other (25 transmissions [5%]). Environmental surfaces frequently served as sources of transmitted strains, and varied across recipient age and gender (see appendix pp 1–2 and p 38 for normalised transmission risk).

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 (appendix pp 21–28). Across samplings, households with higher personal *S aureus* colonisation pressure, higher environmental *S aureus* contamination



(Figure 2 continues on next page)

pressure, and a higher number of strain types across the environment and household members had significantly more transmissions.

Source-recipient pairs were significantly more likely to share a bedroom, bed, towel (hand, face, or bath), and hygiene items (eg, razor, hairbrush) compared with all pairs of household members (appendix pp 21–28). We did separate analyses for transmission recipients and sources, to measure distinct factors that affect colonised sources in transmitting their strains and eligible recipients in becoming colonised with transmitted strains.

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 (appendix pp 21–28). Transmission recipients were more likely to be children, share a bath towel or cosmetics, report a skin and soft tissue infection during the same interval as the transmission, and live in households with higher personal *S aureus* colonisation pressure than non-recipients.

In the multivariable model (appendix pp 12–13), transmission reception was significantly associated with increasing environmental contamination pressure of the transmitted strain, sharing a bedroom with an individual colonised with the transmitted strain, and reporting a skin and soft tissue infection since the previous sampling (table 4). 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* bathing), and home ownership (*vs* renting).

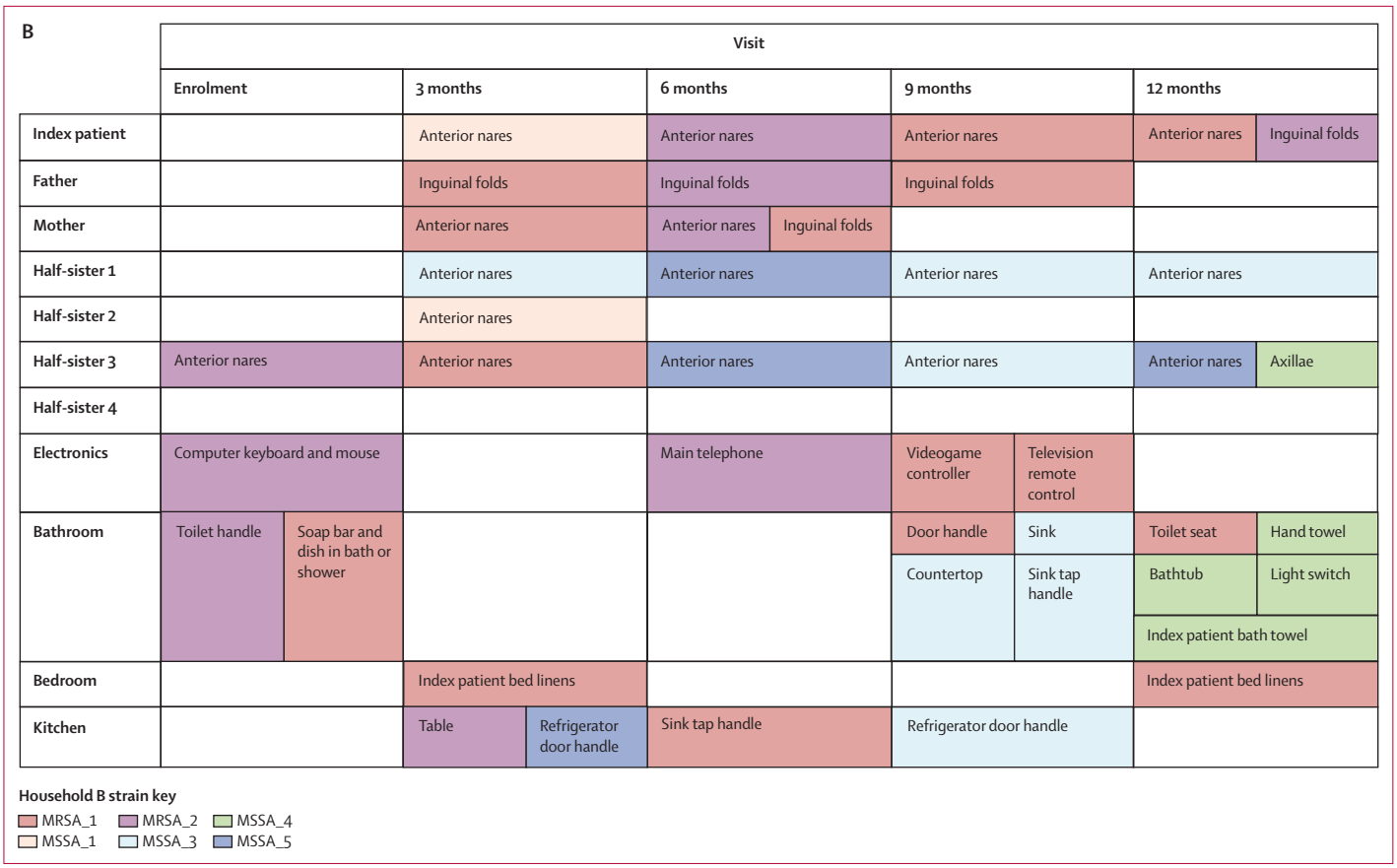


Figure 2: **Longitudinal strain dynamics in two exemplar households**
In both households, the index patient enrolment infection strain was MRSA_1. (A) In household A, the index patient had a skin and soft tissue infection with MRSA_1 3 months before the infection that prompted enrolment. Between the 3-month and 6-month follow-up visits, the index patient had a recurrent skin and soft tissue infection caused by MRSA_1 (the enrolment infection strain). For this infection, the index patient received systemic antibiotics and subsequently performed decolonisation. Example introduction events occurred at the 3-month follow-up visit: novel strain MSSA_7 appeared on half-sister 3, dog 1, and on electronic and bathroom environmental surfaces; novel strain MSSA_6 appeared on electronic, bathroom, and kitchen environmental surfaces. Example transmission events occurred between enrolment and the 3-month follow-up visit, in which strain MSSA_2 was transmitted from potential sources half-sister 2 or bathroom environmental surfaces to the father, mother, half-sister 1, and the kitchen. (B) In household B, the index patient had a skin and soft tissue infection with MRSA_1 1 year before the infection that prompted enrolment. 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 enrolment and the 3-month follow-up visit, 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 follow-up visits, MRSA_2 was transmitted from the potential source kitchen to the index patient, father, mother, and electronics.

In univariate analyses, colonised individuals sharing a bedroom or bath towel or using bar soap for handwashing were significantly more likely to be potential transmission sources (appendix pp 21–28). However, colonised individuals using antibacterial hand soap were significantly less likely to be potential transmission sources.

In the multivariable transmission source model (appendix pp 14–15), although we examined many hygiene and sharing behaviours, sharing a bath towel was the only behaviour 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 4).

A total of 154 pets in 75 households were sampled. 19 pets (16 dogs and three cats) were associated with 22 introductions, ten of which appeared exclusively in pets (appendix p 29 and 39). 35 pets (33%) were transmission recipients. The pet's primary caretaker was a potential source in 13 (19%) of 67 transmission paths from household members to pets. 15 pets served as potential transmission sources across 26 transmission paths to people; in three of these 26 paths, the pet was the exclusive source. Although 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 skin and soft tissue infection) affected their likelihood of experiencing an introduction or transmission event (appendix p 30).

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] By contrast, the design of the present study enables us to truly discern household acquisition dynamics: 96% of household members were enrolled, colonisation samples were obtained five times longitudinally over 1 year from people, environmental surfaces, and pets, and molecular typing with high discriminatory power[22] was done on all recovered *S aureus* isolates. We found 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 shows that MRSA acquisition occurs through household introductions and transmissions. Ng and colleagues[7] reported that in 27 (40%) of 68 households with MRSA-infected index patients and non-MRSA-colonised household contacts at initial screening, at least one household contact acquired colonisation within 3 months.[7] Our study suggests that these observed acquisitions were equally likely to be introductions or transmissions; furthermore, MRSA acquisition in households is driven not by one strain type, but likely by 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 analyses, whereas strain-specific environmental contamination pressure and sharing fomites with colonised individuals were associated with transmission risk assessed in the multivariable model. These factors have previously been correlated with overall *S aureus* colonisation,[5,11,24–26] and we have now shown that introductions from sources outside the household and transmissions within households are distinct epidemiological 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 most *S aureus* introductions occurred in children; moreover, the only activity external to the household that was associated with acquisition in children was daycare attendance in univariate analysis. Although contact sports have been associated with MRSA colonisation[27] and MRSA has been recovered from exercise equipment at fitness centres,[28] sports participation and gym attendance were not significantly associated with introductions in our study. Likewise, employment sites linked to high colonisation risk, such as schools[29] or health-care facilities,[30] were not significantly associated with introductions. However, strain types from such locations may already have established themselves in households before study initiation. Importantly, hand hygiene was shown to be particularly protective against introductions; optimal hand hygiene practices could protect individuals from acquisitions in daily life even when exposure to *S aureus* is high. Interestingly, 28% of all household introductions were exclusively on environmental surfaces. Potential mechanisms for these introductions include intermittently colonised household members who had spontaneously resolved their personal colonisation before the time of sampling, household visitors, or contaminated (and unsampled) fomites brought into the home (eg, from 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-colonised sources. Although sharing a bedroom and towels has previously been associated with increased individual colonisation risk,[24] 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 shows that, in addition to personal contact and a high burden of colonisation among

	Sampling method*	Colonised at ≥1 sampling	Colonised by introduction	Potential transmission source
Electronics				
Television remote control	ESwab	64	16 (25%)	40 (63%)
Main telephone or index cell phone	ESwab	62	18 (29%)	23 (37%)
Computer keyboard and mouse	ESwab	49	22 (45%)	26 (53%)
Videogame controller	ESwab	46	13 (28%)	25 (54%)
Kitchen				
Refrigerator door handle	Contact plate	93	24 (26%)	58 (62%)
Table	Contact plate	72	26 (36%)	33 (46%)
Sink tap handle	ESwab	41	10 (24%)	18 (44%)
Sponge or cloth	ESwab	38	19 (50%)	15 (40%)
Hand towel	ESwab	26	8 (31%)	16 (62%)
Bathroom				
Sink	Contact plate	81	18 (22%)	36 (44%)
Bathtub	Contact plate	77	21 (27%)	40 (52%)
Toilet seat	Contact plate	74	16 (22%)	39 (53%)
Countertop	Contact plate	65	22 (34%)	43 (66%)
Soap bar and dish in bath or shower	Contact plate	16	5 (31%)	13 (81%)
Toilet handle	ESwab	54	14 (26%)	27 (50%)
Light switch	ESwab	47	12 (26%)	28 (60%)
Door handle	ESwab	46	10 (22%)	22 (48%)
Index patient bath towel	ESwab	41	14 (34%)	12 (29%)
Sink tap handle	ESwab	65	16 (25%)	27 (42%)
Hand towel	ESwab	25	11 (44%)	11 (44%)
Bedroom				
Index patient bed sheets and pillowcases	ESwab	121	37 (31%)	61 (50%)

*Eswab (Becton Dickinson, Franklin Lakes, NJ, USA) and Baird-Parker Agar contact plate (Hardy Diagnostics, Santa Maria, CA, USA).

Table 3: **Strain introductions and transmissions by environmental site**

	Odds ratio (95% CrI)	pMCMC
Strain introduction*		
Average monthly low temperature (°F) at time of sampling	0·91 (0·85–0·98)	0·011
Frequent handwashing score†	0·86 (0·74–1·01)	0·064
Pet in household	0·89 (0·75–1·05)	0·190
Transmission recipient‡		
Strain environmental contamination pressure at previous sampling§	3·97 (1·96–8·20)	0·0004
Shares bedroom with individual colonised with transmitted strain at previous sampling	1·33 (1·12–1·58)	0·0008
Environmental contamination pressure of other household strains at previous sampling¶	0·44 (0·23–0·77)	0·003
Home ownership	0·77 (0·63–0·94)	0·009
Interval skin and soft tissue infection	1·32 (1·07–1·64)	0·010
Showers primarily (*vs* taking baths)	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 colonised with transmitted strain at previous sampling	1·16 (0·98–1·35)	0·081
Nights per week spent in household	1·07 (0·96–1·18)	0·214
Transmission source‖		
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)**	0·95 (0·71–1·27)	0·750

For all observations across models, all values are present for all covariates (ie, complete observations with no missing values). CrI=credible interval. pMCMC=Markov chain Monte Carlo p value. *Eligible individuals were those sampled at two consecutive visits who completed the enrolment interview, totaling 2363 observations of 640 individuals in 143 households across samplings. †Aggregate 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). ‡Eligible individuals were those who had completed the enrolment interview, had been sampled at the previous and current sampling, had their environment sampled at the previous sampling, and lived in households with at least one *Staphylococcus aureus* strain present at the previous sampling, providing 2952 observations among 603 household members in 134 households across samplings. §Defined as the number of environmental sites contaminated with the transmitted strain divided by the number of environmental sites sampled in the household at previous sampling. ¶Defined as the 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 previous sampling. ‖Eligible individuals were those who completed the enrolment interview, were colonised with at least one *S aureus* strain at the previous sampling, and lived in households with other individuals not colonised with this strain, yielding 1125 observations of 477 individuals in 139 households across samplings. **The research team rated the overall dwelling clean (above average or average) or dirty (below average or very dirty), considering odour, clutter, and grime per standardised protocol.

Table 4: **Factors remaining in final multivariable models: strain introduction, transmission recipient, and transmission source**

household members,[8,31] environmental contamination plays a substantial role in transmission. Lastly, transmission recipients had a significantly higher incidence of skin and soft tissue infection. Although our sampling interval of 3 months precludes distinguishing cause from effect, acquisition of a novel strain via a transmission event might have often led to development of skin and soft tissue infection.

Although concordant colonisation with MRSA in pets and their owners or veterinary personnel has been described, the directionality of transmission remains unclear.[32] Shahbazian and colleagues[33] associated the presence of pets with increased risk of household environmental MRSA contamination. In the present study, dogs and cats participated in overall household *S aureus* transmission dynamics. 30% of pets were transmission recipients over 12 months, and 33% of these transmission paths to pets were associated with the primary caretaker or someone sharing a bed with the pet. By 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 and colleagues, pets of individuals recently infected with MRSA were not implicated as transmission sources to humans, as discerned by whole-genome sequencing.[34] 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 serve as reservoirs for transmission or reacquisition.[35,36] Future research will illuminate the effect of decolonisation 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 skin and soft tissue infections. Since *S aureus* transmission was associated with interval skin and soft tissue infection, measures to reduce transmission among household members, including providing separate towels and hygiene items for each family member, might also reduce subsequent skin and soft tissue infection. Likewise, improved handwashing could reduce *S aureus* acquisition, as community-based trials providing hand hygiene education materials and alcohol-based hand sanitisers have decreased the incidence of gastrointestinal and respiratory illnesses.[37,38] Although the importance of hand hygiene may seem obvious, compliance remains suboptimal even in high-stakes, controlled settings such

as hospitals, despite education and ready access to hand hygiene products.[39] Individuals in the community face additional barriers, including limited resources. Potentially straightforward public health programmes to implement simple and effective hand hygiene in households and community settings could have far-reaching benefits to prevent a spectrum of infections.[40] Lastly, we found that *S aureus* household environmental contamination significantly predicted transmission. Enhanced environmental disinfection in health-care settings has been shown to reduce pathogen transmission and acquisition,[41] so priority should be given to studies directly testing the effectiveness of targeted surface decontamination in households to reduce *S aureus* transmission and skin and soft tissue infection.

Longitudinal sampling of household members, their environment, and pets, combined with comprehensive molecular typing and personal and household epidemiological data, have allowed for novel delineation of acquisition via strain introduction and transmission, and of features associated with these acquisition modalities. However, this study does have several limitations. For instance, the isolate from interval skin and soft tissue infections was often unavailable, precluding definite association of these incident skin and soft tissue infections with individual acquisition events. While repetitive-sequence PCR allows for a high degree of strain discrimination,[22] it is not as comprehensive as whole-genome sequencing, preventing the analysis of specific genomic signatures associated with transmission. Additionally, the findings of this study may not be generalisable to geographic locales with lower prevalence of MRSA colonisation and lower incidence of skin and soft tissue infection. Finally, since all index patients were children, strain acquisition dynamics may not be generalisable to adult-only households.

In this comprehensive investigation of households, we found that individuals acquire MRSA via introductions from exogenous sources and via within-household transmissions; these routes of acquisition exhibit distinct hygiene and behavioural characteristics, and transmission is significantly associated with skin and soft tissue infection. Introductions and transmission could be mitigated through straightforward changes in household practices, including frequent handwashing and modified sharing behaviours. Prospective studies of high-risk populations should test targeted decolonisation regimens for sources as well as protective hygiene practices for their cognate recipients, combined with targeted decontamination of environmental surfaces.

Contributors

RLM, PGH, SJG, C-ADB, 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, C-ADB, and SAF contributed to acquisition of laboratory data. RLM, PGH, AR, and SAF contributed to statistical analysis. RLM, PGH, SJG, JBW, C-ADB, 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, C-ADB, 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.

Declaration of interests

We declare no competing interests.

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