Clinical Infectious Diseases

MAJOR ARTICLE

HOME$_2$ Study: Household Versus Personalized Decolonization in Households of Children With Methicillin-Resistant *Staphylococcus aureus* Skin and Soft Tissue Infection—A Randomized Clinical Trial

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(See the Editorial Commentary by Knox et al on pages e4578–80.)

Background. A household approach to decolonization decreases skin and soft tissue infection (SSTI) incidence, though this is burdensome and costly. As prior SSTI increases risk for SSTI, we hypothesized that the effectiveness of decolonization measures to prevent SSTI when targeted to household members with prior year SSTI would be noninferior to decolonizing all household members.

Methods. Upon completion of our 12-month observational Household Observation of Methicillin-resistant *Staphylococcus aureus* in the Environment (HOME) study, 102 households were enrolled in HOME$_2$, a 12-month, randomized noninferiority trial. Pediatric index patients with community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) SSTI, their household contacts, and pets were enrolled. Households were randomized 1:1 to the personalized (decolonization performed only by household members who experienced SSTI during the HOME study) or household (decolonization performed by all household members) approaches. The 5-day regimen included hygiene education, twice-daily intranasal mupirocin, and daily bleach-water baths. At 5 follow-up visits in participants' homes, swabs to detect *S. aureus* were collected from participants, environmental surfaces, and pets; incident SSTIs were ascertained.

Results. Noninferiority of the personalized approach was established for the primary outcome 3-month cumulative SSTI: 23 of 212 (10.8%) participants reported SSTI in household approach households, while 23 of 236 (9.7%) participants reported SSTI in personalized approach households (difference in proportions, −1.1% [95% confidence interval, −6.7% to 4.5%]). In multivariable analyses, prior year SSTI and baseline MRSA colonization were associated with cumulative SSTI.

Conclusions. The personalized approach was noninferior to the household approach in preventing SSTI. Future studies should interrogate longer durations of decolonization and/or decontamination of the household environment to reduce household MRSA burden.

Clinical Trials Registration. NCT01814371.

Keywords. methicillin-resistant *Staphylococcus aureus*; skin and soft tissue infection; decolonization; mupirocin; bleach.

Community-associated (CA) methicillin-resistant *Staphylococcus aureus* (MRSA) has caused an epidemic of infections in immunocompetent hosts. Skin and soft tissue infection (SSTI) is the most frequent entity caused by CA-MRSA, and up to 70% of patients will experience recurrent SSTI, engendering burden and frustration for patients and clinicians [1–4]. Moreover, CA-MRSA colonization is a demonstrated risk factor for the development of SSTI. In studies conducted in community settings, 26%–38% of individuals with CA-MRSA colonization experienced subsequent SSTI [5, 6]. To ameliorate this risk, early in the SSTI epidemic, preventive measures traditionally employed in healthcare settings—including decolonization with topical antimicrobials (eg, mupirocin, chlorhexidine, and dilute bleach-water baths)—began to be used in ambulatory patients [7–9]. Initial studies in community settings all focused on decolonization of the index patient exclusively [10–12]. However, MRSA SSTIs cluster in households, particularly in households with children [13–15]. Recent studies demonstrate that in addition

Received 5 March 2020; editorial decision 5 May 2020; accepted 5 June 2020; published online June 10, 2020.

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Clinical Infectious Diseases® 2021;73(11):e4568–77

DOI: 10.1093/cid/ciaa752

to person-to-person transmission, environmental surfaces also serve as reservoirs for household MRSA transmission [16–18]. These observations raised the following question: In households affected by MRSA, who should be prescribed decolonization? To address this question, we previously conducted a randomized clinical trial comparing the effectiveness of decolonization targeted at the index patient alone to decolonization performed by all household members. That trial demonstrated a significantly reduced incidence of SSTI in index patients and household contacts within households performing household decolonization compared to index patient–only decolonization [19].

Though successful in reducing SSTI incidence, decolonizing all household members may pose substantial time and financial burden on families. Furthermore, widespread use may lead to the development of antimicrobial resistance [20–25]. These untoward consequences may be mitigated through targeting select household members. In deciding whom to decolonize, there are several possible approaches. The first is to screen all household members to identify MRSA carriers; this approach, however, is impractical. Additionally, some individuals may be intermittently colonized, or colonized in sites not routinely sampled using typical surveillance approaches, and thus would be falsely identified as "noncarriers." As a history of SSTI predicts subsequent SSTI [26], a second, perhaps more practical approach might target decolonization toward those household members with a history of SSTI. To this end, we conducted a randomized clinical trial to test the primary hypothesis that a 5-day decolonization protocol performed only by household members with a history of SSTI in the prior year would be noninferior to decolonizing all household members in preventing SSTI 3 months following the intervention.

METHODS

Participants

Index patients (N = 150) with CA-MRSA infection, their household contacts, and indoor dogs and cats were enrolled in the Household Observation of MRSA in the Environment (HOME) study and followed for 1 year [18, 27–30]; incidence of SSTI in household members was recorded. After this observational year, households were invited to enroll in the "HOME$_2$ Decolonization Trial." Eligibility required participation in HOME; index patients enrolled in HOME were ≤18 years old, residing ≤80 miles from St Louis Children's Hospital, with a culture-confirmed CA-MRSA SSTI. Exclusion for HOME$_2$ was incident SSTI in all household members. Of 150 HOME households, 130 completed 12-month follow-up (Figure 1). Six

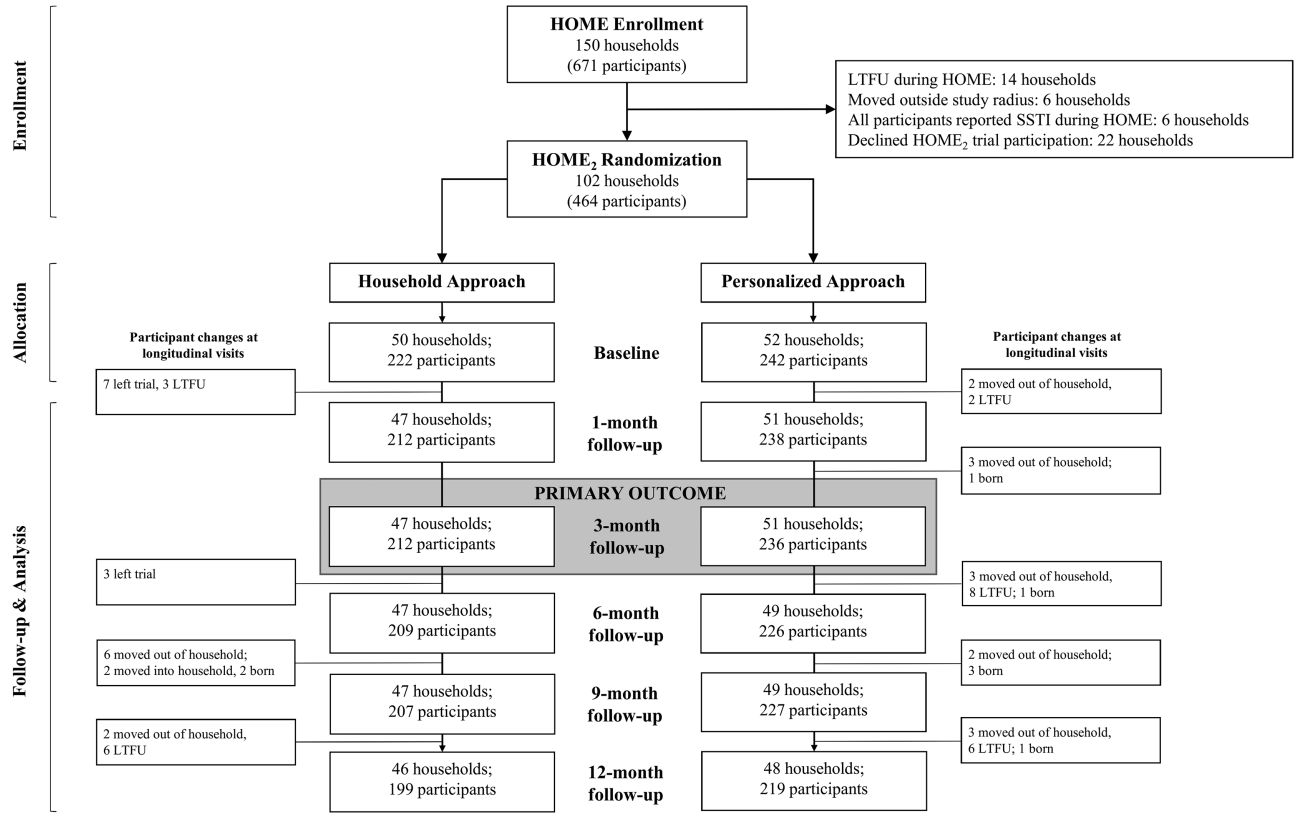

Figure 1. Consolidated Standards for Reporting Trials (CONSORT) flow diagram for the HOME$_2$ decolonization trial, showing study participants with data available for analysis of cumulative skin and soft tissue infection at each time point. Abbreviations: HOME, Household Observation of Methicillin-Resistant *Staphylococcus aureus* in the Environment; LTFU, lost to follow-up; SSTI, skin and soft tissue infection.

households were ineligible for $HOME_2$ (all household members reported SSTI during HOME) and 22 declined participation. From April 2013 through November 2016, index patients, household contacts, and pets from 102 households were enrolled in $HOME_2$ upon written, informed consent (and assent where appropriate) from each household member (and primary caretaker of pets). The Washington University Human Research Protection Office and Animal Studies Committee approved the study methods (ClinicalTrials.gov identifier NCT01814371).

Randomization and Decolonization Regimen

$HOME_2$ was an open-label, randomized noninferiority trial. Households were randomized 1:1 to the "personalized approach," in which decolonization was performed only by household members who experienced SSTI during the 12-month HOME study, or the "household approach," in which decolonization was performed by all household members. All index patients (whose CA-MRSA SSTI prompted HOME enrollment) received decolonization. Block randomization was generated in the Research Electronic Data Capture (REDCap) web application [31] using a minimization algorithm [32] to ensure balanced arms; treatment approaches were balanced by number of household members with SSTI (1 vs >1) and household size (≤4 vs >4 household members). Distinct informed consent documents were used for each treatment approach to reduce risk of crossover (Supplementary Methods) [12].

The decolonization regimen consisted of twice-daily application of a pea-sized amount of 2% mupirocin ointment (Perrigo, Allegan, Michigan) to the anterior nares, plus daily 15-minute dilute bleach-water baths (one-quarter cup of bleach [Clorox, Clorox Company, Oakland, California] per one-quarter tub of water [33]) for 5 days. Participants <1 month of age were excluded from decolonization. All household members performed enhanced hygiene measures (Supplementary Methods). Participants recorded completion, ease or difficulty of the measures, and adverse reactions using a memory aid. Adherence was defined as completing 80% of the assigned regimen (≥4/5 bleach baths and ≥8/10 mupirocin applications).

Data Collection

After randomization, visits were conducted at 1, 3, 6, 9, and 12 months in participants' homes. Trained study staff queried participants (or their guardians, when necessary) about incident SSTI, including date, body site, type of infection (abscess or cellulitis), medical care sought, drainage, and treatment. Surveys also included questions regarding healthcare exposure, antibiotic use, and additional decolonization measures.

To measure *S. aureus* colonization status at each visit, swabs (Eswab, Becton Dickinson, Franklin Lakes, New Jersey) were collected from the anterior nares, axillae, and inguinal folds of all household members and from the nares (minitip Eswab, Becton Dickinson) and dorsal fur (Eswab) of indoor dogs and cats [30]. Up to 21 environmental surfaces (Supplementary Methods) were sampled using Eswabs and contact plates (Baird Parker agar; Hardy Diagnostics, Santa Maria, California) [34].

Microbiological Methods

Broth-enrichment culture-based methods were used to detect *S. aureus* from Eswabs; colony morphology was used to select *S. aureus* from contact plates. Identification and antibiotic susceptibility testing of *S. aureus* isolates were conducted as previously described (Supplementary Methods) [35]. Strain typing was assessed through repetitive sequence-based polymerase chain reaction for isolates from baseline, 1-month, and 3-month samplings and assigned at the household level; strains with ≥95% similarity were considered identical [36, 37].

Sample Size Calculation for Primary Outcome

SSTI incidence 3 months postintervention was chosen as our primary outcome as this is a reasonable amount of time for individuals undergoing decolonization to reacquire the organism from other colonized household contacts and for a subsequent infection to develop. Based on a prior study [19], we anticipated a 9% 3-month SSTI incidence in household approach participants. An absolute difference of 10% is considered clinically equivalent and has been recommended for anti-infective trials [38]; thus, <19% SSTI incidence in personalized approach participants would be considered clinically equivalent. Noninferiority of the personalized approach was defined as the upper limit of the 2-sided 95% confidence interval (CI) for the difference in 3-month SSTI incidence between arms being <10% (Supplementary Methods) [38]. Considering the variance inflation factor due to clustering of participants within households (estimated to be 1.4 based on our prior studies [19]), a total sample of 344 participants (or 86 households) would provide 80% power with $\alpha = .05$ to conclude noninferiority (generated using PASS software; NCSS, Kaysville, Utah). Anticipating 15% attrition between trial enrollment and 3-month follow-up, we enrolled 102 households.

Statistical Analyses of Secondary Outcomes

Analyses were conducted using SPSS version 25 for Windows (IBM SPSS, Chicago, Illinois). Baseline differences between arms were assessed with Fisher exact, Pearson χ^2, and Mann-Whitney *U* tests. Self-reported cumulative SSTI (ie, 1 or more SSTIs reported between initial sampling and each follow-up visit) were compared between arms using Fisher exact test. A Cox proportional hazards model was used, adjusting for MRSA colonization status at baseline sampling, to determine effect of regimen on cumulative SSTI. *Staphylococcus aureus* colonization of participants was compared between baseline and follow-up samplings within each arm with McNemar test and between arms using Fisher exact test. Mean differences in environmental contamination pressure (ie, the number of contaminated surfaces divided by the total number of surfaces sampled per household)

were analyzed between baseline and follow-up samplings within each arm with paired *t* tests. Adherence was compared between arms using Fisher exact test. As exploratory analyses, *S. aureus* carriage in pets and prevalence of mupirocin-resistant *S. aureus* were compared between baseline and follow-up samplings within each arm with McNemar test and between arms using Fisher exact test.

Multivariable generalized mixed-effects logistic regression models were employed to estimate how treatment arm, along with individual and household attributes *a priori* posited to be associated with the outcomes, influenced cumulative SSTI and MRSA colonization in the year following decolonization assignment (Supplementary Methods). These individual-level models were fitted separately for each follow-up sampling using R library "MCMCglmm" [39, 40], with a random intercept for household included to control for clustering within households.

RESULTS

Study Population and Household Demographics

A cohort of 102 pediatric patients (median age, 3.9 years [range, 1.1–17.1 years]) with history of medically attended MRSA SSTI in the past year, household contacts (n = 372 [362 at baseline, 10 enrolled at longitudinal visits]; median age, 25.9 years [range, 0.02–79.0 years]), and pets (n = 95 [in 53 homes]; 79 dogs, 16 cats) were enrolled. Participants were white (331 [70%]), African American (126 [27%]), and multiracial (17 [4%]). Median household size was 4 (range, 2–13) (Table 1). Fifty-two households (n = 248 participants) were randomized to the personalized approach and 50 (n = 226 participants) to the household approach (Figure 1). Participants in the personalized approach arm were more frequently MRSA colonized (63 [26%]) at baseline sampling than participants in the household approach arm (40 [18%]) ($P = .04$).

SSTI

Cumulative SSTI incidence did not significantly differ between participants in the 2 arms (Figure 2A). Noninferiority of the personalized approach was established across all household members at the primary endpoint of 3-month cumulative SSTI: 23 of 212 (10.8%) participants reported SSTI in household approach households, while 23 of 236 (9.7%) participants reported SSTI in personalized approach households (difference in proportions, −1.1% [95% CI, −6.7% to 4.5%]). In total, 89 (19%) participants reported 175 SSTIs over 12 months of follow-up (details are shown in Supplementary Table 1).

In the Cox proportional hazards model, when adjusting for MRSA colonization status at baseline sampling, treatment arm had no effect on hazard of cumulative SSTI over time (adjusted hazard ratio [aHR], 1.0 [95% CI, .6–1.5]; Figure 2B). However, baseline MRSA colonization significantly increased hazard of SSTI (aHR, 2.3 [95% CI, 1.5–3.5]). Time to first SSTI did not differ between treatment arm (household approach: median, 89 days [interquartile range {IQR}, 44–179]; personalized approach: median, 110 days [IQR, 53–220]; $P = .56$).

In the multivariable generalized mixed-effects logistic regression model (Table 2), factors associated with cumulative SSTI included MRSA colonization at baseline sampling (at 6-, 9-, and 12-month follow-up), reporting an SSTI during the prior year (at 1-, 3-, 6-, 9-, and 12-month follow-up), being the index patient (vs a household contact; at 6-month follow-up), and African American race (vs white; at 6-month follow-up). Treatment arm was not significant in the cumulative SSTI model.

MRSA Colonization

MRSA colonization significantly decreased at longitudinal samplings in households assigned the personalized approach and in households assigned the household approach (Figure 3). In the personalized approach arm, MRSA colonization decreased from 26.0% (63 of 242) of household members at baseline to 19.6% (45 of 230), 17.2% (39 of 227), and 17.7% (40 of 226) at 1-, 6-, and 9-month samplings ($P = .03$, $P = .004$, and $P = .01$, respectively). In the household approach arm, MRSA colonization decreased from 18.0% (40 of 222) of household members at baseline to 9.6% (20 of 208), 10.3% (21 of 204), and 8.7% (17 of 196) at 1-, 6-, and 9-month samplings ($P = .01$, $P = .01$, and $P = .001$, respectively). Comparing treatment approaches, the change in MRSA colonization from baseline did not differ significantly between arms at any sampling.

In the multivariable generalized mixed-effects logistic regression model (Table 2), factors associated with MRSA colonization at longitudinal samplings included MRSA colonization at baseline (at 1-, 3-, 6-, 9-, and 12-month follow-up), living in a rented home (at 1- and 3-month follow-up), and increasing environmental MRSA contamination pressure (at 3-, 6-, 9-, and 12-month follow-up). Longitudinal MRSA colonization did not differ between participants in households randomized to the personalized or household approaches (at 1-, 3-, 6-, and 12-month follow-up).

Molecular Epidemiology of Longitudinal Colonization

Of 124 *S. aureus*–colonized participants at baseline who remained colonized at the 1-month sampling despite the decolonization protocol, 82 remained colonized with the same strain, 39 were colonized with a distinct strain, and 3 were colonized with both. Of 31 participants *S. aureus*–colonized at baseline who were not colonized at 1-month sampling but became recolonized at 3-month sampling, 19 were recolonized with their original strain and 12 with a distinct strain. Treatment arm was neither associated with strain persistence nor acquisition of a distinct strain.

Adherence, Adverse Effects, and Mupirocin Resistance

Of 309 participants assigned decolonization measures, 191 of 297 (64%) with follow-up data were adherent with decolonization. Sixty-one of 86 (71%) participants in personalized approach households adhered to the decolonization intervention, compared with 130 of 211 (62%) participants

Table 1. Participant, Household, and Pet Characteristics by Treatment Approach

Participant Characteristics	All Participants (N = 474)	Personalized Approach (n = 248)	Household Approach (n = 226)	*P* Value
Age, years, median (range)	13.6 (0.02–79)	13.4 (0.02–76)	14.2 (0.03–79)	.95
Male sex	216 (46)	114 (46)	102 (45)	.93
Race				
White	331 (70)	169 (68)	162 (72)	.42
African American or multiracial[a]	143 (30)	79 (32)	64 (28)	
Insurance[b,c]				
Private or military	328 (71)	166 (69)	162 (73)	.42
Medicaid or none	135 (29)	74 (31)	61 (27)	
Chronic medical condition[c,d]	225 (50)	107 (46)	118 (54)	.11
Eczema[b,c]	86 (19)	49 (21)	37 (17)	.28
Takes prescription medications[b,c]	135 (30)	68 (29)	67 (31)	.76
SSTI in past year[b,e]	124 (26)	66 (27)	58 (26)	.83
Surgery (including I&D) in past year[b,e]	64 (14)	32 (13)	32 (14)	.79
ED/urgent care visit in past year[b,e]	130 (28)	70 (29)	60 (27)	.61
Hospitalization in past year[b,e]	34 (7)	17 (7)	17 (8)	.86
Antibiotic use in past year[e]	202 (44)	107 (45)	95 (43)	.71
Decolonization in past year[b,e]	210 (46)	115 (48)	95 (43)	.26
Mupirocin in nares	125 (27)	72 (30)	53 (24)	.14
Chlorhexidine washes	58 (13)	30 (13)	28 (13)	1.00
Bleach baths	139 (30)	78 (33)	61 (28)	.26
Colonized with *Staphylococcus aureus* at baseline[b]	219 (47)	105 (43)	114 (51)	.09
MRSA	103 (22)	63 (26)	40 (18)	**.04**
Axillae	25 (5)	11 (5)	14 (6)	.42
Nares	61 (13)	38 (16)	23 (10)	.10
Inguinal folds	55 (12)	37 (15)	18 (8)	**.02**
MSSA	128 (28)	49 (20)	79 (36)	**<.001**
Axillae	38 (8)	11 (5)	27 (12)	**.004**
Nares	105 (23)	42 (17)	63 (28)	**.005**
Inguinal folds	50 (11)	15 (6)	35 (16)	**.001**
Household characteristics	All Households (n = 102)	Personalized Approach (n = 52)	Household Approach (n = 50)	*P* Value
No. persons in household, median (range)	4 (2–13)	4 (2–13)	4 (2–8)	.85
People per 1000 sq ft, median (range)	3.0 (0.4–8.7)	2.9 (0.4–8.3)	3.1 (1.1–8.7)	.22
Owns home[c]	69 (68)	38 (73)	31 (62)	.29
Personal *S. aureus* colonization pressure at baseline[f], mean ± SD	0.23 ± 0.19	0.21 ± 0.16	0.26 ± 0.22	.16
MRSA	0.10 ± 0.13	0.11 ± 0.13	0.08 ± 0.13	.20
MSSA	0.14 ± 0.18	0.09 ± 0.12	0.18 ± 0.22	**.01**
Environmental *S. aureus* contamination pressure at baseline[g], mean ± SD	0.16 ± 0.18	0.14 ± 0.16	0.18 ± 0.21	.24
MRSA	0.06 ± 0.12	0.06 ± 0.10	0.07 ± 0.14	.84
MSSA	0.09 ± 0.16	0.08 ± 0.12	0.11 ± 0.19	.22
Pet characteristics	All Pets (n = 95)	Personalized Approach (n = 48)	Household Approach (n = 47)	*P* Value
Pet type				.79
Dog	79 (83)	39 (81)	40 (85)	
Cat	16 (17)	9 (19)	7 (15)	
Carried *S. aureus* at baseline[b]	21 (26)	10 (24)	11 (28)	.80
MRSA	14 (17)	7 (17)	7 (18)	1.00
Nares	6 (7)	4 (10)	2 (5)	.68
Dorsal fur	10 (13)	4 (10)	6 (16)	.51
MSSA	8 (10)	3 (7)	5 (13)	.47
Nares	2 (2)	0 (0)	2 (5)	.23
Dorsal fur	6 (8)	3 (8)	3 (8)	1.00

Data are presented as no. (%) unless otherwise indicated. Fisher exact test, Pearson χ^2 test, Mann-Whitney *U* test, and Student *t* test were used where appropriate. *P* values ≤.05 were considered significant and are highlighted with bold text.

Abbreviations: ED, emergency department; I&D, incision and drainage; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; SD, standard deviation; SSTI, skin and soft tissue infection.

[a]Multiracial participants include African American/white (n = 14) and African American/white/American Indian (n = 3).

[b]Various characteristics contain missing data: insurance, n = 463; SSTI in past year, surgery, ED visit, hospitalization, decolonization in past year, n = 459; chronic medical condition, takes prescription medications, eczema, n = 452; colonized with *S. aureus* at baseline, n = 464; carried *S. aureus* at baseline, n = 81.

[c]Denotes information retrieved at enrollment into the Household Observation of Methicillin-Resistant *Staphylococcus aureus* in the Environment (HOME) study.

[d]Chronic medical conditions include asthma, seasonal allergies, seizures, heart disease, diabetes, cancer, kidney disease, liver disease, connective tissue disease, gastroesophageal reflux disease, inflammatory bowel disease, immune system problems, depression or bipolar, attention deficit disorder, sickle cell disease, cystic fibrosis, and emphysema.

[e]Denotes characteristics of participants during HOME study year; does not include their HOME enrollment SSTI or details of treatment for that SSTI.

[f]Number of anatomic sites (3 per person) colonized with *S. aureus*, MRSA, or MSSA divided by the total number of anatomic sites sampled per household.

[g]Number of environmental surfaces (up to 21 per house) contaminated with *S. aureus*, MRSA, or MSSA divided by the total number of environmental surfaces sampled per household.

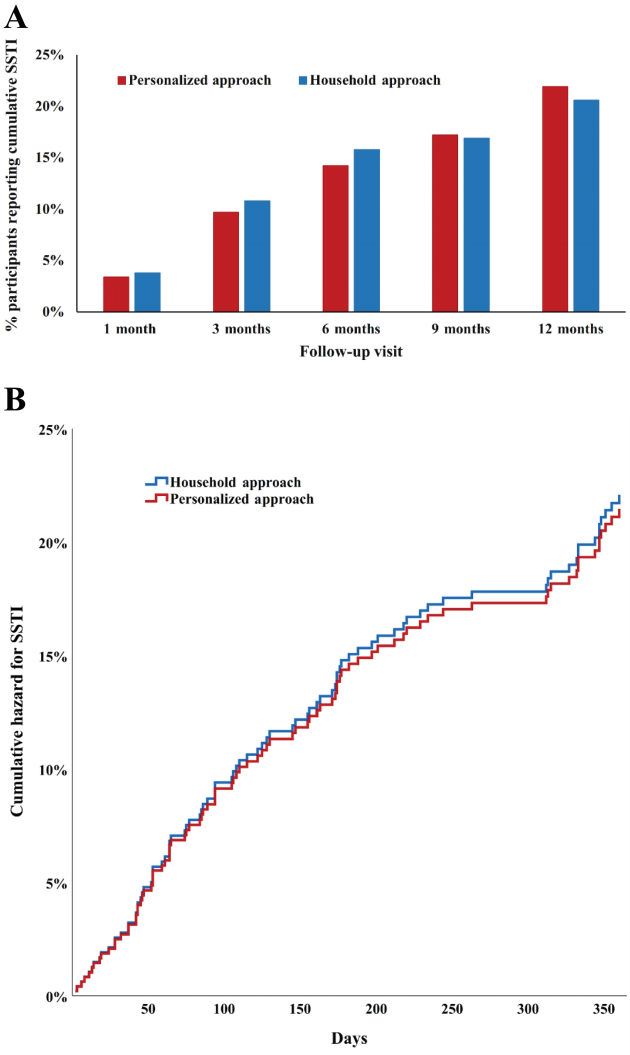

Figure 2. *A,* Cumulative skin and soft tissue infection (SSTI) self-reported by household members following decolonization intervention. Differences in cumulative SSTI over time between the personalized and household decolonization approaches were compared using Fisher exact test ($P > .05$ at each time point). Cumulative SSTI defined as 1 or more SSTIs reported between baseline sampling and each follow-up visit. *B,* Cox proportional-hazard regression analysis for SSTI for up to 1 year between household members assigned the household and personalized decolonization approaches, adjusting for baseline MRSA colonization status. Household members assigned the personalized approach were not more likely to report an SSTI than those assigned the household approach (adjusted hazard ratio [aHR], 1.0 [95% confidence interval {CI}, .6–1.5]). Household members who were MRSA-colonized at baseline sampling were more likely to report an SSTI than those not colonized with MRSA (aHR, 2.3 [95% CI, 1.5–3.5]).

in household approach households ($P = .14$). Minor adverse effects were reported by 143 (48%) participants overall, most commonly runny (41 [14%]) or itchy (25 [8%]) nose with mupirocin application and dry (81 [27%]) or itchy (42 [14%]) skin with bleach baths.

At baseline, 9 (1.9%) participants were colonized with mupirocin-resistant *S. aureus* (Supplementary Table 2); at 1 and 3 months following the intervention, 10 (2.3%) and 8 (1.9%) participants, respectively, were colonized with mupirocin-resistant *S. aureus* ($P = 1.0$ for each). There was no difference in longitudinal prevalence of mupirocin-resistant *S. aureus* colonization between treatment arms.

Effects of Personal Decolonization on Environmental Contamination and Pet Carriage

Within households assigned to either the personalized or household approaches, environmental MRSA contamination pressure did not significantly change after the decolonization intervention (Supplementary Figure 1). Across all households, environmental MRSA contamination pressure was 6.3% (±12.1%) at baseline and 6.3% (±12.3%) at 1-month sampling ($P = .9$). In household approach households, pet MRSA carriage declined postintervention; at baseline sampling, 7 of 39 (18%) pets carried MRSA, decreasing to 0 of 37 (0%) by the 9-month visit ($P = .02$; Supplementary Figure 2). Reductions in pet MRSA carriage in personalized approach households over the same time interval did not reach statistical significance (from 7 of 42 [17%] to 5 of 34 [15%]; $P = 1.0$).

DISCUSSION

Although decolonization with topical antimicrobials reduces the incidence of recurrent SSTIs, particularly when performed by all members of a household compared to the index patient alone, these measures can be cumbersome [19, 41]. Moreover, broad use of these agents may increase selective antimicrobial pressure and may disrupt the microbiota [42]. To decrease this burden, we aimed to compare the effectiveness of these measures, specifically a 5-day regimen of intranasal mupirocin application and dilute bleach-water baths, when performed by only those household members with history of SSTI in the past year (personalized approach) vs all household members (household approach). The personalized approach was noninferior to the household approach in preventing SSTI, while simultaneously reducing the burden for families. Last, environmental MRSA contamination pressure was unaffected by the 5-day decolonization protocol, though higher environmental MRSA contamination pressure was associated with longitudinal MRSA colonization of household members.

Prior studies have demonstrated that MRSA colonization is a predisposing factor for SSTI [5, 6]. Moreover, many individuals with SSTI will experience SSTI recurrences [19, 26, 43]. Indeed, in the present study, both baseline MRSA colonization status and history of SSTI were important predictors of SSTI. While some clinicians prescribe decolonization only for colonized household members [7, 9], routine culturing of all household members is infeasible in a community setting. Thus we posited that a more pragmatic approach would target decolonization measures solely to household members reporting prior SSTI. The success of this personalized approach is amenable to

Table 2. Factors Associated With Cumulative Skin and Soft Tissue Infection and Methicillin-Resistant *Staphylococcus aureus* Colonization at Longitudinal Study Visits, Multivariable Models

	Cumulative SSTI[a], OR (95% CrI)					MRSA Colonization, OR (95% CrI)				
Covariates	1 mo	3 mo	6 mo	9 mo	12 mo	1 mo	3 mo	6 mo	9 mo	12 mo
Personalized approach (vs household approach)	0.89 (.26–2.73)	0.87 (.51–1.55)	0.93 (.63–1.36)	1.05 (.74–1.52)	1.06 (.74–1.52)	1.75 (.81–3.64)	1.69 (.96–3.04)	1.49 (.70–3.52)	**2.49 (1.14–5.56)**	1.70 (.93–3.26)
MRSA colonized at baseline sampling	1.35 (.59–3.27)	1.67 (.96–2.81)	**2.16 (1.37–3.34)**	**1.87 (1.24–2.83)**	**2.05 (1.34–3.13)**	**8.22 (4.60–14.93)**	**4.29 (2.70–6.68)**	**5.22 (3.02–9.11)**	**3.79 (2.17–6.85)**	**3.01 (1.86–4.92)**
Age, y (increase of 1 SD, 16.2 y, from the mean 20.1 y)	1.52 (.99–2.42)	1.00 (.78–1.30)	1.20 (.97–1.47)	1.09 (.90–1.32)	1.02 (.84–1.23)	1.22 (.92–1.65)	0.91 (.72–1.15)	0.82 (.61–1.07)	1.10 (.84–1.47)	1.11 (.89–1.40)
Male sex	0.88 (.43–1.75)	0.84 (.55–1.28)	1.02 (.73–1.46)	1.03 (.74–1.41)	1.10 (.79–1.49)	1.42 (.89–2.23)	1.31 (.87–1.92)	1.54 (.96–2.49)	1.22 (.75–1.96)	1.14 (.77–1.68)
African American or multiracial[b] (vs white)	1.20 (.22–5.37)	1.46 (.70–2.94)	**1.84 (1.09–3.09)**	1.54 (.96–2.51)	1.51 (.92–2.62)	0.67 (.25–1.71)	0.64 (.28–1.36)	1.01 (.36–2.88)	0.52 (.17–1.64)	0.52 (.23–1.22)
Public or no health insurance (vs private or military)	0.44 (.06–2.75)	0.62 (.27–1.42)	**0.39 (.21–.72)**	0.63 (.36–1.05)	0.75 (.44–1.31)	0.88 (.32–2.51)	1.06 (.48–2.43)	0.61 (.19–1.95)	0.92 (.29–2.89)	0.81 (.32–1.97)
Rents home (vs owns)	1.58 (.32–9.03)	1.25 (.56–2.90)	1.35 (.76–2.50)	0.91 (.53–1.53)	0.84 (.48–1.47)	**3.26 (1.07–10.00)**	**2.42 (1.02–5.26)**	0.87 (.28–2.65)	1.80 (.61–5.19)	1.67 (.72–4.47)
People per 1000 sq ft (increase of 1 SD, 1.9 people, from the mean 3.6 people)	1.32 (.65–2.78)	1.12 (.80–1.59)	1.11 (.87–1.42)	1.15 (.91–1.43)	1.11 (.89–1.41)	0.91 (.57–1.46)	0.95 (.66–1.36)	0.86 (.52–1.48)	0.96 (.60–1.53)	1.25 (.88–1.83)
Environmental MRSA contamination pressure[c] at previous sampling (increase of 1 SD, 13.4%, from the mean 6.5%)	0.99 (.54–1.80)	0.93 (.68–1.27)	0.93 (.75–1.12)	0.97 (.81–1.18)	0.93 (.77–1.13)	1.18 (.78–1.79)	**1.37 (1.05–1.85)**	**1.40 (1.03–1.97)**	**1.78 (1.27–2.57)**	**1.38 (1.06–1.85)**
Index patient (vs household contact)	2.18 (.86–5.96)	1.62 (.93–2.74)	**1.71 (1.06–2.79)**	1.36 (.89–2.13)	1.41 (.92–2.17)	1.97 (.99–4.11)	0.98 (.57–1.70)	**0.34 (.15–.74)**	0.71 (.34–1.41)	1.15 (.66–2.00)
SSTI in past year (during HOME study)	**2.51 (1.13–5.84)**	**2.65 (1.62–4.33)**	**2.16 (1.47–3.16)**	**1.95 (1.38–2.77)**	**1.98 (1.38–2.87)**	0.79 (.45–1.41)	1.17 (.72–1.85)	1.17 (.68–2.06)	1.55 (.92–2.78)	1.14 (.71–1.82)
Systemic antibiotics since previous sampling[d]	…	…	…	…	…	2.22 (.98–4.75)	1.03 (.55–1.98)	0.59 (.26–1.32)	0.50 (.20–1.21)	0.92 (.48–1.68)
Additional decolonization with mupirocin ointment to anterior nares since previous sampling[d]	…	…	…	…	…	1.43 (.26–7.71)	1.87 (.37–9.17)	1.70 (.14–20.64)	1.25 (.28–5.52)	0.26 (.05–1.46)
Additional decolonization with chlorhexidine body wash or bleach baths since previous sampling[d]	…	…	…	…	…	1.90 (.92–4.23)	1.14 (.59–2.19)	2.35 (.92–6.20)	0.61 (.25–1.52)	1.24 (.60–2.60)

The cumulative SSTI and MRSA colonization models (Supplementary Methods) are individual-level, multivariable generalized mixed-effects logistic regression models fitted using R library "MCMCglmm"; eligible individuals for each model are those completing follow-up visit and with no missing data for any covariates: 1 month, n = 425; 3 months, n = 414; 6 months, n = 407; 9 months, n = 398; 12 months, n = 381. The odds ratio and 95% credible interval for covariates significantly associated with each outcome (credible interval does not cross 1) are highlighted with bold text.

Abbreviations: CrI, credible interval; HOME, Household Observation of Methicillin-Resistant *Staphylococcus aureus* in the Environment; MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio; SD, standard deviation; SSTI, skin and soft tissue infection.

[a]Defined as 1 or more SSTIs reported between baseline sampling and each follow-up visit.

[b]Multiracial participants are African American/white and African American/white/American Indian.

[c]Defined as the number of environmental surfaces (up to 21 per house) contaminated with MRSA divided by the total number of environmental surfaces sampled per household; the cumulative SSTI model includes environmental MRSA contamination pressure at baseline, not previous, sampling (increase of 1 SD, 12.1%, from the mean 6.5%).

[d]Systemic antibiotics and additional decolonization since previous sampling are not included in cumulative SSTI model as temporality between SSTI and treatment for SSTI cannot be established.

widespread implementation in clinical practice (ie, requiring only history taking) while reducing burden on households.

While both approaches reduced MRSA colonization in the months following the 1-time, 5-day intervention, this effect waned over time. Interestingly, among those from whom carriage was eradicated at the 1-month sampling, one-third who became recolonized at 3 months had acquired a new strain. Furthermore, despite the current intervention, 33% of index patients experienced recurrent SSTI during the 12 months of $HOME_2$. While this SSTI incidence is lower than that experienced by the index patients in the year before $HOME_2$ enrollment (50% [29]), the burden of recurrent SSTI was not entirely eliminated. Taken together, these findings reflect ongoing community exposure to MRSA reservoirs, both within and outside of the household, posing a risk for reacquisition and SSTI. This suggests that a 1-time decolonization regimen performed in homes affected by MRSA is inadequate to prevent SSTI, regardless of who is targeted [10, 11, 19]. One consideration is to prescribe more prolonged or periodic decolonization interventions; prior such trials have enrolled varying populations and examined different decolonization regimens, yielding disparate results [12, 41, 44]. Ultimately,

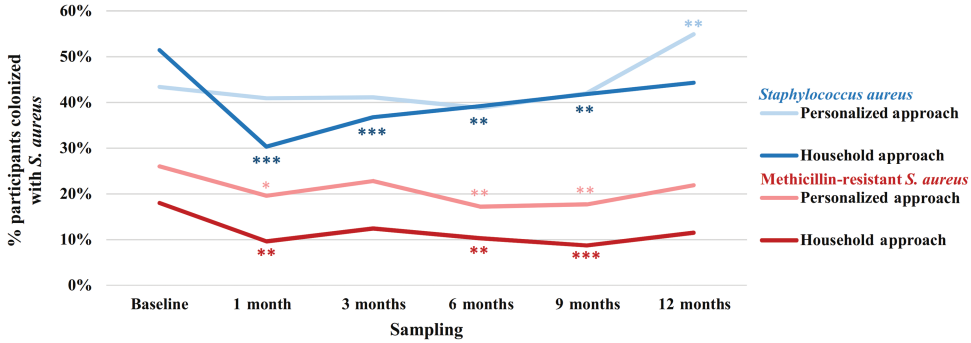

Figure 3. Longitudinal household member *Staphylococcus aureus* colonization. Percentage of household members colonized with *S. aureus* (blue) and methicillin-resistant *S. aureus* (MRSA; red) at 6 sampling intervals over 12 months. 5-day decolonization intervention (personalized approach, light shade; household approach, dark shade) occurred immediately following baseline sampling. *S. aureus* includes MRSA and/or methicillin-susceptible *S. aureus*. Statistically significant changes in colonization at longitudinal samplings compared to baseline sampling within the decolonization approach represented by asterisks (using McNemar test: $^{*}P < .05$, $^{**}P \leq .01$, $^{***}P \leq .001$). Change in colonization between decolonization approaches was compared using Fisher exact test: for *S. aureus*, $P = .01$, $P = .04$, and $P = .003$ at 1-, 3-, and 12-month samplings, respectively; for MRSA: $P > .05$ at all samplings.

further studies and approaches are needed to fully abate community transmission.

The most successful decolonization regimens have included intranasal mupirocin [10, 20, 23], underscoring the importance of persistent nasal colonization [29]. Increasing prevalence of resistance to topical antimicrobials has been associated with their widespread use for treating skin infections and for decolonization in community settings [22, 25, 45]. Additionally, high-level mupirocin resistance predicts failure of decolonization efforts with mupirocin, resulting in persistent staphylococcal carriage [20–24]. While the present trial resulted in no rise in the recovery of mupirocin-resistant strains, monitoring resistance to topical antimicrobials remains a priority.

This study has limitations. The prevalence of MRSA colonization at baseline was higher among participants randomized to the personalized (vs household) approach. To account for this, all analyses of longitudinal MRSA colonization and SSTI adjusted for baseline colonization. Incident SSTI as primary outcome was self-reported, which may have overestimated overall incidence. However, this practice of reporting is common in community-based studies [43, 46]; in addition, all enrolled households had a history of medically attended, culture-confirmed MRSA SSTI, increasing confidence in their ability to recognize and report interval SSTIs. Our study was designed to evaluate effectiveness; accordingly, in this real-world setting, adherence was not optimal, though it was statistically equivalent between study arms. Additionally, our findings may not be generalizable to households affected by methicillin-susceptible *S. aureus* SSTI.

In this pragmatic trial, we aimed to decrease the incidence of SSTI in households affected by MRSA while also decreasing the burden on families. A targeted approach of prescribing decolonization only for those household members with SSTI in the prior year was noninferior to decolonization of all household members. MRSA colonization and prior SSTI were strong predictors of incident SSTI, which may be taken into consideration when counseling families. Last, in the present study, the burden of household environmental MRSA surface contamination was associated with longitudinal MRSA colonization. Thus, future studies are needed to interrogate longer durations of decolonization, decontamination of the household environment, or the integration of both as novel approaches to reduce the burden of MRSA in households.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Acknowledgments. The authors thank Meghan Wallace for assistance with molecular strain typing.

Disclaimer. The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health (NIH) or the Agency for Healthcare Research and Quality (AHRQ).

Financial support. This work was supported by the Children's Discovery Institute of Washington University and St Louis Children's Hospital (to S. A. F.); NIH/National Institute of Allergy and Infectious Diseases (grant number K23-AI091690) to S. A. F.; the National Center for Advancing Translational Sciences at the NIH (grant number UL1-TR002345) to S. A. F.; the AHRQ (grant numbers R01-HS021736 and R01-HS024269) to S. A. F.; and the Burroughs Wellcome Foundation Investigators in the Pathogenesis of Infectious Disease Award (to J. B. W.). The computational analysis was partially funded by the Defense Advanced Research Projects Agency Big Mechanism program (Army Research Office contract W911NF1410333) to A. R.; by the NIH (grant numbers R01HL122712, 1P50MH094267, and U01HL108634) to A. R.; and by a gift from Liz and Kent Dauten) to A. R.

Potential conflicts of interest. D. A. H. reports personal fees from BioVersys AG, outside the submitted work. J. B. W. reports a financial agreement with Aridis Pharmaceutics related to patents owned by the University of Chicago. C. D. B. reports grants from Cepheid, bioMérieux, Luminex, and BioFire, and personal fees from Thermo Fisher Scientific, outside the submitted work. All other authors report no potential conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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