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Effectiveness of measures to eradicate Staphylococcus aureus carriage in patients with community-associated skin and soft-tissue infections: A randomized trial

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ORIGINAL ARTICLE

Effectiveness of Measures to Eradicate *Staphylococcus aureus* Carriage in Patients with Community-Associated Skin and Soft-Tissue Infections: A Randomized Trial

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BACKGROUND. Despite a paucity of evidence, decolonization measures are prescribed for outpatients with recurrent *Staphylococcus aureus* skin and soft-tissue infection (SSTI).

OBJECTIVE. Compare the effectiveness of 4 regimens for eradicating *S. aureus* carriage.

DESIGN. Open-label, randomized controlled trial. Colonization status and recurrent SSTI were ascertained at 1 and 4 months.

SETTING. Barnes-Jewish and St. Louis Children's Hospitals, St. Louis, Missouri, 2007–2009.

PARTICIPANTS. Three hundred patients with community-onset SSTI and *S. aureus* colonization in the nares, axilla, or inguinal folds.

INTERVENTIONS. Participants were randomized to receive no therapeutic intervention (control subjects) or one of three 5-day regimens: 2% mupirocin ointment applied to the nares twice daily, intranasal mupirocin plus daily 4% chlorhexidine body washes, or intranasal mupirocin plus daily dilute bleach water baths.

RESULTS. Among 244 participants with 1-month colonization data, modified intention-to-treat analysis revealed *S. aureus* eradication in 38% of participants in the education only (control) group, 56% of those in the mupirocin group ($P = .03$ vs controls), 55% of those in the mupirocin and chlorhexidine group ($P = .05$), and 63% of those in the mupirocin and bleach group ($P = .006$). Of 229 participants with 4-month colonization data, eradication rates were 48% in the control group, 56% in the mupirocin only group ($P = .40$ vs controls), 54% in the mupirocin and chlorhexidine group ($P = .51$), and 71% in the mupirocin and bleach group ($P = .02$). At 1 and 4 months, recurrent SSTIs were reported by 20% and 36% of participants, respectively.

CONCLUSIONS. An inexpensive regimen of dilute bleach baths, intranasal mupirocin, and hygiene education effectively eradicated *S. aureus* over a 4-month period. High rates of recurrent SSTI suggest that factors other than endogenous colonization are important determinants of infection.

TRIAL REGISTRATION. ClinicalTrials.gov identifier: NCT00513799.

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Over the past decade, the incidence of staphylococcal skin and soft-tissue infections (SSTIs) has increased significantly.¹⁻³ *Staphylococcus aureus* colonization is a demonstrated risk factor for the development of SSTI.⁴⁻⁶ Measures to eradicate *S. aureus* carriage, including intranasal mupirocin and bathing with chlorhexidine antiseptic, have been evaluated in the prevention of nosocomial infections. The effectiveness of these measures has varied across different studies and has been shown to wane over extended periods of time.⁷⁻¹¹

The recent increase in the incidence of SSTI in otherwise healthy individuals is largely attributable to a virulent, community-associated (CA) methicillin-resistant *S. aureus*

(MRSA) clone designated USA300.¹² When this clone first emerged, it represented the majority of CA-MRSA isolates. More recently, similarly virulent strains of methicillin-susceptible *S. aureus* (MSSA) have also been shown by means of genotyping to originate from USA300.^{2,13} Genomic sequencing of the USA300 clone suggests that these strains possess novel gene content and altered regulation of virulence determinants, which may enhance colonization and survival.¹⁴⁻¹⁶ Because of the distinct epidemiology, microbial characteristics, and pathogenesis of contemporary CA *S. aureus* strains, eradication strategies employed in healthcare settings may not be effective in preventing *S. aureus* transmission

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and infection in the community. The paucity of data available to guide the prevention of recurrent *S. aureus* SSTI in community settings, as highlighted by recently published Infectious Diseases Society of America MRSA clinical practice guidelines, has engendered a wide variety of treatment and decolonization practices.^{17,18} Traditional interventions, such as mupirocin or chlorhexidine, are often prescribed,^{17,19} and bathing in dilute bleach water has also been proposed,³ but these measures have not been comprehensively evaluated with a randomized trial in the outpatient setting.

The primary objective of this study was to investigate the effectiveness of decolonization measures in eradicating *S. aureus* carriage from patients with SSTI in the community. The secondary objectives were to determine rates of recurrent SSTI among participants in the study arms and to evaluate the acceptability of and adherence to these eradication measures by study participants. We hypothesized that a decolonization regimen consisting of personal and household hygiene education and application of nasal mupirocin ointment with either chlorhexidine body washes or dilute bleach water baths would be twice as effective as hygiene education alone in eradicating *S. aureus* colonization.

METHODS

Study Design

The St. Louis *Staphylococcus aureus* Reduction Study (StL StaRS) was an open-label, randomized controlled trial at 2 hospitals that compared the effectiveness of 4 regimens to eradicate *S. aureus* carriage from patients with CA-SSTI and *S. aureus* colonization. This study was approved by the Washington University Human Research Protection Office.

Participants

Patients 6 months of age or older with acute, community-onset SSTI were screened from the Emergency Department (ED) and ambulatory wound center at St. Louis Children's Hospital (SLCH) and the Barnes-Jewish Hospital (BJH) ED. At the time of screening, verbal informed consent, demographic information, and colonization swab samples (BBL CultureSwab; Becton Dickinson) from the anterior nares, axilla, and inguinal folds were obtained. Patients were excluded if they had a postoperative wound infection, permanent indwelling catheter, or percutaneous medical device; were pregnant or receiving dialysis; or resided in a long-term care facility. Patients colonized with *S. aureus* (MRSA or MSSA) at one or more of the sampled sites were eligible for enrollment.

Study Intervention and Randomization

Enrollment was conducted in the Clinical Research Center (CRC) at SLCH or BJH from April 2007 through May 2009 after the patient's acute SSTI had healed. The median time from screening to enrollment was 16.5 days (interquartile range, 15.0 days) and did not differ significantly between

treatment arms (Table 1). Written informed consent and assent, when applicable, were obtained at enrollment. Randomization was conducted by B.C.C. with an Internet-based, computer-generated randomization schedule using permutation blocks of 8. The designated intervention for each participant was sealed inside a numbered security envelope by S.A.F. and was opened at the enrollment visit by a research coordinator. Participants were randomized to receive 1 of 4 interventions:

1. Personal and household hygiene education only. This included instructions to discard lotions in jars and replace them with pump or pour bottles; refrain from sharing personal hygiene items (eg, hairbrushes, razors, or towels); wash (in hot water) bed linens at least once weekly and towels and washcloths after each use.

2. Education plus application of 2% mupirocin ointment to the bilateral anterior nares twice daily for 5 days.

3. Education and intranasal 2% mupirocin ointment in addition to daily body washes with 4% chlorhexidine solution (Hibiclens; Mölnlycke Health Care), used as a liquid soap, for 5 days.

4. Education and intranasal 2% mupirocin ointment in addition to daily 15-minute soaks in dilute bleach water (a quarter cup of 6% sodium hypochlorite [Clorox; Clorox Company] per tub of water) for 5 days.

Oral and written instructions and diagrams were provided to study participants. Intranasal application of mupirocin ointment using a sterile cotton applicator was demonstrated by the study staff. Participants or parents were then required to demonstrate the mupirocin application procedure to confirm their understanding. All study materials were supplied to the participants. For participants randomized to the bleach bath arm, a measuring cup marked at one-fourth cup was provided. Decolonization measures were completed by participants at home.

Data Collection at Baseline and Follow-Up

At enrollment, a questionnaire was administered to each participant to collect information regarding medical history, hygiene practices, household factors, employment, and other activities (factors listed in Table 1). Upon completion of the 5-day decolonization protocol, each participant was contacted by telephone to assess their adherence to the protocol, adverse reactions, and ease of performing each protocol step.

Participants were followed up longitudinally, with follow-up visits 1 and 4 months after randomization at the SLCH or BJH CRC. At each follow-up visit, participants had samples collected to detect *S. aureus* colonization in the anterior nares, axilla, and inguinal folds. A survey was administered to ascertain interval SSTI in the participant or a household member. Study participation concluded with a telephone call 6 months after enrollment to ascertain SSTI recurrence; all follow-up was completed by November 2009. Twelve participants were unable to return for follow-up visits because of

TABLE 1. Baseline Characteristics of Study Participants, by Intervention Group

Characteristics	Hygiene education only (n=75)	Education and mupirocin (n=75)	Education, mupirocin, and chlorhexidine (n=75)	Education, mupirocin, and bleach baths (n=75)	P
Age, mean years (±SD)	17.37 ± 16.57	16.52 ± 16.12	18.19 ± 17.37	18.67 ± 15.29	.92
Male sex	41 (55)	38 (51)	23 (31)	37 (49)	.02
Nonwhite race	56 (75)	48 (64)	57 (76)	52 (69)	.35
Health insurance status					.72
Private	22 (29)	26 (35)	23 (31)	29 (39)	
Public	40 (53)	41 (55)	38 (51)	33 (45)	
None	13 (17)	8 (11)	13 (18)	12 (16)	
Colonization					
MRSA only	42 (56)	39 (52)	44 (59)	50 (67)	.31
MSSA only	25 (33)	28 (37)	23 (31)	20 (27)	.56
Both MRSA and MSSA	8 (11)	8 (11)	8 (11)	5 (7)	.79
Baseline sites of colonization ^a					
Anterior nares	52 (69)	51 (68)	49 (65)	54 (72)	.85
Axilla	19 (25)	27 (36)	22 (29)	23 (31)	.56
Inguinal folds	58 (77)	50 (67)	59 (79)	56 (75)	.33
Baseline no. of sites colonized					
1 site	35 (47)	33 (44)	34 (45)	33 (44)	.98
2 sites	26 (35)	31 (41)	27 (36)	26 (35)	.81
3 sites	14 (19)	11 (15)	14 (19)	16 (21)	.77
Prescribed systemic antibiotic(s) at time of acute SSTI	64 (85)	68 (91)	69 (92)	68 (91)	.55
Colonized and/or infected with a mupirocin-resistant <i>S. aureus</i> strain	3 (4)	1 (1)	1 (1)	1 (1)	.56
Time from screening to enrollment, median days (IQR)	17 (15)	17 (15)	16 (13)	16 (15)	.93
Comorbidity					
Any	49 (65)	46 (61)	50 (67)	48 (64)	.92
Asthma	26 (35)	14 (19)	13 (17)	16 (21)	.04
Eczema	28 (37)	15 (20)	32 (43)	19 (25)	.01
Allergies	10 (13)	13 (17)	17 (23)	24 (32)	.03
Hypertension	5 (7)	4 (5)	9 (12)	7 (9)	.46
HIV infection	0 (0)	0 (0)	4 (5)	0 (0)	.01
Takes a prescription medication daily	30 (40)	24 (32)	23 (32)	31 (41)	.43
Has taken antibiotics within past year	40 (54)	42 (58)	45 (65)	41 (56)	.59
Surgery within past year	5 (7)	6 (8)	14 (19)	6 (8)	.05
Emergency department or urgent care visit within past year	30 (40)	27 (36)	27 (36)	36 (48)	.39
Contact with healthcare ^b	20 (27)	21 (28)	18 (24)	20 (27)	.95
Prior SSTI within past year					
Index case	31 (42)	36 (48)	36 (49)	40 (53)	.58
Household member	33 (45)	27 (36)	35 (47)	24 (32)	.24
Permanent home	65 (87)	69 (92)	68 (91)	67 (89)	.74
Crowded home (>2 people per bedroom)	7 (9)	8 (11)	7 (9)	13 (17)	.36
Sports participation	19 (25)	18 (24)	11 (15)	18 (24)	.36
Pet in household	28 (37)	29 (39)	26 (35)	26 (35)	.94

NOTE. Data are no. (%) of participants, unless otherwise indicated. P values are for comparisons across all 4 randomization groups. HIV, human immunodeficiency virus; IQR, interquartile range; MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-sensitive *S. aureus*; SD, standard deviation; SSTI, skin or soft-tissue infection.

^a Participants may have been colonized at more than 1 body site.

^b Participant works in a healthcare facility or lives with someone who works in a healthcare facility.

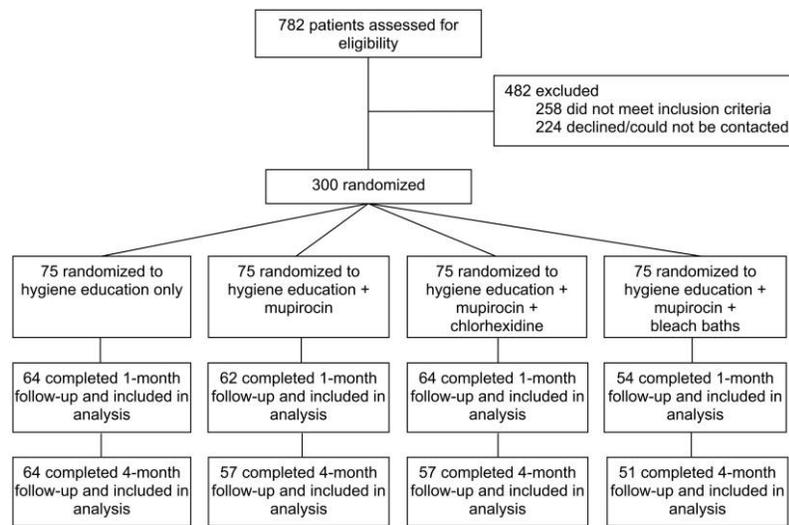


FIGURE 1. Flow of participants through the St. Louis *Staphylococcus aureus* Reduction Study trial.

geographic location. For these participants, the survey was conducted by telephone, and swabs were delivered to the participant's home accompanied by a diagram and detailed instructions for obtaining and returning the culture swab samples (validated by our group and others^{20,21}).

Study Outcomes

The primary outcome measure was eradication of *S. aureus* carriage 1 month after intervention. Eradication was defined as the absence of *S. aureus* carriage at the 3 sampled body sites. Secondary outcomes included *S. aureus* eradication at 4 months; recurrent SSTI at 1, 4, and 6 months; and acceptability of and adherence to the intervention methods.

Laboratory Methods

Swab samples were incubated overnight in tryptic soy broth with 6.5% NaCl (BBL; Becton Dickinson) at 35°C. A sample of broth was plated to trypticase soy agar with 5% sheep blood (BBL; Becton Dickinson) and incubated overnight. *S. aureus* isolates were identified and antibiotic susceptibility testing was performed according Clinical and Laboratory Standards Institute procedures as previously described.^{22,23} Laboratory personnel were blinded to randomization assignments. Follow-up swab samples collected by participants at home all yielded normal flora, which suggested that swab samples were indeed representative of the designated body sites.

Real-time polymerase chain reaction was performed for all recovered *S. aureus* isolates, using established primers, to detect the *mupA* gene encoding high-level mupirocin resistance.²⁴

Statistical Analysis

Based on published data,⁵ we anticipated 50% eradication of *S. aureus* carriage in the control group, who received only

hygiene education. Based on this assumption, 57 participants per group were needed to detect a 50% relative reduction in *S. aureus* colonization at 1 month ($\alpha = 0.05$ and study power at 80%) when comparing each intervention group with the control group. To account for a possible 25% attrition, we enrolled 75 participants in each arm (300 total participants).

Demographic and baseline characteristics were evaluated with descriptive statistics. Outcomes were determined by modified intention-to-treat analysis, including participants who attended longitudinal visits. Statistical analyses were performed using SPSS for Windows, version 17.0 (SPSS) unless otherwise specified. Pearson's χ^2 analyses and analysis of variance (or Kruskal-Wallis test where appropriate) were performed to compare characteristics among participants in the 4 study arms. Statistical significance values for relative risk (RR) and absolute risk reduction (ARR) for *S. aureus* eradication and recurrent SSTI between the control group and the intervention arms were determined by Pearson's χ^2 . Fisher's exact tests were performed using R (R Foundation) in cases of small cell sizes. Potential confounding baseline characteristics that differed significantly between arms ($P \leq .05$) were evaluated with binary logistic regression. All tests for significance were 2-sided, and P values of $\leq .05$ were considered statistically significant. The RR was considered to be significant if the 95% confidence interval (CI) did not include 1.

RESULTS

Baseline Patient Characteristics

Of 782 patients with acute SSTI assessed for eligibility, 300 were enrolled in the trial. Participants were randomly allocated to 4 intervention groups of 75 participants each (Figure 1). Overall, 193 children (64%) and 107 adults (36%) were enrolled. The treatment groups were similarly distributed at baseline with the exception of sex, several comorbidities

(asthma, eczema, allergies, and human immunodeficiency virus infection), and surgery within the past year (Table 1). These factors did not influence the relationship between treatment group and outcomes (data not shown).

Primary and Secondary Outcomes

S. aureus eradication at 1 month. The 1-month colonization evaluation was completed by 244 participants. Modified intention-to-treat analysis revealed significantly greater *S. aureus* eradication with each of the 3 decolonization regimens, compared with the control group, which received only personal and household hygiene education. *S. aureus* eradication occurred in 38% of control subjects. Compared with control subjects, eradication was achieved for 56% of participants who were randomized to education plus mupirocin ($P = .03$ vs control subjects); 55% of those who were randomized to education, mupirocin, and chlorhexidine ($P = .05$); and 63% of those who were randomized to education, mupirocin, and bleach baths ($P = .006$; Table 2).

S. aureus eradication at 4 months. Colonization data were available for 229 participants at 4 months. *S. aureus* was eradicated from 48% of control subjects. Compared with control subjects, eradication was achieved in 56% of participants in the education plus mupirocin group ($P = .40$); 54% in the education, mupirocin, and chlorhexidine group ($P = .51$); and 71% in the education, mupirocin, and bleach baths group ($P = .02$; Table 2).

Body site-specific eradication. Colonization of the nares was significantly reduced at 1 and 4 months in all participants who received mupirocin, compared with control subjects. In addition, inguinal colonization was significantly lower at 1 month in participants who were randomized to bleach baths, compared with those who did not perform bleach baths (Table 3).

Rates of recurrent SSTI. Recurrent SSTI was reported by 20% of participants at 1 month, 36% at 4 months, and 49% at 6 months. There were significantly fewer reports of recurrent SSTI at 1 month by participants who received education, mupirocin, and chlorhexidine (11%) than by control subjects (26%; $P = .03$; all other differences were not significant; Table 4).

Protocol acceptability and adherence. No serious adverse events were reported. Of 283 participants who provided information, 39 reported adverse effects. The most common reactions included dry skin (in 21 [7%] of the participants), rash (9 [3%]), and rhinorrhea or nasal irritation (4 [1%]). A greater number of reactions were experienced by participants who performed chlorhexidine body washes (20%) and bleach baths (25%) than by control subjects (6%; $P = .01$ and $P = .001$, respectively). Mupirocin, chlorhexidine washes, and bleach baths were reportedly easy to perform for 84% (174 of 208), 82% (56 of 68), and 77% (51 of 66) of the participants, respectively. Of those with follow-up information, adherence to protocol assignment was reported by

72% of control subjects; 64% of participants in the education and mupirocin group; 64% of participants in the education and mupirocin group; 70% of participants in the education, mupirocin, and chlorhexidine group; and 62% of participants in the education, mupirocin, and bleach baths group. In groups assigned to multiple interventions, adherence to hygiene measures was consistently lower than was adherence to topical treatments (Table 5).

DISCUSSION

This is, to our knowledge, the first study to compare the effectiveness of multiple approaches for *S. aureus* eradication from multiple body sites in the community. Decolonization regimens employing intranasal mupirocin alone and in combination with chlorhexidine body washes or dilute bleach baths were effective in *S. aureus* eradication 1 month after the intervention, compared with personal and household hygiene education alone. Interestingly, only the regimen that combined hygiene education, intranasal mupirocin, and bleach baths achieved a statistically significant reduction in *S. aureus* colonization rates at 4 months.

The findings of this study are encouraging, because bleach is readily available and very affordable (approximately 40 cents per 5-day course of daily baths, compared with \$10 per 8 fluid ounces of chlorhexidine). Bleach, or sodium hypochlorite, has *S. aureus* antimicrobial activity both in vivo and in vitro and has been used by dermatologists to treat eczema, presumably by suppressing *S. aureus* growth.²⁵⁻²⁸ Variable dilutions of bleach added to bathwater have been recommended.^{3,25,27,28} In this study, we asked participants to add one-quarter cup of bleach to a bathtub full of water. Although this presumably resulted in a range of dilutions among study participants, we wanted to make the intervention easy and practical. Considering typical bathtub sizes and volumes of water used,²⁷ we estimate that most bleach bath participants were exposed to sodium hypochlorite concentrations of 0.002%–0.009%. We believe that soaking in dilute bleach water provided the most exposure for all body parts, especially the inguinal folds, and that longer contact with bleach may have provided a greater antimicrobial effect. In fact, inguinal colonization was significantly reduced in patients in the bleach group, compared with those in the chlorhexidine group. In contrast, chlorhexidine was applied as liquid soap and rinsed off. Used in this manner, chlorhexidine likely provided little residual antimicrobial activity and may have had less contact with the inguinal area, which is a frequently colonized body site.²⁹ The use of chlorhexidine-impregnated cloths, in which chlorhexidine is not rinsed from the skin, may be more effective in *S. aureus* eradication. These cloths have been effective in preventing hospital-acquired infections in intensive care unit settings.^{30,31}

Regardless of the setting (healthcare or community), agreement has not been reached regarding the optimal approach to *S. aureus* decolonization. Numerous decolonization studies, evaluating a variety of regimens, have been conducted in

TABLE 2. Eradication of *Staphylococcus aureus* Carriage at Longitudinal Intervals, by Intervention Group

Variable	Hygiene education only	Education and mupirocin	<i>P</i>	Education, mupirocin, and chlorhexidine	<i>P</i>	Education, mupirocin, and bleach baths	<i>P</i>
One month after intervention							
Eradication	24/64 (38)	35/62 (56)	.03	35/64 (55)	.05	34/54 (63)	.006
RR (95% CI)	...	1.51 (1.02–2.21)		1.46 (0.99–2.15)		1.68 (1.15–2.44)	
ARR (95% CI)	...	19 (2–35)		18 (1–34)		24 (6–40)	
Four months after intervention							
Eradication	31/64 (48)	32/57 (56)	.40	31/57 (54)	.51	36/51 (71)	.02
RR (95% CI)	...	1.16 (0.82–1.63)		1.12 (0.79–1.58)		1.46 (1.07–1.98)	
ARR (95% CI)	...	8 (–10 to 25)		7 (–11 to 24)		21 (3–37)	

NOTE. Data are proportion (%) of participants, unless otherwise indicated. The hygiene education only (control) group was used as the comparator group to determine relative risk (RR), absolute risk reduction (ARR), and *P* values. *P* value represents comparison between the intervention group and the control group. Participants were analyzed by the arm to which they were assigned. CI, confidence interval.

healthcare settings to prevent nosocomial infections, with varying results.^{7–11,32,33} For example, a meta-analysis of topical and systemic antimicrobials by Ammerlaan et al³² concluded that short-term application of nasal mupirocin was highly effective for eradicating MRSA carriage and achieved a 90% success rate 1 week after treatment. However, other meta-analyses have focused on the nondurability of such beneficial effects and have concluded that there is insufficient evidence for the use of topical or systemic therapies for *S. aureus* eradication.^{7,33} As in decolonization studies conducted in health-care settings,^{7–9} we found that CA *S. aureus* eradication achieved at 1 month by the application of mupirocin alone or in combination with chlorhexidine washes was not sustained. Thus, an effective regimen for long-term *S. aureus* eradication remains unclear.

S. aureus colonization at sites other than the anterior nares, including the groin, axilla, and pharynx, has been identified by our group and others as reservoirs for a high burden of *S. aureus* carriage.^{29,34,35} In accordance with this, the reported efficacy of intranasal mupirocin ointment is lower in studies that evaluate multiple body sites for colonization than in those that assess colonization of the nares alone.³² Thus, an

approach that includes decolonization of extra-nasal sites of *S. aureus* carriage may be critical to prevent transmission and infection. Because of the relatively low cost of bleach, and because resistance to mupirocin can develop with widespread use,^{36,37} a prolonged decolonization approach aimed at sustained eradication and consisting of dilute bleach baths without the use of intranasal mupirocin warrants further study. Orally administered antibiotics achieve short-term MRSA eradication rates approaching 60%, but antimicrobial resistance develops more commonly with regimens that include systemic antibiotics.³²

Despite the effectiveness of the studied interventions in reducing *S. aureus* colonization, participants in all study arms experienced a substantial rate of recurrent SSTI. In our cohort, 20% of participants reported recurrent SSTI within a month of study enrollment, which is consistent with other longitudinal studies.^{38,39} Similarly, in a study involving MRSA-colonized soldiers conducted by Ellis et al,⁴⁰ although application of mupirocin to the anterior nares successfully eradicated nasal carriage in the treated soldiers, it did not decrease infection rates in these soldiers or their peers. Because eradication of endogenous colonization alone does not eliminate

TABLE 3. Body Site-Specific Colonization at Longitudinal Intervals, by Intervention Group

Variable	Hygiene education only	Education and mupirocin	<i>P</i>	Education, mupirocin, and chlorhexidine	<i>P</i>	Education, mupirocin, and bleach baths	<i>P</i>
Nasal colonization ^a							
At 1 month	24/52 (46)	14/51 (27)	.049	13/49 (26)	.041	9/54 (17)	.001
At 4 months	26/52 (50)	12/51 (23)	.005	12/49 (24)	.008	8/54 (15)	<.001
Axilla colonization							
At 1 month	5/19 (26)	6/27 (22)	NS	4/22 (18)	NS	2/23 (9)	NS
At 4 months	4/19 (21)	4/27 (15)	NS	3/22 (14)	NS	2/23 (9)	NS
Inguinal colonization ^b							
At 1 month	23/58 (40)	16/50 (32)	NS	19/59 (32)	NS	8/56 (14)	.002
At 4 months	15/58 (26)	12/50 (24)	NS	18/59 (30)	NS	9/56 (16)	NS

NOTE. Data are proportion (%) of participants, unless otherwise indicated. *P* values shown are versus the hygiene education only (control) group, unless otherwise noted. NS, not significant.

^a All participants randomized to receive mupirocin vs control subjects: *P* = .002 at 1 month, *P* < .001 at 4 months.

^b Participants randomized to bleach bath group vs all others: *P* = .004 at 1 month, *P* = .10 at 4 months. Participants randomized to bleach bath group vs participants randomized to chlorhexidine group: *P* = .02 at 1 month, *P* = .07 at 4 months.

TABLE 4. Cumulative Recurrent Skin and Soft-Tissue Infection, by Intervention Group

Variable	Hygiene education only	Education and mupirocin	<i>P</i>	Education, mupirocin, and chlorhexidine	<i>P</i>	Education, mupirocin, and bleach baths	<i>P</i>
One month after intervention							
SSTI reported	17/65 (26)	14/62 (23)	.64	7/63 (11)	.03	12/55 (22)	.58
RR (95% CI)	...	0.86 (0.47–1.60)		0.42 (0.19–0.95)		0.83 (0.44–1.59)	
ARR (95% CI)	...	4 (–10 to 2)		15 (3–28)		4 (–10 to 19)	
Four months after intervention							
SSTI reported	26/64 (41)	20/59 (34)	.44	19/57 (33)	.41	18/52 (35)	.51
RR (95% CI)	...	0.83 (0.52–1.33)		0.82 (0.51–1.32)		0.85 (0.53–1.37)	
ARR (95% CI)	...	7 (–10 to 23)		7 (–10 to 24)		6 (–11 to 23)	
Six months after intervention							
SSTI reported	28/52 (54)	27/52 (52)	.84	23/54 (43)	.25	21/43 (50)	.63
RR (95% CI)	...	0.96 (0.67–1.39)		0.79 (0.53–1.17)		0.91 (0.61–1.35)	
ARR (95% CI)	...	2 (–17 to 20)		11 (–8 to 29)		5 (–15 to 24)	

NOTE. Data are proportion (%) of participants, unless otherwise indicated. The hygiene education only (control) group was used as the comparator group to determine relative risk (RR), absolute risk reduction (ARR), and *P* values. *P* value represents comparison between the intervention group and the control group. Participants were analyzed by the arm to which they were assigned. CI, confidence interval; SSTI, skin or soft-tissue infection.

subsequent infection, an improved understanding of other determinants of CA *S. aureus* pathogenesis, including environmental factors and person-to-person transmission, is needed.

There are several limitations to this study. For logistical reasons, this randomized trial was conducted as an open trial, rather than as a blinded, placebo-controlled trial. Given the objective primary outcome (*S. aureus* eradication as determined by culture), we do not believe the lack of blinding introduced significant bias into the results. Although we did not directly monitor adherence to the measures, 67% of the participants reported adherence with assigned decolonization measures, and reported rates of compliance with therapeutic interventions (mupirocin, chlorhexidine, and bleach) were very high (>90%). In addition, because of the pain and inconvenience of recurrent SSTI, we believe that many patients were motivated to complete the decolonization measures in an attempt to prevent future infection. Household members were not included in this trial and were not asked to perform the decolonization measures. CA *S. aureus* infections have been observed to cluster within households,⁴¹ and study par-

ticipants may have reacquired the organism from close household contacts. We are conducting a separate trial to compare the effectiveness of decolonization interventions directed at all household members with that of interventions directed at the index patient alone. Lastly, the incidence of recurrent SSTI was determined by patient report. We feel this was a valid measure given that each participant had experienced at least one prior SSTI (at the time of screening).

In summary, a regimen of dilute bleach water baths, intranasal mupirocin, and personal and household hygiene education was effective for *S. aureus* eradication in the outpatient setting for individuals with CA-SSTI. Although our results may be generalizable to other diverse populations of children and adults colonized with contemporary *S. aureus* strains, additional studies are needed to evaluate prolonged or intermittent decolonization approaches. Larger multicenter trials evaluating the efficacy and cost-effectiveness of these measures in reducing the morbidity of recurrent SSTI in individuals and communities will be vital to improving the lives of patients who are affected by CA *S. aureus*.

TABLE 5. Adherence to Decolonization Measures, by Intervention Group

Adherence to measures	Hygiene education only	Education and mupirocin	Education, mupirocin, and chlorhexidine	Education, mupirocin, and bleach baths
Hygiene measures	52/72 (72)	50/72 (69)	55/71 (78)	46/68 (68)
Intranasal mupirocin	...	68/72 (94)	68/71 (96)	65/68 (96)
Chlorhexidine	63/70 (90)	...
Bleach baths	66/68 (97)
All assigned measures	52/72 (72)	46/72 (64)	49/70 (70)	42/68 (62)

NOTE. Data are proportion (%) of participants. There was not a statistically significant difference in compliance with the assigned regimens between participants in the 4 randomization arms. Adherence for each protocol component was defined as completion of 3 hygiene steps (discarding lotions in jars, not sharing personal hygiene items, and washing bed linens and towels in hot water), mupirocin application twice daily for 5 days, chlorhexidine body washes daily for 5 days, and bleach baths daily for 5 days.

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