

NIH Public Access

Author Manuscript

Infect Control Hosp Epidemiol. Author manuscript; available in PMC 2012 December 21

Published in final edited form as:

Infect Control Hosp Epidemiol. 2011 September ; 32(9): 872-880. doi:10.1086/661285.

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

Stephanie A. Fritz, MD, MSCI^{1,*}, Bernard C. Camins, MD, MSCR^{2,*}, Kimberly A. Eisenstein, BS^{1,2}, Joseph M. Fritz, MD², Emma K. Epplin, BS^{1,2}, Carey-Ann Burnham, PhD^{1,3}, Jonathan Dukes, MPH², and Gregory A. Storch, MD^{1,2}

¹Department of Pediatrics, Washington University School of Medicine, St. Louis, Missouri, USA

²Department of Medicine, Washington University School of Medicine, St. Louis, Missouri, USA

³Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, Missouri, USA

Abstract

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

Objective—Compare the effectiveness of four regimens for eradicating *S. aureus* carriage.

Design—Open-label, randomized controlled trial. Colonization status and recurrent SSTI were ascertained at one and four 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 (controls) or perform 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 one-month colonization data, modified intention-to-treat analysis revealed *S. aureus* eradication in 38% of participants in the education only (control) group; 56% in the mupirocin group (p=0.03 vs. controls); 55% in the mupirocin/chlorhexidine group (p=0.05); and 63% in the mupirocin/bleach group (p=0.006). Of 229 participants with fourmonth colonization data, eradication rates were 48% in controls; 56% for mupirocin only (p=0.40 vs. controls); 54% for mupirocin/chlorhexidine (p=0.51); and 71% for mupirocin/bleach (p=0.02). At one and four months, respectively, recurrent SSTI was reported by 20% and 36% of participants.

Corresponding author: Stephanie A. Fritz, MD, MSCI, 660 South Euclid Avenue, Campus Box 8116, St. Louis, Missouri 63110, Telephone: (314) 454-4115, Fax: (314) 454-2836, Fritz_S@kids.wustl.edu. *These authors contributed equally to this work

Previous presentation of data: An abstract including preliminary results from this study was presented at the Fifth Decennial International Conference on Healthcare-Associated Infections 2010, Atlanta, GA.

Potential conflicts of interest. B.C.C. receives research support from, serves as a consultant for, and is on the speaker's bureau for Pfizer, Inc. All other authors report no conflicts of interest relevant to this article.

Over the past decade, the incidence of staphylococcal skin and soft tissue infections (SSTI) 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 SSTI in otherwise healthy individuals is largely attributable to a virulent, community-associated methicillin-resistant S. aureus (CA-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-sensitive S. aureus (MSSA) have also been shown to be genotypically USA300 in origin.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 Given 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 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 in eradicating *S. aureus* colonization as hygiene education alone.

METHODS

Study Design

The <u>St</u>. <u>L</u>ouis <u>Staphylococcus aureus R</u>eduction <u>Study</u> (StL StaRS) was an open-label, randomized controlled trial at 2 hospitals comparing 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 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 swabs (BBL CultureSwab; Becton Dickinson, Sparks, MD) from the anterior nares, axilla, and inguinal folds were obtained. Patients were excluded if they had a post-operative 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 1 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 to May 2009 after the patient's acute SSTI had healed. The median time from screening to enrollment was 16.5 days (inter-quartile 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 with pump or pour bottles; refrain from sharing personal hygiene items (e.g., 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, Norcross, GA) (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 (¼ cup of 6% sodium hypochlorite [Clorox[®], Clorox Company, Oakland, CA] 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 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 "¼ 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 past 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 longitudinally with follow-up visits 1 and 4 months after randomization at the SLCH or BJH CRC. At each follow-up visit, participants were sampled for *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 following enrollment to ascertain SSTI recurrence; all follow-up was completed by November, 2009. Twelve participants were unable to return for follow-up visits due to geographic location. For these participants, the survey was conducted by telephone and swabs were delivered to their home

accompanied by a diagram and detailed instructions for obtaining and returning the culture swabs (validated by our group and others20,21).

Study Outcomes

The primary outcome measure was eradication of *S. aureus* carriage 1 month following intervention. Eradication was defined as 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 intervention methods.

Laboratory Methods

Swabs 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 swabs collected by participants at home all yielded normal flora, suggesting that swabs were indeed representative of the designated body sites.

Real-time PCR was performed on all recovered *S. aureus* isolates to detect the *mupA* gene encoding high-level mupirocin resistance using established primers.24

Statistical Analysis

Based on published data,5 we anticipated 50% eradication of *S. aureus* carriage in the control group receiving 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 to 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 17.0 (SPSS, Chicago, IL) unless otherwise specified. Pearson's Chi Square analyses and ANOVA (or Kruskal-Wallis where appropriate) were performed to compare characteristics among participants in the 4 study arms. 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 Chi Square. Fisher's exact tests were performed using "R" (The R Foundation, Wein, Austria) in cases of small cell sizes. Potential confounding baseline characteristics which differed significantly between arms (p-values 0.05) were evaluated with binary logistic regression. All tests for significance were 2-sided, and *P*-values of 0.05 were considered statistically significant. A RR was considered 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 gender, several

comorbidities (asthma, eczema, allergies, and HIV), and surgery in 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 to the control group receiving only personal and household hygiene education. *S. aureus* eradication occurred in 38% of controls. Compared to controls, eradication was achieved in 56% of participants randomized to education plus mupirocin (p=0.03 vs. controls); 55% receiving education, mupirocin, and chlorhexidine (p=0.05); and 63% receiving education, mupirocin, and bleach baths (p=0.006) (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 controls. Compared to controls, eradication was achieved in 56% of participants in the education plus mupirocin group (p=0.40); 54% in the education, mupirocin, and chlorhexidine group (p=0.51); and 71% in the education, mupirocin, and bleach baths group (p=0.02) (Table 2).

Body site-specific eradication—Colonization of the nares was significantly reduced at 1 and 4 months in all participants receiving mupirocin compared to controls. In addition, inguinal colonization was significantly lower at 1 month in participants randomized to bleach baths compared to those not performing 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. Reports of recurrent SSTI by participants receiving education, mupirocin, and chlorhexidine (11%) were significantly lower at 1 month compared to controls (26%, p=0.03; all other differences not significant) (Table 4).

Protocol acceptability and adherence—No serious adverse events were reported. Of 283 participants providing information, 39 reported side effects. The most common reactions included dry skin (21; 7%), rash (9; 3%), and rhinorrhea or nasal irritation (4; 1%). A greater number of reactions were experienced by participants performing chlorhexidine body washes (20%) and bleach baths (25%) compared to controls (6%; p=0.01 and 0.001, respectively). Mupirocin, chlorhexidine washes, and bleach baths were reportedly "easy" to perform for 84% (174/208), 82% (56/68), and 77% (51/66) of participants, respectively. Of those with follow-up information, adherence to protocol assignment was reported by 72% of controls, 64% of participants in the education and mupirocin group, 70% in the education, mupirocin, and chlorhexidine group, and 62% in the education, mupirocin, and bleach baths group. In groups assigned to multiple interventions, adherence to hygiene measures was consistently lower than adherence to topical treatments (Table 5).

DISCUSSION

This is 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 one month following the intervention compared to personal and household hygiene education alone. Interestingly, only the regimen combining hygiene education, intranasal mupirocin, and bleach baths achieved a statistically significant reduction in *S. aureus* colonization rates at four months.

The findings of this study are encouraging, as 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 bath water 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 soaking in dilute bleach water provided the most exposure for all body parts, especially the inguinal folds, and longer contact of bleach may have provided more antimicrobial effect. In fact, inguinal colonization was significantly reduced in patients in the bleach group compared to 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, 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 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 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 and colleagues concluded that short-term application of nasal mupirocin was highly effective for eradicating MRSA carriage, achieving a 90% success rate one week following treatment.32 However, other meta-analyses have focused on the non-durability of such beneficial effects, concluding 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 healthcare settings,7–9 we found that CA-*S. aureus* eradication achieved at one 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 have 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 evaluating multiple body sites for colonization compared with studies assessing colonization of the nares alone.32 Thus, an approach including decolonization of extra-nasal sites of *S. aureus* carriage may be critical to prevent transmission and infection. Given the relatively low cost of bleach, and given that resistance to mupirocin can develop with widespread use,36,37 a prolonged decolonization approach aimed at sustained eradication 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 of MRSA-colonized soldiers by Ellis and colleagues, while 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.40 As eradication of endogenous colonization alone does not eliminate subsequent infections, 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 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, overall, 67% of participants reported adherence with assigned decolonization measures, and reported compliance rates with therapeutic interventions (mupirocin, chlorhexidine, and bleach) were very high (>90%). In addition, due to 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 infections. 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 participants 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 versus the index patient alone. Lastly, 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 community-associated SSTI. Though our results may be generalizable to other diverse populations of children and adults colonized with contemporary *S. aureus* strains, further studies are needed to evaluate prolonged or intermittent decolonization approaches. Larger multi-center 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 affected by community-associated *S. aureus*.

Acknowledgments

We thank Cherie Hill and Dottie Sinclair for assistance with data management. We acknowledge the BJH and SLCH clinical microbiology laboratory technologists for excellent technical assistance and Madeline Snow Martin for performing *mupA* detection. We thank Victoria Fraser, M.D. and David Hunstad, M.D. for their thoughtful reviews of this manuscript. We appreciate the donation of study materials by Mölnlycke Health Care (chlorhexidine solution [Hibiclens[®]]) and Taro Pharmaceuticals (mupirocin ointment).

Financial support. S.A.F. and B.C.C. received salary support from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH), and NIH Roadmap for Medical Research National Institutes of Health (UL1-RR024992 and KL2RR024994) and B.C.C. received grant support from Pfizer, Inc. The trial sponsors had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript. The contents of this manuscript are solely the responsibility of the authors and do not necessarily represent the official view of NCRR or NIH.

REFERENCES

- Hersh AL, Chambers HF, Maselli JH, Gonzales R. National trends in ambulatory visits and antibiotic prescribing for skin and soft-tissue infections. Arch Intern Med. 2008; 168:1585–1591. [PubMed: 18663172]
- Orscheln RC, Hunstad DA, Fritz SA, et al. Contribution of genetically restricted, methicillinsusceptible strains to the ongoing epidemic of community-acquired *Staphylococcus aureus* infections. Clin Infect Dis. 2009; 49:536–542. [PubMed: 19589082]

- Toshkova K, Annemuller C, Akineden O, Lammler C. The significance of nasal carriage of *Staphylococcus aureus* as risk factor for human skin infections. FEMS Microbiol Lett. 2001; 202:17–24. [PubMed: 11506902]
- Ellis MW, Hospenthal DR, Dooley DP, Gray PJ, Murray CK. Natural history of communityacquired methicillin-resistant *Staphylococcus aureus* colonization and infection in soldiers. Clin Infect Dis. 2004; 39:971–979. [PubMed: 15472848]
- Fritz SA, Epplin EK, Garbutt J, Storch GA. Skin infection in children colonized with communityassociated methicillin-resistant *Staphylococcus aureus*. J Infect. 2009; 59:394–401. [PubMed: 19747505]
- Laupland KB, Conly JM. Treatment of *Staphylococcus aureus* colonization and prophylaxis for infection with topical intranasal mupirocin: an evidence-based review. Clin Infect Dis. 2003; 37:933–938. [PubMed: 13130405]
- Perl TM, Cullen JJ, Wenzel RP, et al. Intranasal mupirocin to prevent postoperative *Staphylococcus aureus* infections. N Engl J Med. 2002; 346:1871–1877. [PubMed: 12063371]
- 9. Bode LG, Kluytmans JA, Wertheim HF, et al. Preventing surgical-site infections in nasal carriers of *Staphylococcus aureus*. N Engl J Med. 2010; 362:9–17. [PubMed: 20054045]
- Wendt C, Schinke S, Wurttemberger M, Oberdorfer K, Bock-Hensley O, von Baum H. Value of whole-body washing with chlorhexidine for the eradication of methicillin-resistant *Staphylococcus aureus*: a randomized, placebo-controlled, double-blind clinical trial. Infect Control Hosp Epidemiol. 2007; 28:1036–1043. [PubMed: 17932823]
- Simor AE, Phillips E, McGeer A, et al. Randomized controlled trial of chlorhexidine gluconate for washing, intranasal mupirocin, and rifampin and doxycycline versus no treatment for the eradication of methicillin-resistant *Staphylococcus aureus* colonization. Clin Infect Dis. 2007; 44:178–185. [PubMed: 17173213]
- Kaplan SL, Hulten KG, Gonzalez BE, et al. Three-year surveillance of community-acquired *Staphylococcus aureus* infections in children. Clin Infect Dis. 2005; 40:1785–1791. [PubMed: 15909267]
- McCaskill ML, Mason EO Jr, Kaplan SL, Hammerman W, Lamberth LB, Hulten KG. Increase of the USA300 clone among community-acquired methicillin-susceptible *Staphylococcus aureus* causing invasive infections. Pediatr Infect Dis J. 2007; 26:1122–1127. [PubMed: 18043449]
- Diep BA, Gill SR, Chang RF, et al. Complete genome sequence of USA300, an epidemic clone of community-acquired meticillin-resistant *Staphylococcus aureus*. Lancet. 2006; 367:731–739. [PubMed: 16517273]
- Goering RV, McDougal LK, Fosheim GE, Bonnstetter KK, Wolter DJ, Tenover FC. Epidemiologic distribution of the arginine catabolic mobile element among selected methicillinresistant and methicillin-susceptible *Staphylococcus aureus* isolates. J Clin Microbiol. 2007; 45:1981–1984. [PubMed: 17409207]
- DeLeo FR, Diep BA, Otto M. Host defense and pathogenesis in *Staphylococcus aureus* infections. Infect Dis Clin North Am. 2009; 23:17–34. [PubMed: 19135914]
- Creech CB, Beekmann SE, Chen Y, Polgreen PM. Variability among pediatric infectious diseases specialists in the treatment and prevention of methicillin-resistant *Staphylococcus aureus* skin and soft tissue infections. Pediatr Infect Dis J. 2008; 27:270–272. [PubMed: 18277924]
- Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children: executive summary. Clin Infect Dis. 2011; 52:285–292. [PubMed: 21217178]
- 19. Gorwitz, RJ.; Jernigan, DB.; Powers, JH.; Jernigan, JA. [Accessed January 2, 2011] Participants in the CDC-Convened Experts' Meeting on Management of MRSA in the Community. Strategies for clinical management of MRSA in the community: Summary of an experts' meeting convened by the Centers for Disease Control and Prevention. http://www.cdc.gov/ncidod/dhqp/pdf/ar/ CAMRSA_ExpMtgStrategies.pdf. Published 2006

- Fritz SA, Krauss MJ, Epplin EK, et al. The natural history of contemporary *Staphylococcus aureus* nasal colonization in community children. Pediatr Infect Dis J. 2011; 30:349–351. [PubMed: 21412205]
- Lautenbach E, Nachamkin I, Hu B, et al. Surveillance cultures for detection of methicillin-resistant *Staphylococcus aureus*: diagnostic yield of anatomic sites and comparison of provider- and patient-collected samples. Infect Control Hosp Epidemiol. 2009; 30:380–382. [PubMed: 19239378]
- 22. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing; Sixteenth Informational Supplement. Wayne, PA: Clinical and Laboratory Standards Institute; 2006.
- Fritz SA, Garbutt J, Elward A, Shannon W, Storch GA. Prevalence of and risk factors for community-acquired methicillin-resistant and methicillin-sensitive *Staphylococcus aureus* colonization in children seen in a practice-based research network. Pediatrics. 2008; 121:1090– 1098. [PubMed: 18519477]
- Hogue JS, Buttke P, Braun LE, Fairchok MP. Mupirocin resistance related to increasing mupirocin use in clinical isolates of methicillin-resistant *Staphylococcus aureus* in a pediatric population. J Clin Microbiol. 2010; 48:2599–2600. [PubMed: 20421433]
- Huang JT, Abrams M, Tlougan B, Rademaker A, Paller AS. Treatment of *Staphylococcus aureus* colonization in atopic dermatitis decreases disease severity. Pediatrics. 2009; 123:e808–e814. [PubMed: 19403473]
- Heggers JP, Sazy JA, Stenberg BD, et al. Bactericidal and wound-healing properties of sodium hypochlorite solutions: the 1991 Lindberg Award. J Burn Care Rehabil. 1991; 12:420–424. [PubMed: 1752875]
- Fisher RG, Chain RL, Hair PS, Cunnion KM. Hypochlorite killing of community-associated methicillin-resistant *Staphylococcus aureus*. Pediatr Infect Dis J. 2008; 27:934–935. [PubMed: 18756186]
- 28. Paller, AS.; Mancini, AJ. Eczematous Eruptions in Childhood. In: Paller, AS.; Mancini, AJ., editors. Hurwitz Clinical Pediatric Dermatology. 3rd ed. Philadelphia, PA: Elsevier; 2006.
- Fritz, SA.; Hayek, G.; Mitchell, K.; Garbutt, J.; Fraser, VJ. Community-associated *Staphylococcus aureus* colonization in children with *S. aureus* skin infections and their household members. Final Program of the Infectious Diseases Society of America 47th Annual Meeting; October 29-November 1, 2009; Philadelphia, PA. Abstract 802
- Bleasdale SC, Trick WE, Gonzalez IM, Lyles RD, Hayden MK, Weinstein RA. Effectiveness of chlorhexidine bathing to reduce catheter-associated bloodstream infections in medical intensive care unit patients. Arch Intern Med. 2007; 167:2073–2079. [PubMed: 17954801]
- Popovich KJ, Hota B, Hayes R, Weinstein RA, Hayden MK. Effectiveness of routine patient cleansing with chlorhexidine gluconate for infection prevention in the medical intensive care unit. Infect Control Hosp Epidemiol. 2009; 30:959–963. [PubMed: 19712033]
- Ammerlaan HS, Kluytmans JA, Wertheim HF, Nouwen JL, Bonten MJ. Eradication of methicillinresistant *Staphylococcus aureus* carriage: a systematic review. Clin Infect Dis. 2009; 48:922–930. [PubMed: 19231978]
- Loeb M, Main C, Walker-Dilks C, Eady A. Antimicrobial drugs for treating methicillin-resistant *Staphylococcus aureus* colonization. Cochrane Database Syst Rev. 2003:CD003340. [PubMed: 14583969]
- 34. Yang ES, Tan J, Eells S, Rieg G, Tagudar G, Miller LG. Body site colonization in patients with community-associated methicillin-resistant *Staphylococcus aureus* and other types of *S. aureus* skin infections. Clin Microbiol Infect. 2010; 16:425–431. [PubMed: 19689469]
- Buehlmann M, Frei R, Fenner L, Dangel M, Fluckiger U, Widmer AF. Highly effective regimen for decolonization of methicillin-resistant *Staphylococcus aureus* carriers. Infect Control Hosp Epidemiol. 2008 Jun; 29(6):510–516. [PubMed: 18510460]
- Miller MA, Dascal A, Portnoy J, Mendelson J. Development of mupirocin resistance among methicillin-resistant *Staphylococcus aureus* after widespread use of nasal mupirocin ointment. Infect Control Hosp Epidemiol. 1996; 17:811–813. [PubMed: 8985769]

- Upton A, Lang S, Heffernan H. Mupirocin and *Staphylococcus aureus*: a recent paradigm of emerging antibiotic resistance. J Antimicrob Chemother. 2003; 51:613–617. [PubMed: 12615862]
- Miller LG, Quan C, Shay A, et al. A prospective investigation of outcomes after hospital discharge for endemic, community-acquired methicillin-resistant and -susceptible *Staphylococcus aureus* skin infection. Clin Infect Dis. 2007; 44:483–492. [PubMed: 17243049]
- Duong M, Markwell S, Peter J, Barenkamp S. Randomized, controlled trial of antibiotics in the management of community-acquired skin abscesses in the pediatric patient. Ann Emerg Med. 2010; 55:401–407. [PubMed: 19409657]
- Ellis MW, Griffith ME, Dooley DP, et al. Targeted intranasal mupirocin to prevent colonization and infection by community-associated methicillin-resistant *Staphylococcus aureus* strains in soldiers: a cluster randomized controlled trial. Antimicrob Agents Chemother. 2007; 51:3591– 3598. [PubMed: 17682105]
- Jones TF, Creech CB, Erwin P, Baird SG, Woron AM, Schaffner W. Family outbreaks of invasive community-associated methicillin-resistant *Staphylococcus aureus* infection. Clin Infect Dis. 2006; 42:e76–e78. [PubMed: 16586378]

Fritz et al.



Figure 1.

Flow of Participants through the StL Stars Trial.

\$watermark-text

Fritz et al.

Baseline Characteristics of Study Participants by Protocol Assignment

		Interve	ntion Group		
Characteristics	Hygiene Education Only N =75	Education + Mupirocin N =75	Education + Mupirocin + Chlorhexidine N =75	Education + Mupirocin + Bleach Baths N=75	Α
Age, mean (±SD), years	17.37	16.52	18.19	18.67	0.92
	(16.57)	(16.12)	(17.37)	(15.29)	
Male sex	41 (55)	38 (51)	23 (31)	37 (49)	0.02
Non-white race	56 (75)	48 (64)	57 (76)	52 (69)	0.35
Health insurance status:					0.72
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)	0.31
MSSA only	25 (33)	28 (37)	23 (31)	20 (27)	0.56
Both MRSA & MSSA	8 (11)	8 (11)	8 (11)	5 (7)	0.79
Baseline sites of colonization: ^a					
Anteriornares	52 (69)	51 (68)	49 (65)	54 (72)	0.85
Axilla	19 (25)	27 (36)	22 (29)	23 (31)	0.56
Inguinal folds	58 (77)	50 (67)	59 (79)	56 (75)	0.33
Baseline # of sites colonized:					
1 site	35 (47)	33 (44)	34 (45)	33 (44)	0.98
2 sites	26 (35)	31 (41)	27 (36)	26 (35)	0.81
3 sites	14 (19)	11 (15)	14 (19)	16 (21)	0.77
Prescribed systemic	64 (85)	68 (91)	69 (92)	68 (91)	0.55
antibiotic(s) at time of					
acute SSTI					
Colonized and/or infected with	3 (4)	1 (1)	1 (1)	1 (1)	0.56
a mupirocin-resistant					
S aureus strain					

		Interve	ation Group		
Characteristics	Hygiene Education Only N =75	Education + Mupirocin N =75	Education + Mupirocin + Chlorhexidine N =75	Education + Mupirocin + Bleach Baths N =75	ď
Time from screening to	17 (15)	17 (15)	16 (13)	16 (15)	0.93
enrollment, median days (IQR)					
Comorbidity:	49 (65)	46 (61)	50 (67)	48 (64)	0.92
Asthma	26 (35)	14 (19)	13 (17)	16 (21)	0.04
Eczema	28 (37)	15 (20)	32 (43)	19 (25)	0.01
Allergies	10 (13)	13 (17)	17 (23)	24 (32)	0.03
Hypertension	5 (7)	4 (5)	9 (12)	7 (9)	0.46
HIV	0 (0)	0 (0)	4 (5)	0 (0)	0.01
Takes a prescription	30 (40)	24 (32)	23 (32)	31 (41)	0.43
medication daily					
Has taken antibiotics in past	40 (54)	42 (58)	45 (65)	41 (56)	0.59
year					
Surgery in past year	5 (7)	6 (8)	14 (19)	6 (8)	0.05
Emergency department or					
urgent care visit in past year	30 (40)	27 (36)	27 (36)	36 (48)	0.39
Contact with healthcare b	20 (27)	21 (28)	18 (24)	20 (27)	0.95
Prior SSTI in past year: index	31 (42)	36 (48)	36 (49)	40 (53)	0.58
case					
Prior SSTI in past year:	33 (45)	27 (36)	35 (47)	24 (32)	0.24
household member					
Permanent home	65 (87)	69 (92)	68 (91)	67 (89)	0.74
Crowded home (>2 people per bedroom)	(6) L	8 (11)	7 (9)	13 (17)	0.36
Sports participation	19 (25)	18 (24)	11 (15)	18 (24)	0.36
Pet in household	28 (37)	29 (39)	26 (35)	26 (35)	0.94
NOTE. Data are no. (%) of participants, unle	ess otherwise i	ndicated. <i>P</i> value	s are for comparis	ons across all fou	r randomization groups. Abbreviat

Infect Control Hosp Epidemiol. Author manuscript; available in PMC 2012 December 21.

tion; MRSA, methicillin-resistant S. aureus; MSSA, methicillin-sensitive S. aureus; IQR, inter-quartile range; HIV, human immunodeficiency virus; SSTI, skin or soft tissue infection.

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

 $b_{\rm Participant}$ works in a healthcare facility or lives with someone working in a healthcare facility.

Eradication of Staphylococcus aureus Carriage at Longitudinal Intervals by Intervention

		Interventi	on Group	
	Hygiene Education Only	Education + Mupirocin	Education + Mupirocin + Chlorhexidine	Education + Mupirocin + Bleach Baths
		One Month Follov	ving Intervention	
Eradication N (%)	24/64 (38)	35/62 (56)	35/64 (55)	34/54 (63)
RR (95% CI)	a	1.51 (1.02–2.21)	1.46 (0.99–2.15)	1.68 (1.15–2.44)
% ARR (95% CI)	<i>a</i>	19 (2–35)	18 (1-34)	24 (6-40)
Ρ	<i>b</i>	0.03	0.05	0.006
		Four Months Follo	wing Intervention	
Eradication N (%)	31/64 (48)	32/57 (56)	31/57 (54)	36/51 (71)
RR (95% CI)	<i>a</i>	1.16 (0.82–1.63)	1.12 (0.79–1.58)	1.46 (1.07–1.98)
% ARR (95% CI)	<i>a</i>	8 (-10-25)	7 (-11-24)	21 (3–37)
Ρ	a	0.40	0.51	0.02

veen intervention group and control. Participants were analyzed by the arm to which they were assigned. Abbreviations: RR, relative risk; ARR, absolute risk reduction; CI, confidence interval.

 a . Personal and Household Hygiene Education Only" was used as the comparator group to determine RR, ARR, and *P* values.

Page 15

Table 3

Body Site-Specific Colonization at Longitudinal Intervals by Intervention

		Interventi	on Group			
	Hygiene Education Only (%)	Education + Mupirocin (%)	Education + Mupirocin + Chlorhexidine (%)	Education + Mupirocin + Bleach Baths (%)		
		Baseline Nasa	l Colonization			
Nasal Colonization at 1	24/52 (46)	14/51 (27)	13/49 (26)	9/54		
Month		p=0.049 ^a	p=0.041	p=0.001		
Nasal Colonization at 4	26/52 (50)	12/51 (23)	12/49 (24)	8/54 (15)		
Months		p=0.005	p=0.008	p<0.001		
	All participants ran p=0.002, at 4 montl	domized to receiv hs p<0.001	e mupirocin vs. cor	ntrols: at 1 month		
		Baseline Axilla	a Colonization			
Axilla Colonization at 1	5/19 (26)	6/27 (22)	4/22 (18)	2/23 (9)		
Month		NS	NS	NS		
Axilla Colonization at 4	4/19 (21)	4/27 (15)	3/22 (14)	2/23 (9)		
Months		NS	NS	NS		
	Baseline Inguinal Colonization					
Inguinal Colonization at	23/58 (40)	16/50 (32)	19/59 (32)	8/56 (14)		
1 Month		NS	NS	p=0.002		
Inguinal Colonization at	15/58 (26)	12/50 (24)	18/59 (30)	9/56 (16)		
4 Months		NS	NS	NS		

NOTE. Data are no. (%) of participants unless otherwise noted. Abbreviations: NS, not significant.

 ${}^{a}P$ values shown are vs. education-only control unless otherwise noted.

\$watermark-text

Table 4

Cumulative Recurrent Skin and Soft Tissue Infection by Intervention

		Intervent	ion Group			
	Hygiene Education Only	Education + Mupirocin	Education + Mupirocin + Chlorhexidine	Education + Mupirocin + Bleach Baths		
		One Month Follo	wing Intervention			
SSTI Reported N (%)	17/65 (26)	14/62 (23)	7/63 (11)	12/55 (22)		
RR (95% CI)	a	0.86 (0.47-1.60)	0.42 (0.19-0.95)	0.83 (0.44–1.59)		
% ARR (95% CI)	a	4 (-10-2)	15 (3–28)	4 (-10-19)		
Р	a	0.64	0.03	0.58		
		Four Months Follo	owing Intervention			
SSTI Reported N (%)	26/64 (41)	20/59 (34)	19/57 (33)	18/52 (35)		
RR (95% CI)	a	0.83 (0.52–1.33)	0.82 (0.51–1.32)	0.85 (0.53–1.37)		
% ARR (95% CI)	a	7 (-10-23)	7 (-10-24)	6 (-11-23)		
Р	a	0.44	0.41	0.51		
		Six Months Following Intervention				
SSTI Reported N (%)	28/52 (54)	27/52 (52)	23/54 (43)	21/43 (50)		
RR (95% CI)	a	0.96 (0.67–1.39)	0.79 (0.53–1.17)	0.91 (0.61–1.35)		
% ARR (95% CI)	a	2 (-17-20)	11 (-8-29)	5 (-15-24)		
Р	a	0.84	0.25	0.63		

NOTE. Data are expressed as N (%) or proportion unless otherwise noted. *P* value represents comparison between intervention group and control. Participants were analyzed by the arm to which they were assigned. Abbreviations: SSTI, skin or soft tissue infection; RR, relative risk; ARR, absolute risk reduction; CI, confidence interval.

^a"Personal and Household Hygiene Education Only" was used as the comparator group to determine RR, ARR, and Pvalues.

Table 5

Adherence to Decolonization Measures

Adherence ^{<i>a</i>} to Measures	Hygiene Education Only	Education + Mupirocin	Education + Mupirocin + Chlorhexidine	Education + Mupirocin + 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 expressed as no. (%) of participants unless otherwise noted. There was not a statistically significant difference in compliance with the assigned regimens between participants in the four randomization arms.

^{*a*}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.