Randomized Controlled Trial of Chlorhexidine Gluconate for Washing, Intranasal Mupirocin, plus Rifampin and Doxycycline versus No Treatment for the Eradication of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Colonization

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Running head: Mupirocin and oral antibiotics for MRSA decolonization

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Abstract

Background. Eradication of methicillin-resistant *Staphylococcus aureus* (MRSA) carriage may reduce the risk of MRSA infection, and prevent transmission of the organism to other patients.

Methods. To determine the efficacy of decolonization therapy, patients colonized with MRSA were randomized to receive treatment (2% chlorhexidine gluconate washes, 2% mupirocin ointment intra-nasally, oral rifampin, and doxycycline for 7 days) or no treatment. Follow-up cultures for MRSA were obtained from the nares, perineum, skin lesions, and catheter exit sites monthly for up to 8 months. The primary outcome measure was recurrence or persistence of MRSA at 3 months of follow-up. Univariate and multivariable analyses were done to identify variables associated with treatment failure.

Results. Of 146 patients enrolled in the study, 112 patients (87 treated; 25 not treated) were followed for at least 3 months. At 3 months of follow-up, 64 (74%) of those treated had negative cultures for MRSA as compared to 8 (32%) of those not treated ($P = 0.0001$). This difference remained significant at 8 months of follow-up, at which time 54% of those treated were still culture-negative for MRSA (log-rank test: $\chi^2 = 64.4$; $P < 0.0001$). The results of the multivariable analysis indicated that having a mupirocin-resistant isolate at baseline was associated with treatment failure (RR 9.4, 95% CI 2.8-31.9; $P = 0.0003$), whereas decolonization therapy was protective (RR 0.1, 95% CI 0.04-0.4; $P = 0.0002$). Mupirocin resistance emerged in only 5% of follow-up isolates.

Conclusions. Treatment with topical mupirocin, chlorhexidine gluconate washes, oral rifampin, and doxycycline for 7 days was safe and effective in eradicating MRSA colonization in hospitalized patients for at least 3 months.

Staphylococcus aureus remains one of the most important human bacterial pathogens. Infections due to methicillin-resistant strains (MRSA) have been associated with excess morbidity and mortality, and with increased costs [Cosgrove 2003; Engemann 2003; Kim 2001]. Both community and hospital associated MRSA are clonal in origin, and transmission of a limited number of clones is associated with the majority of disease [Naimi 2003].

Colonization with MRSA generally precedes the development of MRSA infections, and plays a major role in the dissemination of MRSA in healthcare settings [Davis 2004]. Decolonization, primarily with topical mupirocin, has been used with some success in reducing the risk of *S. aureus* infections in select patient populations [Kallen 2005; Tacconelli 2003], but in several studies this approach has not been effective [Kallen 2005; Kalmeijer 2002; Wertheim 2004].

In healthcare facilities, decolonization has also been used, along with other interventions, as an outbreak management strategy While some investigators have suggested that it is a useful strategy [Hill 1988; Tomic 2004], no decolonization regimens have been found to be effective in long-term in hospitalized patients [Roccaforte 1988; Walsh 1993; Muder 1994; Parras 1995; Harbarth 1999], and a recent Cochrane Collaboration review concluded that "there is insufficient evidence to support use of topical or systemic antimicrobial therapy for eradicating MRSA" [Loeb 2003].

This study was designed to determine the efficacy of therapy using a combination of topical and systemic antimicrobial agents (chlorhexidine gluconate washes, intra-nasal mupirocin, plus oral rifampin and doxycycline) for

eradication of MRSA colonization. We were also interested in identifying variables that would predict success or failure of decolonization therapy.

METHODS

Study population and setting. Patients hospitalized in one of eight hospitals (six acute care, one rehabilitation, and one chronic care) in Toronto or Hamilton, Ontario between July 1 2000 and June 30 2003, who were colonized with MRSA were eligible for inclusion in this study provided they were greater than 18 years of age, and were expected to survive for at least three months. Patients were considered to be colonized with MRSA if the organism was recovered in culture from one or more body sites sampled at two separate times, and there was no evidence of infection based on standard criteria [Garner 1988]. Potentially eligible patients were identified by MRSA screening done at each hospital on admission, or as part of outbreak investigation (?REF QMPLS?). Eligible patients who consented to participate in the study had additional baseline (pre-treatment) cultures obtained from the anterior nares, perianal area, any skin lesions, and catheter or medical device exit site(s).

Exclusion criteria were concurrent treatment with antimicrobials for any infection; attempted MRSA decolonization in the previous six months (prior treatment for an MRSA infection was not an exclusion criterion); allergy to one of the study medications; known antimicrobial resistance to one of the study medications (if the isolate was identified as resistant in testing done for the study after treatment was started, the patient was not excluded); inability to take

medications by mouth or feeding tube; pregnancy or breast-feeding; known hepatic cirrhosis, abnormal International Normalized Ratio [INR] due to liver disease, serum aspartate aminotransferase [AST] or alanine aminotransferase [ALT] levels more than five times the upper limit of normal; or planned surgery in the following three months.

The study was approved by the Institutional Review Board at each participating hospital and the University of Toronto.

***Study design*.** This was an open-label, randomized study comparing decolonization treatment with no treatment. Patients were randomized to treatment or no treatment in blocks of eight stratified by hospital in a 3:1 ratio.. Patients randomly assigned to treatment received a seven day regimen including: daily washes with 2% chlorhexidine gluconate, 2% mupirocin ointment (approximately 1 cm) applied to the anterior nares with a cotton-tipped applicator three times daily, rifampin (300 mg) twice daily, and doxycycline (100 mg) twice daily. Compliance with study medications and adverse reactions were monitored.

Baseline demographic and clinical information was obtained by patient interview and review of the medical records. Baseline functional status was assessed using the Katz Index [Katz 1970].

Follow-up cultures for MRSA were obtained from the anterior nares, perianal area, skin lesions, catheter or other medical device exit site(s), and from any other site that had previously yielded MRSA. They were obtained weekly for

four weeks after randomization, and then monthly for an additional seven months. Cllinical data were also obtained to identify any MRSA infections.

***Laboratory methods*.** Specimens for MRSA culture were processed within eight hours of procurement. To optimize the recovery of MRSA, the swabs were incubated overnight in a tryptone-based broth containing 7.5% sodium chloride and 1% mannitol (Difco m Staphylococcus Broth, Becton Dickinson Co., Sparks, Md.), then subcultured onto mannitol-salt agar supplemented with oxacillin (2 µg/ml) (Quelab, Montreal, Que.) incubated at 37°C for up to 48 hours [Gardam 2001]. MRSA was identified using standard methods including a latex agglutination test for detection of PBP 2a (MRSA-Screen, Denka Seiken Co., Tokyo, Japan). Specimens were processed by laboratory staff blinded to the study purpose and treatment allocation.

Susceptibilities to mupirocin, rifampin, and tetracycline were performed by broth microdilution, in accordance with Clinical and Laboratory Standards Institute guidelines [CLSI]. High-level resistance to mupirocin was defined as an MIC ∃ 512 µg/ml; low-level mupirocin resistance as an MIC 8-256 µg/ml [Janssen 1993]. In order to determine whether a repeat isolate from a patient represented relapse with the same strain or acquisition of a new strain, isolates were typed by pulsed-field gel electrophoresis (PFGE) using *Sma*I digests of genomic DNA [Simor JID 2002; McDougal JCM 2003].

***Statistical analysis*.** Descriptive statistics were calculated for baseline demographic and clinical variables. Univariate analysis used Student's t-tests, chi-square and Fisher's exact tests as appropriate.

The primary outcome was eradication of MRSA from all sites three months after completion of therapy in the treatment group and three months following randomization in those not treated. Secondary outcomes included survival analysis to compare the probabilities of remaining free of MRSA colonization over time.in all study patients, and excluding those subjects who acquired a new strain of MRSA during their follow-up period. Log rank tests were used to assess the significance of treatment allocation.

Multivariable logistic regression analysis was performed to assess the relationship of predictor variables of interest to treatment failure at the primary endpoint of three months. Variables included consisted of those identified in the univariate analysis as possibly being associated with treatment failure ($P \# 0.10$), and other variables that had been implicated in previous studies or were biologically plausible. Prior to analysis, predictor variables were assessed for the presence of collinearity; .

All analyses were carried out using SAS Version 9.1 (SAS Institute, Cary, NC). All statistical tests were 2-tailed with a $P \# 0.05$ considered to be statistically significant.

Sample size calculation. We assumed *a priori* that 20% of untreated subjects would have negative cultures for MRSA after three months of follow-up (Harbarth 1999), and that 20% of patients would be lost to follow-up in three months. In order to detect a 30% difference in MRSA decolonzation rates, a sample size of 78 evaluable patients (and 100 enrolled) in the treatment group and 26 evaluable (33 enrollled) in the untreated group were required,

RESULTS

A total of 146 eligible consenting patients were enrolled: 111 randomized to decolonization therapy, and 35 randomized to no treatment (Figure 1). Thirty-four (23%) patients were not evaluable at three months (24 deaths, 4 withdrew consent, 9 lost to follow-up), leaving 112 patients for the analysis of primary outcome (87 in the treatment group, and 25 in the no treatment group). The baseline demographic and clinical characteristics of the two groups were similar (Table 1). There were no significant differences in these characteristics for those not completing three months of follow-up as compared to those who did (data not shown).

At three months following treatment (or randomization for those not treated), 64 of 87 (74%) patients in the treatment group had all follow-up cultures negative for MRSA, as compared to only 8 of 25 (32%) patients in the no treatment group (P=0.0001). Survival analysis (Figure 2A) demonstrated a significant difference in the recovery of MRSA from those treated and not treated over time (P<0.0001). At eight months post-treatment, 54% of those who received decolonization treatment remained culture-negative for MRSA (needs numbers, and comparison to no treatment).

A total of 110 (98%) initial MRSA isolates obtained at baseline (86 from treated patients; 24 from those not treated) were available for antimicrobial susceptibility testing and genotyping by PFGE. Twenty-one (19%) of these

MRSA had high-level resistance to mupirocin, and five (5%) low-level mupirocin resistance.

The most commonly identified strains were CMRSA-2 (46%; identical to or closely resembling USA100 ST5), and CMRSA-1 (24%; USA600 ST45). Only one isolate was identified as CMRSA-7 (USA400 ST1) ?add an no USA300?. This genotype distribution was representative of that seen in hospitalized patients in southern Ontario [Simor JID]. There was no difference in the genotype distribution of the isolates obtained at baseline in those randomized to treatment as compared to those randomized to no treatment. Most (82%) of the 72 patients with MRSA recovered in follow-up cultures, had follow-up strains that were identical to their baseline isolates as determined by PFGE typing. Thirteen (18%) patients had initial and follow-up isolates that represented different strains by PFGE typing (nine in the treatment group and four in those not receiving decolonization therapy). As these cases represented acquisition of a new strain of MRSA rather than failure to eradicate the initial colonizing strain, Kaplan-Meier curves were created excluding these 13 patients (Figure 2B). These also demonstrated a significant difference in the MRSA recovery rates over time in treated vs. untreated patients (log-rank test: χ^2=50.1; P<0.0001).

One (2%) of 61 treated study participants with baseline MRSA isolates that were susceptible to mupirocin had follow-up cultures that yielded MRSA with with an indistinguishable PFGE profile and high-level resistance to mupirocin. In two of these patients, the genotypes as determined by PFGE of the initial and follow-up isolates were distinct, suggesting acquisition of a new strain of MRSA.

In the third patient, the initial and follow-up isolates had indistinguishable PFGE profiles. One of the follow-up mupirocin-resistant isolates in a treated patient also became resistant to tetracycline (was this in a patient with baseline mup resistance?, or new acquisition?? – this kind of implies that treatment may have selected for acquisition of resistant strains – is the rate of mup resistance higher if follow-up strains – if not, I think we should not discuss people who had different resistant strains post; I don't know if it means anything. No patient with a baseline isolate susceptible to rifampin had a subsequent isolate that was resistant. Do we need to point out that no resistance developed in untreated patients? Or whether or not this difference is stat sig?

In univariate analysis, patients who remained colonized with MRSA at three months post-treatment/randomization were more likely to have had a mupirocin-resistant isolate at baseline (40% vs 7%; Relative Risk [RR]=2.89; 95% CI, 1.90-4.39; *P*=0.0002), and were less likely to have been randomized to decolonization therapy (56% vs 89%; RR=0.26; 95% CI, 0.12-0.55; *P*=0.0001) (Table 2). In multivariable analysis, having a mupirocin-resistant isolate at baseline (RR=9.37; 95% CI, 2.76-31.9; *P*=0.0003) remained independently associated with recovery of MRSA in culture by three months of follow-up. Receipt of decolonization therapy was protective, associated with negative cultures for MRSA at three months of follow-up (RR=0.12; 95% CI, 0.04-0.36; *P*=0.0002) (Table 3).

Compliance with decolonization therapy was good, with 102 (92%) completing at least six days of treatment, and the remaining nine subjects

completing two to five days of treatment. Adverse reactions possibly related to medications were reported in 22 (25%) of treated patients. All of these reactions were considered to be mild and included: nausea or vomiting (in 15 patients), diarrhea (9), dyspepsia (5). Antimicrobial therapy was discontinued in four (5%) patients because of adverse effects. Thirty-one study participants died during the study, 25 (23%) of those randomized to receive decolonization therapy, and 6 (17%) randomized to no treatment (P=0.64). No patient developed an MRSA infection during the study.

DISCUSSION

Eradication of MRSA carriage may reduce the risk of subsequent MRSA infection in individual patients, and could decrease MRSA transmission by eliminating a reservoir for the organism [Arnold 2002]. Healthcare workers, generally healthy young adults, who are colonized with *S. aureus* or MRSA may be successfully decolonized with a short course of intra-nasal mupirocin ointment [Doebbeling 1993]. Up to now, however, attempts to eradicate MRSA colonization in hospitalized patients have had very limited success [Boyce 2001]. Although short-term MRSA decolonization has been accomplished in several observational and uncontrolled studies [Hill 1998; Roccaforte 1988; Darouiche 1991; Asensio 1996], randomized controlled trials demonstrating efficacy for long-term eradication of MRSA are lacking. While some negative studies have been under-powered, and others have reported some short-term success, larger trials with longer followup have consistently failed to show efficacy [Walsh 1993;

Muder 1994; Parras 1995; Harbarth 2000; Peterson 1990; Chang 2000; Strausbaugh 1992; Mody 2003 ?add Loeb meta-analysis]. The results of this study, using a combination of topical and oral systemic antimicrobial agents, indicate that a well-tolerated regimen can achieve MRSA decolonization for prolonged periods of time, with infrequent selection for resistance.. At the end of seven days of decolonization treatment, 92% of patients cleared MRSA from all sites, and 74% remained free of MRSA at three months of follow-up. Eight months after treatment, more than half (54%) of those available for follow-up were still MRSA culture-negative.

Although none of the untreated, colonized patients in this study developed MRSA infections, colonization with MRSA in hospitalized patients is not necessarily benign. In a study of intensive care unit patients, the risk of developing MRSA bacteremia was higher in those colonized with MRSA, than was the risk of developing staphylococcal bacteremia in patients colonized with susceptible strains of *S. aureus* [Pujol 1996]. Huang and colleagues found that 29% of 209 hospitalized patients newly identified with MRSA developed a subsequent MRSA infection; these infections occurred a mean of 102 days after the initial MRSA culture [Huang 2003]. Even without infection, implementation of isolation precautions to limit transmission of MRSA may be associated with diminished quality of care and decreased patient safety [Stelfox]. These adverse consequences associated with MRSA colonization would suggest that even partially effective decolonization, such as that achieved in this study, could be useful in reducing the burden of disease caused by MRSA.

Possible explanations for failure to eradicate MRSA colonization in previous studies may include the use of agents with only marginal in vitro activity against the organism, or agents (such as ciprofloxacin and fusidic acid) that induce the development of resistance during therapy [Peterson 1990; Chang 2000]. Alternatively, decolonization may, in fact, succeed but the patient is re-exposed to the organism and becomes colonized with a new strain of MRSA. This occurred in 13 (18%) of the patients in the current study.

In several previous studies, failure to eradicate MRSA carriage has been associated with multiple extra-nasal sites of colonization [Parras 1995; Harbarth 2000]. The gastrointestinal tract is recognized as a potentially important reservoir for the organism [Boyce 2005], and intra-nasal treatment alone is unlikely to eradicate intestinal carriage. In the current study, the presence of MRSA at multiple body sites was not associated with recovery of MRSA in follow-up cultures, possibly because topical treatment was combined with effective oral systemic drugs. Similarly, impaired functional status (as measured by the Katz index), and the presence of medical devices or skin lesions (such as decubitus ulcers) were not associated with re-colonization or persistence of MRSA, despite the association of these variables with MRSA colonization in healthcare facilities [Asensio 1996; Terpenning 1994]. However, it is important to note that the power of this study to identify risk factors was limited.

Because failure of eradication has been reported with mupirocin resistance in prior studies. [Harbarth AAC 1999; Walker 2003], patients known to have a mupirocin resistant isolate at baseline were excluded from our study.

However, the results of mupirocin susceptibility testing were not always available prior to randomization, so that 21 patients colonized with MRSA with high-level mupirocin resistance Were enrolled in the study. As in previous studies, colonization with MRSA with high-level mupirocin resistance was associated with failure of decolonization therapy. The significance of low-level resistance could not be assessed in this study, as only five enrolled subjects had isolates with low-level resistance. Although only one MRSA isolate apparently acquired mupirocin resistance after therapy, the potential for the emergence of such resistance occurring with widespread use of mupirocin is of concern, and emphasizes the importance of using this agent judiciously [Miller 1996].

Fortunately, several novel compounds and investigational agents are now also being studied for MRSA decolonization. Tea tree (*melaleuca alternifolia*) oil applied as a cream and body wash was found to be as safe and effective as the intra-nasal application of mupirocin ointment for clearing MRSA carriage at various body sites in two clinical trials [Dryden 2004]. Mersacidin is a lantibiotic, an antimicrobial peptide, that was able to eradicate MRSA colonization in a murine model [Kruszewska 2004]. Petrolatum-based cream formulations of lysostaphin have been found to be rapidly bactericidal and effective in eradicating staphylococcal nasal colonization in a cotton rat model [Kokai-Kun ?2003]. Further clinical trials are required in order to assess the long-term safety and efficacy of these compounds; in hospitalized patients, combination therapy may need to be studied.

Strengths of the current study include its study design, relatively long follow-up, and inclusion of a sample size adequate for determination of treatment efficacy and to assess variables associated with treatment failure. The use of a broth culture enhanced sensitivity for the detection of MRSA, and the study was also able to examine the risk of emergence of mupirocin resistance in treated study participants. Molecular typing by PFGE enabled us to distinguish relapse from the acquisition of a new strain of MRSA.

The study also has limitations. Although it was a randomized trial, it was not placebo-controlled or double-blind. However, this should not have affected the outcome measurement as MRSA persistence or re-colonization after three months of follow-up was determined by culture without knowledge of allocation to treatment or no treatment. Losses to followup were also significant; although those lost to follow-up were similar to those who were evaluable with regards to demographic and clinical characteristics, it is possible that some unmeasured differences were important. The study included only hospitalized patients with MRSA, and may not be generalizable to other populations, such as residents of nursing homes. Most strains were C-MRSA1 or C-MRSA2, and the results may not be generalizable to all strains of MRSA; in particular, they may not be generalizable to community-associated MRSA

In summary, the results of this study indicate that hospitalized patients colonized with MRSA may be successfully decolonized with a seven-day course of chlorhexidine gluconate washes, intra-nasal 2% mupirocin ointment, oral rifampin and doxycycline. With this treatment, approximately three-quarters of

patients are likely to remain decolonized for at least three months, and more than half will still be MRSA culture-negative up to eight months later. The study reaffirms the clinical significance of high-level mupirocin resistance, and suggests that susceptibility testing should be done in advance if treatment with mupirocin is being considered. The identification of a decolonization regimen that is feasible and relatively successful in the longer term suggests that the role of decolonization therapy as an infection control strategy deserves serious consideration.

How much difference is there at 3 and 8 months if the mup resistant isolates are removed? (for my own interest, not for the paper). Did we look at different strains in univariate analysis – worth commenting on (re potential comparison to CA strains?)?

I'd put chi-square and P values in figure legends, not text

Why does 2A only include those evaluable at 3 months? I would have thought we should include everyone In the survival analysis

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Table 1. Demographic and clinical characteristics at baseline of study patients who completed at least three months of follow-up.

Characteristic	No. (%)		p
	Randomized to treatment N=111	Randomized to no treatment N=??	value
No. with ≥ 3 months of follow-up	87	25	
Mean age, yrs (SD)	77.3 (11.6)	76.2 (12.2)	0.68
Female sex	32 (37)	8 (32)	0.66
Katz index score:			
A	7 (8)	3 (12)	0.29
B	16 (18)	7 (28)	
C	10 (11)	6 (24)	
D	6 (7)	2 (8)	
E	11 (13)	1 (4)	
F	11 (13)	3 (12)	
G	26 (30)	3 (12)	
Dementia	26 (30)	11 (44)	0.19
Stroke	28 (32)	5 (20)	0.23
Chronic lung disease	25 (29)	9 (36)	0.49

Table 1. cont'd.

Characteristic	No. (%)		p value
	Randomized to treatment	Randomized to no treatment	
Cardiac disease	29 (33)	12 (48)	0.19
Diabetes mellitus	23 (26)	5 (20)	0.51
Immunosuppression	7 (8)	3 (12)	0.69
Skin lesions	33 (38)	7 (28)	0.36
Hospitalized in previous 6 months	46 (53)	13 (52)	0.90
Nursing home in previous 6 months	17 (20)	6 (24)	0.65
Surgery in previous 30 days	11 (13)	3 (12)	0.99
Antibiotic treatment in previous 30 days	40 (46)	13 (52)	0.63
Previously treated for MRSA infection	1 (1)	0	1.00
Urinary catheter	19 (22)	8 (32)	0.30
Intravascular catheter	24 (28)	7 (28)	0.97

Table 1. cont'd.

Characteristic	No. (%)		p value
	Randomized to treatment	Randomized to no treatment	
Tracheostomy	5 (6)	2 (8)	0.68
Percutaneous enteral feeding tube	21 (24)	2 (8)	0.08
MRSA recovered from > 1 body site	56 (64)	18 (72)	0.48
MRSA resistant to mupirocin at baseline	16 (18)	5 (20)	0.98
MRSA resistant to rifampin at baseline	3 (3)	0	0.99
MRSA resistant to tetracycline at baseline	1 (1)	0	1.00

Table 2. Comparison of demographic and clinical characteristics of those with and without MRSA at 3 months of follow-up.

Variable	No. (%)		Relative	p
	MRSA isolated at 3 months (n = 40)	MRSA not isolated at 3 months (n = 72)	Risk (95% CI)	value
Mean age, yrs (SD)	76.9 (11.3)	77.1 (11.9)		0.93
Female sex	17 (43)	23 (32)	1.18 (0.87-1.61)	0.26
Katz index (A or B)	30 (75)	40 (56)	1.24 (0.65-2.35)	0.50
Dementia	12 (30)	25 (35)	0.93 (0.72-1.21)	0.61
Stroke	13 (33)	20 (28)	1.06 (0.81-1.39)	0.67
Chronic lung disease	14 (35)	20 (28)	1.11 (0.85-1.45)	0.43
Cardiac disease	13 (33)	28 (39)	0.92 (0.69-1.22)	0.56
Renal disease	10 (25)	16 (22)	1.04 (0.83-1.29)	0.74
Diabetes mellitus	10 (25)	18 (25)	1.00 (0.80-1.25)	1.00
Immunosuppression	2 (5)	8 (20)	0.94 (0.84-1.04)	0.49
Skin lesions	13 (33)	27 (38)	0.93 (0.70-1.22)	0.60

Table 2. cont'd.

Variable	No. (%)		Relative	p
	MRSA isolated at 3 months (n = 40)	MRSA not isolated at 3 months (n = 72)	Risk (95% CI)	value
Hospitalized in previous 6 months	24 (60)	35 (49)	1.34 (0.85-2.11)	0.19
Nursing home in previous 6 months	6 (15)	17 (24)	0.90 (0.75-1.09)	0.31
Surgery in previous 30 days	5 (13)	9 (13)	1.01 (0.87-1.61)	1.00
Antibiotic treatment in previous 30 days	20 (50)	33 (46)	1.11 (0.76-1.64)	0.58
Previously treated for MRSA infection	0	1 (1)	0.99 (0.96-1.01)	1.00
Urinary catheter	11 (28)	16 (22)	1.07 (0.85-1.35)	0.53
Intravascular catheter	9 (23)	12 (31)	1.11 (0.83-1.32)	0.36
Tracheostomy	3 (8)	4 (6)	1.02 (0.92-1.13)	0.68
Percutaneous enteral feeding tube	11 (28)	12 (17)	1.15 (0.93-1.43)	0.17
Any medical device	22 (55)	40 (56)	0.99 (0.64-1.52)	0.95
MRSA recovered from > 1 body site	29 (73)	45 (63)	1.36 (0.76-2.45)	0.28

Table 2. cont'd.

Variable	No. (%)		Relative	p
	MRSA isolated at 3 months (n = 40)	MRSA not isolated at 3 months (n = 72)	Risk (95% CI)	value
MRSA resistant to mupirocin at baseline	16 (40)	5 (7)	2.89 (1.90-4.39)	0.0002
MRSA resistant to rifampin at baseline	2 (5)	1 (1)	1.91 (0.83-4.43)	0.29
MRSA resistant to tetracycline at baseline	0	1 (1)	0.99 (0.97-1.01)	1.00
Randomized to decolonization therapy	23 (56)	64 (89)	0.26 (0.12-0.55)	0.0001

Table 3. Results of multivariable logistic regression analysis to determine variables independently associated with re-colonization with MRSA within three months of follow-up.

Variable	Relative risk (95% CI)	p value
Katz index score[a]	0.45 (0.16-1.31)	0.14
Presence of skin lesions	0.71 (0.27-1.87)	0.48
Presence of a medical device[b]	1.56 (0.62-3.94)	0.35
MRSA recovered from more than 1 body site	1.39 (0.53-3.70)	0.50
Mupirocin-resistant MRSA at baseline	9.37 (2.76-31.87)	0.0003
Randomized to received decolonization therapy[c]	0.12 (0.04-0.36)	0.0002

[a] Katz index score of A or B vs index score C, D, E, F, or G.

[b] Examples of medical devices include: intra-vascular catheter, urinary catheter, tracheostomy, or percutaneous enteral feeding tube

[c] Decolonization therapy consisting of 7 days of treatment with chlorhexidine soap, intra-nasal mupirocin ointment, oral rifampin, and oral doxycycline.