ORIGINAL ARTICLE

Bacterial Infections in Neonates Following Mupirocin-Based MRSA Decolonization: A Multicenter Cohort Study

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OBJECTIVE. To characterize the risk of infection after MRSA decolonization with intranasal mupirocin.

DESIGN. Multicenter, retrospective cohort study.

SETTING. Tertiary care neonatal intensive care units (NICUs) from 3 urban hospitals in the United States ranging in size from 45 to 100 beds.

METHODS. MRSA-colonized neonates were identified from NICU admissions occurring from January 2007 to December 2014, during which a targeted decolonization strategy was used for MRSA control. In 2 time-to-event analyses, MRSA-colonized neonates were observed from the date of the first MRSA-positive surveillance screen until (1) the first occurrence of novel gram-positive cocci in sterile culture or discharge or (2) the first occurrence of novel gram-negative bacilli in sterile culture or discharge. Mupirocin exposure was treated as time varying.

RESULTS. A total of 522 MRSA-colonized neonates were identified from 16,144 neonates admitted to site NICUs. Of the MRSA-colonized neonates, 384 (74%) received mupirocin. Average time from positive culture to mupirocin treatment was 3.5 days (standard deviation, 7.2 days). The adjusted hazard of gram-positive cocci infection was 64% lower among mupirocin-exposed versus mupirocin-unexposed neonates (hazard ratio, 0.36; 95% confidence interval [CI], 0.17–0.76), whereas the adjusted hazard ratio of gram-negative bacilli infection comparing mupirocin-exposed and -unexposed neonates was 1.05 (95% CI, 0.42–2.62).

CONCLUSIONS. In this multicentered cohort of MRSA-colonized neonates, mupirocin-based decolonization treatment appeared to decrease the risk of infection with select gram-positive organisms as intended, and the treatment was not significantly associated with risk of subsequent infections with organisms not covered by mupirocin's spectrum of activity.

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Staphylococcus aureus is the second most common cause of healthcare-associated infections (HAIs) in hospitalized neonates and remains a leading cause of morbidity and excess cost in pediatric settings.[1–3] Decolonization is a strategy to prevent *S. aureus* by reducing the bioburden of skin colonization that may otherwise increase risk of subsequent *S. aureus* infection or transmission. In neonatal intensive care units (NICUs), decolonization primarily has been used to control epidemic and endemic methicillin-resistant *S. aureus* (MRSA).[2] Mupirocin (pseudomonic acid A), a topical antibiotic, is a widely used decolonizing agent and is typically administered in the nares twice daily for 5 days. Mupirocin is highly active against staphylococci and streptococci, but it has poor *in vitro* activity against gram-negative bacilli.[4,5]

Despite calls for more expansive use of mupirocin-based decolonization as a prophylactic infection prevention tool,[6] few studies have evaluated possible unintended consequences of this approach.[7] One potential unintended outcome is pathogen replacement, which is addressed in mupirocin (Bactroban) prescribing information via the caution that application "may result in overgrowth of nonsusceptible microorganisms" but only with prolonged use.[8] Increased susceptibility to infection after systemic antibiotic exposure has been well described in the microbiome literature.[9,10] Antibiotics may either select for or provide sufficient disruption of the protective microbiota to facilitate infections with other pathogens. There is mounting concern that mupirocin, with its specificity for gram-positive organisms, may facilitate infection with nontargeted, gram-negative pathogens.[2,11–13] Gram-negative bacilli are significant NICU pathogens[14]; they are associated with high morbidity and mortality as well as treatment challenges secondary to high-levels of antimicrobial resistance.[15] The possibility of organism replacement after topical antibiotic ointment is particularly salient for infants in

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the NICU, as they are subject to recurrent pathogen introduction events from the healthcare setting and are particularly vulnerable to infections due to naive immune systems, a nascent microbiome, poor skin integrity, and frequent use of invasive devices.[1,16,17]

Our objective was to characterize the intended and unintended outcomes associated with mupirocin use among MRSA carriers in the NICU by estimating (1) the risk of infection with targeted, gram-positive cocci and (2) the risk of infection with nontargeted, gram-negative bacilli.

MATERIALS AND METHODS

Study Design and Population

We conducted a retrospective, multicenter cohort study from January 2007 to December 2014. Data were obtained from 3 tertiary-care NICUs for the portion of the study period when a targeted MRSA decolonization program was employed for MRSA control. Detailed facility data are available in Table 1. We included neonates who were identified as MRSA-colonized by surveillance culture and were, therefore, eligible for decolonization treatment. In addition to decolonization, sites employed other standard elements of NICU infection control practice, including contact precautions for neonates positive for MRSA or other multidrug-resistant organisms and chlorhexidine (CHG) bathing for neonates of higher gestational age (typically >36 weeks).

Definitions and Data Collection

MRSA-colonized neonates were identified via weekly nasal surveillance cultures conducted as part of a targeted decolonization strategy, for which the protocol has been described previously.[18] Neonates entered study observation on the date of first positive MRSA nasal surveillance culture and were followed until outcome occurrence or discharge.

We considered 2 outcomes for 2 separate time-to-event analyses. Outcomes included composites of organisms that were either covered by mupirocin's spectrum of activity (analysis 1) or were not (analysis 2). In analysis 1, we characterized the occurrence of novel gram-positive cocci in sterile culture. This included staphylococci and streptococci species, organisms covered by mupirocin. In analysis 2, we observed neonates for the occurrence of novel gram-negative bacilli in sterile culture. This outcome included Enterobacteriaceae and other gram-negative rods (eg, *Pseudomonas* spp. and *Acinetobacter* spp.) not covered by mupirocin's spectrum of activity. Outcomes were ascertained from clinical cultures obtained during routine care in the NICU. Sterile sites included blood, urine (obtained from urine catheter), cerebrospinal fluid, abscess fluid, and pleural fluid. Neonates were followed for the novel occurrence of an outcome organism in sterile culture, meaning that neonates were observed only for outcome organism species that had not already been detected in clinical culture prior to study entry. This accounted for the possibility of multiple, distinct infections with organisms of interest during admission and eliminated those that originated prior to study entry. For example, in analysis 2, if a neonate was admitted to the NICU with a *Klebsiella pneumoniae*–positive clinical culture and subsequently became MRSA colonized, then he or she would be followed for the occurrence of a non–*Klebsiella pneumoniae* gram-negative organism. Because neonates who had a pre–study-entry positive culture with an outcome organism may have and increased or decreased risk of additional infection with another species within the same outcome type, we included the occurrence of any pre-entry gram-positive cocci or gram-negative bacilli in clinical culture as a potential confounding variable in analysis 1 and analysis 2, respectively. In sensitivity analyses, we restricted our analysis to neonates that were free of all outcome organisms prior to study entry.

Our primary exposure was intranasal mupirocin administration. Mupirocin exposure information was obtained from administrative databases and chart review. A patient was classified as nonexposed from date of first positive MRSA nasal surveillance culture to date of first mupirocin exposure, after which they were considered mupirocin exposed.

Additional sensitivity analyses were performed for each time-to-event analysis to explore the construction of composite outcomes. First, we restricted outcomes to include only bloodstream infections (BSIs) to assess whether our effects were robust when holding the outcome specimen source constant. We additionally conducted a post-hoc sensitivity

TABLE 1. Study Site Description[a]

Site	Calendar Time	Bed Size	Admissions	MRSA-Colonized Neonates	Person Time (Analysis 1)	Person Time (Analysis 2)
Site 1 (St Louis, MO)	Jan 2007–Dec 2014	75	5,653	233	9,523	9,308
Site 2 (Louisville, KY)	Aug 2009–Nov 2013	100	4,303	185	5,649	5,932
Site 3 (Baltimore, MD)	Jan 2007–Dec 2014	45	6,188	104	3,009	3,111
Total	…		16,144	522	18,181	18,351

[a]Calendar time refers to the time period during which targeted decolonization was in place for each site. Admissions reflects neonate admissions during the calendar time period. MRSA-colonized neonates identified during the relevant calendar time that had at least one day of follow up were included in the analytic population. Analysis 1 is a survival analysis of time to gram-positive cocci infection and Analysis 2 is a survival analysis of time to gram-negative bacilli infection.

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analysis in which we further assessed the impact of characterizing outcomes with different organism and specimen type combinations to ensure consistency of results.

Statistical Methods

Bivariate associations between study variables and mupirocin exposure were assessed using χ^2, Fisher's exact, and nonparametric tests. Crude incidence rates were calculated. We conducted survival analyses using Cox proportional hazards regression to assess differences in the occurrence and timing of infection by mupirocin receipt. Mupirocin exposure was time varying as described above. Time at risk was calculated from the date of first MRSA positive culture to outcome or discharge, resulting in risk set comparisons being among those with similar time since initial MRSA-colonization and, therefore, start of eligibility for mupirocin. A priori confounders of interest included calendar year, prestudy entry length of stay, gestational age, birth weight, occurrence of an outcome organism in culture prior to study entry (described above), and study site. The proportional hazards assumption was tested by assessment of Schoenfeld residuals and tests of interaction of primary study variables with time. Data were analyzed using STATA v13.1 (StataCorp, College Station, TX) and R v3.2.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Characteristics of the Study Population

Of 16,144 total neonates admitted to site NICUs throughout the study period, we identified 522 (3.2%) MRSA-colonized neonates. Among these, 246 (47%) were female. Race composition was 59% white, 34% black, and 7% unknown or other. Mupirocin treatment was administered to 380 (73%) of MRSA-colonized neonates between first identification of colonization and discharge or outcome occurrence in analysis 1 and 384 (74%) in analysis 2. Compliance for mupirocin administration after MRSA-positive surveillance screen ranged by site from 69% to 79%. Average time to mupirocin receipt among those treated was 3.5 days (standard deviation, 7.2 days). Distribution of study variables by mupirocin exposure are presented in Table 2.

Primary Survival Analyses

Overall, 37 novel gram-positive cocci infection events were detected during the study period, corresponding to an incidence rate (IR) of 2.0 per 1,000 patient days. The rate of novel gram-positive cocci infection was 64% lower for mupirocin-exposed neonates than for mupirocin-unexposed neonates (1.4 vs 3.9 infections per 1,000 patient days; $P = .001$). Median follow-up time was 22 days (interquartile range [IQR], 8–45 days). The adjusted hazard of gram-positive cocci infection was 64% lower among mupirocin-exposed versus mupirocin-unexposed neonates (HR, 0.36; 95% CI, 0.17–0.76), controlling for length of stay prior to study entry, calendar year, birth weight, gestational age, study site, and whether a gram-positive cocci organism had been identified prior to study entry (Table 3A). Table 2 shows the distribution of observed gram-positive outcome organisms and sterile specimen types by mupirocin exposure. Outcomes included coagulase-negative staphylococci (51%), *S. aureus* (35%), streptococci (14%). Blood cultures were the most common sterile specimen type, accounting for 22 (59%) observed outcomes.

In total, 29 novel gram-negative bacilli infection events were observed, corresponding to a rate of 1.6 per 1,000 patient days. Median follow-up time was 23 days (IQR, 8–49 days). The crude IR of novel gram-negative bacilli infection was not significantly different among mupirocin-exposed and -unexposed neonates (incidence rate ratio [IRR],1.19; 95% CI, 0.49–3.31). Similarly, the adjusted hazard ratio of gram-negative bacilli infection comparing mupirocin-exposed and mupirocin-unexposed neonates was 1.05 (95% CI, 0.42–2.62), controlling for length of stay prior to study entry, calendar year, birth weight, gestational age, study site, and whether a gram-negative organism had been identified prior to study entry (Table 3B). Gram-negative organism and specimen type distribution are shown in Table 2. Enterobacteriaceae, most notably *Klebsiella* spp. (38%), *Escherichia coli* (21%), and *Enterobacter* spp. (14%), were most common. Urine cultures accounted for 21 (72%) of observed gram-negative bacilli outcomes.

Visual inspection of Schoenfeld residuals and tests of interaction of mupirocin exposure with time revealed no evidence that the proportional-hazards assumption had been violated, and no significant time-dependent effects were noted.

Sensitivity Analyses

When restricting to only neonates free of any gram-positive cocci organisms in clinical culture prior to study entry ($n = 439$), the effect of mupirocin exposure on gram-positive cocci infection risk remained highly protective (HR, 0.30; 95% CI, 0.13–0.66). Mupirocin exposure was associated with a nonsignificant protective effect on the hazard of gram-negative bacilli infection among neonates without any gram-negative bacilli identified prior to study entry ($n = 479$; HR, 0.81; 95% CI, 0.32–2.03).

Additional sensitivity analyses ensured consistency of results when restricting the specimen-type and pathogen components included in composite outcomes. First, outcomes were restricted to those found in blood culture alone. The hazard of gram-positive cocci BSI was lower among mupirocin-exposed neonates (HR, 0.37; 95% CI, 0.15–0.88) than in those mupirocin-unexposed, a finding consistent with that for the primary outcome including all sterile specimen sites. The hazard of BSI with gram-negative organisms was, again, not significantly different among mupirocin-exposed versus -unexposed neonates (HR, 0.82; 95% CI, 0.15–4.36). We further assessed the robustness of our findings when altering the organism or sterile specimen type combinations that defined outcomes.

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TABLE 2. Characteristics of Study Population[a]

Analysis 1: Time to Gram-Positive Cocci Infection				Analysis 2: Time to Gram-Negative Bacilli Infection			
Variable	Mupirocin-Treated (n = 380), No. (%)	No Mupirocin Treatment (n = 142), No. (%)	*P*	Variable	Mupirocin-Treated (n = 384), No. (%)	No mupirocin treatment (n = 138), No. (%)	*P*
Gram-positive cocci event	19 (5)	18 (13)	.002	Gram-negative bacilli event	22 (6)	7 (5)	.77
No event	361 (95)	124 (87)		No event	362 (94)	131 (95)	
Event specimen types				Event specimen types			
Blood	10 (53)	12 (66)	.67[a]	Blood	6 (27)	2 (29)	1.00[b]
Urine	5 (26)	3 (17)		Urine	16 (73)	5 (71)	
Other	4 (21)	3 (17)		Other	0 (0)	0 (0)	
Event organisms				Event organisms			
coNS	10 (53)	9 (50)	.28[a]	*Acinetobacter* spp.	1 (5)	0 (0)	1.00[b]
S. aureus	5 (26)	8 (44)		Enterobacteriaceae	19 (86)	6 (86)	
Streptococcus spp.	4 (21)	1 (6)		*Pseudomonas* spp.	2 (9)	1 (14)	
Previous gram-positive cocci in culture	55 (14)	28 (20)	.15	Previous gram-negative bacilli in culture	37 (10)	6 (4)	.05
No previous gram-positive cocci in culture	325 (86)	114 (80)		No previous gram-negative bacilli in culture	347 (90)	132 (96)	
LOS prior to study entry, d (median IQR)	18 (26)	15 (31)	.08[b]	LOS prior to study entry (days) median (IQR)	18 (26)	17 (31)	.22[c]
Gestational age, weeks (median IQR)	30 (9)	32 (10)	.38[b]	Gestational age (weeks) median (IQR)	30 (9)	32 (10)	.20[c]
Birth weight, g (median IQR)	1,100 (949)	1,083 (836)	.71[b]	Birth weight, g (median (IQR)	1,080 (938)	1,120 (884)	.91[c]
Site 1	180 (47)	53 (37)	.12	Site 1	183 (48)	50 (36)	.06
Site 2	127 (33)	58 (41)		Site 2	127 (33)	58 (42)	
Site 3	73 (19)	31 (22)		Site 3	74 (19)	30 (22)	

NOTE. coNS, coagulase-negative staphylococci; LOS, length of stay; IQR, interquartile range.

[a]Characteristics of study population shown by receipt of mupirocin while under observation for each of the specified outcomes. Specimen type and organism variables show distribution of composite outcomes. Other sites refer to sterile sites other than blood and urine, including cerebrospinal fluid, abscess fluid, and pleural fluid. Previous gram-positive cocci and gram-negative bacilli in culture variables refer to the occurrence of positive culture with any outcome organisms (specific to each analysis) prior to study entry (see text). *P* values obtained by chi-square test unless otherwise specified.

[b]*P* value obtained by Fisher's exact test.

[c]*P* value obtained by Kruskal-Wallis test.

TABLE 3A. Clinical Characteristics Associated With Risk of Gram-Positive Cocci Infection Among MRSA-Colonized Neonates Eligible for Mupirocin Treatment (Analysis 1)[a]

Variable	HR	95% CI	aHR	95% CI
Mupirocin treatment	0.43	0.21–0.86	0.36	0.17–0.76
LOS prior to study entry, d	0.99	0.98–1.01	0.98	0.97–1.00
Calendar year	0.94	0.80–1.10	1.00	0.85–1.18
Previous gram-positive cocci in culture	1.03	0.47–2.26	0.93	0.40–2.17
Birth weight, d	1.00	0.99–1.00	1.00	0.99–1.00
Gestational age, weeks	0.94	0.88–1.02	0.89	0.76–1.02
Site				
Site 1	0.86	0.45–1.65	0.72	0.30–1.72
Site 2	0.79	0.38–1.64	0.79	0.24–2.58
Site 3 (Ref)	…	…	…	…

NOTE. MRSA, methicillin-resistance *Staphylococcus aureus*; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; LOS, length of stay.

[a]Estimates obtained via Cox proportional hazards regression. Infection outcomes as measured by novel occurrence of positive sterile site culture with any of specified organisms.

Results were highly robust irrespective of organism or specimen type, demonstrating a strong protective effect for organisms covered by mupirocin (*S. aureus*, coagulase-negative staphylococci, streptococci) and hazard ratios that approach 1 for noncovered organisms. Notably, the rate of *S. aureus* BSI was lower among mupirocin-exposed neonates (IRR = 0.10,

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TABLE 3B. Clinical Characteristics Associated With Risk of Gram-Negative Bacilli Infection Among MRSA-Colonized Neonates Eligible for Mupirocin Treatment (Analysis 2)

Variable	HR	95% CI	aHR	95% CI
Mupirocin treatment	1.13	0.47–2.76	1.05	0.42–2.62
LOS prior to study entry, d	1.00	0.99–1.01	0.99	0.98–1.01
Calendar year	1.01	0.84–1.21	1.04	0.87–1.26
Previous gram-negative bacilli in culture	1.53	0.95–4.86	1.63	0.53–4.98
Birth weight, g	1.00	0.99–1.01	1.00	0.99–1.00
Gestational age, weeks	0.91	0.83–1.00	0.90	0.74–1.10
Site				
Site 1	0.95	0.37–2.43	0.94	0.34–2.66
Site 2	0.56	0.18–1.75	0.62	0.14–2.67
Site 3 (Ref)	…	…	…	…

NOTE. MRSA, methicillin-resistance *Staphylococcus aureus*; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; LOS, length of stay.

[a]Estimates obtained via Cox proportional hazards regression. Infection outcomes as measured by novel occurrence of positive sterile site culture with any of specified organisms.

95% CI: 0.01-0.51) as was the hazard of *S. aureus* BSI in Cox regression analysis (HR = 0.21, 95% CI: 0.04-1.26), though the later was at trend level significance. Additional organisms not covered by mupirocin spectrum activity were included here, including fungi, *Propionibacterium* spp., enterococci, and *Corynebacterium* spp. We did not find any evidence of a significant increase in risk of infection when these additional, noncovered organisms were included as outcomes. Results are shown in Supplementary Figure 1.

DISCUSSION

Data from this large, multicenter cohort suggest that mupirocin treatment for *S. aureus* decolonization decreases the risk of infection with select gram-positive organisms. This finding is consistent with other NICU studies that report reduced risk of MRSA or methicillin-sensitive *S. aureus* after mupirocin treatment.[19–21] We did not find a statistically significant increase in the risk of infection with gram-negative bacilli among MRSA-colonized NICU patients treated with mupirocin. These findings were robust to the type of sterile specimen source used to identify outcomes.

This study addresses growing concern that decolonization treatment may disrupt the microbiologic ecology of the nares and predispose neonates to infections with other organisms. Gram-negative pathogens are of particular concern as they account for a substantial portion of HAIs in the NICU and are associated with high morbidity and mortality.[1,14,22] In the current study, we did not observe a significant increase in the proportion, rate, or hazard of gram-negative bacilli infections with mupirocin treatment. In contrast, Perez-Fontan et al[23] previously reported an increase of gram-negative infections with nasal mupirocin use in adult peritoneal dialysis patients.[23] Similarly, the Mupirocin Study Group[24] conducted a randomized trial of mupirocin use in peritoneal dialysis patients and noted increased occurrence of gram-negative or mixed organism infections. A meta-analysis by van Rijen et al[13] pooled data from 3 trials of surgical and peritoneal dialysis patients and found an increased risk of infection with non–*S. aureus* organisms in those who had received mupirocin treatment. However, adult populations studied to date are likely to be highly distinct from a neonatal population in terms of risk factors, healthcare-associated and outpatient pathogen exposures, as well as microbiome development.

Our study informs distal infectious outcomes associated with mupirocin use as we observed neonates for the duration of their NICU stay, which ranged from days to months. Additional research is needed to assess the more immediate impact of topical antibiotics at the level of the microbiome in hospitalized patients, who may be more susceptible to replacement via repeated exposure to a wide range of healthcare-associated pathogens. Studies of the gut microbiome have shown that antibiotic treatment can disrupt microbial communities and can place recipients at increased risk for colonization with opportunistic pathogens.[25] However, the impact of disruptions in the skin microbiome following antimicrobial use remains poorly understood,[26] particularly for the relatively ubiquitous topical antibiotics. Use of triple antimicrobial ointments has been associated with *Candida* colonization and infection in adult ICU patients.[27] However, a recent study of 15 adults, both outpatient and ICU patients, found that microbial richness did not differ pre- versus postmupirocin treatment, while *S. aureus* body-site colonization decreased over time.[28] The assessment of this issue in neonates remains important because it is possible mupirocin-driven dysbiosis is occurring but is undetectable when clinical infection is the outcome of interest. This factor may be particularly relevant because neonatal microbiomes are evolving and perturbations may impact their long-term composition and stability.

Strengths of our study include the use of data from 3 NICUs that utilize targeted decolonization for MRSA control. The multicentered approach increased the capacity to identify MRSA-colonized and mupirocin-eligible neonates that could

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be observed for both intended and unintended infectious outcomes after mupirocin treatment. The longitudinal nature of the data allowed for estimates of individual-level risk of bacterial infections associated with mupirocin use, accounting for time at risk and establishing temporality between exposure and outcomes. In addition, we accounted for the time-varying nature of mupirocin exposure. This was important as mupirocin was not immediately administered in all cases and characterization of this time as mupirocin-exposed would have underestimated the rate of infection, and therefore, also would be underestimated the relative risk of infection associated with mupirocin exposure. The findings of this study support prior work demonstrating that characterization of time-varying antibiotic exposures has important implications for interpreting antimicrobial-associated infection risk.[29]

Our study has several limitations. First, this was an observational study, and we cannot rule out residual confounding. Although we were not aware of any systematic causes for withheld mupirocin-based decolonization treatment, we attempted to address this issue by comparing only MRSA-colonized neonates at the same time from identification of colonization to maximize comparability between exposure groups. Models were adjusted to control for potential confounders. In particular, adjustment for gestational age, calendar time, and site served to address unit CHG use, secular trends in infection control practice over the study period, and variation in practice by site. Although notable confounding by these variables was not observed, results nevertheless should be interpreted in the context of ongoing, unit-based infection control practices. Postmupirocin infection risk may vary in settings where these practices are not in use. A second limitation is the reliance on clinical culture proxy to define clinically apparent infection outcomes. We limited outcomes to positive sterile site cultures to improve confidence that we were measuring true infection, but this was not verified by chart review. Recognizing that coagulase-negative staphylococci culture positives may, in some cases, reflect skin colonization as opposed to infection, we performed sensitivity analyses focusing on *S. aureus* alone and found a significant decrease in overall rate of *S. aureus* between exposure groups, suggesting that the observed effect was not entirely driven by decreased occurrence of coagulase-negative staphylococci. Third, we continued to observe neonates that had a gram-positive cocci or gram-negative bacilli positive clinical culture prior to study entry for the occurrence of remaining species of outcome organisms. We did so not only to avoid inclusion of infections that originated prior to the beginning of observation but also because an early infection with one organism would not necessarily preclude subsequent risk of overgrowth and infection by another organism. In doing so, we reduce outcome possibilities in neonates with organisms of interest prior to study entry; however, given that we did not observe a significant decrease in the number of events in this subset, we believe this limitation is outweighed by the risk of excluding a potentially high risk group. Moreover, findings were consistent irrespective of the inclusion or exclusion of these neonates. Finally, the absence of a significant finding for mupirocin-associated gram-negative bacilli infection risk does not itself demonstrate absence of an effect. To address this issue, we conducted a post-hoc power analysis using effect sizes obtained from the Mupirocin Study Group.[24] Given a higher proportion of infection with gram-negative or mixed organisms in the mupirocin group (20 of 134 [15%] vs 7 of 133 [5%]; $P = .01$ by Fisher's exact test)[24] and our sample size of 522 neonates, our study would have 87% power to detect a similar effect. Further research is required to elucidate the short- and long-term impacts of topical antimicrobials in a neonatal population. Studies that evaluate outcomes associated with decolonization therapy should consider reporting the overall incidence of infections with any organism to assess unintended consequences.

In this study, we report the risk of bacterial infections following mupirocin decolonization in a NICU population. Our analysis suggests that mupirocin-based decolonization treatment does not facilitate infection with organisms not directly targeted by the approach, but it does appear to be working as intended by reducing risk of infection with gram-positive organisms.

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SUPPLEMENTARY MATERIAL

To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2017.108

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