

Nasal Decolonization: What Agent is Most Effective to Prevent Surgical Site Infections

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INTRODUCTION

US National Data on HAIs, 2009-10

Pathogen	Overall		CLABSI		VAP		SSI	
	No. (%) of pathogens	Rank	No. (%) of pathogens	Rank ^a	No. (%) of pathogens	Rank ^a	No. (%) of pathogens	Rank ^a
<i>Staphylococcus aureus</i>	12,635 (15.6)	1	3,735 (12.3)	2	2,043 (24.1)	1	6,415 (30.4)	1
<i>Escherichia coli</i>	9,351 (11.5)	2	1,206 (4.0)	9	504 (5.9)	6	1,981 (9.4)	3
Coagulase-negative staphylococci	9,261 (11.4)	3	6,245 (20.5)	1	72 (0.9)	...	2,477 (11.7)	2
<i>Klebsiella (pneumoniae/oxytoca)</i>	6,470 (8.0)	4	2,407 (7.9)	5	854 (10.1)	3	844 (4.0)	7
<i>Pseudomonas aeruginosa</i>	6,111 (7.5)	5	1,166 (3.8)	10	1,408 (16.6)	2	1,156 (5.5)	5
<i>Enterococcus faecalis</i>	5,484 (6.8)	6	2,680 (8.8)	3	45 (0.5)	...	1,240 (5.9)	4
<i>Candida albicans</i>	4,275 (5.3)	7	1,974 (6.5)	7	147 (1.7)	...	267 (1.3)	...
<i>Enterobacter</i> spp.	3,821 (4.7)	8	1,365 (4.5)	8	727 (8.6)	4	849 (4.0)	6
Other <i>Candida</i> spp. or NOS	3,408 (4.2)	9	2,465 (8.1)	4	36 (0.4)	...	96 (0.5)	...
<i>Enterococcus faecium</i>	3,314 (4.1)	10	2,118 (7.0)	6	25 (0.3)	...	517 (2.5)	...
<i>Enterococcus</i> spp.	2,409 (3.0)	11	703 (2.3)	12	11 (0.1)	...	685 (3.2)	8
<i>Proteus</i> spp.	2,031 (2.5)	12	232 (0.8)	...	119 (1.4)	...	667 (3.2)	9
<i>Serratia</i> spp.	1,737 (2.1)	13	762 (2.5)	11	386 (4.6)	7	385 (1.8)	...
<i>Acinetobacter baumannii</i>	1,490 (1.8)	14	629 (2.1)	13	557 (6.6)	5	119 (0.6)	...
Other ^a	9,304 (11.5)	...	2,762 (9.1)	...	1,510 (17.8)	...	3,399 (16.1)	...
Total	81,139 (100)		30,454 (100)		8,474 (100)		21,100 (100)	

Epidemiology MSSA and MRSA

Reservoirs

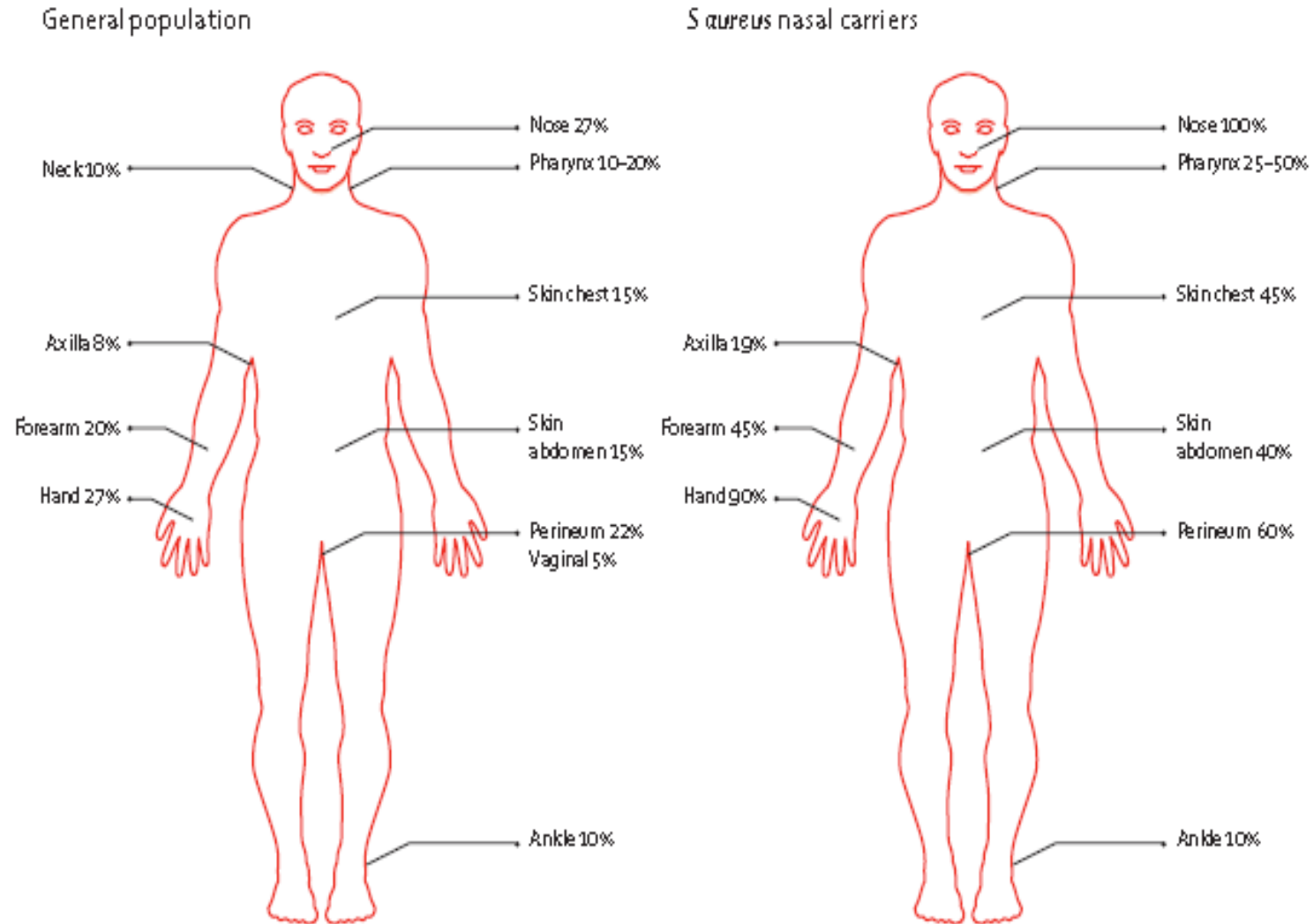
- Humans are the natural reservoirs for *S. aureus*. 20-50% of healthy adults are colonized with *S. aureus*, and 10-20% are persistent carriers. Colonization rates are highest among patients with diabetes, IV drug users, hemodialysis, continuous peritoneal dialysis, dermatologic conditions (eczema and psoriasis), and HIV.
- Nasal colonization with *S aureus* is the single most important determinant of subsequent *S aureus* infections
- Patterns of carriage:

persistent	20% (12-30%)
intermittent	30% (16-70%)
non-carriage	50% (16-69%)



Role of Nasal Carriage in *S. aureus* Infections

Lancet Infect Dis 2005; 5:751



Evaluation of a Strategy of Screening Multiple Anatomic Sites for MRSA at Admission to a Teaching Hospital

<u>Site</u>	<u>% Positive</u>
Nares	73
Rectum	47
Axilla	25
Nares+Axilla	83
Nares+Rectum	91

Randomized Trial of Prophylactic Mupiricin + CHG Shower

- Nasal carriage of *S. aureus* eliminated in 83.4% v. 27.4% in placebo ($p < 0.001$)
- SSI 7.9% v. 8.5% (ns)
- *S. aureus* SSI 2.3% v. 2.4% (ns)
- **In carriers:**
 - any HA staph infection (most SSI) 4% v. 7.7% (OR 7.7% 95% CI 0.25-0.92)
 - 84.6% PFGE match between nares and SSI

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Preventing Surgical-Site Infections in Nasal Carriers
of *Staphylococcus aureus*

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-
- Randomized, double-blinded, placebo-controlled multicenter study of 6,771 patients in The Netherlands (Bode, *NEJM* 2010)
 - Rapid screening for MSSA/MRSA on admission
 - Carriers randomized to mupirocin/CHG soap vs. placebo/bland soap x 5 days

Bode, NEJM 2010 (Continued)

- Results: CHG bathing + mupirocin group had significantly lower SSI rates than the placebo group
- Conclusion: Preoperative identification of *S. aureus* carriers followed by 5 days of intranasal mupirocin plus CHG bathing reduced *S. aureus* SSIs by ~60%

Localization of infection	Mupir + CHG	Placebo	RR (95% CI)
Deep surgical site	4 (0.9)	16 (4.4)	0.21 (0.07-0.62)
Superficial surgical site	7 (1.6)	13 (3.5)	0.45 (0.18-1.11)

Decolonization

	# Studies	OR* 95% CI	Nasal Decolonization Studies (No Bundle)	No Bundle OR* 95% CI
Cardiac Studies	11	0.58 (0.45, 0.77)	6	0.64 (0.45, 0.92)
Orthopedic Studies	11	0.44 (0.33, 0.59)	4	0.49 (0.28, 0.85)
All	20	0.45 (0.34, 0.59)	10	0.53 (0.38, 0.74)

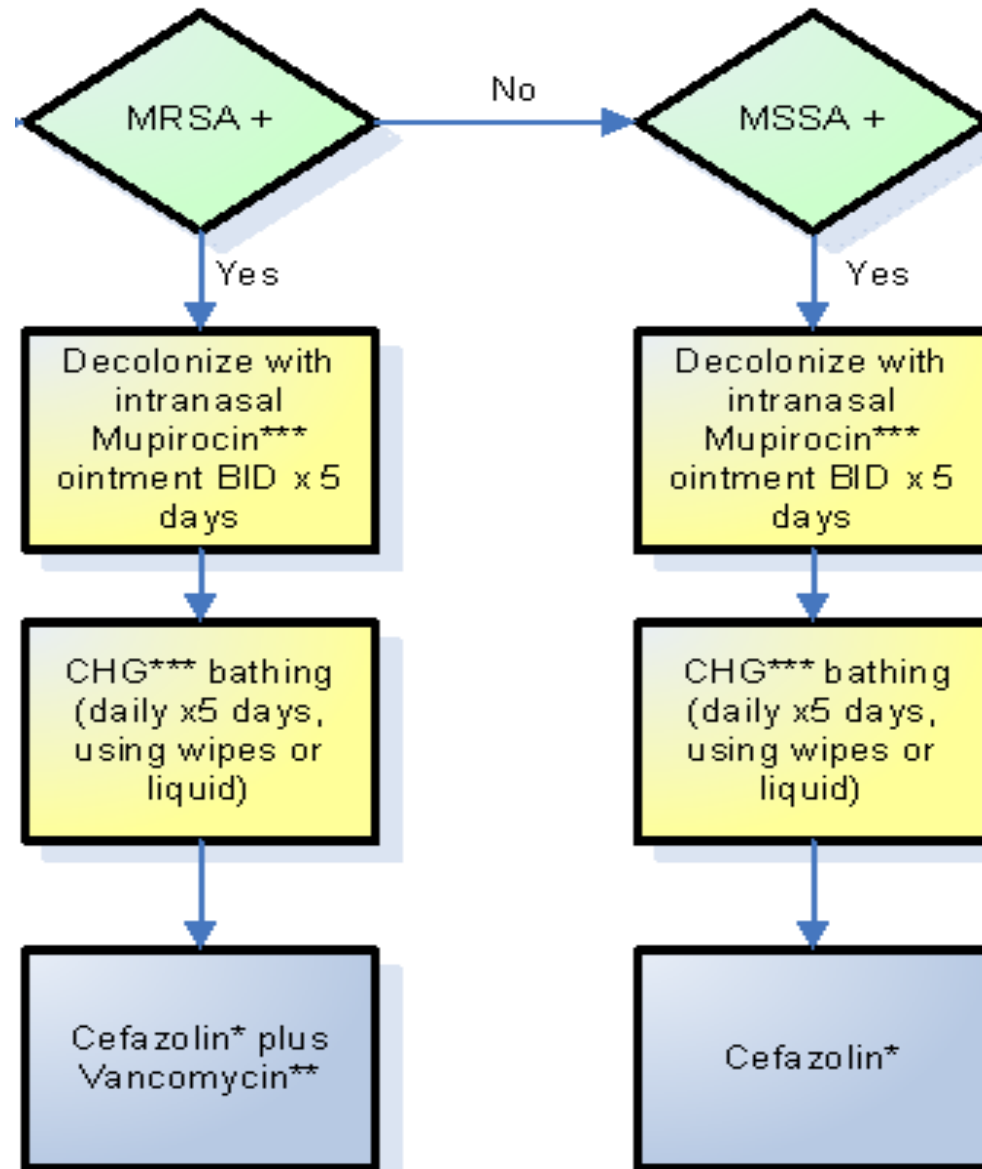
*Pooled Random Effects Odds Ratio (OR)

Original Investigation

Association of a Bundled Intervention With Surgical Site Infections Among Patients Undergoing Cardiac, Hip, or Knee Surgery

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S. aureus Positive



Results: Complex *S. aureus* SSIs

	Pre-Intervention	Intervention	Rate Ratio (95% CI)	P-value
Entire Cohort	28,218	14,316	0.58 (0.37, 0.92)	0.02
Hip/Knee	20,642	11,059	0.48 (0.29, 0.80)	0.005
Cardiac	7,576	3,257	0.86 (0.47, 1.57)	0.63

Nasal Decolonization Strategies

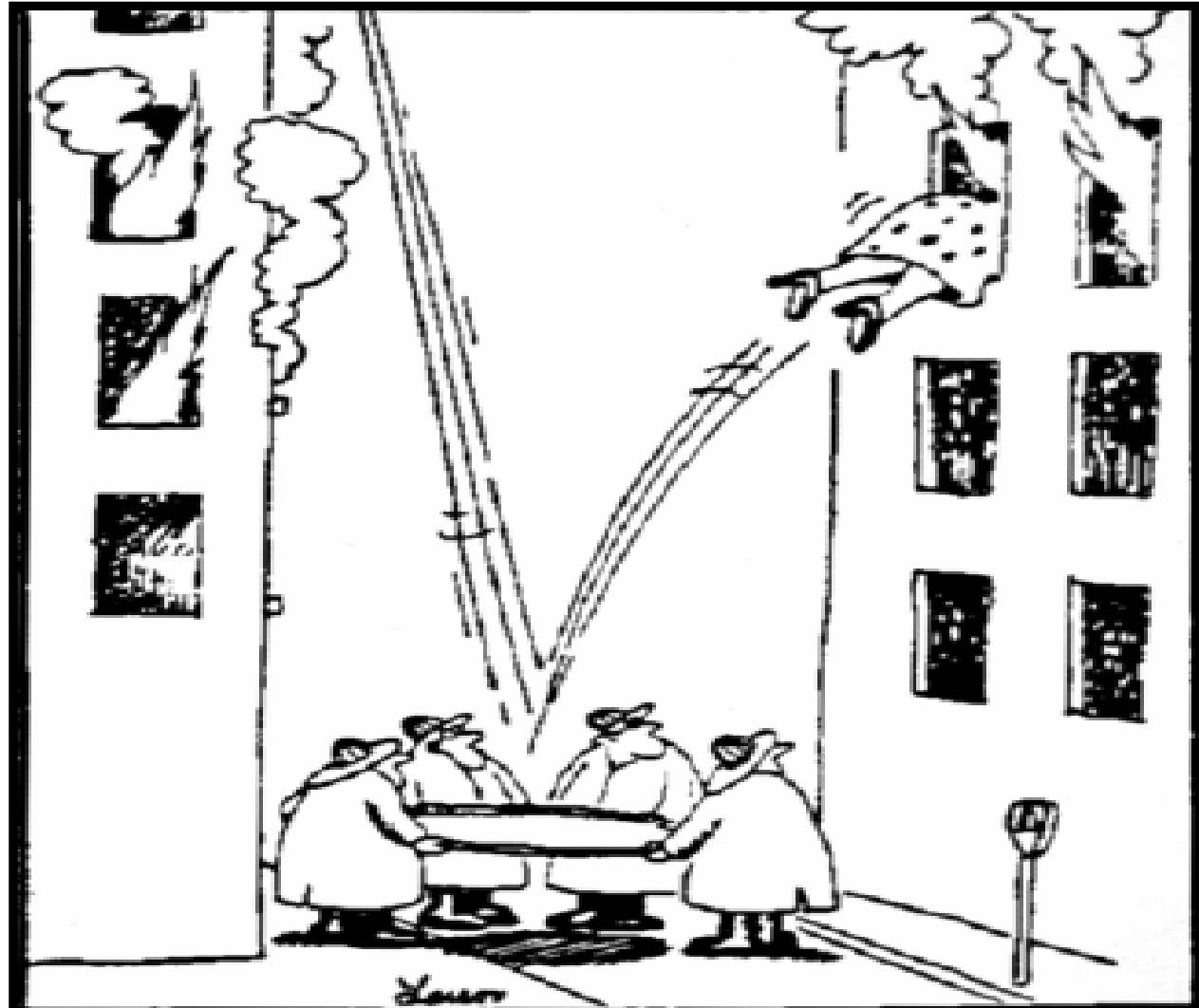
Mupirocin-select studies

- Mupirocin exists in two formulations: a nasal ointment in petrolatum and a generic topical ointment in a polyethylene glycol vehicle. Both have been used for nasal decolonization. Mupirocin is applied to the anterior nares 2 times/day for 5 days.
- Carriage of *S. aureus* was eliminated from 81.3 percent of carriers ($P < 0.001$) who received three to five doses of mupirocin and from 93.3 percent of patients who received six or more doses of mupirocin.

N Engl J Med 2002; 346:1871

Mupirocin(2)

- In a Cochrane review, the authors sought to determine if the use of mupirocin nasal ointment in patients identified as *S aureus* carriers reduced *S. aureus* infections. Only randomized controlled trials comparing mupirocin with no treatment or placebo or alternative nasal treatment were included. They found mupirocin ointment resulted in a significant reduction in *S aureus* infections. (RR 0.55, 95% CI 0.43 to .70)
Cochrane Database Syst Rev 2008; Oct 8;(4):CD006216
- In a systemic review and meta-analysis of published studies limited to controlled clinical trial with the use of mupirocin, the authors demonstrated significant decreases in the incidence of surgical-site infection in nongeneral surgery(cardiac, neurosurgery, and orthopedics). There was no reduction seen in general surgical patients. In all studies, interventions and control groups differed only by the use of perioperative intranasal mupirocin. *Infect Control Hosp Epidemiol* 2005; 26:916



Any Unintended Consequence?

Mupirocin resistance-select studies

- Mupirocin resistance to *S aureus* has now been identified in several studies especially with widespread use over prolonged periods. Am J Kidney Dis 2002; 39:337; Infect Control Hosp Epidemiol 2000; 21:459
- There are two phenotypes of mupirocin resistance: low level mupirocin with MICs from 8 to 64µg/mL, and high-level mupirocin resistance with MICs ≥ 512 µg/mL J Hosp Infect 1997; 35:1-8
- In sensitivity analysis, prior mupirocin exposure was associated with both low-level (OR 6.32; CI 1.58-25.33) and high-level mupirocin resistance (OR 11.18; 95% CI 1.89-66.30). J Hosp Infect 2010; 76:206
- Studies have shown that high-level mupirocin resistance to *S aureus* results in decolonization failure. The association with low-level mupirocin resistance and outcomes of mupirocin decolonization is unclear.

Mupirocin Summary

- Mupirocin has emerged as the topical agent of choice for elimination of *S aureus* nasal carriage.
- However, there is growing evidence of increasing mupirocin resistance and treatment failures, especially with widespread use over long periods of time.
- Therefore, there is renewed interest in evaluating newer agents or alternative methods of decolonization.

Nasal 5%-10% Povidone-Iodine

- Povidone-iodine (PI) is a complex polyvinylpyrrolidone and tri-iodine ions that has been widely used as an antiseptic on skin, wounds, and mucous membranes. PI has broad activity against gram-positive and gram-negative bacteria.
- Hill and Casewell evaluated the in vitro activity of 5% PI as a possible alternative to mupirocin for the elimination of nasal carriage of *S aureus*. The results suggested PI may have a role in the prevention of colonization and infection due to MRSA, including mupirocin-resistant strains. J Hosp Infect 2000; 45:198

Nasal 5% Povidone-Iodine continued

- Phillips et al. conducted a prospective, open label trial of twice daily application of nasal mupirocin ointment for 5 days before surgery compared to 2 applications of a 5% PI solution in each nostril within 2 hours of surgical incision in patients undergoing arthroplasty or spine fusion surgery. Both groups also received CHG bath with 2% cloths the night before and the morning of surgery. In the per protocol analysis, *S aureus* deep surgical site infections (SSI) developed in 5 of 763 surgical procedures in the mupirocin group and 0 of 776 surgical procedures in the PI group ($P=.03$)
- The proportion of postoperative negative nasal cultures was 92% (78 of 85 patients) in the mupirocin group versus only 54% (45 of 84 patients) in the PI group.

Nasal 5% Povidone-Iodine continued

- Limitations of Phillips study:
 - Single site study and results may not be applicable to other sites and populations.
 - They could not perform multivariate analysis due to small sample size.
 - Patients were not followed after discharge to identify late infections.
 - ? Type I error (conclude that a supposed effect or relationship exists when in fact it doesn't.)

Nasal 5% Povidone-Iodine continued

- Bebko and colleagues recently published a preop decontamination protocol to reduce SSIs in orthopedic patients undergoing elective hardware implantations.
- Retrospective quasi-experimental. Authors admit orthopedic service to be a high outlier with regard to SSIs.
- Control group were patients operated from October 1, 2012 to April 30, 2013. Intervention group was May 1, 2013 to December 31, 2013.
- Intervention: application of 2% CHG and oral CHG v the night before and morning of surgery plus intranasal PI solution the morning of surgery.
- Patients were followed for 30 days postop. Patients not available for follow-up within 30 days and those who developed a chronic joint or bone infection at the surgical site were excluded(?).
- MRSA nasal colonization was performed on patients admitted for more than 24 hours as per hospital-wide screening protocol.

Nasal 5% Povidone-Iodine continued

- The SSI rate in the intervention group was significantly lower (1.1%; 4 of 365 patients developed an SSI) than the SSI rate in the control group (3.8%; 13 of 344 patients developed an SSI) (P= .02)
- Multivariate analysis found patients with COPD had more than a 6-fold greater risk of developing an SSI than patients without COPD (OR, 6.76 [95% CI, 2.16-21.19]; P= .001). Likewise, patients who spent more than 2.5 hours in the operating room were 4.59 times more likely to get an SSI than patients who spent less time in the operating room (OR, 4.59 [95% CI, 1.67-12.65]; P= .003). Decontamination was also an independent predictor of not developing an SSI (adjusted odds ratio, 0.24 [95% CI, 0.08-0.77]; P= .02)

Nasal 5% Povidone-Iodine continued

- Limitations of the Bebko study:
 - Retrospective, quasi-experimental (before and after)
 - No randomization
 - High baseline SSI rate
 - Only followed for 30 days post op
 - COPD and length of surgery much stronger predictors of SSI
 - Information regarding MRSA carrier status of patients before decontamination was not collected-therefore did not allow for effect of nasal decolonization

Conclusion:

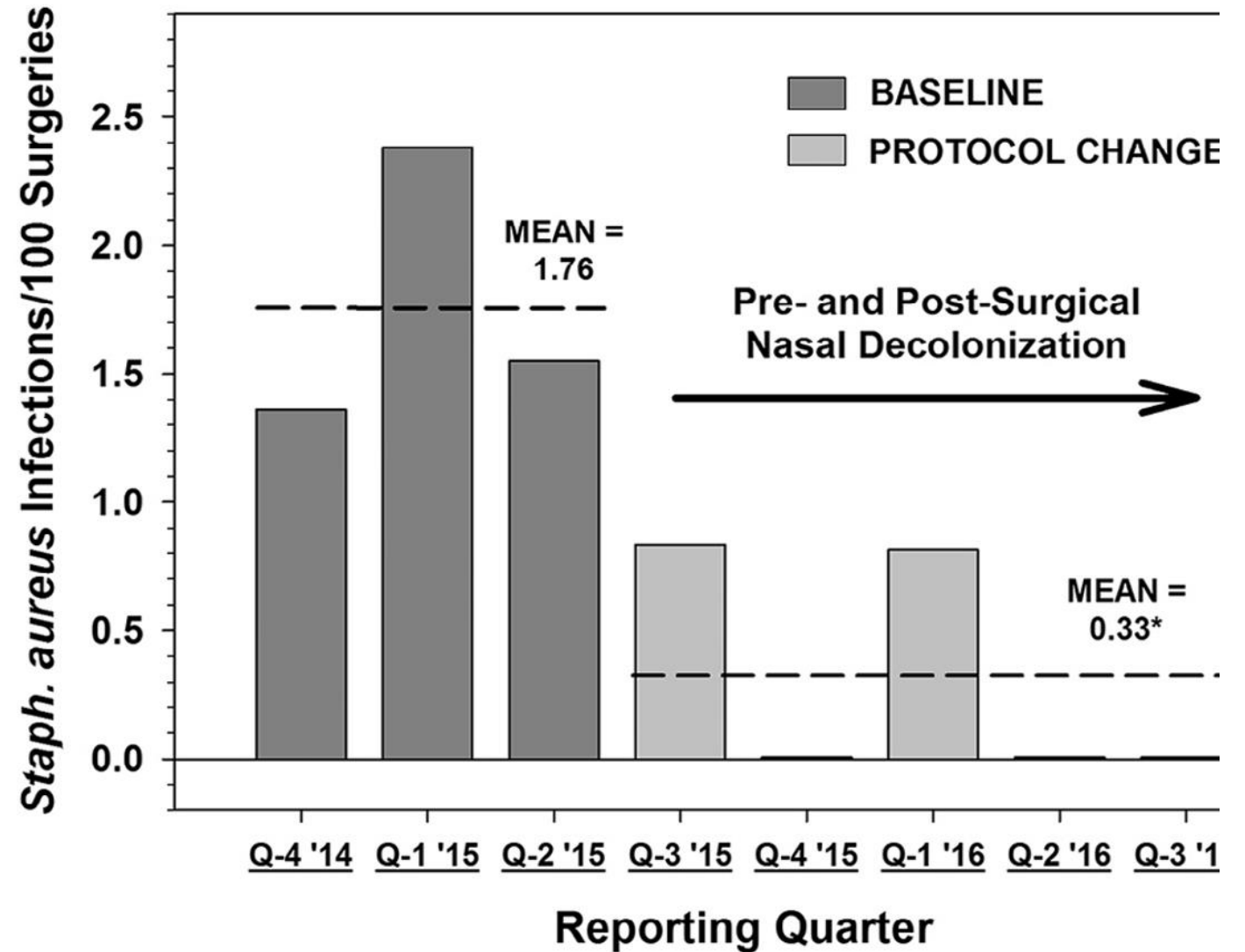
- Although nasal PI may be a potential alternative to nasal mupirocin for prevention of SSIs, more studies are needed. Nasal PI has not been studied in other clinical settings.

Perioperative participation of orthopedic patients and surgical staff in a nasal decolonization intervention to reduce *Staphylococcus* spp surgical site infections

- All patients scheduled for spine surgery were included in the study. Records from 1,073 spine surgical patients undergoing inpatient or outpatient procedures (400 and 673 in the baseline and intervention periods, respectively) were part of the study.
- Authors combined immediate presurgical application of a nonantibiotic alcohol-based nasal antiseptic with existing chlorhexidine bath or wipes in a comprehensive pre and postoperative decolonization protocol.
- After surgery, patients were expected to follow the regular 3 times daily cycle of staff-applied antiseptic application in the postsurgical units until discharge, at which time the patient and family coach were instructed to continue applications for an additional 5-7 days with the remaining antiseptic.

Perioperative participation of orthopedic patients and surgical staff in a nasal decolonization intervention

- Mean infection rates were significantly decreased by 81% from 1.76 to 0.33 per 100 surgeries during the 15-month trial, when compared with the prior 9-month baseline. (P=.036).
- Spine population was not sufficiently large to establish a concurrent control group
- Small, single-center intervention and before and after design needs confirmation



Summary

- Short-term nasal application of mupirocin is still the most effective studied treatment in eradicating *S aureus* nasal carriage, however, increasing mupirocin resistance remains a concern.
- Therefore alternative agents are needed.
- Nasal Povidone-Iodine, and alcohol-based nasal antiseptic are promising new agents, but more studies are needed.
- If pre-surgical decolonization is indicated, intranasal mupirocin plus CHG bathing is recommended since multiple sites are often colonized with *S aureus* in addition to the nares.

**While all changes do not lead to
improvement
all improvement requires change**