

# **Original Article**

# Staphylococcus aureus colonization and surgical site infections among patients undergoing surgical fixation for acute fractures

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### **Abstract**

Objectives: To identify risk factors for methicillin-susceptible (MSSA) and methicillin-resistant *S. aureus* (MRSA) nasal carriage and surgical site infection (SSI) among patients undergoing fracture fixation procedures who were included in a quality improvement protocol involving screening patients for *S. aureus* nasal carriage and treating carriers with intranasal mupirocin and chlorhexidine bathing.

Design: Retrospective cohort study.

Setting: Level 1 trauma center.

Participants: 1,254 adults who underwent operative fixation of 1,298 extremity or pelvis fractures between 8/1/2014 - 7/31/2017.

Methods: We calculated rates of *S. aureus* nasal carriage and SSI. We used multivariable stepwise logistic regression and selected the final models based on Akaike information criterion.

Results: Of the 1,040 screened first procedures, 262 (25.19%) were performed on *S. aureus* nasal carriers: 211 (20.29%) on MSSA carriers and 51 (4.90%) on MRSA carriers. Long-term care facility residence (odds ratio [OR] 3.38; 95% confidence interval [CI] 1.17–9.76) was associated with MRSA nasal carriage. After adjusting for statistically and clinically significant variables, MRSA carriage was significantly associated with any SSI (OR 4.58; 95% CI 1.63–12.88), *S. aureus* SSI (OR 10.11; 95% CI 3.25–31.42), and MRSA SSI (OR 27.25; 95% CI 5.33–139.24), whereas MSSA carriage was not. Among *S. aureus* carriers, any chlorhexidine use was documented for 232 (88.55%), and any intranasal mupirocin was documented for 85 (40.28%) MSSA carriers and 33 (64.71%) MRSA carriers.

Conclusions: MRSA carriage was associated with a significant risk of SSI after operative fracture fixation. Many carriers did not undergo decolonization, suggesting that a simplified decolonization protocol is needed.

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### Introduction

Staphylococcus aureus is a common cause of surgical site infections (SSI) after surgical fixation of acute fractures. <sup>1-4</sup> S. aureus nasal carriage increases the risk for SSI, <sup>5,6</sup> and decolonization of S. aureus carriers can reduce the risk of SSI after elective orthopedic surgery. <sup>7-10</sup> Few orthopedic trauma programs either screen patients for S. aureus carriage or decolonize carriers. <sup>11-13</sup> In addition, few studies have assessed S. aureus nasal carriage rates and the association of S. aureus

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nasal carriage with SSI or wound healing complications among patients undergoing operative fixation for acute fractures. Moreover, the effectiveness of decolonization has not been assessed thoroughly among patients with orthopedic trauma, given in part because the time period from the injuries to the fracture fixations is short.

We implemented a quality improvement intervention that involved screening patients for *S. aureus* and decolonizing carriers with intranasal mupirocin and chlorhexidine bathing to decrease rates of *S. aureus* SSI and wound healing complications among adults undergoing operative fixation of acute pelvis or extremity fractures at a Level 1 trauma center. We aimed to determine the rate of *S. aureus* nasal carriage, identify risk factors for *S. aureus* carriage in this population, and assess if *S. aureus* nasal carriage was associated with

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an increased risk of SSI or wound healing complications. We also assessed compliance with the quality improvement intervention.

### **Methods**

From 8/1/2014 to 7/31/2017, we implemented a quality improvement protocol that involved screening consecutive patients aged 18 years and older for *S. aureus* nasal carriage and decolonization of carriers before they underwent operative fixation of acute pelvis or extremity fractures by one of three fellowship-trained orthopedic trauma surgeons at Iowa Health Care, a Level 1 trauma center. For patients with multiple surgical procedures, we included only the first operation during the study period on each included body region. The University of Iowa Institutional Review Board prospectively approved both the quality improvement initiative and the retrospective cohort study.

Patients were screened for *S. aureus* nasal carriage in the emergency department, after admission to an inpatient ward, or during orthopedic clinic visits when the patients were indicated for operative fixation. Trained nursing staff swabbed patients' nares with a dual-headed Copan swab (COPAN Diagnostics Inc., Murrieta, CA) according to manufacturer's instructions. Swabs were submitted to the on-site clinical microbiology laboratory for polymerase chain reaction testing to identify methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) (Cepheid Inc., Sunnyvale, CA).<sup>14</sup>

### Quality improvement intervention

Patients who did not carry *S. aureus* were to bathe or shower with chlorhexidine the night before and the morning of their procedures; patients who were colonized with MSSA or MRSA were instructed to apply mupirocin to their nares twice daily for five days and to bathe or shower with chlorhexidine once daily for five days before their operations. Surgical interventions were not delayed if the decolonization protocol was not completed.

Patients who were colonized with MSSA were to receive cefazolin for perioperative prophylaxis and those who were colonized with MRSA or whose carrier status was unknown at the time of surgery were to receive both cefazolin and vancomycin in accordance with guidelines.<sup>15</sup>

### Retrospective cohort study

We collected information from the patients' electronic medical records about age, gender, body mass index (BMI), co-morbidities, residence at a long-term care facility (LTCF), injury severity score (ISS), <sup>16</sup> open fractures, Gustilo-Anderson classification, <sup>17</sup> type of operative intervention, *S. aureus* nasal carriage status, antibiotic prophylaxis, compliance with the intervention, essential dates (injury, admission, procedure, discharge), and duration of follow up. We also extracted the information necessary to identify both SSI, as defined by the Centers for Disease Control and Prevention's (CDC) National Healthcare Safety Network (NHSN), <sup>18,19</sup> and wound healing complications, as defined by the Clavien-Dindo classification system. <sup>20</sup>

We used SAS software (version 9.4, SAS Institute, Inc., Cary, North Carolina) and VassarStats (Vassar College, New York) to analyze the data. For the bivariable analyses, we used Chisquared and Fisher's exact tests (categorical variables) and two-sample t-tests (continuous variables), and we used 2x2 tables or logistic regression, when appropriate, to calculate odds ratios

(OR) and 95% confidence intervals (CI). To adjust for clinically and statistically significant variables, we used multivariable stepwise logistic regression and selected the final models based on Akaike information criterion. We considered p-values less than .05 to be significant.

### Results

### S. aureus colonization

The study included 1,254 adults who underwent 1,298 first operative fixation procedures of acute pelvis or extremity fractures during the study period. Of the 1,254 patients, 1,001 (79.82%) were screened for *S. aureus* colonization, of whom 202 (20.18%) patients were colonized with MSSA and 47 (4.70%) were colonized with MRSA.

The 1,001 screened patients underwent 1,040 first procedures. Of these procedures, 211 (20.29%) were performed on MSSA carriers and 51 (4.90%) on MRSA carriers. The following characteristics were more common among patients who were screened than those who were not (n = 253): male sex (P = .0083), mean age of 53 years (P = .0002), malnutrition (P = .0011), heart disease (P < .0001), open fractures (P < .0001), and an ISS > 15 (P < .0001).

### Risk factors for S. aureus colonization

Bivariable analyses of data from the entire cohort of 1,298 first procedures found that any *S. aureus* carriage (MSSA or MRSA) was significantly associated with diabetes and residence in an LTCF (Table 1), but other variables were not. Male gender was the only variable significantly associated with MSSA colonization, whereas older age, diabetes, heart disease, renal disease, and LTCF residence were associated with MRSA carriage (Table 1). The results were similar when we excluded patients whose carrier status was unknown (Supplemental Table 1). Multivariable logistic regression analysis revealed that LTCF residence (OR 3.38; 95% CI 1.17–9.76) was significantly associated with MRSA nasal carriage.

# Compliance with perioperative prophylaxis quality improvement protocol

Patients known to carry MSSA (211) received cefazolin (185; 87.68%), vancomycin (3; 1.42%), cefazolin and vancomycin (21; 9.95%), or neither agent (2; 0.95%) perioperatively. Patients known to carry MRSA (51) received cefazolin (27; 52.94%), vancomycin (3; 5.88%), or both (21; 41.18%) perioperatively. Patients whose S. aureus carriage status was unknown (258) received cefazolin (234; 90.70%), vancomycin (5; 1.94%), both cefazolin and vancomycin (10; 3.88%), or neither agent (9; 3.49%) perioperatively. Patients who carried MSSA were significantly more likely to receive the recommended perioperative antimicrobial prophylaxis than those who carried MRSA (P <.0001) or patients whose carriage status was unknown (P< .0001). The S. aureus decolonization protocol required 5 days to complete, but 198 (75.57%) procedures performed on S. aureus carriers occurred 4 or fewer days after injury onset. At least 1 dose of mupirocin was documented for 85 (40.28%) procedures performed on known MSSA carriers and 33 (64.71%) procedures performed on known MRSA carriers. A preoperative chlorhexidine bath was recorded for 186 (88.15%) procedures performed on known MSSA carriers and 46 (90.20%) procedures performed on known MRSA carriers. We did not assess the effectiveness of the decolonization protocol 386 Megan Ahmann *et al.* 

Table 1. Bivariable analyses of factors associated with Staphylococcus aureus nasal carriage

	Non-carriers & Unknown (n = 1,036)	S. aureus carriage (n = 262)		MSSA carriage (n = 211)		MRSA carriage (n = 51)	
Patient Characteristics	No. (%)	No. (%)	Odds Ratio (95% CI)	No. (%)	Odds Ratio (95% CI)	No. (%)	Odds Ratio (95% CI)
Age, mean (range)	52.47	52.19	1.00	50.35	0.99	59.81	1.02
	(18–98)	(18–97)	(0.99-1.01)	(18–97)	(0.99-1.00)	(19–91)	(1.01–1.03)
BMI, mean (range)	29.26	29.34	1.00	28.85	0.99	31.37	1.03
	(14.65–66.14)	(14.18–75.39)	(0.98–1.02)	(16.21–75.39)	(0.97–1.01)	(14.18–55.01)	(1.00-1.07)
Male gender	536	153	1.31	128	1.45	25	0.84
	(51.74)	(58.40)	(1.00-1.72)	(60.66)	(1.07–1.96)	(49.02)	(0.48-1.48)
Tobacco use	487	112	0.84	89	0.83	23	0.96
	(47.01)	(42.75)	(0.64–1.11)	(42.18)	(0.61–1.11)	(45.10)	(0.55–1.68)
Alcohol use disorder	52	13	0.99	11	1.05	2	0.77
	(5.02)	(4.96)	(0.53–1.84)	(5.21)	(0.54–2.05)	(3.92)	(0.18–3.23)
Illicit drug use (including THC)	61	16	1.04	12	0.95	4	1.37
	(5.89)	(6.11)	(0.59–1.83)	(5.69)	(0.50-1.79)	(7.84)	(0.48–3.90)
Diabetes	109	44	1.72	30	1.30	14	3.02
	(10.52)	(16.79)	(1.17–2.51)	(14.22)	(0.85–2.00)	(27.45)	(1.59–5.72)
Heart disease	152	50	1.37	33	1.01	17	2.87
	(14.67)	(19.08)	(0.96–1.95)	(15.64)	(0.67–1.51)	(33.33)	(1.57–5.24)
Vascular incident	53	17	1.29	12	1.07	5	1.98
	(5.12)	(6.49)	(0.73–2.26)	(5.69)	(0.56–2.03)	(9.80)	(0.76-5.14)
Renal disease	49	19	1.58	10	0.88	9	4.31
	(4.73)	(7.25)	(0.91–2.72)	(4.74)	(0.44–1.76)	(17.65)	(2.01–9.28)
Liver disease	24	11	1.85	8	1.55	3	2.37
	(2.32)	(4.20)	(0.89-3.82)	(3.79)	(0.69–3.45)	(5.88)	(0.70–8.02)
Malnutrition	61	14	0.90	9	0.69	5	1.83
	(5.89)	(5.34)	(0.50-1.64)	(4.27)	(0.34–1.41)	(9.80)	(0.70-4.74)
History of cancer	87	17	0.76	14	0.79	3	0.71
	(8.40)	(6.49)	(0.44–1.30)	(6.64)	(0.44–1.41)	(5.88)	(0.22–2.32)
Immunocompromised or HIV positive	18	2	0.44	1	0.27	1	1.29
	(1.74)	(0.76)	(0.10-1.89)	(0.47)	(0.04–2.01)	(1.96)	(0.17-9.85)
Long-term care facility resident	17	14	3.38	8	1.82	6	6.52
	(1.64)	(5.34)	(1.65–6.96)	(3.79)	(0.80-4.13)	(11.76)	(2.55–16.67)
Open fracture	145	43	1.21	33	1.11	10	1.46
	(14.00)	(16.41)	(0.83–1.75)	(15.64)	(0.74–1.67)	(19.61)	(0.72-2.98)

Note. S. aureus, Staphylococcus aureus; MSSA, methicillin-susceptible Staphylococcus aureus; MRSA, methicillin-resistant Staphylococcus aureus; BMI, body mass index; THC, tetrahydrocannabinol; HIV, human immunodeficiency virus.

because medical record documentation of mupirocin use was limited.

### Surgical site infections: descriptive analyses

We identified 34 SSIs (Table 2) after the 1,298 first procedures, for an overall rate of 2.62%. Of the SSI, 11 (32.35%) were superficial incisional, 13 (38.24%) were deep incisional, and 10 (29.41%) were organ space. The mean duration of clinical follow up was 361.09 days (15–1,292) for procedures complicated by any SSI and 250.43 days (0–1,254) for procedures without SSI. Overall, the follow up period after the initial procedure was 30 days or less for 163 patients (12.56%) and 90 days or less for 380 patients (29.28%).

Of the 34 SSIs, 28 (82.35%) occurred after the 1,040 first procedures among patients who were screened for *S. aureus* nasal carriage, for an SSI rate of 2.69%. Six SSIs occurred after 258 procedures among the 253 unscreened patients, for an SSI rate of 2.33% (P = .74; Figure 1). Eighteen of 34 (52.94%) SSIs were caused by *S. aureus* (9 MSSA, 8 MRSA, and 1 MSSA and MRSA). The rates

of all *S. aureus* SSI, MSSA SSI, and MRSA SSI were 1.39%, 0.77%, and 0.69%, respectively. Four (11.76%) SSIs were caused by gramnegative bacteria, 2 (5.88%) by coagulase-negative staphylococci species, and 5 (14.71%) were polymicrobial. Of the 5 (14.71%) SSIs that were not cultured, 4 (80.00%) were superficial and 1 was deep incisional. Seven of 9 (77.78%) MSSA SSI occurred in screened patients, only 1 of whom (11.11%) carried this organism. All 8 MRSA SSIs occurred among screened patients, 5 (62.50%) of which occurred in *S. aureus* carriers: 1 MSSA carrier and 4 MRSA carriers. The patient whose SSI was caused by both MSSA and MRSA did not carry either organism in her nares.

## Bivariable analysis of risk factors for surgical site infections

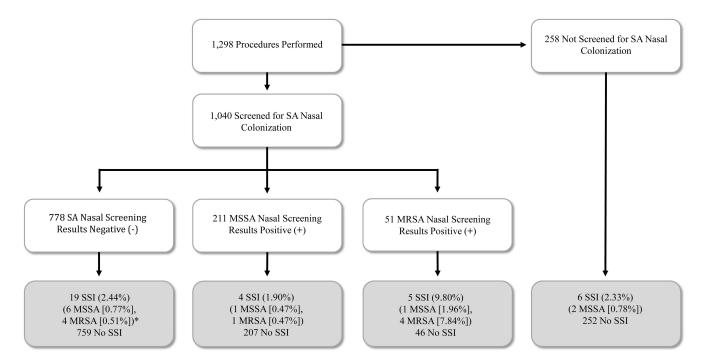
Bivariable analyses of data from the cohort of 1,298 first procedures found that neither the Gustilo-Anderson open fracture classification nor the ISS score were significantly associated with SSI (Table 2). Tobacco use, alcohol use disorder, and MRSA nasal carriage were significantly associated with SSI caused by any

Table 2. Bivariable analyses to identify variables associated with surgical site infections as defined by the National Healthcare Safety Network

No. (%)  57.89 (19-88)  31.70 (19.64-65.52)  16 (47.06)  22 (64.71)  6 (17.65)  2 (5.88)	Odds Ratio (95% CI)  1.01 (1.00-1.03)  1.04 (1.00-1.08)  0.78 (0.39-1.54)  2.18 (1.07-4.45)  4.38 (1.74-10.98)  0.99	No. (%)  58.28 (19-88)  34.82 (19.64-65.52)  6 (33.33)  11 (61.11)  2 (11.11)	Odds Ratio (95% CI) 1.02 (0.99-1.04) 1.07 (1.03-1.12) 0.44 (0.16-1.17) 1.85 (0.71-4.80)	No. (%) 61.56 (49-88) 38.38 (24.22-65.52) 4 (44.44) 5 (55.56)	Odds Ratio (95% CI) 1.02 (0.99-1.06) 1.10 (1.04-1.16) 0.71 (0.19-2.64)
(19-88) 31.70 (19.64-65.52) 16 (47.06) 22 (64.71) 6 (17.65) 2 (5.88)	(1.00-1.03) 1.04 (1.00-1.08) 0.78 (0.39-1.54) 2.18 (1.07-4.45) 4.38 (1.74-10.98)	(19-88)  34.82 (19.64-65.52)  6 (33.33)  11 (61.11) 2	(0.99-1.04) 1.07 (1.03-1.12) 0.44 (0.16-1.17) 1.85 (0.71-4.80)	(49–88) 38.38 (24.22–65.52) 4 (44.44) 5	(0.99–1.06) 1.10 (1.04–1.16) 0.71 (0.19–2.64)
(19.64–65.52)  16 (47.06)  22 (64.71)  6 (17.65)  2 (5.88)	(1.00–1.08) 0.78 (0.39–1.54) 2.18 (1.07–4.45) 4.38 (1.74–10.98)	(19.64–65.52)  6 (33.33)  11 (61.11)  2	(1.03-1.12) 0.44 (0.16-1.17) 1.85 (0.71-4.80)	(24.22–65.52) 4 (44.44) 5	(1.04–1.16) 0.71 (0.19–2.64)
(47.06)  22 (64.71)  6 (17.65)  2 (5.88)	(0.39-1.54) 2.18 (1.07-4.45) 4.38 (1.74-10.98)	(33.33) 11 (61.11) 2	(0.16–1.17) 1.85 (0.71–4.80)	(44.44)	(0.19-2.64)
(64.71) 6 (17.65) 2 (5.88)	(1.07-4.45) 4.38 (1.74-10.98)	(61.11)	(0.71-4.80)		1.46
(17.65) 2 (5.88)	(1.74–10.98)		2 41	(55.55)	(0.39-5.47)
(5.88)	0.00		(0.54–10.73)	0 (0.00)	-
	(0.23–4.21)	1 (5.56)	0.93 (0.12–7.10)	1 (11.11)	2.00 (0.25–16.16)
5 (14.71)	1.30	4	2.17	2	2.15
7	1.42	3	1.09	2	1.56 (0.32–7.54)
3	1.73	2	2.23	1	2.21 (0.27–17.92)
2	1.13	2	2.30	1	2.28 (0.28–18.49)
2	2.33	1	2.16	1	4.61 (0.56–37.93
2	1.02	0	-	0	-
3	1.11	1	0.67 (0.09–5.10)	0	-
	0.899	, versity	1.17		1.39 (0.72–2.66)
7 (20.59)		4 (22.22)	, ,,	1 (11.11)	,
19 (55.88)		7 (38.89)		4 (44.44)	
4 (11.76)		3 (16.67)		2 (22.22)	
4 (11.76)		4 (22.22)		2 (22.22)	
8 (23.53)	1.85 (0.83–4.16)	5 (27.78)	2.31 (0.81–6.54)	3 (33.33)	2.98 (0.74–12.04
4 (11.77)		4 (22.22)		2 (22.22)	
3 (8.82)		1 (5.56)		1 (11.11)	
1 (2.94)		0 (0.00)		0 (0.00)	
0 (0.00)		0 (0.00)		0 (0.00)	
3 (8.82)	2.13 (0.63–7.17)	1 (5.56)	1.26 (0.17–9.65)	0 (0.00)	-
22 (64.71)	0.37 (0.18–0.77)	11 (61.11)	0.32 (0.12–0.85)	5 (55.56)	0.26 (0.07–0.98)
9 (26.47)	2.74 (1.25–5.97)	6 (33.33)	3.77 (1.39–10.18)	4 (44.44)	5.98 (1.59–22.53
9 (26.47)	1.44 (0.66–3.12)	7 (38.89)	2.56 (0.98–6.66)	5 (55.56)	5.02 (1.34–18.83
4 (11.76)	0.68 (0.24–1.95)	2 (11.11)	0.64 (0.15–2.81)	1 (11.11)	0.64 (0.08–5.16)
5 (14.71)	4.57 (1.69–12.33)	5 (27.78)	10.32 (3.53–30.16)	4 (44.44)	21.14 (5.50–81.28
	(14.71)  7 (20.59)  3 (8.82)  2 (5.88)  2 (5.88)  3 (8.82)  7 (20.59)  19 (55.88)  4 (11.76)  4 (11.76)  8 (23.53)  4 (11.77)  3 (8.82)  1 (2.94)  0 (0.00)  3 (8.82)  22 (64.71)  9 (26.47)  4 (11.76)  5	(14.71)     (0.50-3.41)       7     1.42       (20.59)     (0.61-3.31)       3     1.73       (8.82)     (0.52-5.80)       2     1.13       (5.88)     (0.27-4.84)       2     2.33       (5.88)     (0.54-10.14)       2     1.02       (5.88)     (0.24-4.34)       3     1.11       (8.82)     (0.63-1.30)       7 (20.59)     19 (55.88)       4 (11.76)     8       8     1.85       (23.53)     (0.83-4.16)       4 (11.77)     3 (8.82)       1 (2.94)     0 (0.00)       3     2.13       (8.82)     (0.63-7.17)       22     0.37       (64.71)     (0.18-0.77)       9     2.74       (26.47)     (1.25-5.97)       9     1.44       (26.47)     (0.66-3.12)       4     0.68       (11.76)     (0.24-1.95)       5     4.57	(14.71)         (0.50-3.41)         (22.22)           7         1.42         3           (20.59)         (0.61-3.31)         (16.67)           3         1.73         2           (8.82)         (0.52-5.80)         (11.11)           2         1.13         2           (5.88)         (0.27-4.84)         (11.11)           2         2.33         1           (5.88)         (0.54-10.14)         (5.56)           2         1.02         0           (5.88)         (0.24-4.34)         (0.00)           3         1.11         1           (8.82)         (0.33-3.71)         (5.56)           0.899         (0.63-1.30)         4 (22.22)           19 (55.88)         7 (38.89)         4 (11.76)           4 (11.76)         3 (16.67)         4 (22.22)           19 (55.88)         7 (38.89)         4 (11.77)           4 (11.77)         4 (22.22)           8         1.85         5           (23.53)         (0.83-4.16)         (27.78)           4 (11.77)         4 (22.22)           3 (8.82)         1 (5.56)           1 (2.94)         0 (0.00)           0 (0.	(14.71)         (0.50-3.41)         (22.22)         (0.70-6.68)           7         1.42         3         1.09           (20.59)         (0.61-3.31)         (16.67)         (0.31-3.79)           3         1.73         2         2.23           (8.82)         (0.52-5.80)         (11.11)         (0.50-9.89)           2         1.13         2         2.30           (5.88)         (0.27-4.84)         (11.11)         (0.52-10.21)           2         2.33         1         2.16           (5.88)         (0.54-10.14)         (5.56)         (0.28-16.67)           2         1.02         0         -           (5.88)         (0.24-4.34)         (0.00)         -           3         1.11         1         0.67           (8.82)         (0.33-3.71)         (5.56)         (0.09-5.10)           0.899         1.17         (0.73-1.88)           7 (20.59)         4 (22.22)           19 (55.88)         7 (38.89)           4 (11.76)         3 (16.67)           4 (11.76)         4 (22.22)           8         1.85         5         2.31           (23.53)         (0.83-4.16)         (27.7	(14.71)         (0.50-3.41)         (22.22)         (0.70-6.68)         (22.22)           7         1.42         3         1.09         2           (20.59)         (0.61-3.31)         (16.67)         (0.31-3.79)         (22.22)           3         1.73         2         2.23         1           (8.82)         (0.52-5.80)         (11.11)         (0.50-9.89)         (11.11)           2         1.13         2         2.30         1           (5.88)         (0.52-4.84)         (11.11)         (0.52-10.21)         (11.11)           2         2.33         1         2.16         1           (5.88)         (0.54-10.14)         (5.56)         (0.28-16.67)         (11.11)           2         1.02         0         -         0         0           (5.88)         (0.24-4.34)         (0.00)         -         0         0         0         0         -         0

Note. Injury severity score, https://www.mdcalc.com/calc/1239/injury-severity-score-iss; S. aureus, Staphylococcus aureus; SSI, surgical site infection; MSSA, methicillin-susceptible Staphylococcus aureus; MRSA, methicillin-resistant Staphylococcus aureus; BMI, body mass index; THC, tetrahydrocannabinol.

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**Figure 1.** Study Population. Note. SA, *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; SSI, surgical site infection.\*Eighteen procedures had *S. aureus* surgical site infections. The figure includes 1 screened procedure twice because the patient was infected with both MRSA and MSSA.

organism (Table 2). Internal fixation alone was associated with a decreased risk of any SSI but staged internal fixation after external fixation was associated with an increased risk (Table 2).

When we controlled for open versus closed fracture, internal fixation alone was associated with a decreased odds of any SSI after procedures on closed fractures (OR 0.45; 95% CI 0.21–0.95), and staged internal fixation after external fixation was associated with an increased odds of any SSI (OR 2.29; 95% CI 1.02–5.16). In the cohort of 1,298 first procedures, higher BMI, internal fixation alone, staged internal fixation after external fixation, and MRSA nasal carriage were significantly associated with *S. aureus* SSI and with MRSA SSI. The bivariable analyses did not identify statistically significant risk factors for MSSA SSI (data not shown).

# Multivariable analysis of risk factors for surgical site infections

After we adjusted for clinically and statistically significant (see Supplemental Materials) variables, MRSA nasal carriage remained associated with SSI in the cohort of 1,298 first procedures. The odds ratios among MRSA carriers were 4.58 (95% CI 1.63–12.88) for any SSI, 10.11 (95% CI 3.25–31.42) for any *S. aureus* SSI, and 27.25 (95% CI 5.33–139.24) for MRSA SSI.

### Wound healing complications

We identified 47 wound healing complications (Supplemental Table 2) after the 1,298 first procedures, for an overall rate of 3.62%. Thirty-four (72.3%) wound healing complications met the NHSN SSI definition and 19 (40.43%) met the NHSN definition of *S. aureus* SSIs (9 MSSA, 9 MRSA, and 1 MSSA and MRSA). Thirty of 34 (72.34%) Clavien-Dindo grade 3b (required operative procedures under general anesthesia) wound healing complications and 2 of 4 (50%) Clavien-Dindo grade 2 (required pharmacological treatment including antibiotics) wound healing

complications met the NHSN SSI definition. The overall rates of *S. aureus*, MSSA, and MRSA wound healing complications were 1.46%, 0.77%, and 0.77%, respectively. Among the 13 patients with wound healing complications who did not meet the NHSN SSI definition, 12 received antibiotics, 3 had cellulitis, 3 had pin site infections, and 3 had erythema around their surgical wounds.

### **Discussion**

This investigation is one of the largest cohort studies assessing the incidence of *S. aureus* carriage among patients undergoing operative fixation of acute pelvis or extremity fractures. The 20.18% MSSA carriage rate among screened patients was similar to that in other surgical  $(20.2\%-30\%)^{1,9,21-24}$  and non-surgical populations.<sup>25,26</sup> The 4.70% MRSA carriage rate was somewhat higher than that among patients undergoing elective orthopedic operations  $(2.6\%)^{27}$  and those undergoing operations for orthopedic trauma at similar facilities (3%-3.9%).<sup>11,22</sup> Shaw et al. found that the MRSA carriage rate varied from 1.4% among patients with acute orthopedic trauma, to 12.5% among those with non-acute trauma (P=.01).<sup>11</sup> The results of our study and those by Shaw,<sup>11</sup> Saveli (3%),<sup>22</sup> and Shukla  $(3.2\%)^{13}$  suggest that the MRSA carriage rate among patients with orthopedic trauma is higher than that estimated for the general US population (1.5%).<sup>13,22,25</sup>

We obtained similar results with CDC's NHSN SSI definitions<sup>18,19</sup> and the Clavien-Dindo classification.<sup>20</sup> Rates of SSI and wound healing complications caused by MSSA and MRSA were nearly identical; the Clavien-Dindo classification identified 1 additional MRSA-associated wound healing complication. In addition, most patients with wound healing complications that did not meet NHSN SSI definitions were treated with antimicrobial agents.

*S. aureus* was the most common organism causing SSI in our study population. *S. aureus* (1.39%), MSSA (.77%), and MRSA SSI (.69%) rates were similar to rates reported in literature.<sup>2,12</sup>

However, other investigators have reported MRSA SSI rates after fracture fixation surgery as high as 32%–46.5% among patients with complex injuries. <sup>1,2</sup> In addition to differences in injury severity and type, differences in the patient populations and the studies' SSI definitions may help account for variation in the rates of SSI caused by MRSA. <sup>1,2</sup>

We found that MRSA colonization was associated with any SSI, *S. aureus* SSI, and MRSA SSI after operative fracture fixation. Other investigators also have found an association between MRSA colonization and MRSA SSI. For example, Shukla et al. found that patients colonized with MRSA were 2.5 times more likely to acquire *S. aureus* SSI than were non-colonized patients. Stevens et al. found that MRSA carriers were significantly more likely to acquire skin infections than were MSSA carriers. A systematic review of 10 observational studies found that MRSA colonization was associated with a 4-fold increase in the risk of infection compared with MSSA colonization. However, the authors noted that the reason for this difference has not been elucidated.

None of the injury severity indicators we evaluated were associated with a statistically significant increased risk of any SSI. Of the surgical variables evaluated, only staged external fixation followed by internal fixation was associated with any SSI, *S. aureus* SSI, and MRSA SSI. The increased incidence of SSI in patients undergoing staged internal fixation may be explained by selection bias. Orthopedic trauma surgeons are more likely to perform external fixation followed by delayed internal fixation for injuries with greater skeletal and soft tissue injury, though increased injury severity as assessed by the ISS was not associated with SSI. This finding indicates that we should further investigate the effect of delayed internal fracture fixation on SSI risk.

After we controlled for multiple patient variables, MRSA carriage was the only modifiable risk factor associated with SSI in our cohort. In 2009, the American Academy of Orthopaedic Surgeons Patient Safety Committee stated that orthopedic surgeons should consider preoperative screening for MRSA carriage in patients treated with implants.<sup>30</sup> Despite the available data and recommendations, two surveys have shown that practice varies substantially.<sup>31,32</sup> Even though *S. aureus* is an important cause of SSI among patients with orthopedic trauma, screening, and decolonization programs are uncommon and logistically difficult in this patient population.

Our *S. aureus* decolonization protocol was similar to those used before elective orthopedic surgery. We screened about 80% of our patients, which is slightly higher than the 71% Shaw et al. achieved. Although roughly 90% of known *S. aureus* carriers had chlorhexidine baths documented, only about 45% had at least 1 dose of intranasal mupirocin documented. In comparison, 55.2% of known *S. aureus* carriers in our previous study of patients undergoing cardiac operations or total joint replacement had at least three doses of intranasal mupirocin and 85.5% bathed with chlorhexidine. In addition, many *S. aureus* carriers in our study did not receive the recommended perioperative prophylaxis.

Previous studies have shown that *S. aureus* carriage increases the risk of SSI among patients with orthopedic trauma. <sup>13,22</sup> Our study provides preliminary evidence that MRSA carriage may increase the risk of MRSA SSI after operative fracture fixation. Our prior study demonstrated that treatment of *S. aureus* carriers significantly reduced the incidence of *S. aureus* SSI among patients undergoing cardiac operations or total knee and hip arthroplasty. <sup>33</sup> Fewer than 5% of patients in that trial who underwent urgent or emergent procedures used mupirocin and chlorhexidine, which highlights the challenges of decolonizing *S. aureus* carriers before unplanned operations. <sup>33</sup> Our

current study demonstrated that screening patients with orthopedic trauma for S. aureus nasal carriage was feasible but also found that the full 5-day intranasal mupirocin decolonization protocol could not be completed before surgery given the limited time between the injuries and surgical procedures. Given the difficulty of implementing the full mupirocin decolonization protocol and the potentially serious consequences of S. aureus SSI after operative fixation procedures, patients could benefit from a simpler decolonization protocol. For example, quasi-experimental studies of cleansing patients' skin with chlorhexidine before their operations and treating all patients with intranasal povidone iodine decreased the rate of all SSIs among patient undergoing elective orthopedic hardware implantation. <sup>10,34</sup> A single-center retrospective study among patients undergoing orthopedic trauma operations found that the overall S. aureus SSI rate decreased from 1.1% (2 MSSA SSI; 8 MRSA SSI) in the preintervention group to 0.2% (2 MSSA SSI) in the povidone-iodine treated group. 12 Maslow et al. found that patients who used intranasal povidone iodine had fewer side effects than those who used intranasal mupirocin.35 Povidone iodine can be applied as a single dose immediately before the procedure, and it has not caused resistance. Thus povidone-iodine use would eliminate noncompliance and the need to screen patients, the two major barriers to implementation of the intranasal mupirocin protocol.

### Limitations

We were unable to screen about 20% of eligible patients, which may have decreased the power to find an association between *S. aureus* carriage and SSI. In addition, we screened patients' nares, but we did not screen other sites for *S. aureus*. <sup>26,36</sup> Thus, we may have misclassified patients who were colonized with *S. aureus* at extra-nasal sites as non-colonized. Despite including nearly 1,300 procedures, the confidence interval was very large for the association of MRSA carriage with MRSA SSI and the power was not adequate to assess whether decolonization decreased *S. aureus* SSI.

### **Conclusion**

S. aureus was the most common cause of SSI among patients with orthopedic trauma. Although MSSA carriage was over 4 times more common than MRSA carriage, MRSA SSIs were nearly as common as MSSA SSIs. Moreover, MRSA nasal colonization was the only modifiable risk factor associated with MRSA SSI. Given the consequences of SSI in patients who undergo operative fixation of fractures, patient outcomes could be improved with a simple, rapid, and effective S. aureus decolonization protocol that can be completed in the limited time before surgical fixation. We need prospective studies to better evaluate the effectiveness of rapid decolonization protocols with agents such as povidone iodine.

**Supplementary material.** The supplementary material for this article can be found at https://doi.org/10.1017/ice.2024.233

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