G8: Should prophylactic antibiotics be altered for patients who are carriers of methicillin-resistant *Staphylococcus aureus* (MRSA)?

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Response/Recommendation:
Yes. Patients who are carriers of methicillin-resistant *Staphylococcus aureus* (MRSA) should receive an additional antibiotic with activity against MRSA in addition to cephalosporin.

Level of evidence: Limited

Delegate Vote:

Rationale:

Perioperative antibiotic prophylaxis is critical for reducing the risk of periprosthetic joint infections (PJI) and surgical site infections (SSI) in orthopaedic and spinal surgeries (1). Studies have explored the efficacy of combining vancomycin and cefazolin, particularly for preventing methicillin-resistant *Staphylococcus aureus* (MRSA) infections (2). While the addition of vancomycin to cefazolin was not superior to cefazolin and placebo in the prevention of surgical site infection in a population with low prevalence of MRSA colonization (3), the optimal antibiotic regimen that balances efficacy and potential adverse effects in MRSA carriers remains an active area of research.

This systematic review began with an initial screening of 482 article titles and abstracts from PubMed and Web of Science, resulting in 117 relevant studies. After full-text evaluation, 52 studies met the inclusion criteria, with 14 studies selected for data extraction and detailed analysis (4-17) (**Table 1**). There was no study that definitively assessed outcomes in confirmed MRSA carrier patients. Our meta-analysis found that cefazolin alone significantly reduces MRSA infections compared to non-cefazolin regimens ($P < 0.001$) (**Figure 1**). The combination of vancomycin and cefazolin provides superior protection, significantly lowering MRSA infection rates compared to cefazolin alone ($P = 0.002$) (**Figure 2**).

Three studies were not included in our meta-analysis:

1. **Takeuchi et al.** (15)**:** Compared topical vancomycin versus ampicillin in patients undergoing thoracic and/or lumbar fusions. Infection with MRSA occurred in one patient (out of 114) in the ampicillin group, with no MRSA cases reported in the vancomycin group.
2. **Choi et al.** (16)**:** Compared sulfamethoxazole/trimethoprim plus cefazolin or vancomycin (84 patients) versus cefazolin or vancomycin alone (511 patients) in spinal surgery. MRSA infection occurred in one patient in each group.
3. **Kanellakopoulou et al.** (17)**:** Compared teicoplanin (278 patients) versus second-generation cephalosporins, β-lactam/β-lactamase inhibitors, or ciprofloxacin (338 patients) in total hip/knee arthroplasty. MRSA infection was identified in one patient in the teicoplanin group and two in the comparison group (**Table 1**).

Conclusion:

The combination of vancomycin and cefazolin appears to offer superior protection against MRSA infections in orthopaedic and spinal surgeries compared to cefazolin alone. It is

worth noting that most included studies were retrospective cohort studies, and only a few randomized controlled trials were conducted. Moreover, since there are major variations in the patient population, interventions, types of orthopaedic procedures, and outcomes among included studies, it is hard to conclude that adding anti-MRSA agents or switching to anti-MRSA agents would be better than a traditional regimen of surgical antimicrobial prophylaxis (i.e., cefazolin) for MRSA carriers undergoing orthopaedic procedures. The potential risks of dual prophylaxis, such as increased antibiotic resistance and nephrotoxicity, must also be carefully considered. Given the absence of studies specifically addressing confirmed MRSA carriers, further high-quality research is essential to develop definitive guidelines for antibiotic prophylaxis in this patient population.

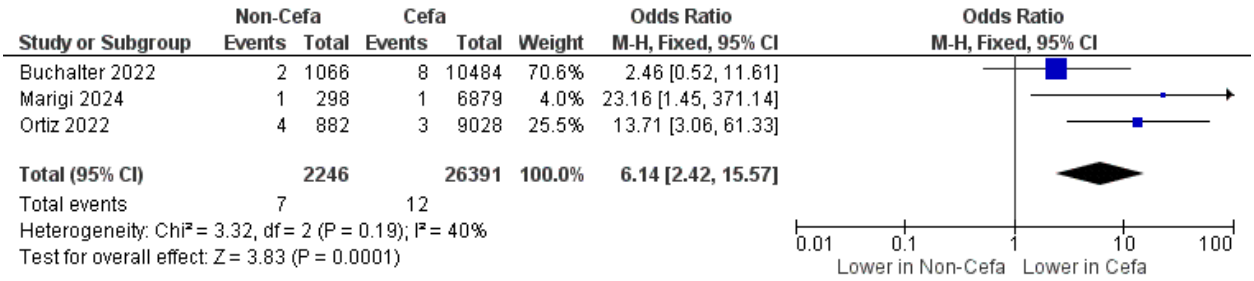

Figure 1. MRSA infections in non-cefazolin vs Cefazolin

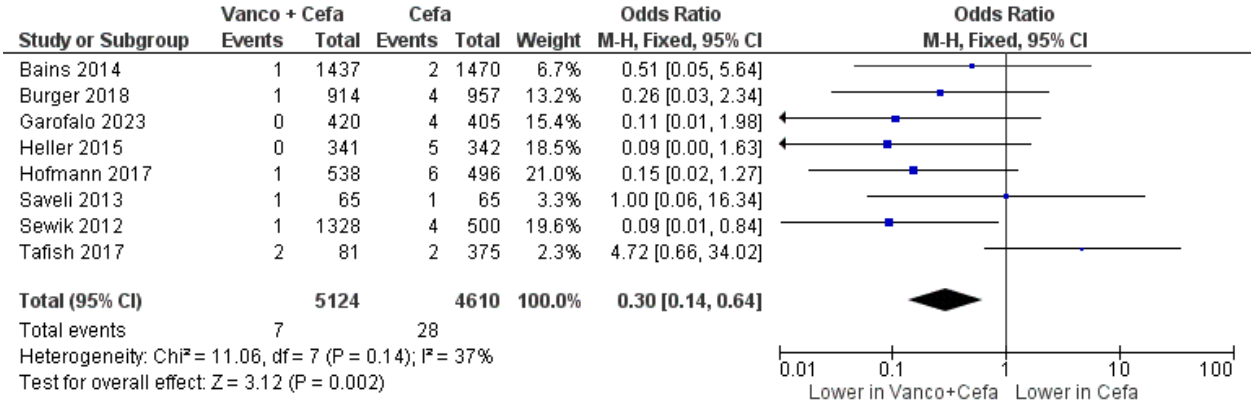

Figure 2. MRSA spell out infections in Vancomycin plus Cefazolin versus Cefazolin

Table 1. Included Studies

Author	**Year**	**Country**	**Type of Procedure**	**CASE**	**Control**	**Sample size**		**Mean age (SD)**		**Gender(M%)**		**MRSA**	
						Case	Control	Case	Control	Case	Control	Case	Control
Heller	2015	USA	posterior instrumented spinal arthrodesis	Vancomycin + Cefazolin	Cefazolin	342	341	55.3 (19.1)	49.1 (20.9	45.3	49.3	0	5(1.5)
Burger	2018	USA	THA,TKA	Vancomycin + Cefazolin	Cefazolin	914	957	59.10 (11.55)	60.31(11.49)	43.04	41.8	1	4
Kanellakopoulou	2008	Greece	THA, TKA	Teicoplanin	second-generation cephalosporin	278	338	67.40(10.74)	70.69(8.01)	25.17	21.79	1	2

					B lactams/ B lactamase inhibitor sciprofloxacin								
Ortiz	2014	USA	THA	vancomycin or clindamycin	Cefazolin	882	9028			294(33)	4071 (45.1)	2	8
Choi	2021	USA	Spinal surgery	sulfamethoxazole/trimethoprim + cefazolin or vancomycin	cefazolin or vancomycin	84	511	62	60.8	44.5	43.4	1	1
Sewick	2012	USA	TJA	Vancomycin + Cefazolin	Cefazolin	1328	500	60.6 (12.5)	59.6 (12.0)	36	44	1	4
Bains	2024	USA	TJA	Vancomycin + Cefazolin	Cefazolin	1,437	1,470	62	62	44	46	1	2
Takeuchi	2018	Japan	thoracic and/or lumbar fusions	Vancomycin	Ampicillin	116	114	66(14)	68(14)	52.58	38.59	0	1
Saveli	2013	USA	Open Fracture Surgery	Vancomycin + Cefazolin	Cefazolin	65	65	40(16)	42(18)	78	66	1	1
Hofmann	2017	USA	THA, TKA	Vancomycin + Cefazolin	Cefazolin	538	496	61.5(11.6)	60.6(12.3)	43.75	39.77	1	6

Marigi	2024	USA	TSA	Vancomycin	Cefazolin	298	6879	69.5(11.4)	68.6 (11.5)	41.6	49.2	1	1
Tafish	2017	USA	Spinal surgery	Vancomycin	Non vancomycin	81	375	50	45	58	66.4	2	2
Garofalo	2023	Italy	TSA	Vancomycin + Cefazolin	Cefazolin	420	405	73(7)	71(7)	31.4	28.6	0	4
Buchalter	2022	USA	TKA	clindamycin and/or vancomycin	Cefazolin	1,066	10484	65.14 (10.2)	65.6 (9.6)	22.8	32.8	4	3

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