# Activity of Oritavancin and Comparator Agents Against Coagulase-Negative Staphylococci Causing Bloodstream Infections in US Medical Centers (2017-2019)

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### Introduction

- Coagulase-negative staphylococci (CoNS) is a common organism group implicated in catheter-related bloodstream infection (BSI) and infective endocarditis.
- Resistance to oxacillin and other  $\beta$ -lactams is widespread among CoNS associated with human infections, restricting therapeutic options mainly to the glycopeptides.
- Prompt appropriate antimicrobial therapy is crucial for suspected or confirmed invasive infections.
- Oritavancin is a lipoglycopeptide agent with a prolonged half-life and concentration-dependent bactericidal activity against clinically relevant Grampositive pathogens.
- The aim of this study was to assess the *in vitro* activity of oritavancin and comparator agents against CoNS causing BSI in US medical centers.

# Methods

- A total of 587 CoNS isolates were consecutively collected during 2017–2019 as part of the SENTRY Antimicrobial Surveillance Program.
- A single isolate per patient was collected in 30 US medical centers located in all 9 US Census Divisions.
- Only isolates determined to be significant by local criteria as the reported probable cause of infection were included in the program.
- Bacterial identification was performed by MALDI-TOF (Bruker Daltonics, Billerica, Massachusetts, USA).
- Antimicrobial susceptibility testing was performed using CLSI broth microdilution methodology in a central laboratory (JMI Laboratories).
- CLSI breakpoints were applied for comparator agents.
- The oritavancin susceptible breakpoint for S. aureus (≤0.12 mg/L) was only used for *in vitro* comparison.

Table 1. Distribution of coagulase-negative Staphylococcus spp. causing BSI in medica
centers (2017–2019)

centers (2017–2019)		
Organisms	No. of isolates	%
S. epidermidis	366	62.4%
S. hominis	77	13.1%
S. capitis	43	7.3%
S. lugdunensis	30	5.1%
S. haemolyticus	25	4.3%
S. pettenkoferi	9	1.5%
S. warneri	8	1.4%
S. simulans	7	1.2%
S. cohnii	6	1.0%
S. auricularis	3	0.5%
S. pseudintermedius	3	0.5%
S. saprophyticus	3	0.5%
S. schleiferi	2	0.3%
S. caprae	1	0.2%
S. pasteuri	1	0.2%
S. sciuri	1	0.2%
Staphylococcus spp.	2	0.3%
Total	587	100.0%

### Results

- The most common species was S. epidermidis (62.4%; 366 isolates) followed by S. hominis (13.1%; 77), S. capitis (7.3%; 43), S. lugdunensis (5.1%; 30), and S. haemolyticus (4.3%; 25). See Table 1. -12 other species included <10 (1.5%) isolates each.
- Overall, 59.1% of isolates were methicillin-resistant (MR). - The highest rate of MR isolates were S. epidermidis (73.2%), followed by S. haemolyticus (68.0%), S. hominis (46.8%), and S. capitis (30.2%; Figure 1). – No MR S. lugdunensis isolate was detected.
- Oritavancin (MIC<sub>50/90</sub>, 0.06/0.12 mg/L) inhibited 96.1% of CoNS at  $\leq$ 0.12 mg/L (Table 2; Figure 2). - Linezolid (MIC<sub>50/90</sub>, 1/1 mg/L; 96.4% susceptible [S]), daptomycin (MIC<sub>50/90</sub>, 0.25/0.5 mg/L; 100%S), and vancomycin (MIC<sub>50/90</sub>, 1/2 mg/L; 100%S) were also active against CoNS.
- Oritavancin displayed similar MIC<sub>50</sub> (0.03–0.06 mg/L) and MIC<sub>90</sub> (0.12–0.25 mg/L) values against S. epidermidis (95.9%S at ≤0.12 mg/L), S. hominis (96.1%S), S. capitis (97.7%S), and S. haemolyticus (84.0%S; Table 2; Figure 2).
- Vancomycin, daptomycin, and linezolid inhibited 100.0%, 100.0%, and 93.9% of MR-CoNS isolates at their susceptible breakpoints, respectively (Figure 3).

### Table 2. Activity of oritavancin and comparators against CoNS causing BSI in US medical centers

Organism grou (no. of isolate

All CoNS (587) MRCoNS (347 5. epidermidis MR-S. epiderma

10 isolates per species); organism included: S. pettenkoferi (9); S. warneri (8); S. simulans (7); S. cohnii (6); S. auricularis (3); S. pseudintermedius (3); S. saprophyticus (3); S. schleiferi (2); S. caprae (1); S. pasteuri (1); S. sciuri (1); and Staphylococcus spp. (2). Organism included: S. pettenkoferi (3); S. warneri (2); S. simulans (1); S. cohnii (4); S. saprophyticus (1); S. caprae (1); and S. sciuri (1).

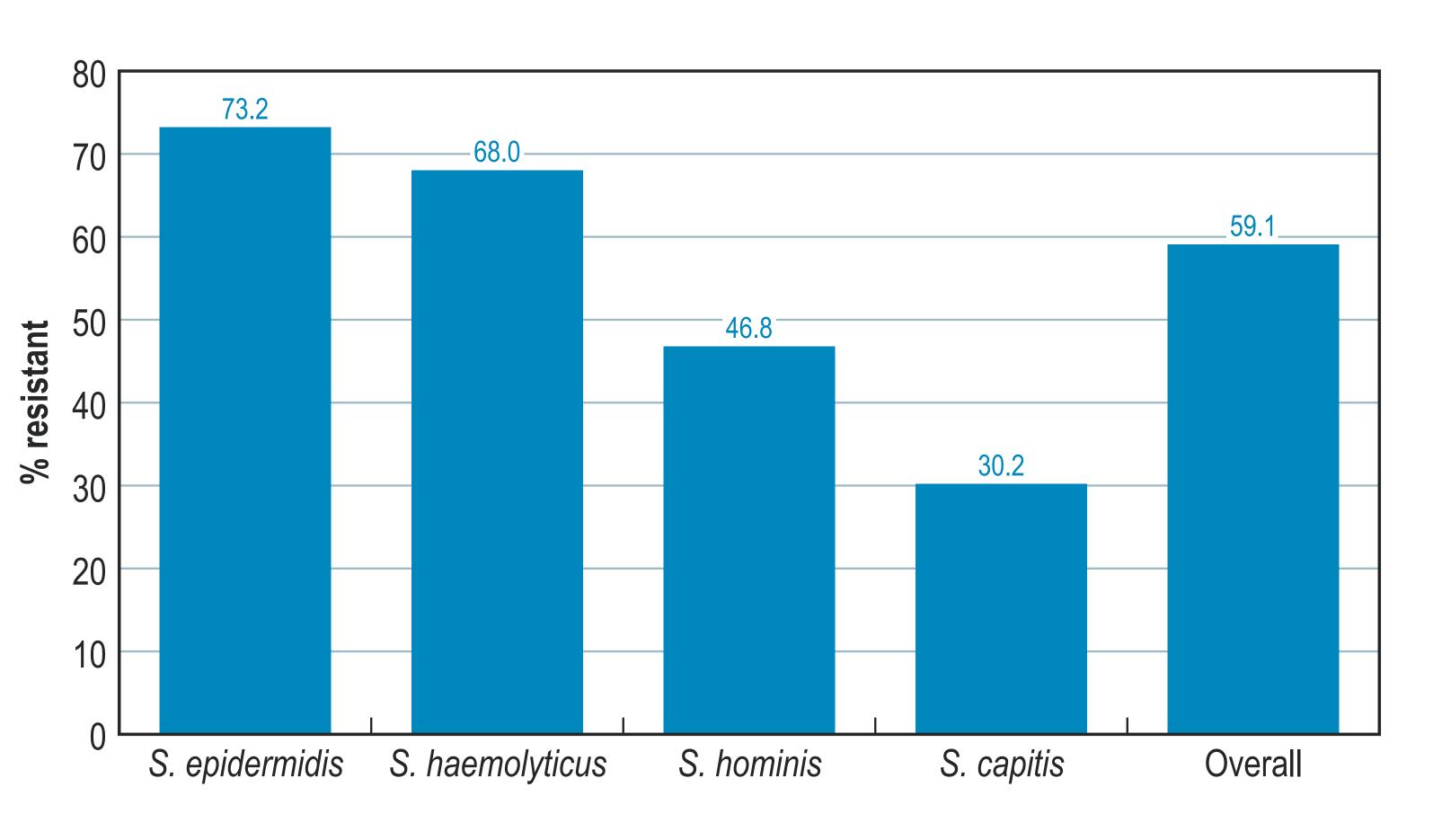
- All S. *lugdunensis* isolates were inhibited by oritavancin at  $\leq 0.015$  mg/L.
- Oritavancin inhibited 94.8% of all MR-CoNS at ≤0.12 mg/L.
- Oritavancin inhibited 95.5%, 94.4%, 92.3%, and 82.4% of MR S. epidermidis, S. hominis, S. capitis, and S. haemolyticus, respectively (Figure 3).

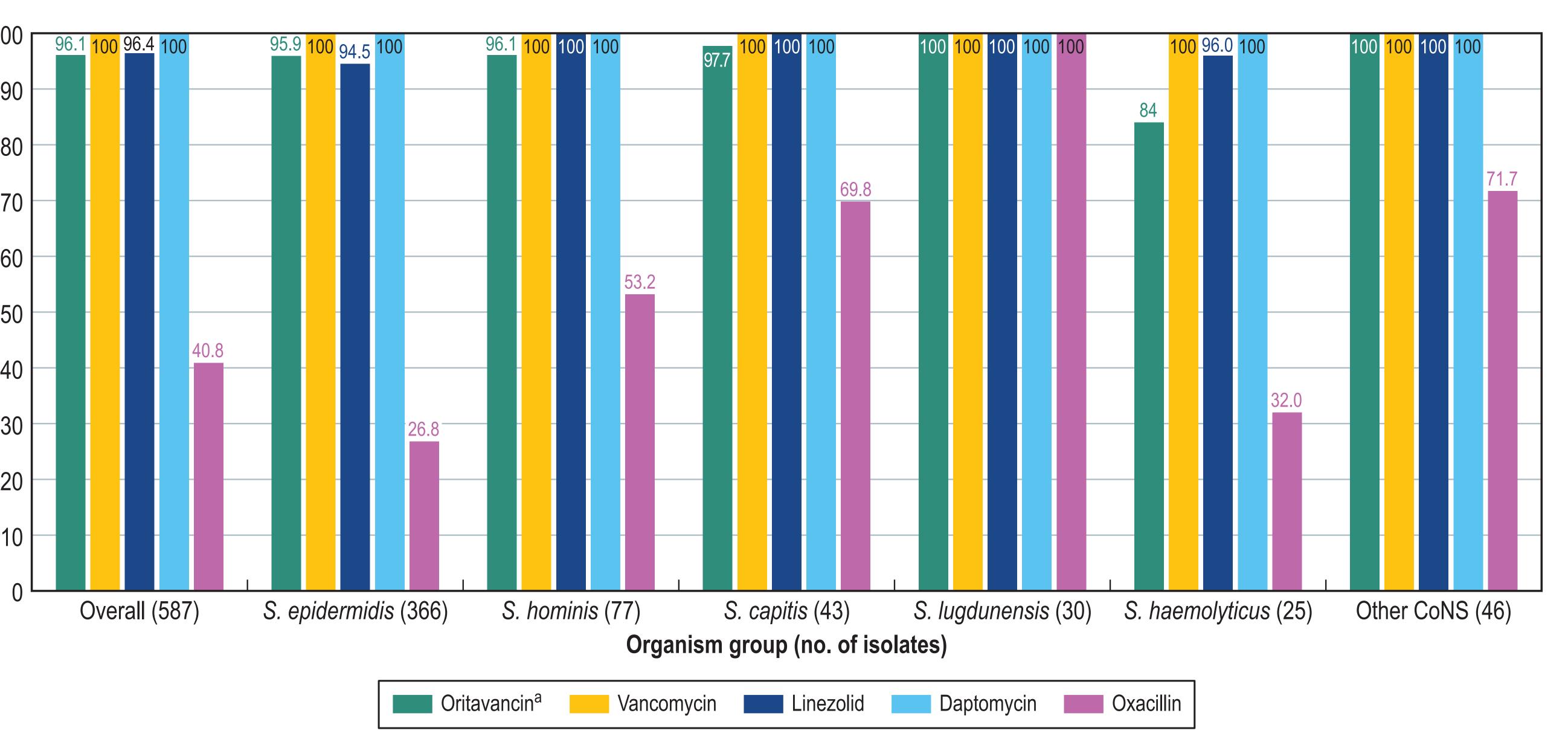
medical centers s	tratifi	ed by a	specie	es and	meth	icillin	resist	ance				
Organism group (no. of isolates)	Oritavancin		Vancomycin		Linezolid			Daptomycin				
	MIC <sub>50</sub>	MIC <sub>90</sub>	CLSI <sup>a</sup> %S	MIC <sub>50</sub>	MIC <sub>90</sub>	CLSI %S	MIC <sub>50</sub>	MIC <sub>90</sub>	CLSI %S	MIC <sub>50</sub>	MIC <sub>90</sub>	CLSI %S
All CoNS (587)	0.06	0.12	96.1	0.06	0.12	100.0	0.06	0.12	96.4	0.06	0.12	100.0
MRCoNS (347)	0.06	0.12	94.8	2	2	100.0	1	2	93.9	0.25	0.5	100.0
S. epidermidis (366)	0.06	0.12	95.9	2	2	100.0	1	1	94.5	0.25	0.5	100.0
MR-S. epidermidis (268)	0.06	0.12	95.5	2	2	100.0	1	1	92.5	0.25	0.5	100.0
S. hominis (77)	0.03	0.12	96.1	1	1	100.0	1	2	100.0	0.25	0.25	100.0
MR-S. hominis (36)	0.03	0.12	94.4	1	2	100.0	1	2	100.0	0.25	0.25	100.0
S. capitis (43)	0.03	0.12	97.7	1	1	100.0	1	1	100.0	0.5	0.5	100.0
MR-S. capitis (13)	0.06	0.12	92.3	1	2	100.0	1	1	100.0	0.5	0.5	100.0
S. lugdunensis (30)	0.008	0.015	100.0	0.5	1	100.0	0.5	1	100.0	≤0.12	0.25	100.0
S. haemolyticus (25)	0.03	0.25	84.0	1	2	100.0	1	2	96.0	0.25	0.5	100.0
MR-S. haemolyticus (17)	0.06	0.25	82.4	1	2	100.0	1	2	94.1	0.25	0.5	100.0
other CoNS (46) <sup>b</sup>	0.03	0.03	100.0	0.03	0.03	100.0	0.03	0.03	100.0	0.03	0.03	100.0
MR- other CoNS (13)°	0.03	0.03	100.0	1	2	100.0	1	2	100.0	0.5	1	100.0

Figure 1. Methicillin resistance rates in CoNS isolates causing BSI in US medical centers (2017 - 2019)

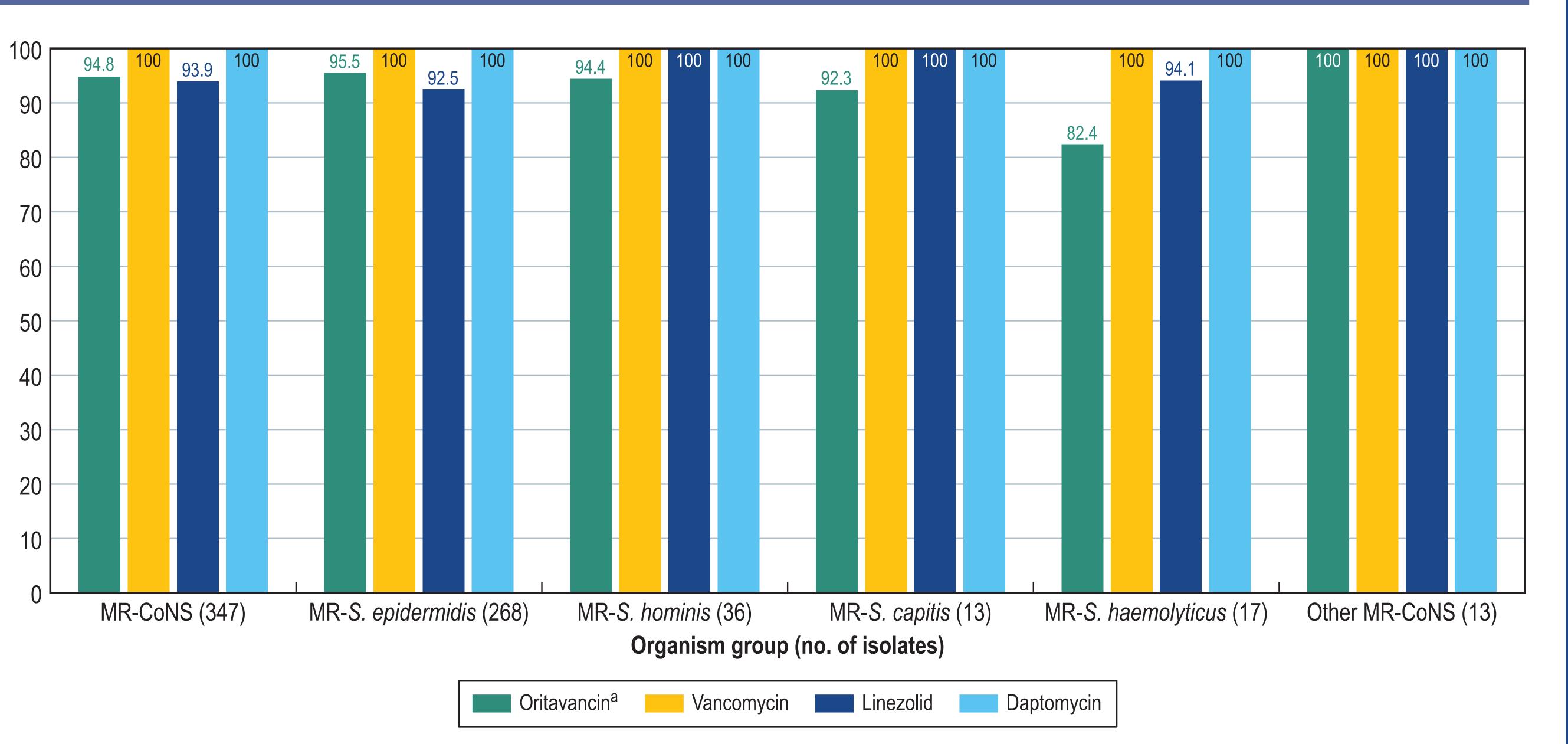
Figure 2. Susceptibility rates of oritavancin and comparators against CoNS stratified by species

Figure 3. Susceptibility rates of oritavancin and comparators against MR-CoNS causing BSI in





<sup>a</sup> The oritavancin susceptible breakpoint published for S. aureus ( $\leq 0.12$  mg/L) was applied to all CoNS isolates (CLSI, 2022).



<sup>a</sup> The oritavancin susceptible breakpoint published for S. aureus (≤0.12 mg/L) was applied to all CoNS isolates (CLSI, 2022).

# Conclusions

- In this collection, 5 species of CoNS caused >90% of all BSI in US medical centers during 2017–2019: S. epidermidis, S. hominis, S. capitis, S. lugdunensis, and S. haemolyticus.
- Overall, oritavancin was highly active and inhibited  $\geq$ 94% of CoNS at  $\leq$ 0.12 mg/L (regardless of methicillin profile).
- Oritavancin displayed  $\geq$ 95% susceptibility at  $\leq$ 0.12 mg/L against S. epidermidis, S. hominis, S. capitis, and S. lugdunensis, and inhibited all S. haemolyticus at  $\leq 1 \text{ mg/L}.$
- The MR rate was elevated overall (59.1%) and varied by CoNS species. – S. epidermidis displayed the highest (73.2%) MR rate.
- Vancomycin, daptomycin, and linezolid were also active against CoNS causing BSI in US medical centers.

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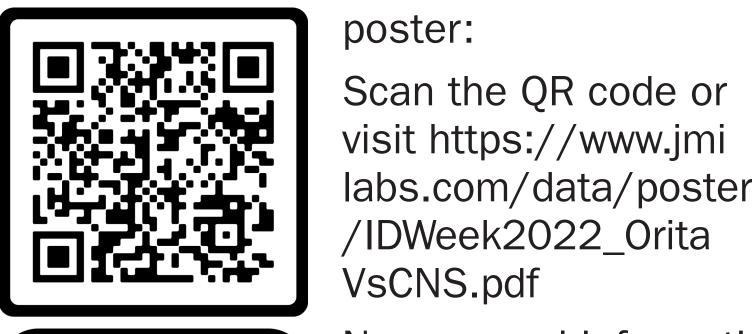
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