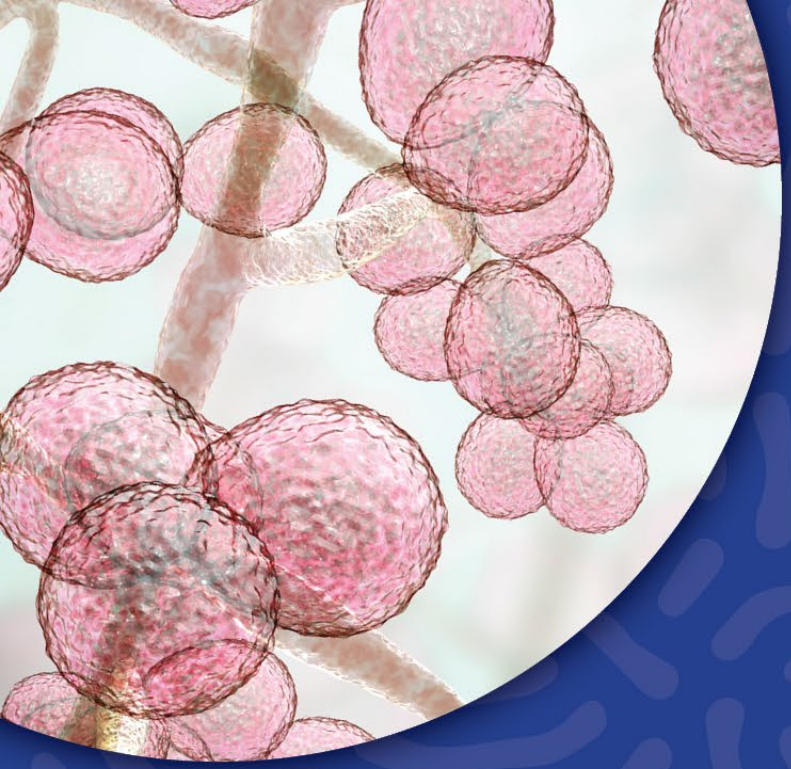

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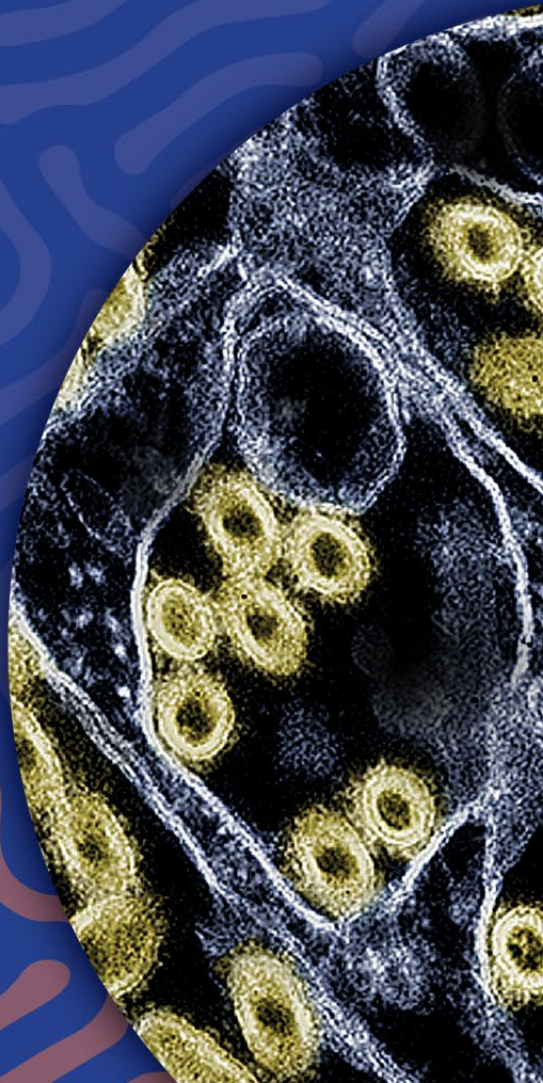

Genomic basis for antibiotic resistance in clinical *Staphylococcus saprophyticus* strains

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Robert Potter, PhD, D(ABMM)

Assistant Director
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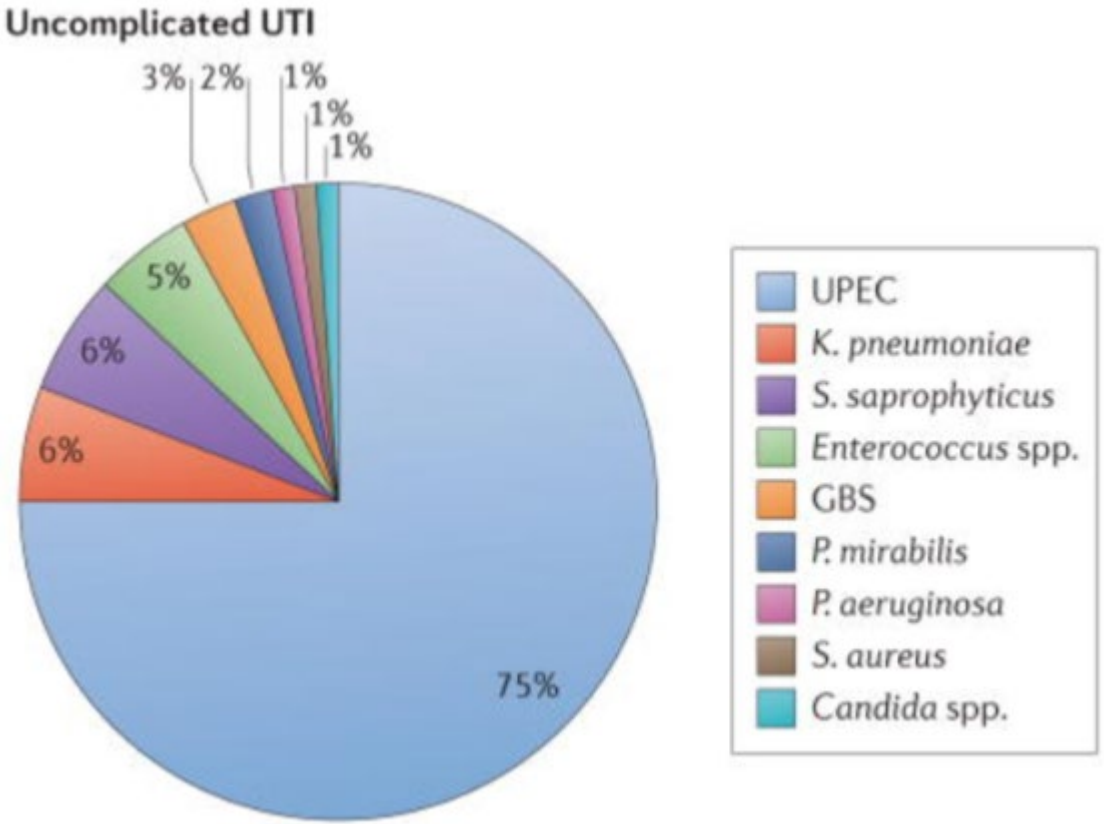
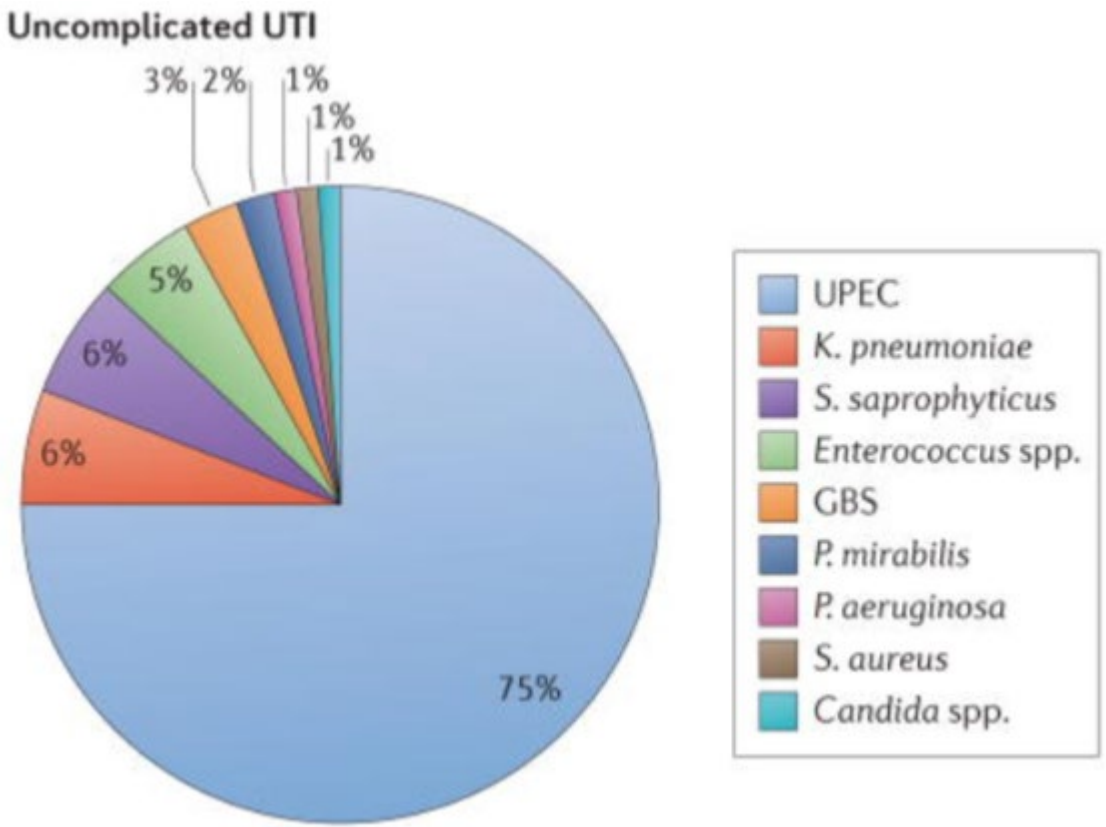
Assistant Professor
Department of Pathology & Laboratory Medicine
The Perelman School of Medicine at the University of Pennsylvania

S. saprophyticus is one of the most common causes of uncomplicated urinary tract infections (UTIs)



PMID: 25853778

S. saprophyticus has a specific association with UTIs in young women



Article

December 9, 1983

Urinary Tract Infections in Young Adult Women Caused by Staphylococcus saprophyticus

Robert H. Latham, MD; Kate Running, WHCS; Walter E. Stamm, MD

» Author Affiliations

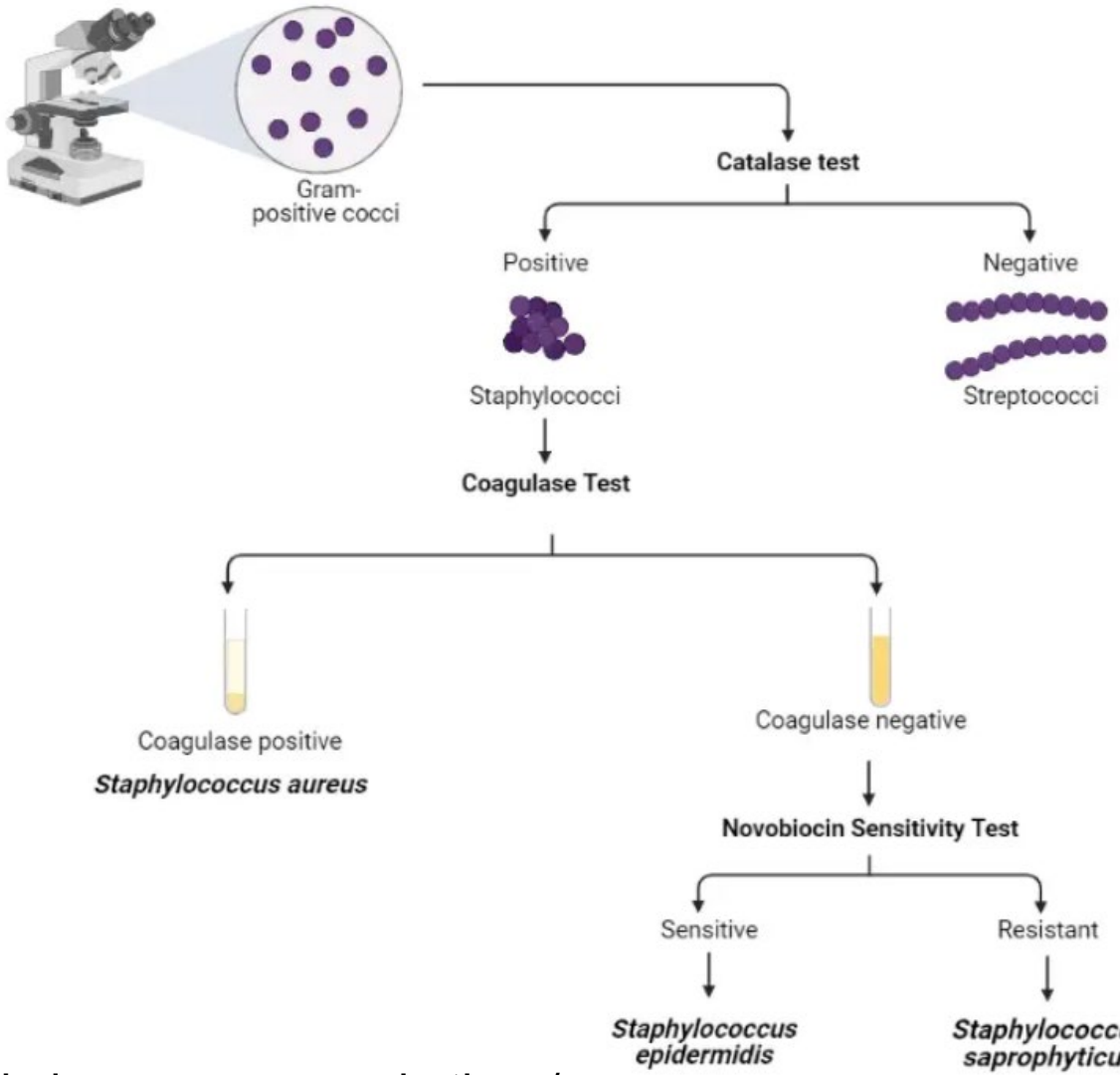
JAMA. 1983;250(22):3063-3066. doi:10.1001/jama.1983.03340220031028

Abstract

We evaluated and compared 81 urinary tract infections (UTIs) with *Staphylococcus saprophyticus* occurring in 72 college women with *Escherichia coli* UTIs. During the 14-month study period, *S saprophyticus* was the second most common cause of UTIs, accounting for 11% of the total. *Staphylococcus saprophyticus* infections occurred more frequently during the late summer and early fall. Age, history of previous UTI, signs and symptoms of infection, and findings on urinalysis were similar in patients with *S saprophyticus* and *E coli* infections. Nine (41%) of 22 *S saprophyticus* infections were localized to the upper urinary tract by the antibody-coated bacteria technique compared with 18 (16%) of 115 infections with *E coli* (*P*=.01). Rectal, vaginal, and urethral colonization with *S saprophyticus* was associated with UTI caused by these organisms, suggesting that their pathogenesis resembles that of *E coli* UTIs. In vitro susceptibility testing showed almost uniform sensitivity of *S saprophyticus* to most antimicrobials used to treat UTIs, but recurrent infections occurred in six of the 72 women despite adequate therapy. Physicians and microbiologists must be aware that *S saprophyticus* is an important cause of UTIs in young women.

PMID: 25853778

S. saprophyticus can be differentiated in the pre-MALDI era from other by novobiocin resistance



https://microbeonline.com/staphylococcus-saprophyticus/

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Identification of *Staphylococcus* isolates to species level is important for antibiotic susceptibility interpretation

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In Vitro Antimicrobial Susceptibility of *Staphylococcus pseudintermedius* Isolates of Human and Animal Origin

Romney M. Humphries,[a] Max T. Wu,[b] Lars F. Westblade,[c] Amy E. Robertson,[d] Carey-Ann D. Burnham,[e] Meghan A. Wallace,[e] Eileen M. Burd,[f,g] Sara Lawhon,[h] Janet A. Hindler[a]

UCLA David Geffen School of Medicine, Los Angeles, California, USA[a]; Landstuhl Regional Medical Center, Landstuhl, Germany[b]; Weill Cornell Medical College, New York, New York, USA[c]; New York-Presbyterian Hospital, Weill Cornell Medical Center, New York, New York, USA[d]; Washington University School of Medicine, St. Louis, Missouri, USA[e]; Emory University School of Medicine, Atlanta, Georgia, USA[f]; Emory Antibiotic Resistance Center, Atlanta, Georgia, USA[g]; Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, Texas, USA[h]

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Evaluation of Surrogate Tests for the Presence of *mecA*-Mediated Methicillin Resistance in *Staphylococcus capitis*, *Staphylococcus haemolyticus*, *Staphylococcus hominis*, and *Staphylococcus warneri*

Romney M. Humphries,[a] Paul Magnano,[b] Carey-Ann D. Burnham,[c] Jennifer Dien Bard,[d,e] Tanis C. Dingle,[f] Katrina Callan,[g] Lars F. Westblade,[g] the Coagulase Negative Staphylococcus *Ad Hoc* Working Group

[a]Department of Pathology, Microbiology and Immunology, Vanderbilt University Medical Center, Nashville, Tennessee, USA
[b]Accelerate Diagnostics, Tucson, Arizona, USA
[c]Department of Pathology and Immunology, Washington University in St. Louis School of Medicine, St. Louis, Missouri, USA
[d]Department of Pathology and Laboratory Medicine, Children's Hospital of Los Angeles, Los Angeles, California, USA
[e]Keck School of Medicine, University of Southern California, Los Angeles, California, USA
[f]Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Alberta, Canada
[g]Department of Pathology and Laboratory Medicine, Weill Cornell Medicine, New York, New York, USA

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CLSI footnote specifies you should not perform susceptibility testing on urine isolates due to routine susceptibility

Table 2C
Staphylococcus spp.
M02 and M07

Table 2C. Zone Diameter and MIC Breakpoints for *Staphylococcus* spp.

(5) Routine testing of urine isolates of *Staphylococcus saprophyticus* is not advised, because infections respond to concentrations achieved in urine of antimicrobial agents commonly used to treat acute, uncomplicated UTIs (eg, nitrofurantoin, trimethoprim - sulfamethoxazole, or a fluoroquinolone).

CLSI footnote specifies you should not perform susceptibility testing on urine isolates due to routine susceptibility

Gap in knowledge on *S. saprophyticus*:

-Best surrogate/breakpoint for methicillin resistance

-Prevalence of non-β-lactam antibiotic resistance and antibiotic resistance genes

Hypothesis:

-Cefoxitin and "*S. epidermidis*" breakpoints will perform best

-Antibiotic resistance will be rare

Created an international cohort of *S. saprophyticus* isolates from academic medical centers

Table 1
Description of the *S. saprophyticus* cohort evaluated

Source	WUSM	CHLA	WCMC	UA	VUMC	IHMA	Total
Urine	35.02%, (97/277)	03.61%, (10/277)	02.89%, (08/277)	02.53%, (07/277)	00.00%, (0/277)	31.77%, (88/277)	75.81%, (210/277)
Blood	01.81%, (5/277)	00.36%, (01/277)	00.36%, (01/277)	01.08%, (03/277)	07.58%, (21/277)	05.42%, (15/277)	16.61%, (46/277)
Sterile Body fluid	00.00%, (0/277)	00.36%, (01/277)	00.00%, (0/277)	00.36%, (01/277)	00.00%, (0/277)	00.36%, (01/277)	01.08%, (03/277)
Wound/Tissue/ Bone	00.00%, (0/277)	00.00%, (0/277)	00.36%, (01/277)	01.08%, (03/277)	00.00%, (0/277)	03.97%, (11/277)	05.42%, (15/277)
Respiratory	00.00%, (0/277)	00.00%, (0/277)	00.00%, (0/277)	00.00%, (0/277)	00.00%, (0/277)	01.08%, (03/277)	01.08%, (03/277)
Total	36.82%, (102/277)	04.33%, (12/277)	03.61%, (10/277)	05.05%, (14/277)	07.58%, (21/277)	42.60%, (118/277)	100.00%, (277/277)

Values represent the number of isolates from each body site and from the different source organizations. Washington University School of Medicine in St. Louis (WUSM), Children's Hospital Los Angeles (CHLA), Weill Cornell Medical Center (WCMC), Vanderbilt University Medical Center (VUMC), University of Alberta (UA), and International Health Management Associates (IHMA).

PMID: 39298933

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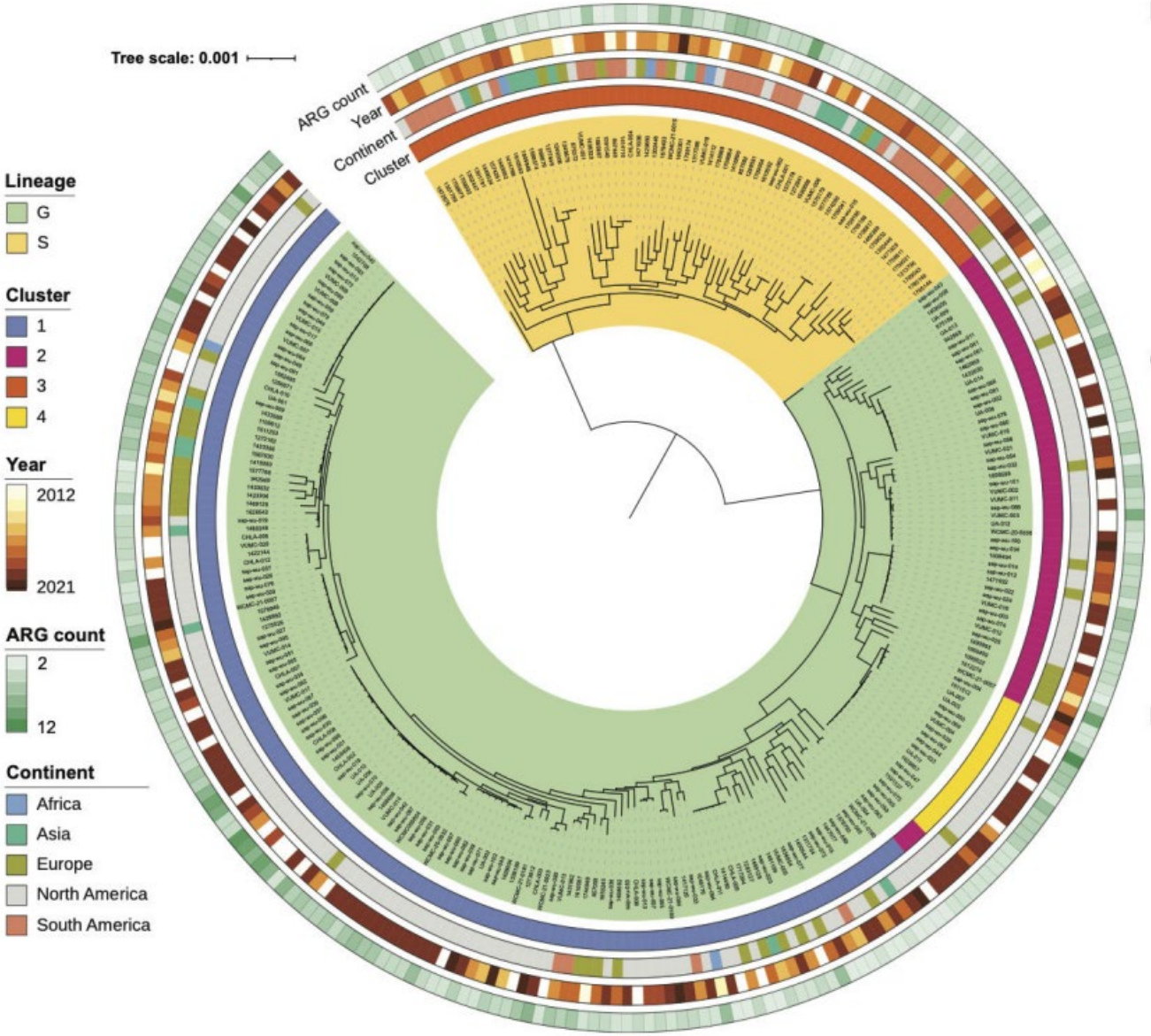
mecA PCR **PBP2A testing** **Antibiotic susceptibility testing** **Illumina WGS**

PMID: 39298933

S. saprophyticus contains two lineages across all geographic sources included in the study



PMID: 31682878

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Slightly better performance by PBP2A *S. aureus* colony culture test compared to latex agglutination

		PBP2A *S. aureus* colony culture test		PBP2' latex agglutination test	
		+	-	+	-
***mecA* PCR**	+	12	2	11	3
	-	0	25	0	25

PMID: 39298933

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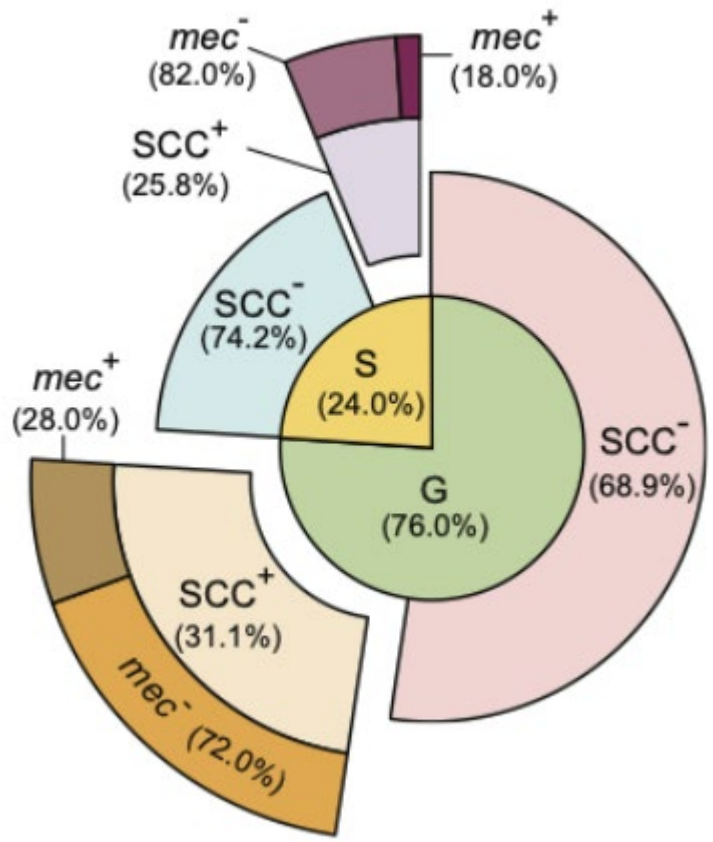
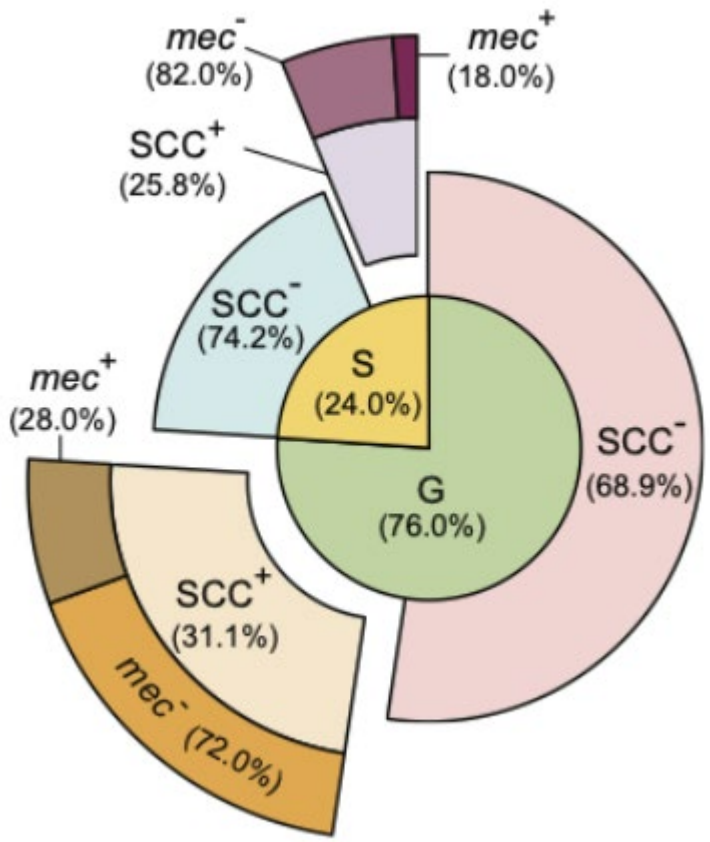
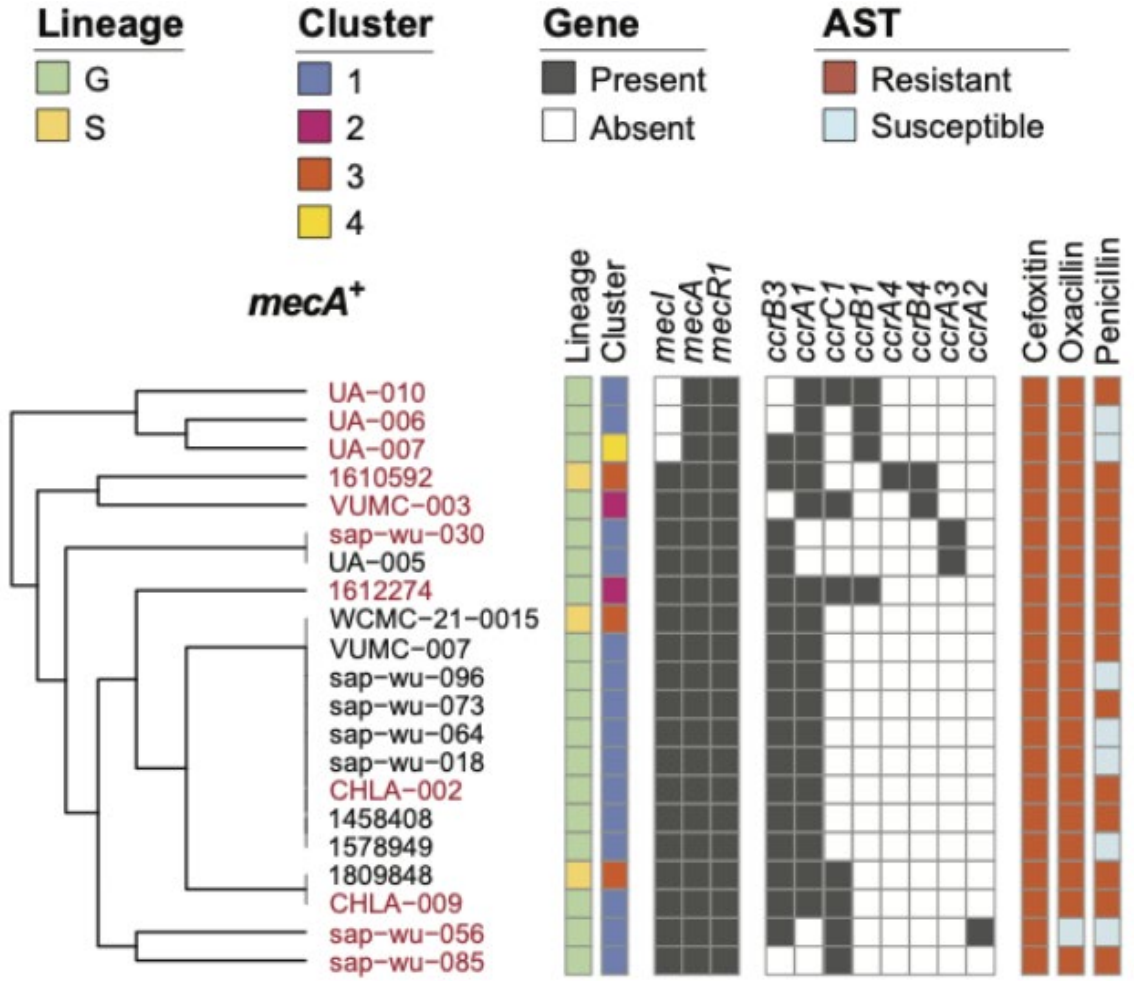
Staphylococcus cassette chromosome (SCC) is more common than *mecA* in *S. saprophyticus*



PMID: 31682878

Various cassette chromosome recombinases (CCR) are associated with *mecA* in *S. saprophyticus*





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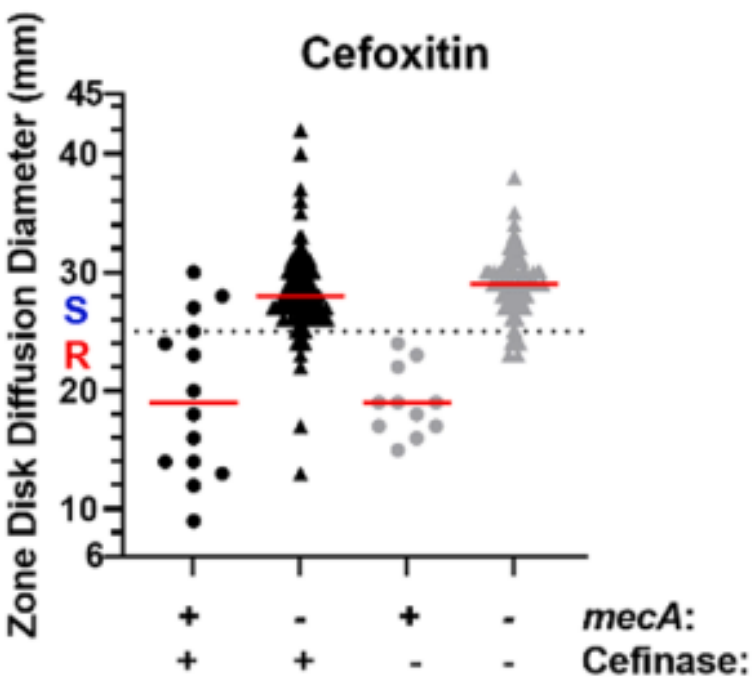
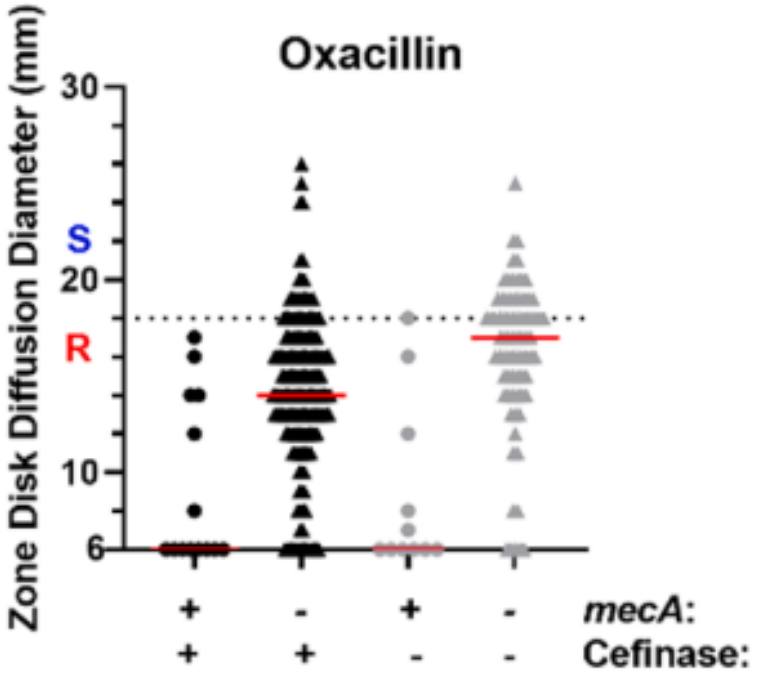
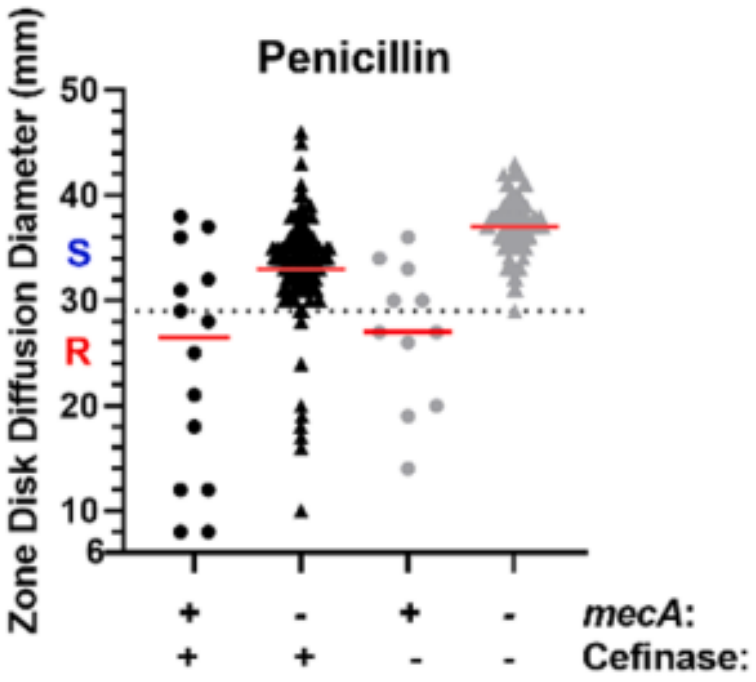
PMID: 31682878

Created an international cohort of *S. saprophyticus* isolates from academic medical centers







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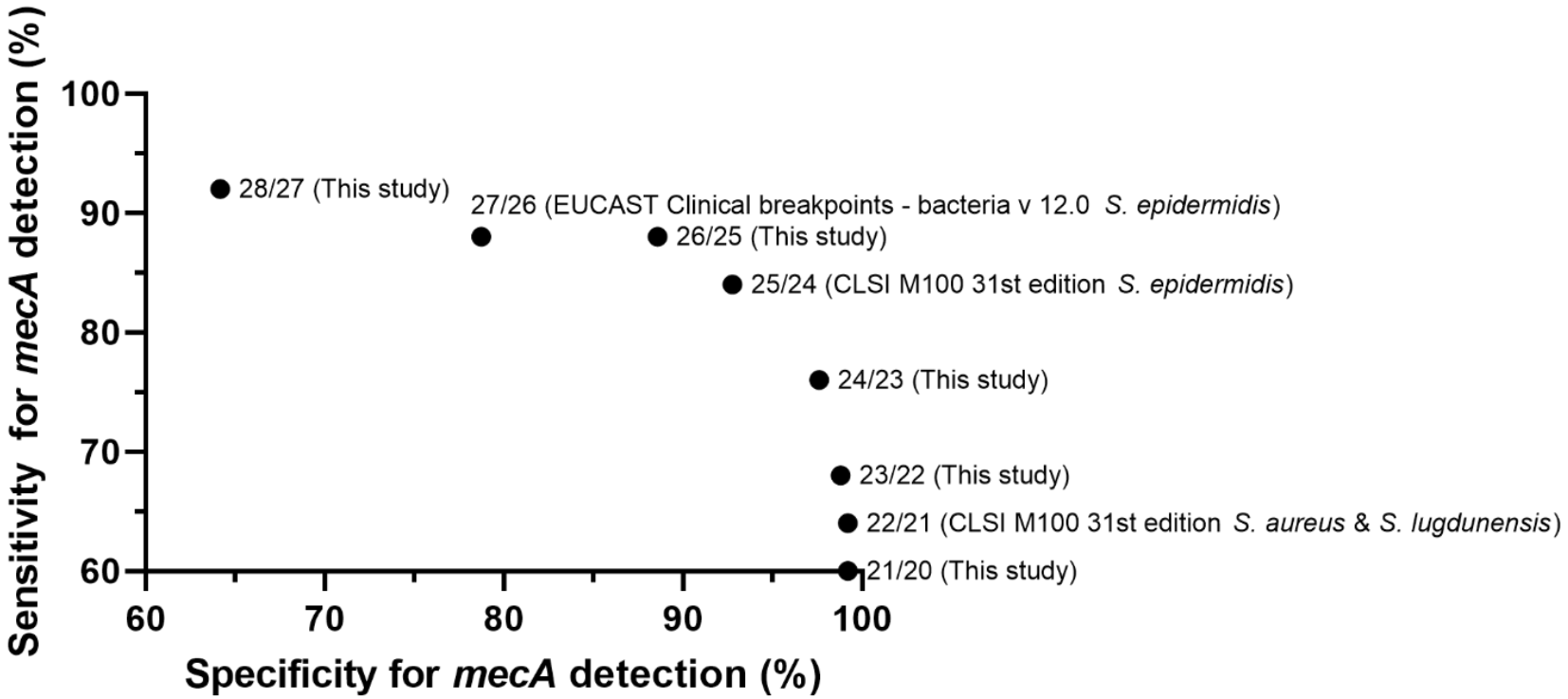
Cefoxitin had better performance characteristics than oxacillin for *S. saprophyticus*

Guidelines	CLSI M100 31st Edition	CLSI M100 31st Edition	CLSI M100 31st Edition	CLSI M100 17th Edition	EUCAST Clinical Breakpoint Tables v. 12.0	EUCAST Clinical Breakpoint Tables v. 12.0	EUCAST Clinical Breakpoint Tables v. 12.0
Organism	*S. aureus* & *S. lugdunensis*	*S. epidermidis* (*Staphylococcus* species except *S. aureus, S. lugdunensis, S. epidermidis, S. pseudintermedius*, and *S. schleiferi*)	*S. epidermidis* (*S. pseudintermedius* & *S. schleiferi*)	*S. aureus* & *S. lugdunensis*	*S. pseudintermedius* & *S. schleiferi*	*S. aureus* and coagulase-negative staphylococci other than *S. epidermidis*	*S. epidermidis*
Disk Content	Cefoxitin (30 µg)	Cefoxitin (30 µg)	Oxacillin (1 µg)	Oxacillin (1 µg)	Oxacillin (1 µg)	Cefoxitin (30 µg)	Cefoxitin (30 µg)
Susceptible Breakpoint (mm)	>22	>25	>18	>18	>20	>22	>27
Resistant Breakpoint (mm)	<21	<24	<17	<17	<20	<22	<27
Number of Isolates testing as Susceptible n (%)	260 (94)	239 (86)	69 (25)	69 (25)	18 (7)	260 (94)	202 (73)
Number of Isolates testing as Resistant n (%)	17 (6)	38 (14)	208 (75)	208 (75)	259 (93)	17 (6)	75 (27)
Category Agreement (%)	268/277(97)	259/277 (92)	91/277 (33)	91/277 (33)	45/277 (16)	268/277(97)	226/277 (82)
Major Error	1/254 (1)	17/254 (7)	185/254 (73)	185/254 (73)	234/254 (92)	1/254 (1)	49/254 (19)
Very Major Error (%)	7/24 (29)	4/24 (16)	1/24 (4)	1/24 (4)	0/24 (0)	7/24 (29)	2/24 (8)

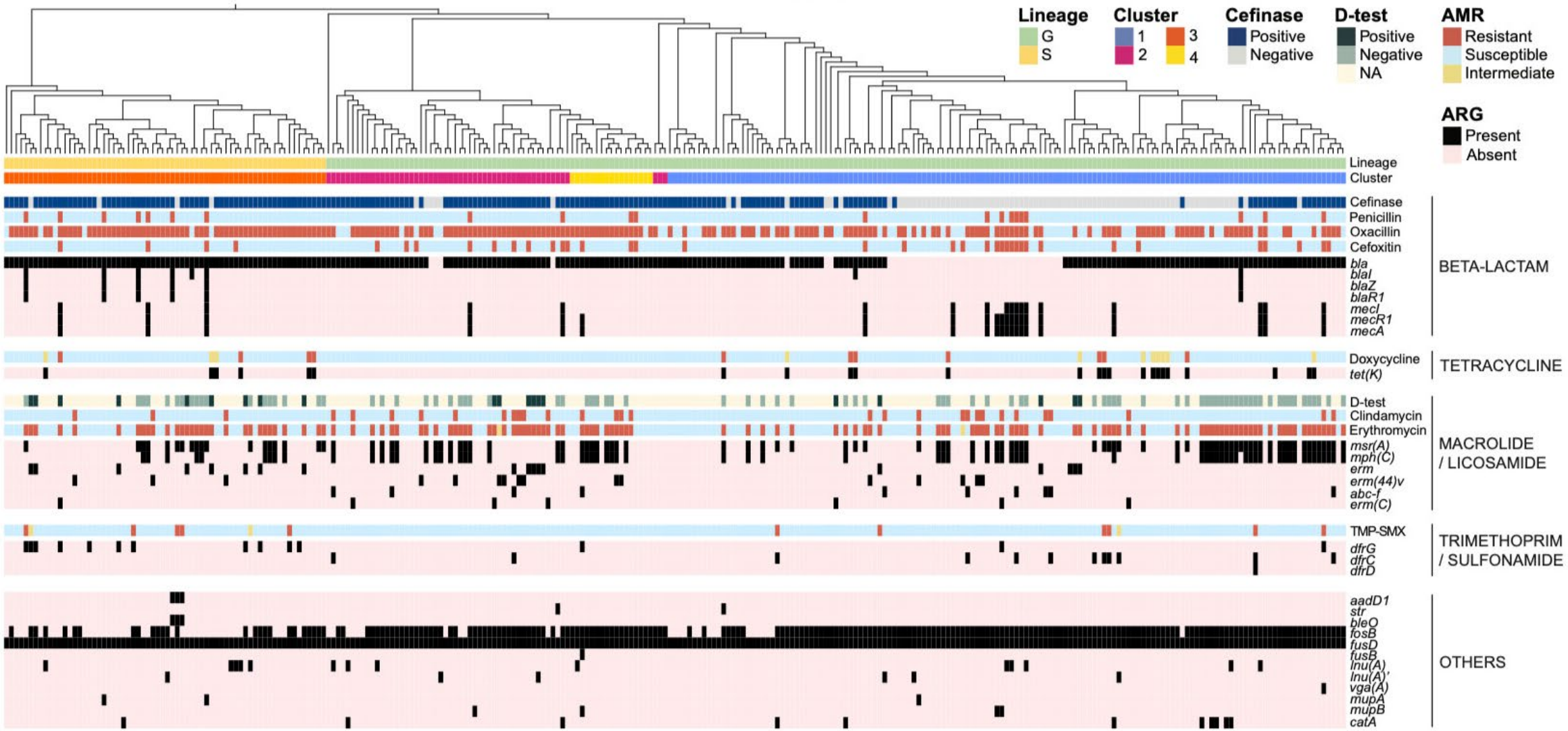
PMID: 39298933

S. saprophyticus contains two lineages across all geographic sources included in the study



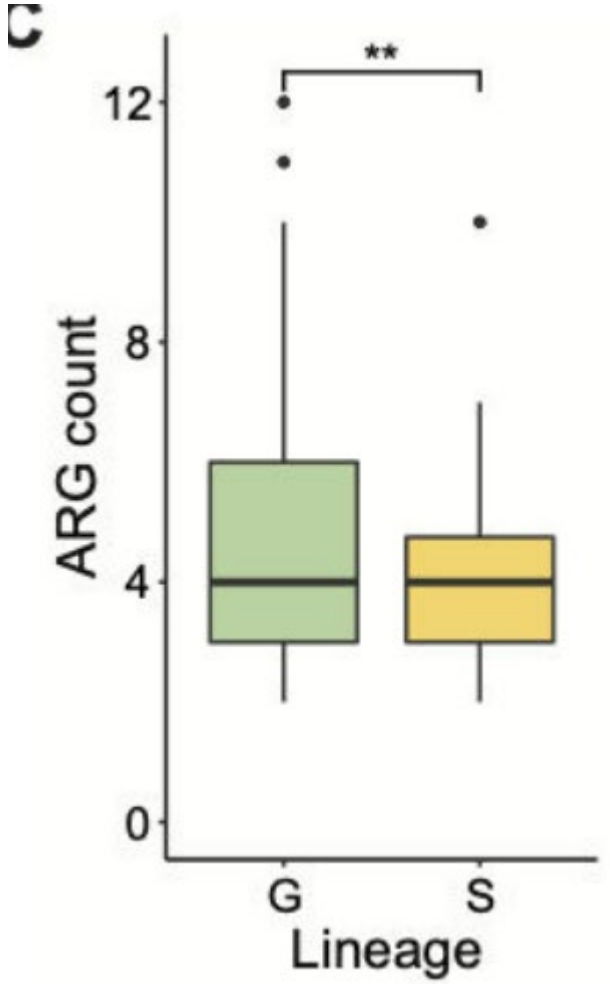
PMID: 39298933

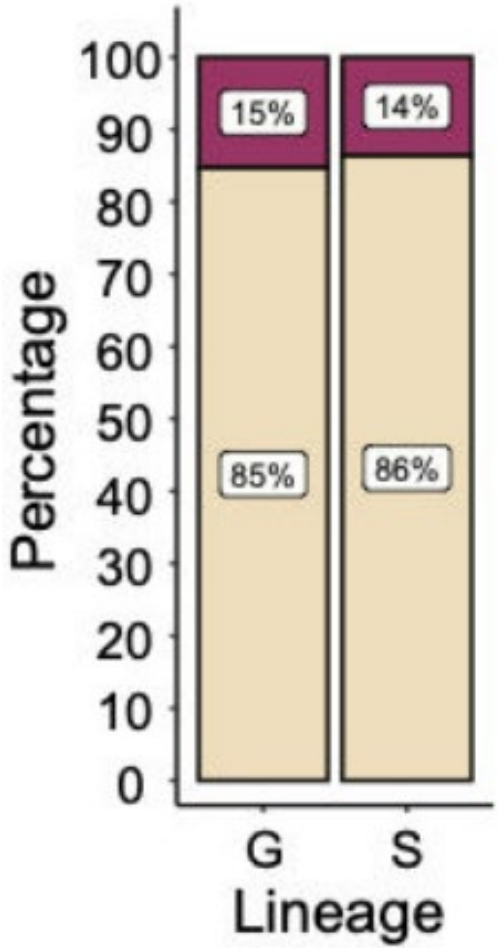
Sporadic nature of antibiotic resistance gene distribution indicates horizontal gene transfer rather than clonal spread



PMID: 31682878

G lineage strains have a higher burden of antibiotic resistance genes compared to S lineage strains

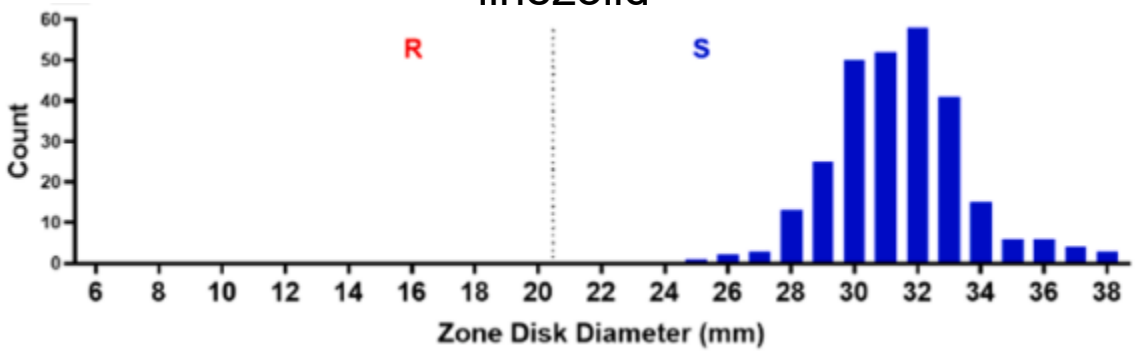




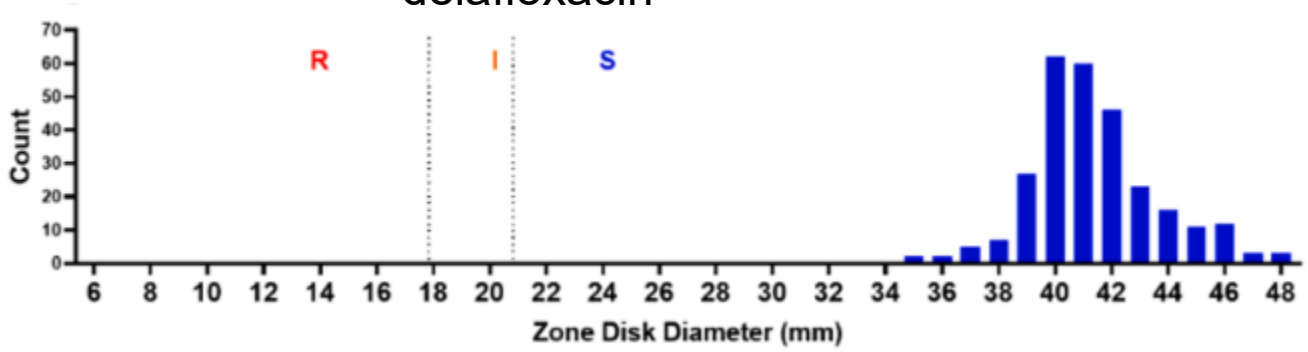
PMID: 31682878

All isolates were susceptible to linezolid, ciprofloxacin, delafloxacin, and rifampin

linezolid



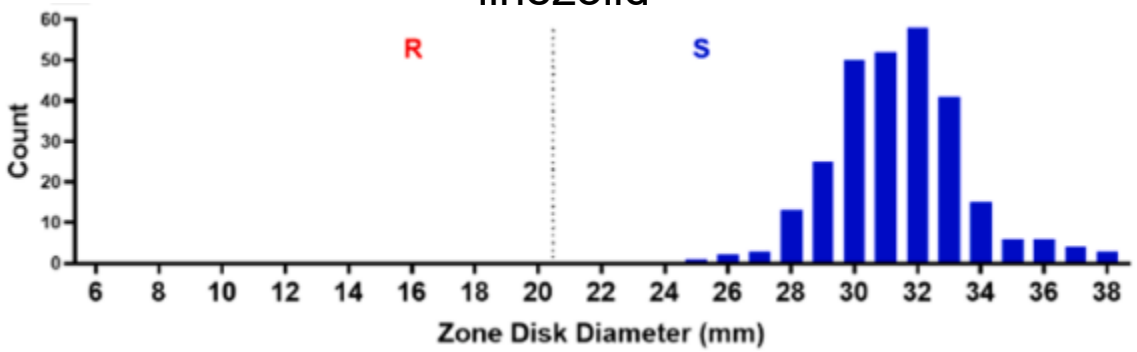
delafloxacin



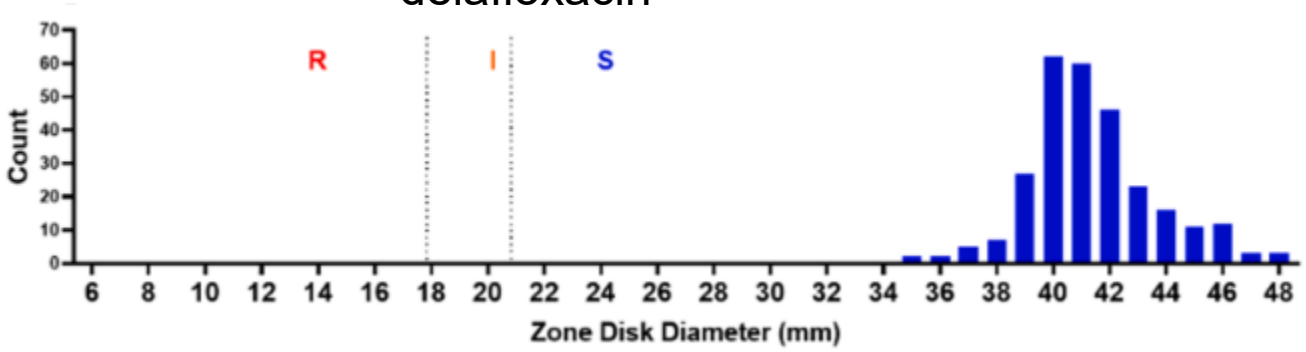
PMID: 39298933

Variable resistance occurred to trimethoprim-sulfamethoxazole and doxycycline

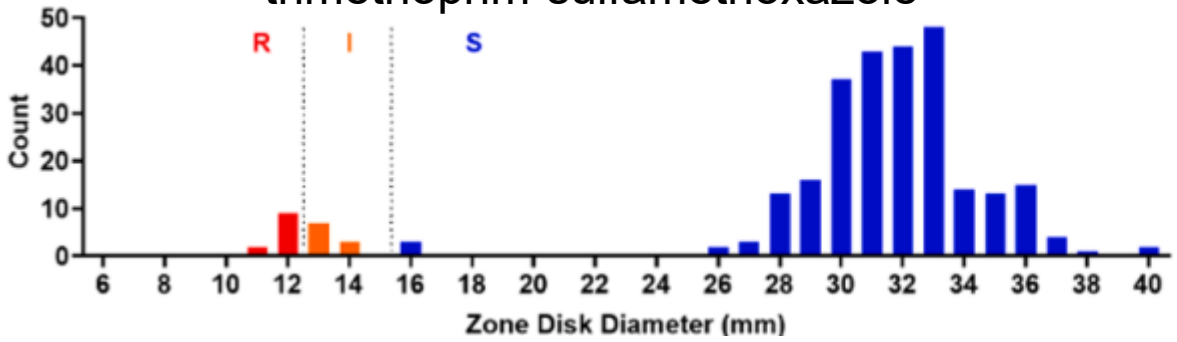
linezolid



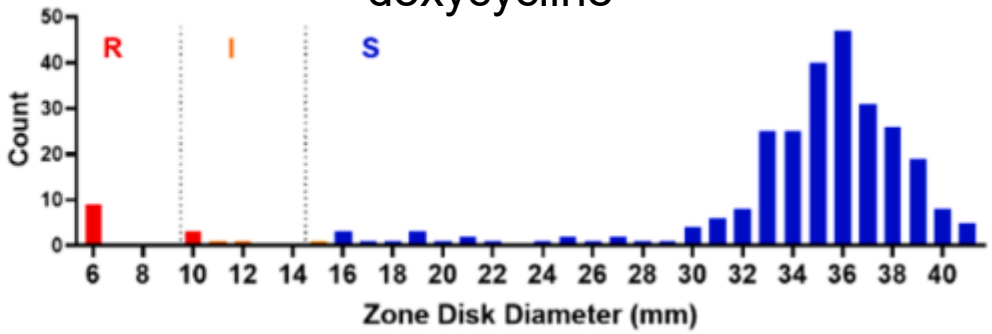
delafloxacin



trimethoprim-sulfamethoxazole



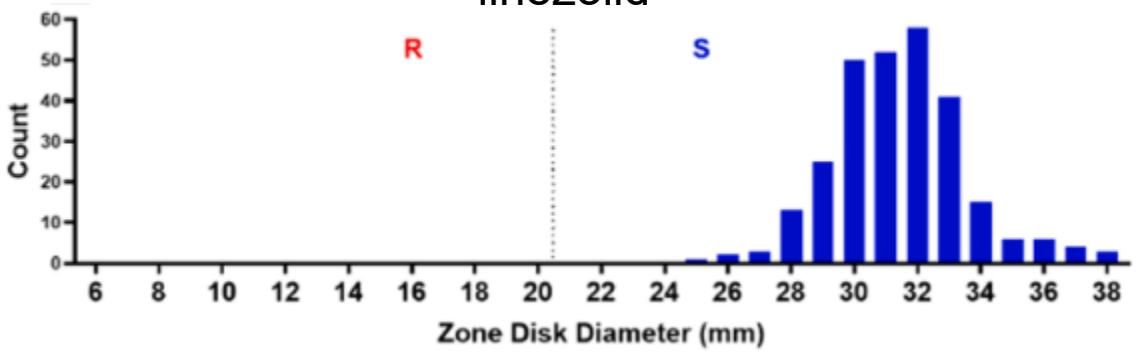
doxycycline



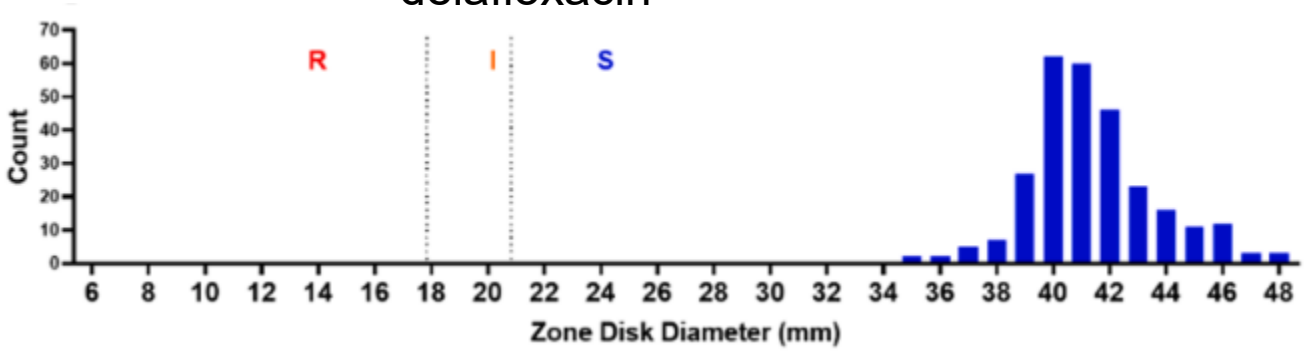
PMID: 39298933

High level of resistance only occurred for erythromycin and clindamycin (which are not used to treat UTIs)

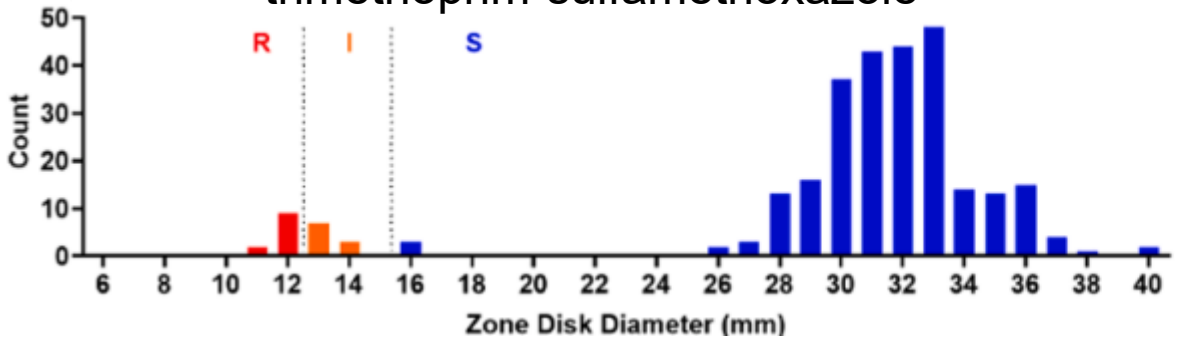
linezolid



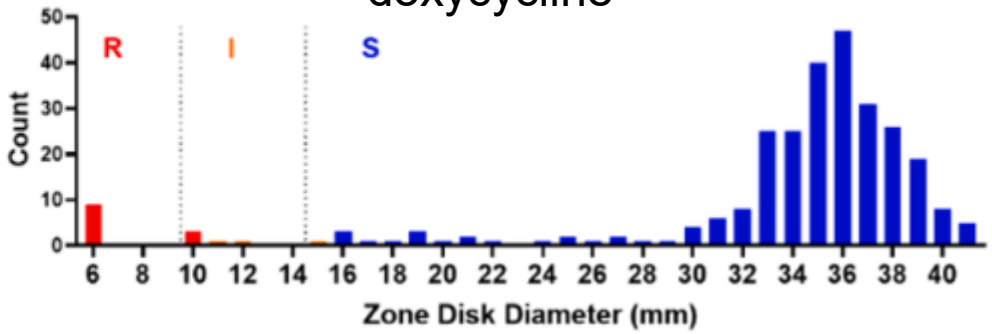
delafloxacin



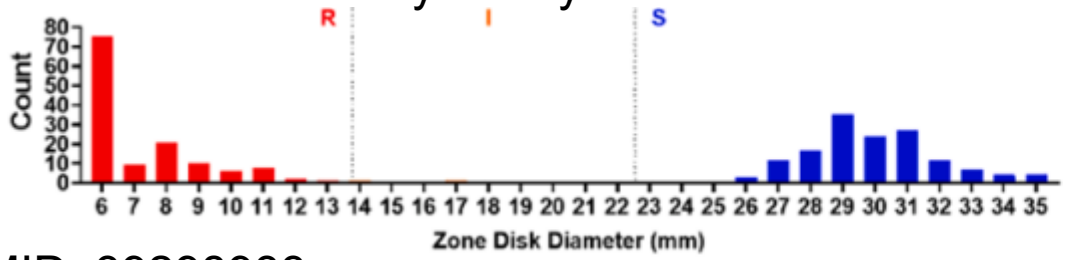
trimethoprim-sulfamethoxazole



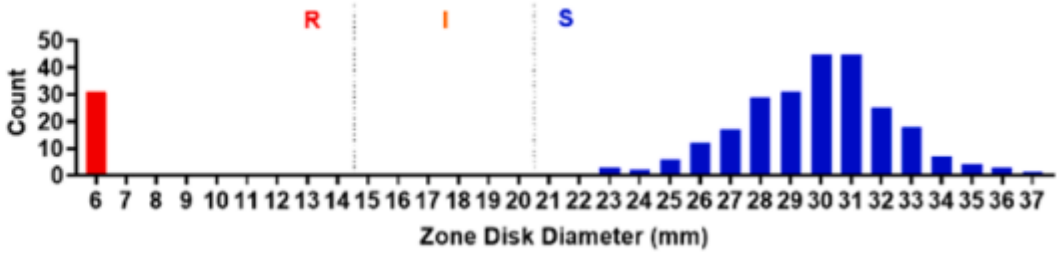
doxycycline



erythromycin

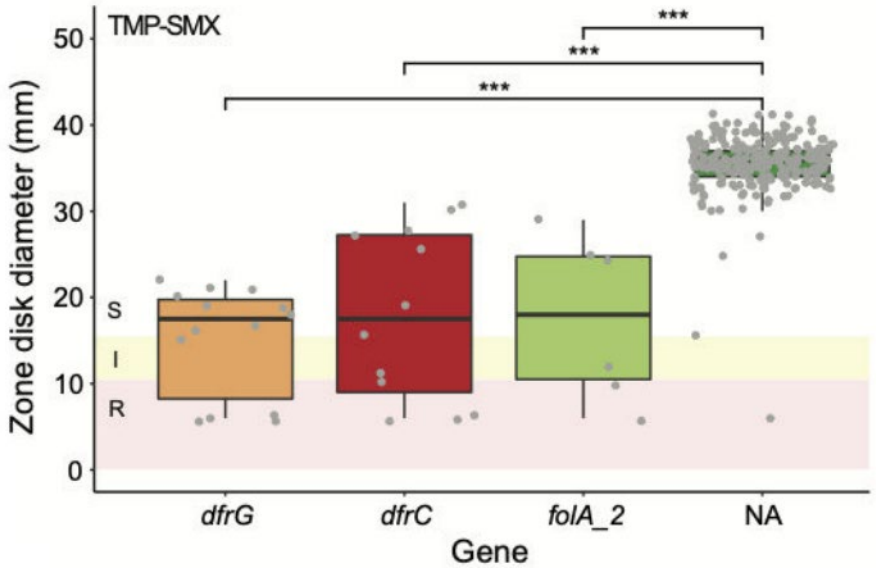


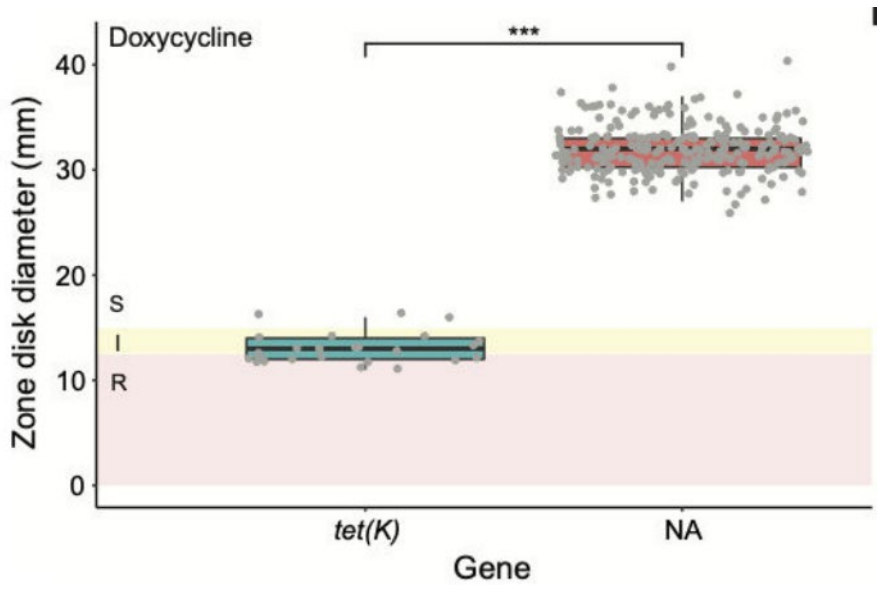
clindamycin

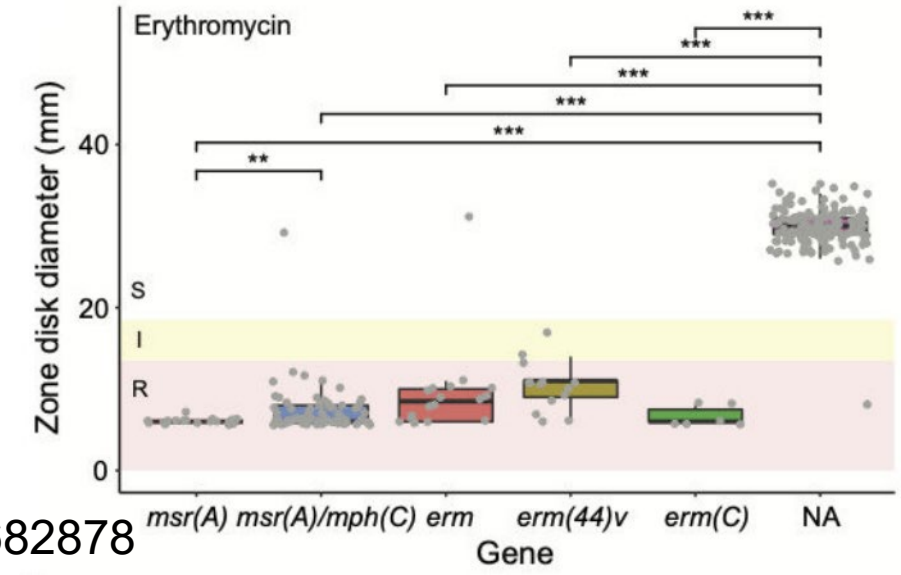


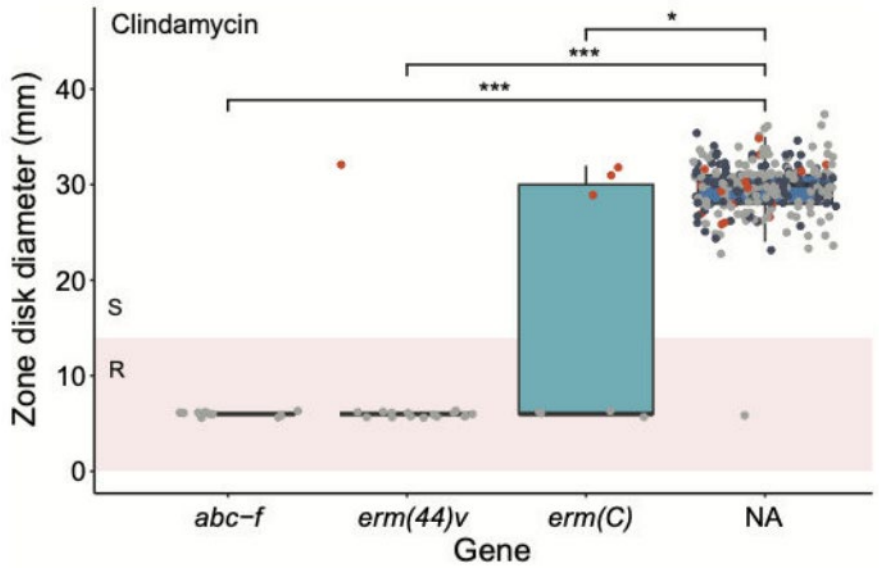
PMID: 39298933

Resistance genes identified that explain variable resistance patterns for all non



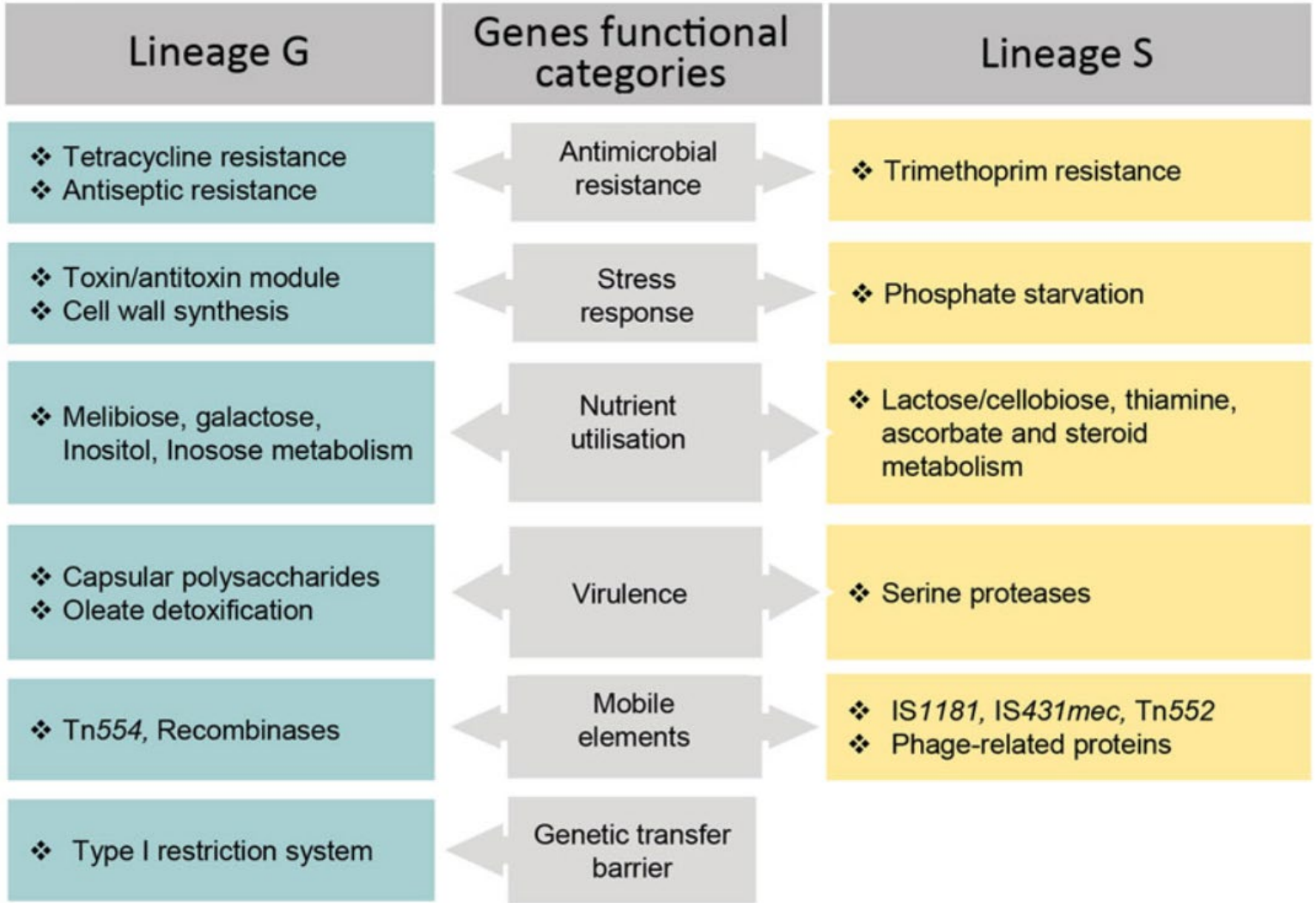






PMID: 31682878

Different evolutionary pressure suspected against the two *S. saprophyticus* lineages, including antibiotic resistance



PMID: 33622483

Conclusions

CLSI footnote is correct. S. saprophyticus is largely susceptible to antibiotics used to treat UTIs

Cefoxitin with S. epidermidis breakpoints gives the best performance for surrogate testing. A new hypothetical breakpoint may work better. PBP2A testing also works well.

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