Does the Nose Know? The Value of MRSA Nares Swab in Skin & Soft Tissue Infections

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Learning Objectives

Recall the current indications for the methicillin-resistant *Staphylococcus aureus* (MRSA) nasal polymerase chain reaction (PCR) test.

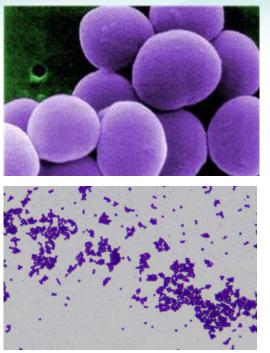
Identify studies that have utilized the MRSA nasal PCR in skin and soft tissue infections (SSTI).

Recognize the clinical utility for the MRSA nasal PCR in SSTI.

Abbreviations

Abbreviation	Definition		
MRSA	Methicillin-resistant Staphylococcus aureus		
PBP	Penicillin-binding protein		
PCR	Polymerase chain reaction		
SSTI	Skin and soft tissue infection		
DFI	Diabetic foot infection		
PNA	Pneumonia		
CAP	Community-acquired pneumonia		
HCAP	Health-care associated pneumonia		
НАР	Hospital-acquired pneumonia		
I&D	Incision and drainage		
VAP	Ventilator-associated pneumonia		
IE	Infective endocarditis		
IDSA	Infectious Diseases Society of America		
ATS	American Thoracic Society		
IV	Intravenous		
PPV	Positive predictive value		
NPV	Negative predictive value		

Staphylococcus aureus



Sources:

Pharmacotherapy. 2018;38(12):1216-1228. Methicillin-Resistant *Staphylococcus aureus*. StatPearls [Internet]. Image: <u>This Photo</u> by Unknown Author is licensed under <u>CC BY-SA-NC</u> Image: <u>This Photo</u> by Unknown Author is licensed under <u>CC BY-SA-NC</u> *Staphylococcus aureus* is a gram-positive bacteria colonized in the:

- Nares
- Throat
- Axillae
- Rectum
- Groin

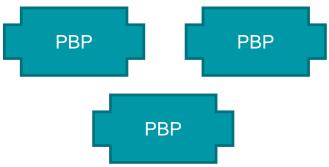
MRSA

Resistance to beta-lactam antibiotics due to the presence of the mecA gene sequence

Sources: Methicillin-Resistant *Staphylococcus aureus*. StatPearls [Internet]. Clin Infect Dis. 2004;39:776-782. Virulence. 2021;12(1):547-569. Annu Rev Biochem. 2015;84:577-601.

MRSA

Resistance to beta-lactam antibiotics due to the presence of the mecA gene sequence



Sources:

Methicillin-Resistant *Staphylococcus aureus*. StatPearls [Internet]. Clin Infect Dis. 2004;39:776-782.

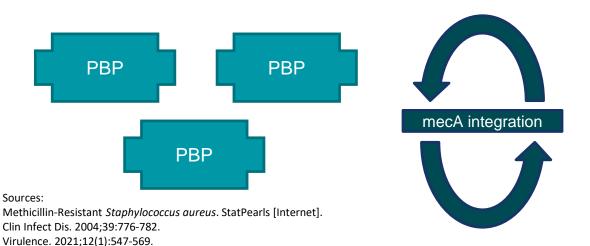
Virulence. 2021;12(1):547-569.

Annu Rev Biochem. 2015;84:577-601.

MRSA

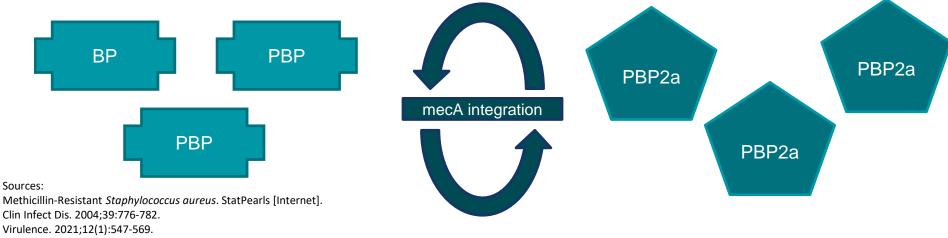
Annu Rev Biochem. 2015;84:577-601.

Resistance to beta-lactam antibiotics due to the presence of the mecA gene sequence



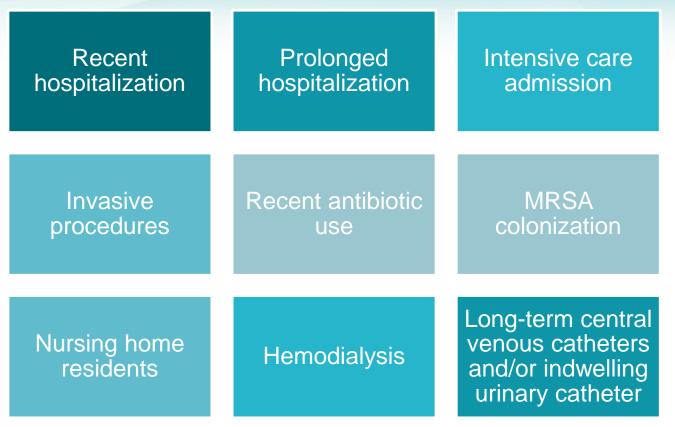
MRSA

Resistance to beta-lactam antibiotics due to the presence of the mecA gene sequence



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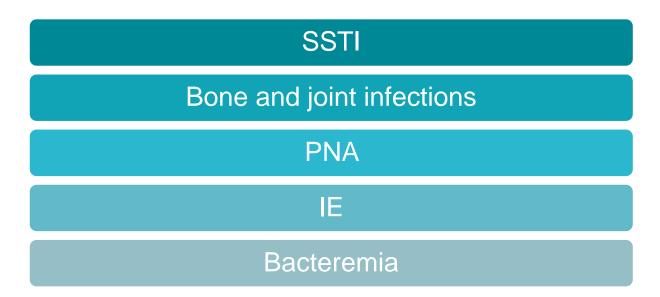
MRSA Risk Factors



Source:

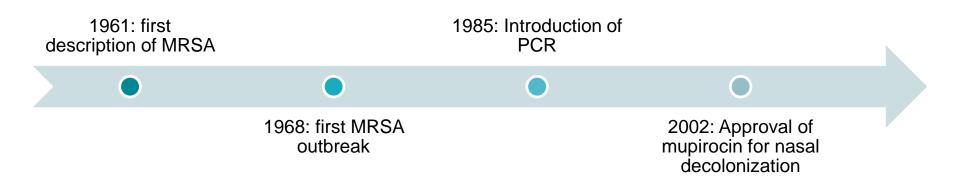
Methicillin-Resistant Staphylococcus aureus. StatPearls [Internet].

MRSA Infection Types



Source: Methicillin-Resistant *Staphylococcus aureus*. StatPearls [Internet].

History of MRSA and Decolonization

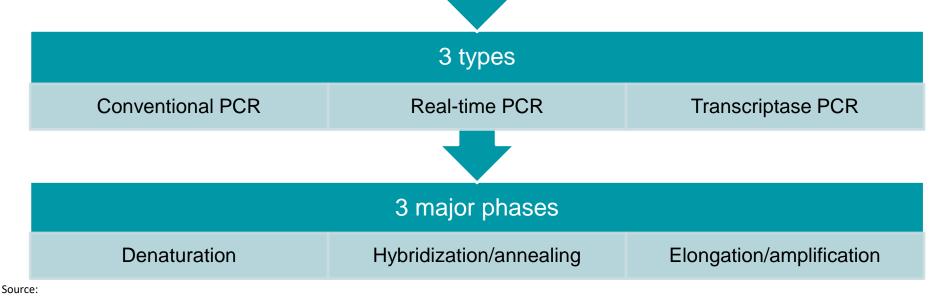


Sources: Methicillin-Resistant *Staphylococcus aureus*. StatPearls [Internet]. Polymerase Chain Reaction (PCR). StatPearls [Internet].

Deoxyribonucleic Acid (DNA) PCR

Introduced in 1985

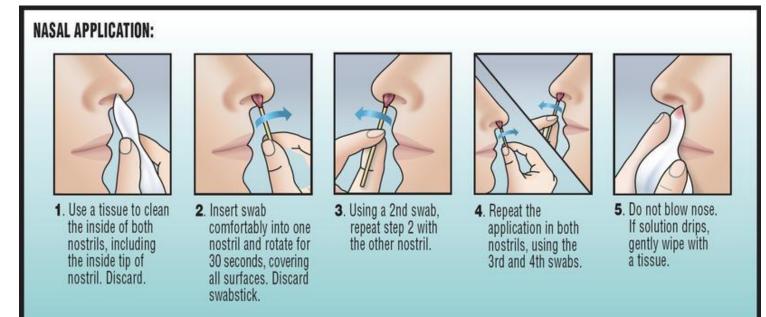
PCR: nucleic acid amplification technique used to denature and renature short segments of DNA or ribonucleic acid (RNA) sequences using DNA polymerase I enzyme



Polymerase Chain Reaction (PCR). StatPearls [Internet].

Testing for MRSA

Positive nasal MRSA DNA PCR indicates presence of MRSA

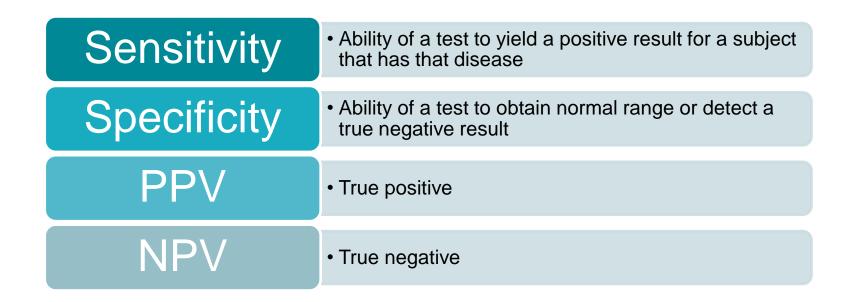


Sources:

Sources: Methicillin-Resistant *Staphylococcus aureus*. StatPearls [Internet]. The Informed Patient - The Ultimate Battle Against MRSA. Wall Street Journal.

Assessing Validity of PCR Tests

McLeod Health



Source:

Diagnostic Testing Accuracy: Sensitivity, Specificity, Predicative Values and Likelihood Ratios. StatPearls [Internet].

Effect of Nasal Sanitizer on Colonization

Ghaddara, et al. 2020 \rightarrow nonblinded, placebo-controlled randomized trial					
Purpose	Methods	Results			
Group 1 (N = 21)					
Assess the efficacy of a one-time povidone-iodine nasal sanitizer	Statistically significant reduction in the mean MRSA concentrations at 1 and 6 hours but not at 12 or 24 hours				
Group 2 (N = 18)	Group 2 (N = 18)				
Determine if repeated dosing would enhance efficacy	Povidone-iodine applied every 12 hours for 5 days with nares cultures obtained at baseline, immediately prior to each treatment dose, and 2 days after the final dose	Povidone-iodine group had lower mean nasal MRSA concentrations during the treatment days, but not statistically significant			

Authors' Conclusions

• Single applications of povidone-iodine may be effective for short-term suppression of *S. aureus*

• Factors leading to lack of sustained reduction: decreased povidone-iodine concentrations, embedded MRSA in the base of hair follicles or mucus, and reinoculation

Source:

Am J of Infect Control. 2020:48:456-459.

McLeod Health Effect of Nasal Sanitizer and Anti-MRSA Agents on MRSA Nasal PCR Validity

Chaudhry, et al. 2020 \rightarrow retrospective, noninferiority, observational cohort study			
Purpose	Methods	Results (Before vs. After PCR)	
Determine whether mupirocin administration affects the reliability of MRSA PCR nasal screens	 Included patients who had a pulmonary infection, had blood and/or respiratory cultures, received intranasal mupirocin, had a MRSA PCR nasal screen result, and had vancomycin administered within 48 hours Predetermined noninferiority margin 5% N = 250 	 Mupirocin (overall): NPV 95% vs. 99%; ARR, -4%; (90% CI, -8% to 0.2%; P = 0.31) Mupirocin (≤ 2 doses): NPV 96% vs. 99%; ARR, -3%; (90% CI, -7% to 2%; P = 0.22) Vancomycin: NPV 98% vs. 96%; ARR, 2%; (90% CI, NR; P = 0.41) 	

Authors' Conclusion

 MRSA PCR may be less reliable if intranasal mupirocin is administered prior to the screen → effort should be made to delay administration of mupirocin until after the MRSA PCR is collected

ARR = absolute risk reduction; CI = confidence interval; NR = not reported

Source:

Am J Health-System Pharm. 2020;77(23):1965-1982.

MRSA – Colonization

Prevalence of MRSA is correlated to PPV and NPV



In infections that have a high prevalence for MRSA, like SSTI, the PPV increases while the NPV decreases



In infections that have a low prevalence for MRSA, like UTI or intra-abdominal infection, the PPV decreases while the NPV increases

Source: Pharmacotherapy. 2018;38(12):1216-1228.

Effect of Colonization on Subsequent MRSA Infection

Davis, et al. 2004 \rightarrow prospective, multicenter, observational cohort study			
Purpose	Methods	Results	
Evaluate the impact of asymptomatic nares MRSA colonization on the development of subsequent MRSA infection	 Included patients who had nare cultures performed within 48 hours after admission to an observed hospital unit N = 758 	 <i>S. aureus</i> colonization at admission, n (%) = 163 (22); MRSA (n = 26), MSSA (n = 137) Subsequent MRSA infection (MRSA vs. MSSA colonization at admission), n/N (%): 5/26 (19) vs. 2/137 (1.5); RR, 13; (95% CI, 2.7-64) Subsequent MRSA infection (MRSA vs. no colonization at admission), n/N (%): 5/26 (19) vs. 12/595 (2); RR, 9.5; (95% CI, 3.6-25) 	

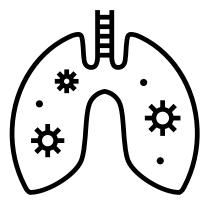
Authors' Conclusion

 MRSA colonization of nares, either present at admission to the hospital or acquired during hospitalization, increases the risk for MRSA infection

RR = relative risk; CI = confidence interval

Source: Clin Infect Dis. 2004;39:776-782.

Evidence for MRSA PCR in Respiratory Infections



MRSA Nasal PCR for PNA

Dangerfield B, et al. 2014 \rightarrow single center, retrospective, cohort study

Purpose	Methods and Design	PNA Classification	Results
 Evaluate the MRSA nasal PCR to predict culture-confirmed MRSA PNA Calculate the sensitivity, specificity, PPV, and NPV of the MRSA nasal PCR 	 January 2009-July 2011 Patients were included if they had confirmed PNA, MRSA nasal PCR, and culture N = 435 		 Sensitivity: 88.0% Specificity: 90.1% PPV: 35.4% NPV: 99.2% 30-day mortality (empiric anti-MRSA antibiotics vs. no empiric anti-MRSA antibiotics): 0 vs. 3 deaths; P = 0.4

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Authors' Conclusion

• Excellent NPV; a negative MRSA nasal PCR can be reasonably used to guide antibiotic de-escalation

Source: Antimicrob Agents and Chemo. 2014;58(2):829-864.

MRSA Nasal PCR for PNA

Parente D, *et al*. 2018 → meta-analysis

Purpose	Methods and Design	PNA Classification	Results
 Evaluate the diagnostic value of MRSA nasal screening in MRSA PNA 	22 studies5163 patients	 Only reported for 11 studies 3 studies (27%) included all PNA types 2 studies (18.2%) included CAP and HCAP 1 study (9%) included HAP 5 studies (45.5%) included VAP 	 All types of PNA Sensitivity: 70.9% Specificity: 90.3% PPV: 44.8% NPV: 96.5%

MRSA Nasal PCR for PNA

Parente D, *et al*. 2018 → meta-analysis

Purpose	Methods and Design	PNA Classification	Results
 Evaluate the diagnostic value of MRSA nasal screening in MRSA PNA 	 22 studies 5163 patients 	 Only reported for 11 studies 3 studies (27%) included all PNA types 2 studies (18.2%) included CAP and HCAP 1 study (9%) included HAP 5 studies (45.5%) included VAP 	 CAP/HCAP Sensitivity: 85.0% Specificity: 92.1% PPV: 56.8% NPV: 98.1% VAP Sensitivity: 40.3% Specificity: 93.7% PPV: 35.7% NPV: 94.8%

MRSA Nasal PCR for PNA

Parente D, et al. 2018 → meta-analysis

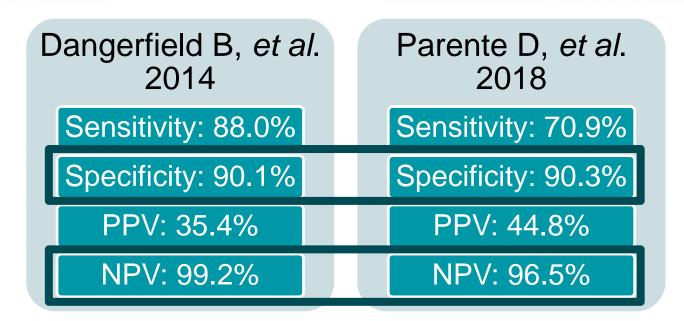
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Authors' Conclusions

- A positive MRSA nares test is not diagnostic of MRSA PNA, but a negative result can rapidly and effectively rule it out
- Valuable tool for antimicrobial stewardship pharmacists to de-escalate empiric anti-MRSA therapy in patients with PNA who are not nasally colonized with MRSA, specifically those with CAP/HCAP

Source.

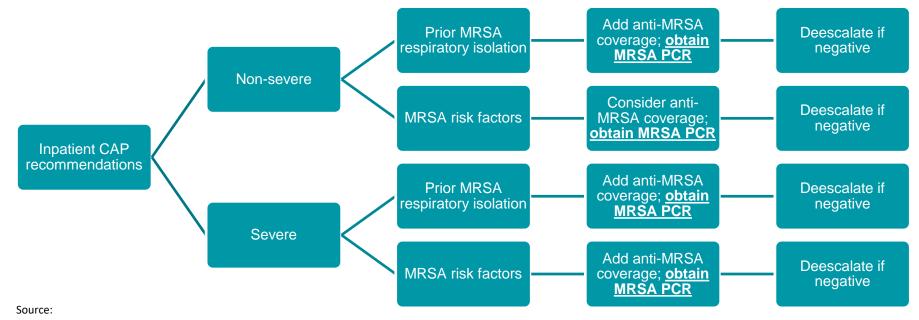
Compare



Sources: Antimicrob Agents and Chemo. 2014;58(2):829-864. Clin Infect Dis. 2018;67(1):1-7.

McLeod Health MRSA Coverage in Respiratory Infections – CAP

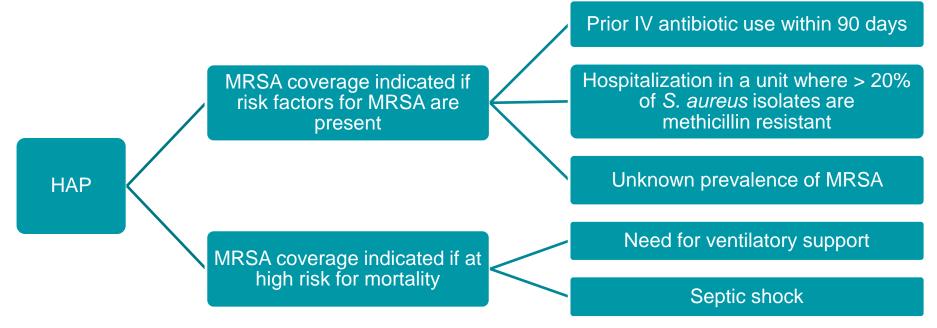
2019 ATS/IDSA CAP Guideline Recommendations



Am J Respir Crit Care Med. 2019;200(7):45-67.

McLeod Health MRSA Coverage in Respiratory Infections – HAP

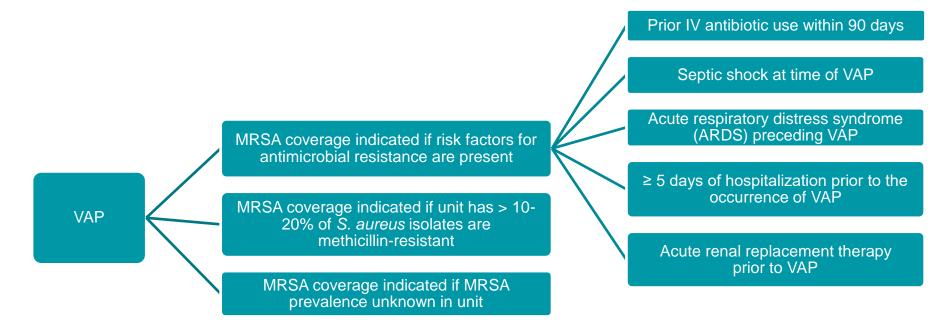
2016 ATS/IDSA Guidelines for the management of HAP/VAP Recommendations



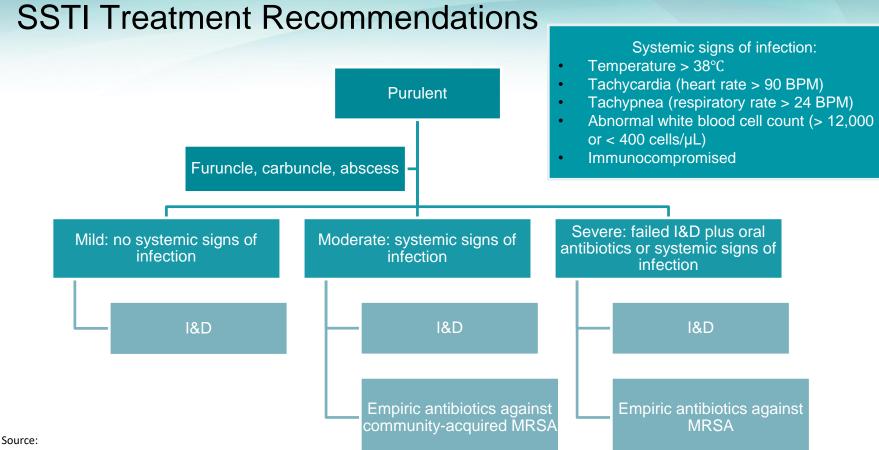
Source: Clin Infect Dis. 2016;63(5):61-111.

McLeod Health MRSA Coverage in Respiratory Infections – VAP

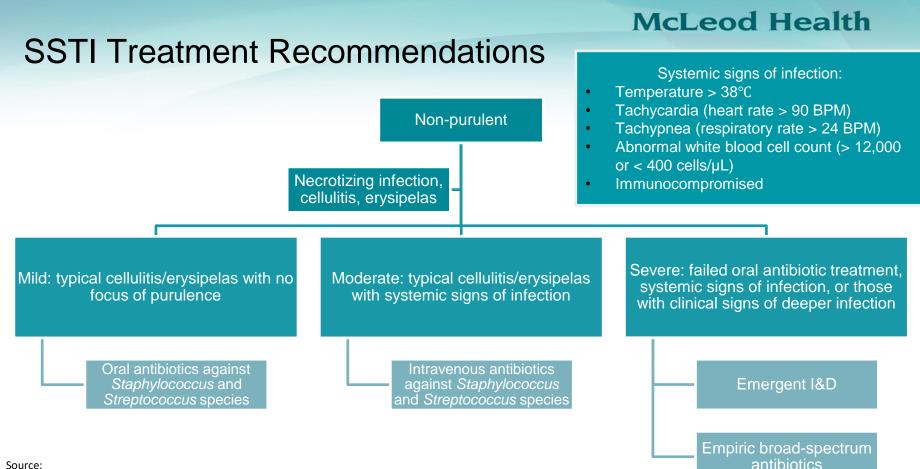
2016 ATS/IDSA Guidelines for the management of HAP/VAP Recommendations



Does the Nose Know? The Value of MRSA Nares PCR in SSTI



Clin Infect Dis. 2014;59(2);10-52.



Source: Clin Infect Dis. 2014;59(2);10-52.



Recommendations for Empiric MRSA Coverage

- Moderate and severe purulent SSTI
- Cellulitis associated with risk factors
- High local MRSA infection rate
- Surgical site infection in patients who have MRSA risk factors
- Necrotizing fasciitis
- Pyomyositis
- Clostridial gas gangrene or myonecrosis
- Febrile neutropenia

Clinical Utility of Negative MRSA Nasal Surveillance PCR in SSTI

Burgoon R, et al. 2022

Study Design and Methods

Retrospective, cohort analysis at a tertiary academic medical center

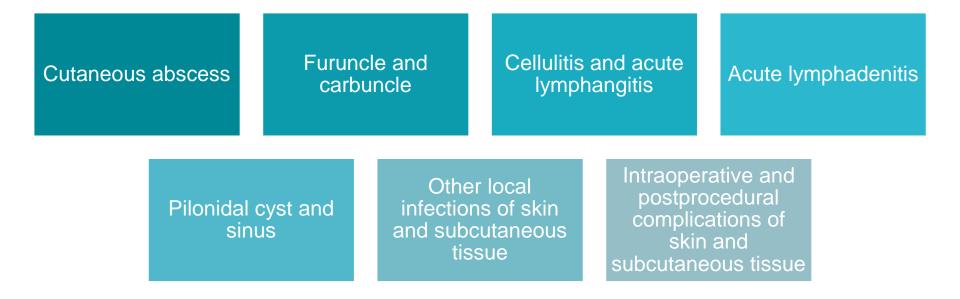
July 2014 – June 2020

Included patients who had a MRSA nasal PCR performed during their hospitalization and had a primary diagnosis of SSTI

Patients separated into two groups (negative MRSA nasal PCR and positive MRSA nasal PCR) in a 2:1 ratio

Source: Am J Infect Control. 2022;50;941-946.

Primary Diagnosis Types



Baseline Characteristics

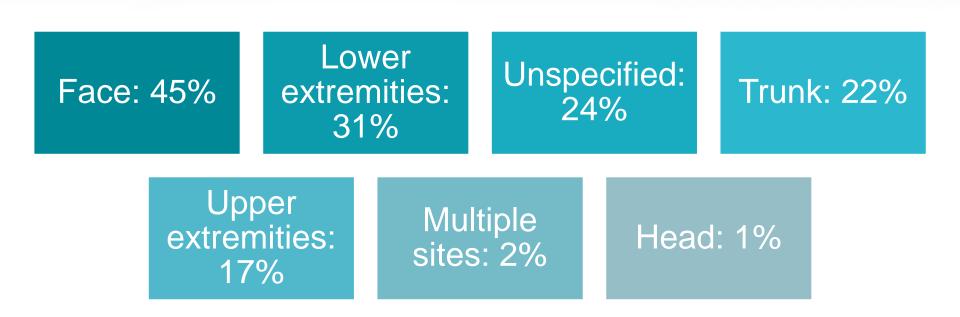
Demographics	MRSA-positive nasal PCR (N = 156)	MRSA-negative nasal PCR (N = 317)	
Age (years), median (IQR)	59 (45-71)	58 (47-69)	
Male, n (%)	88 (56)	180 (57)	
Weight (kg), median (IQR)	78 (68-100)	86 (68-105)	
Height (cm), median (IQR)	173 (163-180)	170 (163-180)	
Race, n (%)			
White	112 (72)	200 (63)	
Black	43 (28)	103 (33)	
Other	1 (1)	14 (4)	
Prior anti-MRSA therapy in 3 months, n (%)	24 (15)	72 (23)	

IQR = interquartile range

Source:

Am J Infect Control. 2022;50;941-946.

SSTI Location



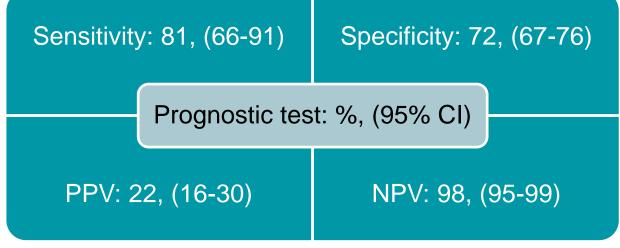
Source: Am J Infect Control. 2022;50;941-946.

Vancomycin Utilization

Outcome	MRSA-positive nasal PCR (N = 156)	MRSA-negative nasal PCR (N = 317)	<i>P</i> -value
Duration of vancomycin therapy (days), median (IQR)	4 (3-6)	3 (2-5)	0.01
Doses of vancomycin administered, median (IQR)	6 (3-10)	5 (3-8)	0.3
Number of vancomycin levels collected, median (IQR)	2 (10-4)	2 (1-3)	0.43

IQR = interquartile range

Prognostic Test Statistics



CI = confidence interval

Source: Am J Infect Control. 2022;50;941-946.

Authors' Conclusions

Potential to decrease the duration of vancomycin therapy using a negative MRSA nasal PCR result

High NPV of MRSA nasal PCR, similar to other studies

Implement a MRSA nasal screening review as an antimicrobial stewardship tool for de-escalating vancomycin therapy

Source: Am J Infect Control. 2022;50;941-946.

Presenter's Critique

McLeod Health

Strengths

- Sample size
- Large time frame
- Multiple SSTI sites were included
- Similar results to previous studies in different infections

Limitations

- Retrospective
- Could not account for anti-MRSA therapy given outpatient or inpatient
- Identification was based on ICD-10 codes

Does a Positive MRSA Nasal Screen Predict the Risk for MRSA SSTI?

Hitchcock AM, et al. 2023

Study Design and Methods

Single-center, retrospective cohort study at a tertiary academic medical center

December 2018 – October 2021

Included patients who had a MRSA nasal screen and wound culture results obtained within 48 hours of starting antibiotic therapy

Excluded patients if they had a history of MRSA infection within 1 year prior to the index admission

Source: Ann of Pharmacotherapy. 2023;57(6):669-676.

Baseline Characteristics

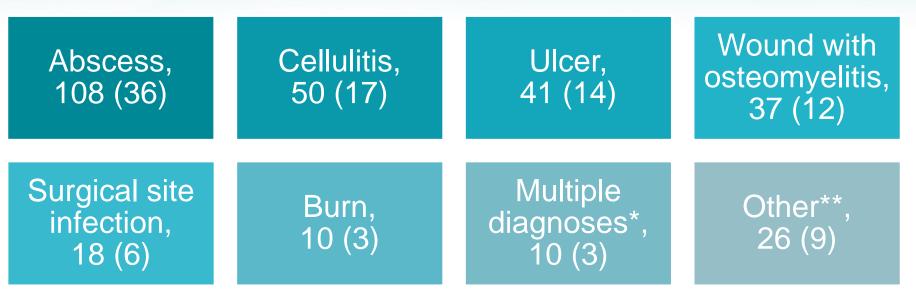
Demographics	N = 300
Male gender, n (%)	181 (60)
Age (years), mean (SD)	56 (15)
Weight (kg), mean (SD)	92 (31)
Residence, n (%)	
Home	276 (92)
Nursing facility	19 (6)
Homeless	5 (2)
Comorbidities, n (%)	
Diabetes	138 (46)
Hemodialysis	6 (2)
Peritoneal dialysis	4 (1)
Persons who inject drugs	31 (10)

Source:

Ann of Pharmacotherapy. 2023;57(6):669-676.

SD = standard deviation

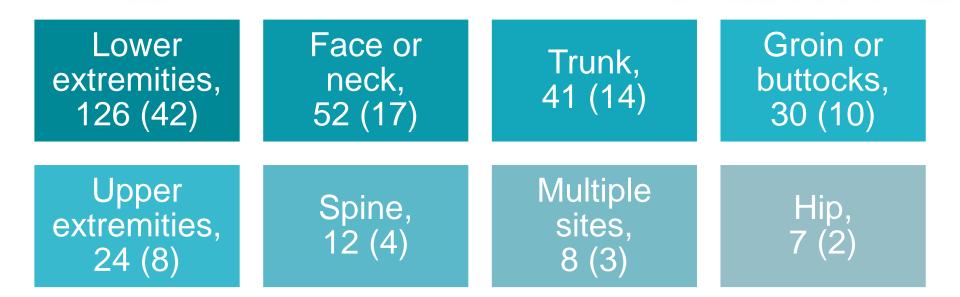
Diagnosis, n (%)



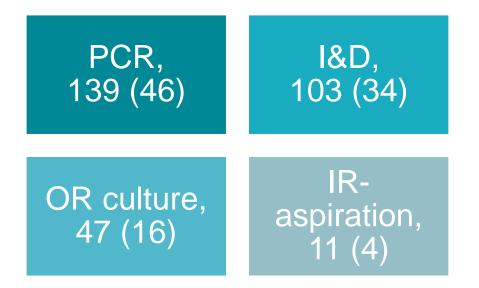
*Multiple diagnoses: patients with > 1 infectious diagnosis in > 1 location during the same encounter **Other diagnoses: gangrene (n = 9), prosthetic infection (n = 9), necrotizing fasciitis (n = 4), septic arthritis (n = 3), pyomyositis (n = 1)

Source: Ann of Pharmacotherapy. 2023;57(6):669-676.

Infection Location, n (%)



Culture Type, n (%)



Source: Ann of Pharmacotherapy. 2023;57(6):669-676.

OR: operating room IR: interventional radiology

Wound Culture and MRSA Nasal Screen Results

	MRSA wound culture (+) (N = 55)	MRSA wound culture (-) (N = 245)	Total (N = 300)	
Total cohort (purulent and non-purulent SSTI)				
MRSA nasal screen (+), n (%)	35 (64)	15 (6)	50 (17)	
MRSA nasal screen (-), n (%)	20 (36)	230 (94)	250 (83)	

Wound Culture and MRSA Nasal Screen Results

	MRSA wound culture (+) (N = 34)	MRSA wound culture (-) (N = 123)	Total (N = 157)	MRSA wound culture (+) (N = 21)	MRSA wound culture (-) (N = 122)	Total (N = 143)
	Purulent SSTI cohort		Non-purulent SSTI cohort			
MRSA nasal screen (-), n (%)	23 (68)	8 (7)	31 (20)	12 (57)	7 (6)	19 (13)
MRSA nasal screen (+), n (%)	11 (32)	115 (93)	126 (80)	9 (43)	115 (94)	124 (87)

Performance Characteristics of MRSA Nasal Screening

Characteristic, %, (95% CI)	Purulent SSTI (n = 157 <i>)</i>	Non-purulent SSTI (n = 143)	Total Cohort (N = 300)
MRSA prevalence	22, (16-29)	15, (10-22)	18, (14-23)
Sensitivity	68, (49-82)	57, (34-77)	64, (50-76)
Specificity	94, (87-97)	94, (88-98)	94, (90-96)
PPV	74, (55-88)	63, (39-83)	70, (55-82)
NPV	91, (85-95)	93, (86-96)	92, (88-95)

CI = confidence interval

Authors' Conclusion

Positive MRSA nasal screen \rightarrow large increase in the probability of MRSA SSTI

Negative MRSA nasal screen \rightarrow small but potentially significant decrease in the probability of MRSA SSTI

Augments existing literature in this area and may improve empiric antibiotic therapy guidance for patients with SSTI

Source: Ann of Pharmacotherapy. 2023;57(6):669-676.

Presenter's Critique

Strengths

- Sample size
- Large time frame
- Included multiple types and locations of SSTI, with purulent vs. nonpurulent noted

Limitations

- Retrospective
- Excluded patients with a history of MRSA infections

Determining the Utility of MRSA Nares Screening in Antimicrobial Stewardship

Mergenhagen KA, et al. 2020

Study Design, Methods, and Inclusion

Retrospective cohort study across Veterans Affairs (VA) medical centers nationwide

January 2007 – January 2018

Included patients who were tested for MRSA colonization via the nares upon admission or inpatient transfer

Total of 245,833 unique patients with 561,325 cultures from a variety of anatomical sites

Source: Clin Infect Dis. 2020;71(5):1142-1180.

Baseline Characteristics

Source: Clin Infect Dis. 2020;71(5):1142-1180.

N = 561,325
540,583 (96)
68 (12)
223,050 (40)
138,647 (25)
90,912 (16)
70,185 (13)
22,446 (4)
4,817 (1)
N = 245,833
237,229 (97)
181,179 (74)
64,654 (26)

SD = standard deviation

Efficacy Characteristics of MRSA Nares Screening by Wound Culture Type

Wound Culture Type	Sensitivity, %, (95% CI)	Specificity, %, (95% CI)	PPV, %, (95% CI)	NPV, %, (95% CI)
Wound site unspecified (n = 136,078)	60, (59-61)	83, (82-83)	34, (34-35)	93, (93-93)
Wound site sterile (n = 72,542)	58, (58-59)	85, (85-86)	36, (36-37)	94, (93-94)

CI = confidence interval

Authors' Conclusion

Negative MRSA PCR taken within 7 days of culture is useful for predicting the absence of MRSA in subsequent clinical culture

MRSA PCR is a stewardship tool to avoid the use or deescalate anti-MRSA therapy

MRSA PCR is not a tool to predict current MRSA infection

Source: Clin Infect Dis. 2020;71(5):1142-1180.

Presenter's Critique

Strengths

- Sample size and nationwide study
- Assessed sterile vs. nonsterile cultures

Limitations

- Retrospective
- Did not assess if patient had been decolonized recently
- Majority of wounds were unspecified

Compare

Burgoon R, <i>et al</i> . 2014	Hitchcock AM, <i>et al</i> . 2023	Mergenhagen KA, <i>et al</i> . 2020
Sensitivity: 81%	Sensitivity: 64%	Sensitivity: 60%
Specificity: 72%	Specificity: 94%	Specificity: 83%
PPV: 22%	PPV: 70%	PPV: 34%
NPV: 98%	NPV: 91%	NPV: 93%

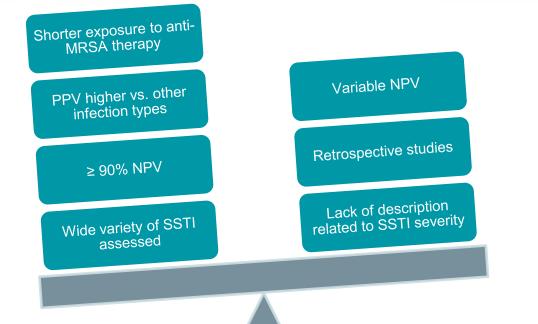
Sources:

Am J Infect Control. 2022;50;941-946.

Ann of Pharmacotherapy. 2023;57(6):669-676. Clin Infect Dis. 2020;71(5):1142-1180.

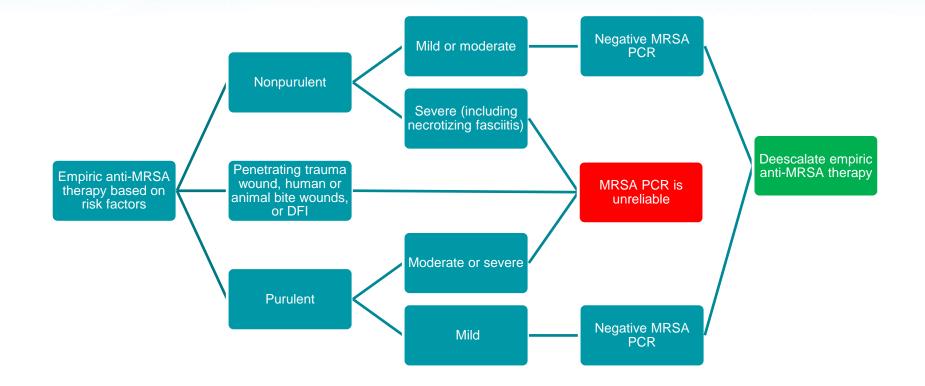
Limitations

Strengths



Strengths and Limitations of Nasal MRSA PCR in SSTI

Proposed Algorithm for the Use McLeod Health of MRSA PCR in SSTI



Future Directions

Correlation Between Patients With McLeod Health MRSA Nares Colonization and MRSA DFI

Brondo, et al. 2022 \rightarrow single-center, retrospective medical record review Purpose **Methods** Results October 2013 – October 2019 To evaluate the utility MRSA Nares Test Results • of MRSA nares testing Negative (N = 176) Patients included had listed diagnosis of diabetes, • ٠ for prediction of MRSA MRSA nares results, and wound, bone, or tissue - Non-MRSA DFI, n (%): 165 (94) in DFI - MRSA DFI, n (%): 11 (6) cultures collected during the same admission N = 200Positive (N = 24)- Non-MRSA DFI, n (%): 10 (42) - MRSA DFI, n (%): 14 (58) MRSA Nares Test Validity Sensitivity: 56% Specificity: 94% PPV: 58% NPV: 94%

Authors' Conclusions

- Expands on prior literature supporting the strong correlation of NPV for MRSA nares and DFI
- Suggest the ability to use a negative MRSA nares test to effectively rule out MRSA DFI, which may allow for faster deescalation of empiric anti-MRSA antibiotic therapy

Source:

Intern J or Low Extrem Wound. 2022;21(4):502-505.

Utility of MRSA PCR Beyond Respiratory Infections

Noeldner HM, et al. 2022 \rightarrow retrospective cohort study across 3 hospitals Purpose **Method and Design** Results To determine the clinical utility • March 2019 – February 2020 Any clinical culture ٠ of MRSA PCR assays beyond 40% of Staphylococcus aureus isolates were MRSA Sensitivity: 67.5% • ٠ respiratory indications by Included patients who had a clinical culture within 3 Specificity: 88.8% ٠ estimating its predictive value days of a MRSA PCR PPV: 11.0% • for clinical cultures from NPV: 99.3% blood, bone, and soft tissue Bone and soft tissue Sensitivity: 55.0% Specificity: 92.7% PPV: 50.0% NPV: 92.7% • **Authors' Conclusion**

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 A negative MRSA PCR obtained within 3 days of a culture has a high NPV for MRSA infections in blood, bone, and soft tissue

Source:

Antimicrob Steward & Healthcare Epidem. 2022;2:1-3.

Assessment Question #1

What classification of pneumonia is a MRSA PCR indicated per the ATS/IDSA guidelines?

- a.CAP b.HCAP c.HAP d.VAP e.a, c
- f. All of the above

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a.CAP

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f. All of the above

Assessment Question #2

Which of the following studies does not assess the MRSA nasal PCR in SSTIs?

a. Parente D, et al. 2018

- b. Burgoon R, et al. 2022
- c. Hitchcock AM, et al. 2023
- d. Mergenhagen KA, et al. 2020

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Assessment Question #3

Which of the following clinical scenarios would the MRSA PCR be unreliable if obtained within 48 hours of presentation, per the presenter's conclusions?

a.Mild cellulitis (nonpurulent SSTI)
b.Moderate erysipelas (nonpurulent SSTI)
c.Moderate SSTI due to a dog bite
d.Mild abscess (purulent SSTI)

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Thank you!

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