University Medical Center New Orleans
LCMC Health

Methicillin Resistant *Staphylococcus aureus* (MRSA) Nares Polymerase Chain Reaction (PCR) Screening within Hospitalized Patients

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Disclosure

The speaker and content reviewers have disclosed that they have no relevant financial disclosures. No one else in a position to control content has any financial relationships to disclose.

Objectives

- Assess implications of MRSA nares PCR for MRSA decolonization within a hospital setting
- Identify infections in which the MRSA nares PCR has a high negative predictive value
- Compare the sensitivity and specificity of the MRSA nares PCR based on cultures from different clinical specimens
- Determine the utility of MRSA nares screening for vancomycin stewardship

Self- Assessment Question 1

1. According to the Centers for Disease Control and Prevention (CDC), 1 in ____ people carry and are colonized by *Staphylococcus aureus* and about 2 in 100 carry methicillin-resistant *Staphylococcus aureus.*

    a. 3
    b. 10
    c. 20
    d. 50

Self- Assessment Question 1

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Methicillin Resistant *Staphylococcus aureus* Infections

Predominant pathogen in healthcare-associated infections

Limited treatment options

- High prevalence influences antimicrobial use
- Contributes to further spread of resistance
- Prevalent MRSA » increased vancomycin use » increased vancomycin resistance (VRE and VRSA)

Prevention of MRSA infections is key in reduction of overall burden

MRSA Colonization

One in 3 people are colonized by *Staphylococcus aureus*

Two in 100 are colonized by methicillin-resistant *Staphylococcus aureus* (MRSA)

Significantly increased risk of invasive MRSA infection

Benefit in identification of colonization status

Willis et al. *American Journal of Health-System Pharmacy*. 2017
Centers for Disease Control and Prevention, Feb 2019

MRSA Nares PCR

Detects and amplifies DNA related to MRSA in the nares

Equal sensitivity to MRSA culture screening

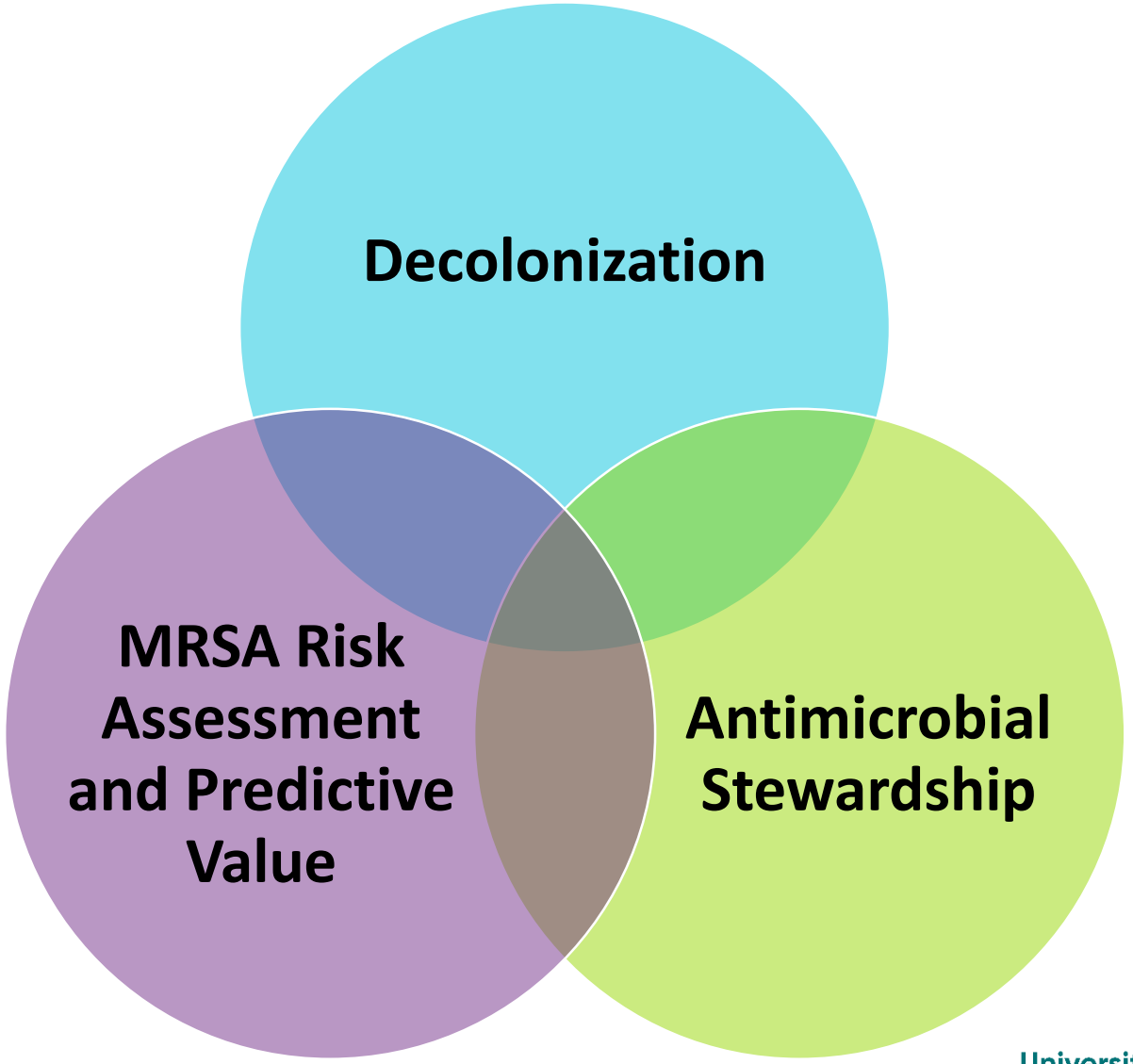
Rapid detection (up to 5 hours) compared to culture methods (1-5 days)

Allows confirmation of MRSA colonization

Kluytmans J. J Hosp Infect. 2007

https://umc.edu/som/Departments%20and%20Offices/SOM%20Departments/Pathology/UMMC%20Lab%20Services/Lab%20Test%20List/Laboratory/images/GBS-PCR-or-MRSA-PCRws.png

Implications of MRSA Nares PCR Utilization



MRSA Nares PCR Implications for:

Decolonization

CDC Recommendation Regarding MRSA Colonization

Prevention Strategies Targeting Colonization

Essential to prevent transmission of *Staphylococcus aureus*

- Decreases contamination of health care personnel and environment

- Reduces bacterial burden and likelihood of transmission

 Centers for Disease Control and Prevention, Feb 2019

MRSA Colonization Prevention Strategies

- Decolonization
  - Intranasal antibiotic (mupirocin)
  - Intranasal antiseptic (povidone-iodine)
- Daily chlorhexidine gluconate (CHG) bathing
  - Decreases pathogen burden on skin
- Active surveillance testing (AST)
  - Detection of MRSA in all patients
  - MRSA nares PCR
- Contact precautions
  - Reduces transmission and contamination

 Centers for Disease Control and Prevention, Feb 2019

Resistance to MRSA Decolonizing Agents

Limitation of mupirocin

- Emerging resistance
- Wide range of incidence depending on geographical location (1%-81%)

Resistance association

- Mupirocin exposure
- Failed decolonization

Alternatives

- Novel antimicrobials: lysostaphin, omiganan pentahydrochloride
- Antiseptics: polyhexanide, **70% ethanol (Nozin® Nasal Sanitizer® Antiseptic)**

Poovelikunnel T, Gethin G, Humphreys H. *J Antimicrob Chemother*. 2015.

Nozin® Nasal Sanitizer® Antiseptic

Non-prescription- ethyl alcohol combined with emollient

Broad spectrum anti-septic with microbial activity when topically applied

Used to reduce nasal carriage of MRSA

Non-selective and does not promote resistance

Has 12-hour persistence and should be applied twice a day

Clinical Applicability of Decolonization and MRSA PCR

Universal decolonization may affect detection and predictive value of MRSA nares PCR

Predictive value allows for clinical decision-making regarding anti-MRSA agent utilization

Unknown how **antiseptic** decolonization affects predictive value

Benefits of MRSA nares PCR	Limitations of MRSA nares PCR

• High negative predictive value for pneumonia
• Substantial evidence for skin and soft tissue infections
	• Lack of data on
	  • **<u>Factors affecting sensitivity</u>**
	  • Many infectious disease states
	  • Optimal timing

MRSA Nares PCR Implications for:

MRSA Risk Assessment and Predictive Value

Self- Assessment Question 2

2. How might decolonization with mupirocin influence MRSA nares PCR results?

   a. Reduction in negative predictive value if administered before PCR
   b. Reduction in positive predictive value if administered before PCR
   c. Increase in positive predictive value if administered after PCR
   d. Increase in negative predictive value if administered after PCR

Self- Assessment Question 2

2. How might decolonization with mupirocin influence MRSA nares PCR results?

   a. Reduction in negative predictive value if administered before PCR
   b. Reduction in positive predictive value if administered before PCR
   c. Increase in positive predictive value if administered after PCR
   d. Increase in negative predictive value if administered after PCR

Evaluation of the reliability of MRSA screens in patients undergoing universal decolonization

Retrospective study

N=125

Evaluated MRSA PCR results based on timing of mupirocin administration

Primary outcome: negative predictive value non-inferiority

Failed to meet non-inferiority with a difference of -3.8% (90% CI -7.8%-0.2%; p=0.31)

	Mupirocin before PCR	Mupirocin after PCR
Negative Predictive Value	95.2%	99%

Chaudhry A, American Journal of Health-System Pharmacy. 2020

Trials Assessing Predictive Value for Various Disease States

	Number of Trials	Range of Negative Predictive Value (NPV)	Range of Positive Predictive Value (PPV)
Respiratory infections	19	76 - 99%	12 - 100%
Skin and soft tissue infections	3	72 - 98%	85 - 93%
Diabetic foot infections	2	89 - 94%	43 - 58%
Prosthetic joint infections	1	74%	90%

Smith MN, *Ann Pharmacother*. 2019.
Lourtet-Hascoëtt J *Diagnostic Microbiology and Infectious Disease*. 2015
Clay TB, Orwig KW, Stevens RA, et al. 2021.
Brondo J et al. Int J Low Extrem Wounds. 2020
Mergenhagen KA et al. Antimicrob Agents Chemother. 2020
Acquisto NM, et al. *Emerg Med J*. 2018.
Terp S. et al. *Clinical Infectious Diseases*. 2014

Determining the Utility of Methicillin-Resistant *Staphylococcus aureus* Nares Screening in Antimicrobial Stewardship

Retrospective cohort study conducted by VA medical centers

All VA patients tested with MRSA nares screening upon admission or transfer from 2007- 2018

Assessed cultures attained within 7 days of MRSA nasal swab

Based on culture, not clinical infection

N=561,325

Mergenhagen KA et al. Clin Infect Dis. 2020

Determining the Utility of Methicillin-Resistant *Staphylococcus aureus* Nares Screening in Antimicrobial Stewardship

Results

Observed Culture	Negative Predictive Value (%)	Positive Predictive Value (%)	Sensitivity (%)	Specificity (%)
Blood	96.5	27.8	68.9	81.9
Intra-abdominal	98.6	18.8	66.1	89.3
Respiratory	96.1	35.0	76.2	80.3
Wound	93.1	34.2	59.8	82.5
Urinary	99.2	7.6	72.5	80.2

Mergenhagen KA et al. Clin Infect Dis. 2020

Determining the Utility of Methicillin-Resistant *Staphylococcus aureus* Nares Screening in Antimicrobial Stewardship

Conclusions

Large cohort of patients and cultures

Confirmed high negative predictive value for all culture types

Suggested that negative MRSA nares screening taken within 7 days of culture may be utilized to de-escalate anti-MRSA agents

Self- Assessment Question 3

3. Which of the following infectious disease states have the most substantial data regarding use of the methicillin resistant *Staphylococcus aureus* polymerase chain reaction (MRSA PCR) for de-escalation?

   a. Bone and joint infections
   b. Pneumonia
   c. Meningeal infections
   d. Intra-abdominal infections

Self- Assessment Question 3

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   b. Pneumonia
   c. Meningeal infections
   d. Intra-abdominal infections

MRSA Nares PCR Implications for:

Antimicrobial Stewardship

Impact of Pharmacist-Driven MRSA PCR Protocols

Trial and Design	Primary Outcome	Results	Conclusion
Willis C et al. American Journal of Health-System Pharmacy. 2017 • Retrospective, pre-post cohort • MRSA PCR protocol for **pneumonia** • N=300	Vancomycin days of therapy (DOT)	Median 2.1 DOT reduction (2.1 days vs 4.2 days, p < 0.0001)	• Reduced vancomycin days of therapy for pneumonia • No difference in rate of AKI and mortality
Pham SN, et al. Hosp Pharm. 2021 • Retrospective, pre-post cohort • MRSA PCR protocol for **pneumonia** • N=210	Anti-MRSA agent days of therapy (DOT)	Mean 1.1 DOT reduction (1.4 vs 2.5 days, p < .001)	• Reduced anti-MRSA days of therapy for pneumonia • No difference in rate of AKI and mortality

Impact of Pharmacist-Driven MRSA PCR Protocols

Future Implications

Assessment of cost reduction

Defining optimal time to de-escalation and attainment of MRSA PCR

Determining predictive value and utility for stewardship within various disease states and populations

Evaluation of the Predictive Value of Methicillin Resistant *Staphylococcus aureus* (MRSA) Nares Polymerase Chain Reaction (PCR) Screening within Hospitalized Patients

Purpose

Evaluate the utility of MRSA nares PCR screening within a wide range clinical specimens and its impact on antimicrobial stewardship

University Medical Center New Orleans

- Academic medical center
- Level I Trauma Center
- 448 beds
- Three intensive care units
  - Burn
  - Trauma
  - Medical
- Urban/underserved population

Study Design

- IRB-approved, retrospective, single center study
- Inclusion criteria: All patients aged ≥18 years tested for MRSA colonization

Nov 2020-Jan 2021

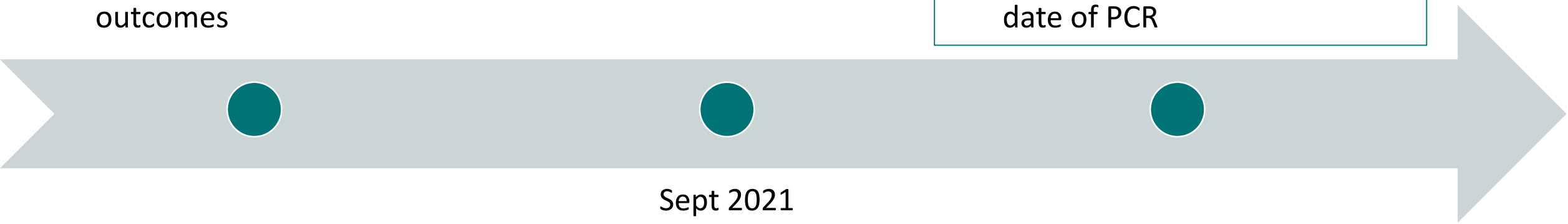
Pre-Intervention

- Comparator arm for antimicrobial stewardship outcomes

Nov 2021-Jan 2022

Post-Intervention

- Assessed patients with cultures taken ± 7 days from date of PCR



Sept 2021

Intervention

- In-house nares implemented

Data Collection

Primary outcome

- Negative predictive value (NPV)

Secondary outcome

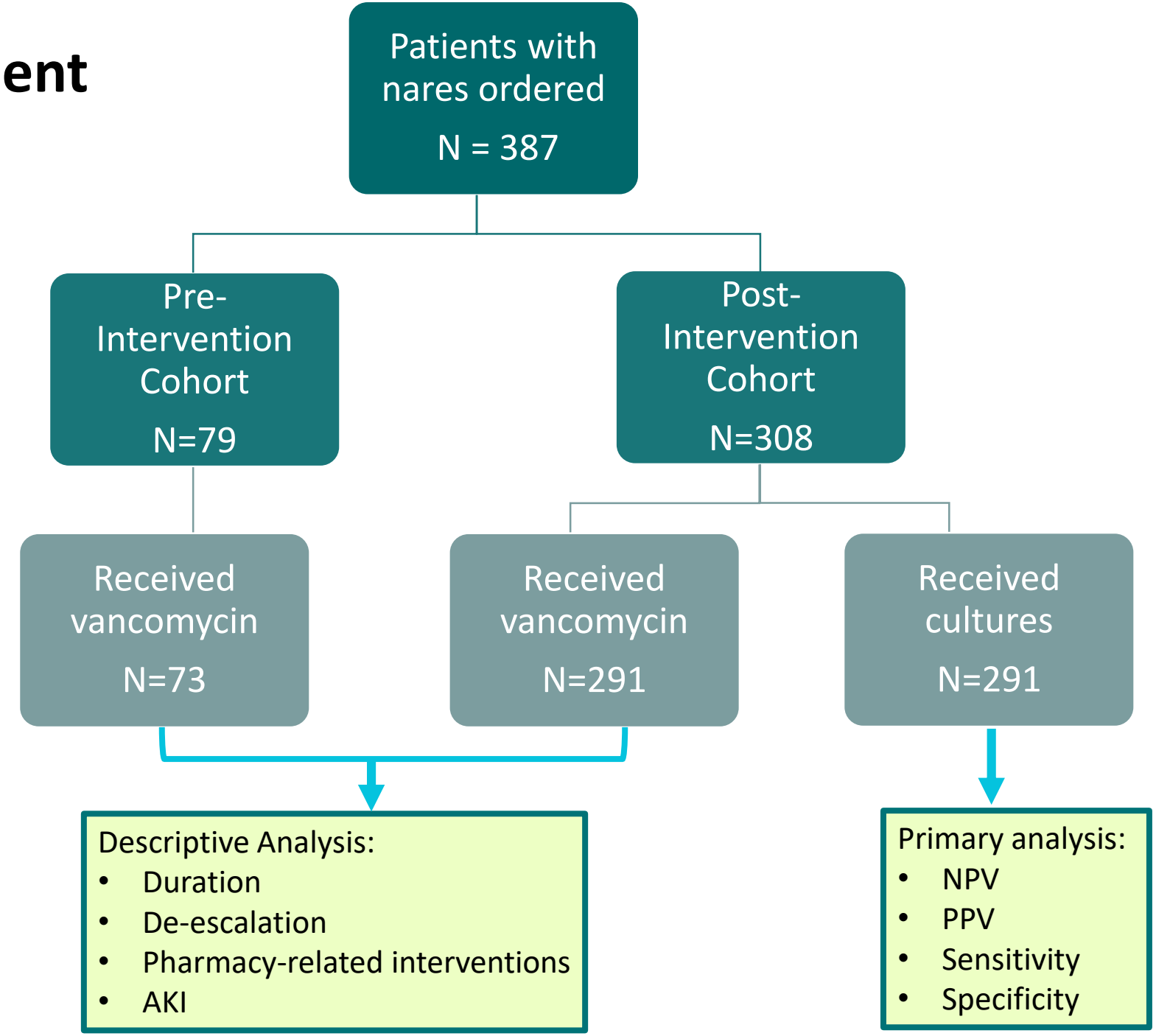
- Positive predictive value (PPV)
- Sensitivity
- Specificity

Descriptive Data

- Vancomycin days of therapy
- Rate of vancomycin de-escalation
- Pharmacy-related interventions
- Acute kidney injury

Results

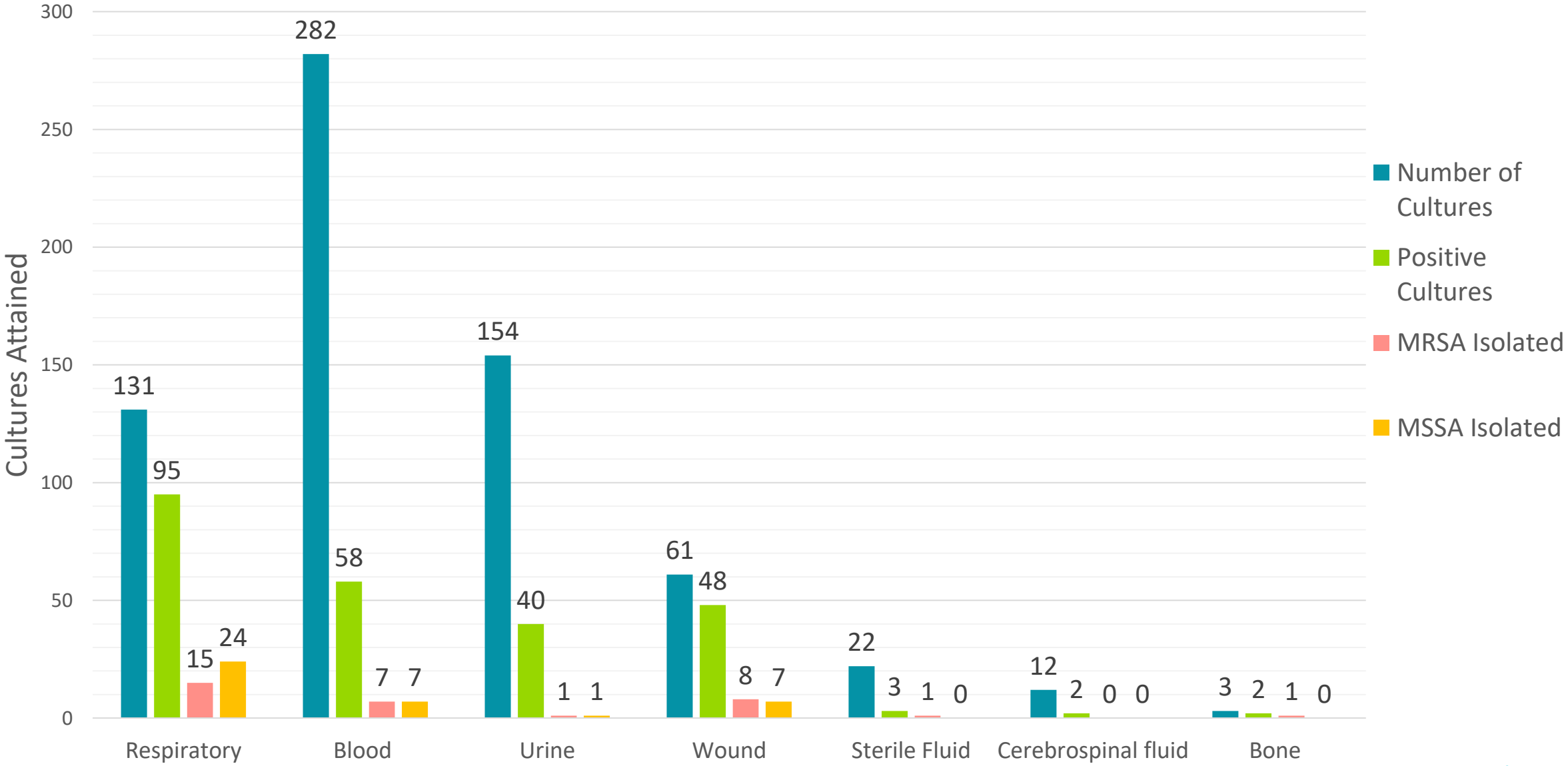
Patient Enrollment



Baseline Characteristics

Demographics	Pre-Intervention Cohort, N=79	Post-Intervention Cohort, N=308
Age, years (±SD)	63 (±15)	54.6 (±15.9)
Weight, kg (IQR)	88 (148-240)	84.3 (145.4-218.2)
Male, n (%)	50 (63)	199 (64.6)
Race/Ethnicity, n (%)		
White/Caucasian	32 (40.5)	99 (32.1)
African American	44 (55.7)	168 (54.5)
Admitted to ICU, n (%)	60 (75.9)	154 (50.9)
Trauma, n (%)	1(1.3)	56 (18.2)
COVID-19 positive, n (%)	20 (25.3)	42 (13.6)
Point of care, n (%)		
Home	59 (74.6)	244 (79.2)
Hospital transfer	18 (22.8)	52 (16.8)
Mortality, n (%)	31 (39.2)	53 (17.2)

Culture Breakdown

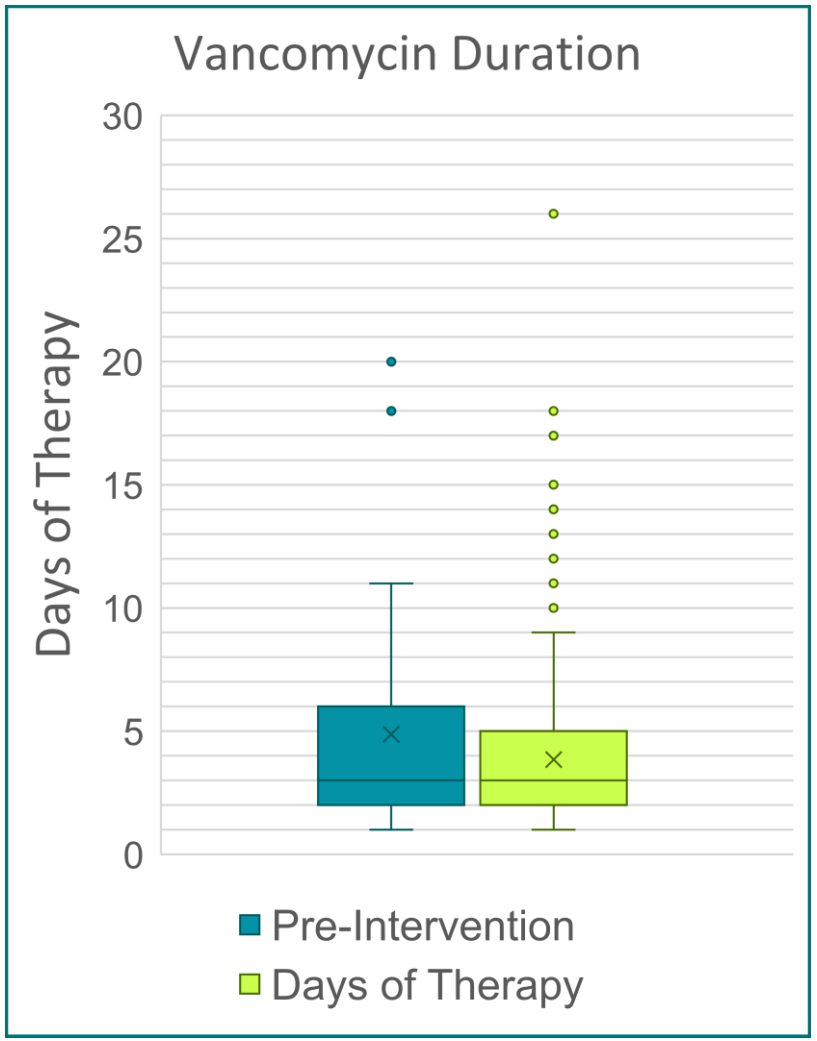


Primary Analysis*

Observed Culture	Negative Predictive Value (%)	Positive Predictive Value (%)	Sensitivity (%)	Specificity (%)	Prevalence (%)
Respiratory (n=131)	99.03	48.15	92.85	88.03	10.68
Blood (n=282)	100	11.48	100	80.36	11.47
Urine (n=154)	100	2.78	100	77.12	0.65
Wound (n=61)	100	50	100	84.9	13.11
Sterile fluid (n=22)	100	20	100	80.95	4.5
Cerebrospinal fluid (n=12)	100	N/A	N/A	91.67	N/A
Bone (n=3)	100	100	100	100	33.3
Total (n=665)	99.8	21.09	96.88	81.67	4.8

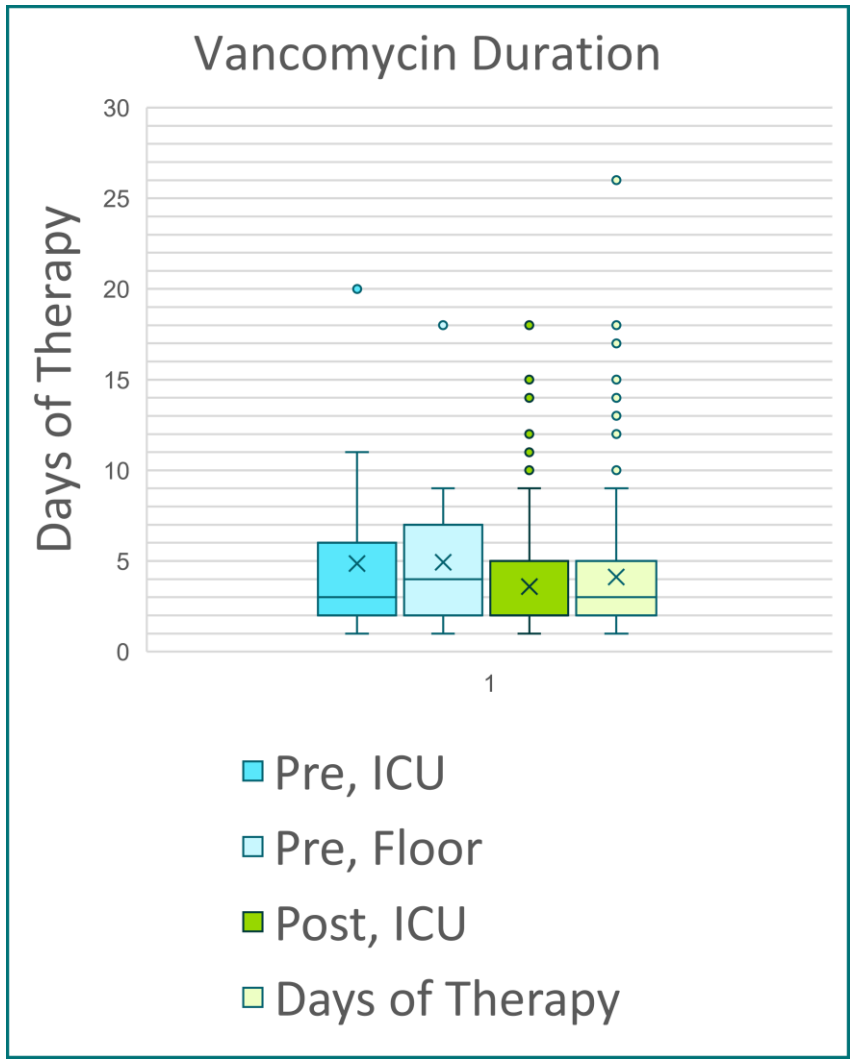
*Within post-intervention cohort

Intervention Analysis



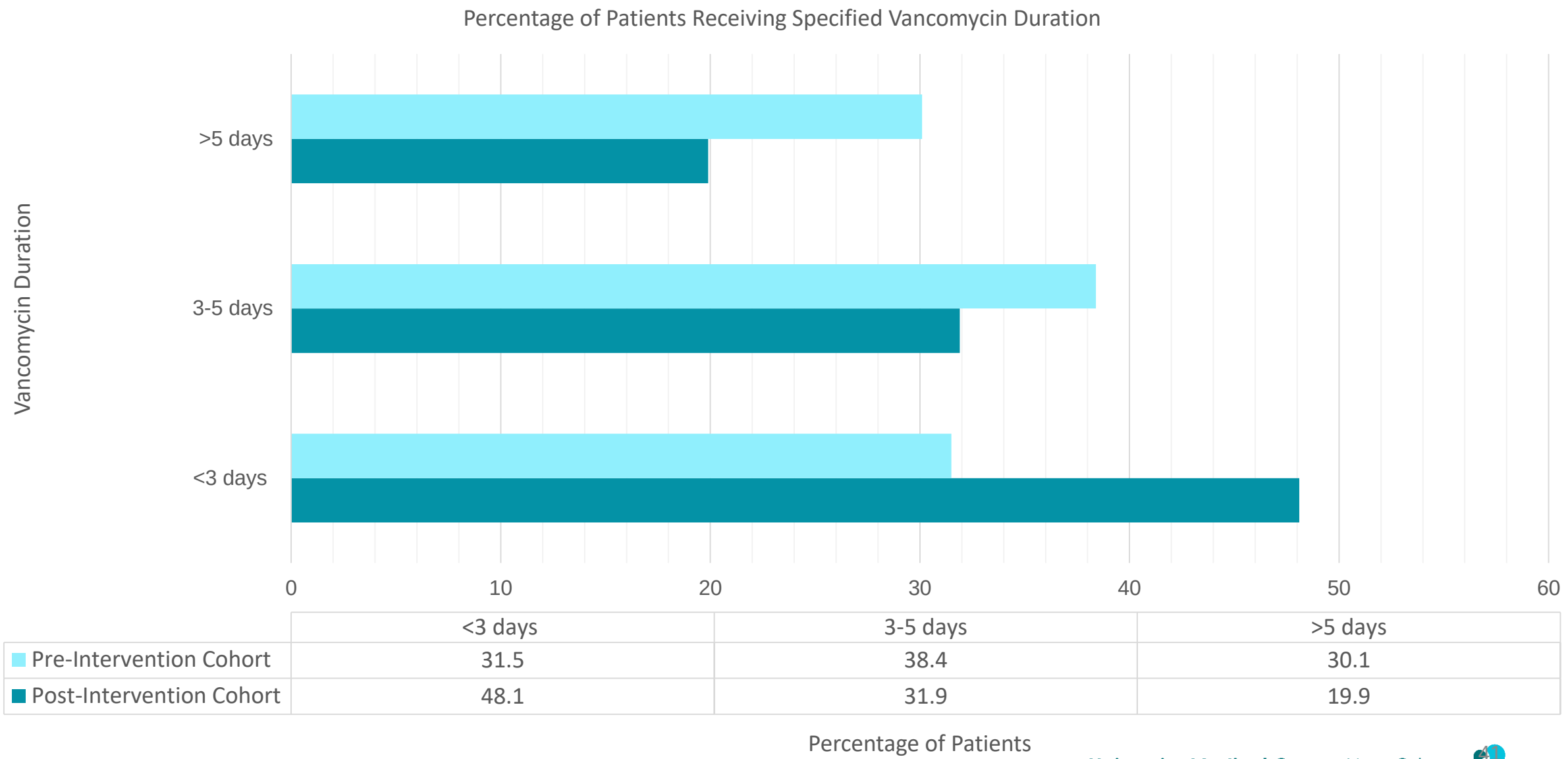
Outcome	Pre-Intervention (n=73)	Post-Intervention (n=291)
Vancomycin duration, days (IQR)	3 (2-6)	3 (2-5)
AKI, n (%)	33 (45.2)	63 (21.6)
Ordered by pharmacy, n (%)	46 (63)	177 (60.8)
Time to result, hours	34.2	2.6

Subgroup Analysis in Patients Receiving Vancomycin



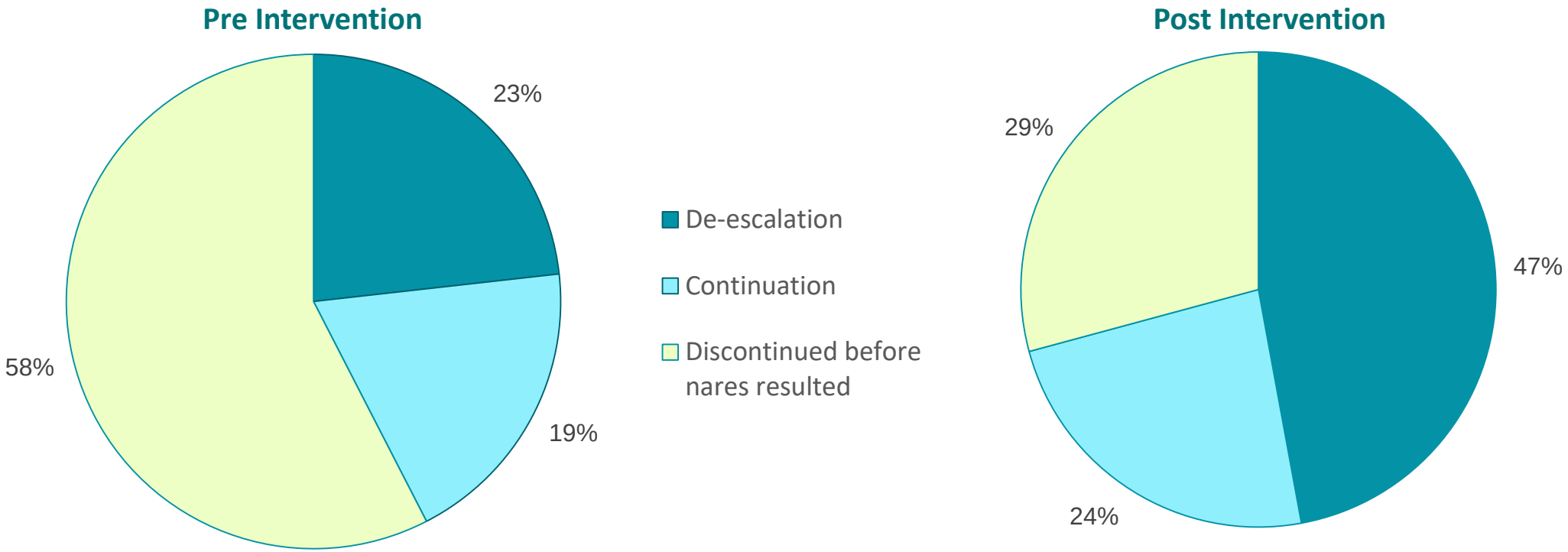
Baseline Characteristic	Pre-Intervention Cohort		Post-Intervention Cohort	
	Floor N=13	ICU N=60	Floor N=138	ICU N=153
Mortality, n (%)	2 (15.3)	28 (46.6)	9 (6.5)	44 (28.7)
Vancomycin duration, days (IQR)	4 (2-5)	3 (2-6)	3 (2-4.8)	2 (2-5)
AKI, n (%)	4 (30.8)	29 (48.3)	22 (15.9)	41 (26.7)

Vancomycin Duration between Cohorts



	<3 days	3-5 days	>5 days
Pre-Intervention Cohort	31.5	38.4	30.1
Post-Intervention Cohort	48.1	31.9	19.9

Vancomycin Management



	Pre intervention cohort (n=73)	Post Intervention cohort (n=291)
Percentage with pharmacist interventions	17.8%	23%

Vancomycin Management

	Total levels (only assessed first three levels)	Inappropriate level drawn (%)	Therapeutic at any time (%)
<3 days of vancomycin N=139	109	10 (9.2)	39 (35.7)
3-5 days of vancomycin N=93	149	21 (14.1)	61 (40.9)
>5 days of vancomycin N=58	151	16 (10.6)	56 (37)

Nozin® Administration and MRSA PCR Results

	MRSA PCR positive N=65	MSSA PCR positive N=67	PCR negative N=176
Average days given before screening	3.5	4.25	5.1
Number of patients given Nozin®	63 (96.9)	59 (88)	162 (92)

Discussion

Primary and Secondary Outcomes

- NPV: ≥ 99%
- PPV: ≤ 50%
- Specificity: ≥ 90%
- Sensitivity: 77-100%

Descriptive Data

- Median duration of vancomycin unchanged
  - Rates of vancomycin de-escalation increased at day 3
  - Decreased percentage of patients receiving 5 days or greater by 10.2%
- Post-Intervention cohort
  - Increased de-escalation
  - Decreased AKI in cohort and subgroup of ICU patients
- Pre-Intervention cohort
  - Vancomycin discontinued before nares result

Strengths

Population

- Tertiary care hospital
- Extensive surgical services
- Large % of ICU patients
- High prevalence of MRSA

Antimicrobial stewardship

- Days of therapy tied to nares ordering
- Impact of pharmacist

Limitations

Study design

- Single center
- Retrospective
- Selection bias
- Small sample size

Culture Data

- Low number of cerebrospinal, sterile, and bone cultures
- Lack of more specific culture data (site, type)

Pharmacist interventions

- Underestimated
- Based off documentation

Conclusions

High total NPV and sensitivity within tertiary care hospital with burn and trauma population

Cultures with low PPV and specificity

- Blood
- Urine
- Sterile fluid
- Cerebrospinal fluid

Outcomes of vancomycin stewardship

- Decrease in AKI
- Increase in pharmacy interventions and de-escalation

Self- Assessment Case

AD, a 74-year-old female with history of T2DM and percutaneous nephrostomy tubes, presented to the ED with complaints of dysuria, hematuria, abdominal pain, and persistent fever. A urinalysis and urine culture were attained with pending results. She was admitted and started empirically on vancomycin and piperacillin/tazobactam with the indication of complicated urinary tract infection.

An MRSA nares PCR was ordered and resulted as negative for both *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus*.

Self- Assessment Case

4. Which statement reflects the most appropriate interpretation and action regarding her negative MRSA PCR result?

   a. The patient is not colonized with MRSA and therefore can be safely de-escalated from vancomycin to piperacillin/tazobactam alone given its high negative predictive value
   b. The patient is not colonized with MRSA but given her presentation should be kept on empiric vancomycin
   c. According to the CDC, it is appropriate to administer nasal antiseptic in a universal de-colonization method despite her negative result
   d. A & C
   e. B & C

Self- Assessment Case

4. Which statement reflects the most appropriate interpretation and action regarding her negative MRSA PCR result?

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   d. A & C
   e. B & C

Acknowledgements

- Catherine Vu, Pharm D., BCIDP
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