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U.S. Department  
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# Impact of Accelerate Pheno™ System on Time to De-escalation of Antimicrobial Therapy

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# Disclaimer

- The material is the result of work supported with resources and the use of facilities at the VA St. Louis Health Care System
- The contents do not represent the views of the U.S. Department of Veterans Affairs or the United States Government
- This study was approved by the Institutional Review Board (IRB) at the VA St. Louis Health Care System



# Background

- Molecular diagnostic tests enable early identification of pathogens and improve timeliness to appropriate definitive therapy
- Accelerate Pheno™ system provides:
  - Organism identification (ID) in ~2 hours
  - Antimicrobial susceptibility testing (AST) in ~7 hours
- Shown to decrease time to ID and AST compared to conventional methods
- Few studies evaluating its impact on the management and outcomes of patients with bloodstream infections



# Literature Review

Study	Intervention	Results
Dare R, et al. (2018)	<ul style="list-style-type: none"><li>• Single center retrospective chart review</li><li>• SOC vs. ADX</li></ul>	<ul style="list-style-type: none"><li>• ↓ time to ID and AST</li><li>• ↓ time to optimal therapy</li><li>• ↓ LOS and total antibiotic DOT</li></ul>
Ehren K, et al. (2020)	<ul style="list-style-type: none"><li>• Quasi-experimental observational study</li><li>• Conventional microbiological diagnostics ± ASP intervention vs. ADX + ASP intervention</li></ul>	<ul style="list-style-type: none"><li>• ↓ time to ID and AST</li><li>• ↓ time to optimal therapy</li><li>• No impact on antibiotic consumption, total antibiotic DOT, LOS, or CDI rate</li></ul>
Banerjee R, et al. (2020)	<ul style="list-style-type: none"><li>• Multicenter, prospective, randomized control trial</li><li>• SOC vs. ADX</li></ul>	<ul style="list-style-type: none"><li>• ↓ time to ID and AST</li><li>• ↓ time to first antibiotic change</li><li>• No impact on LOS, 30-day mortality, or rate of CDI</li></ul>

SOC, standard of care; ADX, Accelerate Pheno™ system; LOS, length of stay; DOT, days of therapy; ASP, antimicrobial stewardship; CDI, *Clostridioides difficile* infection



# Objective and Outcomes

- Objective
  - To identify the impact of the Accelerate Pheno™ system on time to de-escalation of antimicrobial therapy
- Primary Outcome
  - Time to de-escalation of antimicrobial therapy (hours)
    - Difference between the time of first doses of definitive antimicrobial therapy and empiric antimicrobial therapy
      - Definitive therapy- regimen chosen based on definitive ID and AST
      - Empiric therapy- initial antimicrobial therapy administered for  $\geq 2$  doses before organism ID available



# Secondary Outcomes

- Time to organism ID (hours)
- Time to AST (hours)
- Duration of antimicrobial therapy while hospitalized (days)
- Hospital length of stay (days)
- Mortality within 30 days
- Rate of CDI
- Rate of acute kidney injury (AKI)
- Proportion of patients de-escalated from MRSA coverage to non-MRSA coverage
- Proportion of patients de-escalated from antipseudomonal coverage to non-antipseudomonal coverage



# Study Design

- Retrospective quasi-experimental, observational cohort study
- September 1, 2017-August 31, 2019
  - Pre-implementation: September 1, 2017-August 31, 2018
  - Post-implementation: September 1, 2018-August 31, 2019
- Conducted at VA St. Louis Health Care System



# Inclusion and Exclusion Criteria

## Inclusion Criteria

- Age 18-89 years
- Positive blood culture
- Receiving intravenous antimicrobial therapy within 24 hours of blood cultures being drawn

## Exclusion Criteria

- Polymicrobial blood culture
- Positive cultures from another sterile site with a different organism that requires antimicrobial treatment
- Patients expired or on hospice at the time the blood culture resulted
- Patients with a blood culture positive for a fungus





# Statistical Analysis

## Baseline Characteristics and Outcomes

- Baseline characteristics: Descriptive statistics
- Categorical variables: Chi-Square or Fisher's Exact test
- Continuous variables: T-test or Wilcoxon-ranked sum

## Sample Size

- Sample size: At least 45 patients per group
  - Based on clinically meaningful difference, defined as a decrease in time to de-escalation by 24 hours
  - Two-sided  $\alpha=0.05$ ,  $\beta=0.20$

## Multivariate Logistic Regression

- To determine factors associated with de-escalation within 48 hours
- Threshold for univariate  $p < 0.2$
- Significance after regression  $p < 0.05$



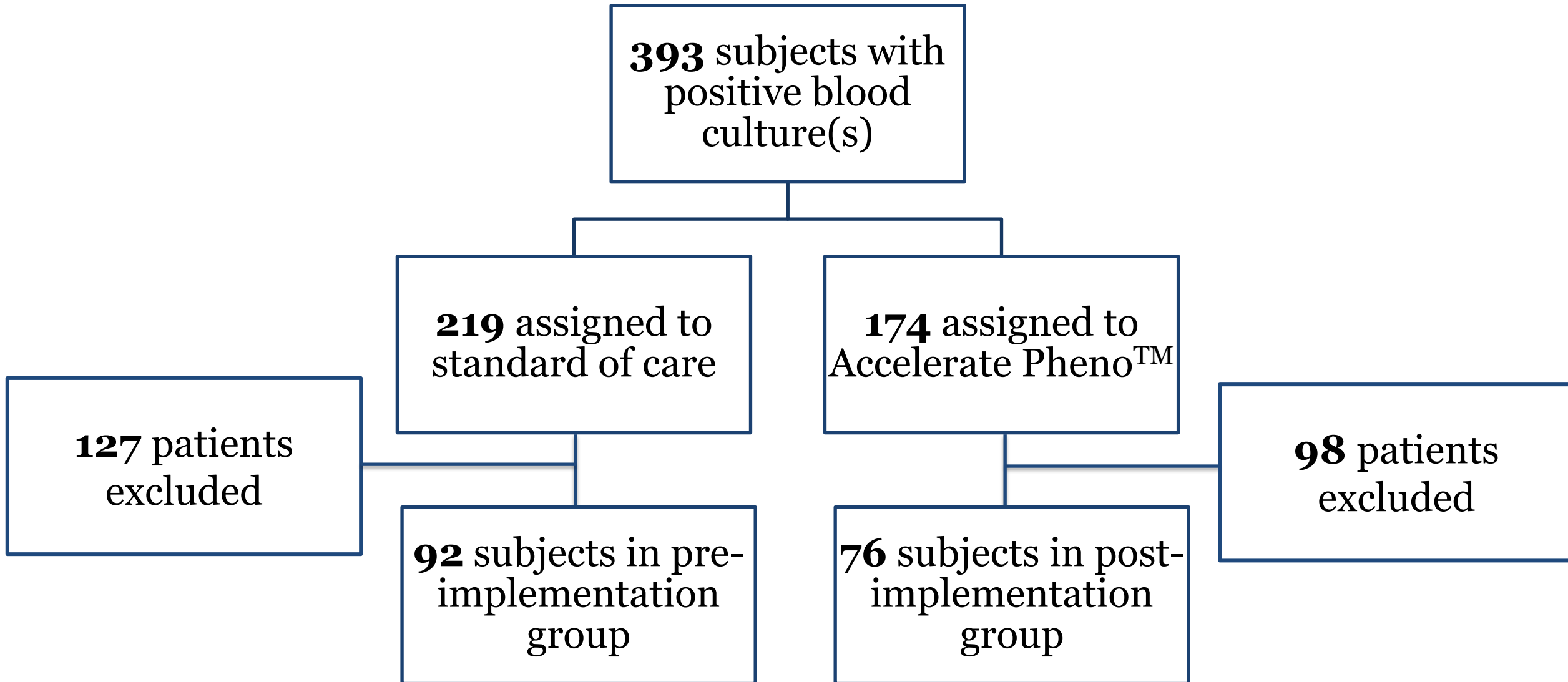
# Logistic Regression Parameters

*Univariate analysis to determine factors independently associated with de-escalation within 48 hours- multivariate logistic regression if  $p < 0.2$*

- Gram-positive infection
- Use of Accelerate Pheno™ system
- Presence of infectious diseases consult
- Presence of pharmacist antimicrobial stewardship note(s)



# Patient Enrollment





# Baseline Characteristics

Variable	Pre-Implementation (n=92)	Post-Implementation (n=76)	P-value
Male, n (%)	89 (96.7)	73 (96.1)	1.000
Age, mean years $\pm$ SD	67.4 $\pm$ 9.1	67.1 $\pm$ 9.3	0.834
Initial SCr (mg/dL), mean $\pm$ SD	1.8 $\pm$ 1.7	2.4 $\pm$ 2.3	0.042
ICU Admission, n (%)	21 (22.8)	13 (17.1)	0.358
Infectious diseases consult, n (%)	43 (46.7)	40 (52.6)	0.447
Pharmacist antimicrobial stewardship notes, n (%)	11 (12.0)	10 (13.2)	0.093



# Organism Identified

Organism	Pre-Implementation (n=92)	Post-Implementation (n=76)
Coagulase-negative <i>Staphylococcus</i> spp.	29 (31.5)	19 (25.0)
<i>Staphylococcus aureus</i>	15 (16.3)	12 (15.8)
<i>Escherichia coli</i>	14 (15.2)	16 (21.1)
<i>Streptococcus</i> spp.	10 (10.9)	4 (5.3)
<i>Klebsiella</i> spp.	9 (9.8)	6 (7.9)
<i>Pseudomonas aeruginosa</i>	2 (2.2)	4 (5.3)
<i>Enterobacter</i> spp.	0 (0)	4 (5.3)
Other	13 (14.1)	11 (14.3)

All values are n (%)



# Empiric Antibiotics

**Pre-Implementation:** n= 150 total empiric antibiotics  
**Post-Implementation:** n= 122 total empiric antibiotics

Antibiotic	Pre-Implementation	Post-Implementation
Vancomycin	56 (37.3)	43 (35.3)
Cefepime	22 (14.7)	22 (18.0)
Piperacillin-tazobactam	19 (12.7)	11 (9.0)
Ceftriaxone	17 (11.3)	16 (13.1)
Metronidazole	9 (6.0)	11 (9.0)
Azithromycin	9 (6.0)	3 (2.5)
Meropenem	8 (5.3)	5 (4.1)
Other	10 (6.7)	11 (9.0)

All values are n (%)



# Definitive Antibiotics

**Pre-Implementation:** n= 75 total definitive antibiotics  
**Post-Implementation:** n= 75 total definitive antibiotics

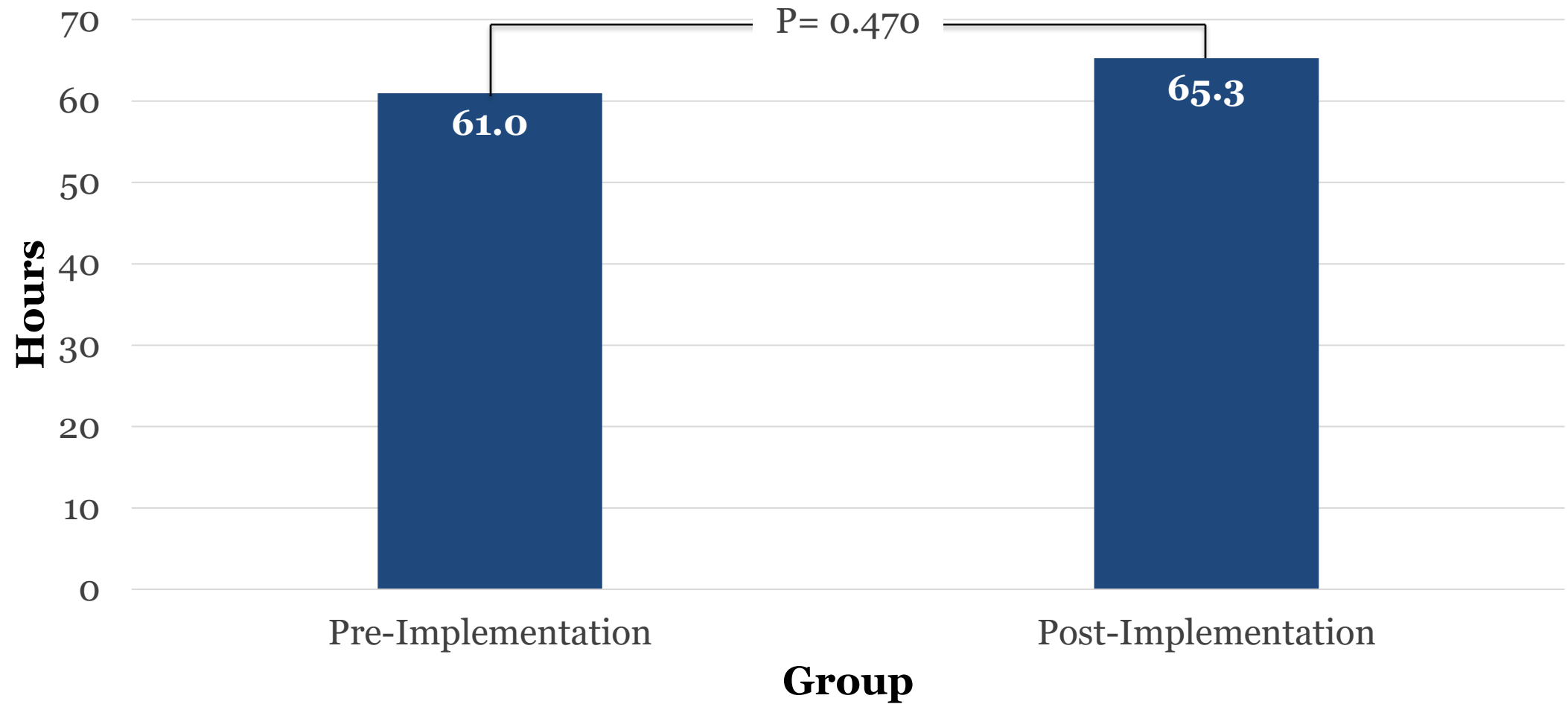
Antibiotic	Pre-Implementation	Post-Implementation
Ceftriaxone	25 (33.3)	20 (26.6)
Vancomycin	13 (17.3)	13 (17.3)
Cefazolin	7 (9.3)	8 (10.7)
Ciprofloxacin	6 (8.0)	8 (10.7)
Metronidazole	4 (5.3)	4 (5.3)
Piperacillin-tazobactam	4 (5.3)	0 (0)
Cefepime	2 (2.7)	7 (9.3)
Azithromycin	2 (2.7)	1 (1.4)
Ampicillin-sulbactam	1 (1.4)	4 (5.3)
Meropenem	1 (1.4)	1 (1.4)
Other	10 (13.3)	9 (12)

All values are n (%)



# Results

## Time to De-escalation of Antimicrobial Therapy







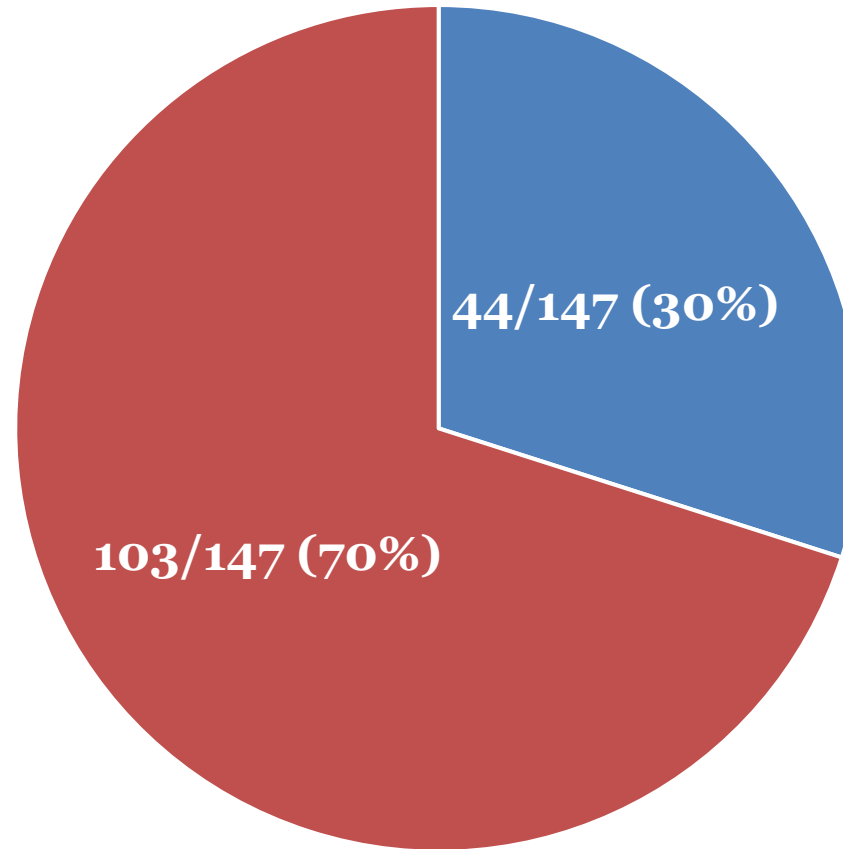
# Results

Secondary Outcomes	Pre-Implementation (n=92)	Post- Implementation (n=76)	P-Value
Time to organism ID, mean hours $\pm$ SD	65.6 $\pm$ 46.4	50.3 $\pm$ 32.3	0.016
Time to AST, mean hours $\pm$ SD	99.0 $\pm$ 39.8	96.7 $\pm$ 28.9	0.674
Total days of antibiotics, mean $\pm$ SD	5.9 $\pm$ 4.5	6.8 $\pm$ 5.4	0.256
Length of stay, mean days $\pm$ SD	7.8 $\pm$ 5.5	8.4 $\pm$ 7.4	0.598
30-day mortality, n (%)	11 (12.0)	7 (9.2)	0.567
De-escalation from MRSA to non-MRSA coverage, n (%)	47 (51.1)	28 (36.8)	0.065
De-escalation from pseudomonal to non-pseudomonal coverage(%)	42 (45.7)	29 (38.2)	0.249
CDI, n (%)	6 (6.5)	1 (1.3)	0.093
AKI, n (%)	9 (9.8)	10 (13.2)	0.492



# De-escalation Within 48 Hours

## De-escalation Within 48 Hours



■ De-escalation  $\leq$  48 hours    ■ De-escalation  $>$  48 hours



# Univariate Results

**Significance:  $p < 0.2$**

Variable	De-escalation $\leq$ 48 hours (n=44)	De-escalation $>$ 48 hours (n=103)	P-Value
Gram-positive infection, n (%)	31 (70.5)	58 (56.3)	0.108
Use of Accelerate Pheno <sup>TM</sup> system, n (%)	18 (40.9)	37 (35.9)	0.567
ID consult, n (%)	20 (45.5)	54 (52.4)	0.439
Pharmacist antimicrobial stewardship note, n (%)	7 (15.9)	9 (8.7)	0.201



# Multivariate Logistic Regression

**Significance:  $p < 0.05$**

<b>Variables</b>	<b>OR (95% CI)</b>	<b>P-Value</b>
Gram-positive infections	1.947 (0.904-4.192)	0.089
Pharmacist antimicrobial stewardship note	2.173 (0.738-6.400)	0.159



# Discussion

- Time to de-escalation of antimicrobial therapy similar between groups
- Time to organism ID was decreased by 16 hours using the Accelerate Pheno™ system
  - However, no difference in time to AST
- Accelerate Pheno™ did not impact duration of antimicrobial therapy, length of hospital stay, or 30-day mortality



# Discussion

- Other studies assessing Accelerate Pheno™ have found significant differences in:

- Time to ID
- Time to AST
- Time to appropriate therapy

Not consistent with this study

Not associated with differences in patient outcomes

Consistent with this study



# Discussion

## Strengths

- Evaluated de-escalation of therapy and other patient outcomes
- Patient demographics evenly matched
- Powered to detect difference in primary endpoint

## Limitations

- Retrospective, single center
- Did not account for outside factors, such as laboratory working hours
- Difficult to capture when AST resulted for Accelerate Pheno<sup>TM</sup>



# Conclusion

- The Accelerate Pheno™ system did not impact time to de-escalation of antimicrobial therapy
- Further antimicrobial stewardship interventions may target:
  - Educating clinical pharmacy specialists and other healthcare providers on the Accelerate Pheno™ system
  - Identifying methods to improve timely communication of test results to healthcare providers



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