DUH ED Blood Culture Algorithm Implementation and Abx Stewardship

Rebecca G Theophanous, MD, FACEP, FAAEM, FAEMUS

EM Ultrasound Faculty

Rebecca.theophanous@duke.edu

Rebekah H Wrenn, PharmD, BCIDP

Manager, Infectious Diseases Pharmacy Programs

Rebekah.wrenn@duke.edu

Duke University School of Medicine

Duke Center for Antimicrobial Stewardship and Infection Prevention

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Disclosures

- None

- Stewardship is a TEAM Effort
  - Jessica Seidelman, MD, MPH leadership with blood culture algorithm
  - Ethan Brenneman, PharmD and Amy Mackowiak, PharmD, BCIDP dedication to the Staphylococcus Blood Culture Algorithm

Questions for the group

- Do you draw blood cultures in your setting?
  - Who orders those blood cultures: MD/DO, APP, or Nurse/Protocol
- Do you have an algorithm for when to obtain blood cultures?
- Do you know your blood culture positivity rate?
- Do you have a protocol for when to send patients to the hospital or ED for evaluation after a positive BCx?

Background

- Blood cultures are commonly ordered for patients with a low risk of bacteremia.
- Liberal ordering of blood cultures increases the risk of false-positives due to contamination
- Increased length of hospital stay
  - Excess antibiotics
  - Avoidable procedures/imaging
  - Unnecessary removal of central venous catheters
- DUH FY22 ~ 11% of blood cultures positive (~4% contaminants)

1. Fabre V, Clin Infect Dis ciaa039. https://doi.org/10.1093/cid/ciaa039.
2. Linsenmeyer K. J Hosp Med 11:336 –340. https://doi.org/10.1002/jhm.2541.
3. Bates DW, JAMA 265:365–369. https://doi.org/10.1001/jama.1991.03460030071031.
4. Doern GV,Clin Microbiol Rev 33:e00009-19. https://doi.org/10.1128/CMR.00009-19.

Background

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A Diagnostic Stewardship Intervention To Improve Blood Culture Use among Adult Nonneutropenic Inpatients: the DISTRIBUTE Study

Valeria Fabre,[a] Eili Klein,[b,c] Alejandra B. Salinas,[a] George Jones,[a] Karen C. Carroll,[d] Aaron M. Milstone,[e,f] Joe Amoah,[e] Yea-Jen Hsu,[g] Avinash Gadala,[f] Sanjay Desai,[h] Amit Goyal,[i] David Furfaro,[j] Jacquelyn Zimmerman,[k] Susan Lin,[l] Sara E. Cosgrove[a]

Implementation of the blood culture algorithm with indications for blood cultures in medicine patients resulted in an 18% and 30% reduction in blood cultures in the ICU and medicine units, respectively, at Johns Hopkins Hospital.

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Objectives

- **Primary Objective**: Introduce a blood culture algorithm to help clinicians feel more comfortable with the indications for ordering blood cultures
- **Secondary Objectives**:
  - Appropriateness of blood cultures based on blood culture algorithm
  - % positivity of blood cultures for unit
  - % positivity of blood cultures considered contaminants for the unit

Phased Implementation

Historical control data (Nov 2020 - Oct 2022)

1) Identified stakeholders
2) Presented algorithm to ED/nursing leadership (buy-in)
3) Final version approved for dissemination

BCx algorithm implementation at DUH ED (Nov 2022)

1) Education of EM faculty/APPs/residents at monthly meetings/conference
2) Education to inpatient teams requesting blood cultures on patient's awaiting inpatient beds in the ED (e.g. medicine, surgery, etc)
3) Education to ED nurses and leadership on BCx algorithm
4) Posting of BCx algorithm in ED pods, in online Duke EM resource folder, and on Duke CustomID page for reference
5) Order set Removal: cellulitis and UTI

Prospective cohort data collection (Nov 2022 – Nov 2023)

NOTE: Outside of Bcx study
BCx bottle shortage – 8/16/24
IV Fluid shortage – 10/2024

Methods: Setting and Population

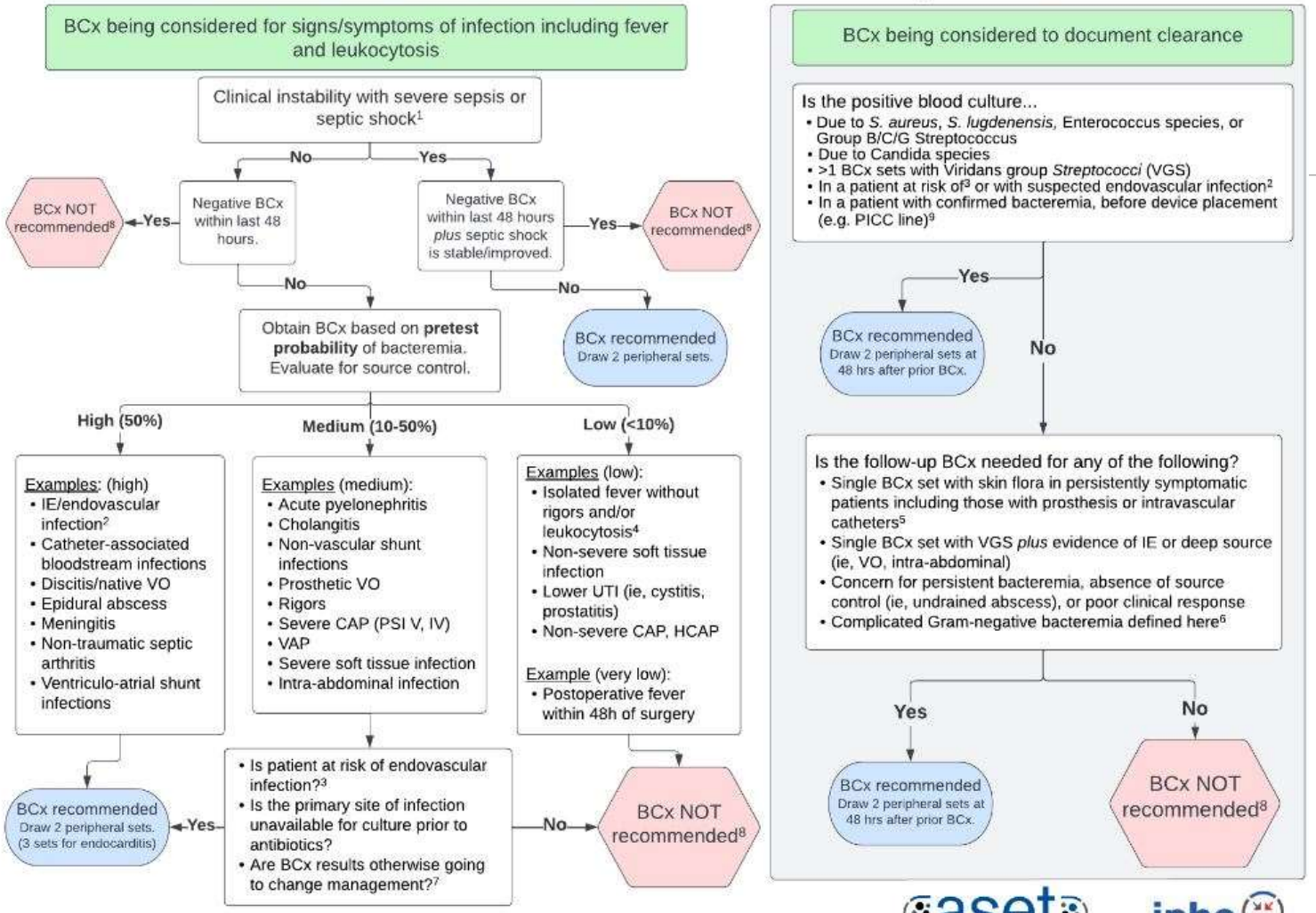
- Setting:
  - DUH ED
- Population:
  - Inclusion criteria:
    - Patient located in the DUH ED at the time of blood culture collection
    - At least 18 years of age
    - Blood culture ordered by DUH ED
  - Exclusion criteria:
    - Neutropenia (ANC < 500)
    - Lung or heart transplant recipients

Algorithm

Now available on customid!

https://www.customid.org/diagnosis-procedure/indications-blood-culture-collection-immunocompetent-adults

Indications for Blood Culture Collection in Immunocompetent Adults



Reference: Fabre et al. *Clin Infect Dis* 2020; 71 (5): 1339-1347.

Abbreviations: BCx, blood culture; IE, infective endocarditis; CAP, community-acquired pneumonia; HCAP, healthcare associated pneumonia; PSI, pneumonia severity index; UTI, urinary tract infection; VAP, ventilator-associated pneumonia; VO, vertebral osteomyelitis; VGS, viridans Group Streptococcus

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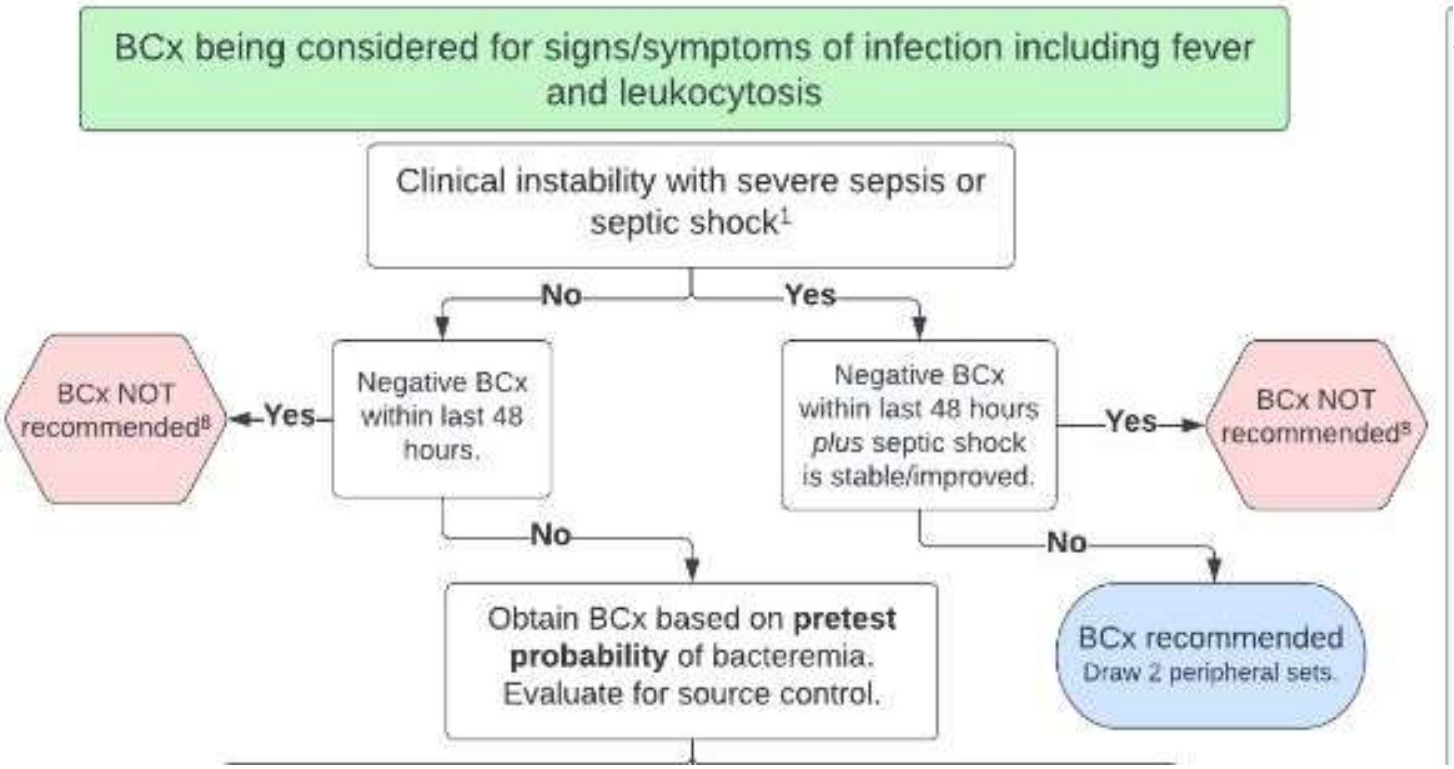
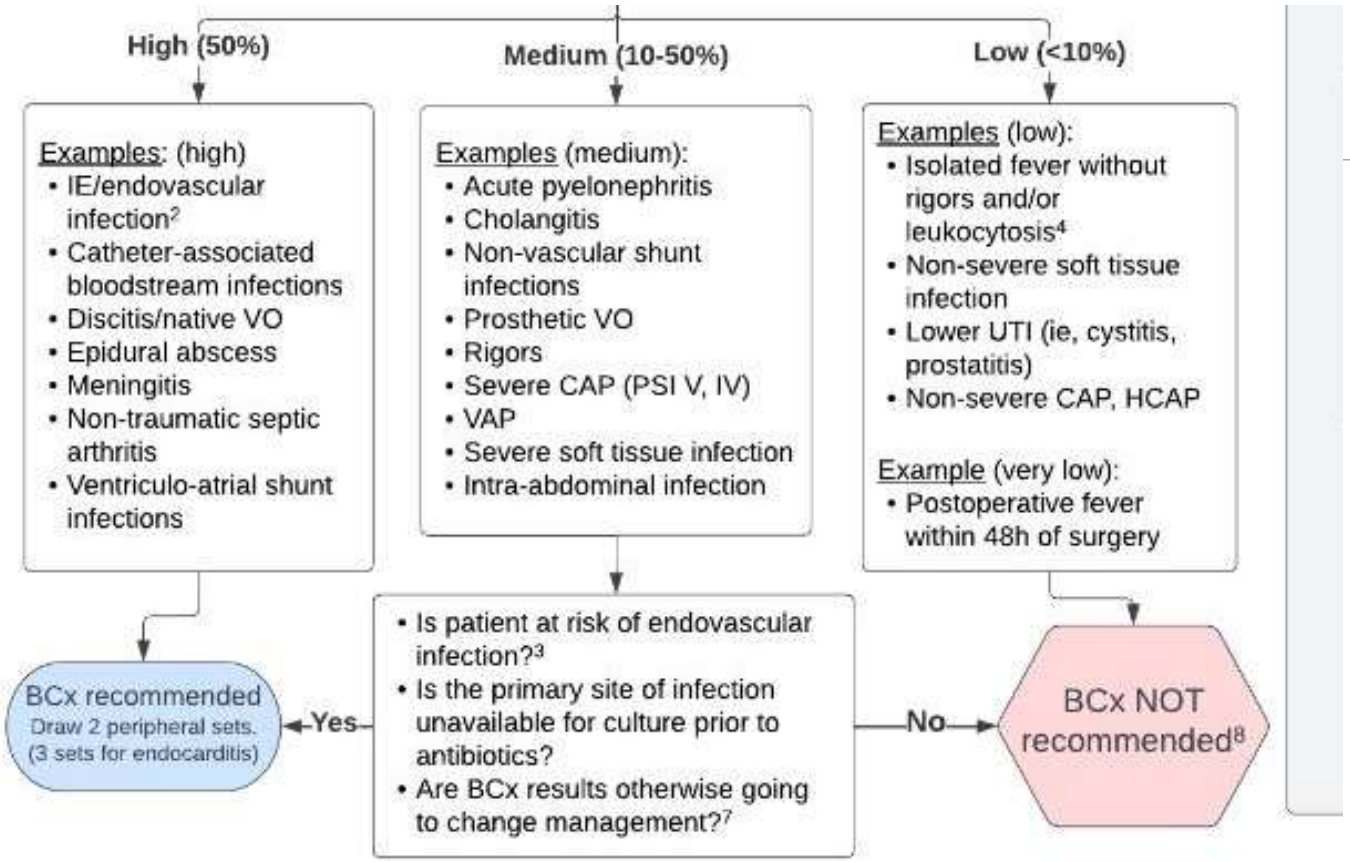
Indications for Blood Culture Collection in Ir





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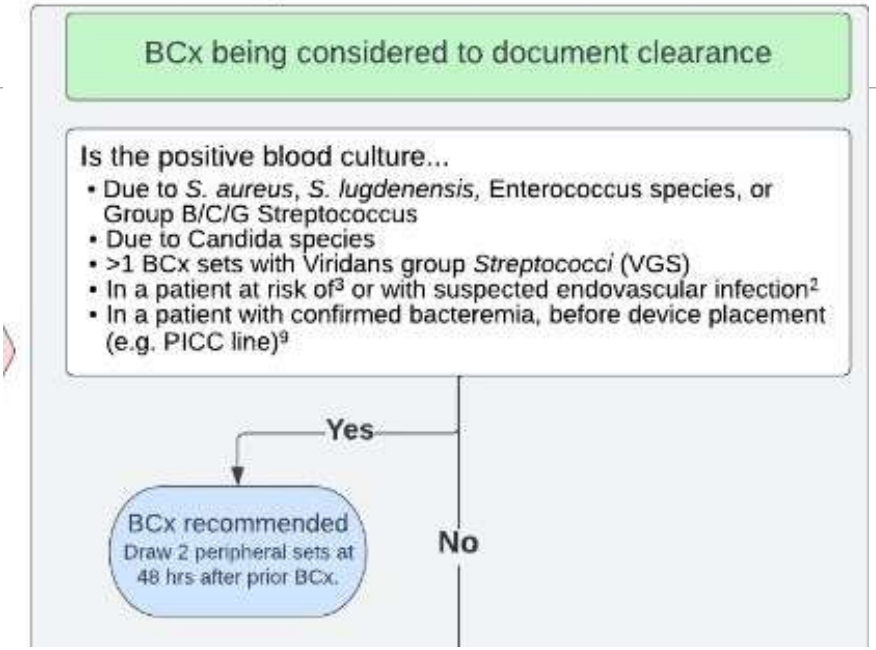
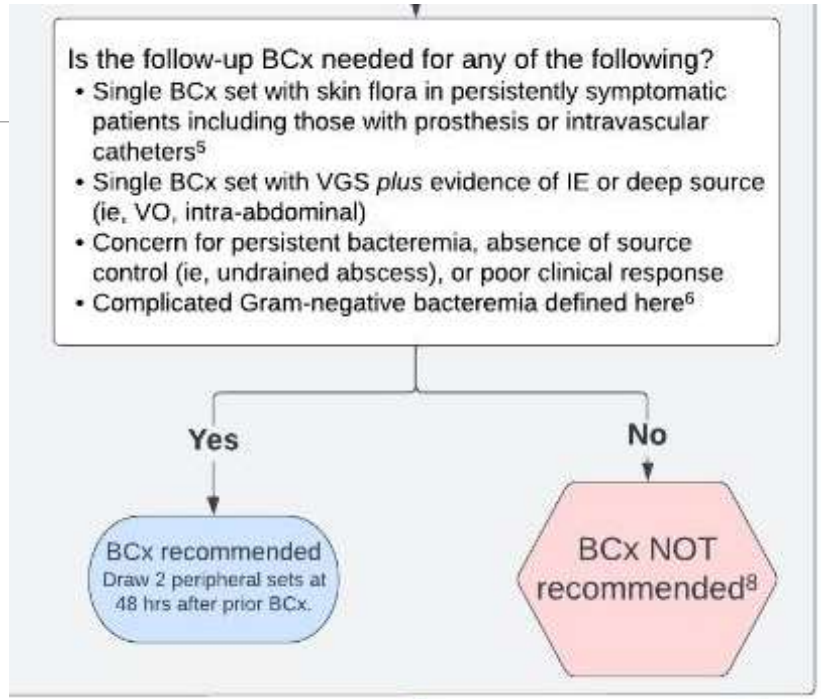
Immunocompetent Adults





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Intervention feedback mechanisms

- Weekly audits of blood culture orders by a committee of 7 ED physicians/APP
  - Standardized collection tool
  - Patient demographics
  - Appropriateness of blood cultures
- Monthly meetings to provide feedback to clinical teams/ED leadership and review adverse events and concerns

Study outcomes

- Primary outcome: blood culture event rates (BCE per 100 ED admissions) pre- and post-intervention
- Secondary outcomes: adverse event rates (30-day ED and hospital readmission and antibiotic days of therapy).

Table 1. Characteristics of patients with blood cultures and blood culture events in the emergency department before and after implementation of a blood culture algorithm.

	Pre-Intervention	Intervention	p-value
Blood culture events	17,809	7,433	
Unique Patients	12,573	5,667	
BCE rate per 100 ED admissions	12.17	10.50	< 0.01*
Maximum WBC [10^9 cells/L (mean, std)] on day of BCE	11.7 (10.4)	11.8 (11.6)	0.50†
Max temperature (^{0}F) recorded on day of BCE	99.4 (1.7)	99.4 (1.7)	0.99†
Patient age (median, IQR)	59.4 (18.1)	59.5 (18.2)	0.73†

Table 2. Distribution of reviewed blood culture events (3478) by clinical indication and further stratified by if the clinical indication followed the blood culture algorithm (appropriate) or not (inappropriate)

Indication	Total (% all indications)	Appropriate Blood Cultures (% row)	Inappropriate Blood Cultures (% of row)
Severe Sepsis or Septic Shock	688 (19.8)	688 (100)	0 (0)
Isolated fever and/or leukocytosis	371 (10.7)	0 (0)	371 (100)
Severe CAP	368 (10.6)	368 (100)	0 (0)
Severe cellulitis or cellulitis in patient with comorbidities	345 (9.9)	338 (98.0)	7 (2.0)
Peritonitis/intraabdominal infection	134 (3.8)	122 (91.0)	12 (9.0)
Acute pyelonephritis	128 (3.7)	107 (83.6)	21 (16.4)
Other-neutropenic fever	101 (2.9)	100 (99.0)	1 (1.0)
Non-severe CAP or HCAP	95 (2.7)	0 (0)	95 (100)
Cholangitis	87 (2.5)	86 (98.9)	1 (1.1)
Suspected infective endocarditis or endovascular infection	80 (2.3)	80 (100)	0 (0)
Lower UTI (cystitis or prostatitis)	78 (2.2)	1 (1.3)	77 (98.7)
Cather-associated bloodstream infection	47 (1.4)	47(100)	0 (0)
Documenting clearance of bacteremia	39 (1.1)	38 (97.4)	1 (2.6)
Non-severe cellulitis	38 (1.1)	0 (0)	38 (100)
Native septic arthritis	36 (1.0)	36 (100)	0 (0)
Meningitis	34 (1.0)	34 (100)	0 (0)
Post cardiac arrest patient	34 (1.0)	34 (100)	1 (0)
Discitis/native vertebral osteomyelitis	31 (0.9)	31 (100)	2 (0)
LVAD patient	31 (0.9)	26 (93.9)	5 (16.1)
Post-op fever within 48 hours of surgery	24 (0.7)	0 (0)	24 (100)
Epidural abscess	9 (.0.3)	9 (100)	0 (0)
Prosthetic vertebral osteomyelitis	5 (0.1)	5 (100)	0 (0)
VAP	3 (0.1)	3 (100)	0 (0)
Grand Total*	3481 (100)	2153 (61.9)	653 (18.7)

*675 blood cultures did not have enough documentation on review to support an appropriate or inappropriate indication.

Legend: Urinary tract infection (UTI), Left ventricular assist device (LVAD), community-acquired pneumonia (CAP), ventilator-associated pneumonia (VAP)

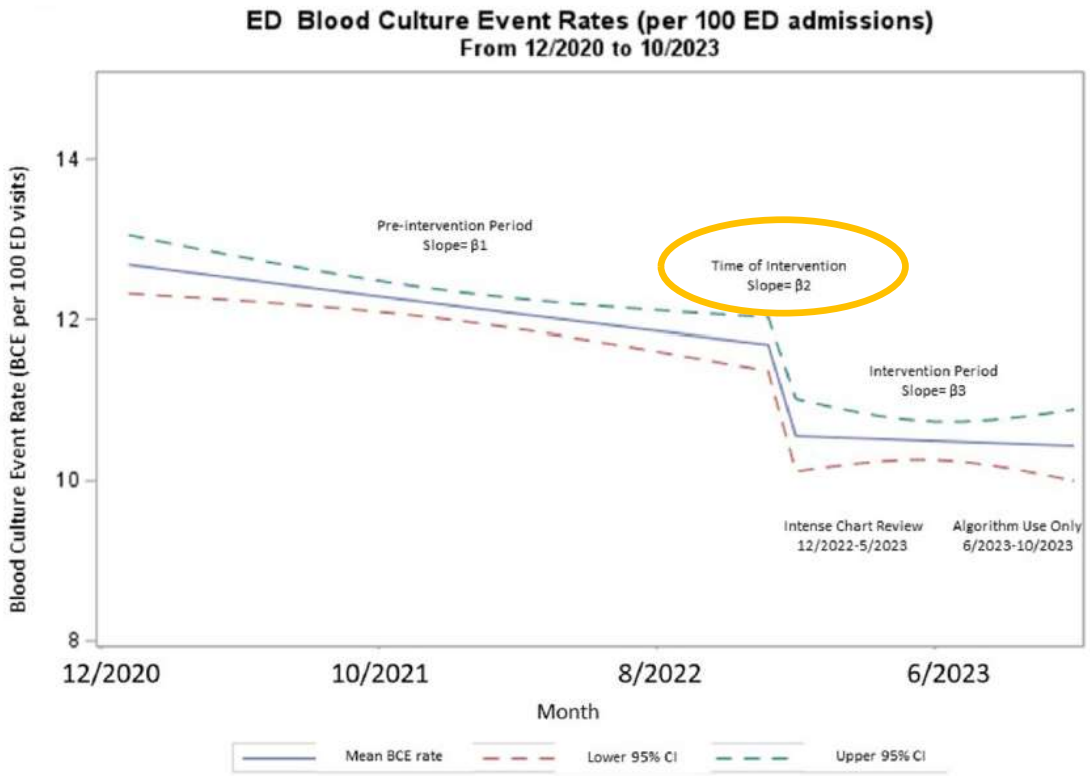
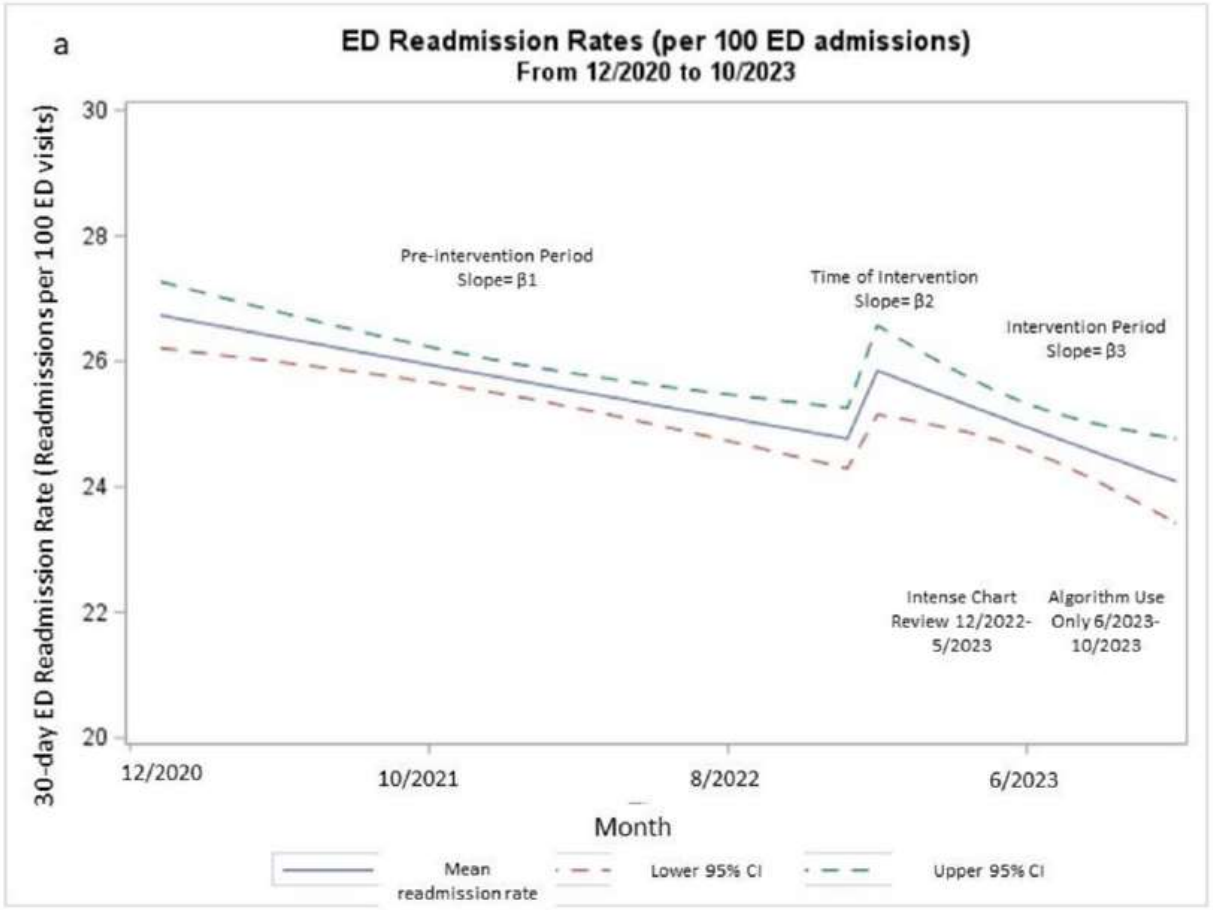


Fig. 1. Monthly blood culture event rate (per 100 ED admissions) for the emergency department before (December 2020-November 2022) and after (December 2022-October 2023) the blood culture algorithm introduction. Intensive chart reviews occurred from December 2022 to May 2023. After that time only the algorithm was used without audit and feedback. β1 = −0.004 (95% CI −0.0057, −0.0014, *P*-value < .01)]. At the time of the intervention there was an acute drop measured by the β2 coefficient −0.16(95% CI −0.38, −0.01, *P*-value .04), followed by a slow increase in slope (β3 = 0.002, 95% CI −0.005, 0.01, *P*-value .54).

Table 3. Outcome measures among the patients who were admitted to the emergency department in the pre-intervention and post-intervention periods. This includes patients who had a blood culture event and those who did not.

Outcome Measure	Pre-intervention (N=17,809)	Intervention (N=7,433)	p-value
Antibiotic days of therapy per 100 ED visits	529	506	<0.01
Average monthly 30-day ED readmissions (%)	1568 (27%)	1591 (25%)	0.08†
30-day hospital readmissions for patients initially seen in the ED (%)	560 (9.0%)	110 (5.0%)	< 0.01†

† t-test



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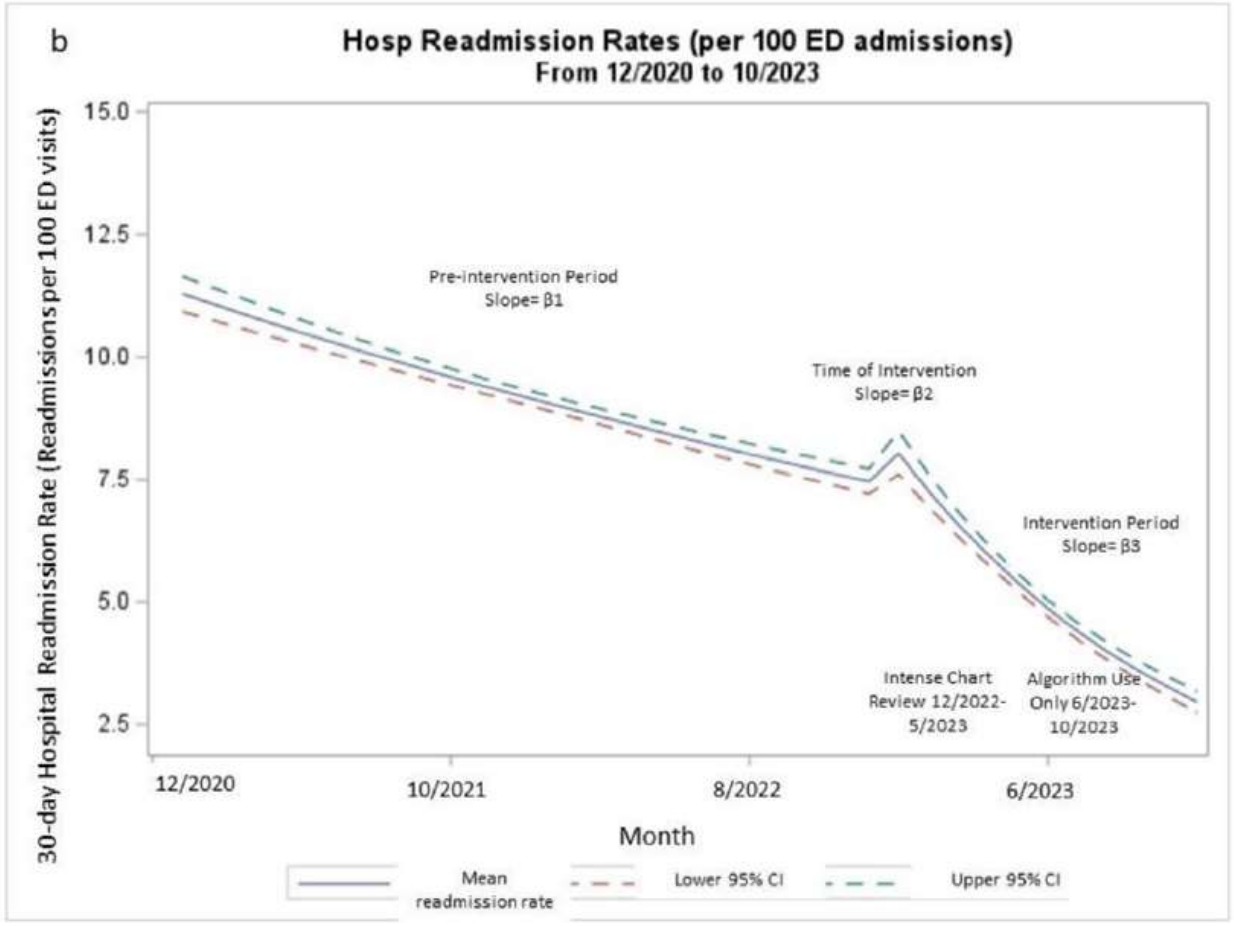

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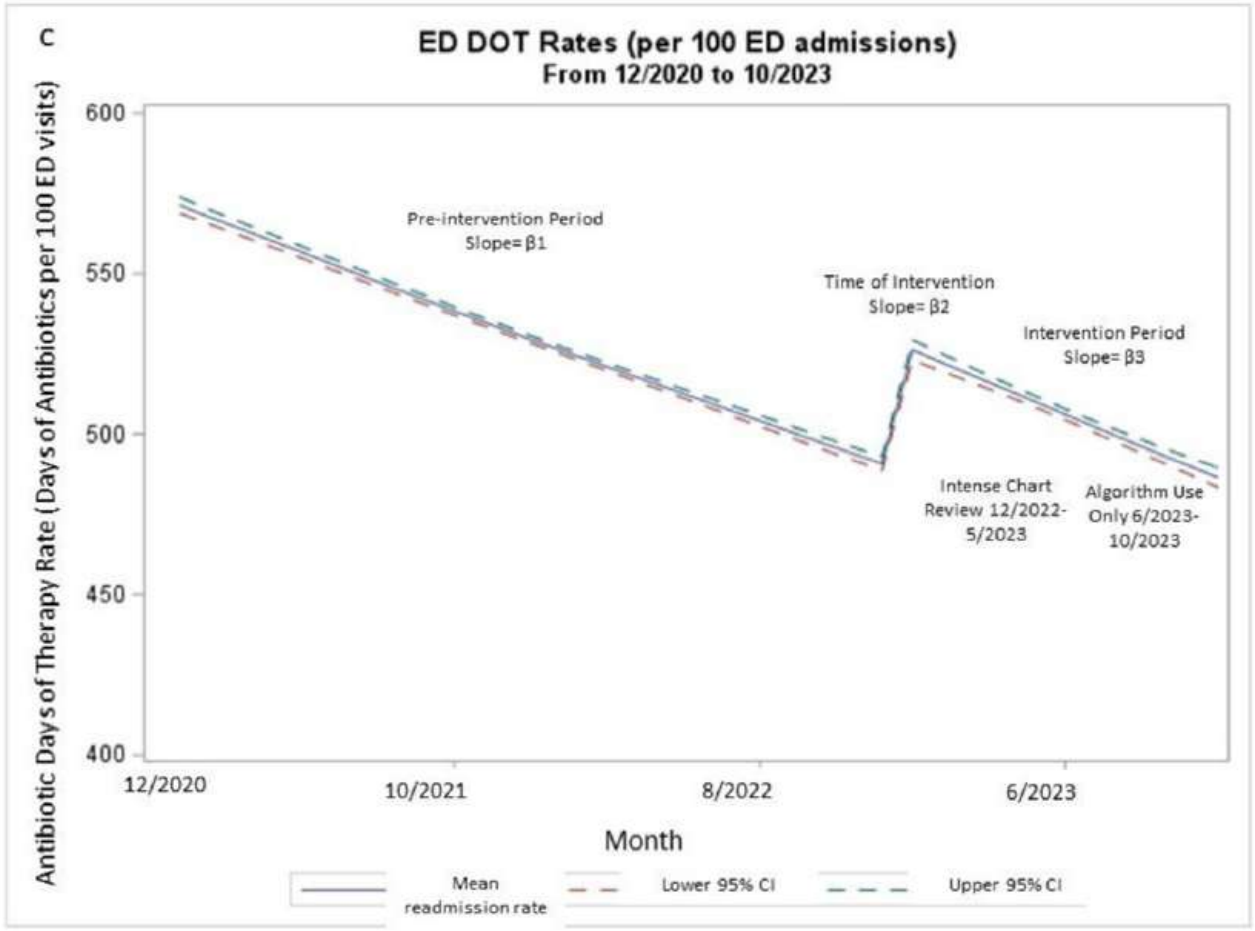

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Study results

- After BCx algorithm implementation, the BCE rate decreased from 12.17 BCE/100 ED admissions to 10.50 BCE/100 ED admissions.
- Of the 3,481 reviewed BCE, we adjudicated 2153 BCE (62%) as appropriate, 653 (19%) as inappropriate, and 675 (19%) as uncertain.
- Adverse safety events were not statistically different pre/post-intervention.

Study results

- The most common indications for appropriate BCE were:
  - severe sepsis/septic shock (17%)
  - severe community-acquired pneumonia (CAP) (11%)
  - severe cellulitis or cellulitis in a patient with comorbidities (10%).
- The most common BCE indications for inappropriate BCE were:
- isolated fever/leukocytosis (26%)
- non-severe CAP (5.4%)
- lower urinary tract infection (5.4%).

Conclusion

- Implementation of an ED BCx algorithm demonstrated a reduction in BCE, without increased adverse safety events.
- Future studies should compare outcomes of BCx algorithm implementation in a community hospital ED without intensive chart review.

Practical points

- Successful BCx algorithm implementation and abx stewardship mechanisms require:
  - Participant education
  - Stakeholder and leadership/administration buy-in
  - Review and feedback mechanisms (cyclical)
  - Collaboration between partners (e.g. pharmacy, ID, EM; physicians, APPs, nursing)
  - Institutional and financial support

Algorithm to Triage ED Discharged Patients with Blood Cultures Positive for *Staphylococcus aureus* or Coagulase-negative Staphylococcus

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Background

Patients may discharge from ED prior to blood culture results

Careful evaluation required to determine if positive cultures represent true infection or contaminants

Difficult to critically evaluate these patients in a high throughput environment

Can stewardship teams assist in standardizing this evaluation and subsequent actions?

Coagulase negative staphylococci (CoNS): *S. epidermidis, S. hominis, S. lugdunensis*, *S. simulans*, etc.

Evidence for Algorithm Based Care of Staphylococcal Infections

Multicenter, open-label, randomized trial conducted in the US and Spain from 2011-2017 compared algorithm-based care to standard-of-care for management of staphylococcal bacteremia

Coagulase-negative Staphylococcal Bacteremia	
Simple	0-3 (+1)[a]
Single blood culture positive for coagulase-negative staphylococci	
Negative follow-up blood culture	
No signs or symptoms of local infection at a catheter site	
No symptoms or signs of metastatic infection	
No indwelling intravascular prosthetic devices	
Uncomplicated	5 (±1)
≥2 blood cultures positive for coagulase-negative staphylococci drawn ≤24 h apart, OR	
Single blood culture positive for coagulase-negative staphylococci, PLUS symptoms or signs of infection at a catheter site	
Complicated	7-28 (±2)
≥2 blood cultures positive for coagulase-negative staphylococci from samples drawn >24 h apart, OR	
Echocardiography with evidence of endocarditis, OR	
Symptoms or signs of metastatic infection	

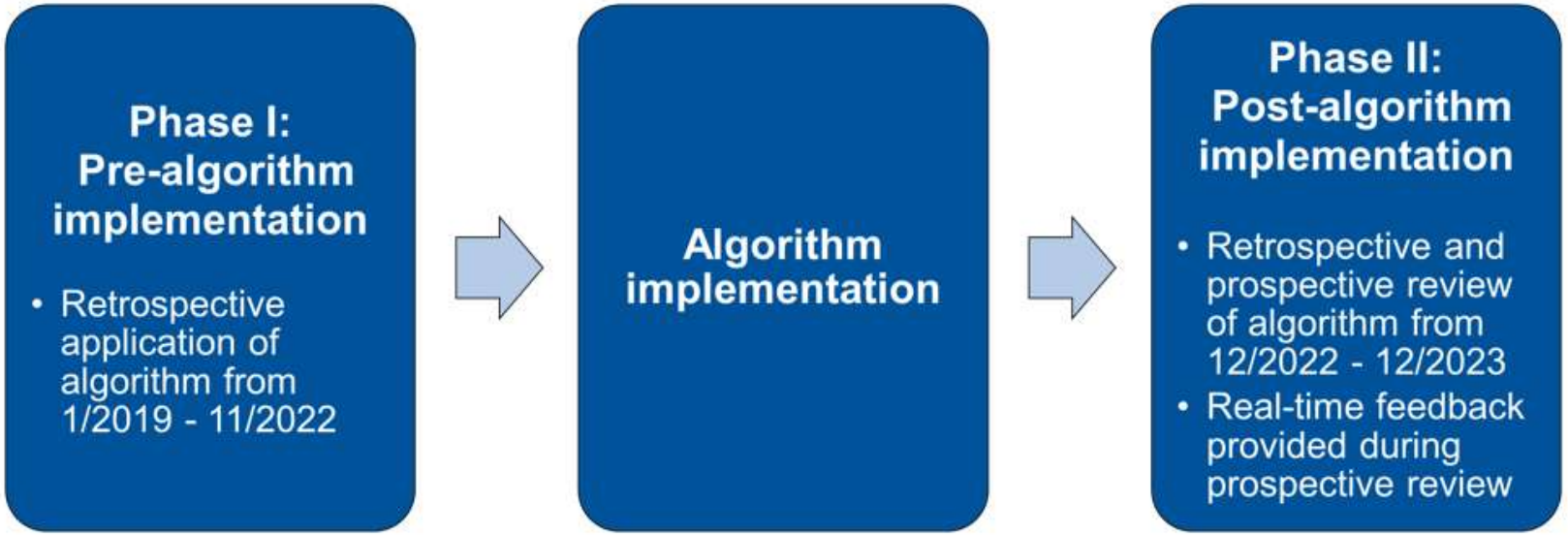
Patients with simple CoNS bacteremia were treated with 0 to 3 days of antibiotics

Outcome	No Antibiotics	Antibiotics
Clinical success at test-of-cure	72/84 (85.7%)	152/176 (86.4%)
Infection-related mortality	0/84 (0%)	0/176 (0%)

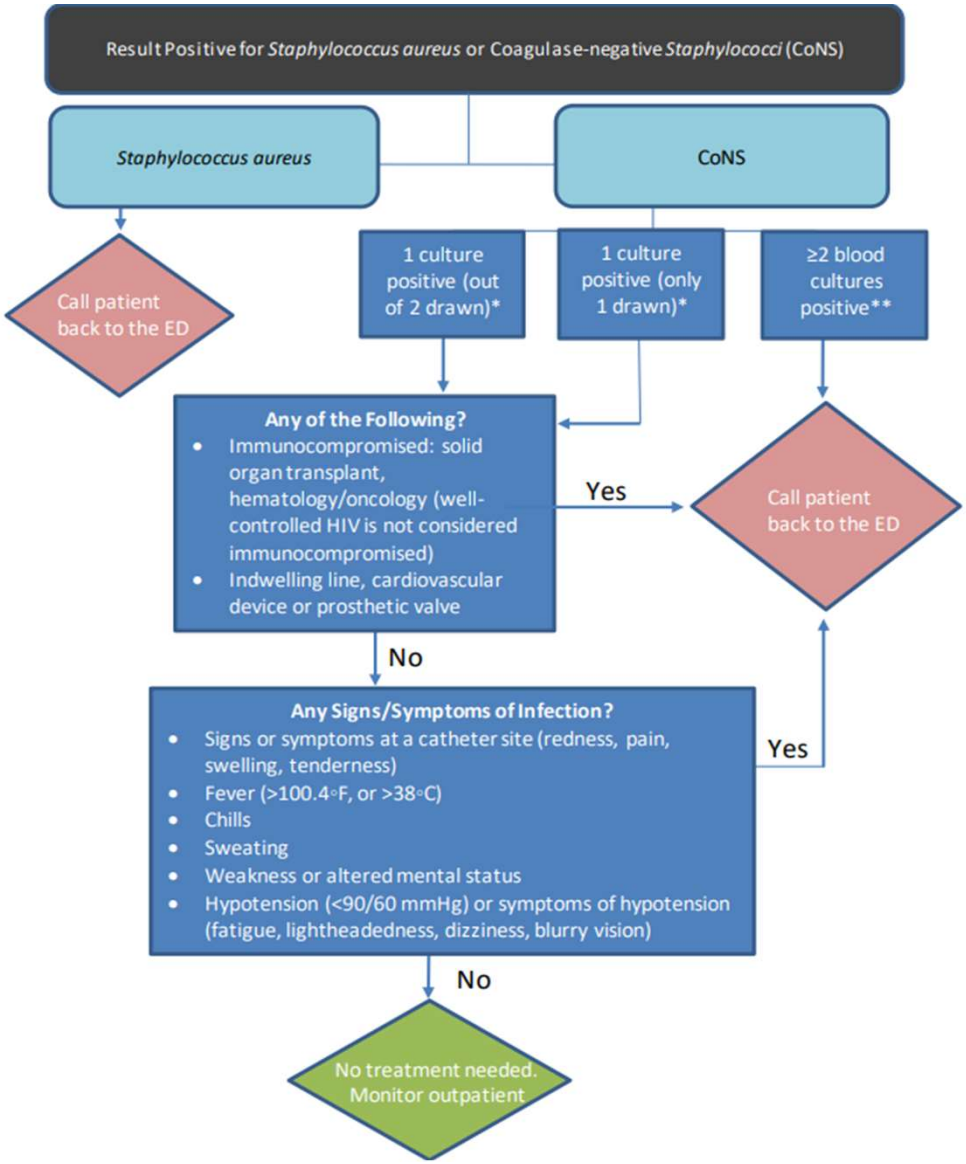
Holland, et al. *JAMA.* 2018; 320(12):1249-1258

DUHS Algorithm Evaluation Methods

- Multi-site, retrospective, and prospective cohort study of pre- and post-implementation of an ED callback decision-making algorithm



DUHS Decision Making Algorithm

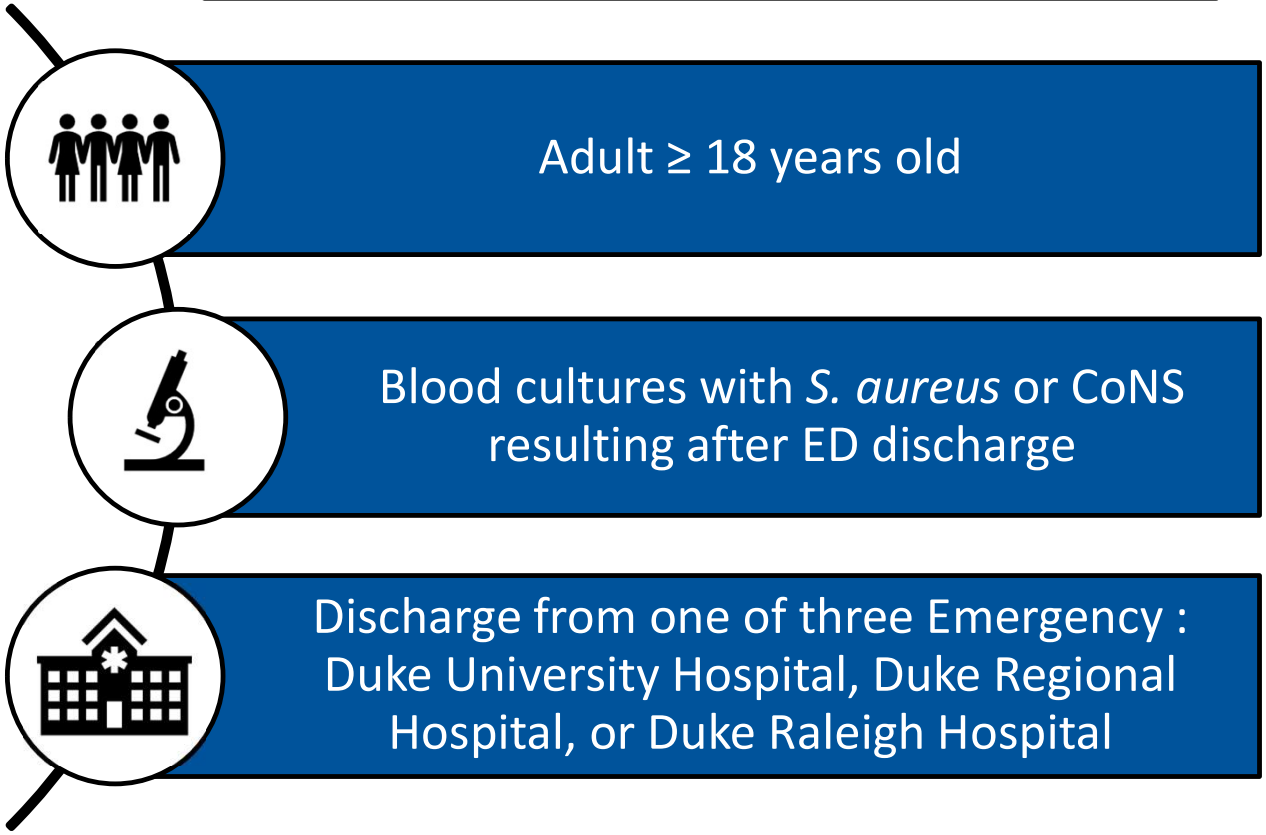


*_Staphylococcus lugdunensis_ has a propensity to cause complicated infections similar to _S. aureus_. Careful evaluation is warranted.

** Two blood cultures positive with different CoNS species may indicate contamination. Evaluate patient carefully for invasive infection.

Methods

Inclusion Criteria



Exclusion criteria

- Growth of non-staphylococcal pathogen in index blood cultures
- Polymicrobial bloodstream infections (unless multiple CoNS species)
- Mortality or return to the ED prior to blood culture growth
- Patients with a directive to not treat infections

Objectives

- **Primary Objectives**: (1) Assess the **difference in the rates of patients called back to the ED in response to a positive blood culture of *S.aureus* or CoNS** before and after implementation of the ED callback algorithm*, and (2) assess the differences in the rates of per-algorithm callback to ED in each implementation period**

- **Key Secondary Objectives:** (1) Compare rates of algorithm adherence pre- and post-implementation and (2) assess the safety of algorithm-based care via the rate of patient infection-related readmission and mortality

- The difference in the rates between pre- and post-implementation periods was estimated with 95% confidence intervals using Newcombe's method. A two-sample z-test for binomial proportions with unpooled variance was used to compare the two rates.

**The differences in the actual callback rate and the callback rate based on the algorithm were estimated with 95% confidence intervals using the Newcombe square-and-add approach and compared using an Asymptotic McNemar's test for paired binomial proportions.

Patient Population

Baseline Patient Characteristic	Pre-Implementation (N = 188)	Post-Implementation (N = 65)
Age, years, mean (SD)	57.7 (18.2)	55.4 (20.9)
Sex - male	91 (48.4%)	30 (46.2%)
Race, n (%)		
-Black	90 (47.9%)	31 (47.7%)
-White	90 (47.9%)	30 (46.2%)
Select infection risk factors		
-Injection drug use	8 (4.3%)	4 (6.2%)
-*S. aureus* infection within past year	17 (9.0%)	3 (4.6%)
-*S. aureus* bacteremia within past year	9 (4.8%)	1 (1.5%)
-Prosthetic material present*	31 (16.5%)	14 (21.5%)
-Immunocompromised**	22 (11.7%)	11 (16.9%)

***Prosthetic material:** indwelling line, cardiovascular device, prosthetic valve, other intravascular prosthetic material

****Immunocompromised** : solid organ transplant, hematology/oncology condition

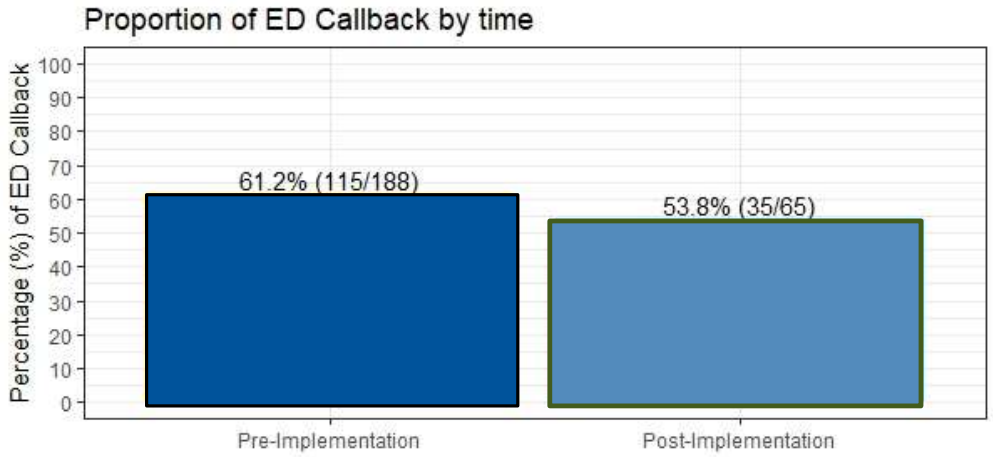
Patient Population

Index Blood Cultures	Pre-Implementation (N = 188)	Post-Implementation (N = 65)
Number of index cultures drawn, median (Q1, Q3)	2 (2, 2)	2 (2, 2)
Number of index cultures with growth 1 2	 154 (81.9%) 34 (18.1%)	 54 (83.1%) 11 (16.9%)
Species identified CoNS (not *S. lugdunensis*) *S. aureus*	 154 (81.9%) 36 (19.1%)	 58 (89.2%) 6 (9.2%)
Time from gram stain to speciation, hours, median (Q1, Q3)	1.6 (1.0, 2.4)	1.5 (0.0, 2.3)
Time from gram stain results to first call, hours, median (Q1, Q3)	2.3 (0.7, 9.6)	6.0 (2.2, 20.0)
Symptoms Upon Call	93 (49.5%)	41 (63.1%)

Rates of Callback to the Emergency Department

Outcome	Pre-Implementation (N = 188)	Post-Implementation (N = 65)	Difference
Rate of ED Callback	115 (61.2%)	35 (53.8%)	**7.32%** 95% CI: (-6.26, 21.05); p = 0.3

$$Rate\ of\ ED\ Callback = \frac{Patients\ called\ back\ to\ ED\ for\ positive\ blood\ cultures\ for\ Staphylococcus\ spp}{Total\ number\ of\ patients\ with\ positive\ blood\ cultures\ for\ Staphylococcus\ spp.after\ ED\ discharge}$$



Rates of Callback to the Emergency Department

The difference in actual and per-algorithm callback rates:

- Pre-algorithm implementation: 15.4% (95% CI: 7.7% to 22.8%, p<0.001)
- Post-algorithm implementation: 4.6% (95% CI: -5.6% to 14.6%, p = 0.55)

Comparative Outcomes, n/n (%)	Pre-Algorithm Implementation			Post-Algorithm Implementation		
	Actual	Per-Algorithm	Difference	Actual	Per-Algorithm	Difference
Rates of patients with ***S. aureus*** told to return to the ED	32/36 (88. 9%)	36/36 (100%)	**-4/36 (11.1%)**	6/6 (100%)	6/6 (100%)	**0/6 (0%)**
Rates of patients with **CoNS** told to return to the ED	85/154 (55.2%)	52/154 (33.8%)	**33/154 (21.4%)**	29/58 (50%)	25/58 (43.1%)	**4/58 (6.9%)**

Rates of Callback to the Emergency Department

Algorithm adherence occurred in 68.6% in the pre-algorithm implementation period versus 84.6% of patients in the post-algorithm implementation period

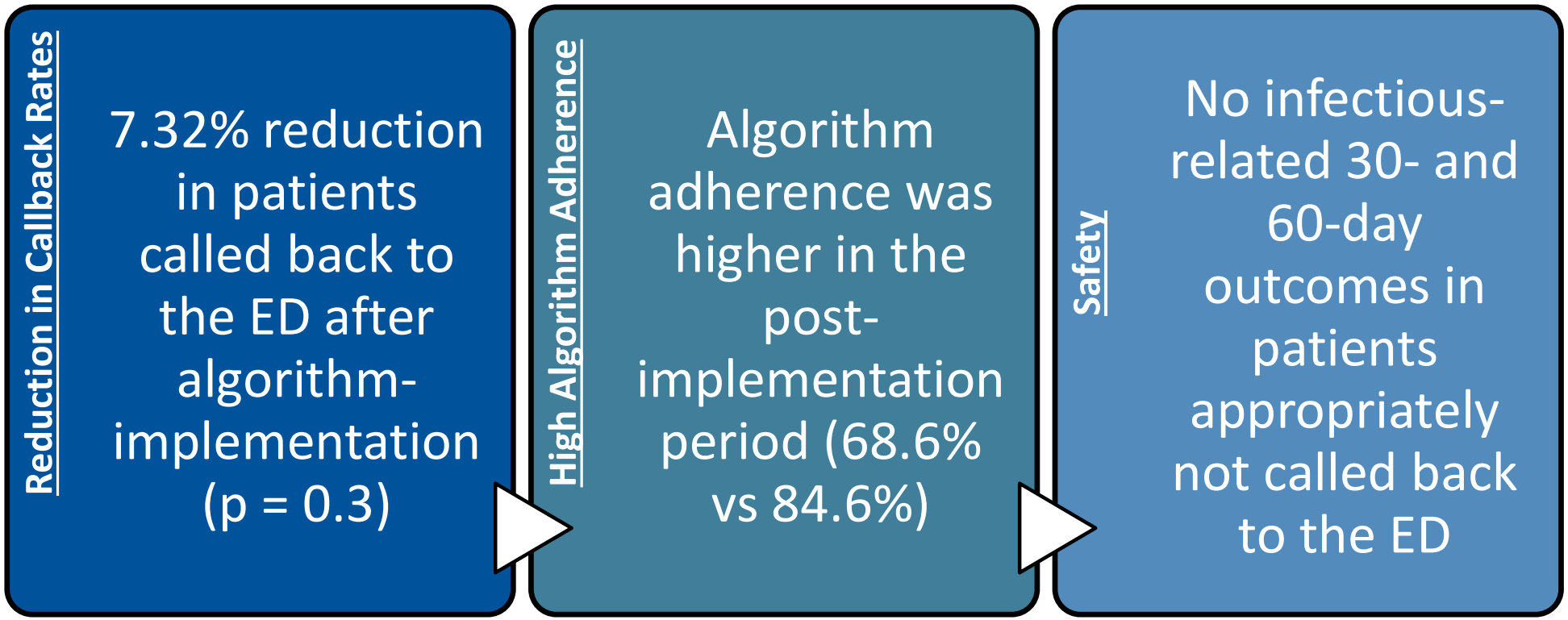
Comparative Outcomes, n/n (%)	Pre-Algorithm Implementation			Post-Algorithm Implementation		
	Actual	Per-Algorithm	Difference	Actual	Per-Algorithm	Difference
Rates of adherence to the algorithm for all patients	129/188 (68.6%)	188/188 (100%)	-59/188 (-31.3%)	55/65 (84.6%)	65/65 (100%)	-10/65 (-15.4%)

Safety of Algorithm – Infection-Related Outcomes

Outcome	Pre-Implementation (N = 188)	Post-Implementation (N = 65)
Infection Related 60-Day ED Visit	5 (2.7%)	0 (0%)
Infection Related 60-Day Admission	9 (4.8%)	1 (1.5%)
Infection Related 30-Day Mortality	4 (2.1%)	0 (0%)
Infection Related 60-Day Mortality	5 (2.7%)	0 (0%)

0 out of 26 (0%) patients appropriately not called back to the ED in the post-implementation period experienced an adverse infection-related outcome

Discussion


Reduction in Callback Rates
7.32% reduction in patients called back to the ED after algorithm-implementation (p = 0.3)
High Algorithm Adherence
Algorithm adherence was higher in the post-implementation period (68.6% vs 84.6%)
Safety
No infectious-related 30- and 60-day outcomes in patients appropriately not called back to the ED

Conclusion

This decision-making algorithm helped providers appropriately triage patients whose blood cultures become positive for *Staphylococcus* spp. after discharge from the ED without any adverse safety outcomes identified

ED Blood Culture Stewardship Conclusion

- Diagnostic and antimicrobial stewardship in the ED is critical
- Implementation of the blood culture algorithm improved clinician comfort in when to appropriately draw blood cultures
  - Significant reductions in blood culture event rates were achieved post-implementation.
  - No increase in adverse safety events indicates the algorithm's effectiveness.
- Implementation of Staphylococcus Call Back Algorithm reduced incidence of call back to ED patients with no safety events

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Rebecca G Theophanous, MD, FACEP, FAAEM, FAEMUS

EM Ultrasound Faculty

Rebecca.theophanous@duke.edu

Rebekah H Wrenn, PharmD, BCIDP

Manager, Infectious Diseases Pharmacy Programs

Rebekah.wrenn@duke.edu

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