

Blood Culture Backwards and Forward

Matthew Pettengill, PhD, D(ABMM)

NACMID, September 2025

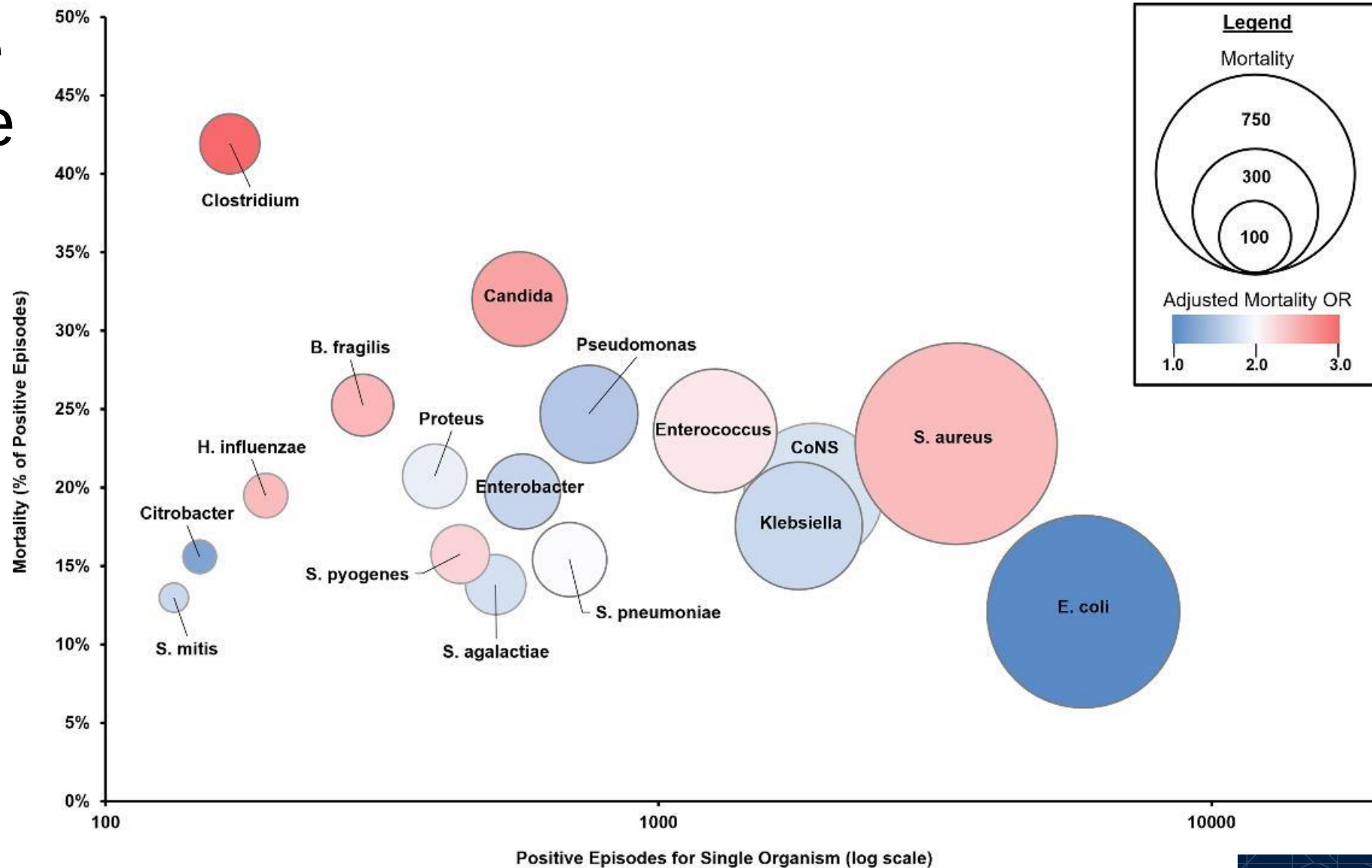
Jefferson Health

- Now >30 hospitals spanning Eastern PA and southern NJ.
- Primary teaching hospital is in Philadelphia PA.



The Importance of Blood Culture

- Bloodstream infections are associated w/ high mortality, ~20% within 30 days.
- How blood cultures are performed can change the mortality risk!



**Preamanalytical
collection
factors**



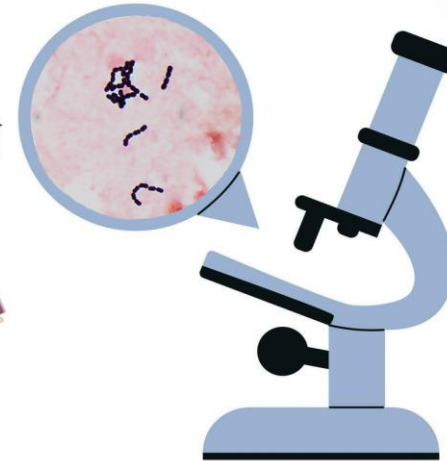
**Physician
ordering
decision**



**Types of blood cultures
and incubation
conditions**



**Time to reporting of Gram
stains and organism
identification**



**Subculture and
AST**

**What can you do
with cumulative
data?**





Physician Ordering Decision

- Many clinicians reflexively order blood cultures for indications such as new fever or leukocytosis even though it has been shown that these, especially in isolation, are not significant predictors of positive cultures (Foong 2022; Lisenmeyer 2016).
- Providers report a desire for more guidance; however, fear of missing bloodstream infections is a significant barrier to diagnostic stewardship of blood cultures (Fabre 2018).
- Excessive collection of blood cultures is associated with other collateral harms such as increased length of stay, health care costs, adverse effects of inappropriate antibiotics, and even anemia from extra blood draws (Fabre 2020a).





Physician Ordering Decision

- We implemented blood culture decision support in response to a blood culture bottle shortage in June 2024 - but we left it in place when the shortage abated.



[Click here to view Interim Guidance for Blood Culture Collection document](#)

There is a critical shortage of blood culture bottles. Please order blood cultures judiciously. See below for recommendations.

Blood Culture orders past 5 days (120h ago, onward)

	Ordered
Culture, Blood Morning collect	07/30/24 1540
Culture, Blood PROCEDURE ONCE	07/30/24 1900
Culture, Blood Once	07/30/24 0851
Culture, Blood Once	07/30/24 0851
Culture, Blood PROCEDURE ONCE	07/30/24 0851
Culture, Blood PROCEDURE ONCE	07/30/24 0851

Which of the following applies to this patient encounter:

- ☐ Initial blood cultures
- ☐ Repeat blood cultures

Blood Culture Collection Guidance
This guidance does not replace clinical judgement/evaluation

High Risk Conditions (Recommended)	Intermediate Risk Conditions (Consider) ¹	Low Risk Conditions (<u>NOT</u> Recommended)
Endocarditis or other possible endovascular infection ²	Acute pyelonephritis	Isolated fever and/or leukocytosis
Severe sepsis/septic shock ³	Cholangitis	Non-severe cellulitis ⁴
Neutropenic fever	Nonvascular shunt infections	Lower UTI (cystitis, prostatitis)
Fever in presence of central venous catheter	Severe vertebral osteomyelitis w/hardware	Non-severe CAP
Isolated fever without source in any infant (<28 days)	Severe CAP/VAP ⁵	Post-operative fever within 48 hours of surgery
High Risk for bacteremia: CLABSI, Native vertebral osteomyelitis/discitis, Epidural abscess, Meningitis, Nontraumatic septic arthritis, Ventriculoarterial shunt infection	Cellulitis with co-morbidities: Advanced HIV, HSCT, history of SOT, hematologic malignancy, on active chemotherapy, in ICU, LTACH patient, ESRD on HD	

See full document for footnotes



 Repeat blood cultures

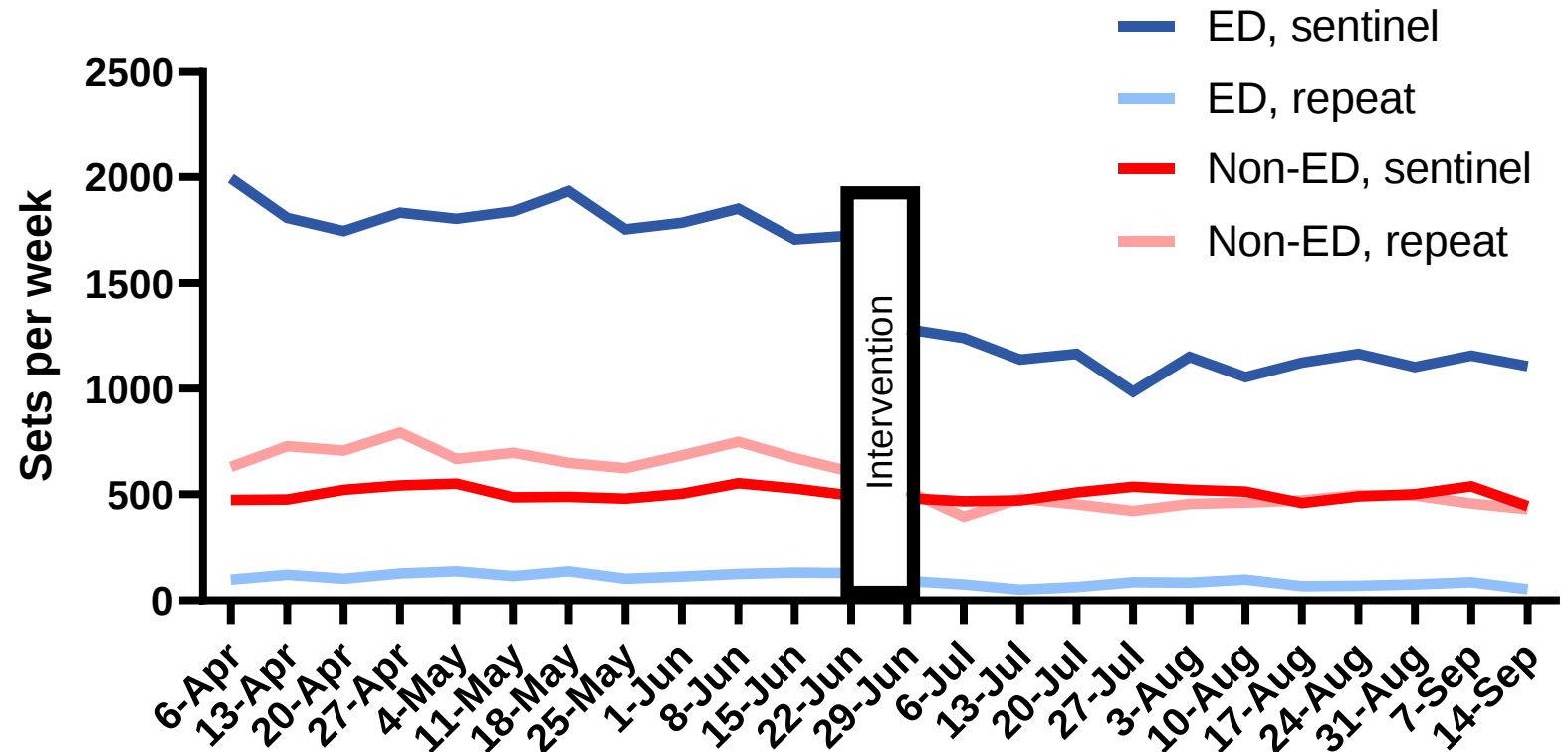
Are Repeat Blood Cultures Indicated? <i>This guidance does not replace clinical judgement/evaluation</i>	
YES	NO
Obtain blood cultures every 48-72 hours until negative in these situations: • <i>S. aureus</i>, <i>S. lugdunensis</i>, <i>Enterococcus spp.</i>, <i>Candida spp.</i> blood stream infection • Catheter-related bacteremia prior to replacing with a new catheter • Infective endocarditis • Blood culture positive for skin flora in symptomatic patient with a vascular / joint prosthesis or central line • Concern for persistent bacteremia without source control (e.g., undrained abscess)	Repeat blood cultures are not routinely indicated in these situations: • Patients with negative blood cultures in the past 72 hours (unless there is a significant clinical deterioration) • Single positive culture with skin flora in asymptomatic patient WITHOUT a vascular / joint prosthesis or central line • Gram negative bacteremia in a patient without a vascular graft or central line who is clinically improving • <i>Strep pneumoniae</i> and beta-hemolytic strep bacteremia

☐ If 'YES' to above, click here to order Repeat blood cultures



Impact of Bcx Decision Support

- Overall, a sustained 25-30% reduction in blood cultures ordered.
- Reduction was primarily from EDs, with a lesser contribution with reduced repeat collections.



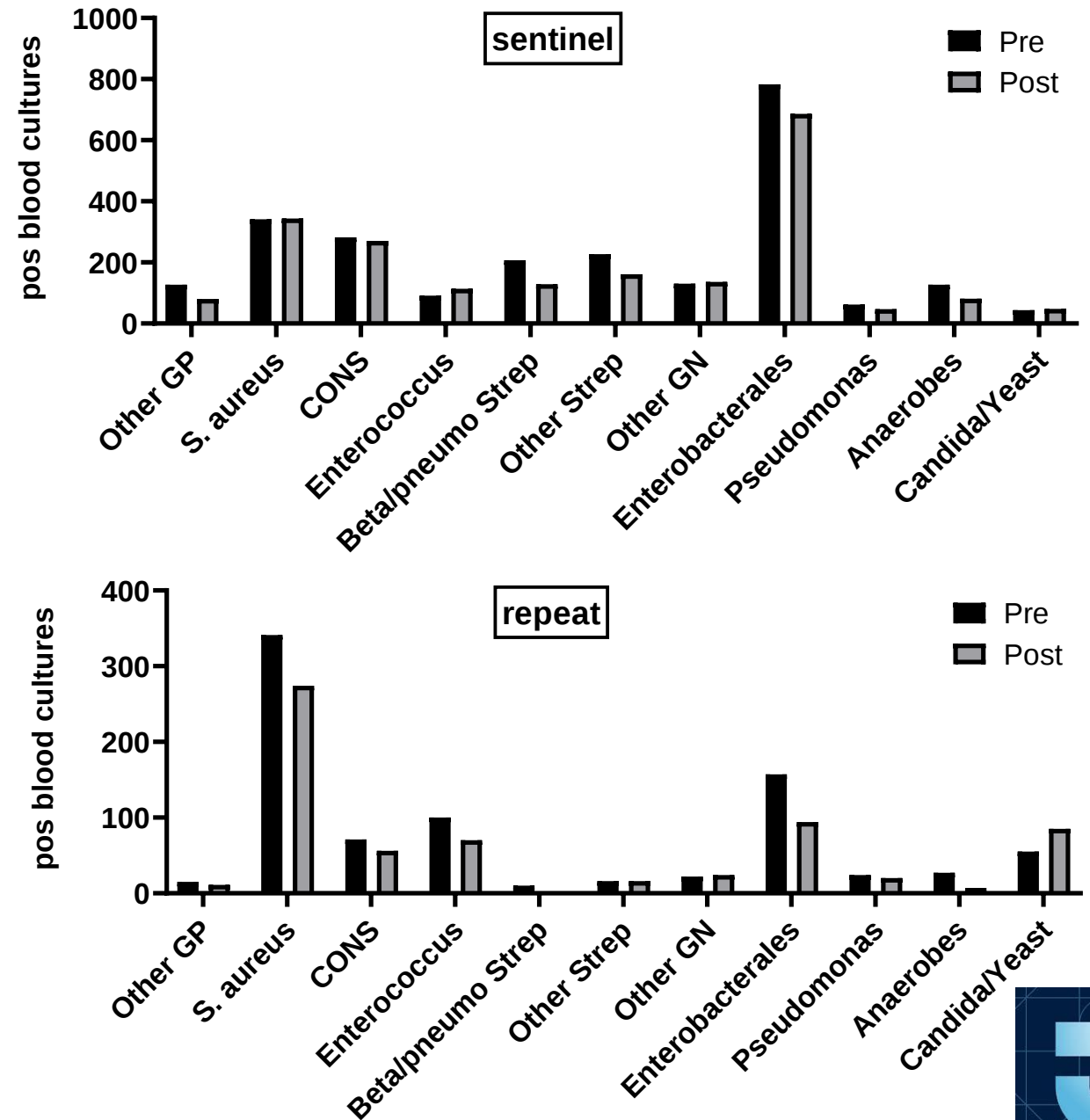


Impact of Bcx Decision Support

- Sentinel Bcx from the floors didn't really change. ED sentinel collections were down 36%, total repeat cultures were down 32%.
- The % of Bcx that were positive was significantly higher with decision support, but the absolute # of positive Bcx was lower – cause for concern?

		sentinel (n)	sent. pos (n)	sent.pos (%)	repeat (n)	rep. pos (n)	rep.pos (%)
12 weeks before	ED	21223	1808	8.52%	1060	78	7.36%
	non-ED	6116	314	5.13%	8511	719	8.45%
	total	27618	2139	7.74%	9569	797	8.33%
12 weeks after	ED	13515	1470	10.88%	559	68	12.16%
	non-ED	6090	339	5.57%	5981	560	9.36%
	total	19873	1820	9.16%	6530	628	9.62%
p value before vs after	ED			<0.0001			0.0013
	non-ED			0.2884			0.0559
	total			<0.0001			0.0047

- There were reductions in the absolute # of Bcx positive for *Streptococcus* and *Enterobacterales*, but not for *S. aureus*.
- Repeat positives went down but this was expected because of proposed reduced frequency of Bcx.
- *S. aureus* staying the same is reassuring – but what of the rest?



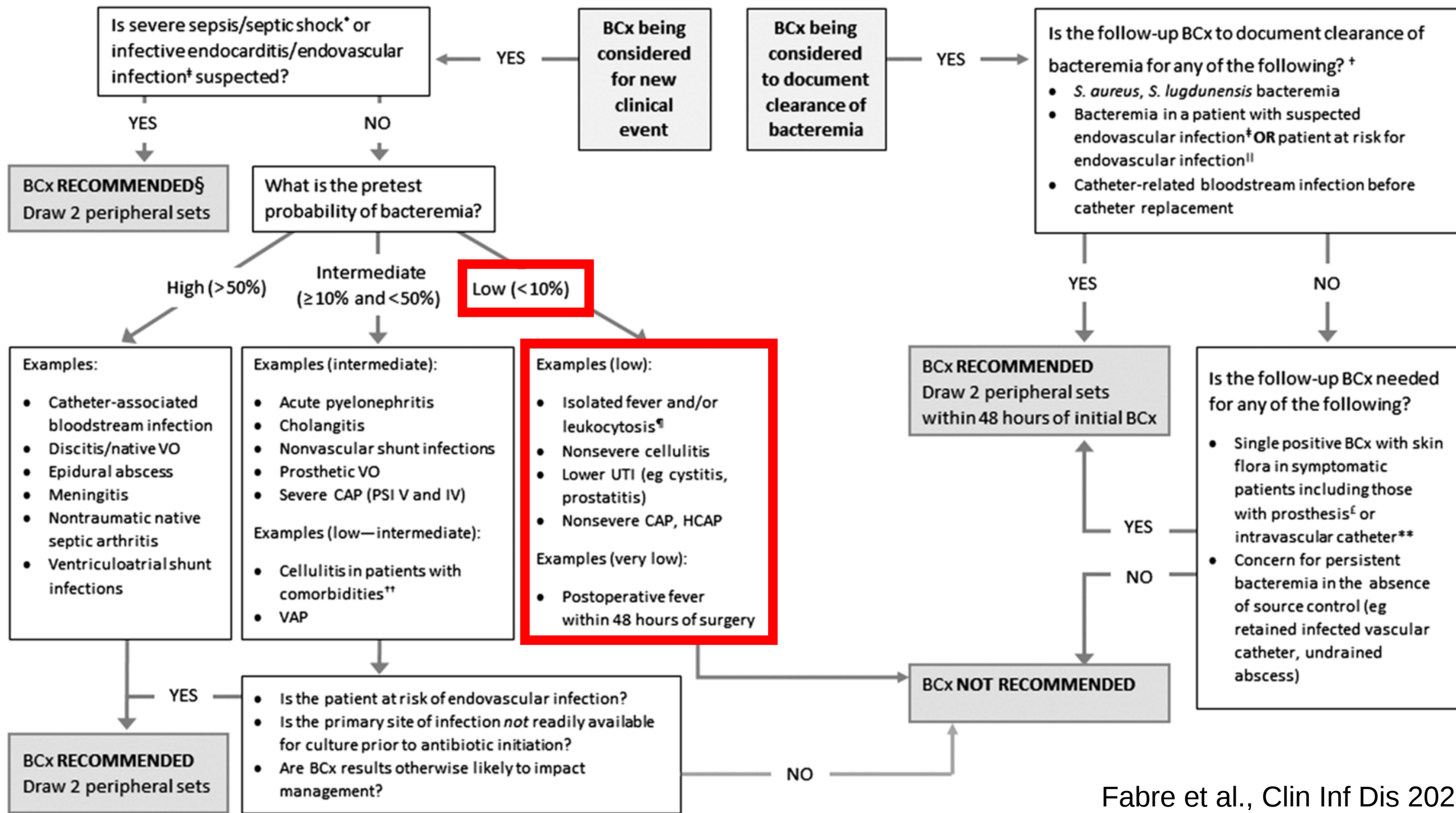


Table 1. Pretest Probability of Bacteremia in Common Clinical Scenarios (Percentages as Reported in the Studies)

< 5% (Very Low)	< 10% (Low)	Between 10% and < 20% (Low-moderate)	Between 20% and < 50% (Moderate)	≥ 50% (High)
Fever within first 48 h of surgery [12–14, 42, 55]	Uncomplicated cellulitis [6, 15–17, 43, 44], including periorbital cellulitis [45, 46]	Cellulitis in patients with severe comorbidities [18, 27, 28]	Severer sepsis	Discitis and VO [39, 40, 47] Epidural abscesses [40, 41] Acute nontraumatic native septic joints [48]
Isolated fever [5, 6]	Lower urinary tract infection [19, 20]	...	Acute pyelonephritis [29, 30, 49, 50]	Meningitis [6]
...	...	...	Cholangitis [32, 33] Pyogenic liver abscess [34]	...
...	CAP [6, 22, 23, 51–53] HCAP [21, 22, 52, 56]	VAP [25, 26]	Severe CAP [31]	...
...	...	...	Nonvascular shunt infections [35]	Ventriculoatrial shunt infections [35]
...	...	...	Severe sepsis [54, 57] Shaking chills in febrile patient [6]	Septic shock [6] Catheter-related bloodstream infections

Abbreviations: CAP, community-acquired pneumonia; HCAP, healthcare-associated pneumonia; VAP, ventilator-associated pneumonia; VO, vertebral osteomyelitis.

What are we missing?

- For our study, you could extrapolate a crude estimate of the % positivity of the cultures not performed:

$$\frac{2139 - 1820}{27618 - 19873} = 4.11\%$$

- Also, the organisms for which we saw reductions, primarily *Enterobacterales* and *Streptococcus*, are commonly associated with the clinical conditions highlighted as low risk: lower urinary tract infection, uncomplicated cellulitis, and community acquired pneumonia.

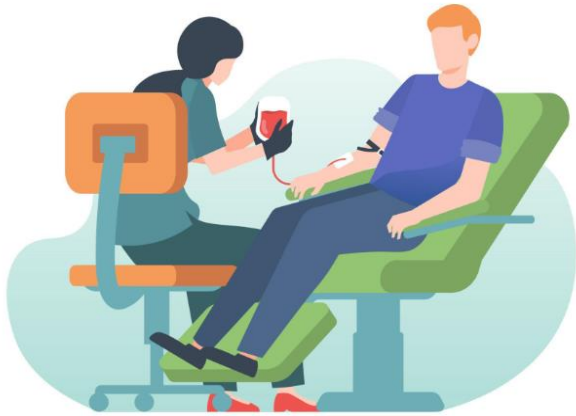
		sentinel (n)	sent. pos (n)
12 weeks before	ED	21223	1808
	non-ED	6116	314
	total	27618	2139
12 weeks after	ED	13515	1470
	non-ED	6090	339
	total	19873	1820



Blood Cx Decision Support Summary

- There is good evidence available on which to base EMR/ordering decision support for blood cultures.
- Depending on the local practices for blood culture ordering, decision support may lead to a dramatic drop in blood cultures.
- Some potentially positive blood cultures will be missed, but these are presumably primarily associated with lower risk conditions.
- As a laboratory stewardship intervention, the cost savings with decision support could be very large (>250K/yr at our institution, just for the blood cx bottles).
- *“In the midst of every crisis lies great opportunity”* – Albert Einstein





Preanalytical Collection Factors

- Blood volume collected for culture has a big impact on the ability to detect organisms causing bloodstream infections.
- IDSA recommends 20 mL per adult collection (10 mL aerobic, 10 mL anaerobic), for 2-4 collections.
- Blood culture contamination also has a negative impact on patient care and is costly in and outside of the lab.
- The CAP requires labs have a system in place to monitor blood culture volumes and contamination rates and report this information back to collecting units.

MIC.22635 Blood Culture Contamination

Phase II



The laboratory monitors blood culture contamination rates and has established an acceptable threshold.

NOTE: The laboratory must determine and regularly review the number of contaminated cultures. Tracking the contamination rate and providing feedback to units and persons drawing cultures has been shown to reduce contamination rates. Other measures for consideration in monitoring blood culture contamination include the types of skin disinfection used, line draws, and the use of diversion devices.

The threshold may be established in collaboration with other relevant institutional groups (eg, infection prevention). The laboratory must perform and record corrective action if the threshold is exceeded.

Evidence of Compliance:

- ✓ Records of contamination rates and corrective action if threshold is exceeded **AND**
- ✓ Records of feedback to responsible parties

MIC.22640 Blood Culture Volume

Phase I



The laboratory monitors blood cultures from adults for adequate volume and provides feedback on unacceptable volumes to blood collectors.

NOTE: Larger volumes of blood increase the yield of true positive cultures. The volume collected must be in accordance with manufacturer instructions (in most systems it is 20 mL, but smaller volumes may be recommended in some systems).

Evidence of Compliance:

- ✓ Records of monitoring of volume at a defined frequency **AND**
- ✓ Records of feedback to responsible parties

Clinical Laboratory Comparison of the 10-ml Isolator Blood Culture System with BACTEC Radiometric Blood Culture Media

JAMES A. KELLOGG,^{1*} JOHN P. MANZELLA,² AND JOHN H. McCONVILLE²

Clinical Microbiology Laboratory¹ and Department of Internal Medicine, Division of Infectious Diseases,² York Hospital, York, Pennsylvania 17405

TABLE 3. Quantitative range of recovery with Isolator

CFU/ml of blood	Detected pathogens	
	No. of positive cultures	% of total isolates
0.1	63	18
0.2	30	8
0.3	18	5
0.4	16	5
0.5	9	3
0.6 to 1.0	40	11
1.1 to 10	74	21
10.1 to 100	59	17
>100	45	13

A single 10mL isolater was performed for the study, so we don't know how many were below 0.1 CFU/mL, at least not quantifiably

Optimized Pathogen Detection with 30- Compared to 20-Milliliter Blood Culture Draws^{▽†}

Robin Patel,^{1,2*} Emily A. Vetter,¹ W. Scott Harmsen,³ Cathy D. Schleck,³
Hind J. Fadel,² and Franklin R. Cockerill III^{1,2}

TABLE 1. Percentage increase for nonconditional pathogens recovered related to the volume of blood cultured

Blood vol (ml)	Increase (%) in nonconditional pathogens recovered in a culture vol of:				
	20 ml	30 ml	40 ml	50 ml	60 ml
10	25.3	35.4	47.7	57.6	63.9
20		8.1	17.9	25.8	30.7
30			9.1	16.4	21.0
40				6.7	10.9
50					4.0

Optimized Pathogen Detection with 30- Compared to 20-Milliliter Blood Culture Draws^{▽†}

Robin Patel,^{1,2*} Emily A. Vetter,¹ W. Scott Harmsen,³ Cathy D. Schleck,³
 Hind J. Fadel,² and Franklin R. Cockerill III^{1,2}

TABLE 1. Percentage increase for nonconditional pathogens recovered related to the volume of blood cultured

Blood vol (ml)	Increase (%) in nonconditional pathogens recovered in a culture vol of:				
	20 ml	30 ml	40 ml	50 ml	60 ml
10	25.3	35.4	47.7	57.6	63.9
20		8.1	17.9	25.8	30.7
30			9.1	16.4	21.0
40				6.7	10.9
50					4.0

In the Patel et al. study the first 10 mL detected 61% of total

Clinical Laboratory Comparison of the 10-ml Isolator Blood Culture System with BACTEC Radiometric Blood Culture Media

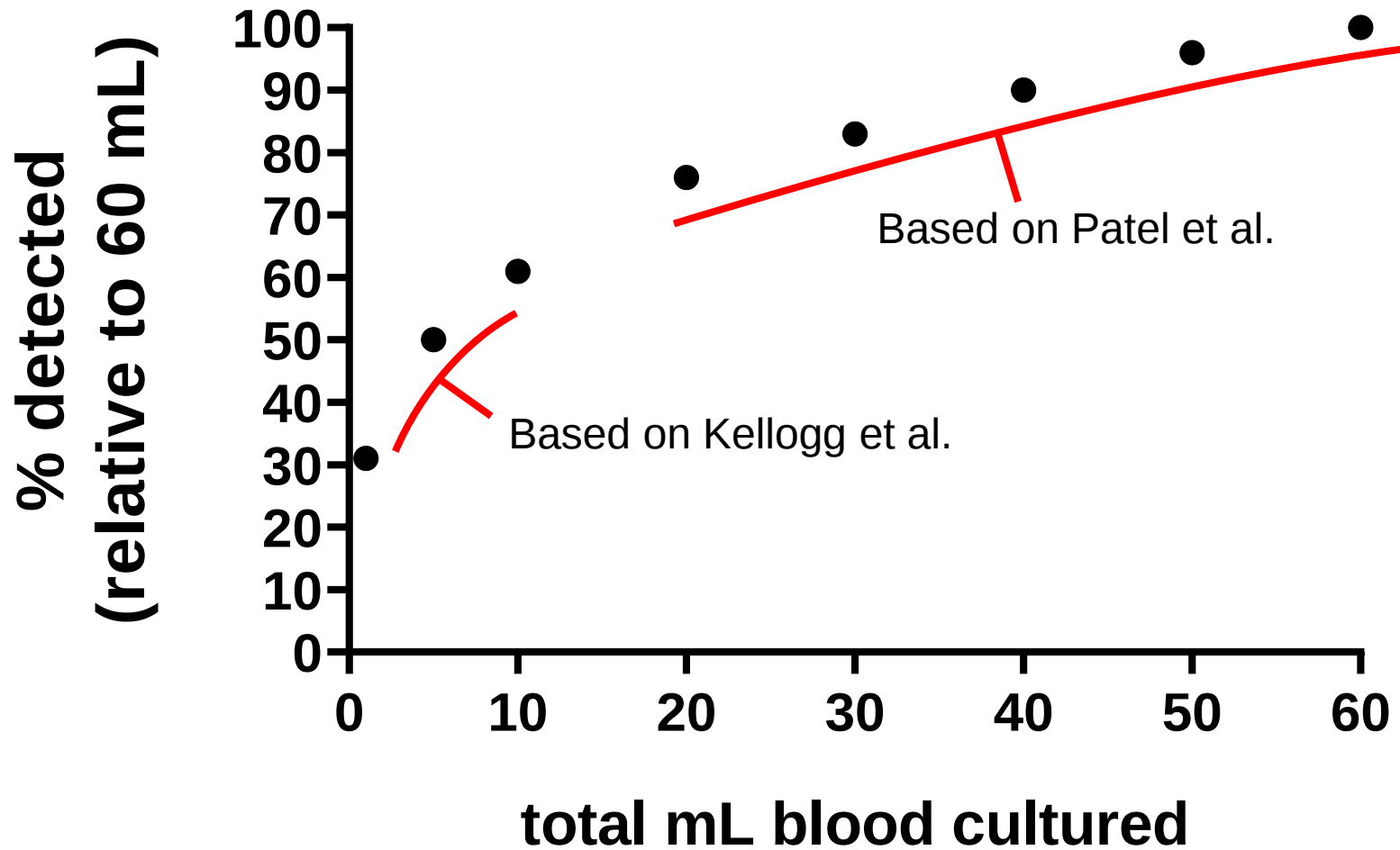
JAMES A. KELLOGG,^{1*} JOHN P. MANZELLA,² AND JOHN H. McCONVILLE²

Clinical Microbiology Laboratory¹ and Department of Internal Medicine, Division of Infectious Diseases,² York Hospital, York, Pennsylvania 17405

TABLE 3. Quantitative range of recovery with Isolator

CFU/ml of blood	Detected pathogens	
	No. of positive cultures	% of total isolates
0.1	63	18
0.2	30	8
0.3	18	5
0.4	16	5
0.5	9	3
0.6 to 1.0	40	11
1.1 to 10	74	21
10.1 to 100	59	17
>100	45	13

Approximately 39% below 0.1 CFU/mL



Extrapolated from Kellogg et al. JCM 1984, and Patel et al. JCM 2011.
This is only an approximation based on two studies, neither of which
used typical collection protocols



T2 Biosystems, Inc.

Thank you for visiting the website for T2 Biosystems, Inc. ("Company"), an in vitro diagnostics company formerly based in Lexington, MA. The Company is no longer operating. Any questions may be submitted by email to: T2@v|pc.com

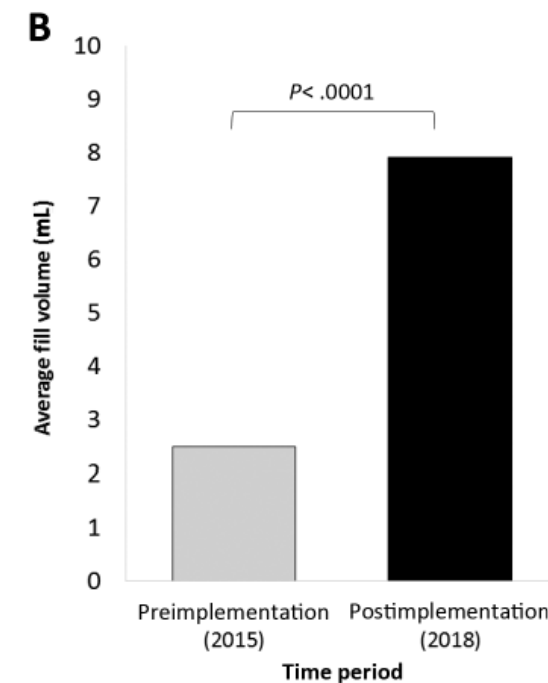
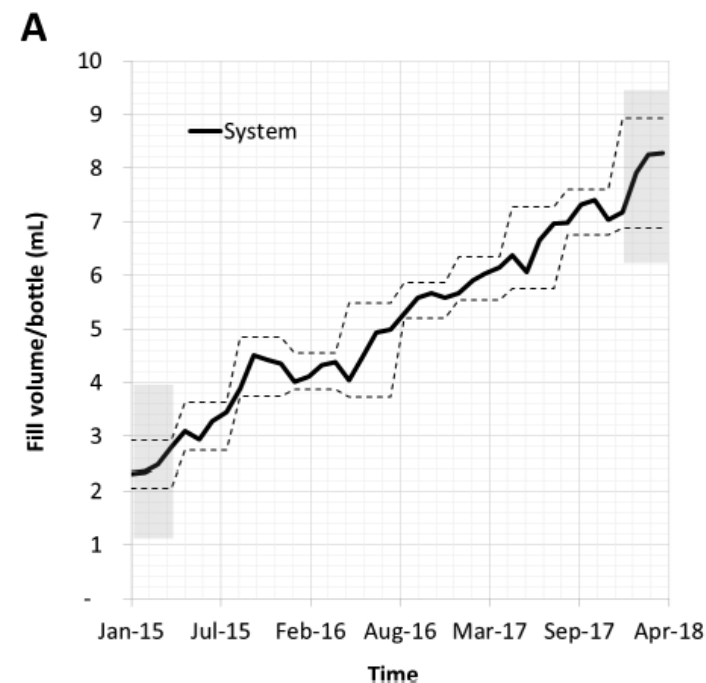
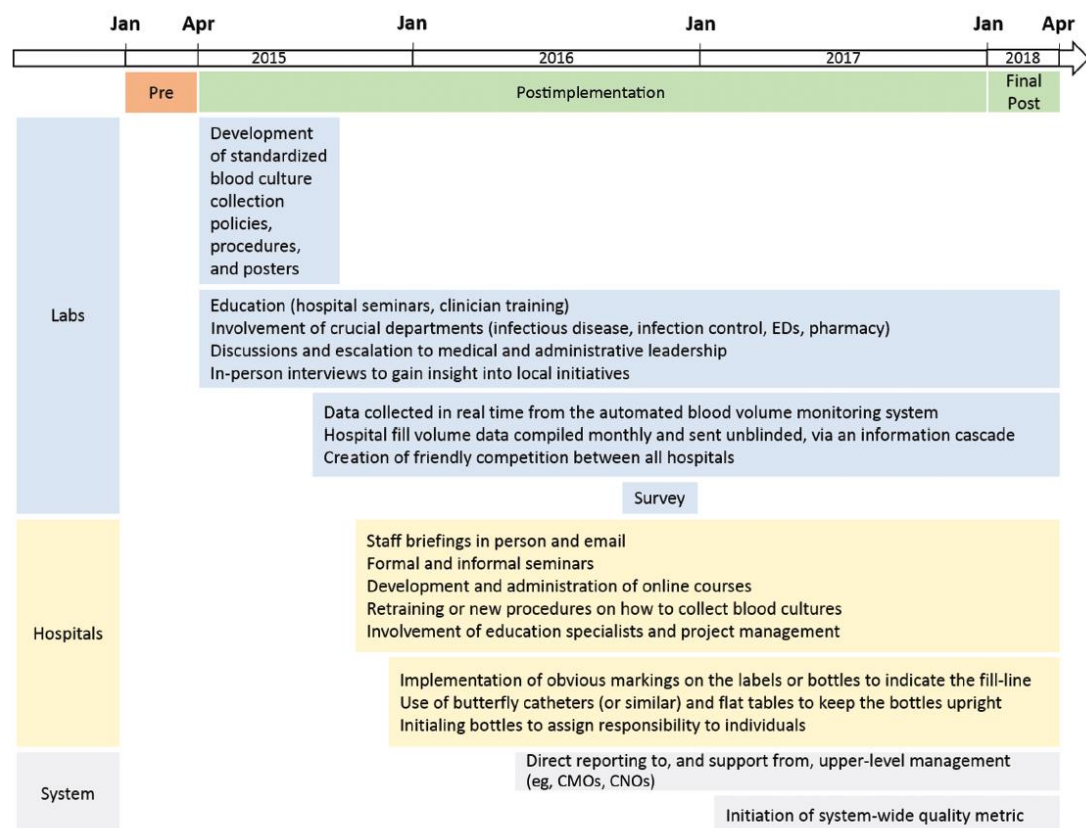
Correspondence can also be sent to:

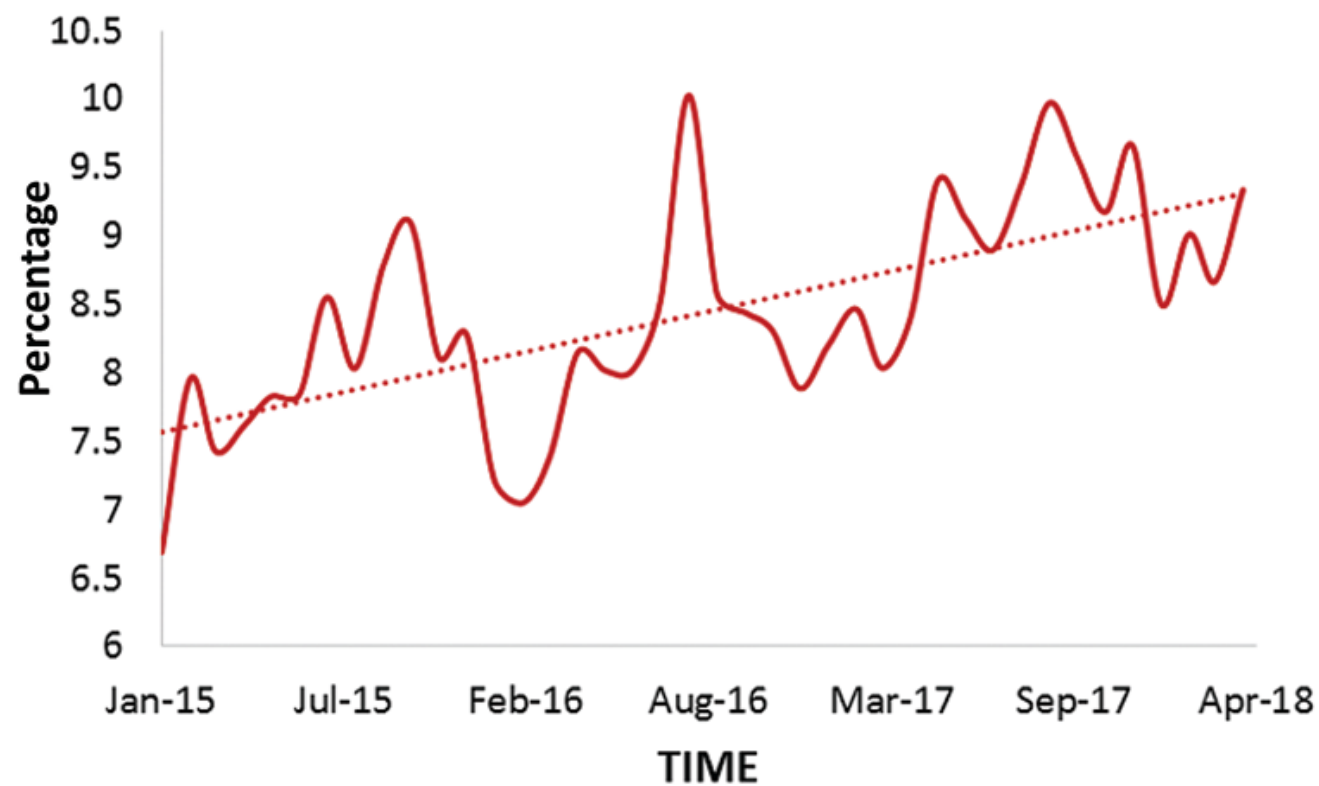
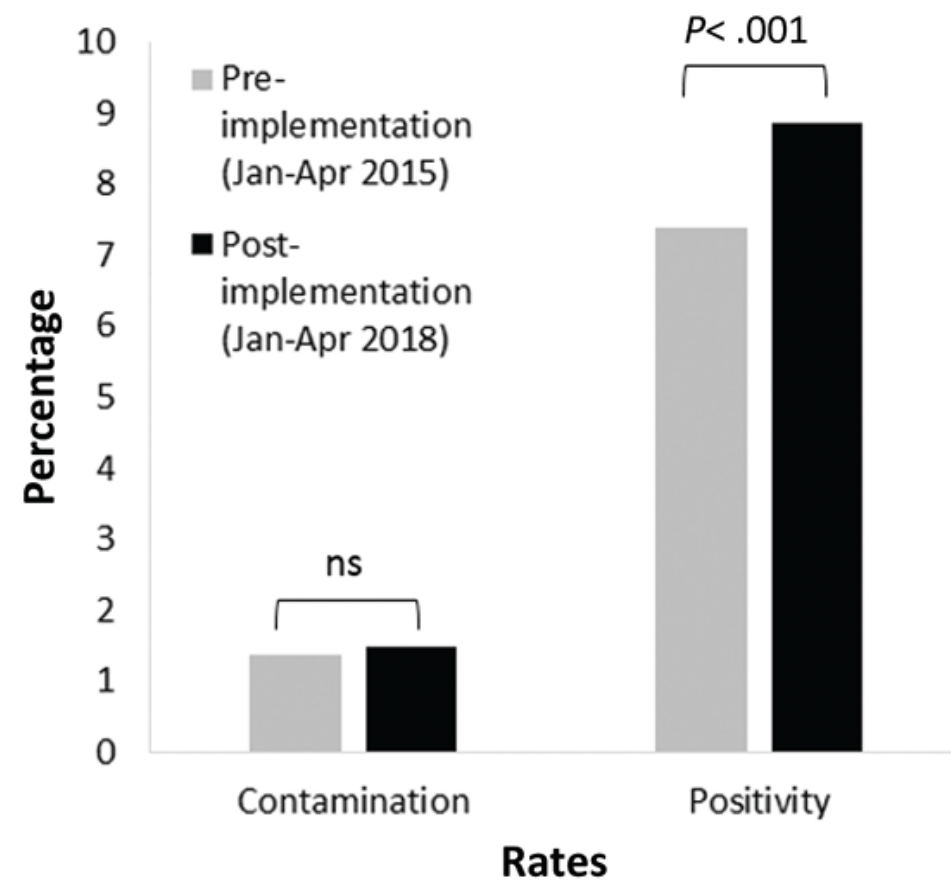
T2 Biosystems, Inc., 124 Washington Street, Ste. 101, Foxboro, MA 02035

LOD was ~ 1 to 8 CFU/mL of blood, depending on the organism, sensitivity ~90% for on panel organisms

Active Monitoring and Feedback to Improve Blood Culture Fill Volumes and Positivity Across a Large Integrated Health System

Reeti Khare,^{1,2} Tarush Kothari,^{2,3} Joseph Castagnaro,³ Bryan Hemmings,^{2,3} May Tso,³ Stefan Juretschko^{1,2}



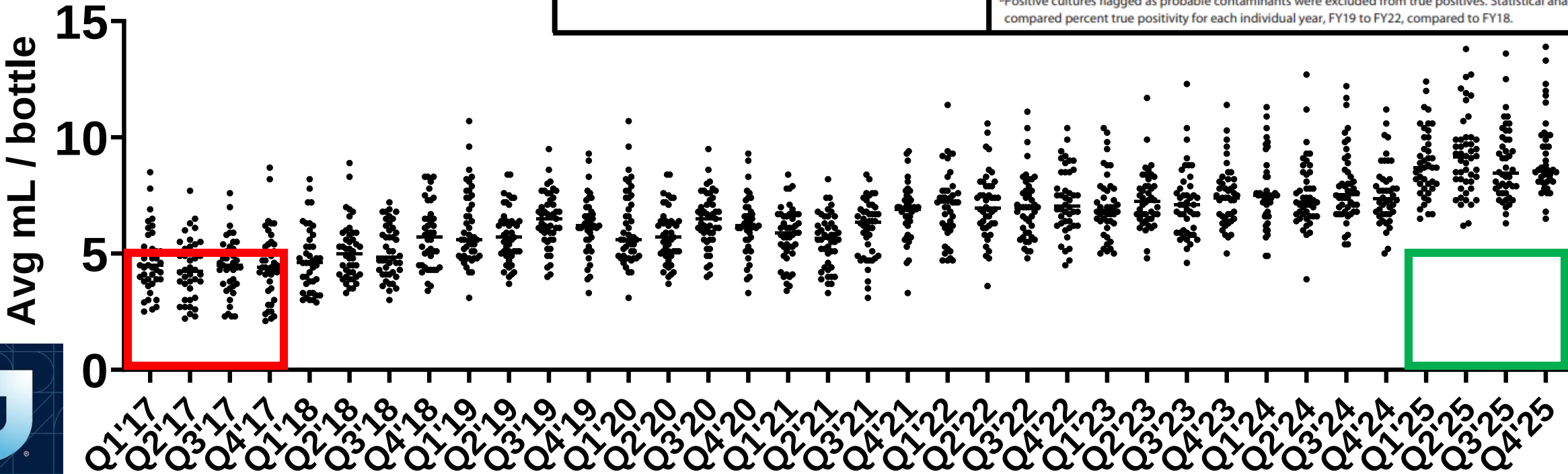
A**B**

$P < .001$



Blood Cx Fill Volume

- Varied educational interventions led by lab
- 2017: majority of TJU CC locations avg <5mL/bottle
- 2025: no TJU CC locations avg <5mL/bottle

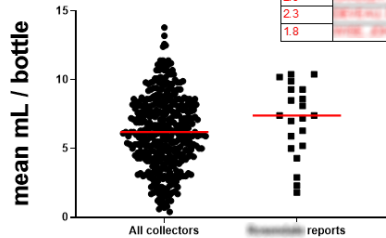


TJUH blood culture collectors who reported to *Capstone Research*: 2020 data

Appropriate blood culture volume is essential for the detection of organisms causing bloodstream infections – 10 mL per bottle is recommended. Data below are only for collectors with at least 25 blood culture collections in 2020. Collectors highlighted in green averaged at least 8 mL, in red averaged <5 mL and need improvement, data for all collectors at TJUH with at least 25 collections are shown for comparison.

★ will receive a gold blood culture pin
★ will receive a silver blood culture pin

mL/bot	Collector
10.4	John Collins
10.4	John Collins
10.2	John Collins
9.9	John Collins
9.3	John Collins
9.3	John Collins
8.6	John Collins
8.5	John Collins
8.1	John Collins
7.4	John Collins
7.4	John Collins
7.2	John Collins
7.0	John Collins
5.9	John Collins
6.3	John Collins
5.2	John Collins
5.0	John Collins
4.3	John Collins
2.9	John Collins
2.3	John Collins
1.8	John Collins



Using Individual Collector Blood Culture Volume Data To Improve Fill Volume

Richard S. Kirby,^a Jenna M. Meloni,^b Karishma B. Naik,^b Matthew D. Minnear,^{b,c} Matthew A. Pettengill^b

^aSidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania, USA
^bDepartment of Pathology and Genomic Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania, USA
^cChildren's Hospital of Philadelphia, Department of Pathology and Laboratory Medicine, Philadelphia, Pennsylvania, USA

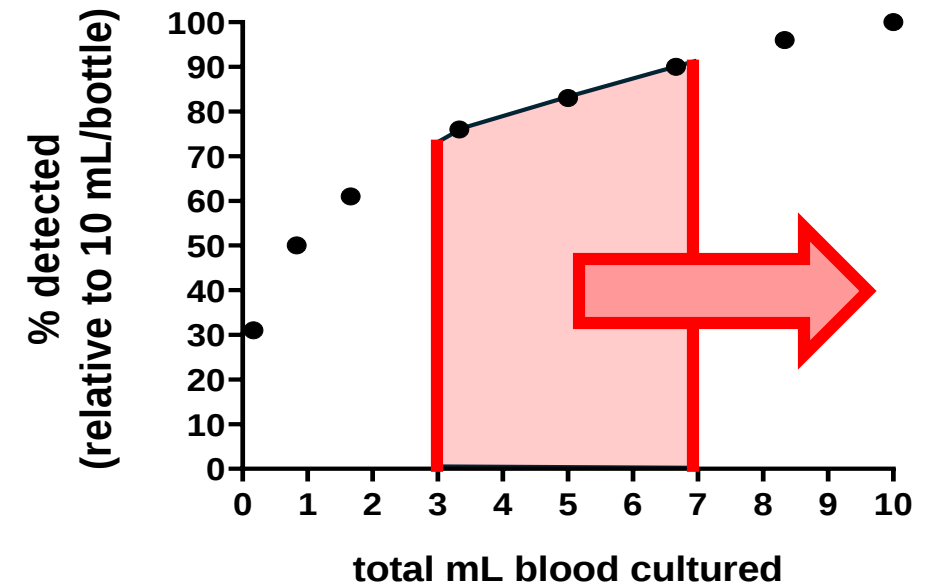
TABLE 1 Blood culture fill volumes and culture positivity by fiscal year of the quality improvement project^a

FY	Total no. of cultures	No. of true positives	No. of true positives/ 50,000	% true positives	Avg BCFV (mL)	P value
FY18	45,261	3,176	3,509	7.00%	4.63	
FY19	46,728	3,303	3,534	7.10%	5.57	0.7603
FY20	50,732	3,648	3,595	7.20%	6.00	0.2960
FY21	50,632	3,830	3,782	7.60%	6.77	0.0011
FY22	48,685	3,866	3,970	7.90%	7.21	<0.0001

^aPositive cultures flagged as probable contaminants were excluded from true positives. Statistical analyses compared percent true positivity for each individual year, FY19 to FY22, compared to FY18.

Blood Culture Bottle Volume Summary

- Standardize and optimize performance for blood culture fill volume, contamination prevention, and turn-around-time of positive results.
- Optimal performance will require not just availability of the latest technology, but availability of technologists to rapidly report Gram stains and organism identifications 24/7.
- We will need to study where blood culture instruments and trained microbiology technologists need to be maintained 24/7, taking into consideration courier route frequency and prioritizing higher volume / higher acuity hubs.



Blood Culture Contamination

- Blood culture contamination has a negative impact on patient care, and several studies have estimated the cost to hospitals for a blood culture contamination event at ~\$5K.
- One way to prevent contaminated blood cultures is to prevent unnecessary blood cultures from being ordered!
- Disinfection of the skin prior to blood culture collection should involve two things you may feel you don't get enough of: *alcohol and time*. Studies have not clearly shown a benefit of disinfectants that add chlorhexidine or iodine compared to alcohol alone – but you do need to give the *alcohol*, or *alcohol-containing* preparation, *time* to work.
- Diversion devices work for reducing blood culture contamination but cost a lot.
- It has been proposed that the target for % Bcx contaminated should be changed from <3% to <1%.



What is a blood culture contaminant?

The Clinical Significance of Positive Blood Cultures in the 1990s: A Prospective Comprehensive Evaluation of the Microbiology, Epidemiology, and Outcome of Bacteremia and Fungemia in Adults

**Melvin P. Weinstein, Michael L. Towns,
Seth M. Quartey, Stanley Mirrett, Larry G. Reimer,
Giovanni Parmigiani, and L. Barth Reller**

Clinical Infectious Diseases 1997;24:584–602
© 1997 by The University of Chicago. All rights reserved.
1058–4838/97/2404–0009\$02.00

*From the Departments of Medicine and Pathology, University of
Medicine and Dentistry of New Jersey–Robert Wood Johnson Medical
School, New Brunswick, New Jersey; Clinical Microbiology Laboratory,
Duke University Medical Center, Departments of Medicine and
Pathology, Duke University School of Medicine, and Institute of
Statistics and Decision Sciences, Duke University, Durham, North
Carolina; and Departments of Pathology and Medicine, Salt Lake City
Veterans Administration Medical Center and University of Utah
Medical School, Salt Lake City, Utah*



What is a blood culture contaminant?

Microorganism (no. of isolates)	No. (%) of isolates per indicated category		
	True pathogen	Contaminant	Unknown
Aerobic and facultative bacteria			
Gram-positive			
<i>Staphylococcus aureus</i> (204)	178 (87.2)	13 (6.4)	13 (6.4)
Coagulase-negative staphylococci (703)	87 (12.4)	575 (81.9)	41 (5.8)
<i>Enterococcus</i> species (93)	65 (69.9)	15 (16.1)	13 (14.0)
Viridans streptococci (71)	27 (38.0)	35 (49.3)	9 (12.7)
<i>Streptococcus pneumoniae</i> (34)	34 (100)	0	0
Group A streptococci (3)	3 (100)	0	0
Group B streptococci (15)	10 (66.7)	3 (20.0)	2 (13.3)
Other streptococci (13)	8 (61.5)	3 (23.1)	2 (15.4)
<i>Bacillus</i> species (12)	1 (8.3)	11 (91.7)	0
<i>Corynebacterium</i> species (53)	1 (1.9)	51 (96.2)	1 (1.9)
<i>Listeria monocytogenes</i> (2)	1 (50.0)	0	1 (50.0)
<i>Lactobacillus</i> species (15)	6 (54.5)	2 (18.2)	3 (27.3)
Other gram-positive bacteria (15)	2 (13.3)	12 (80)	1 (6.7)



What is a blood culture contaminant?

Microorganism (no. of isolates)	No. (%) of isolates per indicated category		
	True pathogen	Contaminant	Unknown
Gram-negative			
<i>Escherichia coli</i> (143)	142 (99.3)	0	1 (0.7)
<i>Klebsiella pneumoniae</i> (65)	65 (100)	0	0
<i>Enterobacter cloacae</i> (25)	25 (100)	0	0
<i>Serratia marcescens</i> (22)	22 (100)	0	0
<i>Proteus mirabilis</i> (16)	16 (100)	0	0
Other Enterobacteriaceae (45)	41 (91)	1 (2.2)	3 (6.7)
<i>Pseudomonas aeruginosa</i> (55)	53 (96.4)	1 (1.8)	1 (1.8)
<i>Pseudomonas</i> species (8)	6 (75)	0	2 (25)
<i>Stenotrophomonas maltophilia</i> (7)	5 (71.4)	0	2 (28.6)
<i>Acinetobacter baumannii</i> (16)	13 (81.2)	1 (6.2)	2 (12.5)
<i>Haemophilus influenzae</i> (3)	3 (100)	0	0
Other gram-negative bacteria (16)	10 (62.5)	3 (18.8)	3 (18.8)



What is a blood culture contaminant?

No. (%) of isolates per indicated category

Microorganism (no. of isolates)	True pathogen	Contaminant	Unknown
Anaerobic bacteria			
<i>Clostridium perfringens</i> (13)	3 (23.1)	10 (76.9)	0
<i>Clostridium</i> species (15)	12 (80)	3 (20)	0
<i>Propionibacterium</i> species (48)	0	48 (100)	0
Other gram-positive anaerobic bacteria (7)	4 (57.1)	2 (28.6)	1 (14.3)
<i>Bacteroides fragilis</i> group (18)	16 (88.9)	0	2 (11.1)
Other gram-negative anaerobic bacteria (5)	2 (40)	2 (40)	1 (20)
Yeasts and fungi			
<i>Candida albicans</i> (30)	27 (90)	0	3 (10)
Other <i>Candida</i> species (15)	15 (100)	0	0
<i>Cryptococcus neoformans</i> (8)	8 (100)	0	0
<i>Torulopsis glabrata</i> (15)	14 (93.3)	0	1 (6.7)
Other yeasts and fungi (4)	2 (50)	1 (25)	1 (25)
Mycobacteria			
<i>Mycobacterium avium</i> complex (16)	16 (100)	0	0
<i>M. tuberculosis</i> (1)	1 (100)	0	0



TJUH definition of Bcx contamination

- Isolated from a single set of multiple sets within 72 hours - AND
- It is either coagulase negative *Staphylococcus* (excluding *S. lugdunensis*, *S. schleiferi*, *S. pseudintermedius*, *S. delphini*), or *Cutibacterium acnes*, or *Bacillus* species not *anthracis*, or most Coryneform Gram positive bacilli (excluding *C. jeikeium*, *C. diphtheriae*, *Arcanobacterium haemolyticum*, see detailed list below from CLSI M45 table 6), or *Micrococcus* spp.
- Coryneform GPR from CLSI M45 table 6: *Arthrobacter*, *Brevibacterium*, *Cellulomonas*, *Cellulosimicrobium*, *Dermabacter*, *Leifsonia*, *Microbacterium*, *Oerskovia*, *Rothia* (except *R. mucilaginosa*), *Trueperella*, and *Turicella*.

Reduction in Blood Culture Contamination Through Use of Initial Specimen Diversion Device

Mark E. Rupp,¹ R. Jennifer Cavalieri,¹ Cole Marolf,¹ and Elizabeth Lyden²

¹Division of Infectious Diseases, and ²Department of Epidemiology, University of Nebraska Medical Center, Omaha

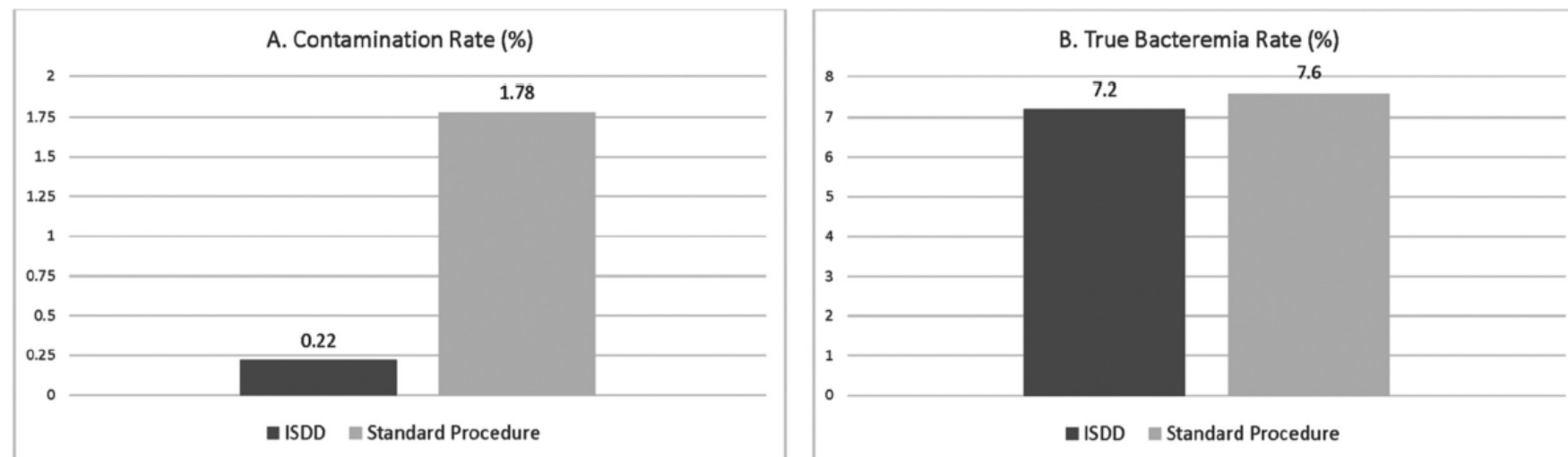
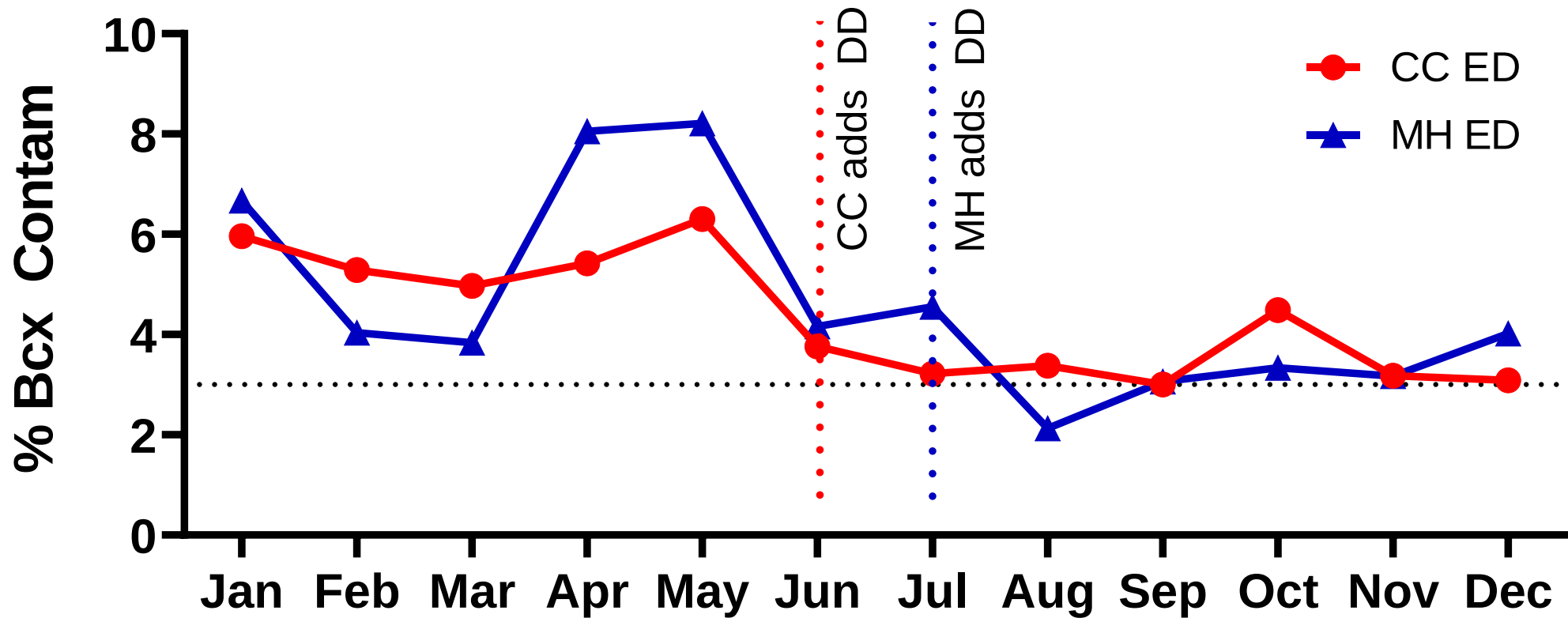


Figure 1. Performance of ISDD vs standard procedure. *A*, Contamination rate. *B*, Detection of true bacteremia. Abbreviation: ISDD, initial specimen diversion device.



Data from a Pennsylvania hospital that implemented diversion devices in two of their EDs. They did not get reliably below 3% contamination. This data is using Steripath in 2021 – in 2024 they switched to Kurin but the contamination levels have remained the same, ~ 3%.

Summary of Bcx Contamination:

- Bcx contamination has negative impact on patient care on hospital finances
- Bcx contamination definition is not standardized, and should be
- The lab is required to monitor Bcx contamination rates and report back to those responsible for collection
- Diversion devices or waste tubes can reduce Bcx contamination



Types of blood cultures and incubation conditions

- The blood cx market is dominated by BD and Biorad – user systems from most recent CAP Bcx survey:
 - BacT/Alert/Biorad 649 labs
 - Bactec BD 633 labs
 - Trek ESP 16 labs
 - Non-automated 21 labs
 - “Other” 21 labs

Okay, I’m going to go on some tangents here related to incubation conditions and how that impacts Bcx sensitivity...



Thermo Scientific Signal Blood-Culture System

Use the Signal™ blood-culture system to detect microbial growth, facilitating the rapid isolation, identification and antimicrobial susceptibility testing of cultured organisms.

One-bottle, manual blood-culture system

Minimizes laboratory costs

Effective with samples as small as 0.1mL

No requirement for special paediatric bottles

Unique broth medium

Enables the recovery of a wide range of aerobes, anaerobes and microaerophilic organisms

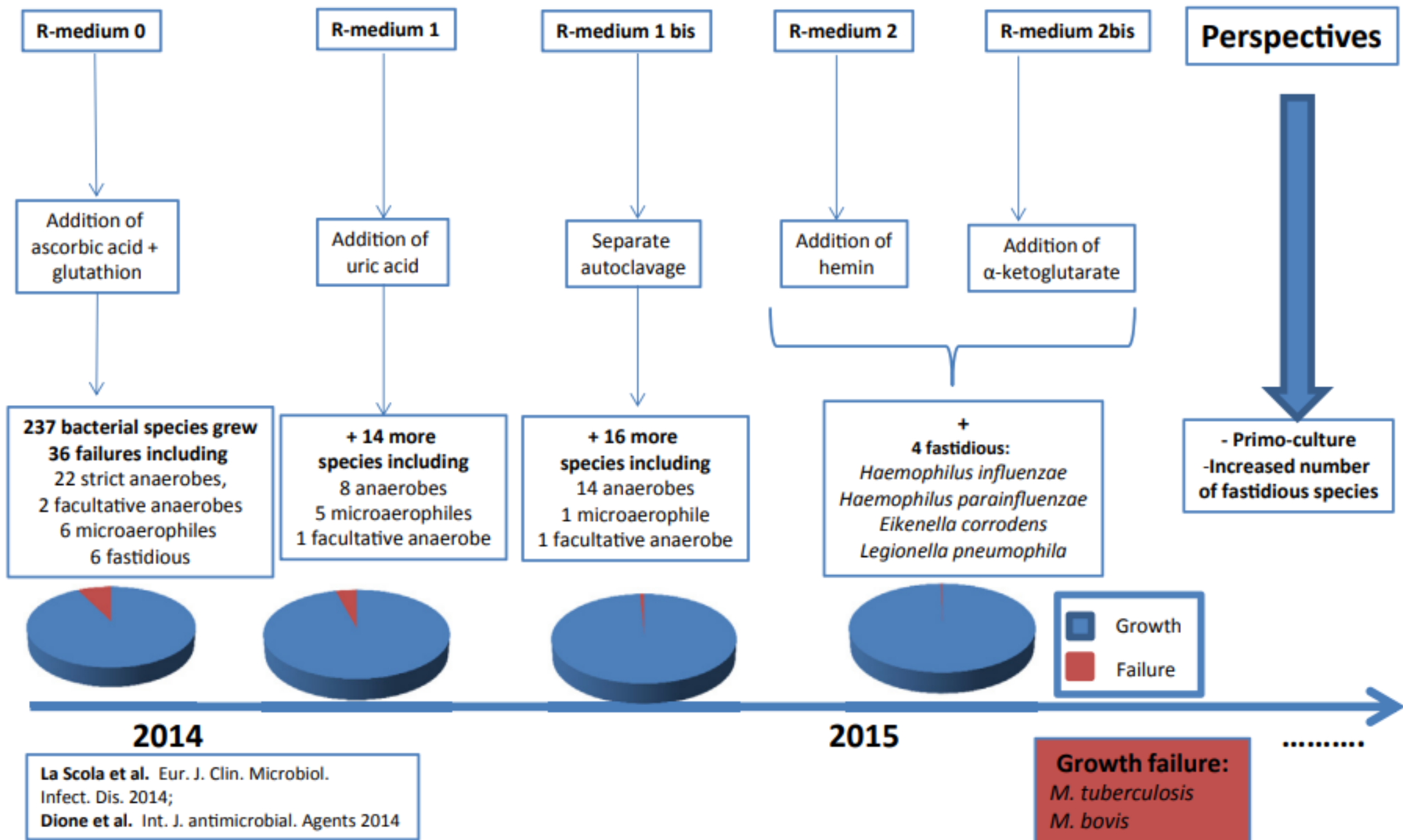


A quasi-universal medium to break the aerobic/anaerobic bacterial culture dichotomy in clinical microbiology

N. Dione, S. Khelaifia, B. La Scola, J. C. Lagier and D. Raoult

Aix Marseille Université, URMITE, UM63, CNRS 7278, IRD 198, INSERM 1095, Marseille, France

Clinical Microbiology and Infection, Volume 22 Number 1, January 2016



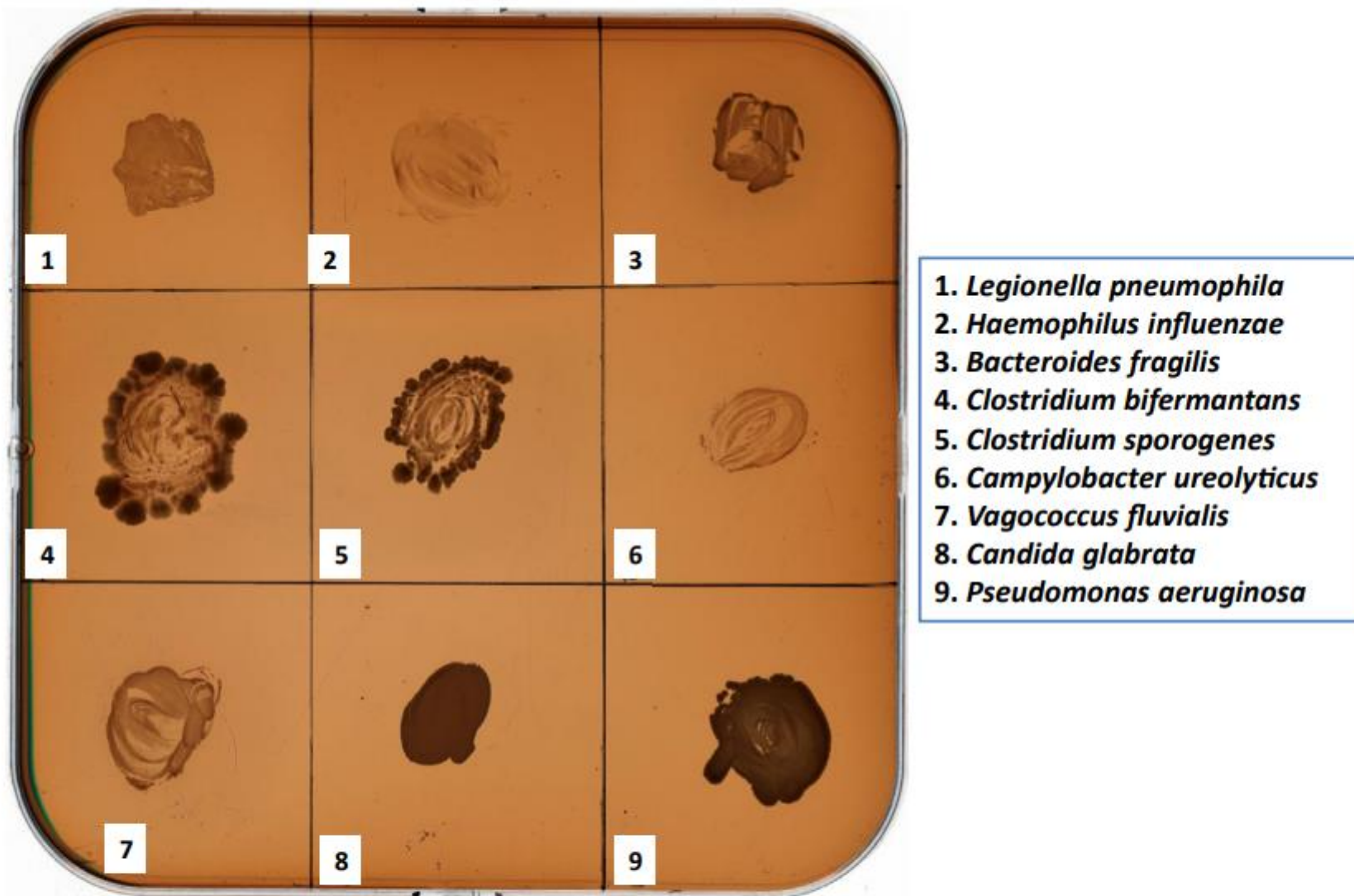


FIG. 2. Impossible petri dish. Concomitant subculture was achieved in same culture medium (R-medium 2bis) of three strict anaerobic species (*Bacteroides fragilis*, *Clostridium bifermentans*, *Clostridium sporogenes*), two fastidious species (*Legionella pneumophila*, *Haemophilus influenzae*), two microaerophiles species (*Vagococcus fluvialis*, *Campylobacter ureolyticus*), one strict aerobe species (*Pseudomonas aeruginosa*) and one fungal species (*Candida glabrata*).

What is the sensitivity of culture for invasive candidiasis?



Journal of
Clinical Microbiology®

MINIREVIEW

May 2018 Volume 56 Issue 5 10.1128/jcm.01909-17
<https://doi.org/10.1128/jcm.01909-17>

Diagnosing Invasive Candidiasis

Cornelius J. Clancy^{a,b}, M. Hong Nguyen^a

^aVA Pittsburgh Healthcare System, Pittsburgh, Pennsylvania, USA

^bUniversity of Pittsburgh, Department of Medicine, Pittsburgh, Pennsylvania, USA

ABSTRACT Cultures are negative in ~50% of invasive candidiasis. Data are emerging for the

Cardiac Fungal Infections:

Review of Autopsy Findings in 60 Patients

JAMES B. ATKINSON, MD, PhD,* DANIEL H. CONNOR, MD,†
MAX ROBINOWITZ, MD,† HUGH A. McALLISTER, MD,† AND
RENU VIRMANI, MD*

An autopsy study of 60 patients with fungal infections of the heart was undertaken. The patients ranged in age from 2 months to 79 years. Fifteen of the patients had undergone cardiac surgery; neoplasms were found in 13, renal failure in eight, bacterial infections in five, liver disease in five, gastrointestinal disorders in five, and immune disease in four; two had been intravenous drug abusers; other miscellaneous disorders were observed in three. The fungal infection was limited to the myocardium in 27 patients and to the endocardium in 17 patients. Myocardium and endocardium were involved in nine patients and pericardium and myocardium in five; two patients had pericarditis alone. The most frequent organism was *Candida* (62 per cent). *Aspergillus* (12 per cent) and *Phycomycetes* (12 per cent) were also found frequently. In 51 patients (85 per cent) other deep organs, usually lung, kidney, brain, or spleen were involved. Cultures for fungus had been positive in 26 patients prior to death, and postmortem cultures were positive in 29 patients. Patients who had undergone cardiac surgery had a higher incidence of endocarditis (93 per cent), with *Candida* (53 per cent) being the most frequent cause. Patients who had received antineoplastic drugs, antibiotics, or corticosteroids had a higher incidence of myocarditis (79 per cent), again most often due to *Candida* (60 per cent). HUM PATHOL 15:935-942, 1984.

Fungal Infection in Surgical Patients

David A. Dean, MD, Kenneth W. Burchard, MD, *Lebanon, New Hampshire*

Invasive fungal infections have become a major source of morbidity and mortality in the modern surgical intensive care unit. Patients at risk for invasion and dissemination are common, and are not as ill as thought previously. Severity of illness (APACHE II score >10, ventilator use for >48 hours), antibiotics, central venous lines, total parenteral nutrition, burns, and immunosuppression are the most common risk factors. Recognition of these risk factors should arouse a high index of suspicion for the diagnosis of invasion or dissemination. Unfortunately, laboratory tests alone lack sensitivity and specificity. Therefore, the diagnosis of invasion and dissemination in the majority of cases requires the acquisition and proper interpretation of clinical evidence. Once the diagnosis is made, early systemic treatment is warranted. Reported toxicity and efficacy supports the use of fluconazole for most patients with invasive fungal infections. However, for the most critically ill patient amphotericin B remains the treatment of choice. *Am J Surg.* 1996;171:374-382.

SUMMARY

Epidemiologically, the incidence of candidemia reported in surgical patients is increasing at an alarming rate, given the difficulty in diagnosis and the high mortality and morbidity rates. Autopsy studies reaffirm this concern, as they demonstrate disseminated candidosis with little antemortem evidence or clues to the diagnosis. Since the 1960s, the risk

Adapted from Weinstein et al., Journal of Clinical Microbiology, 2007

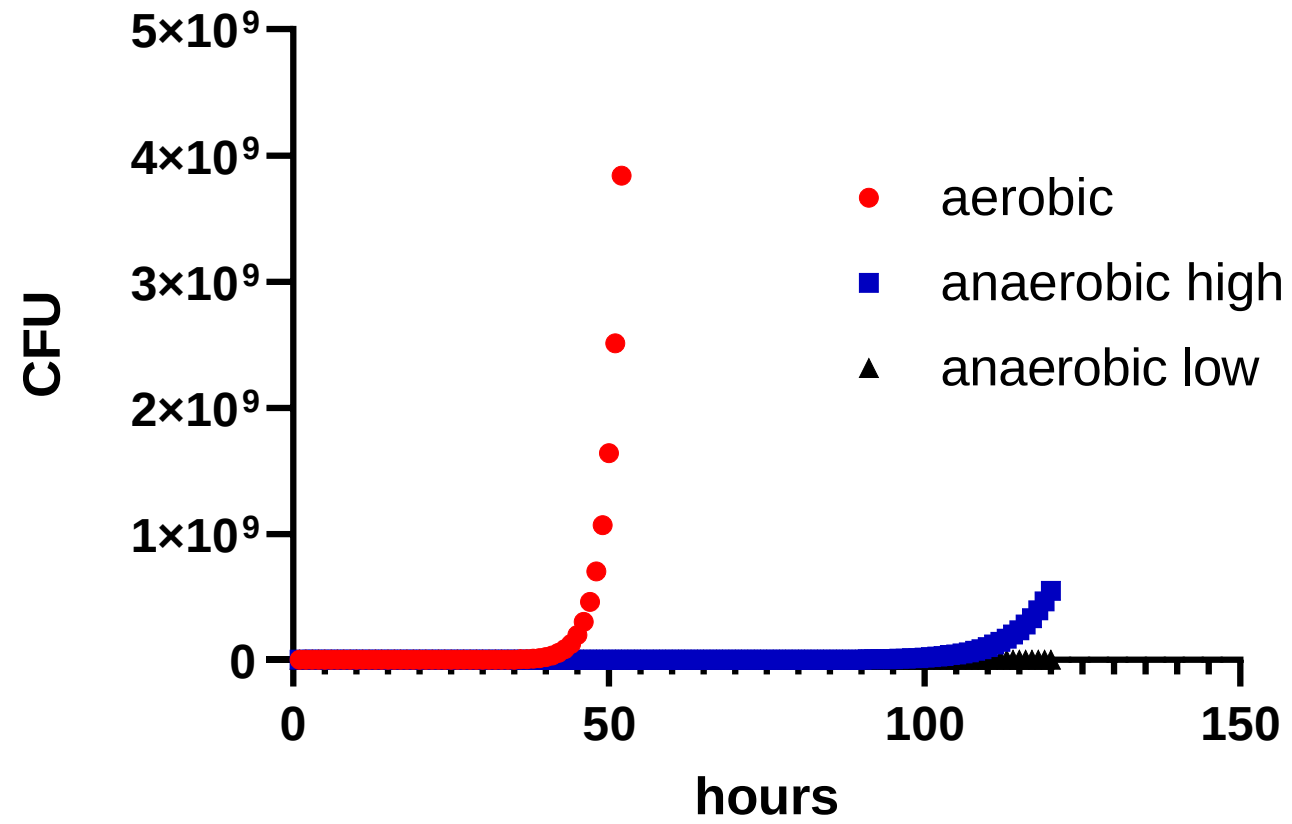
	% detected in first X mL		
	20 mL	40 mL	60 mL
<i>S. aureus</i>	90%	95%	100%
<i>Streptococcus</i> spp.	80%	91%	100%
<i>Enterococcus</i> spp.	71%	89%	100%
<i>E. coli</i>	72%	93%	100%
<i>K. pneumoniae</i>	78%	91%	100%
<i>P. aeruginosa</i>	61%	90%	100%
<i>C. albicans</i>	62%	85%	100%

With less volume collected, the sensitivity of blood culture is especially impacted for non-facultative organisms. But is *Candida* facultative or not?

C. albicans is a facultative organism

- *C. albicans* grows under anaerobic conditions *in vivo* (GI tract) and *in vitro* (anaerobic culture conditions)
- However, it has a much slower doubling time in anaerobic conditions than aerobic
 - Estimates of aerobic growth doubling time range from 98 to 120 minutes
 - For anaerobic conditions estimates range from 248 to 1200 minutes
- The ranges may seem only moderately different, but they are not...

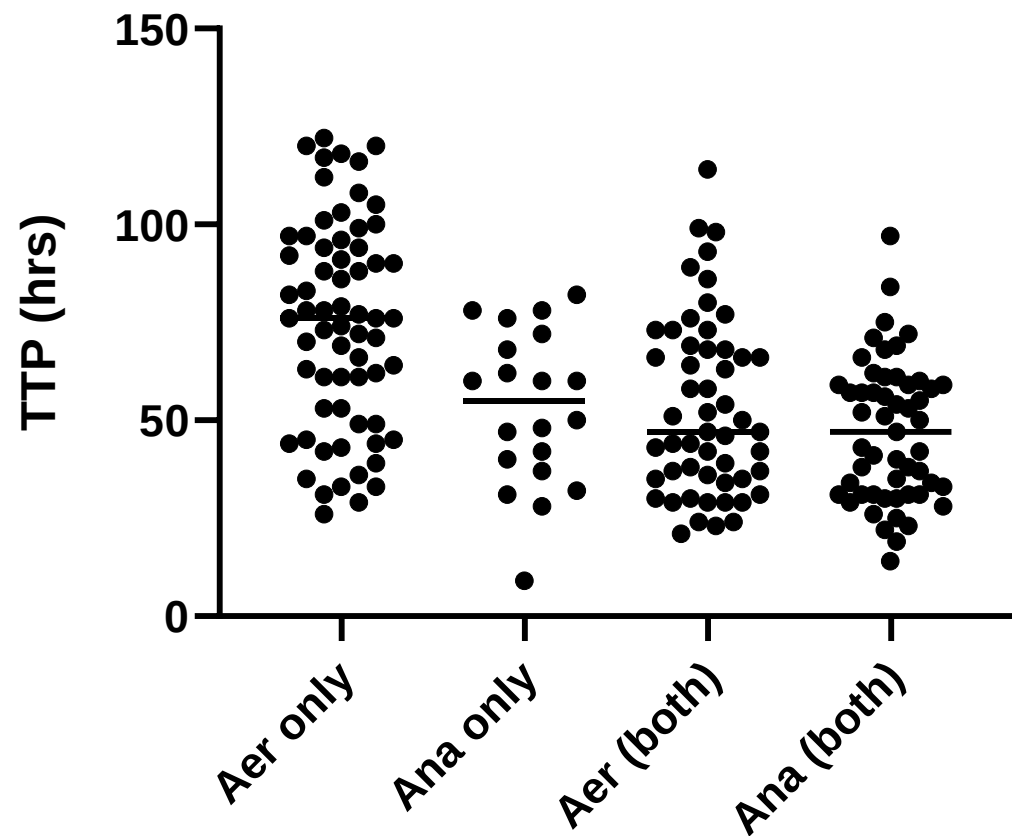
C. albicans aerobic vs anaerobic



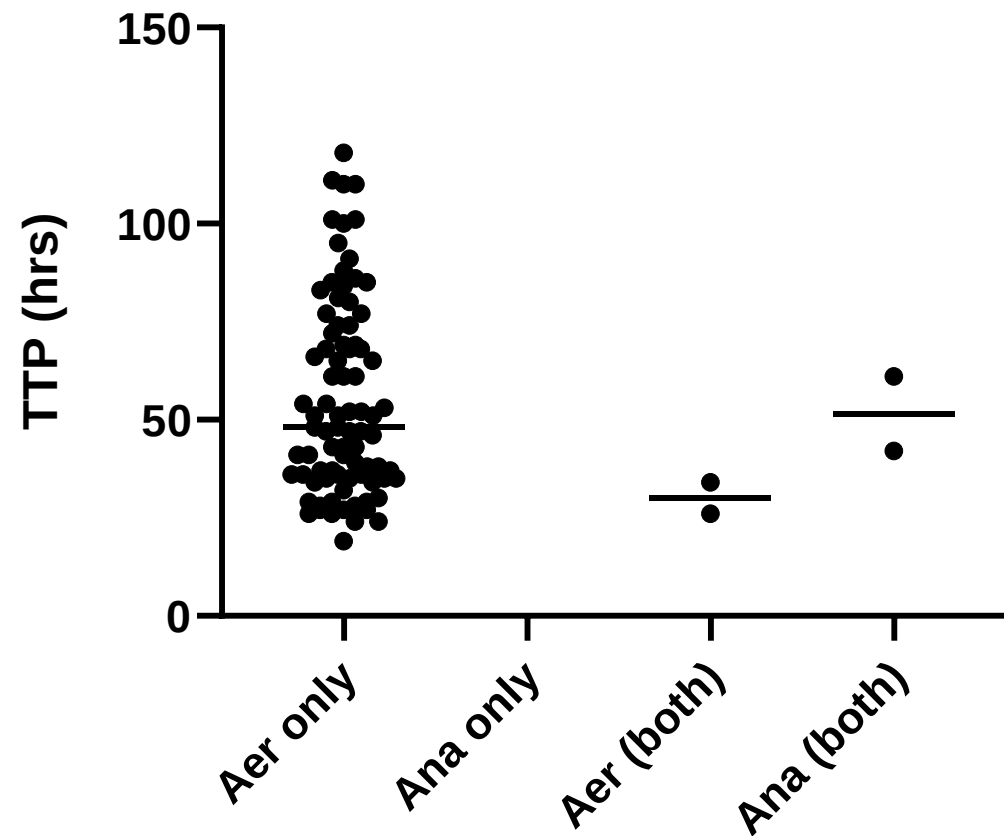
Candida blood cultures

- Potential reasons most *Candida* grow poorly in anaerobic blood culture bottles:
 - Grow better with oxygen
 - Negatively impacted by detergent in lytic anaerobic bottle
 - Resins in aerobic bottle impact antifungal concentration or otherwise favor growth
 - Fill volume is significantly better in aerobic bottles

Candida glabrata

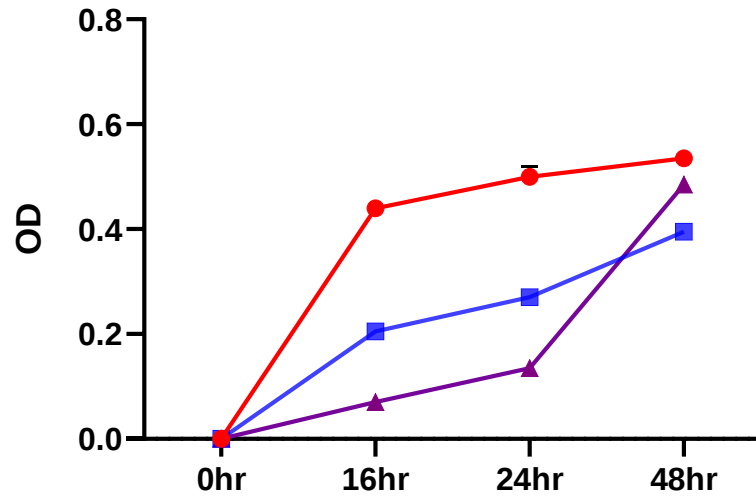


Candida albicans

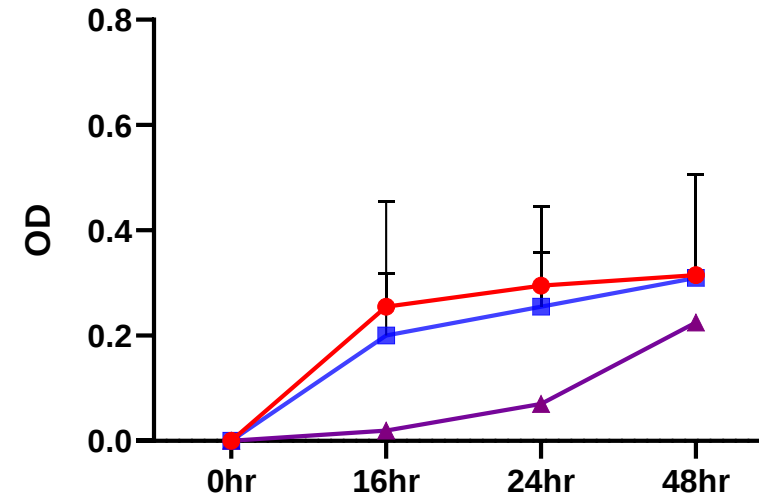


~5 years of data from TJUH

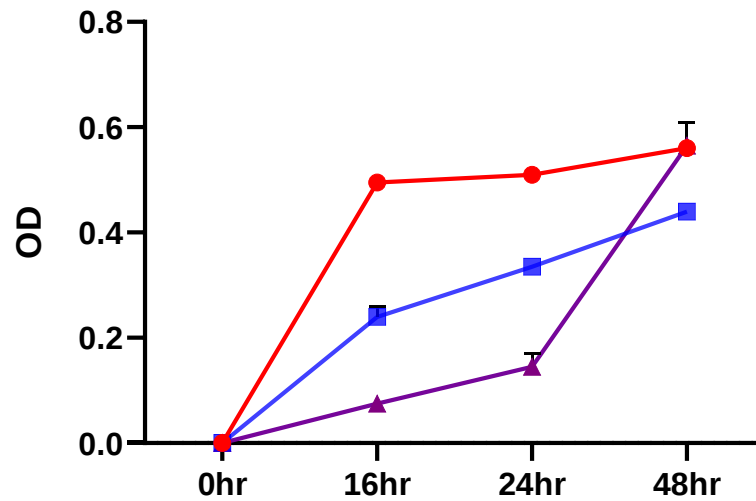
BD aer



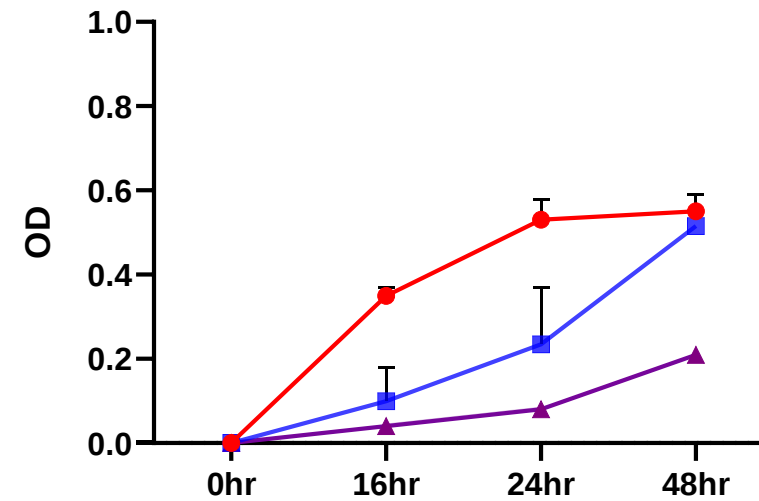
BD ana



BM aer



BM ana



C. glabrata
C. albicans
C. parapsilosis

Is *C. albicans* a facultative organism?

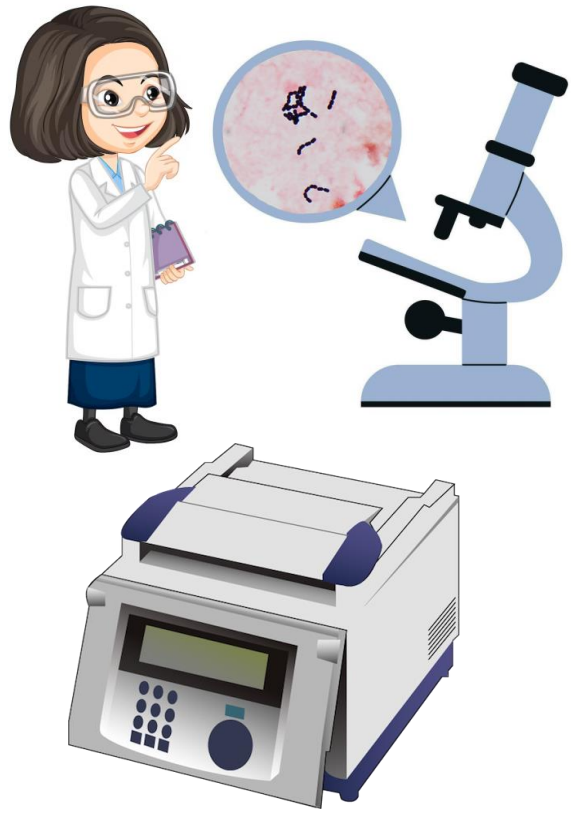
- In the time scale of clinical microbiology cultures – *C. albicans* behaves essentially like a strict aerobe.

Candida blood cultures

- Should we make an orderable double aerobic blood culture?
 - Should enhance the recovery of *Candida* species regardless of the reason they grow poorly in anaerobic bottles.
 - Other important organisms are also functionally strictly aerobic, such as *Pseudomonas*, *Acinetobacter*, *Stenotrophomonas*, *Burkholderia* etc.
- Would need to be restricted to patients with a recently collected routine blood culture.

Summary of my random thoughts on culture conditions:

- Many clinically important organisms grow poorly or not at all in either the aerobic or anaerobic Bcx bottles.
 - This effectively reduces the volume of blood evaluated for growth of these organisms and reduces the sensitivity of Bcx
- It is feasible to make broth media that supports growth of both aerobes and anaerobes – maybe this is the future for mainstream Bcx systems
- Other things can be done to try to enhance growth of strict organisms: Do the Mayo study format collection (30 mL, 2 aerobic bottles, 1 ana), or, not well studied, but maybe an aerobic only collection if prior anaerobic already performed?



Time to reporting of Gram stains and organism identification

- You can significantly reduce the associated mortality by reporting Gram stains and rapid organism identification promptly.
- But most blood cultures flag positive on 2nd or 3rd shift – is anyone available to act on them in the lab?



Blood Cx Speed Matters

Decreased Mortality Associated With Prompt Gram Staining of Blood Cultures

Joan Barenfanger, MD,¹ Donald R. Graham, MD,² Lavanya Kolluri, MD,^{3*} Gaurav Sangwan, MD,³ Jerry Lawhorn,¹ Cheryl A. Drake,¹ Steven J. Verhulst, PhD,⁴ Ryan Peterson,⁶ Lauren B. Moja, PharmD,⁷ Matthew M. Ertmoed, PharmD,⁷ Ashley B. Moja,⁵ Douglas W. Shevlin, MD,¹ Robert Vautrain, MD,^{1*} and Charles D. Callahan, PhD¹

Key Words: Bloodstream infection; Gram staining; Timeliness; Positive blood culture; Outcomes

DOI: 10.1309/AJCPVMDQU2ZJDPBL

Clinical Infectious Diseases

MAJOR ARTICLE

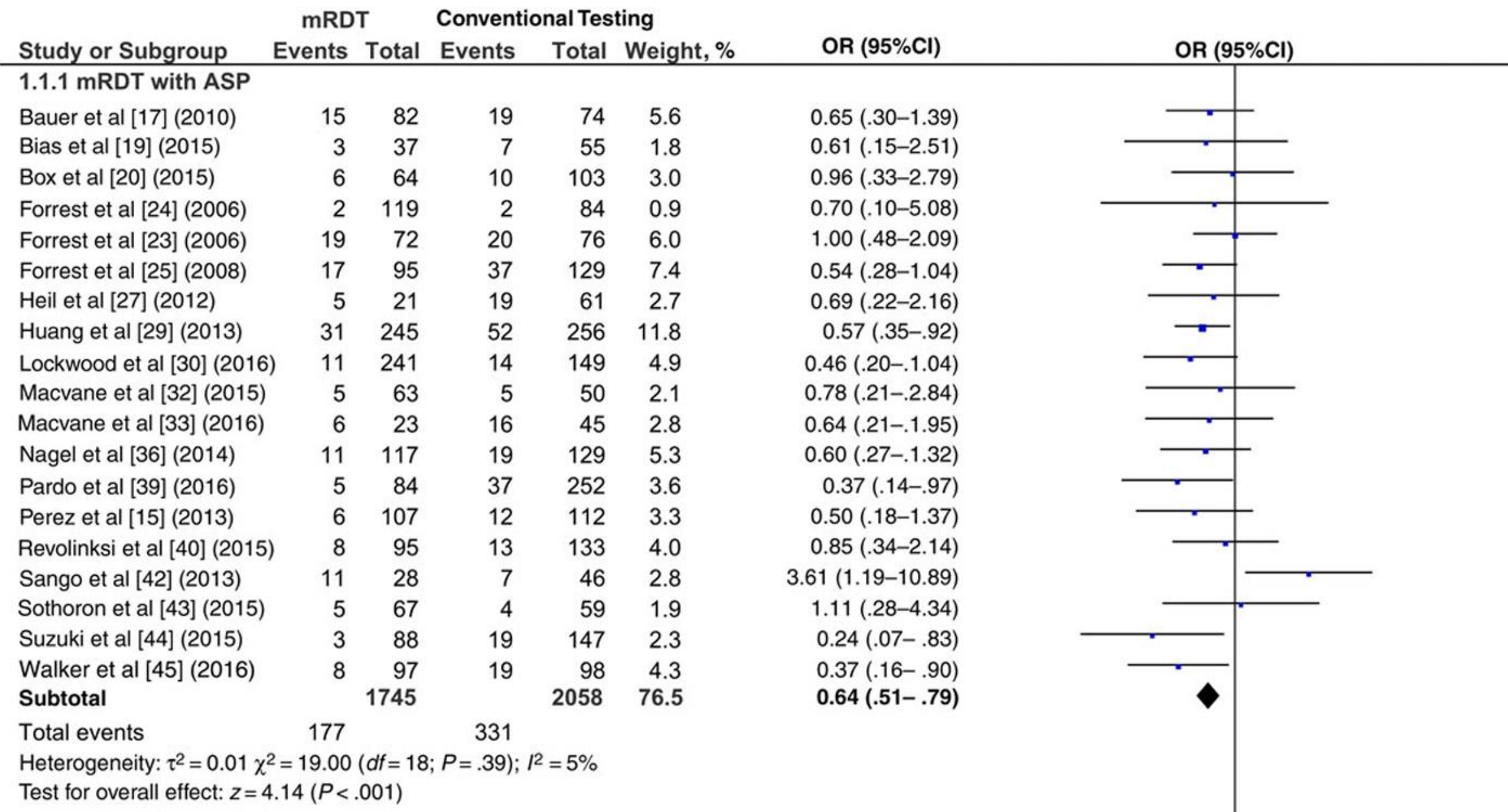


The Effect of Molecular Rapid Diagnostic Testing on Clinical Outcomes in Bloodstream Infections: A Systematic Review and Meta-analysis

Tristan T. Timbrook,^{1,4} Jacob B. Morton,^{1,4} Kevin W. McConeghy,² Aisling R. Caffrey,^{1,2,4} Eleftherios Mylonakis,³ and Kerry L. LaPlante^{1,2,4}

¹Rhode Island Infectious Diseases Research Program, Providence Veterans Affairs Medical Center, ²Center of Innovation in Long Term Services and Supports, Providence Veterans Affairs Medical Center, ³Infectious Diseases Division, Warren Alpert Medical School of Brown University, Providence, and ⁴College of Pharmacy, University of Rhode Island, Kingston





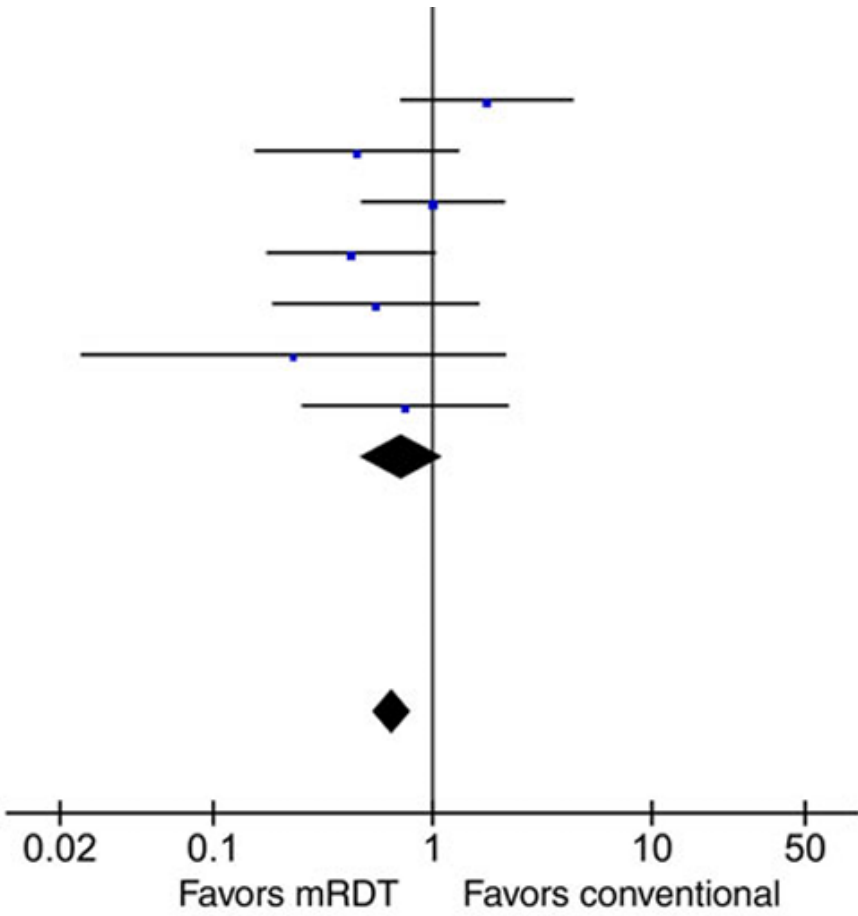
1.1.2 mRDT without ASP

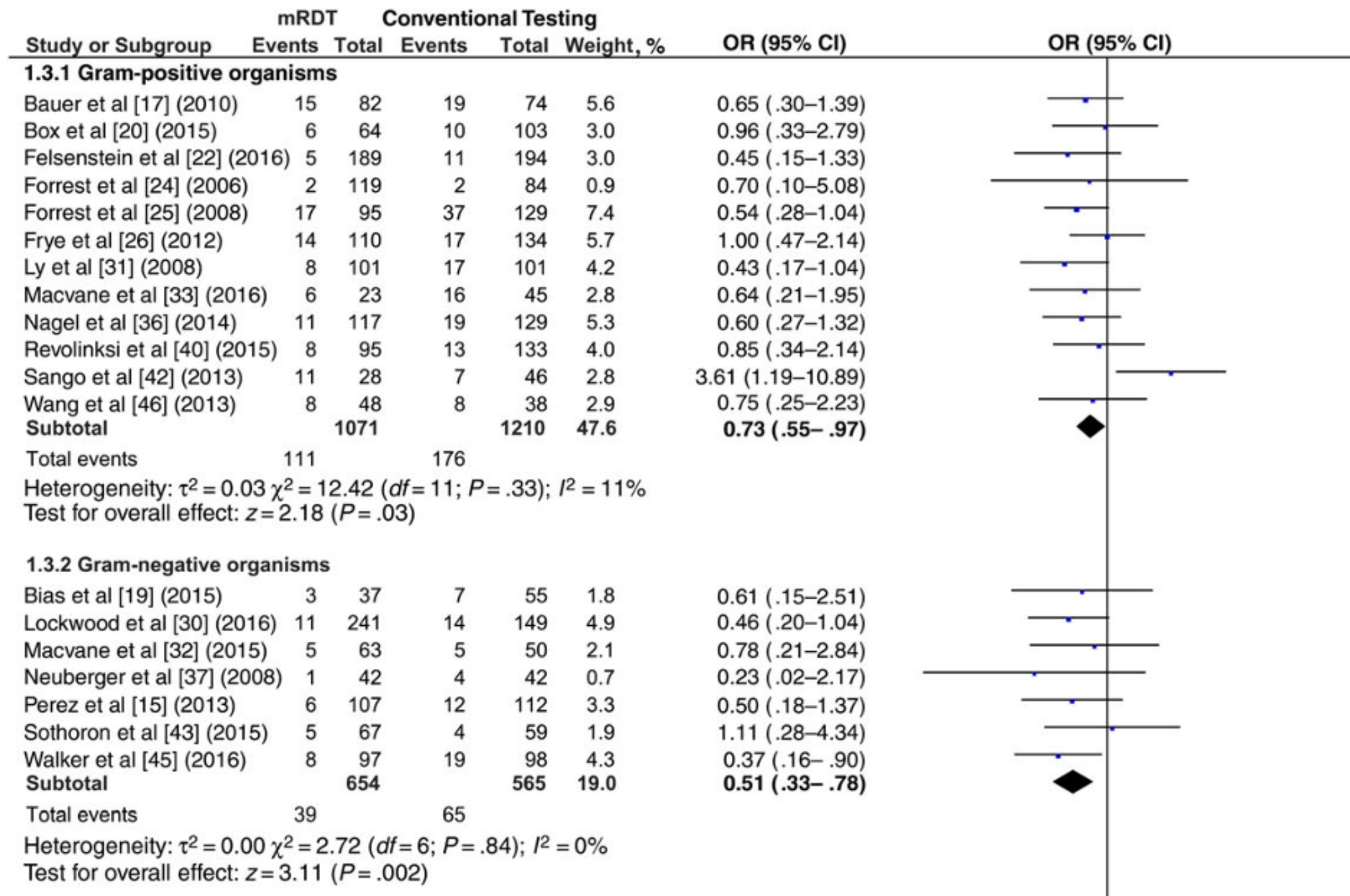
Beuving et al [18] (2015)	14	114	8	109	4.1	1.77 (.71–4.40)
Felsenstein et al [22] (2016)	5	189	11	194	3.0	0.45 (.15–1.33)
Frye et al [26] (2012)	14	110	17	134	5.7	1.00 (.47–2.14)
Ly et al [31] (2008)	8	101	17	101	4.2	0.43 (.17–1.04)
Maslonka et al [34] (2014)	6	55	10	55	2.9	0.55 (.19–1.64)
Neuberger et al [37] (2008)	1	42	4	42	0.7	0.23 (.02–2.17)
Wang et al [46] (2013)	8	48	8	38	2.9	0.75 (.25–2.23)
Subtotal		659		673	23.5	0.72 (.46–1.12)

Total events 56 75
Heterogeneity: $\tau^2 = 0.08$ $\chi^2 = 7.74$ ($df = 6$; $P = .26$); $I^2 = 23\%$
Test for overall effect: $z = 1.46$ ($P = .15$)

Total (95% CI) 2404 2731 100.0 0.66 (.54–.80)

Total events 233 406
Heterogeneity: $\tau^2 = 0.02$ $\chi^2 = 27.22$ ($df = 25$; $P = .34$); $I^2 = 8\%$
Test for overall effect: $z = 4.27$ ($P < .001$)
Test for subgroup differences: $\chi^2 = 0.25$ ($df = 1$; $P = .62$); $I^2 = 0\%$





Part of the incubation is transportation

- BD IFU says blood culture bottles “should be transported as quickly as possible to the laboratory.”
- Biorad says “Inoculated bottles should be transported to the laboratory for testing as quickly as possible, preferably within 2 hours per CLSI*.”
- * “Blood culture bottles/tubes should be sent to the laboratory within 2 hours; delays in entering blood culture bottles into the continuous-monitoring blood culture instruments (particularly if the bottles are incubated at 35 to 37C) may delay or impede detection of growth. Holding bottles at room temperature is not recommended for anything longer than a few hours.” M47

Part of the incubation is transportation

- “The request to positivity times was significantly lower for samples with transit time < 4 h ($p < 0.001$).”
- “A prolonged transit time was associated with a longer length-of-stay in those with a bacteraemia with a significant organism ($p = 0.001$).”

European Journal of Clinical Microbiology & Infectious Diseases (2023) 42:835–842
<https://doi.org/10.1007/s10096-023-04610-z>

ORIGINAL ARTICLE

An assessment of the downstream implications of blood culture collection and transit

Peter J. B. Davies¹  · Timothy P. W. Jones^{1,2} · Mairi Macleod¹

Received: 2 February 2023 / Accepted: 21 April 2023 / Published online: 2 May 2023

Improving the blood culture pathway



A national review of blood culture pathway processes to support better antimicrobial stewardship and improved patient safety

Version 1.1, 8 March 2023

3.2 Time to analyser

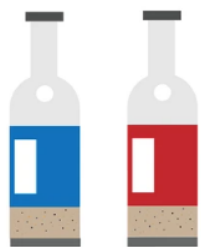
Blood culture systems are monitored for blood cultures from the point at which the blood is placed directly on the analyser. For each hour delay to loading on the blood culture analyser there is both a loss of viability of organisms and an incremental delay to obtaining a result.

Additionally, any delays will cause the temperature of the blood culture to migrate to ambient, also resulting in delays to obtaining a positive culture.

In alignment with laboratory standards, NHS England and NHS Improvement recommends for blood culture sample bottles to be incubated in a blood culture analyser as soon as possible, ideally within a maximum of four hours.

Summary Rapid ID and Speed of Bcx

- Patient **MORTALITY** benefit if performing rapid identification from positive Bcx
- Speed of Bcx overall matters, transportation, loading on instrument, technologists available to respond 24/7, Gram stain report etc...



What can you do with cumulative data?

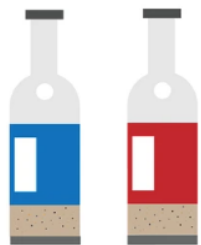
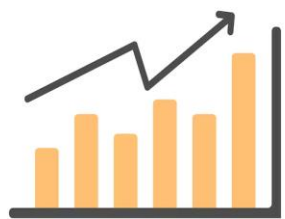
- You could make a source specific antibiogram for isolates from blood cultures.
- May not be worth it – results usually aren't that different from blood than all sources combined.

NM Northwest Region 2022 Blood Antibiogram		Isolates	Ampicillin ^a	Ampicillin/Sulbactam	Cefazolin	Cefepime	Ceftazidime	Ceftriaxone	Ciprofloxacin	Clindamycin	Daptomycin ^c	Levofloxacin	Linezolid ^c	Meropenem ^c	Oxacillin	Penicillin G	Piperacillin/Tazobactam	Sulfamethoxazole/Trimethoprim	Tetracycline	Vancomycin
GRAM POSITIVES																				
Enterococcus species	36	100									100		100							97
Staphylococcus aureus	128			63						63	100		100		63 ^b			96	83 ^d	100
Methicillin-resistant Staphylococcus aureus	47									42	100		100					89	63 ^d	100
GRAM NEGATIVES																				
Escherichia coli	196	54	64	69	81	79	79	71				74		100			97	70		
Klebsiella pneumoniae	50		86 ^b	90 ^b	96	96	96	88				92		100			100	92		
Extended-Spectrum β -Lactamase Enterobacterales (ESBL-E)	41								12			17		100				34		

% Susceptibility

- ≥ 80%
- 70-79%
- ≤ 69%





What can you do with cumulative data?

- Probably more meaningful to make a genotypic antibiogram if you use a molecular panel for positive blood cultures that includes common resistance markers.
- We make one specifically for CTX-M vs. no targets, our ASP group incorporates this data into their positive blood culture guidelines.

Genotypic BCx Gram-negative (TJUH, JMH, JHN)*	# of isolates	% SUSCEPTIBLE															
		Amoxicillin-clavulanate	Ampicillin-sulbactam	Piperacillin Tazobactam	Pip- Tazo +SDD	Ceftriaxone	Cefepime	Cefepime +SDD	Aztreonam	Ertapenem	Meropenem	Ceftazidime avibactam	Gentamicin	Tobramycin	Levofloxacin	Tetracycline	TMP-SMX
Escherichia coli																	
CTX-M detected**	106			b	b		b	b		97	100	99	76	67	23	26	32
No markers detected	490	85	58	94	96	97	100a	100	98	100a	100	100	91	91	81	74	76
Klebsiella pneumoniae																	
CTX-M detected**	52			b	b		b	b		89	93	100	56	44	19	46	19
No markers detected	236	96	83	89	92	98	99	99	98	99	100a	100a	99	98	92	81	92
*3 years of data 2022-2024, **CTX-M ESBL is detected and carbapenemase genes are not detected, a: >=99.5% but <100%, b: Piperacillin-tazobactam and cefepime are not recommended for treatment of CTX-M or other ESBL harboring organisms.																	



Genotypic BCx Gram-negative (TJUH, JMH, JHN)*	# of isolates	% SUSCEPTIBLE															
		Amoxicillin- clavulanate	Ampicillin- sulbactam	Piperacillin Tazobactam	Pip- Tazo +SDD	Ceftriaxone	Cefepime	Cefepime +SDD	Aztreonam	Ertapenem	Meropenem	Ceftazidime avibactam	Gentamicin	Tobramycin	Levofloxacin	Tetracycline	TMP-SMX
<i>Escherichia coli</i>																	
CTX-M detected**	106			b	b		b	b		97	100	99	76	67	23	26	32
No markers detected	490	85	58	94	96	97	100a	100	98	100a	100	100	91	91	81	74	76
<i>Klebsiella pneumoniae</i>																	
CTX-M detected**	52			b	b		b	b		89	93	100	56	44	19	46	19
No markers detected	236	96	83	89	92	98	99	99	98	99	100a	100a	99	98	92	81	92

*3 years of data 2022-2024, **CTX-M ESBL is detected and carbapenemase genes are not detected, a: >=99.5% but <100%, b: Piperacillin-tazobactam and cefepime are not recommended for treatment of CTX-M or other ESBL harboring organisms.



THANK YOU CLINICAL MICROBIOLOGY!



Acknowledgements

- Blood Cx Decision Support:
 - Bryan Hess MD, FIDSA
 - Courtney Comar, PhD D(ABMM)
 - Lizzy Braden, MD
 - Elizaveta Flerova MD
- Blood Cx Volume QI:
 - Sara Goss MLS (ASCP)
 - Jenna Meloni MLS (ASCP)
 - Rich Kirby MD
- Blood Cx Genotypic ABG
 - Bryan Hess MD, FIDSA
 - Courtney Comar, PhD D(ABMM)
 - Madison Leap PharmD

References

- Verway, M. et al. ***Prevalence and mortality associated with bloodstream organisms: a population-wide retrospective cohort study***. J. Clin. Microbiol. 60, e0242921 (2022).
- Foong KS, Munigala S, Kern-Allely S, Warren DK. ***Blood culture utilization practices among febrile and/or hypothermic inpatients***. BMC Infect Dis. 2022 Oct 10;22(1):779. doi: 10.1186/s12879-022-07748-x. PMID: 36217111; PMCID: PMC9552399.
- Linsenmeyer, K., Gupta, K., Strymish, J.M., Dhanani, M., Brecher, S.M. and Breu, A.C. (2016), ***Culture if spikes? Indications and yield of blood cultures in hospitalized medical patients***. J. Hosp. Med., 11: 336-340. <https://doi.org/10.1002/jhm.2541>
- Fabre V, Milstone AM, Keller SC, Carroll KC, Cosgrove SE. ***Prescribers' knowledge, attitudes and perceptions about blood culturing practices for adult hospitalized patients: a call for action***. Infection Control & Hospital Epidemiology. 2018;39(11):1394-1396. doi:10.1017/ice.2018.224
- Fabre V, Sharara SL, Salinas AB, Carroll KC, Desai S, Cosgrove SE. Does ***This Patient Need Blood Cultures? A Scoping Review of Indications for Blood Cultures in Adult Nonneutropenic Inpatients***. Clin Infect Dis. 2020 Aug 22;71(5):1339-1347. doi: 10.1093/cid/ciaa039. PMID: 31942949.
- Fabre V, Klein E, Salinas AB, Jones G, Carroll KC, Milstone AM, Amoah J, Hsu YJ, Gadala A, Desai S, Goyal A, Furfaro D, Zimmerman J, Lin S, Cosgrove SE. ***A Diagnostic Stewardship Intervention To Improve Blood Culture Use among Adult Nonneutropenic Inpatients: the DISTRIBUTE Study***. J Clin Microbiol. 2020 Sep 22;58(10):e01053-20.
- Clancy, Cornelius J, Nguyen, M Hong, ***Diagnosing Invasive Candidiasis***, J Clin Microbiol, 2018 Apr 25;56(5):e01909-17. doi: 10.1128/JCM.01909-17. PMID: 29444828

References

- Atkinson, James, Connor, Daniel; Robinowitz, Max; McAllister, Hugh; Virmani, Renu; ***Cardiac Fungal Infections: Review of Autopsy Findings in 60 Patients***, Human Pathology 1984
- Dean, David; Burchard, Kenneth; ***Fungal Infection in Surgical Patients***, American Journal of Surgery, 1996
- Lee, Andrew; Mirrett, Stanley; Reller, L. Barth; Weinstein, Melvin. ***Detection of Bloodstream Infections in Adults: How Many Blood Cultures Are Needed?***, Journal of Clinical Microbiology, 2007
- Joan Barenfanger, MD, Donald R. Graham, MD, Lavanya Kolluri, MD, Gaurav Sangwan, MD, Jerry Lawhorn, Cheryl A. Drake, Steven J. Verhulst, PhD, Ryan Peterson, Lauren B. Moja, PharmD, Matthew M. Ertmoed, PharmD, Ashley B. Moja, Douglas W. Shevlin, MD, Robert Vautrain, MD, Charles D. Callahan, PhD, ***Decreased Mortality Associated With Prompt Gram Staining of Blood Cultures***, American Journal of Clinical Pathology, Volume 130, Issue 6, December 2008, Pages 870–876
- Tristan T. Timbrook, Jacob B. Morton, Kevin W. McConeghy, Aisling R. Caffrey, Eleftherios Mylonakis, Kerry L. LaPlante, ***The Effect of Molecular Rapid Diagnostic Testing on Clinical Outcomes in Bloodstream Infections: A Systematic Review and Meta-analysis***, Clinical Infectious Diseases, Volume 64, Issue 1, 1 January 2017, Pages 15–23
- Gary V. Doern, Karen C. Carroll, Daniel J. Diekema, Kevin W. Garey, Mark E. Rupp, Melvin P. Weinstein, Daniel J. Sexton, ***Practical Guidance for Clinical Microbiology Laboratories: A Comprehensive Update on the Problem of Blood Culture Contamination and a Discussion of Methods for Addressing the Problem*** Clinical Microbiology Reviews, October 2019
- Melvin P. Weinstein, Michael L. Towns, Seth M. Quartey, Stanley Mirrett, Larry G. Reimer, Giovanni Parmigiani, L. Barth Reller, ***The Clinical Significance of Positive Blood Cultures in the 1990s: A Prospective Comprehensive Evaluation of the Microbiology, Epidemiology, and Outcome of Bacteremia and Fungemia in Adults*** Clinical Infectious Diseases April 1997