# Blood Culture Metrics – Is it Really Quality Over Quantity?

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## Disclosures:

► I have no disclosures.

## Blood Culture Metrics – Learning Goals

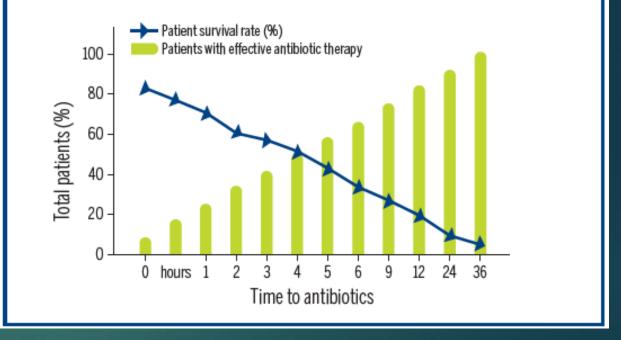
- Understand the general statistical components of clinical laboratory testing and how they can be used to understand blood cultures.
- Identify useful blood culture metrics and how they are calculated.
- Understand how different metrics can give insights into quality issues related to the blood culture process.
- Identify ways to improve blood culture quality and stewardship.

# Sepsis

- Early diagnosis and appropriate treatment make a critical difference when it comes to improving sepsis patient outcomes.
- Chances of survival go down drastically the longer initiation of treatment is delayed.
- Detection and treatment: If a patient receives antimicrobial therapy within the first hour of diagnosis, chances of survival are close to 80%.
  - This is reduced by 7.6% for every hour after.
- Blood cultures are the gold standard test to diagnose bloodstream infections.

### Figure 1: Fast effective antimicrobial therapy increases survival chances

Adapted from Kumar A, et al. Crit Care Med. 2006;34(6):1589-96.15



## Contamination

- ▶ Old (current) "standard" = less than 3% (CLSI, CAP, CDC).
- Movement toward new standard = less than 1%
- Causes:
  - Insufficient antisepsis of draw site.
    - ▶ 30 seconds, 70% alcohol. Allow to dry.
    - Second disinfectant contact with skin for duration recommended by manufacturer. Allow to dry.
    - Do not palpate vein after cleansing draw site.
    - Chlorhexidine should be use with caution in patients <2 months of age. Multiple applications of 70% alcohol are an acceptable alternative.</p>
  - Improper draw type (line, IV start) rather than venipuncture. IV start draws = 3% increase in contamination.
  - Lack of diversion = contaminated skin plug entering bottle.
  - Contaminated supplies via bacteria on surfaces, skin, aerosols (coughing, sneezing, talking).
  - Phlebotomy specialization, training, education insufficient to maintain quality.
- See KHA's resources on contamination reduction.
- CLSI M47-Ed2 (April 2022): Principles and procedures for Blood Cultures.
- Contaminated blood cultures = <u>false positive</u>.

## Lab Test Metrics: 2 x 2 grid

Contamination (false positivity): <sup>1</sup>/<sub>4</sub> of the total picture

	Septic	Healthy
Culture	True	False
Positive	Positive	Positive
Culture	False	True
Negative	Negative	Negative

# Lab Test Metrics: 2 x 2 grid

### Lab test quality:

- Sensitivity: The ability of the blood culture to correctly detect sepsis.
- Specificity: The ability of the blood culture to correctly rule out sepsis.
- Predictive Values: The ability of the blood culture to provide useful information related to detecting or ruling out sepsis.
  - PPV: percentage of positive cultures that actually represent sepsis.
- What can we know? What can be observed?

	Septic	Healthy	
Culture	True	Docitivo	PPV =
Positive	Positive		TP / (TP + FP)
Culture	False	Nogativo	NPV =
Negative	Negative		TN / (FN + TN)
	Sensitivity = TP / (TP + FN)	Specificity = TN / (FP + TN)	

# Lab Test Metrics: 2 x 2 grid expansion

### Lab test quality:

- ► Knowns (Blue)
  - ► True positivity
  - ► False positivity
  - ► Total positivity
    - ► Total Sets drawn
    - ► Total negativity

### Unknowns (Gray)

- Sensitivity
- Specificity
- True/False Negativity
- ► NPV

	Septic	Healthy		
Culture Positive	True Positive	False Positive	Total Positive	PPV
Culture Negative	False Negative	True Negative	Total Negative	NPV
	Total Septic	Total Healthy	Total Sets Drawn	
	Sensitivity	Specificity		

# Blood Culture Metrics: Data, Goals

### <u>Quality targets:</u>

- Knowns (Blue)
  - ► True positivity = 100%
  - False positivity = 0% (<1%)
  - Total positivity = relative increase
  - Total negativity = relative decrease
  - Total Sets drawn = appropriate
  - ▶ <u>PPV = 100%</u>
- Unknowns (Gray) = Process improvement.
- Presumptive:
  - Sensitivity = increase
  - Specificity = increase
  - True Negativity = decrease
  - ► False Negativity = decrease
  - ► NPV = increase

	Septic	Healthy		
Culture Positive	True Positive = 100%	False Positive = 0%	Total Positive = Increase	<u>PPV = 100%</u>
Culture Negative	False Negative = 0%	True Negative = 0%	Total Negative = Decrease	NPV = 100%
	Total Septic	Total Healthy	Total Sets Drawn	
	Sensitivity = 100%	Specificity = 100%		

# Blood Culture Metrics: True Positivity

### Quality targets:

### Positivity:

- True = pathogen isolated
  - ▶ Bacteremia identified.
  - ► Targeted treatment available.
  - ▶ Cost waste avoided.
  - Appropriate length of stay.
  - ▶ Rapid ID = good outcome.
    - ► High quality testing algorithm.
    - ▶ Pharmacy protocols that are organism specific.
    - ► Isolation guidelines reflex from results.

	Septic	Healthy		
Culture Positive	True Positive = 100%	False Positive = 0%	Total Positive = Increase	<u>PPV =</u> <u>100%</u>
Culture Negative	False Negative = 0%	True Negative = 0%	Total Negative = Decrease	NPV = 100%
	Total Septic	Total Healthy	Total Sets Drawn	
	Sensitivity = 100%	Specificity = 100%		

# Blood Culture Metrics: False Positivity

### Quality targets:

### Positivity:

- ► False = contaminant isolated.
  - ► Bacteremia ruled out? Cloudy clinical picture.
  - ► Cost waste:
    - ► Increased length of stay: 1 day.
    - ► Antibiotic charges: 39% increase.
    - ▶ Additional charges: \$5,000-\$8,720.
    - ► Laboratory charges: 20% increase.
    - ► Antibiotic usage: 3 days longer.

	Septic	Healthy		
Culture Positive	True Positive = 100%	False Positive = 0%	Total Positive = Increase	<u>PPV =</u> <u>100%</u>
Culture Negative	False Negative = 0%	True Negative = 0%	Total Negative = Decrease	NPV = 100%
	Total Septic	Total Healthy	Total Sets Drawn	
	Sensitivity = 100%	Specificity = 100%		

# Blood Culture Metrics: Total Positivity

### <u>Quality targets:</u>

### Positivity:

- ► Known:
  - ► true / false positivity.
  - ▶ Total positivity.
  - PPV = true positivity / total positivity.
- PPV = measuring usefulness of blood cultures.
  - Percent chance that positive culture represents a pathogen.
  - 100% PPV = All cultures collected provided useful data (positive for pathogens). Requires 0% contamination.
  - Realistically, contamination >0%, achieve as high PPV as possible.
    - ► Factors in both true positivity and total positivity.

	Septic	Healthy		
Culture Positive	True Positive = 100%	False Positive = 0%	Total Positive = Increase	<u>PPV =</u> <u>100%</u>
Culture Negative	False Negative = 0%	True Negative = 0%	Total Negative = Decrease	NPV = 100%
	Total Septic	Total Healthy	Total Sets Drawn	
۱.	Sensitivity = 100%	Specificity = 100%		

# Blood Culture Metrics: Total Positivity

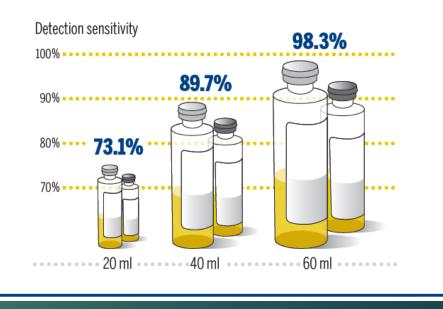
### <u>Quality targets:</u>

### Positivity:

- Total = all positive blood cultures (pathogens and contaminants).
- An evaluation of >6 million cases of severe sepsis found that culture-negative results correlate with an increased number of comorbidities, organ dysfunction, and a higher mortality rate. (Khare).
- % Positivity = Total positive sets / Total sets.
  - ▶ Ranges vary. Khare: 6.69% 9.34%.
  - ► ED vs Inpatient.
  - ▶ Goal = observe relative increase. Peer comparison, trending.
- ► High (true) positivity.
  - Targeted ordering.
  - ► Effective sepsis screening.
  - ▶ Effective laboratory test stewardship.
  - High quality testing:
    - ► Aseptic collection of 40mL of blood + diversion volume.
    - ► Effective microbiology testing protocols.

#### Figure 2: Cumulative sensitivity of blood culture sets<sup>22</sup>

Adapted from Lee A, Mirrett S, Reller LB, Weinstein MP. Detection of Bloodstream Infections in Adults: How Many Blood Cultures Are Needed? J Clin Microbiol 2007;45:3546-3548.



Some studies suggest that each additional milliliter of blood collected can result in a 2%–4% increase in the positivity rate.

# Blood Culture Metrics: Negativity

### Quality targets:

### ► Negativity:

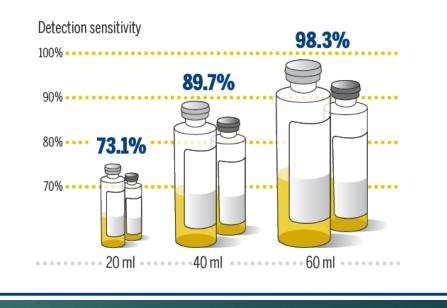
- ► True:
  - Multiple perfectly collected sets.
  - $\blacktriangleright$  60mL + 9mL diverted = 69mL of blood.
  - ► Tested correctly.

### ► False:

- Major hidden issue. False assumption of quality.
- ► Large number of sets with insufficient fill volume.
- ► Underfilling = reduced sensitivity.
  - ► No growth if insufficient CFU incubated.
- ► False negative = unidentified sepsis.
- ► Last line of defense for patient treatment.

#### Figure 2: Cumulative sensitivity of blood culture sets<sup>22</sup>

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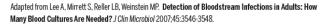
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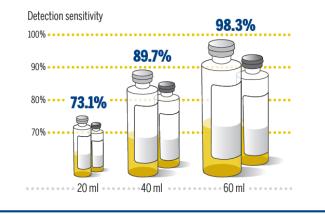
## Blood Culture Metrics: False Negativity

### <u>Quality targets:</u>

- Negativity
  - ▶ False: How big of a problem?
    - ► Khare et al.:
      - To our knowledge, this is the largest multisite study that utilizes long-term continuous monitoring and tracking of BBFV, describes blood collection improvement strategies, and shows sustained improvement in BBFV.
      - Blood culture bottles are routinely underfilled, with as many as <u>40%–85%</u> of blood cultures containing inadequate volume.
      - Using data collected from the automated software, the average BBFV in January 2015 prior to any initiatives (preimplementation) for the 10 hospitals was 2.3 mL (range, 1.6–3.3 mL)
  - Inadequate volume a bottle containing less than 80% of the recommended minimum volume (CLSI M47).
  - Up to 2-4% decrease in positivity per mL omitted?
    - ▶ <1 CFU/mL.
    - > 2 sets 2mL per bottle = 8/40 mL, 1-2% reduction per mL = 32-64%
    - ▶ 90% sensitive (assumed) 64% = 26% sensitivity?
    - ► Low sensitivity, low NPV = unreliable. Cannot assume negative = true negative.
  - Increased positivity = Increase sepsis detection

#### Figure 2: Cumulative sensitivity of blood culture sets<sup>22</sup>

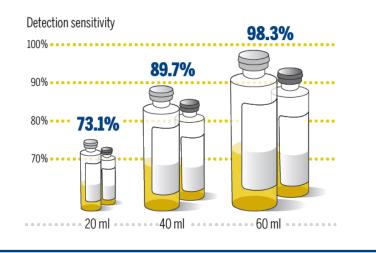




# Blood Culture Metrics: False Negativity

#### Figure 2: Cumulative sensitivity of blood culture sets<sup>22</sup>

Adapted from Lee A, Mirrett S, Reller LB, Weinstein MP. Detection of Bloodstream Infections in Adults: How Many Blood Cultures Are Needed? J Clin Microbiol 2007;45:3546-3548.



### Quality targets:

### Negativity

- Why not reject underfilled bottles, similar to hemolysis?
  - CLSI: Because blood drawn for culture may be irreplaceable, flexibility is warranted. Specimens should be processed even if they are suboptimal.
  - Any chance of detecting sepsis is better than no chance.
  - Reject: incorrectly labeled, broken, damaged, improper collection (clotted, containing anticoagulants).

## Blood Culture Metrics: Goals



### <u>Quality targets:</u>

- Decreasing false negativity:
  - Blood cultures collected before administering antibiotics.
  - Incubation length: (5-7 days).
  - ► <u>Appropriate bottle fill:</u>
    - ▶ 10mL per bottle (8mL minimum) x 2 bottles = 20mL cultured.
    - Plus diversion volume (tube, device) approx. 3mL.
    - ▶ Fill lines on certain bottles.
    - Mark target fill location if no lines available.
      - Reference standard or volume markings.
      - Know bottle target volume (adult and pediatric).
    - Monitor.
    - Provide feedback.
    - ▶ Understand obstacles.

## Blood Culture Metrics: Quality Obstacles

### <u>Improving Blood Bottle Fill Volume (BBFV):</u>

- Understand obstacles. Khare:
  - ▶ (1) Lack of knowledge regarding the sensitivity of blood cultures and its relationship to BBFV.
    - Standard policy, 4 step poster, seminars, training, interviews, surveys, specialized education.
    - Phlebotomy training on the importance of sensitivity.
    - Poor sensitivity = Poor patient outcomes.
  - ► (2) Difficulty for blood drawers to gauge adequate fill volume.
    - Markings or stickers.
    - ► Using butterfly collection.
    - ▶ Visualizing on a flat surface.
  - ▶ (3) Lack of standardized data collection and feedback of metrics.
    - ▶ Data feedback via collector report cards for observable metrics.
  - (4) The low priority placed on BBFV (compared with other hospital sepsis initiatives like the 3- or 6-hour bundle compliance levels).
    - ► Leadership engagement: BBFV as a system quality metric.
    - ► Report card including more metrics than % contamination.

## Blood Culture Metrics: Quality Obstacles

### Improving Blood Bottle Fill Volume (BBFV):

- (3) Lack of standardized data collection and feedback of metrics.
  - Data feedback via collector report cards for observable metrics.
  - ▶ 3 major data points for each collector:
    - ▶ % Contamination.
    - ▶ % Low volume.
    - ▶ % Diversion.
  - Collectors scored based on data points.

BLOOD CULTURE VOLUME CAP			
	Answer	Comment	
Blood Culture Volume Acceptable?	Yes No Peo	liatric	
	No	Denter a comment	
BLOOD CULTURE DISCARD RECEIVED			
	Answer	Comment	
Discard tube received?	Yes No		
	No	O Enter a comment	
		· · · · · · · · · · · · · · · · · · ·	

## Blood Culture Metrics: Quality Obstacles

### Improving Blood Bottle Fill Volume (BBFV):

- (3) Lack of standardized data collection and feedback of metrics.
  - Data acquisition:
    - ▶ % Contamination
      - ▶ Health information system report.
      - Manual calculation.
    - ▶ % Low volume.
      - ▶ Health information system prompt.
        - Comparison to reference standard.
      - Manual monitoring weight or fill volume.
      - ► Automated systems incubators.
    - ▶ % Diversion.
      - ► Health information system prompt.

#### BLOOD CULTURE VOLUME CAP

	Answer	Comment	
Blood Culture Volume Acceptable?	Yes No Pediatric		
	No 🔎	Enter a comment	
BLOOD CULTURE DISCARD RECEIVED			
	Answer	Comment	
Discard tube received?	Yes No		
	No 🔎	Enter a comment	

# Blood Culture Metrics: Goals

### <u>Improving Blood Bottle Fill Volume</u> (BBFV):

- (3) Lack of standardized data collection and feedback of metrics.
  - Example report card:
  - Collectors are educated on meaning and usefulness of metrics.
  - Unblinded data.
  - Possibly Increase standards over time.

Collector (Lab)	Score -	🛛 Draws 斗	% Contamination 💌	% Low Volume 💌	% Diversion 🔽	Contaminants 💌
Collector 1	3	40	0.00%	25.00%	100.00%	0
Collector 2	3	30	0.00%	0.00%	100.00%	0
Collector 3	3	20	0.00%	0.00%	100.00%	0
Collector 4	3	10	0.00%	0.00%	100.00%	0
Collector 5	3	5	0.00%	0.00%	95.00%	0
Collector 6	3	1	0.00%	0.00%	92.00%	0
Collector 7	2	35			94.29%	1
Collector 8	2	30	3.33%	39.00%	100.00%	
Collector 9	2	30	6.67%			2
Collector 10	2	25	8.00%	16.00%	100.00%	2
Collector 11	2	25	4.00%	24.00%	96.00%	1
Collector 12	2	20	10.00%	25.00%	95.00%	2
Collector 13	2	15	6.67%	13.33%	100.00%	1
Collector 14	2	15	6.67%	13.33%	93.33%	1
Collector 15	2	5	0.00%	60.00%	100.00%	0
Collector 16	2	2	0.00%	70.00%	100.00%	0
Collector 17	1	2	0.00%	100.00%	100.00%	0
Collector 18	1	1	100.00%	100.00%	100.00%	1
Collector 19	1	1	0.00%	100.00%	100.00%	0
Collector 20	1	1	0.00%	100.00%	100.00%	0
Collector 21	0	30	6.67%	55.00%	73.33%	2
Collector 22	0	3	33.33%	66.00%	66.00%	1
Grand Total		328	4.88%			16
Remediation Nee	ded		>3%	>40%	<90%	
Pomodiation if:						

Remediation if:

Collector has score 0 or 1 AND substantial # of draws

OR

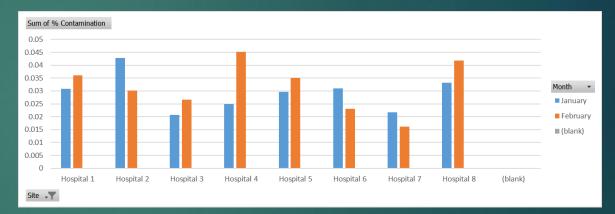
Contamination >3% with >1 contaminants

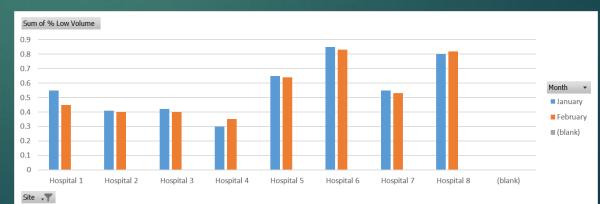
# Blood Culture Metrics: Goals

### <u>Improving Blood Bottle Fill Volume</u> (BBFV):

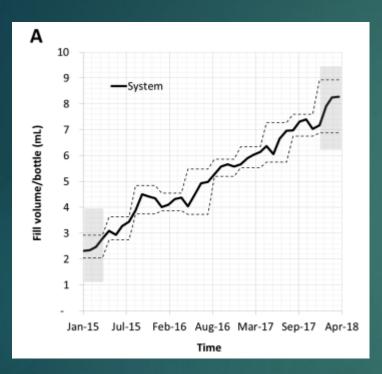
- (4) The low priority placed on BBFV (compared with other hospital sepsis initiatives like the 3- or 6-hour bundle compliance levels).
  - ▶ BBFV as a system quality metric.
    - Positivity is directly correlated with fill volume.
  - Laboratory engagement with sepsis quality groups.
  - Report card including more metrics than % contamination.
  - Peer comparison and trending.

Site	🖵 Total Sets 🔽	% Contamination 🔽	PPV 🔽	% Pos 🔽
Story-Roller	6095	3.90%	64.32%	10.94%
Khare et al. (last 4 months	51620	1.65%	83.14%	9.81%
Rupp et al.	904	1.80%	74.97%	7.19%
Khare et al. (first 4 month	<u>s)</u> 51620	1.34%	80.65%	6.95%
<u>Washer et al.</u>	12904	0.76%	86.67%	5.70%





## Blood Culture Metrics: Positivity



Khare: Figure 2A

### <u>Quality targets:</u>

- Positivity improvement: Convert false negatives to positives!
  - ► Khare:
    - The positivity rate was positively correlated with volume, with each milliliter of additional blood collected correlating with a 0.32% increase in the system-wide blood culture positivity rate. (Less than 2-4%, but still significant).
    - ▶ 20% overall avg. increase in positivity (7.39% 8.85%).
    - The positivity rate for the 10 hospitals improved by as much as 40%, beginning with 6.69% and climbing to 9.34%.
    - Average fill increased: 2.3mL to 8.6mL (3.7-fold)
    - ▶ 7 out of 10 hospitals: 8mL minimum.
      - Inadequate volume a bottle containing less than 80% of the recommended minimum volume (CLSI M47).
    - ▶ 63.2% underfilled (pre) 14.8% underfilled (post)
  - Increased positivity (20%) = Increase sepsis detection
    - Jan-Apr: 2892 pathogens (pre) > 4212 pathogens (post)
    - ▶ 1320 potential false negatives avoided.

## Blood Culture Metrics: Goals

### Stewardship: Monitor, Report, Improve.

- ► False negativity % Bottle underfill rate. Improve through reducing underfilled bottles.
- ▶ True negativity No calculation. Improve collection process and bottle fill volume.
- False positivity % Contamination. Improve through reduction.
- ▶ True positivity Refer to % PPV. Improve through stewardship and reducing contamination.
- Overall positivity / negativity % Positive. Improve through reducing negative cultures, increasing positive cultures.
  - Only culture patients with a high likelihood of sepsis.
  - Culturing healthy patients only increases contamination and decreases positivity.
  - Positivity is directly related to bottle fill volume.

### Contamination is high priority, but there is more to the quality picture.

## Blood Culture Metrics: Example

Site	🚽 Sets Drawn 🖵	Contaminants 星	% Contamination 🖵
Hospital	1 10,000	90	0.90%
Hospital	2 10,000	95	0.95%
Hospital	3 10,000	100	1.00%
Hospital	4 10,000	290	2.90%

### Stewardship goals:

- Reduce cost, patient stay, antibiotic usage, etc. by reducing contamination to <1%.</p>
- ► False positivity issue solved.
- Hospital 1 = best quality? Least waste.
- Factor in overall positivity, fill volume, true positivity, PPV:

## Blood Culture Metrics: Example

Site 💽	Sets Drawn 🖵	Contaminants 🗖 %	Contamination 🗖	Positives 🖵	% Pos 🖵	True Pos 🖵 🤊	6 True Pos 🖵	% PPV 🔽
Hospital 1	10,000	90	0.90%	300	3.00%	210	2.10%	70.00%
Hospital 2	2 10,000	95	0.95%	750	7.50%	655	6.55%	87.33%
Hospital 3	<b>10,000</b>	100	1.00%	900	9.00%	800	8.00%	88.89%
Hospital 4	10,000	290	2.90%	1000	10.00%	710	7.10%	71.00%

Stewardship goal: Increase quality.

- What is quality? Reducing false positives?
  - ► Hospital 4: Highest % false positivity.
    - ▶ 710 vs 210 true positive sets = 500 more cases of sepsis identified, treated.
    - High positivity due to: targeted testing (patients with high probability of sepsis), adequate fill volume, collections before antibiotic administration, 5-7 day incubation.
    - Good test quality, poor value.
    - ▶ Increase quality by reducing contamination (waste costs), while maintaining positivity.
- Contamination is high priority, but there is more to the quality picture.

## Blood Culture Metrics: Example

Site 💽	Sets Drawn 🖵	Contaminants 🗖 %	Contamination	Positives 🖵	% Pos 🖵	True Pos 🖵 %	🛛 True Pos 🖵	% PPV 🔽
Hospital 1	. 10,000	90	0.90%	300	3.00%	210	2.10%	70.00%
Hospital 2	10,000	95	0.95%	750	7.50%	655	6.55%	87.33%
Hospital 3	10,000	100	1.00%	900	9.00%	800	8.00%	88.89%
Hospital 4	10,000	290	2.90%	1000	10.00%	710	7.10%	71.00%

Stewardship goal: Increase quality.

- What is quality? Reducing false positives?
  - ► Hospital 1: Lowest % false positivity.
    - ▶ Least waste, highest quality? Least sepsis identified (70% of positives are useful).
    - Low positivity due to: Poor patient screening, underfilling bottles, drawing after antibiotic administration, 3day incubation.
    - Costs controlled, poor test utility. Increase quality by investigating false negativity. Where is the sepsis?
- Contamination is high priority, but there is more to the quality picture.
- Increase quality = reduce false positives AND false negatives.
- What is a true positive sepsis result worth? What is the utility to cost ratio?

## References:

Blood Culture: A Key Investigation for Diagnosis of Bloodstream Infections. BioMérieux, Inc. 100 Rodolphe Street. Durham, NC 27712.

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- Reeti Khare, Tarush Kothari, Joseph Castagnaro, Bryan Hemmings, May Tso, Stefan Juretschko, Active Monitoring and Feedback to Improve Blood Culture Fill Volumes and Positivity Across a Large Integrated Health System, Clinical Infectious Diseases, Volume 70, Issue 2, 15 January 2020, Pages 262–268, https://doi.org/10.1093/cid/ciz198

## Resources:

- ► Levi Petrey MBA, MLS(ASCP)<sup>CM:</sup>
  - Levi.Petrey@bhsi.com
  - Work: 606-523-8795
  - Personal: 606-524-5384
- Deborah Campbell RN-BC, MSN, CPHQ at KHA.
- Khare et al: Active Monitoring and Feedback to Improve Blood Culture Fill Volumes and Positivity Across a Large Integrated Health System,
  - Clinical Infectious Diseases, Volume 70, Issue 2, 15 January 2020, Pages 262–268.
- CLSI M47-Ed2 (April 2022): Principles and procedures for Blood Cultures.
- Blood culture bottle IFU, other manufacturer resources.
- Questions?