Blood Culture Metrics – Is it Really Quality Over Quantity?

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Disclosures:

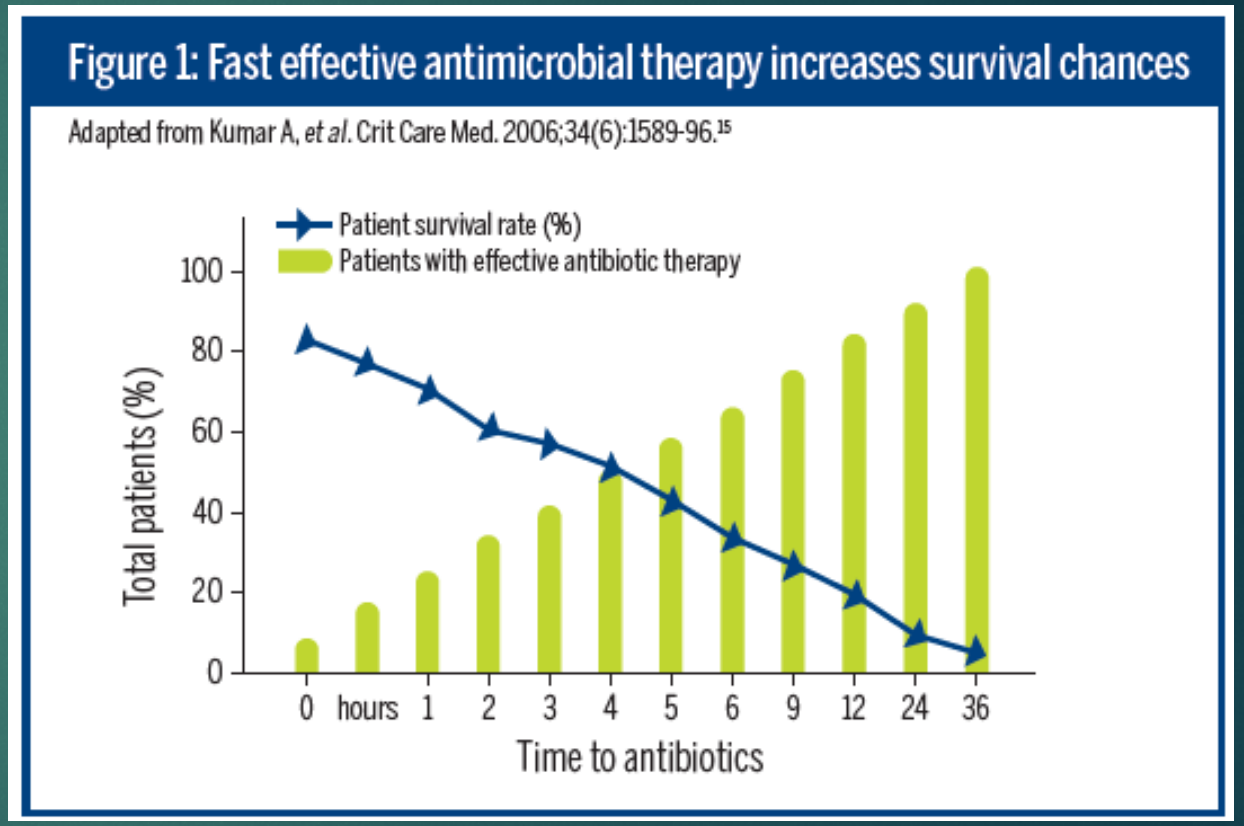
- I have no disclosures.

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.



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.
  - 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):
¼ of the total picture

	Septic	Healthy
Culture Positive	True Positive	False Positive
Culture Negative	False Negative	True 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 Positive	True Positive	False Positive	PPV = TP / (TP + FP)
Culture Negative	False Negative	True Negative	NPV = 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

Quality targets:

- Knowns (Blue)
  - True positivity = 100%
  - False positivity = 0% (<1%)
  - Total positivity = relative increase
  - Total negativity = relative decrease
  - Total Sets drawn = appropriate
  - PPV = 100%
- 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	PPV = 100%
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	PPV = 100%
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	PPV = 100%
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

Quality targets:

- 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	PPV = 100%
Culture Negative	False Negative = 0%	True Negative = 0%	Total Negative = Decrease	NPV = 100%
	Total Septic	Total Healthy	Total Sets Drawn	
	Sensitivity = 100%	Specificity = 100%		

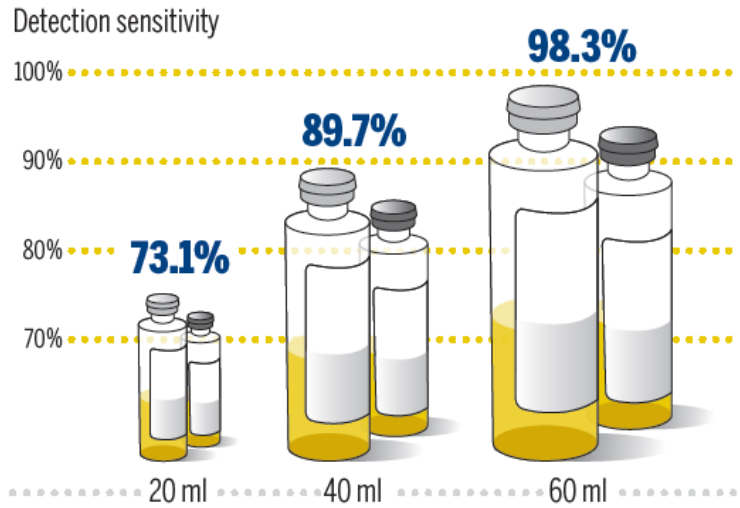
Blood Culture Metrics: Total Positivity

Quality targets:

- 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[22]

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.
    - 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[22]

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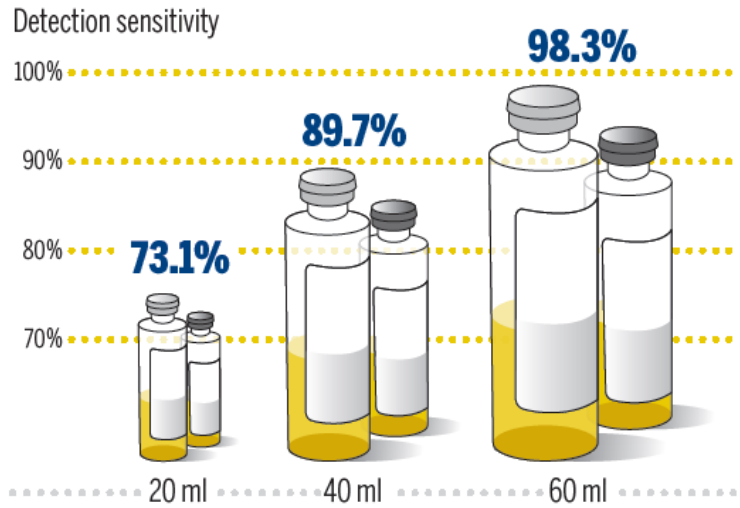

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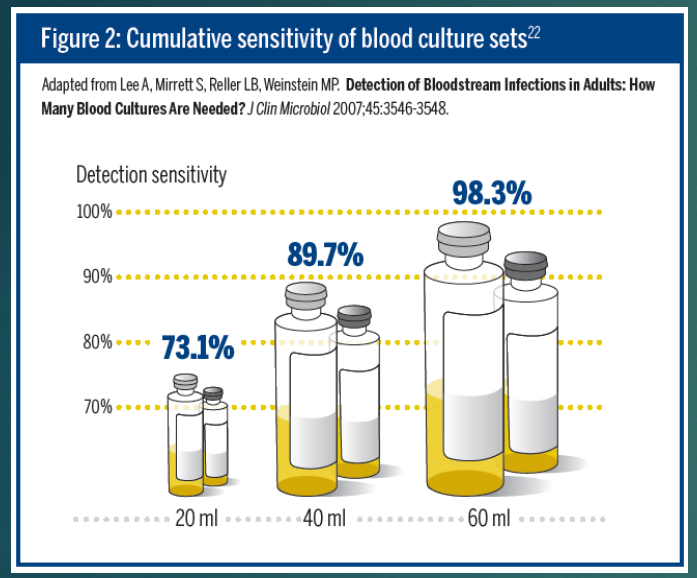
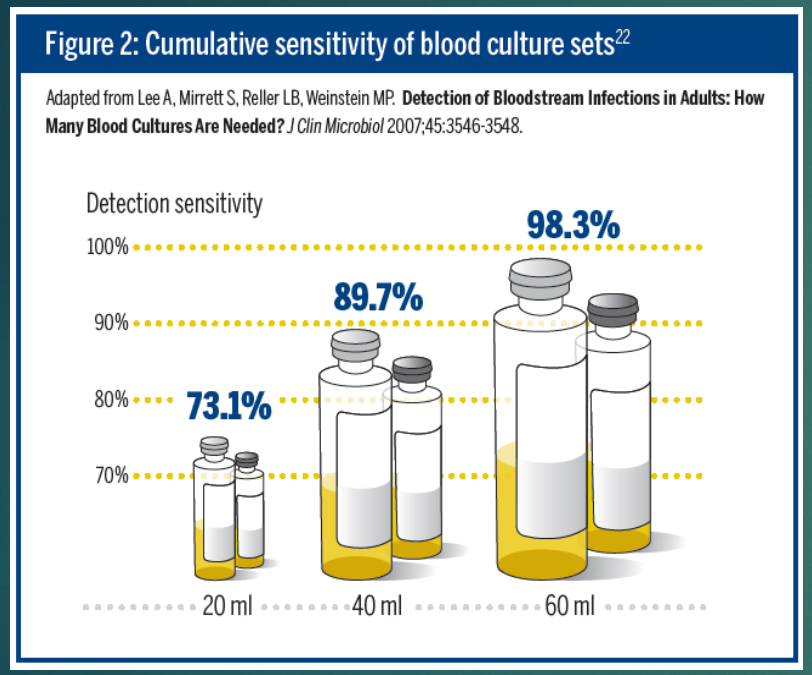
Blood Culture Metrics: False Negativity



Quality targets:

- 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 40%–85% 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

Blood Culture Metrics: False Negativity



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

Quality targets:

- Decreasing false negativity:
  - Blood cultures collected before administering antibiotics.
  - Incubation length: (5-7 days).
  - Appropriate bottle fill:
    - 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

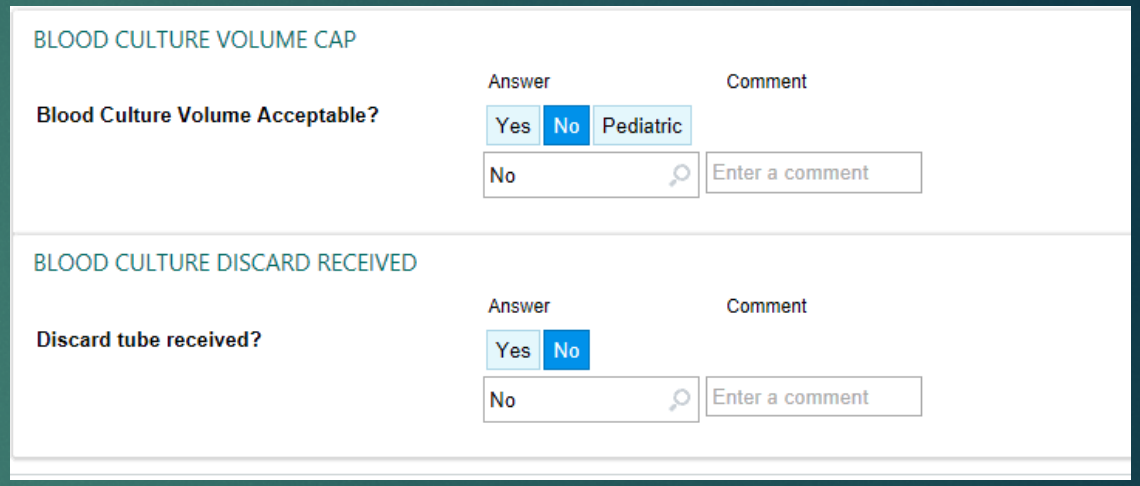
Improving Blood Bottle Fill Volume (BBFV):

- 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):

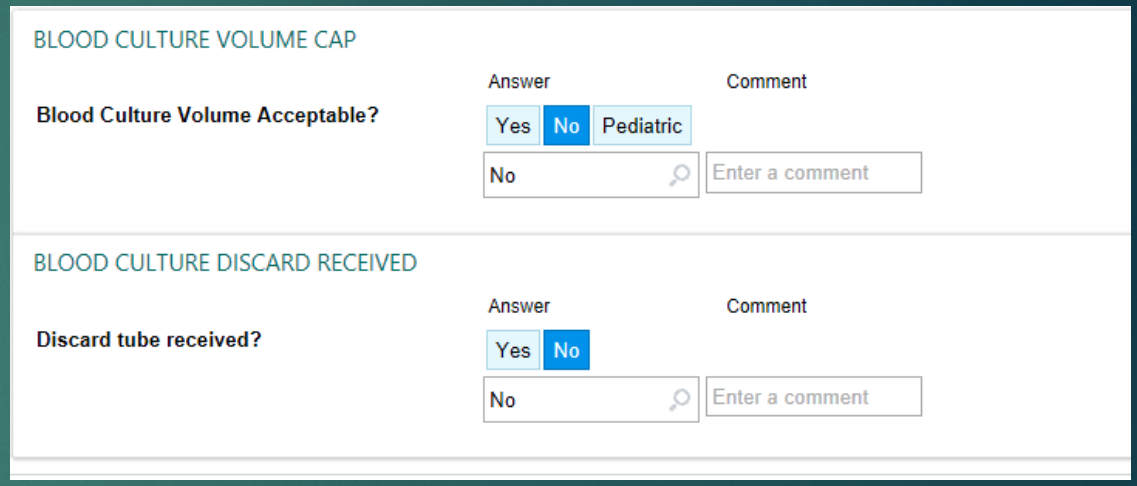
- (3) Lack of standardized data collection and feedback of metrics.
  - Data feedback via collector report cards for observable metrics.
  - 3 major data points for each collector:
    - % Contamination.
    - % Low volume.
    - % Diversion.
  - Collectors scored based on data points.



Blood Culture 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 Metrics: Goals

Improving Blood Bottle Fill Volume (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.

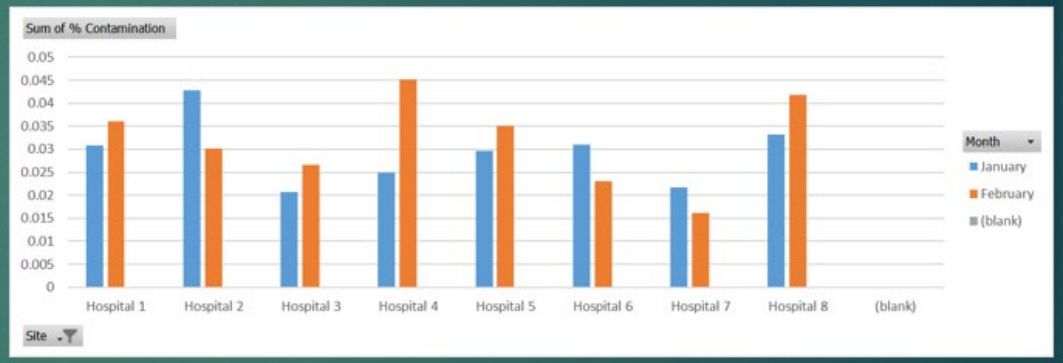
Collector (Lab)	Score	Draws	% Contamination	% Low Volume	% Diversion	Contaminants
Collector 1	3	40	0.00%	25.00%	100.00%	0
Collector 2	3	30	0.00%	0.00%	100.00%	0
Collector 3	3	20	0.00%	0.00%	100.00%	0
Collector 4	3	10	0.00%	0.00%	100.00%	0
Collector 5	3	5	0.00%	0.00%	95.00%	0
Collector 6	3	1	0.00%	0.00%	92.00%	0
Collector 7	2	35	2.86%	41.00%	94.29%	1
Collector 8	2	30	3.33%	39.00%	100.00%	1
Collector 9	2	30	6.67%	35.00%	93.33%	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 Needed			>3%	>40%	<90%	
Remediation if:						
Collector has score 0 or 1 AND substantial # of draws						
OR						
Contamination >3% with >1 contaminants						

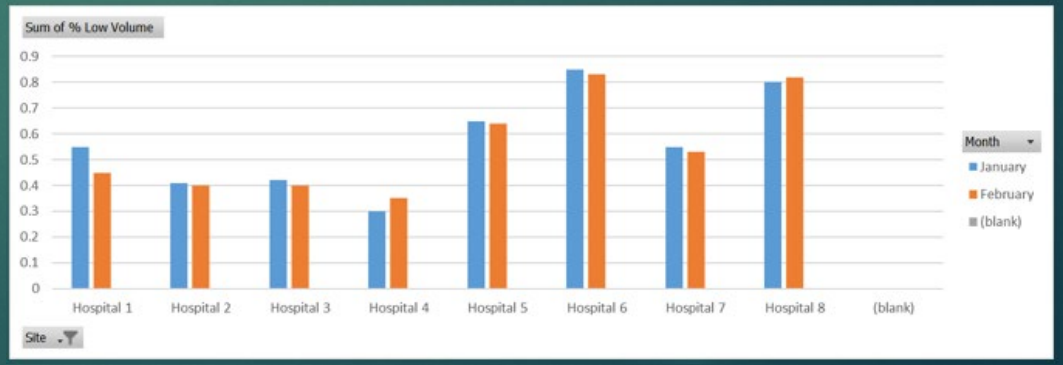
Blood Culture Metrics: Goals

Improving Blood Bottle Fill Volume (BBFV):

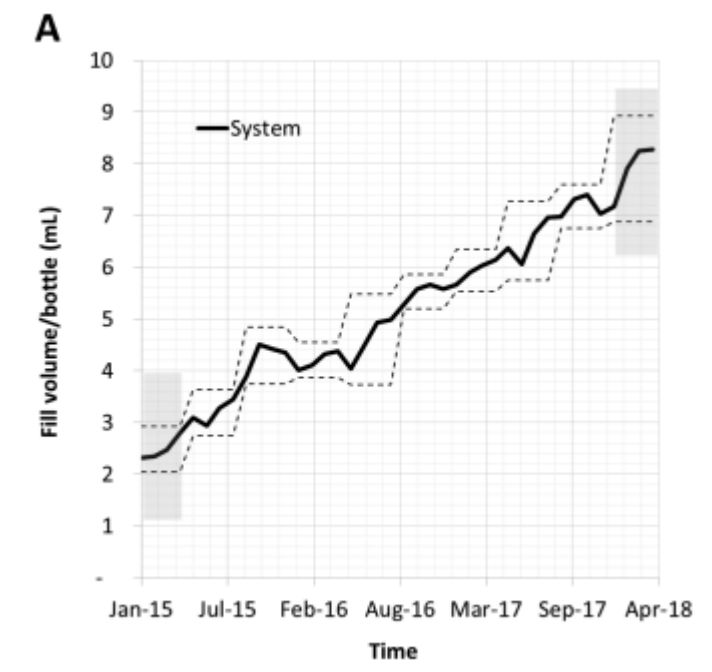
- (4) The low priority placed on BBFV (compared with other hospital sepsis initiatives like the 3- or 6-hour bundle compliance levels).
  - BBFV as a system quality metric.
    - Positivity is directly correlated with fill volume.
  - Laboratory engagement with sepsis quality groups.
  - Report card 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 months)	51620	1.34%	80.65%	6.95%
Washer et al.	12904	0.76%	86.67%	5.70%





Blood Culture Metrics: Positivity



Khare: Figure 2A

Quality targets:

- 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	% 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%.
- 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	% 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 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%
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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, 3-day 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:

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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)$^{CM:}$
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  - 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?