AMERICAN SOCIETY FOR MICROBIOLOGY

BLOOD CULTURE BOTTLE INVENTORY MANAGEMENT AND CLINICAL CONSERVATION DURING SUPPLY SHORTAGES

Endorsed by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of American (IDSA)

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I. Introduction

Critical shortages of blood culture (BC) vials or "bottles" used for BC collection are an infrequent but serious event that can occur due to a variety of supply chain and quality control hurdles. Some shortages may affect a single medium type, while others may broadly impact entire lines of supplies (i.e. aerobic, anaerobic, pediatric, mycobacterial, and fungal bottles) for a given instrument or manufacturer. Acquiring new instrumentation and pivoting to a different supply line from a different manufacturer can take months due to contracting and availability of alternative options. Therefore, managing supplies during such shortages mainly relies on

thoughtful use, stewardship of available reagents, and, during severe shortages may require reducing use below that of standard of care best practices.

Each system's response to BC bottle shortages must be individualized based on the type of shortage, severity of the shortage, baseline clinical practices and utilization, and optimal clinical indications for use for the patients they serve **(Figure 1)**. During mild shortages, institutions may be able to maintain full standard of care testing through conventional management. Conventional management can include no changes to baseline practices or a heightened emphasis on best practices, including diligent supply management to ensure no wastage and implementing diagnostic stewardship programs throughout the system to optimize BC test use. As the severity of a shortage increases or as a system's inventory decreases, more drastic management strategies may be required to ensure patient care while conserving supplies. The interventions employed during mild shortages (conventional to contingency management) should be continued during more severe shortages (contingency to crisis management) in an additive manner. During contingency and crisis management, additional strategies to conserve supplies and reduce testing are typically not supported by standard of care or best practice guidelines. In its most extreme form, crisis management may even include strategies to care for patients in the complete absence of performing BCs.

In this document, we provide practical recommendations for 1) how to approach institution- or system-level coordination to manage BC bottle inventory and patient testing during shortages, 2) optimizing test quality to reduce the need for specimen recollection, and 3) we summarize published guidelines and diagnostic stewardship studies that exemplify common opportunities for stewardship of BCs that can improve patient care during routine practice and may especially be considered for implementation during shortages to help conserve supplies for the most clinically necessary indications. Additionally, 4) we review the test performance data behind some best practice standards that healthcare systems may consider modifying or foregoing to reduce testing during contingency or crisis management. We aim to provide a comprehensive review of best

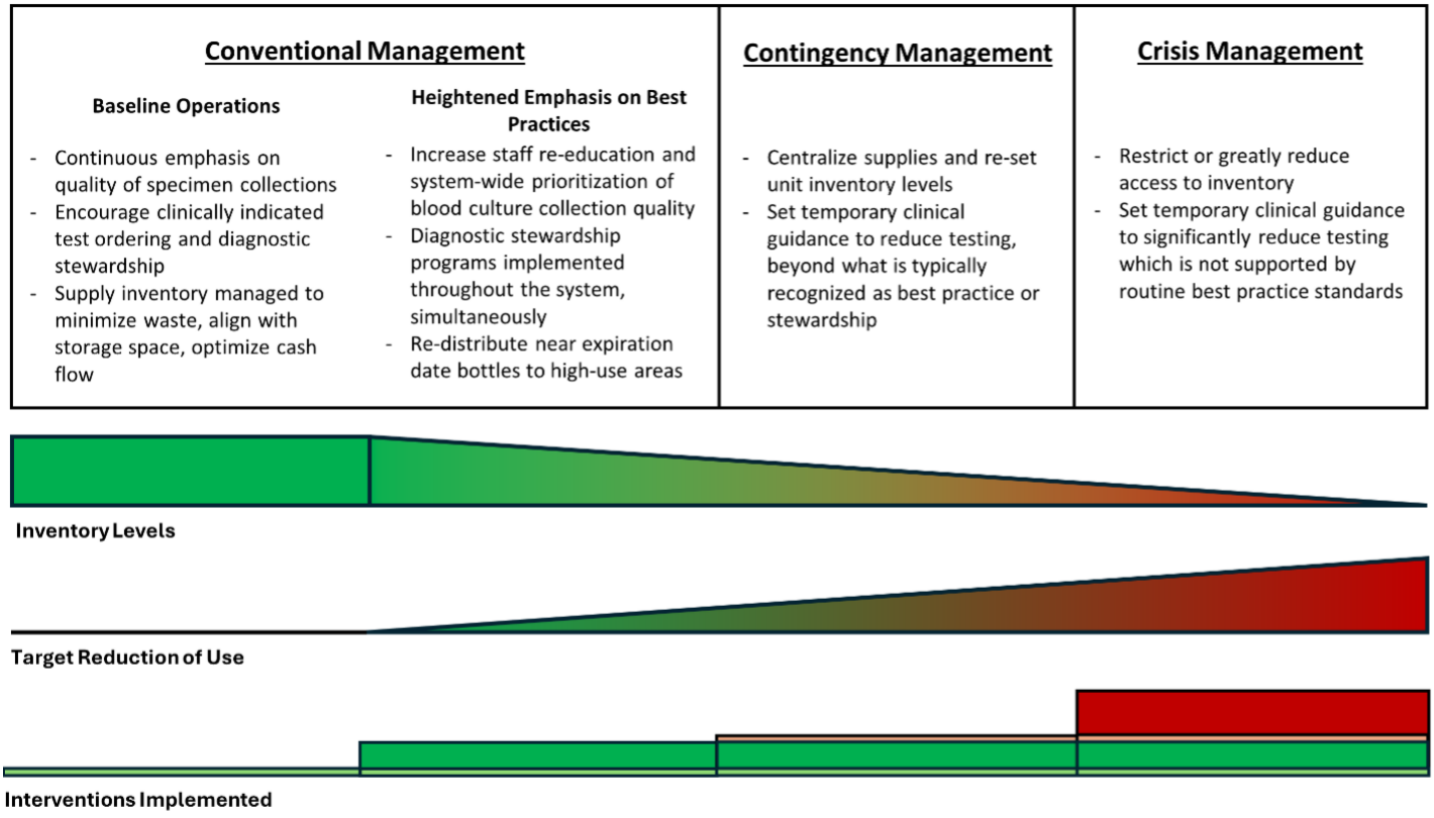

Figure 1. Tiered response categories that may be implemented based on the severity of BC bottle shortages. During BC bottle shortages, healthcare systems should first determine baseline inventory management and clinical utilization practices. Depending on the severity of the BC bottle shortage and target reduction of use required for an individual institution, different interventions may be required. We recommend that first interventions include emphasizing best practices to improve patient care and conserve supplies (conventional management of BC bottle inventory). During severe shortages, best practice interventions may not be sufficient. In those cases, in addition to best practice interventions, systems must identify additional conservation methods that reduce use beyond what is typically recognized as best practice (contingency management) or what is not supported by best practices standards (crisis management).

practices. However, when moving beyond best practices, we encourage users to consider the stage and severity of the shortage in their system **(Figure 1)** and work collaboratively with clinical leadership to weigh the benefits and risks of contingency and crisis management interventions.

II. Approaches to Coordinate Blood Culture Inventory Management and Clinical Conservation Efforts

Avoiding duplicating efforts or creating conflicting plans of action within an institution or healthcare system ("system") is critical. Microbiology laboratories must communicate with hospital leadership and clinical stakeholders to alert them to this critical issue, determine if there are already efforts underway throughout the system to address the shortages and to garner support for the tasks that will be necessary to manage inventory and clinical use during the shortage.

To understand the magnitude of the problem and manage inventory, systems should act promptly to prevent reaching critical inventory levels. Below is an overview of step-wise approaches for how laboratory leaders can help coordinate efforts and collaborate throughout the system to quickly organize a response to BC bottle shortages. These activities are also presented in **Figure 2.** Importantly, while inventory management and clinical guidance efforts are operationally distinct, both are essential to maintaining clinical testing during a shortage. Therefore, we recommend taking steps to coordinate these efforts simultaneously.

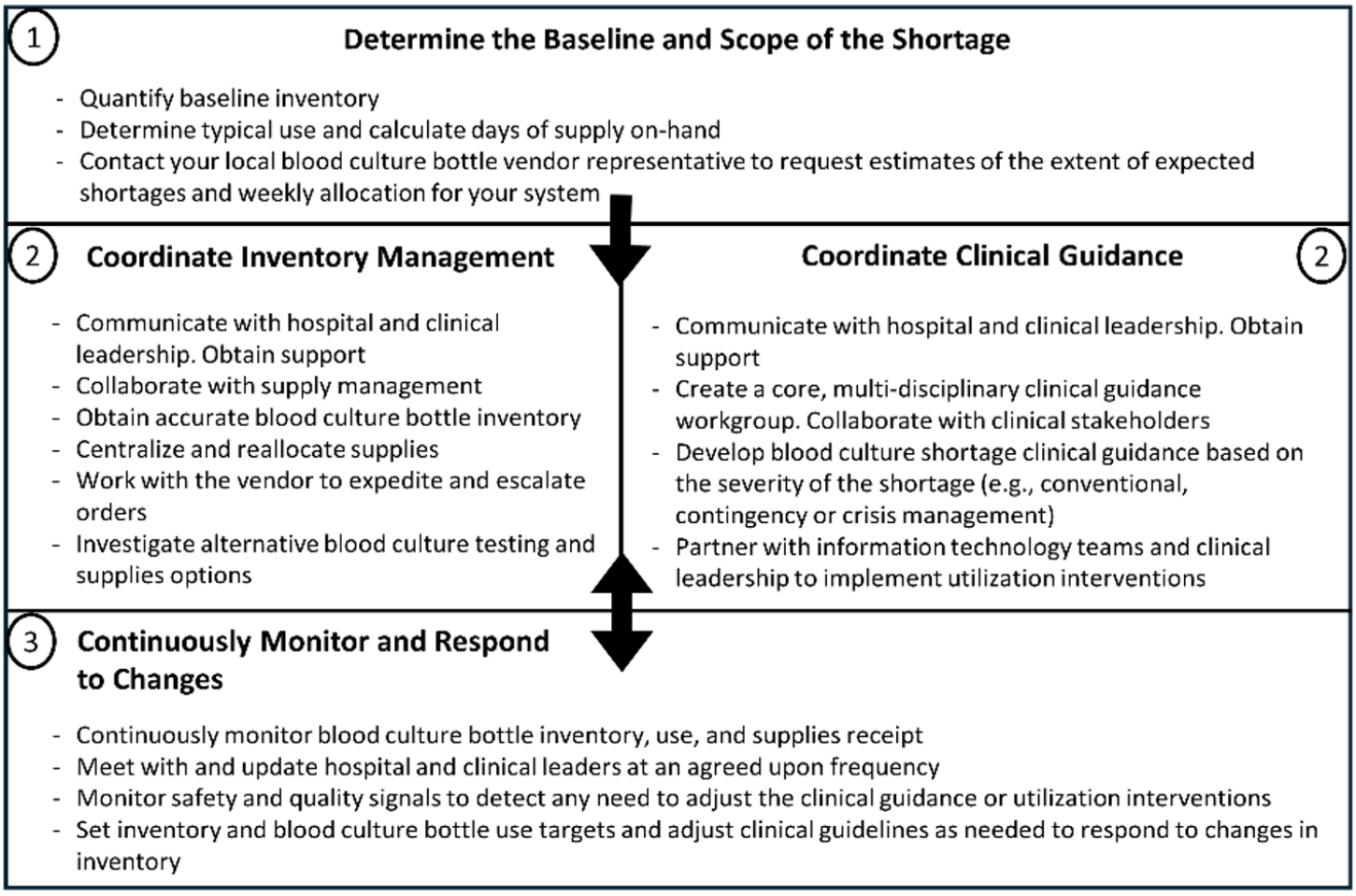

Figure 2. Recommended steps and tasks for laboratories to take to help organize their system's response to a BC bottle shortage. When coordinating a response to BC bottle shortages, we recommend that laboratory leaders first determine the baseline bottle inventory for their system and estimate the extent and scope of the shortage. Next, both inventory management strategies and clinical guidance to reduce use must be coordinated. These activities generally require collaboration with different groups and experts but should be managed at the same time. Depending on the system, laboratory leaders may or may not be delegated to coordinate these responses. Therefore, it is imperative to first communicate with hospital and clinical leadership, determine the status of the system's response, and identify areas in which laboratory expertise is needed. After initial coordination and strategies are developed, an iterative process of monitoring and responding to changes should proceed until the shortage is resolved.

Determine the Baseline Situation and Scope of the Shortage

1. Quantify the inventory on-hand.
   a. Accurate counts include stock in the system's distribution or storage center and unused bottles that were already distributed to the units. To determine the baseline situation, include inventory counts from the primary storage location at minimum. Supplies on the units may be determined subsequently to not delay coordination activities (see **Coordinate Inventory Management** subsection below).

2. Determine typical use and calculate the expected days of supply on-hand.
   a. Weekly or daily average use over the prior month may be sufficient when determining the baseline situation. For long term planning, additional data is recommended to assess seasonality trends (see **Continuously Monitor BC Inventory and Use and Respond to Changes** subsection below).

3. Understand the chain of distribution within your system and determine whether there is one or more distributors working with a single or different hospitals.

4. Contact your local sales representative to request the following information:
   a. Extent of delivery reduction
   b. Estimates for the weekly allocation
   c. Frequency of communication regarding updates/arrange regular check-ins with the representative

Coordinate Inventory Management

1. Communicate the baseline situation and scope of the shortage to hospital leadership. Obtain support to modify routine inventory management procedures.
   a. Determine if other groups or departments are already developing interventions for inventory management. If so, align your efforts and collaborate.

2. Obtain an accurate inventory of all BC bottles in the system, including bottles on the units, if not already done above.
   a. Track the quantities and lot number of each type of bottle (e.g., aerobic, anaerobic, pediatric, mycobacterial or fungal) and the expiration dates of associated lots.

3. Engage the supply management team.
   a. Depending on the institution, BC bottle ordering may be directly managed by the laboratory, through a non-laboratory supply management team or by both teams. In either case, the system's supply management team should be engaged as they can offer unique expertise in working with vendors and managing supply inventory.

5. Centralize and reallocate supplies.
   a. Notify clinical areas of the shortage and of interventions that will be implemented to more stringently manage supplies. Engage unit and nursing leaders.
   b. Engage supply and stocking teams to assist in inventory management to provide information on how and where they stock BC bottles.
   c. Pull supplies back from locations to minimum periodic automatic replacement (PAR) levels.
   · New PAR levels should reflect the stage of supply management (i.e. conventional, contingency, or crisis), BC bottle inventory, and the expected reduction in use based on temporary clinical guidance (See **Coordinate Clinical Guidance** section below)
   d. Remove or reduce inventory from areas that historically have had low levels of BC orders (e.g., most ambulatory clinics).
   e. Redistribute near-expiration date bottles to high-use areas to avoid waste due to expiring.

6. Continuously work with the vendor to minimize delays in supply receipt and escalate orders.

7. Investigate alternative resources. Examples include:
   a. Utilizing alternative BC bottles that are also FDA-cleared for your laboratory's instrumentation (e.g., glass bottles instead of plastic or standard bottles instead of resin bottles). If alternatives are (or become) available, in the United States laboratories must perform test verification studies before implementing different BC bottle types for clinical use.
      - Laboratories should consider the extent of verification needed or ability to streamline the necessary verification based on CLIA requirements, risk assessment, and available supply.

b. Collaborating with neighboring hospitals or systems that use BC systems not affected by the shortage.
   - Laboratories may be able to partner with nearby sites to obtain supplies and send specimens for alternative BC systems with additional capacity. Note, during times of severe shortage, manufacturers that are not directly affected by a shortage also may closely monitor or limit supplies to current customers to ensure supply stability. Therefore, obtaining additional supplies to partner with other laboratories may not be possible.
   - Considerations: feasibility to rapidly transport collected BC bottles, supply stability and availability for the alternative system, method of transferring orders, result and critical value communication (e.g., are the EMRs interfaced?), differences in reporting protocols between laboratories (e.g., antibiotic susceptibility cascades), capacity of the partnering laboratory to work-up additional positive cultures.
     1. Transport collected samples at room temperature.
     2. Transport times must comply with manufacturer recommendations. To accept specimens that exceed the manufacturer's recommended transport time, the performing laboratory must perform test validation to demonstrate acceptable recovery of microorganisms.
     3. Some manufacturers do not state a time limit within which a collected bottle must be loaded onto the continuous monitoring automated BC instrument. Two studies have demonstrated minimal to no impact with transportations times >4 h, but transportation beyond 12 h is not recommended (3-5).

c. Obtaining additional instrumentation for alternative BC system and evaluating alternative blood culturing methods. Inquire with your local vendor representative to determine availability.

d. In some cases, the manufacturer may extend the expiration dates for specific lot numbers of BC bottles. Laboratories or the supply management team may consider sequestering expired BC bottles instead of discarding them upon expiration, in case an extension is granted.

Coordinate Clinical Guidance

1. Communicate the baseline situation and scope of the shortage to hospital leadership. Obtain support to coordinate the development of clinical guidance for BC use during the shortage.

a. Determine if other groups or departments are already developing interventions and clinical guidance. If so, align your efforts and collaborate.

b. Obtain support from clinical leadership, such as Chief of Staff or Chief Medical Officer, to implement a BC shortage clinical guidance, reinforce messaging and restrictions, and for operational resources (e.g., information technology support).

2. Create a multi-disciplinary clinical team to develop BC clinical utilization and conservation strategies. At minimum, the core team should include representatives from antimicrobial stewardship, infectious diseases, infection prevention and control and the laboratory.

a. The multi-disciplinary core team may also include representatives from the emergency department (ED), critical care, surgery, hemato-oncology, pediatrics, nursing and others. If not included in the core team, representative clinical stakeholders should be consulted regarding individual guidelines that will be most relevant to their clinical practices before the guidelines are implemented.

3. The multi-disciplinary clinical team will need to develop BC shortage clinical guidance.

a. Determine baseline BC use practices throughout the system.

b. Identify opportunities to conserve supplies through heightened emphasis on best practices (**Figure 1**).
   - Prioritize and reeducate about best practices for collecting BCs (refer to section **Factors that Increase Test Quality and Reduce Need for Recollection**).
   - Implement diagnostic stewardship programs wherever possible beyond those used at baseline (refer to section **Approaches to Optimize Indications for Blood Culture Ordering**).
   - Implement supply conservation methods that require adjustments in clinical practice. For example: removing the option to order automatically repeating orders ("daily" order frequency); remove specimen orders that enable collection and temporary storage of a BC specimen before a BC is ordered ("extra blood", "hold", or "rainbow" orders).

c. Determine whether BC bottle conservation through best practices and close inventory management will be sufficient to manage testing through the shortage or if contingency or crisis management is required. If contingency or crisis management is required:

- Identify non-standard of care practices that may be employed. Examples: restricting repeat blood culture order frequency; not inoculating body fluid specimens for culture into BC bottles; routinely collecting one set of BCs instead of two sets (refer to sections **Culturing Sterile Body Fluid** and **Recommended Number of Blood Culture Sets**).
- Assess the relative benefits (extent of BC use reduction and extension of BC bottle availability) versus relative risks (reduced detection of blood stream infections, BSIs) of implementing each potential non-standard practice.
- Prioritize and develop specific guidance for test use according to clinical indication based on the performed risk/benefit assessment.

4. Partner with Laboratory Information Systems (LIS) and Hospital Information Systems (HIS) teams to utilize information technology infrastructure to develop tools and operationalize the BC shortage clinical guidance. Examples methods include:
   a. Test order creation or modifications
   b. Best practice alerts, restrictions, and order-based messaging
   c. Identify order sets that contain BCs and determine appropriateness (e.g., default selection for BC)
   d. Create comments or clinical note tools (e.g., SmartPhrases) to streamline clinical documentation relating to BC orders, indications, or instructions (e.g., subspecialist recommendations to the primary team)

5. Use multi-modal communication to communicate BC shortage clinical guidance to all providers and clinical staff.
   a. Ordering providers (including resident physicians), nursing, and phlebotomy teams may need instructions specific to their role in the process. Tailor concise communication for each group.
   b. Use more than one communication tool. Examples include HIS automated messaging, e-mail distribution lists, 'screen saver', network login screen, and working with the graduate medical education office to communicate with resident and fellow trainees.

Continuously Monitor BC Inventory and Use and Respond to Changes

1. Partner with supply chain management and information technology teams to regularly obtain accurate BC bottle inventory, usage, and supplies receipt counts.
   a. Helpful reports include inventory reports, unit-specific inventory distribution, and number of BC specimens received in the laboratory. Measure the daily or weekly average distribution and use.
      - Analytic reports within BC instrument software are often useful resources to obtain daily utilization data.
      - Monitor BC collection by department or location. This data should be shared with the Clinical Guidance team to determine if the implemented interventions have the intended impact on ordering practices.
   b. Create a dashboard to monitor inventory. Recommended metrics include current inventory, current daily use (usually a running 7-day average), and supply days on-hand for each location within the system. Monitor inventory of each type of BC bottle separately.
   c. If the shortage is predicted to extend over several months, long term planning for seasonal variation in test use may be necessary. Consider obtaining historic BC data over the prior 6-12 months, or longer, to identify trends and predict future variability.

2. Determine the appropriate frequency (e.g., daily, weekly) and methods of communication with hospital and clinical leadership. Keep supply management, risk management, patient quality and safety, and hospital executive leadership informed throughout the decision-making process.

3. Continuously collaborate with the Clinical Guidance and Inventory Management teams.
   a. Determine if the employed clinical and inventory interventions are achieving the expected or target impact on supplies.
      - Evaluate need for modifications to the clinical guidance (e.g., clarify implemented interventions, increased messaging or efforts to improve adherence, add new or remove guidance in response to the severity of the shortage and BC inventory).
   b. Monitor safety and quality signals that indicate a need to reassess the initial risk/benefit decisions. Modify clinical guidance accordingly.
   c. Set inventory indicators and thresholds that will signal a need to change clinical utilization
      - Generally, this is based on days of supply on-hand monitoring (e.g., at 10 days of supply, X intervention is introduced; at 6 days of supply, Y intervention).

III. Factors that Increase Test Quality and Reduce Need for Recollection

Diagnosing BSIs is an essential function of clinical microbiology laboratories. There are best practices and expert guidelines from international standards organizations with recommendations on the proper practice of BC collection and testing to diagnose BSIs and infective endocarditis (6, 7). There are several factors that influence the likelihood of detecting bacteremia. These factors include the volume of blood collected, the number of BCs performed, timing compared to antimicrobial therapy initiation, and adherence to proper patient preparation and collection technique. Even when following best practices, fewer than 10% of BCs are typically positive, yet it is estimated that 20-60% of those positive BCs are due to contaminating microorganisms rather than true pathogens (8-10). Key quality practices are highlighted for each subsection below and are summarized in **Summary Box 1.**

Impact of volume of inoculated blood on BC performance

The quantity of microbial pathogens in the blood during a bacteremic episode has been reported to range anywhere from 1 to 10 colony forming units per milliliter of blood in adult patients (11-15). In pediatric patients, the magnitude of bacteremia was reportedly higher (16), but this notion has been an area of controversy. Low level bacteremia is also common in pediatric patients. We refer the reader to a contemporary minireview published on this topic (17). Because of low concentrations of circulating bacteria, a common adage has been that the more blood collected, the higher the likelihood of a positive culture, and this is well described in the literature (18). BC bottles should be inoculated with the maximal (optimal) fill volume recommended by the manufacturer, but should not be overfilled beyond maximum recommended volume. For pediatric patients, weight-based guidelines should be followed to determine optimal and safe blood volume (19).

Active monitoring of BC bottle fill volumes coupled with feedback is an important quality improvement activity for clinical laboratories. It has been shown to improve overall BC positivity. In their multicenter study, Khare et al. found that the baseline average fill volume was 2.3 mL (range 1.6 to 3.3 mL) across all ten hospitals before interventions were implemented (20). Following the interventions, 7/10 hospital sites achieved the recommended fill volume (8 to 10 mL/bottle) following a comprehensive plan including education, monitoring, and real-time feedback. This led to a systemwide increase in overall BC positivity by nearly 40% during the program (initial positivity 6.7% versus 9.3% after intervention).

- BC bottles should be filled with the optimal blood volumes recommended by the manufacturer to optimize pathogen yield.
- Laboratories should have a quality system that monitors BC volumes and provides feedback to collectors.

Timing of BC sampling

It is recommended that BCs be collected before initiation of empiric antimicrobial therapy when there is concern for sepsis or septic shock (21). A study by Scheer et al. reported a 20% decrease in the detection of a pathogen from BC sets collected during antimicrobial therapy compared to those collected before antimicrobial administration (22).

Major guidelines no longer endorse specific timing of BCs when multiple sets are ordered simultaneously or in relation to febrile episodes in the patient, rather emphasizing optimal blood volume sampling and collection before antimicrobial therapy is initiated (6, 19). Previous recommendations suggested that BC sets should be collected 30-60 minutes apart. A study by Fabre et al. determined that the yield of positive BCs was similar between sets collected in short intervals versus those with longer intervals (23). Additionally, a multicenter study by Riedel et al. evaluated the relationship between BC collection times around elevations in body temperature. Among 1,436 patients evaluated, no association between body temperature increases and the time of an initial positive BC was identified. This study concluded that waiting to collect a BC during a febrile episode is not critical for the detection of bacteremia (24).

- For optimal yield, BCs should be collected prior to initiation of antimicrobial therapy whenever possible.
- Multiple BCs may be drawn consecutively without an intervening timeframe between draws.
- Draw timing considerations in relation to fever do not increase yield of BCs.

Minimizing BC contamination

Blood is normally sterile and positive BCs with a known pathogen have a high positive predictive value for infection. However, contamination of BCs with microorganism(s) that are not causing a BSI is a serious problem. Despite the critical role that BCs play in diagnosing bacteremia, in some settings the majority of positive BCs are due to contamination from the skin microbiota during venipuncture (8-10). This is because the skin cannot be sterilized and antiseptic cleansing practices only remove surface microbiota. The bacteria that reside in hair follicles and deeper in the dermis may remain. Therefore, the strategies employed to minimize BC contamination are multifactorial.

Contamination events lead to patient harm through increasing hospital stay, increased exposure to broad-spectrum antimicrobial agents with potential toxicity, and delay in establishing a true diagnosis (10, 25-27). Contaminated BCs are also costly to systems and often lead to repeat BCs and additional diagnostic testing (28).

Proper venipuncture site preparation is crucial to minimize contamination from the skin microbiota. Utilization of antiseptic solutions has a tremendous impact on reducing skin bioburden. Recommendations suggest using chlorhexidine gluconate or iodine tincture for BC specimen collection (29, 30). Chlorhexidine regimens may be favored as the application requires a shorter drying time on the skin to achieve maximum effect compared to iodine.

Timely feedback to the collector regarding contamination rates has been shown to improve overall compliance with proper technique and reduction in contamination rates (31). This has been shown to be effective but is resource intensive and rates can fluctuate back to baseline when feedback is not provided.
A systematic review published in 2012 evaluated practices to reduce BC contamination rates. The authors included studies that focused on dedicated venipuncture for specimen collection, use of phlebotomy teams, and prepackaged specimen collection kits (32). Dedicated venipuncture yielded significantly lower rates of BC contamination than collection from an endovascular catheter. Additionally, BC collection by dedicated phlebotomy teams was associated with reduced BC contamination compared to those collected by non-phlebotomists. Similarly, a single center study by Gander et al. evaluated the effect of personnel on BC collection in the ED. In one ED unit, 2,012 (37%) BCs were collected by dedicated phlebotomists with contamination rates ranging from 2.4 to 3.6% (overall rate 3.1%) whereas the rates of contamination among non-phlebotomy collected specimens ranged from 6.2 to 10.2% (overall rate 7.4%) (33). In a second ED unit without dedicated phlebotomy, the range of BC contamination was similar, ranging from 4.9 to 7.0% (overall rate 5.6%).

Interestingly, another study that evaluated BC contamination rates drawn by phlebotomists and nurses demonstrated that nurses rather than phlebotomists had lower contamination rates (34). The higher contamination rate for phlebotomists (2.3%) versus nurses (0.8%) was postulated to be due to phlebotomists drawing more BCs during the study period as well as drawing more specimens from ICU patients who were deemed more difficult to draw. This evaluation also compared contamination rates by collector in a before-and-after study utilizing a specimen diversion device. The use of the device by phlebotomists was associated with a significant reduction in BC contamination (baseline 2.3% down to 0% with use of the device).

The use of specialized diversion devices to divert the initial volume of blood collected during specimen collection has been shown to significantly reduce contamination rates to less than 1% when correctly used (35-38). Skoglund et al. evaluated the economic impact when specimen diversion devices were employed. The authors detected an 86% reduction in BC contamination by using a specimen diversion device (39). Based on this reduction rate, they calculated a 3% cost savings versus the average total cost per clinical episode in which a BC is drawn.

Minimizing BC contamination reduces downstream resource utilization, including additional BCs, unnecessary administration of antimicrobial therapy, and other diagnostic tests.

- BC contamination is minimized by carefully observing antisepsis of collection sites, collector training, and monitoring of contamination rates coupled with collector education and feedback.
- Use of specimen diversion strategies may help reduce blood culture contamination rates.

Best practices to minimize sample rejection

Most laboratory errors occur in the pre-analytic phase of testing (40, 41). A meta-analysis published in 2023 evaluated blood sample rejection rates in laboratories and found that the leading causes of sample rejection were pre-analytic errors associated with improperly collected specimens, such as using the wrong container, insufficient blood volume, and labeling errors (42). These errors can lead to delays in diagnosis as they typically require repeat specimen collection.

In the event of BC bottle shortage, providers and other clinical staff should be reminded of proper specimen labeling, specimen stability requirements, and transport instructions per institutional policy to minimize sample rejection and supply wastage.

Quality metrics related to BCs

In the US, it is the responsibility of clinical microbiology laboratories to monitor BC specimen acceptability and adequacy in compliance with federal regulations (43). For laboratories that are accredited by the College of American Pathologists, the laboratory is required to monitor the volume of blood collected in BC bottles from adult patients and to provide feedback to collectors (44).

Summary Box 1. Strategies to optimize diagnostic yield of blood cultures and reduce need for recollection

Optimize volume of blood collected

- Blood culture bottle fill volume is the single most critical factor to recover and isolate microorganisms *in vitro*
- Blood culture bottles should be filled with the optimal blood volumes recommended by the manufacturer
- A typical blood culture set comprises of one aerobic bottle and one anaerobic bottle for adult patients

Timing of blood culture sampling

- Blood cultures should be collected **before** initiation of antimicrobial therapy
- Multiple blood cultures may be drawn consecutively without an intervening timeframe between draws
- Draw timing considerations in relation to fever do not increase yield of blood cultures

Minimizing blood culture contamination

- Skin antisepsis should be performed using chlorhexidine gluconate or iodine tincture to minimize the risk of contamination of blood cultures with skin microbiota
- Blood culture contamination is minimized by carefully observing antisepsis of collection sites, collector training, and monitoring of contamination rates coupled with collector education and feedback
- Use of specimen diversion strategies may help reduce blood culture contamination rates

Minimizing sample rejection

- Ensure collectors understand the importance of proper specimen labeling, specimen stability requirements, and transport instructions to minimize sample rejection

Attention to quality metrics related to blood cultures

- The microbiology laboratory is responsible for monitoring the quality metrics tracking blood culture contamination rate and blood culture bottle fill volumes
- A rigorous program to provide feedback to collectors and improve performance on quality metrics improves diagnostic yield of blood cultures

The clinical microbiology laboratory should also monitor BC contamination rates and investigate instances in which rates exceed established thresholds. We refer readers to Palevecino et al., a report by the American Society for Microbiology Laboratory Practices Subcommittee, for comprehensive approaches to calculating and monitoring contamination rates (45). This is an accepted best practice and condition for laboratory accreditation (6, 44). A CAP Q-Tracks study found that laboratories that submitted quarterly BC contamination data for longer periods of time were associated with achieving progressive reductions in institutional contamination rates (46).

IV. Approaches to Optimize Indications for Blood Culture Ordering

Diagnostic stewardship of the BC collection process and clinical indications has been employed at many institutions for various patient populations to optimize BC utilization and improve patient care while minimizing impact on resources. By reducing unnecessary testing, overtreatment of clinically insignificant organisms, overestimation of central line associated BSIs (CLABSIs), unnecessary phlebotomy, and resource waste are avoided. During a time of BC bottle shortage, implementing such diagnostic stewardship strategies can have the added benefit of helping conserve limited supplies for patients who will benefit the most. In the following section, we review interventions that have been employed in published diagnostic stewardship outcome studies (summarized in **Table 1**) and provide references to which we encourage readers to refer for additional collection recommendations and suggestions for algorithms that may fit the needs of their institution. We also summarize published findings from retrospective analyses that describe low yield scenarios for testing, but for which the impact of adjusting collection practices through stewardship may not have been studied. As with most diagnostic stewardship programs, exceptions to recommended routine use may be indicated based on clinical judgement and unique patient situations. Key practices and stewardship activities presented in the referenced studies are highlighted for each subsection and are summarized in **Summary Box 2.**

The approaches below are summarized according to the setting(s) in which the guidelines or stewardship approaches are reported in the cited literature. However, these practices may be more broadly applied to other settings.

General Principles

BCs are the gold standard for diagnosing BSIs and one of the most commonly ordered tests in hospitalized patients. However, ≤10% of BCs recover organisms, and a significant portion of positive cultures represent contaminating microorganisms, suggesting opportunities to optimize test use. A large proportion of BCs are obtained in patients with isolated fever and/or leukocytosis, which do not correlate well with bacteremia (1, 47-53). Thirty to sixty percent of BCs may be inappropriate based on indication (54, 55). Evidence-based guidance and site-specific stewardship studies regarding appropriate use of BCs have been published (1, 2).

Not all infectious syndromes require BCs to be collected for diagnosis. Rather, the pre-test probability of bacteremia within the clinical context of the patient should guide the decision to order BCs. Although BC indications are not standardized, guidelines, scoping reviews and stewardship studies have identified many low yield and high yield clinical indications for BCs. For example, a 2012 paper evaluated the pre-test probability of bacteremia in immunocompetent adults in selected clinical scenarios (56). They classified syndromes as low risk (cellulitis, community-acquired pneumonia), intermediate risk (pyelonephritis) or high risk (severe sepsis, bacterial meningitis, septic shock). Another paper published in 2020 expanded this work and included a more comprehensive evaluation of clinical scenarios taking into account not only the yield of BCs but also the impact of BC results in clinical management (1). A summary of example high yield and low yield clinical indications for BCs that have been studied in different clinical settings is provided in **Table 2.** Many of these studies and study outcomes are further described in the subsections below.

- Pre-test probability of bacteremia and the likelihood of detecting a clinically significant organism should be carefully considered before ordering any test for infectious diseases and is especially important during times of critical supplies shortages.

In a retrospective analysis of all populations in their system (e.g., inpatient, ED, and pediatric, including immunocompromised patients), Humphries et al. evaluated repeat BC yield in their single site as part of de-

veloping a strategic approach to reduce use during a critical shortage of BC bottles in July 2024 (57). They reported that 16.7% of all cultures were repeat collections (drawn >1 h after initial cultures) within 48 h after initial cultures. Only 5% (155/3,088) of repeat cultures performed within the first 48 h of initial cultures yielded different results from the initial cultures. Of these discordant results, 11% (17/155) were due to detection a new organism in the repeat culture when the initial cultures were negative, and 94% (16/17) of those new detections were adjudicated to be likely contaminating microorganisms. Together, these findings suggest that stewardship optimizing when and for which patients repeat cultures are performed may represent a significant method to safely reduce total BC collections

- Repeat BCs within 48 h of initial BCs are of low yield (~5%) in providing new or significant results compared to initial cultures.

Stewardship Approaches for Immunocompetent Adult Patients in the Inpatient Setting

After a scoping review of 50 studies that determined the pre-test probabilities of positive BCs based on reported incidence of bacteremia in selected infectious syndromes and development of an evidence-based algorithm detailing indications for BC use, Fabre et al. found that 24% and 40% of initial BCs collected among intensive care unit (ICU) and medicine ward patients, respectively, and nearly 40% of repeat BCs collected were inappropriate (1). After implementing their evidence-based algorithm coupled with education and provider feedback at their institution, they reported a significant decrease in BC rates across the medical ICU and medicine wards while increasing the rate of BC positivity for true pathogens (54). Other institutions have adopted the algorithm bundled with other interventions in surgical units to improve BC utilization with similar success (58, 59).

- Avoid routine use of BCs in immunocompetent patients with isolated fever or leukocytosis, uncomplicated cellulitis, uncomplicated cystitis or prostatitis, and non-severe pneumonia.
- Avoid routine collection of BCs in response to fever within the first 48 h after surgery (1).
- We refer readers to the scoping review by Fabre et al. as an example algorithm that may be considered to steward BC orders (1).

Although diagnostic stewardship has recently gained more recognition, efforts to reduce unnecessary BCs have been ongoing for decades. Gross et al showed that an overall reduction of BCs may be achieved by optimizing the upfront collection, thus reducing subsequent diagnostic uncertainty (60). When implementing six rules in combination, the average number of BCs per patient discharged from their ICU decreased from 1.2 to 0.3. Their six recommendations for evaluation of suspected sepsis included: always draw two blood samples for initial evaluation; draw two to three samples for suspected sepsis; draw four for initial suspicion of endocarditis, separated by 30min–1hr if antibiotics are to be given that day; BC collection does not need to be timed in relationship to level of fever; draw two samples when documenting persistent bacteremia after initially positive BCs; do not draw BCs for persistent fevers after initial BCs are negative and no change in patient clinical status. Note, some of these six principles are not recommended in more recent studies.

- Optimize initial specimen collection when evaluating suspected sepsis or endocarditis.
- Avoid BC collections for persistent fever after initial BCs are negative in patients with stable or improving clinical status.

Stewardship Approaches for the Emergency Department Setting

Evaluation of BC utility in the ED is limited. However, evidence suggests hospital BC utilization is heavily influenced by ED culture volumes (61). Studies have also demonstrated that contamination rates may be higher in the ED compared to general wards (62). Moreover, the Centers for Medicare and Medicaid Services (CMS) SEP-1 metric has had an unintended consequence of increasing BC orders in discharged healthy ED patients (63). Clinical prediction rules such as the Shapiro decision rule that predict true bacteremia are promising and have been used to develop evidence-based algorithms to reduce unnecessary BCs in the ED (64-67).

- Attention on proper specimen site disinfection protocols can reduce BC contamination if ED does not have dedicated phlebotomists

In a retrospective observational study, implementation of an evidence-based ordering algorithm and a clinical decision support tool into the EMR to remind providers of the ordering criteria and to track the indications

demonstrated a 33.5% reduction in the mean monthly BC utilization in the ED. The criteria for obtaining BCs included hemodynamic instability, immunocompromised status, major and minor Shapiro criteria, and severe community-acquired pneumonia (CAP). The electronic clinical decision tool prompted providers to the algorithm and allowed them to select an indication for ordering BCs (64).

- The Shapiro decision rule and other clinical prediction rules may aid in reducing unnecessary BCs in the ED.

Fabre et al. implemented an evidence-based BC indications algorithm for initial and repeat BCs for nonneutropenic adults in the medical ICU and medicine wards. A significant reduction in BC utilization was observed without negatively impacting the BC ordering component of the CMS SEP-1 core measure (54). Theophanous et al. report applying an algorithm in the ED based on that of Fabre et al, 2020, and demonstrated a decrease from 12.17 to 10.50 BCs per 100 ED admissions postintervention (68).

Stewardship Approaches for the Pediatric Population

Many of the stewardship approaches studied in adult populations may safely be applied to pediatric patients but should be evaluated for appropriateness by each institution. In addition, we summarize published utilization studies and resulting recommendations performed specifically in the pediatric population.
A publication by Woods-Hill et al., provides 19 consensus recommendations for optimizing BC collection in critically ill pediatric patients (2). When applying these recommendations in pediatric ICUs across 14 sites in the US, a 33% reduction in BC use was achieved and no indications of harm were detected (69). We refer readers to the publication for the complete recommendations and highlight a few of their recommendations (2):

- Avoid collecting daily BCs in patients on extracorporeal membrane oxygenation (ECMO), continuous renal replacement therapy (CRRT), and in immunocompromised patients without specific indications of infection.
- Avoid BCs in an asymptomatic patient with a broken, cracked, or accidentally disconnected central venous catheter.
- Avoid BCs in a patient with a new fever in the first 24 hr after surgery, unless there are clinical signs of sepsis.
- Avoid BCs in immunocompetent patients with a viral syndrome that have a new or persistent fever, but no signs of sepsis and no central venous catheter or with a central venous catheter but already have at least one negative BC documented after the start of fever.

In a retrospective analysis by Chand et al., when BCs were collected in non-critically ill patients for evaluation of cellulitis, only 3% of cultures yielded a clinically significant organism (70). The most common pathogen recovered was methicillin susceptible *Staphylococcus aureus*. Additionally, Infectious Diseases Society of America (IDSA) does recommend BC in the evaluation of skin and soft tissue infections in patients with fever and neutropenia but does not recommend BCs for uncomplicated cellulitis (71).

- Avoid routine collection of BCs in non-critically ill patients with cellulitis, but without signs of a serious infection or specific risk factors.

IDSA recommends that pediatric patients with a moderate to severe, presumed bacterial CAP requiring hospitalization have a BC drawn as part of the infection work-up, especially in patients with complicated pneumonia (72). In a single site observational analysis by Kwon et al, investigators found that 69% of BCs collected from previously healthy pediatric patients (6 m-18 y) under evaluation for CAP in their ED did not meet IDSA's recommended criteria for collection (73). Kwon et al. further found that the yield (0.11% bacteremia due to a pathogen) and clinical impact (0% changes in antibiotic regimen) of BCs collected in the ED for evaluation of CAP in their pediatric population were exceedingly low.

- Avoid BCs in patients with mild community acquired pneumonia and non-toxic, immunized patients able to be managed in the outpatient setting (including the ED) (72).
- BCs to document clearance are not necessary for *Streptococcus pneumoniae* in a patient with clinical improvement of CAP (72).
- BCs are not recommended for the evaluation and diagnosis of bronchiolitis (74).

Pediatric patients presenting with acute gastroenteritis do not generally require microbiologic work-up of the etiologic agent, including BCs. The European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Infectious Disease guidelines for the management acute gastroenteritis in children do not include BCs in the evaluation of such cases (75). Note, if the patient presents with symptoms concerning for sepsis associated with a gastrointestinal illness or typhoid fever, sepsis work-up should be activated.

- Avoid BCs in patients presenting with acute gastroenteritis, unless septicemia is suspected.

Stewardship Approaches for Patients with Neutropenia

Many of the strategies discussed in the above sections may be safely applied to immunocompromised patients as well. However, many clinical studies exclude this population. Therefore, a site-specific risk assessment is recommended when considering broader application of diagnostic stewardship approaches to immunocompromised patients, including patients with neutropenia.

The National Comprehensive Cancer Network (NCCN) recommends that neutropenic patients with a new fever should be evaluated for infection, including collection of BCs for initial work-up (76). Additionally, IDSA recommends that an initial fever evaluation in neutropenic patients with cancer include at least two sets of BCs (77). Similarly, for neutropenic patients presenting to emergency care with fever within 6 weeks of receiving chemotherapy, American Society of Clinical Oncology and IDSA recommend collecting two sets of BCs from different anatomic sites as part of the initial diagnostic workup (78).

The optimal workup, timing, and value of repeating BCs after initial fever evaluation in patients with neutropenia is not agreed upon, but overall repeat BC yield appears to be low. IDSA guidelines for fever in neutropenic patients recommended that persistent or recurrent fever of >3 days should prompt an evaluation of source, including collecting a new set of BCs (note, this clinical practice guideline has been archived by IDSA) (77). However, NCCN recommends that after initial work-up, including initial BCs, if the patient is clinically stable, improving, or persistently febrile but otherwise clinically stable, additional BCs are not indicated. If response to therapy evaluation is indicated, cultures may be collected 3-5 days after initiation of therapy (76). Since most positive BCs are detected within the first 48 h and it is expected that effective antimicrobial therapy can require a few days to clear infection, BCs should not be immediately repeated while awaiting results of the initial work-up (79). Meanwhile, Robinson et al. found that only 2% of BCs collected after the first day were positive and that clinically significant microorganisms were rarely recovered from repeat cultures collected after 48 h (79).

Interestingly, in a relatively small retrospective study of 358 BCs collected from admitted adult hematology or oncology patients, Alsfeld et al. found that only 4% of cultures were positive when drawn on patients receiving broad-spectrum antibiotics (80). Among the 4% of positive cultures, none were new pathogen detections, and all were follow-up cultures from a positive culture obtained before broad-spectrum antibiotics. No BCs collected in response to a new fever were positive while on broad-spectrum antibiotics.

- Initial work-up of fever in neutropenic patients should include at least two BCs, e.g., one peripheral and one catheter drawn culture (76).
- Avoid daily BCs in clinically stable patients with persistent fever and neutropenia after initial work-up is performed (76).
- Response to empiric therapy can be evaluated 3-5 days after therapy initiation (76).

The number of BC sets collected for initial work-up of fever and neutropenia in patients with a catheter also offers an opportunity for stewardship. The NCCN 2023 guidelines recommend collecting at least two sets, preferably one peripheral draw and one from the catheter. Notably, it is not recommended to routinely collect sets from each port.

- Avoid collecting multiple BC sets from each port of a single line in adult patients (76).

Summary Box 2. Stewardship approaches to optimize indications for blood cultures according to specific settings.

General Principles

- Pre-test probability of bacteremia and the likelihood of detecting a clinically significant organism should be carefully considered before ordering any test for infectious diseases and is especially important during times of critical supplies shortages
- Repeat blood cultures within 48 h of initial blood cultures are of low yield (~5%) in providing new or significant results compared to initial cultures

Immunocompetent Adult Patients in Inpatient Setting

- Avoid routine use of blood cultures in immunocompetent patients with isolated fever or leukocytosis, uncomplicated cellulitis, uncomplicated cystitis or prostatitis, and non-severe pneumonia
- Avoid routine collection of blood cultures in response to fever within the first 48 h after surgery
- A published algorithm may be considered to steward blood culture collection (1)
- Optimize initial specimen collection when evaluating suspected sepsis or endocarditis
- Avoid blood culture collections for persistent fever after initial blood cultures are negative in patients with stable or improving clinical status

Emergency Department Setting

- The Shapiro decision rule and other clinical prediction rules may aid in reducing unnecessary blood cultures in the ED
- Attention to proper specimen site disinfection protocols can reduce blood culture contamination if ED does not have dedicated phlebotomists

Pediatric Patients

- A published study with 19 recommendations may be considered to steward blood culture collection (2)
- Avoid routine collection of blood cultures in non-critically ill patients with cellulitis, but without signs of a serious infection or specific risk factors
- Avoid blood cultures in patients with mild community acquired pneumonia and non-toxic, immunized patients able to be managed in the outpatient setting (including the ED)
- Blood cultures to document clearance are not necessary for Streptococcus pneumoniae in a patient with clinical improvement of community acquired pneumonia
- Blood cultures are not recommended for the evaluation and diagnosis of bronchiolitis
- Avoid blood cultures in patients presenting with acute gastroenteritis, unless septicemia is suspected

Patients with Neutropenia

- Initial work-up of fever in neutropenic patients should include at least two blood cultures, e.g., one peripheral and one catheter drawn culture
- Avoid daily blood cultures in clinically stable patients with persistent fever and neutropenia after initial work-up is performed.
- Response to empiric therapy can be evaluated 3-5 days after therapy initiation
- Avoid collecting multiple blood culture sets from each port of a single line

Table 1. Summary of select studies with interventions to decrease unnecessary blood culture utilization according to clinical setting.

Clinical setting	Intervention	Outcome	References
Hospitalized, immunocompetent adults	ICU setting: implemented 6 rules to optimize number of blood cultures collected based on clinical scenario	Decreased blood culture orders from 1.2 to 0.3 per patient discharge	Gross et al, 1988 (60)
	Implemented an evidence-based algorithm for blood culture ordering plus education and provider feedback (Fabre et al., 2020) (1)	Decreased blood culture rates from 10.9 to 7.7 blood cultures per 100 patient days in 5 medical units Increased positivity rate of significant pathogens from 8% to 11% postintervention	Fabre et al, 2020 (54)
Emergency Department	Established the Shapiro criteria: Major criteria: temperature > 39.5°C, indwelling vascular catheter, or suspected endocarditis Minor criteria: temperature 38.3-39.4°C, age > 65 y, chills, vomiting, hypotension (systolic blood pressure < 90 mm Hg), neutrophil% > 80, white blood cell count > 18 k/μL, bands > 5%, platelets < 150 k/, or creatinine > 2.0.	Applying 1 major and 2 minor criteria resulted in sensitivity of 97-98% for predicting bacteremia.	Shapiro et al., 2008 (81)
	Implemented blood culture order algorithm incorporating Shapiro criteria (excludes immunocompromised patients)	Decreased average monthly blood cultures by 33.5%	Pawlowicz et al, 2016 (64)
	Implemented blood culture order algorithm (Fabre et al., 2020) (1)	Decreased blood culture events per 100 ED admissions from 12.17 to 10.5 No increase in adverse events	Theophanous et al., 2024 (68)
Pediatrics	ICU setting: Implemented 19 consensus recommendations (Woods-Hill et al., 2021) (2) across 14 sites	Decreased blood culture use by 33% No increase in adverse events	Woods-Hill et al, 2022 (69)
Patients with neutropenia	Adult, non-stem cell transplant: changed clinical practice guideline from daily cultures to clinically guided ordering in setting of ≥3 d of febrile neutropenia	Decreased rate (blood cultures per day of febrile neutropenia beyond 3 d) from 1.4 to 0.7	Robinson et al, 2022 (79)
	Adult bone marrow transplant: Implemented protocol with decreased frequency of blood cultures, e.g., days 1 and 4 vs. for every febrile episode	Decreased number of blood cultures collected per patient by 49% without indication of harm	Serody et al, 2000 (82)

Table 2. Summary of guidelines and scoping reviews on blood culture indications: low versus high yield according to clinical setting.

Clinical Setting	Low Yield/Weak Indications	High Yield/Strong Indications	References
Hospitalized, immunocompetent adults	• Non-septic patients • Isolated fever or leukocytosis • Uncomplicated cellulitis including periorbital cellulitis • Non-severe pneumonia • Daily BCs for persistent fever • Fever in first 48 h after surgery • Cystitis/prostatitis	• Severe sepsis/septic shock • Bacterial meningitis • Shaking chills in febrile patient • Endovascular infections including endocarditis • Catheter-related BSI • Discitis and vertebral osteomyelitis • Epidural abscess • Native joint infection • Ventriculoatrial shunt infection • Nonvascular shunt infection If primary site unavailable for sampling: • Severe CAP • Cholangitis • Pyogenic liver abscess	Stevens et al, 2014 (71) Coburn et al, 2012 (56) Fabre et al, 2020 (1) Fabre et al, 2023 (53)
Emergency Department	• Cellulitis • Simple pyelonephritis • CAP	• Sepsis • Hemodynamic instability • Immunocompromised status • Severe CAP • Endocarditis • Meningitis • Complicated pyelonephritis • See also Shapiro criteria	Long and Koyfman, 2016 (65) Shapiro et al., 2008 (81)
Pediatrics	• Daily surveillance BCs in immunocompromised patients and patients on ECMO or CRRT • Fever in first 24 h after surgery • Immunocompetent patients with viral syndrome and fever and no signs of sepsis or central line • Cellulitis in non-critically ill patient • CAP in an immunized, previously healthy patient • Bronchiolitis • To document clearance of *S. pneumoniae* in patients with clinical improvement of CAP • Acute gastroenteritis	• Sepsis • Complicated pneumonia • Febrile infant 8-60 d old	Kwon et al, 2017 (73) IDSA CID 2011 (77) Stevens et al, 2014 (71) Guarino et al, 2014 (75) Ralston et al, 2014 (74) Pantell et al, 2021 (83)
Patients with neutropenia	• Prior receipt of broad-spectrum antibiotics • Daily BCs for persistent fever in clinically stable patient • Follow-up BCs within 3 d of previous positive • BCs from >1 lumen of a central line	• New fever (≥38.3°C or ≥38.0°C over 1 h period); neutropenia defined as ≤500/μL, or ≤1000/μL and predicted to decline to ≤500/μL over next 48 h	NCCN 2023 (76) Alsfeld et al, 2019 (80) Taplitz et al, 2018 (78)

Abbreviations: BC, blood culture; CAP, community-acquired pneumonia; ECMO, extracorporeal membrane oxygenation; CRRT, continuous renal replacement therapy

V. Culturing Sterile Body Fluids

Best practice recommendations for culturing body fluid specimens include specimen inoculation and incubation using both agar media and broth media, unless the entire specimen is concentrated and inoculated to only agar media (44). BC bottles (aerobic or aerobic and anaerobic) are the preferred broth medium for sterile body fluid culture (84).

As an example of a contingency management strategy during shortages, laboratories that routinely inoculate BC bottles for their cultures of sterile body fluid specimens may consider temporarily switching to use agar media alone or conventional broth media. Published literature demonstrates BC systems can increase detection of pathogens from sterile body fluids by 18-33% when compared to conventional culture media, although recovery of contaminants may also be increased (85-88). Various factors affect the performance of BC system-based cultures, including the type of sterile body fluid, volume of fluid collected and inoculated to bottles, and timing of antibiotic administration relative to specimen collection. Individual laboratories may therefore choose to examine their own positivity rate and pathogen yield from BC bottles compared to conventional agar plates and/or broth media before making a determination.

VI. Recommended Number of Blood Culture Sets

While best practice guidelines recommend routinely collecting at least two sets of BCs, during times of severe supplies shortages many institutions may consider conserving supplies by reducing this practice to collect only one set of BC during crisis management. This section is not intended to recommend for or against reducing BC collections to one set. Rather, as we recognize this will be a common consideration during extreme situations, we aim to summarize published data regarding the performance of single versus multiple set collections that institutions may use when performing a site-specific risk assessment of different methods to conserve supplies.

Examples of society guidelines or best practice standards that recommend collecting more than one BC set:

1. Clinical Laboratory Standards Institute recommends obtaining two to three BC sets per episode within a 24 h period, for both adult and pediatric patients (6).
2. The IDSA/ASM laboratory utilization guide recommends collecting two or three BC sets for the evaluation of each septic episode in adults, with each bottle containing 10 ml of blood (19).
3. National Comprehensive Cancer Network (NCCN) recommends collecting at least two sets of BCs for initial workup of patients with fever and neutropenia (76).
4. American Society of Clinical Oncology (ASCO)/IDSA 2018 guidelines recommend that neutropenic patients presenting to emergency care with fever within 6 weeks of receiving chemotherapy should have at least two sets of BCs collected from different anatomic sites (78).
5. The International Pediatric Fever and Neutropenia Guideline Panel recommends that the evaluation of new fever in neutropenic pediatric patients include BCs collected from all lumens for patients with a central venous catheter. Concurrent peripheral cultures should be considered (89).

Example studies comparing organism recovery from one versus two or more sets of BCs:

1. Humphries et al. reported 93.7% concordance between the first two or first three initial BC sets collected (defined as all BCs collected within 1 h of the first culture) (57). For discrepant cultures, 2.1% of cultures yielded a potential pathogen and 3.6% of cultures yielded a skin commensal in only one of two culture sets. In this study, the analytic sensitivity and specificity of one set versus two sets of BCs was 67-83.4% and 95.3-98.6%, respectively. Second or third culture sets accounted for 45% of total BCs collected during the assessment period. Notably, based on their retrospective review of pathogen recovery in one versus two sets and a site-specific risk assessment, this institution decided to reduce routine collections to only one set, except for patients under evaluation for sepsis, during the July 2024 critical supply shortage.
2. Neves et al. evaluated the likelihood of obtaining a BSI diagnosis in adult patients diagnosed with sepsis, severe sepsis, or septic shock when comparing number of BC sets collected and mass of blood collected (90). In this study 55/345 septic patients had a positive BSI diagnosis based on BCs. Multivariate analysis was performed to determine predictors of obtaining a positive diagnosis by BC. The odds ratio was 1.27 for each BC set collected beyond one set and a 1% increase in positivity rates was observed for each additional

1 mL of blood collected in the bottles (odds ratio 1.01). Both parameters were statistically significant.

3. Comparing the recovery of a pathogen in 80 bacteremic patients with at least three sets of BCs collected within 24 h, the recovery rates were: 80% first collection; 89% first two collections; 99% first three collections, when collecting 10 mL of blood per BC set (91, 92).
4. Another study evaluating 500 episodes of septicemia found that 91.5% of bacteremic episodes were detected by the first BC set and 99.3% within the first two collections, when collecting 15mL of blood per BC set (8, 92).
5. Lee et al. evaluated the recovery rate of organisms adjudicated to represent clinical infection in adults with three or more BC sets collected within 24 h from the first set at two facilities. Pathogen recovery rates in this study were: 73.2% from one set, 87.7% from two sets, 96.9% from three sets, and 99.7% from four sets (93).
6. Cockerill et al. found that collecting 40 mL versus 20 mL of blood increased recovery of pathogens by 21.6% in adult patients without endocarditis (94).
7. Isaacman et al. compared pathogen recovery by number of BCs and volume of blood from a prospectively enrolled, consented pediatric population. A pathogen was detected in 22/288 patients when two BC sets (set = 1 mL in aerobic bottle, 1 mL in anaerobic bottle) versus 19/288 patients when one BC set was collected. This study found that increasing the volume of blood improved pathogen recovery rates more dramatically than did increasing the number of bottles collected (a pathogen was recovered in 24/270 patients when 3 mL of blood was inoculated into each an aerobic and anaerobic bottle). Enrolled patients included those with a higher likelihood of having bacteremia including age 3-36 months, temperature >39.5°C, and/or clinical toxicity. Note, bottles were incubated for 7 days in this study (95).
8. Zalmanovich et al. compared collection of one versus two BCs in pediatric patients in Israel (96). They found that the yield of pathogen recovery from one culture was 1% versus 8.9% from two cultures. However, the authors also noted that there was a significant difference in yield from just the first bottle collected between patients with one versus two BCs (1% for one set, 7.5% for two sets) suggesting a difference in the baseline populations of each group and perhaps higher suspicion of infection driving the collection of multiple BCs. Only aerobic or pediatric aerobic bottles were included and volume inoculated into each bottle was not verified.

VII. Conclusion

Clinical laboratories have experienced BC supply shortages in the past and must be prepared to deal with present and future events. It is imperative for laboratorians to work collaboratively with infectious disease providers, hospital leadership, supply management teams and other stakeholders to manage conservation efforts system-wide. Diagnostic stewardship of BCs is an active field of study with many strategies demonstrating success in recent years. In times of BC bottle shortage, stewardship of BCs is especially critical to ensure that patients presenting with the highest likelihood of BSI or sepsis are appropriately prioritized. However, heightened emphasis on best practices and stewardship may not be enough during severe shortages; contingency and crisis management measures may also be required. The degree of conservation or rationing of bottles required may differ considerably from one hospital to the next. While many different practical approaches, best practice guidelines, and published evidence were discussed herein, each institution must tailor their response based on internal supply and usage data and risk assessment for the patients served.

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