

2026 Consensus Statement 2 by the IDSA and ESCMID on Follow-up Blood Cultures in Patients with SAB

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Executive Summary

Overview

Follow-up blood cultures (FUBC) are a crucial diagnostic and prognostic tool in the management of *Staphylococcus aureus* bacteremia (SAB), facilitating management, informing risk stratification, and guiding antibiotic therapy. However, FUBC are not always obtained and the optimal number and frequency of FUBC are unclear. Their consistent use enables accurate documentation of blood culture clearance and timely adjustments in clinical management.

Clinical question 2

Should follow-up blood cultures (FUBC) be performed until negative in patients with SAB?

Consensus statement for the adult population

- In adult patients with SAB, the panel suggests at least 2 sets of FUBC be obtained at 48 hours after sampling of the first positive blood culture and then repeated as either 1 or 2 sets every 24 to 48 hours until negative to document blood culture clearance (consensus).

Remarks for the adult population

- The term blood culture refers to a set of two bottles (1 aerobic and 1 anaerobic).
- Positive FUBC at ≥ 48 hours after the first positive blood culture should trigger further diagnostic evaluation and source control reassessment as outlined for increased-risk SAB in Consensus Statement 1.
- The FUBC strategy should be individualized with consideration of more intensive monitoring (e.g., FUBC every 24 hours, sampling of 2 sets, negative blood cultures on 2 consecutive days to document clearance) in patients with ongoing signs/symptoms of infection, confirmed or suspected deep-seated focus of infection including endocarditis or other endovascular focus (e.g., intracardiac device or endovascular foreign material), or those with positive FUBC at ≥ 48 hours.
- Blood culture clearance is defined as the point in time when the first negative blood culture is obtained after which no further positive blood cultures for *S. aureus* is documented.
- The day of blood culture clearance should be used as the start date for calculating treatment duration of the bacteremia. In cases where source control occurs after blood culture clearance, the date of focus removal may be counted as the start date of therapy.

Consensus statement for pediatric population

- In pediatric patients with SAB, the panel suggests FUBC be obtained at 48 hours after sampling of the first positive blood culture and then repeated every 24 to 48 hours until negative to document blood culture clearance (consensus).

Remark for the pediatric population

- In collecting FUBC, attention should be given to obtaining appropriate volumes of blood and number of blood culture bottles specific to patient age and weight to optimize sensitivity while minimizing harm. In many young children, one appropriately filled blood culture bottle may provide adequate sensitivity.
- The FUBC strategy should be individualized with consideration of more intensive monitoring (e.g., FUBC every 24 hrs, sampling of 2 sets, negative blood cultures on 2 consecutive days to document clearance) in patients with ongoing signs/symptoms of infection, confirmed or suspected deep focus of infection including musculoskeletal infection, endocarditis or other endovascular focus (e.g., patients with congenital heart disease, intracardiac device or endovascular foreign material), or those with positive FUBC at ≥ 48 hours.
- The day of blood culture clearance should be used as the start date for calculating treatment duration of the bacteremia. In cases where source control occurs after blood culture clearance, the date of focus removal may be counted as the start date of therapy.

Introduction

Background

Follow-up blood cultures (FUBC) are blood cultures obtained after an initial positive blood culture, typically after starting antibiotic therapy. FUBC play a critical role in the management of *Staphylococcus aureus* bacteremia (SAB) by establishing blood culture clearance and identifying patients at increased risk for deep-seated and metastatic foci of infection. While FUBC for SAB are recommended in several guidelines [1, 2], there is considerable variability in practice regarding

sampling frequency, number of sets, and criteria for defining blood culture clearance.[3-5]. This variability, along with the central role of blood cultures as a tool to guide risk stratification and clinical management, highlights the need for a standardized approach to FUBC.

Purpose and specific objectives

This consensus statement was developed in parallel with Consensus Statement 1 to characterize the clinical utility and prognostic significance of FUBC in the management of SAB and to provide guidance on the approach to blood culture sampling and establishing blood culture clearance.

Scope

This consensus statement is intended for use by adult and pediatric healthcare professionals including physicians, advanced practice providers, and pharmacists who care for patients with SAB. The target audience includes but is not limited to infectious diseases specialists, hospitalists, emergency care clinicians, intensivists, and health systems research and policymakers.

Methods

Panel composition

The four chairs of the panel were selected by the leadership of IDSA and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). Twenty-three additional panelists comprised the full panel: Nine from IDSA, 10 from ESCMID, one from the Pediatric Infectious Diseases Society (PIDS), one from the European Society for Paediatric Infectious Diseases (ESPID), one from both IDSA and the Society for Healthcare Epidemiology of America (SHEA), and one from IDSA, the Society of Infectious Diseases Pharmacists (SIDP), and the American Society of Health-System Pharmacists (ASHP). The panel included physicians and pharmacists with expertise in adult and pediatric infectious diseases and microbiology. Panelists were from diverse geographic distributions and years of clinical experience. IDSA staff oversaw all methodological, administrative, and logistical aspects of the guideline. The panel reviewed existing literature and brought in their professional experiences and clinical judgment.

Process

For this question, we selected studies of at least 50 patients with SAB, and which reported clinical outcomes among those with and without FUBC performed. During the initial abstract screening, it became evident that no studies systematically included a comparator group of patients with SAB who did not undergo FUBC. As a result, the inclusion criteria were broadened to encompass studies that either (1) conducted multivariate analyses evaluating the association between positive FUBC and clinically important outcomes, or (2) were considered by the panel to have particularly relevant insights into the role or implementation of FUBC in the management of SAB.

Literature review

A medical librarian (EG) designed the literature searches and Medical Subject Headings (MeSH) terms for Medline (OVID), Embase (OVID), and Cochrane. The formal literature searches were performed in July 2021, July 2023, and January 2025. Searches were limited to studies published in English. We excluded animal studies, conference/meeting abstracts, books/chapters, editorials, or correspondence. Reference lists of related articles and guidelines were reviewed for relevance to supplement the electronic searches. We list in Appendix 1 the search strategies. Title and abstract screening was done by the methodologist (LAK) and verified by two panelists (LS, AJK); full-text screening was done by one panelist (LS) and verified by another (FV).

Consensus statement development

Consensus statements were developed using an iterative, structured process that incorporated input from both topic-specific subgroups and the full multidisciplinary panel. Subgroups drafted preliminary statements based on a comprehensive review of the available literature and expert clinical judgment. The consensus statements were also developed considering the balance of benefits and harms, feasibility, and resource use, while also providing practical advice for implementation and identifying key research gaps. Draft statements were then reviewed and discussed during multiple virtual panel meetings and refined through sequential rounds of asynchronous electronic feedback. Disagreements and areas of limited agreement were systematically identified, documented, and addressed through targeted discussion and revision. Statements were modified iteratively until convergence was achieved. Final consensus for each statement was defined a priori as agreement by >75% of panel members. Consensus statements should be interpreted in the context of evolving evidence and are intended to support, not replace, individualized clinical decision making, while highlighting priorities for future SAB research. Panel members considered whether there was sufficient evidence to support the application of the same guidance to children, or whether available evidence supported development of alternative guidance.

Adults' perspective

Summary of literature review for the adult population

We screened 3,382 titles and abstracts and identified no studies directly comparing outcomes of SAB patients with versus without FUBC. However, our review identified a substantial body of evidence supporting the role of FUBC as an essential tool in the risk stratification as well as the diagnostic and prognostic evaluation of SAB.

Several retrospective studies included sufficient patients without FUBC to allow a limited analysis of how the absence of FUBC impact relapse or mortality. Although these studies are subject to bias—patients with milder illness may be less likely to receive FUBC—these studies generally demonstrate favorable outcomes associated with performance of FUBC [6-8].

Multiple studies have shown that positive FUBC at 48–72 hours are strongly associated with worse outcomes, including SAB-attributable and all-cause mortality. There is some variability in whether this was measured after the first positive blood culture or start of active antibiotic therapy. Key studies and their findings are summarized below [9-13]:

- Minejima 2020 [11]: In 884 North American patients with SAB, when bacteremia duration was considered as a continuous variable in modified Poisson regression analysis, each additional day of bacteremia was associated with an increased 30-day mortality risk by 16% (RR 1.16; 95% CI, 1.10–1.22; $P < .001$).
- Kuehl 2020 [10]: In 987 European patients with SAB, positive blood cultures ≥ 2 days after starting antibiotics was the earliest date associated with a significantly increased 90-day mortality (adjusted HR 1.93; 95% CI, 1.51–2.46; $P < .0001$) and was the timepoint most strongly associated with mortality on bootstrapping analysis.
- Grillo 2022 [13]: In 978 European patients with SAB, positive blood cultures ≥ 2 days after starting antibiotics were associated with increased 30-day mortality on multivariate analysis (adjusted OR 5.67; 95% CI, 3.31–9.69; $P < .001$).
- Papadimitriou-Olivgeris 2023 [12]: In 839 SAB episodes in 779 European patients, positive blood cultures ≥ 48 hours were associated with 28-day mortality after Cox multivariate regression modeling (adjusted OR 1.83; 95% CI, 1.22–2.76; $P = .004$).

- Bae 2024 [9]: In 1936 Southeast Asian patients with SAB, positive blood cultures ≥ 3 days after starting adequate therapy were associated with higher 30-day attributable mortality after competing risk analysis (HR 1.73; 95% CI, 1.31–2.30; $P < .001$).

Positive FUBC at 48–72 hours are also strongly associated with endovascular infection, including infective endocarditis and infected intravascular devices (Supplementary Table 1). Ten studies with more than 100 patients each showed associations between positive FUBC and endocarditis (range of sample sizes: 198–2008; range of OR (95% CI): 1.3 (1.0–1.7) - 45.6 (6.13–339.7)) [13–22].

Similarly, six studies reported associations between positive FUBC and deep-seated or metastatic foci of infection (range of sample size: 127–3147; range of OR (95%CI): 2.4 (1.1–5.4) -6.4 (5.4–19.7)) [22–27]. Additionally, one large study found that positive FUBC after 48–72 hours were associated with relapse post-treatment ($n=18,425$; OR 2.3; 95% CI, 1.9–2.9) [28]. Some studies measured the time to FUBC from the initial blood culture [14–16, 18–20, 24, 26, 28], while others reported from initiation of antibiotic therapy [13] or from appropriate or active antibiotic therapy [17, 21–23, 25, 27].

Intermittent positive and negative FUBC (known as the “skip phenomenon”) have been documented in 4–13% of SAB episodes and have been associated with prolonged bacteremia, confirmed or suspected deep-seated focus of infection including endocarditis, and retained endovascular foreign material (Table 2) [29–34]. While no statistically significant differences in hospital length of stay or mortality have been observed between patients with and without the skip phenomenon, some studies report a trend toward higher mortality [30, 32].

Rationale for the consensus statement of the adult population

Blood cultures are the gold standard for the initial diagnosis of SAB, and FUBC are essential to guide risk stratification in patients with SAB. FUBC are easily integrated into broader diagnostic evaluation for deep-seated or metastatic foci of infection and generally more predictive than most individual risk factors [35]. Positive FUBC ≥ 48 hours are a key prognostic marker that drives further diagnostic evaluation and management decisions, including source control interventions. Similarly, blood culture clearance is an important marker of treatment response while lack of clearance signals the need for additional diagnostic evaluation and/or therapeutic intervention. Because FUBC at 48 hours are central to risk stratification, the panel favored two sets at this specific time point. Consensus was not reached on the optimal number or frequency of subsequent FUBC to confirm blood culture clearance. Practices ranged from a single set every 24 hours to two sets every 24–48 hours. Regarding clearance, some panelists supported two consecutive negative sets collected on different days, while others endorsed one or two negative sets on the same day. Although data are limited, some studies suggest that serial negative blood cultures on 2 separate days are more reliable for predicting clearance compared to a single set [30, 33, 34]. Because intermittent positive and negative blood cultures (“skip phenomenon”) have been associated with prolonged bacteremia, deep-seated foci of infection including endocarditis, or retained endovascular devices, collecting FUBC on at least two different days may be preferable in patients with these scenarios.

Although no definitive evidence establishes the optimal reference point for calculating the duration of antibiotic therapy, most panelists favored using the date of blood culture clearance as start date of the treatment course, aligning with common clinical practice. This approach provides a practical and consistent anchor for calculating treatment duration, helps standardize care, and promotes consistent use of FUBC for risk stratification. While clinical outcomes associated with this practice remain unproven, the panel emphasized the value of consistency in this approach. In some cases,

blood culture clearance may occur prior to a source control procedure to address a deep-seated focus of infection that has a high likelihood of not being controlled by antibiotic therapy alone - in these cases the day of focus removal may be counted as the start date of therapy for that focus of infection (e.g., endocarditis with positive valve tissue cultures at time of surgery). In cases of a superficial focus that undergoes source control (e.g., skin and soft tissue abscess which is incised and drained), the time of blood culture clearance may be counted as the start date of treatment.

Balance of benefits and harm

Potential risks of FUBC include transient anemia, unnecessary antimicrobial treatment triggered by contaminants in blood cultures, and prolonged hospitalization while awaiting blood culture clearance. However, based on the evidence summarized above, the panel concluded that the overall balance of benefits and harms favors performing FUBC until negative to document clearance.

Costs and Feasibility

- Compared to other diagnostic tests, FUBC are low cost and feasible to implement in most settings.
- In lower-resource settings, feasibility may be limited by local phlebotomy or microbiology laboratory capacity and need for transport of blood cultures to regional labs.
- Difficulty obtaining venous access may be a barrier in some patient populations and lead to delayed FUBC.

In the context of SAB, FUBC should be acceptable to most stakeholders and in most care settings where SAB is diagnosed. Additionally, FUBC provide important prognostic and diagnostic information, guide clinical management, and are easily integrated into broader diagnostic evaluation for deep-seated or metastatic foci of infection[35, 36].

Implementation considerations for the adult population

Practical advice

- FUBC should be obtained in any adult with a positive blood culture suspected to be *S. aureus* whether or not antimicrobial therapy has been started.
- The sensitivity of blood cultures for detecting bacteremia is influenced by the volume of blood collected. Underfilled blood culture bottles or only a single blood culture bottle collected instead of a set decreases sensitivity of the testing.
- Because positive FUBC at ≥ 48 hours after the first positive blood culture are central to the risk stratification approach outlined in Consensus Statement 1, and because the sensitivity of 2 blood cultures sets is greater than 1 set, 2 sets of blood cultures should be obtained at 48 hours after sampling of the initial positive blood culture, even if FUBC have been drawn before this time point.
 - FUBC may be obtained earlier than 48 hours after sampling of the first positive blood culture (e.g., at 24 hours) but should not replace repeat cultures at 48 hours.
 - In the event of delayed FUBC collection and documentation of blood culture clearance after 48 hours, an individualized assessment should be made considering time of FUBC collection and clinical response to determine classification of the patient's final diagnosis and guide treatment decisions as outlined in more detail in Consensus Statement 6 and 7.
- Although positive FUBC at ≥ 48 hours are an important predictor of deep-seated or metastatic foci of infection independent of the timing of active antimicrobial therapy,

positive FUBC at ≥ 48 hours of active therapy should raise additional concern for a deep-seated focus of infection and need for source control intervention.

- Tailoring the FUBC strategy to individual clinical scenarios is essential.
 - In patients with scenarios at higher risk of intermittent positive and negative FUBC ("skip phenomenon") including patients with ongoing signs/ symptoms of infection, confirmed or suspected deep-seated focus of infection including endocarditis or other endovascular focus (e.g., intracardiac device or endovascular foreign material), or those with positive FUBC at ≥ 48 hours, negative FUBC on 2 consecutive days may more reliably document clearance.
 - In patients without these scenarios and without concerns for an uncontrolled focus of infection, 2 sets of negative FUBC at 48 hours may be sufficient.
- To improve adherence to the implementation of FUBC, institutions should adopt structured systems to standardize the timing, collection, and interpretation of FUBC. For example:
 - Microbiology laboratories should proactively notify treating clinicians when SAB is first identified, prompting timely FUBC collection.
 - In settings where FUBC in patients with SAB have not been collected, automated reminders or other structures to ensure FUBC collection may support appropriate follow-up.
 - Collaboration between microbiology, phlebotomy services, and infectious diseases consultation teams, when available, can help ensure clear communication and appropriate clinical response to FUBC results.

Barriers

Although FUBC are likely acceptable and feasible, practical challenges may arise in certain settings such as limited phlebotomy or laboratory capacity, or difficulty obtaining venous access in some patient populations. This is highlighted by real-world data indicating that FUBC are inconsistently obtained across clinical settings despite being standard of care [37-40]. Additionally, actions in response to positive FUBC are often variable or poorly defined which may limit impactful implementation. Scarcity of trained infectious disease and medical microbiology providers in certain regions may limit the ability to design and implement the systems needed for consistent implementation of FUBC.

Blood culture systems are highly accurate, with a low false positive rate of 1-2% (typically defined as a positive signal without growth of organisms on terminal subculture) and a low false negative rate of $<1\%$ (typically defined as a negative signal despite organisms growing in terminal subculture) [41]. Nevertheless, higher false positive rates (up to 3%) may be observed due to skin contamination from a peripheral vein during collection with potentially higher rates when sampling from a catheter [36, 42-44]. Prior antibiotic exposure may reduce blood culture growth or extend the time to result and contribute to detection of intermittent bacteremia (e.g., the "skip phenomenon"). While these limitations are uncommon, they also underscore the importance of system-level processes to ensure consistent collection, interpretation, and response to FUBC.

Without systems in place to address these issues, disparities in care may arise between institutions with robust FUBC protocols and those without.

Research needs for the adult population

Several critical questions remain regarding the optimal use of FUBC in adults with SAB, specifically:

- Timing and frequency: The ideal timing and number of FUBC sets needed to reliably document blood culture clearance with acceptable sensitivity have not been established.
- Duration of bacteremia: Research is needed to determine if the duration of bacteremia correlates with specific deep-seated or metastatic foci of infection. Research is also needed to determine whether patients with a long duration of bacteremia (e.g., 7 or 10 days) should have a different diagnostic or therapeutic approach.
- Start date of therapy: Studies should evaluate whether the date of blood culture clearance, date of source control, or date of first appropriate antibiotic should be used to determine start date of therapy including impacts on clinical outcomes and antibiotic stewardship.
- Intermittent positive and negative blood cultures (“skip phenomenon”): Additional investigation is needed to better characterize risk factors for the “skip phenomenon” and to determine the optimal number of negative FUBC to confirm clearance in patients who may be at risk.
- Systems of care: Research is needed to understand the design and implementation of structured systems, including electronic health record systems, which will help support consistent and appropriate FUBC practices.
- Risk Stratification integration: The optimal way to incorporate FUBC in a risk stratification framework remains unclear. Further studies are required to validate the integration of FUBC into the risk stratification framework in Consensus Statement 1.

Pediatrics perspective

Summary of the literature review for the pediatric population

As with adult patients, no studies have examined the impact of FUBC versus no FUBC on clinical outcomes in children with SAB. However, multiple pediatric studies have demonstrated that prolonged SAB—often measured in calendar days of bacteremia—is associated with increased risks of deep-seated foci of infection, metastatic foci, venous thrombosis, and mortality [31, 45-47]. Moreover, positive FUBC [48] in bacteremia with *S. aureus* occur more frequently than in bacteremia with other pathogens, highlighting the potential diagnostic value of FUBC in children with SAB.

While SAB duration in children is typically short (median 1–2 days), [31, 46, 49] even modest prolongation of bacteremia is associated with important clinical findings:

- In a multicenter study of 232 children with MRSA bacteremia, each additional day of bacteremia increased the risk of a composite of mortality or metastatic infection by 50% (95% CI: 26-79%) [46].
- Another multicenter study of 552 pediatric SAB episodes in Australia and New Zealand found that longer SAB duration was independently associated with a composite of mortality, relapse within 90 days, ICU admission, and hospitalization longer than 30 days [49].
- Several studies also link prolonged SAB in children with increased risk of osteoarticular and endovascular infections [31, 45, 47].

A single-center study (n=159) investigated the number of FUBC required to confirm clearance in pediatric patients with SAB [33]. FUBC were drawn daily until clearance was determined; the median number of negative FUBC per child was 2 (IQR 2–3). Intermittent positive and negative blood cultures (“skip phenomenon”) was observed in 4.9% of cases, all with deep-seated infections

like endocarditis or osteomyelitis. Only one child (<1%) had a subsequent positive culture after two consecutive days of negative FUBC. These findings align with adult data, suggesting that positive FUBC in children are strongly associated with serious complications (i.e., deep foci of infection, metastatic infection, and mortality) and support the role of FUBC in pediatric risk stratification.

Rationale for the consensus statement of the pediatric population

Overall, FUBC are a relatively low-cost and potentially high-yield diagnostic tool in children with SAB. Given the strong correlation between the duration of SAB in children and adverse outcomes, the panel suggests obtaining FUBC in all children with SAB to support prognosis and guide diagnostic evaluation. This consensus statement prioritizes the early detection of deep-seated or metastatic foci of infection over concerns about performing unnecessary blood cultures in patients whose bacteremia may already have cleared. The optimal timing of FUBC remain uncertain. Limited evidence suggests that negative FUBC on two consecutive days may reliably predict clearance, although validation studies are needed. Clinicians must remain mindful, however, of the low but non-negligible risk of contamination, the potential for false positive FUBC from skin commensals which may lead to unnecessary testing, treatment changes, and healthcare costs.

Implementation considerations for the pediatric population

Practical advice

- FUBC should be obtained in any child with a positive blood culture suspected to be *S. aureus*, using age- and weight-appropriate blood volumes as recommended by IDSA [50].
- In many young children, one adequately filled blood culture bottle may suffice for diagnostic accuracy as opposed to multiple bottles.
- Given that children typically have shorter durations of SAB than adults, obtaining FUBC earlier than 48 hours after the first positive blood culture was drawn may be appropriate for pragmatic reasons (for example, when other blood samples are being taken), for the convenience of patients, families and practitioners, or to aid management decisions (for example, disposition).
- As in adults, many pediatric clinicians use the first negative culture to mark the start date of effective therapy. In cases in which source control occurs after the date of blood culture clearance, it may be appropriate to consider the date of source control as the start date of therapy. However, the typically short SAB duration in children may reduce the clinical impact of this distinction.

Barriers

- Venipuncture-related anxiety, especially in young children and their caregivers, may limit timely FUBC collection.
- Difficult venous access, particularly in children with medical complexity or multiple prior central lines, can further complicate serial testing.
- Obtaining adequate volumes of blood in very small children may be challenging.

Research needs for the pediatric population

Key pediatric research priorities include:

- Defining the optimal timing, frequency, and number of FUBC needed to confirm clearance in children with SAB.

- Understanding how FUBC results, including intermittently positive cultures, should be incorporated into risk stratification tools tailored to pediatric populations.
- Identifying the clinical and microbiologic parameters associated with delayed clearance of FUBCs. Such information can in turn be used to optimize FUBC practices to individual patient needs.

Limitations

This manuscript was developed using a consensus-based methodology rather than a formal clinical practice guideline process. Although a comprehensive literature review was performed, formal systematic review methods and structured evidence grading were not required. Consensus statements reflect a synthesis of available evidence and expert clinical judgment, particularly in areas where high-quality randomized data and systematic reviews are limited. In this SAB guideline project, where clinical presentations are heterogeneous and many management questions lack definitive trial data, this approach allows translation of imperfect but clinically relevant evidence into practical consensus statements.

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