2026 Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA) and European Society of Clinical Microbiology and Infectious Diseases (ESCMID) on Staphylococcus aureus Bacteremia: Risk Stratification, Diagnostic Evaluation, and Management of Adults and Children

Consensus Statement 2 on Follow-up Blood Cultures in Patients with *Staphylococcus aureus* Bacteremia (SAB)

Author's name	Society	Affiliation
Luke Strnad*	IDSA	Department of Medicine, Division of Infectious Diseases, Oregon Health and Science University (OHSU) and Epidemiology Programs, OHSU/Portland State University School of Public Health; Portland, Oregon, United States
François Vandenesch *	ESCMID	Center for Integrative Research in Infectious diseases and Immunology (CIRI), INSERM U1111, CNRS UMR5308, University of Lyon, ENS Lyon, France
Achim J. Kaasch*	ESCMID	Institute of Medical Microbiology and Hospital Hygiene, Medical Faculty of the Otto von Guericke University Magdeburg, Magdeburg, Germany
J. Chase McNeil	PIDS	Department of Pediatrics, Division of Infectious Diseases, Baylor College of Medicine
Aubrey J. Cunnington	ESPID	Department of Infectious Disease, Section of Paediatric Infectious Disease, and Centre for Paediatrics and Child Health, Imperial College London, London, UK
Marisa Holubar	IDSA	Department of Medicine, Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine; Stanford, California, United States
Bo Shopsin	IDSA	Department of Microbiology and Department of Medicine, Division of Infectious Diseases, NYU Grossman School of Medicine, New York, NY, USA
Cesar Arias	IDSA	Division of Infectious Diseases, Houston Methodist Hospital, Houston, TX, United States; Center for Infectious Diseases, Houston Methodist Research Institute, Houston, TX, United States; Department of Medicine, Weill Cornell Medical College, New York, NY, United States
Thomas Benfield	ESCMID	Department of Infectious Diseases, Copenhagen University Hospital - Amager and Hvidovre, Copenhagen, Denmark
Douglas Black	IDSA	Department of Pharmacy, School of Pharmacy, University of Washington, Seattle, WA, USA

Helen W. Boucher	IDSA	Tufts University and Tufts Medicine, Boston, MA, United States
Vance G. Fowler, Jr.	IDSA	Division of Infectious Diseases, Department of Medicine, Duke University Medical Center, Durham North Carolina USA Duke Clinical Research Institute, Durham, North Carolina, USA
Barbara Hasse	ESCMID	Department of Infectious Diseases and Hospital Epidemiology, University and University Hospital Zurich, Switzerland
Vincent Le Moing	ESCMID	Service des Maladies Infectieuses et Tropicales, CHU de Montpellier
Martin Llewelyn	ESCMID	Department of Global Health and Infection, Brighton and Sussex Medical School, Falmer, East Sussex, UK Department of Infection, University Hospitals Sussex NHS Foundation Trust, Eastern Road, Brighton, UK
Luis Eduardo López Cortés	ESCMID	Infectious Diseases and Microbiology Clinical Unit, University Hospital Virgen Macarena; Department of Medicine, School of Medicine, University of Sevilla; and Biomedicine Institute of Sevilla (IBiS)/CSIC, Seville, Spain. Centro de Investigación en Red de Enfermedades Infecciosas (CIBERINFEC), Instituto de Salud Carlos III, Madrid, Spain
Loren G. Miller	IDSA	Division of Infectious Diseases, Harbor-UCLA Medical Center and the Lundquist Institute at Harbor-UCLA Medical Center, Torrance, CA and the University of California, Los Angeles, Los Angeles, CA
Mical Paul	ESCMID	Infectious Diseases Division, Rambam Health Care Campus, Haifa, Israel The Ruth and Bruce Rappaport Faculty of Medicine, Technion - Israel Institute of Technology, Haifa, Israel
Kyle J. Popovich	IDSA, SHEA	Division of Infectious Diseases Rush University Medical Center, Chicago, IL
Siegbert Rieg	ESCMID	Department of Internal Medicine II, Division of Infectious Diseases, Medical Centre - University of Freiburg, Faculty of Medicine, Freiburg, Germany
Mark E. Rupp	IDSA	Department of Medicine, Division of Infectious Diseases, University of Nebraska Medical Center, Omaha, Nebraska, USA.
Marc H. Scheetz	IDSA	Departments of Pharmacy Practice and Pharmacology, Pharmacometrics Center of

		Excellence, Colleges of Pharmacy and Graduate Studies, Midwestern University, Downers Grove, IL, United States
Alex Soriano	ESCMID	Department of Infectious Diseases, Hospital Clínic of Barcelona, Barcelona, Spain. IDIBAPS, Barcelona, Spain Centro de Investigación en Red de Enfermedades Infecciosas (CIBERINFEC), Instituto de Salud Carlos III, Madrid, Spain
Steven Y.C. Tong	ESCMID	Victorian Infectious Diseases Service, The Royal Melbourne Hospital, at the Peter Doherty Institute for Infection and Immunity, Melbourne, Australia Department of Infectious Diseases, The University of Melbourne at the Peter Doherty Institute for Infection and Immunity, Melbourne, Australia
Winfried V. Kern [+]	ESCMID	Department of Internal Medicine II, Division of Infectious Diseases, Medical Centre - University of Freiburg, Faculty of Medicine, Freiburg, Germany
Catherine Liu[+]	IDSA	Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Center and Division of Allergy and Infectious Diseases, University of Washington, Seattle, Washington
Henry F. Chambers [+]	IDSA	Division of Infectious Diseases, Zuckerberg San Francisco General Hospital, University of California, San Francisco
Lara A. Kahale [+]	IDSA	Clinical Affairs and Practice Guidelines, Infectious Diseases Society of America, Arlington, Virginia, USA

*****Contributed equally as first authors

[+]Contributed equally as last authors

Correspondence: Catherine Liu, Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Center and Division of Allergy and Infectious Diseases, University of Washington, Seattle, Washington**,** practiceguidelines@idsociety.org

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.

Acknowledgments

We would like to acknowledge the contributions of Elena Guadagno, medical librarian, for the creation and execution of question-specific literature searches. We thank Loretta Dzanya and Senam Attipoe for the project coordination. We would also like to acknowledge the following organizations and selected reviewers for providing constructive feedback on the draft manuscript: American Society of Health-System Pharmacists (ASHP), ESCMID, Pediatric Infectious Diseases Society (PIDS), Society for Healthcare Epidemiology of America (SHEA), Society of Infectious Diseases Pharmacists (SIDP), Stan Deresinski, Robert Krause, Andre Kalil, and Justin Searns. The panel also acknowledges the contributions of the Standards and Practice Guidelines Subcommittee.

Luke Strnad (manuscript and subgroup co-lead), François Vandenesch (manuscript co-lead and co-chair at ESCMID), Achim J. Kaasch (manuscript and subgroup co-lead), Bo Shopsin, and Marisa Holubar contributed to screening, data abstraction, conception and design of the analysis, interpretation of data, revision, and final approval of the consensus statement and manuscript. Aubrey Cunnington and J. Chase McNeil served as clinical leads for the pediatrics section and contributed to data abstraction, interpretation of data, revision, and final approval of the consensus statement and manuscript. Catherine Liu (panel chair at IDSA), Henry F. Chambers (co-chair at IDSA), Winfried V. Kern (co-chair at ESCMID), and François Vandenesch (co-chair at ESCMID) oversaw and guided the whole process of consensus statement development and contributed to the interpretation of the data, revision and final approval of the consensus statement and manuscript. Remaining panelists contributed to the interpretation of data, drafting, revision, and final approval of the consensus statement and manuscript. Lara A. Kahale, the current methodologist, contributed to project management, screening, data interpretation, guiding the panel through the drafting of the consensus statement, and drafting the manuscript and supplementary files. Nigar Sekercioglu, the former methodologist was responsible for project management, screening, designing, and supporting the panel through the process.

Disclaimer*:* It is important to recognize that guidelines cannot always account for individual variation among patients. They are assessments of current scientific and clinical information

provided as an educational service; are not continually updated and may not reflect the most recent evidence (new evidence may emerge between the time information is drafted and when it is published or read); should not be considered inclusive of all proper methods of care, or as a statement of the standard of care; do not mandate any course of medical care; and are not intended to supplant clinician judgment with respect to particular patients or situations. Whether to follow guidelines and to what extent is voluntary, with the ultimate determination regarding their application to be made by the clinician in the light of each patient's individual circumstances. While IDSA makes every effort to present accurate, complete, and reliable information, these guidelines are presented "as is" without any warranty, either express or implied. IDSA (and its officers, directors, members, employees, and agents) assume no responsibility for any loss, damage, or claim with respect to any liabilities, including direct, special, indirect, or consequential damages, incurred in connection with these guidelines or reliance on the information presented.

Additional Information: More detailed information on the analysis and development of consensus statements is available in the Supplemental Materials document.

Funding: This guideline has been funded and supported by the Infectious Diseases Society of America.

References

1. Liu, C., et al., *Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children: executive summary.* Clin Infect Dis, 2011. **52**(3): p. 285-92.
2. South Australian expert Advisory Group on Antimicrobial Resistance (SAAGAR), *Staphylococcus aureus Bacteraemia Management Clinical Guideline.* 2023.
3. Liu, C., et al., *Clinical practice variation among adult infectious disease physicians in the management of Staphylococcus aureus bacteremia.* Clinical Infectious Diseases, 2019. **69**(3): p. 530-533.
4. Wood, J.B., et al., *Practice Patterns of Providers for the Management of Staphylococcus aureus Bacteremia in Children: Results of an Emerging Infections Network Survey.* J Pediatric Infect Dis Soc, 2018. **7**(3): p. e152-e155.
5. Westgeest, A.C., et al., *Global Differences in the Management of Staphylococcus aureus Bacteremia: No International Standard of Care.* Clin Infect Dis, 2023. **77**(8): p. 1092-1101.
6. Escrihuela-Vidal, F., et al., *Impact of adherence to individual quality-of-care indicators on the prognosis of bloodstream infection due to Staphylococcus aureus: a prospective observational multicentre cohort.* Clin Microbiol Infect, 2023. **29**(4): p. 498-505.
7. Kim, T., et al., *Clinical significance of follow-up blood culture in patients with a single Staphylococcus aureus-positive blood culture.* Infect Dis (Lond), 2020. **52**(3): p. 207-212.

8. Schenidt Bispo da Silva, S.C., et al., *Pharmacist-led antimicrobial stewardship program in the treatment of Staphylococcus aureus bacteraemia in paediatric patients: a multivariate analysis.* Infect Prev Pract, 2024. **6**(4): p. 100419.
9. Bae, S., et al., *Risk Factors for Infection-Attributable Mortality in Patients With Staphylococcus aureus Bacteremia: A Competing Risk Analysis.* Open Forum Infect Dis, 2025. **12**(1): p. ofae734.
10. Kuehl, R., et al., *Defining persistent Staphylococcus aureus bacteraemia: secondary analysis of a prospective cohort study.* Lancet Infect Dis, 2020. **20**(12): p. 1409-1417.
11. Minejima, E., et al., *Defining the Breakpoint Duration of Staphylococcus aureus Bacteremia Predictive of Poor Outcomes.* Clin Infect Dis, 2020. **70**(4): p. 566-573.
12. Papadimitriou-Olivgeris, M., et al., *Predictors of mortality of Staphylococcus aureus bacteremia among patients hospitalized in a Swiss University Hospital and the role of early source control; a retrospective cohort study.* Eur J Clin Microbiol Infect Dis, 2023. **42**(3): p. 347-357.
13. Grillo, S., et al., *Bloodstream infection and endocarditis caused by Staphylococcus aureus in patients with cancer: a multicenter cohort study.* Infectious Diseases and Therapy, 2022: p. 1-12.
14. Palraj, B.R., et al., *Predicting Risk of Endocarditis Using a Clinical Tool (PREDICT): Scoring System to Guide Use of Echocardiography in the Management of Staphylococcus aureus Bacteremia.* Clinical Infectious Diseases, 2015. **61**(1): p. 18-28.
15. Tubiana, S., et al., *The VIRSTA score, a prediction score to estimate risk of infective endocarditis and determine priority for echocardiography in patients with Staphylococcus aureus bacteremia.* J Infect, 2016. **72**(5): p. 544-53.
16. Finkelstein, R., et al., *Incidence and risk factors for endocarditis among patients with health care-associated Staphylococcus aureus bacteraemia.* Scandinavian Journal of Infectious Diseases, 2012. **44**(12): p. 934-940.
17. Hill, E.E., et al., *Risk factors for infective endocarditis and outcome of patients with Staphylococcus aureus bacteremia.* Mayo Clin Proc, 2007. **82**(10): p. 1165-9.
18. Papadimitriou-Olivgeris, M., et al., *The LAUsanne STAPHylococcus aureus ENdocarditis (LAUSTAPHEN) score: a prediction score to estimate initial risk for infective endocarditis in patients with S. aureus bacteremia.* Frontiers in cardiovascular medicine, 2022. **9**: p. 961579.
19. Gow, N., et al., *The role of echocardiography in Staphylococcus aureus bacteraemia at Auckland City Hospital.* NZ Med J, 2015. **128**(1416): p. 28-35.
20. Longobardo, L., et al., *Risk assessment for infected endocarditis in Staphylococcus aureus bacteremia patients: when is transesophageal echocardiography needed?* European Heart Journal: Acute Cardiovascular Care, 2019. **8**(5): p. 476-484.
21. Chang, F.-Y., et al., *Staphylococcus aureus bacteremia: recurrence and the impact of antibiotic treatment in a prospective multicenter study.* Medicine, 2003. **82**(5): p. 333-339.
22. Gallego Rodriguez, A., et al., *Risk factors for mortality and complications in peripheral venous catheter-associated Staphylococcus aureus bacteraemia: a large multicentre cohort study.* J Hosp Infect, 2024. **152**: p. 13-20.
23. Perez, M.G., et al., *Risk factors for the appearance of secondary foci of infection in children with community-acquired Staphylococcus aureus bacteraemia. Cohort study 2010–2016.* Enfermedades infecciosas y microbiologia clinica (English ed.), 2018. **36**(8): p. 493-497.
24. Wang, X., et al., *Inappropriate empirical antibiotic therapy was an independent risk factor of pediatric persistent S. aureus bloodstream infection.* European Journal of Pediatrics, 2023. **182**(2): p. 719-729.
25. Gasch, O., et al., *Lack of association between genotypes and haematogenous seeding infections in a large cohort of patients with methicillin-resistant S taphylococcus aureus bacteraemia from 21 S panish hospitals.* Clinical Microbiology and Infection, 2014. **20**(4): p. 361-367.

26. Kim, T., et al., *Validation of a new risk stratification system-based management for methicillin-resistant Staphylococcus aureus bacteraemia: analysis of a multicentre prospective study.* European Journal of Clinical Microbiology & Infectious Diseases, 2024. **43**(5): p. 841-851.
27. Kinamon, T., et al., *Risk Factors and Outcomes of Hematogenous Vertebral Osteomyelitis in Patients With Staphylococcus aureus Bacteremia.* Clin Infect Dis, 2023. **77**(9): p. 1226-1233.
28. Albertson, J., et al., *Determination of risk factors for recurrent methicillin-resistant Staphylococcus aureus bacteremia in a Veterans Affairs healthcare system population.* infection control & hospital epidemiology, 2015. **36**(5): p. 543-549.
29. Stewart, J.D., et al., *Intermittent Negative Blood Cultures in Staphylococcus aureus Bacteremia; a Retrospective Study of 1071 Episodes.* Open Forum Infect Dis, 2019. **6**(12): p. ofz494.
30. Fiala, J., et al., *Is a single set of negative blood cultures sufficient to ensure clearance of bloodstream infection in patients with Staphylococcus aureus bacteremia? The skip phenomenon.* Infection, 2019. **47**(6): p. 1047-1053.
31. Cardenas-Comfort, C., et al., *Follow-up Blood Cultures in Children With Staphylococcus aureus Bacteremia.* Pediatrics, 2020. **146**(6).
32. Go, J.R., et al., *The skip phenomenon in Staphylococcus aureus bacteremia: clinical implications.* Diagn Microbiol Infect Dis, 2022. **104**(4): p. 115802.
33. Jang, S., et al., *Clinical Implications of the Skip Phenomenon in Patients with Persistent Staphylococcus aureus Bacteremia.* Microb Drug Resist, 2025. **31**(1): p. 21-25.
34. Van Goethem, S., et al., *Follow-up blood cultures in Staphylococcus aureus bacteremia: a probability-based optimization.* Eur J Clin Microbiol Infect Dis, 2022. **41**(10): p. 1263-1268.
35. van der Vaart, T.W., et al., *The utility of risk factors to define complicated Staphylococcus aureus bacteremia in a setting with low methicillin-resistant S. aureus prevalence.* Clinical Infectious Diseases, 2024. **78**(4): p. 846-854.
36. Dargere, S., H. Cormier, and R. Verdon, *Contaminants in blood cultures: importance, implications, interpretation and prevention.* Clin Microbiol Infect, 2018. **24**(9): p. 964-969.
37. Ariaans, M.B., et al., *Increased overall survival after introduction of structured bedside consultation in Staphylococcus aureus bacteraemia.* European Journal of Clinical Microbiology & Infectious Diseases, 2018. **37**: p. 1187-1193.
38. Joost, I., et al., *Staphylococcus aureus bacteremia in patients with rheumatoid arthritis–Data from the prospective INSTINCT cohort.* Journal of Infection, 2017. **74**(6): p. 575-584.
39. Kim, C.-J., et al., *Impact of antimicrobial treatment duration on outcome of Staphylococcus aureus bacteraemia: a cohort study.* Clinical Microbiology and Infection, 2019. **25**(6): p. 723-732.
40. Strömdahl, M., et al., *Time to Staphylococcus aureus blood culture positivity as a risk marker of infective endocarditis: a retrospective cohort study.* Clinical Infectious Diseases, 2025. **80**(4): p. 727-734.
41. Seifert, H., et al., *MiQ 3a: Blutkulturdiagnostik Sepsis, Endokarditis, Katheterinfektionen, Teil I*, in*:*. 2007, Elsevier, Urban & Fischer.
42. Wilson ML, M.M., Morris A. , *Principles and Procedures for Blood Cultures; Approved Guideline.* 2007. **27**(17).
43. Doern, G.V., et al., *Practical guidance for clinical microbiology laboratories: a comprehensive update on the problem of blood culture contamination and a discussion of methods for addressing the problem.* Clinical microbiology reviews, 2019. **33**(1): p. 10.1128/cmr. 00009-19.
44. Snyder, S.R., et al., *Effectiveness of practices to reduce blood culture contamination: a Laboratory Medicine Best Practices systematic review and meta-analysis.* Clinical biochemistry, 2012. **45**(13-14): p. 999-1011.

45. Bui, R., et al., *The Utilization Of Echocardiography In Children With Staphylococcus aureus Bacteremia.* Journal of the Pediatric Infectious Diseases Society, 2024: p. piae089.
46. Hamdy, R.F., et al., *Epidemiology of Methicillin-Resistant Staphylococcus aureus Bacteremia in Children.* Pediatrics, 2017. **139**(6).
47. Thornley, E.M., et al., *Risk Factors for Persistent Staphylococcus aureus Bacteremia in Children.* Pediatr Infect Dis J, 2024. **43**(11): p. 1040-1045.
48. Puthawala, C.M., et al., *Persistent bloodstream infection in children: examining the role for repeat blood cultures.* J Clin Microbiol, 2024. **62**(11): p. e0099824.
49. Campbell, A.J., et al., *Pediatric Staphylococcus aureus Bacteremia: Clinical Spectrum and Predictors of Poor Outcome.* Clin Infect Dis, 2022. **74**(4): p. 604-613.
50. Miller, J.M., et al., *A Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2018 Update by the Infectious Diseases Society of America and the American Society for Microbiology.* Clin Infect Dis, 2018. **67**(6): p. e1-e94.