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

## Executive Summary on Risk Stratification, Diagnostic Evaluation, and Management of *Staphylococcus aureus* Bacteremia


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## Background

*Staphylococcus aureus* bacteremia (SAB) is a common and complex infection that causes significant morbidity due to its frequent association with deep-seated and metastatic foci of infection. Globally, *S. aureus* is the leading cause of death from bloodstream infection [1]; all-cause 30-day mortality rates range from 15-30% with higher mortality among patients with methicillin-resistant *S. aureus* (MRSA) bacteremia [2-5]. The burden of SAB is increasing in some regions [6, 7] and is further

compounded by growing patient complexity, including increased use of implantable prosthetic devices [8].

The spectrum of disease manifestations in SAB is broad and varies widely in severity, ranging from localized, skin and soft tissue infection (e.g. cellulitis, furuncle) to disseminated infection with multiple metastatic foci. Patients can present with a myriad of clinical syndromes associated with deep-seated foci of infection, examples of which include endocarditis, cardiac device infection, septic thrombophlebitis, osteoarticular infections, pneumonia, and deep tissue abscesses (e.g. epidural, psoas, hepatic, splenic, or renal).

The current paradigm of defining SAB as "complicated" or "uncomplicated" is limited by inconsistent definitions and oversimplification of a complex and heterogeneous disease that is dynamic with an evolving clinical course. Risk factors for complicated SAB are often regarded as having an established diagnosis of deep-seated or metastatic infection, despite low to moderate predictive value which can lead to misclassification and unnecessary prolonged antibiotic use [9]. On the other hand, metastatic seeding may be occult at initial presentation in up to one third of patients [10, 11], and failure to detect these clinically silent foci can result in erroneous labeling as "uncomplicated" SAB and inadequate therapy [11]. As delayed or inadequate source control is strongly associated with poor outcomes such as persistent bacteremia and mortality [5, 12, 13], investigation for deep-seated and metastatic foci of infection is critical.

An alternative framework is needed to guide the diagnostic evaluation and management of SAB that is individualized according to clinical presentation and risk factors for deep-seated and metastatic foci. Additionally, the diagnostic evaluation and management of SAB should be guided by ongoing reassessment of disease evolution and modified accordingly based on a precise clinical diagnosis.

**Scope**

The overall scope of the SAB guideline project (including current and future publications) includes (1) a risk stratification-based approach to evaluation of patients with SAB (2) diagnostic evaluation of SAB; and (3) management of SAB including antibiotic selection and duration of therapy. Available evidence for adults and children with SAB were reviewed and consensus statements developed.

The scope of the current manuscripts includes seven consensus statements focused on risk stratification, diagnostic evaluation (e.g., follow-up blood cultures, echocardiography, [18F]FDG-PET/CT), and duration of therapy. Future manuscripts will address the management of MRSA and methicillin-susceptible *S. aureus* (MSSA) bacteremia.

This guideline project 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, clinical microbiologists, hospitalists, emergency care clinicians, intensivists, and health systems research and policymakers.

**Methods**

This group of clinical questions (1 through 7) of the SAB guideline project was developed as consensus statements rather than following the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology. Infectious Disease Society of America (IDSA) guideline panels develop consensus statements when clinical questions are not optimally structured in PICO format or when there are limited direct comparative data informing those questions. For this guideline project, this was the case despite the comprehensive literature search that was conducted in three databases. The clinically important questions in domains such as risk stratification, follow-up blood cultures, diagnostic evaluation, and duration could not be easily

structured in a PICO format and direct comparative data for populations of interest were limited. The consensus statements were developed considering the balance of benefits and harms, feasibility, and resource use, while also providing practical advice for implementation and identifying key research gaps.

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. 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.

Clinical questions were initially developed with a focus on adult patients. Panelists with expertise in pediatric infectious diseases evaluated the degree to which posed questions could be applied to children and reviewed the relevant pediatric literature when available. Panel members considered whether there was sufficient evidence to support the application of the same consensus statement to children or whether available evidence supported an alternative consensus statement. Each consensus statement is divided into sections containing guidance for adults and children.

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.

## Framework for Risk Stratification and Diagnostic Evaluation and Management of SAB

A risk stratification framework (Consensus Statement 1, Figure 1) is suggested for adult patients that offers a more nuanced and adaptive approach than the terms “complicated” versus “uncomplicated”. Furthermore, it accounts for the heterogeneity and evolving clinical course of SAB. This framework uses a stepwise approach to initially stratify patients as either “low risk” or “increased risk” of deep-seated or metastatic foci of infection and relapse. Diagnostic evaluation leads to a final diagnosis of SAB with or without deep-seated or metastatic foci and ultimately guides treatment decisions. This risk-informed approach stresses the importance of appropriate diagnostic evaluation, minimizing the risk of missed occult infectious foci while avoiding unnecessary prolonged antibiotic exposure in patients without confirmed deep-seated or metastatic foci of infection. The initial evaluation of patients with SAB should include a detailed history of illness and physical exam to assess for risk factors and signs and symptoms of deep-seated or metastatic foci of infection [14], follow-up blood cultures and transthoracic

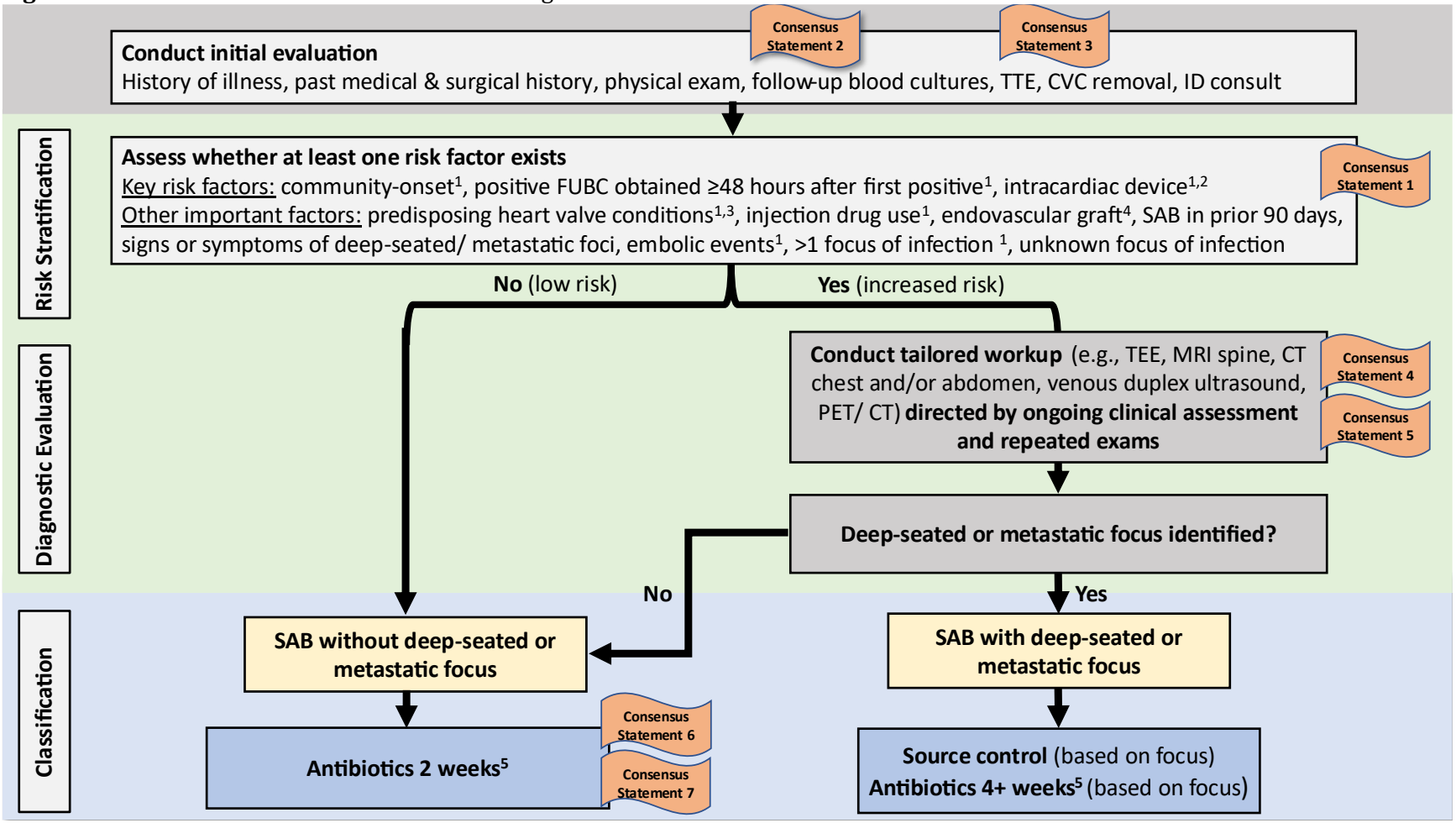
echocardiography (TTE). Prompt removal of central venous catheters is recommended as delayed removal is associated with increased risk of hematogenous complications and relapse [15, 16]. Infectious disease consultation is strongly encouraged to guide diagnostic evaluation and management [17-19].

As detailed in Consensus Statement 1, the panel identified 3 key risk factors consistently associated with increased risk of infection of deep tissue, metastatic foci, or relapse in adults and highlights several other important factors while acknowledging that additional risk factors may exist. Patients classified as low-risk SAB have no risk factors or signs of deep-seated or metastatic foci of infection based on clinical assessment and initial diagnostic evaluation including follow-up blood cultures (Consensus Statement 2) and transthoracic echocardiography (TTE) (Consensus Statement 3). Patients with increased-risk SAB have at least one risk factor. It is important to note that risk exists along a continuum, is dynamic, and may evolve over the course of the patient's care. For example, a patient initially classified as low-risk SAB may be later determined to have increased risk SAB. Thus, ongoing clinical evaluation and repeat physical exams are essential components of risk assessment.

The intensity of the diagnostic evaluation should be guided by risk assessment. While adult patients who are stratified as having low-risk SAB may not require additional evaluation beyond follow-up blood cultures and TTE, patients with increased-risk SAB should have tailored workup directed by patient-specific characteristics, ongoing clinical assessment and repeated exams. Patients with multiple risk factors and persistently positive blood cultures may require more extensive diagnostic evaluation than someone with a single risk factor. A risk-stratified approach to transesophageal echocardiography (TEE) among patients with a negative TTE is provided, taking into consideration the quality and interpretability of TTE, and anticipated impact of TEE findings on management (Consensus Statement 4). Additionally, the guidelines address the potential role of whole-body imaging (e.g. [18F]FDG-PET/CT) in patients with increased risk SAB with an unknown focus after appropriate initial evaluation (Consensus Statement 5).

Establishing a diagnosis of SAB with or without deep-seated or metastatic foci of infection is a critical step to guide duration of therapy and need for source control interventions. Timely source control is associated with earlier clearance of bacteremia and improved mortality [12] and is an essential component in the management of patients with SAB. Consensus Statement 6 suggests a 14-day treatment duration in patients who are stratified as low-risk SAB and classified as without evidence of deep-seated or metastatic foci of infection. Consensus Statement 7 addresses duration of therapy in patients stratified as increased-risk SAB but classified as without evidence of deep-seated or metastatic foci of infection. In such cases, patients with increased-risk SAB can receive 14 days of therapy if there is resolution of signs and symptoms of infection and tailored diagnostic evaluation and ongoing clinical assessment does not reveal a deep-seated or metastatic focus of infection. The panel outlines several scenarios in which longer treatment durations should be considered, particularly when infection cannot be definitively excluded despite a thorough diagnostic evaluation and concern for deep-seated infection remains high. A table of definitions used throughout these guidelines is included in the end of this manuscript and the Supplementary Material of each consensus statement manuscript.

**Figure 1**. Framework for Risk Stratification and Diagnostic Evaluation of SAB in Adult Patients




*Disclaimer: The listed risk factors are based on a review of the literature and expert opinion and do not represent an exhaustive or comprehensive list of all risk factors associated with increased risk SAB.*

**Figure 1.** Framework for Risk Stratification and Diagnostic Evaluation of *Staphylococcus aureus* bacteremia (SAB) in Adult Patients. This framework outlines the approach to risk stratification, diagnostic evaluation, and classification of adult patients into a final diagnosis of SAB with or without deep-seated or metastatic foci. It uses a stepwise approach to guide appropriate diagnostic evaluation, minimizing

the risk of missed occult infectious foci while avoiding unnecessary prolonged antibiotic exposure in patients without confirmed deep-seated or metastatic foci of infection. An initial evaluation is performed in all patients with SAB that enables patients to be stratified into "low-risk" or "increased-risk" SAB. Patients stratified as "increased risk" will undergo tailored diagnostic evaluation based on clinical findings (e.g., symptom/exam-directed imaging) and individual patient characteristics. Due to the dynamic nature of SAB, ongoing clinical assessment is necessary to guide diagnostic evaluation. This approach ultimately supports appropriate classification of patients into a final diagnosis of SAB with or without a deep-seated or metastatic foci of infection enabling treatment decisions to be tailored accordingly. Please refer to Consensus Statements (indicated by flags) for additional detail.

***Footnotes***

***Abbreviations:*** *CT: Computed Tomography; CVC: central venous catheter; DVT: deep vein thrombosis; FUBC: follow-up blood cultures; ID: infectious diseases; MRI: magnetic resonance imaging; PET/CT: Positron Emission Tomography/Computed Tomography; SAB: Staphylococcus aureus bacteremia; TEE: transesophageal echocardiography; TTE: transthoracic echocardiography.*

*[1]Endocarditis increased-risk features for endocarditis: presence of an intracardiac device[2], predisposing heart valve conditions,[3] positive blood culture obtained ≥48 hours after the first positive blood culture, embolic events, more than one non-contiguous focus of infection, community-onset SAB, injection drug use.*

*[2]Intracardiac device: prosthetic heart valve, permanent pacemaker, automatic implantable cardioverter-defibrillator, left ventricular assist device.*

*[3]Predisposing heart valve conditions as defined by 2023 Duke-ISCVID criteria [20].*

*[4]Endovascular graft: synthetic bypass graft in the vessel wall.*

*[5]Longer durations of therapy, guided by the likely focus, may be appropriate in select scenarios (e.g., retained intracardiac device, recently placed endovascular graft, DVT at central venous catheter site), particularly in the setting of prolonged bacteremia, or if diagnostic testing is incomplete or indeterminate. In these situations, reassessment of source control should also be considered.*

**Consensus Statements and Remarks**

**Risk Stratification**

**Clinical Question 1:** In patients with SAB, which risk factors are associated with deep-seated or metastatic foci of infection (e.g., infective endocarditis, osteomyelitis, deep tissue abscess, septic thrombophlebitis, cardiac device-associated infection, septic arthritis,) or relapse of infection?

**Consensus statements for the adult population**

- The panel suggests stratification based on risk factors associated with deep-seated or metastatic foci of infection or relapse of infection and ongoing clinical assessment to guide the diagnostic evaluation, and treatment plan (Figure 1) (consensus).
- Because individual risk factors lack sufficient negative predictive value to exclude deep-seated or metastatic foci of infection, the panel suggests a risk stratification approach using:
    - Key risk factors consistently associated with deep-seated or metastatic foci of infection or relapse of infection: (1) community-onset SAB (2) positive blood culture obtained ≥48 hours after the first positive blood culture, and (3) presence of an intracardiac device **AND**
    - Other important risk factors: predisposing heart valve conditions, injection drug use, endovascular graft, SAB in prior 90 days, signs or symptoms of a deep-seated or metastatic focus of infection, embolic events, more than one non-contiguous focus of infection, and unknown focus (consensus).

**Remarks for the adult population**

- Risk stratification promotes appropriate diagnostic evaluation, enabling classification of patients into SAB with and without deep-seated or metastatic foci of infection. This approach guides individualized patient management decisions including source control interventions, antibiotic choice, and duration of therapy. It aims to establish greater precision in diagnosis to avoid both undertreatment and overtreatment.
- The terms “uncomplicated” and “complicated” SAB are subjective, imprecise, and inadequate to guide management. The panel suggests using terms that refer to the risk of a specific adverse outcome, i.e., “low risk” or “increased risk” of deep-seated or metastatic foci of infection or relapse of infection.
- Validation of the risk stratification framework is needed.

**Consensus statements for the pediatric population**

- The panel suggests that all children with SAB are evaluated for a deep-seated focus of infection (consensus).
- Data are insufficient to define a group of children with SAB who are at low risk of deep-seated or metastatic foci of infection or relapsed bacteremia (consensus).

**Remarks for the pediatric population**

- There are age-related differences in the epidemiology and pathophysiology of SAB and comorbidities, which make it unclear to what extent outcomes and risk factors identified in studies focusing on adults can be directly applied to pediatric practice.
- Children with SAB usually have a clinically or diagnostically identifiable focus of infection, most commonly a musculoskeletal source in community-onset infections.

- Neonates with SAB are less likely to have a focus of infection while also having a higher rate of endocarditis; such patients should be considered separately from older children. The observed higher risk of endocarditis in neonates/premature infants may be at least partly attributable to other comorbidities and/or the need for invasive procedures.
- In all children with SAB, a symptom- and history-based approach to evaluation for the source of bacteremia is warranted.
- Positive blood cultures obtained ≥48 hours after the first positive blood culture may be associated with the presence of deep-seated or metastatic foci of infection (e.g., osteomyelitis, endocarditis, septic thrombophlebitis).

**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.

**Diagnostic Evaluation**

**Clinical question 3:** Should a transthoracic echocardiogram (TTE) be performed in all patients with SAB?

**Consensus statement for the adult population**
- The panel suggests routinely performing TTE in all adults with SAB, since the panel could not identify criteria to clearly define a population at very low risk of infective endocarditis (consensus).

**Remarks for the adult population**
- Although there may exist a group of adult patients with SAB at very low risk of endocarditis for whom TTE may be unnecessary, criteria to define such a population have not been consistently established. As endocarditis is a serious complication among adults with SAB and TTE is non-invasive, minimal risk procedure, decisions to forego TTE in this population should be carefully considered.

**Consensus statement for the pediatric population**
- TTE should be routinely performed in children with SAB who have structural heart disease, prolonged bacteremia, or signs and symptoms suggestive of endocarditis, but may be omitted in the absence of such factors and with low suspicion for endocarditis (consensus).

**Remark for the pediatric population**
- The risk of endocarditis in neonates with SAB may be greater than in older children and requires separate consideration.

**Clinical question 4:** In patients with SAB and a negative TTE, should a transesophageal echocardiogram (TEE) be performed?

**Consensus statements for the adult population**
- The panel suggests performing TEE in adults with SAB who have a negative TTE, even if the TTE is of good quality if any of the following endocarditis increased-risk features are present:
    - Intracardiac device (e.g., prosthetic heart valve, permanent pacemaker, automatic implantable cardioverter-defibrillator, left ventricular assist device)
    - Predisposing heart valve conditions including prior endocarditis
    - Positive follow-up blood cultures≥ 48 hours after the first positive blood culture
    - Embolic events
    - More than one non-contiguous focus of infection (consensus)
- The panel suggests consideration of TEE in adults with SAB with community-onset or injection drug use as an endocarditis increased-risk feature. The decision to perform TEE should be guided by TTE quality and interpretability, presence of other endocarditis

increased-risk features, clinical response, and anticipated impact on management (consensus).
- The panel suggests that TEE may be unnecessary in adults with SAB who have a negative good quality TTE and are without any endocarditis increased-risk features as outlined in below Remarks and Consensus Statement 1 (consensus).

**Remarks for the adult population**
- Features associated with an increased risk of endocarditis include any of the following (Consensus Statement 1):
    - Intracardiac device (e.g., prosthetic heart valve, permanent pacemaker, automatic implantable cardioverter-defibrillator, left ventricular assist device)
    - Predisposing heart valve conditions, including prior endocarditis
    - Positive blood cultures obtained ≥ 48 hours after the first positive blood culture
    - Embolic events
    - More than one non-contiguous focus of infection
    - Community-onset SAB
    - Injection drug use
- There is variability in the literature regarding which patients can be safely classified as low risk for endocarditis who may not require TEE. Clinical prediction scores may help inform the decision to omit TEE but should not replace clinician judgment.

**Consensus statements for the pediatric population**
- The panel suggests not performing TEE in most pediatric patients with SAB and good quality TTE images. TEE has limited additional diagnostic utility over TTE for exclusion of endocarditis in most young children (consensus).
- TEE should be considered in pediatric patients when TTE is negative or indeterminate AND there is high clinical suspicion of endocarditis (consensus).

**Remarks for the pediatric population**
- TEE has limited additional diagnostic utility over TTE for exclusion of endocarditis in most young children.
- Decisions regarding the performance of TEE in children must consider risks associated with the procedure and anesthesia, as well as the size and age of the patient and the availability of experienced personnel. Close consultation with pediatric cardiologists is recommended.

**Clinical question 5:** In patients with *Staphylococcus aureus* bacteremia (SAB) at increased risk for deep-seated or metastatic foci of infection and with an unknown focus after appropriate initial evaluation, should whole-body imaging (e.g., [18F]FDG-PET/CT) be performed?

**Consensus statements for the adult population**
- In adult patients with SAB at increased risk for deep-seated or metastatic foci of infection and with an unknown focus after appropriate initial evaluation, the panel suggests performing either:
    - Whole-body imaging (WBI) (e.g., [18F]FDG-PET/CT) **OR**
    - Combinations of imaging modalities (e.g., thoracic/ abdominal CT, duplex venous ultrasound, etc.) that evaluate the most likely sites of infectious foci (consensus)

**Remarks for the adult population**

- This consensus statement assumes initial diagnostic evaluation including follow-up blood cultures, echocardiography, and symptom/exam-directed imaging (e.g., MRI spine in patient with back pain) has been performed based on risk stratification and as clinically indicated. Please refer to the Executive Summary and Consensus Statements 1, 2, 3, and 4 for additional details regarding risk stratification and diagnostic evaluation.
- Key risk factors for deep-seated or metastatic foci of infection include (1) community-onset, (2) positive blood culture obtained ≥48 hours after the index positive blood culture, and (3) intracardiac device. Please refer to Consensus Statement 1 for additional risk factors.
- Existing evidence for whole-body imaging in the diagnostic evaluation of SAB is limited to observational studies of [18F]FDG-PET/CT, which suggest [18F]FDG-PET/CT may enable earlier detection of occult infectious foci and can inform subsequent treatment modifications. Knowledge gaps exist including:
    - Impact of [18F]FDG-PET/CT on outcomes such as mortality and relapse of infection when compared to symptom/exam-directed imaging or multimodal imaging approaches (e.g., combinations of imaging modalities that evaluate the most likely sites of infectious foci)
- Decisions regarding imaging approach should be guided by the patient's clinical condition and availability of each imaging modality.

**Consensus statement for the pediatric population**

- In pediatric patients with SAB without a focus after appropriate initial evaluation, whole-body imaging (e.g., [18F]FDG-PET/CT or other modality or combination of modalities) should be considered in carefully selected situations (e.g., ongoing SAB and no identifiable focus despite targeted evaluation) (consensus).

**Remarks for the pediatric population**

- It is relatively rare for children to have clinically unsuspected foci of infection associated with SAB.
- Decisions about the choice of imaging in infants and children should be made based on patient age, size, comorbidities, current clinical condition, and availability of each imaging modality.
- There is insufficient evidence to recommend whole-body imaging using [18F]FDG-PET/CT over a combination of other imaging modalities that evaluate the most likely sites of infectious foci. Whole-body imaging using [18F]FDG-PET/CT should be considered in select pediatric patients with SAB if other diagnostic evaluation is unrevealing, taking into consideration the availability of resources.
- Neonates and very young infants in particular have potential for wide dissemination of disease and may require a more cautious approach. Consideration of whole-body imaging may be warranted in neonates with persistent SAB as resources and clinical condition allow.

## Duration of Therapy

**Clinical question 6:** Should patients stratified as low-risk SAB and classified as without deep-seated or metastatic foci of infection after diagnostic evaluation receive antibiotic therapy for 14 days, less than 14 days, or more than 14 days?

**Consensus statement for the adult population**

- In adult patients stratified as low-risk SAB and classified as without deep-seated or metastatic foci of infection after diagnostic evaluation, the panel suggests an antibiotic treatment duration of 14 days rather than longer or shorter courses (consensus).

**Remarks for the adult population**

- The criteria for SAB at low risk of deep-seated or metastatic foci of infection or relapse of infection are defined in Consensus Statement 1.
- This consensus statement assumes that follow-up blood cultures are collected at 48 hours of sampling of the first positive blood culture, and that blood culture clearance is documented as outlined in Consensus Statement 2.
- 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 statements for the pediatric population**

- Data are insufficient to define a population of pediatric patients with SAB who have a low risk of deep-seated or metastatic foci of infection or relapse of infection (consensus).
- In otherwise healthy pediatric patients with SAB and no evidence of deep-seated or metastatic foci of infection after appropriate evaluation, the panel suggests an antibiotic duration of 14 days (consensus).

**Remarks for the pediatric population**

- This consensus statement assumes that follow-up blood cultures are collected at 48 hours of sampling of the first positive blood culture, and that blood culture clearance is documented as outlined in Consensus Statement 2.
- 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.

**Clinical question 7:** Should patients stratified as increased-risk SAB but classified as without deep-seated or metastatic foci of infection after diagnostic evaluation receive antibiotic treatment of 14 days or longer?

**Consensus statement for the adult population**

- In adult patients stratified as increased-risk SAB but classified as without deep-seated or metastatic foci of infection after diagnostic evaluation, the panel suggests antibiotic treatment for 14 days (consensus).

**Remarks for the adult population**

- The criteria for stratification as increased-risk of deep-seated or metastatic foci of infection or relapse of infection are defined in Consensus Statement 1.
- Positive blood cultures obtained ≥ 48 hours after the first positive blood culture is the most robust predictor of adverse outcomes, suggests lack of source control and should prompt additional diagnostic evaluation for deep-seated or metastatic foci of infection. Given this, >14 days of antibiotic therapy should be considered in select patients with prolonged bacteremia especially if the diagnostic evaluation is incomplete or of limited quality.
- 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 the pediatric population**

- In pediatric patients with SAB without deep-seated or metastatic foci of infection after diagnostic evaluation, the panel suggests antibiotic treatment for 14 days (consensus).

**Remarks for the pediatric population**

- There are no established criteria to identify children with increased-risk SAB. Important considerations for risk stratification of children and neonates are noted in Consensus Statement 1.
- Studies informing the optimal duration of therapy in children with SAB are lacking.
- In children with SAB who are at risk for endovascular infection (e.g., congenital heart disease, thrombi, or positive blood cultures obtained ≥ 48 hours after the first positive blood culture) but with a negative diagnostic evaluation, longer than 14 days of therapy may need to be considered, especially if the diagnostic evaluation is incomplete or of limited quality.
- 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.

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**Possible conflicts of interest (COI)**

Evaluation of relationships as potential conflicts of interest is determined by a review process. The assessment of disclosed relationships for possible COIs is based on the relative weight of the financial relationship (i.e., monetary amount) and the relevance of the relationship (i.e., the degree to which an association might reasonably be interpreted by an independent observer as related to the topic or recommendation of consideration).

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**Additional information.** The rationale for each recommendation or consensus statement is detailed in each individual manuscript. More detailed information is available in each manuscript's Supplementary material.

**Table 1:** List of definitions and comments*

| Term | Definitions and comments |
|---|---|
| Disease definition | |
| *Staphylococcus aureus* bacteremia (SAB) | The presence of *S. aureus* in the bloodstream, due to an infectious process. *S. aureus* is rarely a blood culture contaminant. |
| Bacteremic *Staphylococcus (S.) aureus* infection | Most accurate description of the disease. |
| *S. aureus* bloodstream infection (SAB, SABSI, SABI) | Common shorthand for bacteremic *S. aureus* infection. |
| Patient with SAB | Any patient with ≥1 positive blood culture for *S. aureus* due to infection. |
| Start of infection | |
| Onset of bacteremia | The timepoint when the first blood culture positive with *S. aureus* was drawn (recognizing that bacteremia may have been present before its collection). |
| Clinical onset of SAB | The time point when the first clinical symptoms caused by SAB began. |
| Hospital-onset SAB | Onset of bacteremia (first positive blood culture) at ≥48 hours after hospital admission.<br><br>Delayed recognition of community-onset infection may be misclassified as hospital-onset (e.g., no blood cultures drawn until day four of the hospitalization). |
| Community-onset SAB | Onset of bacteremia (first positive blood culture) at <48 hours of admission or before hospitalization.<br><br>Community-acquired SAB is an alternative term, but its use is discouraged. It may be used to differentiate between "community-onset SAB without healthcare-association" (i.e., community-acquired SAB) and "community-onset with healthcare-association". |
| Community-onset SAB with healthcare association | Community-onset SAB with recent healthcare exposure (e.g., attending dialysis clinic, intravenous therapy, wound care, recent hospitalization, nursing home).<br><br>This patient population is exposed to risks associated with healthcare settings (e.g., venous catheters). |
| Site of infection | |
| Portal of entry | The site where *S. aureus* first enters the body.<br><br>An infection is often established at the site of barrier crossing, e.g., a skin and soft tissue infection, a respiratory infection, and, less frequently, a urinary tract infection. However, infection may or may not |

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| | be present at the portal of entry, and in many cases, the portal of entry is unknown. In some cases, direct inoculation of deeper tissues occurs (e.g., trauma, surgery). |
| Infective focus | Body site or device with active infection. Several infective foci can be present.<br>Alternative: "focus of infection". |
| Source of infection | Sometimes used interchangeably with "infective focus" but sometimes used as a synonym for "portal of entry". These other terms are generally preferred due to greater precision. |
| Deep-seated focus of infection | Serious complication of SAB that includes a non-cutaneous and non-intravenous line-associated site of S. aureus infection of deep tissues or infection in sites or organs (e.g., endocarditis, osteomyelitis, splenic abscess, psoas abscess, septic thrombophlebitis, cardiac device-associated infection). |
| Embolic event | Embolic events are a result of dislodgement and travel of fragments of potentially infected material (e.g., thrombus) from a primary infection site through the bloodstream to distant sites, causing infarction or secondary sites of infection. Some examples may include septic embolic to the lungs, cerebral emboli, splenic or renal infarcts and peripheral manifestations such as Janeway lesions and splinter hemorrhages. |
| Metastatic seeding | The process of spreading through the bloodstream to form distant foci of infection. |
| Metastatic focus | Infectious focus that has arisen through metastatic seeding.<br><br>The term implies that there is another primary site or portal of entry (known or unknown) distinct from the metastatic focus from which bacteria have seeded. This term is often used when several foci are present and a sequence of events is likely (e.g., endocarditis with splenic metastatic foci).<br>"Secondary focus" is an alternative term. |
| Primary focus | Original site of infection from which bacteria have seeded.<br><br>In practice, the sequence of events cannot always be determined, and the primary focus may not be known. |
| Contiguous spread | Extension of the infection from an infective focus to adjacent tissues. |
| Superficial focus of infection | Localized, surface-level infection (e.g., skin-soft-tissue infections, cutaneous abscesses, or catheter-related infections). |
| Dominant focus | Focus requiring the longest or most complex treatment when multiple infective foci are present. |
| Classification | |
| Primary bacteremia | A microbiologically documented bloodstream infection without a known source (including an intravenous or arterial line infection).<br><br>The term is most often used when data on the infective focus is not collected, mainly in epidemiological studies. The use of the term is discouraged outside of epidemiological studies. |
| Secondary bacteremia | A local infection leading to bacteremia (e.g., bacteremic skin and soft tissue infection). |

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| | Easily confused with secondary focus; therefore, use is discouraged. |
| Complicated SAB | SAB with infection of deep tissues or organs (e.g., endocarditis and other endovascular structures, osteomyelitis, septic arthritis, myositis, kidney, deep tissue planes), relapse, or infection-related mortality.<br><br>Definitions vary, and the use of this term is discouraged. |
| Uncomplicated SAB | Superficial/removable source with no deep-seated infection, relapse, or infection-related mortality.<br><br>Definitions vary, and the use of this term is discouraged. |
| Low-risk SAB | SAB with no risk factors or signs of deep tissues or metastatic foci of infection (including endocarditis) or relapse. |
| Increased-risk SAB | SAB with at least one risk factor for infection of deep tissues, metastatic foci, or relapse (see Consensus Statement 1). |
| Predisposing heart valve conditions | Previous history of endocarditis, prosthetic valve, previous valve repair, congenital heart disease, more than mild regurgitation or stenosis of any etiology, endovascular intracardiac implantable electronic device, hypertrophic obstructive cardiomyopathy. Refer to 2023 Duke-ISCVID criteria for additional details [20]. |
| Disease Course | |
| Central venous catheter-related infection | SAB that arises from, or is directly associated with, a central venous catheter.<br><br>Diagnosis is usually posed when the same *S. aureus* isolate (based on antibiotic susceptibility) is identified in one of the following scenarios:<br>• Present in both a peripheral blood culture and the catheter tip culture, **or**<br>• Present in both a blood culture and a pus or skin swab from the catheter exit site, **or**<br>• Present in two initial blood cultures—one drawn from a peripheral site and the other through the catheter—with a differential time to positivity (DTTP) of at least 120 minutes (i.e., the catheter-drawn culture becomes positive at least 120 minutes earlier than the peripheral culture), **and**<br>• No other plausible source of infection is identified.<br>Strong clinical suspicion for catheter-related infection: Cultures not obtained, but signs such as pus, redness, pain at exit/tunneled site, or chills during infusion, with no other plausible source. |
| Central-line associated bloodstream infection (CLABSI) | Laboratory confirmed bloodstream infection that develops in a patient with a central line (>48h in place) and the infection is not related to another site of infection. The term CLABSI was designed primarily for surveillance purposes and should not be used to classify clinical diagnoses of SAB. The term CLABSI is non-specific, and surveillance criteria do not clearly characterize the role of the CVC. Thus, patients identified as having a CLABSI may not meet clinical criteria for CVC-related infections. |
| Source control | An intervention to eliminate or control a focus of *S. aureus* infection that would be unlikely to respond to antibiotic therapy alone and would increase risk for ongoing sepsis, spread of infection, or relapse. |

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| | Examples include removal of central line or implanted device, incision and drainage of a skin abscess, interventional drainage of a liver abscess, surgical debridement of an epidural abscess, amputation of an infected diabetic foot, and surgical valve replacement for a perivalvular abscess. |
| Recurrence | Denotes relapse or re-infection. |
| Relapse or relapsed bacteremia | Return of *S. aureus* infection due to unresolved initial infection.<br><br>Often defined as occurring after completion of a course of therapy. Most relapses occur within 90 days after index infection. |
| Re-infection | Another episode *of S. aureus* infection (bacteremic or not) independent from the initial episode of the infection.<br><br>It can be distinguished from relapse by whole-genome sequencing or other genetic markers when these differ between the two isolates. However, same-strain re-infections can occur, e.g., because of colonization. Most recurrences occur more than 90 days after the index infection. |
| Diagnostics | |
| Blood culture set | One aerobic and one anaerobic blood culture bottle from a single draw. |
| Follow-up blood culture | Blood culture drawn after an initial positive blood culture to monitor the duration of blood culture positivity and document the timing of blood culture clearance. |
| Blood culture clearance | Day of sampling of the first negative blood culture after which there are no positive blood cultures with *S. aureus*.<br><br>The date of blood culture clearance is typically sed as a start date for counting the duration of antibiotic therapy (see Consensus Statement 2 for additional details). |
| Time-to-positivity (TTP) | Incubation time of a blood culture for sufficient growth to be detected as "positive" in the blood culture instrument. When several bottles (e.g., aerobic and anaerobic blood culture bottles) are incubated, the shortest time is considered the TTP. TTP is used to calculate the differential time-to-positivity (DTTP) which is used to define CVC-related bloodstream infections (see above). |
| Skip phenomenon | Intermittent blood culture positivity (i.e., negative follow-up blood cultures followed by positive).<br><br>The consecutive blood cultures need to be closely spaced and early in the course of infection to distinguish from relapse (see Consensus Statement 2). |

*The terms defined here reflect both their usage in the literature and the panel's assessment of their appropriateness. This table is intended to promote a shared vocabulary for future research and to guide consistent terminology. It also serves an educational purpose by providing definitions for terms that may be unfamiliar to some but are useful for accurately describing study characteristics.

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