2026 Consensus Statements 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

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

Author's name	Society	Affiliation
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
Winfried V. Kern*	ESCMID	Department of Internal Medicine II, Division of Infectious Diseases, Medical Centre - University of Freiburg, Faculty of Medicine, Freiburg, Germany
François Vandenesch*	ESCMID	Center for Integrative Research in Infectious diseases and Immunology (CIRI), INSERM U1111, CNRS UMR5308, University of Lyon, ENS Lyon, France
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, Hvidovre, Denmark; Department of Clinical Medicine, University of Copenhagen, 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
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
Vance G. Fowler, Jr.	IDSA	Division of Infectious Diseases, Department of Medicine, Duke University Medical Center

		Durham, NC, United States Duke Clinical Research Institute, Duke University, Durham, NC, United States
Barbara Hasse	ESCMID	Department of Infectious Diseases and Hospital Epidemiology, University and University Hospital Zurich, Switzerland
Marisa Holubar	IDSA	Department of Medicine, Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine; Stanford, California, United States
Achim J. Kaasch	ESCMID	Institute of Medical Microbiology and Hospital Hygiene, Medical Faculty of the Otto von Guericke University Magdeburg, Magdeburg, Germany
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
J. Chase McNeil	PIDS	Department of Pediatrics, Division of Infectious Diseases, Baylor College of Medicine, Houston, TX, USA
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, SIDP, ASHP	Departments of Pharmacy Practice and Pharmacology, Pharmacometrics Center of Excellence, Colleges of Pharmacy and Graduate Studies, Midwestern University, Downers Grove, IL, 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
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
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
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
Lara A. Kahale	IDSA	Clinical Affairs and Practice Guidelines, Infectious Diseases Society of America, Arlington, Virginia, USA

*Contributed equally as first 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

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 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.

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.

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.

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].

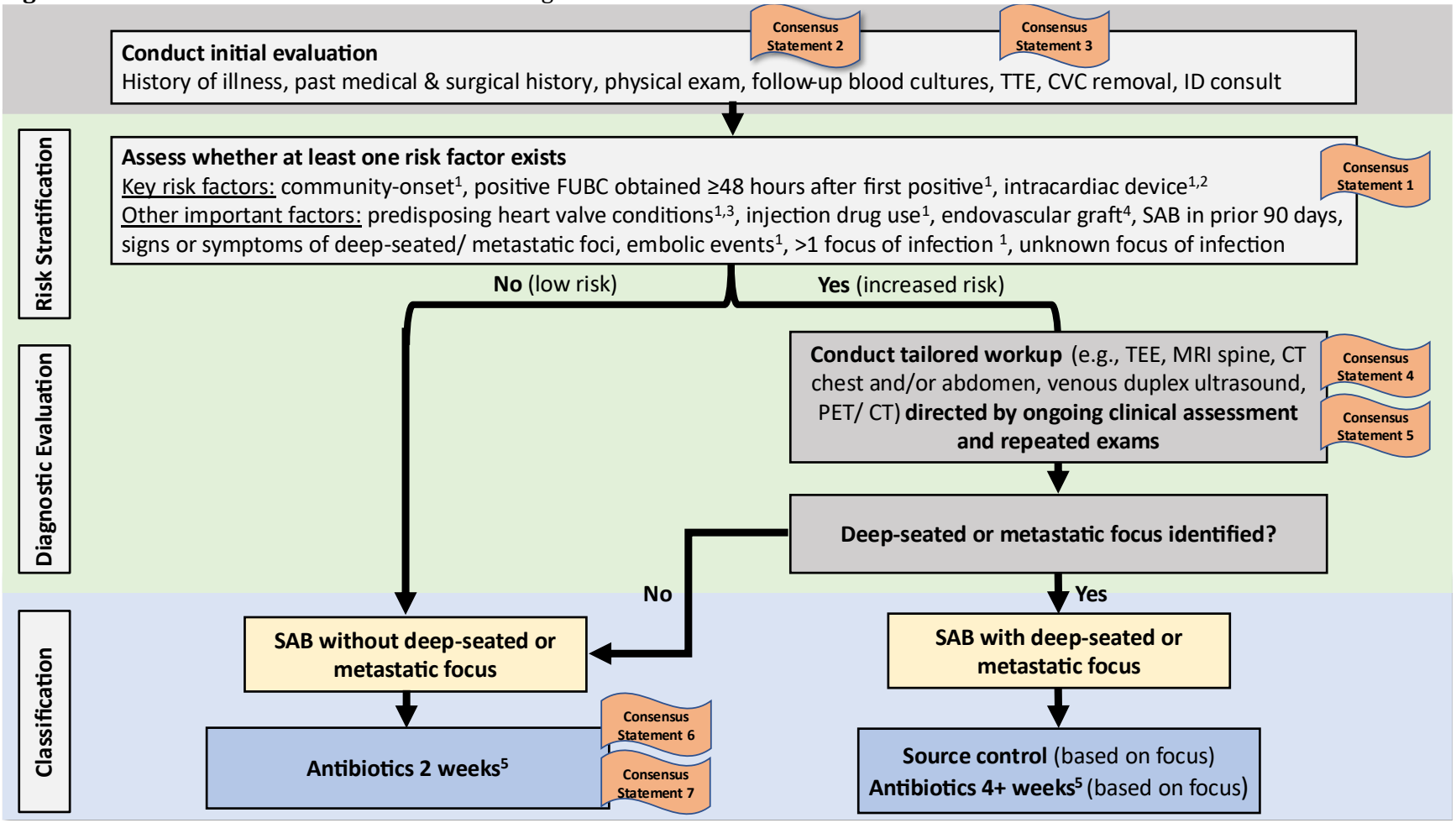
Infectious disease consultation is strongly encouraged to guide diagnostic evaluation and management [17-19].

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.

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.

For this first group of the seven guideline questions, Catherine Liu (panel chair at IDSA), Henry F. Chambers (co-chair at IDSA), François Vandenesch (co-chair at ESCMID), and Winfried V. Kern (co-chair at ESCMID) oversaw and guided the whole process of consensus statement development. Achim J. Kaasch, Luke Strnad, Marisa Holubar, Bo Shopsin, and Francois Vandenesch served in the subgroup for the adult sections for questions 1, 2, 6 and 7. Catherine Liu, Vincent Le Moing, Alex Soriano, Vance G. Fowler, and Loren G. Miller served in the subgroup for the adult sections for questions 3, 4, and 5. Aubrey Cunnington and J. Chase McNeil served as clinical leads for the pediatrics section for all questions. 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. The remaining panelists contributed to the interpretation of data, drafting, revision, and final approval of each consensus statement and manuscript. The entire panel was involved in the development of clinical questions, discussions of the literature, drafting of recommendations or consensus statements, and editing of the manuscripts.

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 the Infectious Diseases Society of America (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. The guidelines represent the proprietary and copyrighted property of IDSA. All rights reserved. No part of these guidelines may be reproduced, distributed, or transmitted in any form or by any means, including photocopying, recording, or other electronic or mechanical methods, without the prior written permission of IDSA. Permission is granted to physicians and health care providers solely to copy and use the guidelines in their professional practices and clinical decision making. No license or permission is granted to any person or entity, and prior written authorization by IDSA is required to sell, distribute, or modify the guidelines, or to make derivative works of or incorporate the guidelines into any product, including, but not limited to, clinical decision support software or any other software product. Except for the permission granted above, any person or entity desiring to use the guidelines in any way must contact IDSA for approval in accordance with the terms and conditions of third-party use, in particular any use of the guidelines in any software product.

Financial support.

This work was supported by the Infectious Diseases Society of America.

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).

The panelists have reported the following disclosures with the indicated companies: **C.A.A.** Serves as a writer for UptoDate and editor in Chief for AAC for the American Society for Microbiology; is named as inventor of a patent application (# 64/002,464); has received a researched grant from Entasis Pharmaceuticals; has served as a standing member of the Microbiology and Infectious Diseases Study Section and Chair of AIRT (Anti-infective Resistance and Targets) with NIH/NIAID; served as a member of the Physician Scientist Development Committee for the American Society for Clinical Investigation and the Anti-infective Pipeline Panel for the World Health Organization. The following relationships were divested prior to joining the panel: Promotional (non-CME) Speakers Bureau for Pfizer, The Medecins Company, Merck, and Actavis; research grants from Merck, The Medecins Company, Actavis, Theravance and MeMed Diagnostics; and advisor for Merck, Theravance, and Bayer Global. **D.B.** serves as an editor for Sanford Guide. **T.B.** serves as a research consultant for MSD and Pfizer; receives an honorarium from GSK; receives research funding from Simonsen Foundation; has received honoraria from Pfizer and Gilead Sciences; has served as an advisor for GSK, Abbvie, Astra Zeneca, Boehring Ingelheim, Janssen, Pfizer, Gilead, MSD, Moderna,

Shionogi; and has received research funding from Medimmune, Innovationsfonden, National Institutes of Allergy and Infectious Diseases, Aarhaus University, Denmark, Roche, Novartis, Bavarian Nordic, Jannsen, MSD, CSL Seqirus, Simonsens Foundation, Gilead, and Lundbeck Foundation. **H.W.B.** serves as an editor for Sanford Guide; serves as Editor, ID Clinics of North America for Elsevier; receives a research grant from NIH's ARLG; has served as an advisor for Actelion, Merck, Cardeas; received remuneration from ABIM and ASM; has received honoraria from NIH and Elsevier; has provided expert testimony for CRICO; has served as Member and Chair, Board of Trustees for Physicians of Tufts Medical Center and College of Holy Cross; and has served as Member of the ID Test Committee and Member and of the ID Board for the American Board of Internal Medicine; and has served as Editor, AAC for ASM. **A.J.C.** receives research funding from NIHR, CARB-X, and UKRI; serves on Conference Organizing Committee and has served as the Chair of Committee for Scientific Affairs and Awards for the European Society for Paediatric Infectious Disease; has served on Conference Organizing Committee for the European Congress on Tropical Medicine and International Health; has received research funding from the European Commission, UK Research and Innovation, European and Developing Countries Clinical Trials Partnership, EU Horizon 2020, and Rosetrees Trust; spouse is a former employee of GlaxoSmithKline. **V.F.** serves as a research consultant for GSK, Akagera, AstraZeneca, and Armata; serves as a research advisor for Basilea and Debiopharm; receives a grant through Duke/DCRI from Basilea, from Exponential Deep Examination // Research of Technologies and Biophotonics, Ltd., AstraZeneca, Contrafect, Merck, Karius, Janssen, and NIH; receives royalties from UpToDate; stock options from Valanbio; patent pending sepsis diagnostic; has served as an advisor for Pfizer, Truis/Cubist/Merck, Novartis, Defined Healthcare Research, Insyght; has served as a consultant for LEK and Novadigm; received research grants from Cubist/Merck, Cerexa/Forest/Actavis/Allergan, Genentech, Medimmune, Medimmune, Advanced Liquid Logic; has coauthored chapters in UptoDate; and has served as an contact PI for an NIH leadership group. **M.H.** serves as a writer for UptoDate; and has received project funding from the World Health Organization. **A.J.K.** receives research funding from the Federal Ministry of Research, Technology and Space (BMFTR), from Ministerium für Wissenschaft, Energie Klimaschutz und Umwelt des Landes Sachsen-Anhalt (MWU); has served as a scientific consultant for the German Center for Infection Research (DZIF), for Staatskanzlei des Landes Sachsen-Anhalt, and Institut für Medizinische und Pharmazeutische Prüfungsfragen (IMPP); has received payments for lectures byLandesärztekammer Sachsen-Anhalt, Donau University Krems, Austria, Limbach Group, Deutsche Gesellschaft für Infektiologie (DGI), and AMEOS KH Labor GmbH; has received research grants from Deutsche Forschungsgemeinschaft (DFG) and served as site principal investigator in clinical studies funded by the European Union; has served as Chairperson for the German Sepsis Society (DSG). **W.V.K.** has received research funding from Baden-Württemberg Federal State Ministry of Science and Art, MSD, BMS, Janssen, Gilead, ViiV; has received honoraria from Gilead; has served as a consultant for Roche, Stiftung Warentest; has received an organizational benefit from Akademie für Infektionsmedzin; and has served as programme director and chair for ESCMID. **V.LM.** has served as a marketing consultant for Sanofi Aventis and Advanz; has served as a research advisor for Pfizer; has received sponsorship from Advanz Pharma; has received funding from ANRS and French Ministry of Health; has served as a scientific advisor for Advanz Pharma; and has served as a marketing advisor for Gilead. **C.L.** receives research funding from SNIPR Biome; has served as a member of an independent efficacy

adjudication committee for Theravance and clinical events committee for DCRI/ ARLG; and has received research funding from NIAID/NIH, Pfizer, University of Queensland, Houston Methodist Hospital, and Johns Hopkins University. **M.J.L.** receives research funding from National Institute for Health Research (NIHR) (UK); has served as an advisor for Genentech; has received remuneration from Pfizer; has served as a research consultant for Infectopharm and Astellas; has served as a member of NIHR Clinical Research Network; and has received research funding from NIHR Research Healthcare Technology Appraisal Panel (UK), Medical Research Council, Joint Programme Initiative on Antimicrobial Resistance, and ESCMID. **E.L.C.** has participated with the Promotional (non-CME) Speakers Bureau for Merck Sharp and Dohme and Angellini; has served as an advisor for Angellini, Glaxosmithkline, Gilead, Correvio, ViiV Healthcare, Merck, Sharp and Dohme, and Menarini; has received research funding from IDIBELL and Instituto de Salud Carols III (Ministry of Health, Social Services and Equality, University of Cologne, Deustschland, and JPI-EC-AMR Joint Transnational, CIDARA; has received an honorarium and other remuneration from Merck Sharp and Dohme; and has served as a consultant for Correvio and Angellini. **J.C.M.** receives research funding from Merck; receives royalties from Up To Date; and has received research funding from Nabriva Therapeutics, NIH, AHRQ, and Allergan. **L.M.** receives research funding from Paratek and Armata; has received research funding from ContraFect, NIH, CDC, AHRQ, GSK, Merck; and has received remuneration from Cepheid, Xbio, Theravance, Gilead, Acchaogen, GSK, and Genentech. **M.P.** serves as editor for ESCMID; receives academic funding from ERANET JPIAMR; has received a research grant through Rambam Health Care Campus from Pfizer; has received academic funding from H2020-JTI-IMI2-2017, IMI, EU, 7th FP, The Israel National Institute for Health Policy Research, Israel Ministry of Science, Israel Science Foundation, the European Commission, Shionogi, and Israel Ministry of Health. **K.J.P.** receives research funding from NIH; has served as a member of the Society for Healthcare Epidemiology of America; has served as a member of CDC/American Hospital Association/Health Research and Educational Trust and SHEA/CDC; and has received research funding from NIAID and CDC. **S.R.** receives honoraria for lectures from Akademie für Infektionsmedizin, Med Update GmbH, streamedup! GmbH, Forum für medizinische Fortbildung, Meet The Experts Academy, Deutscher Apotheker-Verlag, Deutsches Beratungszentrum für Hygiene, Pfizer, bioMériux, GSK, and Falk Foundation; serves as an elected member of the Steering Committee of The German Society for Infectious Diseases (DGI); has served on the Promotional (non-CME) Speakers Bureau for MSD and Pfizer; has received remuneration from Astellas, Falk Foundation, MedUpdate GmbH; has served as an Executive Committee member of the German Infectious Diseases Society; has received research funding from DLR/Innovationsfonds GBA, BMBF, the Federal Ministry of Education and Research, from the German Research Foundation and the European Union, and from University Medical Center Freiburg; and has received honoraria from Dt. Apotheker-Verlag, Deutsches Beratungszentrum für Hygiene, and Paul-Ehrlich Society for Chemotherapy. **M.R.** serves as a content reviewer for UptoDate and DynaMedex; serves as a member of the scientific advisory board for Citius Pharmaceuticals; serves on an editorial board for a SHEA journal (ASHE); has served as a consultant for XBiotech, CR Bard, 3M, Teleflex, Allecra, and Medpace; has received research funding from Magnolia, ContraFect, NIH/DCRI; and was a liaison to CDC for SHEA. **M.S.** receives lecture honoraria from various universities; serves as chair of advisory board for DoseMe; receives research grants from NIH/FDA, University of Pennsylvania, and University of Michigan; serves on the Board of Directors with the American College of Clinical

Pharmacy; serves as Associate Editor for International Journal of Antimicrobial Agents; is a co-owner of SafeGate Therepeutics, LLC; and owns a patent; has provided expert testimony for Chambless, Higdon, Richardson, Katz & Griggs, LLP, for Hall, Booth, Smith, P.C., for Reminger Co., L.P.A., and for Taylor, English, Duma, LLP; has served as a legal consultant for Duke ARLG, Chambless, Higdon, Richardson, Katz& Griggs, LLP, for Hall, Booth, Smith, P.C., and for Reminger Co., L.P.A.; has served as a consultant or advisor for Innoviva, Abbvie, Guidepoint Global, Roche, Spero, Seikagaku Corporation, Meitheal Pharmaceuticals, Inc., Chattem, Inc., Xellia, Duke/ARLG, ARK, Cidara, Third Pole Therapeutics, F2G, Merck, Takeda, Nevakar, Achaogen, Paratek, Bayer, SuperTrans Medical, University of Michigan, Premier Healthcare Solutions, iFAST, DoseMe, Inc, Lykos Therapeutics; has received research funding from Cystic Fibrosis Foundation, Allecra, Nevakar, Hauser, DHHS/FDA/OAGS/DAO, NIAID, Midwestern University Intramural, Cubist Pharmaceuticals, Illinois Department of healthcare, CARE Foundation, International Institute for Nanotechnology Seed Project; received remuneration from NIH, ASHP, SuperTrans Medical, Cystic Fibrosis Foundation, Taylor, English, Duma, LLP, Allecra, Merck, SIGA Technologies, CARE Foundation, Astellas, Allergan, UIC, Premier Inc.; and has received honoraria from St. Jude, Monash University, SHEA, Roosevelt University, ACCP, MAD-ID, NIH, University of Cincinnati. **A.S.** serves on the Promotional (non-CME) Speakers Bureau for Shionogi, Menarini, and Pfizer; receives research funding from Gilead and Advance Pharma; has served as a research and marketing advisor for Pfizer; has served as a research consultant for Pfizer and Advance Pharma; has served on the Promotional (non-CME) Speakers Bureau for Merk Sharp and Dohme, Angelini, Novartis, and Gilead; has received research funding from Fondos de Investigación Sanitari, Gilead, and Pfizer; and has served on the Promotional (non-CME) Speakers Bureau for Gilead. **B.S.** receives funding from Analog Devices; has served on the advisory board for Basilia Pharmaceutica; has served on the advisory board for MicroGenDx; has served as a panel member for ARLG; has received research grants from NIAID and DARPA; and has served as a consultant for Pfizer and Regeneron. **L.S.** has received research funding from NID/NIAID/DMID. **H.C.**'s spouse has stocks in Merck; has stock in Moderna; serves on a Data Safety Monitoring Board for Merck; serves as a consultant for GSK; receives funding from NIH; serves as an editor of the Sanford Guide to Antimicrobial Therapy; has served as a past editor on Antimicrobial Agents and Chemotherapy with ASM; receives research funding from NIH/NIAID; has provided expert testimony for Lilly and Nexus; had stock in Merck; has served as an advisor to TAXIS, Theravance, Allergan, Anacor, Genetech, Cempras, and Quorum; has received past research funding from NIH, Allergan, The Medicine Company, and Genentech. **S.Y.C.T.** serves as a research advisor for AstraZeneca; receives research funding from NHMRC and NIH; receives royalties from UpToDate; has served as an advisor for Roivant; has served as a member of ESCMID; has received research funding from BHP, Minderoo, Macquarie Group, Pratt Foundation, NHMRC, and MRFF; has served as a member of an expert writing group for Therapeutic Guidelines: Antibiotic; and has served as a steering committee member for WikiGuidelines. **F.V.** serves as co-funder and medical director of Weezion; receives funding from the French National Research Agency; and has received research funding from bioMérieux, European community, FINOVI Foundation, Boaster Technology Research Agency, and Ministry of Health.

No disclosures were reported from **B.H.**

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. 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. 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). 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. 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

	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. 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 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. 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). "Secondary focus" is an alternative term.
Primary focus	Original site of infection from which bacteria have seeded. 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). 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). 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. 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. 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. Diagnosis is usually posed when the same *S. aureus* isolate (based on antibiotic susceptibility) is identified in one of the following scenarios: • Present in both a peripheral blood culture and the catheter tip culture, **or** • Present in both a blood culture and a pus or skin swab from the catheter exit site, **or** • 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** • No other plausible source of infection is identified. 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.

	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. 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. 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*. 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). 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.

References

1. GBD Antimicrobial Resistance Collaborators, *Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019.* Lancet, 2022. **400**(10369): p. 2221-2248.
2. Bai, A.D., et al., *Staphylococcus aureus bacteraemia mortality: a systematic review and meta-analysis.* Clin Microbiol Infect, 2022. **28**(8): p. 1076-1084.
3. Austin, E.D., et al., *Reduced Mortality of Staphylococcus aureus Bacteremia in a Retrospective Cohort Study of 2139 Patients: 2007-2015.* Clin Infect Dis, 2020. **70**(8): p. 1666-1674.
4. Kourtis, A.P., et al., *Vital Signs: Epidemiology and Recent Trends in Methicillin-Resistant and in Methicillin-Susceptible Staphylococcus aureus Bloodstream Infections - United States.* MMWR Morb Mortal Wkly Rep, 2019. **68**(9): p. 214-219.
5. 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.
6. Lam, J.C., et al., *Epidemiology and Outcome Determinants of Staphylococcus aureus Bacteremia Revisited: A Population-Based Study.* Infection, 2019. **47**(6): p. 961-971.
7. Jokinen, E., et al., *Trends in incidence and resistance patterns of Staphylococcus aureus bacteremia().* Infect Dis (Lond), 2018. **50**(1): p. 52-58.
8. Souli, M., et al., *Changing characteristics of Staphylococcus aureus bacteremia: results from a 21-year, prospective, longitudinal study.* Clinical Infectious Diseases, 2019. **69**(11): p. 1868-1877.
9. 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.
10. Cuijpers, M.L., et al., *Complicating infectious foci in patients with Staphylococcus aureus or Streptococcus species bacteraemia.* Eur J Clin Microbiol Infect Dis, 2007. **26**(2): p. 105-13.
11. Holland, T.L., et al., *Effect of algorithm-based therapy vs usual care on clinical success and serious adverse events in patients with staphylococcal bacteremia: a randomized clinical trial.* Jama, 2018. **320**(12): p. 1249-1258.
12. 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.
13. Chong, Y.P., et al., *Treatment duration for uncomplicated Staphylococcus aureus bacteremia to prevent relapse: analysis of a prospective observational cohort study.* Antimicrobial agents and chemotherapy, 2013. **57**(3): p. 1150-1156.
14. Tong, S.Y.C., et al., *Management of Staphylococcus aureus Bacteremia: A Review.* Jama, 2025.
15. El Zakhem, A., et al., *Central line-associated bloodstream infections caused by Staphylococcus aureus in cancer patients: clinical outcome and management.* Annals of medicine, 2014. **46**(3): p. 163-168.
16. Walker, T.M., I.C. Bowler, and P. Bejon, *Risk factors for recurrence after Staphylococcus aureus bacteraemia. A retrospective matched case-control study.* J Infect, 2009. **58**(6): p. 411-6.
17. Pliakos, E.E., P.D. Ziakas, and E. Mylonakis, *Economic Analysis of Infectious Disease Consultation for Staphylococcus aureus Bacteremia Among Hospitalized Patients.* JAMA Netw Open, 2022. **5**(9): p. e2234186.
18. Goto, M., et al., *Association of infectious diseases consultation with long-term postdischarge outcomes among patients with Staphylococcus aureus bacteremia.* JAMA network open, 2020. **3**(2): p. e1921048-e1921048.
19. Vogel, M., et al., *Infectious disease consultation for Staphylococcus aureus bacteremia–a systematic review and meta-analysis.* Journal of Infection, 2016. **72**(1): p. 19-28.

20. Fowler, V.G., et al., *The 2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis: Updating the Modified Duke Criteria.* Clin Infect Dis, 2023. **77**(4): p. 518-526.