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

Consensus Statement 7 on Duration of Antibiotic Therapy in Patients with Increased-Risk *Staphylococcus aureus* Bacteremia without Evidence of Deep-Seated or Metastatic Foci of Infection

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Executive Summary

Overview

The optimal duration of therapy for patients with *Staphylococcus aureus* bacteremia (SAB) is unknown. Management of SAB should be guided by risk stratification to direct both diagnostic

evaluation and antibiotic treatment (Consensus Statement 1). Patients classified as having SAB without deep-seated or metastatic foci of infection may be candidates for shorter courses of treatment. Here, we evaluate the optimal duration of therapy for patients initially stratified as increased risk but ultimately classified as SAB without deep-seated or metastatic foci of infection after diagnostic evaluation.

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 are 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.

Introduction

Background

The optimal duration of therapy for patients with *Staphylococcus aureus* bacteremia (SAB) is unknown. In Consensus Statement 6, the panel suggests 14 days of effective antibacterial therapy for patients with low-risk SAB. Here, we address the question of whether extending antibiotic therapy beyond two weeks improves outcomes in patients with increased-risk SAB if evaluation for deep-seated or metastatic foci is negative.

Historically, clinicians have relied on classifications such as "complicated" versus "uncomplicated" SAB to guide treatment duration. As noted in Consensus Statements 1 and 6, these terms lack consistent definitions and may not adequately capture the spectrum of risk. As a result, many patients who fall outside strict low-risk criteria but have no identifiable deep-seated or metastatic infection have been managed with extended antibiotic courses (≥4 weeks), despite limited evidence supporting this practice.

Given the potential harms of unnecessarily prolonged therapy, including drug toxicity, catheter-associated complications, and increased healthcare utilization, the panel seeks to determine whether a 14-day course is appropriate in patients with increased-risk SAB but negative diagnostic evaluation for deep-seated or metastatic infection.

Purpose and objectives

The objective of the panel was to review the relevant literature to develop guidance on the optimal duration of antibiotic therapy for patients stratified as increased-risk SAB but classified as without deep-seated or metastatic foci of infection after diagnostic evaluation. This consensus statement builds on the risk stratification framework developed in Consensus Statements 1 and integrates literature, clinical judgement, and expert consensus to propose an appropriate treatment duration.

Scope

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

Methods

Panel composition

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

Process

This consensus statement was developed in parallel with the risk stratification framework outlined in Consensus Statements 1. We considered randomized controlled trials, observational studies,

large series, or meta-analyses that included at least 50 individuals with at least one of the following criteria: Community onset of bacteremia, positive follow-up blood cultures at 48-96 hour, persistent fever 72 hours or more after starting active antibiotic therapy, and implanted prostheses or intravascular foreign bodies but without evidence of infective endocarditis upon echocardiography (transthoracic echocardiogram (TTE) and/or transesophageal echocardiography (TEE)) or evidence of metastatic infection or visceral nidus of infection (i.e., pneumonia, splenic abscess) on clinical evaluation or diagnostic workup (based on symptoms, signs, and clinical judgement and radiologic evaluation).

Literature review

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

Consensus statement development

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

Results

Adults' perspective

Summary of the literature review for the adult population

We screened 3,476 titles and abstracts and identified no studies directly addressing this clinical question. Seven studies provided limited outcome data on treatment durations >14 days in cohorts where at least some patients met our criteria for increased-risk. These provide indirect evidence on treatment duration and are summarized below and in Supplementary Table 1.

This body of evidence, composed entirely of cohort studies, is difficult to synthesize due to heterogeneity in patient populations and limited clarity regarding the presence of deep-seated infections warranting prolonged therapy (e.g., endocarditis).

Studies favoring longer therapy

Two studies suggested improved outcomes with longer durations, but both included some patients with endocarditis and some without echocardiographic evaluation for endocarditis.

- Abbas 2020 [1]: In 305 patients classified as "complicated SAB," defined by the presence of any of the following factors: endocarditis, implanted prosthesis, duration of SAB more than two days, and fever more than three days, more than 14 days of antibiotic therapy was associated with improved survival (adjusted Hazard Ratio (aHR) 0.32, 95% Confidence Interval (CI) 0.16-0.64). No benefit of prolonged therapy was observed in the 225 patients without these factors (aHR 0.85; 95% CI 0.41–1.78).
- Asgeirsson 2011 [2]: In 183 patients with "complicated SAB", defined as those with a non-removable focus of infection, an unknown focus of infection, or persistent bacteremia after three days of antibiotics, the authors found those who did not relapse received a longer median duration of therapy (median 30.0 days; (IQR) 13.3 - 45.8) compared to those who did relapse (median 14.0 days; interquartile range (IQR) 4.0 - 28.0.) Of note, echocardiography rates were not reported.

Studies finding no difference between ≤ 14 days compared to > 14 days of therapy

Three cohort studies found no statistically significant differences in outcomes between ≤ 14 days versus > 14 days of therapy.

- Kreisel 2006 [3]: In 397 patients with at least one blood culture positive for *S. aureus* (46% community-onset, 14% endocarditis), recurrence rates did not differ between those who received ≤14 days compared to > 14 days of therapy (Relative Risk (RR) 0.68; 95% CI 0.44–1.04). Logistic regression excluding patients with endocarditis yielded similar results (n = 341; Odds Ratio (OR) 0.58; 95% CI 0.32 – 1.05).
- Platts 2022 [4]: In 281 patients with at least one blood culture positive for *S. aureus* (49% community-onset, 6% endocarditis, 12% unknown focus), recurrence was 8.5% in those who received ≤14 days vs. 3.8% who received >14 days of therapy (p-value =0.12).
- Fätkenheuer 2004 [5]: In 229 patients with at least one blood culture positive for *S. aureus* (22% community-onset, 6% endocarditis) there was no difference in survival for those treated with ≤ 14 days compared to > 14 days of therapy; patients with and without deep-seated or metastatic foci of infection were not analyzed separately.

These observational studies varied in the definitions of "high-risk" patients, the composition of the cohorts (e.g., including or excluding endocarditis), and the subgroups analyzed, which limits conclusions. It may, thus, be possible that some patients with increased-risk SAB but classified as without deep-seated or metastatic foci of infection after diagnostic evaluation would benefit from more than two weeks of therapy, but current data do not allow confident identification of those patients.

Immunocompromised populations

Immunocompromising conditions often prompt clinicians to use longer durations of antibiotic therapy even in those without evidence of a deep-seated infection because of a perceived risk of poor outcomes. Shibata 2024 [6] compared outcomes for immunocompromised patients who received ≥28 days of antibiotic therapy to those who received < 28 days of therapy for SAB. Immunocompromised was defined as the presence of hematological or solid tumor malignancies requiring chemotherapy or radiation therapy, diabetes requiring medication, hemodialysis, or a chronic inflammatory condition, and/or receipt of immune-modulating medications; all patients underwent echocardiography. After propensity-score matching, they found no difference in 90-day all-cause mortality (long: 4/21 (19.0%) vs short: 2/21 (9.5%), p-value = 0.33) and recurrence

(long: 2/21 (9.5%) vs short: 0/21 (0%), p-value = 0.22). Small sample size and selection bias to treat sicker patients for longer durations limit interpretation but these data may suggest that the presence of immunocompromise alone may not warrant prolonged durations of therapy.

Patients with prosthetic material

In patients with indwelling prosthetic material, clinicians often prescribe longer durations of antibiotic therapy without evidence of infection of the prosthetic material. This is due to concern for poorer outcomes related to potential occult infection involving the prosthesis, even in the absence of clinical or diagnostic evidence of a deep-seated infection or suspected prosthetic joint infection. van Der Waart 2024 found that prosthetic material was associated with "complicated SAB" (OR 2.3; 95% CI 1.5–3.6), however sensitivity analyses excluding infected prostheses showed no association (OR 0.9; 95% CI 0.6–1.4) [7]. Blank 2025 studied 247 adults with SAB and prosthetic hip and/or knee joints. This study showed a low risk of prosthetic joint infection within 6 months (<1%) after SAB treatment, regardless of therapy duration [8]. These data may suggest that longer therapy is not warranted solely due to the presence of uninfected prosthetic joints.

Rationale for the consensus statement for the adult population

Balance of benefits and harm

Extended antibiotic therapy carries important risks, including adverse drug events (e.g., allergic reactions, nephrotoxicity, gastrointestinal intolerance), prolonged hospitalization with associated complications such as deconditioning, venous thromboembolism, and healthcare -associated infections, including catheter-related bloodstream infections. Based on the above evidence, the panel concluded that the balance of benefits and harms favors a 14-day antibiotic course over longer durations even in patients with increased-risk SAB but classified as without deep-seated or metastatic foci of infection after diagnostic evaluation for most patients (see Practical Advice below). This approach aims to maximize the likelihood of clinical cure, prevent relapse or dissemination, reduce mortality, and minimize treatment-related harm.

The panel prioritizes the prevention of serious complications from undetected device-related or endovascular infection. While direct evidence is lacking, there are some scenarios (e.g., retained intracardiac device, recently placed endovascular graft, or DVT at a central venous catheter site) where infection is challenging to exclude using physical examination and all currently available imaging modalities. In these cases, additional source control and/or >14 days of antibiotic therapy targeting the suspected focus should be considered. Variability in approaches may exist in how the adverse effects of prolonged antibiotics, such as toxicity and hospital burden, are weighed by patients and systems. This makes the benefit-harm balance context-dependent.

Costs

- Shorter therapy may yield moderate-to-substantial savings but carries the risk of relapse or readmission. Conversely, longer therapy, particularly intravenous, can increase inpatient and outpatient costs.

Feasibility

- This consensus statement is feasible in settings with access to diagnostic tools needed to evaluate for deep-seated infection. In low-resource settings, limited diagnostics may challenge this approach.

Implementation Considerations for the adult population

Practical advice

- Patients stratified as increased-risk SAB should be treated with 14 days of therapy if there is improvement of signs and symptoms of infection and tailored diagnostic evaluation and ongoing clinical assessment do not reveal a deep-seated or metastatic focus of infection.
- Patients stratified as increased-risk SAB based on positive blood cultures obtained ≥ 48 hours after the first positive blood culture should have additional evaluation for deep-seated or metastatic foci of infection if no focus was identified on initial tailored diagnostic evaluation (Consensus Statement 5).
- Patients stratified as increased-risk SAB based on positive blood cultures obtained ≥ 48 hours after the first positive blood culture should have duration of therapy guided by clinical course, tailored diagnostic evaluation, and likely focus of infection. Two examples:
    - A 14-day course of therapy may be acceptable in a patient with a removable focus (e.g., central venous catheter, skin, and soft tissue abscess) with clinical improvement and rapid clearance of bacteremia following source control (e.g., catheter removal or abscess drainage) and no evidence of deep-seated or metastatic infection on tailored diagnostic evaluation.
      > 14 days of therapy may be appropriate in the setting of prolonged bacteremia and an incomplete or indeterminate diagnostic evaluation for deep-seated or metastatic foci of infection. In this case, duration of therapy may be guided by the likely focus of infection (e.g., treatment as "presumed endocarditis" in a patient with a bicuspid aortic valve with 5 days of SAB and an indeterminate TTE for whom TEE is unavailable).

In certain increased-risk scenarios (e.g., retained intracardiac device, recently placed endovascular graft, or DVT at a central venous catheter site), infection may be difficult to exclude despite thorough diagnostic evaluation, particularly when suspicion for deep-seated infection remains high (e.g., positive FUBC ≥48 hours). In these cases, additional source control and/or >14 days of antibiotic therapy targeting the suspected focus should be considered.

- If any focus of infection is identified which merits > 14 days of therapy, then this focus should dictate the final duration of therapy.
- All patients with SAB should be educated about signs and symptoms warranting medical re-evaluation, including those suggestive of previously undetected deep-seated or metastatic infection. Standardized discharge instructions and early post-discharge follow-up may also be considered.

Barriers

- Diagnostic limitations: Access to advanced imaging may be limited in some settings that may restrict the ability to use a risk-stratified diagnostic evaluation to determine the optimal duration of therapy for individual patients.
- Evidence gaps: Limited published data directly addressing specific patient populations may lead to over- or under-treatment.
- Resource constraints: Lack of access to Infectious Disease consultation in certain regions may limit the ability to use a risk-stratified diagnostic evaluation to determine the optimal duration of therapy for individual patients.
- Advocacy and education: Successful implementation will require clinical advocates and broader education to promote uptake and integration into practice.

Research needs for the adult population.

- Prospective studies are needed to evaluate clinical outcomes of patients with increased-risk SAB and classified as without deep-seated or metastatic foci of infection after diagnostic evaluation who are treated with 14 days of therapy.
- Prospective studies are needed to identify which patients stratified as increased-risk SAB and classified as without deep-seated or metastatic foci of infection may still benefit from >14 days of therapy.
- Research is needed to explore whether advanced diagnostics can adequately exclude infection of intracardiac devices, endovascular grafts, and DVTs at the site of a previous catheter to allow for shorter durations of therapy for SAB in the presence of these risk factors. Conversely, prospective studies are needed to evaluate whether prolonged therapy with SAB in the presence of these risk factors lowers the rate of relapse or mortality.
- Research should explore clinical, microbiologic, and imaging features that can reliably guide risk stratification and duration decisions.

Pediatrics perspective

Summary of the literature review for the pediatric population

As discussed in Consensus Statement 6, there is a notable lack of comparative studies evaluating different antibiotic durations for pediatric SAB. No studies have directly compared 14-day versus longer (>14-day) regimens in pediatric SAB. In children with evidence of deep-seated or metastatic foci of infection, treatment duration is generally guided by the underlying source of infection. As noted in Consensus Statement 1, most pediatric SAB cases are associated with identifiable infectious foci, and therefore, there is little evidence base for stratifying risk of deep-seated or metastatic foci of infection or relapse of infection in children without evidence of these complications after diagnostic evaluation.

Rationale for the consensus statement for the pediatric population

- As discussed in Consensus Statement 1, the panel considers that neonates, children with congenital or acquired heart disease, immunocompromised children, those with comorbidities which make diagnostic evaluation less reliable, and those with ongoing bacteremia >=48 hrs of initiation of appropriate treatment, are likely to be at higher risk of deep-seated or metastatic foci of infection or relapse of infection. In most cases, these foci will be detectable on diagnostic evaluation.
- For children who have undergone a thorough diagnostic evaluation and have no evidence of deep-seated or metastatic foci of infection, a 14-day course of antibiotics is considered reasonable. However, both shorter and longer durations have been reported in a retrospective study [9]. Decisions regarding shorter durations of therapy in children at increased risk should be individualized and made with close clinical follow-up.
- Children with congenital heart disease represent a high-risk subgroup for deep-seated SAB, including endocarditis[10, 11]. These patients often require complex surgical repairs involving prosthetic materials, which may further increase infection risk. In such cases—especially those with complex anatomy or vascular grafts—longer treatment durations may be warranted even when imaging does not show definitive evidence of infection, due to the limited sensitivity of echocardiography in this group of patients. In one cohort of 216 children with complex congenital heart disease and *S. aureus* infection, 44 had positive blood cultures; of these, 29.5% met Duke criteria for endocarditis, and three had no echocardiographic evidence of vegetations visible [12].

- Similarly, in children with ongoing bacteremia (e.g., positive blood cultures 48–72 hours after starting appropriate antibiotics) extended treatment (such as 4-6 weeks of therapy) should be considered even if other evaluations are negative, taking into account the specific clinical scenario. Multidisciplinary collaboration is critical in managing these complex scenarios.

Implementation Considerations for the pediatric population

Practical advice

- Implementation of this consensus statement is feasible in most pediatric settings. However, treatment duration should be tailored based on clinical response, laboratory and imaging results, and shared decision-making with families.
- In general, if any focus of infection is identified found which merits > 14 days of therapy , then this focus should dictate the final treatment choice and duration of therapy.
- Parents/guardians of children with SAB should be educated about signs and symptoms warranting medical re-evaluation, including those suggestive of previously undetected deep-seated or metastatic infection. Early post-discharge follow-up may be beneficial for these children.
- Extended treatment may be considered in children who have not shown expected clinical and laboratory evidence of resolution of infection by 14 days of treatment.

Barriers

- Identification of children who do not have deep-seated or metastatic foci of infection may be limited by the availability of investigations such as MRI and echocardiography, particularly for the youngest children and neonates.
- Prolonged antibiotic therapy in children presents unique challenges. Peripheral intravenous access can be difficult and distressing; central line placement may require sedation, anesthesia, or transfer to specialized centers.
- Antibiotic adherence may also be inconsistent. As such, a pragmatic, individualized approach is required, balancing clinical needs with patient/family preferences and treatment feasibility.

Research needs for the pediatric population

Further studies are needed to better define the optimal duration of therapy for pediatric SAB and to identify which children, despite appearing at low risk, might still benefit from extended treatment. Comparative effectiveness research and prospective observational studies will be key in closing these evidence gaps.

Limitations

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

Acknowledgments

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

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

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

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

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