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SEPSIS AND SEPTIC SHOCK: CURRENT DEFINITIONS, DIAGNOSIS AND MANAGEMENT - A NARRATIVE REVIEW OF INTERNATIONAL GUIDELINES

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ABSTRACT

Sepsis and septic shock remain leading causes of in-hospital and global mortality, and international recommendations changed substantially with the 2026 Surviving Sepsis Campaign (SSC) update. This narrative review summarizes the Sepsis-3 definitions and diagnostic criteria, current concepts of sepsis immunopathology, and the SSC 2026 recommendations for adults on resuscitation, antimicrobial therapy, vasopressors and adjunctive care. Global Burden of Disease estimates attribute 48.9 million incident cases and 11.0 million sepsis-related deaths to 2017, equal to 19.7% of all deaths. Sepsis is identified by suspected infection with an acute increase of at least 2 SOFA points, and septic shock by a vasopressor requirement to maintain a mean arterial pressure (MAP) of at least 65 mm Hg with lactate > 2 mmol/L despite adequate fluid resuscitation, which carries hospital mortality above 40%. SSC 2026 recommends antimicrobial therapy within 1 hour in septic shock, at least 30 mL/kg of crystalloid in the first 3 hours (conditional), norepinephrine as the first-line vasopressor, an initial MAP target of 65 mm Hg, and NEWS, NEWS2, MEWS or SIRS rather than qSOFA as a single screening tool. Most recommendations are conditional and rest on low or very low certainty of evidence. The review is non-systematic, relies on a limited set of guideline and consensus documents, and does not replace clinical judgement or local protocols.

Keywords: sepsis; septic shock; Sepsis-3; SOFA; Surviving Sepsis Campaign; vasopressors; fluid resuscitation; critical care.

INTRODUCTION

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection [1]. It is not a single disease but a syndrome that can follow infection at any site and in patients of any age, and it is the final common pathway to death from many infectious diseases. Septic shock is the subset of sepsis in which circulatory, cellular and metabolic abnormalities are profound enough to substantially increase mortality [1]. The burden is large. Global Burden of Disease estimates reported 48.9 million incident sepsis cases and 11.0 million sepsis-related deaths worldwide in 2017, representing 19.7% of all global deaths; age-standardized incidence fell by 37.0% and mortality by 52.8% between 1990 and 2017, yet more than 40% of cases occurred in children under 5 years of

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age [2]. The burden is highest in low- and middle-income settings, where diagnostic and critical care resources are most limited [2].

The first consensus definitions (Sepsis-1, 1991) described sepsis as a systemic inflammatory response syndrome (SIRS) caused by infection, graded into sepsis, severe sepsis and septic shock [1,4]. The 2001 revision (Sepsis-2) kept this framework and added a broader list of diagnostic signs, but SIRS criteria remained non-specific, since they also occur in non-infectious states and in many hospitalized patients who never develop sepsis [1,5]. The Sepsis-3 task force (2016) therefore redefined sepsis as organ dysfunction rather than inflammation. Organ dysfunction is identified by an acute increase of at least 2 points in the Sequential Organ Failure Assessment (SOFA) score due to infection; the baseline score is assumed to be zero in patients without known pre-existing dysfunction, and a SOFA score of 2 or more is associated with an in-hospital mortality of about 10% [1]. The term "severe sepsis" was dropped as redundant. Septic shock is identified clinically by the need for vasopressors to maintain a mean arterial pressure (MAP) of at least 65 mm Hg and a serum lactate level above 2 mmol/L despite adequate fluid resuscitation, and carries a hospital mortality above 40% [1,6]. For rapid bedside identification outside the intensive care unit, the task force proposed qSOFA, which scores one point each for respiratory rate of at least 22/min, altered mentation and systolic blood pressure of 100 mm Hg or less [1]. Parallel to clinical definitions, current immunological work shows that sepsis is characterized by concurrent hyperinflammation and immunosuppression rather than a simple sequence from one to the other, and that patients are biologically heterogeneous, which may explain why many trials of single-target immunomodulatory therapies have failed [9,10].

The Surviving Sepsis Campaign (SSC) has issued consensus guidelines since 2004, and they have been revised repeatedly and now address adults and children separately [3,7,8]. The 2026 adult edition retains the Sepsis-3 framework but, for screening, recommends against using qSOFA as a single tool, favouring NEWS, NEWS2, MEWS or SIRS instead [3]. Its 2026 adult update contains 129 statements, 46 of them new, developed by a 69-member panel from 23 countries, 38% of whom had experience in low- and middle-income settings [3]. This article aims to summarize the current definition, diagnostic criteria, pathophysiological concepts and adult management principles of sepsis and septic shock in the light of Sepsis-3 and the SSC 2026 guidelines, reporting the strength of each recommendation and the certainty of its evidence.

MATERIALS AND METHODS

This is a narrative (non-systematic) literature review. No patient data were collected, so ethical approval and informed consent were not required. Targeted web searches were carried out in October 2026 using the terms "sepsis", "septic shock", "Sepsis-3", "Surviving Sepsis Campaign 2026", "sepsis epidemiology" and "sepsis immunology". Priority was given to international consensus definitions, the most recent SSC guidelines, global burden estimates and review articles on immunopathology published in peer-reviewed journals. Ten sources were included in the reference list [1–10]. From each source we extracted definitions, diagnostic criteria, epidemiological figures and, for the

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SSC 2026 guidelines, the wording, direction and strength of each recommendation together with the stated certainty of evidence. The full text of the SSC 2026 guideline [3] could not be retrieved automatically because of access limits; its recommendations were therefore extracted from the summary of recommendations published by the Society of Critical Care Medicine and cross-checked against the guideline abstract. The historical definitions [4,5] and the 2021 and pediatric guidelines [7,8] are cited for context and were not appraised in detail.

No formal database strategy, dual screening or risk-of-bias assessment was applied, and the selection of sources may therefore be incomplete or subject to selection bias. Findings concern adult patients; pediatric sepsis is outside the scope of this article [8]. All numerical values and recommendations should be verified against the original publications before clinical use.

RESULTS

In 2017, an estimated 48.9 million incident sepsis cases and 11.0 million sepsis-related deaths occurred worldwide, accounting for 19.7% of all deaths [2]. Between 1990 and 2017, age-standardized incidence decreased by 37.0% and mortality by 52.8% [2]. More than 40% of all cases occurred in children younger than 5 years, and the highest burden was recorded in sub-Saharan Africa, Oceania, and South, East and South-East Asia [2]. The main burden indicators are shown in Figure 1.

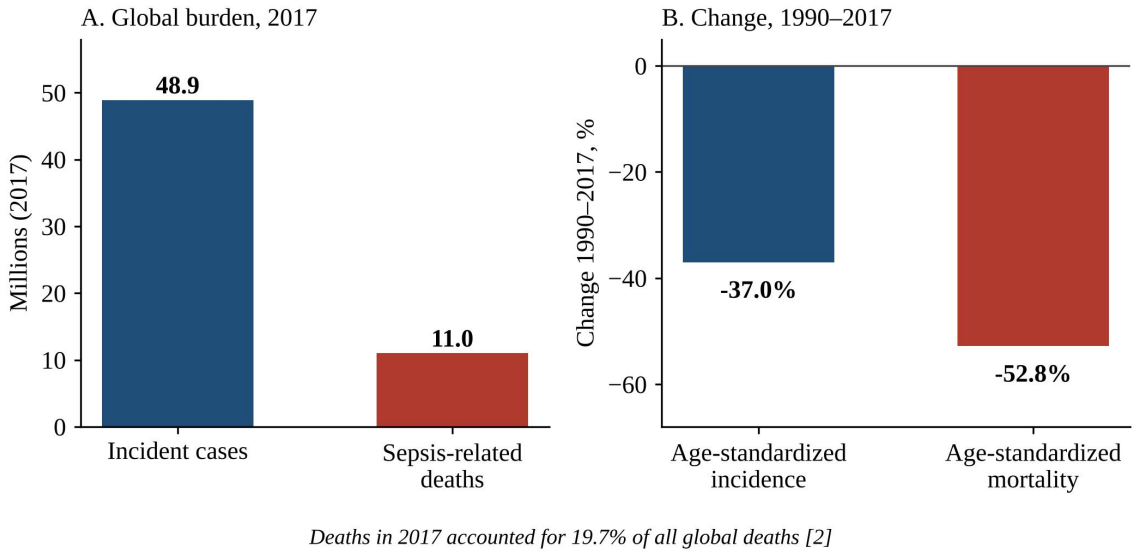


Figure 1. Global burden of sepsis: incidence and deaths in 2017 (A) and change in age-standardized rates, 1990–2017 (B) [2]

The Sepsis-3 criteria are summarized in Table 1. Severe sepsis is no longer used as a separate category, and SIRS criteria are no longer required for diagnosis [1]. Among intensive care patients in Australia and New Zealand with infection and new organ failure, about one in eight did not meet two SIRS criteria despite a prolonged and severe course,

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which illustrates the limited sensitivity of SIRS [1]. Sepsis is a clinical diagnosis: no single biomarker or test can confirm or exclude it, and failure to meet SOFA or qSOFA thresholds is not a reason to delay investigation and treatment of infection [1,3].

Table 1. Sepsis-3 definitions and associated in-hospital mortality [1]

Condition	Clinical criteria	In-hospital mortality
Sepsis	Suspected or confirmed infection and an acute increase in SOFA score of at least 2 points	Above 10%
Septic shock	Sepsis with vasopressors required to maintain MAP of at least 65 mm Hg and lactate above 2 mmol/L despite adequate fluid resuscitation	Above 40%

The baseline SOFA score is assumed to be zero in patients without known pre-existing organ dysfunction [1]. qSOFA (respiratory rate of at least 22/min, altered mentation, systolic blood pressure of 100 mm Hg or less) requires no laboratory tests and identifies patients with suspected infection at higher risk when at least two criteria are present [1]. However, for screening of acutely ill hospitalized patients, SSC 2026 recommends NEWS, NEWS2, MEWS or SIRS rather than qSOFA as a single screening tool (strong recommendation, moderate certainty) [3]. A systematic review of studies on septic shock definitions, covering 44 studies and 166,479 patients, found marked variation in thresholds for blood pressure, fluid volume, vasopressor use and lactate [6].

In sepsis the immune response to infection fails to return to homeostasis: persistent hyperinflammation and immunosuppression coexist, and anti-inflammatory as well as pro-inflammatory responses are activated from the earliest stage [1,9,10]. Cardiovascular, neuronal, autonomic, hormonal, bioenergetic, metabolic and coagulation pathways are also altered, each with prognostic significance, yet organ dysfunction is not usually accompanied by widespread cell death [1]. Raised lactate may reflect cellular dysfunction, but it can also result from inadequate oxygen delivery, impaired aerobic respiration, accelerated aerobic glycolysis and reduced hepatic clearance [1]. Sepsis is also clinically and biologically heterogeneous, with patient age, comorbidity, trauma, medications and the source of infection all modifying the picture [1]. Stratifying patients into subgroups with similar clinical and pathobiological features, using biomarkers or functional defects, is considered key to selecting immunomodulatory treatments [9,10].

Sepsis and septic shock are medical emergencies, and treatment and resuscitation should begin immediately [3]. For sepsis-induced hypoperfusion or septic shock, SSC 2026 suggests at least 30 mL/kg of intravenous crystalloid within the first 3 hours (conditional recommendation, low certainty), calculated on actual body weight, or on adjusted or ideal weight when body mass index exceeds 30 kg/m² [3]. Frequent reassessment during fluid administration is advised, because both insufficient and excessive fluid are harmful [3]. Fluid choices are summarized in Table 2.

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Table 2. SSC 2026 recommendations on fluid type [3]

Question	Recommendation	Strength; certainty of evidence
First-line fluid	Crystalloids	Strong; moderate
Type of crystalloid	Balanced crystalloids over 0.9% saline	Conditional; moderate
Albumin	Crystalloids alone (no albumin)	Conditional; moderate
Starches	Do not use	Strong; high
Gelatin	Do not use	Conditional; moderate

Saline is suggested in sepsis with traumatic brain injury; albumin may be appropriate in patients who received large volumes of crystalloid or have cirrhosis, but should be avoided in traumatic brain injury [3]. To guide resuscitation, SSC 2026 favours dynamic measures (passive leg raising, stroke volume, stroke volume or pulse pressure variation) over physical examination or static parameters (conditional; low), and suggests capillary refill time as an adjunct to other perfusion indicators (conditional; low) [3]. Serial lactate measurement is used, but fluids need not be continued until lactate normalizes [3]. In hypotension, a crystalloid bolus is given first and a vasopressor is added if hypotension persists; in unstable shock both may be given concurrently [3]. If hypoperfusion persists after 30 mL/kg, a liberal or restrictive strategy is chosen according to patient and institutional factors, and after the acute phase active fluid removal is suggested in septic shock (conditional; very low) [3].

Antimicrobial therapy should start as soon as septic shock is recognized, ideally within 1 hour (strong recommendation, very low certainty), and blood cultures should be drawn before antimicrobials whenever possible (strong; low) [3]. The timing depends on clinical context (Table 3).

Table 3. SSC 2026 timing of antimicrobial therapy [3]

Clinical situation	Timing	Strength
Possible or definite septic shock	Immediately, within 1 hour	Strong
Probable or definite sepsis without shock	Immediately, within 1 hour	Strong
Possible sepsis without shock	Rapid assessment; start within 3 hours if concern persists	Conditional
Low likelihood of infection without shock	Defer therapy and monitor	Conditional

Certainty of evidence is very low in all rows [3]. Other recommendations [3]: empirical cover for multidrug-resistant (MDR) organisms only when MDR risk is high (colonization or prior infection, prolonged broad-spectrum antibiotic use, long stay in a unit with high MDR prevalence); anaerobic cover only with risk factors such as intra-abdominal or pelvic infection, necrotizing soft tissue infection, head and neck infection, or CNS abscess or empyema; routine empirical antifungal therapy is not recommended; extended infusion of

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beta-lactams after an initial loading dose is preferred over bolus (strong; moderate); procalcitonin together with clinical assessment may inform when to stop therapy, but clinical assessment alone suffices to decide whether to start; and de-escalation is strongly recommended when the pathogen and susceptibilities are known and conditionally suggested when no pathogen is identified, with shorter courses when source control is adequate. Where source control is needed, intervention is suggested ideally within 6 hours of diagnosis (conditional; very low) [3].

Norepinephrine is the first-line vasopressor in septic shock (strong recommendation against dopamine, epinephrine and selepressin as first choice) [3]. The initial MAP target is 65 mm Hg (strong; moderate), and a target of 60–65 mm Hg is suggested for patients aged 65 years or older (conditional; low) [3]. Further recommendations are listed in Table 4.

Table 4. SSC 2026 recommendations on vasopressors [3]

Question	Recommendation	Strength
First-line vasopressor	Norepinephrine over dopamine, epinephrine, selepressin, vasopressin and angiotensin II	Strong (vs dopamine, epinephrine, selepressin); conditional (vs vasopressin, angiotensin II)
Rising norepinephrine dose	Add vasopressin	Conditional
Low MAP despite norepinephrine and vasopressin	Add epinephrine	Conditional
Terlipressin	Do not use	Conditional

Additional practical points [3]: vasopressors may be started through a peripheral vein without waiting for central access (conditional; very low); because holding MAP exactly at 65 mm Hg is impractical, a range of about 5 mm Hg is used; invasive arterial pressure monitoring is advised for patients on medium- to high-dose, escalating or multiple vasopressors, or when non-invasive readings are unreliable; norepinephrine may be preferred with tachyarrhythmia and epinephrine with bradyarrhythmia; an inotrope (dobutamine or epinephrine alone) is suggested when perfusion remains impaired despite adequate fluid and blood pressure; levosimendan and short-acting beta-blockers (esmolol, landiolol) are suggested against. Evidence was insufficient to make a recommendation on methylene blue as rescue therapy in refractory shock or on oral midodrine [3].

SSC 2026 suggests intravenous corticosteroids in septic shock (conditional; low) [3]; the 2021 guideline gave hydrocortisone 200 mg/day as the usual regimen [7]. Other recommendations are as follows [3]: transfusion: restrictive rather than liberal strategy (strong; moderate); glucose control: start insulin at glucose of 180 mg/dL (10 mmol/L) or above (strong; moderate); thromboprophylaxis: pharmacological prophylaxis unless contraindicated, low-molecular-weight heparin preferred over unfractionated heparin (both strong; moderate); adding mechanical prophylaxis is not required; nutrition: start enteral feeding within 72 hours (conditional; very low); stress-ulcer prophylaxis: proton pump

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inhibitors when risk factors for gastrointestinal bleeding exist (conditional; moderate); respiratory support: high-flow nasal cannula rather than conventional oxygen in acute hypoxemic respiratory failure; in ARDS, tidal volume 6 mL/kg and plateau pressure not above 30 cm H2O (both strong; high), higher PEEP and prone positioning for more than 12 hours daily in moderate to severe ARDS, and venovenous ECMO in experienced centres for severe ARDS when conventional ventilation fails; kidney: avoid renal replacement therapy without a clear indication in acute kidney injury (conditional; moderate).

SSC 2026 suggests against: antipyretics or external cooling to improve outcome (except for symptom control, neurocritical care or post-cardiac-arrest care); intravenous vitamin C; intravenous immunoglobulins; blood purification techniques including polymyxin B hemoperfusion; vitamin D and probiotics; and sodium bicarbonate for hemodynamic improvement, although it is suggested when pH is 7.2 or lower with stage 2–3 acute kidney injury [3].

The main time-critical and numerical targets of SSC 2026 discussed above are brought together in Table 5.

Table 5. Summary of key SSC 2026 targets for adults with sepsis and septic shock [3]

Parameter	Target	Strength; certainty of evidence
Start of antimicrobials in septic shock	Within 1 hour of recognition	Strong; very low
Blood cultures	Before antimicrobials whenever possible	Strong; low
Initial crystalloid volume	At least 30 mL/kg within the first 3 hours	Conditional; low
Initial MAP target	65 mm Hg (60–65 mm Hg if aged 65 years or older)	Strong; moderate (conditional; low if aged 65 or older)
Source control	Ideally within 6 hours of diagnosis	Conditional; very low
Insulin initiation	Glucose of 180 mg/dL (10 mmol/L) or above	Strong; moderate
Enteral nutrition	Start within 72 hours	Conditional; very low
Tidal volume in ARDS	6 mL/kg; plateau pressure not above 30 cm H2O	Strong; high
Transfusion	Restrictive rather than liberal strategy	Strong; moderate

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DISCUSSION

The Sepsis-3 framework shifted the definition of sepsis from inflammation to organ dysfunction and remains the basis of the SSC 2026 guideline [1,3]. Two practical consequences stand out. First, the diagnosis is clinical, so no threshold or biomarker should delay assessment and treatment of suspected infection [1,3]. Second, the guideline's preference for NEWS, NEWS2, MEWS or SIRS over qSOFA as a screening tool shows that a score designed for risk stratification outside the intensive care unit is not accepted as a stand-alone screening test [1,3]. The core of management has not changed: early recognition, timely antimicrobials and hemodynamic resuscitation [3]. The SSC 2026 text adds details such as extended beta-lactam infusion, dynamic indicators and capillary refill time for guiding fluids, peripheral initiation of vasopressors and a limited role for procalcitonin [3]. Many practices in earlier editions, such as the 1-hour antimicrobial target in septic shock, still rest on very low certainty evidence, and most recommendations in the 2026 guideline are conditional [3]. This means that bedside judgement and local resources remain decisive, which is particularly relevant where the burden is greatest and critical care capacity is limited [2,3].

The immunological literature explains why single-target anti-inflammatory strategies have mostly failed: sepsis combines hyperinflammation and immunosuppression in a heterogeneous population [9,10]. Biomarker-guided patient stratification is therefore a research priority rather than a current recommendation [9,10].

Limitations. This is a narrative review based on a small set of sources, and the SSC 2026 recommendations were taken from a secondary summary because the full text was not accessible [3]. Pediatric sepsis, which accounts for a large share of global cases [2,8], is not covered.

In conclusion, sepsis is defined by life-threatening organ dysfunction (SOFA increase of at least 2 points) due to infection, and septic shock by vasopressor dependence with lactate above 2 mmol/L, with hospital mortality above 40% [1]. According to SSC 2026, priorities for adults are early recognition, antimicrobial therapy within 1 hour in septic shock, at least 30 mL/kg of crystalloid (balanced solutions preferred) guided by dynamic reassessment, norepinephrine as the first-line vasopressor with an initial MAP target of 65 mm Hg, and source control within about 6 hours when needed [3]. Because most recommendations are conditional and the certainty of evidence is low or very low, treatment should be individualized and aligned with local protocols [3]. Future work should address biomarker-based phenotyping, wider access to critical care in low-resource settings and updated reviews of the guideline full text.

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