SPECIAL REPORT

Surviving Sepsis Campaign Guidelines 2021: highlights for the practicing clinician

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ABSTRACT

The 2021 Surviving Sepsis Campaign Guidelines provided evidence-based recommendations for adult patients with sepsis and septic shock. This iteration of the guidelines placed increased emphasis on a diverse, global perspective, as well as on the long-term sequelae of sepsis experienced by patients and their families. The guidelines encompassed the following sections: 1) screening and early treatment; 2) infection; 3) hemodynamic management; 4) ventilation; 5) additional therapies; and 6) goals of care and long-term outcomes. In this review, we provide a summary of key recommendations of interest to the practicing clinician, which are either novel or require a change in practice, as well as those for which the evidence has substantially evolved in the 5 years since the 2016 iteration of the Guidelines. Rather than reviewing the underlying evidence, we emphasize the practical aspects of interpretation, dissemination, and implementation of these recommendations in the clinical setting.

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Introduction Despite advances in rapid recognition and resuscitation, sepsis remains a major cause of morbidity and mortality worldwide, underscoring the need for continued research, education, and knowledge translation activities.[1,2] Since its inception in 2002, the Surviving Sepsis Campaign (SSC) has played a central role in improving the care of patients with sepsis. As a collaboration between the Society of Critical Care Medicine and the European Society of Intensive Care Medicine, with endorsement from many other national and international societies, the SSC Guidelines represent the currently accepted standard for sepsis care in adults.[3]

The 2021 Guidelines build upon and advance the earlier versions in important ways. Firstly, they address sepsis as a global health threat. To this end, the leadership explicitly sought to increase diversity in the representative panelists as well as the recommendations themselves to ensure they would be applicable in both high- and low-resource settings. Secondly, while remaining intensive care unit (ICU)-focused, the 2021 Guidelines acknowledged the long-term impact of sepsis, including physical, psychological, and mental problems experienced by sepsis survivors and their families. A new section of the Guidelines was developed to address long-term outcomes and goals of care in sepsis, with an expanded patient and public involvement in the panel to provide input on the Guidelines and ensure they were consistent with patient and family needs, values, and preferences for care.

In this paper, we outline the noteworthy aspects of each section of the 2021 Guidelines that represent a change from previous practice, address an important clinical question not previously discussed, or remain an area of persistent clinical challenge. Of note, we do not address issues related to the COVID-19 pandemic,

as the SSC developed recommendations specific to COVID-19 in a separate guideline.[4,5]

Improved methodology The structure of the 2021 Guidelines was expanded to include medical librarians, systematic reviewers, methodologists, as well as patient and family representatives. The main advances in the Guidelines' methodology included the use of an iterative, systematic process to assist the diversified panel in developing and prioritizing guideline questions, the inclusion of dedicated guideline methodologists within each subgroup, the use of the evidence-to-decision framework to capture the panel view and develop recommendations, and the robust disclosure and management of the panelists' potential conflicts of interest, both intellectual and financial. Additionally, patient and family member representatives assisted in the selection of the PICO (population, intervention, comparator, and outcome) questions to be addressed, identification of key outcomes, and ensuring the recommendations were consistent with their true experiences with sepsis, most prominently in the section on the goals of care and long-term outcomes.

Relevant to the practicing clinician is the distinction between "strong" and "weak" recommendations in Grading Recommendations, Assessment, Development, and Evaluation (GRADE), the methodologic approach used in creating the Guidelines.[6] "Strong" recommendations indicate that on balance, the effects, resource considerations, acceptability, and feasibility greatly favor the recommended approach, and it should be adopted in almost all circumstances. On the other hand, "weak" recommendations indicate that in a minority of circumstances, patients and clinicians may reasonably choose the alternative option, usually because the effects are more closely balanced, or the evidence is less certain. Thus, the strength of a recommendation refers not only to the quality or certainty of evidence, but has implications for the clinical application of the recommendation as well.[7] We encourage readers to access the executive summary and full text of the SSC 2021 Guidelines for more details.[3,8]

Screening and early treatment

Sepsis screening Sepsis represents a potentially life-threatening organ dysfunction due to dysregulated response to infection, and hospital mortality in septic shock often exceeds 40%.[2] Efforts on early recognition and treatment are aimed to reduce morbidity and mortality. With respect to early recognition, the SSC Guidelines issued a strong recommendation for using performance improvement programs, which include screening for sepsis and standard operating procedures for treatment. Multiple tools have been used for sepsis screening, including the quick Sequential (Sepsis-related) Organ Failure Assessment (qSOFA), commonly used since the publication of the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3).[9] However, due to its poor sensitivity and the concern that missed sepsis diagnoses would worsen patient outcomes, the SSC Guidelines issued a strong recommendation against using it as a single screening tool. Lactate level measurement has also been proposed as a screening tool for sepsis. While as a single measure it has a poor predictive value, an elevated serum lactate level is associated with adverse outcomes in a variety of conditions. The SSC Guidelines issued a weak recommendation for measuring lactate levels during sepsis screening, and an elevated lactate level should prompt a thorough clinical assessment of the patient.

Initial resuscitation Early and appropriate fluid resuscitation has been a pillar in the treatment of sepsis. However, controversy existed regarding what constitutes an "adequate" volume of fluids in the initial phase. Previous iterations of the SSC Guidelines issued a strong recommendation to use a fixed volume of 30 ml/kg in the first 3 hours. However, the 2021 SSC Guidelines downgraded this to a weak recommendation due to the limited quality of evidence supporting this practice. The panel considered 3 large randomized controlled trials (RCTs) of early-goal directed therapy in sepsis.[10-12] While not part of the study protocol, most study participants received approximately 30 ml/kg of fluids prior to randomization, suggesting this to be "usual care" in most settings.[13] In addition, 1 RCT from a resource-limited setting showed worse outcomes with a sepsis protocol incorporating a larger volume of fluids in comparison with usual care.[14] Lastly, retrospective data from the subset of patients with end-stage kidney disease and congestive heart failure, who might be expected to do worse with higher fluid volumes, actually showed that these patients had improved outcomes if given adequate intravenous (IV) resuscitation for the first 3 hours.[15]

After the initial resuscitation phase, fluid management becomes a bigger challenge, as there is an increasing risk of fluid overload, which is associated with worse outcomes necessitating a more cautious approach. The objective of any fluid is to improve cardiac output and oxygen delivery, that is, "fluid-responsiveness."[16] This can be achieved using dynamic measures, such as passive leg raise, stroke volume (SV), SV variation, pulse pressure variation, and echocardiography. Existing evidence on these techniques demonstrated inconsistent effects, and the studies themselves were conducted in high-resource settings, limiting their generalizability. Thus, the SSC Guidelines issued a weak recommendation for using dynamic measures to guide resuscitation beyond the initial stage, including the use of capillary refill time as an adjunct or when other advanced methods are not available.

Serum lactate level, often considered to be a marker of tissue and organ hypoperfusion, can also be elevated for other reasons.[17,18] However, with adequate resuscitation and restoration of perfusion, serum lactate levels usually decrease.[17]

The SSC Gguidelines suggested incorporating serial lactate level measurements into the resuscitation process, noting clinicians should not use this method in isolation. Rather, a rising or persistently elevated lactate level should prompt clinicians to perform a thorough clinical assessment to determine the need for further resuscitation.

Mean arterial pressure The 2021 Guidelines issued a strong recommendation to target a mean arterial pressure (MAP) of 65 mm Hg in patients with septic shock. A meta-analysis of 2 RCTs showed no benefit of higher MAP, as compared with MAP greater than or equal to 65 mm Hg in early resuscitation of septic patients.[19]

Admission to intensive care unit Finally, it was recognized that the admission of critically ill patients in general, and specifically those with sepsis, within 6 hours to the ICU leads to better outcomes.[20,21] On this basis, the 2021 Guidelines included a weak recommendation for ICU admission to take place within 6 hours from the decision to admit. If the admission is delayed for any reason, other guideline recommendations should be carried out to the greatest extent possible wherever the patient is.

Infection **Timing of antimicrobials** Given the association between time to appropriate antimicrobials and mortality in sepsis, especially in patients with septic shock, the recommendations for timing of antimicrobials were classified according to the probability of sepsis, and the presence or absence of shock. In patients with confirmed or probable sepsis, the 2021 Guidelines included a strong recommendation for administering empiric antimicrobials within 1 hour. In situations where sepsis is possible, but not definite or probable, patients with shock should receive antimicrobials within 1 hour (being "too sick to miss"), and those without shock should undergo rapid assessment of the infectious vs noninfectious causes of acute illness, ideally deciding on and administering antimicrobials (if appropriate) within 3 hours. In situations where patients are at a low probability of infection and have no signs of shock, the 2021 Guidelines included a weak recommendation for continued observation and monitoring for signs of sepsis, without administering empiric antimicrobials.

Biomarkers to start antibiotics The 2021 Guidelines recommended to obtain microbiologic cultures before starting antimicrobials, so long as it does not substantially delay the initiation of antimicrobials. The Guidelines included a weak recommendation against adding procalcitonin to a standard clinical evaluation, given a lack of benefit demonstrated in RCTs.

Antimicrobial choice The 2021 Guidelines advocated for assessing the patient's risk of infection and individualizing the choices for each patient based on the most likely organism and local antimicrobial resistance patters. For example, for patients at a high risk for methicillin-resistant *Staphylococcus aureus* (MRSA) infection, clinicians should use empiric MRSA coverage (strong recommendation). The full Guidelines present risk factors for the abovementioned infections that should prompt empiric coverage. Of note, the panel made no recommendation with respect to empiric antiviral coverage, noting that such data are sparse and rapidly evolving, and addressed in the SSC COVID-19 Guidelines.[4,5]

Delivery of antimicrobials, pharmacokinetics, and pharmacodynamics Appropriate delivery of antimicrobials is essential to achieve the desired effect while minimizing toxicity. Moderate-quality evidence suggested that prolonged infusions of β-lactams, which increase time in the therapeutic range, may reduce mortality. Accordingly, the 2021 Guidelines included a weak recommendation for this approach, acknowledging that it may require more resources and not be feasible in all settings. The Guidelines also included a best practice statement to optimize dosing strategies using pharmacokinetic and pharmacodynamic data for each drug.

Source control Alongside the antimicrobials, the 2021 Guidelines included best practice statements for emergent source control in patients with sepsis or septic shock as soon as possible, and for prompt removal of intravascular access devices when considered a possible source of infection.

De-escalation and discontinuation of antimicrobials The 2021 Guidelines included a weak recommendation for a daily assessment of antimicrobial de-escalation, noting that very low-quality evidence showed an association between de-escalation of antimicrobials and shorter hospital stay and lower short term-mortality. Furthermore, de-escalation may reduce costs and antimicrobial resistance. While not specifically addressing the duration of treatment in any single case, the Guidelines included a weak recommendation to use shorter, rather than longer, durations of antimicrobial therapy in patients with adequate source control. The panel noted that RCTs in a variety of infections evidence that shorter durations generally show little to no difference in outcomes, especially in patients who have demonstrated clinical improvement. In situations where the optimal duration of antimicrobials is unclear despite adequate source control, the Guidelines included a weak recommendation to use procalcitonin level measurements, alongside clinical evaluation, as part of criteria for antibiotic discontinuation, citing low-quality evidence that suggested this approach may reduce mortality as compared with bedside clinical evaluation alone. This stands in contrast to the weak recommendation against using procalcitonin

levels to guide the initiation of antibiotics in the first place.

Hemodynamic management **Fluid management** There has been substantial development of the evidence base for fluid choice in sepsis. The 2021 Guidelines included a strong recommendation for using crystalloids as first-choice fluids in resuscitation, a strong recommendation against using starches, and a weak recommendation against using gelatins. There are numerous crystalloid solutions available, usually classified into "balanced" (eg, Ringer's lactate) and "nonbalanced" (eg, 0.9% normal saline). Several trials compared balanced and nonbalanced crystalloids, and low-quality evidence suggests that balanced crystalloids may reduce mortality in septic patients. Given the similar cost and convenience of both types of crystalloids, the Guidelines included a weak recommendation for using balanced solutions over saline. The role of albumin remains controversial; while there is some evidence that it may improve patient outcomes, this remains uncertain, and given its higher cost, the Guidelines suggested its use only in patients who have received large volumes of crystalloids but require further fluid resuscitation. Two large trials released since the publication of the Guidelines compared balanced solutions and normal saline in critically ill patients.[22,23] The patients in these trials did not specifically have sepsis or septic shock; however, subgroup analyses of patients admitted with sepsis did not demonstrate any differences in mortality. While other trials specifically evaluating fluid choice in sepsis are ongoing,[24] the totality of the pooled evidence to date still supports a weak recommendation for balanced crystalloids over saline, but it is increasingly clear that, for most patients, the magnitude of the effect is small.[25]

The panel noted there was insufficient evidence to make a recommendation on the use of restrictive vs liberal fluid strategies in the first 24 hours of resuscitation in patients with sepsis, and stated that fluids should generally only be given in patients with signs of hypoperfusion. The subsequent publication of the CLASSIC (Conservative vs Liberal Fluid Therapy in Septic Shock) trial, which compared restrictive vs standard IV fluid therapy in patients with septic shock, did not show a difference between these 2 approaches in patient mortality or adverse events up to 90 days.[26] This suggests that either approach remains reasonable and the panel's suggestion to give fluids only in patients with signs of hypoperfusion continues to be a prudent approach to ongoing fluid therapy. Future trials may provide more evidence on the optimal dose of fluids and timing of vasopressor initiation in septic patients.

Vasoactive agents and inotropes The 2021 Guidelines continued to recommend the use of norepinephrine over other vasopressors including dopamine (high-quality evidence), vasopressin (moderate-quality evidence), epinephrine (low-quality evidence), selepressin (low-quality evidence), and angiotensin II (very low-quality evidence). The panel noted that norepinephrine is not readily available in all regions, and that in such cases epinephrine or dopamine would be a reasonable alternative despite the higher risk of arrhythmia—but also encouraged efforts to improve the availability of norepinephrine. In patients on norepinephrine who continue to have inadequate MAP, the Guidelines included a weak recommendation for adding vasopressin, without a specific dose at which it should be initiated. For practical purposes, the panel noted this is often done when the dosing is in the range of 0.25–0.5 μg/kg/min, but this was not a formal evidence-based recommendation, and may vary between clinicians, patients, and centers. Despite scant evidence, the Guidelines included a weak recommendation for using epinephrine as a third-line agent in patients on norepinephrine and vasopressin, in part because it may be useful in patients with concomitant myocardial dysfunction, as described below.

The 2021 Guidelines addressed the role of inotropes in patients with cardiac dysfunction with persistent hypoperfusion despite adequate volume status and blood pressure. Two alternative strategies were suggested. Firstly, dobutamine could be added (as was done in the early-goal directed therapy trials); alternatively, the patient could switch from norepinephrine to epinephrine, which has more β-agonist activity. A weak recommendation was made against levosimendan; a calcium-sensitizing drug appears to be no better than dobutamine in septic patients, and may delay weaning and result in more tachyarrhythmias.

Monitoring and intravenous access The 2021 Guidelines included a weak recommendation to start peripheral vasopressors to restore MAP, rather than delaying vasopressors until central access is obtained. Despite very low quality of evidence, persistent hypoperfusion can be dangerous, even though observational evidence suggests that short (<6 hours) durations of peripheral vasopressors, in veins at or proximal to the antecubital fossa, are associated with a low risk of complications. The Guidelines also suggested the use of invasive monitoring of blood pressure in patients with septic shock, so long as the practice and resources are available, as cuff pressures can be inaccurate, especially in extreme physiologic states, including septic shock.

Ventilation **High-flow nasal cannula and noninvasive ventilation** Sepsis can lead to multiorgan dysfunction, including respiratory failure. The 2021 Guidelines revisited and updated several previous recommendations on the management of hypoxemic respiratory failure in patients with sepsis, and made 2 new recommendations. First, based on low-quality evidence, a weak recommendation suggested using high-flow nasal oxygenation

(HFNO) over noninvasive ventilation (NIV) in patients with sepsis-induced hypoxemic respiratory failure. This was based on an RCT that compared HFNO directly with NIV in septic patients with hypoxemic respiratory failure. Little to no difference in intubation was found, but HFNO improved survival at 90 days and increased ventilator-free days at 28 days in comparison with NIV.[27] Similarly to previous iterations of the SSC Guidelines, no recommendation was made for the use of NIV as compared with invasive mechanical ventilation when managing patients with sepsis-induced respiratory failure.

Extracorporeal membrane oxygenation The second new recommendation addressed the use of veno-venous extracorporeal membrane oxygenation (VV-ECMO) in patients with sepsis-induced severe acute respiratory distress syndrome (ARDS). A meta-analysis of 2 RCTs including sick patients with severe ARDS refractory to conventional strategies of management showed a reduction in mortality with VV-ECMO in individuals treated at expert centers.[28] Accordingly, the Guidelines included a weak recommendation for using VV-ECMO for sepsis-induced severe ARDS when conventional mechanical ventilation fails, in centers with appropriate infrastructure and experience.

Neuromuscular blocking agents Owing to new evidence, updates were made to the recommendation regarding the use of neuromuscular blocking agents (NMBAs) in patients with sepsis-induced moderate-to-severe ARDS. Since the 2016 Guidelines, results of several RCTs have been published, including 1 large trial.[29] Continuous NMBA infusion reduced mortality when compared with deep sedation without continuous neuromuscular blockade, but showed little to no difference in comparison with a light sedation strategy using intermittent boluses. Therefore, the 2021 Guidelines included a weak recommendation for using intermittent NMBA boluses over a continuous infusion in patients with sepsis-induced moderate-to-severe ARDS.

Oxygenation targets The panel was unable to issue a recommendation on the oxygenation targets in patients with sepsis-induced hypoxemic respiratory failure. Although 3 RCTs were included in the meta-analyses, there was little to no difference in mortality, ventilator-free days, or the length of ICU stay. While meta-analyses of RCTs in patients in other clinical settings were identified, the panel judged these to be too indirect to formulate recommendations.[30] As there are ongoing trials assessing this question, the panel elected not to issue a recommendation at this time.

Lung protective ventilation and proning Many recommendations remained unchanged from the 2016 Guidelines. These include recommendations on using low tidal volume ventilation in adults with sepsis-induced ARDS (strong recommendation) and in septic patients without ARDS (weak recommendation). Recommendations on ventilatory parameters in septic patients with moderate-to-severe ARDS remained the same, including recommendations to target plateau pressures of 30 cm H_2O or less (strong recommendation), use higher positive end expiratory pressure (PEEP) (weak recommendation), and use prone ventilation for at least 12 hours per 24-hour period (strong recommendation).

Recruitment maneuvers The 2021 Guidelines included 2 additional RCTs on the use of recruitment maneuvers in the updated meta-analysis. These studies examined the effect of incremental PEEP strategy for lung recruitment, followed by a decremental PEEP titration. A subgroup analysis showed increased mortality at 28 days with incremental PEEP strategy vs reduced 28-day mortality with traditional recruitment maneuvers (eg, 30–40 cm H_2O for 30–40 seconds). Therefore, the 2021 Guidelines suggested using traditional recruitment maneuvers, but recommended against using an incremental PEEP titration strategy in adults with sepsis-induced moderate-to-severe ARDS.

Additional therapies

The additional therapy section of the SSC Guidelines focused on supportive therapies, whether directly related to sepsis or complications of sepsis-related critical illness. There are many changes in this section, as these therapies often have a rapidly evolving evidence base.

Corticosteroids Corticosteroids have been part of the SSC Guidelines since the first iteration in 2004. Results of the meta-analysis on corticosteroid use in septic shock have upgraded the quality of evidence from low to moderate.[31] Evidence showed that corticosteroid use resulted in faster resolution of shock, at the expense of a possible increase in neuromuscular weakness, while the effect on mortality was somewhat unclear. The 2021 Guidelines included a weak recommendation to use corticosteroids in adults with septic shock and an ongoing requirement for vasopressor therapy despite adequate fluid resuscitation, and proposed using 200 mg/day of hydrocortisone, either divided into 6-hour doses or as a continuous infusion.

Vitamin C The 2021 Guidelines issued a new weak recommendation against the use of intravenous vitamin C for sepsis or septic shock. Initial optimism for this therapy, based on observational data, has been tempered by meta-analyses of RCTs,[32] including the recently published LOVIT (Lessening Organ Dysfunction with Vitamin C) trial.[33]

Bicarbonate As in the 2016 Guidelines, the panel issued a weak recommendation against

the routine use of bicarbonate therapy in sepsis-induced lactic acidosis; however, it may be reasonable to use bicarbonate therapy in septic patients with metabolic acidosis (pH ≤7.2) and acute kidney injury. This weak recommendation was primarily driven by a subgroup analysis of an RCT in which these populations showed a large treatment effect.[34]

Blood purification techniques In previous iterations, the SSC Guidelines did not issue a recommendation on the use of hemoperfusion therapies in sepsis. However, the 2021 Guidelines included a suggestion not to use polymyxin B hemoperfusion in the treatment of sepsis or septic shock. One new RCT informed an updated meta-analysis that demonstrated harm.[35] The hemoperfusion literature in sepsis has been conflicting—beneficial effects typically came only from older studies in a single region, and updated data were sufficient for the panel to state that the resources and potential for harm warranted a weak recommendation against polymyxin hemoperfusion. The panel pointed to a lack of sufficient evidence to make a recommendation about other forms of hemoperfusion therapy.

Red blood cell transfusion targets and immunoglobulin Regarding red blood cell transfusion targets, although the quality of evidence was downgraded to moderate based on the inclusion of a new RCT, the 2021 Guidelines included a strong recommendation for restrictive over liberal strategies (typically defined as a trigger of 7.0 g/dl, in addition to clinical status) similarly to the previous iteration.[36] The 2021 Guidelines included a weak recommendation against the use of immunoglobulins, given the low quality evidence and associated costs.[37]

Stress ulcer prophylaxis The 2021 Guidelines included a single recommendation for stress ulcer prophylaxis in patients with risk factors, and pointed to a higher quality of evidence (upgraded to moderate) but a weaker level of recommendation due to possible adverse effects. For venous thromboembolism prophylaxis, recommendations for pharmacologic prophylaxis remained unchanged, with the exception that a weak recommendation for using mechanical in addition to pharmacologic prophylaxis was changed to a suggestion against adding mechanical prophylaxis to pharmacologic prophylaxis, based on new data.[38]

Renal replacement therapy Regarding renal replacement therapy (RRT), a previous weak recommendation for either continuous or intermittent RRT did not change. Evidence against the use of early RRT in patients with acute kidney injury but no definitive indications was strengthened to moderate with the addition of 2 new RCTs, supporting a weak recommendation for the initiation guided by standard dialysis indications.[39,40]

Glucose control The 2021 Guidelines approached questions related to glycemic control from a different perspective, asking at what threshold insulin therapy should be initiated. The Guidelines added a recommendation to start insulin when blood glucose levels in 2 consecutive measurements were higher than 10 mmol/l, based upon a network meta-analysis suggesting a lower risk of hypoglycemia when this threshold was used.

Nutrition Finally, several recommendations around nutrition made in 2016 were not addressed in this iteration of the Guidelines. The 2021 Guidelines included only a single weak recommendation for early (within 72 hours) initiation of enteral nutrition, based on the addition of a new RCT to 4 previous studies.[41]

Long-term outcomes and goals of care The 2021 Guidelines included a new section on long-term outcomes and goals of care. In the 2016 Guidelines, the goals of care and palliative care were addressed as single recommendations. Given the novel nature of these recommendations, the patient panel played a crucial role in developing this section of the Guidelines. The quality of evidence for all PICO questions in this section was low or very low, highlighting that post-ICU care is a new area of focus for sepsis research.

Several recommendations were relevant to early phases of sepsis care. With respect to the goals of care discussions, in which clinicians discuss the care preferences and available treatment options with patients and/or families, the 2021 Guidelines included a best practice statement to ensure that patients only receive care that is concordant with their values. Low-quality evidence showed that early discussions (within 48 hours of ICU admission) may improve perception of the quality of communication, patient-centeredness of care, and reduce the length of ICU stay, which may be due to patients not receiving unwanted, invasive treatments. The literature review did not identify any clinical trigger for goals of care discussions that clearly and consistently outperformed routine discussions. Instead, the Guidelines recommended an early-ICU goals of care discussion, with recurrent discussions preferably based upon patient/family request and clinical changes likely to impact patient morbidity and mortality, including the need for additional treatments.

Surprisingly, the use of routine, formal, palliative care consults was not associated with a consistent benefit, and in some cases demonstrated harm to the family mental health outcomes.[42] As symptom management and holistic care are crucial to the care experience of patients and families, the panel made a best practice statement to incorporate palliative care principles to address patient symptoms and suffering, and formal palliative care consultations when expert input is required.

Many recommendations in this section aimed to improve long-term patient outcomes after

the initial resuscitative phase of sepsis. Recognizing that sepsis survivors often have significant cognitive dysfunction, early (within-ICU) cognitive therapy has been studied as preventative treatment. However, the evidence was insufficient to make a recommendation for or against cognitive therapy.[43] The 2021 Guidelines included a best practice statement to screen and make appropriate referrals for patients with sepsis and their families for economic and social supports, on the basis of evidence that patients without these supports in the community have worse outcomes. Very low-quality evidence supported a weak recommendation to offer sepsis-specific education to patients and their families, as a low-cost intervention that can help recognize complications early.

The 2021 Guidelines strongly emphasised the risks patients face during transitions of care, such as from the ICU to the ward or from the ward to home, including a best practice statement to engage the patient and the family in shared decision-making for post-ICU care and hospital discharge planning. There was very low-quality evidence that a critical care transition program (eg, ICU nurse or physician follow-up on the ward after the end of ICU stay) may reduce readmission or death. The 2021 Guidelines included best practice statements for medication reconciliation at ICU and hospital discharge, and providing patients and families with information on sepsis, including the diagnosis, treatments, and long-term sequelae, as part of the discharge plan.

Lastly, while there has been a proliferation of post-ICU clinics, there was only very low-quality evidence that these may improve psychological symptoms, and little evidence of their impact on other important patient outcomes. Similarly, while post-ICU rehabilitation programs possibly improve the quality of life and depressive symptoms, the evidence was of very low quality. Therefore, the 2021 Guidelines included a weak recommendation for post-ICU clinics and ICU-specific rehabilitation programs, and a best practice statement to assess the risk of potential physical, cognitive, and emotional sequelae in sepsis survivors and to follow them after hospital discharge. There was insufficient evidence to make any recommendations on the duration of the follow-up after discharge.

Conclusions The 2021 SSC Guidelines provide evidence-based recommendations for the treatment of adult patients with sepsis, based upon the current best available evidence.

ARTICLE INFORMATION

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