Executive Summary: Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-associated Organ Dysfunction in Children 2019

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American Academy of Pediatrics; American Association of Critical-Care Nurses; American College of Emergency Physicians; American Thoracic Society; Canadian Critical Care Society; European Society of Intensive Care Medicine; European Society of Paediatric and Neonatal Intensive Care; Scandinavian Society of Anaesthesiology and Intensive Care Medicine; ; Society of Critical Care Medicine; UK Sepsis Trust; World Federation of Pediatric Intensive and Critical Care Societies][balanceTBD]

The following non-sponsoring organizations (without formal liaison appointees) endorse this guideline: [TBD]

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INTRODUCTION

In 2001, the Surviving Sepsis Campaign (SSC) began to develop evidenced-based guidelines and recommendations for the resuscitation and management of patients with sepsis. With the 2016 edition, the Society of Critical Care Medicine and European Society of Intensive Care Medicine recommended a separate task force be dedicated to guideline formulation for children.

The objective of the *Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-associated Organ Dysfunction in Children* is to provide guidance for the care of children with septic shock and other sepsis-associated organ dysfunction. Recommendations are intended to guide "best practice" rather than to establish a treatment algorithm or to define standard of care, and cannot replace the clinician's decision-making capability when presented with a patient's unique set of clinical variables.

METHODS

This executive summary briefly reviews the methodology, with additional details provided in the complete guidelines document published in *Pediatric Critical Care Medicine* <add link to url> and *Intensive Care Medicine* <add link to url>.

Definitions and Scope

The scope of these guidelines includes all patients from ≥37 weeks' gestation at birth to 18 years with severe sepsis or septic shock as defined by the 2005 International Pediatric Sepsis Consensus Conference (1) or inclusive of severe infection leading to

life-threatening organ dysfunction. Practically, all children with septic shock or other sepsis-associated acute organ dysfunction are included in this scope with the exception of premature babies who have distinct pathology, biology, and therapeutic considerations. Even though these guidelines are not intended to address the management of infection when there is not associated acute organ dysfunction, we recognize that sepsis exists as a spectrum and some children without known acute organ dysfunction may still benefit from similar therapies as those with known organ dysfunction.

The intended users of these guidelines are health professionals caring for children in a hospital, emergency, or other acute care setting. However, many of the recommendations are likely to apply to the care of children in other settings and will need to be adapted to specific environments and resource availability. In addition, these guidelines were largely developed without consideration of the availability of health care services, though we realize that medical care is necessarily carried out within the confines of locally available resources.

Selection and Organization of Panel Members

The selection of panel members was based on their expertise in specific aspects of pediatric sepsis, with broad International and multi-professional representation representing diverse geographic settings and health care systems. Three members from the lay public were also included.

Panelists were divided into the following subgroups: 1) recognition and management of infection, 2) hemodynamics and resuscitation, 3) ventilation, 4)

endocrine and metabolic therapies, and 5) adjunctive therapies. A sixth subgroup reviewed research priorities. Each subgroup was supported by a trained methodologist.

Question Development and Outcome Prioritization

The panel selected topics addressed in the 2016 adult SSC guidelines that were relevant to children, as well as other key topics important to children with sepsis. The PICO format, which describes the population (P), intervention (I), control (C), and outcomes (O), was used for all guideline questions. For practical reasons, we excluded several issues pertaining to general acute or critical illness that were not specific for sepsis (e.g., head-of-bed positioning during invasive mechanical ventilation) and have been addressed in other guidelines (e.g., Pediatric Acute Lung Injury Consensus Conference [PALICC]) (2). However, topics with particular relevance to children with septic shock or other sepsis-associated acute organ dysfunction were included in this guideline, even if there was evaluation of similar or overlapping topics in previous publications. The final list of PICO questions is provided as eTable 1 in the supplement to the complete guidelines.

Search Strategy and Evidence Summation

Professional medical librarians assisted with the literature searches and utilized a combination of controlled vocabulary (e.g., “sepsis,” “bacterial infections,” “critical illness,” “intensive care units,” “pediatrics”), key words (e.g., “toxic shock,” “blood poisoning,” “acute infection,” “PICU,” “child”), and qualifiers specific to each PICO question. Only English language studies were included. As this was the inaugural

version of these guidelines for children, all publications through May 1, 2017 were considered. Key studies published after the conclusion of the initial literature search were incorporated into the evidence synthesis if identified by panel members as important and relevant even if they were not part of the initial literature review.

Formulation of Recommendations

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) principles guided the assessment of quality of evidence from high to very low and were used to determine the strength of recommendations. The GRADE approach to assess the quality of evidence is based on the evaluation of six domains: 1) risk of bias, 2) inconsistency, 3) indirectness, 4) imprecision, 5) publication bias, and 6) other criteria, followed by assessment of the balance between benefit and harm, patients' values and preferences, cost and resources, and feasibility and acceptability of the intervention (3).

The panel initially considered research focused on pediatric patients using the following hierarchy of evidence: systematic reviews, randomized controlled trials, prospective observational studies**,** retrospective observational studies, case-control studies, and large case series. Research focusing on children with septic shock and other sepsis-associated organ dysfunction was prioritized, though studies inclusive of more general pediatric populations (e.g., all PICU patients) were considered for some questions on a case-by-case basis. If there were insufficient data in children with sepsis or general pediatric illness, data from adult studies was considered using a pre-specified framework to guide appropriateness of indirect evidence.

Each of the subgroups used the Evidence-to-Decision (EtD) framework to facilitate transition from evidence to recommendations. The EtD framework ensured that panel members took into consideration not only the quality of evidence and magnitude of effect, but also balance between benefits and harms, patients' values and preferences, resources, cost, acceptability, and feasibility (4).

We classified recommendations as strong or weak using the language "We recommend…" or "We suggest…," respectively. We judged a strong recommendation in favor of an intervention to have desirable effects of adherence that will clearly outweigh the undesirable effects. The implications of calling a recommendation strong are that most patients would accept that intervention and that most clinicians should use it in most situations. However, a strong recommendation does not imply a standard of care, and circumstances may exist in which a strong recommendation cannot or should not be followed for an individual patient. We judged a weak recommendation in favor of an intervention to have desirable consequences of adherence that will probably outweigh the undesirable consequences, but confidence is diminished either because the quality of evidence was low or the benefits and risks were closely balanced. We anticipate that a weak recommendation, while still relevant for most patients in most settings, will be more heavily influenced by clinical circumstances and patients' values than a strong recommendation. We permitted strong recommendations (for or against an intervention) based on low or very low quality of evidence when there was either strong physiologic rationale to support benefit or uncertain benefit but very likely or certain harm (5).

Best practice statements (BPS) were offered when the evidence could not be summarized using GRADE methodology but the benefit or harm was deemed

unequivocal. In addition, when evidence was insufficient to make a recommendation, but the panel felt that some guidance may be appropriate, we issued an “in our practice” statement. The “in our practice” statements were developed through a survey of all panelists in that group to ascertain their state of current practice in an attempt to describe current variation in care. These should not be construed as recommendations.

Voting Process

Panel members convened to review evidence and discuss recommendations at key international meetings, a stand-alone meeting in November 2018, and numerous web-based conference calls. Panelists then indicated agreement or disagreement (or abstention if conflict of interest present) with each recommendation. Up to 3 rounds of voting were conducted in an attempt to achieve consensus. Acceptance of a statement required votes from 75% of panel members with a 80% agreement threshhold.

Conflict of Interest Policy

Conflict-of-interest disclosures were sought from all panelists prior to commencing activities, with updates annually and as needed. There was no industry input into or support of the guideline development process. Only librarians and a supporting project manager received compensation for their work.

RECOMMENDATIONS

The consensus recommendations of the *Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-associated*

Organ Dysfunction in Children are summarized in Table 1 of this executive summary. The rationale and evidence profiles supporting each recommendations are presented in the complete guidelines <add link to URL>s. The panel provided 76 statements on the management and resuscitation of children with septic shock and other sepsis-associated organ dysfunction, including 5 strong recommendations, 49 weak recommendations, and 9 best practice statements. For 13 questions, no recommendations could be made, but, for 10 of these, “in our practice” statements were provided. In addition, 49 research priorities were identified (see complete guidelines).

CONCLUSIONS

Although most aspects of care had relatively low quality of evidence resulting in the frequent issuance of weak recommendations, these guidelines regarding the management of children with septic shock and other sepsis-associated organ dysfunction should provide a foundation for consistent care to improve outcomes and inform future research.

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