Sepsis and septic shock

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Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children

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International Guidelines for Management of Sepsis and Septic Shock 2021

Updated global adult sepsis guidelines, released in October 2021 by the Surviving Sepsis Campaign (SSC), place an increased emphasis on improving the care of sepsis patients after they are discharged from the intensive care unit (ICU) and represent greater geographic and gender diversity than previous versions.

In 2001, the Surviving Sepsis Campaign (SSC) was formed by the Society of Critical Care Medicine (SCCM), European Society of Intensive Care Medicine (ESICM), and the International Sepsis Forum.

A primary aim of the SSC was to develop evidenced-based guidelines and recommendations for the resuscitation and management of patients with sepsis.

The initial guidelines were published in 2004 and have been reviewed and updated every four years thereafter.

Sepsis is a clinical syndrome characterized by systemic inflammation due to infection.

There is a continuum of severity ranging from sepsis to septic shock,

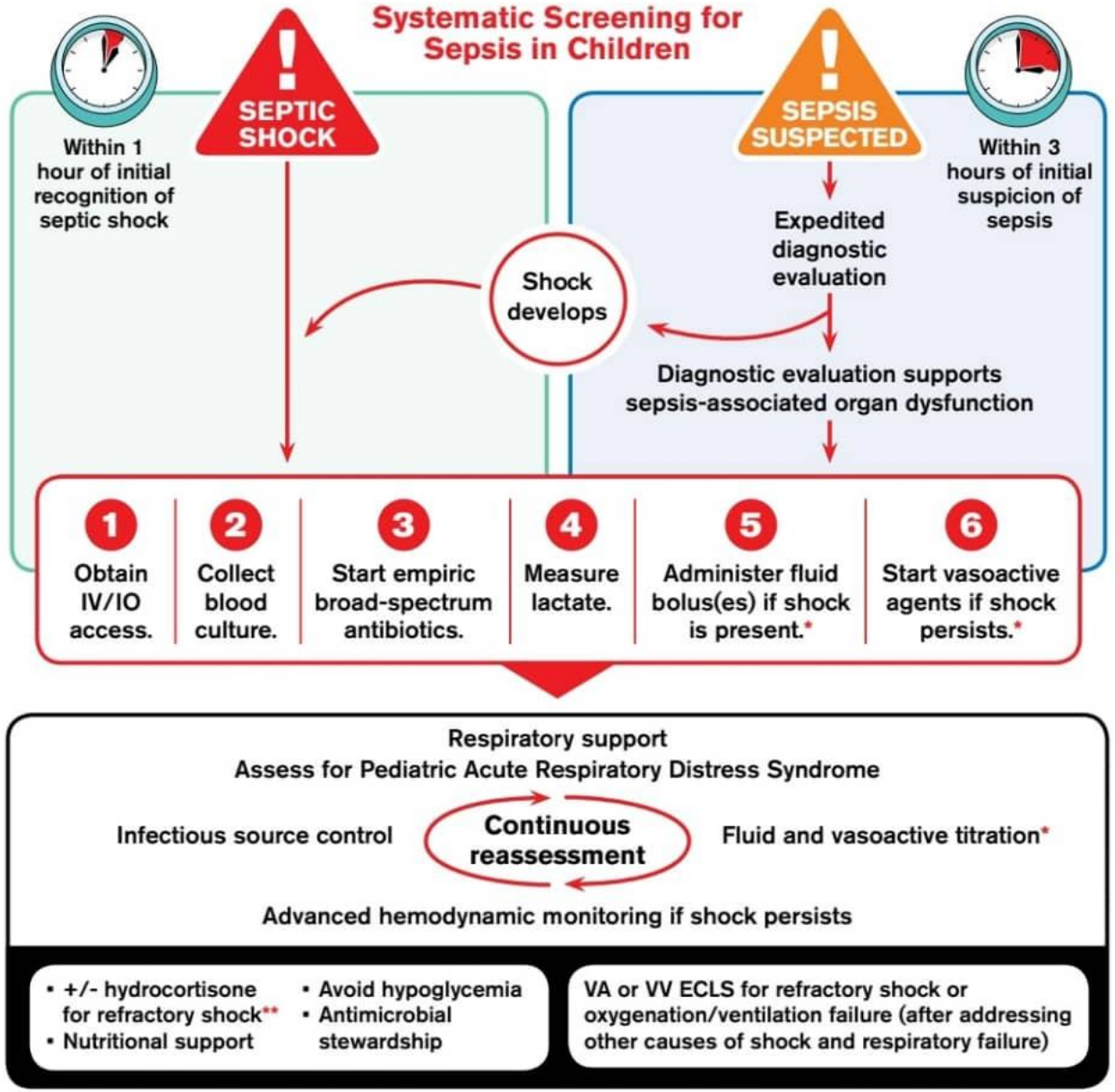
mortality has been estimated to be ≥10 percent and ≥40 percent when shock is present .

septic shock in children as severe infection leading to cardiovascular dysfunction (including hypotension, need for treatment with a vasoactive medication, or impaired perfusion) .

“sepsis- associated organ dysfunction” in children as severe infection leading to cardiovascular and/or noncardiovascular organ dysfunction.

Initial Resuscitation Algorithm for Children

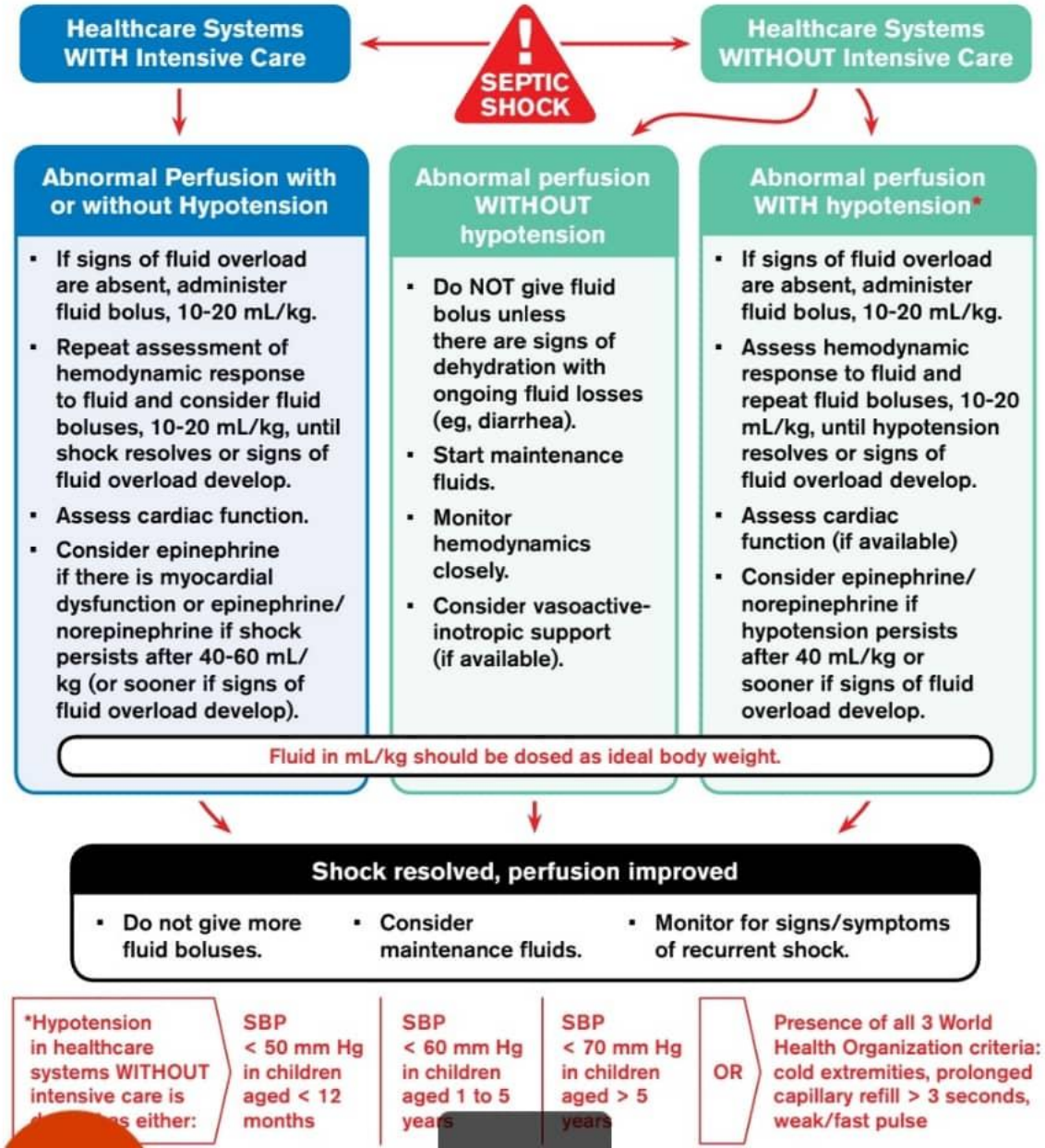
Surviving Sepsis Campaign



*See fluid and vasoactive algorithm. Note: Fluid bolus should be omitted from bundle if a) fluid overload

Fluid and Vasoactive-Inotrope Management Algorithm For Children

Surviving Sepsis Campaign



SCREENING, DIAGNOSIS, AND SYSTEMATIC MANAGEMENT RECOMMENDATIONS TABLE

RECOMMENDATION #1	STRENGTH & QUALITY OF EVIDENCE
In children who present as acutely unwell, we ***suggest implementing*** systematic screening for timely recognition of septic shock and other sepsis-associated organ dysfunction. **Remarks:** Systematic screening needs to be tailored to the type of patients, resources, and procedures within each institution. Evaluation for the effectiveness and sustainability of screening should be incorporated as part of this process.	• Weak • Very Low-Quality of Evidence

RECOMMENDATION #2	STRENGTH & QUALITY OF EVIDENCE
We were unable to issue a recommendation about using blood lactate values to stratify children with suspected septic shock or other sepsis-associated organ dysfunction into low- versus high-risk of having septic shock or sepsis. However, ***in our practice***, if lactate levels can be rapidly obtained, we often measure blood lactate in children when evaluating for septic shock and other sepsis-associated organ dysfunction.	Insufficient

RECOMMENDATION #3	STRENGTH & QUALITY OF EVIDENCE
We ***recommend implementing*** a protocol/guideline for management of children with septic shock or other sepsis-associated organ dysfunction.	Best Practice Statement

RECOMMENDATION #4	STRENGTH & QUALITY OF EVIDENCE
We ***recommend obtaining*** blood cultures before initiating antimicrobial therapy in situations where this does not substantially delay antimicrobial administration.	Best Practice Statement

ANTIMICROBIAL THERAPY RECOMMENDATIONS TABLE

RECOMMENDATION #5	STRENGTH & QUALITY OF EVIDENCE
In children with septic shock, we ***recommend*** starting antimicrobial therapy as soon as possible, within one (1) hour of recognition.	• Strong • Very Low-Quality of Evidence

RECOMMENDATION #6	STRENGTH & QUALITY OF EVIDENCE
In children with sepsis-associated organ dysfunction but without shock, we ***suggest*** starting antimicrobial **therapy as soon as possible** after appropriate evaluation, within three (3) hours of recognition.	• Weak • Very Low-Quality of Evidence

RECOMMENDATION #7	STRENGTH & QUALITY OF EVIDENCE
We ***recommend*** empiric broad-spectrum therapy with one or more antimicrobials to cover all likely pathogens.	Best Practice Statement

RECOMMENDATION #8	STRENGTH & QUALITY OF EVIDENCE
Once the pathogen(s) and sensitivities are available, we ***recommend*** narrowing empiric antimicrobial therapy coverage.	Best Practice Statement

Recommendation #9	Strength & Quality of Evidence
If no pathogen is identified, we ***recommend*** narrowing or stopping empiric antimicrobial therapy according to clinical presentation, site of infection, host risk factors, and adequacy of clinical improvement in discussion with infectious disease and/or microbiological expert advice.	Best Practice Statement

Recommendation #10	Strength & Quality of Evidence
In children without immune compromise and without high risk for multidrug-resistant pathogens, we ***suggest against*** the routine use of empiric multiple antimicrobials directed against the same pathogen for the purpose of synergy. **Remarks:** In certain situations, such as confirmed or strongly suspected group B streptococcal sepsis, use of empiric multiple antimicrobials directed against the same pathogen for the purpose of synergy may be indicated.	• Weak • Very Low-Quality of Evidence

Recommendation #11	Strength & Quality of Evidence
In children with immune compromise and/or at high risk for multidrug-resistant pathogens, we ***suggest*** using empiric multi-drug therapy when septic shock or other sepsis-associated organ dysfunction is present/suspected.	• Weak • Very Low-Quality of Evidence

Recommendation #12	Strength & Quality of Evidence
We ***recommend*** using antimicrobial dosing strategies that have been optimized based on published pharmacokinetic/ pharmacodynamic principles and with consideration of specific drug properties.	Best Practice Statement

RECOMMENDATION #13	STRENGTH & QUALITY OF EVIDENCE
In children with septic shock or sepsis-associated organ dysfunction who are receiving antimicrobials, we ***recommend*** daily assessment (e.g., clinical, laboratory assessment) for de-escalation of antimicrobial therapy. **Remarks:** This assessment should include a review of the ongoing indication for empiric antimicrobial therapy after the first 48 hours that is guided by microbiologic results and in response to clinical improvement and/or evidence of infection resolution. This recommendation applies to patients being treated with empiric, targeted, and combination therapy.	Best Practice Statement

RECOMMENDATION #14	STRENGTH & QUALITY OF EVIDENCE
We ***recommend*** determining the duration of antimicrobial therapy according to the site of infection, microbial etiology, response to treatment, and ability to achieve source control.	Best Practice Statement

SOURCE CONTROL RECOMMENDATIONS TABLE

RECOMMENDATION #15	STRENGTH & QUALITY OF EVIDENCE
We ***recommend*** that emergent source control intervention be implemented as soon possible after a diagnosis of an infection amenable to a source control procedure is made. **Remarks:** Appropriate diagnostic testing to identify the site of infection and microbial etiology should be performed, and advice from specialist teams (e.g., infectious diseases, surgery) should be sought, as appropriate, in order to prioritize interventions needed to achieve source control.	Best Practice Statement

RECOMMENDATION #16	STRENGTH & QUALITY OF EVIDENCE
We ***recommend*** removal of intravascular access devices that are confirmed to be the source of sepsis or septic shock after other vascular access has been established and depending on the pathogen and the risks/benefits of a surgical procedure.	• Strong • Low-Quality of Evidence

FLUID THERAPY RECOMMENDATIONS TABLE

RECOMMENDATION #17	STRENGTH & QUALITY OF EVIDENCE
In healthcare systems with availability of intensive care, we ***suggest*** administering up to 40–60mL/kg in bolus fluid (10–20mL/kg per bolus) over the first hour, titrated to clinical markers of cardiac output and discontinued if signs of fluid overload develop, for the initial resuscitation of children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Low-Quality of Evidence

RECOMMENDATION #18	STRENGTH & QUALITY OF EVIDENCE
In healthcare systems with no availability of intensive care and in the *absence of hypotension*, we ***recommend against*** bolus fluid administration while starting maintenance fluids.	• Strong • High-Quality of Evidence

RECOMMENDATION #19	STRENGTH & QUALITY OF EVIDENCE
In healthcare systems with no availability of intensive care, if hypotension is present, we ***suggest*** administering up to 40mL/kg in bolus fluid (10–20mL/kg per bolus) over the first hour with titration to clinical markers of cardiac output and discontinued if signs of fluid overload develop. **Remarks:** Clinical markers of cardiac output may include heart rate, blood pressure, capillary refill time, level of consciousness, and urine output. In all settings, the need for fluid administration should be guided by frequent reassessment of clinical markers of	• Weak • Low-Quality of Evidence

RECOMMENDATION #19	STRENGTH & QUALITY OF EVIDENCE
In healthcare systems with no availability of intensive care, if hypotension is present, we ***suggest*** administering up to 40mL/kg in bolus fluid (10–20mL/kg per bolus) over the first hour with titration to clinical markers of cardiac output and discontinued if signs of fluid overload develop. **Remarks:** Clinical markers of cardiac output may include heart rate, blood pressure, capillary refill time, level of consciousness, and urine output. In all settings, the need for fluid administration should be guided by frequent reassessment of clinical markers of	• Weak • Low-Quality of Evidence

cardiac output, serial blood lactate measurement and advanced monitoring, when available. Signs of fluid overload that should limit further fluid bolus therapy may include clinical signs of pulmonary edema or new or worsening hepatomegaly.

RECOMMENDATION #20	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** using crystalloids, rather than albumin, for the initial resuscitation of children with septic shock or other sepsis-associated organ dysfunction. **Remarks:** Although there is no difference in outcomes, this recommendation takes into consideration cost and other barriers of administering albumin compared with crystalloids.	• Weak • Moderate-Quality of Evidence

RECOMMENDATION #21	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** using balanced/buffered crystalloids, rather than 0.9% saline, for the initial resuscitation of children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Very Low-Quality of Evidence

RECOMMENDATION #22	STRENGTH & QUALITY OF EVIDENCE
We ***recommend against*** using starches in the acute resuscitation of children with septic shock or other sepsis-associated organ dysfunction.	• Strong • Moderate-Quality of Evidence

RECOMMENDATION #23	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** using gelatin in the resuscitation of children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Low-Quality of Evidence

HEMODYNAMIC MONITORING RECOMMENDATIONS TABLE

RECOMMENDATION #24	STRENGTH & QUALITY OF EVIDENCE
We were ***unable to issue a recommendation*** about whether to target mean arterial blood pressure (MAP) at the 5th or 50th percentile for age in children with septic shock and other sepsis-associated organ dysfunction. However, ***in our practice***, we target MAP to between the 5th and 50th percentile or greater than 50th percentile for age.	Insufficient In Our Practice

RECOMMENDATION #25	STRENGTH & QUALITY OF EVIDENCE
We ***suggest not using*** bedside clinical signs in isolation to categorize septic shock in children as "warm" or "cold".	• Weak • Very Low-Quality of Evidence

RECOMMENDATION #26	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** using advanced hemodynamic variables, when available, in addition to bedside clinical variables to guide the resuscitation of children with septic shock or other sepsis-associated organ dysfunction. **Remarks:** Advanced hemodynamic monitoring may include cardiac output/cardiac index, systemic vascular resistance, or central venous oxygen saturation (Scvo2).	• Weak • Low-Quality of Evidence

RECOMMENDATION #27	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** using trends in blood lactate levels, in addition to clinical assessment, to guide resuscitation of children with septic shock and other sepsis-associated organ dysfunction. **Remarks:** In children with an elevated blood lactate, repeat testing that reveals a persistent elevation in blood lactate may indicate incomplete hemodynamic resuscitation and should prompt efforts, as needed, to further promote hemodynamic stability.	• Weak • Very Low-Quality of Evidence

VASOACTIVE MEDICATIONS RECOMMENDATIONS TABLE

RECOMMENDATION #28	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** using epinephrine, rather than dopamine, in children with septic shock.	• Weak • Low-Quality of Evidence

RECOMMENDATION #29	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** using norepinephrine, rather than dopamine, in children with septic shock.	• Weak • Very Low-Quality of Evidence

RECOMMENDATION #30	STRENGTH & QUALITY OF EVIDENCE
We were ***unable to issue a recommendation*** for a specific first-line vasoactive infusion for children with septic shock. However, in our practice, we select either epinephrine or norepinephrine as the first-line vasoactive infusion guided by clinician preference, individual patient physiology, and local system factors.	Insufficient

RECOMMENDATION #31	STRENGTH & QUALITY OF EVIDENCE
We were ***unable to issue a recommendation*** about initiating vasoactive agents through peripheral access in children with septic shock. However, in our practice, we often or sometimes administer a dilute concentration of the initial vasoactive medication through a peripheral vein if central venous access is not readily accessible.	Insufficient

RECOMMENDATION #32	STRENGTH & QUALITY OF EVIDENCE
We **suggest** either adding vasopressin or further titrating catecholamines in children with septic shock who require high-dose catecholamines. **Remarks:** No consensus was achieved on the optimal threshold for initiating vasopressin. Therefore, this decision should be made according to individual clinician preference.	• Weak • Low-Quality of Evidence

RECOMMENDATION #33	STRENGTH & QUALITY OF EVIDENCE
We were unable to issue a recommendation about adding an inodilator in children with septic shock and cardiac dysfunction despite other vasoactive agents. However, in our practice, we sometimes use inodilators in children with septic shock and evidence of persistent hypoperfusion and cardiac dysfunction despite other vasoactive agents.	Insufficient

VENTILATION RECOMMENDATIONS TABLE

RECOMMENDATION #34	STRENGTH & QUALITY OF EVIDENCE
We were ***unable to issue a recommendation*** about whether to intubate children with fluid-refractory, catecholamine-resistant septic shock. However, in our practice, we commonly intubate children with fluid-refractory, catecholamine-resistant septic shock without respiratory failure.	Insufficient

RECOMMENDATION #35	STRENGTH & QUALITY OF EVIDENCE
We ***suggest not to use*** etomidate when intubating children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Low-Quality of Evidence

RECOMMENDATION #36	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** a trial of noninvasive mechanical ventilation (over invasive mechanical ventilation) in children with sepsis-induced pediatric ARDS (PARDS) without a clear indication for intubation and who are responding to initial resuscitation.	• Weak • Very Low-Quality of Evidence

RECOMMENDATION #37	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** using high positive end-expiratory pressure (PEEP) in children with sepsis-induced PARDS. **Remarks:** The exact level of high PEEP has not been tested or determined in PARDS patients. Some RCTs and observational studies in PARDS have used and advocated for use of the ARDS-network PEEP to Fio2 grid though adverse hemodynamic effects of high PEEP may be more prominent in children with septic shock.	• Weak • Very Low-Quality of Evidence

RECOMMENDATION #38	STRENGTH & QUALITY OF EVIDENCE
We ***cannot suggest for or against*** the use of recruitment maneuvers in children with sepsis-induced PARDS and refractory hypoxemia. **Remarks:** If a recruitment maneuver is considered, the use of a stepwise, incremental and decremental PEEP titration maneuver is preferred over sustained inflation techniques that have not been optimized through direct testing in PARDS patients. All PARDS patients must be carefully monitored for tolerance of the maneuver.	Insufficient

RECOMMENDATION #39	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** a trial of prone positioning in children with sepsis and severe PARDS. **Remarks:** Research trials in adults with ARDS and children with PARDS have emphasized prone positioning for at least 12 hours per day, as tolerated.	• Weak • Low-Quality of Evidence

RECOMMENDATION #40	STRENGTH & QUALITY OF EVIDENCE
We ***recommend against*** the routine use of inhaled nitric oxide (iNO) in all children with sepsis-induced PARDS.	• Strong • Low-Quality of Evidence

RECOMMENDATION #41	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** using iNO as a rescue therapy in children with sepsis-induced PARDS and refractory hypoxemia after other oxygenation strategies have been optimized.	• Weak • Moderate-Quality of Evidence

RECOMMENDATION #42	STRENGTH & QUALITY OF EVIDENCE
We were **unable to issue a recommendation** to use high-frequency oscillatory ventilation (HFOV) versus conventional ventilation in children with sepsis-induced PARDS.	Insufficient
However, **in our practice**, there is no preference to use or not use HFOV in patients with severe PARDS and refractory hypoxia.	In Our Practice

RECOMMENDATION #43	STRENGTH & QUALITY OF EVIDENCE
We suggest using neuromuscular blockade in children with sepsis and severe PARDS. **Remarks:** The exact duration of neuromuscular blockade to use in severe PARDS patients has not been determined to date. Most of the adult RCT data and pediatric observational data support treatment for 24–48 hours after ARDS onset.	• Weak • Very Low-Quality of Evidence

CORTICOSTEROIDS RECOMMENDATIONS TABLE

RECOMMENDATION #44	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** using IV hydrocortisone to treat children with septic shock if fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability.	• Weak • Low-Quality of Evidence

RECOMMENDATION #45	STRENGTH & QUALITY OF EVIDENCE
We **suggest** that either IV hydrocortisone or no hydrocortisone may be used if adequate fluid resuscitation and vasopressor therapy are not able to restore hemodynamic stability.	• Weak • Low-Quality of Evidence

ENDOCRINE & METABOLIC RECOMMENDATIONS TABLE

RECOMMENDATION #46	STRENGTH & QUALITY OF EVIDENCE
We ***recommend against*** insulin therapy to maintain a blood glucose target at or below 140mg/dL (7.8 mmol/L).	• Strong • Moderate-Quality of Evidence

RECOMMENDATION #47	STRENGTH & QUALITY OF EVIDENCE
We were ***unable to issue a recommendation*** regarding what blood glucose range to target for children with septic shock or other sepsis-associated organ dysfunction. However, ***in our practice***, there was consensus to target blood glucose levels below 180mg/dL (10 mmol/L) but there was not consensus about the lower limit of the target range.	Insufficient In Our Practice

RECOMMENDATION #48	STRENGTH & QUALITY OF EVIDENCE
We were ***unable to issue a recommendation*** as to whether to target normal blood calcium levels in children with septic shock or sepsis-associated organ dysfunction. However, ***in our practice***, we often target normal calcium levels for children with septic shock requiring vasoactive infusion support.	Insufficient In Our Practice

Recommendation #49	Strength & Quality of Evidence
We ***suggest against*** the routine use of levothyroxine in children with septic shock and other sepsis-associated organ dysfunction in a sick euthyroid state.	• Weak • Low-Quality of Evidence

Recommendation #50	Strength & Quality of Evidence
We ***suggest*** either antipyretic therapy or a permissive approach to fever in children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Moderate-Quality of Evidence

NUTRITION RECOMMENDATIONS TABLE

RECOMMENDATION #51	STRENGTH & QUALITY OF EVIDENCE
We were ***unable to issue a recommendation*** regarding early hypocaloric/trophic enteral feeding followed by slow increase to full enteral feeding versus early full enteral feeding in children with septic shock or sepsis-associated organ dysfunction without contraindications to enteral feeding. However, in our practice, there is a preference to commence early enteral nutrition within 48 hours of admission in children with septic shock or sepsis-associated organ dysfunction who have no contraindications to enteral nutrition and to increase enteral nutrition in a stepwise fashion until nutritional goals are met.	Insufficient

RECOMMENDATION #52	STRENGTH & QUALITY OF EVIDENCE
We ***suggest not withholding*** enteral feeding solely on the basis of vasoactive-inotropic medication administration. **Remarks:** Enteral feeding is not contraindicated in children with septic shock after adequate hemodynamic resuscitation who no longer require escalating doses of vasoactive agents or in whom weaning of vasoactive agents has started.	• Weak • Low-Quality of Evidence

RECOMMENDATION #53	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** enteral nutrition as the preferred method of feeding and that parenteral nutrition may be withheld in the first 7 days of PICU admission in children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Moderate-Quality of Evidence

RECOMMENDATION #54	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** supplementation with specialized lipid emulsions in children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Very Low-Quality of Evidence

RECOMMENDATION #55	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** the routine measurements of gastric residual volumes (GRVs) in children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Low-Quality of Evidence

RECOMMENDATION #56	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** administering enteral feeds through a gastric tube, rather than a postpyloric feeding tube, to children with septic shock or other sepsis-associated organ dysfunction who have no contraindications to enteral feeding.	• Weak • Low-Quality of Evidence

RECOMMENDATION #57	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** the routine use of prokinetic agents for the treatment of feeding intolerance in children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Low-Quality of Evidence

RECOMMENDATION #58	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** the use of selenium in children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Low-Quality of Evidence

Recommendation #59	Strength & Quality of Evidence
We ***suggest against*** the use of glutamine supplementation in children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Low-Quality of Evidence

Recommendation #60	Strength & Quality of Evidence
We ***suggest against*** the use of arginine in the treatment of children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Very Low-Quality of Evidence

Recommendation #61	Strength & Quality of Evidence
We ***suggest against*** using zinc supplementation in children with septic shock and other sepsis-associated organ dysfunction.	• Weak • Very Low-Quality of Evidence

Recommendation #62	Strength & Quality of Evidence
We ***suggest against*** the use of ascorbic acid (vitamin C) in the treatment of children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Very Low-Quality of Evidence

Recommendation #63	Strength & Quality of Evidence
We ***suggest against*** the use of thiamine to treat children with sepsis-associated organ dysfunction.	• Weak • Low-Quality of Evidence

Recommendation #64	Strength & Quality of Evidence
We ***suggest against*** the acute repletion of vitamin D deficiency (VDD) for treatment of septic shock or other sepsis-associated organ dysfunction.	• Weak • Very Low-Quality of Evidence

BLOOD PRODUCTS RECOMMENDATIONS TABLE

RECOMMENDATION #65	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** transfusion of RBCs if the blood hemoglobin concentration is greater than or equal to 7 g/dL in hemodynamically stabilized children with septic shock or other sepsis-associated organ dysfunction. **Remarks:** According to the 2018 Transfusion and Anemia Expertise Initiative (TAXI) guidelines, for the purposes of RBC transfusion, "hemodynamically stabilized" is defined as a MAP higher than 2 sds below normal for age and no increase in vasoactive medications for at least 2 hours.	• Weak • Low-Quality of Evidence

RECOMMENDATION #66	STRENGTH & QUALITY OF EVIDENCE
We ***cannot make a recommendation*** regarding hemoglobin transfusion thresholds for critically ill children with unstable septic shock.	Insufficient

RECOMMENDATION #67	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** prophylactic platelet transfusion based solely on platelet levels in nonbleeding children with septic shock or other sepsis-associated organ dysfunction and thrombocytopenia.	• Weak • Very Low-Quality of Evidence

RECOMMENDATION #68	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** prophylactic plasma transfusion in nonbleeding children with septic shock or other sepsis-associated organ dysfunction and coagulation abnormalities. **Remarks:** Prophylactic plasma transfusion refers to situations in which there is an abnormality in laboratory coagulation testing but no active bleeding.	• Weak • Very Low-Quality of Evidence

PLASMA EXCHANGE, RENAL REPLACEMENT AND EXTRACORPOREAL SUPPORT RECOMMENDATIONS TABLE

RECOMMENDATION #69	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** using plasma exchange (PLEX) in children with septic shock or other sepsis-associated organ dysfunction without thrombocytopenia-associated multiple organ failure (TAMOF).	• Weak • Very Low-Quality of Evidence

RECOMMENDATION #70	STRENGTH & QUALITY OF EVIDENCE
We ***cannot suggest for or against*** the use of PLEX in children with septic shock or other sepsis-associated organ dysfunction with TAMOF.	Insufficient

RECOMMENDATION #71	STRENGTH & QUALITY OF EVIDENCE
We ***suggest using*** renal replacement therapy to prevent or treat fluid overload in children with septic shock or other sepsis-associated organ dysfunction who are unresponsive to fluid restriction and diuretic therapy.	• Weak • Very Low-Quality of Evidence

RECOMMENDATION #72	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** high-volume hemofiltration (HVHF) over standard hemofiltration in children with septic shock or other sepsis-associated organ dysfunction who are treated with renal replacement therapy.	• Weak • Low-Quality of Evidence

RECOMMENDATION #73	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** using venovenous ECMO in children with sepsis-induced PARDS and refractory hypoxia.	• Weak • Very Low-Quality of Evidence

RECOMMENDATION #74	STRENGTH & QUALITY OF EVIDENCE
We ***suggest*** using venoarterial ECMO as a rescue therapy in children with septic shock only if refractory to all other treatments.	• Weak • Very Low-Quality of Evidence

IMMUNOGLOBULINS AND PROPHYLAXIS RECOMMENDATIONS TABLE

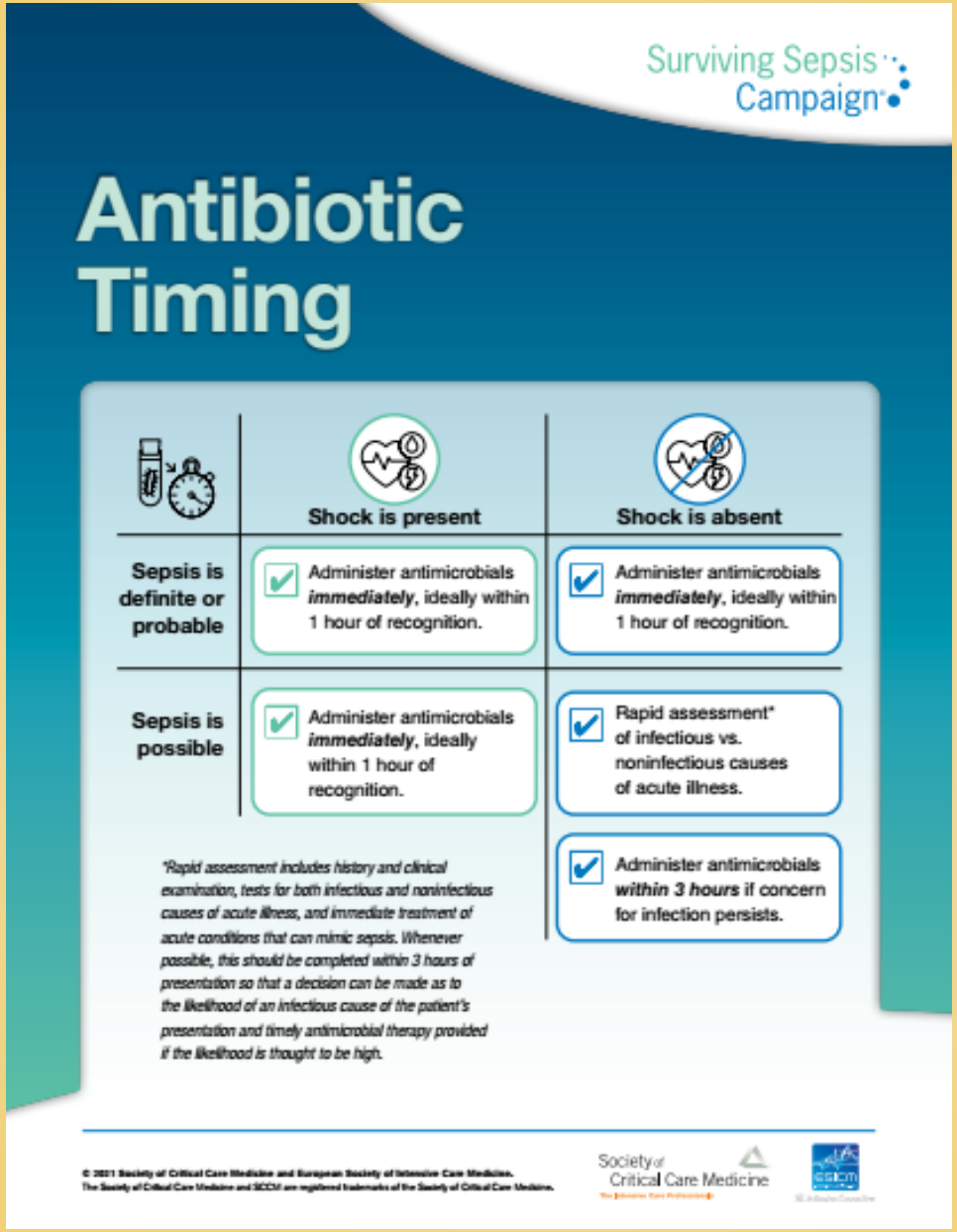
IMMUNOGLOBULINS

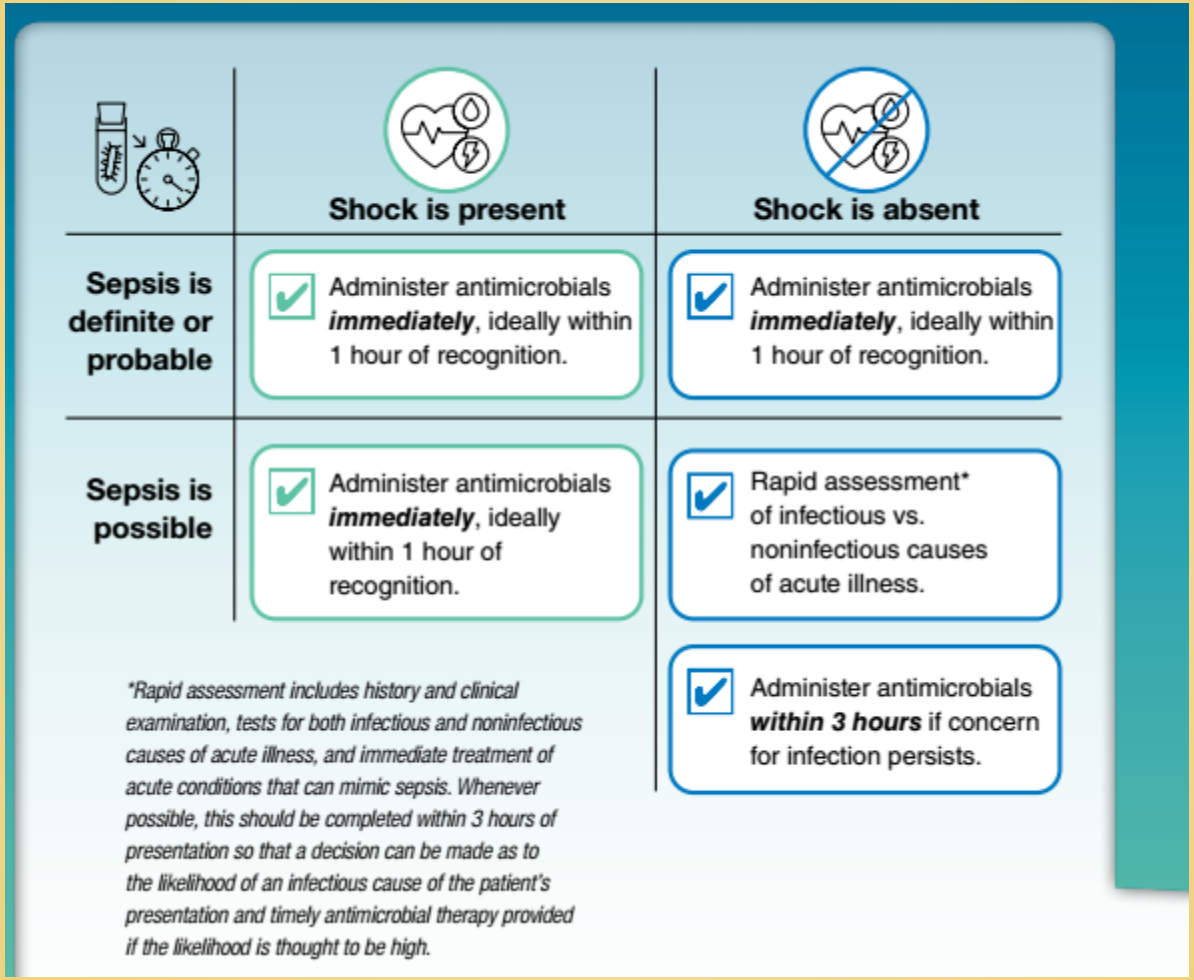
RECOMMENDATION #75	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** the routine use of IV immune globulin (IVIG) in children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Low-Quality of Evidence

PROPHYLAXIS

RECOMMENDATION #76	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** the routine use of stress ulcer prophylaxis in critically ill children with septic shock or other sepsis-associated organ dysfunction, except for high-risk patients.	• Weak • Very Low-Quality of Evidence

RECOMMENDATION #77	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** routine deep vein thrombosis (DVT) prophylaxis (mechanical or pharmacologic) in critically ill children with septic shock or other sepsis-associated organ dysfunction, but potential benefits may outweigh risks and costs in specific populations.	• Weak • Low-Quality of Evidence


Surviving Sepsis Campaign
Antibiotic Timing
Shock is present
Shock is absent
Sepsis is definite or probable
Administer antimicrobials immediately, ideally within 1 hour of recognition.
Administer antimicrobials immediately, ideally within 1 hour of recognition.
Sepsis is possible
Administer antimicrobials immediately, ideally within 1 hour of recognition.
Rapid assessment* of infectious vs. noninfectious causes of acute illness.
Administer antimicrobials within 3 hours if concern for infection persists.
*Rapid assessment includes history and clinical examination, tests for both infectious and noninfectious causes of acute illness, and immediate treatment of acute conditions that can mimic sepsis. Whenever possible, this should be completed within 3 hours of presentation so that a decision can be made as to the likelihood of an infectious cause of the patient's presentation and timely antimicrobial therapy provided if the likelihood is thought to be high.
Society of Critical Care Medicine


Shock is present
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2021 RECOMMENDATIONS ON
SCREENING FOR PATIENTS WITH SEPSIS AND SEPTIC SHOCK

Surviving Sepsis Campaign

For hospitals and health systems, we **recommend** using a performance improvement programme for sepsis, including sepsis screening for acutely ill, high-risk patients and standard operating procedures for treatment.

MODERATE — Screening

VERY LOW — Standard operating procedures

MODERATE

We **recommend against** using qSOFA compared to SIRS, NEWS, or MEWS as a single screening tool for sepsis or septic shock.

VERY LOW

For adults suspected of having sepsis, we **suggest** measuring blood lactate.

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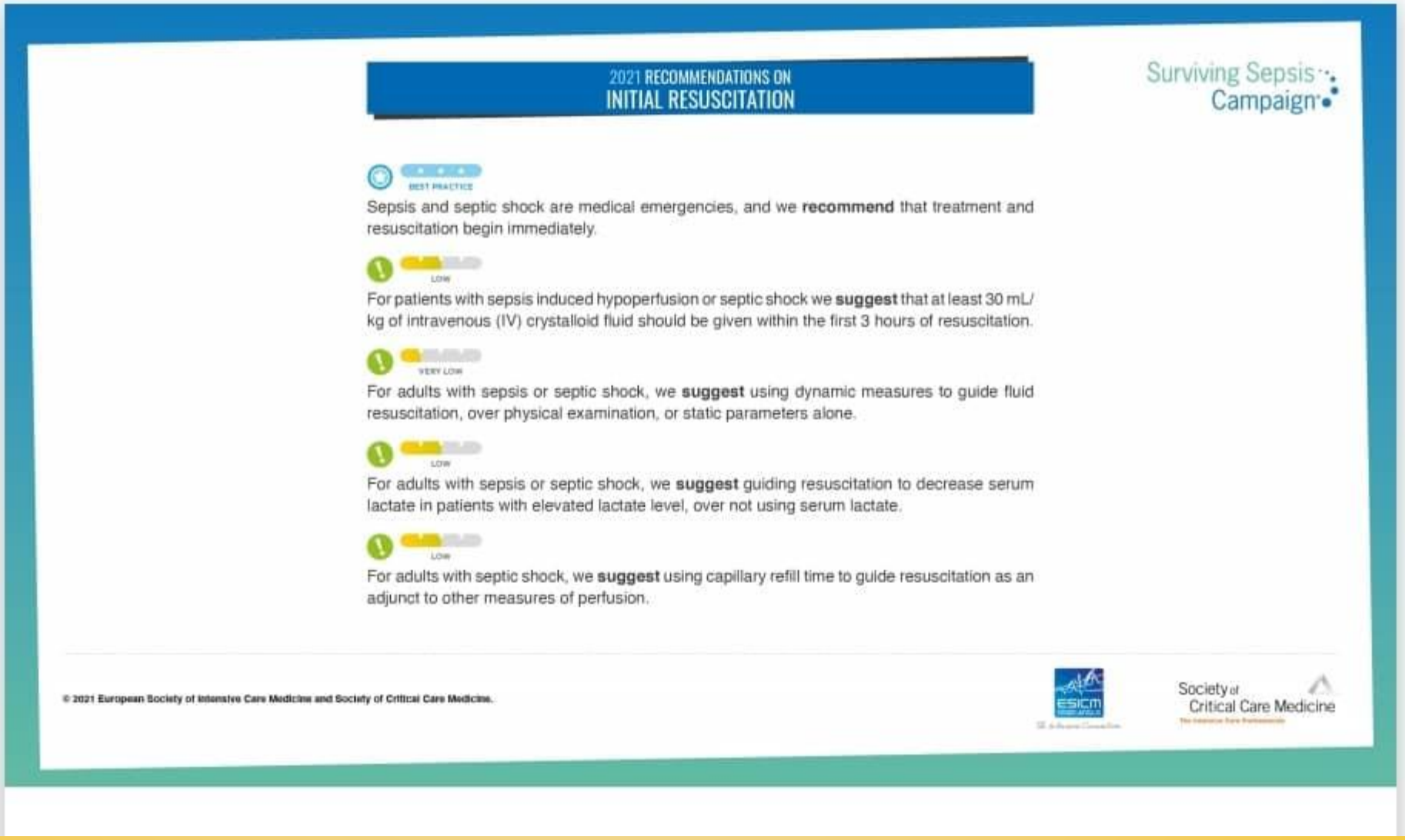
2021 RECOMMENDATIONS ON
INITIAL RESUSCITATION
Surviving Sepsis Campaign
BEST PRACTICE
Sepsis and septic shock are medical emergencies, and we **recommend** that treatment and resuscitation begin immediately.
LOW
For patients with sepsis induced hypoperfusion or septic shock we **suggest** that at least 30 mL/kg of intravenous (IV) crystalloid fluid should be given within the first 3 hours of resuscitation.
VERY LOW
For adults with sepsis or septic shock, we **suggest** using dynamic measures to guide fluid resuscitation, over physical examination, or static parameters alone.
LOW
For adults with sepsis or septic shock, we **suggest** guiding resuscitation to decrease serum lactate in patients with elevated lactate level, over not using serum lactate.
LOW
For adults with septic shock, we **suggest** using capillary refill time to guide resuscitation as an adjunct to other measures of perfusion.
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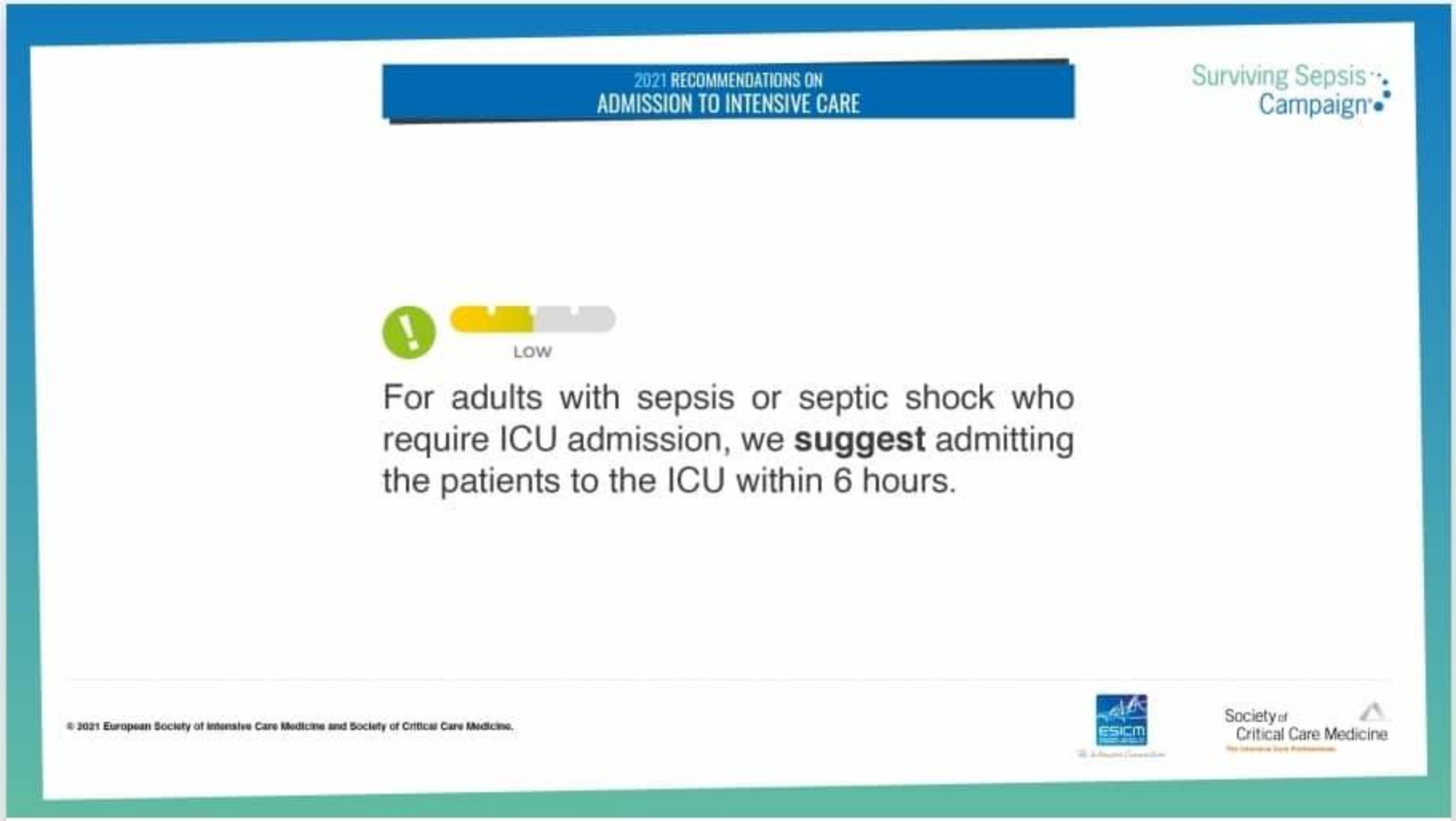
2021 RECOMMENDATIONS ON
ADMISSION TO INTENSIVE CARE
Surviving Sepsis Campaign
LOW
For adults with sepsis or septic shock who require ICU admission, we **suggest** admitting the patients to the ICU within 6 hours.
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2021 RECOMMENDATIONS ON
HEMODYNAMIC MANAGEMENT
Surviving Sepsis Campaign
MODERATE
For adults with sepsis or septic shock, we recommend using crystalloids as first-line fluid for resuscitation.
LOW
For adults with sepsis or septic shock, we suggest using balanced crystalloids instead of normal saline for resuscitation.
MODERATE
For adults with sepsis or septic shock, we suggest using albumin in patients who received large volumes of crystalloids.
HIGH
For adults with sepsis or septic shock, we recommend against using starches for resuscitation.
MODERATE
For adults with sepsis and septic shock, we suggest against using gelatin for resuscitation.
For adults with septic shock, we recommend using norepinephrine as the first-line agent over other vasopressors.
HIGH Dopamine
MODERATE Vasopressin
LOW Epinephrine
LOW Selepressin
VERY LOW Angiotensin 2
MODERATE
For adults with septic shock on norepinephrine with inadequate mean arterial pressure levels, we suggest adding vasopressin instead of escalating the dose of norepinephrine.
LOW
For adults with septic shock and inadequate mean arterial pressure levels despite norepinephrine and vasopressin, we suggest adding epinephrine.
LOW
For adults with septic shock, we suggest against using terlipressin.
LOW
For adults with septic shock and cardiac dysfunction with persistent hypoperfusion despite adequate volume status and arterial blood pressure, we suggest either adding dobutamine to norepinephrine or using epinephrine alone.
LOW
For adults with septic shock and cardiac dysfunction with persistent hypoperfusion despite adequate volume status and arterial blood pressure, we suggest against using levosimendan.
VERY LOW
For adults with septic shock, we suggest invasive monitoring of arterial blood pressure over non-invasive monitoring, as soon as practical and if resources are available.
VERY LOW
For adults with septic shock, we suggest starting vasopressors peripherally to restore mean arterial pressure rather than delaying initiation until a central venous access is secured.
There is insufficient evidence to make a recommendation on the use of restrictive versus liberal fluid strategies in the first 24 hours of resuscitation in patients with sepsis and septic shock who still have signs of hypoperfusion and volume depletion after the initial resuscitation.
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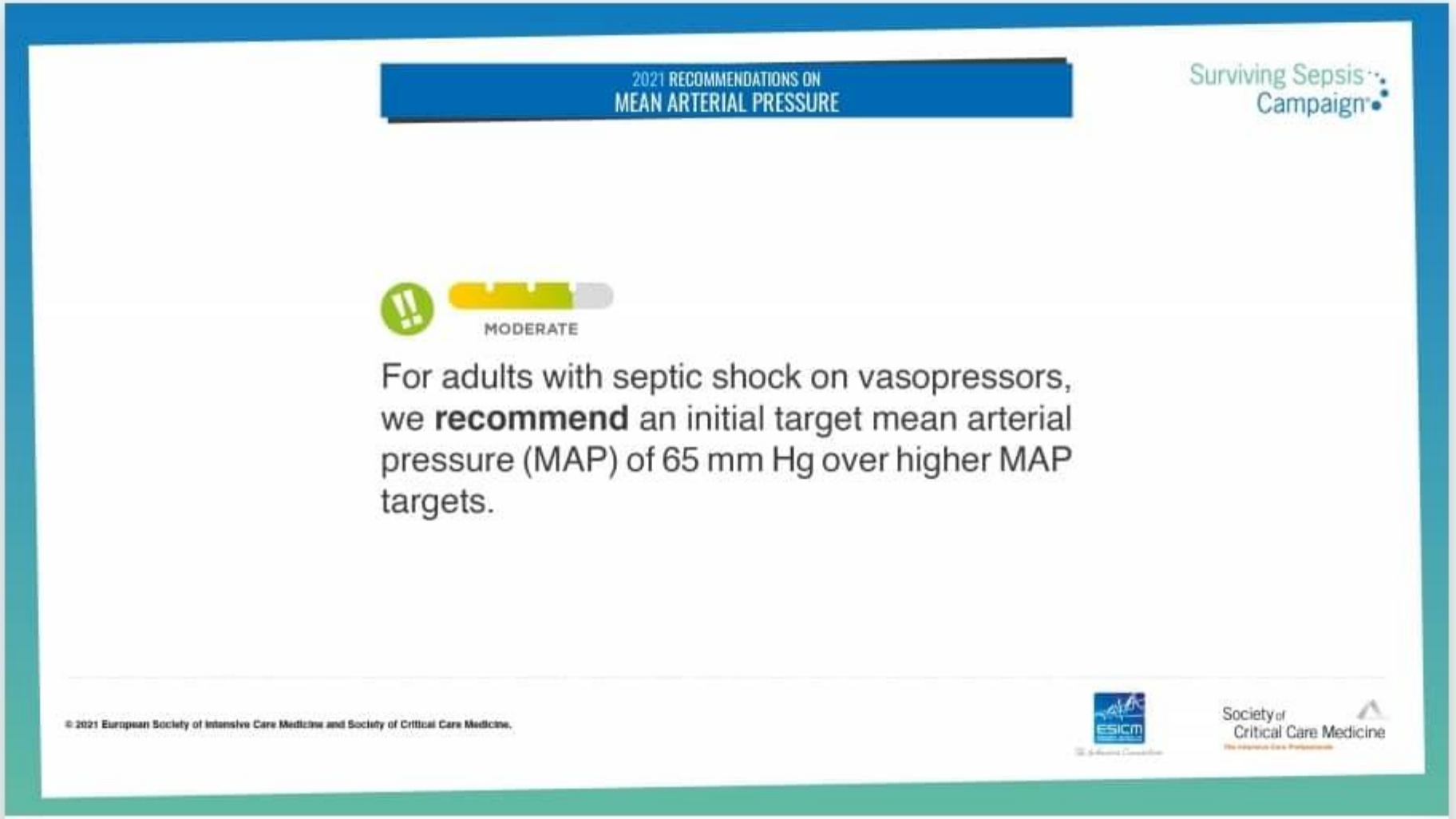
2021 RECOMMENDATIONS ON
MEAN ARTERIAL PRESSURE
Surviving Sepsis Campaign
MODERATE
For adults with septic shock on vasopressors, we **recommend** an initial target mean arterial pressure (MAP) of 65 mm Hg over higher MAP targets.
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2021 RECOMMENDATIONS ON
INFECTION
1/2
Surviving Sepsis Campaign
BEST PRACTICE
For adults with suspected sepsis or septic shock but unconfirmed infection, we recommend continuously re-evaluating and searching for alternative diagnoses and discontinuing empiric antimicrobials if an alternative cause of illness is demonstrated or strongly suspected.
For adults with possible septic shock or a high likelihood for sepsis, we recommend administering antimicrobials immediately, ideally within one hour of recognition.
LOW Septic shock
VERY LOW Sepsis without shock
BEST PRACTICE
For adults with possible sepsis without shock, we recommend rapid assessment of the likelihood of infectious versus non-infectious causes of acute illness.
VERY LOW
For adults with possible sepsis without shock, we suggest a time-limited course of rapid investigation and if concern for infection persists, the administration of antimicrobials within 3 hours from the time when sepsis was first recognized.
VERY LOW
For adults with a low likelihood of infection and without shock, we suggest deferring antimicrobials while continuing to closely monitor the patient.
VERY LOW
For adults with suspected sepsis or septic shock, we suggest against using procalcitonin plus clinical evaluation to decide when to start antimicrobials, as compared to clinical evaluation alone.
BEST PRACTICE
For adults with sepsis or septic shock at high risk of MRSA, we recommend using empiric antimicrobials with MRSA coverage over using antimicrobials without MRSA coverage.
LOW
For adults with sepsis or septic shock at low risk of MRSA, we suggest against using empiric antimicrobials with MRSA coverage, as compared with using antimicrobials without MRSA coverage.
VERY LOW
For adults with sepsis or septic shock and high risk for multidrug resistant (MDR) organisms, we suggest using two antimicrobials with gram-negative coverage for empiric treatment over one gram-negative agent.
VERY LOW
For adults with sepsis or septic shock and low risk for multidrug resistant (MDR) organisms, we suggest against using two gram-negative agents for empiric treatment, as compared to one gram-negative agent.
VERY LOW
For adults with sepsis or septic shock, we suggest against using double gram-negative coverage once the causative pathogen and the susceptibilities are known.
LOW
For adults with sepsis or septic shock at high risk of fungal infection, we suggest using empiric antifungal therapy over no antifungal therapy.
LOW
For adults with sepsis or septic shock at low risk of fungal infection, we suggest against empiric use of antifungal therapy.
We make no recommendation on the use of antiviral agents.
MODERATE
For adults with sepsis or septic shock, we suggest using prolonged infusion of beta-lactams for maintenance (after an initial bolus) over conventional bolus infusion.
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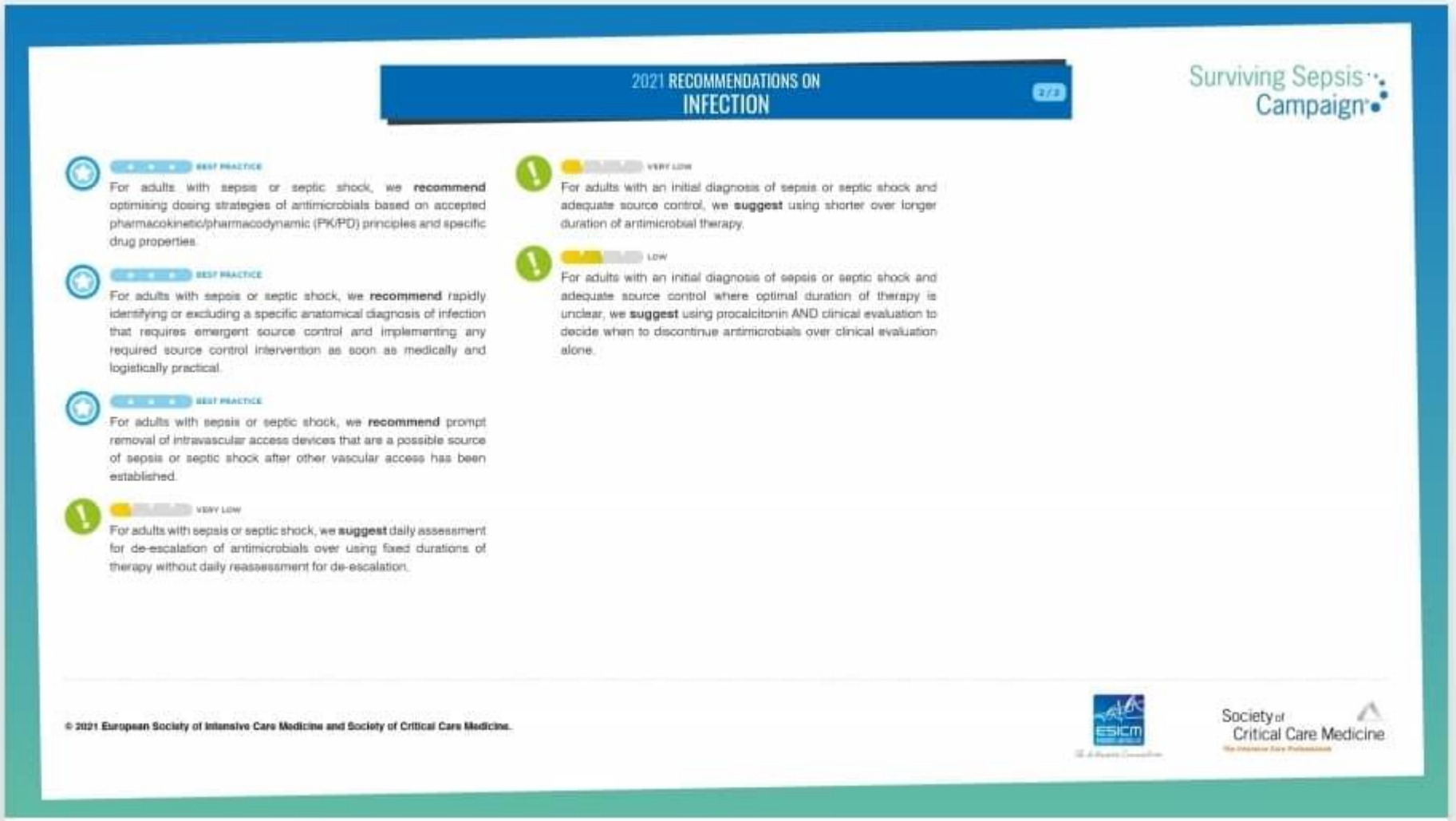
2021 RECOMMENDATIONS ON
INFECTION
2 / 3
Surviving Sepsis Campaign
BEST PRACTICE
For adults with sepsis or septic shock, we recommend optimising dosing strategies of antimicrobials based on accepted pharmacokinetic/pharmacodynamic (PK/PD) principles and specific drug properties.
BEST PRACTICE
For adults with sepsis or septic shock, we recommend rapidly identifying or excluding a specific anatomical diagnosis of infection that requires emergent source control and implementing any required source control intervention as soon as medically and logistically practical.
BEST PRACTICE
For adults with sepsis or septic shock, we recommend prompt removal of intravascular access devices that are a possible source of sepsis or septic shock after other vascular access has been established.
VERY LOW
For adults with sepsis or septic shock, we suggest daily assessment for de-escalation of antimicrobials over using fixed durations of therapy without daily reassessment for de-escalation.
VERY LOW
For adults with an initial diagnosis of sepsis or septic shock and adequate source control, we suggest using shorter over longer duration of antimicrobial therapy.
LOW
For adults with an initial diagnosis of sepsis or septic shock and adequate source control where optimal duration of therapy is unclear, we suggest using procalcitonin AND clinical evaluation to decide when to discontinue antimicrobials over clinical evaluation alone.
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2021 RECOMMENDATIONS ON
ADDITIONAL THERAPIES
Surviving Sepsis Campaign
MODERATE
For adults with septic shock and an ongoing requirement for vasopressor therapy we **suggest** using IV corticosteroids.
LOW
For adults with sepsis or septic shock we **suggest against** using polymyxin B hemoperfusion.
There is insufficient evidence to make a recommendation on the use of other blood purification techniques.
MODERATE
For adults with sepsis or septic shock we **recommend** using a restrictive (over liberal) transfusion strategy.
LOW
For adults with sepsis or septic shock we **suggest against** using intravenous immunoglobulins.
MODERATE
For adults with sepsis or septic shock, and who have risk factors for gastrointestinal (GI) bleeding, we **suggest** using stress ulcer prophylaxis.
MODERATE
For adults with sepsis or septic shock, we **recommend** using pharmacologic venous thromboembolism (VTE) prophylaxis unless a contraindication to such therapy exists.
MODERATE
For adults with sepsis or septic shock, we **recommend** using low molecular weight heparin over unfractionated heparin for VTE prophylaxis.
LOW
For adults with sepsis or septic shock, we **suggest against** using mechanical VTE prophylaxis, in addition to pharmacological prophylaxis, over pharmacologic prophylaxis alone.
LOW
In adults with sepsis or septic shock and AKI, we **suggest** using either continuous or intermittent renal replacement therapy.
MODERATE
In adults with sepsis or septic shock and AKI, with no definitive indications for renal replacement therapy, we **suggest against** using renal replacement therapy.
MODERATE
For adults with sepsis or septic shock, we **recommend** initiating insulin therapy at a glucose level of ≥ 180mg/dL (10mmol/L).
LOW
For adults with sepsis or septic shock we **suggest against** using IV vitamin C.
LOW
For adults with septic shock and hypoperfusion-induced lactic acidemia, we **suggest against** using sodium bicarbonate therapy to improve hemodynamics or to reduce vasopressor requirements.
LOW
For adults with septic shock and severe metabolic acidemia (pH ≤ 7.2) and acute kidney injury (AKIN score 2 or 3), we **suggest** using sodium bicarbonate therapy.
VERY LOW
For adult patients with sepsis or septic shock who can be fed enterally, we **suggest** early (within 72 hours) initiation of enteral nutrition.
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2021 RECOMMENDATIONS ON
VENTILATION
Surviving Sepsis Campaign
There is insufficient evidence to make a recommendation on the use of conservative oxygen targets in adults with sepsis-induced hypoxemic respiratory failure.
LOW
For adults with sepsis-induced hypoxemic respiratory failure, we **suggest** the use of high flow nasal oxygen over non-invasive ventilation.
There is insufficient evidence to make a recommendation on the use of non-invasive ventilation in comparison to invasive ventilation for adults with sepsis-induced hypoxemic respiratory failure.
HIGH
For adults with sepsis-induced ARDS, we **recommend** using a low tidal volume ventilation strategy (6 mL/kg), over a high tidal volume strategy (>10 mL/kg).
MODERATE
For adults with sepsis-induced severe ARDS, we **recommend** using an upper limit goal for plateau pressures of 30 cm H2O, over higher plateau pressures.
MODERATE
For adults with moderate to severe sepsis-induced ARDS, we **suggest** using higher PEEP over lower PEEP.
LOW
For adults with sepsis-induced respiratory failure (without ARDS), we **suggest** using low tidal volume as compared to high tidal volume ventilation.
MODERATE
For adults with sepsis-induced moderate-severe ARDS, we **suggest** using traditional recruitment maneuvers.
MODERATE
When using recruitment maneuvers, we **recommend against** using incremental PEEP titration/strategy.
MODERATE
For adults with sepsis-induced moderate-severe ARDS, we **recommend** using prone ventilation for greater than 12 hours daily.
MODERATE
For adults with sepsis induced moderate-severe ARDS, we **suggest** using intermittent NMBA boluses, over NMBA continuous infusion.
LOW
For adults with sepsis-induced severe ARDS, we **suggest** using Veno-venous (VV) ECMO when conventional mechanical ventilation fails in experienced centres with the infrastructure in place to support its use.
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