2021 RECOMMENDATIONS ON ADDITIONAL THERAPIES

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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
ADMISSION TO INTENSIVE CARE

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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

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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 INFECTION

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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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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 INITIAL RESUSCITATION

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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 LONG-TERM OUTCOMES AND GOALS OF CARE

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BEST PRACTICE

For adults with sepsis or septic shock, we **recommend** discussing goals of care and prognosis with patients and families over no such discussion.

LOW

For adults with sepsis or septic shock, we **suggest** addressing goals of care early (within 72 hours) over late (72 hours or later).

For adults with sepsis or septic shock, there is insufficient evidence to make a recommendation on any specific standardized criterion to trigger goals of care discussion.

BEST PRACTICE

For adults with sepsis or septic shock, we **recommend** that the principles of palliative care (which may include palliative care consultation based on clinician judgement) be integrated into the treatment plan, when appropriate, to address patient and family symptoms and suffering.

LOW

For adults with sepsis or septic shock, we **suggest against** routine formal palliative care consultation for all patients over palliative care consultation based on clinician judgement.

VERY LOW

For adult survivors of sepsis or septic shock and their families, we **suggest** referral to peer support groups over no such referral.

VERY LOW

For adults with sepsis or septic shock, we **suggest** using a handoff process of critically important information at transitions of care over no such handoff process.

For adults with sepsis or septic shock, there is insufficient evidence to make a recommendation on the use of any specific structured handoff tool over usual handoff processes.

BEST PRACTICE

For adults with sepsis or septic shock and their families, we **recommend** screening for economic and social support (including housing, nutritional, financial, and spiritual support), and make referrals where available to meet these needs.

VERY LOW

For adults with sepsis or septic shock and their families, we **suggest** offering written and verbal sepsis education (diagnosis, treatment, and post-ICU/post-sepsis syndrome) prior to hospital discharge and in the follow-up setting.

BEST PRACTICE

For adults with sepsis or septic shock and their families, we **recommend** the clinical team provide the opportunity to participate in shared decision making in post-ICU and hospital discharge planning to ensure discharge plans are acceptable and feasible.

VERY LOW

For adults with sepsis and septic shock and their families, we **suggest** using a critical care transition programme, compared to usual care, upon transfer to the floor.

BEST PRACTICE

For adults with sepsis and septic shock, we **recommend** reconciling medications at both ICU and hospital discharge.

BEST PRACTICE

For adult survivors of sepsis and septic shock and their families, we **recommend** including information about the ICU stay, sepsis and related diagnoses, treatments, and common impairments after sepsis in the written and verbal hospital discharge summary.

BEST PRACTICE

For adults with sepsis or septic shock who developed new impairments, we **recommend** hospital discharge plans include follow-up with clinicians able to support and manage new and long-term sequelae.

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For adults with sepsis or septic shock and their families, there is insufficient evidence to make a recommendation on early post-hospital discharge follow-up compared to routine post-hospital discharge follow-up.

For adults with sepsis or septic shock, there is insufficient evidence to make a recommendation for or against early cognitive therapy.

BEST PRACTICE

For adult survivors of sepsis or septic shock, we **recommend** assessment and follow-up for physical, cognitive, and emotional problems after hospital discharge.

VERY LOW

For adult survivors of sepsis or septic shock, we **suggest** referral to a post-critical illness follow-up programme if available.

VERY LOW

For adult survivors of sepsis or septic shock receiving mechanical ventilation for >48hours or an ICU stay of >72 hours, we **suggest** referral to a post-hospital rehabilitation programme.

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2021 RECOMMENDATIONS ON MEAN ARTERIAL PRESSURE

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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
SCREENING FOR PATIENTS WITH SEPSIS AND SEPTIC SHOCK

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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.

Screening

Standard operating procedures

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

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

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2021 RECOMMENDATIONS ON VENTILATION

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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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