

Multimedia Appendix 1 – Definitions of sepsis, severe sepsis or septic shock [7,15]

<p>Sepsis</p>	<p>Presence (probable or documented) of infection with systemic manifestation:</p> <p>General variables: Fever >38.3°C, hypothermia < 36°C, heart rate > 90 bpm or more than two SD above the normal value for age, tachypnea, altered mental status, significant oedema or positive fluid balance >20 ml/kg over 24 hours, hyperglycaemia with a plasma glucose > 140 mg/dl or 7.7mmol/L in the absence of diabetes mellitus</p> <p>Inflammatory variables: Leukocytosis (WBC count > 12,000 μl^{-1}), leukopenia (WBC count < 4,000 μl^{-1}), normal WBC with greater than 10% immature forms, plasma C-reactive protein more than two SD above the normal value, plasma procalcitonin more than two SD above the normal value</p> <p>Hemodynamic variables: Arterial hypotension (SBP <90 mmHg, mean BP <65 mmHg, or reduction in SBP >40 mmHg from baseline) persisting for at least 1 hour, despite adequate fluid resuscitation</p> <p>Organ dysfunction variables: Arterial hypoxemia ($\text{PaO}_2/\text{FiO}_2 < 300$), acute oliguria (urine output <0.5 ml $\text{kg}^{-1}/\text{h}^{-1}$ for at least 2 h) creatinine increase $\geq 0.5 \text{ mg dL}^{-1}$, coagulation abnormalities (INR >1.5 or activated partial thromboplastin time >60 s), ileus (absent bowel sounds), thrombocytopenia (platelet count <100,000/μL), hyperbilirubinemia (plasma total bilirubin >4 mg dL^{-1} or 70 mmol L^{-1})</p> <p>Tissue perfusion variables: Hyperlactatemia (>3 mmol/L^{-1}), decreased capillary refill or mottling</p>
<p>Severe sepsis</p>	<p>Sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion:</p> <p>Altered mental state</p> <p>Arterial hypoxemia ($\text{PaO}_2/\text{FiO}_2 < 300$)</p> <p>Acute kidney injury (urine output < 0.5 ml/kg/h for at least 2h or creatinine increase > 0.5 mg/dL)</p> <p>Thrombocytopenia (platelet count < 100.000/μl)</p> <p>Coagulopathy (INR > 1.5 or aPTT > 60 s)</p> <p>Hyperbilirubinemia (total plasma bilirubin > 2 mg/dl)</p> <p>Hyperlactatemia (> 1 mmol/L)</p> <p>Sepsis-induced hypotension</p> <p>Decreased capillary refill or mottling</p>
<p>Septic shock</p>	<p>Sepsis-induced hypotension (SBP < 90 mmHg or MAP <</p>

	70 mmHg or SBP decrease > 40 mmHg) persisting despite adequate fluid resuscitation
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Abbreviations C: Celsius; bpm: beats per minute; SD: standard deviation; ml: milliliter; kg: kilogram; mg: milligram; dl: deciliter; mmol: millimol; L: liter; WBC: white blood cell; μ l: microliter; SBP: systolic blood pressure; mmHg: millimeter of mercury; MAP: mean arterial pressure; aPTT: activated partial thromboplastin time; SBP: systemic blood pressure; MAP: mean arterial pressure; PaO₂/FiO₂: ratio of arterial oxygen partial pressure to fractional inspired oxygen; INR: international normalized ratio, INR: international normalized ratio.