

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

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

	70 mmHg or SBP decrease > 40 mmHg) persisting despite adequate fluid resuscitation
--	--

**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;  $\mu$ 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; PaO<sub>2</sub>/FiO<sub>2</sub>: ratio of arterial oxygen partial pressure to fractional inspired oxygen; INR: international normalized ratio, INR: international normalized ratio.