Our recommendation focuses on adults with septic shock and ongoing requirement for vasopressor therapy. We defined ongoing requirement as a dose of norepinephrine or epinephrine ≥ 0.25 mcg/kg/min for at least 4 h after initiation to maintain the target MAP. The dose of hydrocortisone is typically 200 mg/day. No dose response benefit was seen in a prior systematic review and meta-analysis [480].

Blood Purification

Recommendations

59. For adults with sepsis or septic shock, we **suggest against** using polymyxin B haemoperfusion
Weak recommendation; low quality of evidence

60. There is **insufficient evidence to make a recommendation** on the use of other blood purification techniques

Rationale

Haemoperfusion refers to the circulation of blood through an extracorporeal circuit that contains an adsorbent containing cartridge. The previous guidelines made no recommendation regarding the use of blood purification techniques [12, 13]. The updated literature search for guideline identified one new relevant RCT [481].

The most widely investigated technique involves the use of polymyxin B-immobilised polystyrene-derived fibers. Randomised trials of this technique have been previously summarised in a systematic review and meta-analysis [482]. An updated meta-analysis of all available RCTs (Supplementary Appendix 5) demonstrated a possible reduction in mortality (RR 0.87; 95% CI 0.77–0.98, low quality), however this finding was challenged by sensitivity analyses: after excluding high risk of bias trials the risk ratio is 1.14 (95% CI 0.96–1.36); and after excluding trials published prior to 2010 we observed higher mortality with haemoperfusion (RR 1.23; 95% CI 1.04–1.46). Overall, the quality of evidence is judged as low (Supplementary Appendix 5).

Substantial uncertainty as to any beneficial effect exists and the frequency of undesirable effects is reported in few trials. Polymyxin B haemoperfusion is expensive, resource intensive, potentially reduces health equity, and is infeasible in low-income economies. All considered, the panel issued a weak recommendation against the use of polymyxin B haemoperfusion therapy.

We did not identify new evidence on other modalities such as haemofiltration, combined haemoperfusion and haemofiltration or plasma exchange. Accordingly, no recommendation regarding the use of these modalities is made. This is unchanged from the 2016 guidelines. Since the analysis new data has emerged, but at this stage was not sufficient for us to re-consider the recommendation [483].

Further research is needed to determine the effect of various blood purification techniques on patient outcomes.

Red blood cell (RBC) transfusion targets

Recommendation

61. For adults with sepsis or septic shock, we **recommend** using a restrictive (over liberal) transfusion strategy
Strong recommendation; moderate quality of evidence

Remark

A restrictive transfusion strategy typically includes a haemoglobin concentration transfusion trigger of 70 g/L; however, RBC transfusion should not be guided by haemoglobin concentration alone. Assessment of a patient's overall clinical status and consideration of extenuating circumstances such as acute myocardial ischaemia, severe hypoxemia or acute haemorrhage is required

Rationale

The previous guidance was informed by two RCTs [484, 485]. The Transfusion Requirements in Septic Shock (TRISS) trial addressed a transfusion threshold of 70 g/L versus 90 g/L in 1000 septic shock patients after admission to the ICU. The results showed similar 90-day mortality, ischaemic events, and use of life support in the two treatment groups with fewer transfusions in the lower-threshold group. The Transfusion requirements in in Critical Care trial (TRICC), which compared a restrictive transfusion threshold of 70 g/L versus 100 g/L in 838 euvolemic ICU patients, demonstrated no difference in the primary outcome (30-day mortality). In the subgroup of 218 patients with sepsis or septic shock 30-day mortality was similar in the two groups (22.8% in the restrictive group vs. 29.7% in the liberal group, $p = 0.36$).

Our literature search identified a recent systematic review and meta-analysis of RCTs [486] and one new RCT: The Transfusion Requirements in Critically Ill Oncologic Patients (TRICOP) trial [487]. This trial randomised 300 adult cancer patients with septic shock to either a liberal (haemoglobin threshold, < 90 g/L) or restrictive strategy (haemoglobin threshold, < 70 g/L) of RBC transfusion. At 28 days after randomisation, the mortality rate in the liberal group was 45% 67 patients versus 56% 84 patients in the restrictive group (HR 0.74; 95% CI 0.53–1.04; $p = 0.08$) with no differences in ICU and hospital length of stay. At 90 days after randomisation, mortality rate in the liberal group was lower (59% vs 70%) than in the restrictive group (hazard ratio, 0.72; 95% CI 0.53–0.97).

Our update of the meta-analysis showed no difference in 28-day mortality (OR 0.99 95% CI 0.67–1.46, moderate quality). This is due to the inclusion of the TRICOP study where lower 28 mortality was observed with a liberal