

Appendix 1: Core set of adjustment factors

Step	Method	Potential confounders identified
1. Preliminary searches to identify potential prognostic factors on mortality in patients with sepsis	1. PubMed search: (sepsis[Title]) AND "prognostic factor"[Title] 2. Embase: 'prognostic factor':ti AND 'sepsis':ti 3. Search in Uptodate 4. Initial discussion with review team members	1. Hypertriglyceridemia 2. Positive fluid balance 3. Red cell distribution width 4. Duration of SIRS before organ failure 5. Heart-type fatty acid-binding protein 6. D-dimer 7. Low serum level of high-density lipoprotein cholesterol 8. Serum N-terminal pro-brain natriuretic peptide level 9. Immunosuppression 10. Cancer 11. Liver diseases 12. Alcohol dependence 13. Non-urinary source of infection 14. Inappropriate or late antibiotic coverage
2. Identify prognostic models for mortality in patients with sepsis	We considered factors included in the SOFA prognostic model	1. PaO ₂ 2. FiO ₂ 3. On mechanical ventilation 4. Platelets, ×10 ³ /μL 5. Glasgow Coma Scale 6. Bilirubin, mg/dL (μmol/L) 7. Mean arterial pressure OR administration of vasoactive agents required 8. Creatinine, mg/dL (μmol/L) (or urine output
3. Final list of key additional prognostic factors	We defined the final list of core set of adjustment factors by consensus	1. Age 2. Severity score at baseline (SOFA, SAPS II, APACHE II score) 3. Comorbidities: immunosuppression, pulmonary diseases, cancer, liver diseases, alcohol dependence 4. Non-urinary source of infection 5. Inappropriate or late antibiotic coverage