

Additional File 1. Detailed inclusion and exclusion criteria

Inclusion Criteria:

Admission to surgical or medical intensive care unit within 48 hours prior to enrollment

Age \geq 18 years

Diagnosis of severe sepsis, defined by:

Presence of proven or suspected infection (as indicated by order for antibiotics, excluding antibiotics ordered for perioperative prophylaxis)

AND

At least two of the following criteria present within 24 hours prior to enrollment: heart rate $>$ 90 beats/minute, respiratory rate $>$ 20 breaths/minute, white blood cell count $<$ 4 or $>$ 12 cells/ μ L \times 10³, or body temperature $<$ 36.0°C or $>$ 38.0°C

AND

At least one of the following criteria present within 24 hours prior to enrollment: mean arterial pressure $<$ 65 mmHg or systolic blood pressure $<$ 90 mmHg, requirement for vasopressors, lactate above normal limits, PaO₂/FiO₂ $<$ 250, creatinine $>$ 2.0 mg/dl (in patients with normal baseline renal function), bilirubin $>$ 2.0 mg/dl, platelet count $<$ 100,000, or INR $>$ 1.5 (in patients not being treated with warfarin)

Exclusion Criteria:

Previous diagnosis of hematological or immunological disease (e.g. lymphoma, leukemia, myelodysplastic syndrome, HIV)

History of chronic infection with hepatitis B or C virus

Treatment with chemotherapy within 3 months

Treatment with oral or intravenous corticosteroids within 3 months

Treatment with therapeutic hypothermia in the intensive care unit prior to enrollment

Transferred directly to the intensive care unit from another hospital