Supplementary Appendix

Table S1: Average Adherence Rate to Combined and Individual Bundle Targets over the total Program Duration of 3.5 years in Severe Sepsis Patients (N=8387)

	% Not Applied	% Not Applicable	% Applied
Combined resuscitation & management bundle targets	39.9	0	60.1
Combined resuscitation bundle targets	34.9	0	65.1
Combined management bundle targets	13.4	0	86.6
Resuscitation bundle			
Blood cultures	13.4	0	86.6
Antibiotics	5.9	0	94.1
Lactate measurement	2.7	1.2	96.1
Mixed Venous Saturation measurement	22.2	32.1	45.7
Optimization fluid status	0.8	9.3	89.9
Vasopressors in fluid refractory hypotension	1.5	23.1	75.5
Management bundle			
Protective mechanical ventilation	2.9	35.8	61.3
Activated protein C	6.6	89.0	4.4
Normoglycaemia	3.8	26.2	70.0
Glucocorticoids	3.6	42.9	53.5

Addendum 1
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Endorsing organizations

Netherlands Society of Medical Microbiology (NVMM)
Netherlands Society for Intensive Care (NVIC)
Netherlands Society for Internal Medicine (NIV)
Netherlands Society for Anesthesiology (NVA)

Addendum 2

Severe Sepsis and Septic Shock screening document

Question 1: Is there a clinical proven or suspected infection: yes/no

Question 2: Are 2 or more of the following SIRS criteria present: yes/no

- Temperature: ≥38°C or ≤36°C
- Tachycardia: >90 beats/min
- Tachypnea: >20/min or $PaCO_2$ <4.3 kPa
- Leucocytes: <4 x10^9 /L or 12 x10^9 /L or more than 10% bands

Question 3: Does the patient meet criteria of 1 or more organ dysfunctions: yes/no

- Cardiovascular: SBP <90 mmHg, MAP ≤65 mmHg or drop of SBP >40 mmHg
- Respiratory: Bilateral infiltrations and PaO_2/FiO_2 <40kPa
- Renal: Acute oliguria (<0.5 mL/kg/hour) or creatinine >176 mcmol/L
- Blood coagulation: INR>1.5 or aPTT>60 sec or trombocytopenia (<100,000/mm^3)
- Metabolic: Serum lactate: hyperlactatemia (> 4 mmol/L)
- Hepatic: Bilirubin: hyperbilirubinemia (Total Bilirubin > 34 mmol/L)
- Cerebral: Acute altered mental status or reduced consciousness

In case of triple yes: Severe Sepsis or Septic Shock

Record location (ICU, Emergency Department, General Ward) of diagnosis and time/date

Addendum 3

Severe Sepsis and Septic Shock Resuscitation Bundle:

To be achieved <6 hours after severe sepsis or septic shock diagnosis

1. Measure serum lactate.
2. Obtain at least 2 sets of blood cultures before administration of antibiotics.
3. Administer broad-spectrum antibiotic within three hours of admission to the emergency department and within one hour of admission to other hospital units.
4. Measure and achieve central venous oxygen saturations above 70%.
5. In the event of persistent hypotension despite fluid resuscitation (septic shock) and/or lactate level above 4 mmol/L: Achieve a central venous pressure above 8 mm Hg.
6. In the event of hypotension (systolic blood pressure <90 mmHg or Mean Arterial Pressure <65 mmHg) and/or serum lactate above 4 mmol/L (36 mg/dL): Administer an initial minimum of 1L of crystalloid (or 0.5 L of colloid equivalent) in 30 minutes. Initiate vasopressor therapy for hypotension not responding to initial fluid resuscitation to maintain mean arterial pressure above 65 mm Hg.

Severe Sepsis and Septic Shock Management Bundle:

To be achieved <24 hours after severe sepsis diagnosis

7. Maintain inspiratory plateau pressures below 30 cm H_20 for mechanically ventilated patients.
8. Administer low-dose steroids in accordance with a standardized ICU policy.
9. Drotrecogin alfa (activated) in accordance with a standardized ICU policy*.
10. Maintain glucose control above lower limit of normal (>4.0 mmol/l, 72 mg/dL), but less than 8.3 mmol/L (150 mg/dL).

*After the publication of negative results in the study Prowess Shock (2012) the guideline concerning the administration of activated protein C (drotrecogin alfa activated, aPC) was withdrawn[16]. After withdrawal of activated protein C participants were instructed to register this target as not applicable.

Time Zero of Severe Sepsis and/or Septic Shock Diagnosis

Locations of patient screening were the Emergency Department (ED), general wards or the ICU. For patients enrolled from the ED, the time of presentation was defined as the time of diagnosis. For patients admitted to the ICU from the general wards the time of diagnosis on the ward was used. For patients in the ICU at the time of diagnosis, the time of ICU admission was used.