**Online Supplement**

**Compliance with the National SEP-1 Quality Measure and Association with Sepsis Outcomes: A Multicenter Retrospective Cohort Study**

**eTable. Sensitivity Analyses: Association of SEP-1 Failure with In-Hospital Mortality**

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|  | **Primary Model** | | **Sensitivity Analysis** | |
|  | | **SEP-1 Failure**  *Adjusted OR [95% CI]*  *(p-value)* | **SEP-1 Failure For Any Reason Other than Antibiotic Delay**  *Adjusted OR [95% CI]*  *(p-value)* | **Antibiotic Time > 3 hours**  *Adjusted OR [95% CI]*  *(p-value)* |
| Severe Sepsis Alone  (n=714) | | 1.31 [0.79, 2.19]  (p=0.299) | * 1. [0.62, 1.65]   (p=0.956) | 1.82 [0.96, 3.46] (p=0.066) |
| Septic Shock Alone  (n=137) | | 1.21 [0.32, 4.50]  (p=0.780) | 1.46 [0.39, 5.41]  (p=0.573) | 3.76 [0.15, 92.5]  (p=0.418) |
| Community-Onset Severe Sepsis or Septic Shock (n=776) | | 1.45 [0.87, 2.41]  (p=0.154) | 1.14 [0.70, 1.85]  (p=0.593) | 1.97 [1.01, 1.85]  (p=0.048) |
| Explicit Presenting Symptoms (Severe Sepsis or Septic Shock)  (n=507) | | 2.11 [1.02, 4.37]  (p=0.044)\* | 1.52 [0.77, 3.01]  (p=0.225) | 3.35 [1.08, 10.4] (p=0.037)\* |
| Vague Presenting Symptoms (Severe Sepsis or Septic Shock)  (n=344) | | 0.91 [0.48, 1.75]  (p=0.785) | 0.82 [0.44, 1.52]  (p=0.520) | 1.50 [0.71, 3.17]  (p=0.290] |

\*Indicates statistically significant results.

Numbers in each cell represent the adjusted odds ratio for in-hospital death on multivariate analysis, with 95% confidence intervals and p-values.

The primary model examined SEP-1 failure (on any part of the measure) as the primary exposure of interest. The sensitivity analysis separated time-to-antibiotics and failure on any other part of the SEP-1 bundle.

**Appendix A: CMS Definitions for Severe Sepsis / Septic Shock**

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| Severe Sepsis\* |
| 1. Documentation of Suspected or Confirmed infection 2. Systemic Inflammatory Response Syndrome Criteria (two or more):    * Temperature > 38.3 C or < 36.0 C; Heart rate > 90 beats per minute; Respiration > 20 per minute; White blood cell count > 12 or < 4 x 103/µL or > 10% bands 3. ≥ 1 Organ dysfunction:    * Systolic blood pressure < 90 mmHg (or decrease by > 40 mmHg) or Mean arterial blood pressure <65 mmHg    * Lactate > 2.0 mmol/L    * Respiratory distress requiring initiation of mechanical ventilation or noninvasive positive pressure ventilation    * Creatinine > 2.0 mg/dL, or urine output < 0.5 mL/kg/hour for 2 hours    * Bilirubin > 2 mg/dL    * Platelet count < 100,000 x 109/L    * INR > 1.5 or aPTT > 60 seconds |
| Septic Shock |
| Severe sepsis +   1. Persistent hypotension after 30 cc/kg of intravenous fluids, or 2. Initial lactate ≥ 4.0 mmol/L |

\*All 3 sets of criteria (documentation of suspected infection, SIRS, and organ dysfunction) must be present within 6 hours of each other. Time zero is the date/time on which the last sign of severe sepsis within that 6 hour window is noted. Alternatively, severe sepsis criteria are met if there is provider documentation of suspected or confirmed severe sepsis or septic shock.

**Appendix B: The CMS SEP-1 Measure**

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| Severe Sepsis Bundle: |
| 1. Measure lactate level within 3 hours 2. Blood cultures (prior to antibiotics) within 3 hours 3. Broad spectrum antibiotics within 3 hours 4. Remeasure lactate if initial lactate elevated (>2.0 mmol/L) within 6 hours |
| Septic Shock Bundle |
| *For Sepsis with Hypotension, Initial Lactate ≥4.0 mmol/L, or Provider Documentation of Septic Shock*   1. Fluids (30 cc/kg normal saline or lactated ringers fluids) within 3 hours   *For Septic Shock With Persistent Hypotension After 30 cc/kg of Fluids:*   1. Vasopressors to target MAP ≥ 65 mmHg within 6 hours   *For Septic Shock (Persistent Hypotension or Initial Lactate ≥4.0 mmol/L)*   1. Document repeat volume status and tissue perfusion assessment within 6 hours:  * Repeat focused exam: vital signs, cardiopulmonary, capillary refill, pulse and skin findings, OR * 2 of the following: Measure central venous pressure, central venous oxygen saturation, bedside cardiovascular ultrasound, or passive leg raise or fluid challenge |

The SEP-1 measure is “all-or-nothing”: failure in any one bundle component means overall failure; no partial credit is given.