**Patient Safety Post-Comment Web Meeting (Spring 2021 Cycle)**

**Comments on Severe Sepsis and Septic Shock: Early Management Bundle (SEP-1)**

Submitted by the Infectious Diseases Society of America with endorsement from the American College of Emergency Physicians, American Hospital Association, Pediatric Infectious Disease Society, Society for Healthcare Epidemiology of America, Society of Hospital Medicine, and Society of Infectious Disease Pharmacists

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NQF, CMS, and the SEP-1 measure stewards deserve due credit for creating SEP-1, which has helped raise awareness of sepsis and improved the standard of care for this deadly disease.  However, data have emerged over the past 6 years that have identified problems that, if rectified, would significantly strengthen SEP-1 and reduce unintended measure consequences.

***The Infectious Diseases Society of America is joined by the following five organizations in strongly urging that SEP-1 not be re-endorsed unless and until the bundle is revised: American College of Emergency Physicians, American Hospital Association, Pediatric Infectious Disease Society, Society for Healthcare Epidemiology of America, Society of Hospital Medicine, and Society of Infectious Disease Pharmacists.***

**The goals for the major revisions we request are:**
- Focus the bundle on the subset of patients most likely to benefit from rapid and aggressive interventions, i.e., those with septic shock, not those without shock
- Minimize antibiotic overuse and adverse effects by eliminating patients with sepsis without shock from the bundle, and redefining the goals for time to antibiotic delivery
- Eliminate bundle elements that do not contribute to improved patient outcomes, such as measuring serial lactates
- Streamline the reporting process to focus on clinical outcomes
- Make reporting electronic with data that is easily extractable from the electronic health record
- Get input and support for intended changes from all the professional organizations that are most affected by the measure

Below, we summarize our major concerns that were addressed in an IDSA position paper published in 2020 and endorsed by five major professional societies [1]. For the purposes of this letter, "sepsis" and "severe sepsis" are used interchangeably hereafter and are distinguished from "septic shock."

1. **Despite massive investments by US hospitals to implement, assess compliance with, and report data on the SEP-1 core measure, our analysis of published literature indicates that these SEP-1 activities have not improved outcomes for patients.**
   - Much of the evidence used to support the SEP-1 measure comes from before-after studies or studies of association that reported lower mortality rates in sepsis patients who received bundle compliant care versus those who did not. These studies are at high risk for confounding due to failure to adequately adjust for factors that influenced bundle compliance and outcomes leading to misleading claims of lower mortality [1].

- More rigorous analyses using interrupted time series models and detailed clinical data for risk adjustment demonstrate that SEP-1 did lead to changes in the processes of care (50% increase in lactate checks, 10% increase in broad spectrum antibiotics, and a 30% increase in infusion of 30mL/kg fluids within 3 hours of culture orders) but no improvement in sepsis-associated mortality [2]. These data support the concern that SEP-1 forces clinicians and hospitals to focus on a low yield set of processes and interventions. These processes and interventions constrain practice but have not clearly led to better outcomes for patients.

2. **SEP-1's requirement to immediately administer antibiotic therapy to all patients with possible sepsis risks increasing excessive and unwarranted antibiotic administration.**
   - The signs and symptoms of sepsis are non-specific and mimicked by many non-infectious conditions. At least one third of patients treated with antibiotics for possible sepsis turn out to have non-infectious conditions. A forced rush to treatment therefore exposes many patients to the risk of antibiotics without benefit. This in turn exacerbates the public health crisis of antibiotic resistance [3, 4, 5].

3. **SEP-1 conflates the urgency of antibiotic administration for sepsis and septic shock.**
   - SEP-1 stipulates the same time-to-antibiotic goals for sepsis and septic shock, but the association between time-to-antibiotics and mortality is much stronger for septic shock than for sepsis.
   - The perception that any delays in antibiotic therapy led to worse outcomes for patients with sepsis, regardless of severity-of-illness, contributes to inappropriate antibiotic prescribing and is the wrong message for providers [3].

4. **The current SEP-1 time-zero is complex, subjective, and not evidence based.**
   - The SEP-1 time zero definition requires documentation of suspected infection, SIRS criteria, and one of more than 8 potential organ dysfunction criteria within a limited time window. The complexity of the current time zero definition contributes to variability in abstraction and therein undermines the validity of the measure [6].
   - The original early-goal directed therapy trial that served as the inspiration for SEP-1 focused on patients with septic shock, as defined by refractory hypotension or lactate levels ≥4 mmol/L [7]. The sepsis bundle has since been extrapolated to a much broader set of patients, but there are no high-quality studies demonstrating the benefit of immediate antibiotics in patients whose only signs of organ dysfunction are abnormal creatinine, bilirubin, coagulopathy, or mildly elevated lactate levels at the thresholds specified in the time zero definition.

5. **Serial lactate measurements have not been shown to consistently improve clinical outcomes in patients with sepsis [8].**
   - The lack of benefit of this bundle component is further supported by a recent randomized controlled trial of patients with septic shock that showed no difference in mortality between fluid resuscitation based on physical exam (capillary refill time) versus serial lactate measurements [9].

**Concrete suggestions to revise SEP-1 are as follows**:

1. **Sepsis without shock should be removed from SEP-1.**
   - Limiting SEP-1 to septic shock will focus the measure on the patients in whom the evidence best supports the potential benefit of immediate antibiotics.

- This will also reduce the risk of harm from unnecessary antibiotics (or unnecessarily broad antibiotics) by allowing clinicians more time and discretion in relatively stable patients to determine if infection is present versus one of the many conditions that can mimic infection.
- We note that this view is further emphasized in a separate statement by the American College of Emergency Medicine [10].

2. **SEP-1 should include a clear and reproducible definition of time-zero**.
   - The current SEP-1 time-zero definition is complex and subjective. SEP-1 should have an evidence-based time-zero that can be easily recorded from an electronic health record such as the time when vasopressors were initiated, sustained measures of hypotension, or the time of antibiotic order. This will increase reliability of time zero identification and reduce the burden of abstraction.

3. **Serial lactate measurements should be removed from SEP-1.**
   - Requiring repeat lactate measurements in all patients with initial mildly elevated lactate levels is not evidence-based and a poor use of resources.

**Over the long term, we believe that sepsis quality measurement should transition to an electronic measure focusing on outcomes rather than processes.** We appreciate the opportunity to work with CMS and the IMPAQ group on developing an objective risk-adjusted electronic outcome measure that can help drive further innovations and improvements in sepsis care.

Until a validated outcome measure is established, however, we strongly recommend updating SEP-1 with the suggestions outlined above and believe that a decision by NQF against re-endorsing this measure will encourage the measure stewards to make these important updates to the measure. The impact of a CMS measure is substantially enhanced if stakeholders have confidence that the measure truly improves outcomes, does not lead to unintended consequences, and has minimal reporting burden.

It should be noted that the American Medical Association has also issued formal comments (May 27, 2021) to NQF recommending removal of endorsement due to ongoing concerns over the lack of alignment with current evidence and the potential for negative unintended consequences such as incentivizing antibiotic overuse. **The fact that multiple professional societies are calling for change now suggests many well informed and thoughtful clinicians support the need for a substantial update of this high-stakes measure.**

Thank you for your consideration.

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