

The 2018 Surviving Sepsis Campaign's Treatment Bundle: When Guidelines Outpace the Evidence Supporting Their Use

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Those who cannot remember the past are condemned to repeat it.

—George Santayana

Inadvertent catastrophes often arise from good intentions. One recent medical care example of this phenomenon was the 2002 Centers for Medicare & Medicaid Services (CMS) National Hospital Quality Measure for the initial management of community-acquired pneumonia.¹ This measure called for obtaining blood cultures and administering antibiotics within 4 hours of emergency department (ED) triage in patients being admitted with pneumonia, even if pneumonia was not clearly present on arrival. These metrics had little evidentiary basis but led to an institutional-fostered culture of overdiagnosis and overtreatment.² Eventually, many recognized the downstream harms of antibiotic overuse and misuse,² prompting the loss of the National Quality Forum measure endorsement and the measure's subsequent removal as a CMS quality metric. Have we learned from this folly or does a new sepsis guideline promote similar time-based treatment strategies with little direct supporting evidence?

The most recent iteration of the Surviving Sepsis Campaign treatment bundle now exists, published simultaneously in *Critical Care Medicine* and *Intensive Care Medicine* by Levy et al.³ The newest guidelines from this group propose a novel 1-hour care bundle, in contrast to the National Quality Forum 0-500 and the Sepsis CMS Core measures that defined 3- and 6-hour target care bundles. The Surviving Sepsis Campaign group argues that the temporal nature of sepsis means benefit from even more rapid identification and intervention. They identify the start of the bundle as patient arrival at triage, when sepsis may or may not be present. Items to be successfully initiated within this brief window include the following:

- Measure lactate level and remeasure if the initial lactate level is greater than 2 mmol/L.
- Obtain blood cultures before administration of antibiotics.
- Administer broad-spectrum antibiotics.
- Begin rapid administration of crystalloid at 30 mL/kg for hypotension or lactate level greater than or equal to 4 mmol/L.
- Start vasopressors if the patient is hypotensive during or after fluid resuscitation to maintain mean arterial pressure level greater than or equal to 65 mm Hg.

Although no one would argue against an appropriate and timely recognition plus resuscitation for patients presenting with septic shock, this is not the mandate that such a guideline will promote. First, although triage is a reliable, extractable time stamp, it is likely a poor surrogate for many patients for the onset of sepsis. Think of the parable of the drunk who searches for lost keys beneath a lamp because “that is where I can see”; starting where things one thinks are easiest to measure may not really aid the task at hand (getting the right care started when needed). Next, by condensing the 3- and 6-hour bundles into a single 1-hour treatment directive, the authors create an operational challenge with the potential of leading to downstream patient harms. To achieve compliance with these new recommendations, most EDs, already challenged by the current 3-hour bundle,⁴ will likely use strategies such as those in the 2002 CMS pneumonia measure efforts, applying this 1-hour bundle broadly to the majority of patients presenting with a suspected infection in the event a sepsis or septic shock diagnosis is later entertained.⁵

Like the pneumonia quality measure, this resource-heavy care flows from an overreaching interpretation of evidence. First, the authors assume that all earlier treatment is better; in this case, a 1-hour bundle is superior to 3- and 6-hour bundles from previous guidelines. This contention stems from data sets reporting clinical improvements associated with earlier completion of the sepsis bundle,⁶⁻¹¹

some even citing an increased mortality for every hour's delay.⁸ However, these were all observational cohorts that separated patients by the time to intervention and usually after a clear start signal, such as shock or an elevated lactate level. The methodological limits of these approaches include inability to define causation, only association, and no ability to detect the granular differences that 1 hour versus 2 or 3 hours to complete makes on overall care, septic or nonseptic patients alike. The only prospective randomized controlled trial evaluating early antibiotic administration in an undifferentiated cohort of patients with suspected infection found no benefit.¹² Furthermore, the temporal benefits identified in these observational trials existed in the sickest subset of patients with septic shock, suggesting that when they are applied to a general ED population, overall benefit will be diluted and net harm (from overtreatment) may occur.⁸

The second assumption is that bundled and structured care is superior to individualized treatment guided by the bedside clinician. The evidentiary support of structured bundled sepsis care has its roots in early goal-directed therapy, pushed to the forefront by Rivers et al¹³ in 2001. Newer large trials have demonstrated that early aggressive approaches in many forms produce outcomes improved from the past and without differences between the approaches; simply put, the specifics of care are less important than early and ongoing care guided at the bedside by the treating clinician using a collection of tools.¹⁴⁻¹⁶ A high-quality meta-analysis of these trials confirmed their individual results, reinforcing the notion that good care can happen in many forms.¹⁷ When examining patients with severe sepsis and septic shock from 2000 to 2012 in Australia and New Zealand, Kaukonen et al¹⁸ observed a reduction in mortality from 35% to 18.4% during the 12-year period, despite the study's occurring in a region that did not endorse use of the previous Surviving Sepsis Campaign or bundled care measures. Despite that evidence consistently fails to find a benefit of a single treatment strategy, the Surviving Sepsis Campaign continues to promote recommendations that bypass the individual clinician's judgment.

The third assumption is that all components of the bundle are equally effective and must be applied with equal consistency. When Seymour et al⁸ examined the individual components of the sepsis bundle, they noted that although time to antibiotic administration showed temporal benefits similar to those of completion of the entire bundle, time to administration of the fluid bolus did not. Barochia et al¹⁹ analyzed 8 trials studying bundled care, noting an association between higher sepsis bundle compliance and improved survival, but also observing that only antibiotic

use was consistently associated with these improved outcomes, not the rest of the bundled components. Andrews et al²⁰ discovered that in adult patients presenting with septic shock, early fluid boluses caused harm. Although this study occurred in Zambia with a setting and population different from those of most industrialized countries, it reminds us that the singular optimal resuscitation strategy is still undefined. Despite these findings, the Surviving Sepsis Campaign continues to recommend an empiric fluid bolus of 30 mL/kg for all patients presenting with hypotension or an elevated lactate level, independent of the clinician judgment.

Finally, the new Surviving Sepsis Campaign guidelines view the problem of identification and treatment of sepsis from a limited perspective. By examining only the patients later determined to have sepsis, the authors ignored patients without sepsis who were exposed to the risks associated with broad-spectrum antibiotics and large-volume fluid resuscitation. The approach suggested in the guideline eschews concern about effect on the other ED patients whose care will suffer as resources are diverted to meet another time-based metric. Each of us has been witness to shortcomings of zealous mandated sepsis care, such as the patient presenting with suspected pneumonia in whom a fluid bolus meeting the target of 30 mL/kg unmasks and worsens the real cause, acute heart failure. How many patients will receive broad-spectrum antibiotics and large-volume fluid resuscitations needlessly? How many patients do we screen to identify the few who may benefit from aggressive care?

Although well intentioned, the current sepsis bundles and the potential penalties associated with noncompliance lay a heavy weight on ED care absent evidence that a net benefit will follow. The proposed Surviving Sepsis Campaign abbreviated bundle heightens the burden by further restricting the time allotted for the identification and treatment of patients with suspected sepsis, all without any evidence of benefit or knowledge of the logistic consequences or cost. A more thoughtful approach to both the identification and management of patients with sepsis is needed, one that engages all stakeholders and experts, including the emergency medicine clinicians who treat most patients hospitalized with sepsis and who will be responsible for implementing these recommendations. A better strategy will identify more meaningful time stamps, focus less on the exact volume of fluid administered, and concentrate on identifying the subgroup of septic patients who will benefit from timely, appropriate care while limiting the diagnostic noise and logistic burdens that come with oversensitive screening tools. Absent this reevaluation and reconstructing, we may look back on our current

efforts with the same sense of embarrassment and regret once experienced with the pneumonia quality metric.

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