

Component-Level Analysis of the SEP-1 3-Hour Bundle and its Association With 30-day Mortality after Sepsis

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Introduction

Sepsis is the most common cause of death in hospitalized patients. The “sepsis-3” classification defines sepsis as an infection with life-threatening organ dysfunction¹ (**Table 1**). In 2015, CMS released the “SEP-1” treatment protocol which is a multicomponent 3-hour and 6-hour resuscitation treatment plan for patients with the diagnosis of either severe sepsis or septic shock² (**Table 2**). This study focused on the 3-hour treatment metrics including fluid administration in appropriate candidates, antibiotics, blood culture before antibiotics, blood culture after antibiotics, initial lactate, and repeat lactate. While previous studies have demonstrated an association between the lack of antibiotics and patient mortality, research on the other components of the treatment protocol is less clear³. The purpose of this study was to understand the most commonly missed steps or “fallouts” in the CMS-directed 3-hour bundle and their effect on patient mortality.

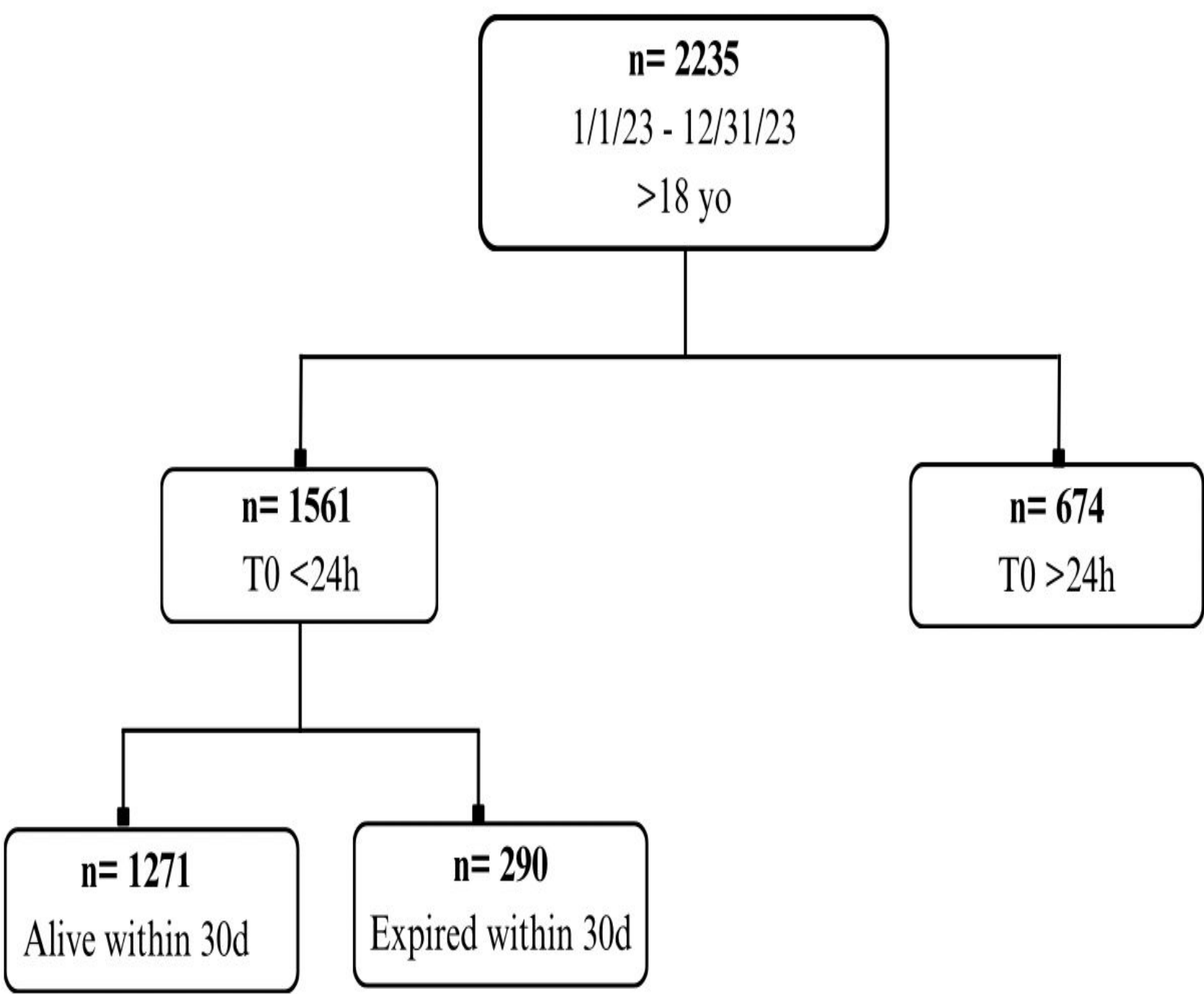
Table 1. Definition of Sepsis	
Sepsis is defined by the presence of all three criteria below, occurring within 6 hours of each other.	
Criteria	Description
1. Suspected or Confirmed Infection	Evidence or strong clinical suspicion of infection.
2. ≥2 SIRS (Systemic Inflammatory Response Syndrome) Criteria	- Temperature >38.3°C (100.9°F) or <36°C (96.8°F) - Heart rate >90 beats/min - Respiratory rate >20 breaths/min - White blood cell count >12,000/μL or <4,000/μL
3. ≥1 Sign of Organ Dysfunction*	- Lactic acid >2 mmol/L - Hypotension** - Acute respiratory failure - Creatinine >2 mg/dL - Urine output <0.5 mL/kg/h for 2 hours - Bilirubin >2 mg/dL - Platelet count <100,000/μL - INR >1.5 or aPTT >60 seconds - New need for invasive or noninvasive mechanical ventilation (eg, ETT, BIPAP)
* Criteria adapted from clinical guidelines on organ dysfunction in sepsis.	
** Persistent hypotension despite adequate fluid resuscitation may indicate septic shock.	

Table 2. Treatment Overview of the 3-Hour Sepsis Bundle		
Following identification of severe sepsis or septic shock, initiate the following interventions within the specified time frames:		
Time Frame	Intervention	Description
Within 3 Hours of Presentation	Lactic acid measurement	Collect initial lactic acid specimen.
	Blood cultures	Obtain prior to initiating antibiotics.
	IV antibiotics	Administer broad-spectrum antibiotics based on suspected or identified source.
	Fluid resuscitation	Administer 30 mL/kg crystalloid fluid bolus (0.9% NS or LR) if hypotension** is present or if initial lactic acid level is ≥4 mmol/L.
Within 6 Hours of Presentation	Repeat lactic acid measurement	If initial lactic acid >2 mmol/L, repeat the test to assess for resolution or persistence of lactic acidosis.
** Hypotension defined as systolic blood pressure <90 mm Hg or mean arterial pressure <65 mm Hg after fluid resuscitation.		

Methods

A retrospective chart analysis was performed for 1561 patients (18 years and older) with sepsis onset within 24 hours of arrival to the emergency department at a major academic hospital in metro Detroit between January-December 2023. An automated algorithm was developed to establish sepsis “time zero” based on both structured data and unstructured clinical notes using a rule-based natural language processing (NLP) approach. In addition, the algorithm determines the timing of diagnostic tests and treatments as specified by the CMS SEP-1 protocol. Multivariable linear regression was used to determine the association between each SEP-1 component and 30-day mortality while adjusting for age, race, and gender. Race included 5 categories: white or caucasian, black or african american, asian, other, and ND.

Figure 1. Consort diagram of the study population.



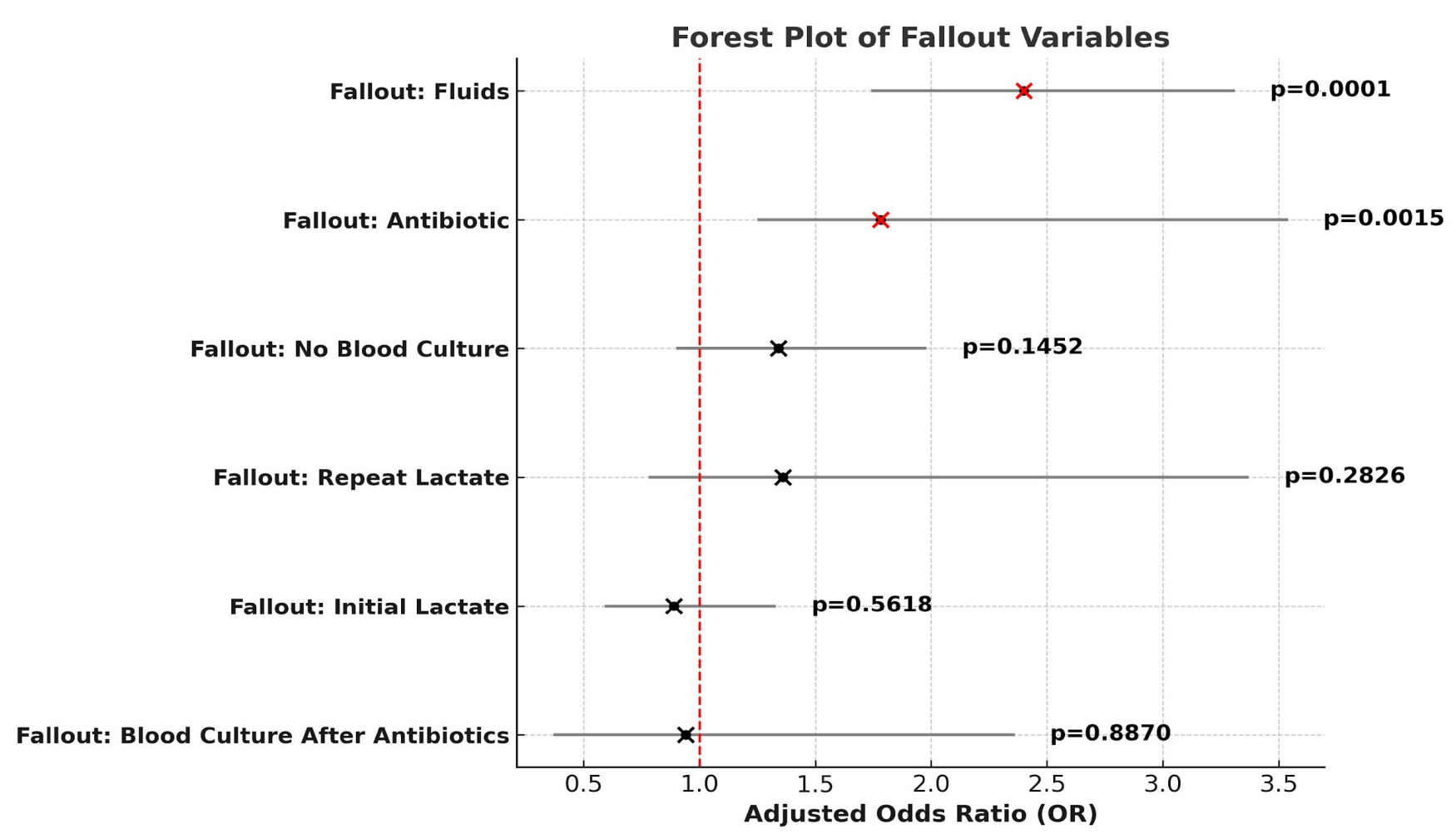
Results

Each year in age was significantly (adj OR: 1.04, 95% CI: 1.02-1.05) associated with 30-day mortality after sepsis. Race across all 5 categories was not statistically significant. Among the six components of the 3-hour SEP-1 bundle, failure to administer antibiotics (adj OR: 1.78, 95% CI: 1.24-2.54) and appropriate volume of IV fluids (adj OR: 2.40, 95% CI: 1.74-3.31) were significantly association with 30-day mortality.

Figure 2: Demographics of the study cohort with respect to 30-day mortality

Variable	All	30 d mortality	Presumed alive
Sample, n	1561	290	1271
Age, median (IQR)	69 (57-79)	75 (65-83.25)	68 (55-78)
Female, n [%]	722 (46.25)	149 (51.38)	573 (45.08)
Race, n (%)			
White/Caucasian	1020 (65.34)	196 (67.59)	824 (64.83)
Black/AA	403 (25.82)	71 (24.48)	332 (26.12)
Asian	38 (2.43)	3 (1.03)	35 (2.75)
Other	90 (5.77)	15 (5.17)	75 (5.90)
ND	10 (0.64)	5 (1.72)	5 (0.39)

Figure 3: Adjusted Odds Ratios for each fallout category with respect to 30-day mortality



Conclusions

It is essential to have a comprehensive treatment plan for sepsis given it is one of the major causes of death in hospitalized patients worldwide. Some key takeaways from our study include:

- Need for early identification and management of sepsis, particularly in regards to fluids and antibiotics administration, two treatment metrics of the SEP-1 3-hour bundle.
- Demographic factors like age have a higher association with 30-day mortality after sepsis.
- Appropriate volume of fluids as part of the sepsis treatment in addition to antibiotics.
- Our findings can be used by other healthcare systems to optimize the delivery of the SEP-1 3-hour bundle.
- Limitations:
 - Patients from one hospital system.
 - Our study looked at fluids overall.

References

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3. Seymour CW, Gesten F, Prescott HC, et al. Time to Treatment and Mortality during Mandated Emergency Care for Sepsis. *N Engl J Med.* 2017;376(23):2235-2244. doi:10.1056/NEJMoa1703058

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