Impact of Host Response Sepsis Diagnostic Implementation on Length of Stay and Mortality in an Emergency Department

Nancy Jacobson MD[1,2], Mathew Chinn MD[1,2], Tom Carver MD FACS[1,2], Jamie Aranda MD[1,2], Tom Aufderheide MD[1,2], Wei-Jien Tan[3], Nathan Ledeboer PhD[1,2]

1.Foedtert Hospital, Milwaukee, WI, USA; 2. Medical College of Wisconsin, Milwaukee, WI, USA 3. Cytovale, Inc. S. San Francisco, CA, USA.

Introduction

Sepsis, a dysregulated host immune response to infection leading to life-threatening organ dysfunction[1], is a common, fast-moving condition, with a substantial unmet need for the rapid diagnosis and delivery of precision therapies to prevent resultant morbidity and mortality[2]. Current guidelines stress quick intervention[3], yet undifferentiated patients with signs and symptoms of infection present to the Emergency Department (ED) and physicians are tasked with sepsis diagnosis often before adequate, objective diagnostic and prognostic data are available. A new cellular host response test, recently cleared by the U.S. Food and Drug Administration (FDA) for early detection of sepsis, can aid in addressing this gap.

In August 2024 Froedtert Hospital and Medical College of Wisconsin (MCW), a 766 bed facility with >75,000 ED visits per year, implemented a process for sepsis care including a novel host-response sepsis diagnostic (HRSD) in the Emergency Department (ED). The test was not applied via a standard protocol. Rather, it was ordered at discretion of the provider. As a result, test ordering was about 37.8% of suspected infection patients and some providers ordered frequently, while others did not, which created a natural comparison (tested vs untested in the same hospital and time period). This study sought to evaluate the outcomes of patients for whom the providers utilized the process for sepsis care featuring the HRSD (Tested) to those of patients for whom the providers did not use the process (Untested).

Methods

Host Response Sepsis Diagnostic (HRSD)

- The HRSD, the Cytovale IntelliSep test, is FDA cleared (21 CFR 866.3215, 2022),
- Semi-quantitative test, assesses cellular host response via deformability cytometry
- Indicated for use in adult patients with signs and symptoms of infection who present to the ED.
- Performed on a K2 EDTA anticoagulated whole blood sample <10 min.
- interpretation bands based on the probability of sepsis with organ dysfunction manifesting within3d: Band 1 (low), Band 2, and Band 3 (high)[4,5].

Scientific Theory of Operation

- Biophysical properties shift with degranulation, neutrophil extracellular trap (NET) formation[6,7], or maturity that occurs during the dysregulated immune activation associated with sepsis[8,9].
- The test measures thousands of cells using microfluidic deformability cytometry combined with high-speed imaging and machine learning[6,10].

Study Design & Setting

- Alerting and ordering workflow: manual vitals populate alert logic; RN selects Positive Sepsis Screen, confirms with MD and orders HRSD via ANI (the EHR ordering interface) (Fig-1).
- In this ED setting, specific treatment pathways are recommended based on the HRSD result for a patient (Fig-2).
- The timeframe of the study included patients presenting between 8/21/2024 and 5/21/2025
- The analysis focused on a Suspected Infection Population based on provider action, defined as patients with an ED blood culture order or an HRSD order or both.
- Propensity matching used to create comparable Tested and Untested groups based on observed covariates.
- Sepsis status determined by discharge Sepsis ICD-10 codes included.

Figure 1: Alerting and test ordering workflow

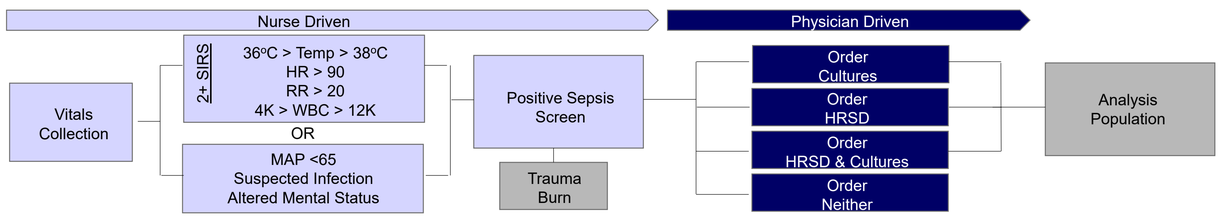
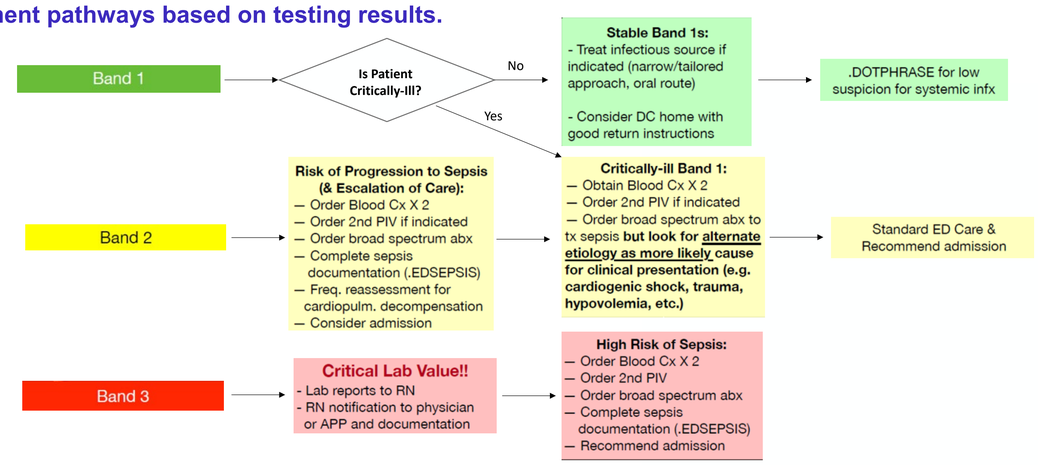


Figure 2: Treatment pathways based on testing results.



Results

- ED census: 61,567
- Suspected Infection Population: 6,040 patients
- HRSD or Both Ordered 37.8% (2,284)
- Cultures only Order 62.2% (3,756)
- Median HRSD laboratory turnaround time <45min
- Tested patients with a Sepsis ICD-10 had a propensity-matched Hospital Length of Stay (HLOS) 2.22 days shorter than Untested patients with a Sepsis ICD-10
- Sepsis mortality among Tested patients was estimated to be 3.3% lower than Sepsis mortality among Untested patients when propensity matching was performed

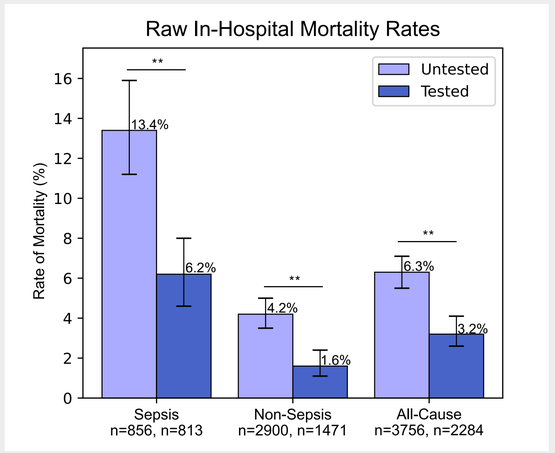
Ordering of Tests	N	Column %
Blood Culture Only	3,756	62.2%
Both Same Time	863	14.3%
HRSD First	840	13.9%
HRSD Only	452	7.5%
Both, Blood Culture First	129	2.1%
All	6,040	

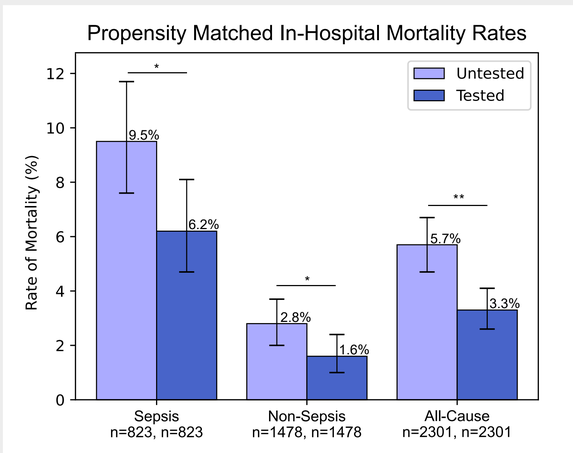
Length of Stay*

	Raw						Propensity Matched		
	Median			Mean			Mean		
	Untested	Tested	Difference	Untested	Tested	Difference	Untested	Tested	Estimated Effect
Hospital Length of Stay	5 days n = 3260	4 days n = 1744	1 day	8.21 days n = 3260	6.38 days n = 1744	1.83 days p: < 0.001	8.32 days n = 1744	6.38 days n = 1744	1.93 days p: < 0.001
Sepsis Hospital Length of Stay	7 days n = 800	5 days n = 771	2 days	9.67 days n = 800	7.39 days n = 771	2.28 days p: < 0.001	9.61 days n = 771	7.39 days n = 771	2.22 days p: < 0.001
Non- Sepsis Hospital Length of Stay	5 day n = 2460	4 day n = 973	1 day	7.74 days n = 2460	5.59 days n = 973	2.15 days p: < 0.001	7.29 days n = 973	5.59 days n = 973	1.70 days p: < 0.00 1

*Top 2.5% of all HLOS trimmed from analysis due to limit the impact of outliers

Mortality (In-Hospital^)





^Discharged patients assumed to survive, *p < 0.05, **p < 0.01

Conclusions

In a suspected infection population, HRSD -Tested patients appeared to have shorter HLOS and lower rate of mortality than Untested patients. These differences were robust following propensity matching. Further investigation, including prospective cohorts, is warranted to further evaluate these findings.

Acknowledgements

We would like to thank the nursing staff of the Froedtert Hospital ED and the physicians of the Medical College of Wisconsin Department of Emergency Medicine for their tireless efforts in adopting new processes and technologies to improve the care of our patients who present with signs or suspicion of infection. We also thank the Lab Director, and the clinical laboratory staff of Wisconsin Diagnostics Laboratories who have worked with us to implement this test. Finally, we thank the Froedtert Hospital Quality and Safety team that works to ensure we are providing the best possible care to our patients.

References

[1] Singer, *JAMA*, 2016
[2] Wang, *Crit Care Med* 2017.
[3] Surviving Sepsis Campaign Declarations. 'Barcelona Declaration' [cited 2020].
[4] Guillou, *PLOS One* 2021.
[5] O'Neal, *Crit Care Exp.* 2021.
[6] Sorrells, *Diagnostics.* 2023.
[7] Granger, *Leuk. Bio.* 2017.
[8] Camicia, *SHOCK* 2014.
[9] Czaikoski. Plos One 2017.
[10] Crawford, *Respir Crit Care Med.* 2018.