Title: Effect of Early-Stage Protocolized Implementation of a Novel Host-Response Test on Discharges, Hospital Free Days, and Returns at Four EDs in a Health System

Authors

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Background

There is a major unmet need in emergency departments for diagnostics that aid in rapid sepsis risk assessment of potentially infected patients [1-3]. In this study, we evaluated the results of implementation of a novel host response test (HR) as part of the protocolized screening and guideline-directed treatment pathway process for patients at risk of sepsis, in four geographically distinct EDs within a health system.

Methods

The HR test, which generates an Index based on the state of immune activation stratified into 3 interpretation bands (Band 1- 3) of increasing sepsis likelihood [4], was integrated into the protocolized response to suspected infection at four EDs in Baton Rouge, LA (S1, 9/24/2024 :1/24/2025), Lafayette, LA (S2, 9/24/2024 :1/24/2025), (Jackson, MS (S3, 8/27:12/27/2024) and Monroe, LA (S4, 8/27: 12/27/2024). At all sites, screening and ordering was achieved through 2 mechanisms, a triage-based nurse-driven protocol, and a later physician-driven protocol. Guideline-directed treatment pathways based on the results of the HR test were adopted by the health system.

Patients with missing data for discharge disposition were omitted from this analysis. ED returns were ruled as those who had an ED encounter within 30 days of their original encounter, excluding encounters with discharge ICD-10 diagnosis codes related to mental health (F1-99), substance abuse (F10-19), chronic pain (G89), sickle cell disease (D57), end of life care (Z51.5), injury/poisoning (S1-99,T1-88), or external morbidity (V1-99, Y1-99). Return-adjusted hospital free days was calculated by further subtracting a patient's length of stay for ed returns within 30 days from the original encounter, or by setting it to zero for mortalities on such returns.

Results

This study consisted of 4650 patients with 758, 764, 1930, and 1198 from sites 1-4, respectively. Of these 2546 (54.8%), 1194 (25.7%), and 910 (19.6%) returned HR results of Bands 1-3, respectively. From month 1 (M1) to month 4 (M4), a 12.3% and 8.2% increase in rates of ED discharge was observed in Band 1 (M1 22.0%, M4 34.3%, $p < 0.01$) and Band 2 (M1 10.5%, M4 18.7%, $p < 0.05$, Fig1A), respectively. During this period, no significant change to rates of ED return was observed across any Band. Additionally, an overall 1 day increase in median return-adjusted hospital free days was observed across the entire cohort from M1 to M4 (M1 26.0, M4 27.0, $p < 10^{-4}$), with a significant 1-day increase (M1 27.0, M4 28.0, $p < 10^{-4}$) and 2-day increase (M1 25.0, M4 27.0, $p < 0.05$, Fig1B) in Bands 1-2, respectively.

Conclusion

These findings suggest that the addition of a host response test as an aid in risk stratification to protocolized screening and treatment of those presenting to the ED suspected of infection may lead to improved rates of ED discharge and hospital-free days in geographically diverse EDs.

References

1. CDC.2024.
2. Finfer. NEJM. 2013.
3. Paoli. CCM. 2018.
4. US FDA 510(k) Clearance Letter for IntelliSep Test. 2022.

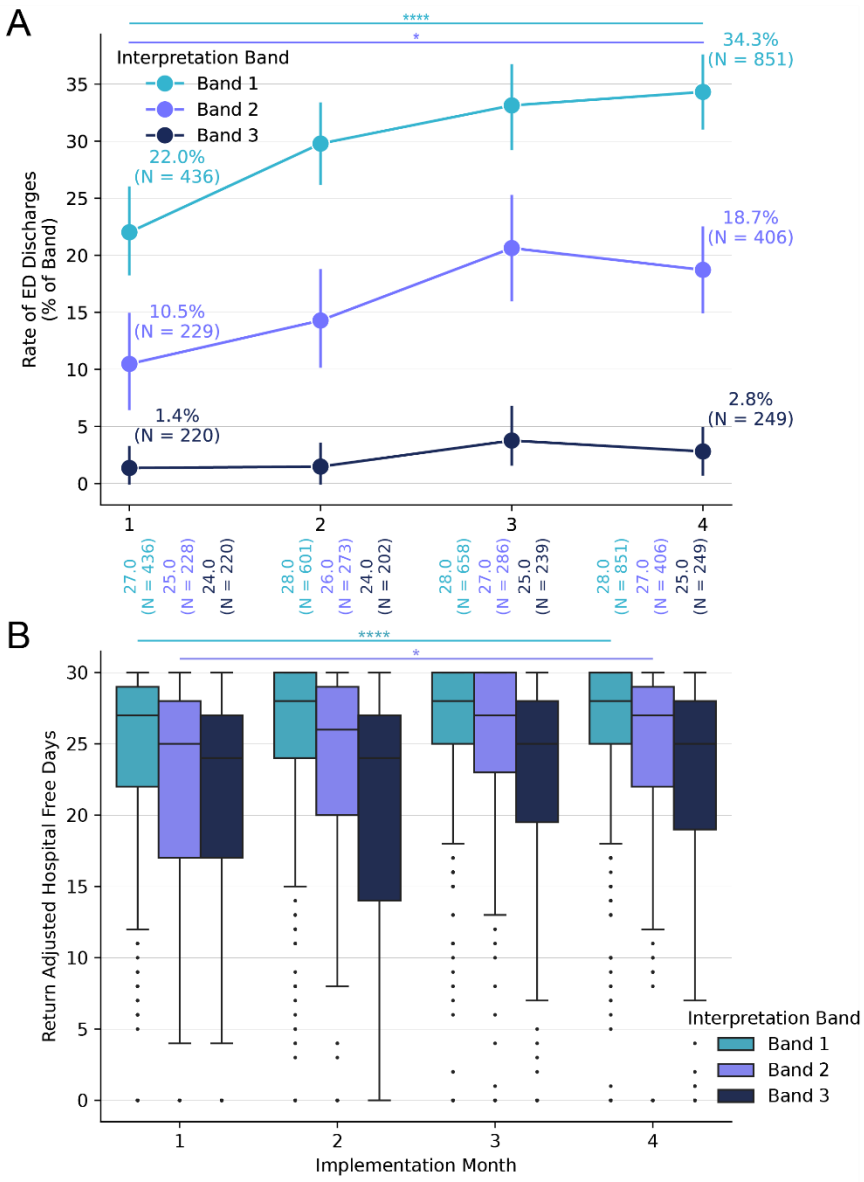

Figure 1 – (A) Rate of ED discharges among survivors across implementation time span (B) Return adjusted hospital free days across implementation time span. After hospital free days for returns within 30d, these returns were removed from the analysis to avoid double counting. N's show the total number of patients in each band at a given month. (* and **** indicate $p < 0.05$, and $p < 0.0001$, respectively.)

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INTRODUCTION

Sepsis, a dysregulated host immune response to infection leading to life-threatening organ dysfunction[1], is a common, fast-moving condition, and the leading cause of in-hospital death. Most cases develop in the community and present to Emergency Departments (ED)[2], where urgent action is required to prevent resultant morbidity and mortality[3]. However, there is a major unmet need in for diagnostics that aid in rapid sepsis risk assessment of potentially infected patients[4-6]. In this study, we evaluated the results of implementation of a novel host response test (HR) as part of the protocolized screening and guideline-directed treatment pathway process for patients at risk of sepsis, in four geographically distinct EDs within a health system.

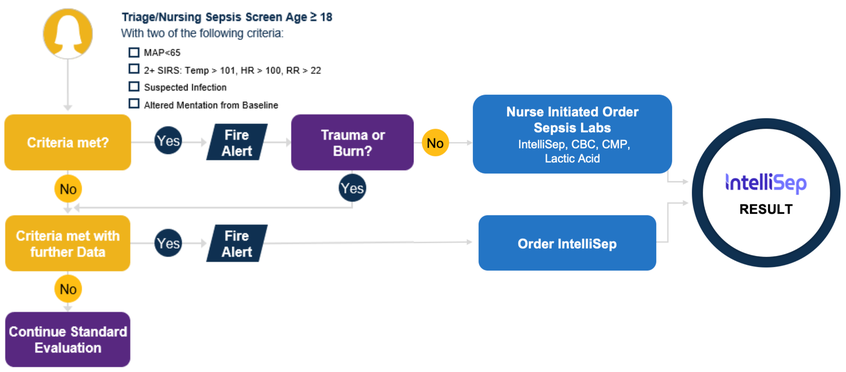

Figure 2: Schematic of nurse-driven protocol implemented for IntelliSep ordering in the ED.

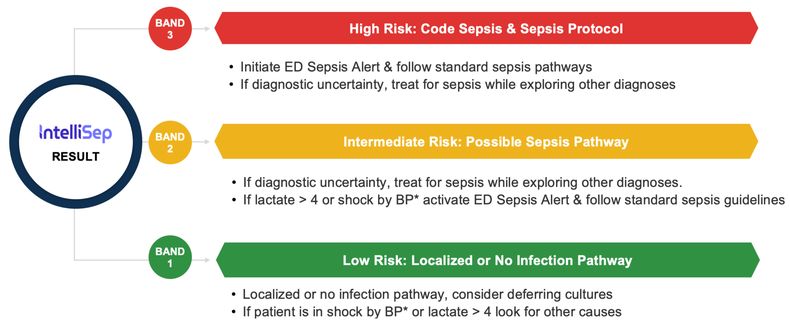

Figure 3: IntelliSep-informed treatment pathways for use in the ED.

(A) (B)

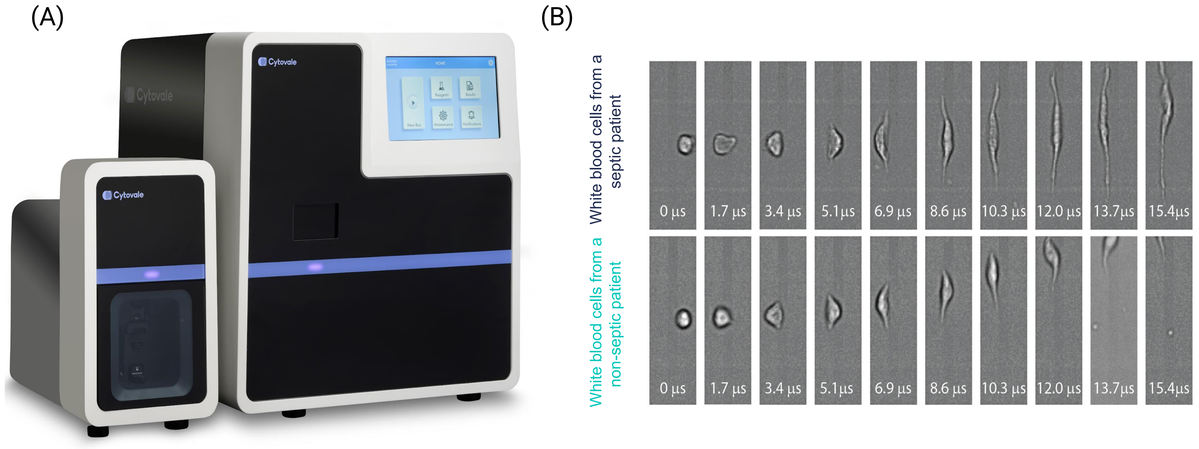

Figure 1: (A) Photograph of the Cytovale system, a benchtop instrument on which the IntelliSep test is performed (inset) the IntelliSep microfluidic cartridge; (B) Time series of cell deformation for a representative leukocyte of a septic Band 3 patient (top) and a non-septic Band 1 patient (bottom).

The IntelliSep Test

The Cytovale IntelliSep test is an FDA cleared, semi-quantitative test that assesses cellular host response via deformability cytometry of leukocyte biophysical properties and is intended for use in conjunction with clinical assessments and laboratory findings to aid in the early detection of sepsis with organ dysfunction manifesting within the first 3 days after testing . It is indicated for use in adult patients with signs and symptoms of infection who present to the ED. The test is performed on a K2 EDTA anticoagulated whole blood sample.

The test results in the IntelliSep Index (ISI), a single score between 0.1-10.0, in <10 minutes. The score is stratified into three discrete interpretation bands based on the probability of sepsis with organ dysfunction manifesting within the first three days after testing: Band 1 (low), Band 2, and Band 3 (high)[7].

Biophysical properties such as deformability, density, and size of neutrophils and monocytes are thought to shift with degranulation, neutrophil extracellular trap (NET) formation[8,9], or maturity that occurs during the dysregulated immune activation associated with sepsis[10,11]. As such, these properties differ in cells from septic patients when compared to quiescent white blood cell (Fig. 1-B).

METHODS

Study Design and Setting

- IntelliSep test was integrated into the protocolized response to suspected infection at four EDs in Baton Rouge, LA (S1, 9/24/2024 :1/24/2025), Lafayette, LA (S2, 9/24/2024 :1/24/2025), Jackson, MS (S3, 8/27:12/27/2024) and Monroe, LA (S4, 8/27: 12/27/2024).
- At all sites, screening and ordering was achieved through 2 mechanisms, a triage-based nurse-driven protocol (Fig. 2) and a later physician-driven protocol.
- Guideline-directed treatment pathways based on the results of the HR test were adopted by the health system (Fig 3).
- ED returns were ruled as those who had an ED encounter within 30 days of their original encounter, excluding encounters with discharge ICD-10 diagnosis codes related to mental health (F1-99), substance abuse (F10-19), chronic pain (G89), sickle cell disease (D57), end of life care (Z51.5), injury/poisoning (S1-99,T1-88), or external morbidity (V1-99, Y1-99).
- Return-adjusted hospital free days was calculated by further subtracting a patient's length of stay for ed returns within 30 days from the original encounter, or by setting it to zero for mortalities on such returns.

RESULTS

- This study consisted of 4650 patients with 758, 764, 1930, and 1198 from sites 1-4, respectively.
- Of these 2546 (54.8%), 1194 (25.7%), and 910 (19.6%) returned HR results of Bands 1-3, respectively.
- From month 1 (M1) to month 4 (M4), a 12.3% and 8.2% increase in rates of ED discharge was observed in Band 1 (M1 22.0%, M4 34.3%, $p < 0.01$) and Band 2 (M1 10.5%, M4 18.7%, $p < 0.05$, Fig. 4A), respectively. No significant change in discharge was observed in Band 3 (1.4% M1, 2.8% M3)
- During this period, no significant change to rates of ED return was observed across any Band.
- From M1 to M4, a significant 4.3% reduction in mortality of Band 1 patients was observed (10.6% M1, 6.3% M4, $p < 0.05$)
- Additionally, an overall 1 day increase in median return-adjusted hospital free days was observed across the entire cohort from M1 to M4 (M1 26.0, M4 27.0, $p < 10^{-4}$), with a significant 1-day increase (M1 27.0, M4 28.0, $p < 10^{-4}$) and 2-day increase (M1 25.0, M4 27.0, $p < 0.05$, Fig. 4B) in Bands 1-2, respectively.

A B

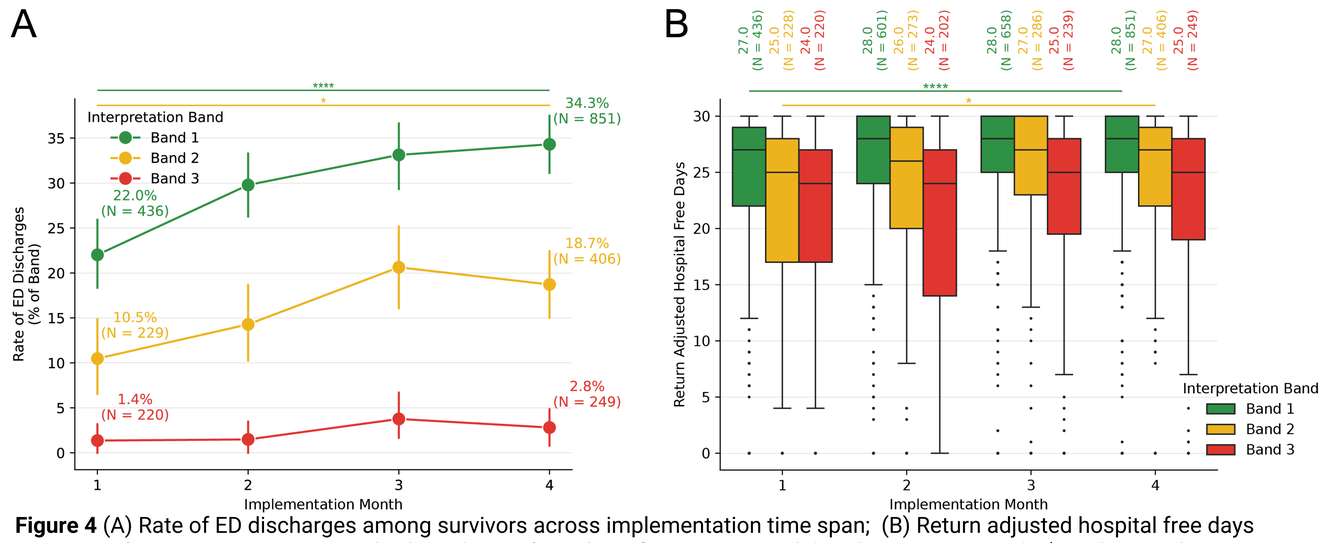

Figure 4 (A) Rate of ED discharges among survivors across implementation time span; (B) Return adjusted hospital free days across implementation time span. N's show the total number of patients in each band at a given month. (* and **** indicate $p < 0.05$, and $p < 0.0001$, respectively.)

CONCLUSIONS

These findings suggest that the addition of a host response test as an aid in risk stratification to protocolized screening and treatment of those presenting to the ED suspected of infection may lead to improved rates of ED discharge and hospital-free days in geographically diverse EDs.

ACKNOWLEDGEMENTS

REFERENCES

1. Singer *JAMA* 2016.
2. Wang *Crit Care Med* 2017.
3. Surviving Sepsis Campaign Declarations. 'Barcelona Declaration' [cited 2020].
4. CDC.2024.
5. Finfer. NEJM. 2013.
6. Paoli. CCM. 2018.
7. O'Neal Crit Care Exp. 2024.
8. Sorrells, Diagnostics. 2023.
9. Granger Leuk. Bio. 2017.
10. Camicia SHOCK 2014.
11. Czaikoski. Plos One 2017.