

Title Evaluation of early stage implementation results of a cellular host-response test in an emergency department setting

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Sepsis is a life-threatening emergency requiring urgent intervention to achieve optimal outcomes[1-3]. In the emergency department (ED), there is a critical unmet need for novel diagnostics to aid in timely sepsis risk stratification of patients with nonspecific signs of infection. In this study, we evaluated performance of a commercial cellular host-response test to risk-stratify patients and change relevant resource utilization for patients with suspicion of infection 3 months after implementation in an ED setting.

The rapid (<10 minute) cellular host-response test, which generates an Index based on the state of immune activation stratified into 3 interpretation bands (Band 1-Band 3) of increasing sepsis likelihood[4], was integrated into an existing ED workflow for patients presenting to the ED of a large academic medical center in Louisiana, USA, with suspected infection. Blood cultures, antibiotic administration, outcomes, and host-response test results of patients were analyzed for the first 3 months after (August - October 2023) implementation of the test. For the case of blood culture and antibiotics, data was also obtained and analyzed from July 2023, prior to test implementation.

1275 patients had been assayed using the test, with 608 (47.7%) in Band 1, 361 (28.3%) in Band 2, and 306 (24.0%) in Band 3. Patients who had tests ordered (on average 14 tests/day) comprised 2.34% of all patients seen in the ED and 39.35% of patients who had a sepsis best-practices alert fire. A significant reduction in length of stay among survivors was observed in patients from August 2-20 (mean 5.24 days) to October 14-31 (mean 3.77 days, $p < 0.05$, Fig-1A). From July 1 to October 31 a continual reduction of 5% of total blood cultures ($N=1036$, 15.8% of ED encounters - July; $N=692$: 10.8% of ED encounters -October) and a 15% reduction of antibiotics/100 visits (19.7 doses/100-visits July, 16.7 doses/100-visits October, $p < 0.0001$, Fig-1B/C) was observed.

This study's findings suggest this cellular host-response test may improve risk stratification and resource utilization for those presenting to the ED with suspected infection.

Figures

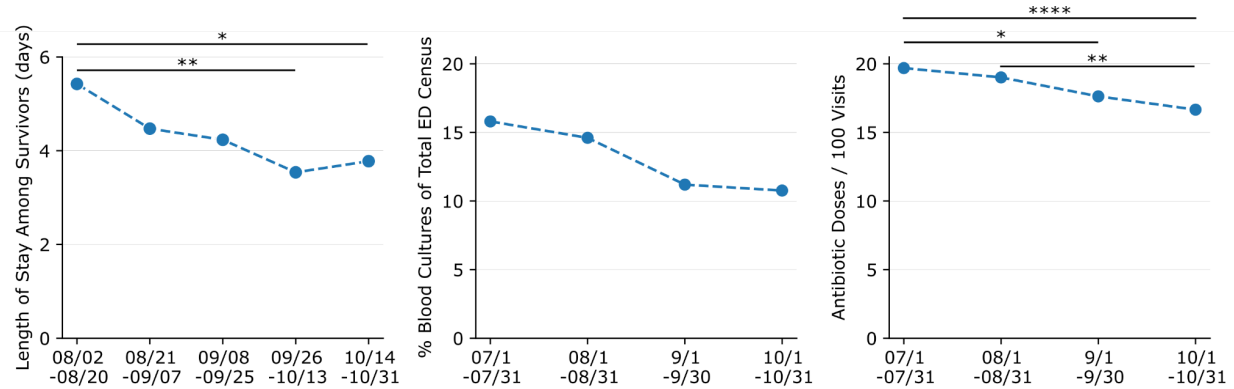


Figure 1 (A) Mean length of stay among survivors from 08/2 to 10/31, (B) percent of blood cultures of total ED cases from 7/1 to 10/31, and (C) antibiotic doses per 100 visits for patients in the ED from 7/1 to 10/31 (*, **, and **** indicate $p < 0.05$, $p < 0.01$, and $p < 0.0001$, respectively).

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Evaluation of Early-Stage Implementation Results of a Cellular Host-Response Test in an Emergency Department Setting

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Introduction

Sepsis, a dysregulated host immune response to infection leading to life-threatening organ dysfunction¹, 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 mortality². Current guidelines stress quick intervention³, 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. As such, diagnostics to aid the ED in rapid sepsis risk assessment of potentially infected patients are needed. In this study, we evaluated performance of a commercial cellular host-response test to risk-stratify patients and change relevant resource utilization for patients with suspicion of infection 3 months after implementation in an ED setting.

Methods

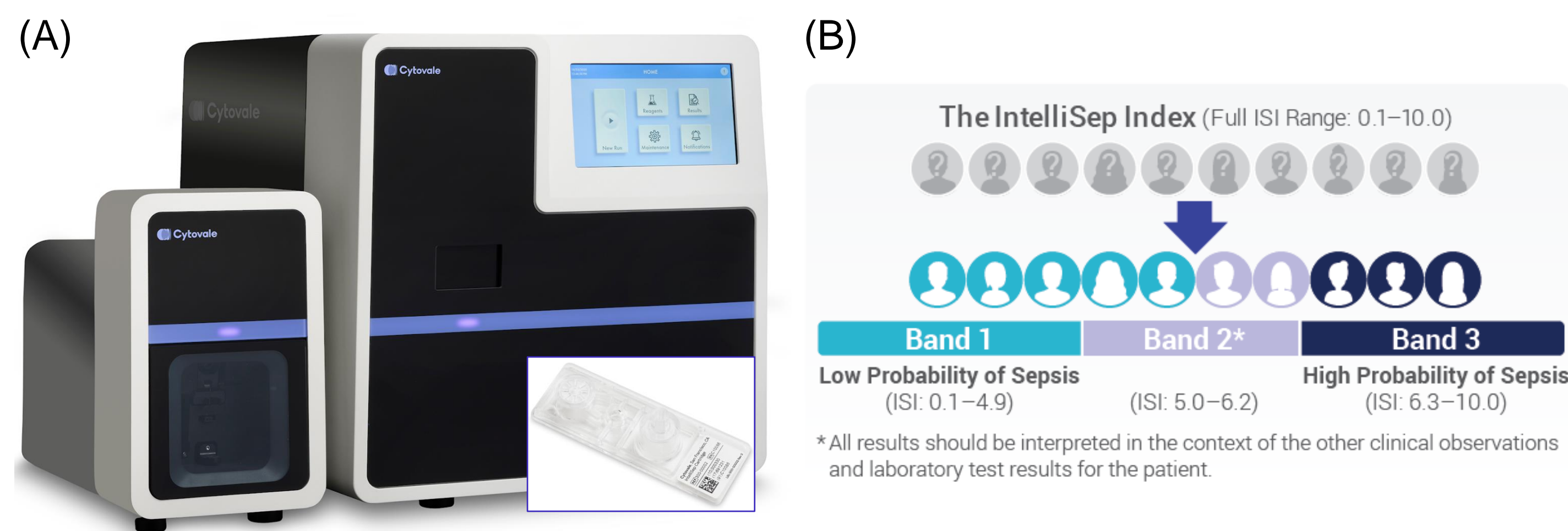


Figure 1: (A) Photograph of the Cytovale system, a benchtop instrument on which the IntelliSep test is performed (inset the IntelliSep microfluidic cartridge); (B) The IntelliSep reported result: the IntelliSep Index and Interpretation Bands.

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)^{4,5} (Fig. 1-B).

Scientific Theory of Operation

Biophysical properties such as deformability, density, and size of neutrophils and monocytes are thought to shift with degranulation, neutrophil extracellular trap (NET) formation^{6,7}, or maturity that occurs during the dysregulated immune activation associated with sepsis^{8,9} (Fig. 2-A). As such, these properties differ in cells from septic patients when compared to quiescent white blood cell (Fig. 2-B).

The IntelliSep test utilizes a microfluidic deformability cytometry technique in combination with technological advances in high-speed imaging and machine learning, to measure the biophysical properties of thousands of individual leukocytes in rapid succession, enabling rapid assessment of immune activation signatures and sepsis risk stratification^{6,10}.

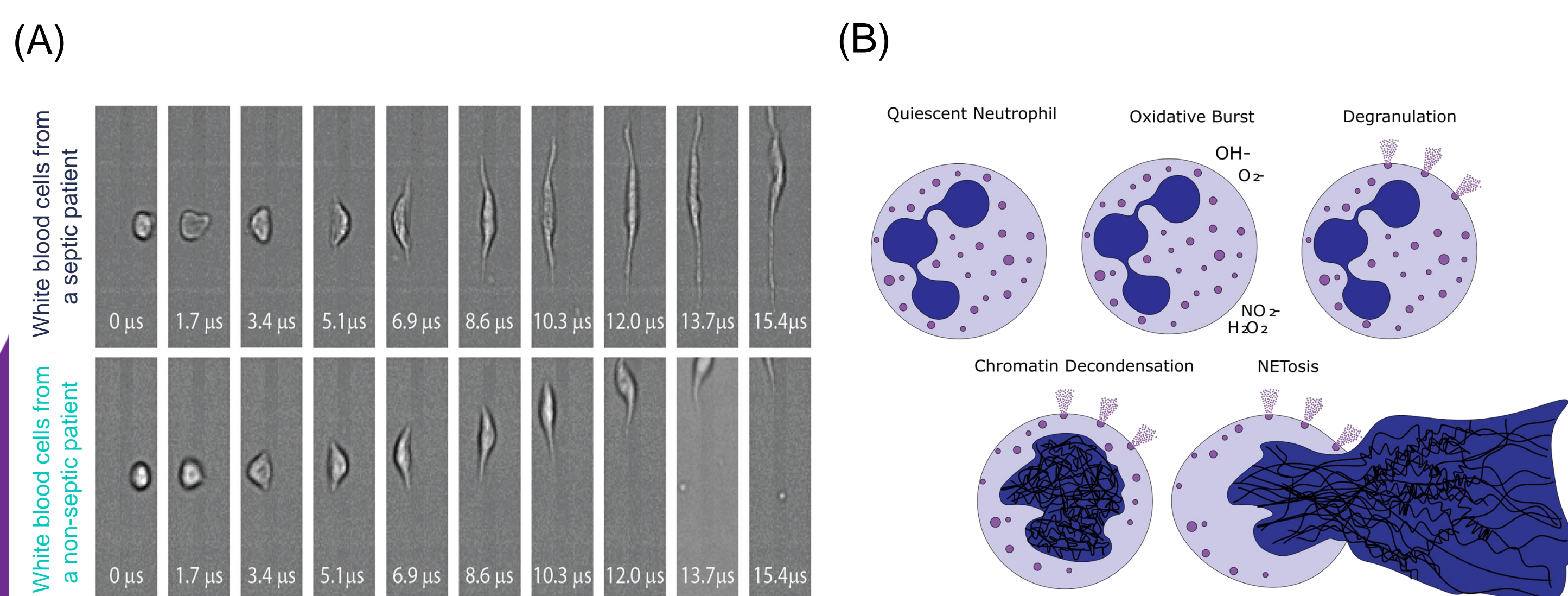


Figure 2: (A) Time series of cell deformation for a representative leukocyte of a septic Band 3 patient (top) and a non-septic Band 1 patient (bottom); (B) Neutrophil extracellular traps (NETs) formation is a rapid active process mediated by NETosis, involving chromatin decondensation and nuclear membrane disintegration¹¹.

Study Design & Setting

- The IntelliSep test was integrated into an existing ED workflow for patients presenting to the ED of a large academic medical center in Louisiana, USA, with suspected infection.
- Blood cultures, antibiotic administration, outcomes, and host-response test results of patients were analyzed for the first 3 months after (August - October 2023) implementation of the test.
- For the case of blood culture and antibiotics, data was also obtained and analyzed from July 2023, prior to test implementation.

Results & Discussion

- 1277 sequential patients assayed using the test were included in this study, with 610 (47.8%) in Band 1, 361 (28.2%) in Band 2, and 306 (24.0%) in Band 3.
- Patients who had tests ordered (on average 14 tests/day) comprised 6.3% of all patients seen in the ED and 49.6% of patients who had a sepsis best-practices alert (BPA) fire (Figure 3).
- A significant 1.47 day reduction in length of stay among survivors ($p < 0.05$, Figure 4A) was observed in patients from initial implementation (August 1-19 (mean 5.24 days)) to full implementation (October 14-31 (mean 3.77 days)).
- From baseline (July 1) to full implementation (October 31) a 15% reduction of antibiotics/100 visits was observed (19.7 doses/100-visits July, 16.7 doses/100-visits October, $p < 0.0001$, Figure 4B).
- From initial implementation (August 1-19) to full implementation (October 14-31) a continual reduction of 19% of total blood cultures among those with an IntelliSep ordered (62% Aug – 41% Oct, $p < 0.001$) was observed (Figure 5A). Across Interpretation Bands, rates of blood culture orders fell approximately two-fold in Bands 1 (38% Aug – 16% Oct, $p < 0.001$) and 2 (77% Aug – 44% Oct, $p < 0.05$) but were unchanged in Band 3 (Figure 5B).

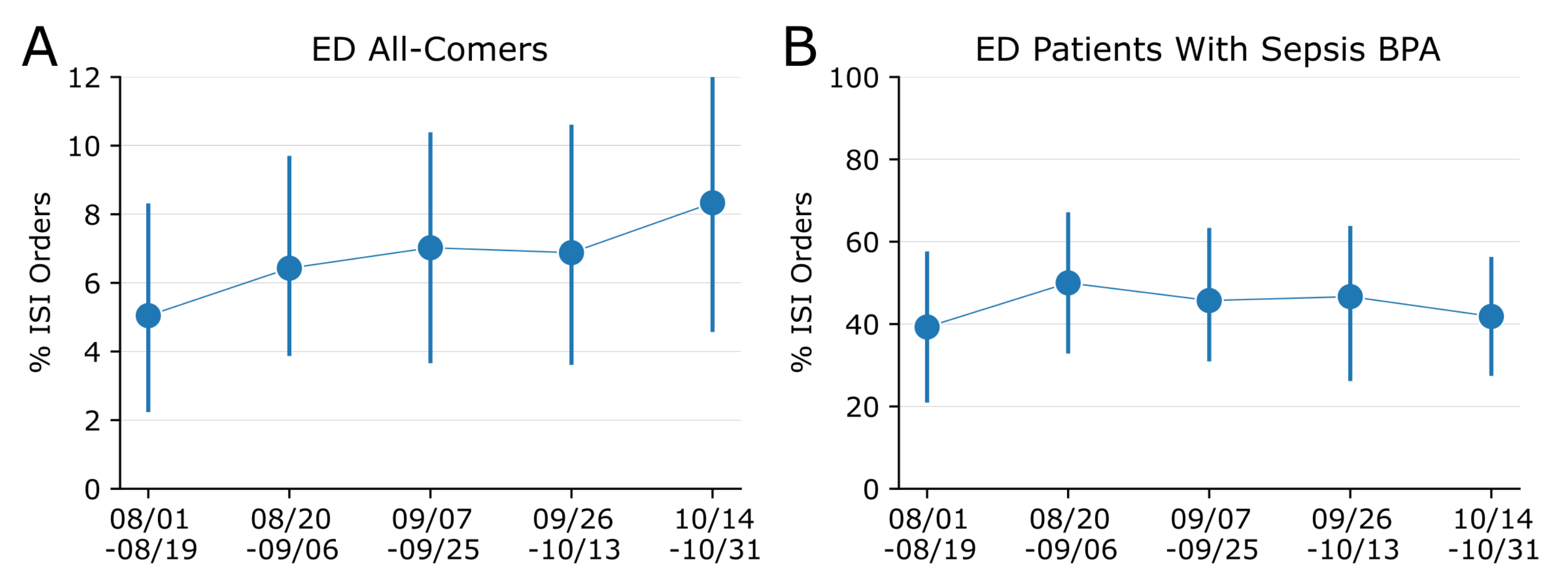


Figure 3: Attachment rates of ISI orders across time with a denominator of (A) all patients in the ED and (B) all patients who had a sepsis BPA fire.

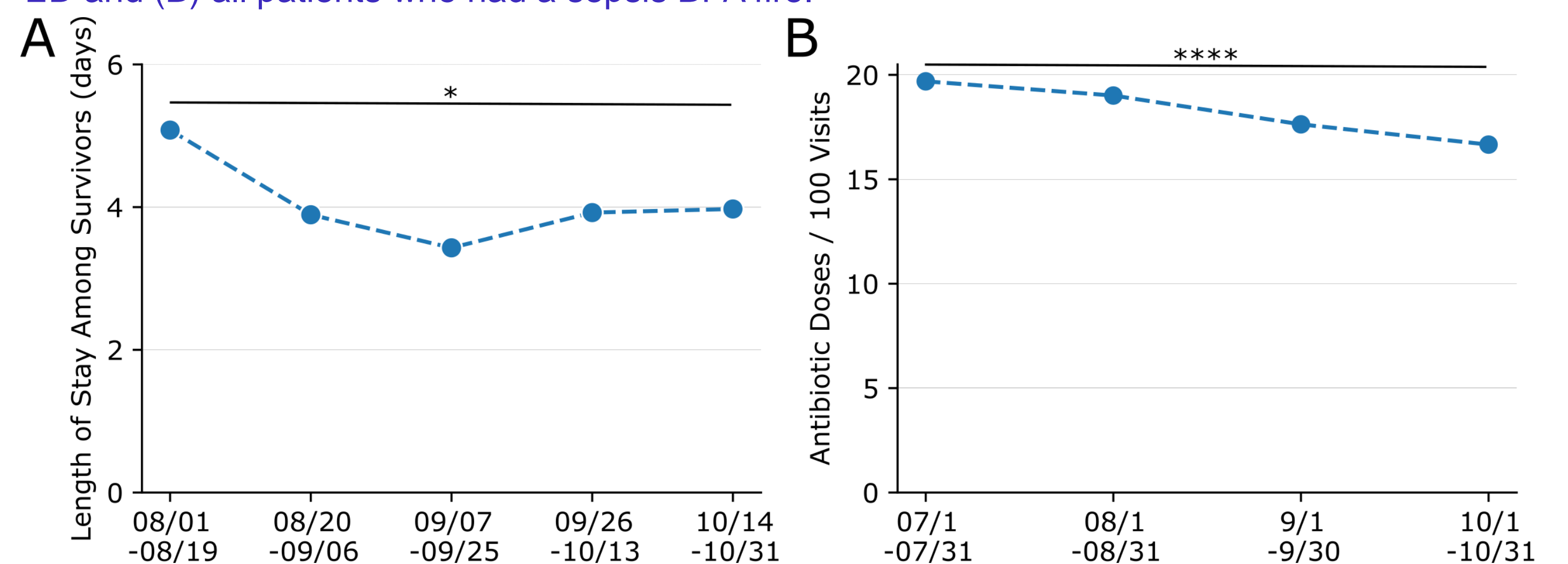


Figure 4: (A) Length of stay among survivors and (B) antibiotic doses per 100 visits for all-comers to the ED (* and **** indicate $p < 0.05$ and $p < 10^{-4}$, respectively).

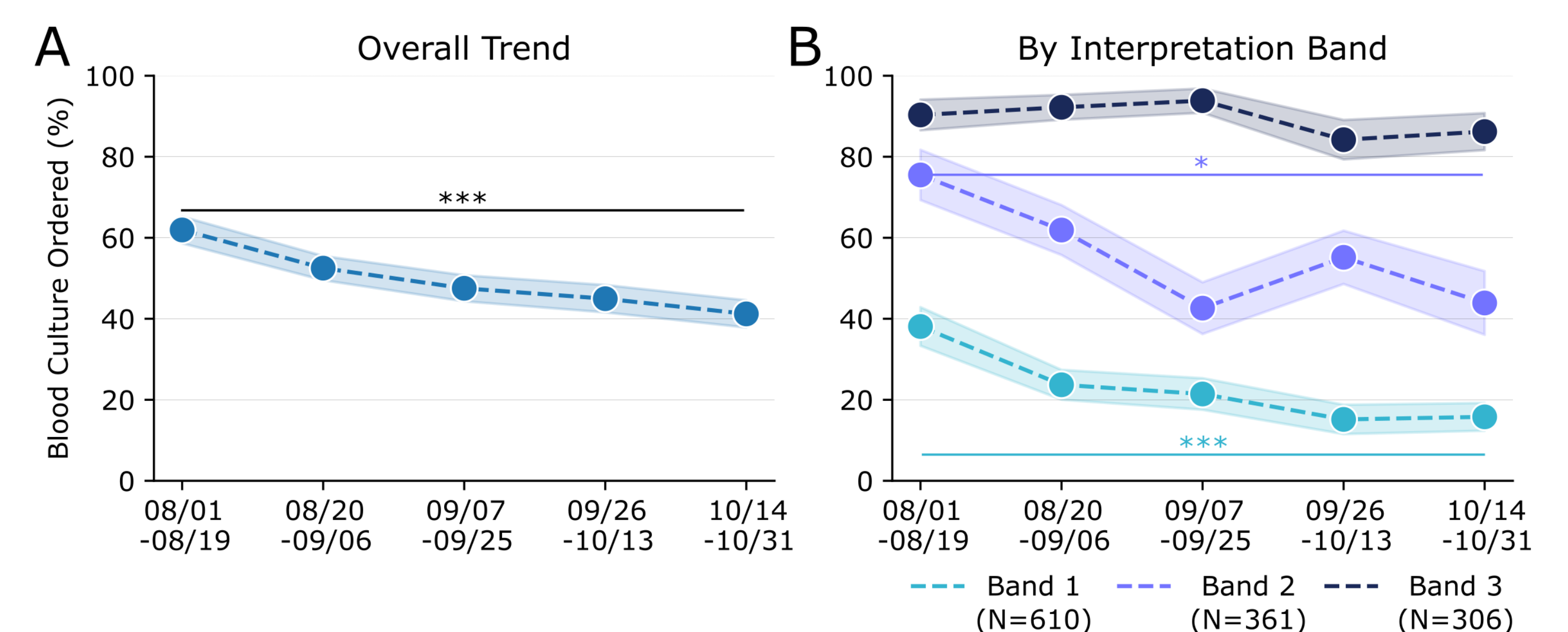


Figure 5: Rate of blood cultures ordered across time for (A) all patients with an ISI ordered and (B) across interpretation band. (* and *** indicate $p < 0.05$ and $p < 0.001$, respectively)

Conclusions

This study's findings suggest this cellular host-response test may improve risk stratification and resource utilization for those presenting to the ED with suspected infection.

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