Title Evaluation of a cellular host response test for risk-stratifying patients presenting to the ED with signs or suspicion of urinary tract infection

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Objectives
Urinary tract infections (UTIs) are a leading cause of bacterial infections in the US and account for a significant portion of antibiotic consumption and healthcare costs. UTIs occur across a broad spectrum of disease from uncomplicated lower UTI to pyelonephritis, and sepsis.These infections are difficult to accurately diagnose due to the high rates of asymptomatic bacteriuria (ASB) and nonspecific symptoms such as altered cognition. In this study, we evaluated the potential of a novel cellular host response test to risk stratify patients with suspected UTI for localized UTI, sepsis, or no infection.

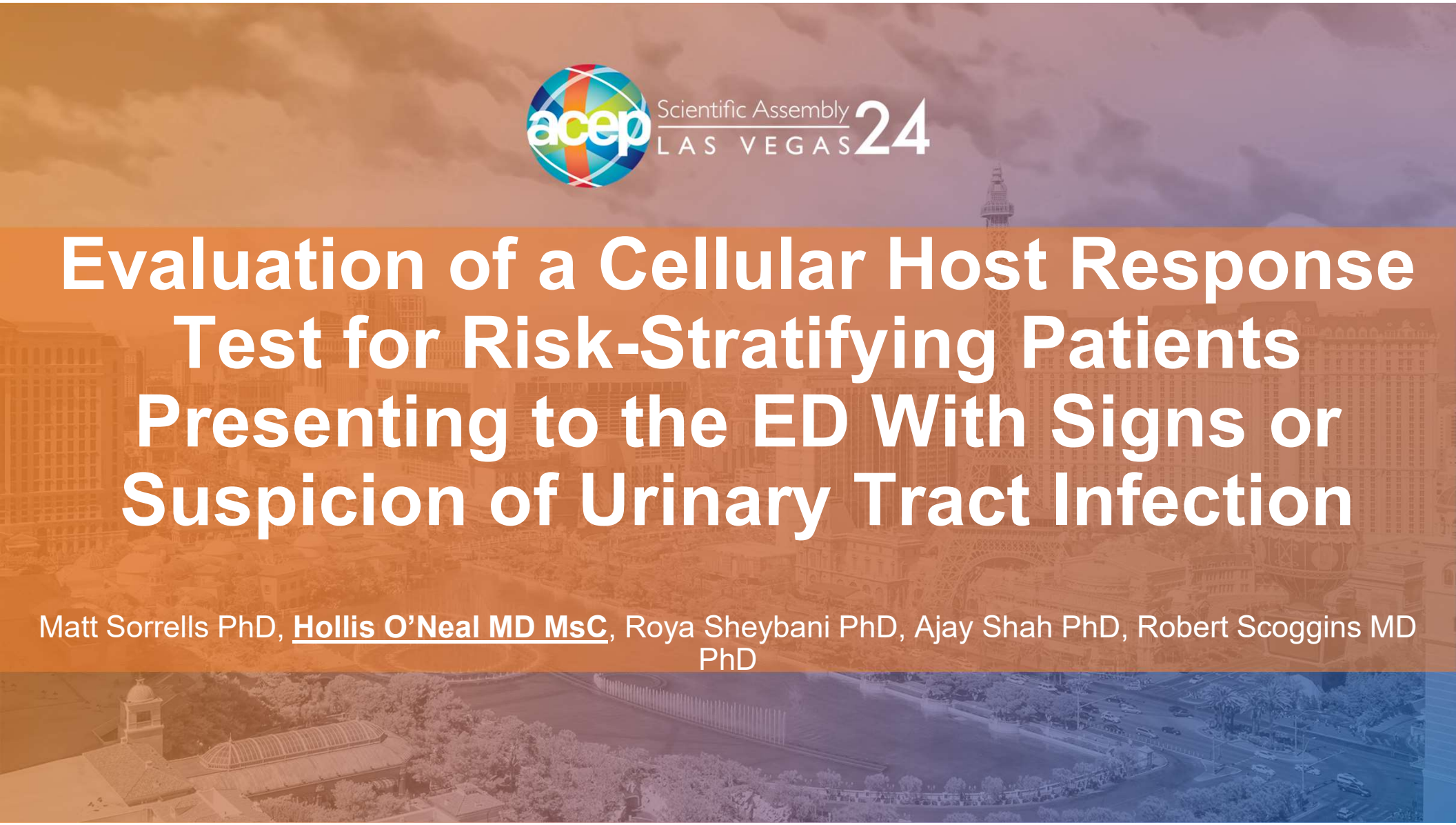
Methods
The cellular-host response test evaluated in this study is a semi-quantitative in-vitro test that uses deformability cytometry to assess leukocyte biophysical properties from whole blood in <10 minutes. The test generates the IntelliSep Index (ISI), a single score between 0.1 and 10.0, stratified into 3 interpretation bands (Band 1,Band 2, Band 3) that represents the probability of the clinical syndrome of sepsis from low to high risk. Adult patients presenting to the ED with signs or suspicion of infection were prospectively enrolled at multiple US sites (Feb. 2016 – Oct. 2021). EDTA-anticoagulated blood was assayed, and patients were followed by retrospective chart review. Presence of infection and organ dysfunction were confirmed through blinded retrospective physician adjudication. This population was subsampled to those suspected of UTI as detailed in Figure 1. Within this cohort, we evaluated risk stratification performance and resource allocation potential of the test through trend analysis across interpretation bands.

Results
The 399 patients included in the analysis were stratified by the ISI as 223 (55.9%) in Band 1, 97 (24.3%) in Band 2, and 79 (19.8%) in Band 3. Comparing Band 3 to Band 1, an approximate 7-fold increase in blood culture positivity (27.8% Band 3, 4.0% Band 1, $p < 10^{-4}$), 2-fold increase in length of stay among survivors (medians 4.5 days Band 3, 2.0 days Band 1, $p < 10^{-4}$), 2-fold increase in maximum SOFA score within 3 days of enrollment (medians Band 1, 3.0 Band 3 and 1.5 $p < 10^{-4}$), 5-fold increase in all-cause 28 day mortality (13.9% Band 3, 2.7% Band 1, $p < 0.001$), and a 9.5-fold increase in infection-associated mortality (0.4% Band 1, 3.8% Band 3, $p < 0.05$) were observed. Finally, though rates of antibiotic administration increased from Bands 1-3 (44.1% Band 1, 74.4% Band 3, $p < 10^{-4}$), patients in Band 1(low-risk population) comprised 49% of all patients who were administered antibiotics. Given the short length of stay, and low risk of mortality in Band 1, there may be an opportunity to safely reduce antibiotics in this large group of patients.

Conclusion

Our findings show that this cellular host response test may aid clinicians in risk stratifying patients suspected of UTI with the potential to improve resource allocation during treatment and championing antibiotic stewardship initiatives.

Figure 1 Summary of inclusion criteria. 1545 patients were retrospectively enrolled from 5 studies from 2016-2021. Patients were matched to common enrollment criteria of 2+ SIRS criteria (with 1 being WBC or temperature) or order for a culture of bodily fluid, and, SARS-CoV-2(-) or not tested (N = 1196). This subset was downselected to patients that are non-infected or have single source genitourinary infections (N = 788), and finally were downselected to patients with a positive urinalysis (PUA) and/or urine culture ordered (N = 399). PUA was defined as UA being positive for nitrates, leukocyte esterase, bacteria, or white blood cell levels greater than 10 cells/μL.



Evaluation of a Cellular Host Response Test for Risk-Stratifying Patients Presenting to the ED With Signs or Suspicion of Urinary Tract Infection

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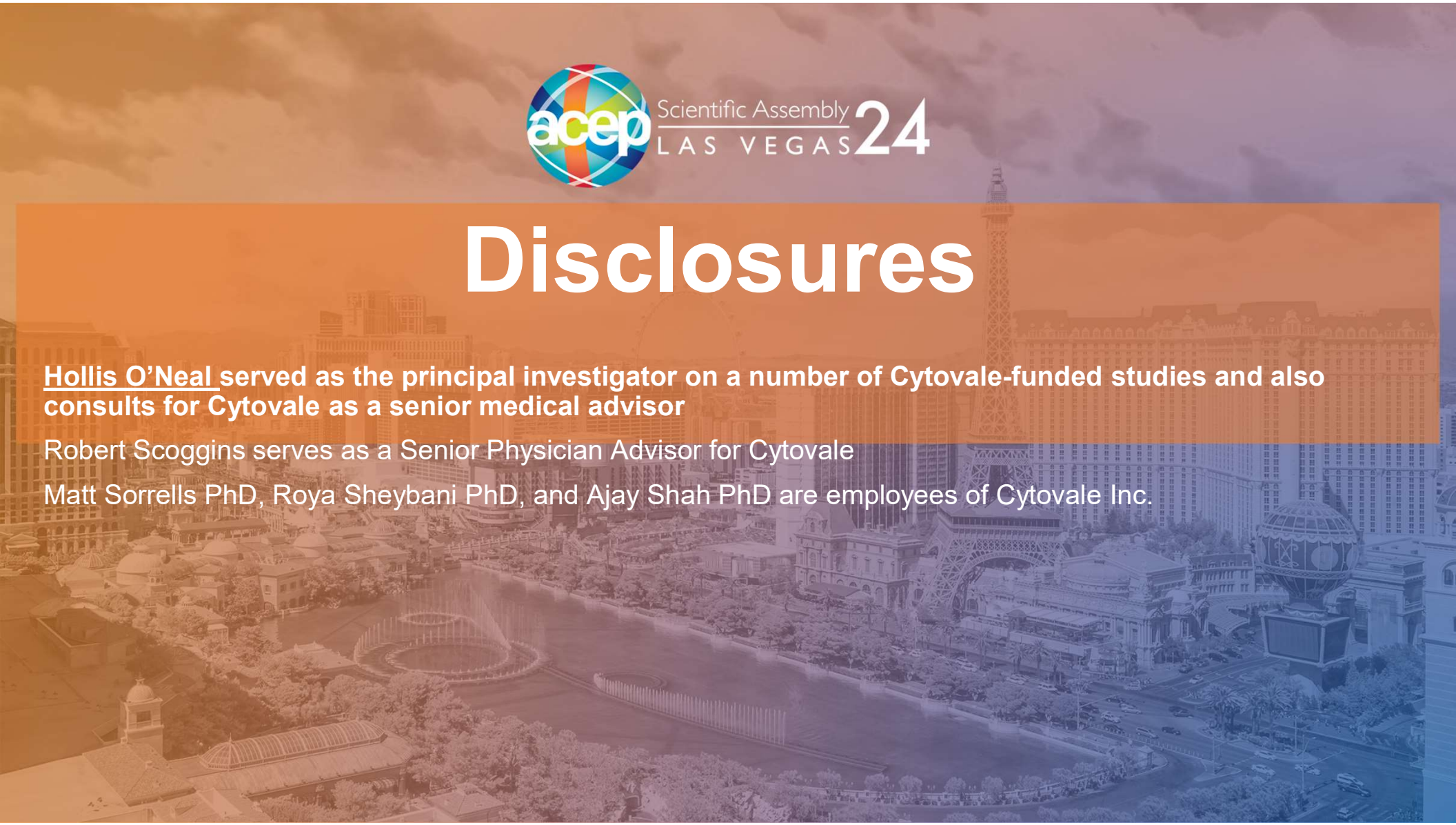


Disclosures

Hollis O'Neal served as the principal investigator on a number of Cytovale-funded studies and also consults for Cytovale as a senior medical advisor

Robert Scoggins serves as a Senior Physician Advisor for Cytovale

Matt Sorrells PhD, Roya Sheybani PhD, and Ajay Shah PhD are employees of Cytovale Inc.

Urinary Tract Infections

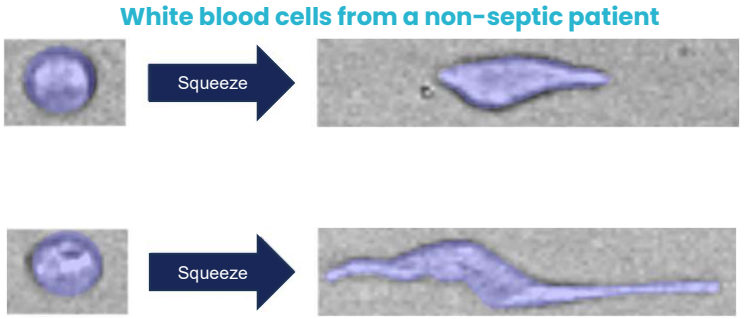
- Urinary tract infections (UTIs) are a leading cause of bacterial infections in the US and account for a significant portion of antibiotic consumption and healthcare costs.
- UTI represents a broad spectrum of disease, from uncomplicated lower UTI to pyelonephritis, urosepsis, and uroseptic shock. Asymptomatic bacteriuria (noninfectious bacterial growth in the urine) is also common.
- Especially in an ED setting, Urosepsis is difficult to accurately distinguish from simple urinary tract infection or asymptomatic bacteriuria (ASB) due to insensitive and nonspecific symptoms.
- In this study, we evaluated the potential of a novel cellular host response test to risk stratify patients with suspected UTI for risk of poor outcomes.

The IntelliSep Test (FDA Cleared)

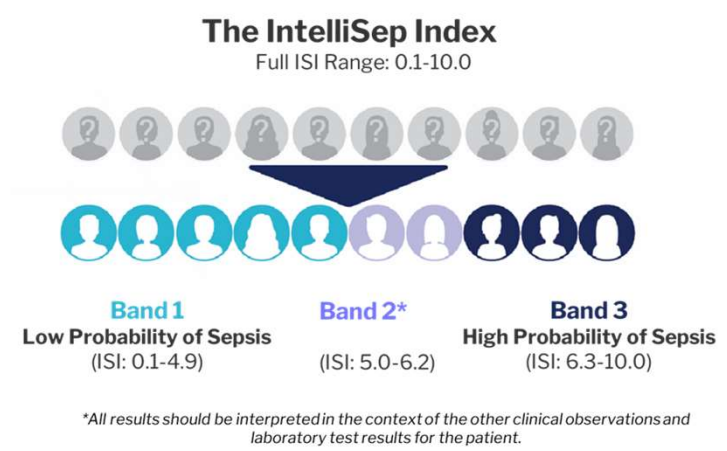
90 sec
Hands-on Time

100uL
K2 EDTA Whole Blood

< 10 min
Blood to Score



- FDA cleared, semi-quantitative test that assesses cellular host response to aid in the early detection of sepsis with organ dysfunction manifesting within the first 3 days after testing for adults presenting to the ED with signs and symptoms of infection.
- Microfluidic junction “squeezes” leukocytes from patient whole blood sample, allowing the discrimination of septic and non-septic patients through leukocyte deformability cytometry.
- Generates an IntelliSep Index (ISI) value and discrete interpretation bands based on the probability of sepsis in less than 10 min.

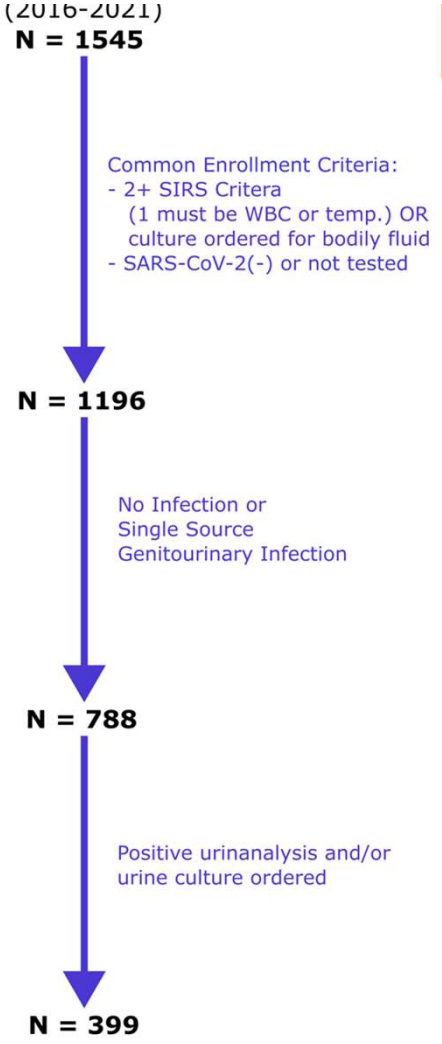


Study Objective

- Evaluate the potential of the IntelliSep test to aid in risk stratification and resource utilization in patients presenting to the ED with suspected UTI.

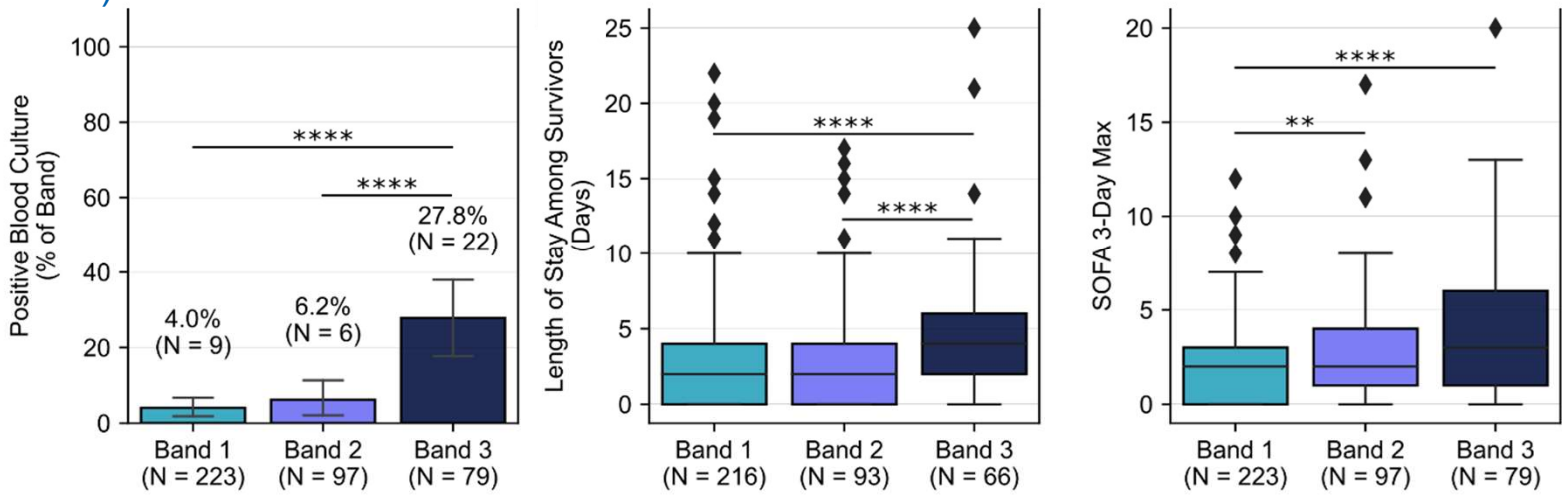
Study Design

- Adult patients presenting to the ED with signs or suspicion of infection were prospectively enrolled at multiple US sites (Feb. 2016 – Oct. 2021).
- EDTA-anticoagulated blood was assayed, and patients were followed by retrospective chart review.
- Presence of infection and organ dysfunction determined through blinded retrospective physician adjudication.
- Population subsampled to those suspected of UTI (only), with 399 patients included in final analysis.



Risk Stratification Across Bands

- The 399 patients in the analysis were stratified by the ISI as 223 (55.9%) Band 1, 97 (24.3%) Band 2, and 79 (19.8%) Band 3.
- From Band 1 to Band 3:
  - Approximate 7-fold increase in blood culture positivity (27.8% Band 3, 4.0% Band 1, $p < 10^{-4}$)
  - 2-fold increase in length of stay among survivors (Band 1 – median 2.0 d, Band 3 – median 4.5 d)
  - 2-fold increase in maximum SOFA score within 3 days of enrollment (Band 1 – median 1.0, vs Band 3 – median 3.0)

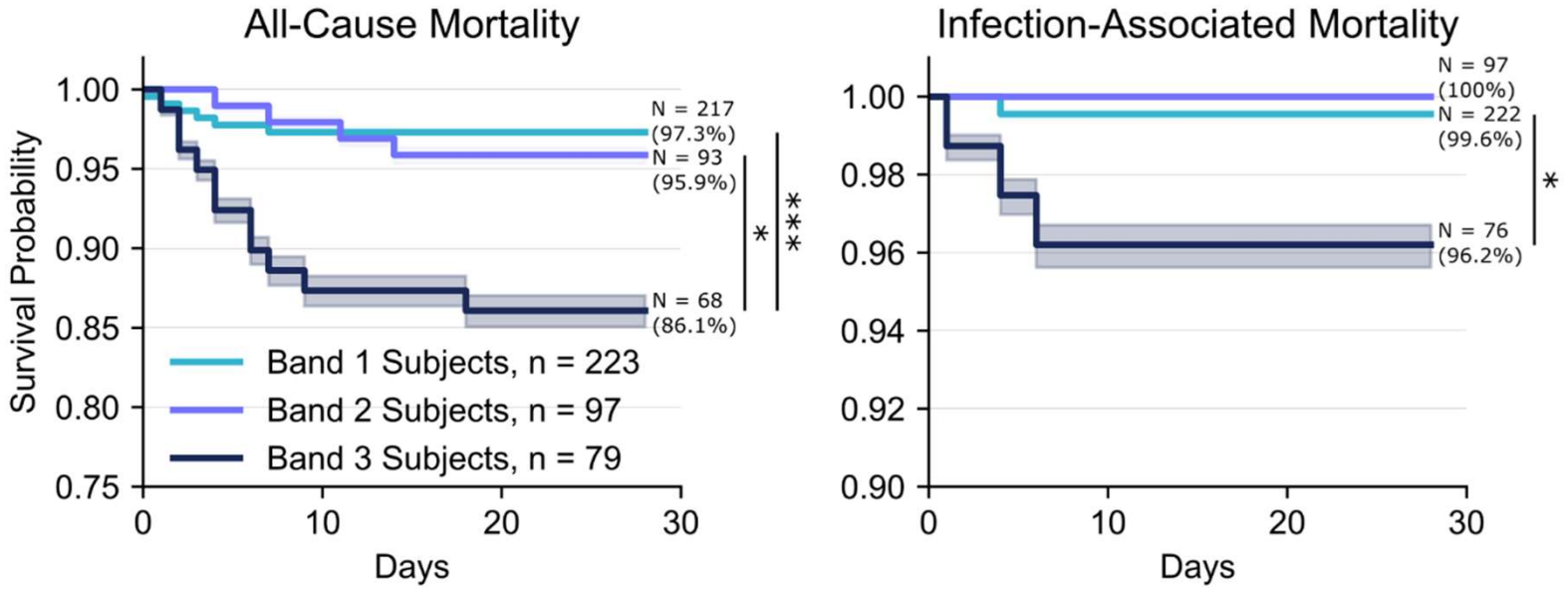


** and **** indicate $p < 0.01$ and $p < 0.0001$

Stratification of Mortality

From Band 1 to Band 3

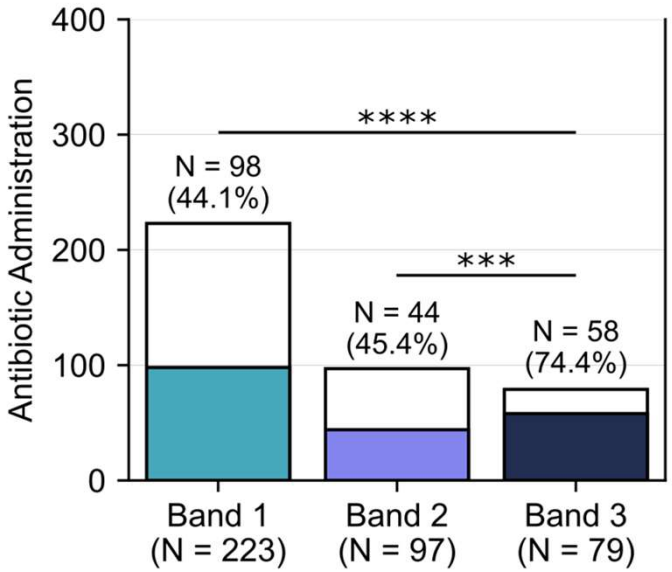
- 5-fold increase in all-cause 28-day mortality (13.9% Band 3, 2.7% Band 1, $p < 0.001$)
- 9.5-fold increase in infection-associated mortality (0.4% Band 1, 3.8% Band 3, $p < 0.05$)



* and *** indicate $p < 0.05$ and $p < 0.001$

Resource Allocation and ABX Stewardship

- Increase in percentages of antibiotic administration across interpretation bands.
- Band 1 accounted for nearly half (49%) of antibiotic administrations, showing potential for improved resource allocation and stewardship.



Conclusions

The results of this study suggest that, in this population of patients with signs or suspicion of UTI, the cellular host response test, IntelliSep, can provide effective risk stratification information, to aid in rapidly distinguishing those at highest and lowest risk for adverse outcomes.

If applied to a population in clinical use, the ISI may be able to assist clinicians in determining those patients in whom aggressive therapy is warranted and those in whom a more conservative approach is acceptable, until a diagnosis can be confirmed.