Can We Deliver Patient-Centered Sepsis Care While Achieving SEP-1 Targets?

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Cytovale

Agenda

- The Challenge of Sepsis and SEP-1 Compliance
- Cytovale Cellular Host Response Test: IntelliSep
- IntelliSep Clinical Data

The Challenge of Sepsis

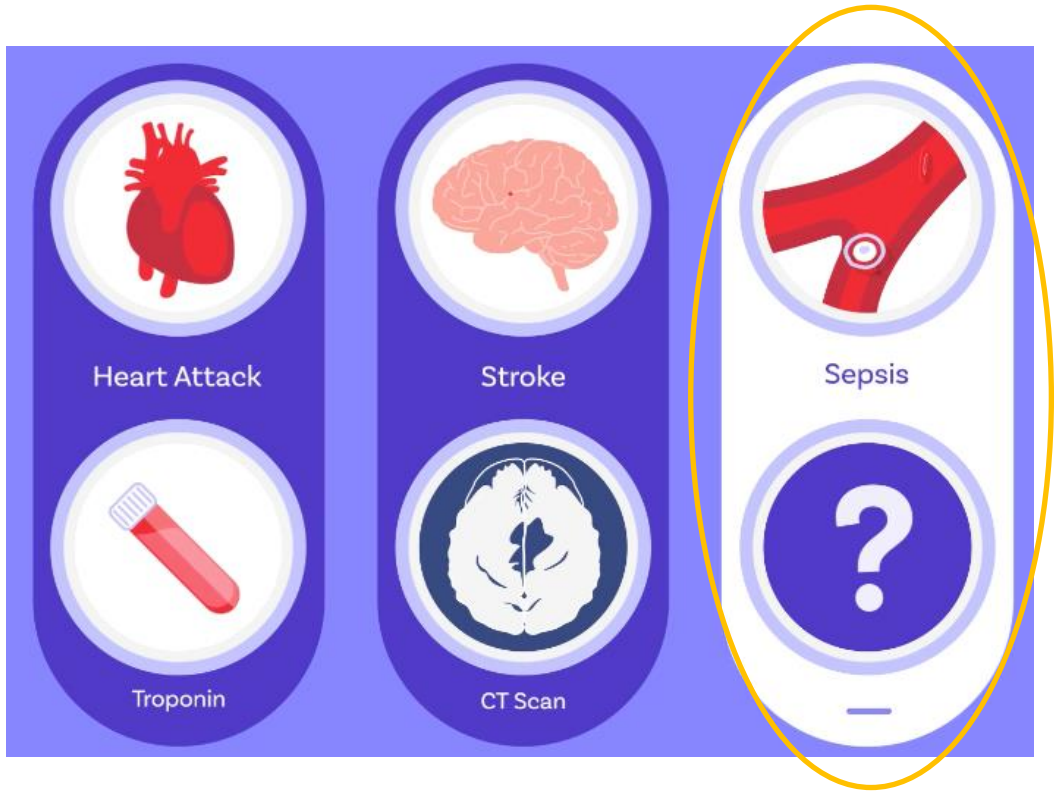
Sepsis is a Medical Emergency That Needs An Objective, Rapid, Early Detection Tool

Sepsis is the leading cause of death in U.S. hospitals[1]

80%
Of sepsis cases present to ED[2-3]

2x
Number of Stroke & Heart Attack cases

1 in 5
Of 150M+ ED patient visits are at risk of sepsis



Sepsis has **2x** cases than Stroke & Heart Attack **combined**

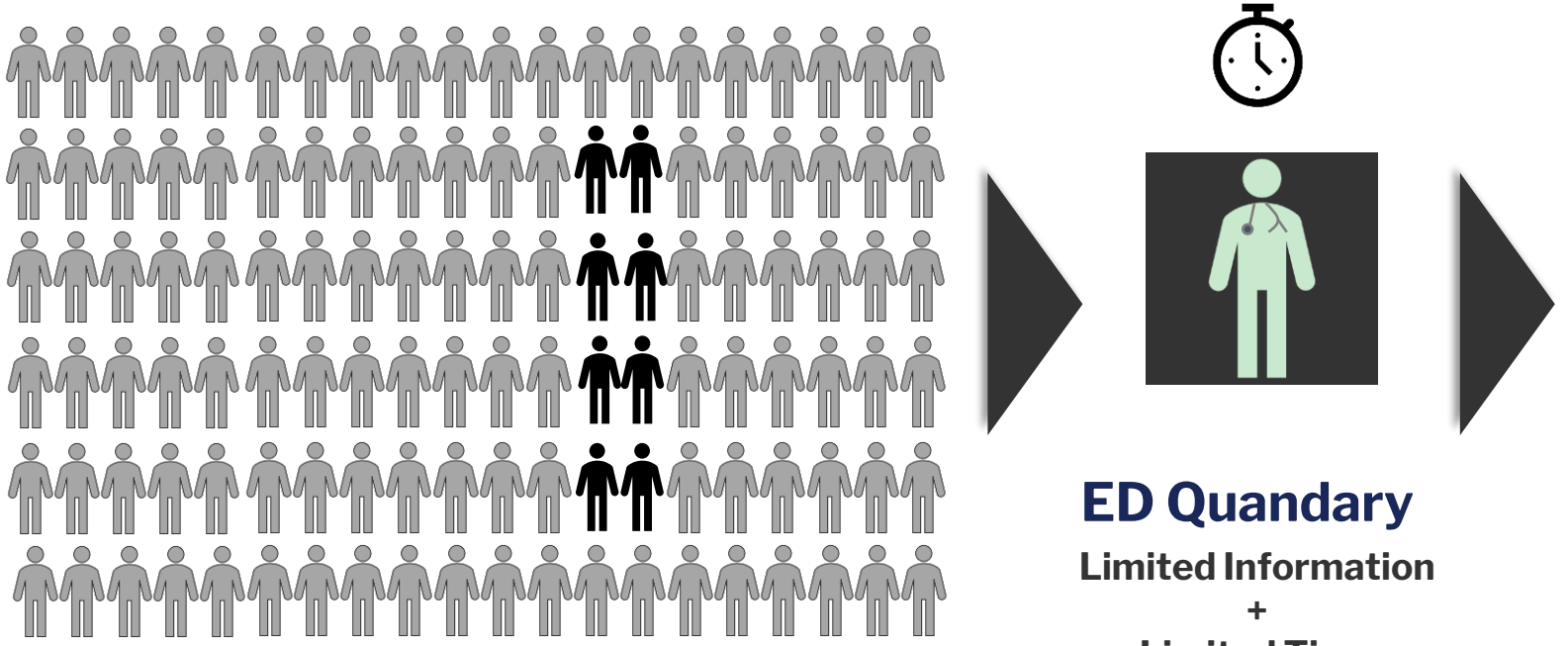
Today, no standardized care pathway exists to evaluate potentially septic patients because there's **no objective, actionable early detection tool available**

[1]"Sepsis: Clinical Information." Centers for Disease Control and Prevention, 2020. https://www.cdc.gov/sepsis/clinicaltools/. Accessed Jan 30, 2023.
[2]Wang HE, Jones AR, Donnelly JP. Revised national estimates of emergency department visits for sepsis in the United States. Crit Care Med. 2017;45:1443-1449.
[3]Rhee C, Dantes R, Epstein L, et al. Incidence and trends of sepsis in US hospitals using clinical vs claims data, 2009-2014. JAMA. 2017;318:1241-1249.

Challenge of Potentially Infected Patients in the ED

80% of Sepsis patients present to the ED

However, sepsis patients are **masked** by a much larger cohort of suspected infection patients



ED Quandary

Limited Information
+
Limited Time

Challenging Situation for ED

- **Under diagnosis/ Missed Treatment**
  - Rapid clinical deterioration/ risks of organ damage
  - Potential for readmission
  - Quality metrics -> reimbursement
- **Over diagnosis/ Over Treatment**
  - Increased costs/resource utilization
  - ED Throughput
  - IV vs Oral Abx

SEP-1 Compliance Mandate

CMS SEP-1 Compliance

- CMS Hospital Quality Initiative based on Surviving Sepsis Guidelines
- Early Management Bundle, Severe Sepsis/Septic Shock Measure (SEP-1) Began measuring Compliance in 2015
- Compliance Measured as follows:

$$\text{SEP-1 Compliance} = \frac{\text{Patients Receiving Sepsis Bundle Delivery within time thresholds*}}{\text{Patients Diagnosed or Likely to have been Septic}}$$

** All or nothing (e.g. Must receive all elements in specified time or no credit given)*

SEP-1 Bundle Delivery – All or nothing

SEP-1 Compliance = Received Bundle / Dx as Septic

Severe Sepsis Bundle	Septic Shock Bundle
Blood Cultures Collection (w/in 3h)	Blood Cultures Collection (w/in 3h)
Broad Spectrum Abx Admin (w/in 3h)	Broad Spectrum Abx Admin (w/in 3h)
Serial Lactate (w/in 3h, 6h)	Serial Lactate (w/in 3h, 6h)
	Fluid Administration w/in 3h
	Vasopressors w/in 6h (if hypotension persists)

SEP-1: Patients Diagnosed as Septic

SEP-1 Compliance = Received Bundle / Dx as Septic

- ICD-10-CM Principal or Other Discharge Diagnosis Code of Sepsis, Severe Sepsis, or Septic Shock
- Chart Abstraction (20% or a minimum)
  - Provider documentation of “Sepsis”
  - Documentation of Suspected Infection, 2+ SIRS, Organ Dysfunction (*details in “time zero” slide*)

When does the SEP-1 clock start?
(aka When is *time zero*?)

- Documentation by a provider of Severe Sepsis or Septic Shock

OR

- Last point where all 3 conditions met (w/in 6h of each other)*:
  1. Documentation referencing an infection
  2. 2 or more SIRS Criteria (not associated with other known shock)
     (e.g. Temperature > 38°C or < 36°C, Heart Rate >90bpm, Respiratory Rate >20 bpm, White Count > 12,000 or < 4,000 or > 10% bands)
  3. New onset organ dysfunction (w/in 24h of presentation)
     (e.g. Lactate >2, SBP < 90 mmHg or MAP < 65 mmHg, Respiratory support, Creatinine level, Bilrubin level, Urine output, Platelet count, Cognitive fxn)

**additional requirements for Septic Shock*

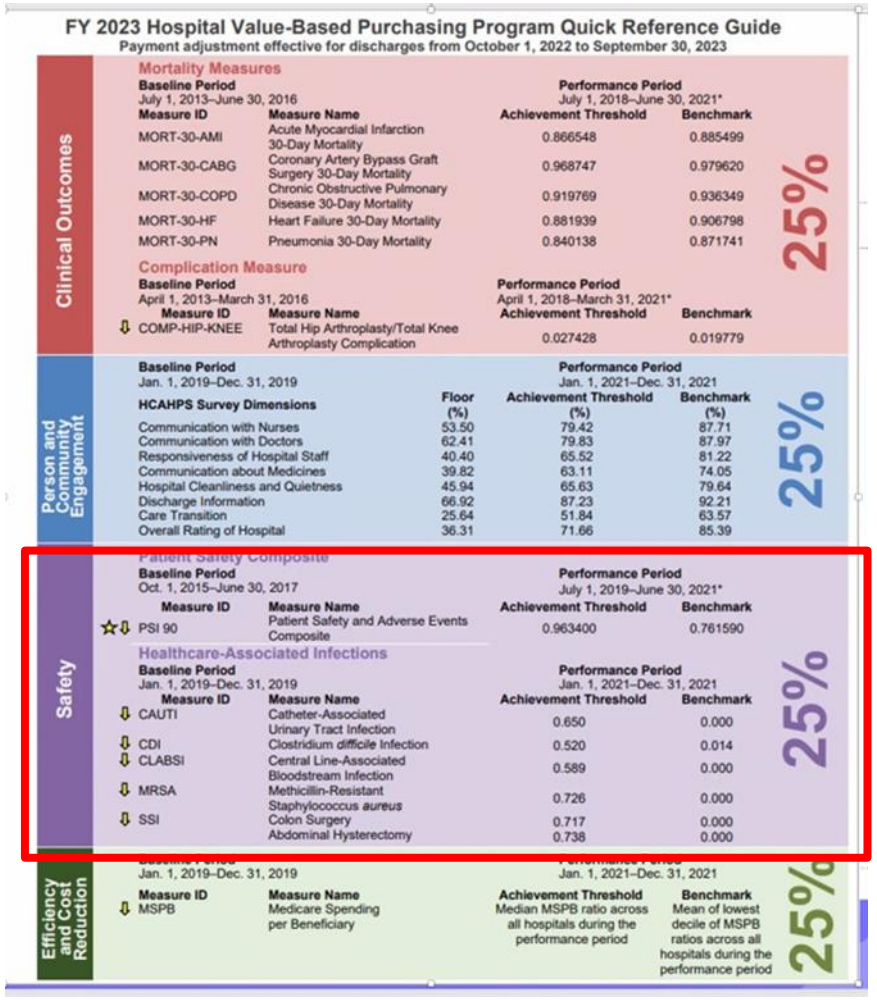
2023 Changes

- After tracking SEP-1 Compliance rates since 2015, CMS will now integrate SEP-1 Compliance into the Value Based Purchasing (VBP) Program
- It will become part of the Safety Metrics (25% of total), alongside 6 others (25%/7 ~4%)
- VBP targeted to 2.8% of total CMS spend

Case Study: Community Hospital in the West

250 beds
~$1.8B Rev/yr
60% CMS

Potential Impact
~$1M/y



FY 2023 Hospital Value-Based Purchasing Program Quick Reference Guide

Payment adjustment effective for discharges from October 1, 2022 to September 30, 2023

Clinical Outcomes — 25%

Mortality Measures

Baseline Period: July 1, 2013–June 30, 2016 | Performance Period: July 1, 2018–June 30, 2021*

Measure ID	Measure Name	Achievement Threshold	Benchmark
MORT-30-AMI	Acute Myocardial Infarction 30-Day Mortality	0.866548	0.885499
MORT-30-CABG	Coronary Artery Bypass Graft Surgery 30-Day Mortality	0.968747	0.979620
MORT-30-COPD	Chronic Obstructive Pulmonary Disease 30-Day Mortality	0.919769	0.936349
MORT-30-HF	Heart Failure 30-Day Mortality	0.881939	0.906798
MORT-30-PN	Pneumonia 30-Day Mortality	0.840138	0.871741

Complication Measure

Baseline Period: April 1, 2013–March 31, 2016 | Performance Period: April 1, 2018–March 31, 2021*

Measure ID	Measure Name	Achievement Threshold	Benchmark
⇩ COMP-HIP-KNEE	Total Hip Arthroplasty/Total Knee Arthroplasty Complication	0.027428	0.019779

Person and Community Engagement — 25%

Baseline Period: Jan. 1, 2019–Dec. 31, 2019 | Performance Period: Jan. 1, 2021–Dec. 31, 2021

HCAHPS Survey Dimensions	Floor (%)	Achievement Threshold (%)	Benchmark (%)
Communication with Nurses	53.50	79.42	87.71
Communication with Doctors	62.41	79.83	87.97
Responsiveness of Hospital Staff	40.40	65.52	81.22
Communication about Medicines	39.82	63.11	74.05
Hospital Cleanliness and Quietness	45.94	65.63	79.64
Discharge Information	66.92	87.23	92.21
Care Transition	25.64	51.84	63.57
Overall Rating of Hospital	36.31	71.66	85.39

Safety — 25%

Patient Safety Composite

Baseline Period: Oct. 1, 2015–June 30, 2017 | Performance Period: July 1, 2019–June 30, 2021*

Measure ID	Measure Name	Achievement Threshold	Benchmark
☆⇩ PSI 90	Patient Safety and Adverse Events Composite	0.963400	0.761590

Healthcare-Associated Infections

Baseline Period: Jan. 1, 2019–Dec. 31, 2019 | Performance Period: Jan. 1, 2021–Dec. 31, 2021

Measure ID	Measure Name	Achievement Threshold	Benchmark
⇩ CAUTI	Catheter-Associated Urinary Tract Infection	0.650	0.000
⇩ CDI	Clostridium difficile Infection	0.520	0.014
⇩ CLABSI	Central Line-Associated Bloodstream Infection	0.589	0.000
⇩ MRSA	Methicillin-Resistant Staphylococcus aureus	0.726	0.000
⇩ SSI	Colon Surgery	0.717	0.000
	Abdominal Hysterectomy	0.738	0.000

Efficiency and Cost Reduction — 25%

Baseline Period: Jan. 1, 2019–Dec. 31, 2019 | Performance Period: Jan. 1, 2021–Dec. 31, 2021

Measure ID	Measure Name	Achievement Threshold	Benchmark
⇩ MSPB	Medicare Spending per Beneficiary	Median MSPB ratio across all hospitals during the performance period	Mean of lowest decile of MSPB ratios across all hospitals during the performance period

Note: 2024 may differ from the above

What are we compared to?

Pay for Performance

(Relative to benchmark of other hospitals)

OR

Pay for Improvement

(Relative to baseline performance of your hospital)

SEP-1 Compliance Rates

Average SEP-1 Bundle Compliance Rate[1]

50%

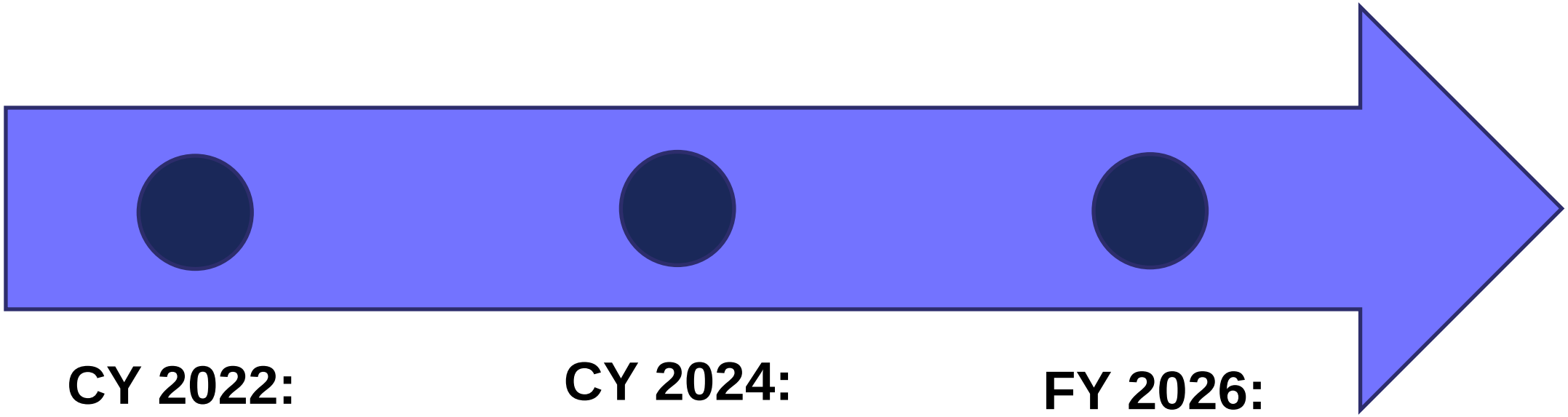
SEP-1

Compliance Failure Driven By:

- Failure to Identify Sepsis
- Incomplete Bundle Delivery
- Failure to Deliver Bundle In Time

[1] www.medicare.gov/care-compare

Timeframe



CY 2022:
Baseline Period

CY 2024:
Performance Period

FY 2026:
SEP-1 Performance impacts payments

How do we detect sepsis today?

Provider judgement often a key determinant of initiation of sepsis care…

How good are providers at recognizing sepsis?

Critical Care Providers (2016 study)[1]

- Background/Methods
  - 94 Critical Care Providers
    - 90% academic
    - 83% felt strongly or somewhat confident in their ability to apply consensus sepsis definitions
  - Each presented 5 case vignettes (including initial presentation and subsequent hospital course)
  - 1 "control" case of septic shock with gram negative bacteremia included for baselining
  - Asked to classify as: SIRS, Sepsis, Severe Sepsis, Septic Shock or None

- Findings
  - Considering all cases, overall interrater "***agreement was poor"***
  - For 4/5 test cases (removing the control case), agreement was ***"nearly random"***

[1]*Rhee et al. Critical Care (2016) 20:89; DOI 10.1186/s13054-016-1266-9*

Provider judgement often a key determinant of initiation of sepsis care…

How good are providers at recognizing sepsis?

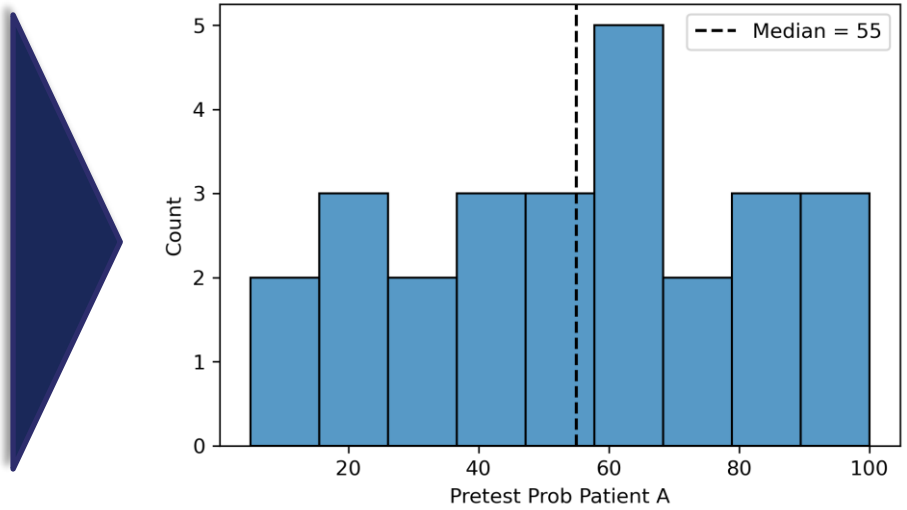
Providers with Sepsis Expertise – primarily ED (2023 study)[1]

Background/Methods

- 26 Providers involved in sepsis research
  - 92% academic environment
  - 56% Emergency Medicine, 22% Critical Care, 11% Lab Medicine, 11% ID/Pharmacy
- Each presented 2 case vignettes (Presentation, Initial Labs – including CBC, Lactate)
- Asked to provide a likelihood of sepsis (0%-100%)

Findings

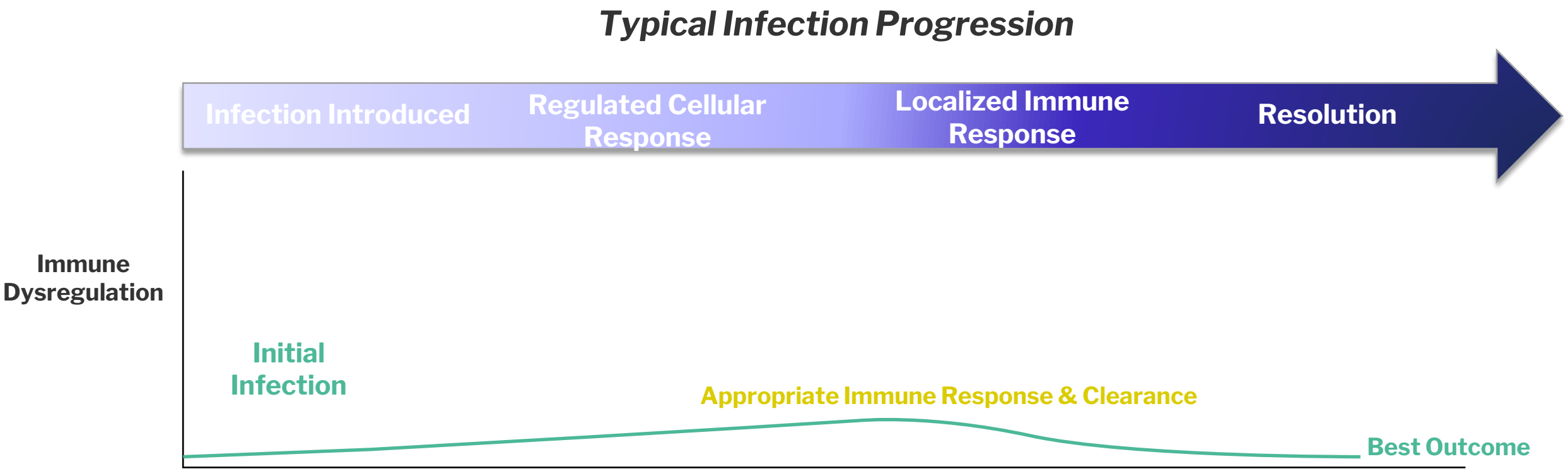
- Perceived likelihood of sepsis ranged 10-90% for both cases
- Very Low level of agreement for either case



[1]Kraus et.al. SAEM 2023, Manuscript under development

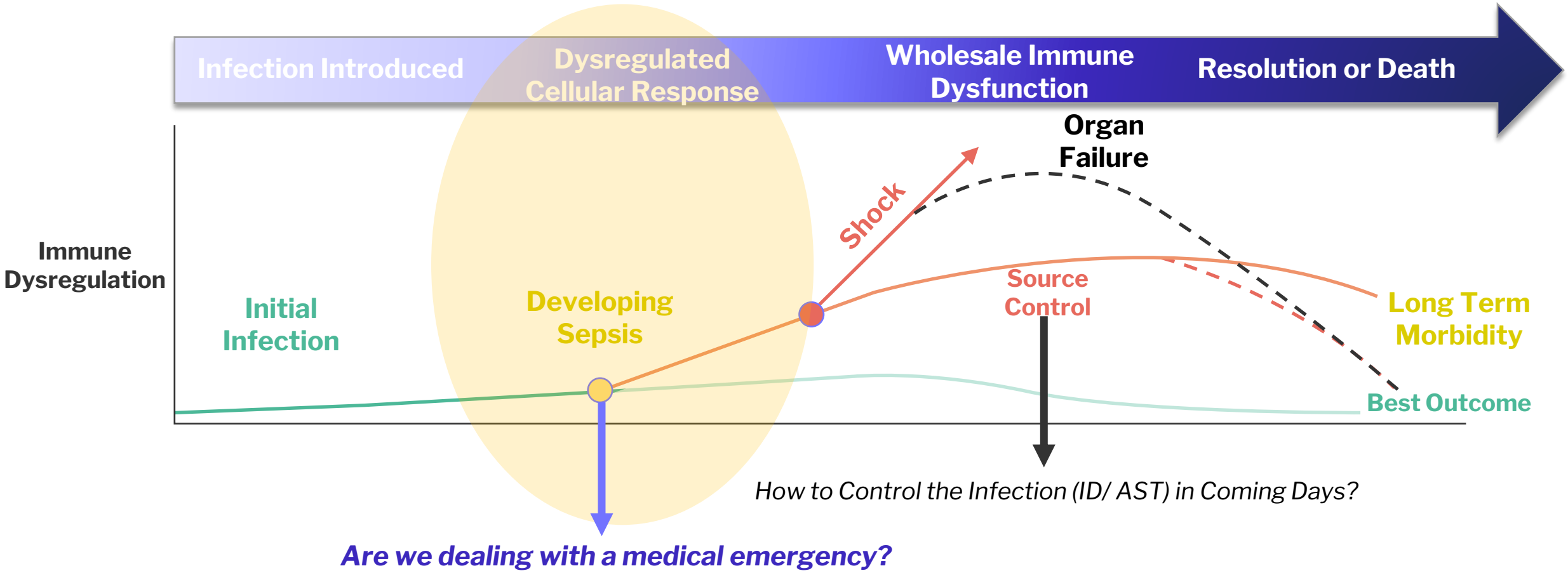
Cytovale Cellular Host Response Test: IntelliSep

Sepsis is Not an Infection



Sepsis is a Dysregulated Immune Response to Infection

Infection Progression – Dysregulated Immune Response[1-2]

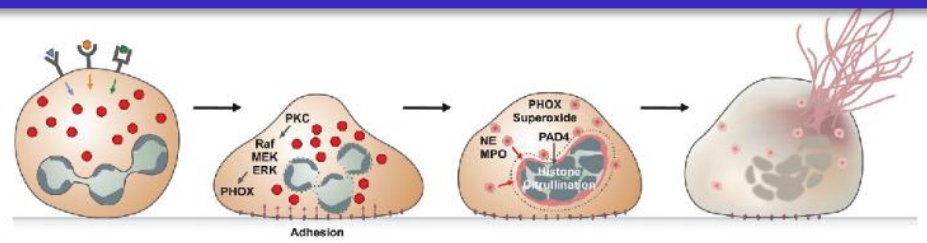


[1]Graphic adapted from Prof. Mervyn Singer, ECCMID 2022
[2]Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):801–810. doi:10.1001/jama.2016.0287

Dysregulated Immune Cell Response Is the Causal Link Underlying Sepsis

Activation state is measurable by cell mechanics

Neutrophil Extracellular Trap (NETs) Formation[1]

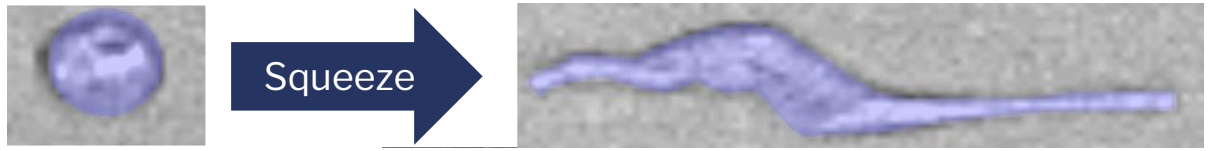


Brinkmann, J. Cell Biology, 2012

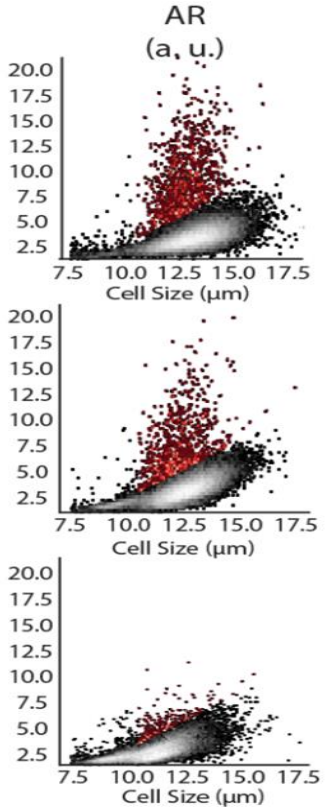
Squeezing Cells Reveals Nuclear Architecture

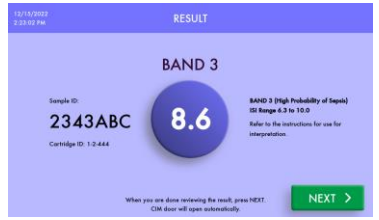
White blood cells from a healthy donor

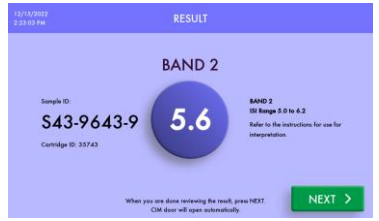
White blood cells from a septic patient

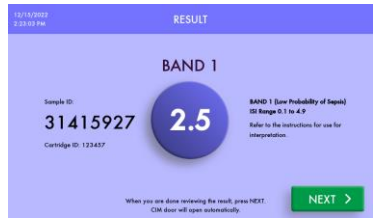


From Video to IntelliSep Index









[1]*Sorrells M, Seo Y, Magnen M, et al., Biophysical Changes of Leukocyte Activation (and NETosis) in the Cellular Host Response to Sepsis . Diagnostics. 2023; 13(8):1435. https://doi.org/10.3390/diagnostics13081435*

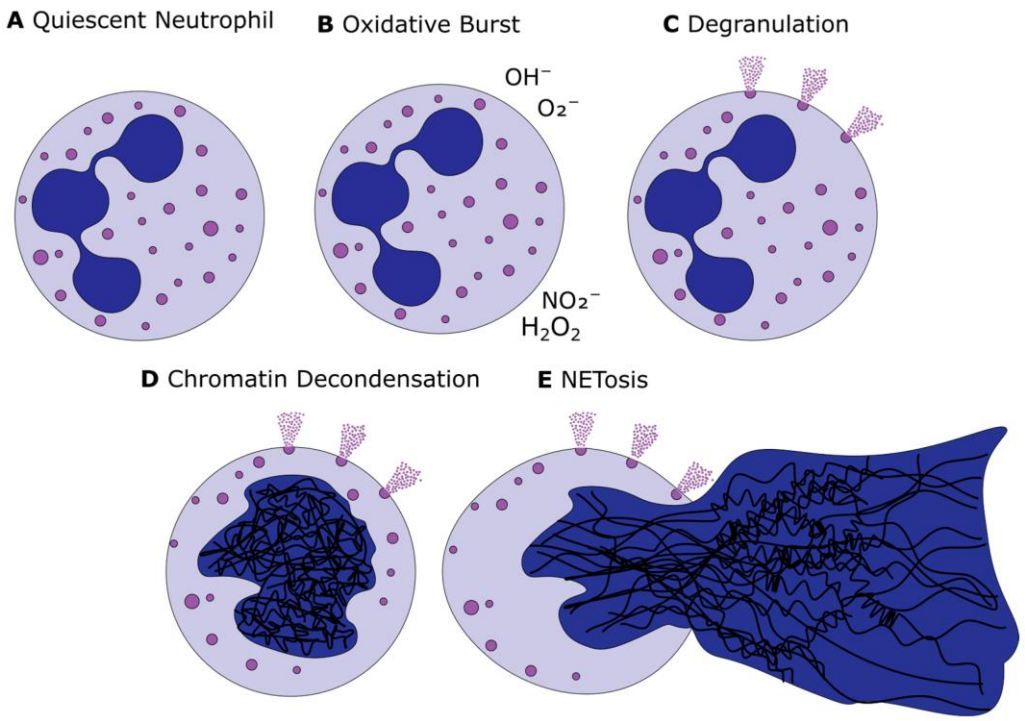
Dysregulated Immune Response = Activated Cells in Circulation

Neutrophil extracellular traps (NETs) Overview

- During immune activation, leukocytes respond by releasing **neutrophil extracellular traps (NETs)** into the extracellular space which physically capture and kill or impair invading microbes[1-3]
- An increase in NET formation has been **documented in septic patients**, and high concentrations of NETs have been shown to be **associated with tissue damage.**

The ability to measure these biophysical changes that signal immune dysregulation could be key in **guiding better clinical care in sepsis[4].**

NETs Formation Visual[5]

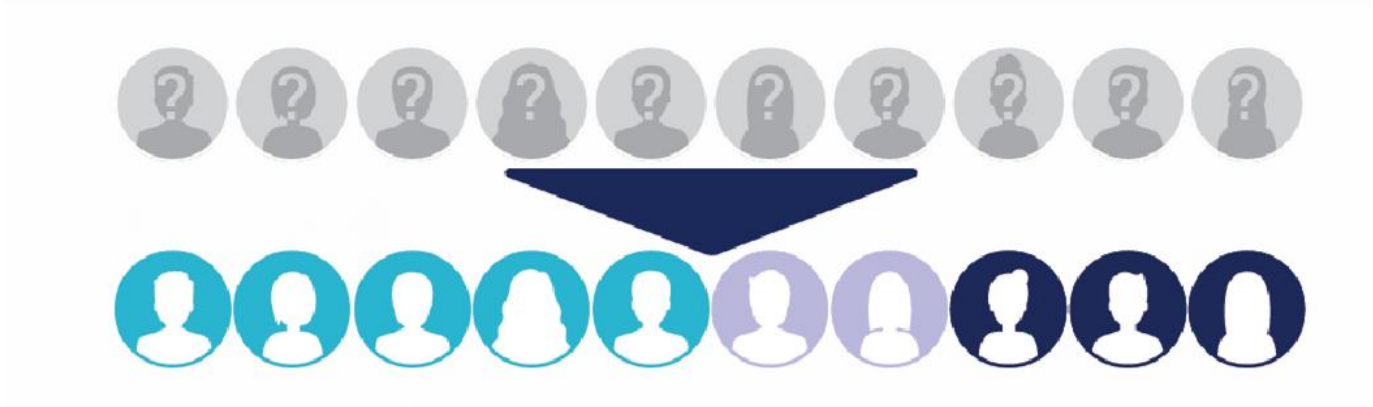


[1]Mayadas TN, Cullere X, Lowell CA. The Multifaceted Functions of Neutrophils. Annu Rev Pathol Mech Dis. 2014;9: 181–218. doi:10.1146/annurev-pathol-020712-164023
[2]Brinkmann V, Reichard U, Goosmann C, Fauler B, Uhlemann Y, Weiss DS, et al. Neutrophil extracellular traps kill bacteria. science. 2004;303: 1532–1535.
[3]Granger V, Faille D, Marani V, Noël B, Gallais Y, Szely N, et al. Human blood monocytes are able to form extracellular traps. Journal of Leukocyte Biology. 2017;102: 775–781. doi:10.1189/jlb.3MA0916-411R
[4-5]Sorrells M, Seo Y, Magnen M, et al., Biophysical Changes of Leukocyte Activation (and NETosis) in the Cellular Host Response to Sepsis . Diagnostics. 2023; 13(8):1435. https://doi.org/10.3390/diagnostics13081435

Providing a Probability of Sepsis in <10 Minutes

The IntelliSep Index

ISI Range: 0.1-10.0



Band 1
Low Probability of Sepsis
(ISI: 0.1-4.9)

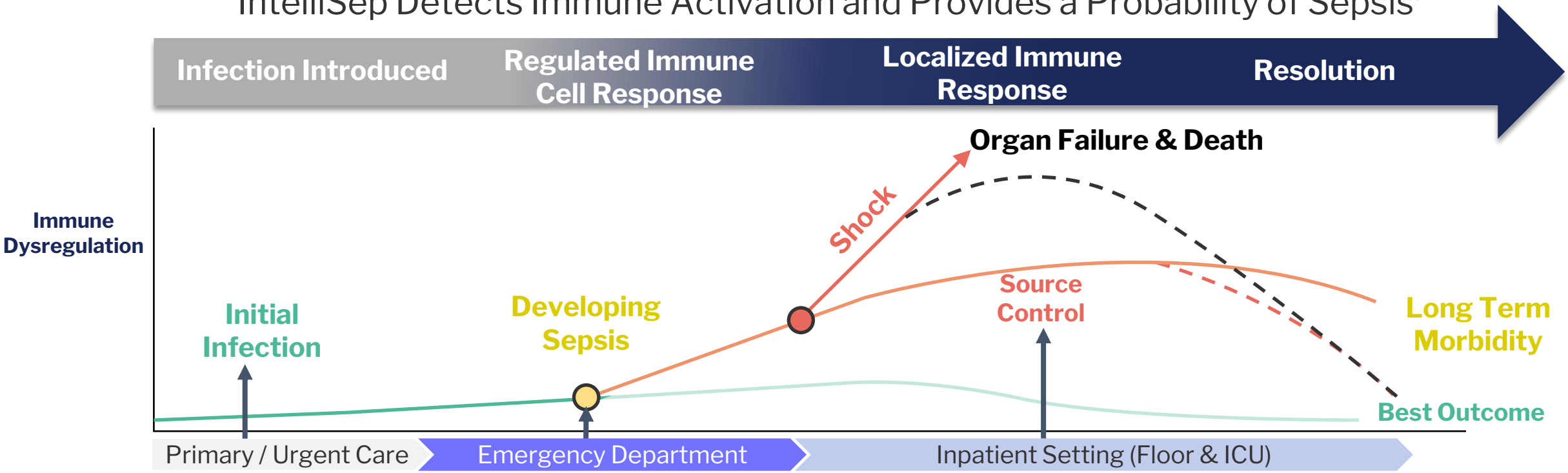
Band 2*
(ISI: 5.0-6.2)

Band 3
High Probability of Sepsis
(ISI: 6.3-10.0)

**All results should be interpreted in the context of the other clinical observations and laboratory test results for the patient.*

IntelliSep Addresses: Is This a Medical Emergency?

IntelliSep Detects Immune Activation and Provides a Probability of Sepsis*



Key Question

Is There a Treatable Infection?

MeMed

Is this a Medical Emergency?

Cytovale

How To Control the Infection (ID / AST) in Coming Days?

T2Biosystems, BIOFIRE, SPECIFIC, KARIUS, ACCELERATE DIAGNOSTICS, BD, BRUKER

IntelliSep is focused on specifically measuring the dysregulated host response

*Graphic adapted from Prof. Mervyn Singer, ECCMID 2022

[1]Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):801–810. doi:10.1001/jama.2016.028

How is IntelliSep Different?

Key advantages in speed, workflow and cost structure

	ED Sepsis Triage Need	IntelliSep
Workflow Considerations	**Time to Answer –** Use in ED triage requires a turn-around time of less than 30 min – KOL Panel (*Kraus et.al. JACEP Open 2023*)	**<10 minutes** ability to report alongside CBC
	Throughput – ED volumes vary during the day and could require 5-10 samples to be tested per hour	**>12 Samples/hr/placement** (Typical placement: 2 systems)
	Fits into Clinical Workflows – Ideal solution should not require a new sample or expensive tube (e.g PaxGene tube)	**Whole Blood** 510(k) cleared with K2 EDTA tube
Clinical Considerations	**Indicated Population –** Should include the broad set of patients that the ED intends to screen for sepsis	**Signs and Symptoms of Infection** 510(k) cleared for use in adults
	Use Setting – 80% of sepsis patients present to the ED, Indication for use should match this use case	**ED Presentation** 510(k) cleared for ED Triage
	Healthy Reference Range – All healthy patients should receive the low scores	**Entirely in Band 1 *** (low likelihood of sepsis)
	Race Agnostic – Technology and training set should provide similar results across different races	**Yes**

*Outlier (n=1) removed

See IntelliSep instructions for use for all cleared claims and performance data.

IntelliSep Data

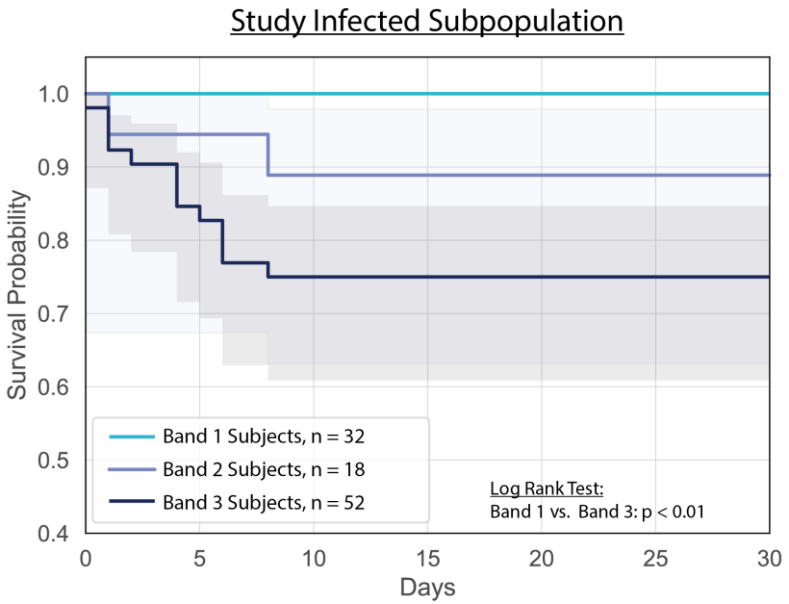
IntelliSep Performance Proven Across Multiple Studies

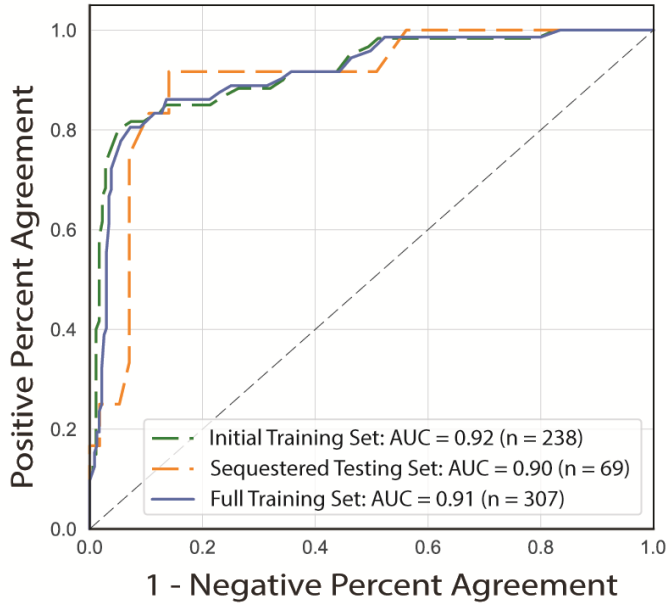
	2016 SQuISH	2019 Be-SQuISH-ED	2020 SQuISH-COVID	2021 CV-SQuISH-ED
Study Objective	Evaluate the system and initial sepsis model	Apply locked model to intended use population	Apply locked model to novel pathogen SARS-COV-2	Multi-center validation study for FDA Clearance
Population	**300+ Patients** Signs of infection & organ dysfunction in ED	**255 Patients** Signs or suspicion of infection in the ED	**282 Patients** Signs or suspicion of respiratory infection in ED	**~600 Patients** Signs or suspicion of infection in the ED
Key Findings	Sepsis: NPV = 96% Observed appropriate risk stratification in severity of illness and resource use Mortality: > 5-fold delta	Sepsis: NPV = 97% Severity Risk Stratification	Severity Risk Stratification Mortality: > 10-fold delta	Demonstrated the performance of IntelliSep, against blinded physician adjudication, in the early detection of sepsis
Journal	PLOS ONE	Critical Care Explorations — Society of Critical Care Medicine	PLOS ONE	*Manuscript In Development*

Data Supported by Over 2,000 Patients

SQuISH-ED: System Evaluation & Algorithm Development

- Population of patients presenting to the ED with signs of infection organ dysfunction (N = 307, population sepsis prevalence 23%)
- Significant differences were observed in severity of illness across the Bands when compared to Sequential Organ Failure Assessment (SOFA) and APACHE II.
- No significant differences in baseline demographics (age, sex, and race) across Interpretation Bands.
- Study enabled the development of the ISI diagnostic algorithm targeting clinically actionable performance.





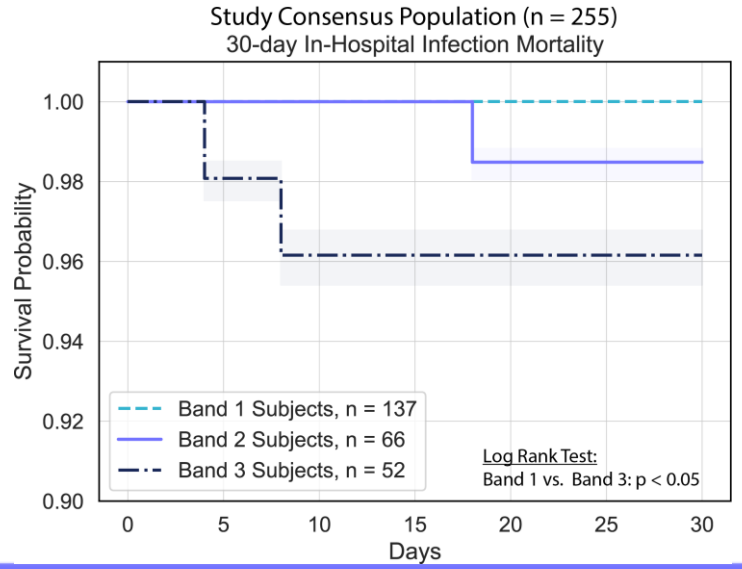
Test Characteristics	Value (95% CI)
AUC	0.91 (0.87 – 0.95)
Positive Percent Agreement (sensitivity): Band 1 vs. else	90.3 (81.0 – 96.0)
Negative Percent Agreement (specificity): Band 3 vs. else	95.3 (86.4 – 98.5)
Negative Predictive Value: Band 1 vs. else	95.9 (88.3 – 99.1)
Positive Predictive Value: Band 3 vs. else	82.8 (71.1 – 90.0)
LR+	15.7
LR- (1/LR-)	0.07 (14.3)

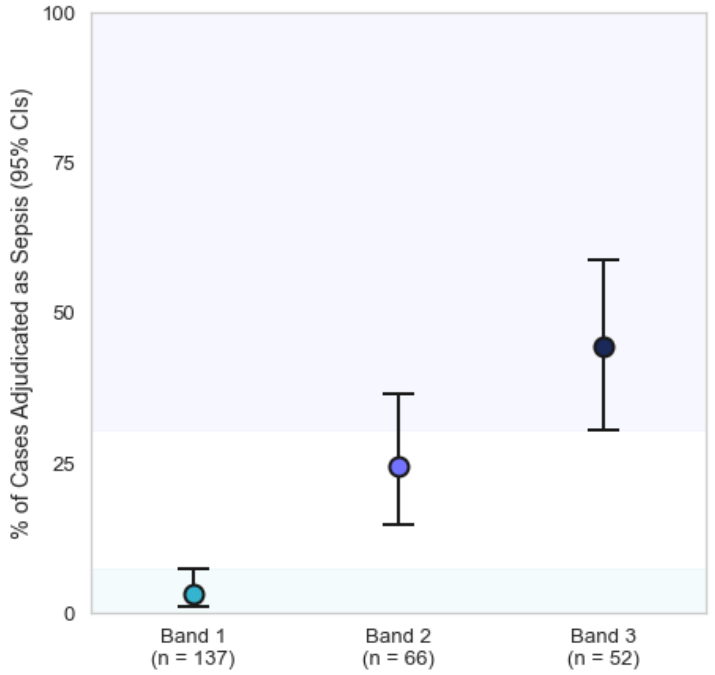
Guillou, Lionel, et al. "Development and validation of a cellular host response test as an early diagnostic for sepsis." PloS one 16.4 (2021): e0246980.

See IntelliSep instructions for use for all cleared claims and performance data.

ße-SQuISH-ED: Sepsis Diagnosis in Intended Use Population

- In a population of patients presenting to the ED with signs or suspicion of infection defined as:
  - 2+ SIRS criteria where one must be aberration of WBC or temperature **OR** an order for culture of body fluid (blood, urine, sputum, etc.)
- Test performance was compared to consensus retrospective physician's adjudication (N = 255, population sepsis prevalence 17%)
- Significant differences were observed in severity of illness across the Bands when compared to Sequential Organ Failure Assessment (SOFA) and APACHE II.





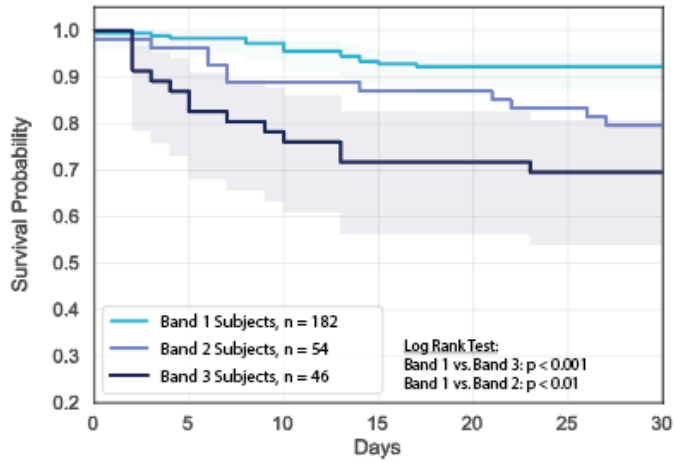
Test Characteristics	Value (95% CI)
AUC	0.84 (0.79 – 0.90)
Positive Percent Agreement (sensitivity): Band 1 vs. else	90.7 (77.9 – 97.4)
Negative Percent Agreement (specificity): Band 3 vs. else	86.3 (72.1 – 94.7)
Negative Predictive Value: Band 1 vs. else	97.1 (84.2 – 99.4)
Positive Predictive Value: Band 3 vs. else	44.2 (29.1 – 60.1)
LR+	3.91
LR- (1/LR-)	0.15 (6.7)

O'Neal Jr, Hollis R., et al. "Assessment of a Cellular Host Response Test as a Sepsis Diagnostic for Those With Suspected Infection in the Emergency Department." Critical Care Explorations 3.6 (2021).
See IntelliSep instructions for use for all cleared claims and performance data.

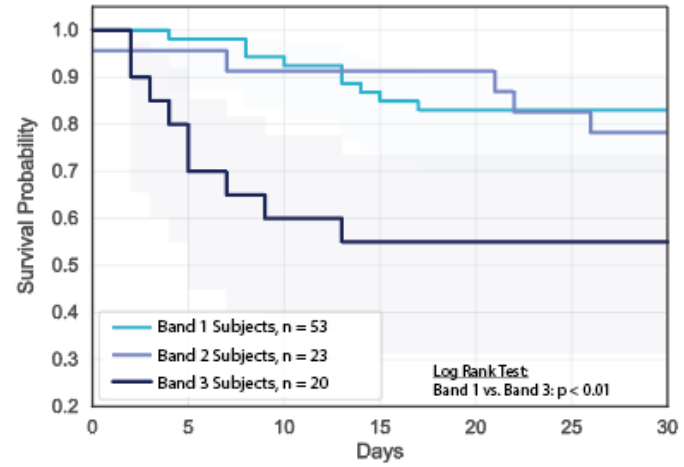
SQuISH-COVID: Morbidity & Mortality Risk

- In a population of patients presenting to the ED with signs or suspicion of respiratory infection.
- Significant differences in survival were observed across the bands, with a greater than 10-fold difference in 7-day mortality between Band 1(1.6%) and Band 3 (19.6%) patients.
- Bands were observed to correlate strongly with severity of illness metrics (mortality, SOFA and APACHE II scores) and hospital care metrics (hospital admission, ICU admission and transfer, positive blood cultures, and antibiotic administration).
- Band 3 patients were more likely to need supplemental oxygen, vasopressors, and ICU admission within 3-day of ED presentation, compared to Band 1 patients.
- Appropriate risk-stratification of patients independent of demographic groups (age, sex, race) or common comorbidities (hypertension, diabetes, obesity).

Study Population



SARS-CoV-2(+) Subpopulation



O'Neal Jr, Hollis R., et al. "Assessment of a Cellular Host Response Test to Risk-stratify Suspected COVID-19 Patients in the Emergency Department Setting." PloS one 17.3 (2022).

See IntelliSep instructions for use for all cleared claims and performance data.

Case Example 1

42-year-old female hx of CVA (intracranial hemorrhage), diabetes, autoimmune disease (SLE, PA) and hypertension.

Presenting with one week of body aches and new cough.
Temperature = 100.6 °F
HR = 125 beats/min
RR = 20 breaths/min
SPO_2 = 100%
SBP/DBP = 152/81
Emergency Severity Index (ESI) = 2

- SOFA (worst values for day of presentation) = 3
- APACHE II (worst values for day of presentation) = 6
- Blood cultures negative

Patient at Triage 8:09 am

Blood Cx Ordered 8:27 am

CBC Ordered 8:36 am

Lactate Ordered 8:36 am

WBC = 6.4 ×10^3cells/µL
Lactate = 1.4 mmol/L

She was found to have a left lower lobe consolidation on CXR.

Admission to Floor 1:37 pm

8 am | 9 am | 10 am | 11 am | 12 pm | 1 pm

Fluids Ordered/Dispensed

Antibiotics Ordered/Dispensed

IntelliSep Index = 8.1 (Band 3)

ED Diagnosis: pneumonia of the left lower lobe due to infectious organism, hemoptysis, and dyspnea.

Patient developed ARDS on Day 3 and required escalation to ICU level of care.

She clinically declined from her respiratory dysfunction and was intubated on day 4.

She gradually improved with IV antibiotics and mechanical ventilation. She was eventually discharged to rehab after a 16-day hospital stay (9 ICU days) with discharge dx of ARDS, pneumonia due to infectious organism, and severe sepsis.

Unanimous retrospective adjudication of sepsis

Note: Cases are sourced from IntelliSep observational clinical studies (NCT04933760). Study personnel in every tier of the process were blinded to the IntelliSep test results.

Case Example 2

73-year-old female hx of CVA, hyperthyroidism, dementia, diverticulosis, impaired fasting glucose, leukopenia, transient ischemic attack, and hypertension.

Presenting with altered mentation. Noted to have cognitive decline over past 1-2 years.
- Temperature = 98.1 °F
- HR = 102 beats/min
- RR = 20 breaths/min
- SPO_2 = 99%
- SBP/DBP = 130/98

Emergency Severity Index (ESI) = 2

Patient at Triage
11:02 am

CBC Ordered
11:02 am

Urine Cx Ordered
11:05 am

WBC = 3.4 ×10^3cells/µL
Lactate = not collected

IntelliSep Index = 2.3 (Band 1)

- SOFA (worst values for day of presentation) = 3
- APACHE II (worst values for day of presentation) = 6
- Urine culture positive for mixed morphotypes

Admission to Floor
5:12 pm

Antibiotics Ordered/Dispensed

ED Diagnosis: urinary tract infection without hematuria, Alzheimer's dementia with behavioral disturbance, and agitation.

Patient received a new antipsychotic an antibiotics, however, upon retrospective chart review, urine colonization and asymptomatic bacteriuria was suspected.

Discharged to nursing home after 9 days, with discharge dx of acute metabolic encephalopathy, volume depletion, and acute cystitis.

Unanimous retrospective adjudication of <u>not</u> infection

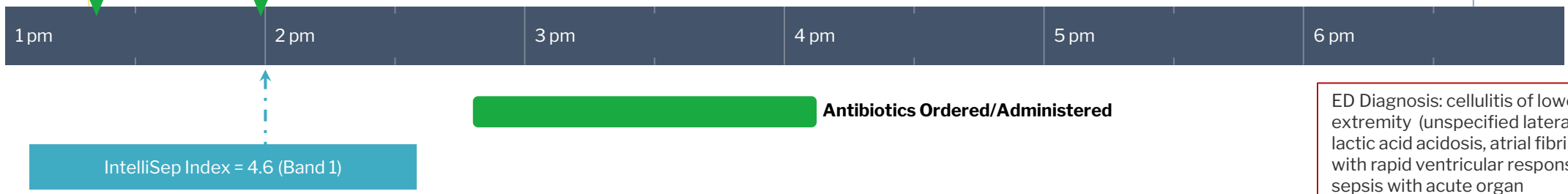
Note: Cases are sourced from IntelliSep observational clinical studies (NCT04933760). Study personnel in every tier of the process were blinded to the IntelliSep test results.

Case Example 3

Presenting with generalized weakness and presumed cellulitis.
Temperature = 97.1 °F
HR = 136 beats/min
RR = 26 breaths/min
SPO_2 = 99%
SBP/DBP = 184/116
Emergency Severity Index (ESI) = 2

- SOFA (worst values for day of presentation) = 4
- APACHE II (worst values for day of presentation) = 22
- Blood cultures negative.

67-year-old male
hx of atrial Fibrillation, chronic kidney disease, CHF, hypertension.



ED Diagnosis: cellulitis of lower extremity (unspecified laterality), lactic acid acidosis, atrial fibrillation with rapid ventricular response, sepsis with acute organ dysfunction, and septic shock

Determined to have uncontrolled atrial fibrillation (due to noncompliance with medication) which resulted in hypotension and elevated lactate along with associated hepatic/renal lab abnormalities.
No clinically relevant cellulitis present despite chronic venous stasis dermatitis.

Rapid correction of hemodynamic abnormalities with rate control and diuresis.
Discharged home after 3 days, with discharge dx of acute on chronic systolic heart and venous stasis dermatitis of both lower extremities.

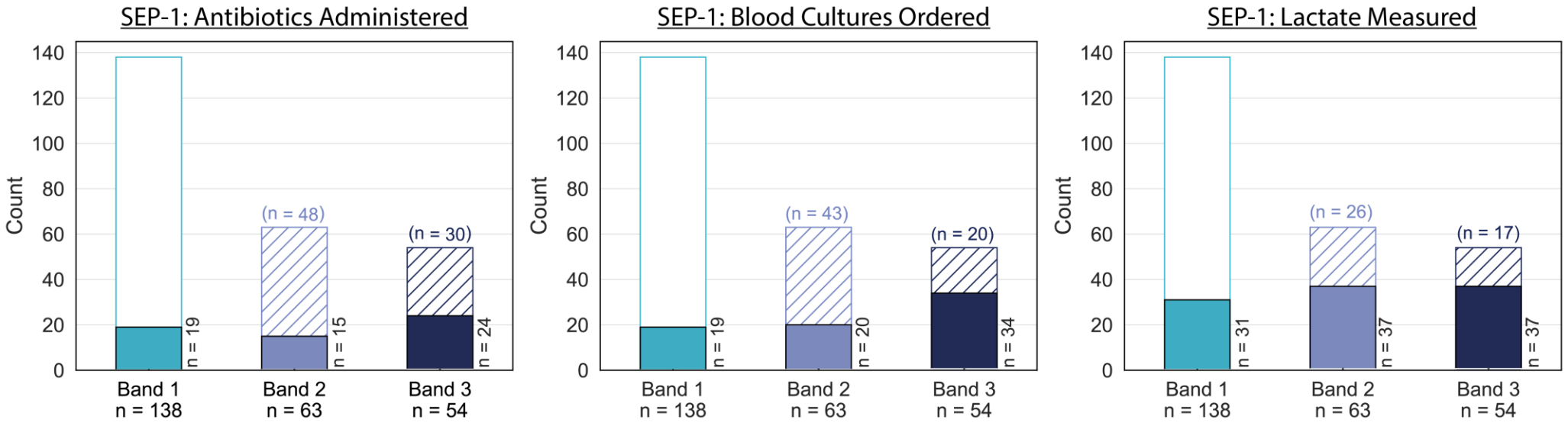
Unanimous retrospective adjudication of <u>not</u> infection

Note: Cases are sourced from IntelliSep observational clinical studies (NCT04933760). Study personnel in every tier of the process were blinded to the IntelliSep test results.

IntelliSep and SEP-1

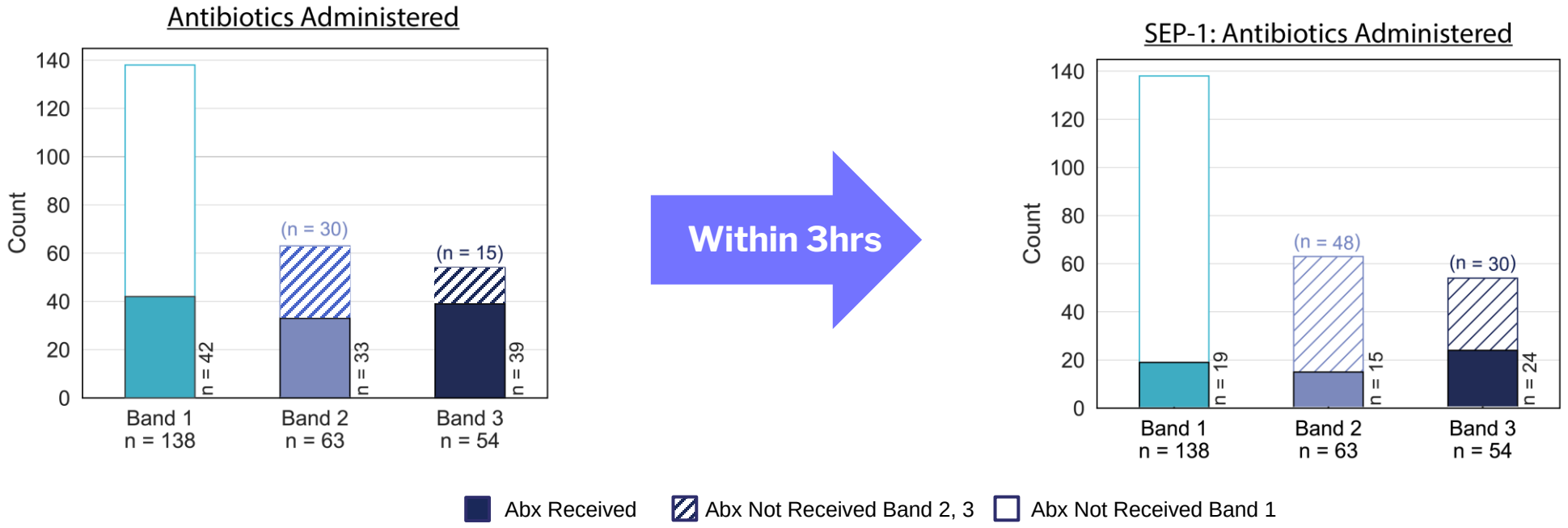
ISI vs. Receiving Elements of SEP-1 3-hour Bundle in 3-hours (ßе-SQuISH-ED)

- The Sepsis CMS core measure (SEP-1) requires measuring of serum lactate, obtaining blood cultures prior to antibiotics, and administering antibiotics within 3-hours of presentation for those presenting with severe sepsis (i.e., sepsis with organ dysfunction).
- SEP-1 Compliance Rate =46.5% in ßе-SQuISH-ED Study
- By providing a rapid, quantitative measure of immune activation, the ISI may have the potential to offer ED clinicians an aid for rapid risk stratification of patients presenting with signs and symptoms of infection and guide appropriate compliance with the Medicare sepsis quality measure while promoting antimicrobial stewardship aims.



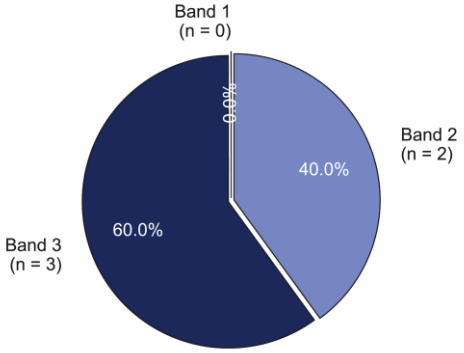
ISI vs. Antibiotics Delivery
(ße-SQuISH-ED)

- Antibiotics delivered to more Band 1 patients (n=42) than those in Band 2 (n=33) or Band 3 (n=39) patients
- There may be an opportunity to focus nursing and other resources on higher risk patients rather than spreading them equally across different interpretation bands
- Late delivery of Antibiotics to Band 2 and Band 3 patients contributed to low SEP-1 compliance performance
- Improved recognition of Sepsis may enable more rapid delivery of SEP-1 Bundle elements to highest risk patients

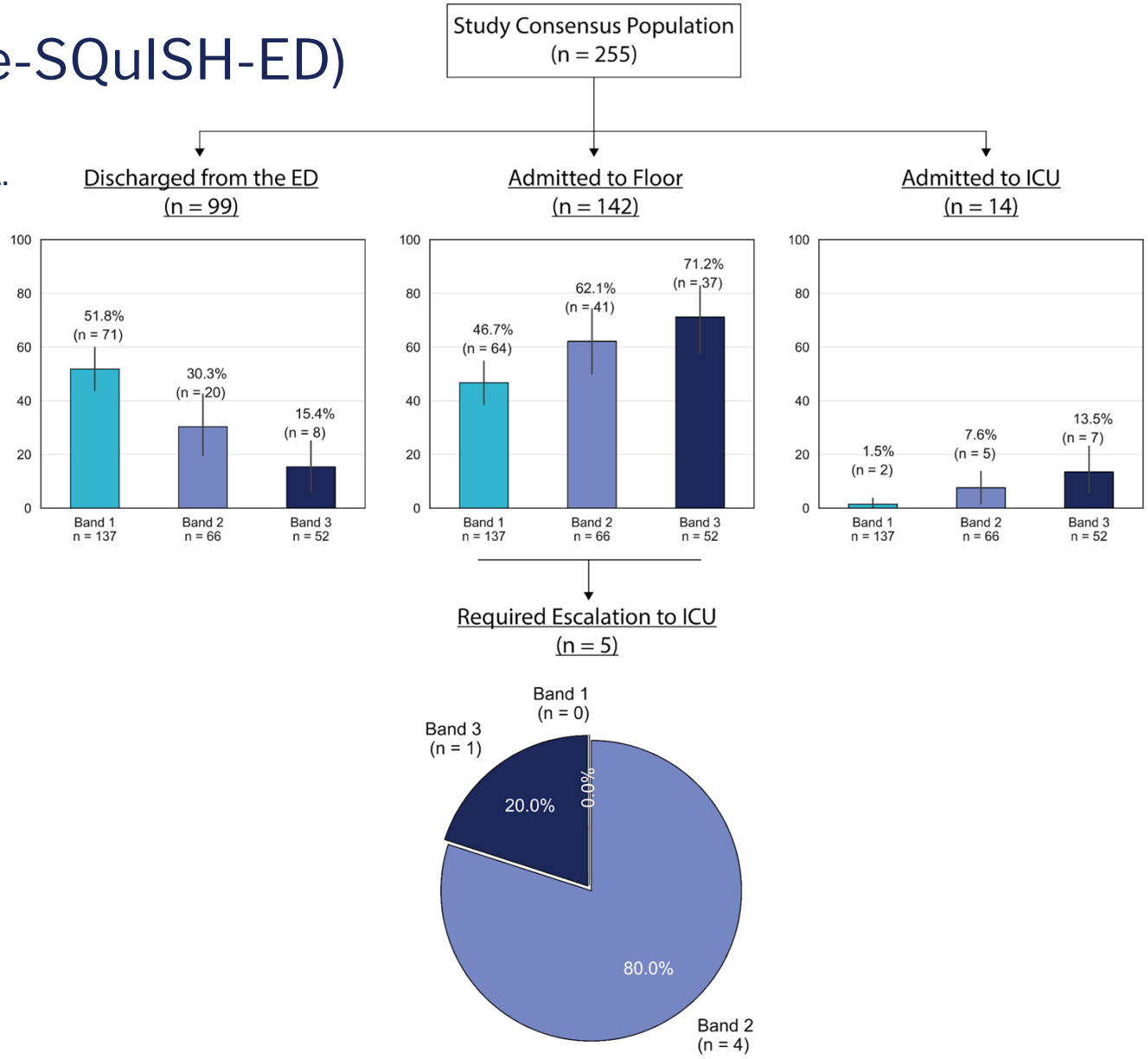


ISI vs. Hospital Resources (ße-SQuISH-ED)

- A significantly higher percentage of subjects in Bands 2 and 3 were admitted to the hospital compared to those in Band 1.
- A significantly higher percentage of subjects in Bands 2 and 3 were directly admitted to the ICU compared to those in Band 1.
- 163 study subjects were initially admitted to the Floor, of which 5 subjects required escalation to ICU care (typically within 3 days of admission):
  - All of these subjects were in the ISI Bands 2 and 3.
- 5 study subjects returned to the ED within 7-days of discharge with an ED return diagnosis of sepsis. All of these subjects were in the ISI Bands 2 and 3.



ED Return Due to Sepsis (within 7-days)



Cytovale System

Easily Integrated into Existing Lab Workflows

System

CLIA Moderate

3 ft bench space
1-day installation
No calibration required
PM every 90 days

Enlarged View

Cytovale System Specifications:

1. **Sample Preparation Module (SPM):** 16" wide, 15" tall, 18" deep, 40 lbs
2. **Cell Imaging Module (CIM):** 21.5" wide, 22.5" tall, 24" deep, 170 lbs
3. **Imaging Analysis Module (IAM):** 7.0" wide, 18.2" tall, 26.5" deep, 65 lbs
4. **Reagents**
5. **IntelliSep Cartridge (single-use)**

Process

<10 MINUTES TOTAL

Starts with a simple purple-top tube → Aliquot 100µl sample into preparation tube → Sample loaded into SPM → White blood cells separated and suspended for analysis (*90 seconds processing time*) → Sample then transferred to the cartridge (contains precision microfluidics) for analysis → CIM captures images of cells under stress at high magnification, analyzed using ML algorithm (*~5 minutes processing time*) → **IntelliSep Score Reported**

Questions?

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