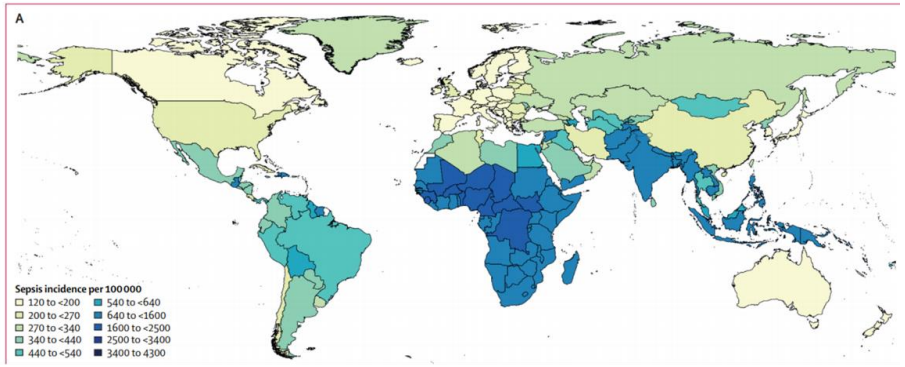
Immunexpress

ICD-10-PCS Code Request For SeptiCyte RAPID – Gene Expression Assay

March 8th 2022

Sepsis Background



Rudd K, et al. Lancet 2020:395;200-211.

A Global Issue

48.9 million cases

11.0 million deaths

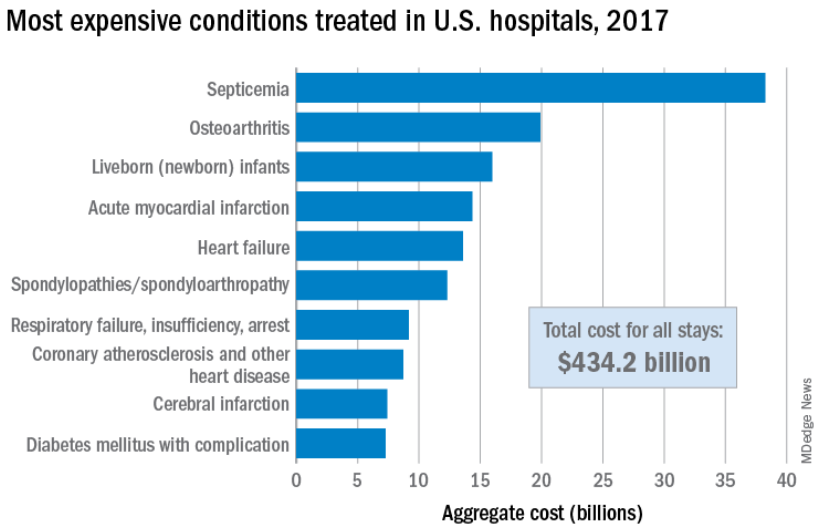
19.7% of all global deaths

World Health Organization

W.H.O. calls for global action on sepsis - cause of 1 in 5 deaths worldwide (2020)

In The U.S.:

- The #1 cause of in-hospital deaths
- Contributes to 1 in every 2-3 in-hospital deaths
- Most expensive condition (~ $57.5 billion), with only 5.8% of hospital stays
- Total cases increasing
- Mortality unchanged



Note: Based on data from the Healthcare Cost and Utilization Project's National Inpatient Sample.
Source: Agency for Healthcare Research and Quality

Importance of Rapid Detection of Sepsis

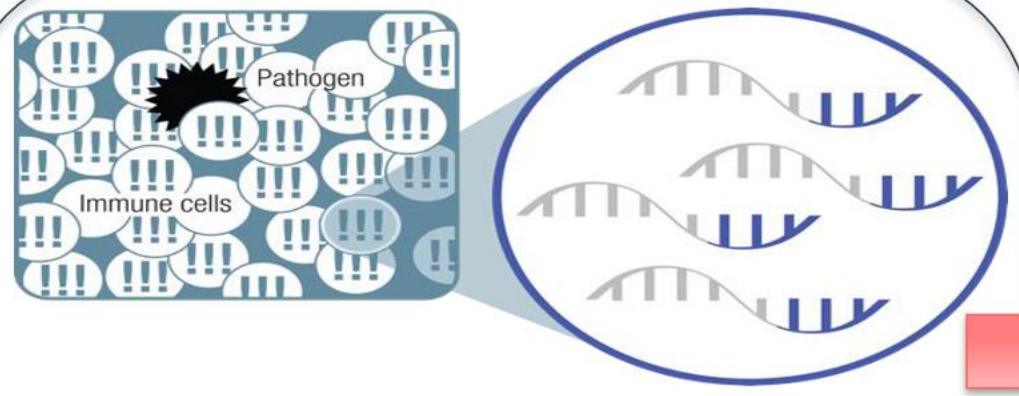
Early and appropriate identification of sepsis is the main factor for patient outcome

Factors hindering early identification

Low Sensitivity & Specificity of Diagnostic Options	Blood Cultures	Antibiotic Administration
• No test to differentiate sepsis from non-infectious causes • Non-specific biomarkers- Lactate, CRP, PCT • Non-specific - SOFA score & SIRS criteria	• Only 10-12% positivity in undifferentiated patients • Prone to false negatives and false positives • 24- 48 hour turn around time	• Delays in sepsis recognition impedes timely appropriate antibiotic administration

The SeptiCyte RAPID Solution - technology

SeptiCyte RAPID aids in differentiating infection-positive (sepsis) from non-infection negative systemic inflammation in patients suspected of sepsis on their first day of ICU admission.



Measures Host Response Signals

- Measures mRNA in White Blood Cells (WBCs)
- Quantifies expression in multiple WBC genes
- Specific to infection in systemic inflammation
- Independent of type of pathogen causing sepsis (Gram-positive or gram-negative bacteria, viral, fungi/yeast, parasite)
- Not reliant on finding pathogen in blood sample

1 hour

Likelihood of Sepsis: SeptiScore 0 - 15

Clinical Interpretation of Result

- Results reported as SeptiScore
- 4 discrete interpretation bands
- Increasing likelihood of sepsis
- Independent of severity
- Actionable information in ~100% *suspected* sepsis patients

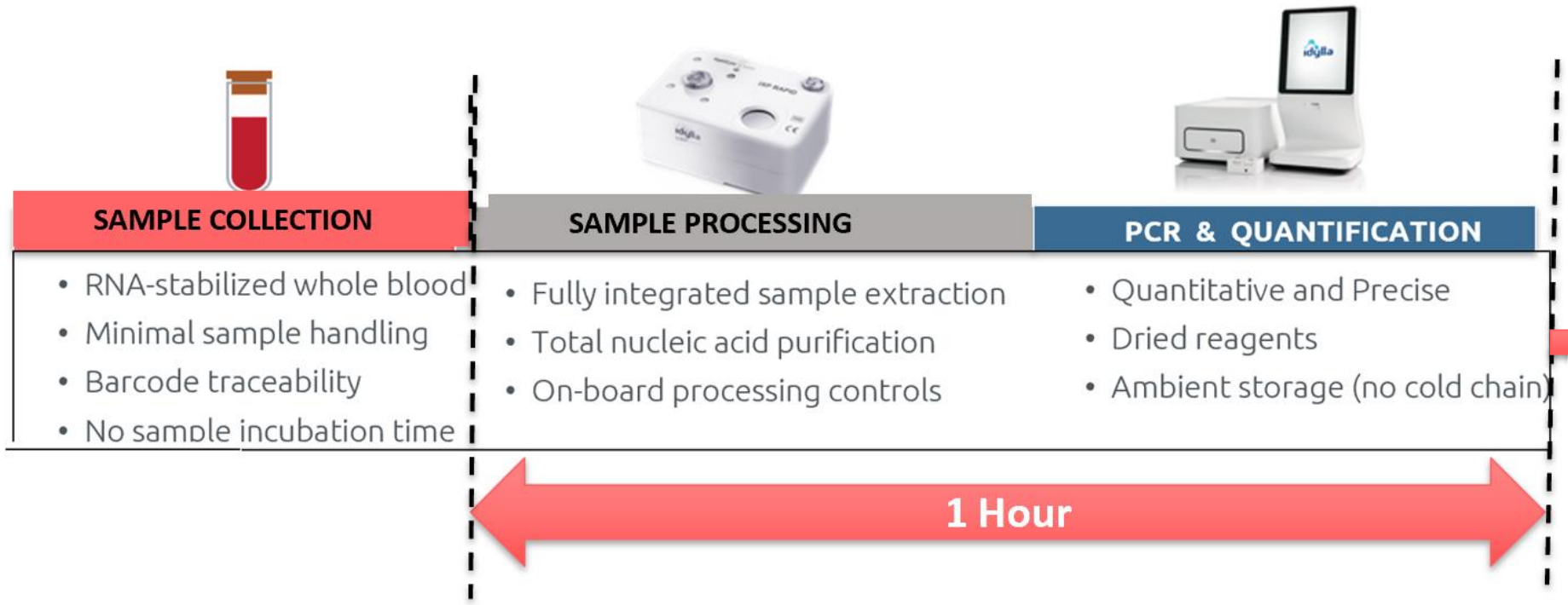
SeptiCyte RAPID Solution – FDA 510 K cleared US IVD Intended Use

- **SeptiCyte® RAPID** is a gene expression assay using reverse transcription polymerase chain reaction to measure the relative expression levels of host response genes isolated from whole blood collected in a PAXgene Blood RNA Tube.
- **SeptiCyte® RAPID** is used in conjunction with clinical assessments, vital signs and laboratory findings as an aid to differentiate infection-positive (sepsis) from infection-negative systemic inflammation in patients suspected of sepsis on their first day of ICU admission.

Existing ICD-10 – PCS codes do not describe a host response gene expression assay to differentiate sepsis from SIRS

SeptiCyte RAPID Solution - workflow

- Single use, disposable, multi-chambered cartridge
- All steps completely automated and integrated
- Automatically generated test report, linkable to EHR



Test Report

TEST RESULT REPORT

idylla by BIOCARTIS

Sample ID	IXP_IVD_120_TC4		
Sample type	RNA-stabilized whole blood		
Cartridge ID	55520626		
Test type	IXP-RAPID_IVD/1.20	TTP Version	1.23
Lot ID	00005552	Expiration date	05 Aug 2022

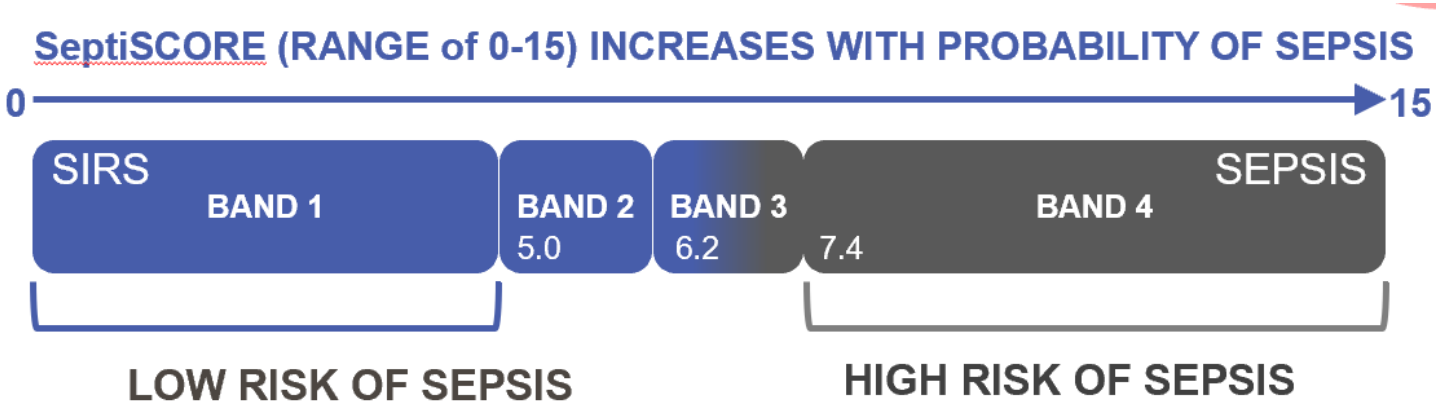
Instrument serial number	VIRT_INST_26.0_5
Instrument software version	26.0
Console Serial Number	C00000DAR
Console software version	4.4.0.630
Test request completed	02 Dec 2021 (14:37)
Test started	02 Dec 2021 (14:39)
Test ended	02 Dec 2021 (14:49)
Test status	Released result: Automatic, 02 Dec 2021 (14:49)
Operator	datanasova

Test Result (1) In Vitro Diagnostic Medical Device. For use in diagnostic procedures.

SeptiCyte® RAPID

SeptiCyte® RAPID Test Result	HIGH RISK OF SEPSIS
SeptiScore® (0 – 15)	9.4
Sepsis Probability Band (1 – 4)	Band 4
Sepsis Probability (0 - 100%)	79.7 - 80.6%
SIRS Probability (0 - 100%)	19.4 - 20.3%
Sample Processing Control (SPC)	PASS
Cq of Sample Processing Control	32.22
Quality Status	The test targets and control have been properly amplified. The test result is VALID.
Test Interpretation	See test limitation notes summarized below
Note [1]	Sepsis probability estimated from a clinical trial of 386 subjects with diagnosis by a panel of 3 physicians.
Note [2]	Predictive values depend on the prior sepsis probability and prevalence.
Note [3]	Increased scores were observed in African Americans relative to other racial/ethnic groups, in the clinical study of patients suspected of sepsis. For African-American subjects, only Band 4 showed a higher likelihood of Sepsis versus SIRS.

SeptiCyte RAPID Performance (FDA 510k Clinical Validation Results)



BAND 1	Performance
Cohort size ((N)	378
Sensitivity	0.94
Sepsis probability	≤ 9.4%
SIRS probability	≥ 90.6%
Likelihood Ratio	0.15

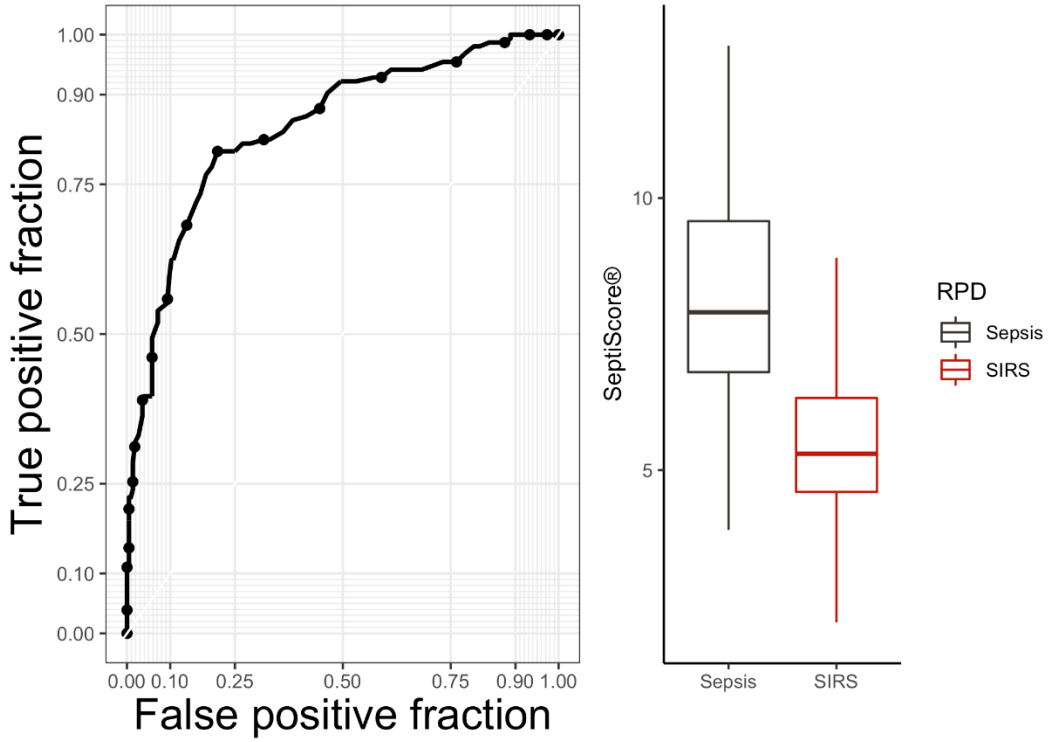
BAND 4	Performance
Cohort size (n)	378
Specificity	0.90
Sepsis probability	≥ 80.7%
SIRS probability	≤ 19.3%
Likelihood Ratio	6.05

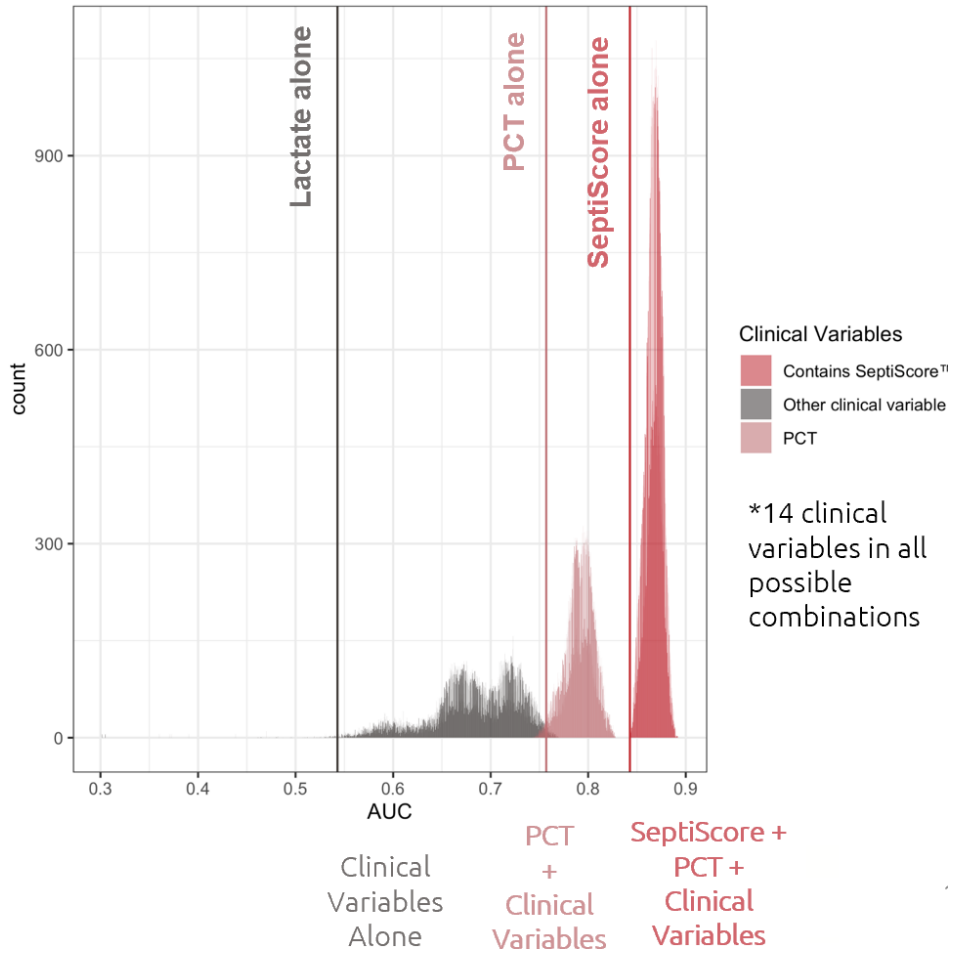
SeptiCyte RAPID results (SeptiScore) strongly discriminate sepsis from infection-negative systemic inflammation (i.e., SIRS).

Grady · Intermountain Healthcare · Johns Hopkins Medicine · Northwell Health · Amsterdam UMC Universitair Medische Centra · Utrecht University · RUSH · Loyola Medicine

Immunexpress

SeptiCyte RAPID Differentiate Sepsis vs SIRS & Outperforms Procalcitonin (PCT), Lactate & Other Clinical Variables

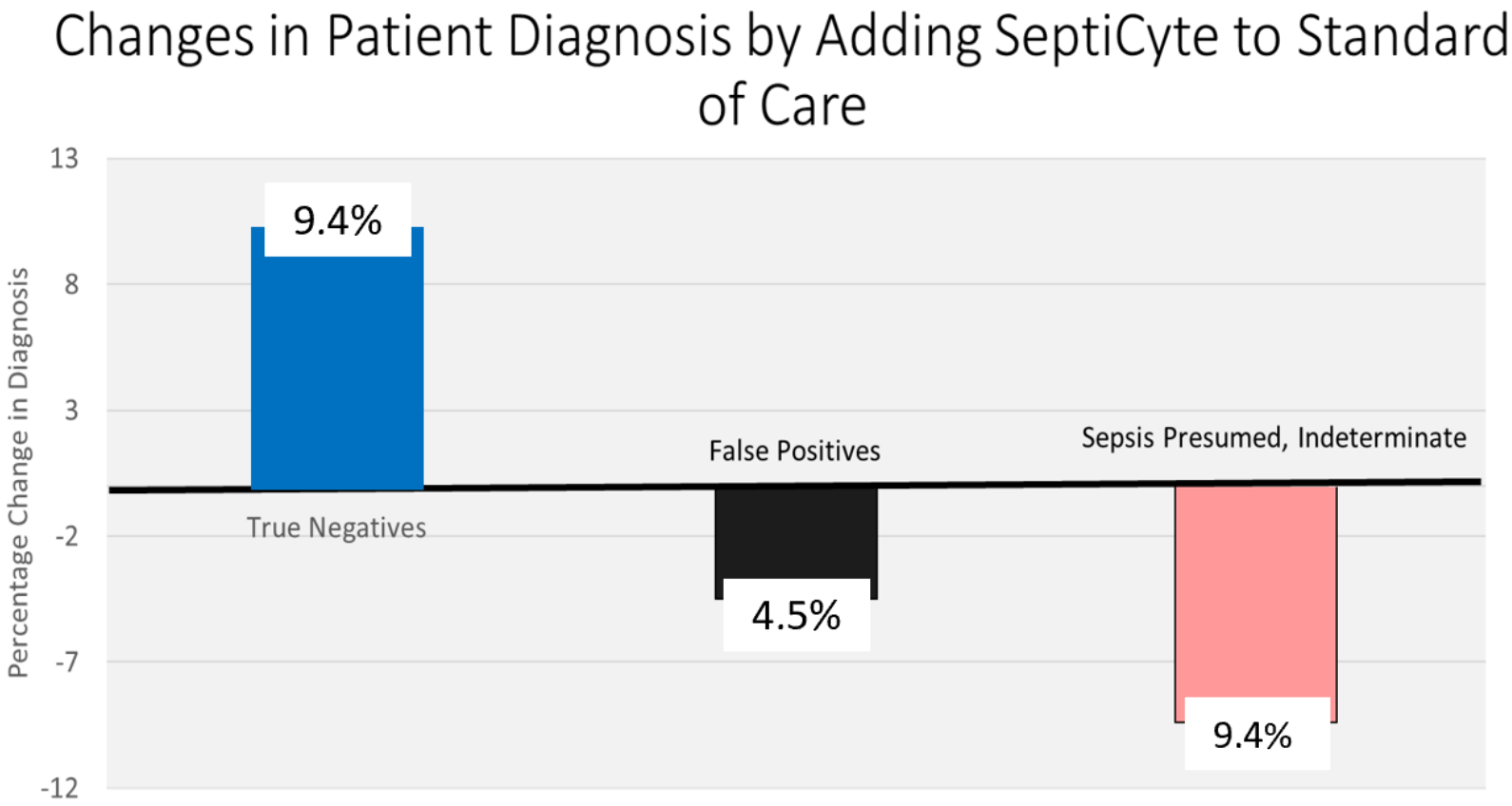




- SeptiScore strongly discriminates sepsis and SIRS (AUC > 0.84)
- SeptiScore significantly outperforms PCT and Lactate alone and in combination with commonly measured clinical variables in prospectively collected and tested samples

E.Hassan et al. Comparison of lactate, procalcitonin and a gene signature assay alone or in combination to differentiate sepsis from infection negative systemic inflammation in ICU patients. IDWeek 2021

SeptiCyte® Impact on Changing Patient's Diagnosis



- 265 adult ICU admissions[1]
- SeptiCyte impact evaluated by 3 sepsis experts
- 25% overall change in patient diagnosis[2]

1. Miller et al. Am J Respir Crit Care Med 2018;198:903-913
2. McHugh et al IDWeek 2018 A2022

SeptiCyte RAPID relationship to Surviving Sepsis Campaign* 2021 Recommendations for Timing of Antibiotics*

Low Sepsis Probability

Low Likelihood of infection & Without Shock

- Defer antimicrobials
- Continuing closely monitor the patient.

0 SeptiScore Range 15

Intermediate (Possible Sepsis)

Is Shock Present?

No (*Possible Sepsis without Shock*)

Yes (*Possible Sepsis Shock*)

Possible Sepsis Without Shock:
- Rapid assessment of infectious vs non-infectious causes of illness.
- If infection concern persists, administer antimicrobials with 3 hours of recognition.

0 SeptiScore Range 15

High (Probable Sepsis)

Possible Septic Shock or High Likelihood of Sepsis

- Administer antimicrobials Immediately, ideally with one hour of recognition.

0 SeptiScore Range 15

*Surviving Sepsis Campaign International Guidelines For Management of Sepsis & Septic Shock, authored by 60 global sepsis experts & endorsed by 23 critical care & infectious disease societies

Immunexpress

SeptiCyte RAPID Turnaround Time Facilitates Compliance With CMS SEP-1 3 hour Resuscitation Bundle

1 hr bundle

Antimicrobials started ideally within 1 hour if shock present (High Probability)

1 hr Turn Around Time

SepticyteRAPID

3 hr bundle

Antimicrobials started ideally within 3 hours if shock absent with infection concern (Intermediate Probability)

Serum Lactate, Blood Cultures, Fluids

6 hr bundle

ICU Admission
Vasopressors for persistent hypotension
Corticosteroids w ongoing vasopressor needs

Surviving Sepsis Campaign Guidelines	With high likelihood of sepsis, administer antimicrobials ideally within 1 hour (pg 16)	Sepsis without shock administer antimicrobials within 3 hours (pg 17)
Level of Recommendation	Strong Recommendation, New from previous guidelines	
SeptiCyte RAPID	1 hour turnaround time aids in early ABX administration	

Proposed SeptiCyte RAPID Clinical Utility

- **Satisfies rapid turnaround for CMS SEP-1 compliance & aligns with 2021 International Surviving Sepsis Campaign Guidelines**.
  - Aids sepsis probability determination
  - Decreases delay differentiating sepsis from infection negative systemic inflammation
  - Improves sepsis bundle compliance
  - Decreased mortality

- Diagnostic Stewardship
  - Rapid, accurate and early sepsis diagnostic work up
  - Prompts for evaluation of alternative diagnoses
  - Not impacted by early antibiotic administration

- Antibiotic Stewardship
  - Early appropriate initiation of antibiotics
  - Early cessation of antibiotics if infection negative systemic inflammation

A unique ICD-10-PCS code for SeptiCyte RAPID would…

1) Assist in diagnosis and reporting of sepsis
2) Facilitate claims for providers
3) Impact ease and accuracy of sepsis coding
4) Standardize sepsis research studies or assessments

Ultimately driving adoption in the sepsis clinical workflow to improve healthcare and economic outcomes.

SeptiCyte™ RAPID

Where Coders Can Find SeptiCyte RAPID ?

SeptiCyte RAPID could be found…

1) Ordered within the Sepsis Bundle

2) Results reported in Patient Lab tests

3) Results reported or discussed by physician in progress notes or discharge report.

Sepsis Order Sets or Bundles – 2 models

Inclusive

Developed by multidisciplinary sepsis team. Reviewed by medical staff, nursing and pharmacy. Physician marks a box in the order sheet to cover initial laboratory evaluation. Physician must enter others as needed:

- ❑ Sepsis initial evaluation laboratory tests:

Includes CBC, Diff, platelets, Lactate, urine for UA and culture, blood culture and SeptiCyte RAPID

Other, add as needed:

- ❑ BUN and Creatinine
- ❑ CRP
- ❑ Troponin
- ❑ PCT

Individual

Physician orders tests individually under a sepsis order set. eg:

Laboratory Tests

- ❑ CBC, diff and platelets
- ❑ Bilirubin
- ❑ Lactate
- ❑ BUN and Creatinine
- ❑ CRP
- ❑ SeptiCyte RAPID
- ❑ Troponin
- ❑ PCT
- ❑ IL6
- ❑ ESR
- ❑ Glucose
- ❑ d-Dimer
- ❑ INR
- ❑ Urine for UA and culture
  Blood Culture

SeptiCyte™ RAPID

A Unique Code For SeptiCyte RAPID Should Be Included in the ICD-10 PCS

- Immunexpress received FDA clearance for SeptiCyte® RAPID, November 2021. It is the 1st host response gene signature assay for differentiating sepsis from SIRS.
- SeptiCyte® RAPID has demonstrated excellent ability to differentiate sepsis from infection negative systemic inflammation, generating strong analytical & clinical data.
- Current ICD-10 codes do not describe a host response gene signature assay for differentiating sepsis from SIRS. All other diagnostic tests in this category are for pathogen identification or non-specific single biomarkers.
- Inclusion of a unique code will assist in diagnostic reporting purposes

SeptiCyte RAPID can address a critical unmet diagnostic challenge in sepsis workflow and enable more precise sepsis coding