Enhancing the Standard of Sepsis Care

T2Biosystems®

Our mission is to fundamentally change the way medicine is practiced through **transformative culture-independent diagnostics** that improve the lives of patients around the world

T2 Biosystems Mission Statement

In the Battle Against Sepsis, Every Hour Counts

WHO WE ARE

T2 Biosystems offer the first and only FDA-cleared diagnostic tests for the detection of sepsis-causing bacterial and fungal pathogens, **direct from whole blood**.

WHAT WE DO

Species ID **within 3 to 5 hours of the first blood draw** and independent of a positive blood culture.

HOW WE ENHANCE THE STANDARD

T2 Panels detect the presence, or absence, of targeted species in 3 to 5 hours**,** often **before the second dose** of empiric therapy.

WHY IT MATTERS

We enable change - timely results that inform therapeutic and clinical interventions when patients need it most.

“70% of today’s medical decisions depend on laboratory test results[1]”

…“In order to influence outcomes, a laboratory test must be ordered, conducted, returned with **results on a timely basis**, appropriately interpreted, and **affect a decision** for further diagnosis or treatment that results in **changes in outcomes**[2]”

1. https://www.cdc.gov/csels/dls/strengthening-clinical-labs.html
2. The Lewin Group. The Value of Laboratory Screening and Diagnostic Tests for Prevention and Health Care Improvement. http://www.lewin.com/content/dam/Lewin/Resources/Site_Sections/Publications/Lewin_Value_LabTesting_Sept_2009.pdf.

“1 in 3 patients who dies in a hospital has sepsis[1]”

…“Despite a progressive increase in mortality rate with increasing delays, only 50% of septic shock patients received **effective antimicrobial therapy** within 6 hours of documented hypotension.[2]”

1. https://www.cdc.gov/sepsis/what-is-sepsis.html
2. Kumar A, et al., Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006 Jun;34(6):1589-96. doi: 10.1097/01.CCM.0000217961.75225.E9. PMID: 16625125.

Enhance the Standard of Sepsis Care

Independent Meta-analysis of 14 Controlled Studies

Utilization of T2MR for Identification of Bloodstream Pathogens as Compared to Blood Culture

FASTER TIME TO DETECTION

- Time to detection **81 hours faster** with T2MR
- Time to species identification **77 hours faster** with T2MR

TARGETED THERAPY SOONER

- Patients testing negative on T2MR de-escalated from empirical therapy **7 hours faster**
- Patients testing positive on T2MR received targeted antimicrobial therapy **42 hours faster**

REDUCED LENGTH OF STAY

- Length of ICU stay **5 days shorter** with T2MR
- Length of hospital stay **4.8 days shorter** with T2MR

Title: Antimicrobial and Resource Utilization with T2 Magnetic Resonance for Rapid Diagnosis of Bloodstream Infections: Systematic Review with Meta-analysis of Controlled Studies (2021)

Authors: Maddalena Giannella, George A. Pankey, Renato Pascale, Valerie M. Miller, Larry E. Miller, Tamara Seitz

Journal: Expert Review of Medical Devices (Independent peer-reviewed)

T2Bacteria 11-center, Prospective Pivotal Trial

T2Bacteria Clinical Sensitivity for the Identification of Bloodstream Infections as Compared to Blood Culture

FASTER TIME TO DETECTION

- Time to detection ~ **32.5 hours faster** with T2Bacteria than BC
- Time to species identification **~ 65.7 hours faster** with T2Bacteria than BC

HIGH SENSITIVITY AND NPV

- T2Bacteria Panel clinical **sensitivity was 90%** and Negative Predictive Value **(NPV) was 99.7%**
- Findings suggest that T2Bacteria is more sensitive than BC, esp. in the presence of antimicrobial treatment

ENHANCING THE STANDARD OF CARE: A CLOSER LOOK AT DISCORDANT RESULTS

- T2Bacteria+ / Blood Culture– occurred in n=146 samples, or 10% of study patients
- 60% (88/146) were characterized as probable (n=62) or possible (n=26); 78% received prior antimicrobials
- The remaining 40% (58/146) were defined as ‘false positives’, however with T2Bacteria’s low LoD, more infections at smaller concentrations will be identified compared to BC

Title: Performance of the T2Bacteria Panel for Diagnosing Bloodstream Infections (2019)

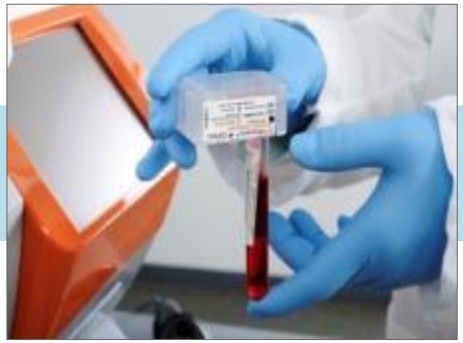
Authors: M. Hong Nguyen, MD; Cornelius J. Clancy, MD; A. William Pasculle, ScD; Peter G. Pappas, MD; George Alangaden, MD; George A. Pankey, MD; Bryan H. Schmitt, DO; Altaf Rasool, MD; Melvin P. Weinstein, MD; Raymond Widen, MD;Diana R. Hernandez, PhD; Donna M. Wolk, PhD; Thomas J. Walsh, MD; John R. Perfect, MD; Mollie N. Wilson, MS; and Eleftherios Mylonakis, MD

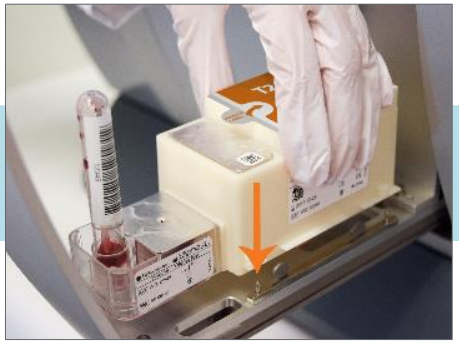
Journal: Annals of Internal Medicine

Simple to Use Platform

Fully-automated T2Dx® Instrument

- Results within 3 to 5 hours
- No upfront sample purification or extraction
- T2MR technology is not inhibited by prior antimicrobial administration1





Species-specific results enable targeted therapy

1. T2Candida and T2Bacteria Instructions for Use, refer to Performance Characteristics: Interfering Substances

T2 Biosystems Comprehensive Sepsis Test Panels

T2Bacteria®

Sensitivity: 90%[2]
Specificity: 98%[2]

E. faecium
S. aureus
K. pneumoniae
P. aeruginosa
E. coli

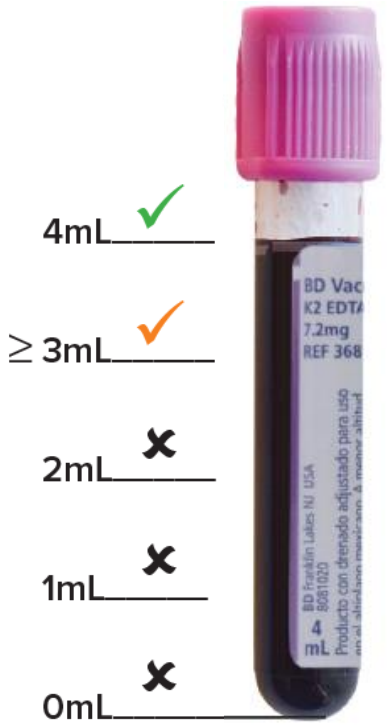
FDA-Cleared
CE-marked
2-11 CFU/mL LoD

T2Candida®

Sensitivity: 91%[1]
Specificity: 99%[1]

C. albicans
C. tropicalis
C. parapsilosis
C. krusei
C. glabrata

FDA-Cleared
CE-marked
1-3 CFU/mL LoD



New Technology Add-on Payment by CMS

"The T2Bacteria Test Panel represents a **substantial clinical improvement over existing technologies** because it reduces the proportion of patients on inappropriate therapy, thus reducing the rate of subsequent diagnostic or therapeutic intervention as well as length of stay and mortality rates caused by sepsis causing bacterial infections."

- United States CMS FY 2020 inpatient prospective payments system final rule

The payment of up to $97.50 per eligible patient who meets Medicare IPPS criteria, is in addition to the current diagnosis-related group (MS-DRG) reimbursement

1. https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/QualityInitiativesGenInfo/Downloads/RoadmapOverview_OEA_1-16.pdf

T2MR Technology Enhancing Standard-of-Care

CLINICAL IMPACT - Independent Meta-Analysis demonstrating the clinical utility of T2Bacteria and T2Candida as a faster diagnostic method of species ID, leading to targeted therapy sooner and a reduced number of patient days in the hospital

NTAP APPROVAL - The T2Bacteria Panel represents a **substantial clinical improvement** over existing technologies, improving stewardship while reducing LOS, mortality, and inappropriate antimicrobial utilization

CLABSI IMPACT - New guidelines positively impact hospital reimbursement rates by not penalizing institutions for implementing non-culture tests to improve and advance patient care, by **not increasing CLABSI rates** for patients tested with T2

BREAKTHROUGH DEVICE - T2Resistance Panel, which detects 13 resistance genes from both gram-positive and gram-negative pathogens without the wait for blood culture, received **"Breakthrough Device"** designation from the FDA

EXPANDED ACCESS - The Innovative Technology contract with Vizient Inc. was awarded due to the impact of our products on improving patient care

ACTIVE PIPELINE - BARDA contract providing funding for the **development of new products** based on T2MR technology

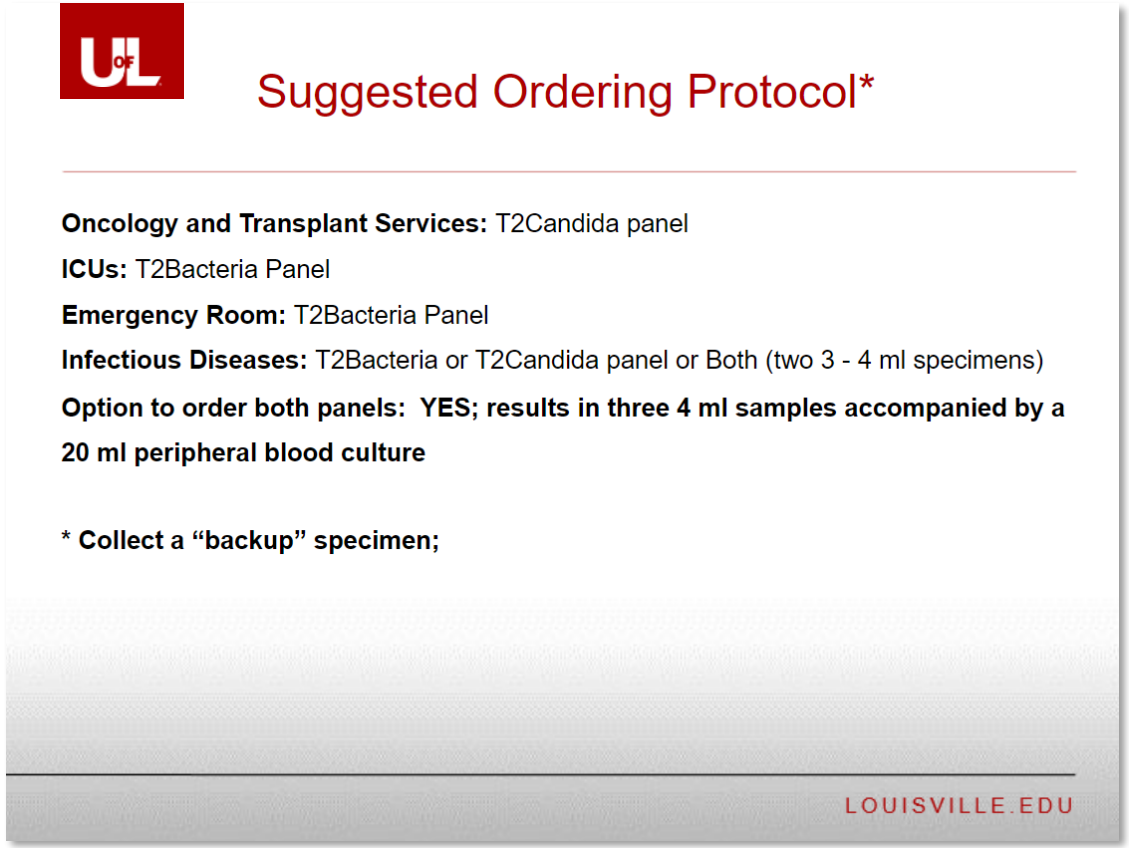
Example of Patient Selection Criteria

T2Bacteria & T2Candida Ordering Protocol in Current Practice at University of Louisville[1]

- Testing restricted to high-risk patients
  - Intensive Care Units
  - Transplant (BMT and Solid Organ)
  - Emergency Room
  - Can be orderable by Infectious Diseases personnel

*A standard blood culture (aerobic/anaerobic) must be collected and accompany the T2 specimen (3-4 ml in a separate tube). T2 specimens will not be tested if received without an accompanying blood culture set.

Note: Once a patient has been on antibiotics (>3 days/per IDSA guidelines) and continue to show signs of sepsis or are hemodynamically unstable, T2Candida can be considered following a negative T2Bacteria test result.



Ahuja A, McCarty T, Snyder J, (2021). World Microbe Forum: Industry & Science Symposium Culture Independent Rapid Diagnostics Impact on Sepsis Management. https://www.t2biosystems.com/world-microbe-forum-industry-science-symposium/

T2Bacteria Case Study 1: Anti-Pseudomonal De-Escalation

Example of how T2Bacteria result was used interventionally to direct therapy

- Patient receiving dialysis became unresponsive and developed sepsis
- Started on broad-spectrum antibiotics
  - vancomycin and piperacillin-tazobactam
- T2Bacteria rapid *S. aureus* result led to de-escalation of gram-negative therapy (pip-tazo)
- Blood culture later confirmed *S. aureus* result
- Bacterial infection cleared and patient was discharged

Conclusion: Knowledge of *S. aureus* present and not *E. coli, E. faecium, P. aeruginosa*, or *K. pneumoniae* in blood allowed immediate de-escalation of unnecessary nephrotoxic therapy. T2Bacteria was used interventionally to assist the clinical team in selecting a targeted treatment while meeting antimicrobial stewardship goals.

T2Bacteria Case Study 2: Reported Escalation of Therapy

Example of how T2Bacteria result was used interventionally to escalate and direct therapy

- Nursing home patient presented to hospital with pneumonia
- Patient was started on broad-spectrum therapy (vancomycin, ceftazidime, and clindamycin)
- Blood cultures were negative and T2Bacteria positive for *K. pneumoniae*
- T2Bacteria result directed antibiotic therapy (hospital antibiogram-directed meropenem with discontinuation of vancomycin and clindamycin)
- After meropenem was initiated WBC declined from 25 to 10 in 24 hours
- The patient improved and was transferred back to the nursing home

Conclusion: Knowledge of *K. pneumonia* present and not *S. aureus, E. coli, E. faecium,* or *P. aeruginosa*, in blood allowed immediate escalation and optimization of therapy.

T2Candida Case Study 1: Lee Health, Florida

Example of how T2Candida result improved timely and accurate diagnosis of secondary candidemia in critically ill COVID-19 patient.

- Patient was admitted to hospital with PCR-confirmed COVID-19
  - patient required oxygen support via nasal cannula, chest radiograph showed bibasilar infiltrates, initial blood cultures were negative
- On hospital day 14, patient developed a new fever and escalated on day 15 and 16
- On day 16 additional blood cultures were obtained, along with a T2Candida test, which was positive for *C. albicans/C. tropicalis* - 29 hours prior to the positive result of blood culture for yeast
- Evening of day 16, patient was given targeted anidulafungin
- By hospital day 18, patient defervesced
- Patient improved and was discharged

Conclusion: highlights a utilization opportunity for T2Candida in the diagnosis of candidemia and rapid initiation of antifungal therapy in critically ill patients with COVID-19, where species ID and targeted treatment were enabled 29 hours sooner with T2Candida.

Cubillos, A., et al., Utilization of a Novel Diagnostic Assay to Improve Turnaround Time and Accurate Diagnosis and Treatment of Secondary Candidemia in a Critically Ill Immunososupressed COVID-19 Patient, Poster Presentation, CAP, 2021.

T2Candida Case Study 2: Univ. of Louisville, Kentucky

Example of how T2Candida result was utilized to target treatment in oncology patient

- Oncology patient presenting with persistent spiking fevers
- Broad-spectrum treatment was administered; port in place
- All blood cultures were negative; spiking fevers continued
- Plan was to remove the port and hope that the offending organism had been treated
- T2Candida tested positive for *C. albicans/tropicalis*, the port was removed and the patient was placed on targeted antifungals
- Fever terminated; patient was discharged

Conclusion: T2Candida helped to determine an actual bloodstream fungal infection, and helped to target the species and treatment for *Candida albicans/tropicalis,* allowing the port to be removed with justification as the source, following the identification of the species.

Ahuja, A, McCarty T, Snyder J, (2021). World Microbe Forum: Industry & Science Symposium Culture Independent Rapid Diagnostics Impact on Sepsis Management. Access presentation: https://www.t2biosystems.com/world-microbe-forum-industry-science-symposium/, slides of interest are at 30:00 and 31:30 respectively

WITH SEPSIS, EVERY HOUR COUNTS.

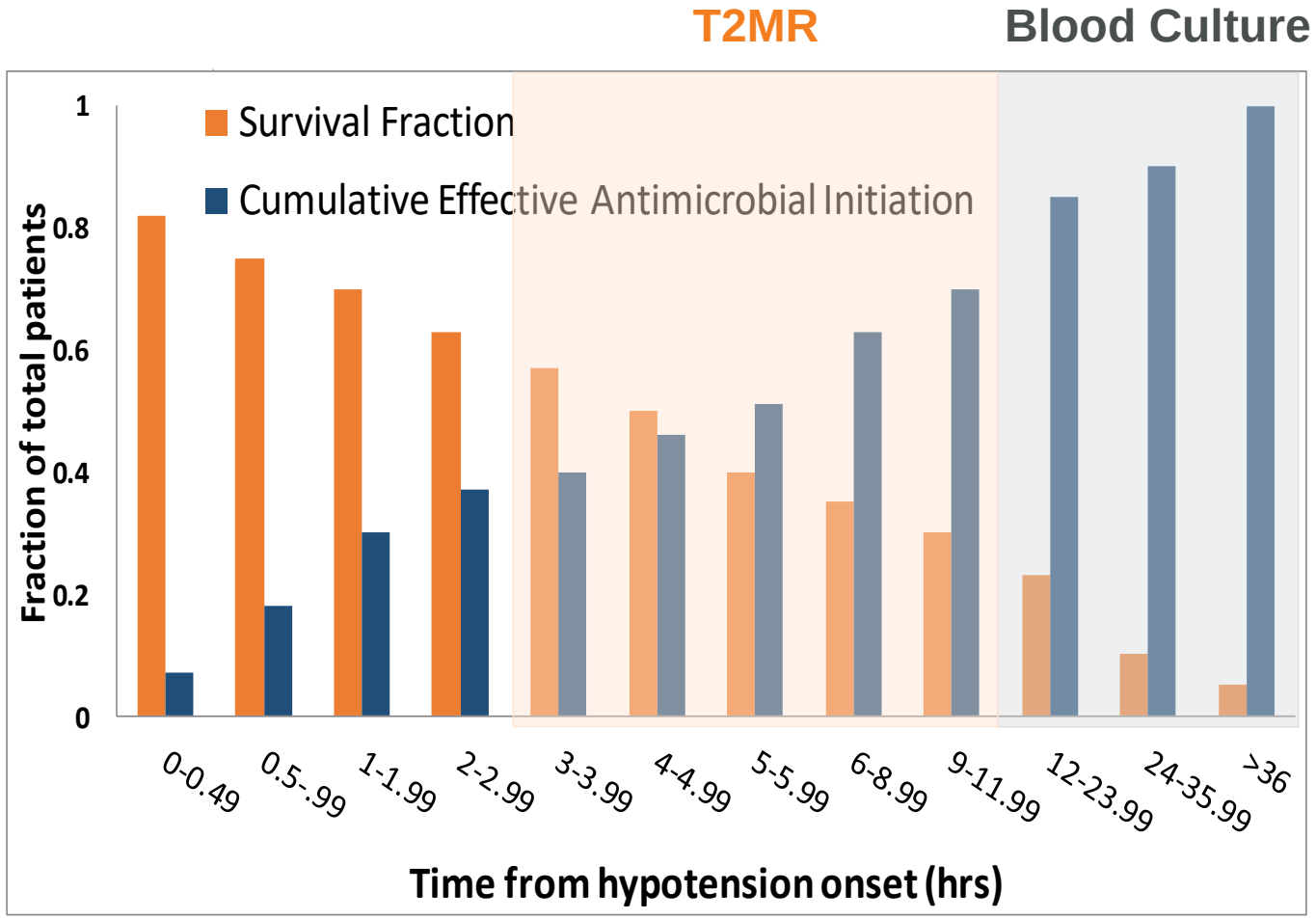
Species ID **before** the second dose of empiric therapy

with T2Biosystems®

Appendix

Time to Appropriate Therapy Impacts Survival

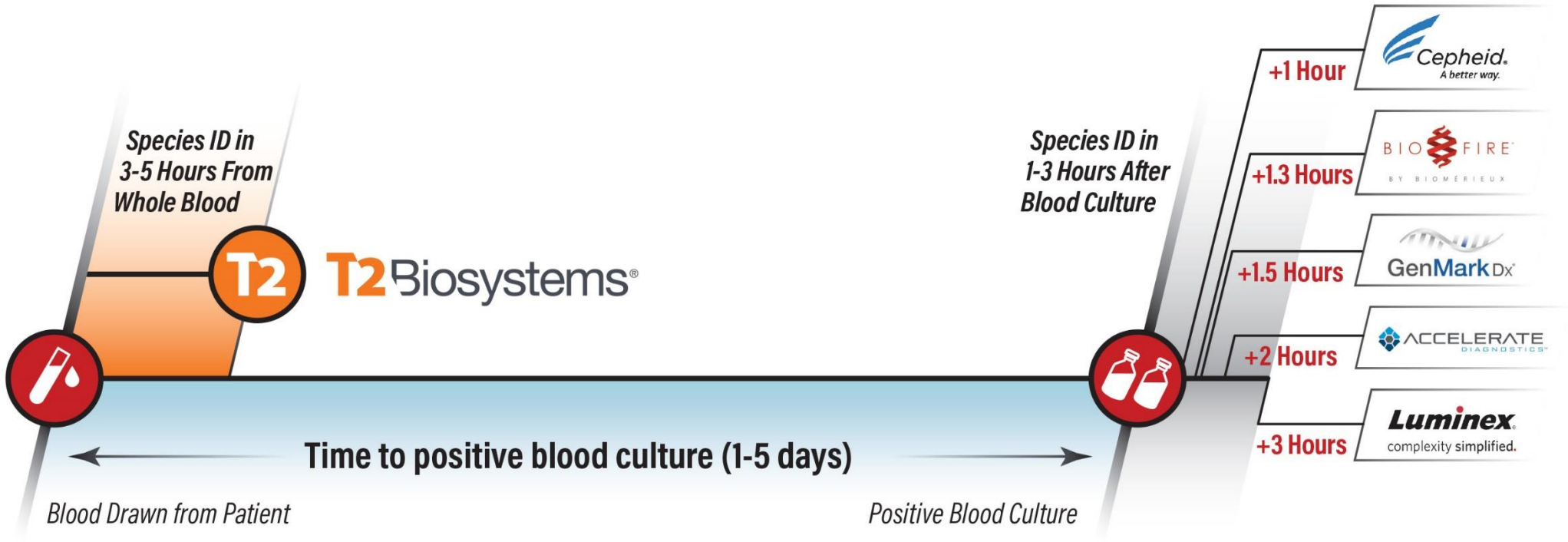
- Key predictor of survival and length of stay (LoS) for patients with bacteremia is time to effective therapy
- As many as 80% of sepsis deaths could be prevented with rapid diagnosis and treatment
- For every hour delay in time to appropriate therapy:
  - Survival decreases by 7.6% during septic shock[1]
  - Relative odds of death increase by 4.0% during bacteremia[2]
- Reducing time to effective therapy has resulted in significant reductions in LoS, up to 8 days[3-5]
- Appropriate and rapid delivery of targeted antibiotics is critical for surviving sepsis[6]



Kumar A. et al., Crit Care Med 2006, 34:1286, N=2731

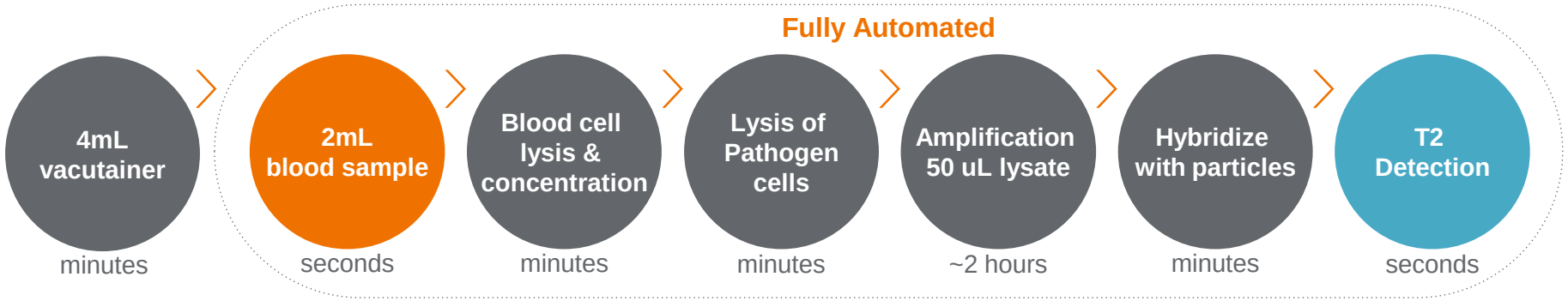
(1) Kumar et al. Crit Care Med 2006. (2) Seymour et al. NEJM 2017. (3) Huang et al. Clin Infect Dis 2013. (4) Perez et al. Arch Pathol Lab Med 2013. (5) Perez et al. J Infect 2014. (6) Rhodes et al CCM 2017.

Why Wait Days for Results?

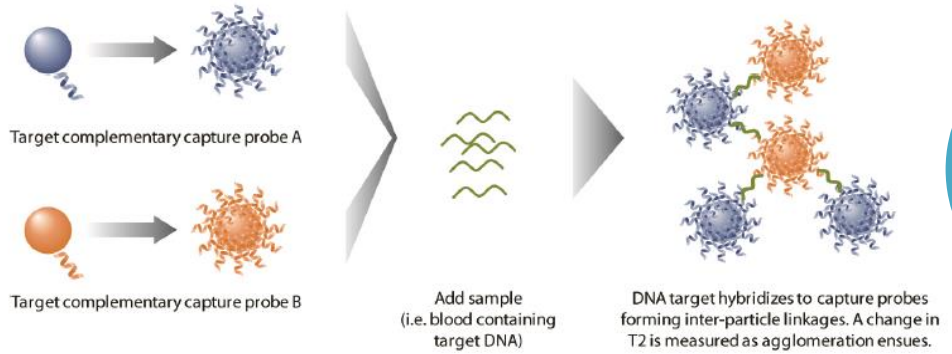


*T2 Biosystems' diagnostic panels are the **only FDA-cleared** tests that provide species identification, **directly from whole blood** and within **3-5 hours of the first blood draw**, which is often before the second dose of broad-spectrum antibiotics is delivered, enabling clinicians to target therapy faster than current standard of care.*

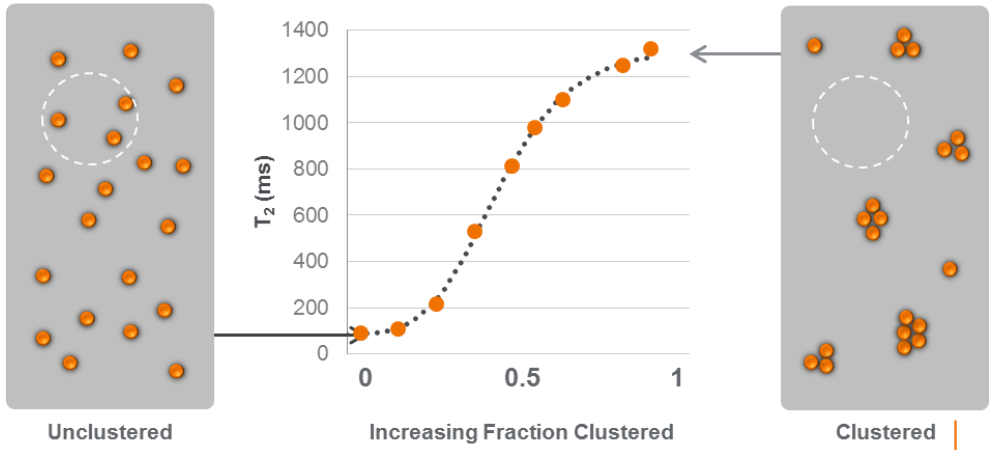
T2Dx Instrument Workflow – T2Bacteria/T2Candida



- Proprietary methodology enabling inhibition-free DNA amplification in complex clinical matrices (plasma, blood, sputum, urine, etc.)
- No background interference (e.g. human DNA, antibiotics, etc) simplifies process and eliminates extraction & purification of targets
- T2 Magnetic Resonance (T2MR) enables measurement direct from patient sample enables higher sensitivity
- T2MR detector can be configured to detect many different target types (e.g., small molecules, proteins, clotting reactions)

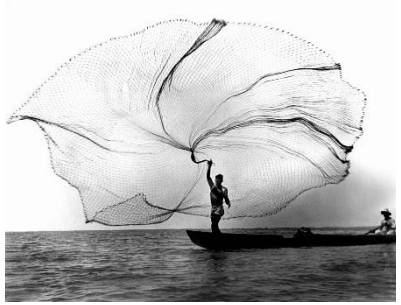


T2 Detection



Neely, L. A., Audeh, M., Phung, N. A., et al (2013). T2 magnetic resonance enables nanoparticle-mediated rapid detection of candidemia in whole blood. Science translational medicine, 5(182), 182ra54-182ra54.

T2Candida Panel Criteria: Who to Test?



Suggested Criteria for T2Candida use[1]:

≥ 1% Prevalence of Candidemia

T2Candida Panel Performance[2]:

- Sensitivity = 91.1%
- Specificity = 99.4%

T2Candida Panel Predictive Value (candidemia prevalence 1-20%)[1]:

- PPV = 31-92% → *Early detection*
- NPV = 98-99.7% → *Possible de-escalation*

POTENTIAL PATIENT SELECTION CRITERIA – T2Candida Panel

Current physical situation:

- Sepsis, or
- Septic shock, and/or
- 3+ days in ICU, or
- T2Bacteria Panel negative, or
- **Considering antifungal therapy**

Underlying condition:

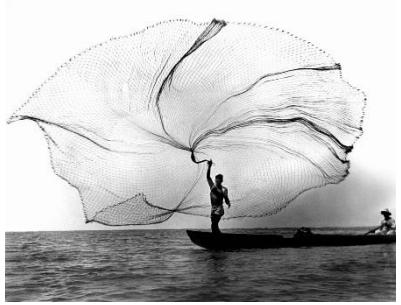
- Neutropenic w/o antifungal prophylaxis
- Pancreatitis
- Gastrointestinal/hepatobiliary surgery
- Trauma and burn

Implanted devices:

- Dialysis access
- TPN
- CVC

1. Nguyen MH and Clancy CJ. (2018). PCR-Based Methods for the Diagnosis of Invasive Candidiasis: Are They Ready for Use in the Clinic?. Current Fungal Infection Reports. 12. 10.1007/s12281-018-0313-1.
2. Mylonakis E, et al. (2015). T2 Magnetic Resonance assay for the rapid diagnosis of candidemia in whole blood: a clinical trial. Clinical Infectious Diseases, 2015: ciu959.

T2Bacteria Panel Criteria: Who to Test?



Suggested Criteria for T2Bacteria Use:

- Suspect bloodstream infection and risk of progression to sepsis exists
- Starting empiric therapy

T2Bacteria Panel Performance:

- Sensitivity = 90%
- Specificity = 98.0%

POTENTIAL PATIENT SELECTION CRITERIA – T2Bacteria Panel

Current physical situation:

- Suspect bloodstream infection or
- Sepsis, or
- Septic shock, and/or
- Starting empiric therapy, and/or
- qSOFA ≥ 2, or
- Elevated PCT or Lactate > 2

Underlying condition:

- Complicated UTI
- Post-op | GI/hepatobiliary surgery | SOT
- IV drug user
- Febrile neutropenic
- Cellulitis
- HAP/VAP
- Immunocompromised/elderly (LTAC)

Implanted devices:

- Dialysis access
- CVC/PICC
- Prosthetic valves

1. Nguyen H, et al. Performance of the T2Bacteria Panel for Diagnosing Bloodstream Infections: A Diagnostic Accuracy Study. J Antimicrob Chemother. 2019. Ann Intern Med. doi:10.7326/M18-2772