Novel Technologies in Microbiology

BENEFITS BEYOND THE LAB

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Disclosures

- **Advisory Board/Consultant**
  - Accelerate Diagnostics
  - Merck
  - Paladin Labs
- **Research Support**
  - Accelerate Diagnostics
  - Bio-Rad
- **Honorarium**
  - Merck

Objectives

By the end of this session, you should be able to:

1. Describe **advances in microbiology diagnostics** and the paradigm shift associated with them
2. Discuss the **clinical impact of novel technologies in microbiology** beyond the laboratory
3. Outline **future microbiology technologies** that have the potential to improve patient care

Traditional **NEW**

TECHNOLOGIES

1. Specimen Processing
2. Incubation
3. Microbial Identification
4. Nucleic Acid Amplification Tests
5. Novel Technologies
6. Point of Care Testing

in Microbiology

BEFORE: 8-4pm LAB

NOW: 24/7 LAB

FUTURE: 24/7 LAB & POC

in Microbiology

Clinical Impact of These New Technologies:

1. Lab function
2. Antimicrobial stewardship
3. Infection control
4. Patient outcomes

Novak et al. Clin Lab Med 2013;33:567-588

1. Lab Function

Productivity (workload/staff full time equivalent)

Turn-around-times

Quality

2. Antimicrobial Stewardship

Faster time to appropriate antimicrobial

Earlier discontinuation of antimicrobials

& reduction of associated adverse events and costs

3. Infection Control

Earlier initiation/discontinuation of precautions

Reduction in nosocomial transmission/outbreaks

4. Patient Outcome

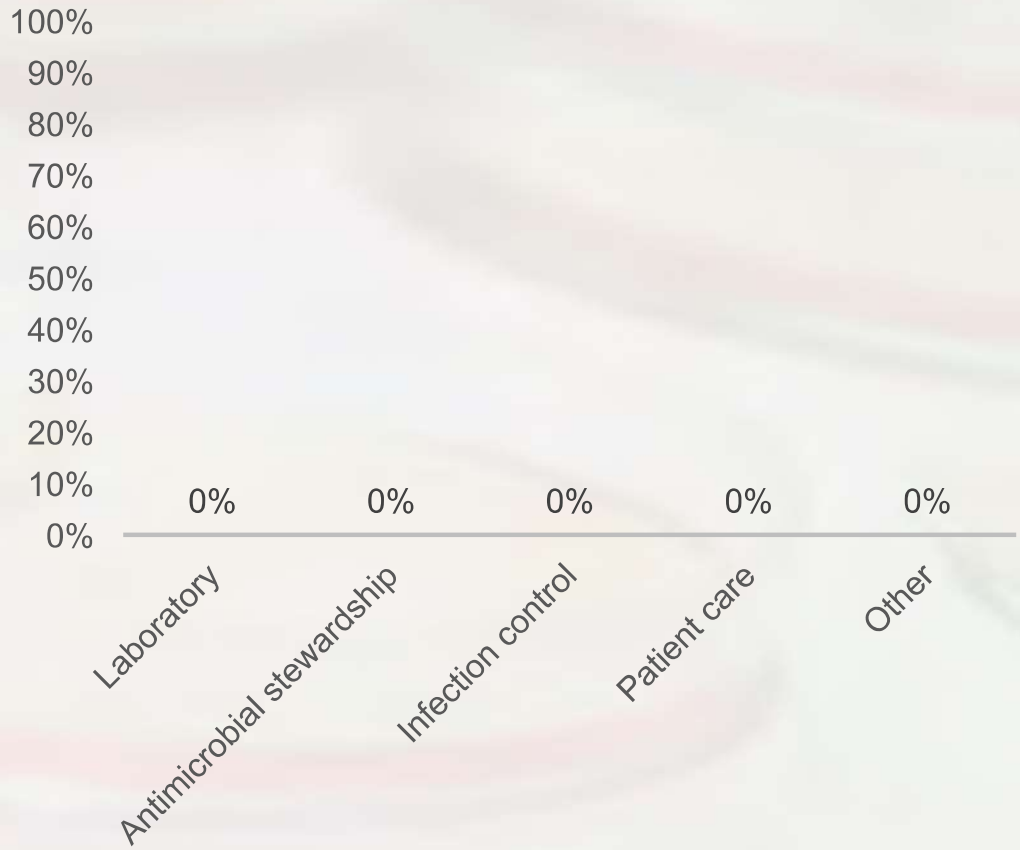
Improved patient flow/bed management

Shorter duration of admission

Reduced morbidity/mortality

Which are is your **Primary Affiliation**?

1. Laboratory
2. Antimicrobial stewardship
3. Infection control
4. Patient care
5. Other



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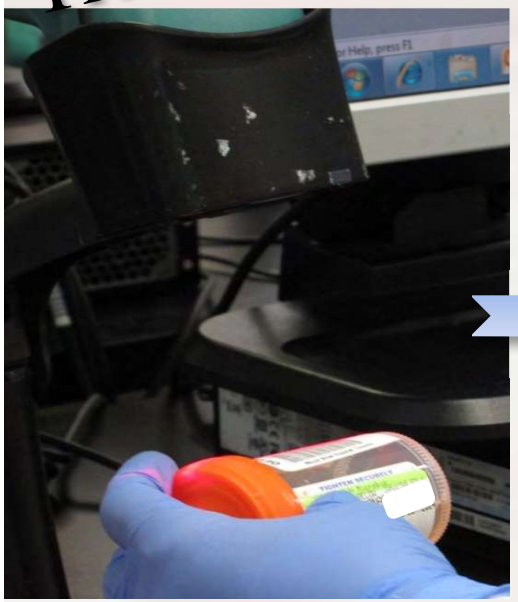
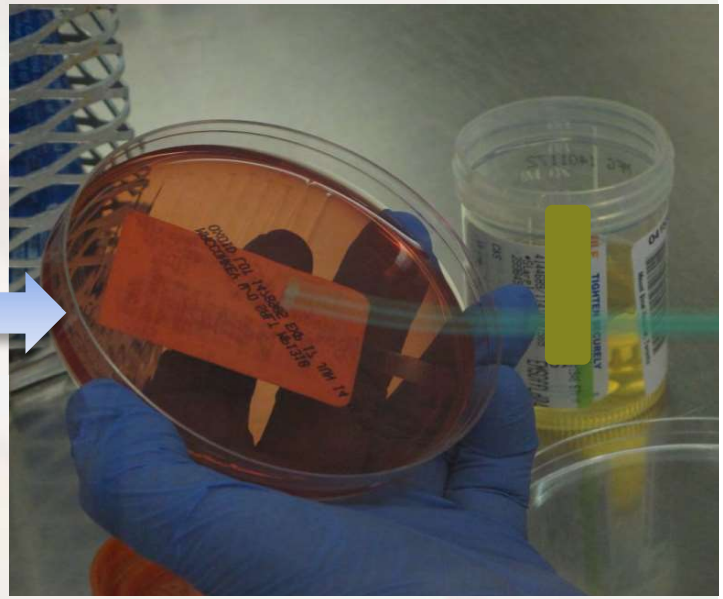
Traditional

❶ Specimen Processing





Traditional Specimen Processing and Streaking

2006

NEW

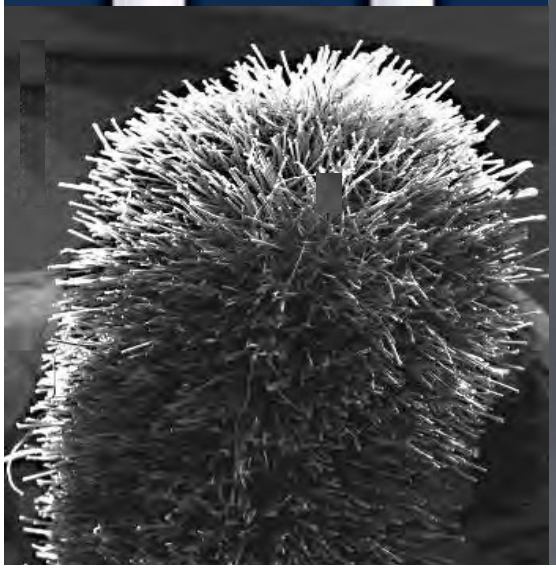
InoqulA (BD)

2008

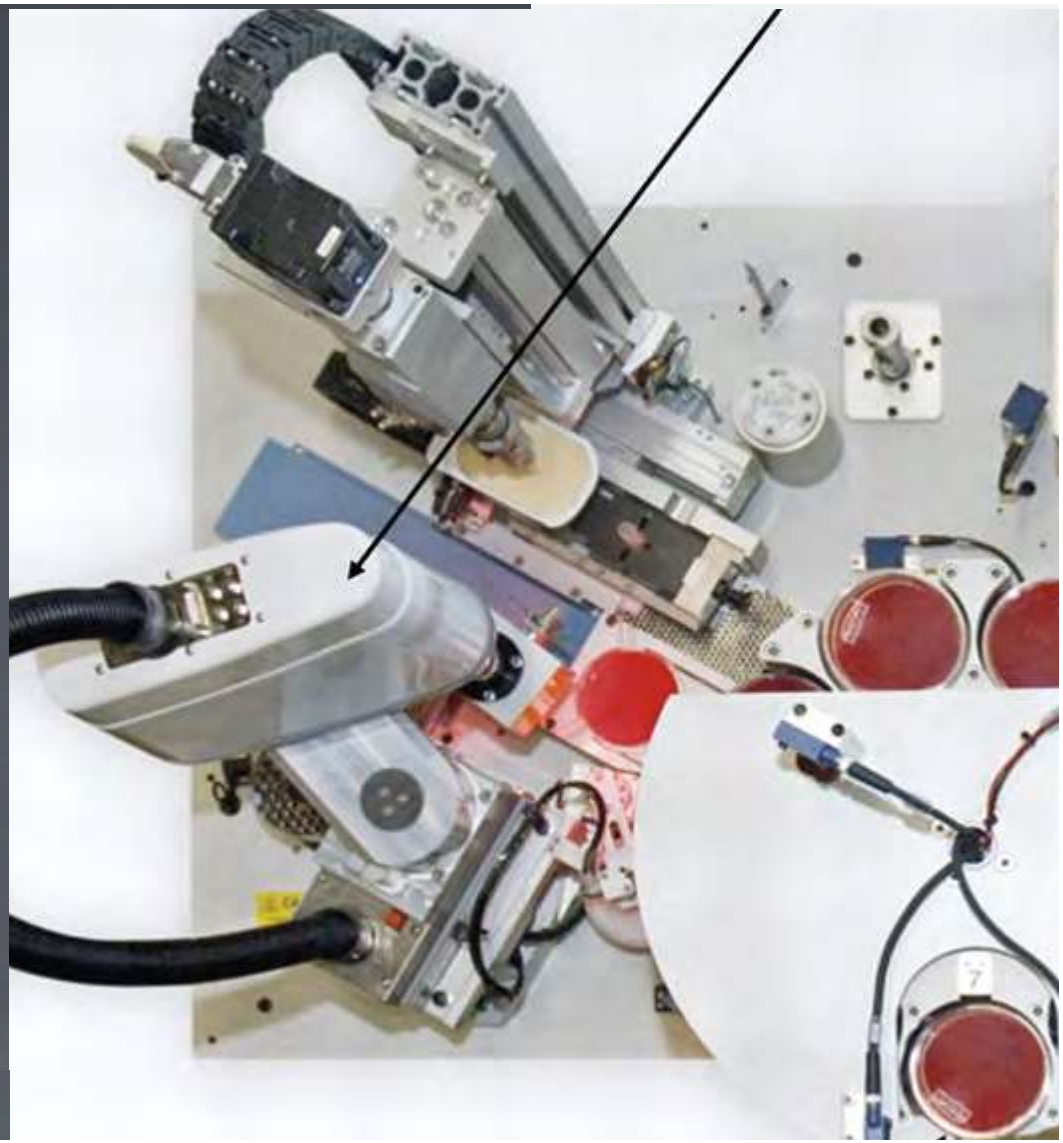
NEW

WASP (Walk-away Specimen Processor), Copan

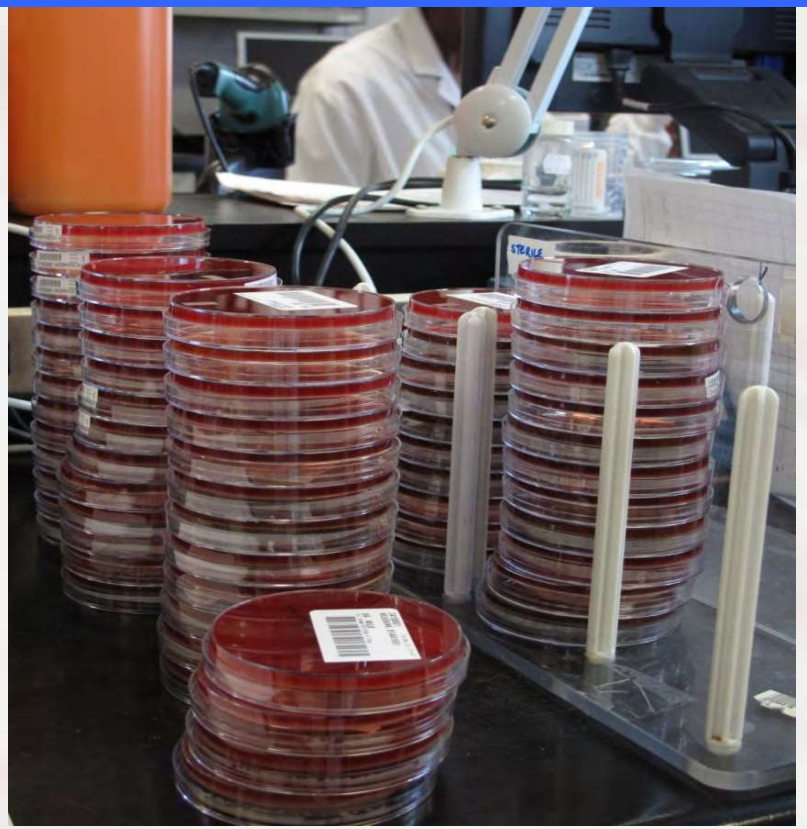

NEW




LOT
eSwab
liquid amies
preservation medium
For Universal Specimen Processing:
Culture - Amplification - Direct Testing
Name
Hospital No.
Age/DOB



❷Incubation



Traditional Specimen Incubation, Sorting, and Reading

Smart Incubators

NEW

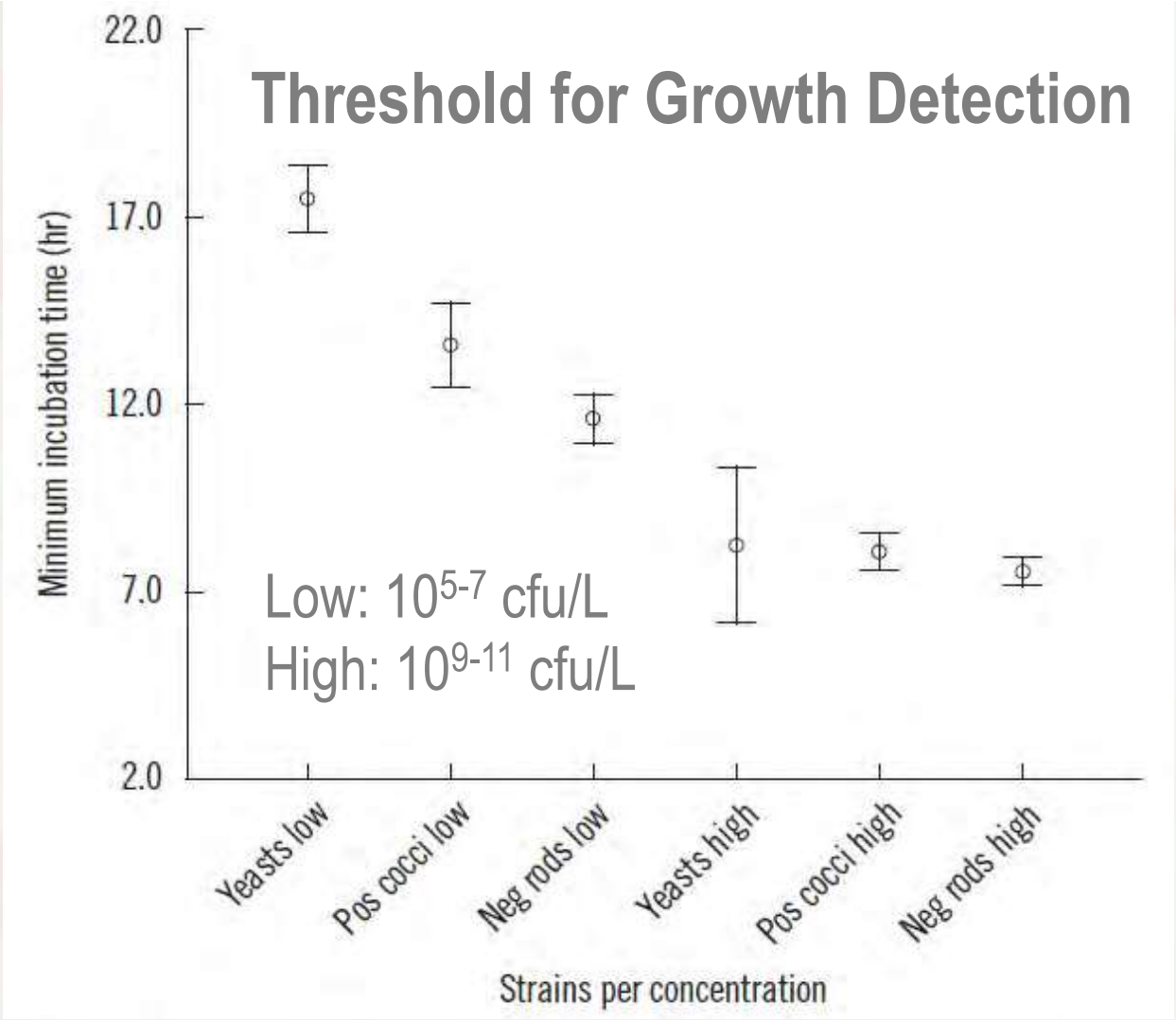
- Space efficient O_2 and CO_2 incubators
- Digital microbiology capabilities with artificial intelligence enabling:
  - Detection of growth and no growth and sorting of plates accordingly at set incubation times
  - Detection of specific colours, colony counts, zones of inhibition
- Remote reading of digital images

NEW

TLA = total laboratory automation

WASPLab (Copan)

NEW

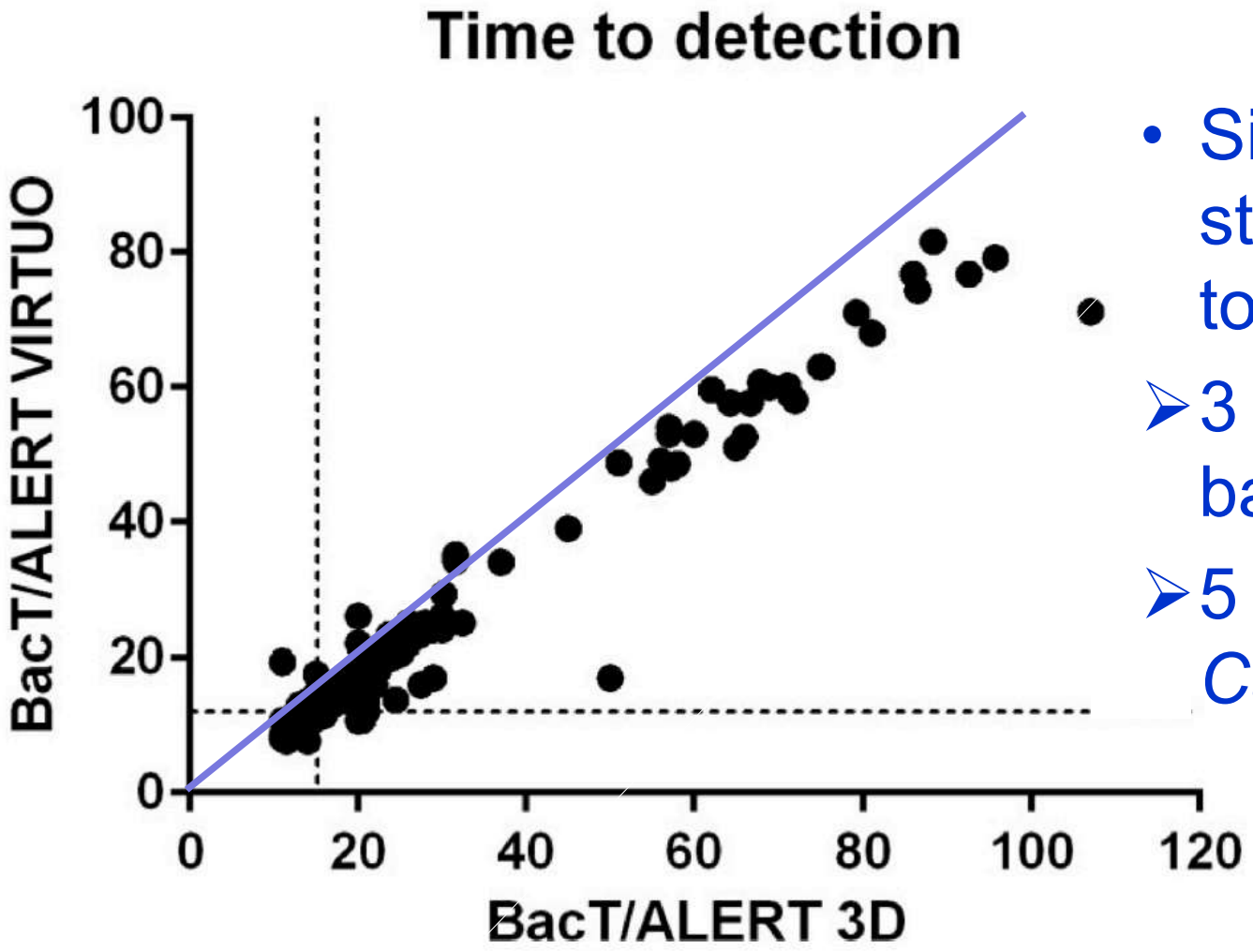


Mutters et al. Ann Lab Med 2014;34:111-117

Virtuo (bioMérieux)

NEW

- Robotic automatic receiving and sorting positives from negative blood cultures
- Automated blood volume detection



- Simulated BC study: ↓ time to detection by:
  - ➢ 3 hours for bacteria
  - ➢ 5 hours for *Candida* spp.

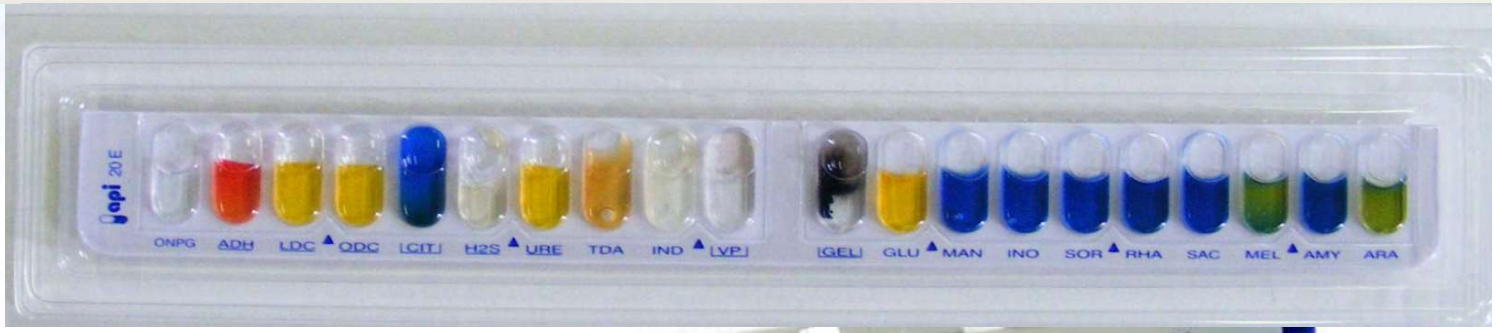
Altun et al. JCM 2016;54(4):1148-1151

Outcomes Related to Delays in Appropriate Therapy

- Delay to effective antimicrobial therapy is the **single strongest predictor of survival in septic shock**
  - Effective antimicrobial therapy within the first hour:
    - associated with 80% survival
  - For every additional hour delay in the first 6 h:
    - survival dropped an average of 7.6%

A. Kumar. Crit Care Med 2006; 34:1589–1596

Traditional ❸ Microbial Identification

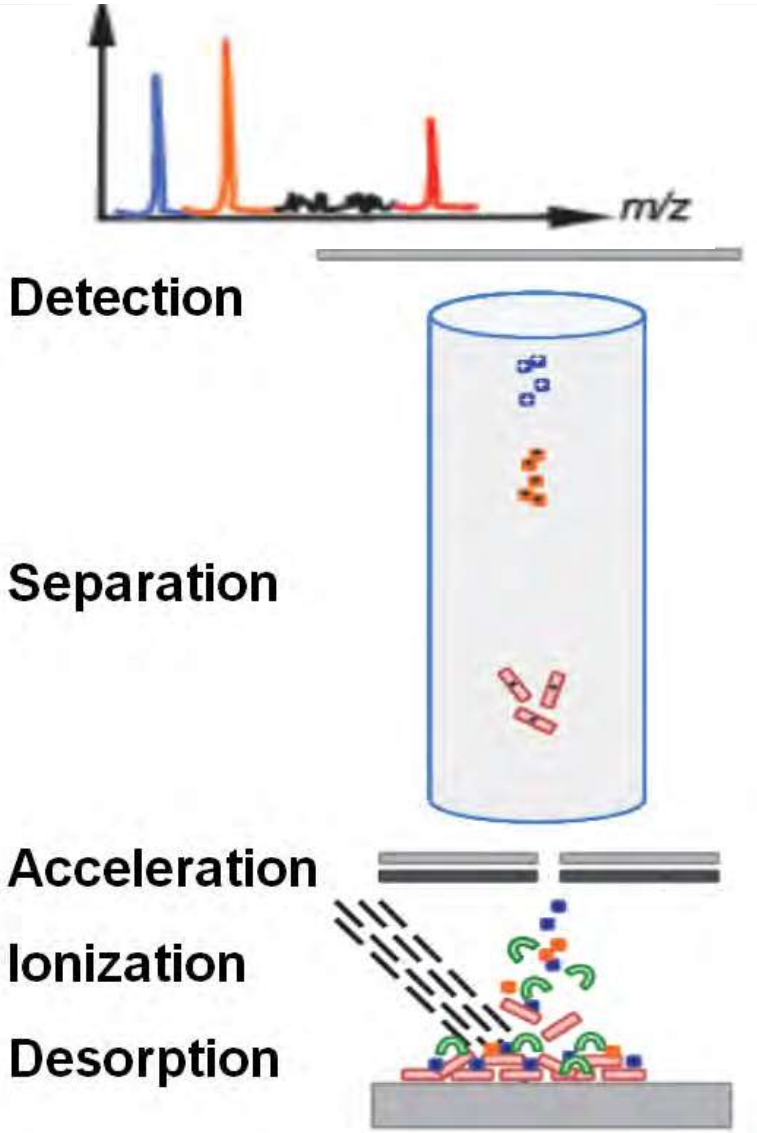


Traditional Specimen Incubation, Sorting, and Reading

MALDI-TOF

NEW

- Matrix-assisted laser desorption ionization-time of flight
- Accurate
- Fast turn-around-time (~5 min)
- Low hands-on time
- Inexpensive

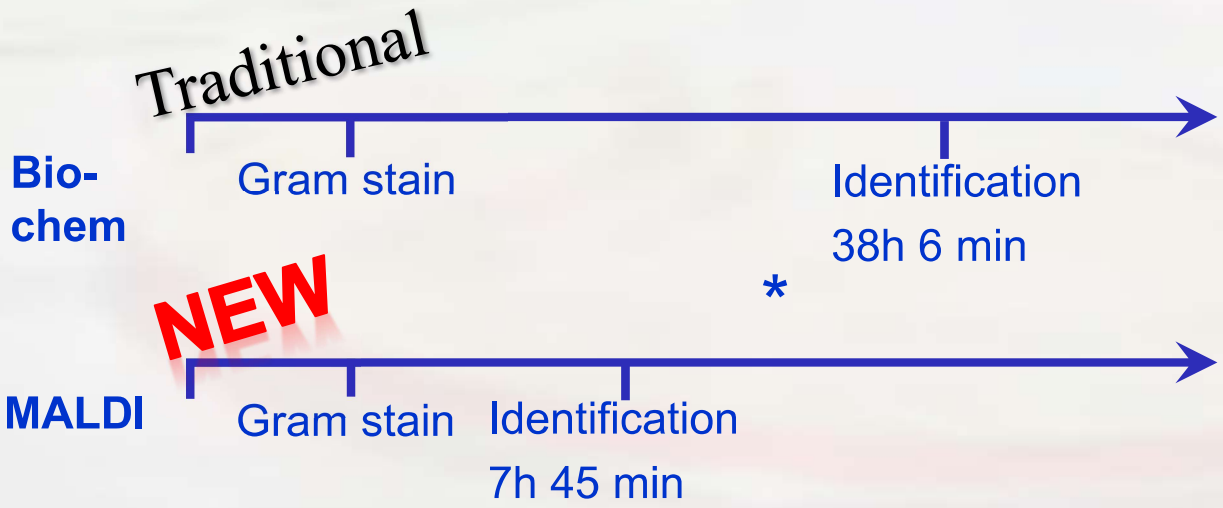


Vitek MS (bioMérieux)

Bruker MALDI Biotyper (BD)

BC: MALDI-TOF from Short Incubation Cultures or Positive Filtrate/Sediment

- ↓ time to ID by 25-31* hrs



*Matic et al. AMMI CACMID 2017, P23

Verroken et al. PLOS One 2016;11(5)

Lockwood et al. ICHE 2016;37(4):425-432

Huang et al. CID 2013;57(9):1237-45

Arch Pathol Lab Med 2013;137(9):1247-54

Integrating Rapid Diagnostics and Antimicrobial Stewardship in Two Community Hospitals Improved Process Measures and Antibiotic Adjustment Time

Ashley M. Lockwood, PharmD;[1] Katherine K. Perez, PharmD;[1,2] William L. Musick, PharmD;[1] Judy O. Ikwuagwu, PharmD;[1] Engie Attia, PharmD;[1] Oyejoke O. Fasoranti, PharmD;[1] Patricia L. Cernoch, MT;[1] Randall J. Olsen, MD, PhD;[1,2] James M. Musser, MD, PhD[1,2]

- Pre-post quasi-experimental study assessing impact of implementation of MALDI-TOF on **Gram-negative blood cultures**
- 1 year period, 151 pts PRE vs 242 pts POST
- **PRE:** Gram stain called to ward
- **POST:** Gram stain called to ward and ID and susc. results called to pharmacist-on-call 24/7 (with ID pharmacist available as backup)

Lockwood et al. ICHE 2016;37(4):425-432

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	PRE	POST	
• Time to ID results ↓	32 h	6 h	P<0.001
• Time to susc. results ↓	48 h	22 h	P<0.001
• Time to appropriate tx ↓	71 h	30 h	P<0.001
• % adjust tx	64%	84%	P<0.001
• Mortality if not on active tx at time to positivity (20%) ↓	26%	2%	P=0.006

Lockwood et al. ICHE 2016;37(4):425-432

Impact of Rapid Organism Identification via Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Combined With Antimicrobial Stewardship Team Intervention in Adult Patients With Bacteremia and Candidemia

Angela M. Huang,[1,2] Duane Newton,[5,6] Anjly Kunapuli,[1,2] Tejal N. Gandhi,[3] Laraine L. Washer,[3,4] Jacqueline Isip,[1,2] Curtis D. Collins,[1,2] and Jerod L. Nagel[1,2]

- Pre-post quasi-experimental study assessing impact of implementation of MALDI-TOF on **all positive blood cultures**
- 3 m period, 256 pts PRE vs 245 pts POST
- **PRE:** Gram stain called to ward
- **POST:** Gram stain, ID, and susc. results called to an ASP member 0600-1130

Huang et al. CID 2013;57(9):1237-45

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	PRE	POST	
• Time to AST results ↓	84 h	56 h	P<0.001
• Time to effective tx ↓	30 h	20 h	P=0.02
• Time to optimal tx ↓	90 h	47 h	P<0.001
• Recurrence same BSI ↓	6%	2%	P=0.04
• LOS ICU ↓	15 d	8 d	P=0.01
• Mortality ↓	20%	13%	P=0.02

Huang et al. CID 2013;57(9):1237-45

Impact of MALDI-TOF-MS-based identification directly from positive blood cultures on patient management: a controlled clinical trial

M. Osthoff[1,7], N. Gürtler[1,7], S. Bassetti[2], G. Balestra[3], S. Marsch[3], H. Pargger[4], M. Weisser[1], A. Egli[5,6],

- Prospective controlled trial assessing independent impact of MALDI-TOF MS (same ASP) for ID for **all positive blood cultures**
- Allocated by weekday to conventional ID vs MS
- Conventional arm: n=200
- MS arm: n=168

Osthoff et al. CMI 2017;23(2):78-85

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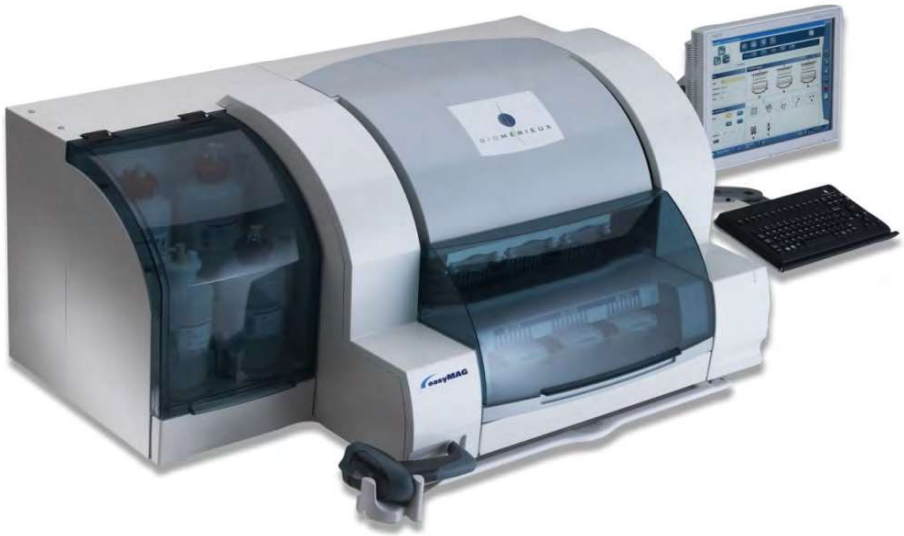
	CONV	MS	
• IV abx for contaminants ↓	7.5 d	4.8 d	P=0.04
• Time to active tx ↓	6.7 h	3.7 h	P=0.003
• ICU admission ↓	37.2%	23.1%	P=0.02
• Length of stay	17.9 d	16.1 d	P=0.3
• IV antimicrobials	13.2 d	12.9 d	P=0.9

Osthoff et al. CMI 2017;23(2):78-85

Traditional 4 Nucleic Acid Amplification



Step 1: Extraction

Step 2: Amplification (Step 3) (& Detection)

Random Access Automated PCR

NEW

- Sensitive
- Low risk of contamination
- Fast turn-around-time (~1-1.5 hrs)
- Low hands-on-time

Singleplex

Multiplex

SHORT REPORT Open Access

Rapid detection of glycopeptide-resistant enterococci: impact on decision-making and costs

Gabriel Birgand[1,2,3*], Raymond Ruimy[4], Michael Schwarzinger[1,2], Isabelle Lolom[3], Gisèle Bendjelloul[3], Nadira Houhou[5], Laurence Armand-Lefevre[4], Antoine Andremont[4], Yazdan Yazdanpanah[1,2,6] and Jean-Christophe Lucet[1,2,3]

- Compared conventional chromogenic agar to Cepheid Xpert *vanA/vanB* for workup of contacts on different wards during an outbreak of VRE

Birgand et al. Antimicrobial Resistance and Inf Control 2013;2:30

	Agar	Xpert *vanA/vanB*
	Investigation of the first case in the diabetology unit (n=31 patients)	Investigation of a secondary case in the nephrology unit (n=22 patients)
Turn-around time (h)		
From sample reception, to inoculation or preparation	2.3 (2.2– 2.4)	1.3 (0.5 – 2.3)
From inoculation or preparation, to results	65.5 (65.5– 65.5)	1 (0.9-1.1)
Overall loss of income (€)	13,968.70 to 85,175.00	0
Overall cost of the strategy (€)	14,302.20 to 86,175.50[g]	870.40 to 2,611.20[g]

Birgand et al. Antimicrobial Resistance and Inf Control 2013;2:30

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Birgand et al. Antimicrobial Resistance and Inf Control 2013;2:30

Impact of Early Detection of Respiratory Viruses by Multiplex PCR Assay on Clinical Outcomes in Adult Patients

- Resp FilmArray Assay (Biofire, bioMérieux) (20 pathogens)
- Pre-post study comparing CONV PCR to FilmArray

	CONV PCR	FILMARRAY	
TAT dx flu ↓	7.7 h	1.7 h	P<0.015
TAT dx non-flu ↓	13.5 h	1.5 h	P<0.0001
Admission ↓	multivariate model		P=0.046
LOS ↓	multivariate model		P=0.04
Duration of abx ↓	multivariate model		P=0.03
#CXR ↓	multivariate model		P=0.005

Rappo et al. CID 2016;54(8)2096-2103

Benefits of Adding a Rapid PCR-Based Blood Culture Identification Panel to an Established Antimicrobial Stewardship Program

- BC FilmArray Assay (Biofire, bioMérieux) (24 pathogens)
- Pre-post study CONV vs CONV+ASP vs FilmArray+ASP
- N~100 in each arm

	Bch	Bch+ASP	FA+ASP	
Time to org ID ↓	57h	54h	17h	P<0.0.001
Time to effective tx ↓	15h	13h	5h	P<0.0001
Rate de-escalation ↓	34%	57%	52%	N/A
Time to de-escalation ↓	63h	61h	48h	P=0.03
Mortality, 30d re-admission, ICU LOS, post-culture LOS, cost				NS

MacVane et al. JCM 2016;54(10)2455-2463

Randomized Trial of Rapid Multiplex Polymerase Chain Reaction–Based Blood Culture Identification and Susceptibility Testing

- BC FilmArray Assay (Biofire, bioMérieux) (24 pathogens)
- Randomized CONV (MS) vs FilmArray vs FilmArray+ASP
- N~200 in each arm

	MS	FA	FA+ASP	
Time to org ID ↓	22.3h	1.3h	1.3h	P<0.001
Piperacillin-tazo ↓	56h	44h	45h	P=0.01
Narrow spectrum abx ↑	25%	11%	8%	P=0.01
Time to escalation ↓	24h	6h	5h	P=0.04
Time to de-escalation ↓	34h	38h	21h	P<0.001
Mortality, LOS, cost				NS

Benerjee et al. CID 2016;61(7):1071-80

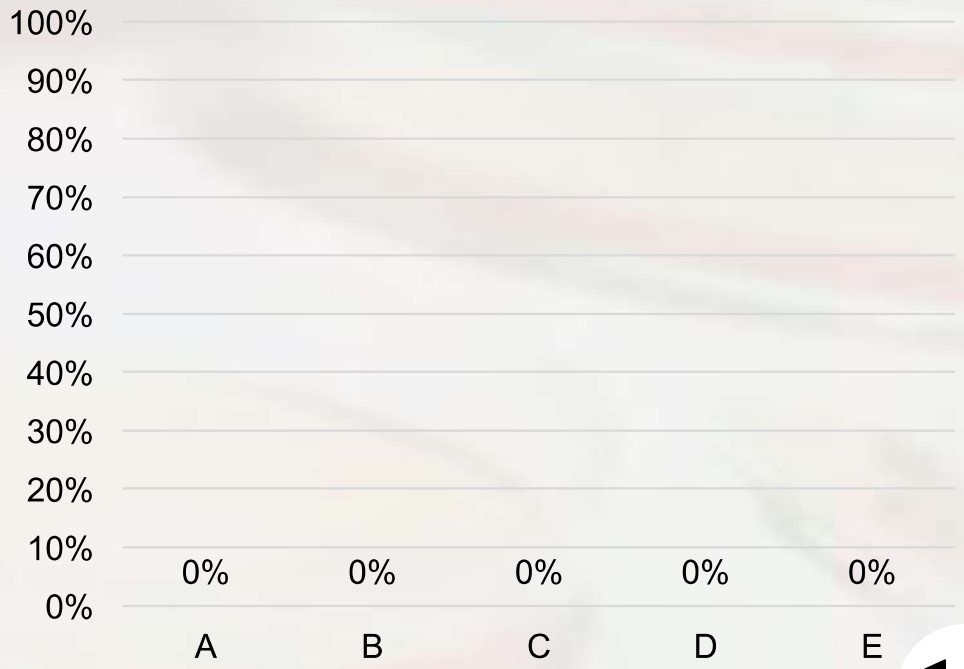
Traditional **NEW**

TECHNOLOGIES

1. Specimen Processing
2. Incubation
3. Microbial Identification
4. Nucleic Acid Amplification Tests
5. Novel Technologies
6. Point of Care Testing

Is your laboratory using **automation technologies**?

A. YES – specimen processor(s)
B. YES – specimen processor(s) and smart incubators
C. No – but expecting to in the near future
D. No
E. Not sure



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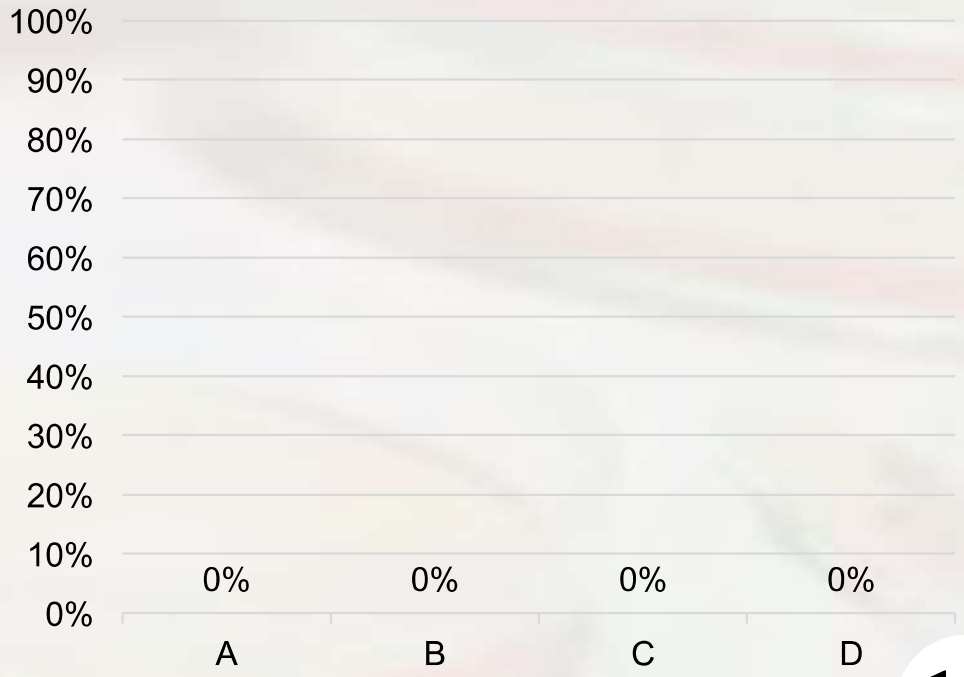
Is your laboratory using **MALDI-TOF MS** for bacterial identification?

A. YES

B. No – but expecting to in the near future

C. No

D. Not sure



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Is your laboratory using **random access automated PCR**?

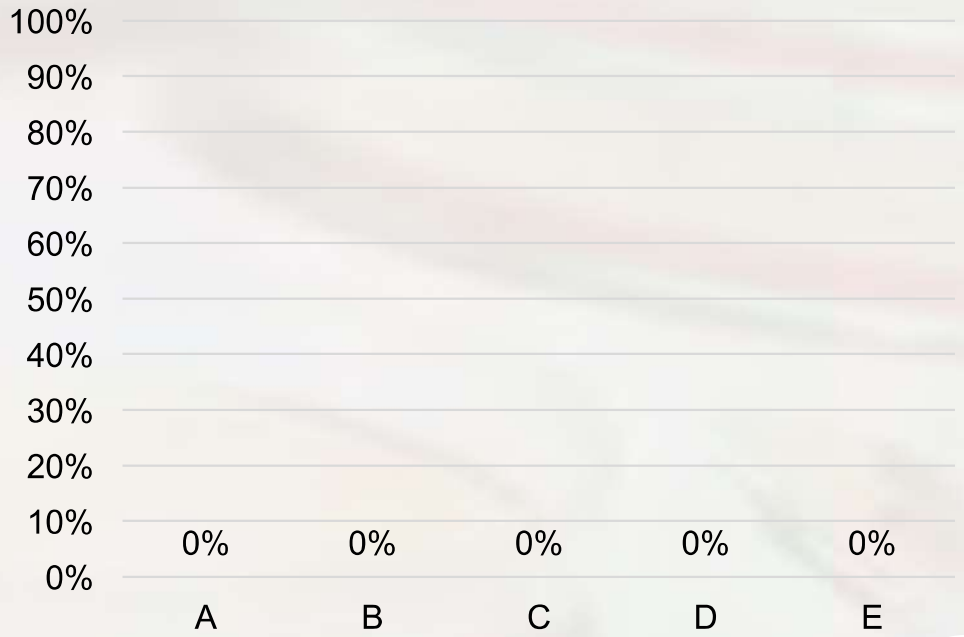
A. YES – singleplex

B. YES – singleplex and multiplex

C. No – but in the near future

D. No

E. Not sure



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Traditional **NEW**

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❺ Novel Technologies

- ID by Magnetic Resonance
- ID and AST by Automated microscopy
- AST by Resonate Mass Measurement
- AST by Laser Scattering

NEW

T2 Magnetic Resonance Detection (T2 Biosystems)

- uses **magnetic resonance technology**
  - superparamagnetic nanoparticles coated with target-specific binding agents cluster around the target, altering water molecules and their T2 relaxation signal
- detects DNA, cells, proteins directly from specimens without extraction or amplification
- fast and simple
- a low limit of detection (1-3 CFU/mL vs. 100-1000 CFU/mL for PCR) not impacted by the presence of antimicrobials

Mylonakis et al. CID 2015;60(6):892-9

T2 Magnetic Resonance Assay for the Rapid Diagnosis of Candidemia in Whole Blood: A Clinical Trial

- **T2Candida Panel** (detects *C. albicans*, *C. parapsilosis*, *C. tropicalis*, *C. krusei* and *C. glabrata*)
- Included patient samples and spiked blood
  - Mean time to positive results: 4.4h +/- 1h from receipt
  - Mean time to negative results: 4.2h +/- 0.9h from receipt
- 99.4% specific, 91.1% sensitive

➢ **12% (n=25) of pos. results were T2+/cult-**

Wilson et al, IDWeek 2016 (Poster 1569)

T2 Magnetic Resonance Improves Timely Management of Candidemia

- Pre-post-test quasi-experiment
- n=87 pre-T2 vs n=55 post-T2
- T2 associated with improvement in:
  - Time to ID: 42h (30-66) vs 25h (6-43), P=0.01
  - Time to app. tx: 40h (13-55) vs 27h (2-47), P=0.01
  - Shorter ICU LOS: 13d (6-21) vs 6d (4-13), P=0.009
- No significant difference in all-cause in-hospital mortality, 33% vs 39.5% P=0.49

T2 Magnetic Resonance Detection (T2 Biosystems)

- **T2Bacteria Panel** currently in clinical trials (detects *S. aureus, E. faecium, E. coli, K. pneumoniae, P. aeruginosa, Acinetobacter baumannii*)

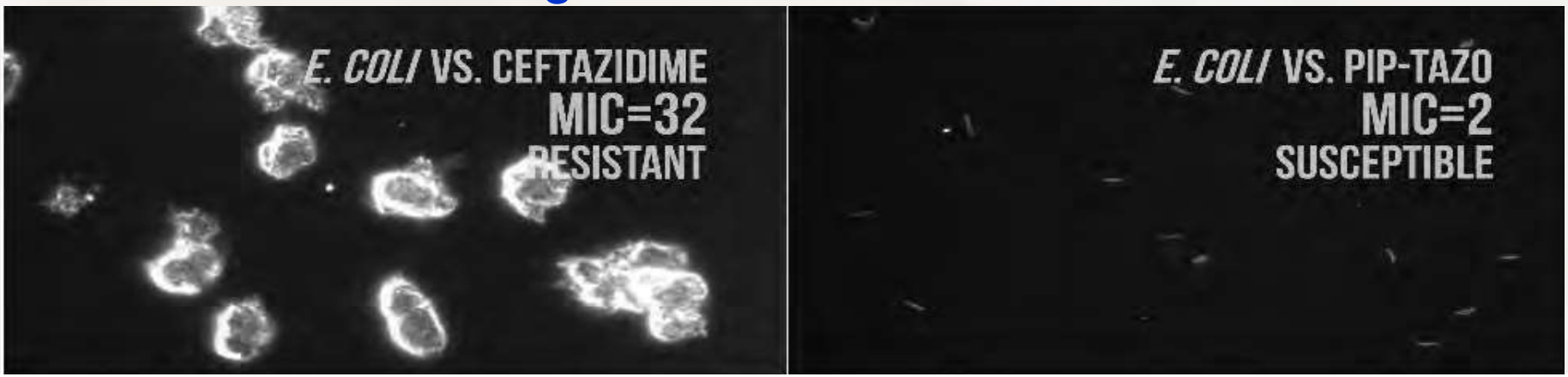
Automated Microscopy

ACCELERATE DIAGNOSTICS

~7 hour AST

Automated Microscopy

- FISH based identification
- Time-lapse imaging of bacterial growth
- Propriety image analysis algorithm
- Translation of bacterial morphokinetics into rapid MIC results from a single abx conc.



Evaluation of the Accelerate *pheno*™ System versus current blood culture ID/AST methods and potential impact on antimicrobial stewardship and patient management

Stephen P Kidd, Jasper Ellis, Simon Munro, Gemma Lockyer, Kordo Saeed, Matthew Dryden, Nick Cortes, Claire Thomas & Nicki Hutchinson
Hampshire Hospitals NHS Foundation Trust, Basingstoke & North Hampshire Hospital, Aldermaston Road, Basingstoke, RG24 9NA – stephen.kidd@hhft.nhs.uk

- Prospective pilot on 51 patients from ED/ICU pre-selected by microbiologist vs Vitek 2 (Bch) ID and disc diffusion
- Of those tested in the Accelerate pheno System
  - 5 (10%) had escalation of abx
  - 3 (6%) changed to oral
  - 2 (4% had descalation

	Bch	**Acc Dx**
Time to optimal tx ↓	24h	7h

ECCMID 2017

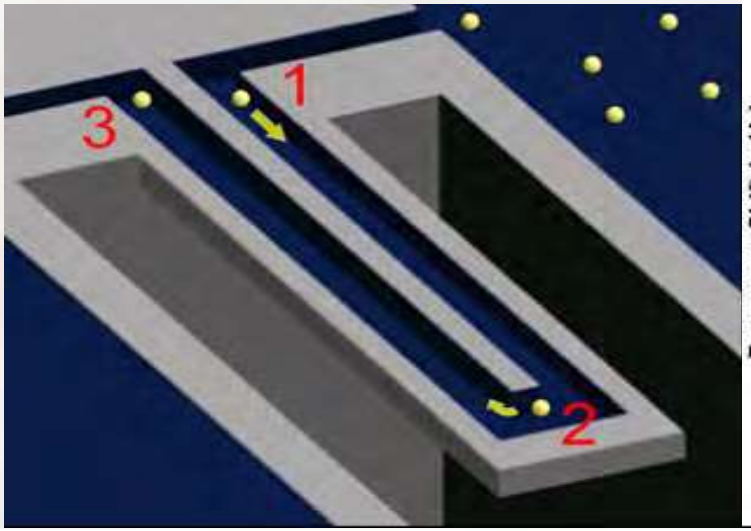
Resonate Mass Measurement

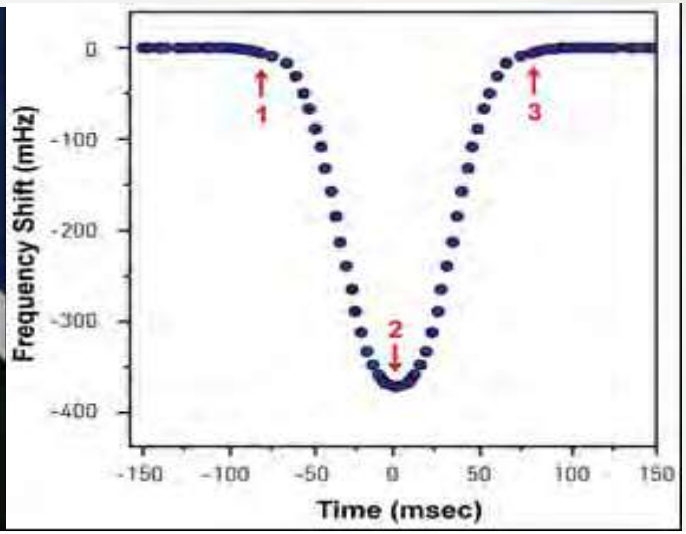
LifeScale

<3 hr AST

Resonate Mass Measurement

- Microbes suspended in broth pass them through a microfluidic channel
- Mass (and growth curve) measured by the change in resonate frequency





Laser Scattering

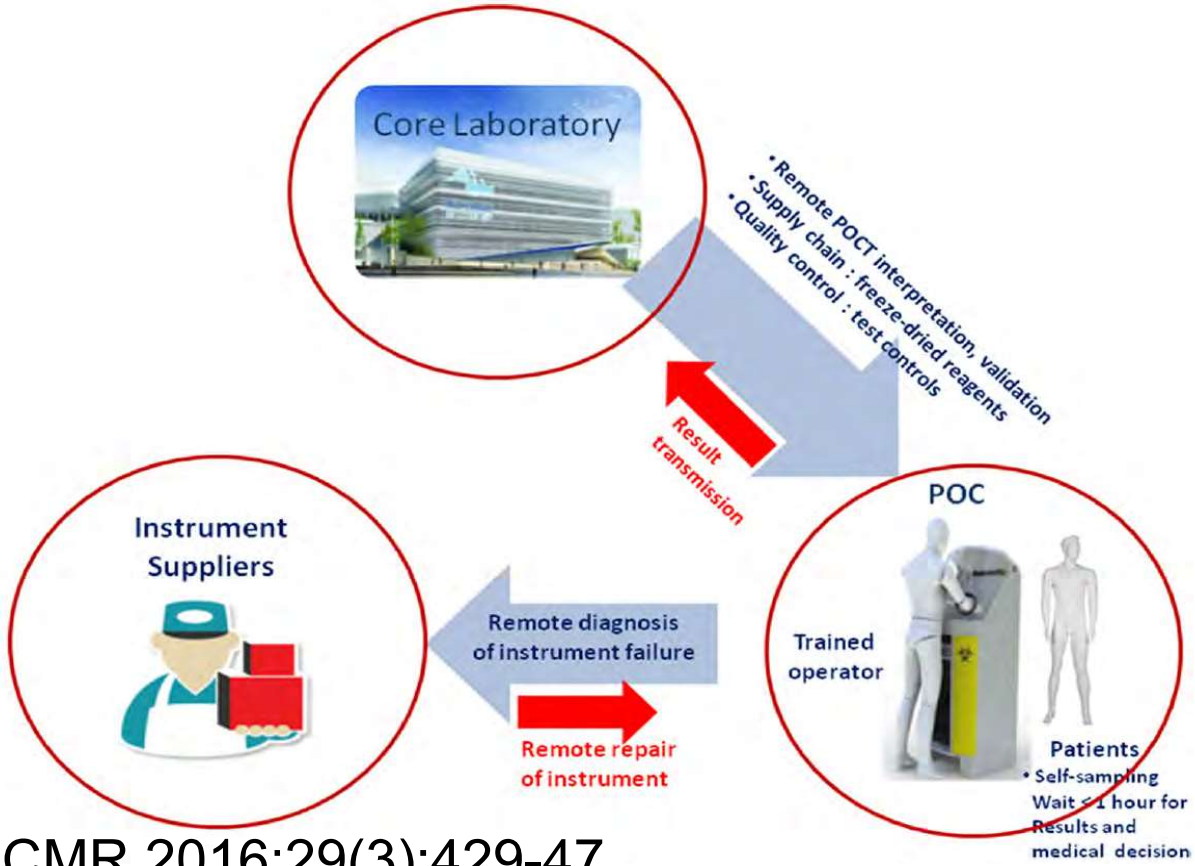
- rapid detection and real-time quantification of bacteria in fluid using optical measurements based on laser scattering

BACTERIOSCAN

3100R platform

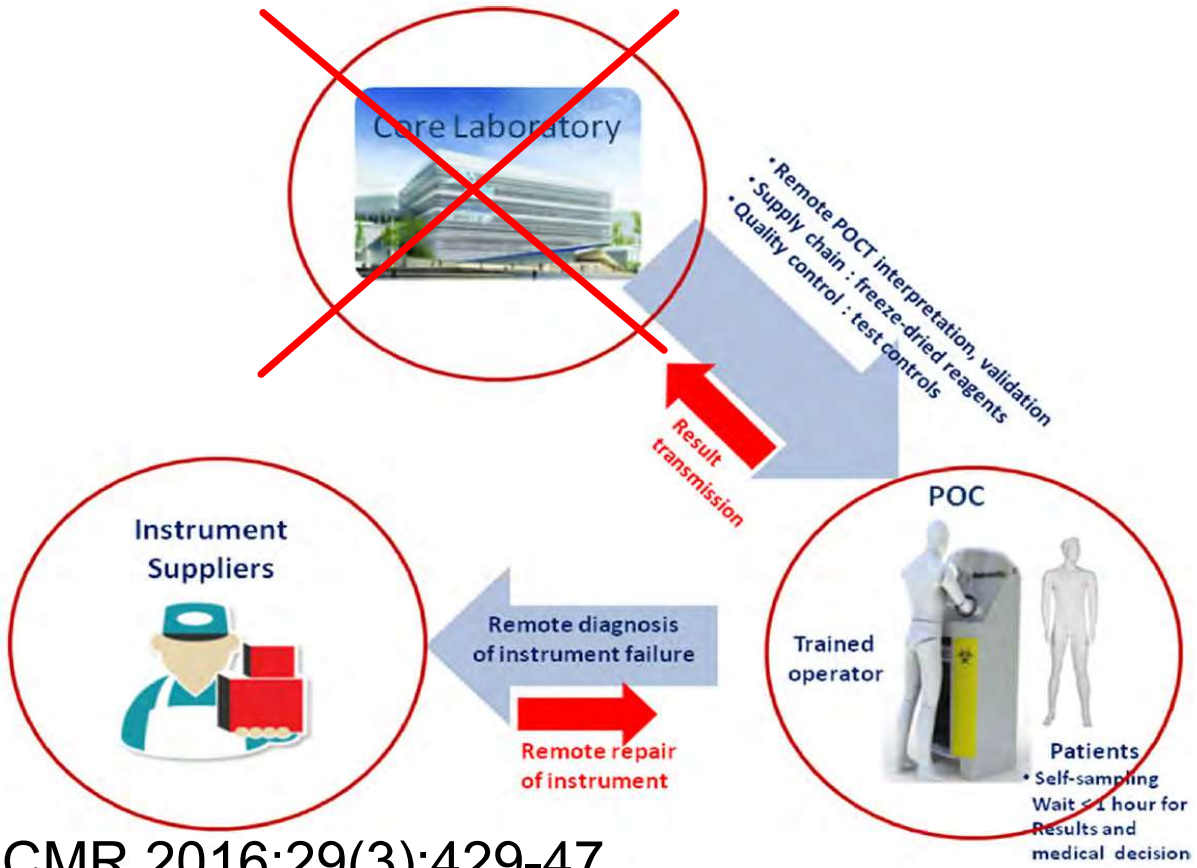
4-6 hr AST

❻ Point of Care Tests



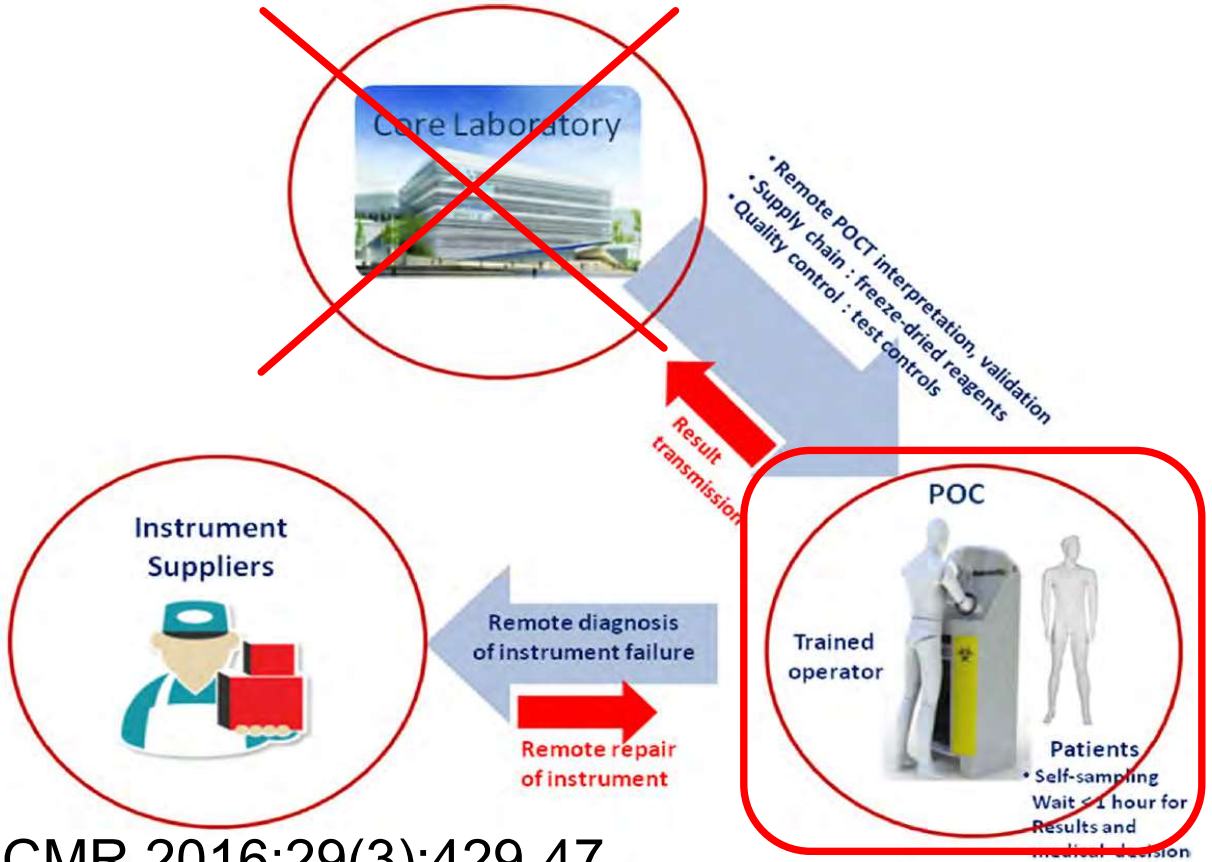
Drancourt et al. CMR 2016;29(3):429-47

❻ Point of Care Tests



Drancourt et al. CMR 2016;29(3):429-47

❻ Point of Care Tests



Drancourt et al. CMR 2016;29(3):429-47

PCR based

(results in ~20 min)

cobas Liat System, Roche

GeneXpert Omni, Cepheid

PCR based

(results in ~60 min)

GenePOC, GenePOC Diagnostics


FUTURE
xagenic
Novel Technology:
ultrasensitive
nanostructured
microelectrode
arrays (results in
~20 min)
Xagenic

The Value of Outcomes Data in the Practice of Clinical Microbiology

Gary V. Doern, Editor in Chief, *Journal of Clinical Microbiology*
University of Iowa Carver College of Medicine, Department of Pathology, Clinical Microbiology Division, Iowa City, Iowa, USA

With this editorial, I would make a plea that going forward, clinical microbiologists begin to embrace the importance of data which [redacted] oratory as the ultimate measure of the utility of new technologies. This will require the performance of objective, systematic, controlled [redacted], the results of which must then be [redacted]

Doern GV. JCM 2014;52(5):1314-5


FUTURE