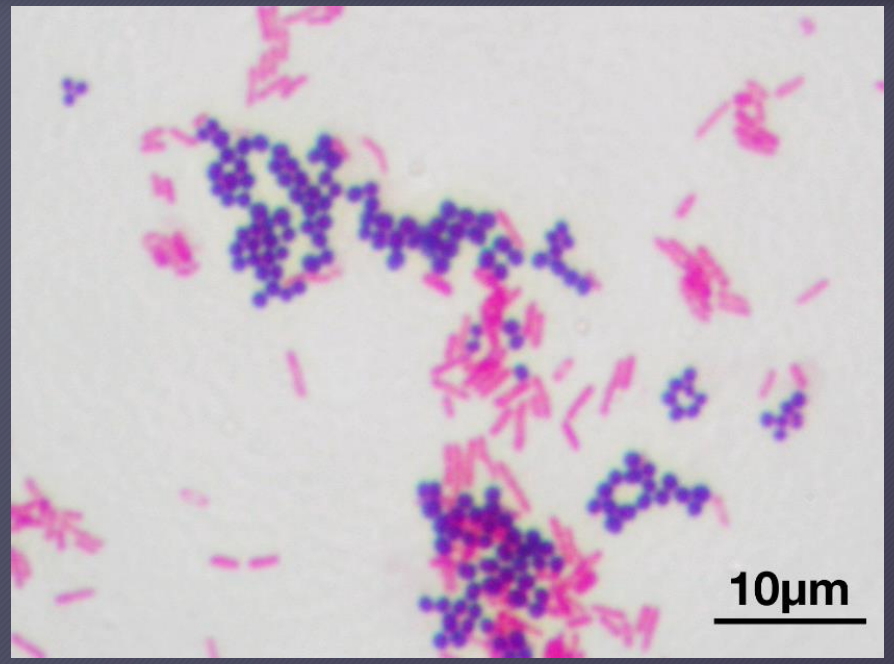
Need for Speed:
Blood Culture Rapid Diagnostics & Antimicrobial Stewardship

Ashley Wilde, PharmD
Director, Infectious Diseases Clinical Programs and Research
Norton Infectious Diseases Institute

Objectives

- State the blood culture processing steps followed in a clinical microbiology lab
- Describe the integration of blood culture rapid diagnostics into clinical practice at Norton Healthcare
- Describe the impact of the Norton Healthcare Rapid Bacteremia Response Program

Microbiology Circa 1884



Hans Christian Gram publishes staining method

Benz Patent Motor Car

Dailmer AG https://www.daimler.com/company/tradition/company-history/1885-1886.html Accessed 2/28/17

Gram, HC. Fortschritte der Medizin. 1884;**2**:185–9

By Y tambe via Wikimedia Commons from Wikimedia Commons

Blood Cultures

Patient with suspected infection

Blood Cultures

Patient with suspected infection

Blood cultures obtained

Blood Cultures

Patient with suspected infection

Blood cultures obtained

Incubation

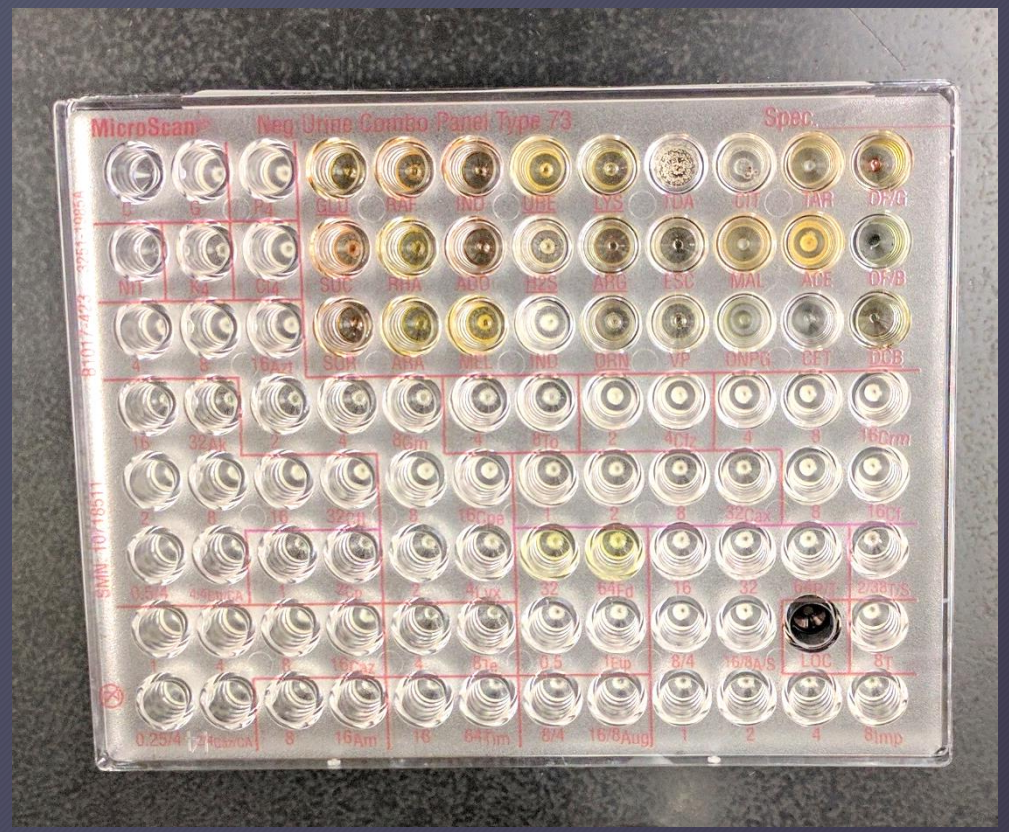
Blood Culture Incubator

Gram Stain

Plating

Plate Reading

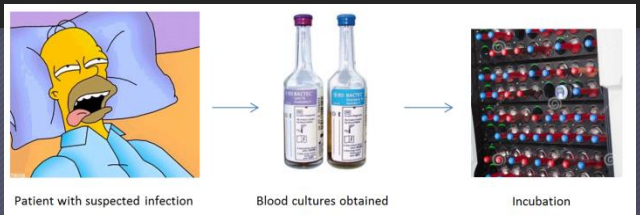
Susceptibility Panels and Purity Plates



Loading Panels

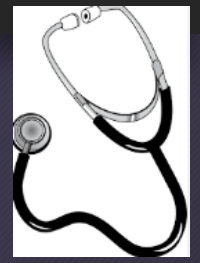
MicroScan

Blood Cultures – NHC Pre-2017



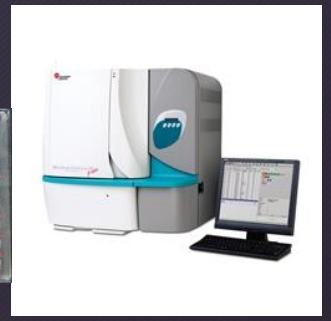
Positive
Blood Culture

Gram stain called
to nurse



Nurse contacts prescriber
with result

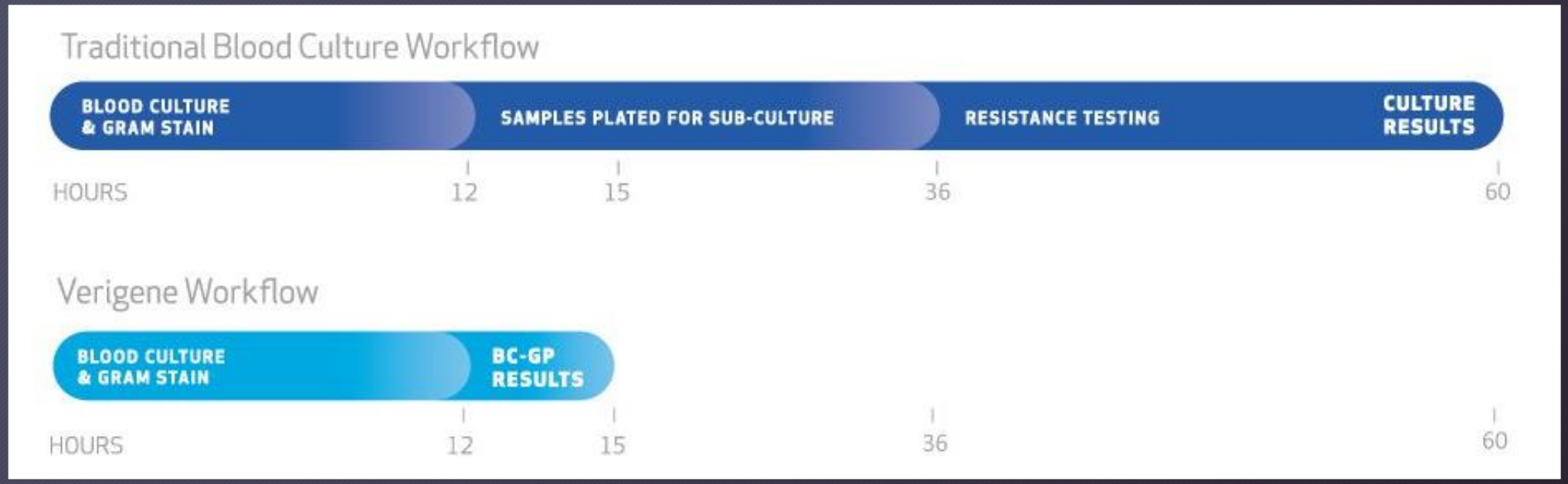
Plated ~24 h



Susceptibilities
(Microscan) resulted
~24 h

Verigene

- Gold nano-particles to identify small parts of DNA or RNA from positive blood cultures
- ~2-3 hour turn around time



Verigene System

Gram Negative Bacteria	Gram Positive Bacteria
Escherichia coli	*Staphylococcus* species
Klebsiella pneumoniae	*Staphylococcus aureus*
Klebsiella oxytoca	*Staphylococcus epidermidis*
Pseudomonas aeruginosa	*Staphylococcus lugdunensis*
Acinetobacter species	*Streptococcus* species
Proteus species	*Streptococcus pneumoniae*
Citrobacter species	*Streptococcus agalactiae*
Enterobacter species	*Streptococcus pyogenes*
	Streptococcus anginosus group
Resistance genes	*Enterococcus faecalis*
CTX-M (ESBL)	*Enterococcus faecium*
KPC (carbapenemase/CRE)	*Listeria* species
NDM (carbapenemase/CRE)	
OXA (carbapenemase/CRE)	**Resistance genes**
VIM (carbapenemase/CRE)	mecA (methicillin resistance)
IMP (carbapenemase/CRE)	vanA/vanB (vancomycin resistance)

Benefits of Blood Culture Rapid Diagnostics

- Early de-escalation
  - Contaminant (Coagulase negative staph) vs true infection
  - Targeted therapy (MSSA vs MRSA)
- Faster time to appropriate therapy and isolation
  - Pseudomonas
  - Acinetobacter
- Faster time to contact isolation
  - ESBLs
  - Carbapenem-resistant Enterobacteriaceae

Limitations of Verigene

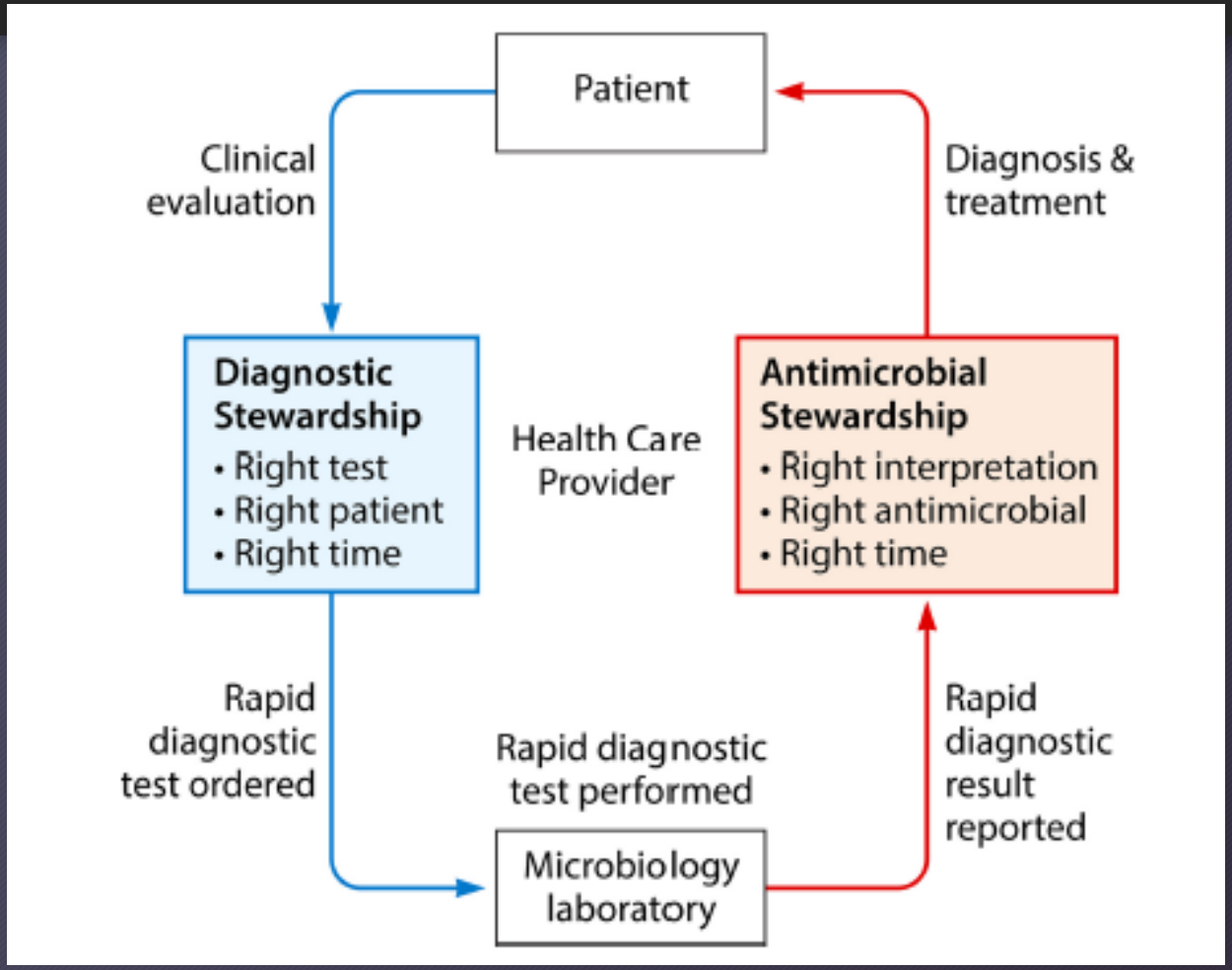
- Most antibiotic susceptibilities remain unknown
- Does NOT replace full ID and susceptibility
- Some complicated interpretations
  - Ex: Staphylococcus genus, non-aureus, non-epidermidis, non-lugdunensis, mecA positive
- Difficulty with polymicrobial specimens

Knowledge is Power, Right?

- Dr. Raymond Bartlett, clinical pathologist, 1974
- “Our technical capabilities are exceeding our ability to apply them effectively and economically to human problems.”
- The microbiology lab today is “faced with a superabundance of academic information and pressure to perform exhaustive, expensive, clinically irrelevant [testing].”

Messacar K, et al. J Clin Microbiol 2017;35:715-23
https://bestsellingcarsblog.com/1975/01/usa-1974-ford-pinto-and-plymouth-valiant-dominate
https://www.autosafety.org/ford-pinto-fuel-tank/

Diagnostic and Antimicrobial Stewardship



Messacar K, et al. J Clin Microbiol 2017;35:715-23

Role of Antimicrobial Stewardship with Rapid Diagnostics

Clinical Infectious Diseases

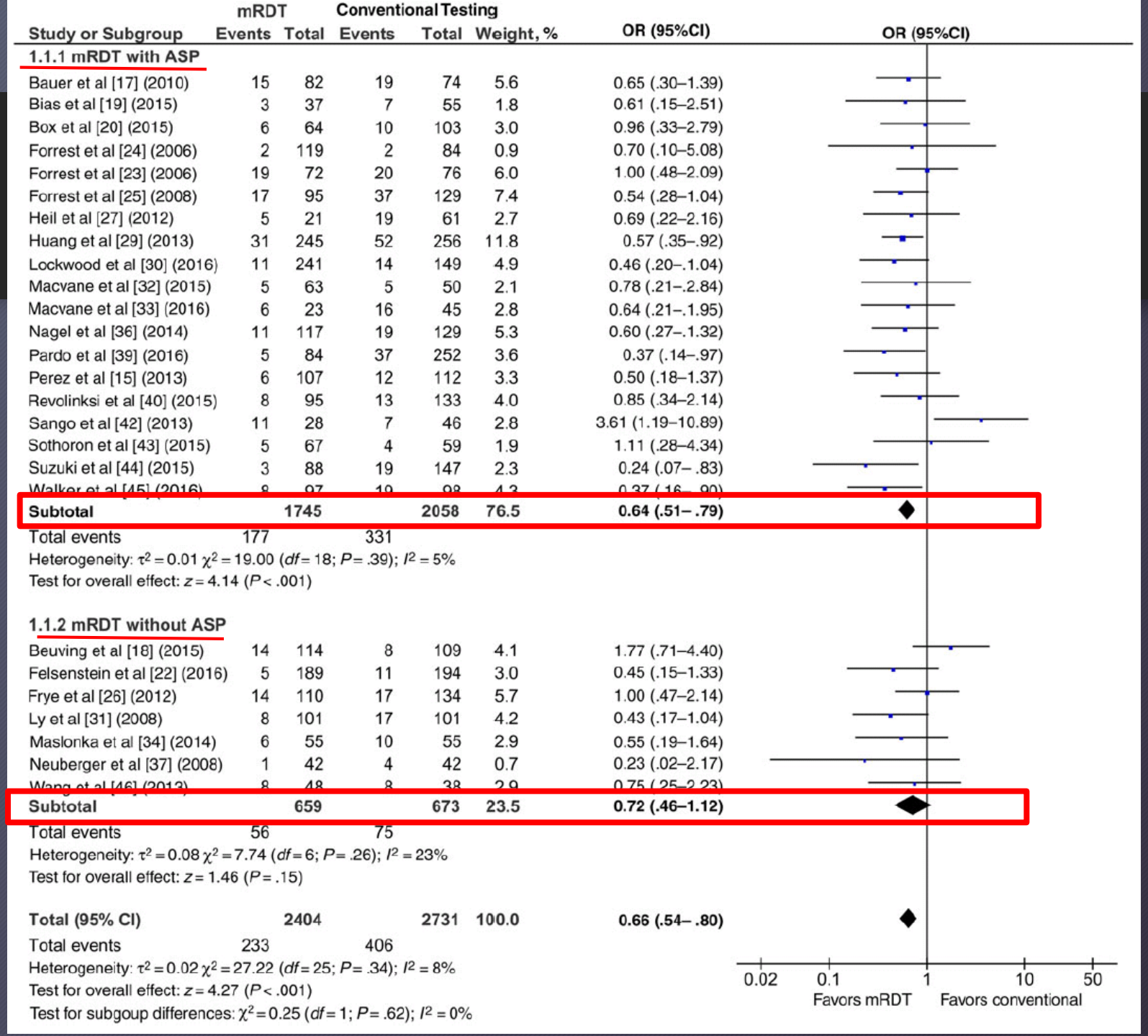
MAJOR ARTICLE

The Effect of Molecular Rapid Diagnostic Testing on Clinical Outcomes in Bloodstream Infections: A Systematic Review and Meta-analysis

Tristan T. Timbrook,[1,4] Jacob B. Morton,[1,4] Kevin W. McConeghy,[2] Aisling R. Caffrey,[1,2,4] Eleftherios Mylonakis,[3] and Kerry L. LaPlante[1,2,4]

[1]Rhode Island Infectious Diseases Research Program, Providence Veterans Affairs Medical Center, [2]Center of Innovation in Long Term Services and Supports, Providence Veterans Affairs Medical Center, [3]Infectious Diseases Division, Warren Alpert Medical School of Brown University, Providence, and [4]College of Pharmacy, University of Rhode Island, Kingston

Timbrook TT, et al. Clin Infect Dis 2017;64:15-23



- Odds ratio for mortality risk was reduced if…..
- Number needed to treat to prevent 1 death at 30 days: **20**

Timbrook TT, et al. Clin Infect Dis 2017;64:15-23

Implementation of Rapid Diagnostics

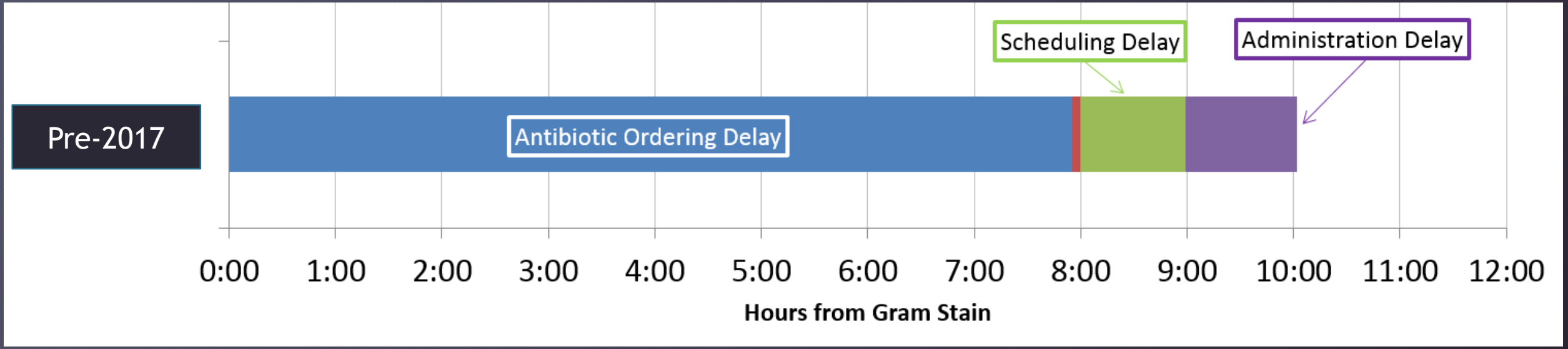
- Batched testing versus on-demand testing
- Communication of result
  - How should results be reported?
    - EMR
    - Wording - more is not always better
  - Who should receive results?
    - Nurse
    - Provider
    - Infectious diseases specialist
  - How will results be interpreted?
    - Acceptance of medical staff of diagnostic results
    - Acceptance of recommendations

Integrating ASP with Rapid Diagnostics

- Low resource – guideline or protocol

- High resource – personalized antimicrobial stewardship decision support
  - Site of infection
  - Antibiotic allergies
  - Prior antibiotic exposure
  - Past culture and susceptibilities
  - Drug-drug interactions
  - Dosing customization

Time from Gram Stain to Antibiotic: Pre-2017



Rapid Bacteremia Response Program (RBRP)

Positive Blood Culture

Gram stain called to central pharmacy

Pharmacists evaluates antibiotics
Orders first dose stat antibiotic per protocol, if needed

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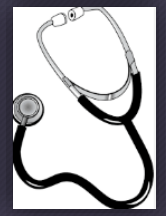
Verigene

ASP or Central pharmacy



Pharmacist notifies prescriber with result and recommendation

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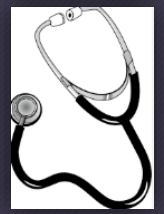
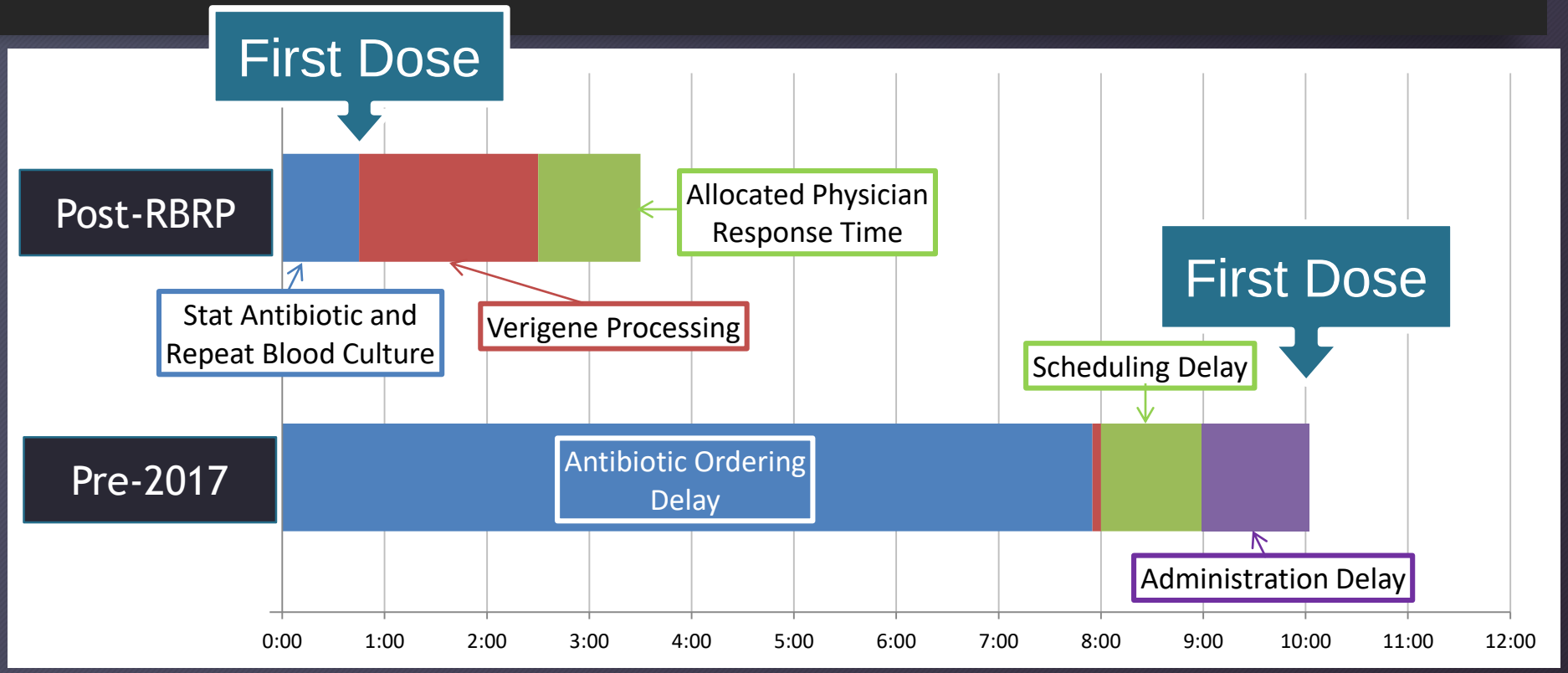


Pharmacist notifies prescriber with result and recommendation

Plated

ID and susceptibilities

Direct Patient Impact



Norton Healthcare RBRP – First Year

- 2282 positive blood cultures, 2046 Verigene results
- Stat antibiotic given to 781 patients (34.2%)
- Time from Gram stain to start of antibiotic infusion
  - Baseline historical data: 10-12 hours
  - Median time after RBRP: 51 minutes
  - Fastest time to antibiotic:

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Pharmacist Interventions from Verigene Results

	Verigene Results n=2046
Adjusted based on RBRP*	1139 (55.7%)
Escalated spectrum	455 (22.2%)
Dose optimization	264 (12.9%)
De-escalated spectrum	429 (21%)
Contact isolation orders	135 (6.6%)

* may have more than one adjustment

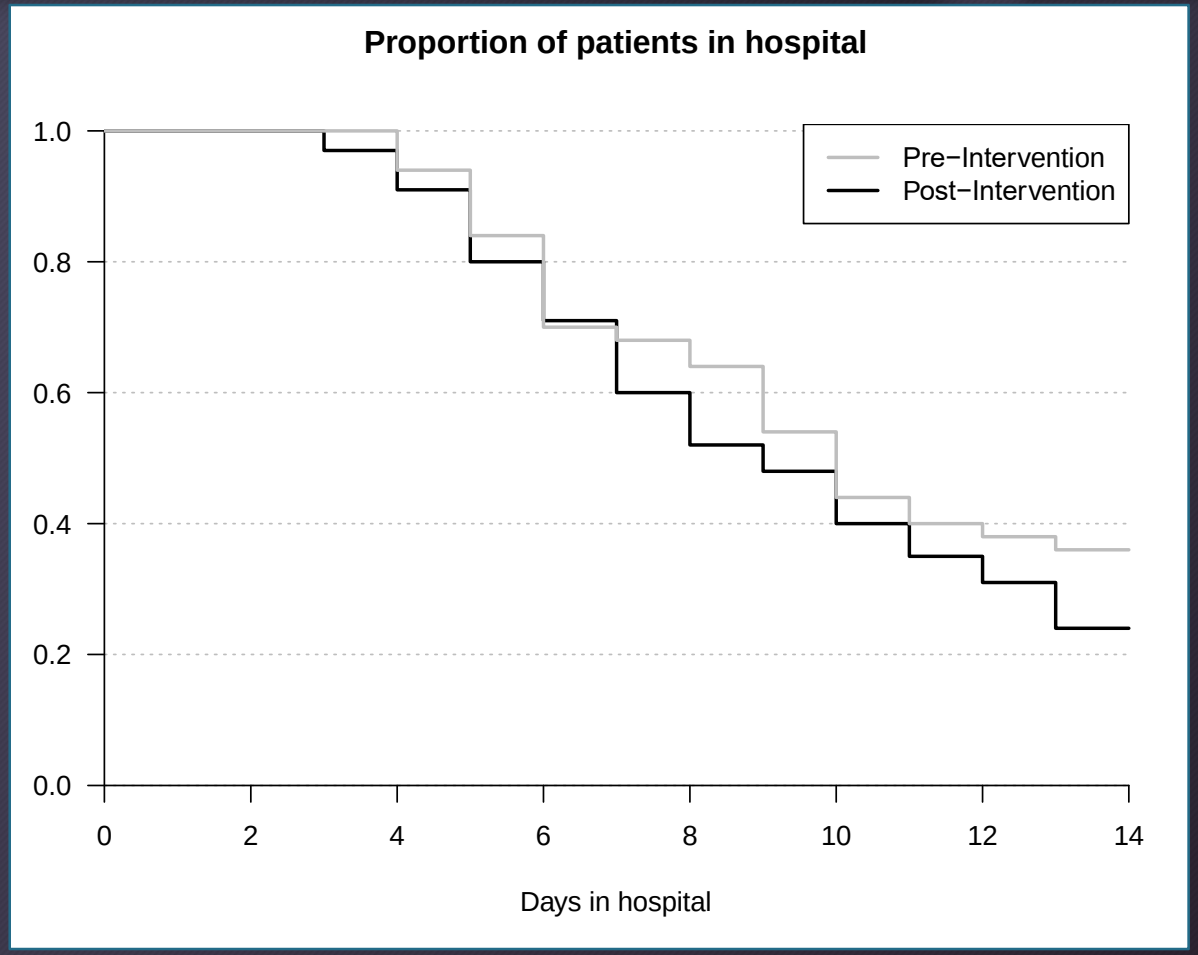
- GPC in clusters
  - 92% had repeat blood cultures – 2.4 fold increase from baseline

Is Faster Better?

Tesla Model S P100D

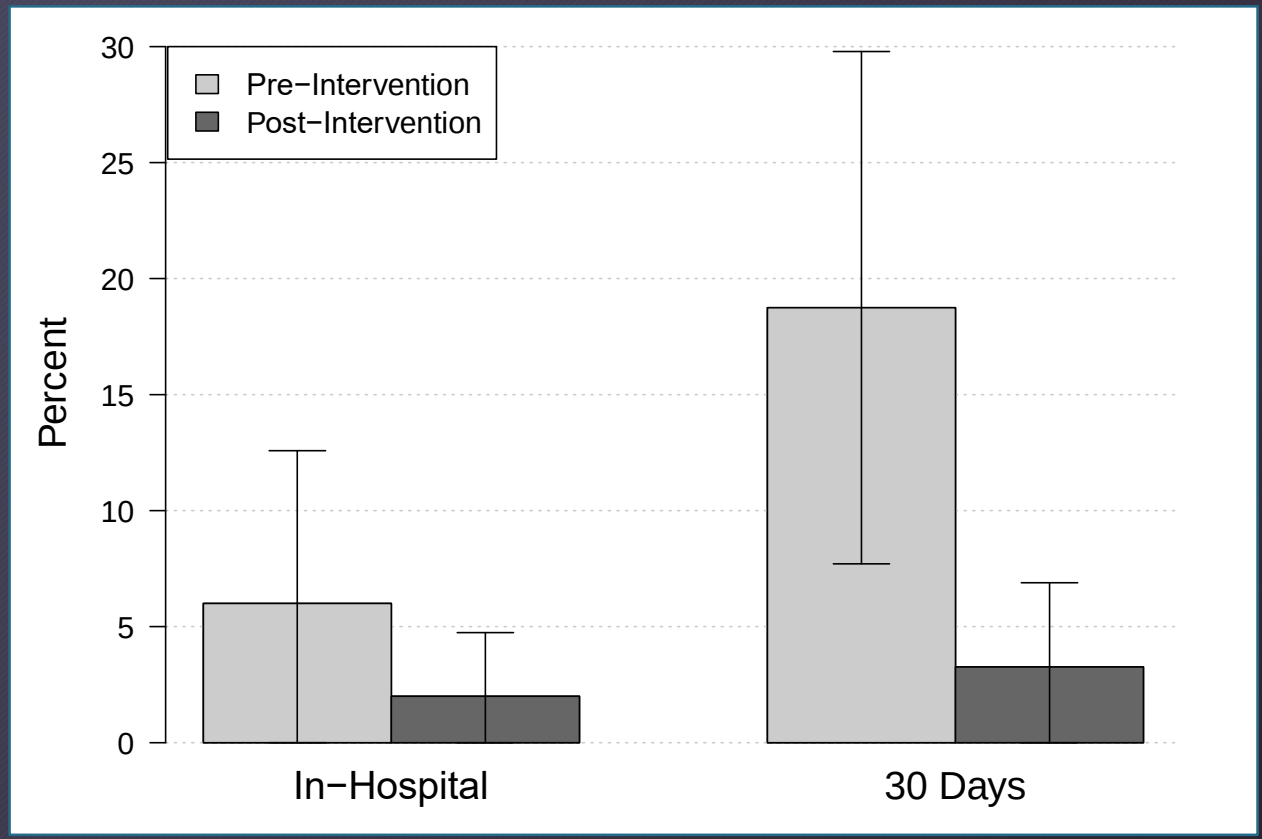
Community-onset *Staphylococcus aureus* Bacteremia

- 50 pre-RBRP; 100 post-RBRP
- Reduced length of stay (LOS)
- Median LOS
  - Pre-RBRP: 9 (IQR: 6-15) days
  - Post-RBRP: 9 (IQR: 6-13) days
  - Adjusted hazard ratio:
    - 0.49
    - 95% CI: 0.26 – 0.92; p=0.026



Community-onset *Staphylococcus aureus* Bacteremia

- 30-day mortality was reduced by 93%
  - Pre-RBRP: 9 (19%)
  - Post-RBRP: 3 (3%)
  - Adjusted odds ratio: 0.072, 95% CI: 0.009 – 0.365, p=0.004
- Number needed to treat to prevent 1 death at 30 days: 7



2019 ASHP Best Practice Award

Conclusions

- Rapid diagnostics have revolutionized the clinical microbiology laboratory
- Selection and implementation of rapid diagnostic tools should be tailored to institutional needs
- Antimicrobial stewardship programs are key to achieving benefits

Tesla. https://www.tesla.com/models Accessed 6/27/22

Acknowledgements

- Alan Junkins, PhD, D(ABMM), Chief of Microbiology, Norton Healthcare
- Norton Healthcare microbiology staff
  - Brent Cox
  - Susie Hancock