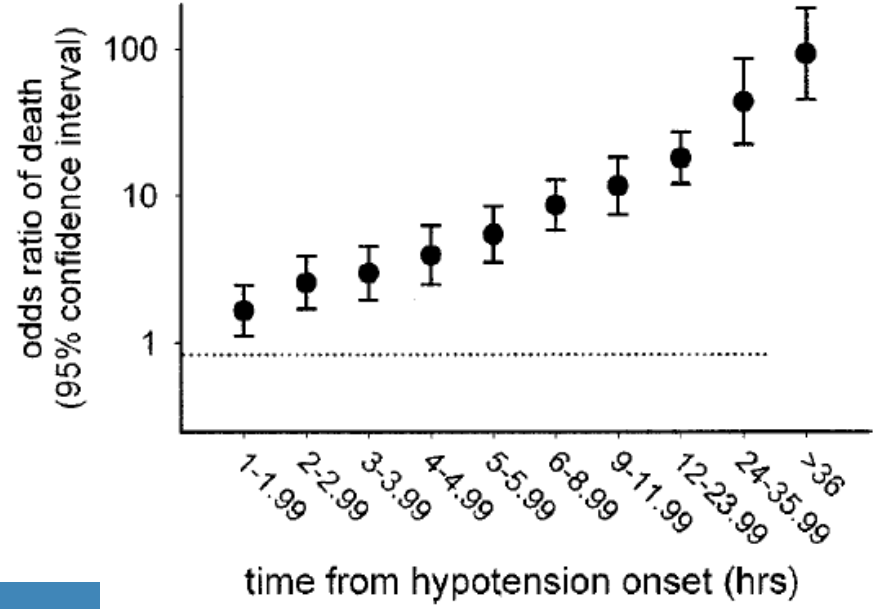
Rapid diagnostics and antibiotic stewardship

Ritu Banerjee, MD, Ph.D
Vanderbilt University Medical Center

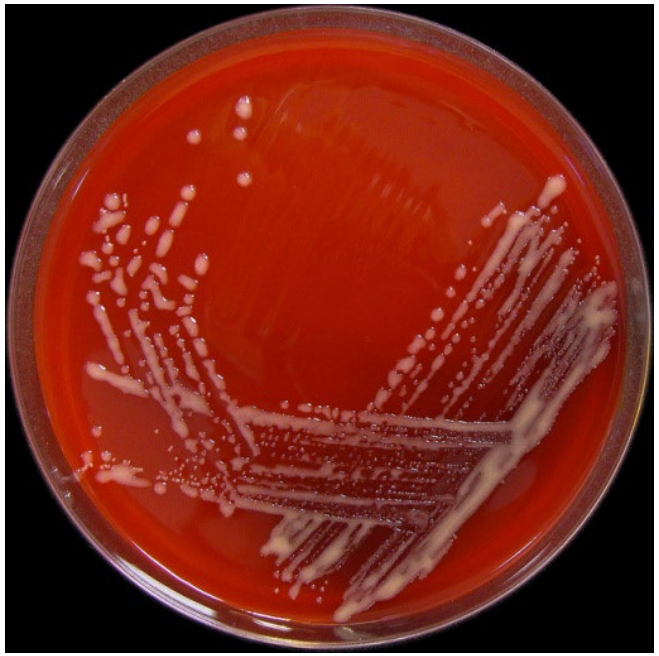
Sepsis



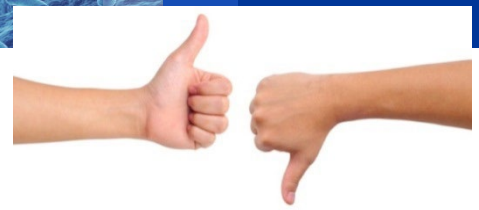
What antibiotic should I prescribe?

Conventional bacterial blood cultures and AST

- Standard methods are SLOW
- Results take >2 days AFTER positive culture
- Empiric antibiotics before pathogen ID/susceptibility



Observational Studies: Rapid blood culture dx and outcomes



Test	ASP	Decrease TOT*	Mortality benefit	ΔLOS (days)	Cost savings	Study
PNA FISH	Y	Y	Y	N	-	Forrest 2008
Xpert MRSA	Y	Y	Y	-6.2	21K	Bauer, 2010
MALDI-TOF	Y	Y	Y	-1.8	19K	Perez, 2013
MALDI-TOF	Y	Y	Y	-2.8	-	Huang, 2013
Verigene GP	Y	Y	N	-21.7	60K	Sango, 2013
mecA PCR	Y	Y	-	-3	-	Nguyen, 2010
PNA FISH	N	N	-	N	-	Holtzman, 2011
Verigene	N	Y	Y	-	Y	Suzuki, 2015
BCID	Y	Y	-	-	-	Messacar, 2016
MALDI-TOF	Y	Y	N	N	-	Malcolmson, 2016
BCID	Y	N	N	N	-	Tseng, 2018
Accelerate Pheno	Y	Y	-	-	-	Robinson, 2021
Metaanalysis (31 studies)	Y/N	Y	Y (ASP only)	Y	-	Timbrook, 2017

TOT, time to optimal therapy

Clinical impact of rapid blood culture diagnostics: RCTs

Test	Org.	SS	ASP	Decreased TOT*	Mortality benefit	ΔLOS (days)	Cost savings	Study
1. Same day Microscan	All	573	N	Y	Y	N	Y	Doern, 1994, US
2. Multiplex PCR	All	250	N	Y	N	N	-	Beuving, 2015, Netherlands
3. BCID	All	617	Y	Y	N	N	N	Banerjee, 2015, US
4. MALDI-TOF	All	425	Y	Y	N	N	-	Ostoff,2017, Switzerland
5. Accelerate Pheno	GN	448	Y	Y	N	N	N	Banerjee, 2020, US
6. MALDI-TOF	All	3127	Y	N	N	N	N	MacGowan 2020, England and Wales
7. QMAC-dRAST	All	89	Y	Y	N	N	N	Kim, 2021, Korea
8. Accelerate Pheno	GN	205	Y	Y	N	-2	-	Christensen, 2022, US

* TOT, time to optimal therapy

Blood Culture IDentification (BCID) trial
Single center, prospective RCT

Patients with positive blood cultures
(n = 617)

Stratified randomization (age, ICU, transplant svc)

Control
(n = 207)

- Gram stain called to service
- Standard culture and susceptibility (1-3 d)
- Baseline testing: MALDI-TOF, PBP2a

BCID
(n = 198)
TEST ALONE

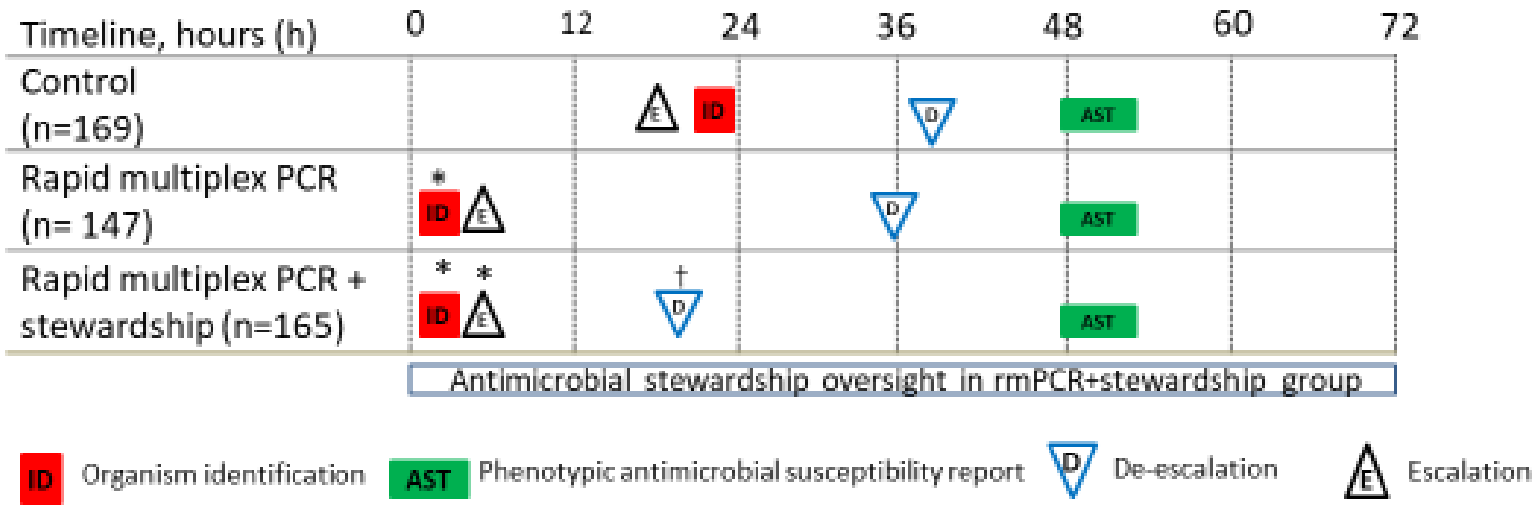
- Gram stain called to service
- Standard culture and susceptibility (1-3 d)
- BCID plus lab call with comments (1 h)

BCID plus stewardship
(n = 212)
TEST PLUS ID RECS

- Gram stain called to service
- Standard culture and susceptibility (1-3 d)
- BCID plus lab call with comments (1 h)
- ID MD/pharmacist call with specific tx recs

Banerjee et al, (2015) CID 61: 1071

Comparison of median time to identification, susceptibility results, and time to antibiotic modifications



Among subset of patients with organisms on BCID panel (n=481)
*significant vs. control
†significant vs. control and BCID

Banerjee et al, (2015) CID 61: 1071

Clinical Outcomes

Outcome	Control (n= 207)	BCID (n=198)	BCID + Stewardship (n=212)	P – value
Length of stay (days)	8 (5,15)	8 (5,15)	8 (5,16)	0.60
ICU within 14 days	16 (7.7%)	5 (2.5%)	10 (4.7%)	0.06
30-day mortality	22 (10.6%)	20 (10.1%)	18 (8.5%)	0.74
30-day readmission[1]	6 (2.9%)	6 (3%)	8 (3.8%)	0.88
Toxicity/ adverse drug rxn	3 (1.4%)	3 (1.5%)	2 (0.9%)	0.82
Blood cx clearance in 3d	147 (71%)	131 (66%)	146 (69%)	0.79
C. difficile/ MDRO[2] in 30d	15 (7.2%)	16 (8.1%)	21 (9.9%)	0.62
Overall costs[3]	$65,450 ($27,192)	$66,887 ($23,935)	$68,729 ($29,064)	0.78

[1] with same organism; [2]VRE, MRSA, ESBLs, Gram-negatives resistant to ≥ 3 drug classes;
[3]Mean (median) among inpatients with available data (n= 544)

Banerjee et al, (2015) CID 61: 1071

RAPIDS GN Trial

RAPIDS-GN
Antibacterial Resistance Leadership Group

Prospective Randomized Controlled Trial

Patients with Gram-negative bacilli in blood culture bottle (n = 500)

Randomization in lab

Control (n = 250)

- Gram stain called to service
- Standard subculture and AST
- Baseline AS

Rapid testing (n = 250)

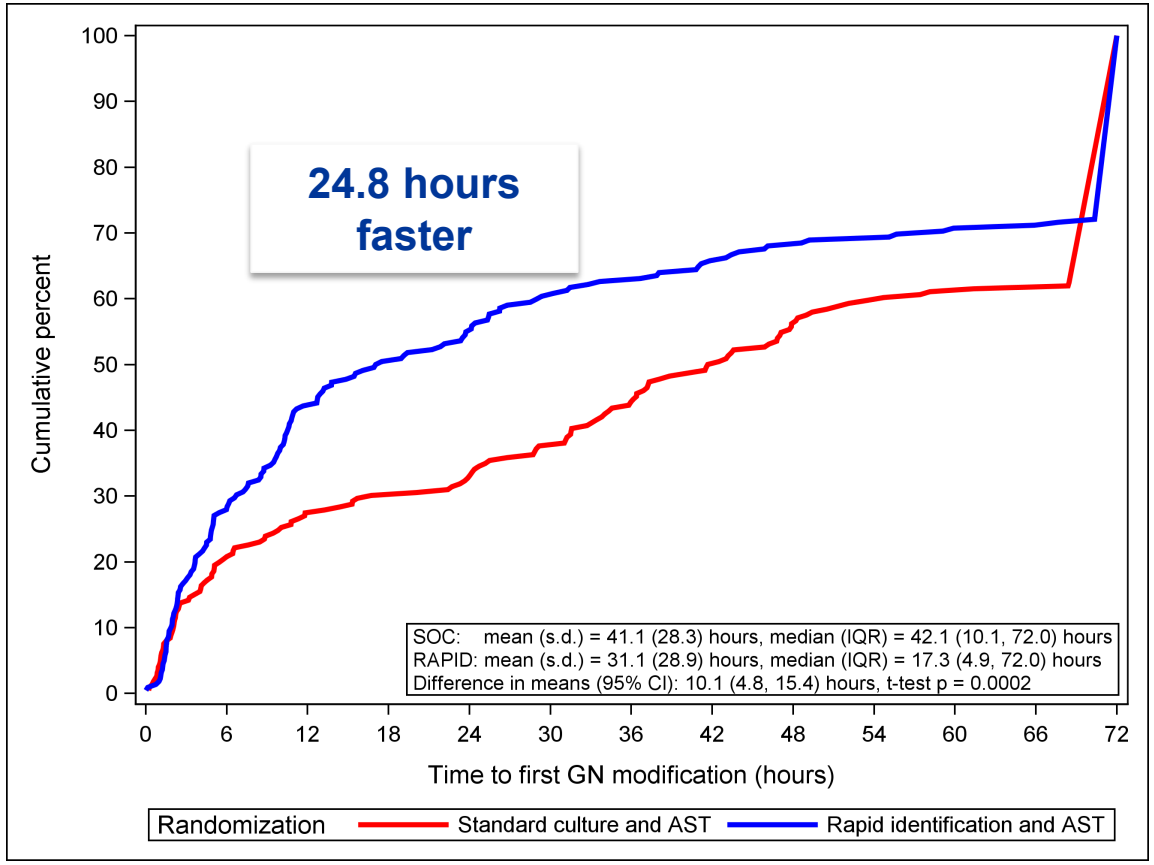
- Gram stain called to service
- Standard subculture and AST
- Rapid test + lab call with ID
- Baseline AS

AS, antimicrobial stewardship; ID, identification; AST, antimicrobial susceptibility testing

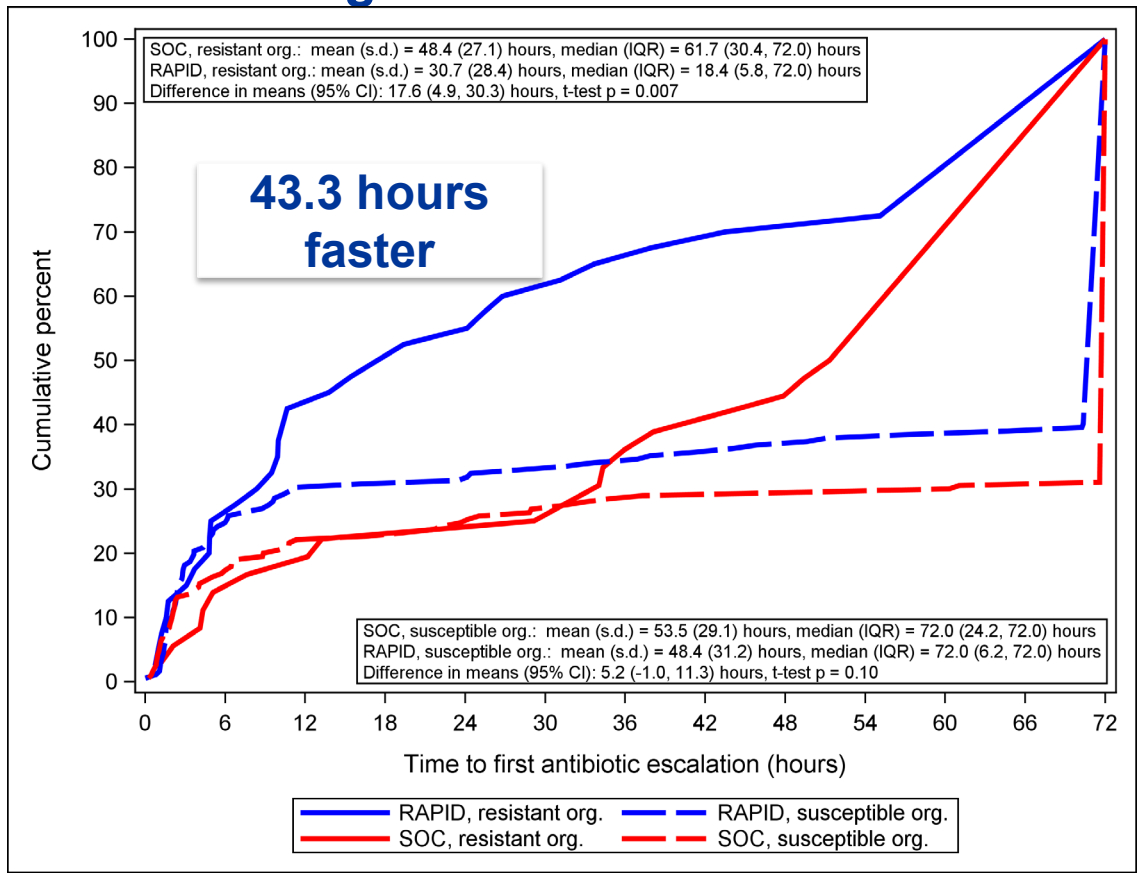
RAPIDS GN trial

RAPIDS-GN
Antibacterial Resistance Leadership Group

Time to Gram neg antibiotic change



Resistant Organisms: Time to abx escalation



Lessons learned from blood culture trials

- Rapid blood culture diagnostics **implemented with stewardship** can optimize treatment of bloodstream infections
  - Faster antibiotic modifications
  - More judicious antibiotic use

- **Context and study design** are important
  - Local resistance rates, antibiotic prescribing patterns, patient populations, availability of ASPs, lab practices
  - Clinical benefits seen in observational studies were not replicated in RCTs
  - Endpoints

Selection of endpoints for clinical utility studies

- Laboratory
  - TAT for organism ID and AST result
  - Workflow efficiencies
- Infection control
  - Time to isolation
  - Turnover of isolation rooms
- Antibiotic stewardship
  - Broad vs. narrow spectrum abx
  - Abx escalation/de-escalation
  - Time to effective treatment
  - # stewardship recs and % accepted
- Mortality
- LOS
- Readmissions
- MDRO acquisition
- Adverse Events
- Cost/cost avoidance
- Population-level impact on AMR

ID diagnostics: unmet needs

- Direct from specimens (pathogen and resistance)
- Faster methods, POC
- Rule in or out bacterial infection
- Distinguish colonization vs. infection