Fighting Resistance with Rapidity: Antimicrobial Stewardship and Rapid Diagnostics

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Disclosure

- **I have no actual or potential conflicts of interest in relation to this program or presentation**

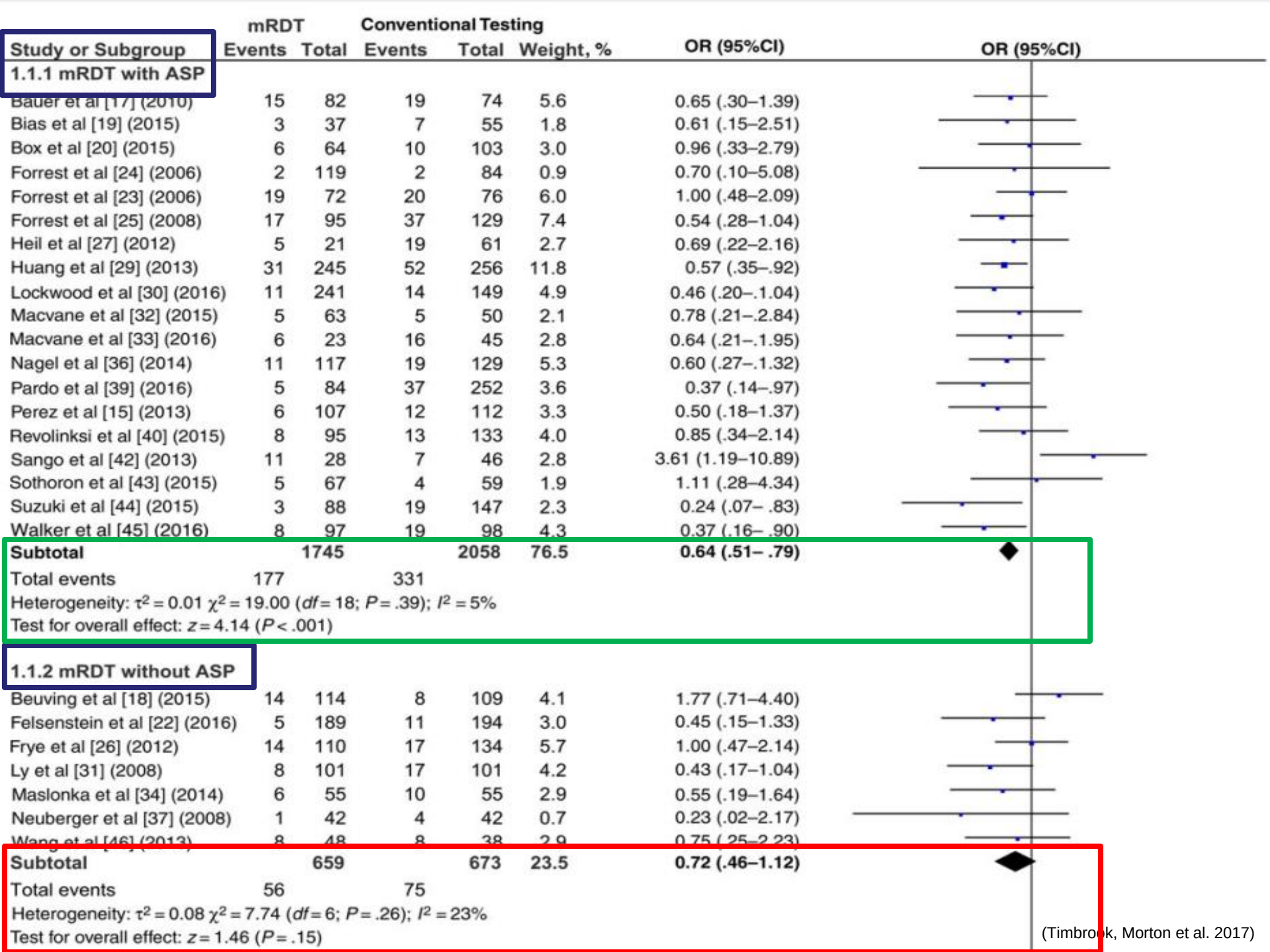
Objectives

- Review impact and knowledge of rapid diagnostic tests (RDTs)
- Discuss diagnostic stewardship and its components
- Examine the RDT and antimicrobial stewardship (ASP) relationship
- Identify limitations and future directions of RDTs and ASPs

Stewardship Guidelines

- **Recommend implementing syndrome-based interventions**
- **Endorses the use of RDTs in bloodstream infections (BSIs) with ASP intervention**
  - **“Weak” recommendation with moderate quality evidence**

(Barlam, Cosgrove et al. 2016)



(Timbrook, Morton et al. 2017)

RDT Knowledge

- **Electronic survey of 224 ID PharmDs**
  - **87.9% with ≥0.5 FTE for ASP**
  - **73% with RDT for <3 years**
- **Multiplex PCR most common RDT @ 42.1%**
  - **58% reported familiarity with multiplex PCR**
- **ONLY 32.5% had assessed outcomes related to RDT implementation**

(Foster, Kuper et al. 2017)

RDT Knowledge

- **Electronic survey of 156 physicians**
- **60% would adjust therapy based on RDT result**
- **29.4% had viewed the ASP website for RDT interpretation guide**
  - **Significantly better knowledge scores for those who had viewed guide**

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(Donner, Campbell et al. 2017)

Diagnostic Stewardship

Goal	Key question	Key considerations and potential strategies
Right test	Is the test appropriate for the clinical setting?	Sensitivity and specificity Predictive values Testing volumes Diagnostic yield Laboratory feasibility Cost Clinical impact
Right patient	Will the clinical care of the patient be affected by the test result?	Laboratory test utilization committee Automatic laboratory reflex CPOE decision support Appropriate use criteria Indication selection Prior authorization Benchmarking Specimen rejection
Right time	Will the result be available in time to optimally affect care?	Time to specimen receipt Centralized vs point-of-care testing On-demand vs batched testing Specimen preparation time Run time Result reporting time

(Messacar, Parker et al. 2017)

Diagnostic Stewardship

Parameter	Cost ($) per patient[a] Preintervention (n = 233)	Intervention (n = 247)	P value
Cost accounting system			
ICU	13,783 (41,235)	11,023 (24,666)	0.279
Acute care	9,977 (12,463)	9,901 (11,050)	0.566
Pharmacy	5,172 (14,743)	5,501 (10,388)	0.169
Respiratory/pulmonary	3,211 (9,158)	3,139 (10,409)	0.435
Blood procedures	2,724 (11,346)	3,399 (9,987)	0.005
Laboratory	2,188 (4,671)	1,998 (2,537)	0.182
Imaging service	2,177 (3,815)	2,155 (3,514)	0.337
Operating room	1,407 (5,529)	1,790 (7,435)	0.771
Cardiac services	929 (4,740)	924 (5,274)	0.179
Emergency service	698 (1,693)	910 (2,150)	0.851
Anesthesia	224 (813)	207 (574)	0.512
Nephrology	690 (2,463)	958 (2,667)	0.266
Other[c]	1,816	596	NS[d]
Total[b]	44,996 (88,119)	42,501 (56,604)	0.209
MALDI-TOF device, reagent, and antimicrobial stewardship pharmacist time (intervention period only)	0	79	
Pharmacist time	0	36	
MALDI lease (3 mo)		40	
Isolate identification and personnel costs		3	
Vitek for organism identification (3 mo; preintervention only)[e]	23	0	
Total (cost accounting plus incremental costs for intervention)	45,019	42,580	NS

(Patel, Kaakeh et al. 2017)

Diagnostic Stewardship

Core Element	How RDT impacts or fulfills core element
Leadership Support • financial support	• Financial backing required from administration for initial fixed and variable costs associated with implementation of RDT
Accountability • physician leader responsible for ASP	• Accountable for RDT implementation and outcomes • Can prioritize use of RDT as daily ASP activities • Advocate resource utilization to appropriately implement, track, and report results
Drug Expertise • pharmacist leader to improve antibiotic utilization	• ASP pharmacist generally performs daily ASP interventions • Help streamline process for antibiotic administration from pharmacy in timely manner • Helps collect and analyze data
Actions • implement specific intervention to improve antibiotic use	• Prospective audit and feedback on positive blood cultures • Considered advanced activity per Playbook as diagnosis and infection-specific intervention • Align with local needs • Measurable outcomes

Diagnostic Stewardship

Core Element	How RDT impacts or fulfills core element
Tracking/Monitoring • process measures • monitoring compliance with specific intervention in place	• Considered intermediate activity to monitor a specific intervention per Playbook • RDT provides a tangible outcome to monitor and is targeted • Event is not too frequent resulting in extensive data collection • Outcomes include: mortality, LOS, time to appropriate therapy, time to optimal therapy
Reporting • share outcomes with key stakeholders	• Outcomes shared with key stakeholders • C-suite: confirms continual ASP support, demonstrate follow through for accountability core element • Pharmacy Director use reporting as demonstration of pharmacy activities and impact • Other stakeholders: various subgroups within hospital that may benefit – ie ED, ICU
Education • can perform education to clinicians	• Provided at RDT roll out to improve acceptance rates • RDT data may be provided to improve confidence in ASP when making recommendations with RDTs

RDT & ASP

Goal	Key question	Key considerations and potential strategies[a]
Right interpretation	Will the clinician understand the test result?	Result report language Selective reporting of relevant results AS prospective audit and feedback AS real-time decision support
Right antimicrobial	Will the clinician appropriately modify antimicrobials based on the test result?	Clinical practice guidelines EMR-based decision support with result reporting AS prospective audit and feedback AS real-time decision support
Right time	Will the clinician act upon the test result promptly?	EMR reporting Results called with readback reporting AS prospective audit and feedback AS real-time decision support

(Messacar, Parker et al. 2017)

RDT & ASP Outcomes

- Time to effective therapy
- Time to optimal therapy
- Duration of therapy
- SAAR
- Infection control
- Patient isolation
- Clinical cure
- Mortality
- Cost

RDT & ASP & Microbiology

- **Laboratory verification of RDT**
- **Communication of RDT results**
- **Interface with LIS and EMR**
- **Reporting of RDT and traditional culture results**

RDT & ASP

Blood Culture Assay	Pathogens Detected	Resistance Markers	Turnaround Time (After Blood Cultures Turn Positive)
PNA-FISH	*Staphylococcus aureus*, CoNS, *Enterococcus faecalis*, other enterococci, *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Candida albicans, Candida parapsilosis, Candida glabrata, Candida krusei, Candida tropicalis*	No	1.5–3 h
*Quick*FISH	*S. aureus*, CoNS, *E. faecalis*, other enterococci, *E. coli, K. pneumoniae, P. aeruginosa*	No	<30 min
MALDI-TOF[a]	Gram-positive and gram-negative bacteria, yeast, fungi, filamentous fungi, mycobacteria	In development	10–30 min
Gene Xpert MRSA/SA	*S. aureus*	*mecA*	<1 h
Verigene gram-positive blood culture (BC-GP)	*S. aureus, Staphylococcus epidermidis, Staphylococcus lugdunensis, Streptococcus anginosus group, Streptococcus agalactiae, Streptococcus pneumoniae, Streptococcus pyogenes, E. faecalis, Enterococcus faecium, Staphylococcus* spp., *Streptococcus* spp., *Listeria* spp.	*mecA, vanA, vanB*	2.5 h
Verigene gram-negative blood culture (BC-GN)[b]	*Escherichia coli, Shigella* spp., *K. pneumoniae, Klebsiella oxytoca, P. aeruginosa, Serratia marcescens, Acinetobacter* spp., *Proteus* spp., *Citrobacter* spp., *Enterobacter* spp.	KPC, NDM, CTX-M, VIM, IMP, OXA	2 h
FilmArray blood culture identification (BC ID)	*S. aureus, Staphylococcus* spp., *S. agalactiae, S. pneumoniae, S. pyogenes, Streptococcus* spp., *Enterococcus* spp., *Listeria monocytogenes, Hemophilus influenza, Neisseria meningitides, Enterobacter cloacae* complex, *E. coli, K. pneumoniae, K. oxytoca, P. aeruginosa, Serratia marcescens, Acinetobacter baumanii, Proteus* spp., *C. albicans, C. glabrata, C. krusei, C. parapsilosis, C. tropicalis*	*mecA, vanA, vanB*	1 h

RDT limitations

- Not universal organism coverage
- Lack of resistance determinants
- Solely genotypic resistance markers
- No direct-from-specimen bacterial RDTs
- Few non-blood RDTs
- Costs
- Cannot replace conventional microbiology

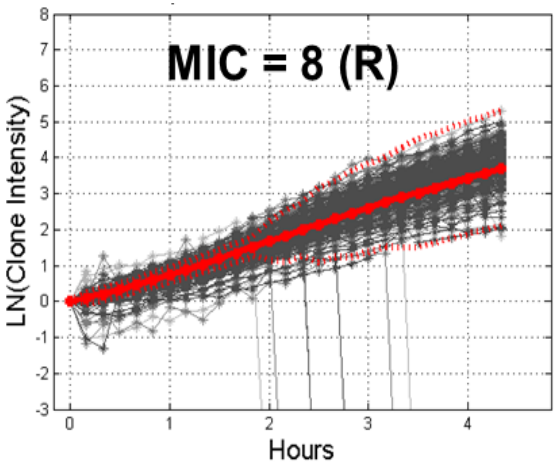
Future of RDTs & ASP

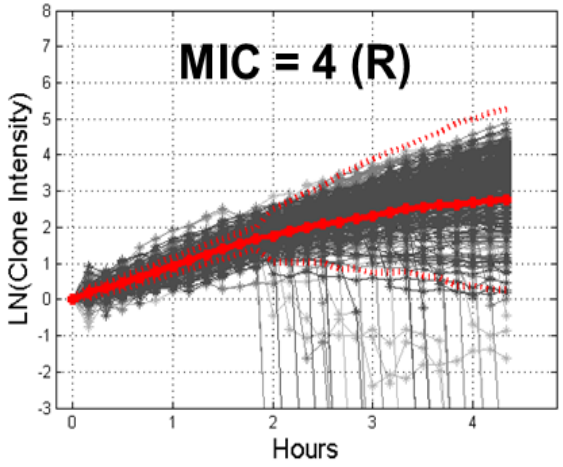
- **Improve study design of RDT + ASP studies**
- **Direct-from-blood/specimen assays**
- **Total laboratory automation**
- **Registrational trials incorporating RDTs**
- **Pharma pairing with diagnostic companies**

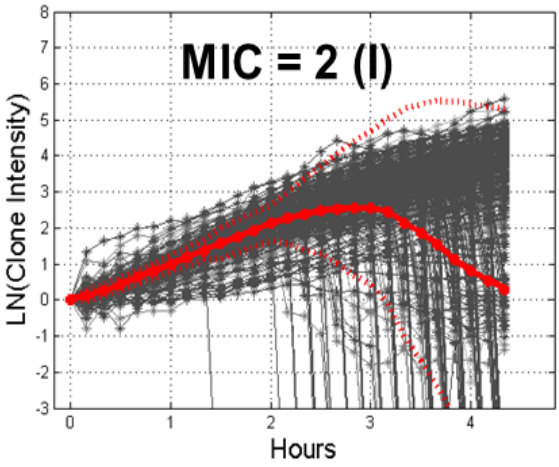
Accelerate Pheno™ BC Kit

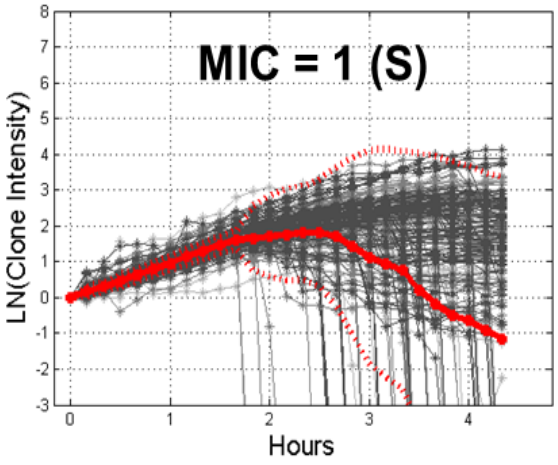
- **Identification and susceptibility directly from positive blood cultures within 7 hours**
- **Morphokinetic cellular analysis**
  - **ID and AST based on established reference values for mass, shape, growth pattern, and growth rate**

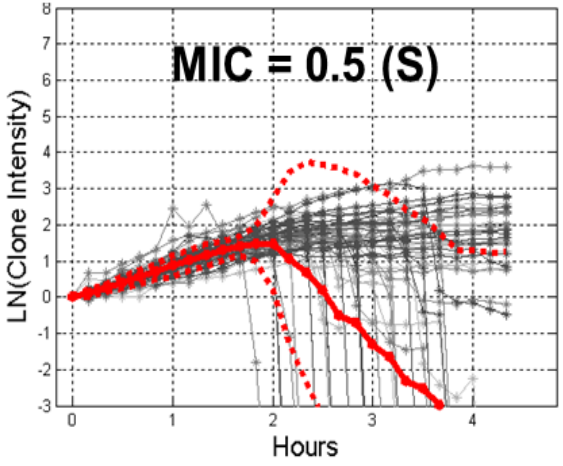
Accelerate Pheno™ BC Kit

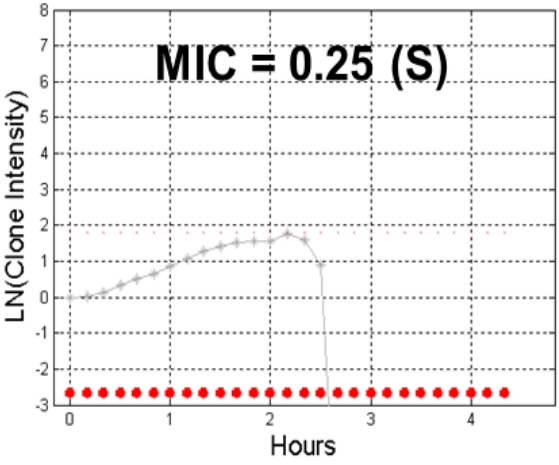












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Accelerate Pheno™ BC Kit

Gram-Positive	Sens.	Spec.
S. aureus	97.9	98.5
Coag-negative Staph spp.	95.3	98.2
S. lugdunensis	97.5	99.9
E. faecium	98.0	99.1
E. faecalis	97.0	99.9
Streptococcus spp.	97.2	97.6
Gram Positive Total	**97.0**	**98.9**

Antibiotic	EA%	CA%
Ceftaroline	94.9	99.5
Daptomycin	98.1	99.6
Vancomycin	97.2	97.9
Erythromycin	98.3	96.6
Linezolid	98.9	99.6
Ampicilin	100.0	100.0
TMP-SMX	96.0	96.0
Doxycycline	94.4	95.8

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Gram-Negative	Sens.	Spec.
Escherichia coli	97.3	99.7
Klebsiella spp.	96.1	99.6
Citrobacter spp.	96.8	99.3
Enterobacter spp.	97.3	99.5
Proteus spp.	97.7	99.6
Serratia marcescens	100	99.9
Pseudomonas aeruginosa	100	99.4
Acinetobacter baumannii	98.6	99.7
Gram Negative Total	**97.6**	**99.6**

Antibiotic	EA%	CA%
Amikacin	93.8	93.8
Gentamicin	99.5	98.7
Tobramycin	96.3	96.0
Ertapenem	98.8	98.5
Meropenem	96.7	96.9
Cefazolin	95.7	85.6
Cefepime	96.2	95.5
Ceftazidime	92.4	92.1
Ceftriaxone	94.7	96.4
Cipro	98.4	98.4
Aztreonam	96.4	97.6
Amp-Sulb	91.0	82.7
Pip-Taz	91.0	90.8
Colistin	94.9	97.6

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Antimicrobial Agent	AXDX Reportable MIC Ranges					
	E. coli	*Klebsiella* spp.	*Enterobacter* spp.	*Proteus* spp.	*S. marcescens*	*Citrobacter* spp.
Amikacin	4-128	4-128	4-128	4-128	4-128	4-128
Gentamicin	1-32	1-32	1-32	1-32	1-32	1-32
Tobramycin	1-32	1-32	1-32	1-32	1-32	1-32
Cefepime	1-32	1-32	1-32	1-32	1-32	1-32
Ceftazidime	2-32	2-32	2-32	1-32	1-32	2-32
Ceftriaxone	0.25-8	0.25-8	0.25-8	0.5-8	0.5-8	0.25-8
Cefazolin-CLSI	0.5-16	0.5-16				
Ertapenem	0.12-4	0.12-4	0.12-4	0.12-4	0.12-4	0.12-4
Meropenem	0.25-8	0.25-8	0.5-8	0.25-8	0.25-8	0.25-8
Ciprofloxacin	0.25-8	0.25-8	0.5-8	0.25-8	0.25-8	0.25-8
Amp-sulb	2-64	2-64		4-64		
Pip/tazo	4-256	4-256	4-256	4-256	4-256	4-256
Aztreonam	1-32	1-32	1-32	1-32	1-32	1-32
Colistin	**0.5-8**	**0.5-8**	**0.5-8**			**0.5-8**

Limitations

- Does not cover all organisms
- ID and AST affected by low clone counts and loss of camera focus
- COST
  - 1 sample per module at a time
  - $120,000 for system with 1 module
  - $80,000 each additional module
  - $250/sample
  - ~$15,000 in yearly maintenance

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