MOLECULAR DIAGNOSTICS FOR PNEUMONIA: A BREATH OF FRESH AIR IN THE SMOG OF CULTURE?

Potential impact of molecular methods on diagnosis and antibiotic stewardship for patients with lower respiratory tract infections

Blake W. Buchan, PhD, D(ABMM)
Assistant Professor, Dept. of Pathology
Associate Director, Clinical Microbiology
and Molecular Diagnostics
The Medical College of Wisconsin

Disclosures

Research support	Meeting/travel support	Consulting/honoraria
◦ **BioFire Diagnostics**	◦ **BioFire Diagnostics**	◦ **BioFire Diagnostics**
◦ **Curetis**	◦ ChromaCode	◦ ChromaCode
◦ **Accelerate**	◦ Alere	◦ Luminex
◦ Quidel	◦ iCubate	◦ Genmark
◦ ChromaCode		
◦ Luminex		
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◦ Alere		
◦ iCubate		

BOLD: Products discussed today

Objectives

- Provide an overview of lower respiratory tract infections (LRTIs)
- Recognize the shortcomings of culture-based methods for diagnosis of LRTIs
- Understand the correlation between molecular and culture-based results
- Realize the potential impact of molecular tests on antimicrobial stewardship and patient care

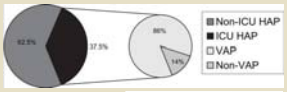
Respiratory Illness

- Fourth leading cause of death worldwide
  - Respiratory symptoms are leading reason for unscheduled outpatient healthcare visit
    - Account for ~3.0% of all physician visits, 2.3M/yr in US
    - May lead to more severe illness
      - Asthma exacerbation, LRTIs (pneumonia, bronchiolitis, etc.)
  - Prevalence
    - Seasonal distribution, spike in colder months
  - Organisms
    - Viral – Most common
    - Bacterial
    - Fungal

Loffelholz et al. *Int. J. Microbiol. 2010*
Naghavi et al. *Lancet. 2015 Jan 10;385(9963):117-71*
Hing et al. *National Health Statistics Report. 2010*

Respiratory Illness

- Epidemiology - Inpatient
  - Hospital acquired pneumonia (HAP)
    - Affects ~1% of all hospital admissions
    - Accounts for 15-18% of all nosocomial infections (2nd to UTI)
      - Mortality highly variable based on underlying condition
  - Ventilator acquired pneumonia (VAP)
    - Second most common nosocomial infection in ICUs
    - Affects 9-27% of patients with mechanical ventilation
      - 1.2-8.5/1,000 vent days; 9-13% mortality, **50% of abx utilized in ICU**
  - Organisms
    - Most commonly bacterial, rarely viral/fungal
      - Pooling of secretions/biofilm/impaired clearance
      - Microaspiration and direct inoculation of bacteria to LRT



Organism	%
P. aeruginosa	24.4
S. aureus	20.4
Enterobacteriaceae	14.1
Streptococcus spp	12.1
Haemophilus	9.8
Acinetobacter	7.9
Neisseria spp	2.6
S. maltophilia	1.7
Others	4.7

Kalanuria et al. *Critical Care.* 2014
Kalil et al. *Clin. Infect. Dis.* 2016
Rotstein et al.. *Can J Infect Dis Med Microbiol* 2008

Practice and Consequences

- Prognosis/Mortality
  - Dependent on severity index, early empiric antibiotics, laboratory diagnosis

Table 5. Variables associated with early (≤2 days), late (≥3 days) and total mortality[a]

Variable	% mortality			Multivariate OR (95% CI)			Multivariate p value		
	Early	Late	Total	Early	Late	Total	Early	Late	Total
PSI risk class									
Low-risk (classes I, II, IID	0.2	1.9	2.1	13.0 (4.0–42.6)	6.1 (4.0–9.3)	7.3 (4.9–10.9)	<0.01	<0.01	<0.01
High-risk (classes IV, V)	3.1	12.1	15.2						
Empirical antibiotic									
No IDSA/ATS first choice	1.2	8.1	9.3	–	0.6 (0.5–0.8)	0.7 (0.5–0.9)	NS	<0.01	0.02
IDSA/ATS first choice	1.7	5.8	7.4						
Aetiological diagnosis									
No	1.8	7.2	8.9	–	0.5 (0.3–0.8)	0.5 (0.3–0.8)	NS	<0.01	<0.01
Yes	1.3	6.4	7.7						

Garau J et al. Clin Microbiol Infect. 2008 Apr;14(4):322-9

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Laboratory Challenges – Diagnosis of LRTI

- Bacterial "pathogens"
  - Common pathogens are often upper respiratory flora/colonizers
- Specimen
  - Sputum/ETA
    - More likely to contain URT/oral flora → poor PPV
    - Difficult to manipulate → viscosity impacts plating reliability/quantitation
  - BAL
    - "Clean" LRT specimen but susceptible to sampling bias, invasive
- Organisms and thresholds
  - Conditional – *S. pneumoniae, H. influenzae, M. catarrhalis, P. aeruginosa, S. aureus, Enterobacteriaceae*
    - Quant: PSB ≥10^3 BAL≥10^4, SPU/ETA ≥ 10^5-10^6
    - Semi-quant: "Significant" quantity (2+), predominance, > NOF, ≥ 3 pathogens is MPI

≥48-72 h for ID/AST

ATS HAP/VAP Guidelines 2017

Focus on minimizing exposure to unnecessary abx through de-escalation and shorter abx courses to treat LRTIs

- Target initial empiric broad-spectrum therapy
  - Use of local antibiogram to inform therapy – requires rapid, accurate, ID
  - Use of prevalence/risk-based risk for MRSA therapy
    - >20% prevalence, hx of IV abx, > 5 days since admission, or critically ill
- Laboratory Dx
  - Guidelines focus on sensitivity over specificity
  - Recommend non-invasive, semi-quant Cx

Molecular test could support goal of ATS through rapid result and high sensitivity/NPV

European HAP/VAP Guidelines 2016

Focus on minimizing exposure to unnecessary abx through de-escalation and shorter abx courses to treat LRTIs

- Target initial empiric therapy
  - Narrow-spectrum therapy (e.g. Ceftriaxone, Moxifloxacin)
    - Low-risk and early onset HAP/VAP
    - <5 days into admission, no septic shock, low prevalence of hospital MDRO (<25%)
  - Broad-spectrum therapy (e.g. Pip/Tazo, Cefepime)
    - High-risk or late onset HAP/VAP
- Laboratory Dx
  - Guidelines focus on specificity over sensitivity
  - Recommend invasive, quantitative Cx

Semi-quantitative result required to support European guidelines

Molecular Options (Targeted)

- MRSA
  - ~60% of ICU patients meet IDSA criteria for empiric anti-MRSA therapy
    - ~5% culture prevalence, ~8% NAAT prevalence

S. aureus		Culture	
		Positive	Negative
NAAT	Positive	71	73
	Negative	1	438

Sensitivity: 98.6% **NPV: 99.8%**
Specificity: 85.7% PPV: 49.3%

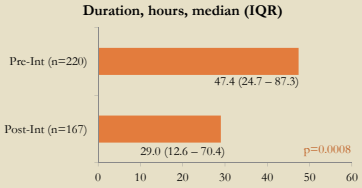
MRSA		Culture	
		Positive	Negative
NAAT	Positive	28	20
	Negative	1	534

Sensitivity: 96.6% **NPV: 99.8%**
Specificity: 96.3% PPV: 58.3%

~65% of "false positive" specimens had *S. aureus* on culture plate, not reported due to laboratory policy
- ~50% of patients had *S. aureus* reported in culture from subsequent specimen

Molecular Options (Targeted)

- MRSA
  - Impact of NAAT on anti-MRSA therapy



Pharmacist recommend **de-escalation** for **27% of patients** with negative result
- Co-morbidity
- Potential BSI, wait for BC result

Pharmacist recommendation **accepted in 92% of cases**

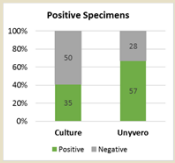
Molecular Options (Panels)

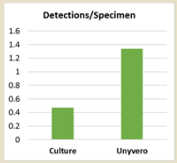
	FilmArray Pneumo	Unyvero LRT	Accelerate Respiratory
Regulatory	FDA-review	FDA-cleared	Development
Technology	NAAT	NAAT/array	Microscopy/FISH
Specimen	Sputum, ETA, BAL	Sputum, ETA	?
Bacterial targets	18	20	?
Viral targets	8	0	0
Resistance	7	17 (FQ, *shv*, *tem*, *ermB*)	Phenotypic
Result	Semi-quantitative	Qualitative	Quantitative
Workflow	Sample-Result	2-step (Lysis, Analysis)	2 step ?
Time to result	~ 1 hour	4.5-5.5 h	8-12 h ?

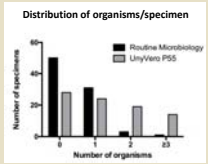


Unyvero: Overview

- **Qualitative** multiplex MolDx
  - Study #1: 85 Sputum or ETA specimens (HAP, VAP, CAP)
    - Results compared to semi-quant SOC culture report







Positive: ≥ 1 "pathogen"
Negative: No growth, NOF, mixed growth/doubtful significance

Unyvero: Overview

Target Organism	Routine laboratory	True Positive (Routine and Unyvero P55)	False Positive (Unyvero P55 only)	False Negative (Routine only)	Sensitivity (%)	Specificity (%)
S. aureus	4	4	5	0	100.0	93.8
S. pneumoniae	3	1	2	2	33.3	97.6
A. baumannii	0	0	3	0	–	96.5
P. aeruginosa	11	11	12	0	100.0	83.8
H. influenzae	7	6	6	1	85.7	92.3
M. catarrhalis	1	1	2	0	100.0	97.6
S. maltophilia	5	4	16	1	80.0	80.0
E. cloacae cplex	0	0	4	0	–	95.3
E. aerogenes	0	0	1	0	–	98.8
E. coli	3	3	12	0	100.0	85.4
K. pneumoniae	3	3	4	0	100.0	95.1
K. oxytoca	0	0	2	0	–	97.6
K. varticola	0	0	0	0	–	100.0
M. morganii	0	0	0	0	–	100.0
Proteus spp	0	0	2	0	–	97.6
S. marcescens	1	1	6	0	100.0	92.9
C. freundii	0	0	1	0	–	98.8
L. pneumophila	0	0	0	0	–	100.0
M. pneumoniae	0	0	0	0	–	100.0
Overall (average)	34	78	4	88.8	94.9	

- Overall concordance:
  - 67% (57/85) of specimens
- Discordance
  - 86% (24/25) of discordant specimens reported as
    - NOF
    - Non-significant growth
    - Mixed growth/doubtful significance

Abx? Low abundance?

Drive abx overutilization?

Unyvero: Overview

- **Analysis of 14 randomly selected specimens**
  - Compare Cx, Unyvero, quantitative 16S NGS
    - Single pathogen reported by Cx → also reported by Unyvero and accounted for majority of sequencing reads
    - NOF reported by Cx → Unyvero positive, NGS demonstrated a mixture of reads without a predominating organism

Specimen number & type	Routine Culture Result	Unyvero P55 Result	16S rRNA Sequencing Results
347 ETT	*P. aeruginosa*	*P. aeruginosa* (+ + +)	*Pseudomonas* spp. 79.6% *Others 20.4%*
346 ETT	*P. aeruginosa*	*P. aeruginosa* (+ + +) *S. marcescens* (+ + +) *S. aureus* (+ +) *S. maltophilia* (+ +)	*Pseudomonas* spp. 38.4% *Streptococcus* spp. *(not including S. pneumoniae) 17.1%* *Neisseria* spp. 16.4% *Serratia* spp. 12.5% *Stenotrophomonas* spp 1.6% *Others 14.0%*
360 ETT	Normal respiratory flora	*S. maltophilia* (+ +)	*Acinetobacter* spp. 3.4% *Pseudomonas* spp. 1.2% *Mixed commensal genera*

"These data suggest broad agreement of NGS with routine culture rather than Unyvero"

Unyvero: Overview

- **Resistance markers**
  - B-lactamase – SHV, TEM
  - ESBL – CTX-M
  - Carbapenemase – KPC, VIM, IMP, NDM, OXA-48, 23, 24, 58
  - Alt PBP – *mecA, mecC*
  - Macrolide – *ermB*
  - FQ – GryA83, GyrA87
  - Sulfonamide – *sul1*
- Unyvero detected ≥ 1 resistance marker in 72% of specimens
  - Includes 14/28 (50%) of specimens with no organism detected
- Excluded SHV, TEM, *sul1*, *ermB* (ubiquitous in pathogens and flora)
  - Unyvero → 18 detections
  - Culture→10 isolates with corresponding resistance

Unyvero: Overview

Table 3
Number of potentially significant resistance mechanisms detected by routine microbiology versus Unyvero P55.

	ESBL producer	MRSA	Fluoroquinolone resistance	Carbapenem resistance
Routine Microbiology	n = 2 bla_{CTX-M}	none detected	n = 4 1 x *E. coli*, 3 x *P. aeruginosa*	n = 4 4 x *P. aeruginosa*, no enzyme detected
Unyvero P55	n = 2 bla_{CTX-M}	n = 4 (*mecA* + *S. aureus*)	n = 12 7 x *P. aeruginosa* 5 x *E. coli*	n = 0
Concordance	1/2	0/4	3/12	0/4

* We presumed potential presence of MRSA when both *S. aureus* and *mecA* or *mecC* were detected in the specimen.

- ESBL
  - 1 FP
  - 1 FN
  - 1 culture-negative
- MRSA
  - 2 MSSA – *mecA* likely in CoNS
  - 2 culture-negative
- FQ
  - 5 culture-negative
  - 7 *gyrA* detected, phenotypically susceptible

C. Özenguvı et al. Biomolecular Detection and Quantification 13 (2017) 1–6

FA-Pneumo: Overview

- Semi-quantitative multiplex MolDx
  - 18 bacterial agents (15 reported semi-quantitatively) in addition to 9 viral agents
  - 7 genetic markers of antibiotic resistance
- Addresses problem of relative abundance for bacterial targets in resp. specimens
- AMR
  - $10^{3.5}$ to $>10^{6.5}$, reported semi-quantitatively in "bins"

FA-Pneumo was in categorical agreement with culture results for 10/13 bacteria reported by culture method (based on significance threshold of 10^4)

Molecular quantitation by FA-Pneumo was 1 $\log_{10}$ higher than culture for 11/13 culture positive targets

Figure 1. Qualitative comparison of LRTI and culture in BAL (n=73)

All targets		Culture result			
		ND/NR	10^3	10^4	10^5 or >
LRTI result	ND	1074	0	0	0
	10^4	3	3	1	0
	10^5	2	0	2	1
	10^6	0	0	0	0
	10^7 or >	3	0	1	5

ND/NR=Not detected or not reported

Essential agreement
Categorical agreement
LRTI "overestimation"
LRTI "underestimation"
Agreement based on 10^4 CFU/mL threshold for clinical significance in BAL

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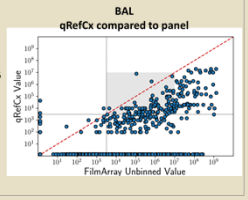
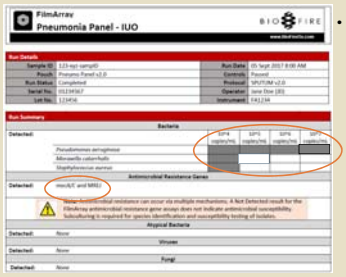


FA-Pneumo: Report



- Summary of bacteria detected and relative abundance
  - Result report applicable regardless of the changing guidance for specimen type, or quantitative vs. semi quantitative reporting
  - Added benefit for sensitive detection of resistance markers for infection control/isolation

E.g. *S. aureus* may not clinically significant but MRSA still infection control concern

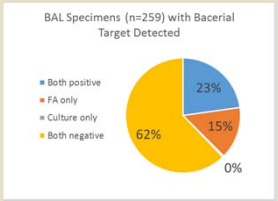
Study design

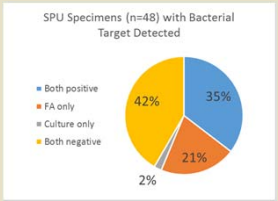
- Prospective comparison of FA-Pneumo to Laboratory SOC
  - Adult inpatients with signs/symptoms of respiratory infection
  - Composite SOC
    - Bacterial culture – Quant/Semiquant/Qual according to site protocol
      - "True" quantitative culture comparison conducted by reference lab (multiple dilutions, replicate plating)
    - Viral/atypical NAAT
      - Based on SOC orders - Resp panel, Flu/RSV only, LDT for CMV, etc.
    - In depth chart review
      - Specific symptoms and comorbidities
      - Abx start/stop date and time
      - Time to SOC result
      - Discharge or 14 day Dx - Infectious (bacteria, virus etc.) vs. non-infectious (allergy, asthma, COPD)

We want to know specifically how FA compares to routine standard of care and potential impact!

Bacterial Targets: Overview

- Number of specimens with on-panel target detected

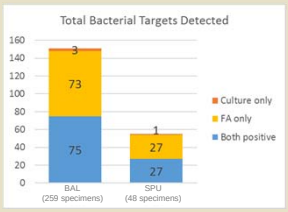




FilmArray detected a bacterial target in 65% more BAL and 57% more SPU specimens than routine culture

Bacterial Targets: Overview

- Total number of on-panel targets detected



- Failure to recover in culture
  - Fastidious organisms (*H. flu*)
  - Abx onboard prior to specimen collection
- Overgrowth/outcompeted
  - Pseaer, Enterobacteriaceae, NOF
- Not reported in SOC culture
  - Multiple pathogens isolated
  - Below Cx threshold
  - Other pathogen "predominant"

Significance of additional targets?

FilmArray detected 94% more targets in BAL and 96% more targets in SPU specimens compared to routine culture

Bacterial Targets: Performance

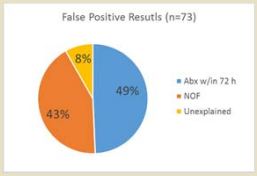
- FA vs. SOC culture report (BAL)

"sensitivity" "specificity"

Target	SOC+/FA+	SOC+/FA-	SOC-/FA+	SOC-/FA-	Total	PPA	NPA
A. baumannii	1	0	0	258	259	100%	100%
E. cloacae cplx	7	0	4	248	259	100%	98.4%
E. aerogenes	3	0	1	255	259	100%	99.6%
E. coli	1	1	1	254	259	50.0%	99.6%
H. influenzae	4 20%	0	16	236	259	100%	93.7%
K. oxytoca	2	0	3	251	259	100%	98.8%
K. pneumoniae	8	0	3	247	259	100%	98.8%
M. catarrhalis	2 25%	0	6	249	259	100%	96.9%
Proteus sp.	2	0	2	254	259	100%	99.2%
P. aeruginosa	18	1	6	234	259	94.7%	97.5%
S. marcescens	3	0	0	256	259	100%	100%
S. agalactiae	1	0	6	253	259	100%	97.6%
S. pneumoniae	2	0	3	254	259	100%	98.8%
S. pyogenes	0	0	1	258	259	100%	99.6%
S. aureus	21 50%	1	21	216	259	95.5%	91.1%

Bacterial Targets: Discordance

- FA vs. SOC culture report (BAL)



- Unexplained → 3/6 (50%) were *S. aureus* quantified at 10^4/mL
  - ~10^5 in Cx – Not detected or not reported/below threshold
  - (2) *P. aeruginosa* 10^5, abx not recorded; (1) *H. influenzae* 10^6
- NOF
  - 10/31 (32%) quantified at 10^4/mL
  - 13/31 (42%) contained ≥ 1 more predominant target(s) recovered in Cx → not reported per lab policy?
- Abx → Useful to detect these?
  - Prevent premature discontinuation of Abx based on negative Cx
  - Allow appropriate de-escalation (e.g. pip/tazo to amox for *H. flu*)

Bacterial Targets: Correlation

- Composition of positive specimens – Correlation of predominant target detection

60

97

Targets	SOC 0	SOC 1	SOC 2	SOC 3	SOC 4
FA 1	31	29/29 (100%)	-	-	-
FA 2	5	11/13 (85%)	8/9 (89%)	1/1 (100%)	-
FA 3	-	1/1 (100%)	2/2 (100%)	-	-
FA 4	1	1/1 (100%)	1/1 (100%)	-	0/1 (0%)
FA 5	-	-	-	-	
FA 6	-	1/1 (100%)	-	-	-

Predominant organism agreement

- At least 1 target detected FA+Cx
  - 55/59 (93%) of specimens
- > 1 target detected by FA or SOC
  - 26/30 (87%) of specimens

FA: Staaur 10^6, Entclo 10^5 → Cx: Entclo 10^5
FA: Staaur 10^6, Entclo 10^4 → Cx: Entclo 10^4

Both patients on anti-staphylococcal abx at time of collection

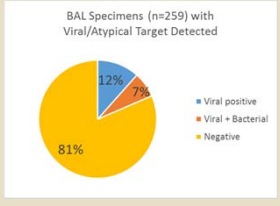
FA: Strpne 10^7, Pseaer 10^5 → Cx: Pseaer 10^4 Strpne "few"

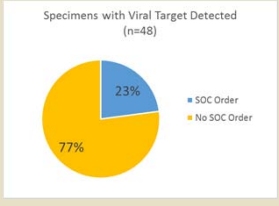
No NOF, No Abx…abundance of Pseaer outcompete?

FA: Staaur 10^5, Kleoxy 10^4, Sermar 10^4, Pseaer 10^4
Cx: Kleoxy 10^4, Sermar 10^4, Pseaer 10^4, Staaur 10^5

Viral Targets: Overview

- Number of specimens with on-panel target detected





FilmArray detected a viral target in 19% of BAL.

77% of positive specimens did not have SOC order

Viral Targets: Performance

- Number of specimens with on-panel target detected

Target	FA+	SOC Order	SOC Agree	FA No Bacteria
hRV/EV	17	6/17 (35%)	6/6 (100%)	7/17 (41%)
CoV	9	2/9 (22%)	2/2 (100%)	7/9 (78%)
FluA	5	0/5 (0%)	n/a	3/5 (60%)
PIV	3	1/3 (33%)	1/1 (100%)	2/3 (66%)
FluB	2	1/2 (50%)	1/1 (100%)	1/2 (50%)
RSV	2	0/2 (0%)	n/a	2/2 (100%)
hMPV	1	0/1 (0%)	n/a	0/1 (0%)
AdV	1	0/1 (0%)	n/a	1/1 (100%)
Legionella	1	0/1 (0%)	n/a	1/1 (100%)
Mycoplasma	1	0/1 (0%)	n/a	1/1 (100%)
CoV+hMPV	1	1/1 (100%)	1 (100%)	0/1 (0%)
hRV/EV+PIV	3	0/3 (0%)	n/a	1/3 (33%)
hRV/EV+CoV	1	0/1 (0%)	n/a	0/1 (0%)
hMPV+FluA+CoV	1	0/1 (0%)	n/a	1/1 (100%)
None Detected	211	79/211 (37%)	76/79 (96.2%)	129/211 (61%)

- Only 95/259 (37%) of specimens had SOC order for viral/atypical NAAT
  - 11/48 (22%) of those that were positive

~80% Missed diagnosis b/c not in differential …but are they clinically significant?

- 27/48 (56%) specimens with a viral detection were **negative** for bacterial targets

FluA: No SOC orders, uncommon HAI, specific therapy available

Others: <20% SOC orders, no specific therapy, Serious infection in compromised patients, Infection control/cohorting

hRV/EV: 35% SOC orders, no specific therapy, 41% had no bacteria detected explanation for symptoms, DC Abx

Impact of FA result on Management

- Time to result and antibiotic adjustments

Potential Intervention	Description
Appropriate antimicrobial escalation	Clinically significant organism(s) or resistance mechanisms were identified on **SOC and FA** • FA would result in more rapid initiation of appropriate antimicrobials
Appropriate antimicrobial de-escalation	Clinically significant organism(s) or resistance mechanisms **not** identified on **SOC and FA** • FA would result in more rapid discontinuation or de-escalation of one or more antimicrobial agents
Inappropriate* antimicrobial escalation/continuation	Clinically insignificant organism(s) or resistance mechanisms were identified on **FA but not SOC** • FA would result in inappropriate initiation or continuation of one or more antimicrobial agents • FA would result in inappropriate broadening of spectrum of antimicrobial therapy
Inappropriate* antimicrobial de-escalation	Clinically significant organism(s) were identified via **SOC but not FA** • FA would result in inappropriate discontinuation or de-escalation of one or more antimicrobial agent
No change in therapy	Concordant FA and SOC results and antibiotics appropriate for identified organism(s) • No escalation or de-escalation possible based on FA results

*Based on SOC culture as gold standard

Impact of FA result on Management

- Time to result and antibiotic adjustments

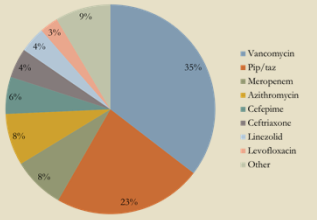
Potential Change, no.	Antimicrobials	Patients	Hours
Appropriate de-escalation/discontinuation	206	122 (48%)	18,284.07
Appropriate escalation/initiation	5	5 (2%)	184.66
Inappropriate de-escalation/discontinuation	6	6 (2%)	-
Inappropriate escalation/continuation	42	42 (17%)	-
No change	-	78 (31%)	-
Unable to assess*	-	16	-

* Date or time not included for antimicrobials, concomitant infection present (cannot determine which antimicrobials are used for LRTI versus other infection), etc.

- Antibiotic adjustment could be made on 165/243 (68%) evaluable patients
  - 10 patients fell into multiple categories
- Multiple antibiotic interventions could be made/patient (avg 1.48/patient)
  - >18,000 antibiotic hours saved (avg. 6.2 d/patient, 3.8 d/abx)

Impact of FA result on Management

- Appropriate de-escalation/discontinuation (% of total changes)



- Includes 122 patients with negative agreement between FA and SOC Cx
- Vanc and Pip/tazo account for 58% of antimicrobial adjustments
  - D/C based on negative FA result for MRSA and *Enterobacteriaceae*

It was assumed that all antimicrobials were prescribed for LRTI, unless concomitant infection was noted in discharge or 14-day diagnosis
Antimicrobials targeted toward anaerobic infections (not on-panel targets) and those not utilized for pneumonia (e.g. daptomycin) were not included

Impact of FA result on Management

- Time to result and antibiotic adjustments

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- FA false negative results
  - 3/6 were failed organism detection by FA
    - *S. aureus* 10^3 CFU/mL in SOC Cx
    - *E. coli* 10^3 CFU/mL in SOC Cx
      - *K. pneumoniae* also 10^3 in SOC Cx, not treated
    - *P. aeruginosa* "few" in SOC Cx

} below threshold for clinical significance in BAL may not treat.

Impact of FA result on Management

- Time to result and antibiotic adjustments

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* Date or time not included for antimicrobials, concomitant infection present (cannot determine which antimicrobials are used for LRTI versus other infection), etc.

- FA false negative results
  - 3/6 resistance mechanism not detected by FA
    - CTX-M not detected, ESBL organism (2)
    - *mecA* not detected, MRSA in Cx

} Multiple ESBL classes. Education of test limitations!

Impact of FA result on Management

- Time to result and antibiotic adjustments

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- FA false positive results – assuming Cx as gold standard these would be potential inappropriate escalation
  - 38 specimens positive by FA but negative by Cx
  - FA detection may have variable impact
    - Continuation of abx in spite of improving clinical course → Cx negative result may have resulted in earlier D/C
    - Narrowed therapy based on ID to complete course for LRTI (e.g. *H. flu* vs. *P. aeruginosa*)
    - Historic reference in case of clinical relapse → Cx neg you never know etiology

Conclusions

- MolDx are capable of detecting bacterial pathogens in clinical specimens with **high sensitivity**
  - Detect potential pathogens in 60-70% more specimens, not subject to NOF, fastidious growth, Abx
  - Excel at complex specimens with multiple pathogens or those with higher viscosity
- Semi-quantitative results may aid interpretation, esp. for complex/polymicrobial specimens
  - FA-Pneumo results in relative agreement with qCulture results
- Results are clinically actionable
  - Abx adjustment in >60% of patients ~ 3-4 days sooner than culture
  - 50% of patients could have therapy narrowed
- Inclusion of viral targets enables detection of pathogens not high on differential
  - Viral agent detected in ~20% of specimens
  - ~30% of these had a SOC order capable of detecting the agent

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