

IS THE JUICE WORTH THE SQUEEZE?

RAPID IDENTIFICATION AND ANTIMICROBIAL SUSCEPTIBILITY TESTING USING THE ACCELERATE PHENO™ SYSTEM

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Lifespan



BROWN
Alpert Medical School

DISCLOSURES

- K Chapin Clinical Advisory/Consulting for Accelerate
- All other authors no conflicts

BACKGROUND

- Rapid identification (ID) and antimicrobial susceptibility testing (AST) have the power to appropriately guide antibiotic therapy and optimize healthcare outcomes
- The Microbiology lab at Rhode Island Hospital performs:
 - 50,000-60,000 blood cultures/year
 - 700,000 tests/year
 - 24h/7d
- High volume and varied tech capabilities (55) does not favor methods with multiple hands-on manipulations for rapid ID and AST

BACKGROUND

- The purpose of this study was to prospectively evaluate the Accelerate Pheno™ system (Pheno) for blood cultures positive for Gram negative rods (GNR) in the context of:
 - routine laboratory workflow
 - accuracy with current identification and AST methods
 - identify medically actionable benefits as part of:
 - business plan for the lab
 - stewardship plan for implementation

ACCELERATE PHENO™ SYSTEM



20"/43 cm

3 feet/ 32 cm

- FDA cleared Feb 2017
- Direct from positive blood culture
- ID in 90 minutes
- AST in ~ 7 hrs
 - GN 15 antibiotics
 - GP 8 antibiotics
- Entire process contained in 1 kit



WHAT IS THE SCIENCE?



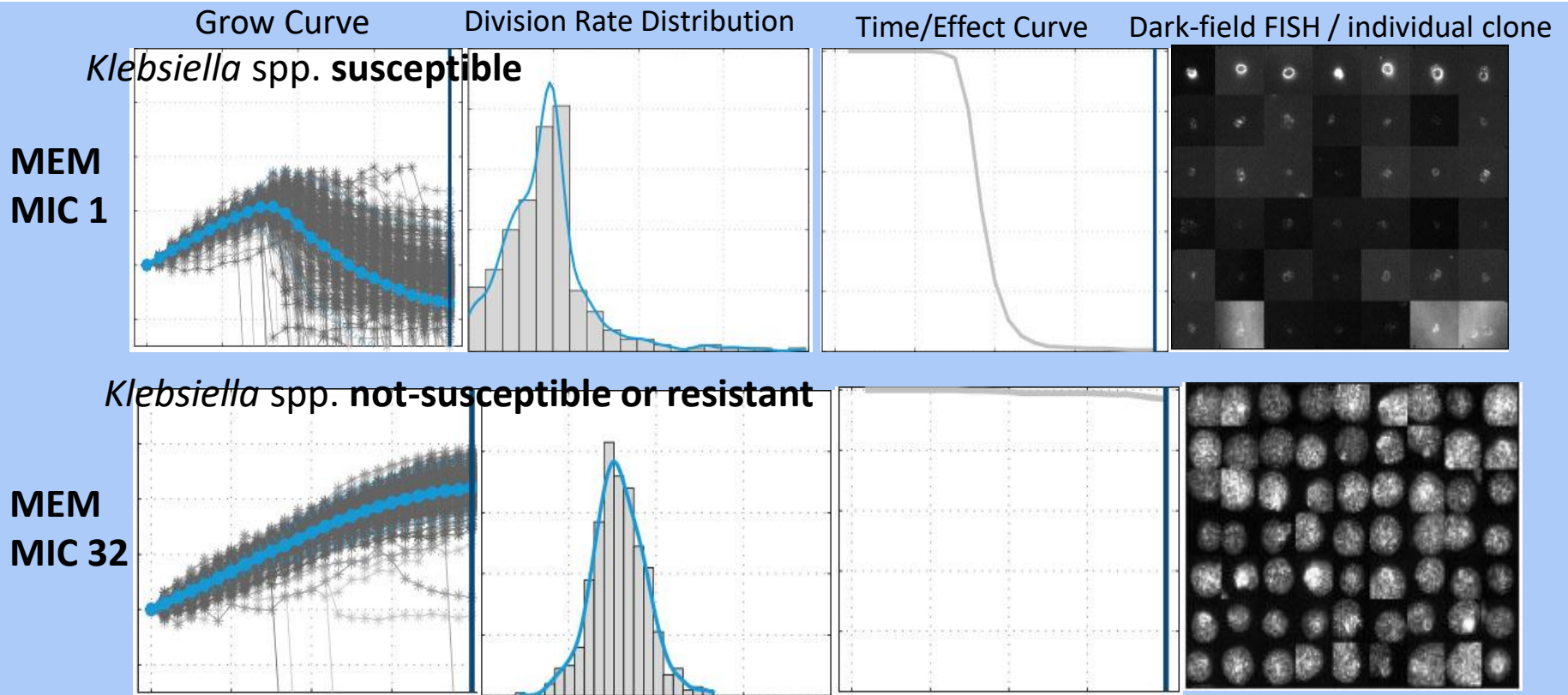
- Automated sample prep and bacterial immobilization to enable microscopy-based, single-cell analysis for ID and AST
- ID performed using fluorescence in situ hybridization (FISH)
 - target organism specific rRNA sequences with several mono-labeled DNA probes
- Colocalization of target probe with universal probe signal confirms the presence/identity of target while differentiating non-specific staining

WHAT IS THE SCIENCE?



- The MIC and categorical interpretation are generated using morphokinetic cellular analysis by dark-field microscopy of individual, live, growing, immobilized bacterial cells
 - in near real-time (q 10 min)
 - in presence (test) and absence (control) of a single concentration of antimicrobial agent
- Data analysis: billions of data points per run and growth curve algorithm analysis used to predict susceptibility

ACCELERATE PHENO™ SYSTEM



AST- Morphokentic Cellular Analysis

- Bacteria are grown up to 4 hrs in presence of single concentration of antibiotic.
- Growth response is measured using time-lapse imaging.
- **MICs determined by matching growth patterns to reference growth profiles that correlate to MICs**

STUDY ASSESSMENT PROTOCOL

- From January to August 2018, Pheno was prospectively evaluated from 100 blood cultures determined as GNR based on Gram stain
- Per protocol:
 - Positive bottles are stained, read and subbed to media for next day bench reading
 - During the study period, technologists (1st and 2nd shifts) were trained and Pheno performed as part of the routine workflow
 - After gram stain return to bottle and withdraw specimen for plate subbing and pheno inoculation

ACCELERATE PHENO™ SYSTEM

Identification	SAM	TZP	CPM	CAZ	CRO	ETP	MEM	AMK	GEN	TOB	CIP	ATM
<i>E. coli</i>	X	X	X	X	X	X	X	X	X	X	X	X
<i>Klebsiella</i> spp.	X	X	X	X	X	X	X	X	X	X	X	X
<i>Enterobacter</i> spp.		X	X	X	X	X	X	X	X	X	X	X
<i>Proteus</i> spp.	X	X	X	X	X	X	X	X	X	X	X	X
<i>Citrobacter</i> spp.		X	X	X	X	X	X	X	X	X	X	X
<i>S. marcescens</i>		X	X	X	X	X	X	X	X	X	X	X
<i>P. aeruginosa</i>		X	X	X			X	X	X	X	X	X
<i>A. baumannii</i>		X						X				

***Klebsiella* spp.**

K. oxytoca, K. pneumoniae

***Enterobacter* spp.**

E. cloacae, E. aerogenes

***Proteus* spp.**

P. mirabilis, P. vulgaris

***Citrobacter* spp.**

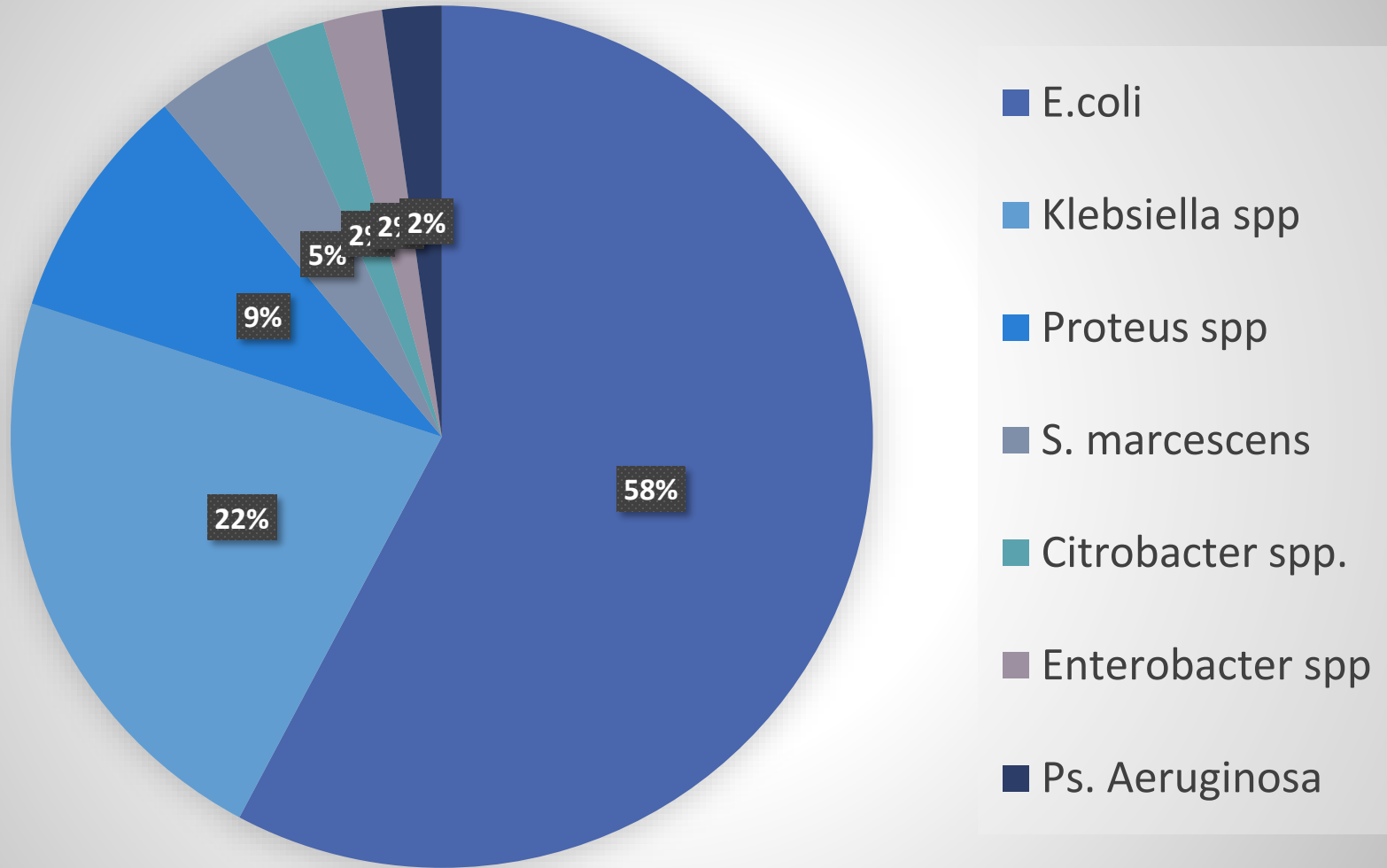
C. freundii, C. koseri

STUDY ASSESSMENT PROTOCOL

- Pheno provided automated ID/AST results, which were recorded and compared to laboratory standard of care:
 - MALDI-TOF ID and VITEK[®] 2 AST
- Tabulated:
 - Time points for all ID/AST results
 - Accuracy of ID/AST comparisons
 - Chart review was performed to assess underlying:
 - Diagnosis
 - Antibiotic use and assessment
 - Length of stay (LOS)
 - Mortality

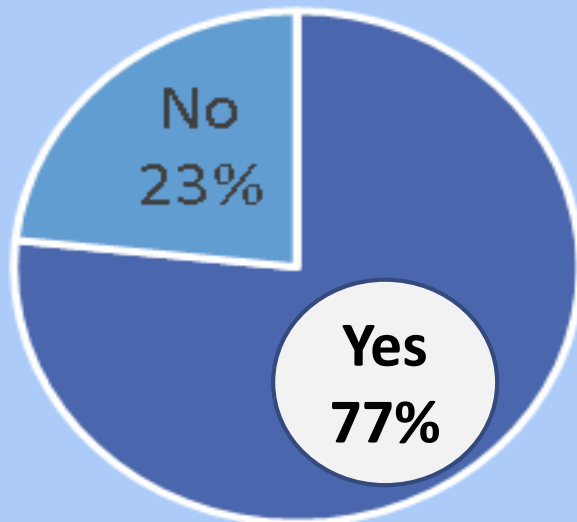
Jan – May 2018 had **585** Positive Blood cultures at RIH
65 (11%) Pheno tests on Blood Cultures with Single morphology of GNRs on GS

Single organism = 56 (86%) ; > 1 organism = 9 (14%) → 70% with an ID/AST



PRELIMINARY POTENTIAL STEWARDSHIP IMPACT DATA

Was there a change in atbx
after Vitek AST reported?



■ Yes ■ No

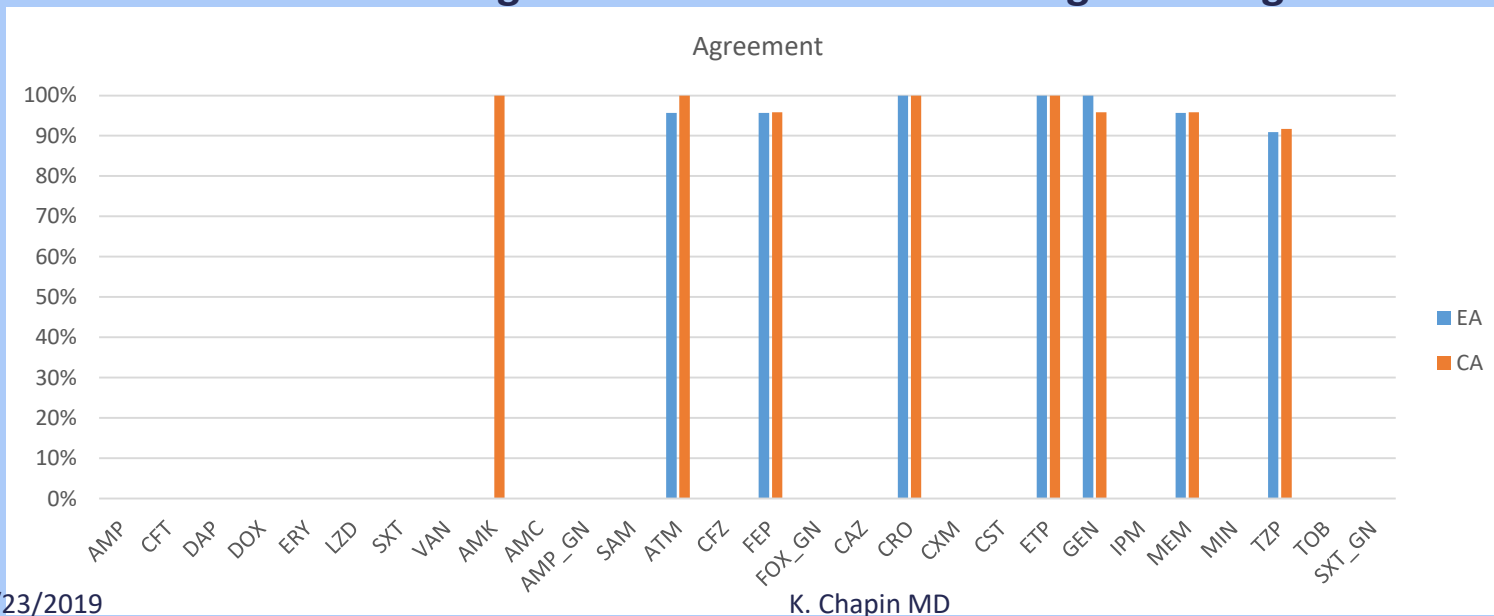
Where was change
NOT happening?

- Surgical Service
- Those already on appropriate antibiotics

YES!!

RESULTS 100: PHENO DATA

- Pheno gave interpretable ID/AST results for **76% of specimens**
- Identification
 - 81 specimens monomicrobial/ID sensitivity **100%** and specificity **100%**
 - 19 polymicrobial/ID sensitivity **83.3%** and specificity **100%**
- Susceptibility
 - **96.7% Essential Agreement and 96.3% Categorical Agreement**



100 PROSPECTIVE GNR RESULTS

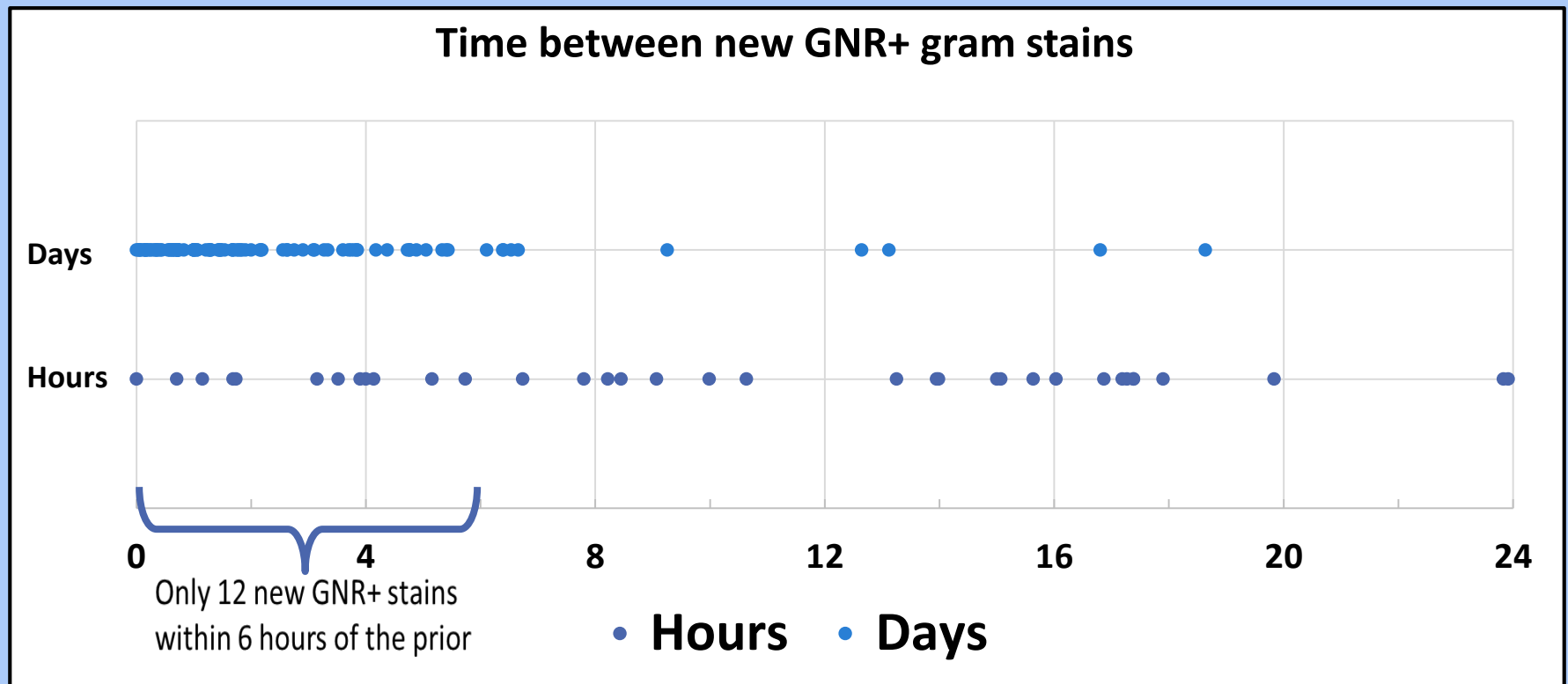
76% CORRECT ID/AST

TABLE 1

PH MALDI/VITEK	Pheno	PH MALDI/VITEK	Pheno	PH MALDI/VITEK	Pheno	PH MALDI/VITEK	Pheno
1 BURK	indeterminate	26 PR	PR	51 ENT, ECOC	ENT	76 BACT	Strep - no AST
2 PR	PR	27 KL	KL	52 EC	EC	77 EC	EC
3 KL	kl	28 KL, CIT	KL	53 HAF	no result	78 PR	PR, SA - no AST
4 KL, ECOC	error	29 EC	EC	54 EC	EC	79 KL	KL
5 KL, ECOC	EC, KL - no AST	30 CIT	CIT	55 EC	EC	80 EC, CONS	no result
6 KL	KL	31 SER	SER	56 EC	EC	81 EC, ECOC	EC
7 HFLU	no result	32 PA	indeterminate	57 KL	KL	82 KL	KL
8 PR	PR	33 KL, PR	KL, PR - no AST	58 EC	EC	83 EC	no result
9 KL	KL	34 EC	EC	59 EC	EC	84 KL	KL
10 BACT	indeterminate	35 KL	KL	60 ENT, PANT, SPHING	ENT	85 EC	EC
11 EC	EC	36 MORAX, MICCOC	indeterminate	61 EC, KL, ENT, CLOS	EC	86 KL	FNT
12 EC	EC	37 PR	PR	62 PFL, SPHING	indeterminate	87 ENT	indeterminate
13 EC	EC	38 KL, CLOS, BACT	KL	63 EC	EC	88 BACT	KI
14 EC	error	39 PANT	no result	64 PA	KL	89 EC	EC
15 EC	EC	40 EC	EC	65 EC	EC	90 ENT	ENT
16 CLOST	indeterminate	41 EC	EC	66 EC	EC	91 SAL	no result
17 EC	EC	42 PR	PR, SER - no AST	67 CIT	CIT	92 CIT, CORYN	CIT
18 PA	PA	43 SER, CDUB	SER	68 KL	KL	93 KL, SER	SER
19 EC	EC	44 EC	EC	69 KL	KL	94 EC	EC
20 BACT	no result	45 KL	KL	70 PA	PA	95 BACIL	no result
21 EC	EC	46 EC	EC	71 ENT	ENT	96 EC	EC
22 EC	EC	47 EC	EC	72 PA, EC, BACT	PA	97 EC	EC
23 EC, CONS	EC	48 KL	KL	73 PAST	no result	98 AB, PANT, CONS	AB
24 EC	EC	49 SER	SER	74 EC	EC	99 ENT	ENT
25 EC	EC	50 BACT	no result	75 PA	PA	100 EC, CONS	EC

TIMING OF NEW GNR+ GRAM STAINS

- Assessment of timing distribution of positive blood cultures/gram stains and Pheno AST allowed assessment of instrument needs



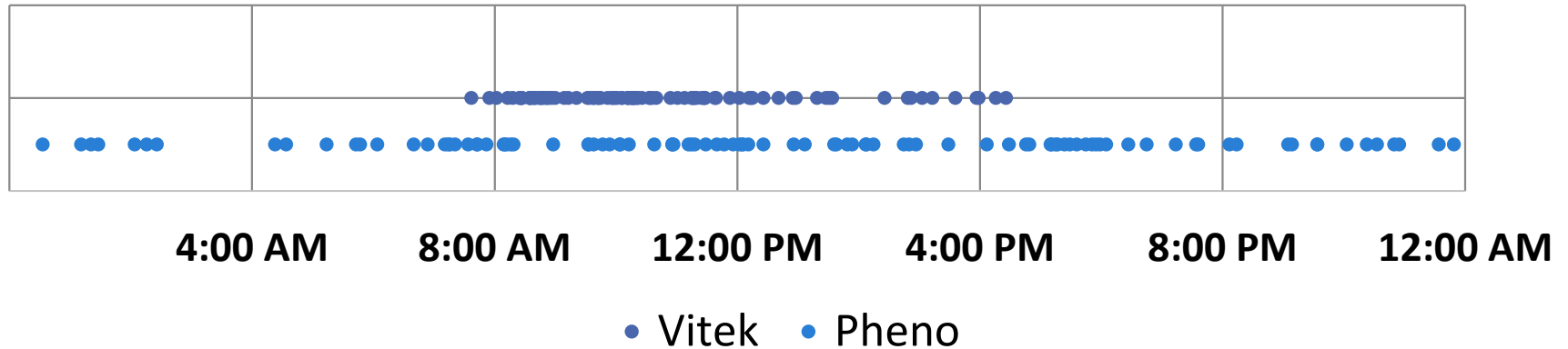
RESULTS PHENO LAB PARAMETERS

- Comparison of average time from Gram stain to final AST:
 - Pheno was 8.4 hours and
 - VITEK 48.3 hours (**p<0.0001**)

- Easily incorporated into routine workflow

TIMING OF AST RESULTS

Time of AST result



Time distribution of Pheno results would allow 2/3 of patients to have same day AST intervention

FINAL RESULTS : CLINICAL DATA

Mortality due to GNR sepsis was 17%



RESULTS

CHART REVIEW AND STEWARDSHIP OPPORTUNITIES

- 17% mortality
- LOS 9.1 days
- Over 50% of GNR infections were due to:
 - UTI or uncomplicated sepsis and
 - 20% were polymicrobial
- De-escalation from broad-spectrum antibiotics:
 - could have occurred in 79% of patients
 - Antibiotic changes were delayed in 40% and
 - Discharge was delayed in 11% because of pending standard protocol AST results
- Cost of one septic patient RI \$28,000

CONCLUSIONS



- Diagnostic management including microbiology and antimicrobial stewardship programs (ASPs) providing rapid ID/AST and active consultation respectively, could have major impact on this GNR septic patient population with high mortality
- Pheno was easily incorporated into routine micro workflow and gave results for almost 80% of all GNR
- Stewardship currently reviews all GNR blood cultures and agreed that they could incorporate Pheno results into daily consults

BUSINESS PLAN SUPPORT

Support data for Accelerate Pheno testing Implementation K. Chapin MD 11/2018

Sepsis Background:
Over 60,000 bloodstream infections/year US
Blood stream infections are the **leading cause of mortality** due to infection in US,
resulting in increased length of stay (LOS), and increased expenditures
Rapid diagnostic testing and timely result reporting especially in conjunction with
antimicrobial stewardship programs (ASP) has shown **improved outcomes** for
patients in terms of:

- Mortality*
- LOS*
- Readmissions*
- Adverse drug reactions
- Overall hospital costs

* **Lifespan quality measures**
Increasing bacterial resistance for the most common blood stream infections means
targeted antimicrobial therapy is even more critical

New Technology – rapid Identification and susceptibility testing (AST)

A recently FDA-cleared rapid ID/AST and susceptibility platform, Accelerate Pheno,
currently available and 2 instruments exist at Lifespan
The Microbiology Laboratory **prospectively evaluated 100 patients with Gram negative bacteremia**. Data was compared to current ID/Susceptibility methods,
to final ID and full susceptibility result was calculated, and retrospective chart review
was performed to assess diagnosis, antibiotic use and LOS to identify ASP
opportunities.

Time difference between current methods vs. Pheno was 48.3 hours versus 8.4 hours
(p < 0.0001)

Mortality in this population was 17%
79% could have had antibiotics de-escalated with reduction of adverse events
40% had delayed appropriate antibiotic changes due to TAT of current methods
11% of patients had delayed discharge due to pending standard antibiotic
susceptibility results

Current data shows that the best combination for cost expenditures, quality of life/mortality is
the combination of rapid microbiology results in conjunction with ASP
**Costs for testing (based on current contracts provided) and Sepsis Patients (based on data
generated from Mylonakis 2018)**

**Lifespan Labs currently perform approximately 50,000 blood cultures for potential
sepsis per year.**
Approximately 250 – 300 are Gram negative rod(GNR) bacteremias
Cost for 1 Pheno test \$250
Cost to run 300 patients @ \$250 = \$75,000/year
Cost for 1 septic patient \$28,000

**Hospital Costs for 1 septic patient based on Quality score and most savings in hospital costs was
approximately \$28,000**

Conclusions:
This patient population exhibits a very high mortality (sepsis from GNR bacteremia)
This patient population has high hospital expenditures (Average LOS 9.1 days)

Benefits of implementing a rapid ID and Susceptibility methods with Antimicrobial stewardship program
antibiotic therapy, decrease LOS, and reduce overall costs. Mortality can only be assessed based
on prospective implementation.

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APPROVED

FINALIZING STAGES

- Both acute care hospitals will use Pheno for GNR
- Retrain and train our remaining micro staff
- AMS interventions tracking planned

AMS Interventions

- Intervention made: yes/no
- Intervention type: de-escalation, escalation, initiation, etc
- Intervention outcomes: accepted/rejected
- Date/Time intervention

Process Measures

- Time to effective therapy
- Time to de-escalation

Other Metrics

- Source of BSI
- LOS

CPT CODE SPECIFIC FOR PHENOTEST BC KIT

Accelerate PhenoTest™ BC kit, Accelerate Diagnostics, Inc	●00X XU	Infectious disease (bacterial and fungal), organism identification, blood culture, using rRNA FISH, 6 or more organism targets, reported as positive or negative with phenotypic minimum inhibitory concentration (MIC)-based antimicrobial susceptibility	April 1, 2019	July 1, 2019	CPT [®] 2020
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Will help with cost justification and comparisons to current methods
ID 87077 and AST 87186 reimbursement from CMS = \$20.64



THANK YOU