PACE Program Title:

Forecasting the Emerging Technologies of the Laboratory of the Future

THREE TECHNOLOGY TRENDS THAT WILL CHANGE THE MICROBIOLOGIST'S WORLD!

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OUTLINE

- The host will be the new platform for assessment of infection
  - There is a need for better markers of infection status
  - A Couple of Host response solutions

- Is sequencing ever going to come to my lab?

- Is AI going to take over my lab?
  - But what about the practice of core clinical Microbiology?

THE HOST WILL BE THE NEW PLATFORM FOR ASSESSMENT OF INFECTION

Sepsis Is A Medical Emergency That Needs Actionable Risk Stratification

Sepsis is the leading cause of death in hospitals worldwide

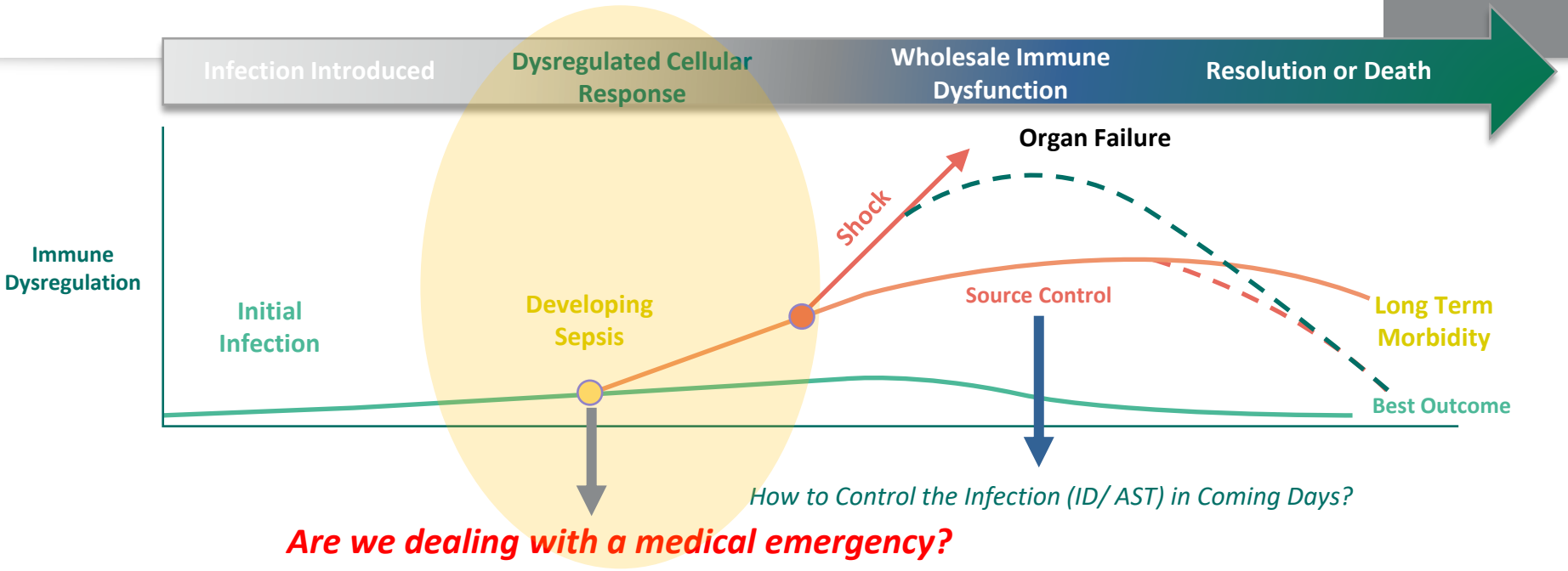
80%
Of sepsis cases present to ED

2x
Number of Stroke & Heart Attack cases

1 in 5
Of 150M+ ED patient visits are at risk of sepsis

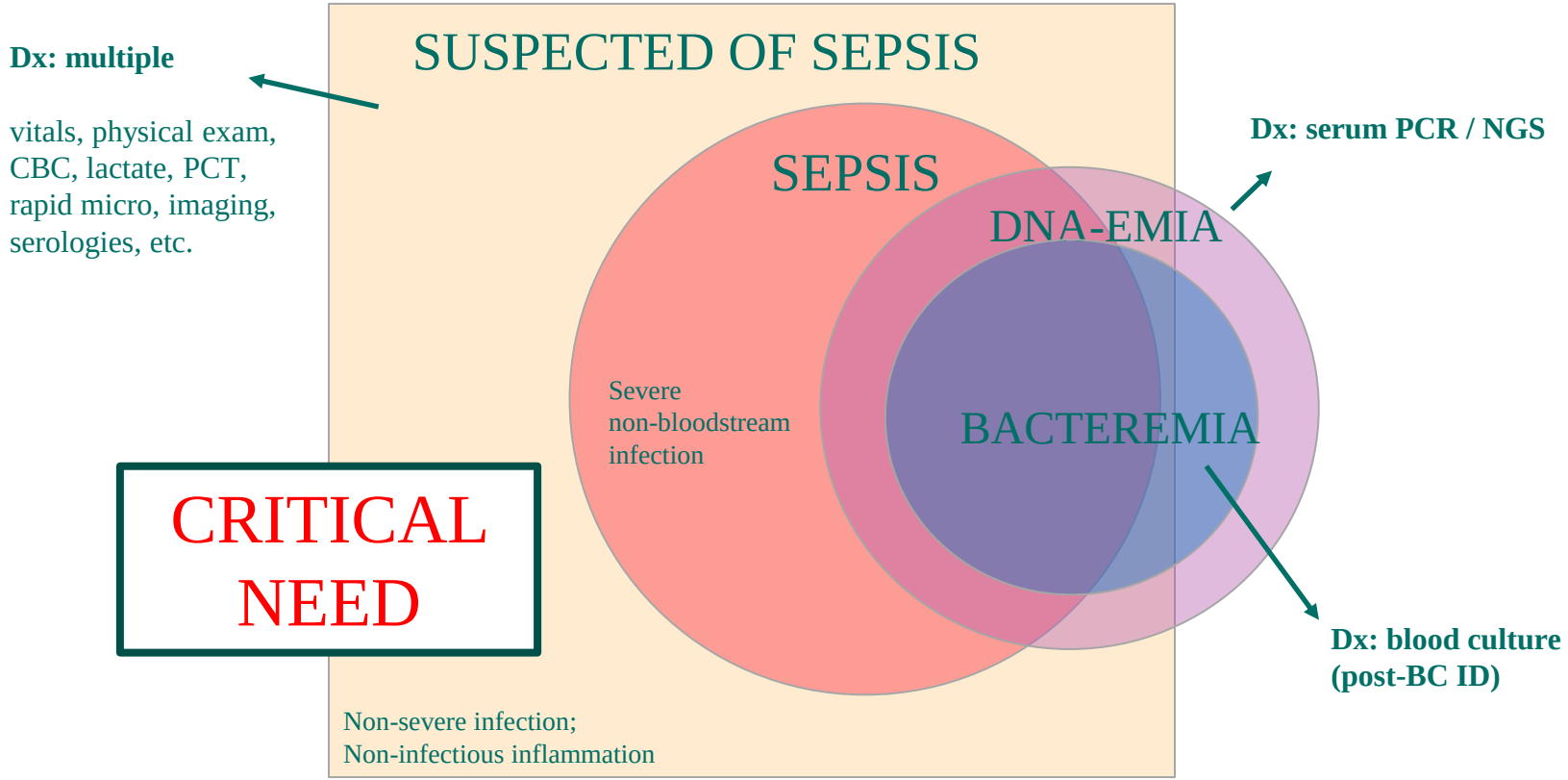
Sepsis Poses A Medical Emergency

This dysregulated immune response makes sepsis a medical emergency



Are we dealing with a medical emergency?

BACTEREMIA DIAGNOSTICS ARE NOT SEPSIS DIAGNOSTICS



THERE IS A NEED FOR BETTER MARKERS OF INFECTION STATUS

A Case Study Illustrating the Need

Study Objectives

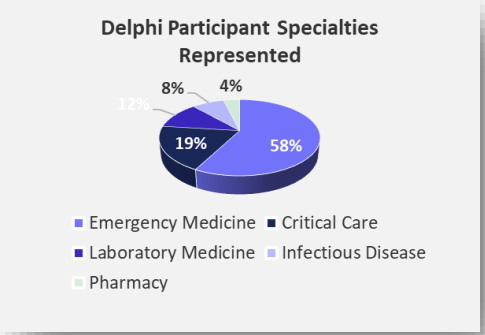
1. **Develop guiding statements** around (1) use of a hypothetical Rapid Sepsis Test (performance characteristics mirror IntelliSep) and (2) direction on clinical use and incorporation into hospital workflow of **IntelliSep**

2. **Gain consensus on statements** with experts across specialties involved in sepsis research and clinical care of sepsis patients

Study Approach

- **Expert Participant Group:**
  - 26 participants – involved in sepsis research and clinical care; majority from academic centers
  - Representative of: Emergency Medicine, Critical Care, Laboratory Medicine, ID, Pharmacy

- **Study Method:**
  - **Modified Delphi approach**, consisting of 2 rounds of questionnaires *(100% participation)*
  - Both questionnaires split into **two sections**: **(1) need statements for a rapid sepsis test** (performance characteristics provided), **(2) clinical action statements based on ISI bands** associated with hypothetical patient cases
  - Participants asked to evaluate majority of statements using a **five-point Likert scale**
  - **Level of agreement for each statement assessed** post-questionnaire



1 Kraus et.al. Manuscript under review

How consistent is the perception of Sepsis Risk?

Patient Description:

- 72 year-old female nursing home patient
- Past medical history of dementia, hypertension and dyslipidemia
- Presented to the emergency department after nursing home staff noted her to have altered mentation
- Somnolent on the morning evaluation; on repeat evaluation several hours later, the patient remained in bed & very difficult to arouse
- At baseline, able to transfer from bed to bedside commode and wheelchair without difficulty, and is typically bright and communicative. This morning she was arousable only to physical stimulus and spoke incoherently.

On arrival to the Emergency Department:

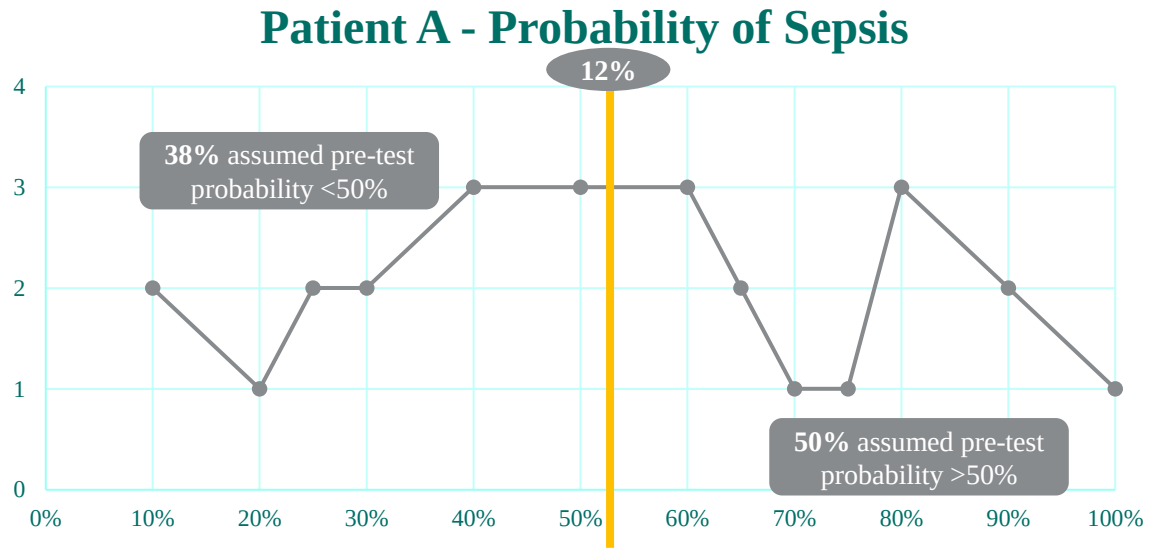
- Temperature: 97.8F, Pulse: 84, Respiratory rate: 16, Blood pressure 98 / 62 mmHg, Oxygen saturation 95% on room air.
- She opened her eyes and moaned incoherently to physical stimulus. An evaluation in the emergency department, including imaging studies, was significant for a:
- WBC of 9.8k, BUN 32, creatinine 1.9 (baseline 0.8), Lactate of 2.8 mmol/L
- Urinalysis (cath specimen) with + nitrites, 6-10 WBC / HPF, 0-5 RBC / HPF and many bacteria on microscopic exam

Little Agreement of Sepsis Risk amongst respondents

- Provided 2 example cases of potential diagnostic dilemmas and asked about pre-test probability of sepsis for these cases (1 presented here)
- Probability ranged from 10% to 100% for the same case, with little agreement

Providers don't currently "Know sepsis when they see it"

%	Votes
10%	2
20%	1
25%	2
30%	2
40%	3
50%	3
60%	3
65%	2
70%	1
75%	1
80%	3
90%	2
100%	1



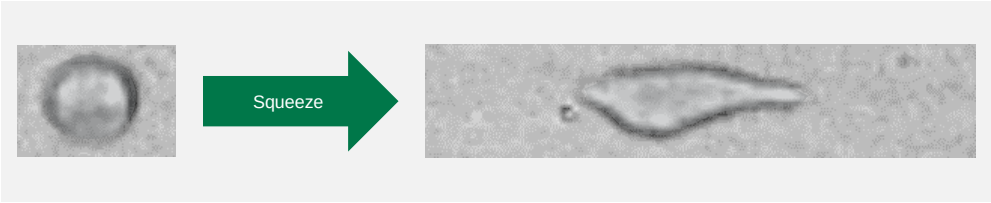
A COUPLE OF HOST RESPONSE SOLUTIONS

INTELLISEP: AIMING TO PROVIDE A WINDOW INTO DYSREGULATED IMMUNITY AND PHENOTYPIC CELLULAR SHIFTS

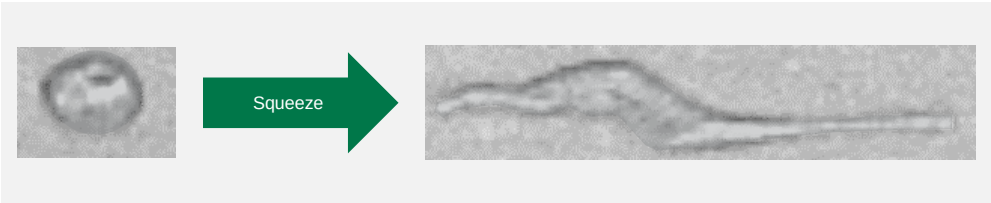
- IntelliSep interrogates biophysical properties of white blood cells (mainly neutrophils and monocytes) that may signal a **Dysregulated Host Response**
- 10,000 white blood cells are **exposed to a controlled deformation process (squeezed)** and **imaged**
- Squeezing cells **reveals the nuclear architecture** and **level of Immune Activation**
- The cell mechanics are analyzed and interpreted by the Cytovale system's **machine learning algorithm**

Images from Cytovale System

White Blood Cells from a **Healthy Donor**



White Blood Cells from a **Septic Patient**



INTELLISEP INDEX (ISI): 3 DISCRETE BANDS

IntelliSep

IntelliSep may provide actionable, clinical guidance around sepsis risk in under 10 minutes with three distinct bands – **The IntelliSep Index**

Green Band (0.1-4.9)
Suggest exploring other diagnoses or conservative care

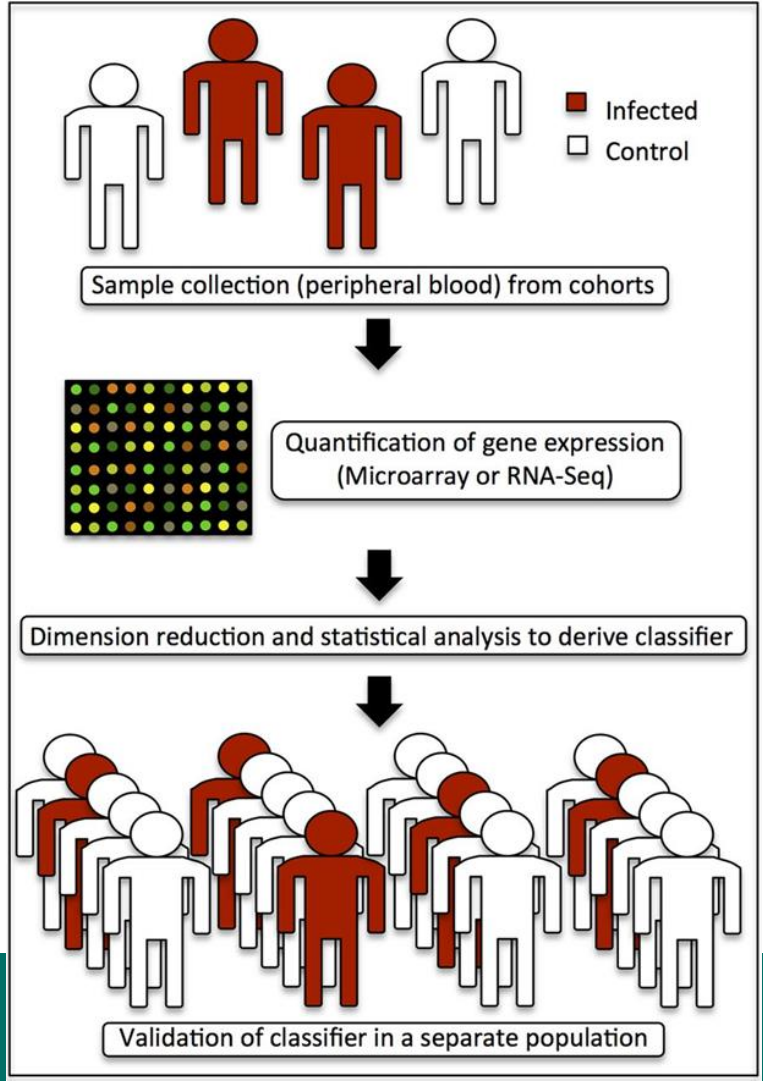
Yellow Band (5.0-6.2)
Slow down, additional workup may be appropriate for this patient

Red Band (6.3-10.0)
Likely warrants immediate and aggressive management

The ISI provides 3 key pieces of information regarding a patient's result:

1. A **single value (between 0.1-10.0)** indicating a patient's level of immune activation and corresponding level of having sepsis or developing sepsis over the next 72 hours
2. A **corresponding color band**, for ease of interpretation around sepsis risk
3. A **description** of the value/band results

A BETTER APPROACH TO BIOMARKER DEVELOPMENT



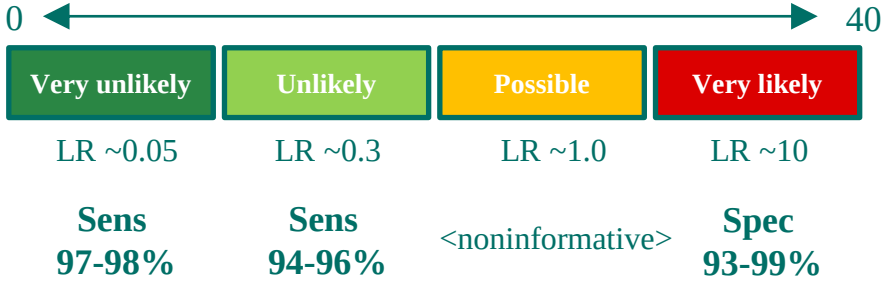
Holcomb ZE et al. J Clin Microbiol. 2017

HOSTDX™ SEPSIS: PRESENCE, TYPE, AND SEVERITY

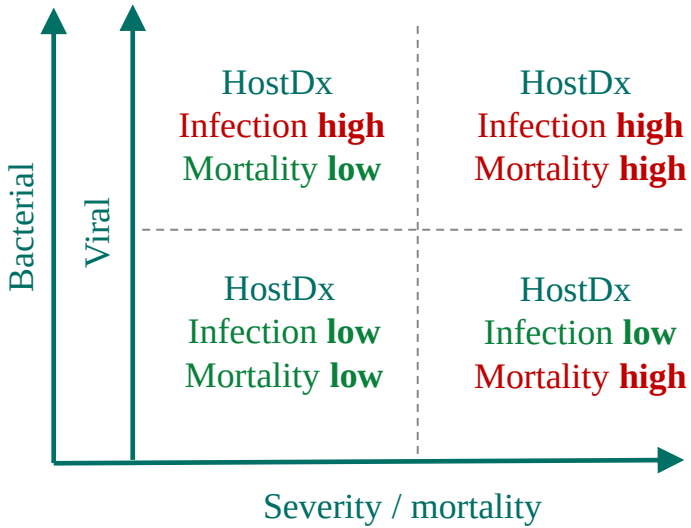
HostDx Sepsis puts out not one but three scores:

1. Bacterial infection,
2. Viral infection, and
3. Severity (30-day Mortality)

Each score is broken into 4 interpretation bands:

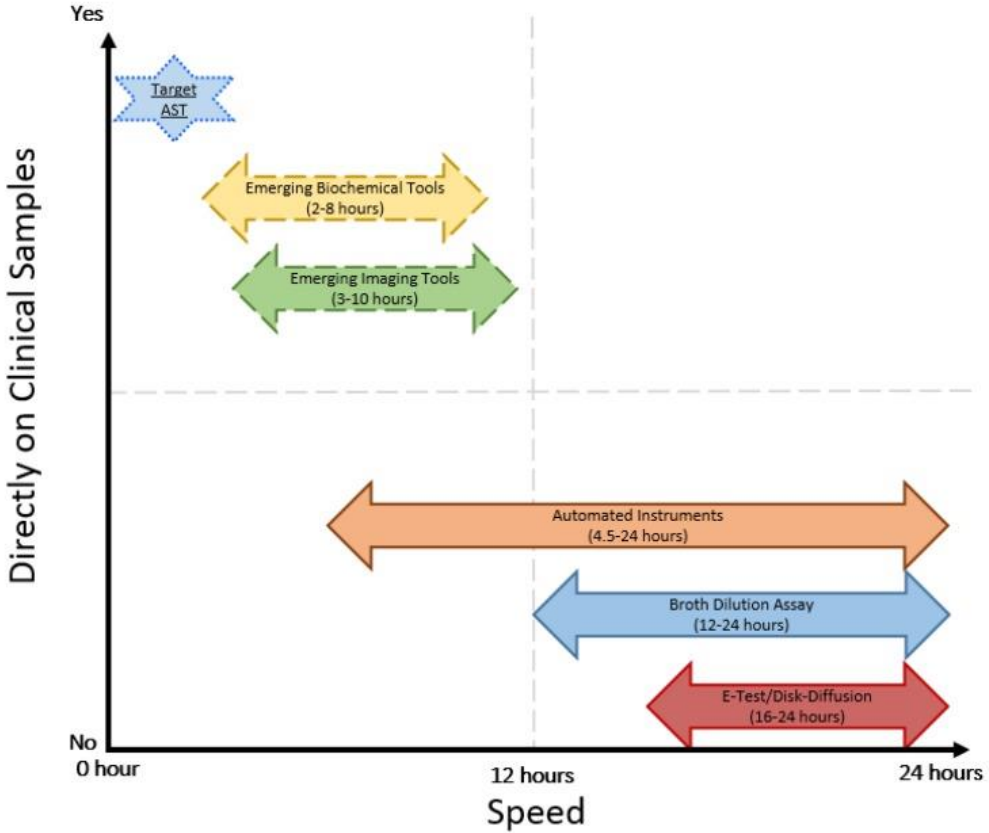


Highly actionable output



IS SEQUENCING EVER GOING TO COME TO MY LAB?

WHERE ARE WE AND WHERE DO WE NEED TO GO?

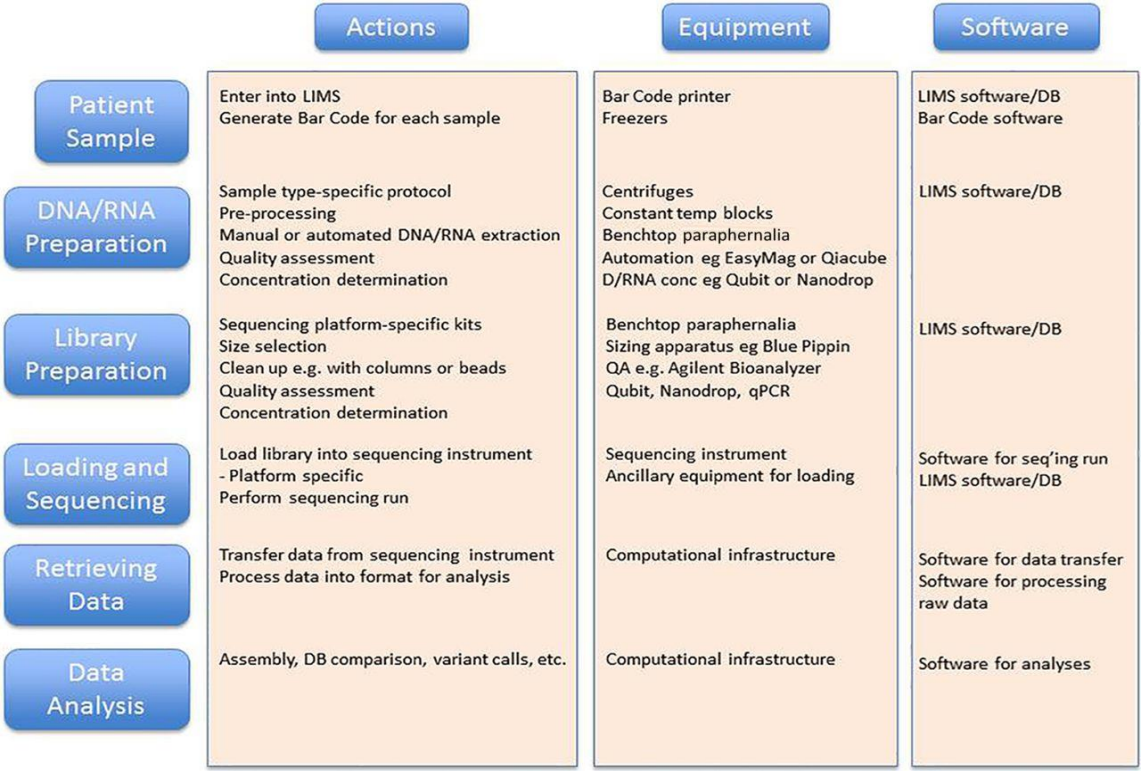


BACTERIAL 16S SEQUENCING

- 178 Specimens tested over 10 months
  - 13 (7.3%) had no bacterial culture order
  - 163 tested by both culture and sequencing

RESULT	NUMBER	PERCENT OF TOTAL	CLINICALLY VALUABLE RESULT FROM SEQUENCING
Specimens tested by sequencing and culture	163	100%	N/A
Negative by both tests	86	52.8%	No
Culture and sequencing positive for same organism (culture result available before sequencing)	34	20.9%	No, culture result was obtained first
Sequencing positive only for a previously diagnosed infection (patient was being treated, which prevented growth on culture)	7	4.3%	No, infection had already been identified and effective treatment initiated
Specimens with multiple organisms identified by culture and sequencing was indeterminate	5	3.1%	No, sequencing does not work if multiple organisms are present
Culture positive, sequencing negative	22	13.5%	No
Sequencing positive, culture negative (patient was on antibiotics that would prevent bacterial growth in culture)	7	4.3%	Yes
Sequencing positive, culture negative	1	0.6%	Yes

NGS workflow



Brittany Goldberg et al. mBio 2015; doi:10.1128/mBio.01888-15

VERIFICATION/VALIDATION

- The entire process of NGS (extraction to bioinformatics pipeline) must be verified
- Must be of suitable size to demonstrate performance on SNPs, insertions, deletions, etc..
  - CAP introduced 10 specimen MINIMUM requirement in 2016.
  - Significant opportunity to help labs in this area
- Supplementary/Confirmatory testing should also be included
- Ongoing QC should be considered
- Cost of verification significant – man oncology labs report verification studies costing $250,000-$300,000
  - Updates to verification can cost $50,000-$70,000

REAL OR CONTAMINATION ?

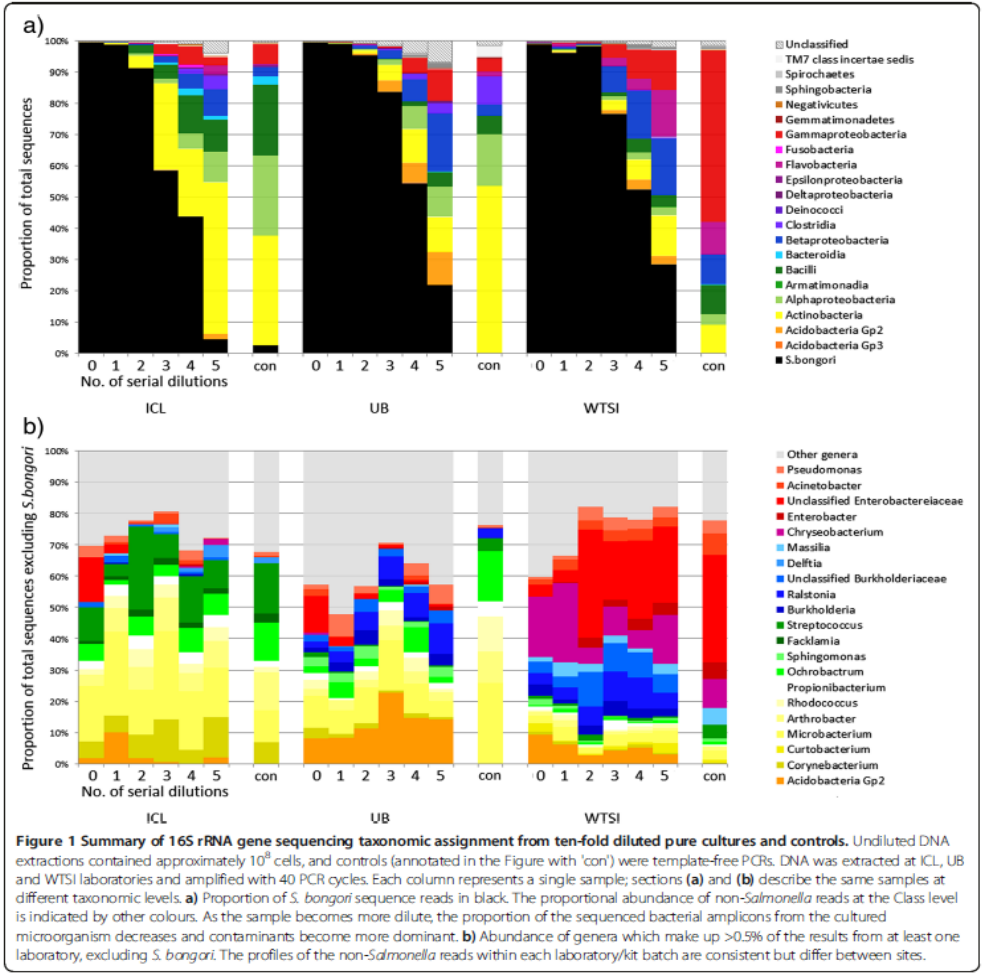


Figure 1 Summary of 16S rRNA gene sequencing taxonomic assignment from ten-fold diluted pure cultures and controls. Undiluted DNA extractions contained approximately 10^8 cells, and controls (annotated in the Figure with 'con') were template-free PCRs. DNA was extracted at ICL, UB and WTSI laboratories and amplified with 40 PCR cycles. Each column represents a single sample; sections **(a)** and **(b)** describe the same samples at different taxonomic levels. **a)** Proportion of *S. bongori* sequence reads in black. The proportional abundance of non-*Salmonella* reads at the Class level is indicated by other colours. As the sample becomes more dilute, the proportion of the sequenced bacterial amplicons from the cultured microorganism decreases and contaminants become more dominant. **b)** Abundance of genera which make up >0.5% of the results from at least one laboratory, excluding *S. bongori*. The profiles of the non-*Salmonella* reads within each laboratory/kit batch are consistent but differ between sites.

Salter et al, BMC Biology 2014. 12:87

NOT ALL SOFTWARE IS CREATED EQUAL

Table 1. Numbers of false positives from the full datasets

	Resistance gene	SRST2	ResFinder	KmerResistance
UK hospital (number of tests = 858)	*aac(3)-IIa*	1	—	—
	aac(6′)Ib-cr	1	2	2
	bla_{CTX-M}[a]	12	12	12
	bla_{TEM}[a]	4	4	3
	qnrB[a]	1	1	1
Denmark pig farm (number of tests = 2592)	*aac(6′)-aph(2″)*	6	7	2
	aadA[a]	6	6	6
	aadE	—	4	1
	ant(6)-Ia	5	—	—
	aph(3′)-I[a]	2	2	—
	aph(3′)-III	3	4	—
	bla_{CTX-M}[a]	3	—	—
	bla_{TEM}[a]	3	3	—
	cat[a]	1	1	—
	dfrA1	1	1	—
	dfrG	1	1	—
	erm(B)	10	7	—
	lnu(B)	1	—	—
	str	—	3	—
	strA/strB	1	1	—
	sul2	—	1	—
	tet(A)	1	1	—
	tet(B)	1	1	1
	tet(L)	—	2	—
	tet(M)	6	3	—

[a]Different alleles were detected.

Clausen PTLC et al. JAC. 2016; 71.

ANTIMICROBIAL RESISTANCE

TABLE 4 Derivation set results[a]

Antimicrobial agent	No. of isolates resistant by phenotype: Susceptible by genotype	No. of isolates resistant by phenotype: Resistant by genotype	No. of isolates susceptible by phenotype: Susceptible by genotype	No. of isolates susceptible by phenotype: Resistant by genotype	Total no. of isolates	Very major error rate (%)	Major error rate (%)	Sensitivity (95% CI)	Specificity (95% CI)
Penicillin	4	438	59	0	501	0.8	0	0.99 (0.98–1.00)	1.00 (0.92–1.00)
Methicillin	1	158	341	1	501	0.2	0.2	0.99 (0.96–1.00)	1.00 (0.98–1.00)
Ciprofloxacin	7	165	326	3	501	1.4	0.6	0.96 (0.91–0.98)	0.99 (0.97–1.00)
Erythromycin	1	133	366	1	501	0.2	0.2	0.99 (0.95–1.00)	1.00 (0.98–1.00)
Clindamycin	0	88	89	0	177[c]	0	0	1.00 (0.95–1.00)	1.00 (0.95–1.00)
Tetracycline	0	28	473	0	501	0	0	1.00 (0.85–1.00)	1.00 (0.99–1.00)
Vancomycin	0	0	501	0	501	0	0	N/A[d]	1.00 (0.99–1.00)
Fusidic acid	3[b]	38	458	2	501	0.6	0.4	0.93 (0.79–0.98)	1.00 (0.98–1.00)
Trimethoprim	5	10	308	0	323	1.5	0	0.67 (0.39–0.87)	1.00 (0.98–1.00)
Gentamicin	0	7	494	0	501	0	0	1.00 (0.60–1.00)	1.00 (0.99–1.00)
Mupirocin	0	2	174	2	178	0	1.1	1.00 (0.20–1.00)	0.99 (0.96–1.00)
Rifampin	1	2	498	0	501	0.2	0	0.67 (0.13–0.98)	1.00 (0.99–1.00)
Overall	22	1,069	4,087	9	5,187	0.2	0.4	0.98 (0.97–0.99)	1.00 (0.99–1.00)

[a] Comparison of results for individual antimicrobial agents for 501 [illegible] genotypic prediction method. The result (resistant or susceptible) b susceptibility using the v2.0 genotypic prediction method.
[b] Two isolates had two nonsynonymous mutations in fusA not prev observed phenotypes.
[c] One isolate failed to grow for clindamycin testing.
[d] N/A, not applicable.

TABLE 5 Validation set results[a]

Antimicrobial agent	No. of isolates resistant by phenotype: Susceptible by genotype[b]	No. of isolates resistant by phenotype: Resistant by genotype	No. of isolates susceptible by phenotype: Susceptible by genotype	No. of isolates susceptible by phenotype: Resistant by genotype[b]	Total no. of isolates	Very major error rate (%) (95% CI)	Major error rate (%) (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Penicillin	3 (2)	379	84	25 (9)	491	0.6 (0.1–1.8)	5.1 (3.3–7.4)	0.99 (0.98–1.00)	0.77 (0.68–0.84)
Methicillin	2 (1)	55	432	2 (1)	491	0.4 (0.05–1.5)	0.4 (0.05–1.5)	0.96 (0.87–0.99)	1.00 (0.98–1.00)
Ciprofloxacin	6 (4)	64	420	1 (0)	491	1.2 (0.4–2.6)	0.2 (0.05–1.1)	0.91 (0.82–0.96)	1.00 (0.98–1.00)
Erythromycin	4 (2)	79	405	3 (3)	491	0.8 (0.2–2)	0.6 (0.1–1.8)	0.95 (0.87–0.98)	0.99 (0.98–1.00)
Clindamycin	2 (2)	77	2	0	81	2.5 (0.3–8.6)	0.0 (0–4.4)	0.97 (0.90–1.00)	1 (0.20–1.00)
Tetracycline	0	18	471	2 (2)	491	0.0 (0–0.7)	0.4 (0.05–1.5)	1.00 (0.78–1.00)	1.00 (0.98–1.00)
Vancomycin	0	0	491	0	491	0.0 (0–0.7)	0.0 (0–0.7)	N/A[c]	1.00 (0.99–1.00)
Fusidic acid	4 (4)	39	448	0	491	0.8 (0.2–2)	0.0 (0–0.7)	0.91 (0.77–0.97)	1.00 (0.99–1.00)
Trimethoprim	2 (2)	1	197	2 (1)	202	1.0 (0.1–3.5)	1.0 (0.1–3.5)	0.33 (0.02–0.87)	0.99 (0.96–1.00)
Gentamicin	2 (2)	2	487	0	491	0.4(0.05–1.5)	0.0 (0–0.7)	0.50 (0.09–0.91)	1.00 (0.99–1.00)
Mupirocin	0	2	489	0	491	0.0(0–0.7)	0.0 (0–0.7)	1.00 (0.20–1.00)	1.00 (0.99–1.00)
Rifampin	0	5	486	0	491	0.0 (0–0.7)	0.0 (0–0.7)	1.00 (0.46–1.00)	1.00 (0.99–1.00)
Overall	25 (19)	644	4,410	35 (16)	5,112	0.5 (0.3–0.7)	0.7 (0.5–0.9)	0.97 (0.95–0.98)	0.99 (0.99–1.00)

[a] Comparison of susceptibility results for 491 bacteremia and carriage isolates by phenotype (Phoenix/disc diffusion consensus result) and genotype prediction tool v2.0. The result (resistant or susceptible) by phenotype refers to Phoenix or disc diffusion consensus results, and the result by genotype refers to the predicted susceptibility using the v2.0 genotypic prediction method.
[b] Figures in parentheses are numbers of isolates with discrepant phenotype confirmed on repeat testing.
[c] N/A, not applicable.

Gordon NC et al. JCM. 2014; 52.

EXPERT INTERPRETATION

[redacted]

SPECIMEN TYPE: PLASMA

SPECIMEN INFORMATION

PATIENT INFORMATION

INSTITUTION INFORMATION

[redacted]

TEST RESULTS

MICROORGANISM NAME	DNA MOLECULES PER MICROLITER (MPM)*	REFERENCE INTERVAL (MPM)**
Trypanosoma cruzi	40,078	< 10
Cytomegalovirus (CMV) (Human herpesvirus 5)	9,587	< 10
Staphylococcus aureus	1,139	< 10
Escherichia coli	238	< 17
Prevotella melaninogenica	203	< 10
Neisseria sicca	115	< 10
Streptococcus anginosus (Streptococcus anguinosis/milleri group)	115	< 10
Streptococcus mitis (Streptococcus mitis group)	106	< 14
Streptococcus intermedius (Streptococcus anguinosis/milleri group)	87	< 10
Bacteroides fragilis (Bacteroides fragilis group)	83	< 10
Bacteroides uniformis (Bacteroides fragilis group)	63	< 10
Fusobacterium nucleatum	50	< 10

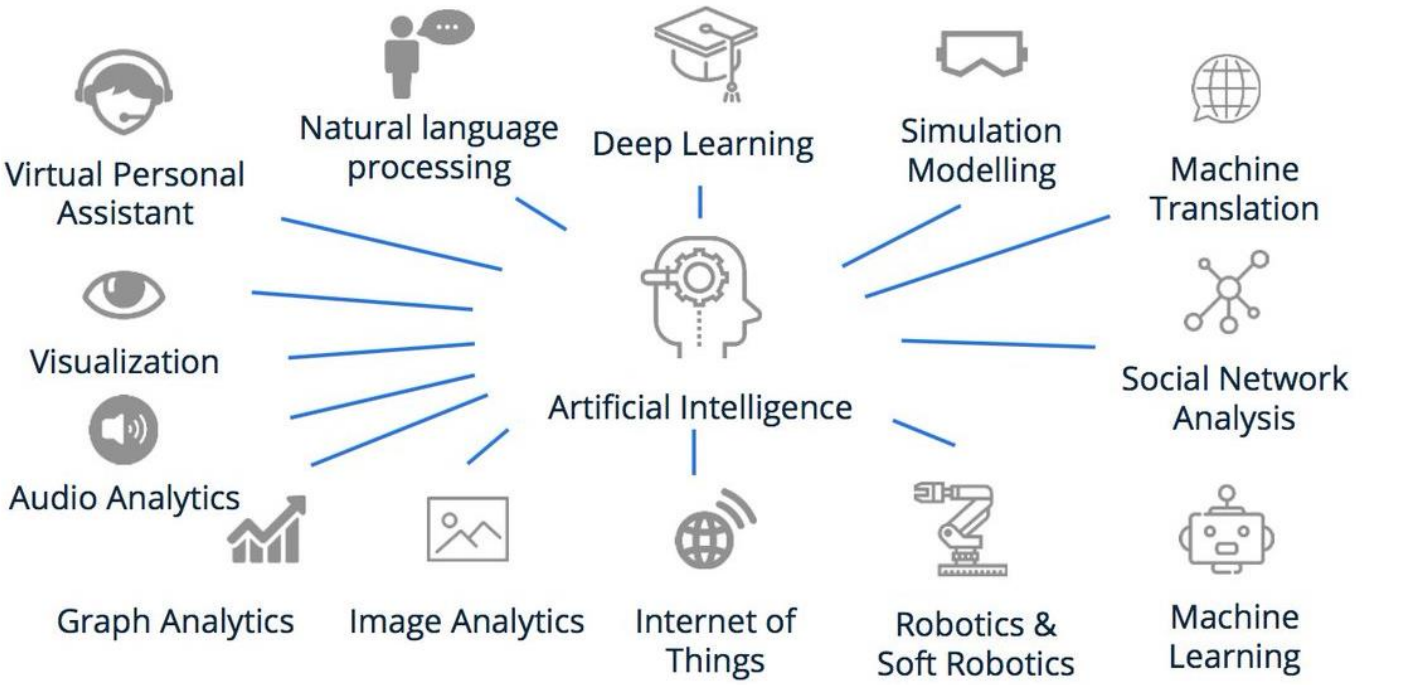
* Molecules per microliter = number of DNA fragments present in one microliter of plasma

** Reference Interval = the 97.5th percentile MPM concentration detected in PPT plasma from a cohort of asymptomatic donors

Karius Medical staff are available to answer any questions about these results Phone: (866) 452-7487 | Email: medical@kariusdx.com

IS AI GOING TO TAKE OVER MY LAB?

WHAT ARE THE APPLICATIONS OF AI?

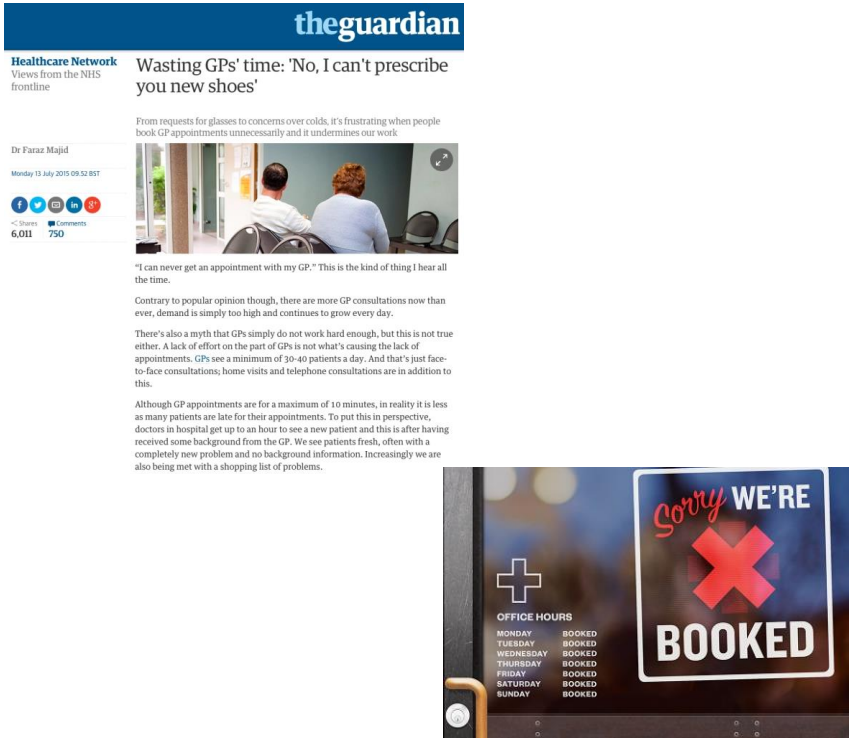


WHICH AREAS OF MEDICINE WILL AI MOST IMPACT?

- Every area will be impacted
- Strengths of AI
  - Pattern recognition
    - Radiology
    - Pathology
    - GI – Identification of polyps during colonoscopy
    - Scheduling - University College in London
  - Liberation from typing notes
    - Natural language recognition to synthesize notes
- Liabilities of AI
  - Data Privacy and Security
  - Embedded bias in datasets
  - Potential to worsen inequities
  - Lack of transparency of algorithms to patients

- By 2021 AI will generate $6.7 billion in revenue, globally
- By 2025, between 100 million and 2 billion genomes will be sequenced

IMPACT TO PROVIDER SCHEDULING



theguardian

Healthcare Network
Views from the NHS frontline

Wasting GPs' time: 'No, I can't prescribe you new shoes'

From requests for glasses to concerns over colds, it's frustrating when people book GP appointments unnecessarily and it undermines our work

Dr Faraz Majid

Monday 13 July 2015 09.52 BST

Shares 6,011 Comments 750

"I can never get an appointment with my GP." This is the kind of thing I hear all the time.

Contrary to popular opinion though, there are more GP consultations now than ever, demand is simply too high and continues to grow every day.

There's also a myth that GPs simply do not work hard enough, but this is not true either. A lack of effort on the part of GPs is not what's causing the lack of appointments. GPs see a minimum of 30-40 patients a day. And that's just face-to-face consultations; home visits and telephone consultations are in addition to this.

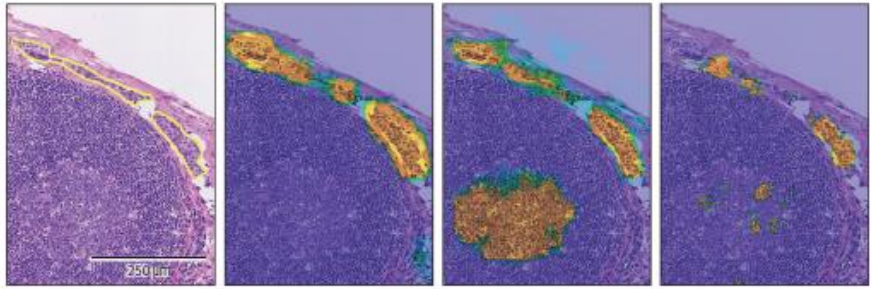
Although GP appointments are for a maximum of 10 minutes, in reality it is less as many patients are late for their appointments. To put this in perspective, doctors in hospital get up to an hour to see a new patient and this is after having received some background from the GP. We see patients fresh, often with a completely new problem and no background information. Increasingly we are also being met with a shopping list of problems.

- Scheduling is challenging
  - Patients want to be seen quickly, but often do not show for appointments
  - No show rates can be as high as 33%, making clinic scheduling difficult
- University College, London
  - Using AI evaluation of patient social media networks can predict if patient will show up for clinic with 99% accuracy

IMPACT TO PATHOLOGY

- DeepMind evaluation of breast cancer metastasis
  - LYNA (lymph node assistant) compared to 11 pathologists for evaluation of lymph node metastases
  - AUC for LYNA was 99% compared to 62% for pathologists
    - Difference attributed to amount of time the pathologist could spend evaluating slide versus LYNA evaluating every part of the slide

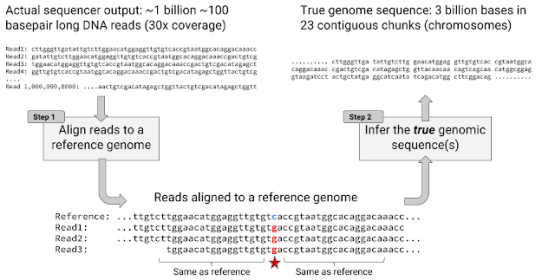
Codename[a]	Task 1: Metastasis Identification FROC Score (95% CI)[c]	Task 2: Metastases Classification AUC (95% CI)[c]	*P* Value for Comparison of the Algorithm vs Pathologists WTC[d]	Algorithm Model Deep Learning	Architecture	Comments
VISILAB II	0.116 (0.063-0.177)	0.651 (0.549-0.742)	>.99	✓	3-layer CNN	Self-designed network architecture
Anonymous I	0.097 (0.049-0.158)	0.628 (0.530-0.717)	>.99		Random Forests[23]	
Laboratoire d'Imagerie Biomédicale I	0.120 (0.079-0.182)	0.556 (0.434-0.654)	>.99		SVM[22]	Used various color and texture features
Pathologist WOTC	0.724 (0.643-0.804)	0.966 (0.927-0.998)				Expert pathologist who assessed without a time constraint
Mean pathologists WTC		0.810 (0.750-0.869)				The mean performance of 11 pathologists in a simulation exercise designed to mimic the routine workflow of diagnostic pathology with a flexible 2-h time limit



Ehteshami-Bejnordi B et al. 2017. JAMA. 318(22)

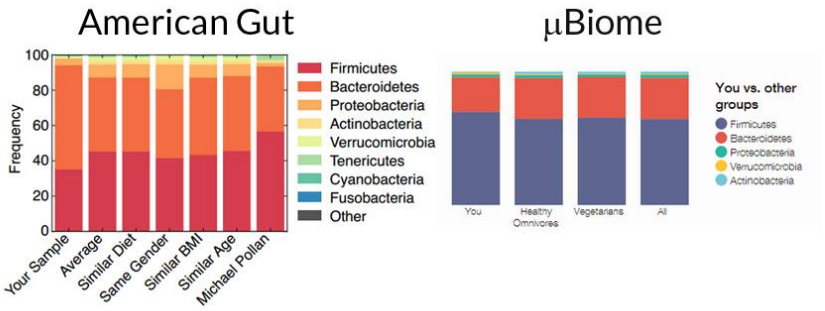
GENOMIC HEALTH

- High throughput sequencing allows whole genome to be sequenced in less than a week at a cost of $1000-10,000
- DeepVariant
  - Google AI open source gene reconstruction tool
  - Able to distinguish SNPs versus random errors
- Deep Genomics and Sophia Genetics
  - Use genome data to determine best drug therapies
  - Analyze mutations from patient specimen and determine the impact of the mutation on a genome wide level
- Gene Editing
  - Edit out genes that may cause disease or introducing genes that can prevent disease
    - eg RoundUp resistant crops….



AI IN PREDICTIVE MEDICINE, THE EXAMPLE OF THE MICROBIOME

- Microbiome analysis generates massive amounts of data
  - We're still learning how to use the microbiome to improve health
  - Changes in microbiome that affect your health happen over longer periods of time – A Glacial development for microbes
  - Who tests your microbiome can significantly impact the results and will need to monitor data over extended period to follow impact on health

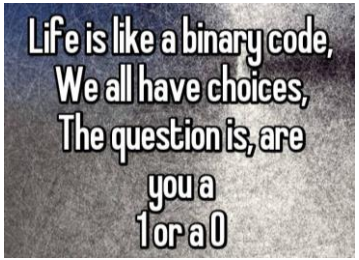


BUT WHAT ABOUT THE PRACTICE OF CORE CLINICAL MICROBIOLOGY?

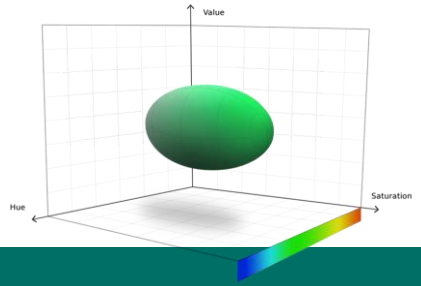
HAI SCREENING - REPRESENTATIVE IMAGES FROM VRE SCREENING

	Negative	Positive	Break through growth
Colorex VRE			
Oxoid VRE			

THREE TYPES OF READING ALGORITHMS



- Binary
  - Simple yes or no answers – ie Growth versus no growth
  - Can occur on any media type
  - Most useful when screening large populations which are largely negative
- Color Recognition
  - Combines binary growth/no growth with color recognition
  - Useful for chromogenic media and media that uses color to differentiate colony types
  - Can be tuned and optimized for each lab
- Deep Colony
  - Machine learning, individual analysis of each colony type
  - Can be useful to help assign preliminary identification to colonies
  - Can help quantify different populations and assign significance



VRE RECTAL SWAB SCREENING WITH COPAN PHENOMATRIX SOFTWARE (N=104,730 SAMPLES)

Performance of digital imaging of VRE plates compared to manual reading

Clinical test site	No. of specimens tested	Results (no.)[a]				Performance (% [95% CI])[b]		PPV[c] (%)	NPV[c] (%)	Prevalence
		MP/AP	MN/AN	MN/AP	MP/AN	Sensitivity	Specificity			
1	11,438	1,474	9,129	835	0	100 (99-100)	91.6 (91-92)	64	100	12.9%
2	75,518	2,822	64,535	8,161	0	100 (99-100)	88.8 (88-89)	26	100	3.7%
3	17,774	2,107	14,315	1,352	0	100 (99-100)	91.4 (91-92)	61	100	11.8%
Total	104,730	6,403	87,979	10,348	0	100 (99-100)	89.5 (89-90)	38	100	6.1%

[a]MP/AP, manual Pos automation Pos; MN/AN, manual Neg/automation Neg; MN/AP, manual Neg/automation pos; MP/AN, manual Pos/automation Neg.

[b] CI, confidence interval.

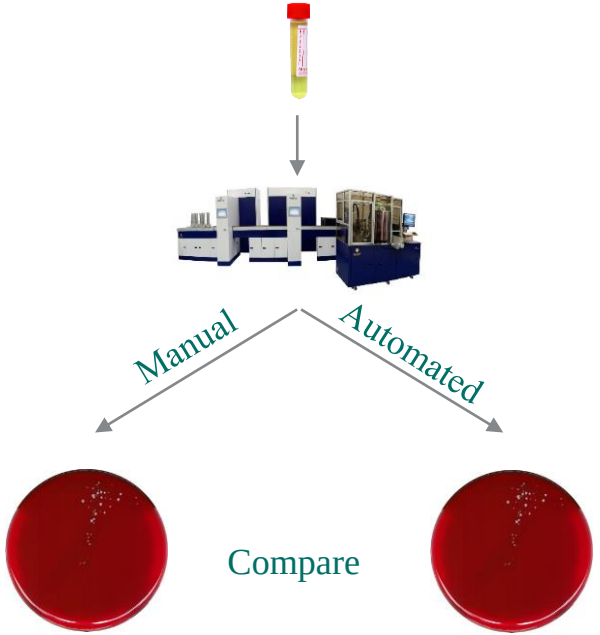
[c]PPV, Positive Predictive Value; NPV. Negative Predictive Value

INCORPORATING INTO THE LABORATORY

- Negative Specimens
  - Batch viewing images
  - Batch report
- Non-negative Specimens
  - Still requires Technologist
  - View on HD monitor
    - Positive vs Matrix or Yeast
  - Standard of care

CAN WE USE THIS SOFTWARE TO ANALYZE URINE USING NON-CHROMOGENIC PLATES?

- 3 sites
- Specimens
  - Urines (Plated Blood, MacConkey, CNA)
- Algorithm results
  - POS >10 colonies on any plate
  - Neg ≤ 10 colonies in all 3 agars
- Reference method
  - Manual reading
  - Site specific procedures for results
- Discrepant analysis
  - Images reviewed by supervisor



How well does it work on Urines?

Performance of WASPLab™ digital imaging software compared to manual reading of BAP, MAC and CNA

	No. of specimens tested	Results (no.)[a]				Performance (% [95% CI])[b]	
		MP/AP	MN/AN	MN/AP	MP/AN	PPA[c]	NPA[c]
Site 1	5201	2960	1101	1099	41	98.6 (98-99)	50.0 (48-52)
Site 2	5513	1620	3392	500	1	99.9 (99-99)	87.2 (86-88)
Site 3	2751	1108	1184	393	66	94.4 (93-96)	75.1 (73-77)
Total	13465	5688	5677	1992	108	98.1 (97-98)	74.0 (73-75)

[a]MP/AP, manual Pos automation Pos; MN/AN, manual Neg/automation Neg; MN/AP, manual Neg/automation pos; MP/AN, manual pos/automation Neg.

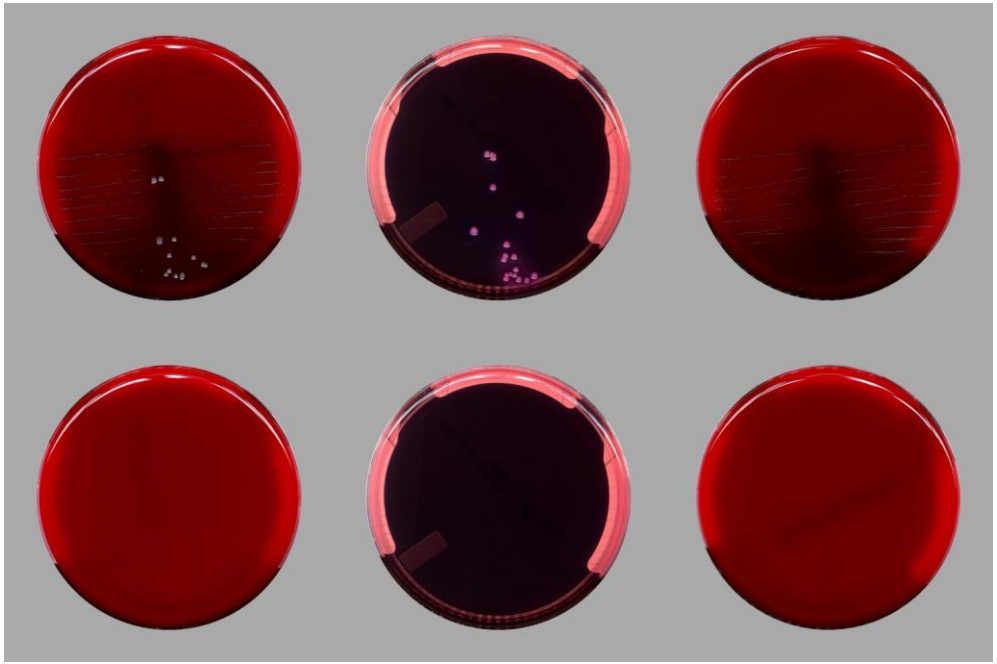
[b] CI, confidence interval.

[c]PPA, Positive Percent Agreement; NPA, Negative Percent Agreement

FALSE POSITIVE EXAMPLE
SW POS, HUMAN NSG

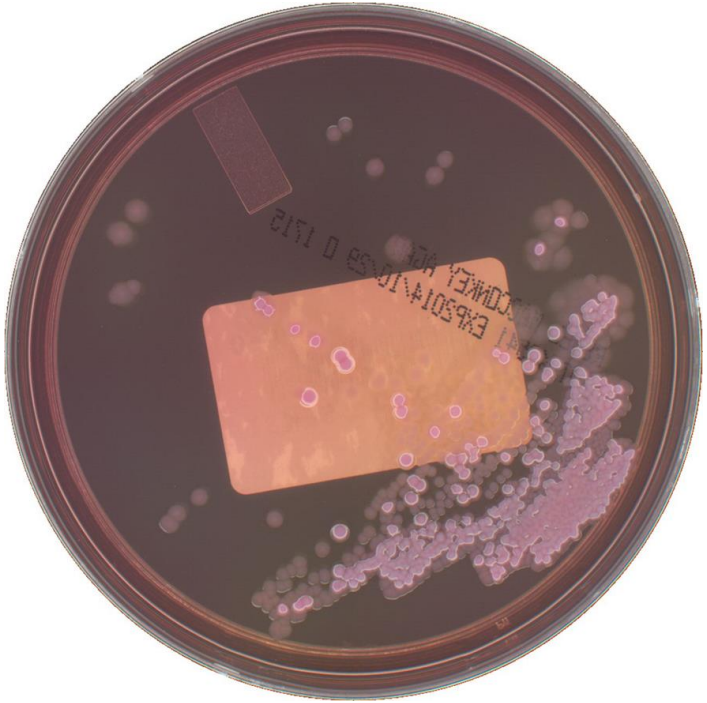
T18H

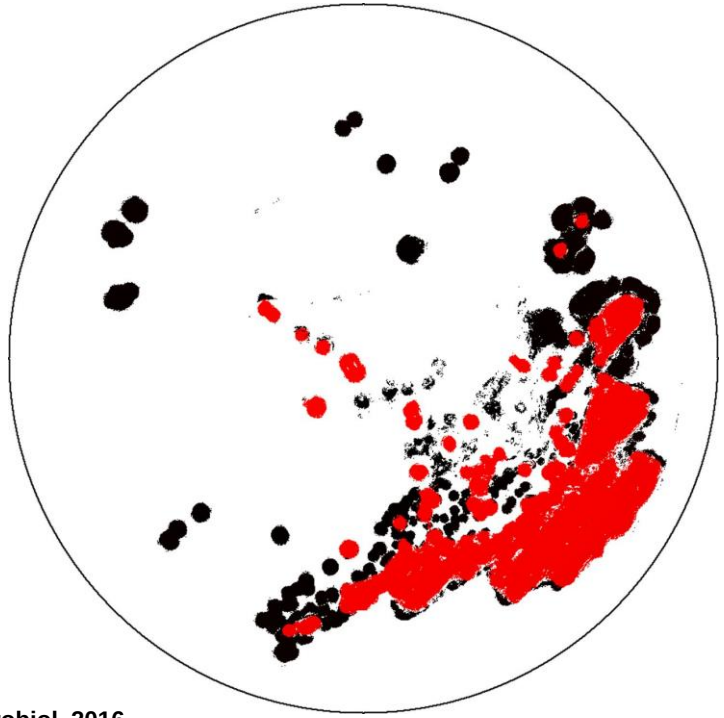
T0



BLOOD MAC CONKEY CNA

APAS COLONY MORPHOLOGY RECOGNITION – SEPARATION OF LACTOSE FERMENTERS





John Glasson et al. J. Clin. Microbiol. 2016.

PERFORMANCE OF APAS ON URINE CULTURES (N=509 SAMPLES)

TABLE 2 Organisms detected by APAS compared with those by the routine laboratory reports

Organism	No. of cases detected by APAS	No. of cases reported by the laboratory
Escherichia coli	339	341
Enterococcus faecalis	38	38
Klebsiella pneumoniae	21	21
Proteus mirabilis	19	19
Pseudomonas aeruginosa	18	19
Staphylococcus saprophyticus	14	14
Klebsiella oxytoca	8	8
Staphylococcus epidermidis	7	7
Streptococcus agalactiae	6	6
Enterobacter aerogenes	5	5
Citrobacter koseri	5	5
Enterobacter cloacae complex	3	3
Morganella morganii	3	3
Viridans streptococci	3	3
Candida albicans	2	2
Citrobacter freundii	2	2
Staphylococcus, coagulase negative	2	2
Acinetobacter spp.	1	1
Aerococcus urinae	1	1
Candida spp.	1	1
Enterococcus faecium	1	1
Raoultella spp.	1	1
Serratia liquefaciens	1	1
Serratia ureilytica	1	1
Staphylococcus aureus	1	1
Staphylococcus haemolyticus	1	1
Staphylococcus hominis	1	1
Streptococcus dysgalactiae	1	1
Total	506	509

TABLE 1 Colony identification performance by APAS compared with that of a reference panel

Colony morphologies on blood agar	Examples of colony morphology	Sensitivity (%)	Specificity (%)
Coliform-like colonies	*Escherichia coli*	98.9	83.9
Swarming colonies	*Proteus mirabilis*	97.2	99.9
Granular Gram-negative colonies	*Pseudomonas aeruginosa*	67.7	92.5
Staphylococcus-like colonies	*Staphylococcus* spp.	94	83.8
Small beta-hemolytic colonies	*Streptococcus agalactiae*	92.4	89.3
Small colonies	Enterococci, lactobacilli, corynebacteria	90	73.7
Colony morphologies on MacConkey agar			
Lactose fermenters	*Escherichia coli*	99.2	98.1
Non-lactose fermenters	*Proteus* spp.	92.6	95.9

John Glasson et al. J. Clin. Microbiol. 2016.

IS THERE ANY VALUE OR IS THIS JUST COOL TECHNOLOGY?

What Does AI Mean in the Context of the Clinical Laboratory and Pathology?

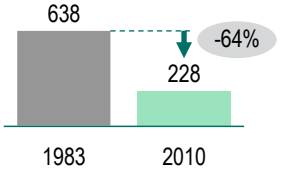
Macro trends are driving the need for automation

Key market trends

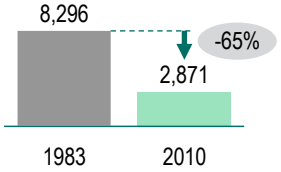
- Lack of experienced technologists, supervisors, pathology and microbiology PhDs
- Decreased financial incentive for in-patient testing and increased incentive for shorter LOS
- Increasing volume and lab consolidation pressures
- Pricing and reimbursement pressure
- Need for sample traceability/ chain of custody
- Need for better coordination between the lab – physician – pharmacist

The biggest driver of automation is the lack of qualified microbiologists and med techs

Number of med tech programs US



Med tech enrollment US annual



Lab professionals eligible for retirement US 2010, percent