CURRENT TRENDS IN AMR AND AST

Alex van Belkum

Belgrade, 27 March 2019

PIONEERING DIAGNOSTICS

USE OF ANTIBIOTICS DRIVES RESISTANCE UP

One example out of many: Meropenem at the hospital

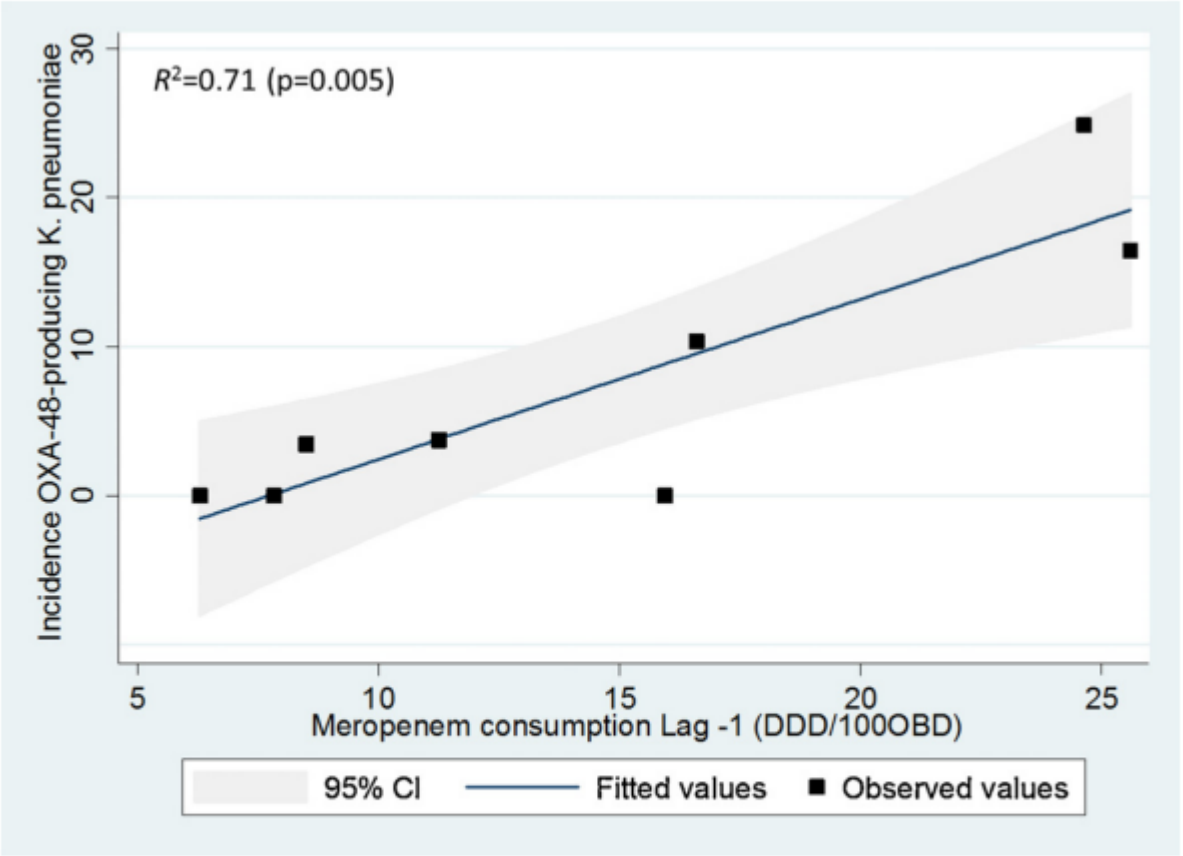
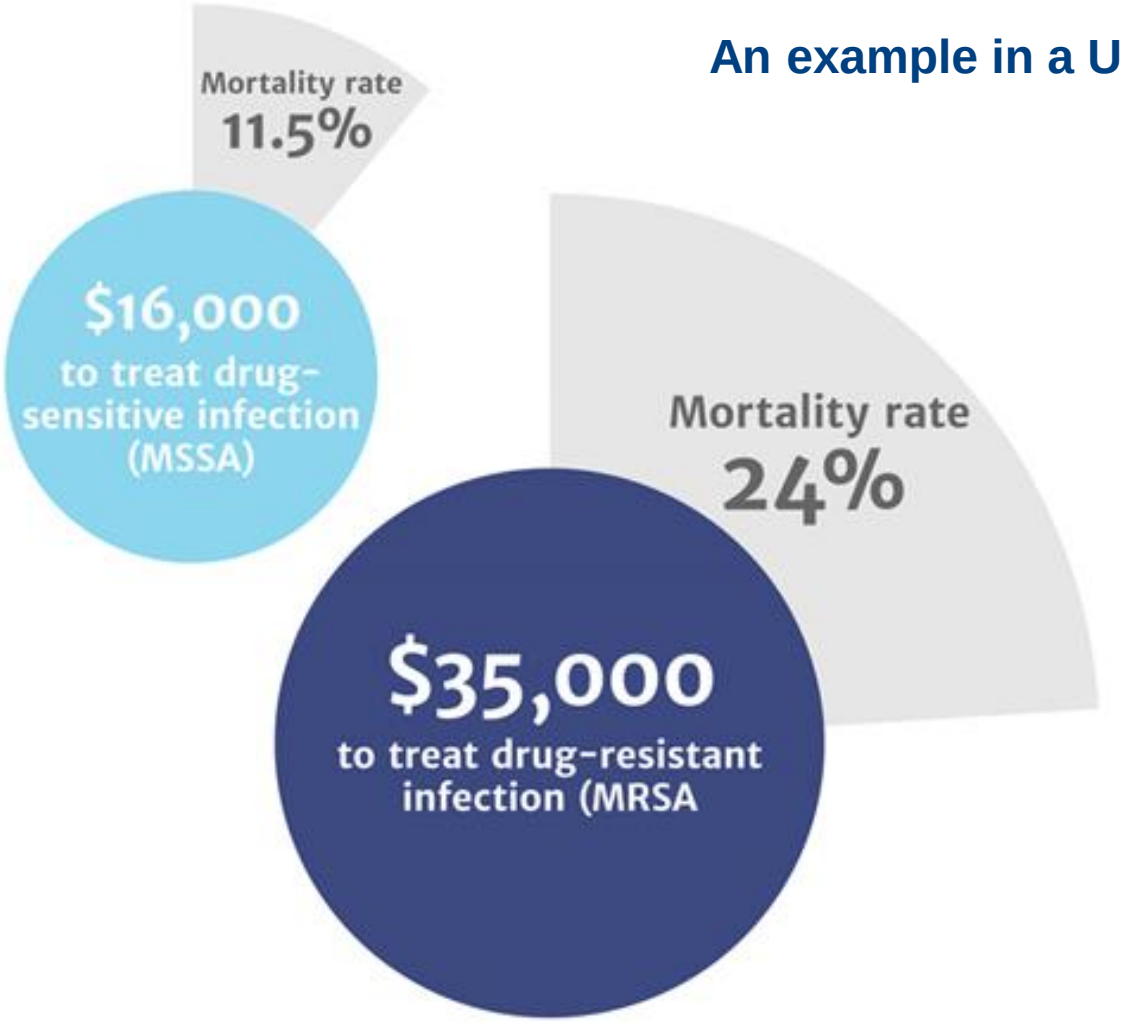


Fig. 1. Cross-correlation between meropenem consumption lag −1 (the preceding year) and the incidence rate of OXA-48-producing *Klebsiella pneumoniae* in a West London renal unit from 2008–2009 to 2013–2014.

Source : M. Gharbi et al. / International Journal of Antimicrobial Agents 46 (2015) 150–15

A RESISTANT INFECTION IS MORE LIKELY TO BE LETHAL AND CERTAINLY MORE COSTLY

An example in a US hopital



Source : Filece GA ey al. 2010. Infection Control& Hospital epidemiology 31 (4à

WHO PRIORITY PATHOGEN LIST!

ANTIMICROBIAL SUSCEPTIBILITY TESTING

AST IS A MICROBIOLOGICAL PROCEDURE THAT DETERMINES THE CONCENTRATION OF ANTIBIOTIC REQUIRED TO INHIBIT THE GROWTH OF OR KILL A MICROORGANISM.

THIS CAN BE ACCOMPLISHED VIA GROWTH-BASED (PHENOTYPIC) METHODS OR (ON A MORE SURROGATE LEVEL) VIA MOLECULAR MEANS (PROTEO/LIPIDO/GLUCO/GENOTYPIC).

BARRIERS TO ANTIMICROBIAL SUSCEPTIBILITY TESTING

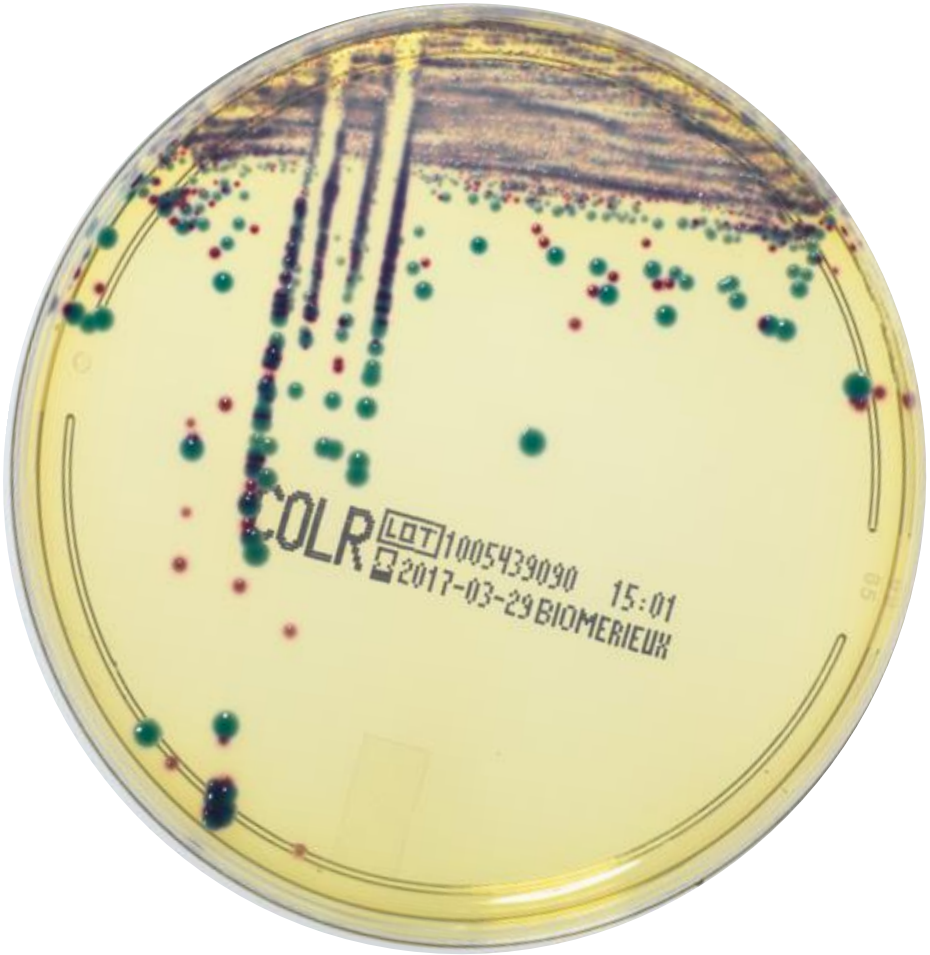
MICROBIOLOGY

- SMALL NUMBERS OF CELLS
- SLOW GROWTH
- LAG TIME
- HETEROGENEITY OF ANTIBIOTIC RESISTANCE
- INDUCTION OF RESISTANCE
- LOW LEVEL RESISTANCE
- CIDAL VERSUS STATIC ANTIBIOTICS
- DETECTION OF NEW MECHANISMS

TECHNOLOGY

- NEED FOR ID AND AST AT THE SAME TIME (?)
- SPEED – PHENOTYPIC AST IN LESS THAN 4 H IS A CHALLENGE.
- MANDATORY DAILY QC TESTING (IRRESPECTIVE OF METHOD)
- RECURRING ISSUES AND DEVELOPMENT DELAYS IN SEMI AUTOMATED AST (MICROSCAN, PHOENIX, VITEK2)
- POOR QUALITY OF ASSAYS FROM SOME MANUFACTURERS
- RECURRING ISSUES WITH GRADIENT TEST QUALITY
- INFLUX OF NEW PHENOTYPIC METHODS – DIFFICULT TO ASSESS.

NO NEED FOR SAMPLE PROCESSING AT ALL??



Screening of Colistin-resistant Enterobacteriaceae from rectal swabs and stools

IMPROVING “OLD FASHIONED” AST: MORE DRUGS IN A SINGLE ASSAY

VITEK® 2 OPUS AST CARD

Test more antibiotics

Save time
Increase efficiency with less offline tests

Easy transition (Same set up and same VITEK®2)

REPORT APPROPRIATE ANTIBIOTICS FOR BETTER TREATMENT DECISIONS

MOLECULAR AMR DIAGNOSTICS


www.drw-ltd.com


www.biocartis.com


www.cepheid.com


www.nanosphere.com


www.molecular.roche.com


www.check-points.com


www.optigene.co.uk


www.curetis.com


www.alere-i.com


www.epistem.co.uk


www.meridianbioscience.co.uk


www.rheonix.com


www.enigmadiagnostics.com


www.atlasgenetics.com


www.micronics.net


www.dnae.co.uk


www.optigene.co.uk

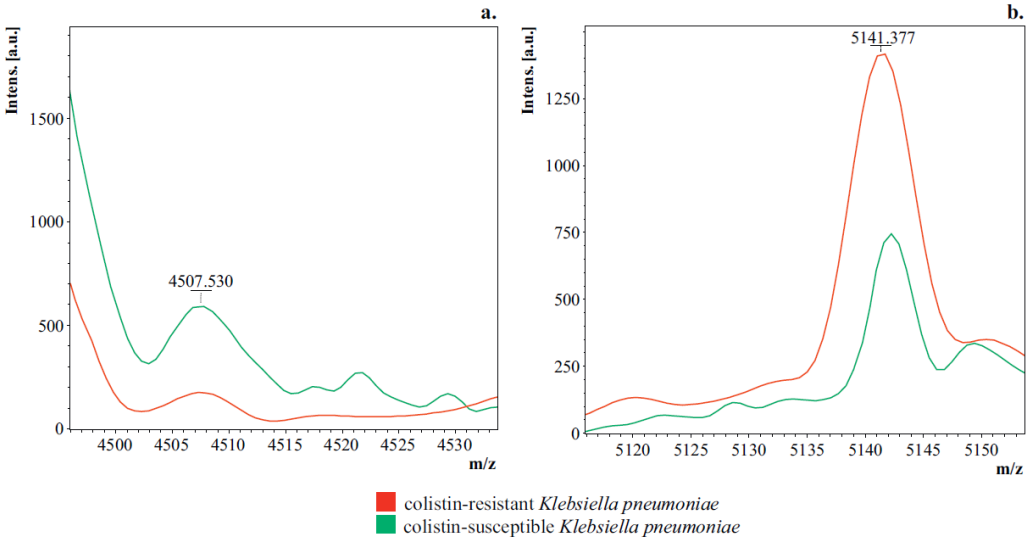

www.alere.com


www.quantumdx.com


www.me-med.com

RESISTANCE DETECTION BY MALDI TOF MS

1. Detection of degradation or modification of antibiotics.
2. Use of incorporation of stable-isotope labeled amino acids.
3. MS mediated nucleic acid sequencing (Iridica, Abbott).
4. Direct detection of resistance (associated) factors (including next gen MS and pre-purification methods).
5. Changes in metabolic patterns.
6. Quantitation of MALDI detectable compounds.
7. Application of next gen MS methods

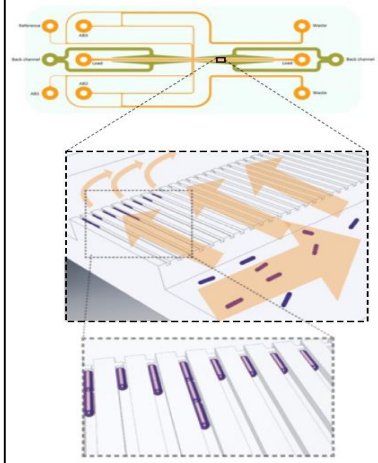


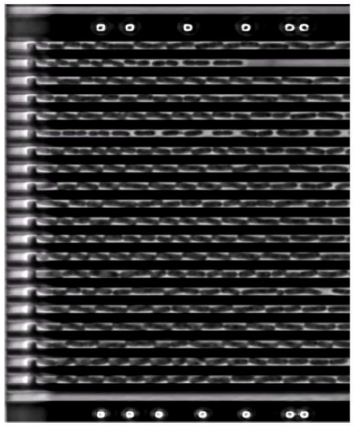
Giordano C, Barnini S. Rapid detection of colistin-resistant Klebsiella pneumoniae using MALDI-TOF MS peak-based assay. J Microbiol Methods. 2018 Dec;155:27-33.

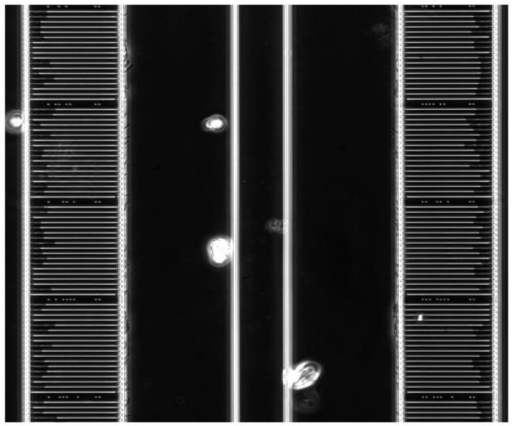
POTENTIALLY INVASIVE NEW TECHNOLOGY

MICROFLUIDICS AND SINGLE CELL HANDLING.
TRANSCRIPTOMICS.
NEXT GENERATION MASS SPECTROMETRY.
(FLOW) CYTOMETRY.
CANTILEVERS.
ISOTHERMAL MICRO-CALORIMETRICS.
MAGNETIC BEAD ROTATION.
MICRODROPLETS.
NMR.
MICROSOUND.
METABOLOMICS (ROS AND CELLULAR RESPIRATION).
RAMAN, IR AND OTHER SPECTROSCOPIES.
BACTERIOPHAGES.
REAL-TIME, VIDEO ENHANCED MICROSCOPY.
APOPTOSIS MARKERS.
ELECTRONIC NOSES.
IMPEDANCE MARKERS.
ETC ETC

FASTEST AST??????

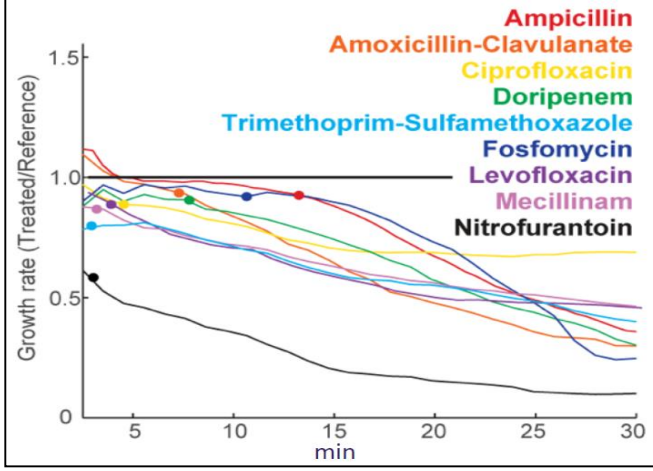


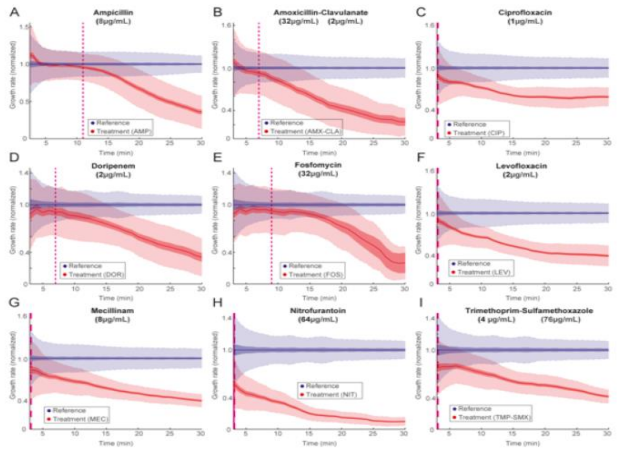




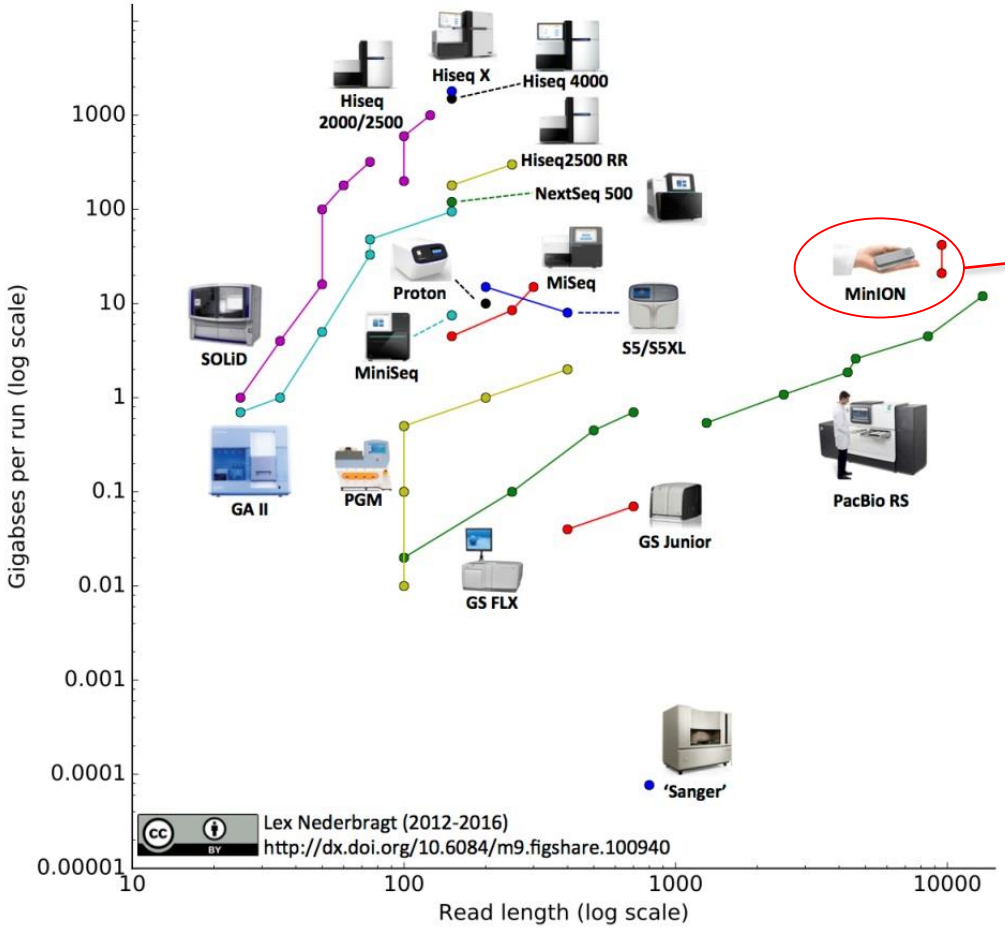
Confidential

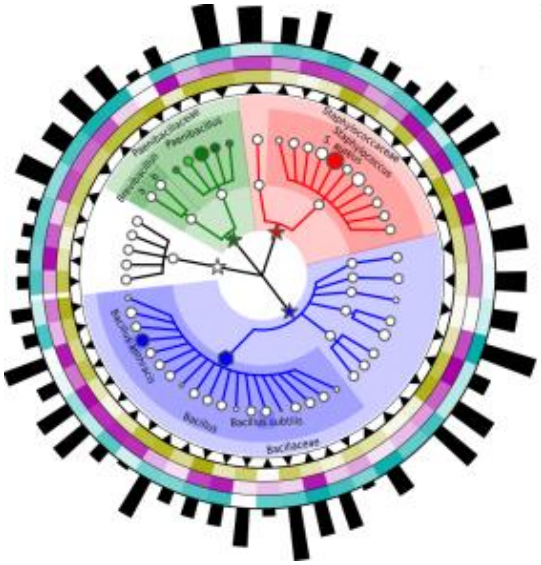
Reference: Baltekin et al. PNAS 2017





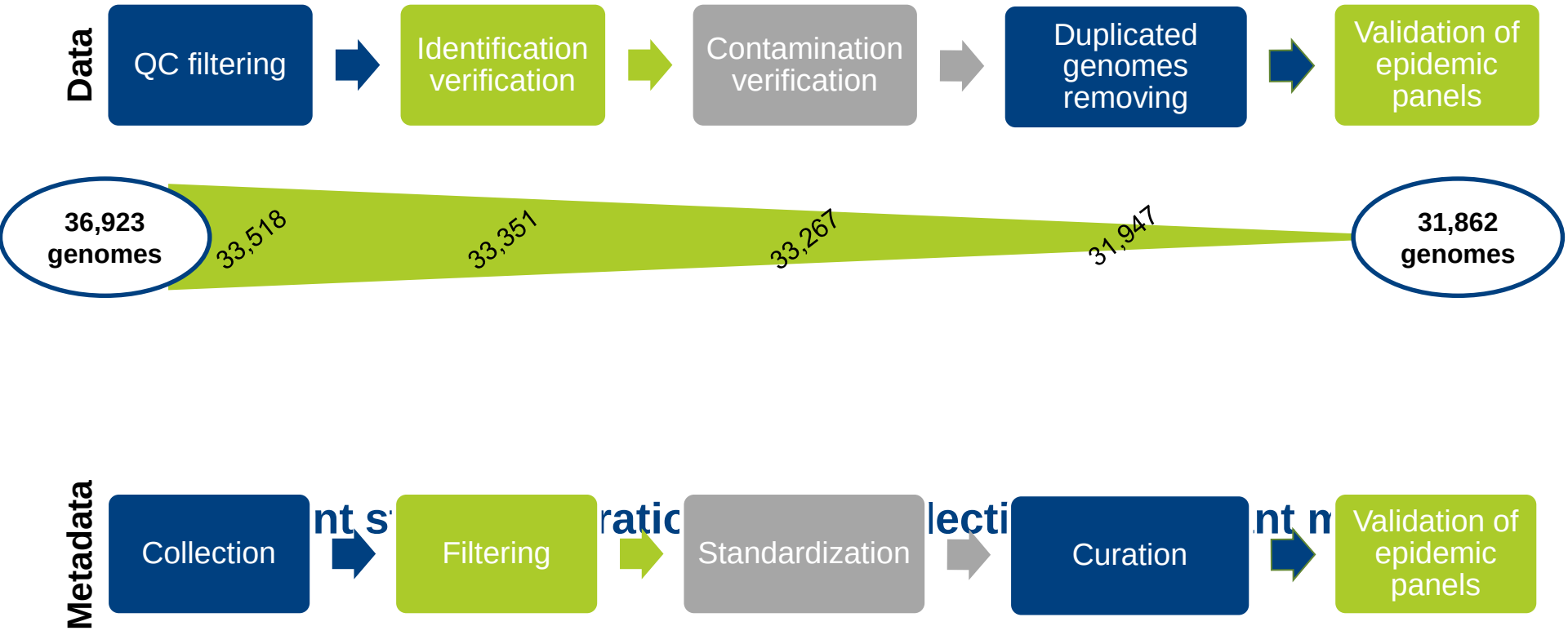
NGS TECHNOLOGY AND SOFTWARE PACKAGES FOR INTERPRETATION



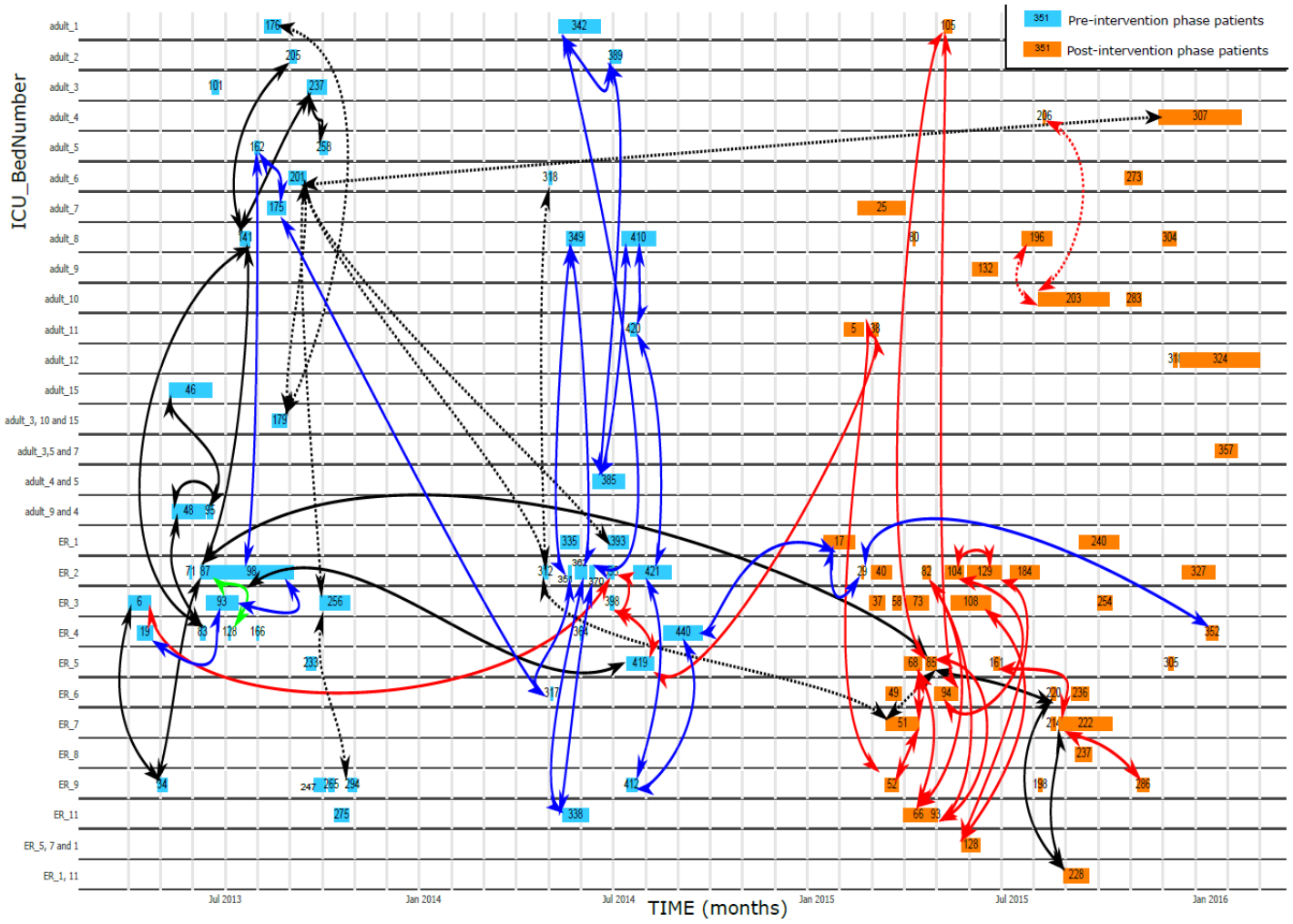


DATA AND DATABASES: QUALITY AND CLEANSING

- **Different steps of filtering for the selection of genomes of quality**

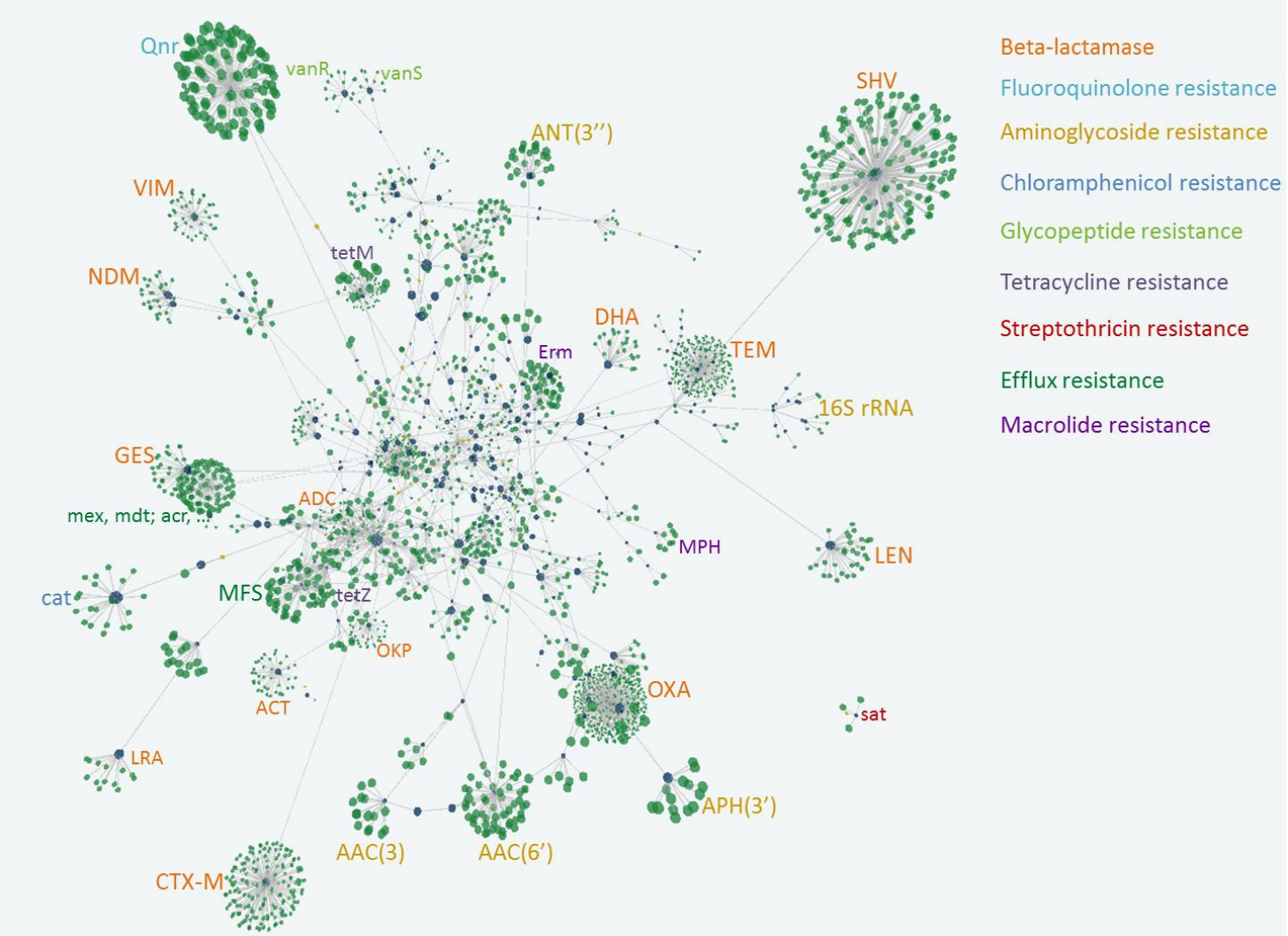


GENOMIC CHARACTERIZATION OF PSEUDOMONAS AERUGINOSA FROM A REFERRAL HOSPITAL'S ICUS IN JAKARTA



UNRAVELLING COMPLEX EPIDEMIOLOGIES

ANTIBIOTIC RESISTANCE GENE CATALOGUE



Provided by Stéphane Schicklin

Salmonella Typhi AS A GENOMIC AST MODEL

Antimicrobial resistance category	Presence of gene(s) and WGS-res profile	No. of isolates with indicated phenotype		Sensitivity (%)[b]	Specificity (%)[c]
		Resistant	Susceptible		
Ampicillin resistance	Total	263	273		
	bla_{TEM-1B}	262	7		
	Truncated bla_{TEM-1B}	0	2		
	No bla_{TEM-1B}	1	264		
	WGS-res profile: resistant	262	7	99.6	97.4
	WGS-res profile: susceptible	1	266		
Co-trimoxazole resistance[d]	Total	233	303		
	dfrA7 + *sul1* + *sul2*	205[e,i]	4[f,i]		
	dfrA7 + *sul1* only	26	22[g]		
	sul2 only	1[e,i]	55[h,j]		
	None of three	1	222		
	WGS-res profile: resistant	231	26	99.1	91.4
	WGS-res profile: susceptible	2	277		
Chloramphenicol resistance	Total	250	286		
	catA1	248[j]	7[j]		
	Truncated *catA1*	0	1[j]		
	No *catA1*	2	278		
	WGS-res profile: resistant	248	7	99.2	97.6
	WGS-res profile: susceptible	2	279		
Ceftriaxone resistance	Total	1	535		
	$bla_{CTX-M15}$	1	0		
	No $bla_{CTX-M15}$	0	535		
	WGS-res profile: resistant	1	0	100.0	NA
	WGS-res profile: susceptible	0	535		

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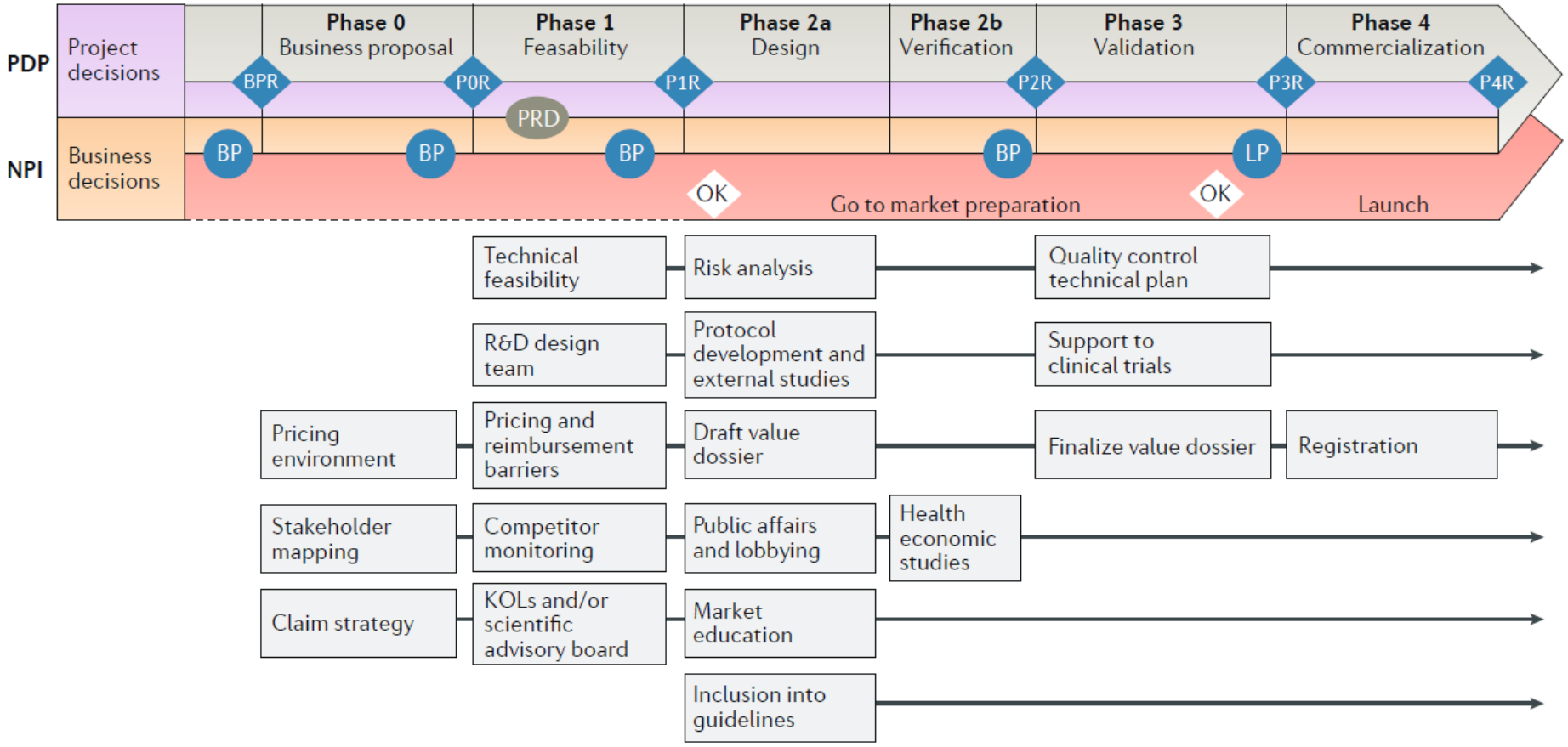
RESEARCH ARTICLE
Clinical Science and Epidemiology

Salmonella enterica Serovar Typhi in Bangladesh: Exploration of Genomic Diversity and Antimicrobial Resistance

PRODUCT DEVELOPMENT IS SCIENCE



Van Belkum et al, Nat Rev Microbiol 2018

ACKNOWLEDGMENTS

- Marie Françoise Gros and Claude Mabilat for (many) slides.
- The Point Prevalence Surveillance team.
- Marc van Nuenen for BioFire slides.
- Victoria Girard for any MALDI TOF MS stuff.
- Mike Dunne for (post-retirement) AST activities.
- François Vandenesch et al for *S. aureus* genomics.
- Fondation Mérieux and Tanmoy for *S. typhi* collaboration.

The presenter's virtual lab is funded by bMx, but mostly by various EU H2020 grants and a little bit of JPIAMR money