MALATTIE INFETTIVE: I CASI CLINICI COMPLESSI, LA CONDIVISIONE DEL SAPERE
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Venezia-Mestre, 31 ottobre 2015
Presidente: Prof. Enzo Raise

Le sepsi da *Klebsiella pneumoniae*: aspetti epidemiologici, metodiche di rilevazione e interpretazione dell'antibiogramma

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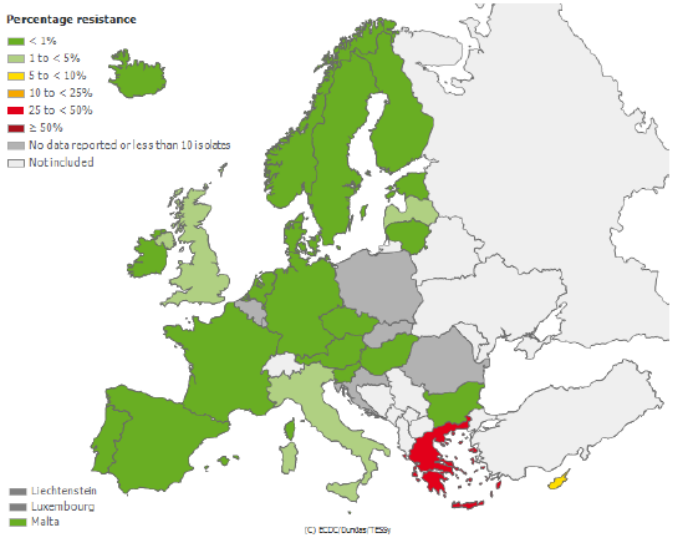
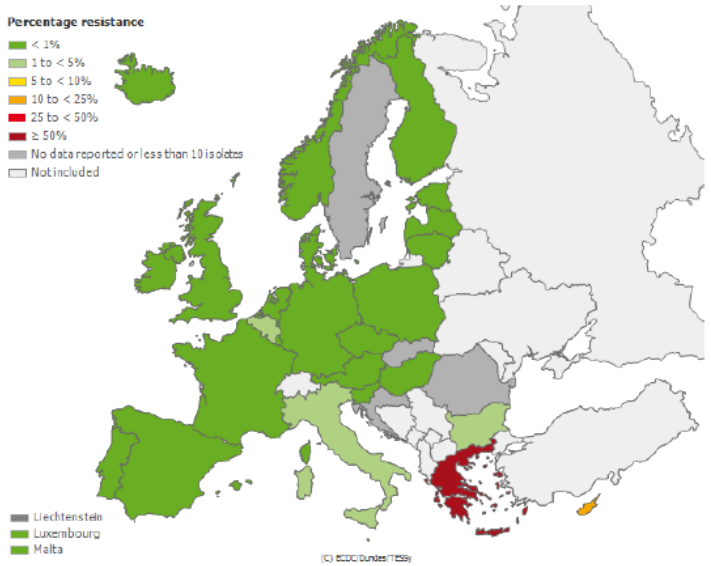
Epidemiologia

Proportion of Carbapenems Resistant (R+I) *Klebsiella pneumoniae* Isolates in Participating Countries in 2008

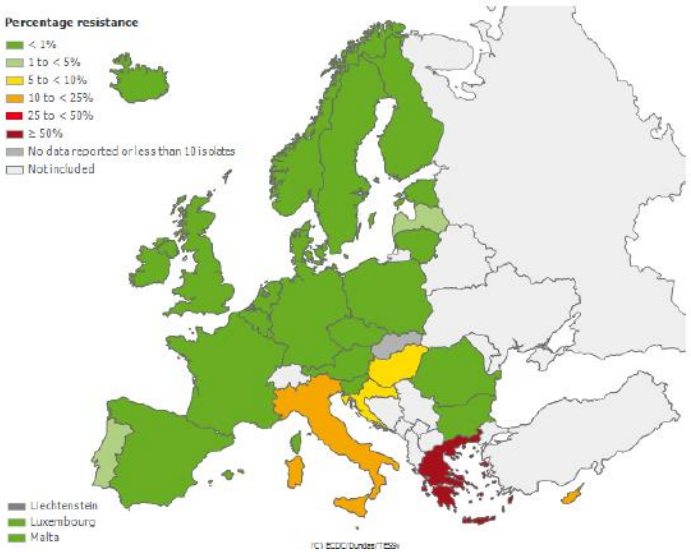


Proportion of Carbapenems Resistant (R+I) *Klebsiella pneumoniae* Isolates in Participating Countries in 2009

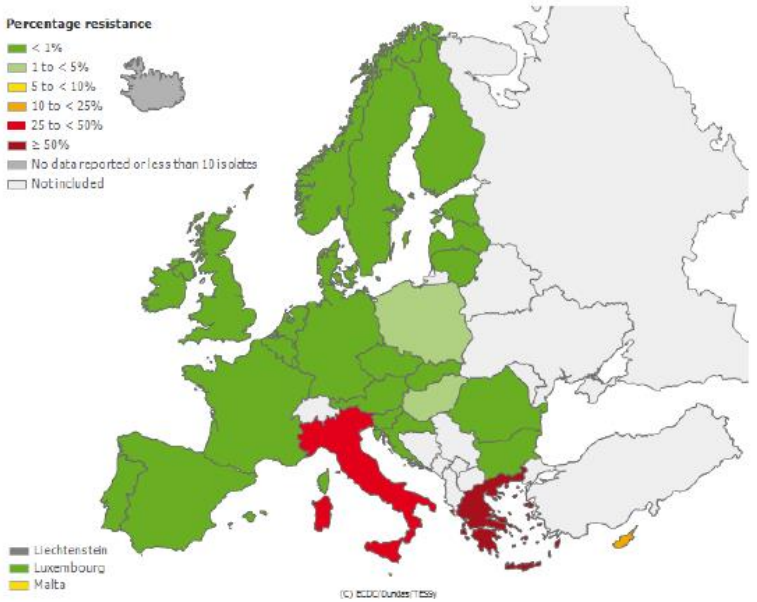


Epidemiologia

Proportion of Carbapenems Resistant (R+I) *Klebsiella pneumoniae* Isolates in Participating Countries in 2010

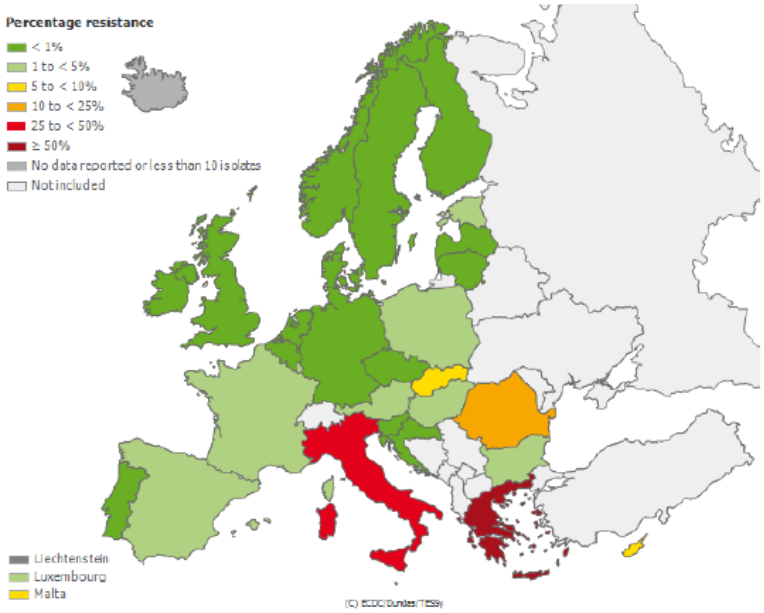


Proportion of Carbapenems Resistant (R+I) *Klebsiella pneumoniae* Isolates in Participating Countries in 2011

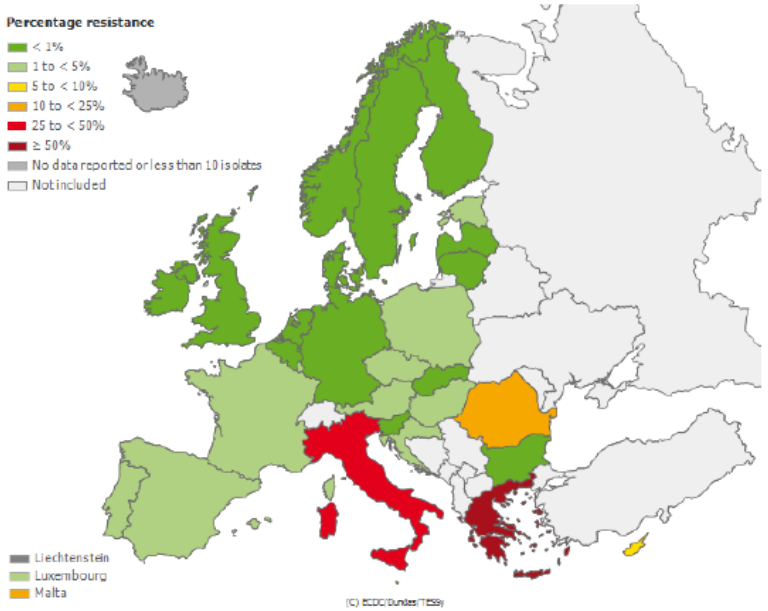


Epidemiologia

Proportion of Carbapenems Resistant (R+I) *Klebsiella pneumoniae* Isolates in Participating Countries in 2012

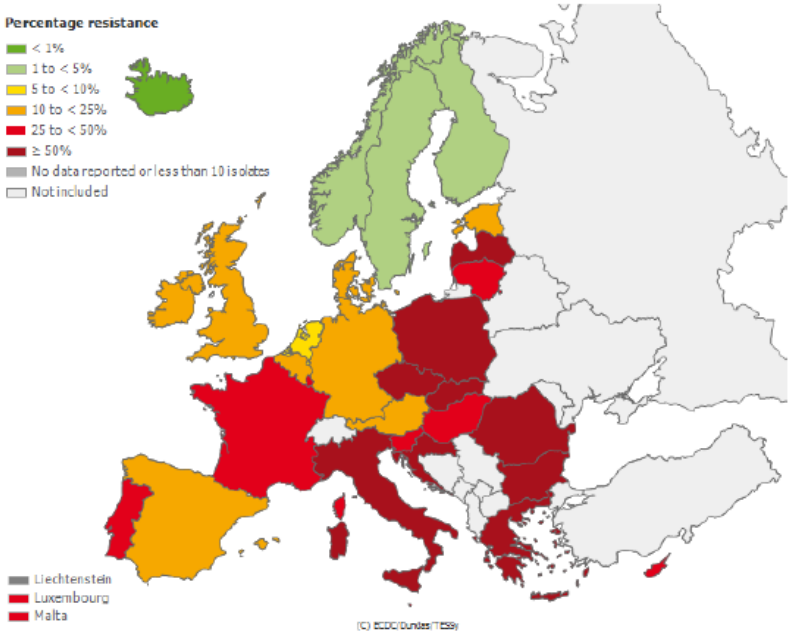


Proportion of Carbapenems Resistant (R+I) *Klebsiella pneumoniae* Isolates in Participating Countries in 2013

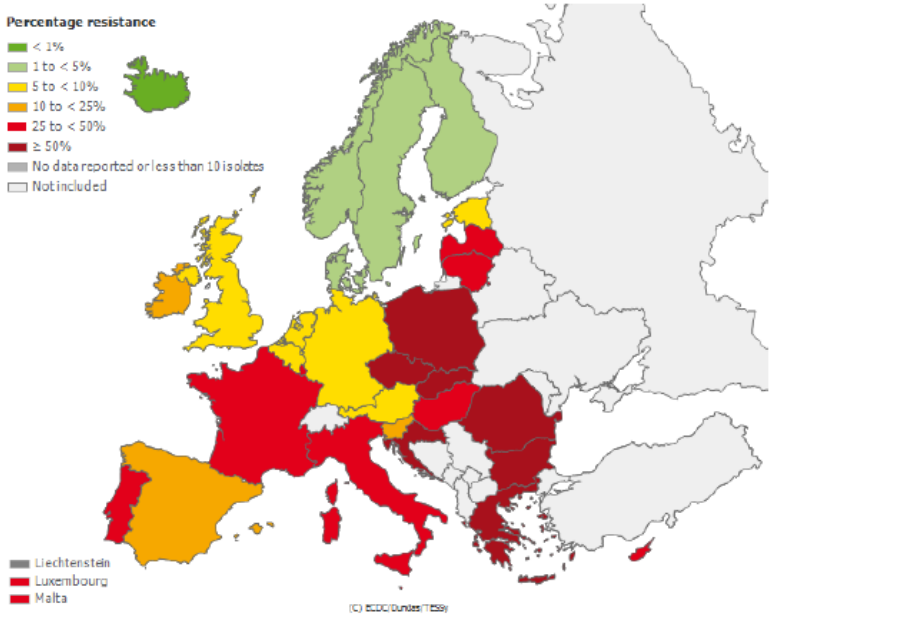


Epidemiologia

Proportion of 3rd gen. cephalosporins Resistant (R+I) *Klebsiella pneumoniae* Isolates in Participating Countries in 2013

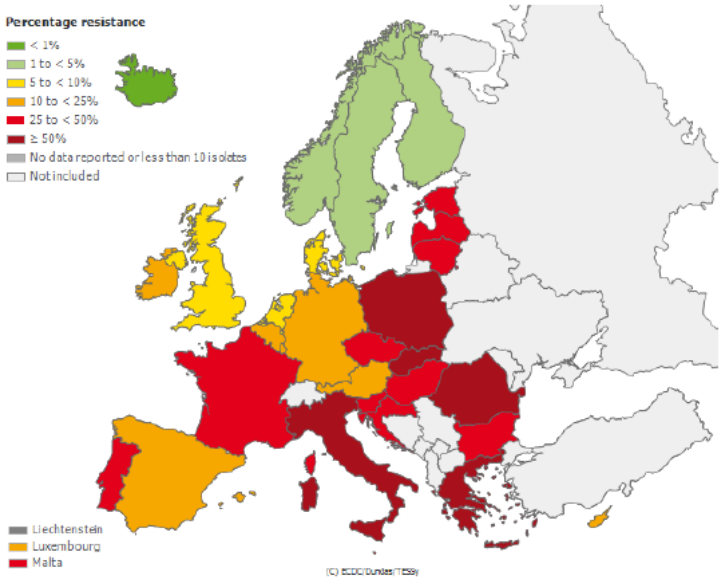


Proportion of Aminoglycosides Resistant (R) *Klebsiella pneumoniae* Isolates in Participating Countries in 2013

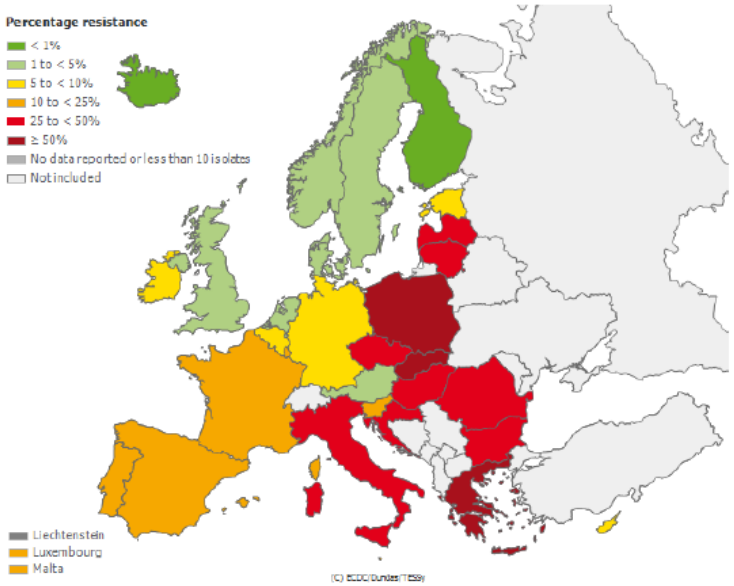


Epidemiologia

Proportion of Fluoroquinolones Resistant (R) *Klebsiella pneumoniae* Isolates in Participating Countries in 2013



Multidrug-resistant Klebsiella pneumoniae Isolates in Participating Countries in 2013 (Resistant to Third-generation Cephalosporins, Fluoroquinolones and Aminoglycosides)



Negli Stati Uniti …

March 2013

CDC Vitalsigns™

On this Page

4% & 18%

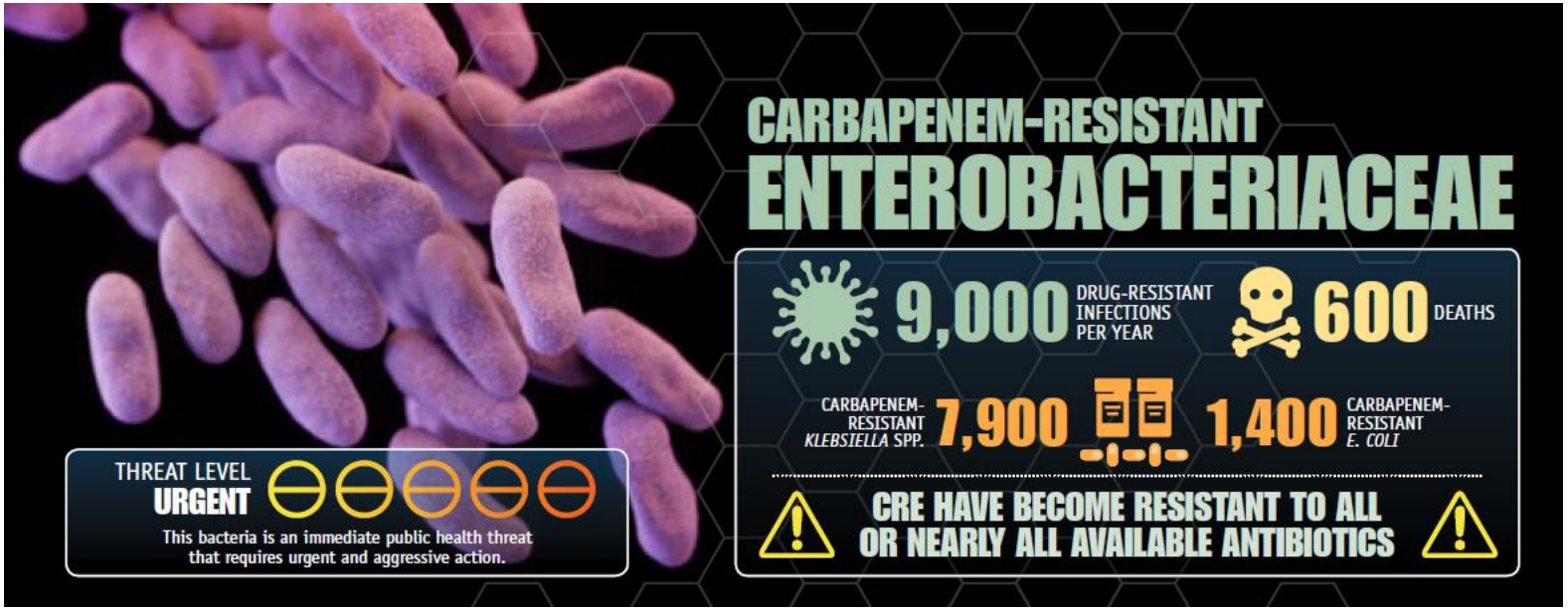
About 4% of US hospitals had at least one patient with a CRE (carbapenem-resistant Enterobacteriaceae) infection during the first half of 2012. About 18% of long-term acute care hospitals* had one.

42

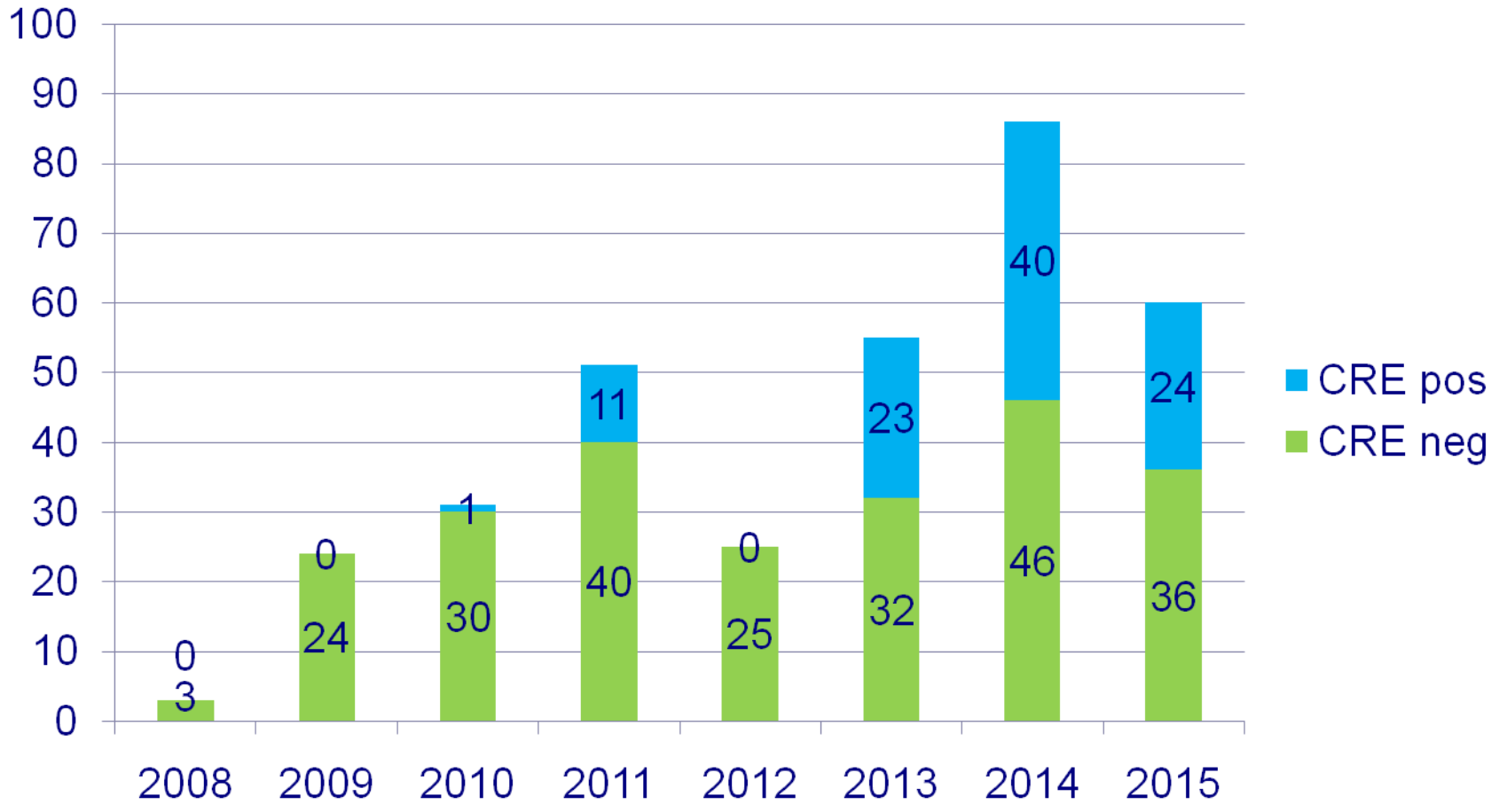
One type of CRE infection has been reported in medical facilities in 42 states during the last 10 years.

1 in 2

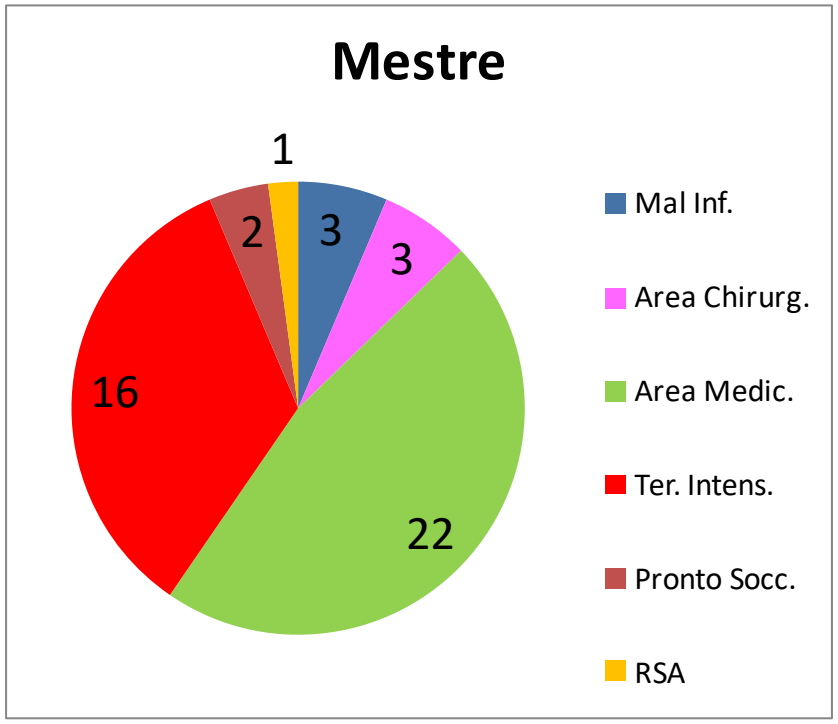
CRE germs kill up to half of patients who get bloodstream infections from them.

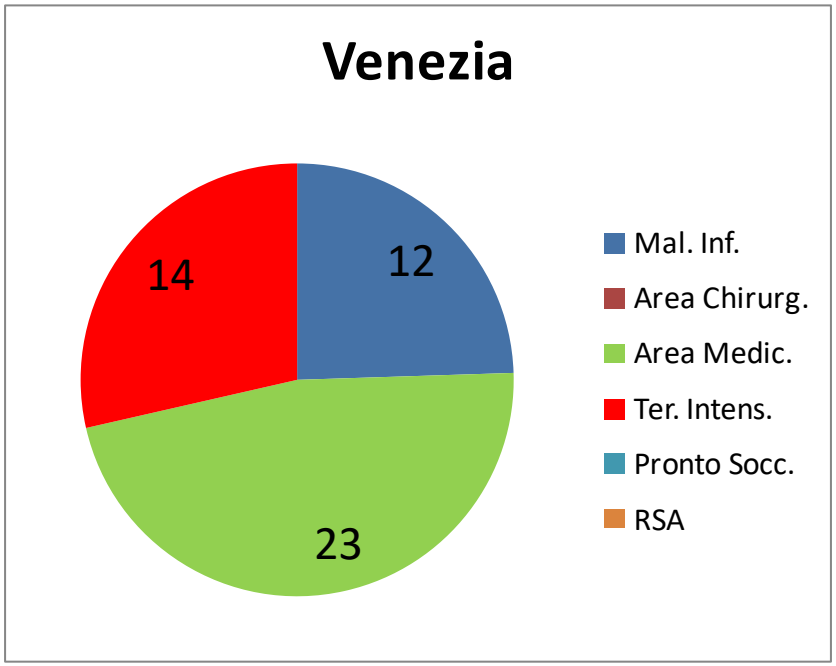

CARBAPENEM-RESISTANT
ENTEROBACTERIACEAE
9,000 DRUG-RESISTANT INFECTIONS PER YEAR
600 DEATHS
CARBAPENEM-RESISTANT *KLEBSIELLA* SPP. 7,900
1,400 CARBAPENEM-RESISTANT *E. COLI*
CRE HAVE BECOME RESISTANT TO ALL OR NEARLY ALL AVAILABLE ANTIBIOTICS
THREAT LEVEL
URGENT
This bacteria is an immediate public health threat that requires urgent and aggressive action.

Episodi di batteriemia da *K. pneumoniae* ULSS12



Episodi di batteriemia da *K. pneumoniae* CRE per sede





Diagnostica delle sepsi da *K. pneumoniae*

- **Prima delle emocolture o contemporaneamente a loro**
- **Ad emocolture positive**

Diagnostica delle sepsi da *K. pneumoniae*

SeptiFast Test ® Roche

Gram (-) bacteria	Gram (+) bacteria	Fungi
Escherichia coli	*Staphylococcus aureus*	*Candida albicans*
Klebsiella pneumoniae/oxytoca	CoNS[a] *(S. epidermidis, S. haemolyticus*	*Candida tropicalis*
Serratia marcescens	*Streptococcus pneumonia*	*Candida parapsilosis*
Enterobacter cloacae/aerogenes	*Streptococcus viridans*	*Candida glabrata*
Proteus mirabilis	*Streptococcus pyogenes*	*Candida krusei*
Pseudomonas aeruginosa	*Streptococcus agalactiae*	*Aspergillus fumigatus*
Acinetobacter baumannii	*Enterococcus faecium*	
S. maltophilia	*Enterococcus faecalis*	

TABLE 3. **Comparison of Septi*Fast* and BactAlert results**

Microorganisms	Total	Positive only with Septi*Fast*	Positive only with BactAlert	Positive with both methods (% concordance)
B. capillosus[*]	1	0	1*	0
C. albicans	1	0	0	1 (100)
CoNS	6	0	6[†]	0
E. coli	20	4	1	15 (70)
E. faecalis	1	1	0	0
*E. fergusonii**	1	0	1*	0
Enterobacter cloacae	1	0	0	1 (100)
K. pneumoniae	3	1	0	2 (67)
*M. morganii**	1	0	1*	0
P. aeruginosa	1	0	1	0
Proteus mirabilis	1	0	0	1 (100)
S. aureus	5	1	1	3 (60)
Stenotrophomonas maltophilia	1	0	0	1 (100)
Streptococcus species	3	0	0	3 (100)
S. pneumoniae	6	3	0	3 (50)
*P. stuartii**	1	0	1*	0
Total	53	10	13	30

*Not detectable by Septi*Fast*.
[†]Sample contamination.

In fact, despite its limitations, Septi*Fast* could be useful as an adjunct to traditional culture methods to facilitate detection of BSIs (22), especially in cases where BC is negative but BSI is strongly suggested. For these clinical conditions, we wish to further investigate the use of Septi*Fast*.

Avolio et al. Shock. 2010

TABLE 2. **Comparison of BC and Septi*Fast* results**

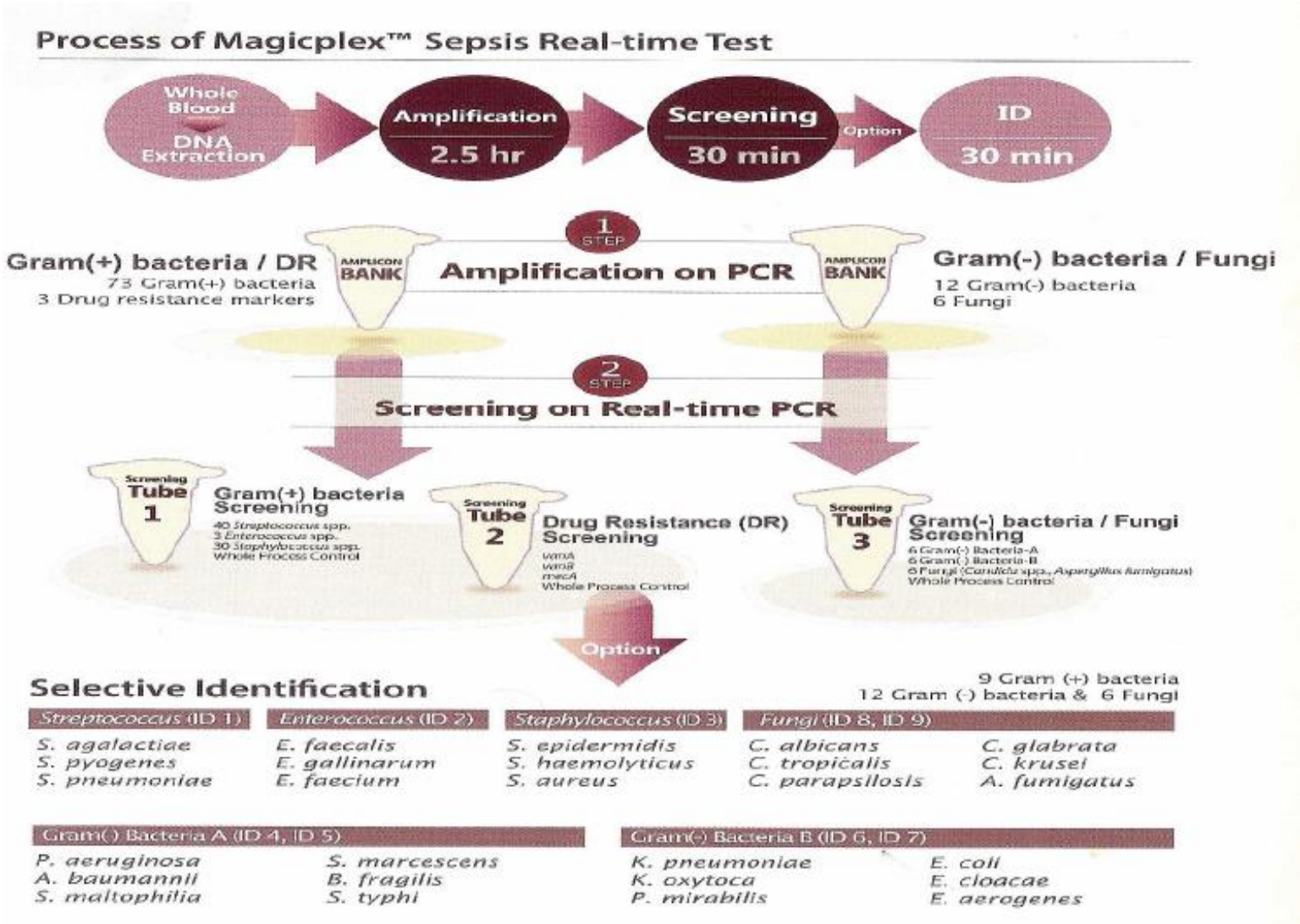
	Septi*Fast* positive, %	Septi*Fast* negative, %	Total, %
BC positive, %	30 (21)	13 (9)	43 (30)
BC negative, %	10 (7)	91 (63)	101 (70)
Total, %	40 (28)	104 (72)	144 (100)

	Septi*Fast vs* BC
Sensitivity	90,9%
Specificity	90,1%
PPV	75,0%
NPV	96,8%

Avolio et al. Shock. 2010

Diagnostica delle sepsi da *K. pneumoniae*

Magicplex Sepsis Realtime Test Seegene



Diagnostica delle sepsi da *K. pneumoniae*

Bactec® per anaerobi

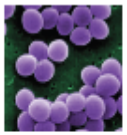
Bactec® per aerobi

Metodiche Molecolari

Spettrometria di massa

Metodiche Molecolari

- BioFire BCID

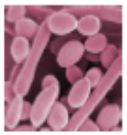


Gram-Positive Bacteria

Enterococcus
Listeria monocytogenes
Staphylococcus
Staphylococcus aureus
Streptococcus
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes

Gram-Negative Bacteria

Acinetobacter baumannii
Haemophilus influenzae
Neisseria meningitidis
Pseudomonas aeruginosa
Enterobacteriaceae
Enterobacter cloacae complex
Escherichia coli
Klebsiella oxytoca
Klebsiella pneumoniae
Proteus
Serratia marcescens



Yeast

Candida albicans
Candida glabrata
Candida krusei
Candida parapsilosis
Candida tropicalis

Antibiotic Resistance Genes

mecA – methicillin resistant
vanA/B – vancomycin resistant
KPC – carbapenem resistant

Simple: 2 minutes of hands-on time

Easy: No precise measuring or pipetting required

Fast: Turnaround time of about 1 hour

Comprehensive: 27 target BCID Panel

Metodiche Molecolari

- Verigene

Pannello	Organismo/Gene	
Bacterial Targets	*Acinetobacter* spp. *Citrobacter* spp. *Enterobacter* spp. *Proteus spp.* *E. coli* *Klebsiella pneumoniae* *Klebsiella oxytoca* *Pseudomonas aerogenes* *Serratia marcescens*	
Resistance Marker	CTX-M	VIM
	KPC	IMP
	NDM	OXA (48/23/40/58)

Spettrometria di massa

Antibiotics solution:
1 mg/ml Ertapenem in H_2O per tube 10 µl are needed.
For inhibition: prepare a solution containing 1 mg/ml Ertapenem and 2 mg/ml APBA Use this instead of the Ertapenem solution

Cultures: fresh over night culture
Negative control: Known carbapemen sensitive strain
Positive control: known KPC^+ strain

Assay setup:
fill 10 µl Ertapenem in an 1.5-ml tube (Eppendorf)
take a 1-µl-inoculating loop of bacteria from the plate and resuspend in the antibiotics solution
close the tube

Incubation:
3 h at 37°C under agitation
(e.g. Eppendorf-Shaker at 900 rpm)

Spettrometria di m

Preparation
centrifuge tube for 2 min at 13.000 rpm
spot 1 µl of the supernatant onto a polished steel target after drying overlay with 1 µl HCCA (10 mg/ml in OS)
air dry again
for calibration use a special Antibiotics Standard Protocol

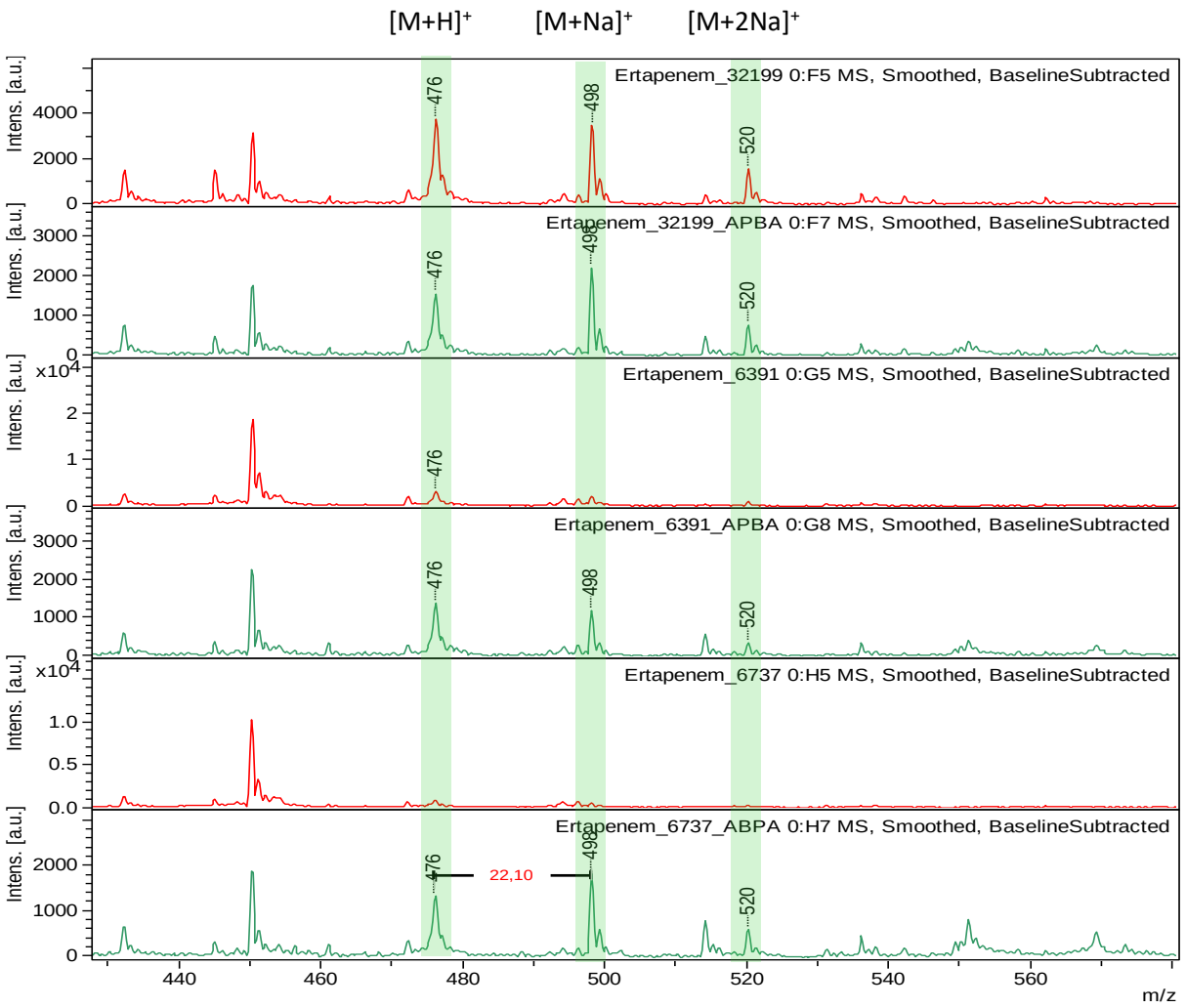
Measurements
parameter file will have to be optimized
mass range 100 Da to 1000 Da
aquisition of 240 shots with 40 shots per each position

Evaluation

	$[M + H]^+$	$[M + Na]^+$	$[M + 2 Na]^+$
Ertapenem	476,5	498,5	520,5
Ertapenem hydrol.	494,5	516,5	538,5
Ertapenem hydrol./decarboxyl.	450,5		

Spettrometria di massa

Ertapenem: 1 mg/ml
APBA: 2 mg/ml



Carbapenem sensitive strain plus Ertapenem

Carbapenem sensitive strain plus Ertapenem/APBA

Carbapenem resistant strain plus Ertapenem

Carbapenem resistant strain plus Ertapenem/APBA

Carbapenem resistant strain plus Ertapenem

Carbapenem resistant strain plus Ertapenem/APBA

MALDI Biotyper

MBT Resist

J Clin Microbiol. 2013 Nov;51(11):3741-8. doi: 10.1128/JCM.01536-13. Epub 2013 Sep 4.

MALDI biotyper-based rapid resistance detection by stable-isotope labeling.

Sparbier K[1], Lange C, Jung J, Wieser A, Schubert S, Kostrzewa M.

Eur J Clin Microbiol Infect Dis. 2013 Dec 14. [Epub ahead of print]

Rapid detection of antibiotic resistance based on mass spectrometry and stable isotopes.

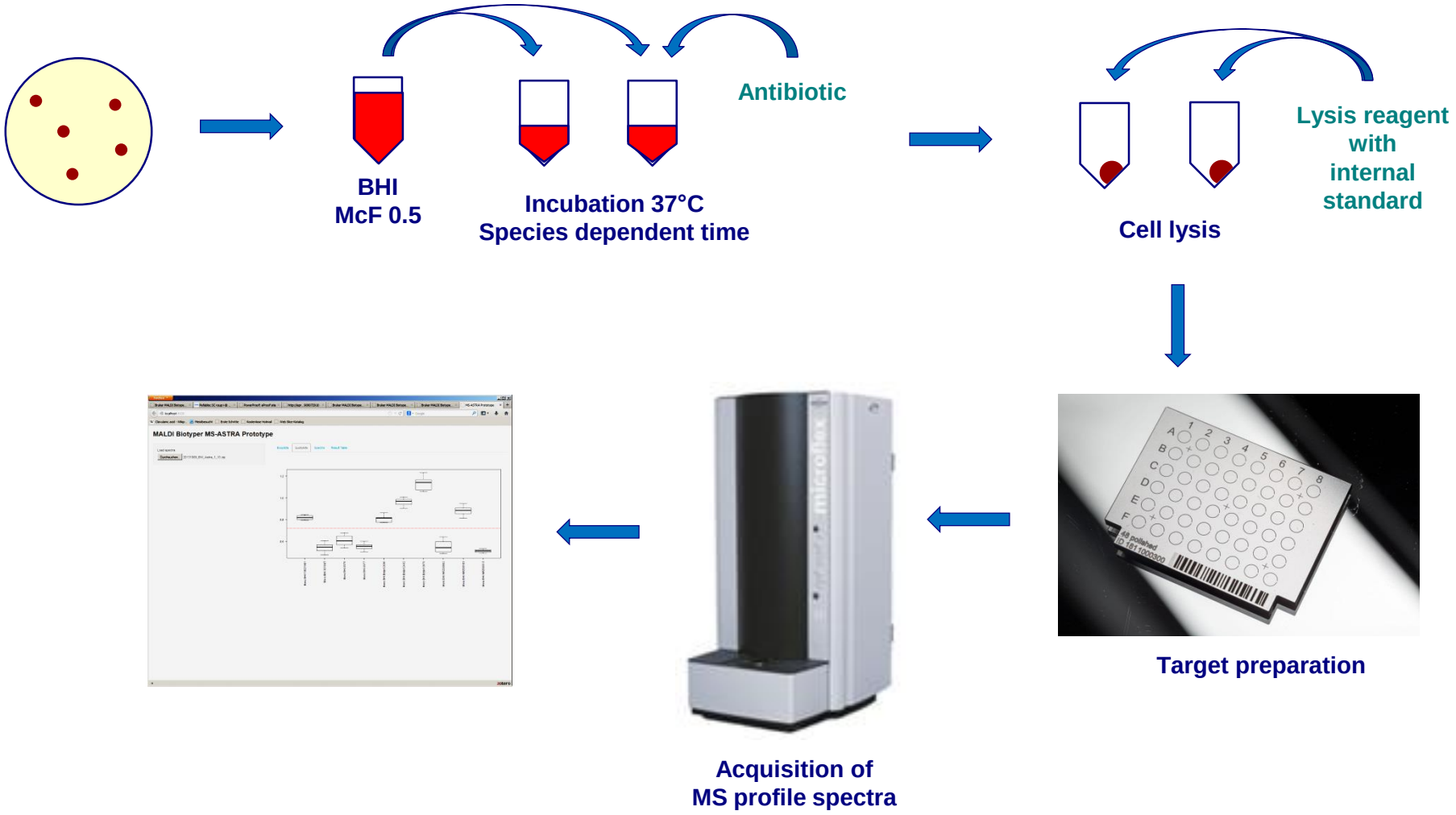
Jung JS[1], Eberl T, Sparbier K, Lange C, Kostrzewa M, Schubert S, Wieser A.

MBT-RESIST assays established successfully

• *Staphylococcus aureus*	Oxacillin, Cefoxitin
• *Pseudomonas aeruginosa*	Ciprofloxacin, Tobramycin, Meropenem (LMU)
• *Klebsiella pneumoniae*	Meropenem
• *E. coli*	Cefotaxime (LMU)

MALDI Biotyper – Resistance detection

Quantitative growth monitor



Can Carbapenem Susceptibility of I or R Detect KPC-Producers?

Method	Sens/Spec (%) for Detection of KPC-mediated R*		
	Imipenem	Meropenem	Ertapenem
Ref BMD	94/93	94/98	97/89
Disk Diffusion	42/96	71/96	97/82
Etest	55/96	58/96	90/84
Vitek Legacy	55/96	52/98	N/A
Vitek 2	71/98	48/96	94/93
MicroScan	74/96	84/98	100/89
Phoenix	81/96	61/98	N/A

*N = 76 *K. pneum*, *K. oxy*, *E. coli*; 31 KPC-producers & 45 non-KPC producers

Phenotypic Tests for Carbapenemase Activity

- Modified Hodge Test
  - 100% sensitivity in detecting KPC; also positive when other carbapenemases are present
  - 100% specificity

Procedure described by Lee et al. CMI, 7, 88-102, 2001.

Test di conferma

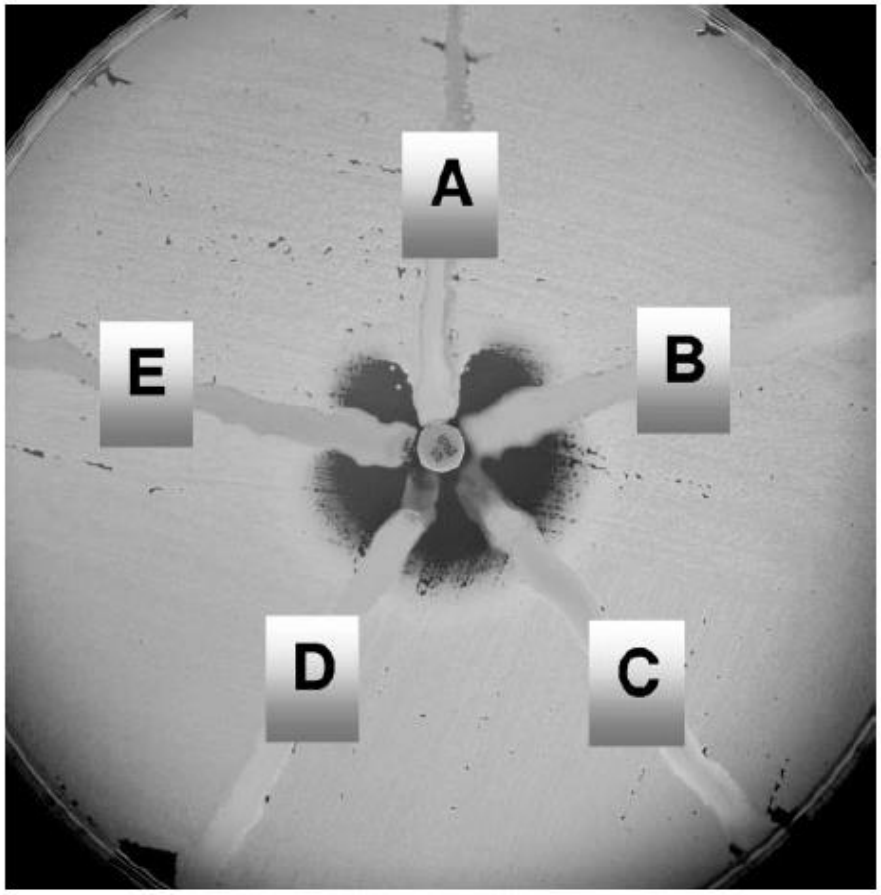


FIG. 1. The modified Hodge test Mueller-Hinton agar plate was inoculated with a 1:10 dilution of a 0.5 McFarland suspension of *E. coli* ATCC 25922 and streaked for confluent growth using a swab. A 10-μg imipenem disk was placed in the center, and each test isolate was streaked from the disk to the edge of the plate. Isolate A is a KPC producer and positive by the modified Hodge test. Isolates B, C, D, and E do not produce a carbapenemase and are negative by the test.

Modified Hodge Test

- reasonably good for KPC
- may miss NDM-1
- Nonspecific (high-level AmpC-producers)

Test di conferma

Rapid Detection of Carbapenemase producing *Enterobacteriaceae*

Patrice Nordmann, Laurent Poirel, and Laurent Dortet

To rapidly identify carbapenemase producers in *Enterobacteriaceae,* we developed the **Carba NP test**. The test uses isolated bacterial colonies and is based on in vitro hydrolysis of a carbapenem, imipenem.
It was 100% sensitive and specific compared with molecular-based techniques.
This rapid (<2 hours), inexpensive technique may be implemented in any laboratory.

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 18, No. 9, September 2012

Carba-NP

Table 1. Carbapenemase-producing clinical enterobacterial isolates subjected to the Carba NP test*

Ambler class, carbapenemase type	Species	β-Lactamase	No.	MIC range, mg/L			Carba NP test result
				IMP	ERT	MER	
Class A							
KPC-type	*Klebsiella pneumoniae*	KPC-2	27	0.5–>32	4–>32	1–>32	+
		KPC-3	3	0.5–8	4–>32	1–8	+
	Klebsiella ozaenae	KPC-3	1	>32	>32	2	+
	Escherichia coli	KPC-2	5	0.5–4	0.5>32	0.5–2	+
	Enterobacter cloacae	KPC-2	7	1–24	1.5–32	0.75–16	+
	Enterobacter aerogenes	KPC-2	1	8	>32	8	+
	Citrobacter freundii	KPC-2	2	8–>32	1.5–>32	1.5–3	+
	Serratia marcescens	KPC-2	2	>32	>32	>32	+
	Salmonella spp.	KPC-2	1	4	1	0.25	+
NMC-A	*E. cloacae*	NMC-A	1	16	>32	16	+
SME-type	*S. marcescens*	SME-1	1	32	4	12	+
		SME-2	1	32	4	12	+
GES-type	*E. cloacae*	GES-5	1	>32	>32	>32	+
IMI-type	*Enterobacter asburiae*	IMI-2	1	>32	>32	>32	+
Class B							
NDM-type	*K. pneumoniae*	NDM-1	16	0.5–>32	2–>32	1–>32	+
		NDM-4	1	>32	>32	>32	+
	E. coli	NDM-1	7	1–16	3–>32	1–16	+
	E. cloacae	NDM-1	1	2	16	2	+
	C. freundii	NDM-1	1	>32	>32	>32	+
	Providencia stuartii	NDM-1	1	12	0.38	1.5	+
	Proteus rettgeri	NDM-1	1	3	0.5	1.5	+
VIM-type	*K. pneumoniae*	VIM-1	15	0.5–>32	0.5–>32	0.38–>32	+
		VIM-19	1	8	16	4	+
	E. coli	VIM-1	2	1.5–3	0.38–1.5	0.5–1	+
		VIM-2	2	2–4	0.5–1.5	0.38–0.5	+
		VIM-19	1	8	16	4	+
	E. cloacae	VIM-1	4	1–>32	0.38 to >32	0.5–>32	+
	S. marcescens	VIM-2	1	>32	>32	>32	+
IMP-type	*K. pneumoniae*	IMP-1	5	0.5–8	2–4	1–8	+
		IMP-8	2	0.5–1	0.5–1	0.5	+
	E. coli	IMP-1	2	0.5	3–4	0.5–1	+
		IMP-8	1	6	8	3	+
	E. cloacae	IMP-1	12	8–>32	>32	2–>32	+
		IMP-8	2	0.75–1.5	0.5–1	0.5–1	+
	S. marcescens	IMP-1	2	8–>32	>32	2–>32	+
		IMP-11	1	8	>32	2	+
Class D							
OXA-48 type	*K. pneumoniae*	OXA-48	15	0.38–>32	0.38–>32	0.38–>32	+
		OXA-181	2	0.5-1	2–4	0.5–1	+
	E. coli	OXA-48	6	0.38–3	0.5–16	0.12–1	+
	E. cloacae	OXA-48	3	0.5–1	0.5–16	0.5–1.5	+
	P. rettgeri	OXA-181	1	8	1	2	+

*IMP, imipenem; ERT, ertapenem; MER, meropenem; KPC, *K. pneumoniae* carbapenemase; NMC-A, non–metallo-enzyme carbapenemase; SME, *S. marcescens* enzyme; GES, Guiana extended-spectrum β-lactamase; IMI, imipenem-hydrolysing β-lactamase; NDM, New Delhi metallo-β-lactamase; VIM, Verona integron–encoded metallo- β-lactamase; IMP, imipenemase; OXA-48, oxacillinase-48.

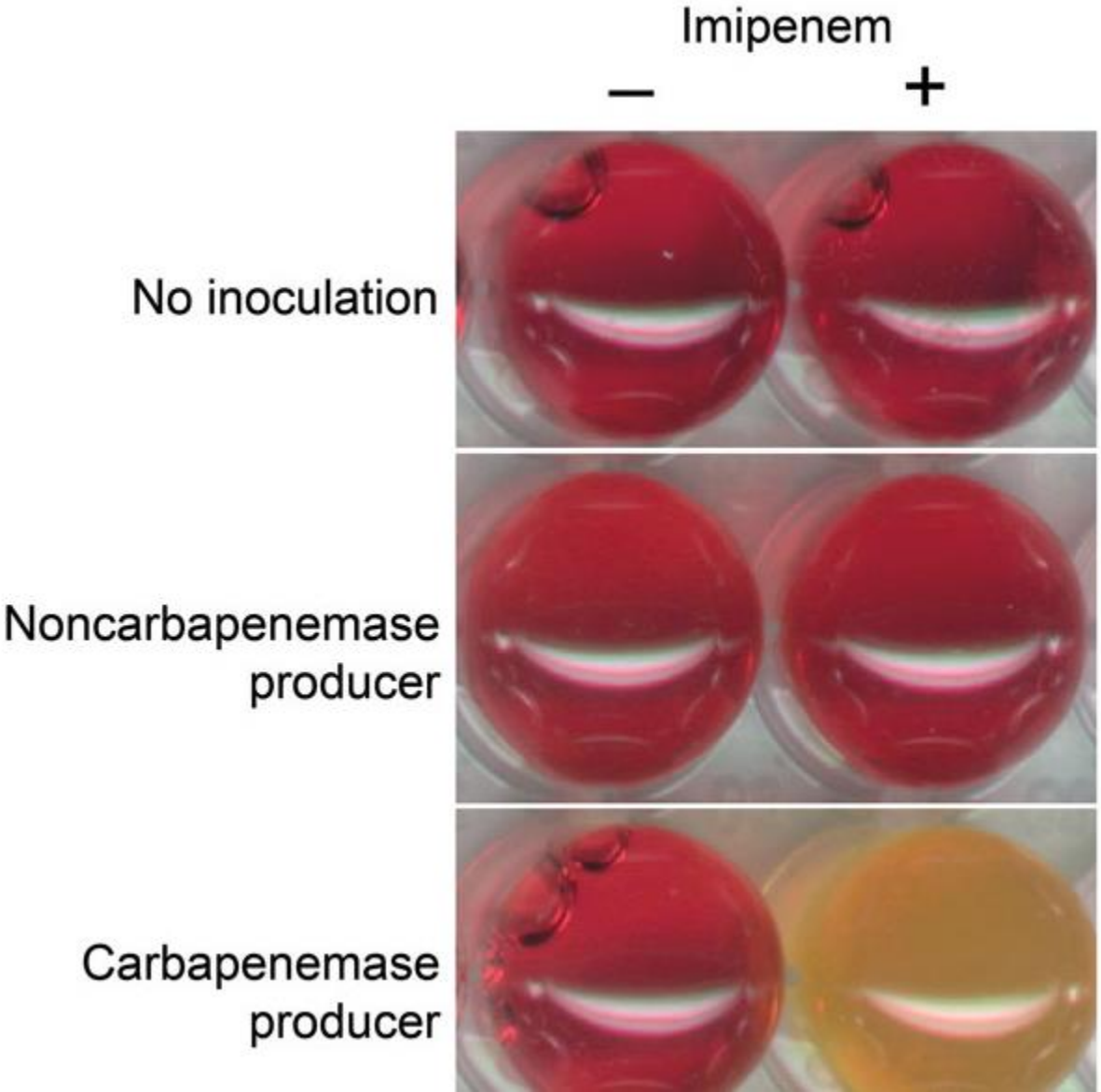
Carba-NP

Table 2. Non–carbapenemase-producing clinical enterobacterial isolates subjected to the Carba NP test*

β-Lactamase type, species	β-Lactamase	No.	MIC, mg/L			Carba NP test result
			IMP	ERT	MER	
ESBLs						
Klebsiella pneumoniae	CTX-M-3	1	0.12	0.12	0.12	–
	CTX-M-14	1	0.12	0.12	0.12	–
	CTX-M-15	3	0.12	0.12	0.12	–
Escherichia coli	CTX-M-1	1	0.12	0.12	0.12	–
	CTX-M-3	1	0.12	0.12	0.12	–
	CTX-M-14	2	0.12	0.12	0.12	–
	CTX-M-15	2	0.12	0.12	0.12	–
	VEB-1	1	0.12–0.25	0.12	0.12	–
Enterobacter cloacae	CTX-M-15	3	0.12	0.12	0.12	–
	VEB-1	1	0.12	0.12	0.12	–
Plasmid-mediated AmpC or chromosomal AmpC + decreased membrane permeability						
K. pneumoniae	DHA-1	1	>32	>32	>32	–
	DHA-2	1	0.12	0.5	0.12	–
E. coli	Extended-spectrum cephalosporinase	1	0.12	0.12	0.12	–
	CMY-2	1	0.12	0.12	0.12	–
	CMY-10	1	0.12	0.38	0.12	–
	DHA-1	1	0.12	0.12	0.12	–
	ACC-1	1	0.12	0.12	0.12	–
	Overexpressed cephalosporinase	1	16	>32	2	–
Proteus mirabilis	ACC-1	1	0.25	0.12	0.12	–
E. cloacae	Overexpressed cephalosporinase	7	0.12–16	1–>32	0.12–>32	–
Enterobacter aerogenes	Overexpressed cephalosporinase	1	1	4	0.75	–
Morganella morganii	Overexpressed cephalosporinase	2	1.5–2	0.12	0.5	–
ESBL + decreased membrane permeability						
K. pneumoniae	CTX-M-15	8	0.25–8	1–>32	1–>32	–
	SHV-28	1	1	4	1	–
	SHV-2a	1	0.25	2	0.38	–
Enterobacter sakazakii	CTX-M-15	1	0.25	1.5	0.25	–
Citrobacter freundii	TEM-3	1	1	8	1	–

*IMP, imipenem; ERT, ertapenem; MER, meropenem; ESBLs, extended-spectrum β-lactamases.

Carba-NP


Imipenem
–
+
No inoculation
Noncarbapenemase producer
Carbapenemase producer

RAPIDEC® CARBA NP

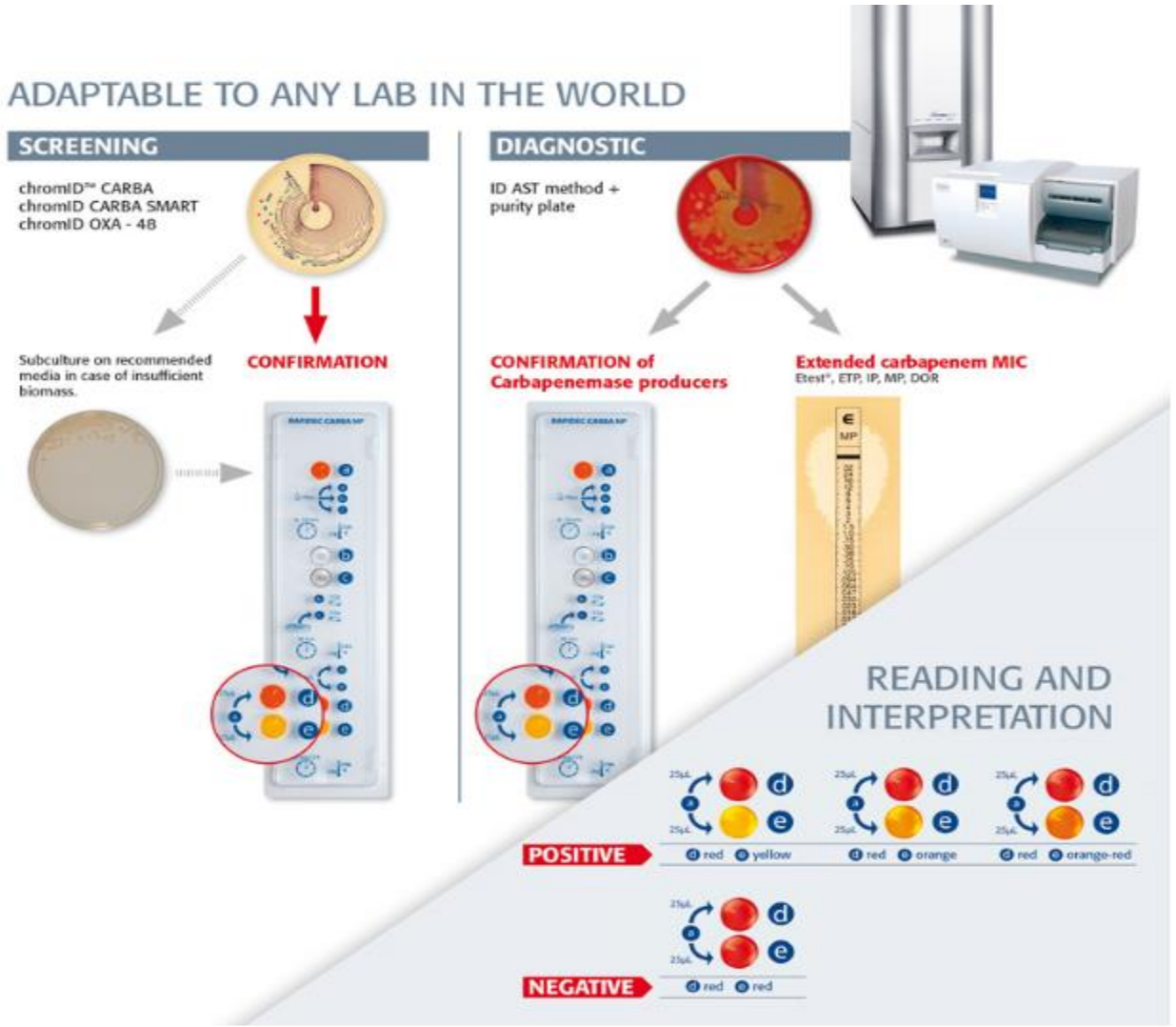
NEW, high medical value test confirms Carbapenemase-producing bacteria in agar cultures.

The test gives reliable results in under 2 hours, making it the quick and easy way to control carbapenemase producers and meet diagnostics and screening challenges, improving patient management and controlling HAI.

Results in 30 mins-2 hours

Cost-effective, all-in-one solution

Highly specific and sensitive



EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases

EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance

EUCAST, December 2012

Eucast

Table 1. Clinical breakpoints and screening cut-off values for carbapenemase-producing Enterobacteriaceae.

Carbapenem	MIC (mg/L)		Disk diffusion zone diameter (mm)	
	S/I breakpoint	Screening cut-off	S/I breakpoint	Screening cut-off
Meropenem[1]	≤2	>0.125	≥22	<25[2]
Imipenem	≤2	>1	≥22	<23
Ertapenem[3]	≤0.5	>0.125	≥25	<25

[1]Best balance of sensitivity and specificity.

[2]In rare cases OXA-48-producers have zone diameters of 24-26 mm, so 27 mm may be used as a screening cut-off during outbreaks, but with significant reduction in specificity.

[3]High sensitivity, but low specificity and therefore not recommended.

Eucast

Table 2. Interpretation of phenotypic tests (carbapenemases in **bold type**) with in-house or commercial disks or tablets.

β-lactamase	Synergy observed as increase in meropenem zone diameter (mm) with 10µg disk				Temocillin MIC > 32 mg/L
	DPA/EDTA	APBA/PBA	DPA+APBA	CLX	
MBL	≥5	-	-	-	NA[1]
KPC	-	≥4	-	-	NA[1]
MBL+KPC[2]	Variable	Variable	≥5	-	NA[1]
OXA-48-like[3]	-	-	-	-	Yes
AmpC + porin loss	-	≥4	-	≥5	NA[1]
ESBL + porin loss	-	-	-	-	No

Abbreviations: MBL=metallo-β-lactamase, KPC=*Klebsiella pneumoniae* carbapenemase, DPA=dipicolinic acid, EDTA=ethylenediaminetetraacetic acid, APBA= aminophenyl boronic acid, PBA= phenyl boronic acid, CLX=cloxacillin.

[1] Temocillin is recommended only in cases where no synergy is detected, in order to differentiate between ESBL + porin loss and OXA-48-like enzymes.

[2] There are no published reports with commercial disks or tablets containing double inhibitors (DPA or EDTA plus APBA or PBA), and in-house tests have not been evaluated in multi-centre studies. This phenotype is rare outside of Greece and confers high-level resistance to carbapenems.

[3] In the absence of a temocillin MIC, high-level resistance to piperacillin-tazobactam (MIC>32 mg/L) may indicate OXA-48 as ESBLs tend to confer lower MICs.

GeneXpert®

Xpert® Carba-R
On-demand detection and differentiation of KPC, NDM, VIM, IMP-1 and OXA-48 (now covering OXA-181 & OXA-232)

Xpert Carba-R Assay to Detect Carbapenem-Resistant Bacteria

Cartridge detects five classes of carbapenem resistance genes:

- – bla_{KPC}
- – bla_{NDM}
- – bla_{VIM}
- – bla_{OXA-48}
- – bla_{IMP-1}

• Sample: Rectal Swabs

Time to result: 48 minutes

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Accuracy of different methods for susceptibility testing of gentamicin with KPC carbapenemase-producing *Klebsiella pneumoniae*

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ABSTRACT

Performance of Vitek2, Etest, and TREK broth microdilution (BMD) panels was evaluated versus reference CLSI BMD for gentamicin susceptibility testing with 57 bloodstream isolates of KPC-producing *Klebsiella pneumoniae*. Compared with reference BMD, the Essential Agreement and Categorical Agreement for TREK panels, Vitek2, and Etest were 91.2%, 31.6%, and 61.4%, respectively, and 86%, 21%, and 52.6%, respectively. Four very major discrepancies occurred with Vitek2. In these 4 strains, gentamicin resistance was associated with the presence of an *armA* aminoglycoside resistance determinant.

Table 1
Results of gentamicin susceptibility testing with 57 KPC-KP using reference BMD, BMD with TREK panel, Vitek2, and Etest.

Method	MIC (μg/mL)				Category (%)			EA (%)	CA (%)	mD (%)	MD (%)	VMD (%)
	≤1	2	4	>4	S	I	R					
BMD reference	46	6	1	4	52	1	4	NA	NA	NA	NA	NA
BMD TREK panel	11	35	7	4	46	7	4	52 (91.2)	49 (86)	8 (14)		
Vitek2	10	5	42	0	15	42	0	18 (31.6)	12 (21)	41 (71.9)		4 (100)
Etest	4	23	26	4	27	26	4	35 (61.4)	30 (52.6)	27 (47.4)		

Interpretation of MIC results was according to EUCAST breakpoint table (EUCAST, 2014).

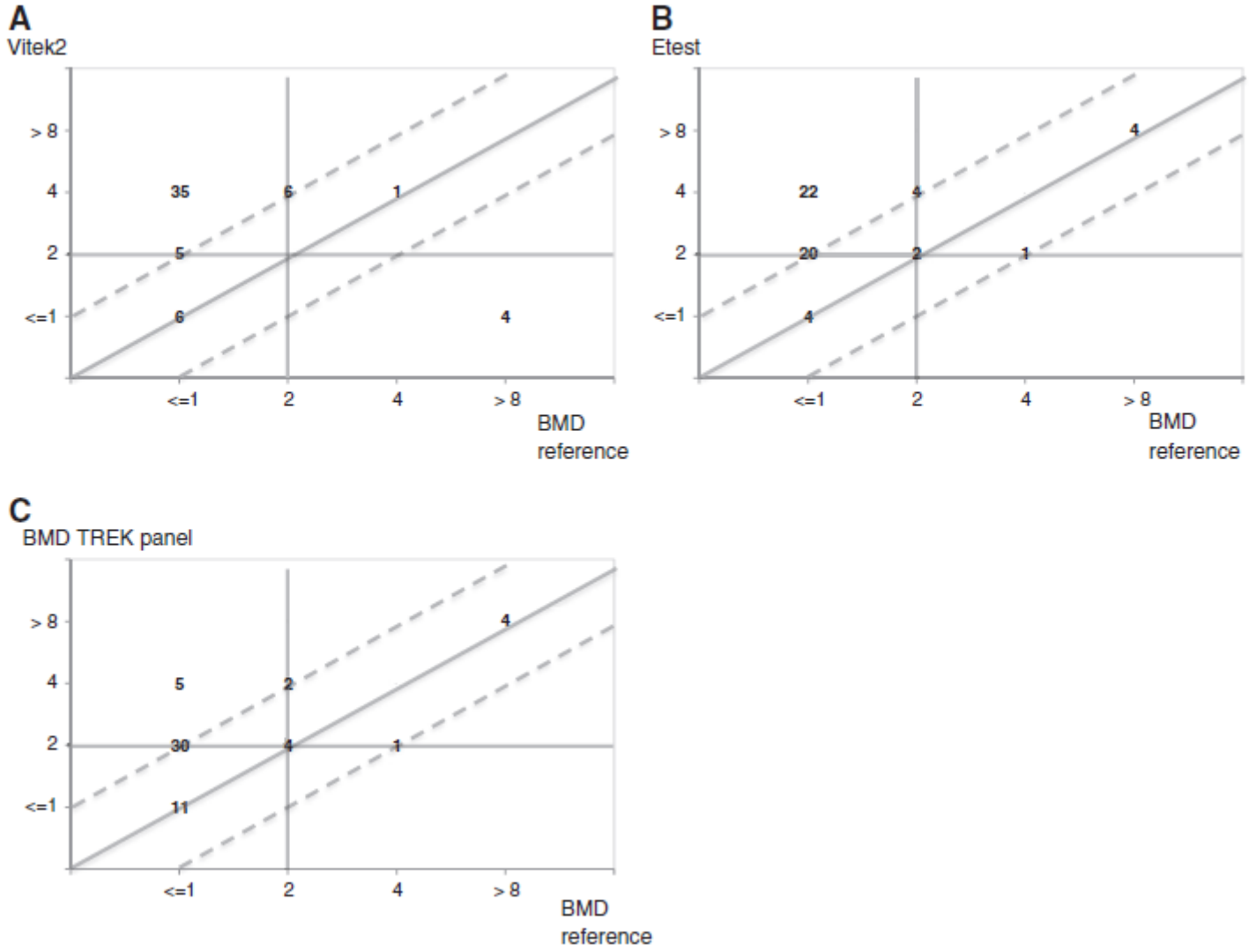

Fig. 1. Scattergram of gentamicin MICs for 57 KPC-KP tested measured by BMD and Vitek2 (A), by BMD and Etest (B), and by TREK panels (C). MICs were indicated in μg/mL.

Tigeciclina : Sensititre vs E-test
(20 ceppi)

		E-test						
		0.25	0.5	0.75	1.5	2	3	4
SENSITITRE	0.25	1		1	1			1
	0.5	1		2	6	1		
	1		1		2	2	1	
	4					1		

Tigeciclina : Sensititre vs Vitek

(20 ceppi)

		VITEK					
		≤0.5	1	2	4	8	≥8
SENSITITRE	0.25		2	2			
	0.5	2		3	4		
	1			2		1	3
	4				1		

MIC di K. pneumoniae CRE

	0.25	≤0.5	0.5	≤1	1	2	4	>4	8	>8	16	32	64	>64	% I+R
Colistina		27			1				1	29					51
Gentamicina				10		32	17	4							33
Meropenem	1					3	11		8		1	11	23	5	93
Tigeciclina	5		33		19	4	2								10

RAPID COMMUNICATIONS

Colistin resistance superimposed to endemic carbapenem-resistant *Klebsiella pneumoniae*: a rapidly evolving problem in Italy, November 2013 to April 2014

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Consecutive non-replicate clinical isolates (n=191) of carbapenem non-susceptible Enterobacteriaceae were collected from 21 hospital laboratories across Italy from November 2013 to April 2014 as part of the European Survey on Carbapenemase-producing Enterobacteriaceae (EuSCAPE) project. *Klebsiella pneumoniae* carbapenemase-producing *K. Pneumoniae* (KPC-KP) represented 178 (93%) isolates with 76 (43%) respectively resistant to colistin, a key drug for treating carbapenamase-producing Enterobacteriaceae.

KPC-KP colistin-resistant isolates were detected in all participating laboratories. This underscores a concerning evolution of colistin resistance in a setting of high KPC-KP endemicity.

EuSCAPE: European Survey on Carbapenemase-producing Enterobacteriaceae; KPC: *Klebsiella pneumoniae* carbapenemase; KPC-KP: KPC-producing *K. pneumoniae*.

The peripheral laboratories are numbered on the map according to alphabetical order.

Proportions of colistin-resistant isolates among KPC-KP per peripheral laboratory:. 1, Alessandria: 1/10; 2, Ancona: 8/10; 3, Ferrara: 1/4; 4, Florence: 5/10; 5, Foggia: 4/10; 6, Lecco: 2/9; 7, Milan: 1/10; 8, Modena: 3/7; 9, Neaples: 3/8; 10, Perugia: 5/10; 11, Reggio Calabria: 4/10; 12, Rome: 4/9; 13, Rome: 2/4; 14, Rome: 6/7; 15, San Remo: 4/8; 16, Siena: 6/8; 17, Treviso: 1/7; 18, Turin: 5/9; 19, Udine: 2/8; 20, Venice: 8/10; 21, Vercelli: 1/10.

Grazie per l'attenzione