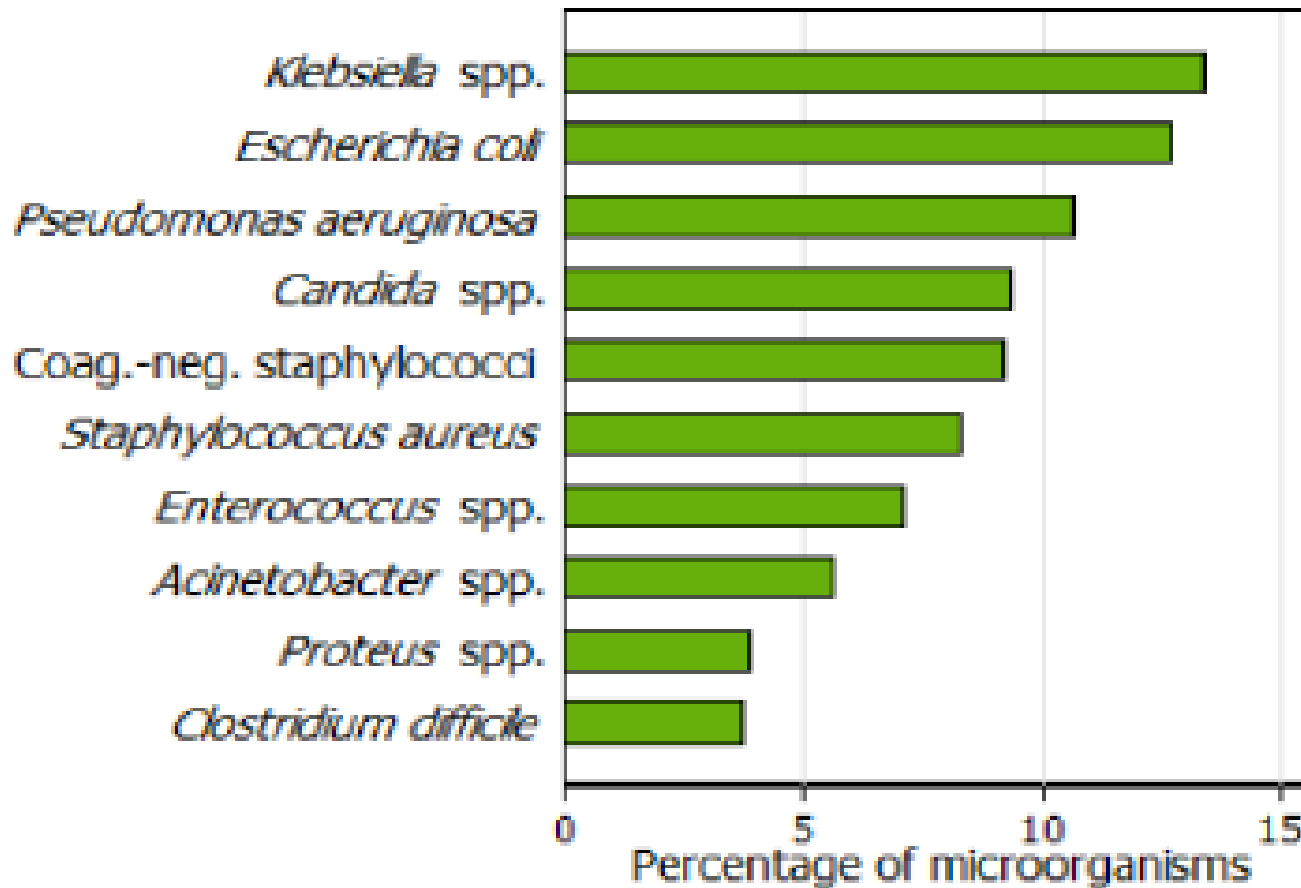


“Epidemiologia dei patogeni ospedalieri multi resistenti in Italia”

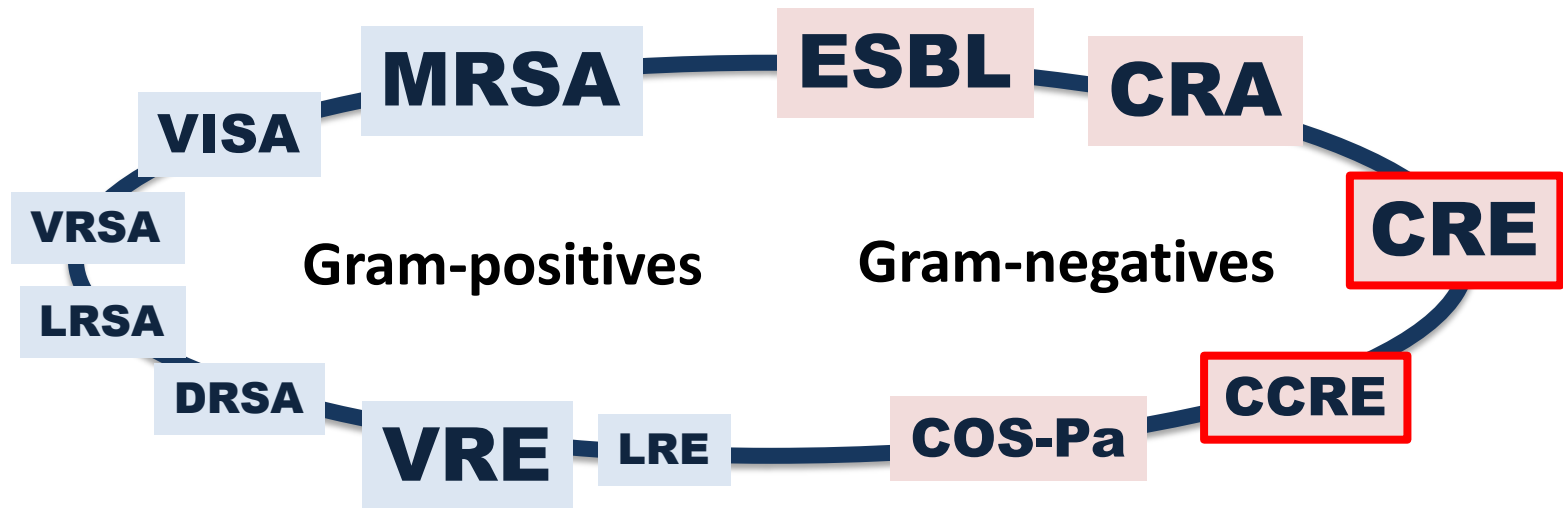
Fabio Arena



Top ten pathogens causing HAIs in Italy



The growing alphabet of MDR pathogens



MRSA = methicillin-R *S. aureus*

VISA = vancomycin-I *S. aureus*

VRSA = vancomycin-R *S. aureus*

LRSA = linezolid-R *S. aureus*

DRSA = daptomycin-R *S. aureus*

VRE = vancomycin-R enterococci

LRE = linezolid-R enterococci

ESBL = extended-spectrum β -lactamases

CRA = carbapenem-R *Acinetobacter*

COS-Pa = colistin-only *S. P. aeruginosa*

CRE = carbapenem-R Enterobacteria

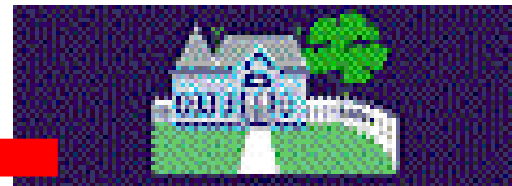
CCRE = colistin+carbapenem-R Enterobacteria

The epidemiological versatility of MRSA

Hospital-associated (HA) MRSA



Hospital



Community

Community-associated (CA) MRSA

Livestock-associated (LA) MRSA

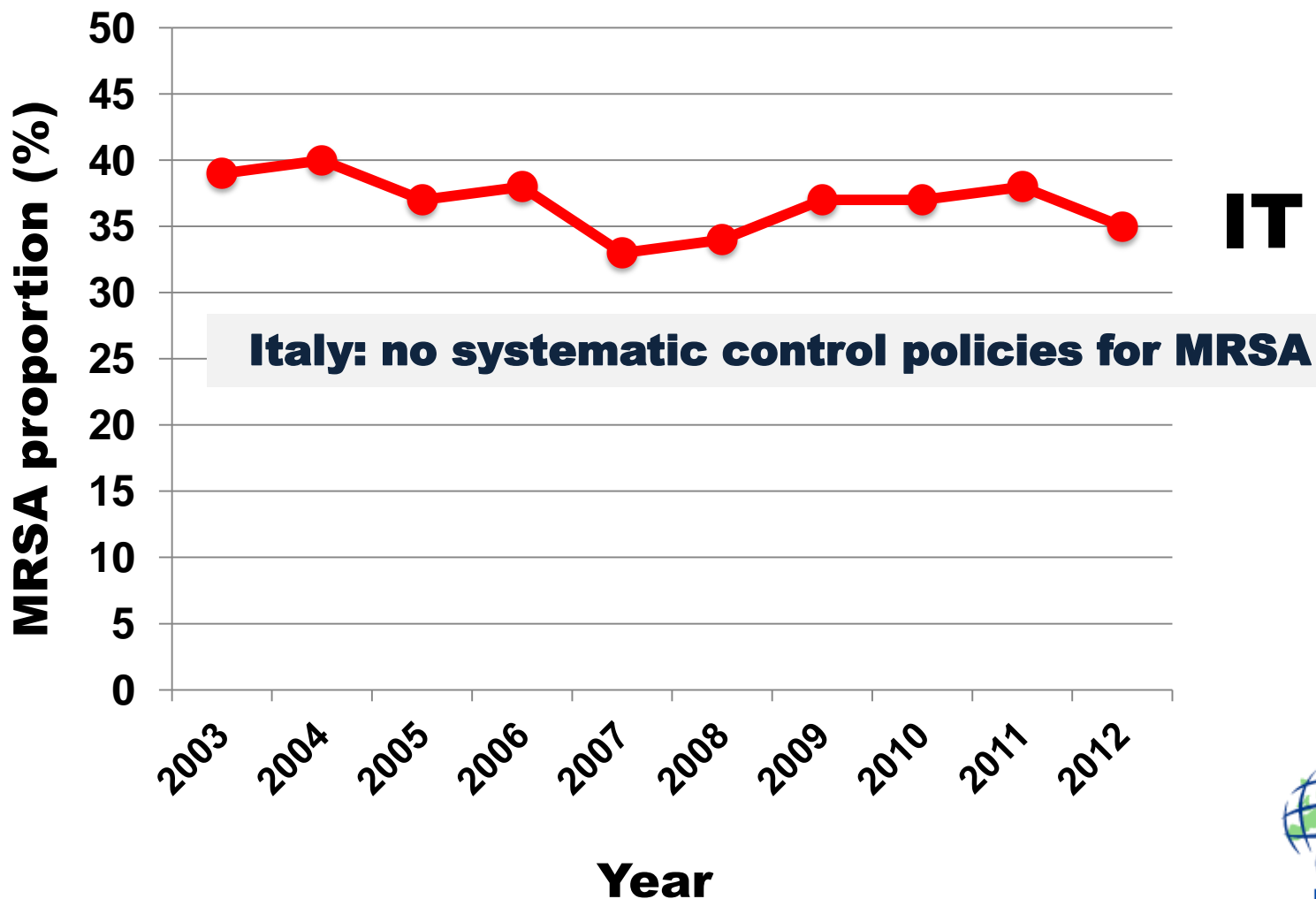


De Leo *et al* – Lancet 2010

Voss *et al* – EID 2005

Garcia-Alvarez *et al* - Lancet ID 2011

MRSA trends in Europe



IT

Studio multicentrico sulla prevalenza di MRSA a livello nazionale condotto nel 2012 (64 centri distribuiti sul territorio nazionale)

(15 giugno-15 luglio e 15 settembre 15 novembre 2012)



	n°	MRSA	MSSA
BSI	465	39%	61%
LRTI	451	40%	60%
SSSI	768	36%	64%
altro	99	28%	72%
TOTALE	1783	37%	63%

Necessità di coprire MRSA nella terapia empirica delle infezioni a possibile eziologia stafilococcica

Studio multicentrico sulla prevalenza di MRSA a livello nazionale condotto nel 2012 (64 centri distribuiti sul territorio nazionale)

(15 giugno-15 luglio e 15 settembre 15 novembre 2012)

Tabella 2		MRSA	MSSA	TOT
NORD (29)	BSI	69	132	201
	LRTI	100	137	237
	SSTI	125	281	406
		294 (34%)	550	844 (47.3%)
CENTRO(15)	BSI	71	103	174
	LRTI	65	64	129
	SSTI	87	148	235
		223 (41%)	315	538 (30%)
SUD E ISOLE (19)	BSI	43	47	90
	LRTI	19	66	85
	SSTI	61	66	127
		123 (40%)	179	302 (17%)

Anti-MRSA agents

Old drugs

- **Vancomycin**
- **Teicoplanin**
- **Cotrimoxazole**
- **Doxycycline**

New drugs

- **Linezolid**
- **Daptomycin**
- **Tigecycline**
- **Ceftaroline**

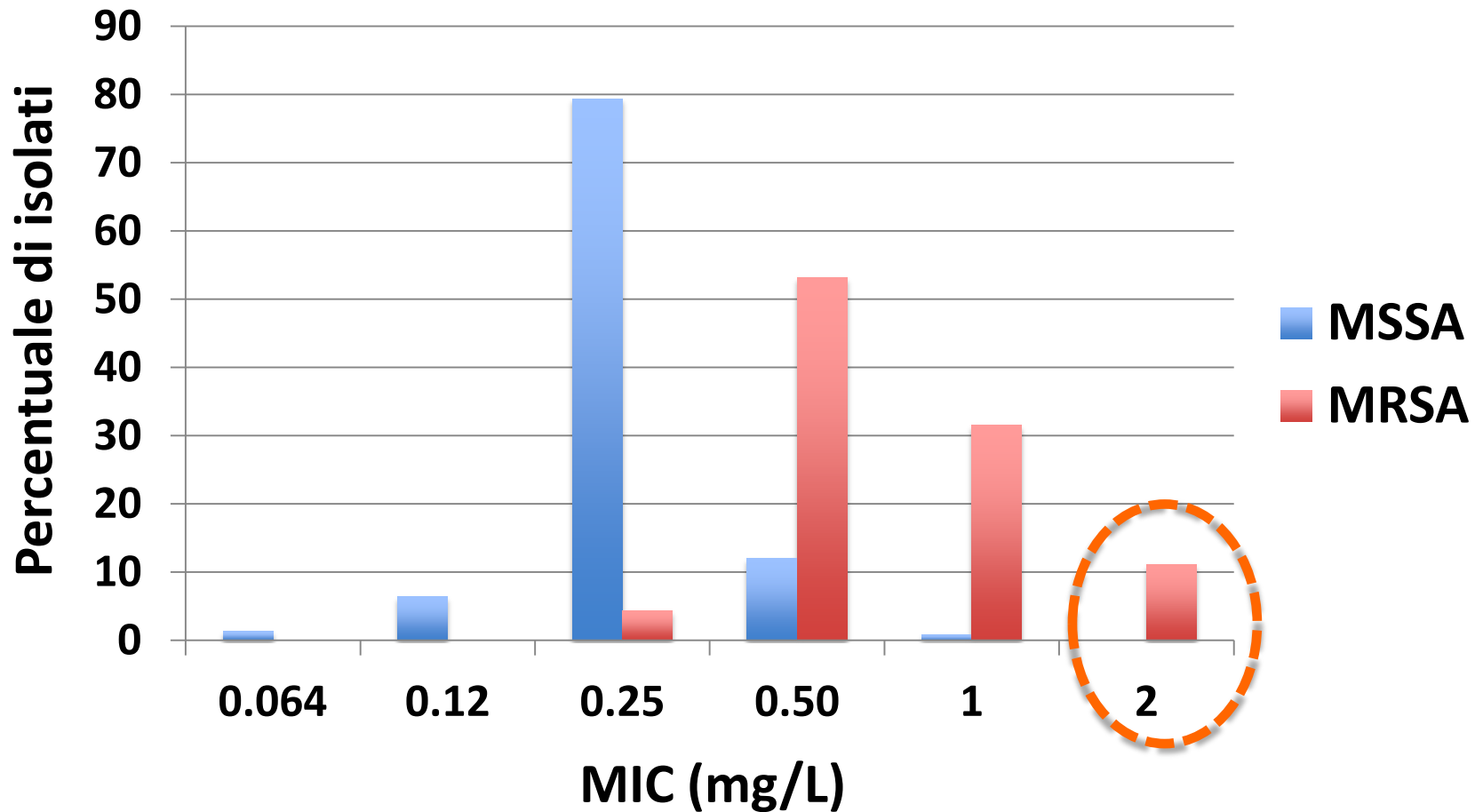
Lo studio PREMIUM

- ◆ **Studio europeo multicentrico (UK, SP, PT, BE, CH, IT) su epidemiologia e antibiotico-sensibilità di patogeni batterici isolati da cSSTI e CAP**
- ◆ **Raccolta ceppi: febbraio – maggio 2012**



- ◆ **Centri italiani partecipanti: 16**
- ◆ **Totale ceppi raccolti: 1058
(738 da cSSTI e 320 da CAP)**

Studio PREMIUM-IT: MIC di ceftarolina per MSSA (N=233) e MRSA (N=162)



Challenging resistant Gram-negatives in the last decade

Early 2000s

- ◆ *P. aeruginosa* XDR Outbreaks
- ◆ ESBL enterics Epidemic
- ◆ *Acinetobacter* XDR Outbreaks

Early 2010s

- ◆ *P. aeruginosa* XDR Outbreaks
- ◆ ESBL enterics Endemic (also community)
- ◆ *Acinetobacter* XDR Endemic
- ◆ CRE Epidemic

Carbapenem-R *Acinetobacter*, Italy

AMCLI-CoSA – Italian national surveillance 2011

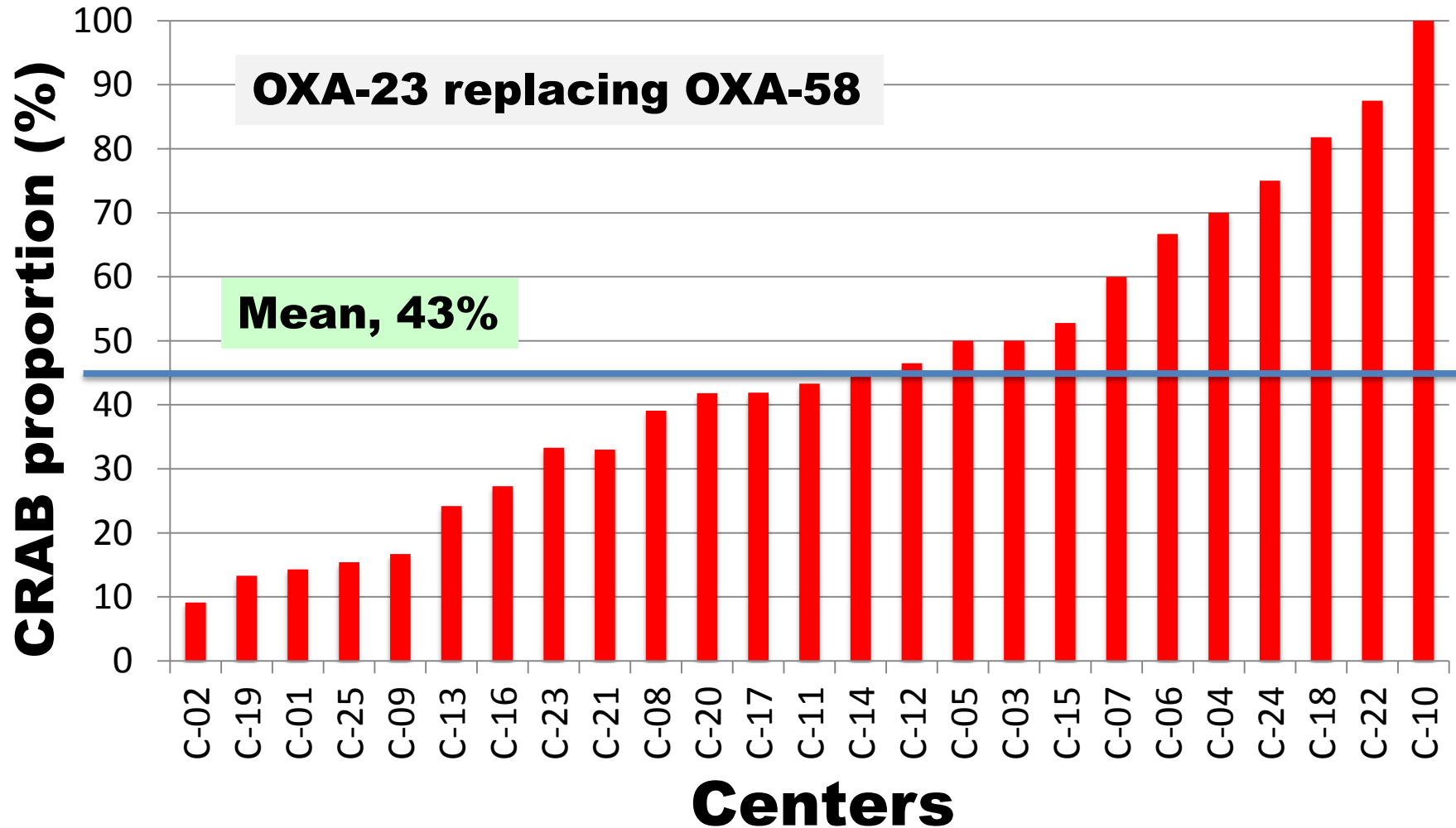


**Nationwide cross-sectional survey, 2011
(6 weeks / 25 centers / N=585 isolates)**

CRAB detected in ALL CENTERS

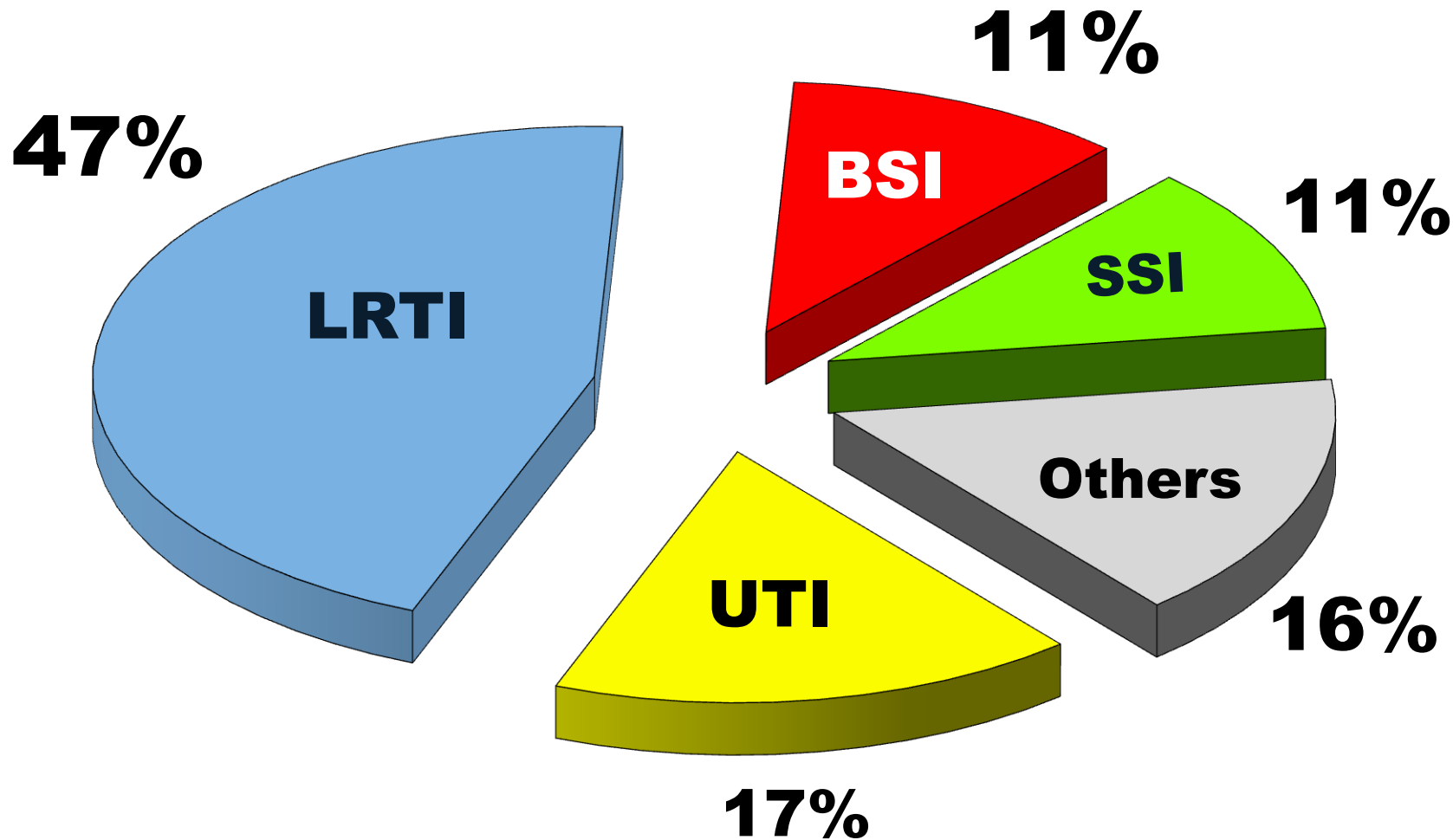
CRAB proportion by center – Italian surveillance

AMCLI-CoSA – Italian national surveillance 2011











Carbapenem-R *Acinetobacter*, Italy - 2011

AMCLI-CoSA – Italian national surveillance 2011






MICs collezione Italiana CRAB

ANTIBIOTICO	MICs			
	MIC range	MIC ₅₀	MIC ₉₀	
PIP/TAZ	128/4 - >128/4	>128/4	>128/4	
SXT	≤0.5/9.5 - >4/76	>4/76	>4/76	
IMIPENEM	4 - >16	>16	>16	
MEROPENEM	2 - >64	64	>64	
DORIPENEM	2 - >8	>8	>8	
GENTAMICINA	≤1 - >4	>4	>4	
AMIKACINA	≤4 - >16	>16	>16	
COLISTINA	≤0.5 - 2	≤0.5	≤0.5	

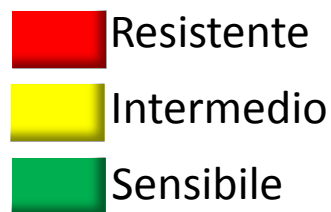
218 isolati con fenotipo XDR/COS

98% R a fluorochinoloni+aminoglicosidi+carbapenemi

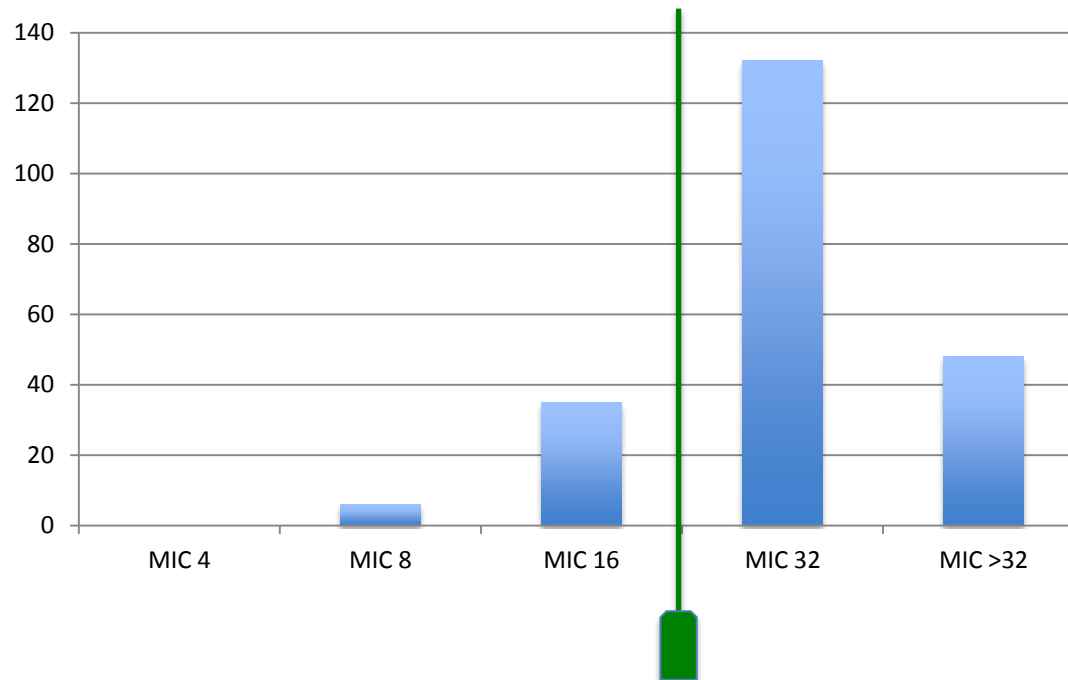
 Resistente
 Intermedio
 Sensibile

MICs collezione Italiana CRAB

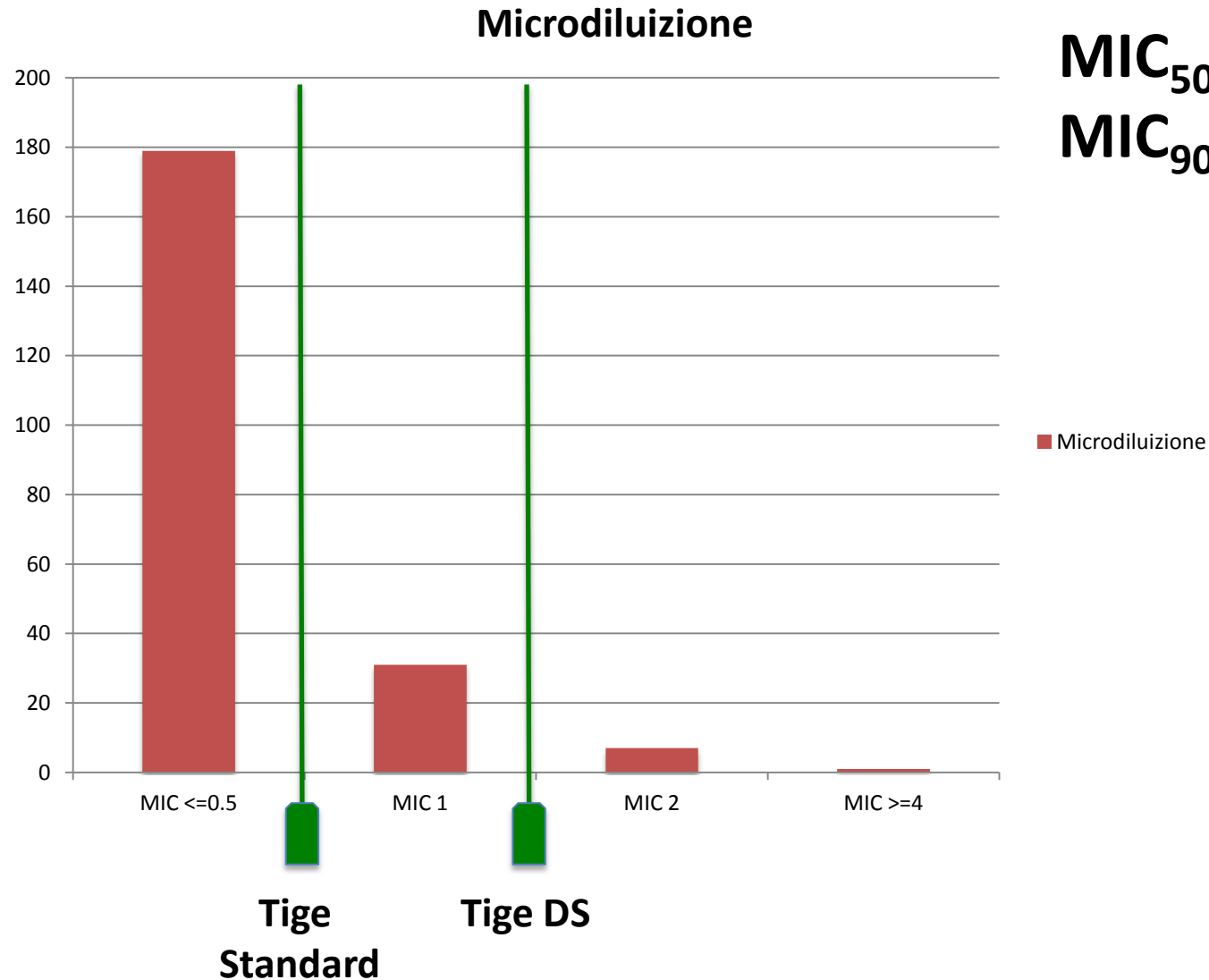
ANTIBIOTICO	MICs			CLSI	
	MIC range	MIC ₅₀	MIC ₉₀	%S	%R
AMP/SUL	≤4 - >16	16	>16	4	80
CEFTAZIDIME	4 - >128	64	128	1	95.9
CEFEPIME	8 - >32	32	>32	2.5	81.7



CEFEPIME



Test di sensibilità alla Tigeciclina



Carbapenem-resistance mechanisms in *K. pneumoniae*, Italy

AMCLI-CoSA – Italian national CRE surveillance 2011



**Cross-sectional survey, 2011
(6 weeks, N=1964 consecutive
nonreplicate *K. pneumoniae*
isolates from 25 centers)**

Carbapenem-resistance mechanisms in *K. pneumoniae*, Italy

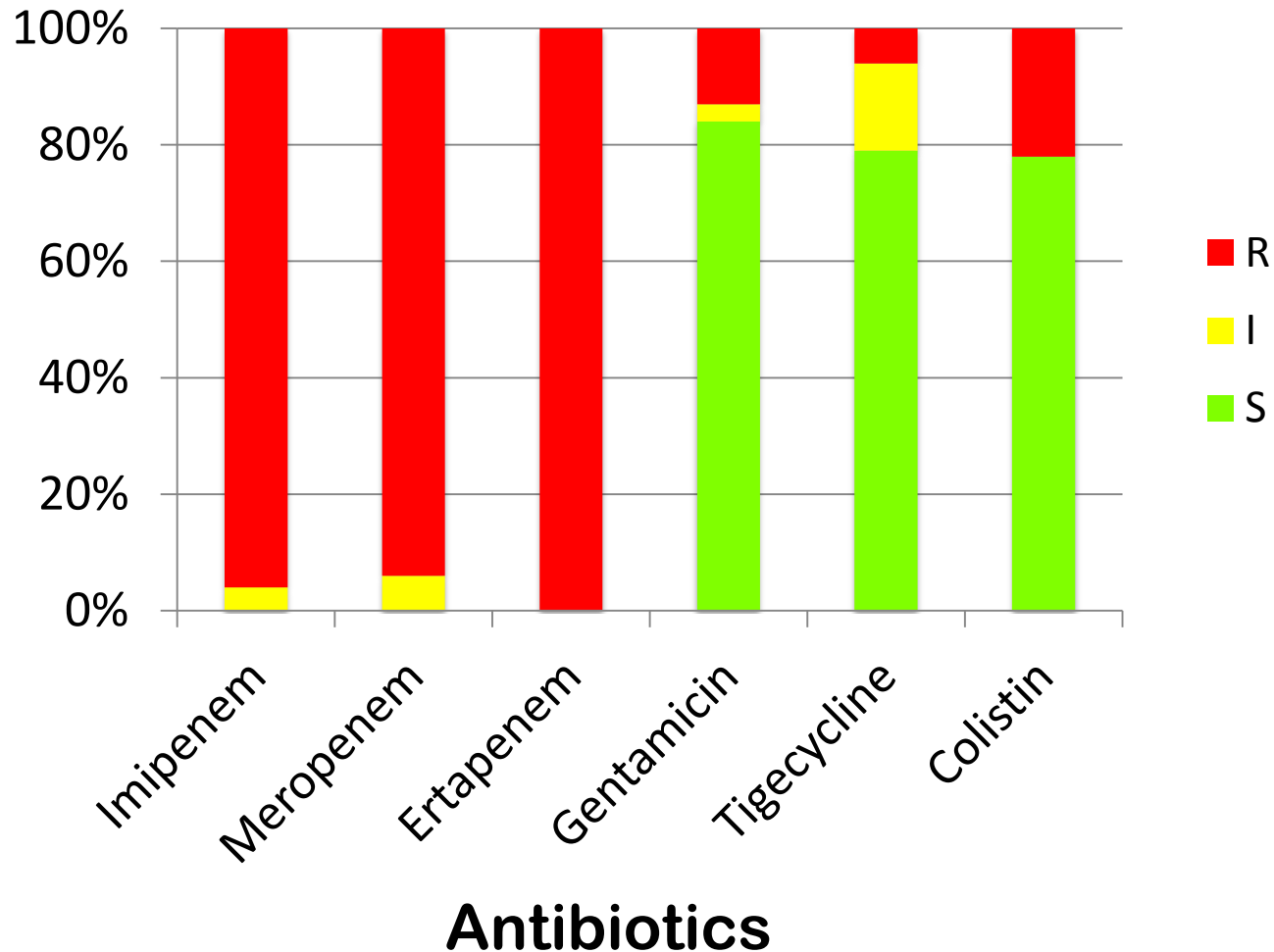
AMCLI-CoSA – Italian national CRE surveillance 2011



**Cross-sectional survey, 2011
(6 weeks, N=1964 consecutive
nonreplicate *K. pneumoniae*
isolates from 25 centers)**

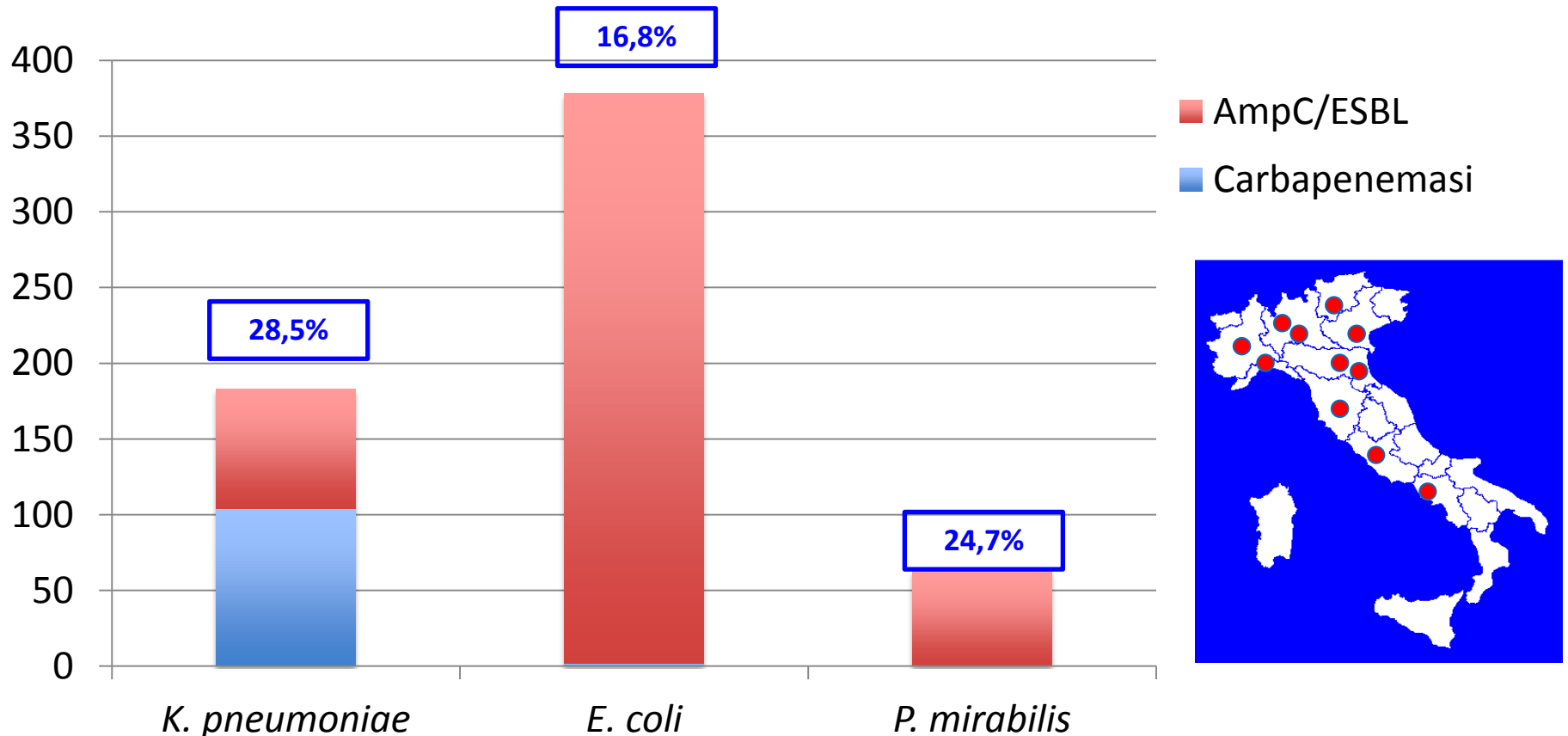
- ◆ Carbapenem-NS *K. pneumoniae* (n=234) detected in 23 of 25 centers
- ◆ 95% carbapenemase producers
- ◆ 87% KPC, 7% VIM, 1% OXA-48

Antimicrobial susceptibility of KPC-Kp (Italian nationwide surveillance, n=204 isolates)

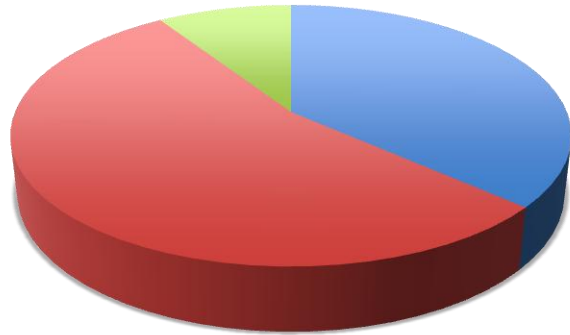


2013 AMCLI-COSA Surveillance (1/15-Oct) 12/14 centers

Consecutive non-replicate isolates of *E. coli*, *K. pneumoniae*, *P. mirabilis*, with MIC for 3GC or/and ERT >1



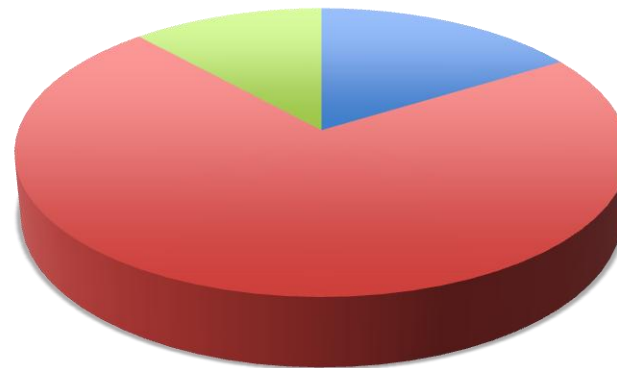
Inpatients (n. 1354)



- *K. pneumoniae*
- *E. coli*
- *P. mirabilis*

Number of resistant to 3GC or CARB= 402/1354 (29,7%)

Number of resistant to 3GC or CARB= 222/1792 (12,4%)



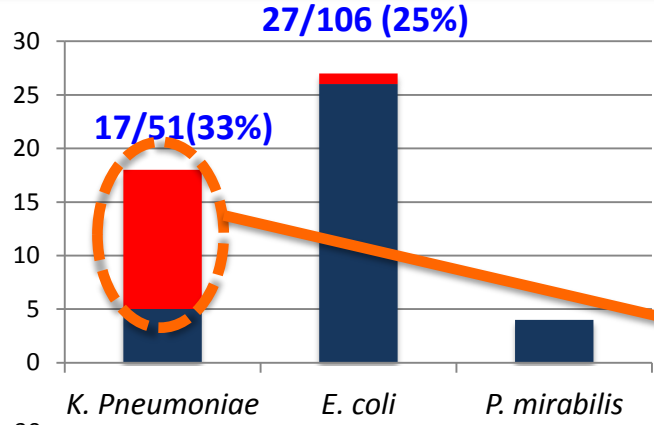
- *K. pneumoniae*
- *E. coli*
- *P. mirabilis*

Outpatients (n. 1792)

Inpatients (n. 1354)

Outpatients (n. 1792)

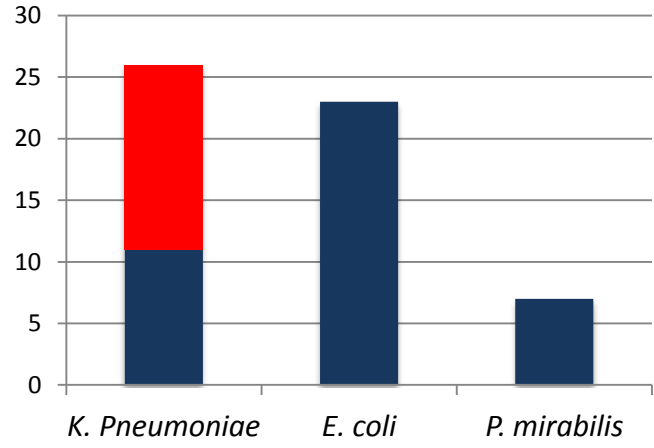
Blood



4 *E. coli* ESBL produttori

12 CARB.-R out of 51 (23,5%)

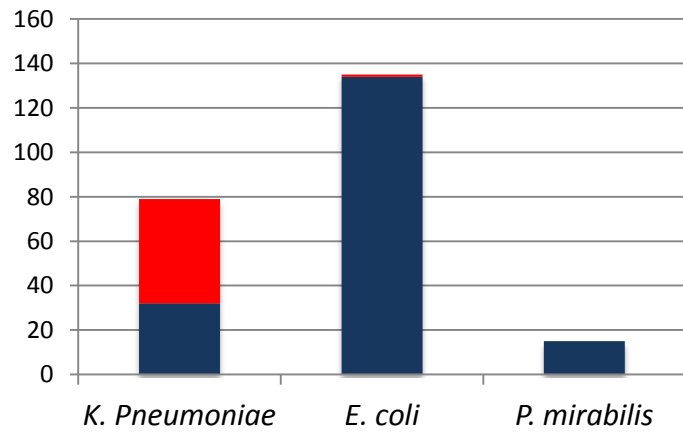
Respiratory



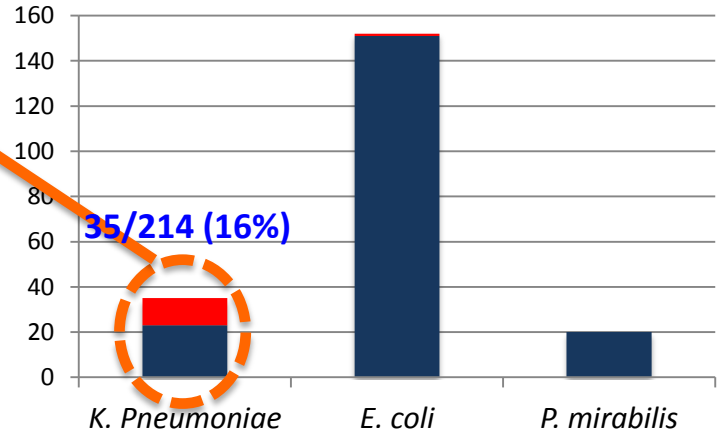
1 *E. coli* ESBL produttore
1 *K. pneumoniae* CARB-R

12 CARB.-R out of 214 (5,6%)

Urine



160/1286 (12%)



CARB-R
3GC-R

Collezione isolati BSI collaborazione “AOU Careggi”-Università Cattolica



late 2011-13

95 *K. pneumoniae*
KPC isolates
ST512
ST258
ST101

Sviluppo di un checkerboard modificato per il test della sinergia

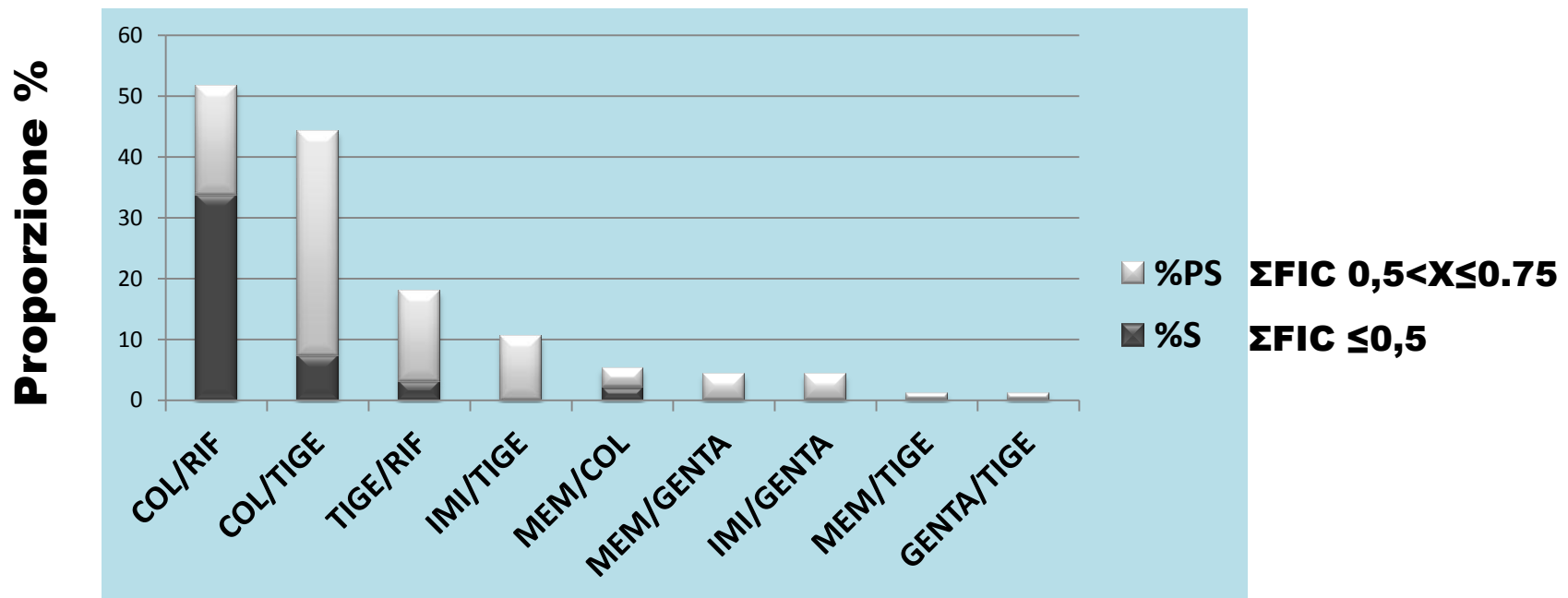
COL ₁₆	COL ₈	COL ₄	COL ₂	COL ₁	COL _{0,5}	COL _{0,25}	RIF ₁₂₈	RIF ₆₄	RIF ₃₂	RIF ₁₆	MEM ₁₂₈	RIF ₁₂₈	TIGE _{10,5}
MEM ₁₂₈	MEM ₆₄	MEM ₃₂	MEM ₁₆	MEM ₈	IMI ₁₂₈	IMI ₆₄	IMI ₃₂	IMI ₁₆	IMI ₈	IMI ₄	MEM ₁₂₈	RIF ₁₂₈	TIGE _{10,5}
TIGE ₈	TIGE ₄	TIGE ₂	TIGE ₁	TIGE _{0,5}	TIGE _{0,25}	TIGE _{0,125}	MEM ₃₂	RIF ₆₄	IMI ₃₂	IMI ₁₆	MEM ₃₂	RIF ₆₄	GENTA ₁₆
GENTA ₁₆	GENTA ₈	GENTA ₄	GENTA ₂	GENTA ₁	GENTA _{0,5}	GENTA _{0,25}	TIGE _{10,5}	TIGE _{10,5}	TIGE _{10,25}	TIGE _{10,125}	MEM ₃₂	RIF ₆₄	TIGE _{10,5}
MEM ₃₂	MEM ₃₂	MEM ₃₂	MEM ₃₂	COL ₁₆	TIGE _{10,5}	TIGE _{10,25}	TIGE _{10,5}	MEM ₃₂	MEM ₃₂	IMI ₃₂	IMI ₃₂	RIF ₆₄	IMI ₃₂
TIGE _{10,5}	TIGE _{10,25}	GENTA ₁₆	GENTA ₁₆	RIF ₆₄	COL ₁₆	COL ₁₆	GENTA ₁₆	COL ₁₆	COL ₁₆	TIGE _{10,25}	TIGE _{10,25}	GENTA ₁₆	GENTA ₁₆
MEM ₆₄	MEM ₆₄	MEM ₆₄	MEM ₆₄	COL ₈	TIGE _{10,5}	TIGE _{10,25}	TIGE _{10,5}	MEM ₆₄	MEM ₆₄	IMI ₆₄	IMI ₆₄	RIF ₆₄	IMI ₆₄
TIGE _{10,5}	TIGE _{10,25}	GENTA ₁₆	GENTA ₁₆	RIF ₆₄	COL ₈	COL ₈	GENTA ₁₆	COL ₈	COL ₈	TIGE _{10,25}	TIGE _{10,25}	GENTA ₁₆	GENTA ₁₆
MEM ₂₂	MEM ₂₂	MEM ₂₂	MEM ₂₂	COL ₁	TIGE _{10,5}	TIGE _{10,25}	TIGE _{10,5}	MEM ₂₂	MEM ₂₂	IMI ₂₂	IMI ₂₂	RIF ₆₄	IMI ₂₂
TIGE _{10,5}	TIGE _{10,25}	GENTA ₁₆	GENTA ₁₆	RIF ₆₄	COL ₁	COL ₁	GENTA ₁₆	COL ₁	COL ₁	TIGE _{10,25}	TIGE _{10,25}	GENTA ₁₆	GENTA ₁₆
MEM ₁₀	MEM ₁₀	MEM ₁₀	MEM ₁₀	COL _{0,5}	TIGE _{10,5}	TIGE _{10,25}	TIGE _{10,5}	MEM ₁₀	MEM ₁₀	IMI ₁₀	IMI ₁₀	RIF ₆₄	IMI ₁₀
TIGE _{10,5}	TIGE _{10,25}	GENTA ₁₆	GENTA ₁₆	RIF ₆₄	COL _{0,5}	COL _{0,5}	GENTA _{10,5}	COL _{0,5}	COL _{0,5}	TIGE _{10,25}	TIGE _{10,25}	GENTA ₁₆	GENTA ₁₆

— Sector 1, MICs of single drugs

— Sector 2, **test 9** dual combinations (Σ FIC indexes)

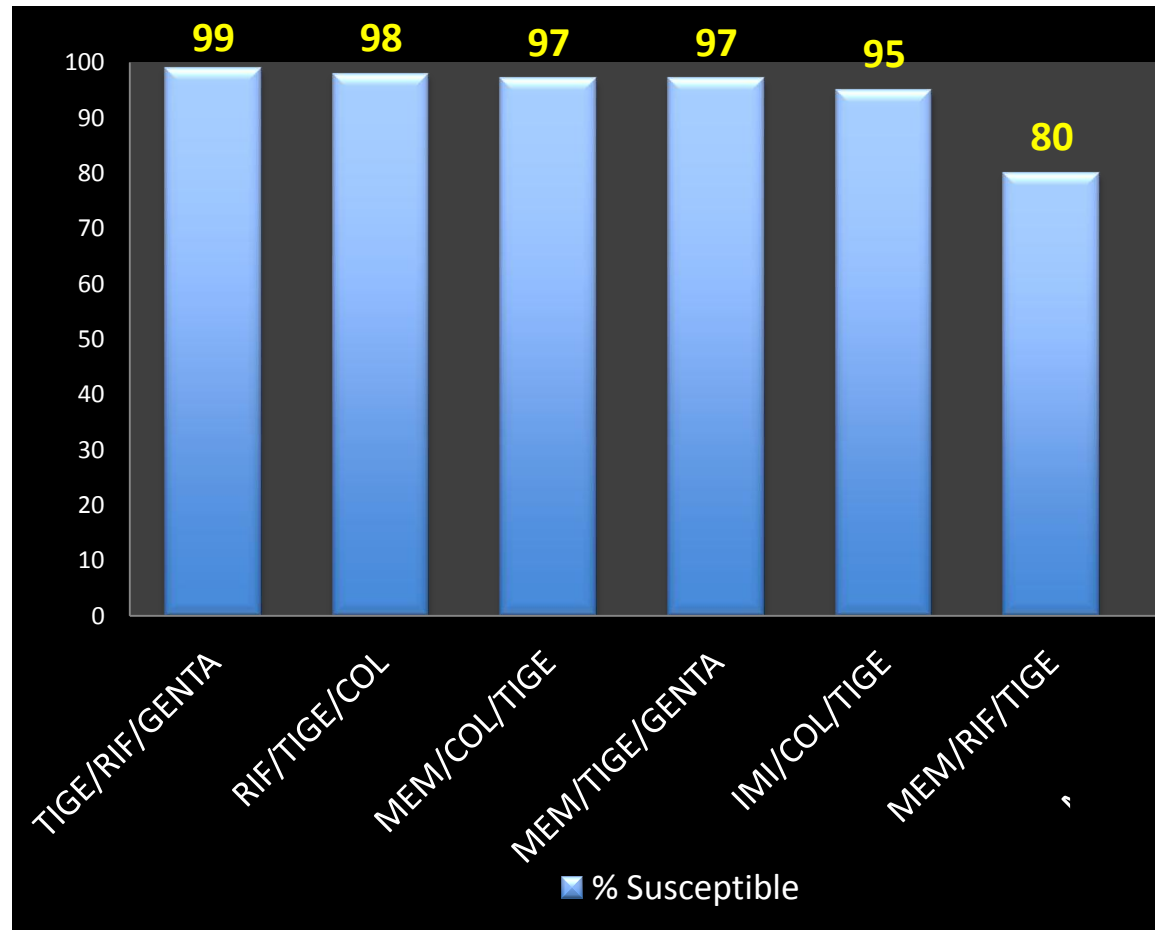
— Sector 3, **test 8** three-drug combinations

Proporzione dei sinergismi osservata con le varie combinazioni tra antibiotici



Combinazione di antibiotici

Association (3 drugs)



Meropenem+Tigeciclina+Colistina

Meropenem+Tigeciclina+Gentamicina

Conclusions

- MRSA in HAI and CAI but new drugs retain good activity
- Dynamic evolution of resistance in Gram-negatives pathogens
- *Acinetobacter baumannii* XDR endemic
- Need to cover KPC-Kp in empiric therapy of BSI?
- KPC-Kp relevant also in outpatients
- Synergy data are increasing
- COL-RIF and TIGE-COL high activity