Acinetobacter baumannii e *Pseudomonas aeruginosa* MDR

Alberto Farese

Malattie Infettive e Tropicali

AOU Careggi

- Speaker per conto di
  - Gilead
  - Pfizer

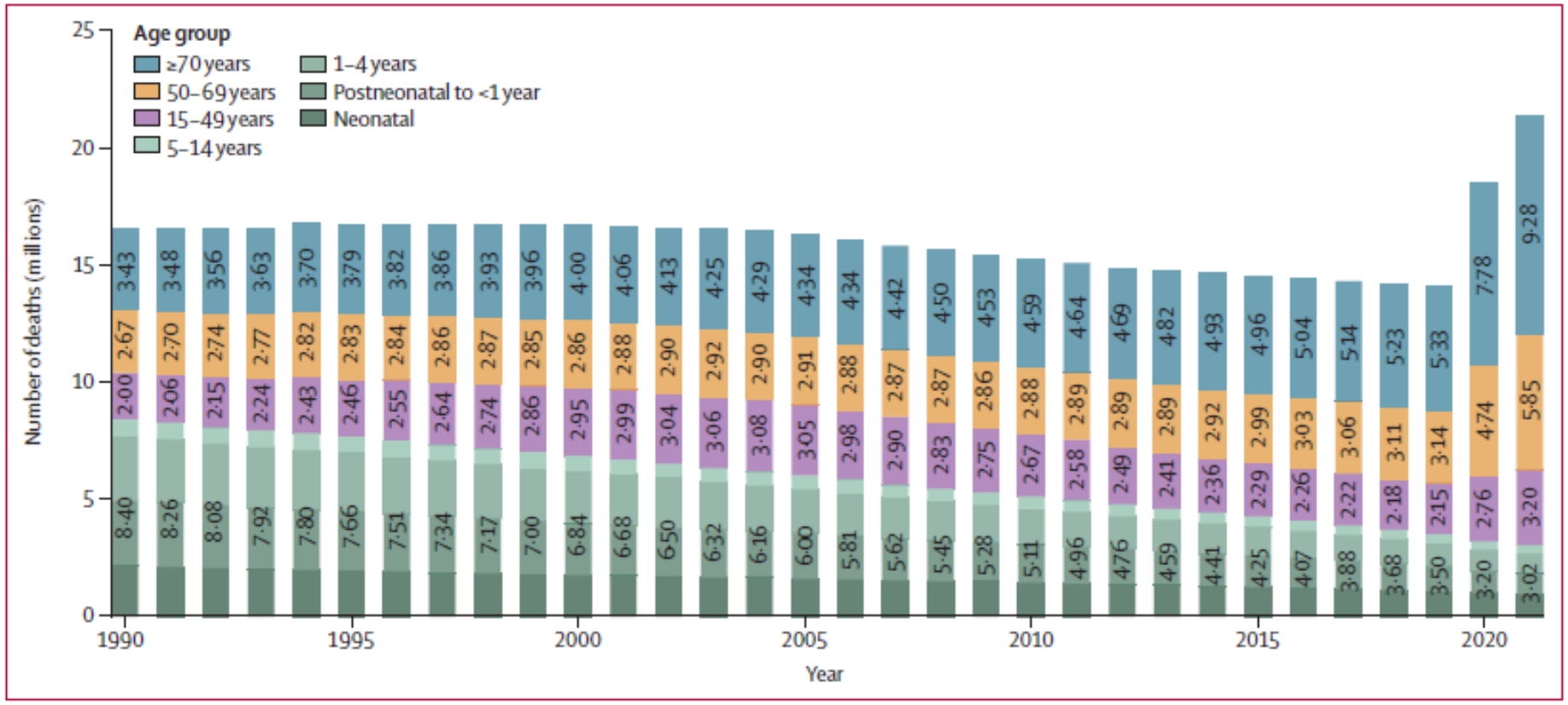
Lancet 2024; 404: 1199–226

Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050

GBD 2021 Antimicrobial Resistance Collaborators*

- Morti e DALY attribuibili e associabili a resistenza antimicrobica a batteri in 204 Paesi dal 1990 al 2021
- In particolare a 22 patogeni, 84 combinazioni antibiotico-patogeno e 11 sindromi infettive
- Fonti: cause di morte, dimissioni ospedaliere, dati microbiologici, letteratura, profili di resistenza, dati di vendita farmaco, survey sull'uso di antibiotici, sorveglianza di mortalità, linkage data, dati assicurativi e precedenti dati sull'argomento
- Analisi di 520 milioni di record o isolati
- Modello statistico per stimare il burden

Decessi per sepsi per gruppi di età



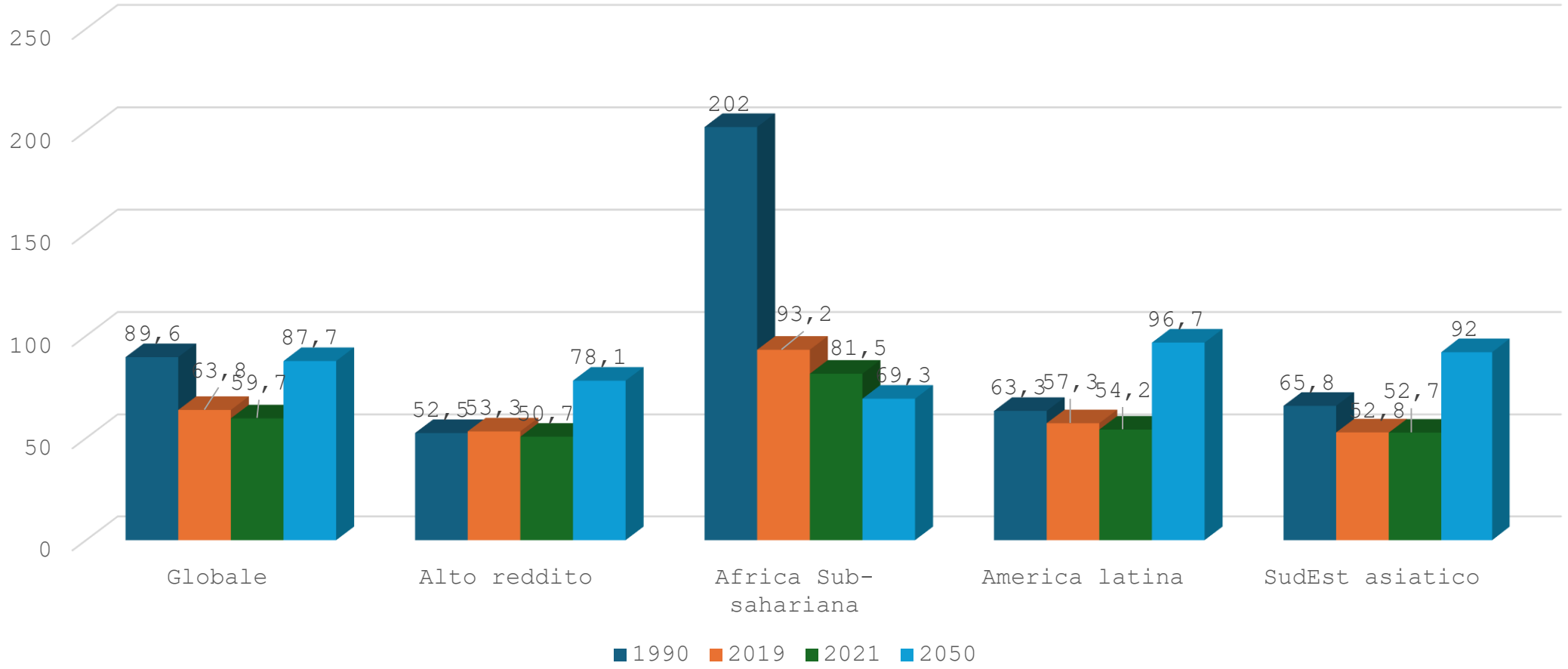
3,43-9,28

2,67-5,85

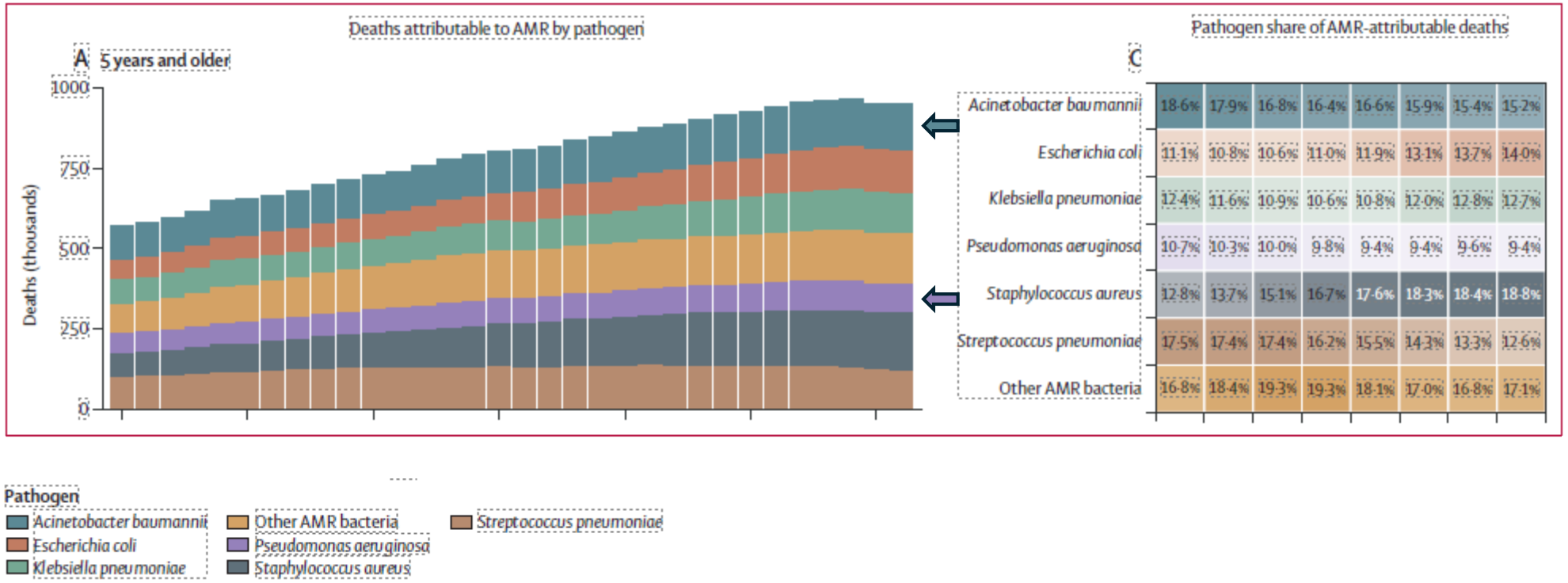
2,00-3,20

3,43-9,28

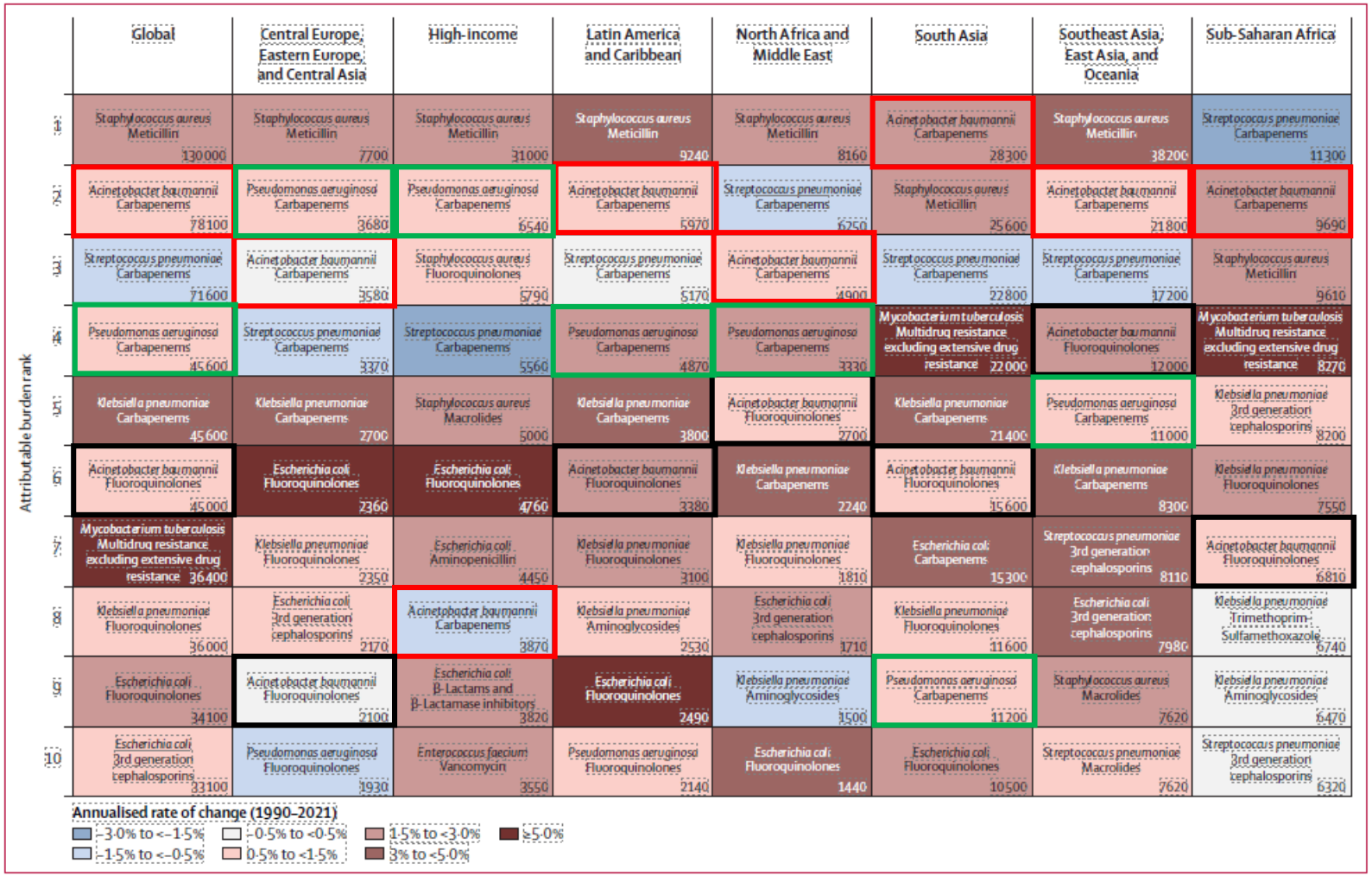
Decessi associati a AMR (tasso x 100.00)



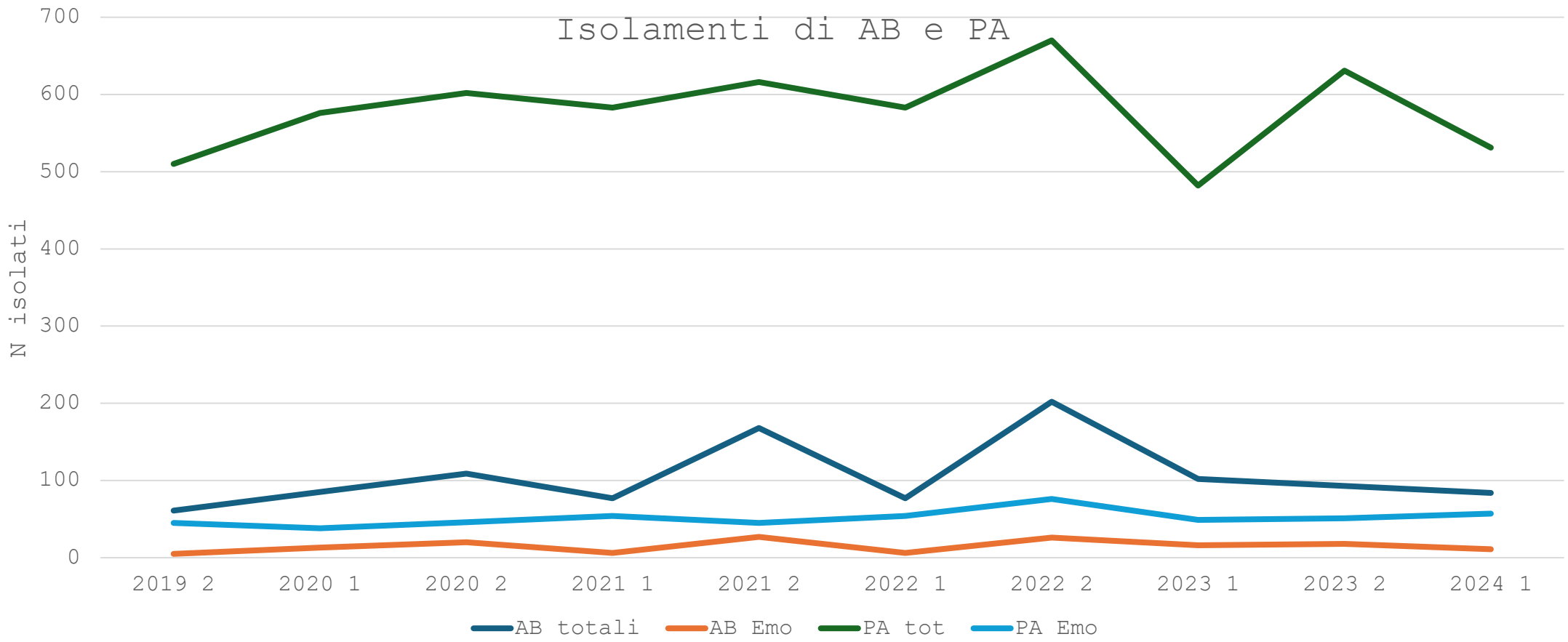
Decessi attribuibili per patogeno 1990-2021



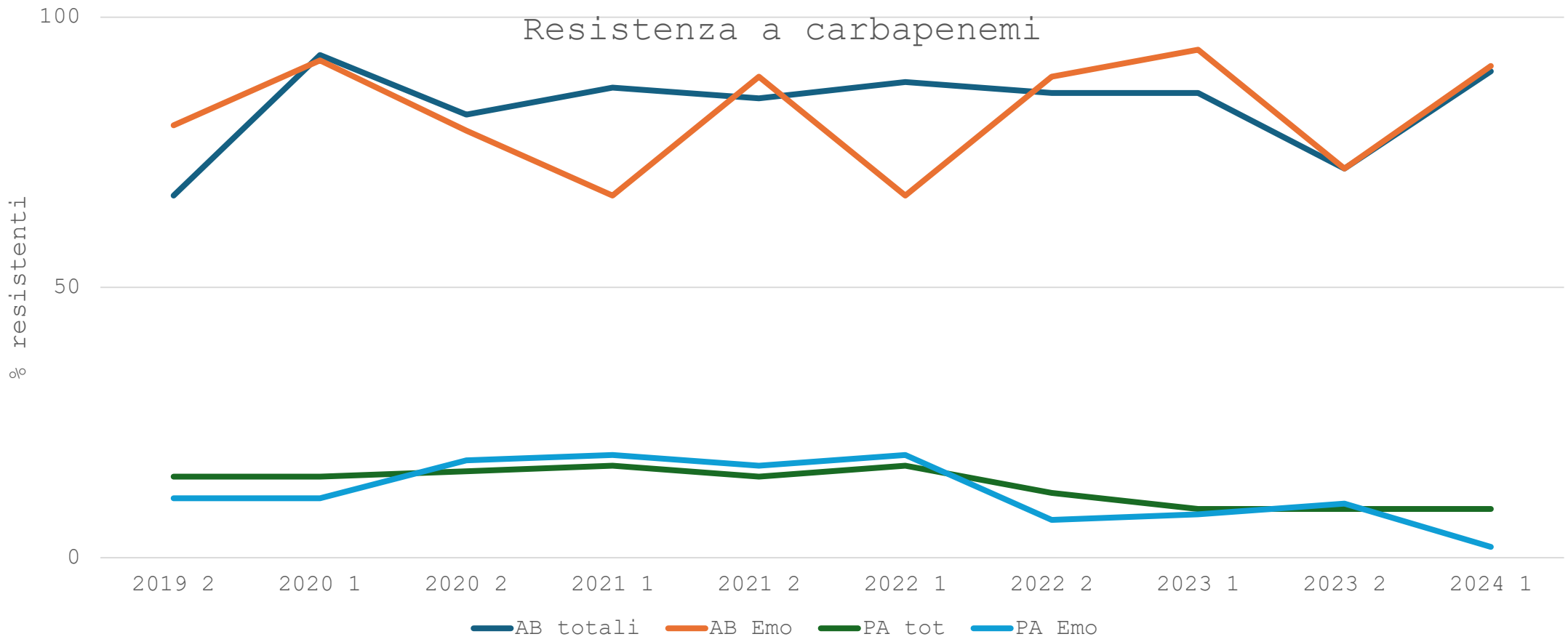
Top ten killer (decessi attribuibili) nel 2021



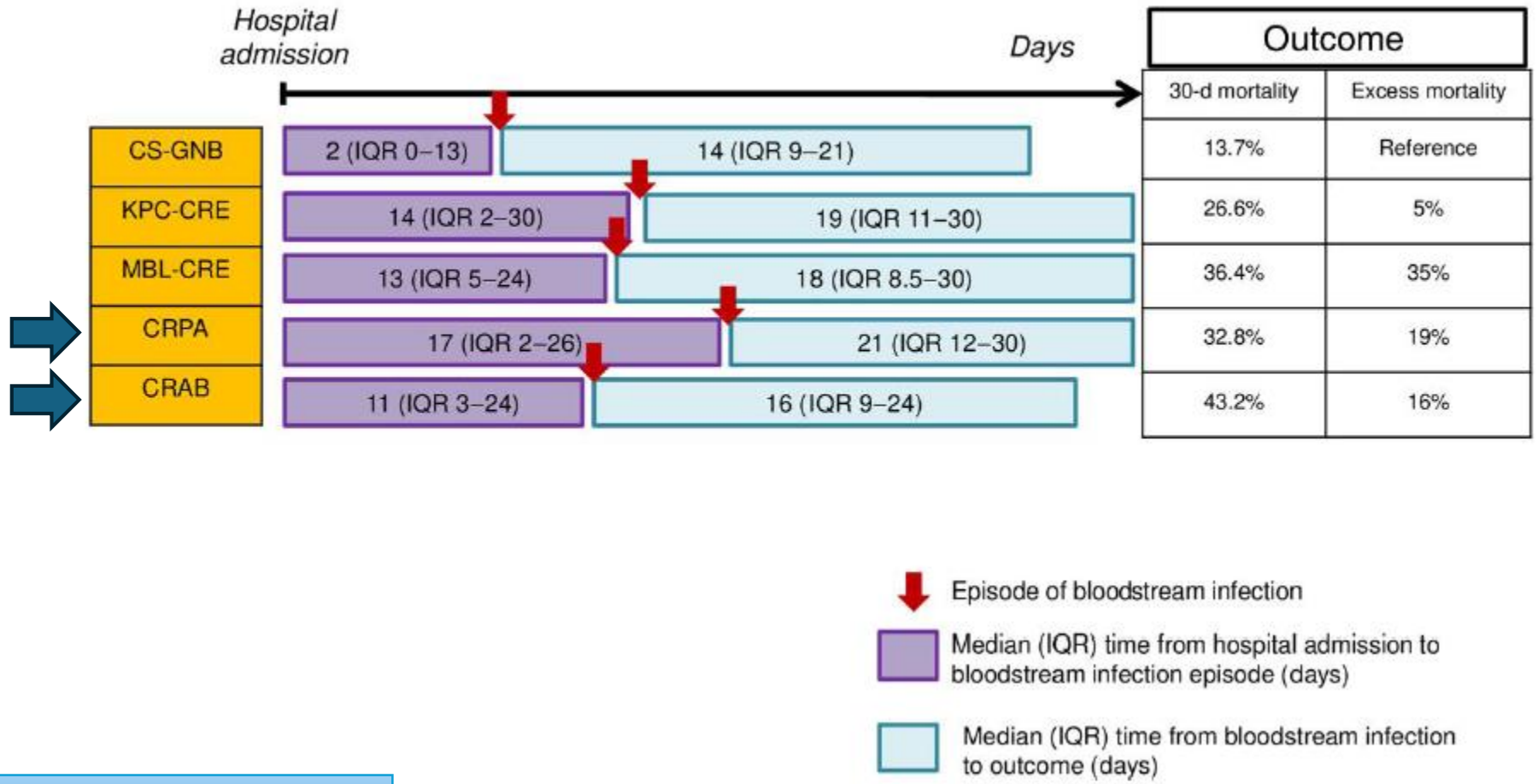
Casistica AOU Careggi



Casistica AOU Careggi

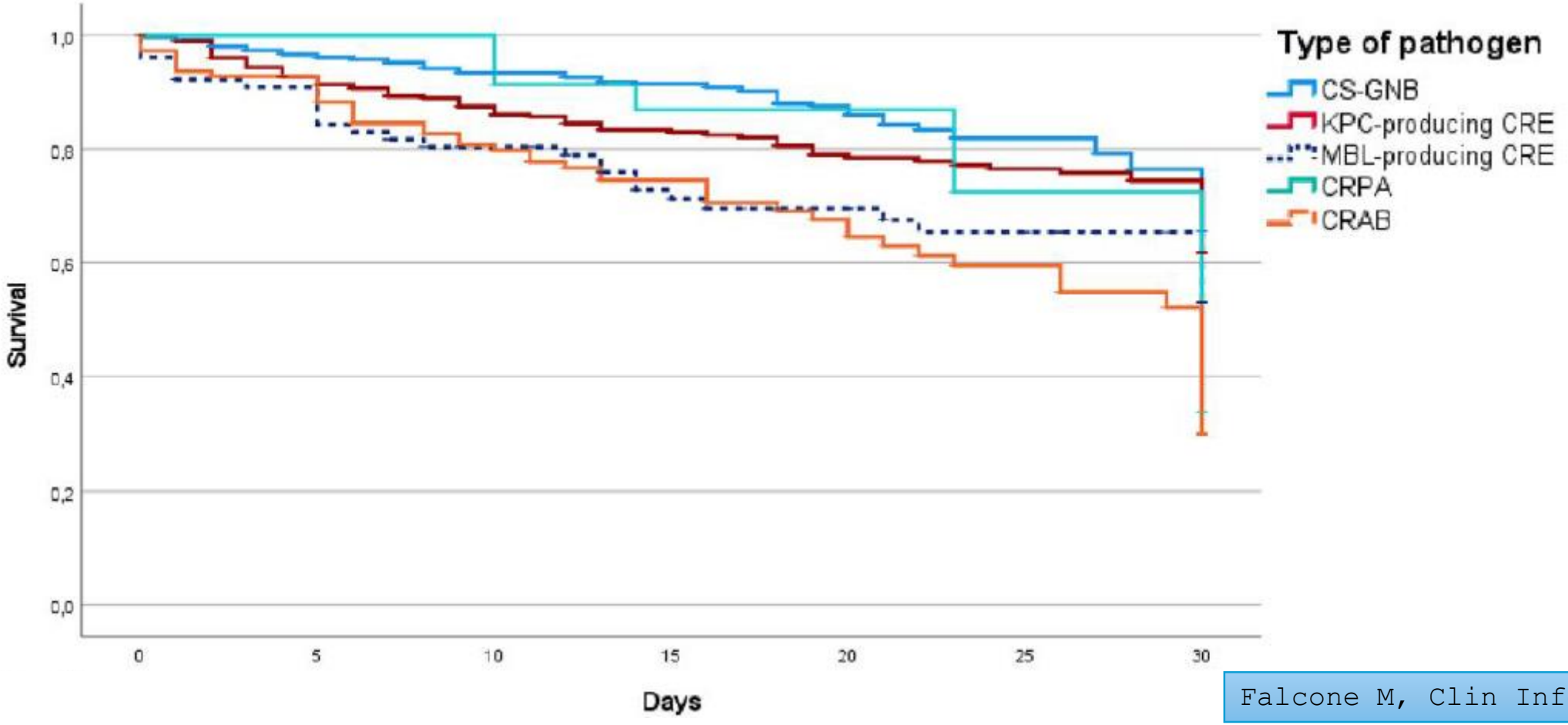


Mortalità attribuibile a Gram negativi resistenti a carbapenemi



Falcone M, Clin Infect Dis 2023

Curve di sopravvivenza per patogeno



Falcone M, Clin Infect Dis 2

Attività dei nuovi antibiotici contro i bacilli Gram negativi

	ESBL	KPC	MBL	AmpC	OXA-48	DTR-PA	CRAB	S. maltophilia
Aztreonam/avibactam								
Cefepime/enmetazobactam								
Cefepime/taniborbactam								
Cefepime/zidebactam								
Cefiderocol								
Ceftazidime/avibactam								
Ceftolozane/tazobactam								
Imipenem/relebactam								
Cefepime/nacubactam								
Meropenem/vaborbactam								
Eravacycline								

CRAB: cosa dicono le linee guida

ESCMID guidelines Paul M. CMI 2022	• CRAB susceptible to sulbactam and HAP/VAP, we suggest ampicillin sulbactam. • For patients with CRAB resistant to sulbactam, a polymyxin or high-dose tigecycline can be used if active *in vitro*. • We conditionally recommend against cefiderocol for the treatment of infections caused by CRAB.
SIMIT, SITA, GISA, AMCLI, SIM Tiseo G, Int J Antimicrob Agents 2022	• There are no convincing data about the optimal antibiotic therapy against CRAB infections. Consultation by infectious diseases specialists is needed in patients with CRAB infections. • The use of recently approved cefiderocol should be appropriately evaluated to prevent the emergence of resistant isolates.
IDSA Tamma PD, Clin Infect Dis 2024	• The preferred regimen is sulbactam-durlobactam in combination with a carbapenem (ie, imipenem-cilastatin or meropenem). • An alternative regimen is high-dose ampicillin-sulbactam in combination with at least 1 other agent (ie, polymyxin B, minocycline > tigecycline, or cefiderocol), if sulbactam-durlobactam is not available. • Cefiderocol should be limited to the treatment of CRAB

Durlobactam/sulbactam

- Durlobactam inibisce le betalattamasi di classe A (KPC, SHV, TEM, CTX-M), C (AmpC, P99, PDC) e D (OXA-10, 23, 24/40, 48) che sono prevalenti in CRAB; non inibisce le classi B
- Quindi solo i CRAB che producono MBL non risentono dell'attività di durlobactam
- Farmaco di scelta (in combinazione con carbapenemi) per il trattamento di CRAB secondo le linee guida IDSA 2024

Efficacia di durlobactam/sulbactam

- Studio ATTACK
  - Durlobactam/sulbactam vs colistina, entrambi con imipenem/cilastatina
  - Arruolati 125 CRAB da HAP o VAP
  - Mortalità a 28 giorni 19 vs 32%
  - Nefrotossicità 13 vs 38%
  - SAE 40 vs 49%
  - Interruzioni di trattamento 11 vs 16%

Kaye KS, Lancet Inf Dis 2023

Perché con un carbapenemico?

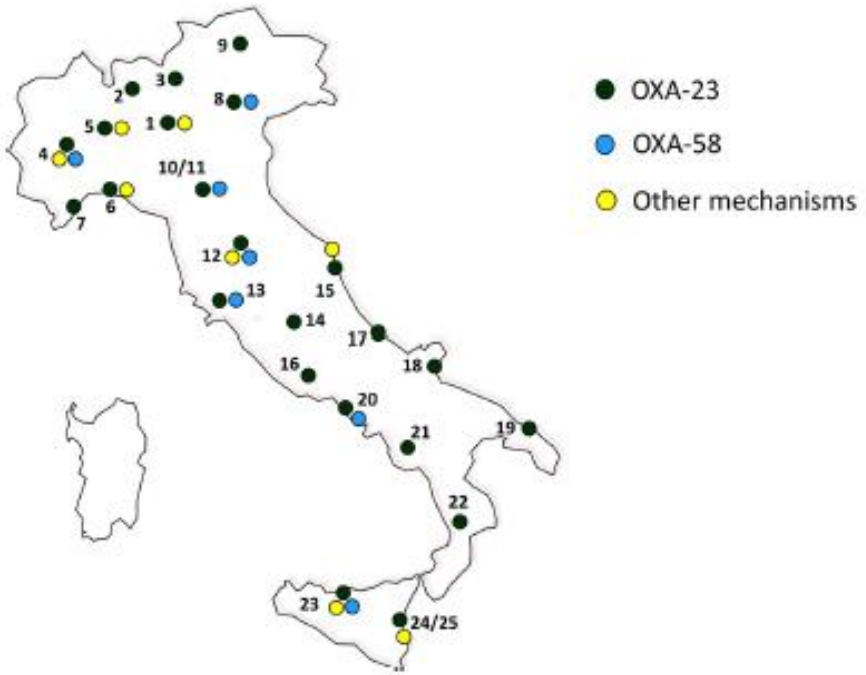
- Studio ATTACK
- Frequenti infezioni polimicrobiche
- Azione su PBP2 (carbapenemi) e PBP3 (sulbactam)
- L'aggiunta di imipenem mostra una riduzione della MIC di due diluizioni di sulbactam-durlobactam.

Iovleva A, Antimicrob Agents Chemother 20
Miller AA, Antimicrob Agents Chemother 20

Cefiderocol

- Stabile in presenza di carbapenemasi OXA-51
- Stabile in presenza di carbapenemasi OXA-23/24/40/58
- Emergenza di resistenza durante il trattamento con vari meccanismi
  - Mutazioni nei recettori del sideroforo
  - Mutazioni di β-lattamasi ADC con idrolisi del cefiderocol
  - Presenza di PER-like β-lattamasi

Oxa-23

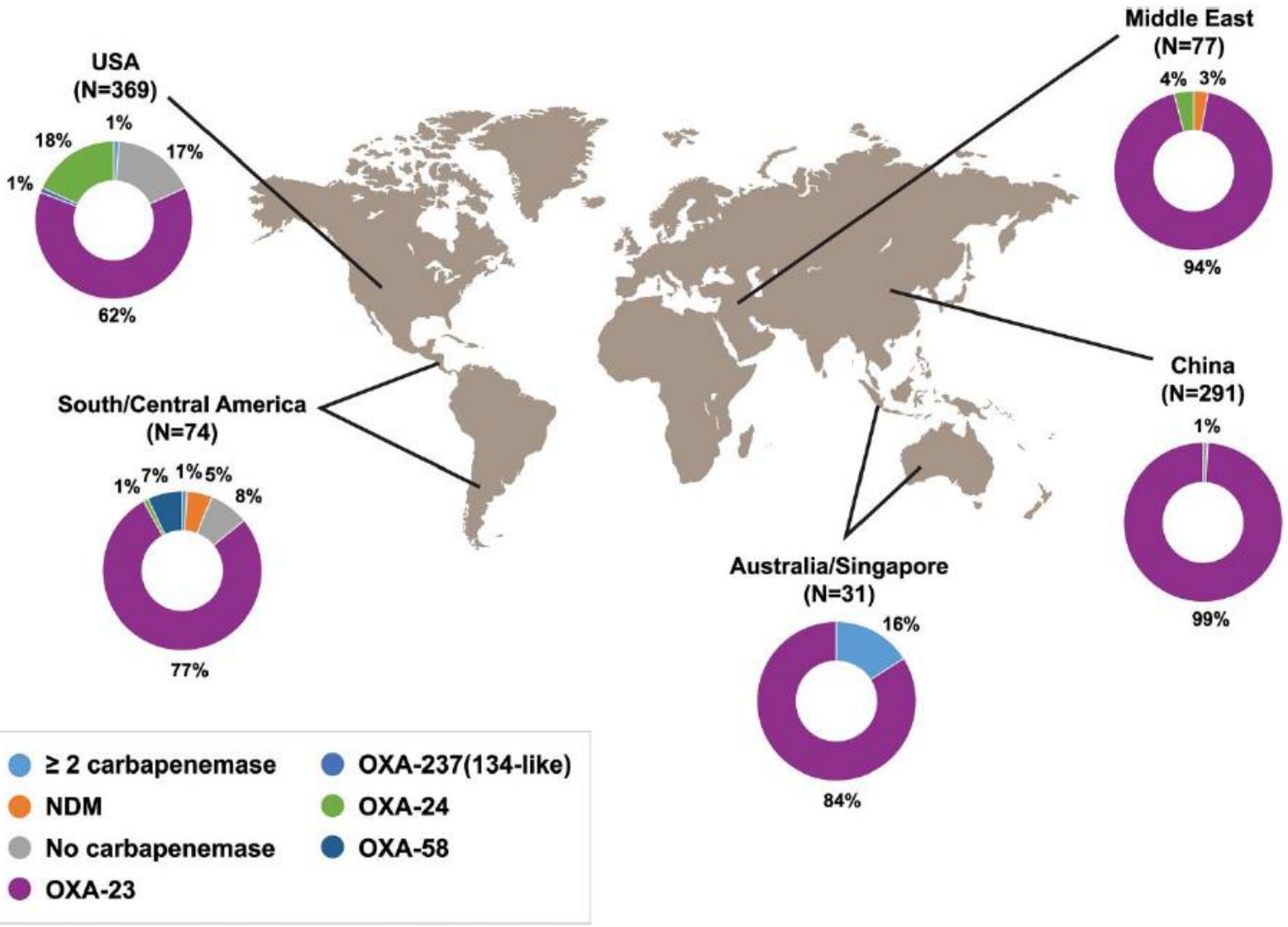


Principe L, JCM 2014
Seifert H, Antibiotics 2023

Antimicrobial Agent	$bla_{OXA\text{-}23\text{-}like}$ (n = 227)				
	MIC_{50}	MIC_{90}	MIC range	%S	%R
Cefiderocol [a,b]	0.5	4	0.06 -≥ 64	82.4	17.6
Ceftazidime [a]	≥64	≥64	2 -≥ 64	-	-
Ceftazidime/avibactam [a]	≥16/4	≥16/4	2/4 -≥ 16/4	-	-
Ceftolozane/tazobactam [a]	≥16/4	≥16/4	1/4 -≥ 16/4	-	-
Ciprofloxacin	≥8	≥8	0.12 -≥ 8	0.4 [c]	99.6
Colistin	1	2	0.5 -≥ 8	96.0	4.0
Imipenem/relebactam	≥16/4	≥16/4	8/4 -≥ 16/4	0.0	100.0
Meropenem	≥32	≥32	8 -≥ 32	0.0	99.6
Meropenem/vaborbactam [a]	≥16/8	≥16/8	8/8 -≥ 16/8	-	-
Minocycline [a]	8	≥16	0.25 -≥ 16	-	-
Piperacillin/tazobactam [a]	≥128/4	≥128/4	≥128/4 -≥ 128/4	-	-

Cefiderocol MIC	No. of Isolates with Respective MIC	Carbapenem Resistance Mechanism	No. of Isolates with Respective Mechanism
4 mg/L	32	upregulated $bla_{OXA\text{-}51}$	2
		$bla_{OXA\text{-}23}$	16
		$bla_{OXA\text{-}23}$ + upregulated $bla_{OXA\text{-}51}$	7
		$bla_{OXA\text{-}23+GES\text{-}11}$	1
		$bla_{OXA\text{-}23+GES\text{-}12}$	1
		$bla_{OXA\text{-}40\text{-}like}$	3
		$bla_{NDM\text{-}1}$	1
		$bla_{OXA\text{-}23+NDM\text{-}1}$	1
8 mg/L	9	$bla_{OXA\text{-}23}$	7
		$bla_{NDM\text{-}1}$	1
		$bla_{IMP\text{-}26}$	1
16 mg/L	1	$bla_{OXA\text{-}23}$	1
32 mg/L	5	$bla_{OXA\text{-}23}$	1
		$bla_{OXA\text{-}40\text{-}like+GES\text{-}11}$	1
		upregulated $bla_{OXA\text{-}51}$	1
		$bla_{OXA\text{-}23+NDM\text{-}1+PER\text{-}7}$	1
		$bla_{NDM\text{-}1}$	1
>32 mg/L	10	$bla_{OXA\text{-}23}$	8
		$bla_{OXA\text{-}40\text{-}like}$	1
		$bla_{OXA\text{-}23+NDM\text{-}1}$	1

OXA-23



Wang M, CID 2023

Efficacia di cefiderocol

Riferimento	Tipo di infezione	Comparatore	Mortalità cefiderocol	Mortalità colistina	p
Pascale R, JAC Antimicrob Res, 2021	**Tutti**	**Colistina**	**55%**	**58%**	**p=0.7**
Falcone M, Antimicrob Agents Chemother 2022	**Tutti**	**Colistina**	**34%**	**55.8%**	**p=0.018**
Bavaro D, Infect Dis Ther 2023	**BSI**	**Colistina**	**40%**	**59%**	**p= 0.04**
Russo A, Int J Antimicrob Agents 2023	**VAP batteriemica**	**Colistina**	**31.5%**	**98.1%**	**p<0.001**
Mazzitelli M, Microorganisms 2023	**Tutti**	**Colistina**	**43.3%**	**41.2%**	**p=0.130**
Rando E, JAC Antimicrob Resist. 2023	**VAP**	**+++ colistina**	**44%**	**67%**	**p= 0.011**

Mortalità BSI vs HAP/VAP

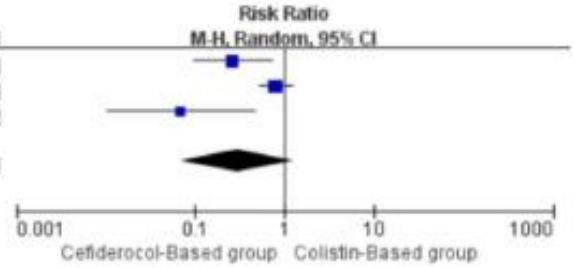
Riferimento	Mortalità complessiva	Mortalità BSI	Mortalità HAP/VAP
Bavaro DF, Antibiotics 2021	3/9 (33.3%)	2/6 (33.3%)	1/2 (50%)
Pascale R, JAC Antimicrob Resist 2021	23/42 (54.8%)	15/27 (55.6%)	8/14 (57.1%)
Falcone M, Antimicrob Agents Chemother 2022	16/47 (34%)	**7/27 (25.9%)**	7/12 58.3%)
Calò F, J Infect Public Health 2023	19/38 (50%)	**7/16 (43.8%)**	10/16 (62,5%)
Giannella M, Open Forum Infect Dis 2023	69/147 (46.9%)	**15/39 (38,5%)**	52/96 (54.2%)
Piccica M, J Antimicrob Chemother 2023	52/142 (36.6%)	**5/19 (26%)**	35/81 (43%)

Metanalisi cefiderocol vs *colistin based regimens*

a

Study or Subgroup	Cefiderocol-Based group Events	Total	Colistin-Based group Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Dalfino 2023	4	40	19	50	35.1%	0.26 [0.10, 0.71]
Pascale 2021	17	42	33	65	40.5%	0.80 [0.51, 1.24]
Russo 2023	1	19	41	54	24.3%	0.07 [0.01, 0.47]
Total (95% CI)		**101**		**169**	**100.0%**	**0.30 [0.07, 1.27]**
Total events	22		93			

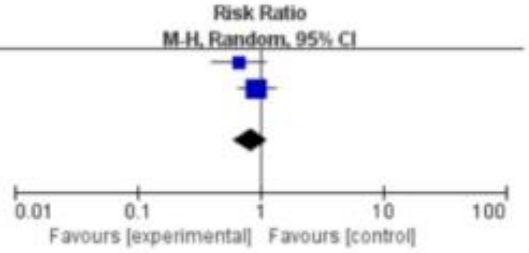
Heterogeneity: Tau² = 1.30; Chi² = 12.73, df = 2 (P = 0.002); I² = 84%
Test for overall effect: Z = 1.63 (P = 0.10)



b

Study or Subgroup	Cefiderocol-Based group Events	Total	Colistin-Based group Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Dalfino 2023	14	40	26	50	34.7%	0.67 [0.41, 1.11]
Pascale 2021	23	42	38	65	65.3%	0.94 [0.66, 1.32]
Total (95% CI)		**82**		**115**	**100.0%**	**0.84 [0.61, 1.14]**
Total events	37		64			

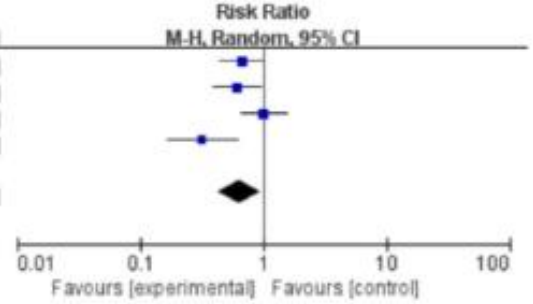
Heterogeneity: Tau² = 0.01; Chi² = 1.17, df = 1 (P = 0.28); I² = 15%
Test for overall effect: Z = 1.13 (P = 0.26)



c

Study or Subgroup	Cefiderocol-Based group Events	Total	Colistin-Based group Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Bavaro 2023	17	43	44	75	27.6%	0.67 [0.44, 1.02]
Falcone 2022	16	47	43	77	26.4%	0.61 [0.39, 0.95]
Mazzitelli 2023	26	60	22	51	27.1%	1.00 [0.65, 1.54]
Russo 2023	6	19	53	54	18.9%	0.32 [0.17, 0.62]
Total (95% CI)		**169**		**257**	**100.0%**	**0.64 [0.43, 0.95]**
Total events	65		162			

Heterogeneity: Tau² = 0.11; Chi² = 8.51, df = 3 (P = 0.04); I² = 65%
Test for overall effect: Z = 2.22 (P = 0.03)



Zhan Y, BMC Infectious Diseases

Eravaciclina

- Tetraciclina alogenata sintetica
- Attiva su MRSA, VRE, Enterobacterales produttori di ESBL, carbapenemasi, *Acinetobacter baumannii* MDR, *S. maltophilia*
- Alto volume di distribuzione
- Non attiva su *P. aeruginosa*
- Opzione alternativa per il trattamento di CRE secondo le linee guida IDSA 2024 se betalattamici inefficaci o non tollerati
- Approvata per cIAI

Efficacia di eravaciclina

- 24 pazienti con COVID19 e VAP da CRAB
- 17 successo clinico, 6 deceduti (25%), 1 fallimento clinico

Jackson MNW, Pharmacother 2023

- 27 pazienti trattati con eravaciclina vs BAT
- Maggior mortalità (33% vs 15%)
- Minor eradicazione microbiologica (17% vs 59%)
- Maggior durata della VM (10.5 vs 6.5 g

Scott CJ, Ann Pharmacother 2022

- "Despite its promising intrinsic activity, in the absence of supportive clinical data it is unlikely that eravacycline will become a key component of the treatment strategies against carbaper
resistant *A. baumannii* infections."

Iovleva A, Drugs 2025

Pseudomonas aeruginosa DTR: cosa dicono le linee guida

ESCMID guidelines Paul M. CMI 2022	• In patients with severe infections due to DTR-CRPA, we suggest therapy with ceftolozane-tazobactam if active *in vitro*. • Insufficient evidence is available for imipenem-relebactam, cefiderocol and ceftazidime-avibactam at this time. • In patients with non-severe or low-risk CRPA infections, under the consideration of antibiotic stewardship, we consider it good clinical practice to use the old antibiotics, chosen from among the *in vitro* active antibiotics on an individual basis and according to the source of infection.
SIMIT, SITA, GISA, AMCLI, SIM Tiseo G, Int J Antimicrob Agents 2022	• In patients with invasive infections ceftolozane/tazobactam and ceftazidime/avibactam are currently the first-line options for targeted treatment. • Imipenem/cilastatin-relebactam and cefiderocol might be potential alternatives, as well as colistin-based therapy.
IDSA Tamma PD, Clin Infect Dis 2024	• For infections isolates not susceptible to any carbapenem agent but susceptible to traditional β-lactams, the administration of a traditional agent as high-dose extended-infusion therapy is suggested. • For critically ill patients or those with poor source control with *P. aeruginosa* isolates resistant to carbapenems but susceptible to traditional β-lactams, use of newer β-

Ceftolozano/tazobactam

Resistance Mechanisms	Outer Membrane Porin Loss	β-lactamase Enzyme	Efflux Pump	Efflux Pump
	OprD	AmpC	MexXY	MexAB
Ceftolozane	●	●	●	●
Ceftazidime	●	○	●	○
Cefepime	●	◐	○	○
Piperacillin/ tazobactam	●	○	●	○
Imipenem	○	●	●	●
Meropenem	◐	●	○	◐

● Not affected ◐ Partially affected ○ Affected

Castanheira M, AAC 2014

Meccanismi di resistenza di *P. aeruginosa*

- Intrinsic resistome
  - AmpC
  - Mex AB e Mex XY
  - Low outer membrane permeability
- Mutational resistome
  - 36 geni coinvolti
  - Modifica del target
  - Iperproduzione pompe di efflusso
  - Iperproduzione β-lattamasi
  - Perdita di porine specifiche
- Horizontally acquired resistome
  - β-lattamasi di classe A e classe D

Horcajada JP, Clin Microbiol 2019

Gene(s)	Resistance mechanism	Antibiotics affected
gyrA	Quinolone target modification (DNA gyrase)	Fluoroquinolones
gyrB	Quinolone target modification (DNA gyrase)	Fluoroquinolones
parC	Quinolone target modification (DNA topoisomerase IV)	Fluoroquinolones
parE	Quinolone target modification (DNA topoisomerase IV)	Fluoroquinolones
pmrA, pmrB, phoQ, cprS, colR, colS	Lipopolysaccharide modification (addition of the 4-amino-4-deoxy-L-arabinose moiety to the lipid A portion)	Polymyxins
parR	Lipopolysaccharide modification (addition of the 4-amino-4-deoxy-L-arabinose moiety to the lipid A portion)	Polymyxins
	OprD downregulation	Imipenem, meropenem
	MexEF-OprN hyperproduction	Fluoroquinolones
	MexXY hyperproduction	Fluoroquinolones, aminoglycosides, cefepime
parS	Lipopolysaccharide modification (addition of the 4-amino-4-deoxy-L-arabinose moiety to the lipid A portion)	Polymyxins
	OprD downregulation	Imipenem, meropenem
	MexEF-OprN hyperproduction	Fluoroquinolones
	MexXY hyperproduction	Fluoroquinolones, aminoglycosides, cefepime
mexR, nalC, nalD	MexAB-OprM hyperproduction	Fluoroquinolones, ceftazidime, cefepime, piperacillin-tazobactam, meropenem, ceftazidime-avibactam
nfxB	MexCD-OprJ hyperproduction	Fluoroquinolones, cefepime
mexS	MexEF-OprN hyperproduction	Fluoroquinolones
	OprD downregulation	Imipenem, meropenem
mexT	MexEF-OprN hyperproduction	Fluoroquinolones
	OprD downregulation	Imipenem, meropenem
cmrA, mvaT, PA3271	MexEF-OprN hyperproduction	Fluoroquinolones
mexZ, PA5471.1, amgS	MexXY hyperproduction	Fluoroquinolones, aminoglycosides, cefepime
oprD	OprD porin inactivation	Imipenem, meropenem
ampC	AmpC structural modification	Ceftolozane-tazobactam, ceftazidime-avibactam
ampD, ampDh2, ampDh3, ampR, dacB, mpl	AmpC hyperproduction	Ceftazidime, cefepime, piperacillin-tazobactam
ftsI	β-Lactam target modification (PBP3)	Ceftazidime, cefepime, piperacillin-tazobactam, ceftolozane-tazobactam, ceftazidime-avibactam, meropenem
fusA1	Aminoglycoside target modification (elongation factor G)	Aminoglycosides
glpT	Inactivation of transporter protein GlpT	Fosfomycin
rpoB	Rifampin target modification, RNA polymerase β-chain	Rifampin

Ceftolozano/tazobactam vs ceftazidime/avibactam

	Ceftolozane–tazobactam group	Ceftazidime–avibactam group	Unadjusted OR (95% CI)	Unadjusted p value	Adjusted OR* (95% CI)	Adjusted p value
All patients (n=420)						
Clinical success	128 (61%)	109 (52%)	1·50 (1·00–2·26)	0·053	2·07 (1·16–3·70)	0·013
30-day mortality	48 (23%)	50 (24%)	0·94 (0·59–1·51)	0·81	0·77 (0·41–1·53)	0·49
90-day mortality	79 (38%)	77 (37%)	1·04 (0·70–1·56)	0·84	0·95 (0·56–1·61)	0·86
Recurrence within 30 days	31 (15%)	44 (21%)	0·65 (0·39–1·09)	0·099	0·50 (0·25–0·99)	0·048
Recurrence within 90 days	53 (25%)	65 (31%)	0·73 (0·47–1·15)	0·18	0·62 (0·34–1·11)	0·11
Emergence of resistance†	38 (22%)	40 (23%)	0·96 (0·58–1·60)	0·89	0·95 (0·56–1·63)	0·86
Pneumonia subgroup (n=350)						
Clinical success	110 (63%)	89 (51%)	1·68 (1·08–2·62)	0·022	2·34 (1·23–4·47)	0·0098
30-day mortality	39 (22%)	41 (23%)	0·93 (0·56–1·56)	0·79	0·97 (0·49–1·94)	0·95
90-day mortality	59 (34%)	66 (38%)	0·84 (0·55–1·30)	0·44	0·81 (0·46–1·42)	0·45
Recurrence within 30 days	26 (15%)	40 (23%)	0·58 (0·33–1·01)	0·055	0·44 (0·20–0·97)	0·041
Recurrence within 90 days	45 (26%)	61 (35%)	0·62 (0·38–1·01)	0·055	0·48 (0·24–0·94)	0·033
Emergence of resistance†	30 (21%)	37 (26%)	0·78 (0·45–1·35)	0·38	0·75 (0·42–1·35)	0·34

OR is presented using the ceftolozane–tazobactam cohort as the reference such that an OR greater than 1 corresponds to a greater odds of the outcome for patients who received ceftolozane–tazobactam and an OR less than 1 corresponds to lower odds of the outcome for patients who received ceftolozane–tazobactam. OR=odds ratio.
*Controlled for age (≥65 years or <65 years), immunocompromising conditions, infection site, suboptimal dosing, Sequential Organ Failure Assessment score (≥8 or <8), Charlson Comorbidity Index (≥5 or <5), time to treatment initiation, concomitant infections, prolonged infusions, and receipt of renal replacement therapy using conditional logistic regression analyses. For the overall cohort, infection site was also included, but not for the pneumonia subgroup. †Based on the number of patients whose baseline isolates were confirmed to be susceptible by the local study site testing methods (n=173 for ceftolozane–tazobactam and n=177 for ceftazidime–avibactam overall; n=144 for ceftolozane–tazobactam and n=147 for ceftazidime–avibactam in the pneumonia subgroup).

Table 2: **Primary and select secondary outcomes among all patients and patients with pneumonia**

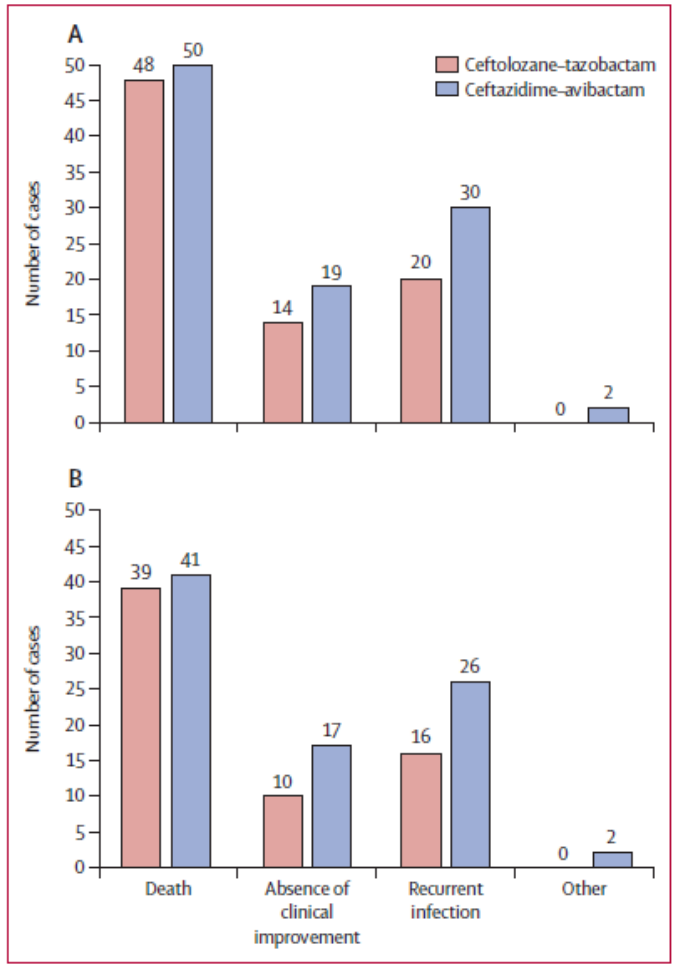
Shields RK, Lancet Infect Di

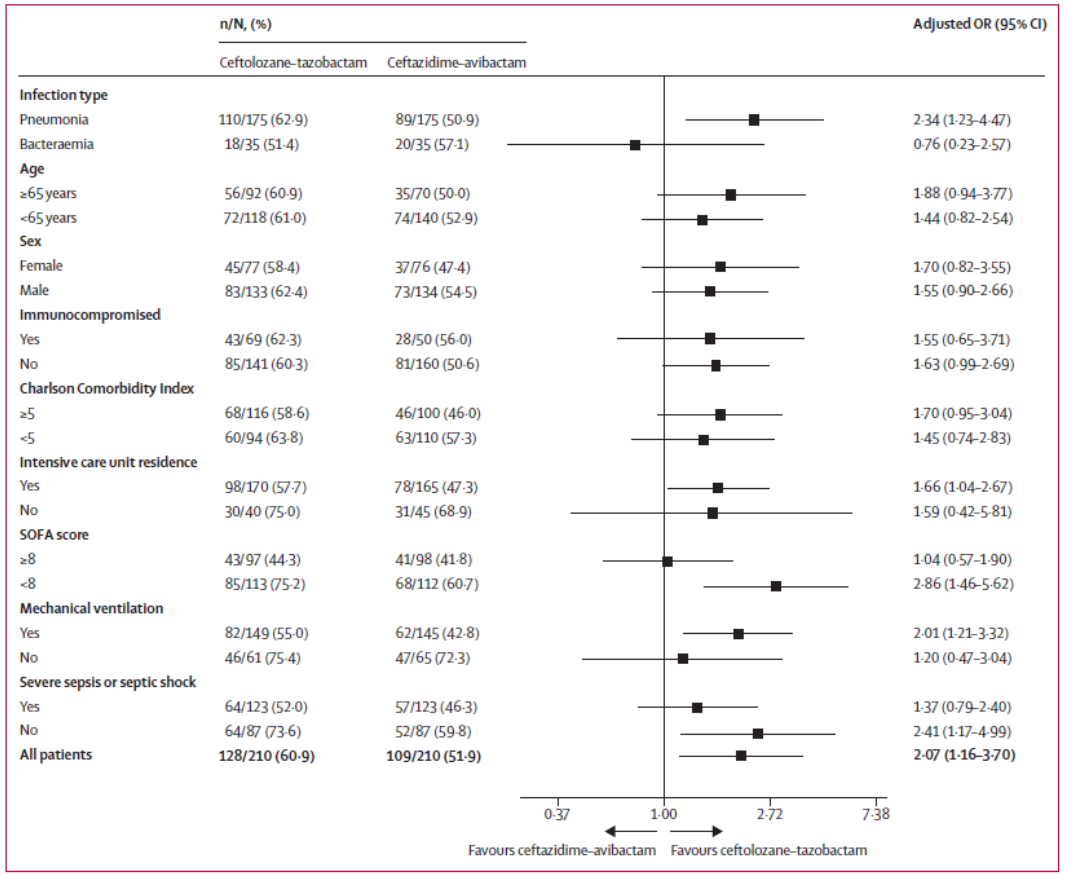
Penetrazione polmonare

Antibiotico	AUC $_{ELF/plasma}$
Ceftazidime/avibactam 2/0,5 g ogni 8 ore o 3/1 g ogni 8 ore	31-32% (ceftazidime) 32-35% (avibactam)
Ceftolozano/tazobactam	50% (ceftolozano) 62% (tazobactam)

Nicolau DP, JAC 2015
Caro L, J Antimicrob Chemother 2020

Ceftolozano/tazobactam vs ceftazidime/avibactam





	n/N, (%)		Adjusted OR (95% CI)
	Ceftolozane–tazobactam	Ceftazidime–avibactam	
Infection type			
Pneumonia	110/175 (62·9)	89/175 (50·9)	2·34 (1·23–4·47)
Bacteraemia	18/35 (51·4)	20/35 (57·1)	0·76 (0·23–2·57)
Age			
≥65 years	56/92 (60·9)	35/70 (50·0)	1·88 (0·94–3·77)
<65 years	72/118 (61·0)	74/140 (52·9)	1·44 (0·82–2·54)
Sex			
Female	45/77 (58·4)	37/76 (47·4)	1·70 (0·82–3·55)
Male	83/133 (62·4)	73/134 (54·5)	1·55 (0·90–2·66)
Immunocompromised			
Yes	43/69 (62·3)	28/50 (56·0)	1·55 (0·65–3·71)
No	85/141 (60·3)	81/160 (50·6)	1·63 (0·99–2·69)
Charlson Comorbidity Index			
≥5	68/116 (58·6)	46/100 (46·0)	1·70 (0·95–3·04)
<5	60/94 (63·8)	63/110 (57·3)	1·45 (0·74–2·83)
Intensive care unit residence			
Yes	98/170 (57·7)	78/165 (47·3)	1·66 (1·04–2·67)
No	30/40 (75·0)	31/45 (68·9)	1·59 (0·42–5·81)
SOFA score			
≥8	43/97 (44·3)	41/98 (41·8)	1·04 (0·57–1·90)
<8	85/113 (75·2)	68/112 (60·7)	2·86 (1·46–5·62)
Mechanical ventilation			
Yes	82/149 (55·0)	62/145 (42·8)	2·01 (1·21–3·32)
No	46/61 (75·4)	47/65 (72·3)	1·20 (0·47–3·04)
Severe sepsis or septic shock			
Yes	64/123 (52·0)	57/123 (46·3)	1·37 (0·79–2·40)
No	64/87 (73·6)	52/87 (59·8)	2·41 (1·17–4·99)
All patients	**128/210 (60·9)**	**109/210 (51·9)**	**2·07 (1·16–3·70)**

"Therefore, these data provide support for the preferential use of ceftolozane–tazobactam over ceftazidime–avibactam for the treatment of multidrug resistant and DTR *P aeruginosa*, particularly for patients with pneumonia and when the local epidemiology of *P. aeruginosa* or susceptibility testing results suggest that both agents are viable t

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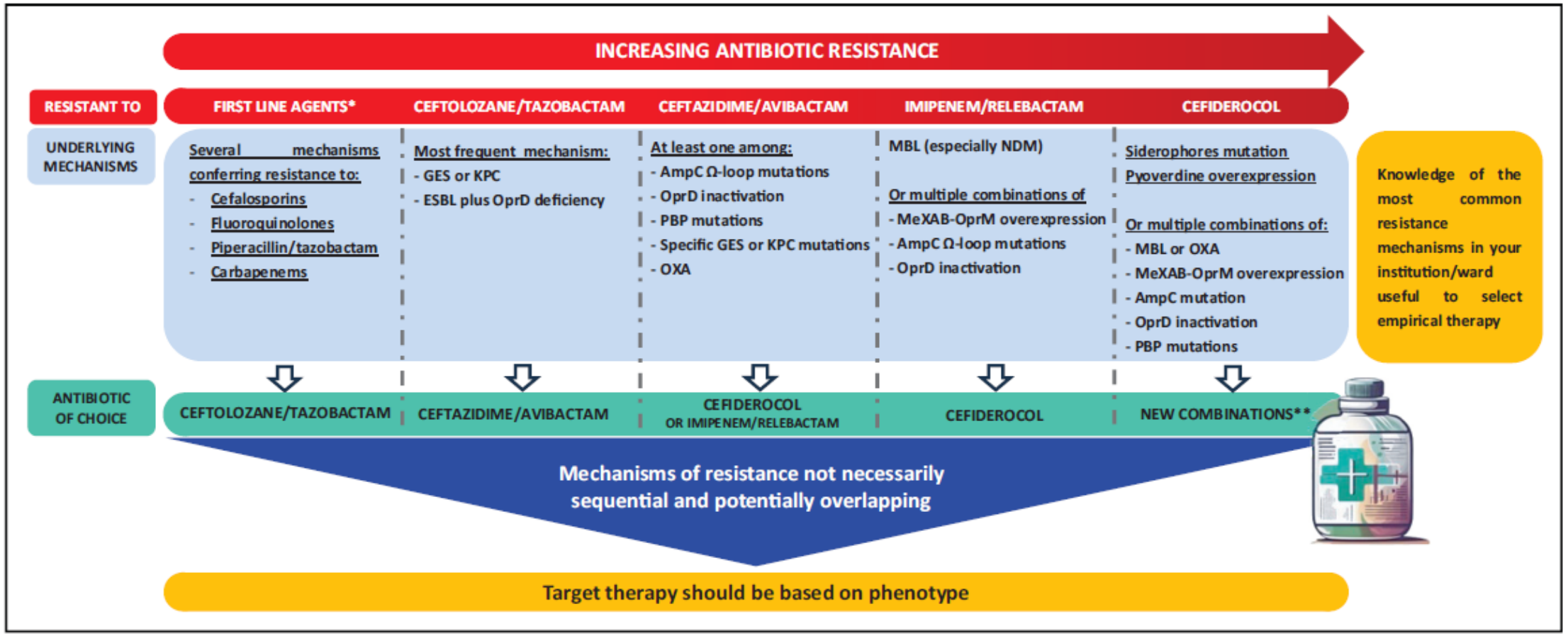
Terapia anti-*Pseudomonas* secondo il meccanismo di resistenza



*Resistenza a cefalosporine, fluorochinoloni, piperacillina/tazobactam, carbapenemi (DTR-PA)
**Cefepime/zidebactam, cefepime/taniborbactam, aztreonam/avibactam

Falcone M, Curr Opin Infect D

Conclusioni

- Infezioni gravi con alta letalità
- Importanza dell'epidemiologia locale per impatto e pattern di resistenza
- Importanza di conoscere i meccanismi di resistenza
- Importanza di diagnostica microbiologica e di avere MIC puntuali (specialmente per cefiderocol)
- Da valutare la collocazione di eravaciclina per CRAB
- In attesa di durlobactam-sulbactam per CRAB e