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Controle de Infecção e  
Epidemiologia Hospitalar  
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*Ciência para a saúde da população brasileira desde 1906*

# Disseminação de enterobactérias resistentes a carbapenêmicos e o impacto nas IRAS: existe alguma luz no fim do túnel? Impacto Nacional

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# Sumário

- ▶ Situação Atual no Brasil
- ▶ Impacto nas IRAS
- ▶ Luz no Fim do Túnel

# Situação Atual no Brasil: Problemas para Determinar

- ▶ Sistema de Informação que integre os resultados microbiológicos dos Hospitais do Sistema Único de Saúde (SUS).
- ▶ Sistematização no Controle de Qualidade dos Laboratórios de Microbiologia dos Hospitais.
- ▶ Definição dos cut offs dos testes de susceptibilidade aos antimicrobianos com base na realidade Nacional.
- ▶ Atenção as Políticas de Monitoramento Desenvolvidas.
- ▶ Retorno aos Hospitais dos Resultados dos Sistemas de Vigilância Desenvolvidos.
- ▶ Sistematização na Divulgação dos Resultados dos Sistemas de Vigilância Desenvolvidos.
- ▶ Políticas de Prevenção e Controle que envolva a participação de Toda a Sociedade.
- ▶ Políticas de Monitoramento do Consumo de Antimicrobianos no SUS.

Agência Nacional de Vigilância Sanitária (Anvisa)  
Rede Nacional de Monitoramento da Resistência Microbiana em  
Serviços de Saúde - Rede RM: Resistência Microbiana em IPCSL  
relacionada a CVC em UTI (2012)

Para classificação do micro-organismo como sensível, intermediário ou resistente a determinado antimicrobiano, aproximadamente 34,3% dos serviços de saúde utilizaram os critérios estabelecidos pelo “Clinical Laboratory Standards Institute” (CLSI), enquanto que 8,1% e 0,2% dos serviços de saúde seguiram aqueles recomendados pela Nota Técnica da Anvisa 01/2010 e pelo “European Committee on Antimicrobial Susceptibility Testing” (EUCAST), respectivamente. Lamentavelmente, 2,2% das unidades de saúde afirmaram utilizar outra metodologia para análise dos seus resultados, enquanto 55,2% das unidades de saúde não informaram quais as recomendações técnicas eram seguidas pelos seus respectivos laboratórios de microbiologia, pois os formulários utilizados pelo estado de São Paulo, que concentra a maior parte das notificações, não questionavam à época, a informação da metodologia utilizada. O mesmo pode ser observado nos dados referentes às UTIs pediátrica e neonatal.



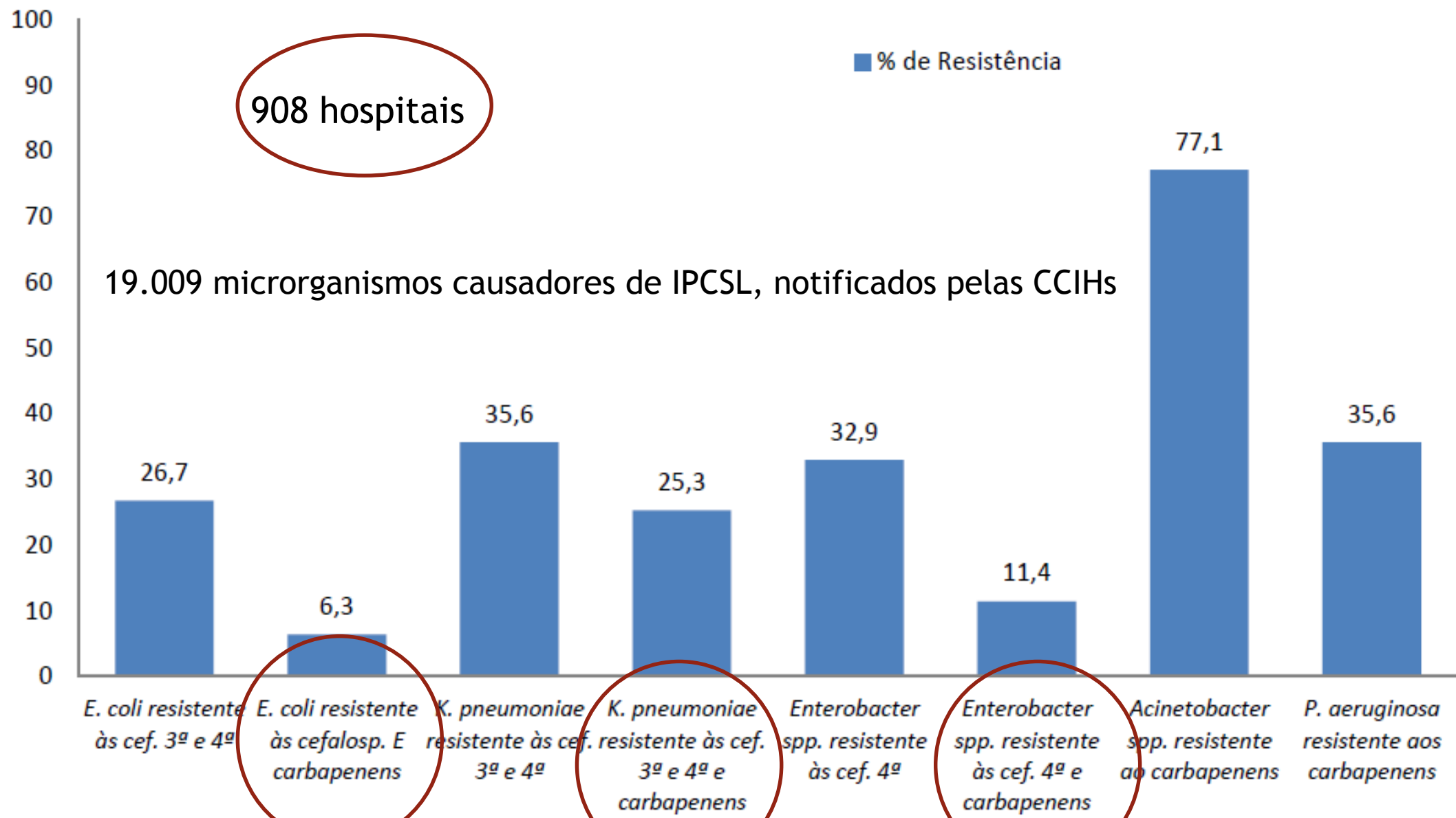
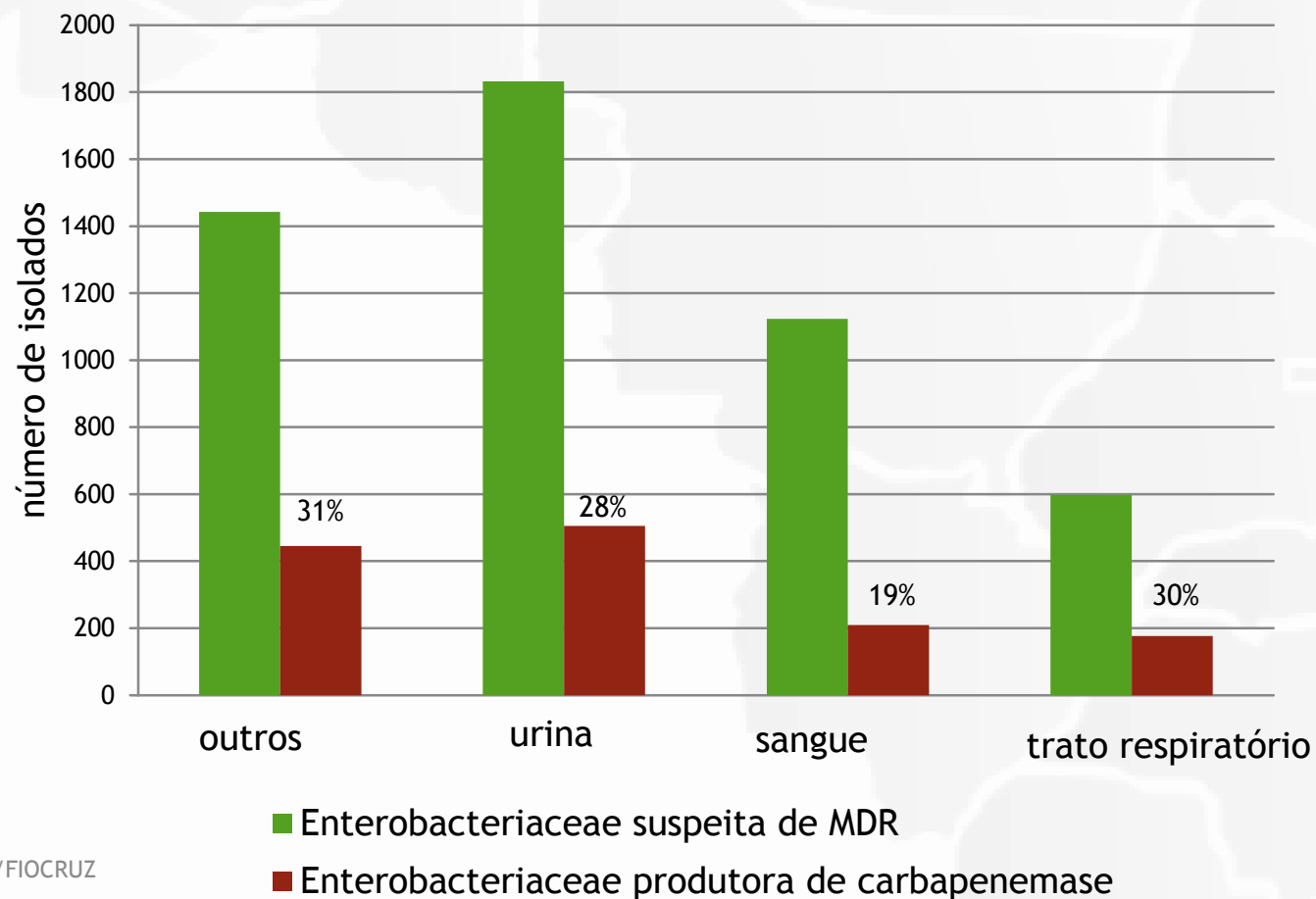


Figura 5. Porcentagens dos fenótipos de resistência entre os bacilos Gram-negativos mais frequentemente notificados como agentes etiológicos de IPCSL em pacientes adultos hospitalizados em UTIs (Brasil, 2012).

Tabela 4. Porcentagens de resistência e sensibilidade entre os micro-organismos mais frequentemente notificados como agentes etiológicos de IPCSL em pacientes adultos hospitalizados em UTIs de acordo com a região geográfica (Brasil, 2012).

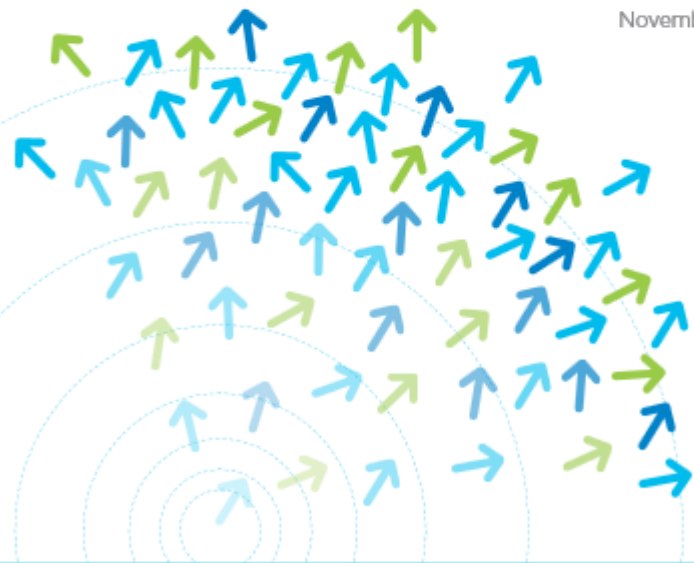
Microorganismos <sup>a</sup>	Norte	Nordeste	Centro-Oeste	Sul	Sudeste	N Total (%)
<i>Escherichia coli</i>						1126
Sensível às cefalosporinas de amplo espectro e carbapenens	100 (57,1)	103 (68,2)	59 (58,4)	169 (74,4)	323 (68,4)	754 (66,9)
Resistente às cefalosporinas de amplo espectro, mas sensível aos carbapenens	66 (37,7)	44 (29,1)	28 (27,7)	56 (24,7)	107 (22,7)	301 (26,7)
Resistente às cefalosporinas de amplo espectro e carbapenens	9 (5,1)	4 (2,6)	14 (13,9)	2 (0,9)	42 (8,9)	71 (6,3)
<i>Klebsiella pneumoniae</i>						2363
Sensível às cefalosporinas de amplo espectro e carbapenens	71 (43,0)	134 (37,6)	77 (32,5)	113 (45,7)	528 (38,9)	923 (39,1)
Resistente às cefalosporinas de amplo espectro, mas sensível aos carbapenens	87 (52,7)	130 (36,5)	61 (25,7)	94 (38,1)	469 (34,5)	841 (35,6)
Resistente às cefalosporinas de amplo espectro e carbapenens	7 (4,2)	92 (25,8)	99 (41,8)	40 (16,2)	361 (26,6)	599 (25,3)

# Frequência de Enterobacteriaceae produtoras de carbapenemases KPC-2, NDM-1 e OXA-48-like por material clínico, Serviços de Saúde Brasileiros, LAPIH, 2007 - jun 2014 (n=4996)



Recommendations  
for the control of  
Multi-drug resistant  
Gram-negatives:  
**carbapenem resistant  
Enterobacteriaceae**

November 2013



AUSTRALIAN COMMISSION  
ON SAFETY AND QUALITY IN HEALTH CARE

- Both CLSI and EUCAST now have lower clinical breakpoints for the carbapenems, but none were specifically set to ensure high sensitivity to the presence of carbapenemases.

Laboratories using semi-automated methods for susceptibility testing should also undertake or seek molecular confirmation of all Enterobacteriaceae with a meropenem minimum inhibitory concentration (MIC) of  $> 0.25$  mg/L, especially from high-risk patients or units.

All suspected CRE isolates should be subjected to molecular screening for at least the known suite of carbapenemase gene families that have so far been seen in Enterobacteriaceae in Australia: IMP, VIM, OXA-48 and OXA-48-like, KPC and NDM.



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

Version 1.0  
December 2013

### 2.4.1 Screening for carbapenemase-production

Carbapenem MICs for carbapenemase-producing Enterobacteriaceae may be below the clinical breakpoints (10, 11, 13). However, the ECOFF values as defined by

Table 1. Clinical breakpoints and screening cut-off values for carbapenemase-producing Enterobacteriaceae (according to EUCAST methodology).

Carbapenem	MIC (mg/L)		Disk diffusion zone diameter (mm) with 10 µg disks	
	S/I breakpoint	Screening cut-off	S/I breakpoint	Screening cut-off
Meropenem <sup>1</sup>	≤2	>0.12	≥22	<25 <sup>2</sup>
Imipenem <sup>3</sup>	≤2	>1	≥22	<23
Ertapenem <sup>4</sup>	≤0.5	>0.12	≥25	<25

<sup>1</sup>Best balance of sensitivity and specificity

<sup>2</sup>In some cases zone diameters for OXA-48-producers are up to 26 mm, so <27 mm may be used as a screening cut-off in countries where OXA-48 is endemic, but at the expense of lower specificity.

<sup>3</sup>With imipenem, the separation between the wild-type and carbapenemase-producers is relatively poor. Imipenem is therefore not recommended for use as a stand-alone screening test compound.

<sup>4</sup>High sensitivity but low specificity, and therefore not recommended for routine use.



## C2. Triagem de enterobactérias produtoras de carbapenemases

Ao realizar TSA de enterobactérias isoladas de pacientes hospitalizados, o laboratório deverá testar simultaneamente ertapenem, imipenem e meropenem. Caso seja utilizado

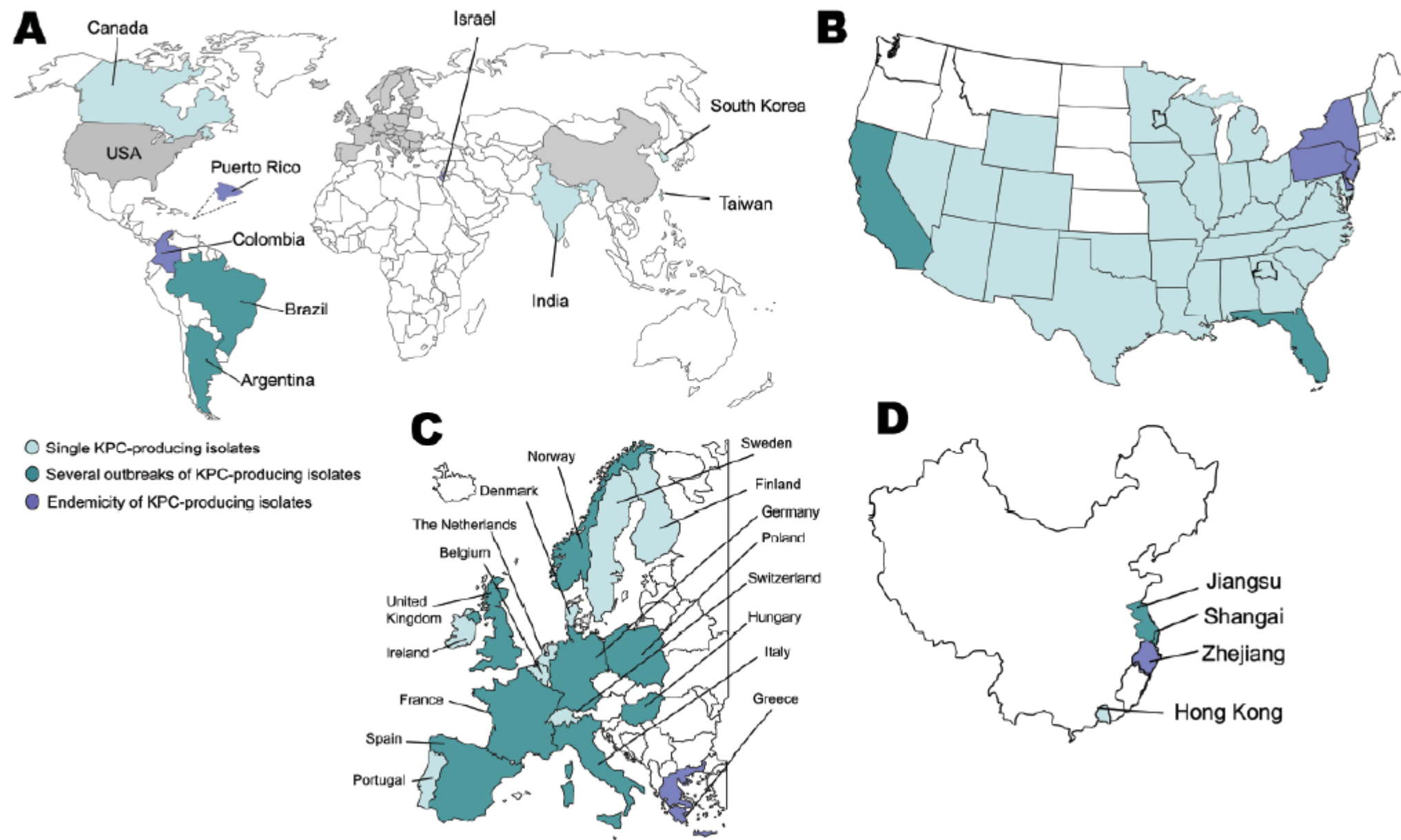
NOTA TÉCNICA Nº 01/2013

MEDIDAS DE PREVENÇÃO E CONTROLE DE  
INFECÇÕES POR ENTEROBACTÉRIAS  
MULTIRESISTENTES.

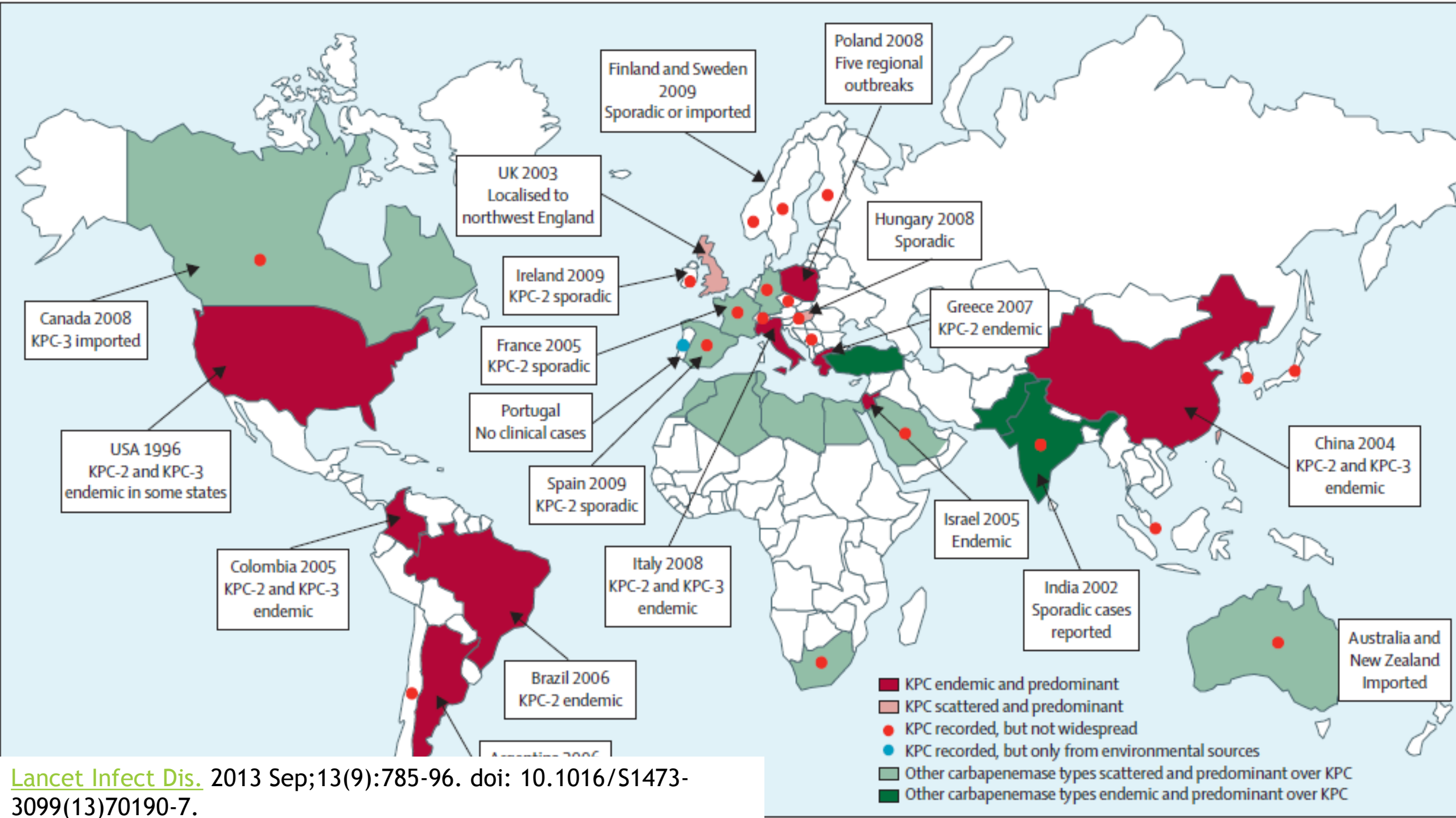
Isolados com diâmetro de halo de inibição  $\leq 22$  mm ou com CIM  $\geq 2$   $\mu\text{g/mL}$  para imipenem e/ou meropenem, e isolados com diâmetro do halo de inibição  $\leq 24$  mm, ou CIM  $\geq 1$   $\mu\text{g/mL}$  para ertapenem deverão ser testados, de modo suplementar, com discos de meropenem e imipenem com e sem adição de EDTA, cloxacilina (CLOXA) e ácido fenilborônico (AFB).

## C3. Utilização do teste de Hodge modificado, potenciadores e inibidores para detecção de carbapenemases

O teste de Hodge modificado, amplamente utilizado em laboratórios de diagnóstico microbiológico em todo o Brasil, apresenta baixa sensibilidade para detecção de NDM ( $\leq 50\%$ ); portanto, até que mais evidências científicas sejam acumuladas este teste não deve ser utilizado para detecção de carbapenemases, em particular NDM<sup>28, 29</sup>.



[Emerg Infect Dis.](#) 2011 Oct;17(10):1791-8. doi: 10.3201/eid1710.110655.  
**Global spread of Carbapenemase-producing Enterobacteriaceae.**  
[Nordmann P<sup>1</sup>](#), [Naas T](#), [Poirel L](#).







2014



**Table A2.20 *Klebsiella pneumoniae*: Resistance to carbapenems<sup>a</sup>**  
**Region of the Americas**

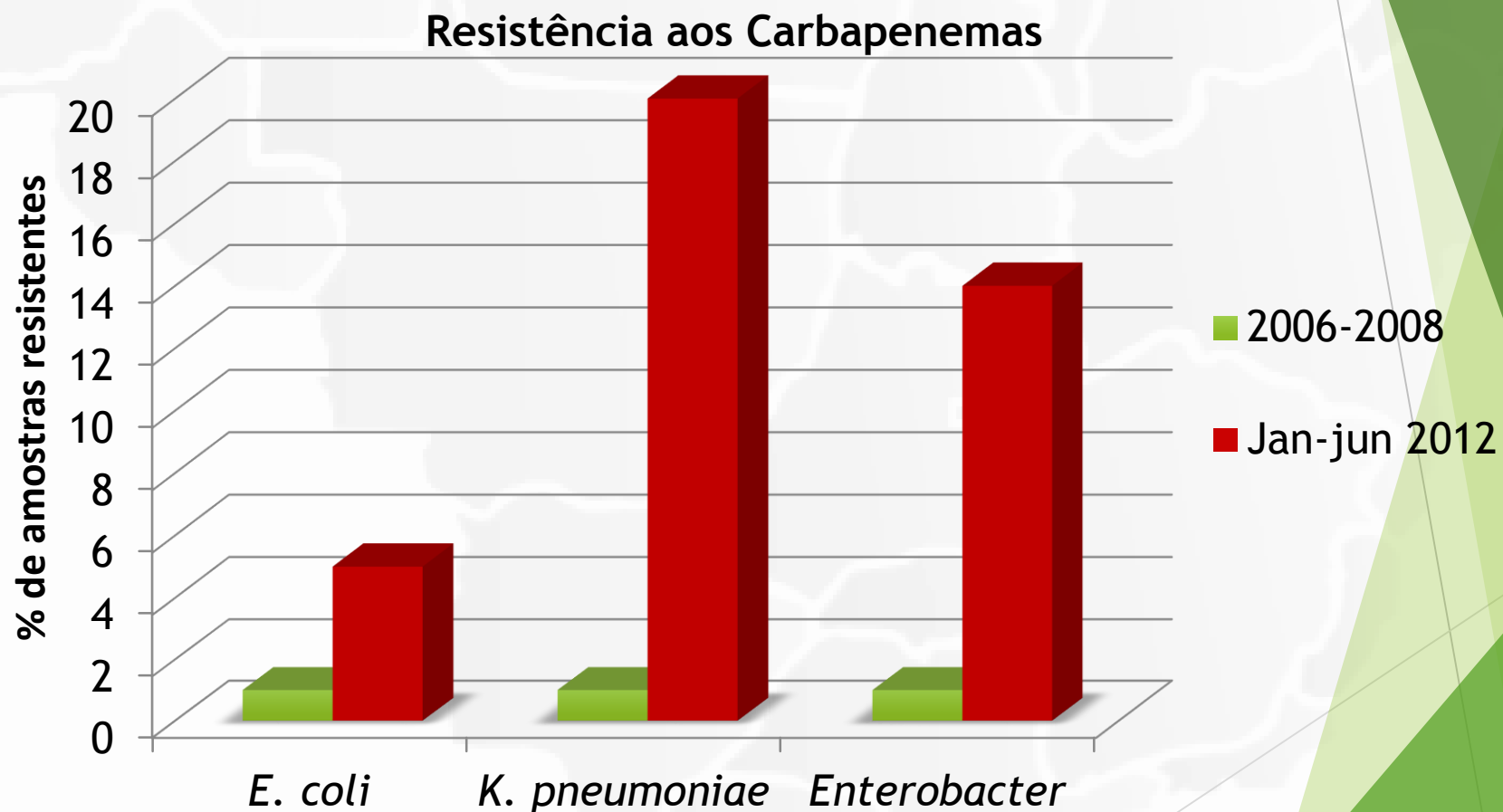
Countries, territories and other areas or groupings	Data source <sup>b, c, d</sup>	Resistance (%)	No. tested isolates	Type of surveillance, population or samples <sup>c</sup>	Period for data collection	Year of publication or report
Antigua and Barbuda	No information obtained for this report					
Argentina	National data	6 (imi); 8 (mem)	1622	Hospital isolates	2010	2013
Bahamas	No information obtained for this report					
Barbados	No information obtained for this report					
Belize	No information obtained for this report					
Bolivia (Plurinational State of)	National data	4 (imi); 5 (mem)	1176	Hospital isolates	2010	2013
Brazil	National data not available					2013
Brazil	Publication (143)	0 (imi); 1.6 (etp)	63	Clinical isolates	2009	2011
Canada	National data	0	226	Sentinel hospitals	2011	2013
Chile	National data not available					2013
Colombia	National data	6 (imi); 7 (mem)	4561	Hospital isolates	2010	2013
Costa Rica	National data not available					2013
Cuba	National data	5 (imi); 6 (mem)	39	Hospital isolates	2009	2013
Dominica	No information obtained for this report					
Dominican Republic	National data	0	2021	Hospital isolates	2009	2013
Ecuador	National data	2	933	Hospital isolates	2010	2013
El Salvador	National data	2	490	Hospital isolates	2010	2013



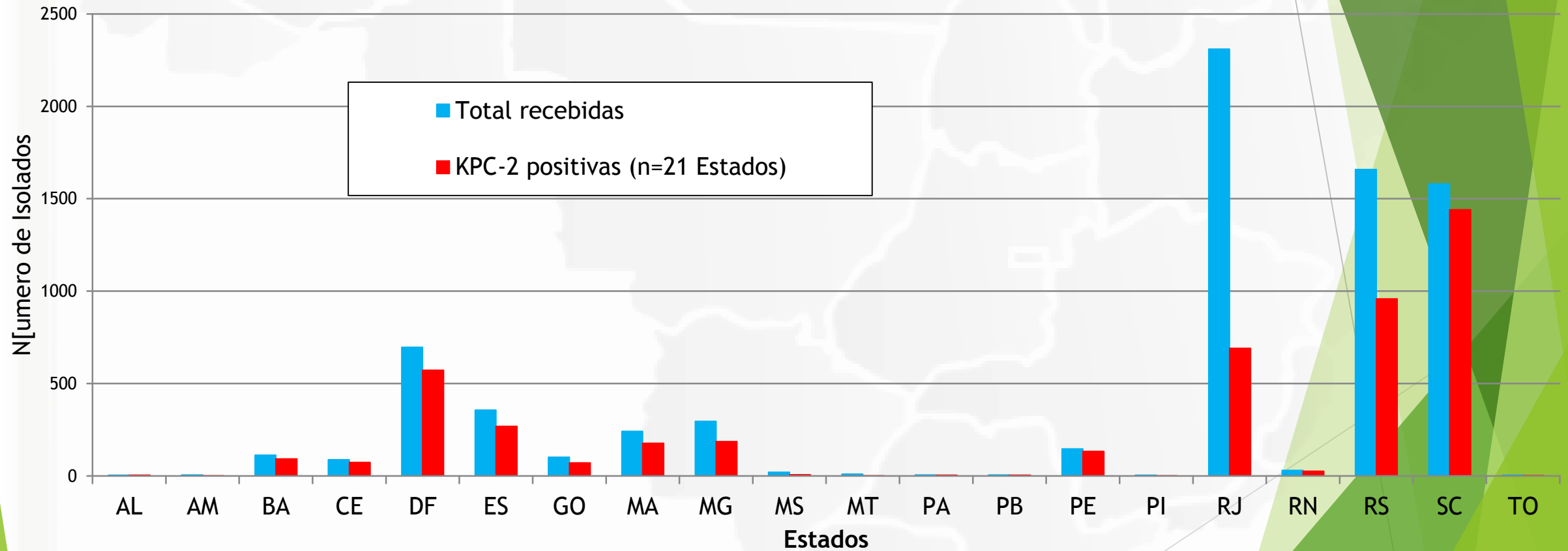


# Dados da Rede de Monitoramento da ANVISA

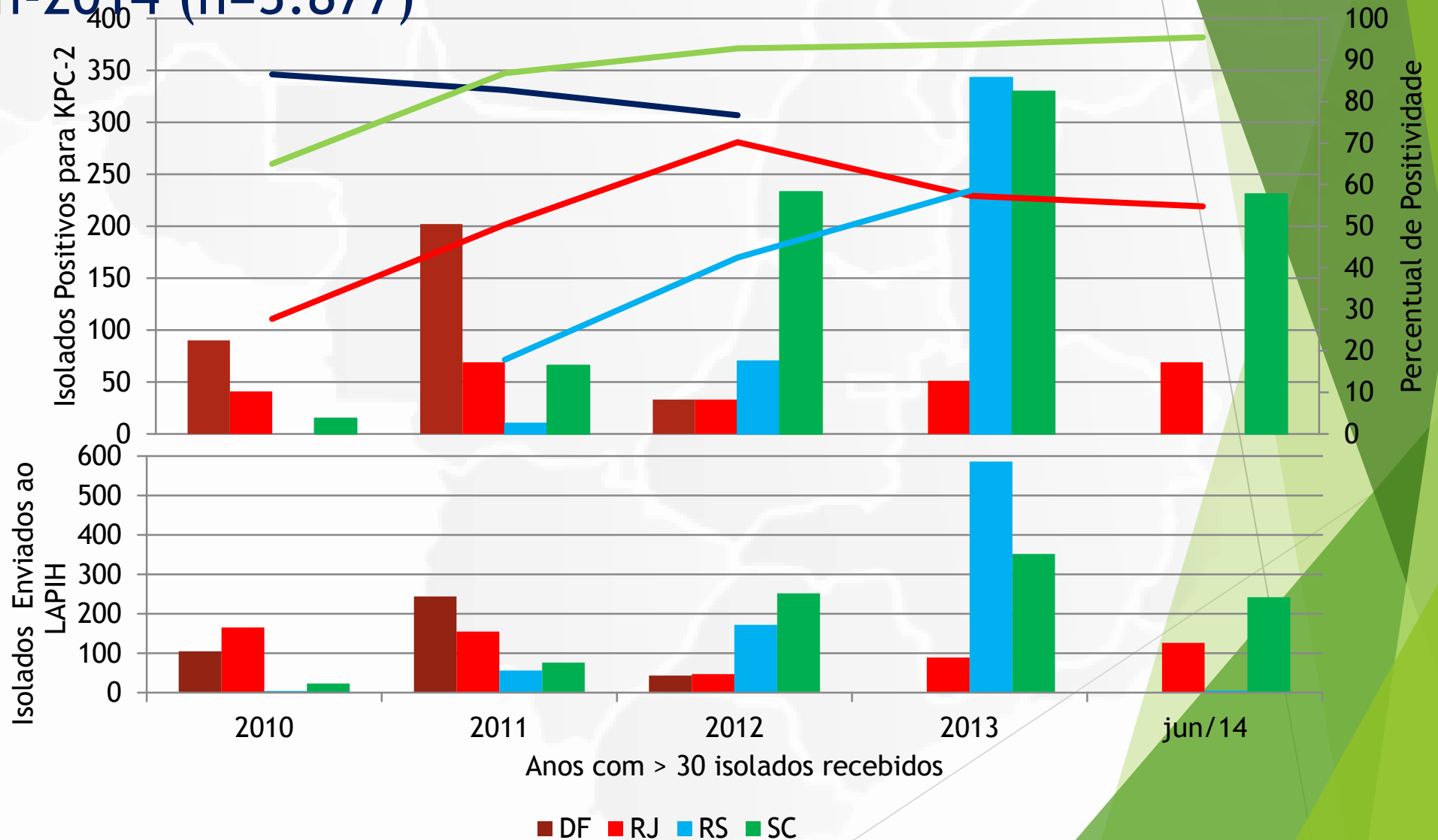
## 2006 a 2012



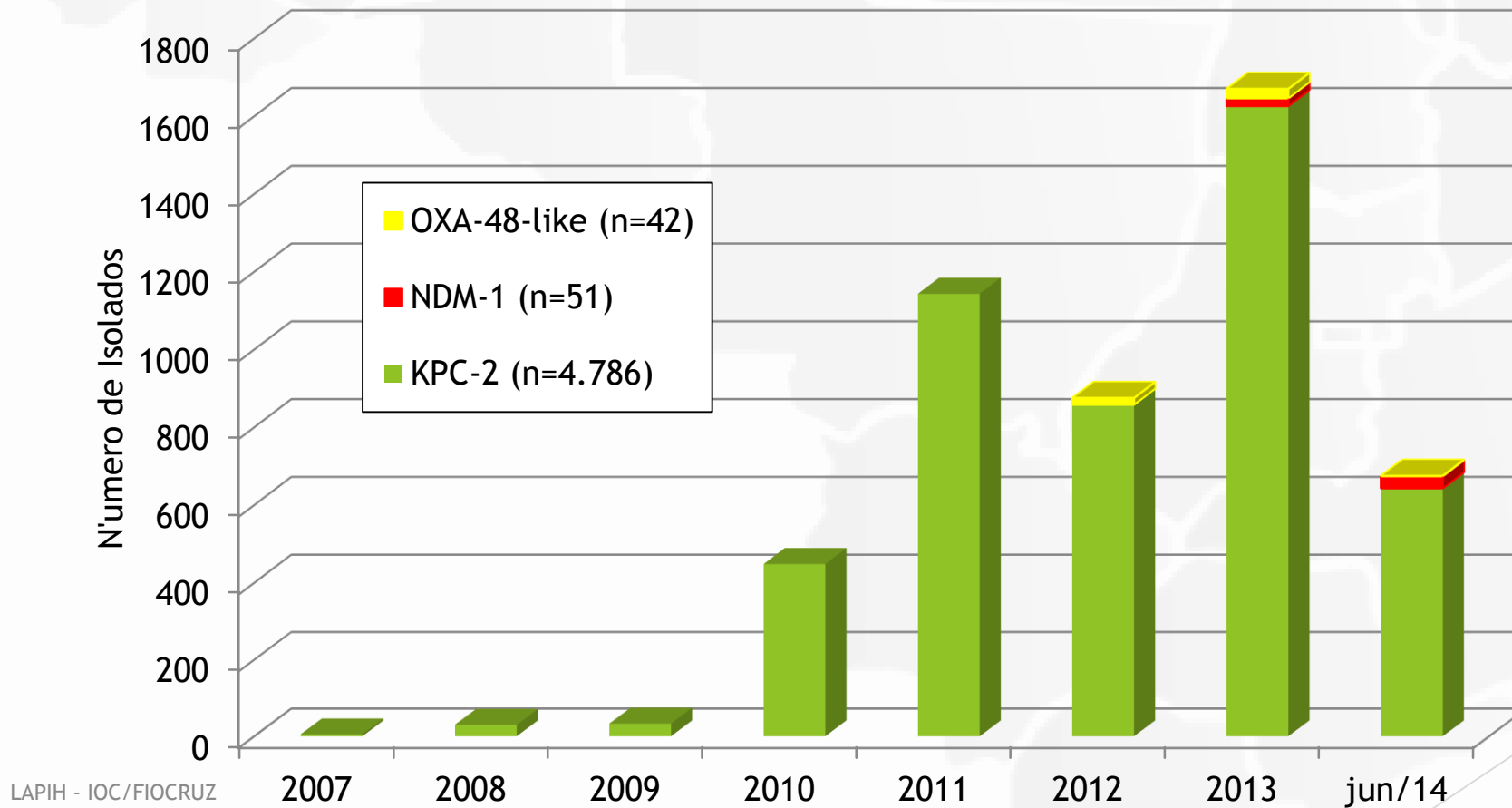
# Enterobactérias dos Serviços de Saúde Brasileiros Investigadas pelo LAPIH quanto à Produção de Carbapenemase KPC-2, Material Clínico e de Vigilância, LAPIH, 2007 a jun-2014 (n=7.677)



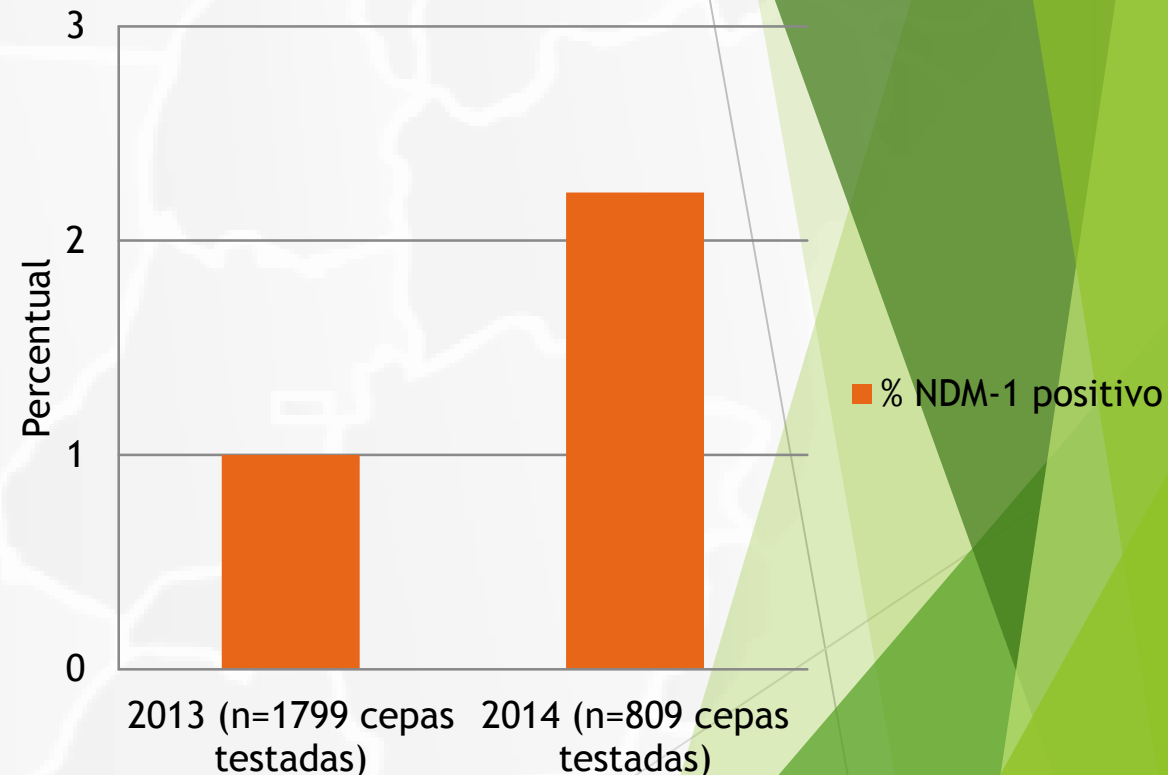
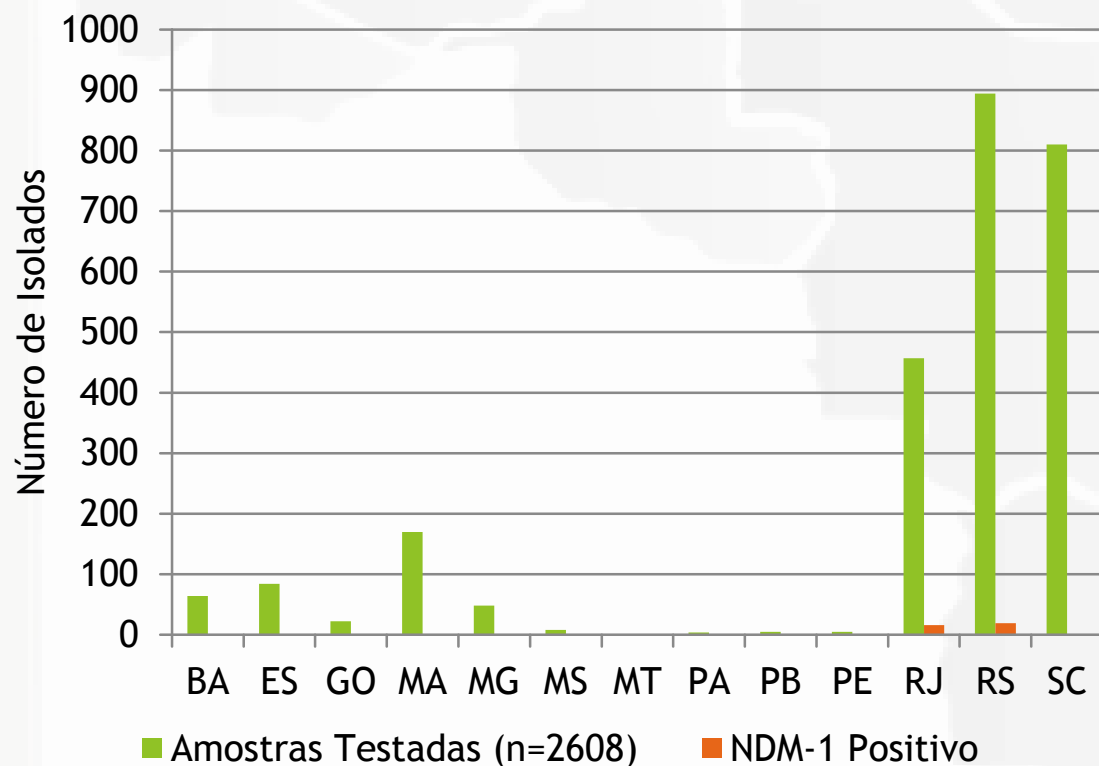
# Evolução da KPC-2 Enterobacteriaceae em Estados Brasileiros, Materias Clínicos enviados ao LAPIH, 2010 a Jun-2014 (n=3.877)



# Enterobacteriaceae produtoras de carbapenemases KPC-2, OXA-48-like, NDM-1, Serviços de Saúde do Brasil, LAPIH

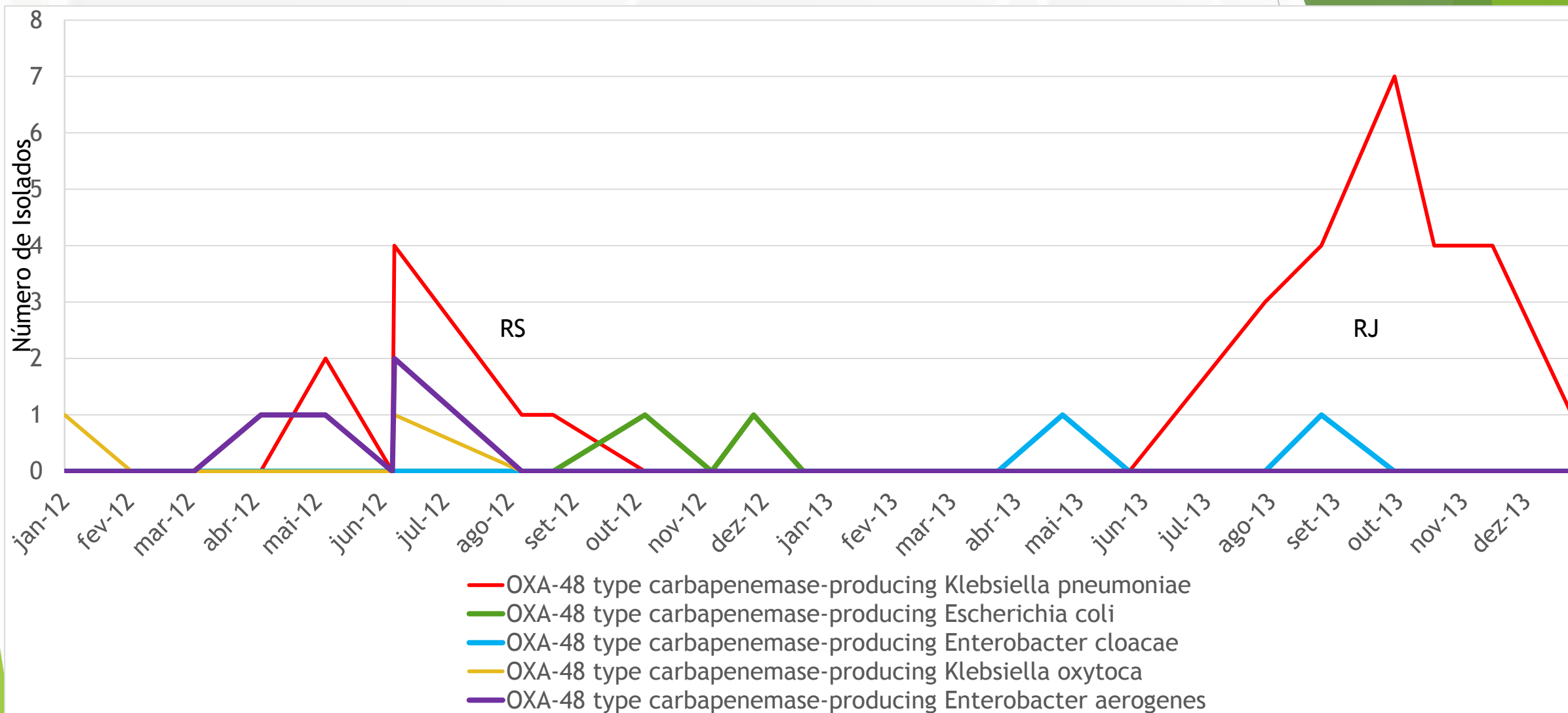


# Enterobactérias dos Serviços de Saúde Brasileiros Investigadas pelo LAPIH quanto à Produção de Carbapenemase NDM-1, 2013 e jun-2014

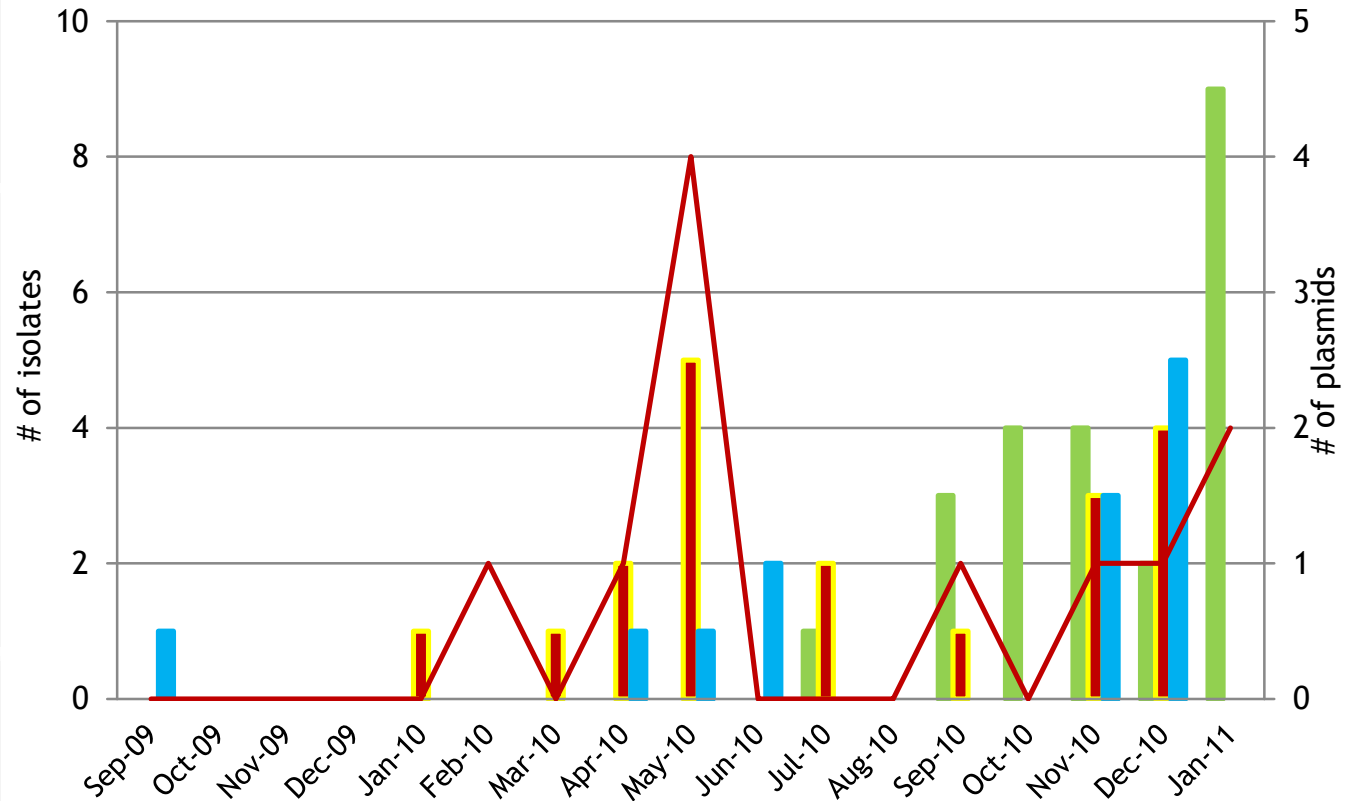
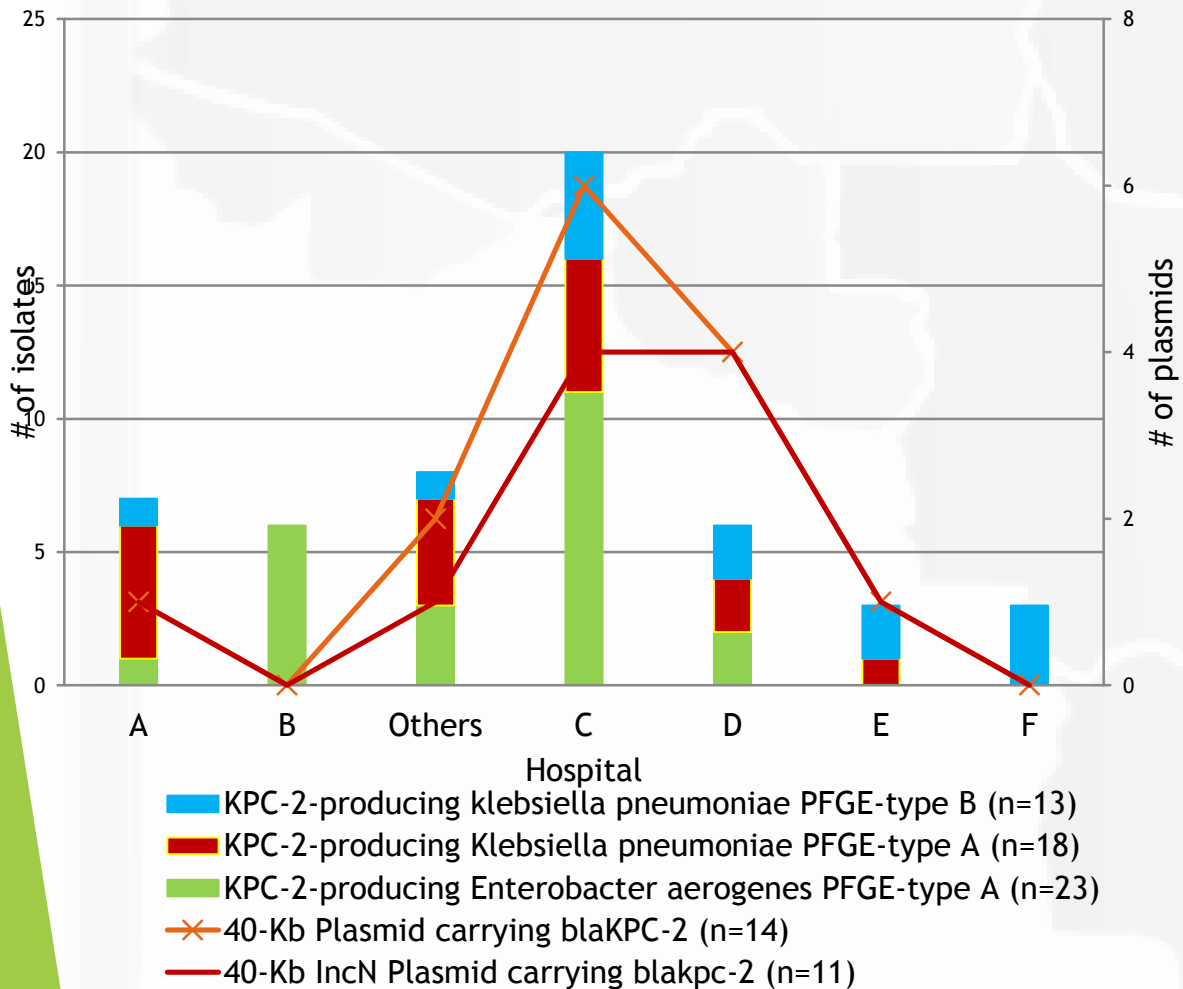




# Enterobactérias Produtoras de Carbapenemases OXA-48-like, Serviços de Saúde Brasileiros, LAPIH - 2012 a 2014 (n=38)



# Likely multicenter plasmid outbreak among clonal KPC-2-producing Enterobacteriaceae species.



Half of KPC-2-producing *K. pneumoniae* (n=20) was recovered from blood, while 70% (n=19) of KPC-2-producing *Enterobacter* spp. was recovered from rectal swabs and none from blood. Thirteen percent (5/39) of *K. pneumoniae* and 33% (9/27) of *E. aerogenes* had polymyxin B MIC >2 µg/ml

ECMID, 2015

Gomes MZR, Tavares CP, Pereira PS, Cassiano I, Lobato LC, Faria Junior CL, Tassinari WS, Asensi MD, Assef APAC

LAPIH - I OC/FIOCRUZ

**RESEARCH ARTICLE**

**Open Access**

# A hospital-based matched case–control study to identify clinical outcome and risk factors associated with carbapenem-resistant *Klebsiella pneumoniae* infection

Luci Correa<sup>1,3\*</sup>, Marines Dalla Valle Martino<sup>2</sup>, Itacy Siqueira<sup>2</sup>, Jacyr Pasternak<sup>2</sup>, Ana Cristina Gales<sup>3</sup>, Claudia Vallone Silva<sup>1</sup>, Thiago Zinsly Sampaio Camargo<sup>4</sup>, Patricia Faria Scherer<sup>4</sup> and Alexandre Rodrigues Marra<sup>4</sup>

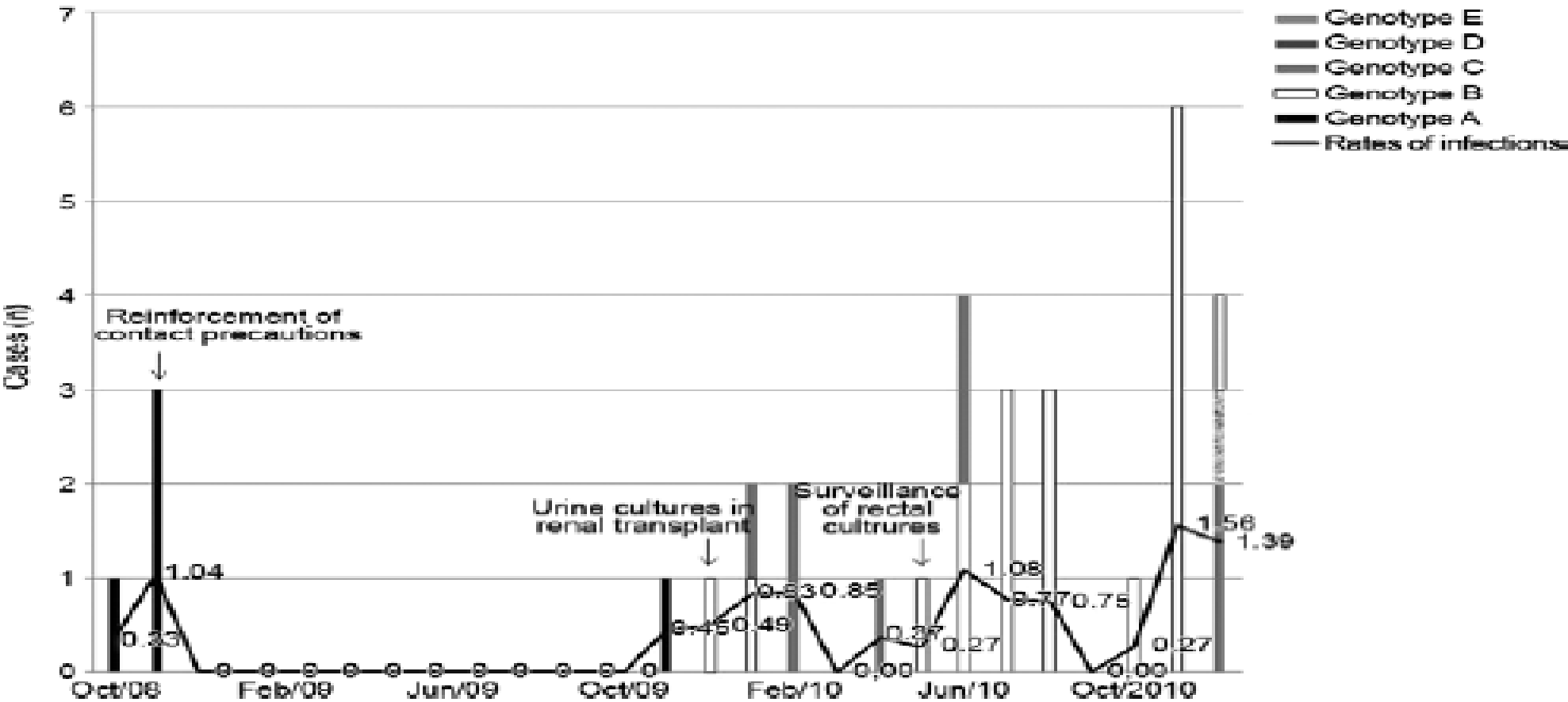
**Table 3 Resistant mechanisms detected in different strains**

Strain	GES	CTX-M 2	ompK35	ompK36
1	NEG	POS	>2072	>2072
2	NEG	POS	>2072	NA
3	NEG	POS	>2072	>2072
4	NEG	POS	>2072	NA
5	NEG	POS	1000	>2072
6	NEG	POS	>2072	NA
7	NEG	POS	>2072	1000
8	NEG	POS	1000	1000
9	POS	POS	1000	>2072
10	NEG	POS	1000	NA
11	NEG	POS	1000	NA
12*	NEG	NEG	1000	NA
13*	NEG	POS	1000	1000
14	NEG	NEG	1000	1000
15	NEG	POS	NA	1000
16	NEG	POS	>2072	1000
17	NEG	POS	1000	NA

\* The isolates 12 (susceptible strain) and 13 (resistant strain) are from the same patient.

Outbreak of carbapenem-resistant *Klebsiella pneumoniae*: two-year epidemiologic follow-up in a tertiary hospital

Graziella Hanna Pereira<sup>1, \*</sup>; E Fanti<sup>1</sup>; Anna S Levin<sup>3</sup>

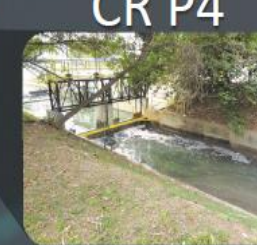
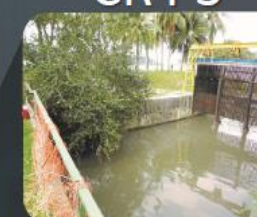
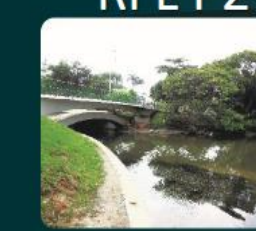
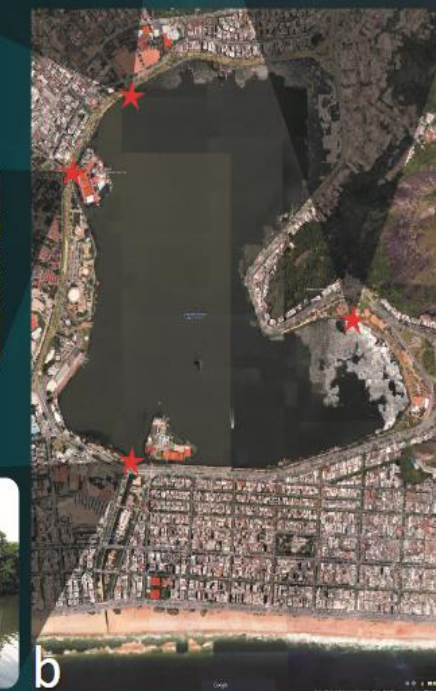
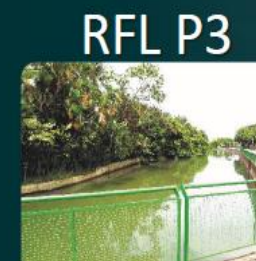
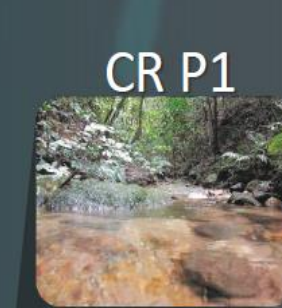
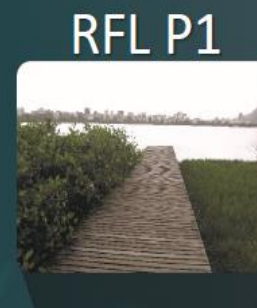
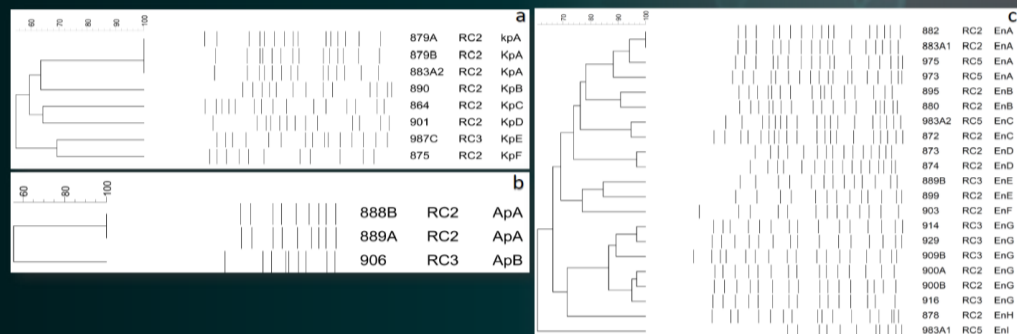


Monthly distribution of genotypes and rates of infection per 1,000 patients-days of carbapenem-resistant *Klebsiella pneumoniae* and interventions measures, from October 2008-December 2010 in Hospital Brigadeiro, state of São Paulo, Brazil.





**Genetic polymorphism:** The PFGE analysis, displayed 6 clonal groups among *K. pneumoniae* isolates, 2 among *A. punctata* isolates and 9 among *Enterobacter* sp. The same clonal groups of *Enterobacter* sp. were observed in different points, including in Flamengo Beach (Figure 4).



# KPC-producing Bacteria detected in Aquatic Ecosystem from Rio de Janeiro

C.F.M. Araujo<sup>1</sup>, D.M. Silva<sup>2</sup>, M.T. Carneiro<sup>2</sup>, M.D. Asensi<sup>1</sup>, V. Zahner<sup>1</sup>, A.P.D'A. Carvalho-Assef<sup>1</sup>.  
<sup>1</sup>Laboratório de Pesquisa em Infecção Hospitalar (LAPIH) – IOC/FIOCRUZ – Brazil;  
<sup>2</sup>Departamento de Saneamento e Saúde Ambiental (DSSA) – ENSP/FIOCRUZ – Brazil;

Acknowledgment:

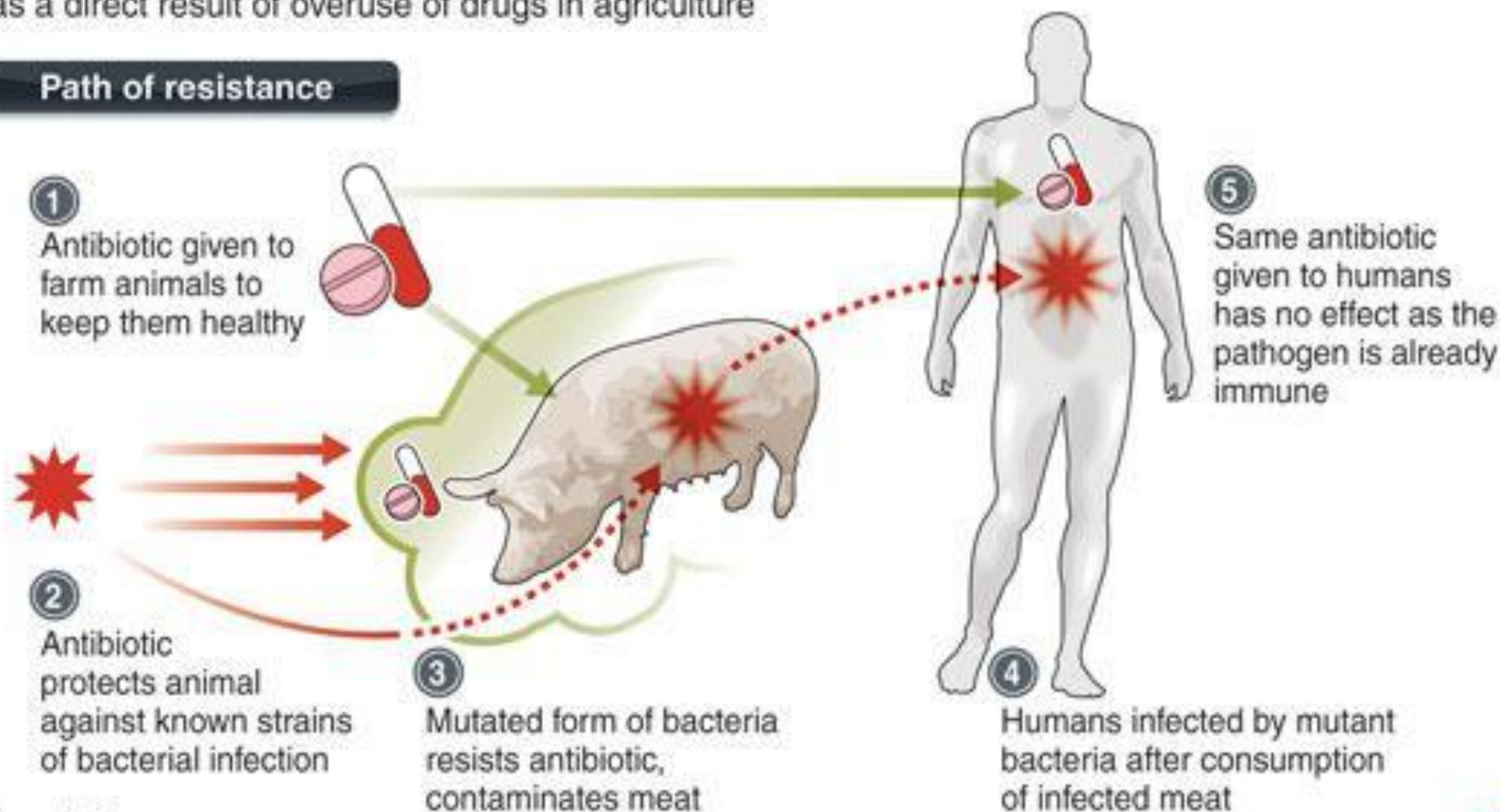




# Drugs, animals and mutations

The World Health Organization has detected increased bacterial resistance to antibiotics as a direct result of overuse of drugs in agriculture

## Path of resistance





Report 714

## Antibiotic use in Brazilian broiler and pig production: an indication and forecast of trends

March 2014

The conclusion on antibiotic use in Brazilian livestock are:

- There is no information available about used/sold quantities of veterinary antibiotics in Brazil.
- Growth promoters (AGP's) are commonly used on pig and broiler farms producing for the home market.
- Production for the EU market at present is without the use of growth promoters and completely separated from other production
- Based on qualitative information, the therapeutic use of antibiotics in Brazilian broiler production is estimated to be substantially lower than the average on Dutch broiler farms in 2011. There is no estimation for antibiotic use in Brazilian pig production.

The expectations for Brazilian veterinary antibiotic use in the next 3 to 5 years are:

- Monitoring of veterinary use will start in the future, but it might take 5 – 10 years to establish adequate monitoring systems. There is currently debate about extending the existing monitoring from 17 to 140 substances, including all antibiotics (Proposal Ordinance nr. 137, 2011).
- There will be an increasing pressure by EU and other markets regarding veterinary use of antibiotics. Brazil will accept more stringent regulations on antibiotics to keep the market.
- There will be an increasing pressure from the Brazilian Ministries of Health and of Agriculture. The expectation is that many 'critical' antibiotics will be banned.
- An on-going advantage of Brazil compared to Europe will be the strongly integrated animal production chain, with strict external (and internal) biosecurity measures for each production step. The use of antibiotics is strictly regulated within the integrations.
- A shift to further intensification of production in the Central West region of Brazil, with much larger farms, a hot climate and more mechanical ventilation, could put some pressure on the good animal health status and increase the need for therapeutic use of antibiotics in pig and broiler production.
- The use of AGP's in Brazilian broiler and pig production for the home market will probably go on, due to the expected economic benefits. In addition, there is a high pressure from pharmaceutical companies, which due to interviewees would hinder a reduction of use and restructuring of animal production systems.

ANTIMICROBIAL RESISTANCE IN *CAMPYLOBACTER* SPP ISOLATED FROM  
BROILER FLOCKS

Suzete Lora Kuana<sup>1</sup>; Luciana Ruschel dos Santos<sup>2</sup>; Laura Beatriz Rodrigues<sup>2</sup>; Anderlise Borsoi<sup>1</sup>;  
Hamilton Luis do Souza Moraes<sup>1</sup>; Carlos Tadeu Pippi Salle<sup>1</sup>; Vladimir Pinheiro do Nascimento<sup>1\*</sup>

**Table 1.** Antimicrobial resistance of *Campylobacter* spp. strains isolated from broiler flocks

Antimicrobial drug	Number of strains	Diameter (mm)	S%	I%	R%
Amoxicillin	15	0-32	73	0	27
Ampicillin	12	14-44	82	0	18
Ceftiofur	9	0-24	34	33	33
Colistin	20	9-32	80	20	0
Doxycycline	10	12-30	90	0	10
Enrofloxacin	17	0-30	17	12	71
Erythromycin	10	11-30	90	0	10
Spiramycin	10	13-30	60	20	20
Estreptomicina	14	10-30	86	0	4
Gentamicin	11	23-30	100	0	0
Lincomycin-Spectinomycin	5	31	100	0	0
Lincomycin	12	0-30	17	33	50
Neomycin	6	0-28	50	0	50
Norfloxacin	14	0-38	72	14	14
Penicilin	12	0-26	58	0	42
Tetracycline	14	0-40	57	0	43

S= sensitive I= intermediate R= resistant.



CTX-M-2–Producing *Salmonella* Typhimurium Isolated  
from Pediatric Patients and Poultry in Brazil

Sueli A. Fernandes,<sup>1</sup> David L. Paterson,<sup>2,3</sup> Ângela C. Ghilardi-Rodrigues,<sup>1</sup>  
Jennifer M. Adams-Haduch,<sup>2</sup> Ana T. Tavechio,<sup>1</sup> and Yohei Doi<sup>2</sup>

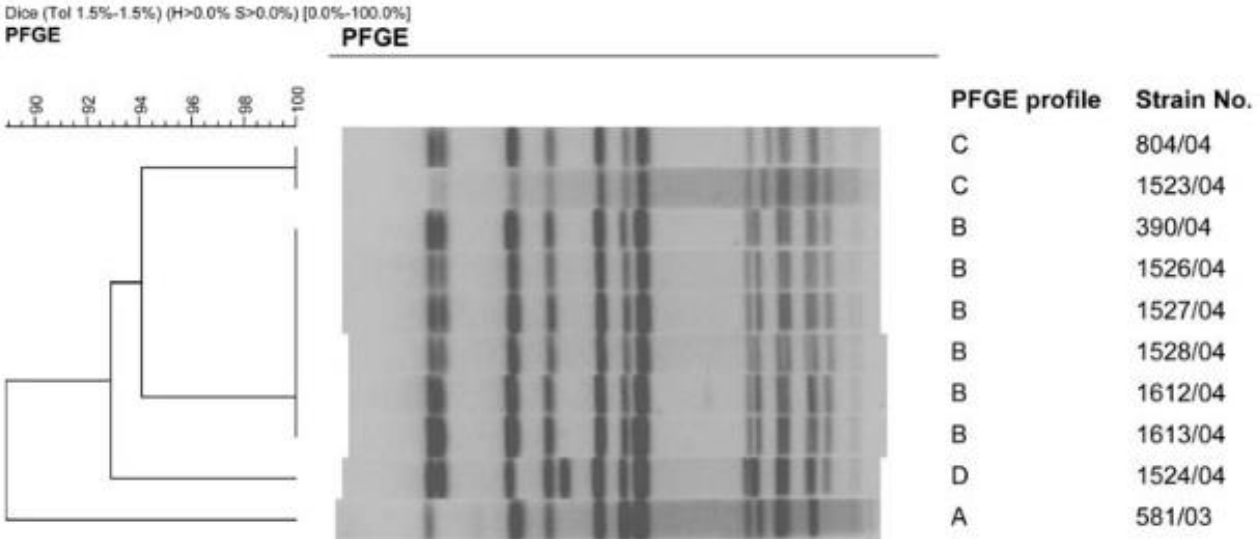


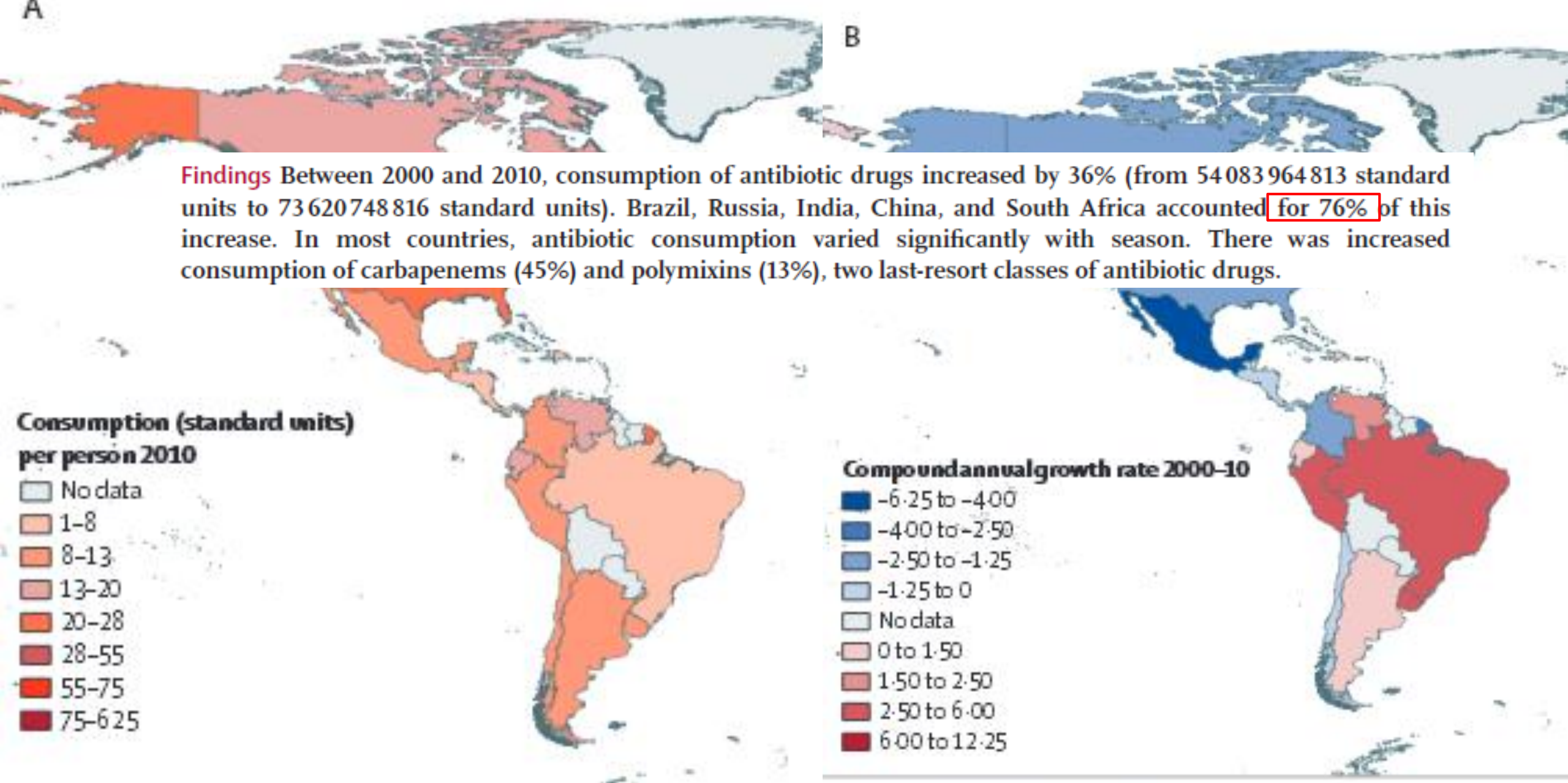
FIG. 1. Dendrogram for *Salmonella* Typhimurium isolates generated by pulsed-field gel electrophoresis (PFGE).

Isolate	Origin	City	AMP	CAZ	CPM	CTX	CRO	Additional resistance	PFGE	ESBL
581/03	Patient	Porto Alegre	≥ 256	24	≥ 32	≥ 32	≥ 32	AMC <sup>a</sup> ATM CO SF SFT TT	A	CTX-M2
390/04	Patient	São Paulo	≥ 256	8	≥ 32	≥ 32	≥ 32	AMC <sup>a</sup> ATM ET SF SFT TT	B	CTX-M2
804/04	Poultry	São Paulo	≥ 256	8	≥ 32	≥ 32	≥ 32	ATM ET SF SFT TT	C	CTX-M2
1523/04	Drag swab	Porto Alegre	≥ 256	12	≥ 32	≥ 32	≥ 32	AMC ATM ET SF SFT TT	C	CTX-M2
1524/04	Drag swab	Porto Alegre	≥ 256	8	≥ 32	≥ 32	≥ 32	ATM ET SF SFT TT	D	CTX-M2
1526/04	Drag swab	Porto Alegre	≥ 256	16	≥ 32	≥ 32	≥ 32	AMC ATM ET GN SF SFT TT	B	CTX-M2
1527/04	Drag swab	Porto Alegre	≥ 256	12	≥ 32	≥ 32	≥ 32	AMC ATM ET SF SFT TT	B	CTX-M2
1528/04	Drag swab	Porto Alegre	≥ 256	12	≥ 32	≥ 32	≥ 32	AMC <sup>a</sup> ATM ET SF SFT TT	B	CTX-M2
1612/04	Drag swab	Porto Alegre	≥ 256	12	≥ 32	≥ 32	≥ 32	AMC <sup>a</sup> ATM ET SF SFT TT	B	CTX-M2
1613/04	Drag swab	Porto Alegre	≥ 256	12	≥ 32	≥ 32	≥ 32	AMC <sup>a</sup> ATM ET SF SFT TT	B	CTX-M2

<sup>a</sup>Intermediate resistance.

AMC, amoxicillin/clavulanic acid; AMP, ampicillin; ATM, aztreonam; CAZ, ceftazidime; CTX, cefotaxime; CRO, ceftriaxone; CPM, cefepime; CO, chloramphenicol; ET, streptomycin; GN, gentamicin; SFT, trimethoprim/sulfamethoxazole; SF, sulfonamide; TT, tetracycline; MIC, minimum inhibitory concentration; PFGE, pulsed-field gel electrophoresis; ESBL, extended-spectrum  $\beta$ -lactamase.





**Figure 2: Consumption of antibiotics in 2010**

	Class	Status	Advantages	Caveats
Ceftazidime-avibactam (AstraZeneca/Forest, Wilmington, DE, USA)	Cephalosporin-BLI	Phase 3	Furthest advanced BLI combination; uses well-established cephalosporin at high doses (up to 2 g plus 0.5 g avibactam every 8 h)	Occasional resistance if other enzymes are also present. <sup>16</sup> Strains with metallo-carbapenemases, rather than KPC enzymes, are resistant
Ceftaroline-avibactam (AstraZeneca/Forest, Wilmington, DE, USA)	Cephalosporin-BLI	Entering phase 3	Also covers methicillin-resistant <i>Staphylococcus aureus</i> but (unlike ceftazidime-avibactam) not <i>Pseudomonas aeruginosa</i>	Higher doses might be needed than used for ceftaroline alone. Strains with metallo-carbapenemases, rather than KPC enzymes, are resistant
Plazomicin ACHN-490 (Achaogen, San Francisco, CA, USA)	Aminoglycoside	Completed phase 2	Active versus most isolates with KPC enzymes; <sup>17</sup> evades aminoglycoside-modifying enzymes	Compromised by rRNA methylases, which sometimes accompany KPC enzymes in China, <sup>18</sup> although these are not present in typical ST258-KPC strains elsewhere
Eravacycline TP-434 (Tetraphase, Watertown, MA, USA)	Tetracycline	Completed phase 2	Active vs Enterobacteriaceae with KPC or other carbapenemases <sup>19</sup>	Efficacy of tetracyclines in severe infections is debated
Imipenem-MK7655 (Merck, Summit, NJ, USA)	Carbapenem-BLI	Phase 2	Uses a well established carbapenem <sup>20</sup>	Strains with metallo-carbapenemases, rather than KPC enzymes, are resistant
Aztreonam-avibactam (AstraZeneca/Forest, Wilmington, DE, USA)	Monobactam-BLI	Phase 1	Also covers Enterobacteriaceae with metallo-carbapenemases <sup>16</sup>	Spectrum mostly confined to Enterobacteriaceae
Biapenem-RPX7009 (Rempex, San Diego, CA, USA)	Carbapenem-BLI	Phase 1	Novel boronate inhibitor; biapenem is less compromised than other carbapenems vs Enterobacteriaceae with metallo-carbapenemases	Resistance can arise in isolates with high biapenem minimum inhibitory concentrations, probably owing to hyperproduction of KPC enzymes
BAL30072 (Basilea, Basel, Switzerland)	Monosulfactam	Phase 1	Stable to metallo-carbapenemases and OXA-48 carbapenemases as well as KPC enzymes <sup>21</sup>	Vulnerable to the SHV extended-spectrum $\beta$ -lactamases, which often accompany KPC enzymes (eg, in ST258 <i>K. pneumoniae</i> ) <sup>22</sup>

BLI =  $\beta$ -lactamase inhibitor. KPC = *Klebsiella pneumoniae* carbapenemase.

**Table 2: Drugs in clinical development that are active against Enterobacteriaceae with *Klebsiella pneumoniae* carbapenemases**

## Update of the molecular epidemiology of KPC-2-producing *Klebsiella pneumoniae* in Brazil: spread of clonal complex 11 (ST11, ST437 and ST340)

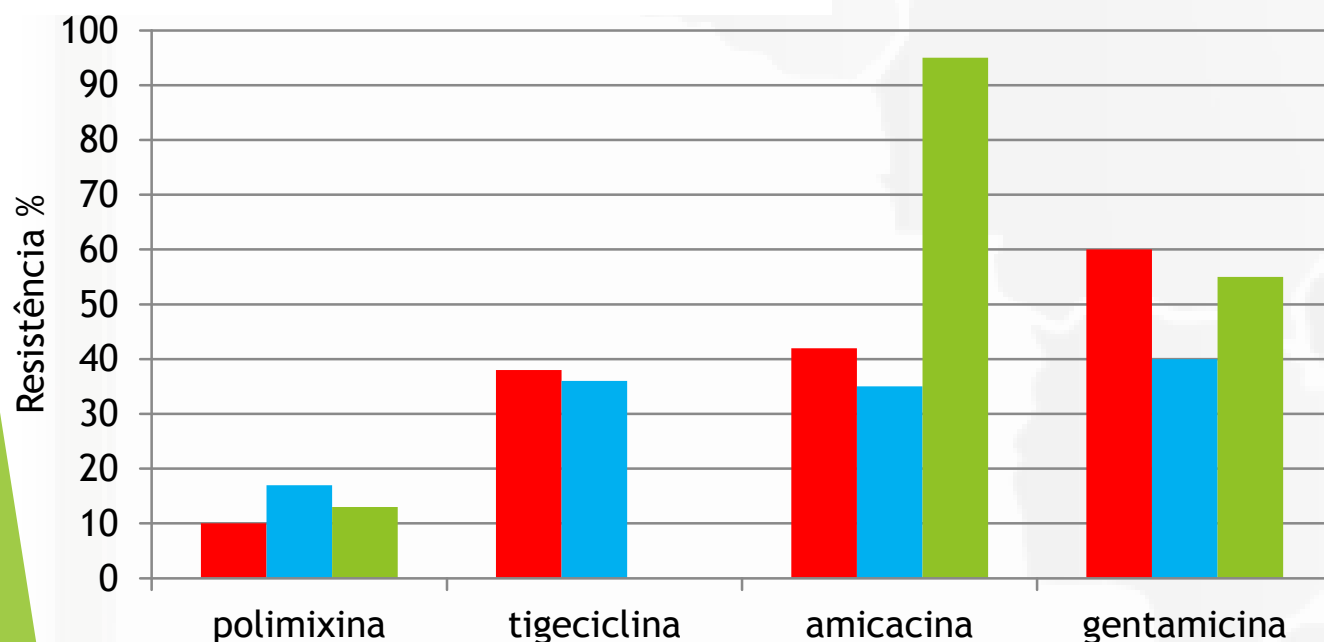
Polyana Silva Pereira, Carlos Felipe Machado de Araujo, Liliane Miyuki Seki, Viviane Zahner, Ana Paula D'Alincourt Carvalho-Assef and Marise Dutra Asensi\*

### Clonal dissemination of OXA-370- producing *Klebsiella pneumoniae* in Rio de Janeiro, Brazil

Polyana Silva PEREIRA<sup>a</sup>, Mirla BORGHI<sup>a</sup>, Carlos Felipe Machado de ARAÚJO<sup>a</sup>, Caio Augusto

Martins AIRES<sup>a</sup>, Jane Cleide Ribeiro OLIVEIRA<sup>b</sup>, Marise Dutra ASENSI<sup>a</sup>, Ana Paula D'Alincourt

CARVALHO-ASSEF<sup>a</sup> #.



■ KPC-2 *K. pneumoniae* (n=113)

■ KPC-2 other *Enterobacteriaceae* (n=83)

■ OXA-48-like *K. pneumoniae* (n=22)

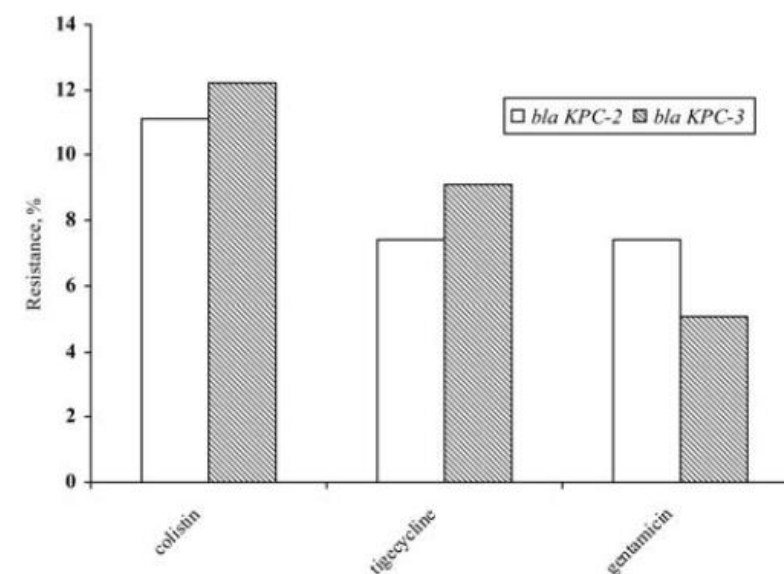
LAPIH - IOC/FIOCRUZ

## Outbreak of carbapenem-resistant *Klebsiella pneumoniae*: two-year epidemiologic follow-up in a tertiary hospital

Graziella Hanna Pereira<sup>1, \*</sup>, Doroti O Garcia<sup>2</sup>, Marcelo Mostardeiro<sup>1</sup>, Karina SVN Fanti<sup>1</sup>, Anna S Levin<sup>3</sup>

## Predictors of Mortality in Bloodstream Infections Caused by *Klebsiella pneumoniae* Carbapenemase-Producing *K. pneumoniae*: Importance of Combination Therapy

Mario Tumbarello,<sup>1</sup> Pierluigi Viale,<sup>2</sup> Claudio Viscoli,<sup>3</sup> Enrico Maria Trecarichi,<sup>1</sup> Fabio Tumierto,<sup>2</sup> Anna Marchese,<sup>4</sup> Teresa Spanu,<sup>5</sup> Simone Ambretti,<sup>6</sup> Francesca Ginocchio,<sup>3</sup> Francesco Cristini,<sup>2</sup> Angela Raffaella Losito,<sup>1</sup> Sara Tedeschi,<sup>2</sup> Roberto Cauda,<sup>1</sup> and Matteo Bassetti<sup>3,7</sup>



**Figure 1.** Colistin, tigecycline, and gentamicin resistance rates among *Klebsiella pneumoniae* isolates harboring the *bla*<sub>KPC-2</sub> and *bla*<sub>KPC-3</sub> genes. Abbreviation: KPC, *Klebsiella pneumoniae* carbapenemase.



Update of the molecular epidemiology of KPC-2-producing *Klebsiella pneumoniae* in Brazil: spread of clonal complex 11 (ST11, ST437 and ST340)

Polyana Silva Pereira, Carlos Felipe Machado de Araujo, Liliane Miyuki Seki, Viviane Zahner, Ana Paula D'Alincourt Carvalho-Assef and Marise Dutra Asensi\*

According to CLSI 2011 breakpoints,<sup>7</sup> most of the isolates were resistant to  $\beta$ -lactams, such as cefotaxime (93.8%), ceftazidime (87.6%) and piperacillin/tazobactam (100%). All isolates were non-susceptible to ertapenem ( $MIC_{50} >32$  mg/L,  $MIC$  range 2–>32 mg/L), 99.1% to imipenem ( $MIC_{50} >32$  mg/L,  $MIC$  range 1–>32 mg/L) and 99.1% to meropenem ( $MIC_{50} >32$  mg/L,  $MIC$  range 0.5–>32 mg/L). We observed elevated resistance to



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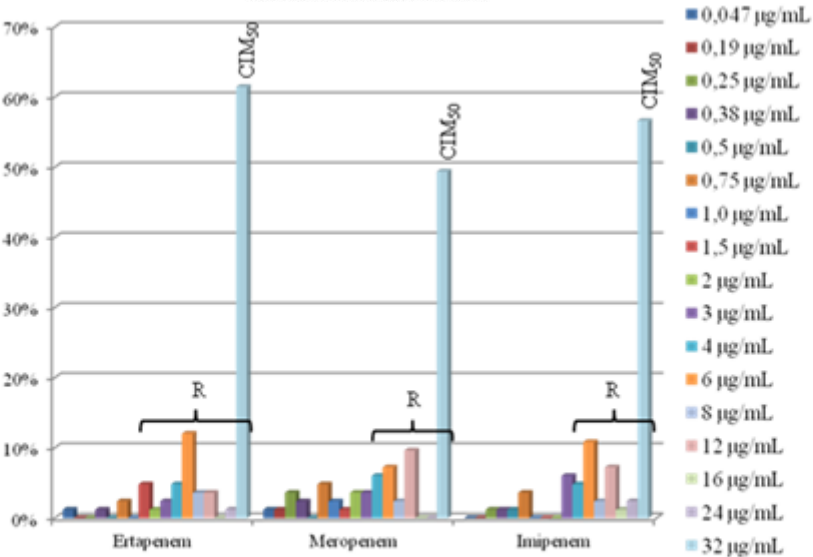


Gráfico 4.4. Concentração inibitória mínima de ertapenem, meropenem e amostras de *Enterobacteriaceae* produtoras de KPC-2.

Predictors of Mortality in Bloodstream Infections Caused by *Klebsiella pneumoniae* Carbapenemase-Producing *K. pneumoniae*: Importance of Combination Therapy

Mario Tumbarello,<sup>1</sup> Pierluigi Viale,<sup>2</sup> Claudio Viscoli,<sup>3</sup> Enrico Maria Trecarichi,<sup>1</sup> Fabio TumiETTO,<sup>2</sup> Anna Marchese,<sup>4</sup> Teresa Spanu,<sup>5</sup> Simone Ambretti,<sup>6</sup> Francesca Ginocchio,<sup>3</sup> Francesco Cristini,<sup>2</sup> Angela Raffaella Losito,<sup>1</sup> Sara Tedeschi,<sup>2</sup> Roberto Cauda,<sup>1</sup> and Matteo Bassetti<sup>3,7</sup>

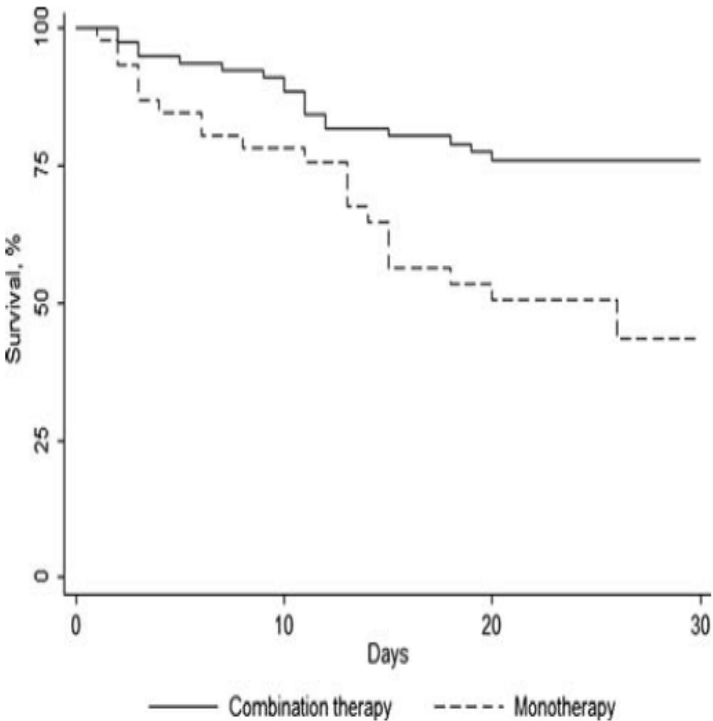


Figure 2. Kaplan-Meier curves showing the impact of combination therapy (solid line) versus monotherapy (dotted line) on 30-day mortality of patients with *Klebsiella pneumoniae* carbapenemase-producing *K. pneumoniae* isolate bloodstream infections ( $P=.002$ ).

Table 4. Outcomes of the 36 Bloodstream Infections Treated With Combination Therapy Including Meropenem Stratified by Meropenem Minimum Inhibitory Concentration

Meropenem MIC (mg/L)	Total	No. (%)	
		Nonsurvivors	Survivors
1	1	0	1 (100)
2	4	0	4 (100)
4	10	2 (20)	8 (80)
8	4	1 (25)	3 (75)
≥16	17	6 (35.2)	11 (64.7)
Total	36	9 (25)	27 (75)

Abbreviation: MIC, minimum inhibitory concentration.

against the isolate is essential in these cases. Indeed, even though all of the patients included in this cohort received at

# Clinical epidemiology of the global expansion of *Klebsiella pneumoniae* carbapenemases



L Silvia Munoz-Price, Laurent Poirel, Robert A Bonomo, Mitchell J Schwaber, George L Daikos, Martin Cormican, Giuseppe Cornaglia, Javier Garau, Marek Gniadkowski, Mary K Hayden, Karthikeyan Kumarasamy, David M Livermore, Juan J Maya, Patrice Nordmann, Jean B Patel, David L Paterson, Johann Pitout, Maria Virginia Villegas, Hui Wang, Neil Woodford, John P Quinn

	USA <sup>125</sup> (2009)	Crete <sup>76</sup> (2009)	USA <sup>21</sup> (2009)	USA <sup>126</sup> (2010)	Israel <sup>127</sup> (2010)	USA <sup>23</sup> (2010)	USA <sup>128</sup> (2010)	Israel <sup>129</sup> (2011)	Israel <sup>130</sup> (2011)	Italy <sup>131</sup> (2011)	Italy <sup>70</sup> (2012)	Greece <sup>132</sup> (2012)	Spain <sup>133</sup> (2012)
Increased hand hygiene precautions	Yes	Yes	Yes	Yes*	..	..	Yes	..	Yes	Yes*	Yes	Yes*	Yes
Increased compliance with gowns and gloves	Yes	Yes	Yes	Yes*	Yes	Yes	Yes	Yes	Yes	Yes*	Yes	Yes*	Yes
Rectal surveillance initiated	Yes	..	Yes	Yes†	Yes	Yes	Yes	Yes	Yes	Yes*	..	Yes‡	Yes
Grouping of KPC-positive patients	Yes	..	Yes	Yes†	Yes	Yes	Yes	Yes	Yes	Yes†	Yes	Yes†	Yes
Grouping of staff caring for KPC-positive patients	Yes	..	Yes	Yes†	Yes	Yes	Yes	Yes	Yes	Yes†	..	Yes‡	..
Education on hospital epidemiology of KPC among health-care workers	Yes	Yes	..	..	..	Yes	Yes	Yes	Yes	Yes*	Yes	..	Yes
Increased environmental cleaning	Yes	Yes	..	..	..	Yes	Yes	Yes	Yes	Yes*	Yes	Yes†	Yes
Cultures of environmental surfaces in patients' rooms	..	Yes	..	..	..	Yes	Yes	..	..	..	Yes	Yes*	Yes
Daily chlorhexidine baths	..	..	..	..	..	Yes	Yes	..	..	..	..	..	Yes
Regular infection control reports of new cases to affected units	..	..	..	..	Yes	Yes	Yes	Yes	Yes	..	..	Yes†	..
Flagging of cases in hospital database	..	..	..	..	Yes	..	..	Yes	Yes	..	..	..	..
Closing the ICU	Yes	..	..	Yes*	..	..	..	..	..	..	..	..	..
Surveillance cultures obtained from staff	..	..	..	..	..	..	..	..	..	..	..	..	Yes
Dedicated equipment for KPC-positive patients	..	..	Yes	..	..	..	..	..	Yes	..	Yes	..	..
Decreased antibiotic use or antibiotic restriction	..	..	..	Yes*	..	..	..	..	Yes	..	..	..	..
Outbreak improved or controlled	Yes	Yes	Yes	Yes, during second phase	Yes	Yes	Yes	Yes	..	Yes, during second phase	No	Yes, during second and third phases	Yes

ICU=intensive care unit. KPC=*Klebsiella pneumoniae* carbapenemase. ..=not reported. Symbols represent bundles that were implemented in a staggered fashion: \* first phase; †second phase; ‡third phase.

**Table 3: Infection control interventions for the containment of Enterobacteriaceae positive for *Klebsiella pneumoniae* carbapenemase**

# Conclusão:

- ▶ Resultados Fragmentados
- ▶ Enfrentamento Mundial