Epidemiology of Bacterial Resistance

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Disclosures

- Consultant, Scientific Advisor and Speaker's Bureau, Consulting fee and Speaker honorarium
  - AstraZeneca,
  - Bayer,
  - BD,
  - MSD,
  - Pfizer

- WHO, Consultant
- Brazilian Ministry of Health, Consultant
- Brazilian Committee on Antimicrobial Susceptibility Testing, General Coordinator

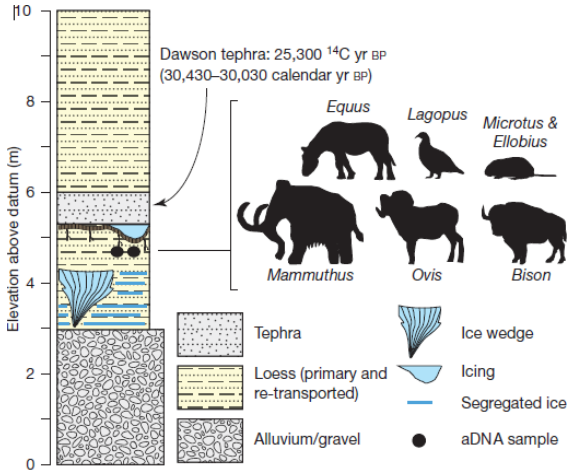
Why is bacterial resistance a major threat to public health worldwide?

LETTER

doi:10.1038/nature10388

Antibiotic resistance is ancient

Vanessa M. D'Costa[1,2]*, Christine E. King[3,4]*, Lindsay Kalan[1,2], Mariya Morar[1,2], Wilson W. L. Sung[4], Carsten Schwarz[3], Duane Froese[5], Grant Zazula[6], Fabrice Calmels[5], Regis Debruyne[7], G. Brian Golding[4], Hendrik N. Poinar[1,3,4] & Gerard D. Wright[1,2]



OPEN ACCESS Freely available online

PLoS one

Antibiotic Resistance Is Prevalent in an Isolated Cave Microbiome

Kirandeep Bhullar[1], Nicholas Waglechner[1], Andrew Pawlowski[1], Kalinka Koteva[1], Eric D. Banks[2], Michael D. Johnston[2], Hazel A. Barton[2], Gerard D. Wright[1]*

1 M.G. DeGroote Institute for Infectious Disease Research, Department of Biochemistry and Biomedical Sciences, McMaster University, Hamilton, Ontario, Canada, 2 Department of Biology, University of Akron, Akron, Ohio, United States of America

Bacteria bonanza found in remote Amazon village

Genes for antibiotic resistance among those found in most-diverse human microbiome.

Robin Hanbury-Tenison/Robert Harding

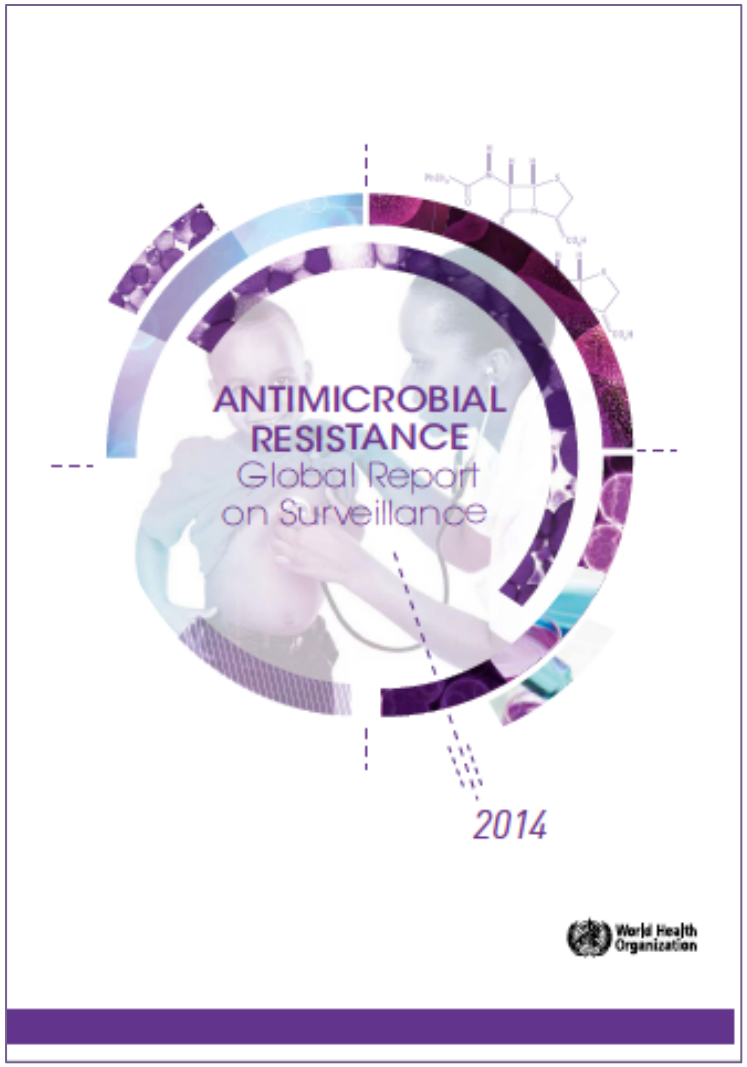
Louise Murray/Science Photo Library

Figure 2: Antibiotic resistance in nature, such as that identified in polar bears in Svalbard, is likely anthropogenic

Laxminarayan et al. The Lancet Infect Dis. S1473-3099(13)70318-9.

http://www.nature.com/news/bacteria-bonanza-found-in-remote-amazon-village-1.17348

Resistência Bacteriana: Problema de Saúde Pública Mundial



- **Bacterial resistance (MDR) reported in all regions**
- **Limited therapeutic options;**
- **Negative impact on clinical outcomes of patients infected by MDR pathogens.**
- **MDR = ↑cost**

http://www.who.int/drugresistance/publications/infographic-antimicrobial-resistance-20140430.pdf?ua=1

Neisseria gonorrhoeae
Resistance to extended-spectrum cephalosporins

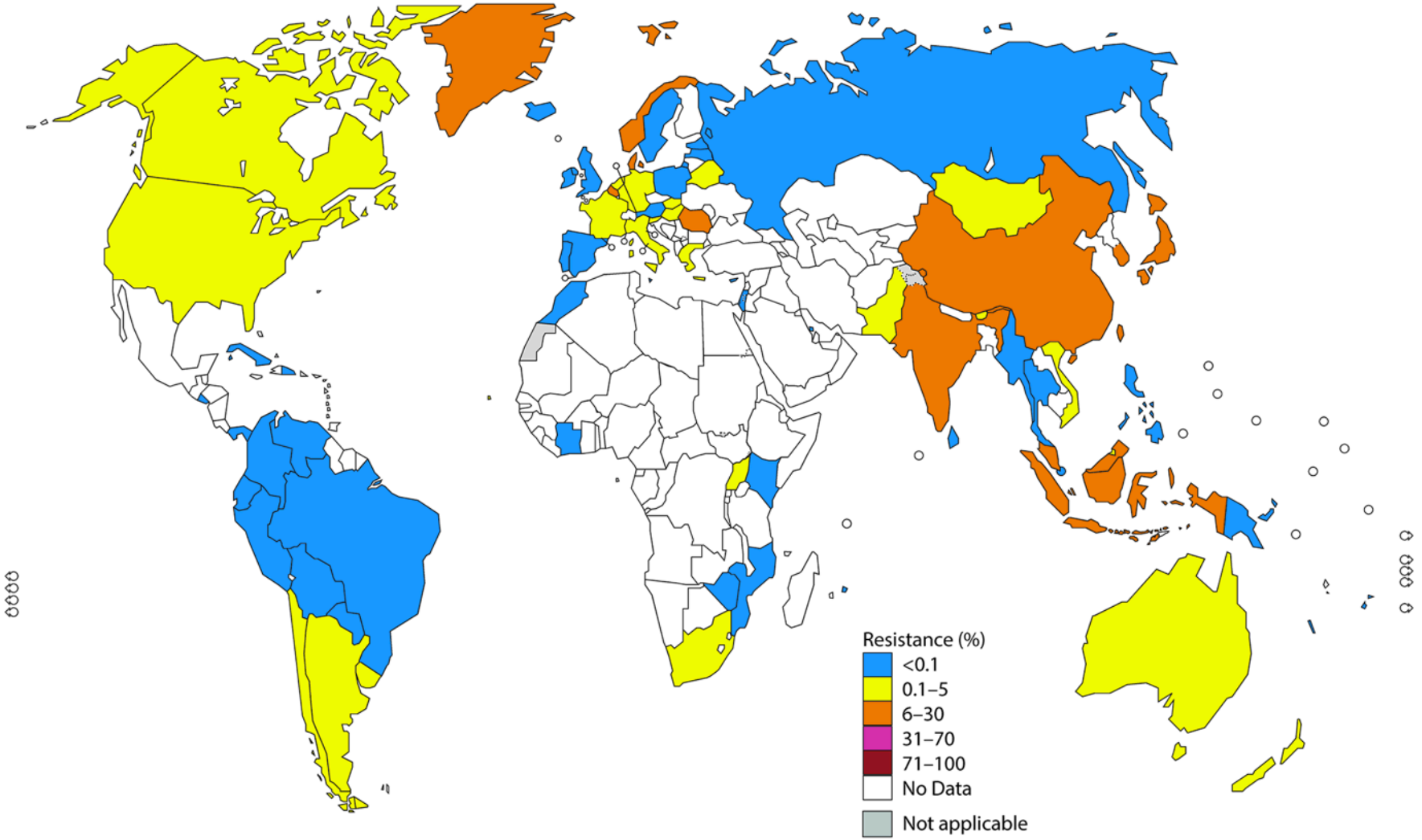


Fig 1. The percentage (%) of isolates with decreased susceptibility or resistance to extended-spectrum cephalosporin (ESC) (cefixime and/or ceftriaxone) according to the most recent World Health Organization (WHO) Gonococcal Antimicrobial Surveillance Programme (GASP) data (2014 for most countries, but for a few countries, only 2011±2013 data were available). Note: The areas in grey are disputed territories (e.g., Western Sahara, Jammu, and Kashmir), and no antimicrobial resistance (AMR) data are available from these regions.

https://doi.org/10.1371/journal.pmed.1002344.g001

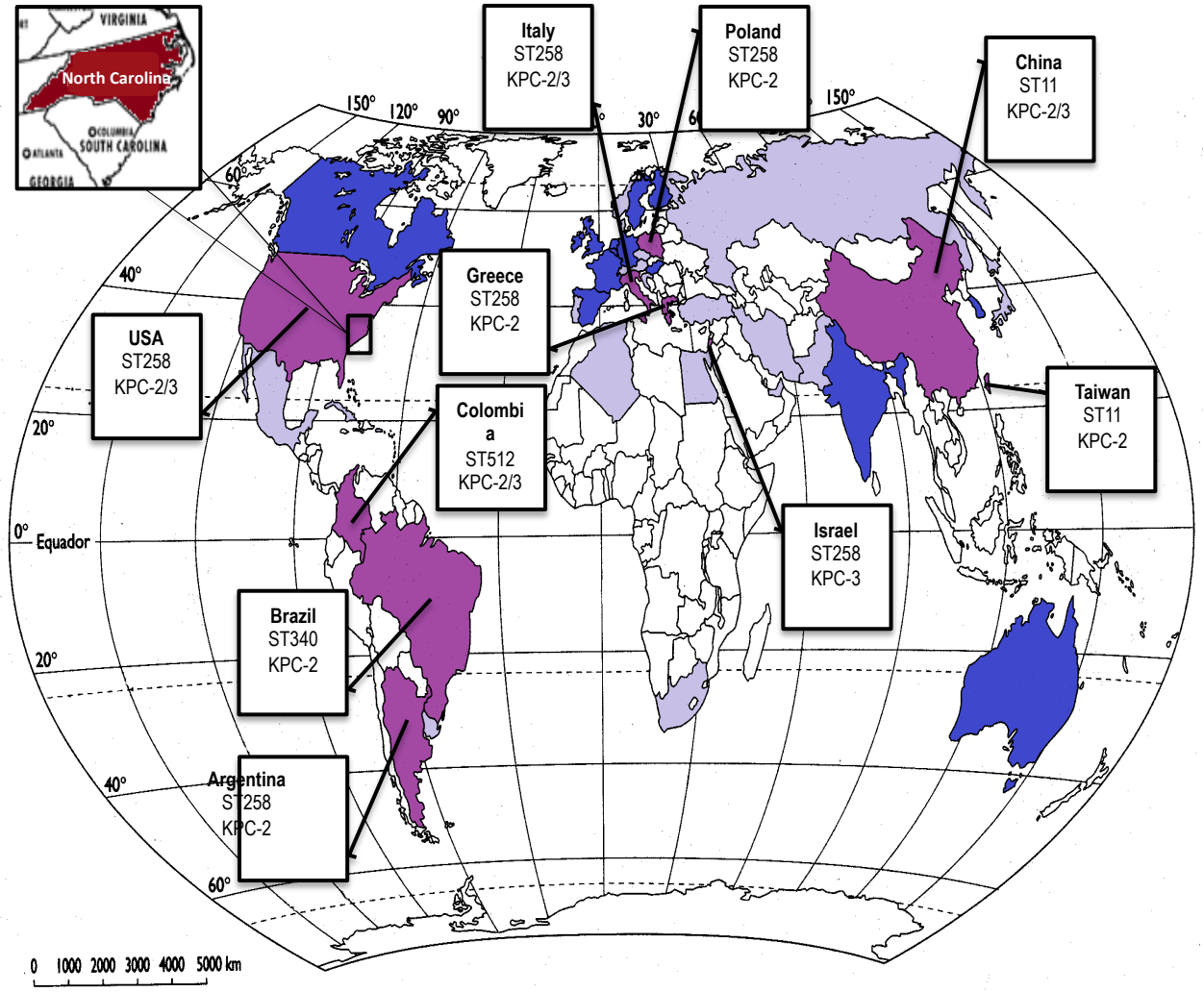
Enterobactérias produtoras de MCR-1 (mobile colistin resistance)

FIGURE 4

Countries (n = 30) reporting presence of *mcr-1* in samples of animal, environmental or human origin (data collected till 27 June 2016)

Xavier et al. Euro Surveill. 2016;21(27):pii=30280. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2016.21.27.30280

KPC (*Klebsiella pneumoniae* carbapenemase)



Yigit et al.Antimicrob Agents Chemother. 2001 Apr;45(4):1151-61.
Munoz-Price et al. Lancet Infect Dis. 2013 Sep; 13(9): 785–796.
DeLeo Proc Natl Acad Sci U S A. 2014 Apr 1; 111(13): 4988–4993.
Lee et al. Front. Microbiol. 7:895. doi: 10.3389/fmicb.2016.00895.

Distribuição Mundial de NDM

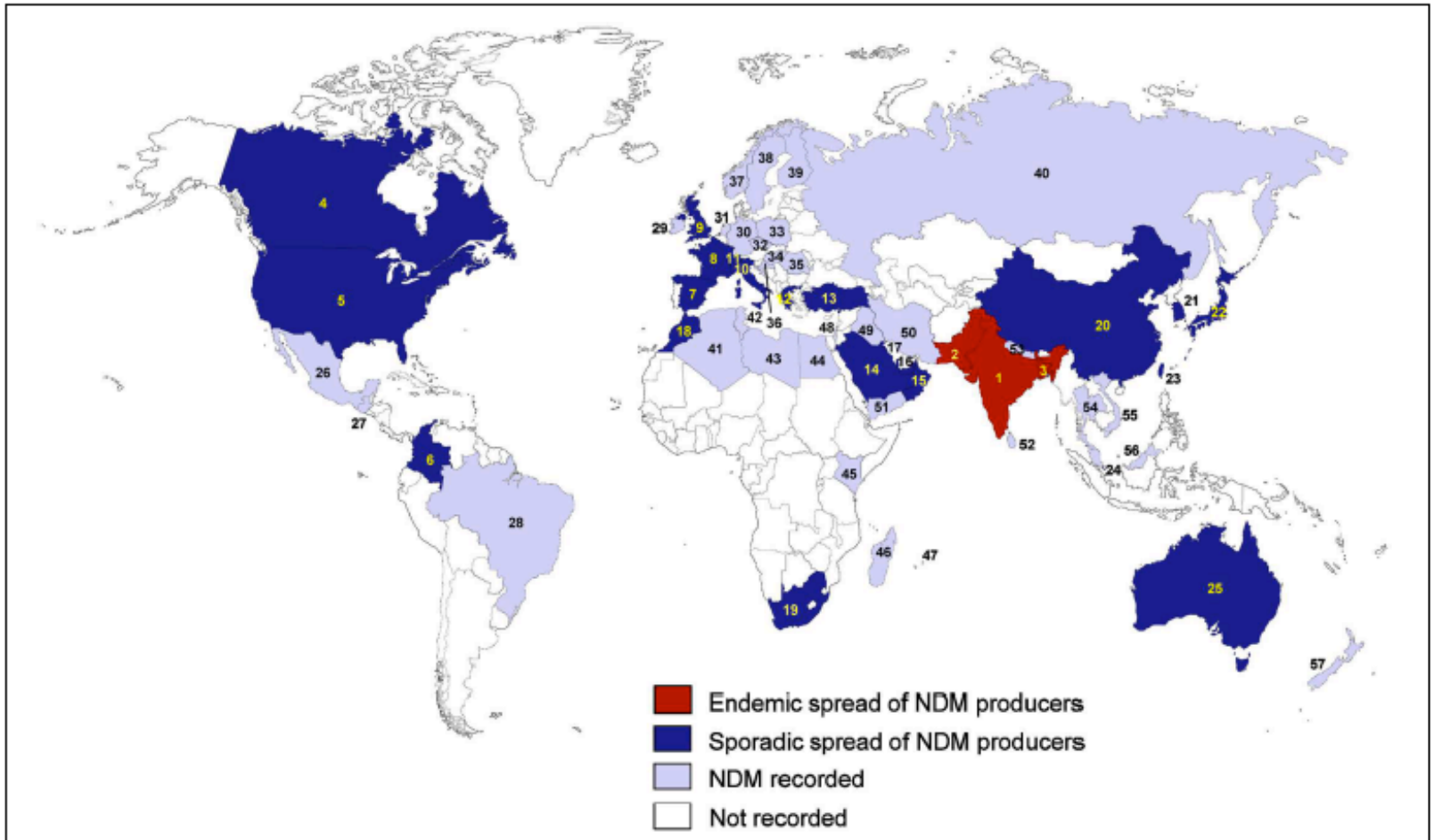
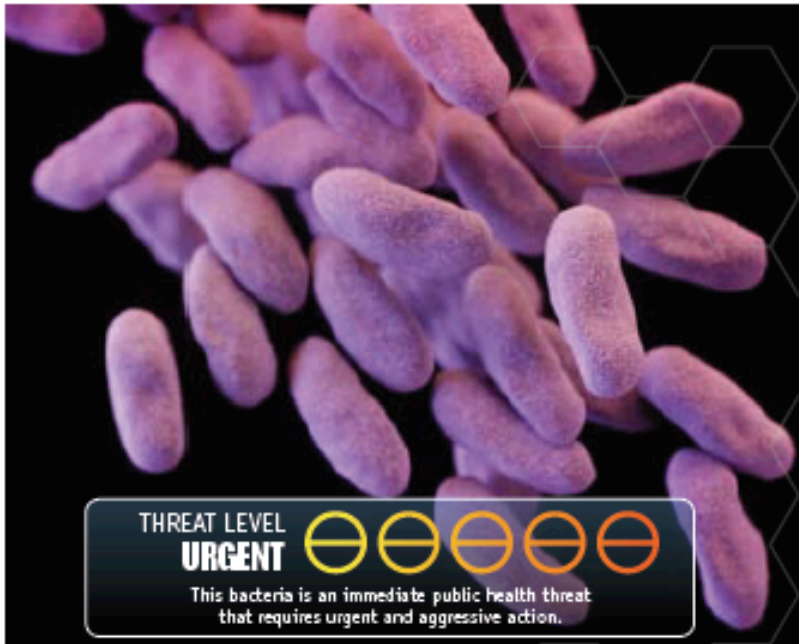


FIGURE 3 | Epidemiological features of NDM-producing *K. pneumoniae*. (1) India; (2) Pakistan; (3) Bangladesh; (4) Canada; (5) USA; (6) Colombia; (7) Spain; (8) France; (9) UK; (10) Italy; (11) Switzerland; (12) Greece; (13) Turkey; (14) Saudi Arabia; (15) Oman; (16) United Arab Emirates; (17) Kuwait; (18) Morocco; (19) South Africa; (20) China; (21) South Korea; (22) Japan; (23) Taiwan; (24) Singapore; (25) Australia; (26) Mexico; (27) Guatemala; (28) Brazil; (29) Ireland; (30) Germany; (31) Netherlands; (32) Czech Republic; (33) Poland; (34) Hungary; (35) Romania; (36) Croatia; (37) Norway; (38) Sweden; (39) Finland; (40) Russia; (41) Algeria; (42) Tunisia; (43) Libya; (44) Egypt; (45) Kenya; (46) Madagascar; (47) Mauritius; (48) Israel; (49) Iraq; (50) Iran; (51) Yemen; (52) Sri Lanka; (53) Nepal; (54) Thailand; (55) Vietnam; (56) Malaysia, (57) New Zealand.

Lee et al. Front. Microbiol. 7:895. doi: 10.3389/fmicb.2016.00895.



CARBAPENEM-RESISTANT ENTEROBACTERIACEAE

9,000 DRUG-RESISTANT INFECTIONS PER YEAR

600 DEATHS

CARBAPENEM-RESISTANT *KLEBSIELLA* SPP. **7,900**

1,400 CARBAPENEM-RESISTANT *E. COLI*

THREAT LEVEL
URGENT

This bacteria is an immediate public health threat that requires urgent and aggressive action.

CRE HAVE BECOME RESISTANT TO ALL OR NEARLY ALL AVAILABLE ANTIBIOTICS

Untreatable and hard-to-treat infections from carbapenem-resistant Enterobacteriaceae (CRE) bacteria are on the rise among patients in medical facilities. CRE have become resistant to all or nearly all the antibiotics we have today. Almost half of hospital patients who get bloodstream infections from CRE bacteria die from the infection.

RESISTANCE OF CONCERN

- Some Enterobacteriaceae are resistant to nearly all antibiotics, including carbapenems, which are often considered the antibiotics of last resort.
- More than 9,000 healthcare-associated infections are caused by CRE each year.
- CDC laboratories have confirmed at least one type of CRE in healthcare facilities in 44 states.
- About 4% of U.S. short-stay hospitals had at least one patient with a serious CRE infection during the first half of 2012. About 18% of long-term acute care hospitals had one.

PUBLIC HEALTH THREAT

An estimated 140,000 healthcare-associated Enterobacteriaceae infections occur in the United States each year; about 9,300 of these are caused by CRE. Up to half of all bloodstream infections caused by CRE result in death. Fortunately, bloodstream infections account for a minority of all healthcare-associated infections caused by Enterobacteriaceae. Each year, approximately 600 deaths result from infections caused by the two most common types of CRE, carbapenem-resistant *Klebsiella* spp. and carbapenem-resistant *E. coli*.

	Percentage of Enterobacteriaceae healthcare-associated infections resistant to carbapenems	Estimated number of infections	Estimated number of deaths attributed
Carbapenem-Resistant *Klebsiella* spp.	11%	7,900	520
Carbapenem-resistant *E. coli*	2%	1,400	90

For more information about data methods and references, please see technical appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

AR-Threat, CDC, 2013.

Bloodstream Infections Caused by Multidrug-Resistant Gram-Negative Bacteria Are Due Primarily to Patients with Hospital-Acquired Infections

Joshua T. Thaden,[a] Yanhong Li,[b] Felicia Ruffin,[a] Stacey A. Maskarinec,[a] Jonathan M. Hill-Rorie,[a] Lisa C. Wanda,[a] Shelby D. Reed,[b] Vance G. Fowler, Jr.[a,b]

Division of Infectious Diseases, Duke University, Durham, North Carolina, USA[a]; Duke Clinical Research Institute, Duke University, Durham, North Carolina, USA[b]

2009-2015, 891 adult inpatients with Gram-negative BSI at a single US institution were prospectively enrolled (292 MDR – 33%)

Only history of Gram-negative infection was associated with MDR BSI versus non-MDR BSI (OR: 1.60; 95% CI, 1.19-2.16; P= 0.002).

Patients with MDR BSI had increased BSI recurrence (1.7% vs 0.2%) and longer hospital stay (10 vs 8 days, P= 0.0005)

Unadjusted mean costs were 1.62 times higher in MDR than in non-MDR BSI ($59,266 versus $36,452; P= 0.003)

Interestingly, the increased cost of MDR BSI was noted even after we adjusted for appropriate empirical antibiotic therapy.

Antimicrob Agents Chemother 61:e01709-16. https://doi.org/10.1128/AAC.01709-16.

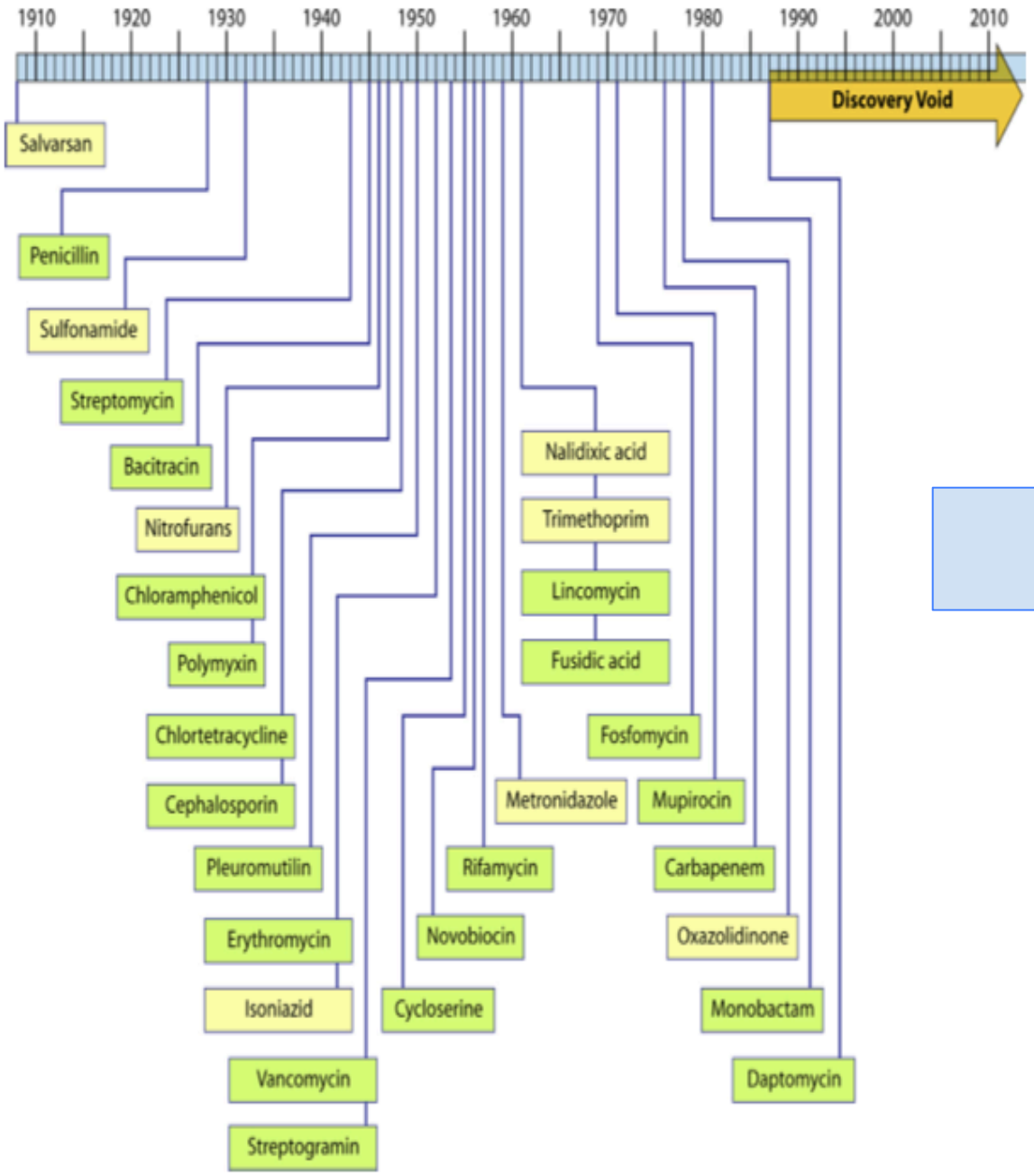


FIG. 1. Illustration of the "discovery void." Dates indicated are those of reported initial discovery or patent.

Void Discovery

Lynn L. Silver. *Clin. Microbiol. Rev.* 2011, 24(1):71.

World Health Organization

WHO PRIORITY PATHOGENS LIST FOR R&D OF NEW ANTIBIOTICS

Priority 1: CRITICAL#

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

Enterobacteriaceae*, carbapenem-resistant, 3rd generation cephalosporin-resistant

Priority 2: HIGH

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella *spp.*, fluoroquinolone-resistant

Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

Streptococcus pneumoniae, penicillin-non-susceptible

Haemophilus influenzae, ampicillin-resistant

Shigella *spp.*, fluoroquinolone-resistant

 # Mycobacteria (including *Mycobacterium tuberculosis*, the cause of human tuberculosis), was not subjected to review for inclusion in this prioritization exercise as it is already a globally established priority for which innovative new treatments are urgently needed.

* Enterobacteriaceae include: *Klebsiella pneumonia, Escherichia coli, Enterobacter* spp., *Serratia* spp., *Proteus* spp., and *Providencia* spp, *Morganella* spp.

Epidemiology of Bacterial Resistance

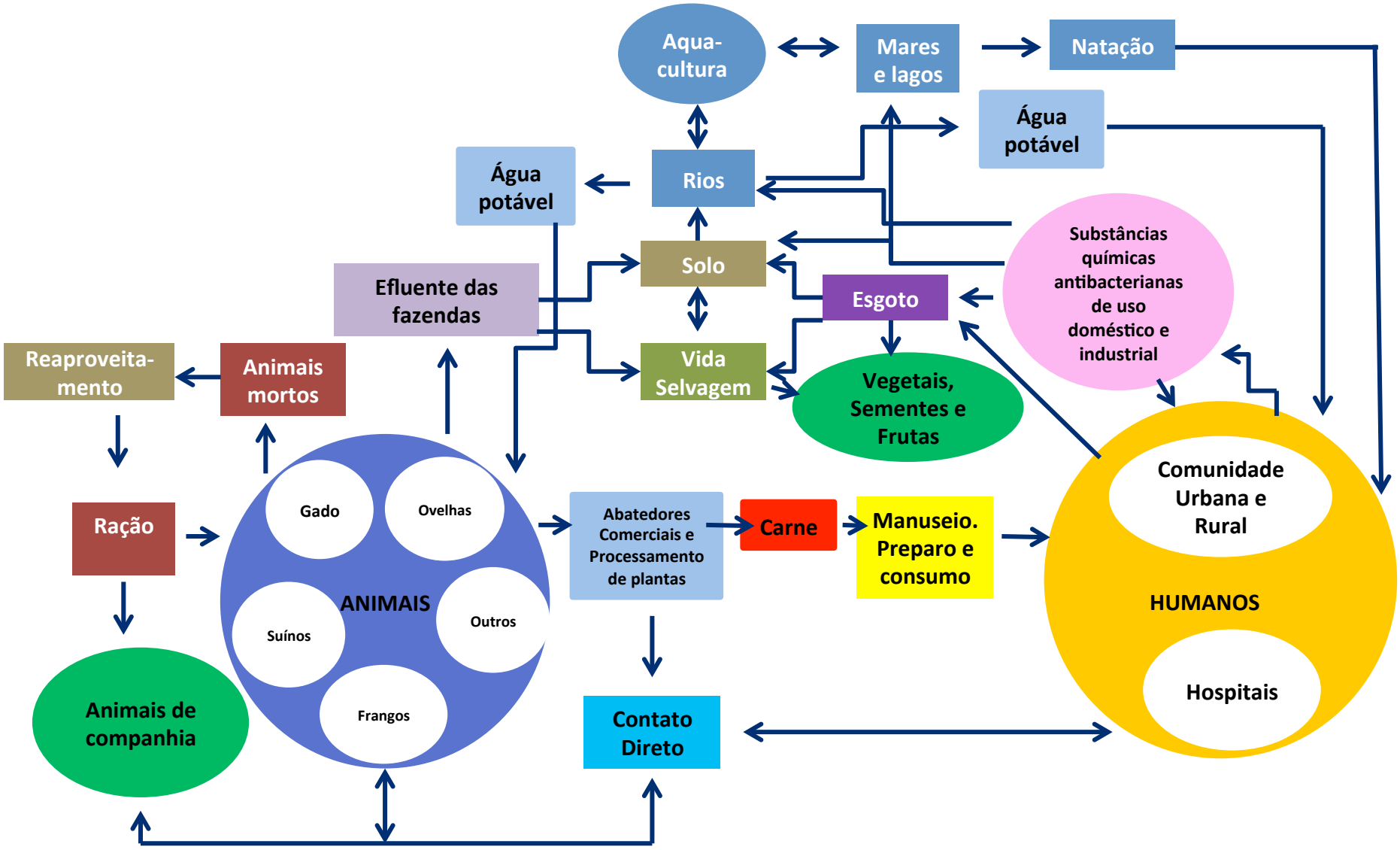
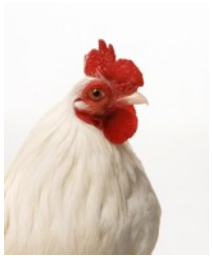
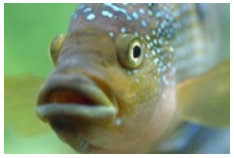


Figura adaptada http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/pubs/amr-ram_final_report-rapport_06-27-eng.pdf

Spread of Resistant Bacteria





Direct contact

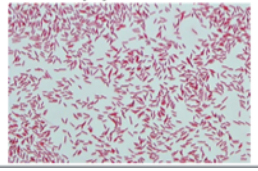
Food chain

Colonização
Infecção

Escherichia coli

Salmonella spp.

Campylobacter



Extended-Spectrum β-Lactamase Genes of *Escherichia coli* in Chicken Meat and Humans, the Netherlands

Ilse Overdevest, Ina Willemsen, Martine Rijnsburger, Andrew Eustace, Li Xu, Peter Hawkey, Max Heck, Paul Savelkoul, Christina Vandenbroucke-Grauls, Kim van der Zwaluw, Xander Huijsdens, and Jan Kluytmans

ESBL Genes of *E. coli* in Chicken Meat and Humans

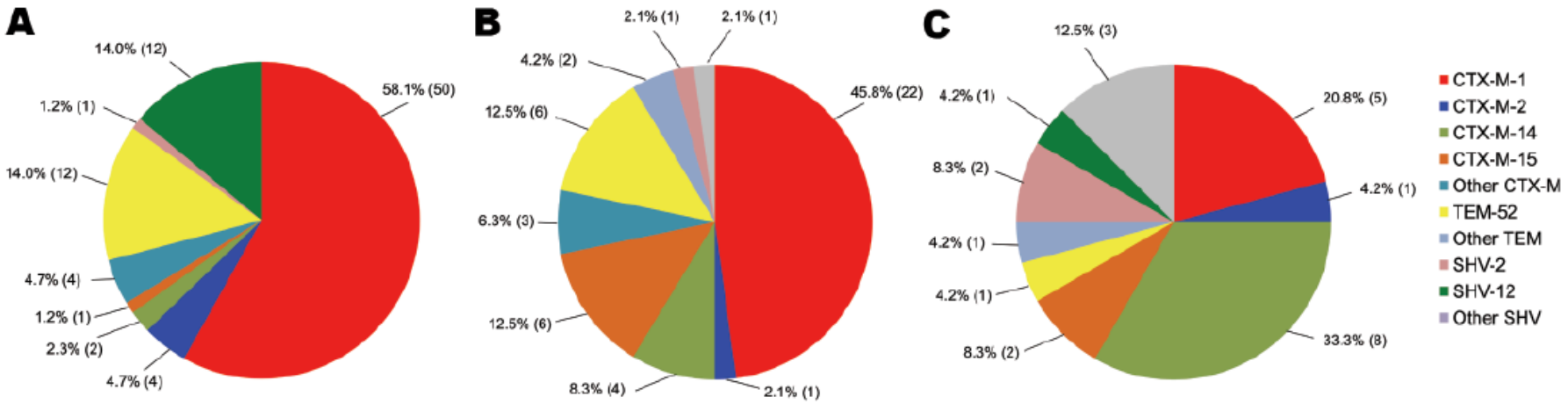
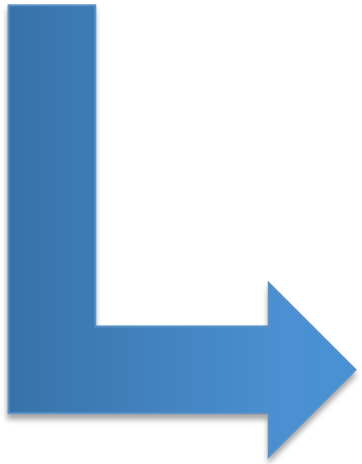


Figure 1. Distribution of extended-spectrum β-lactamase genes in chicken meat (A), human rectal swabs (B), and human blood cultures (C), the Netherlands. Values in parentheses are no. positive.

Overdevest I et al Emerg Infect Dis. 2011 Jul;17(7):1216-22.

“Indirect Factors”

- Socio-economic factors
  - Governance
    - Education
    - Drinking water & Basic Sanitation
    - GPD expediture on health and education
    - Corruption



Impacts infra-structure of health care facilities

Research & Development

RESEARCH ARTICLE

Geographical Variability in the Likelihood of Bloodstream Infections Due to Gram-Negative Bacteria: Correlation with Proximity to the Equator and Health Care Expenditure

David Fisman[1☯], Eleni Patrozou[2☯], Yehuda Carmeli[3], Eli Perencevich[4], Ashleigh R. Tuite[1], Leonard A. Mermel[5*], and the Geographical Variability of Bacteremia Study Group[¶]

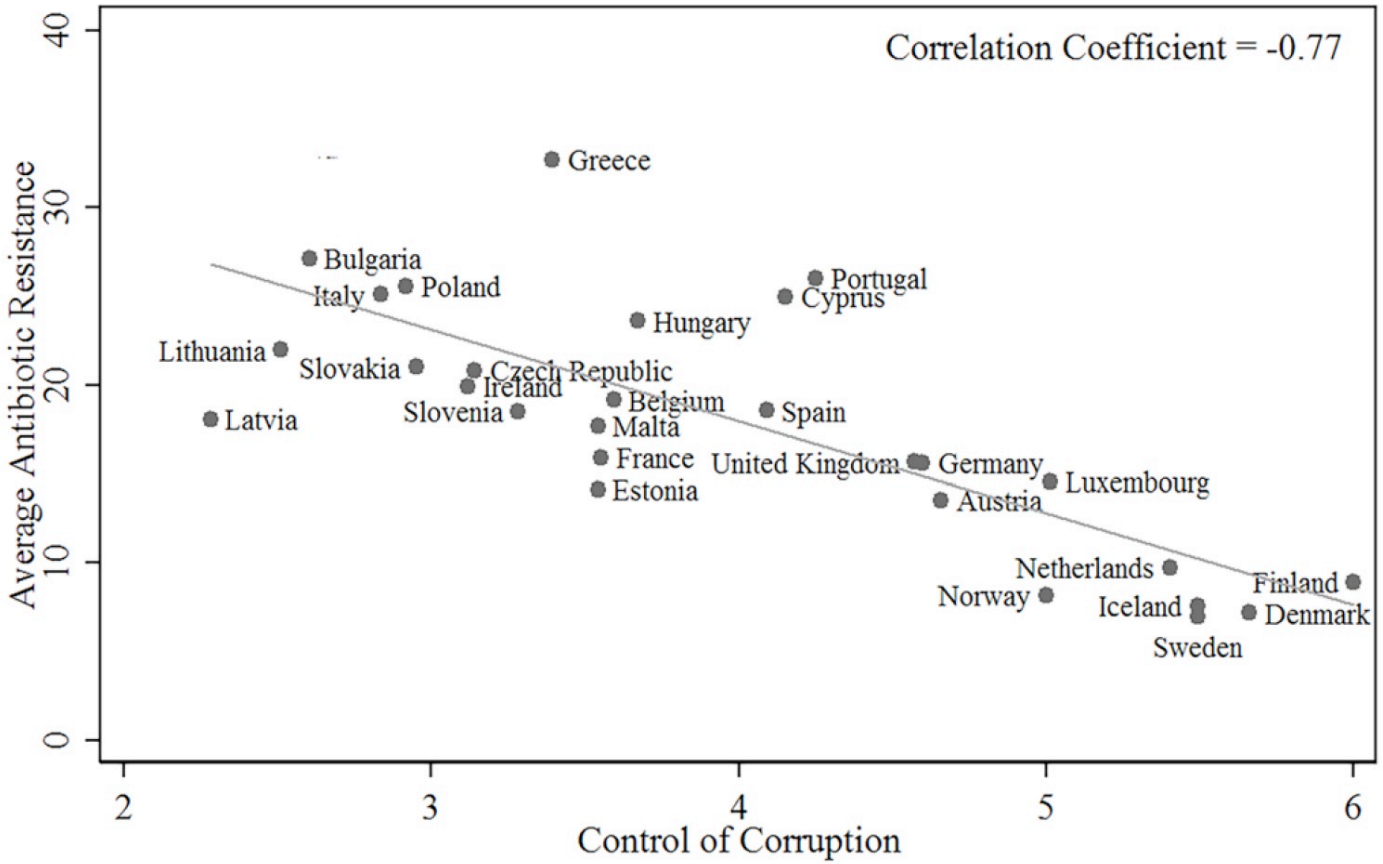
Table 4. Univariable and Multivariable Meta-Regression Models Predicting Log (Odds) of Bloodstream Infection due to Gram Negative Bacteria.

	Univariable Models			Multivariable Models		
Characteristic	Coefficient	95% CI	P-Value	Coefficient	95% CI	P-Value
Longitude	0.003	0.0001 to 0.005	0.042	–	–	–
Latitude	−0.008	−0.013 to 0.003	0.004	–	–	–
Latitude^2	−0.0004	−0.0006 to −0.0001	0.017	−0.0005	−0.0009 to −0.0007	0.024
Log_{10}(Per-Capita GDP)	−0.416	−0.628 to −0.204	0.001	–	–	–
% GDP on Healthcare	−0.079	−0.114 to −0.044	<0.001	−0.077	−0.118 to −0.035	0.002
Income Inequality (Gini Coefficient)	−0.654	−3.290 to 1.981	0.61	–	–	–
Population Density	−0.0003	−0.002 to 0.001	0.72	–	–	–
Mean Annual Temperature	0.040	0.014 to 0.065	0.004	−0.039	−.093 to 0.013	0.148
Mean Annual Precipitation	0.0003	−0.0001 to 0.0007	0.17	–	–	–

RESEARCH ARTICLE

Antimicrobial Resistance: The Major Contribution of Poor Governance and Corruption to This Growing Problem

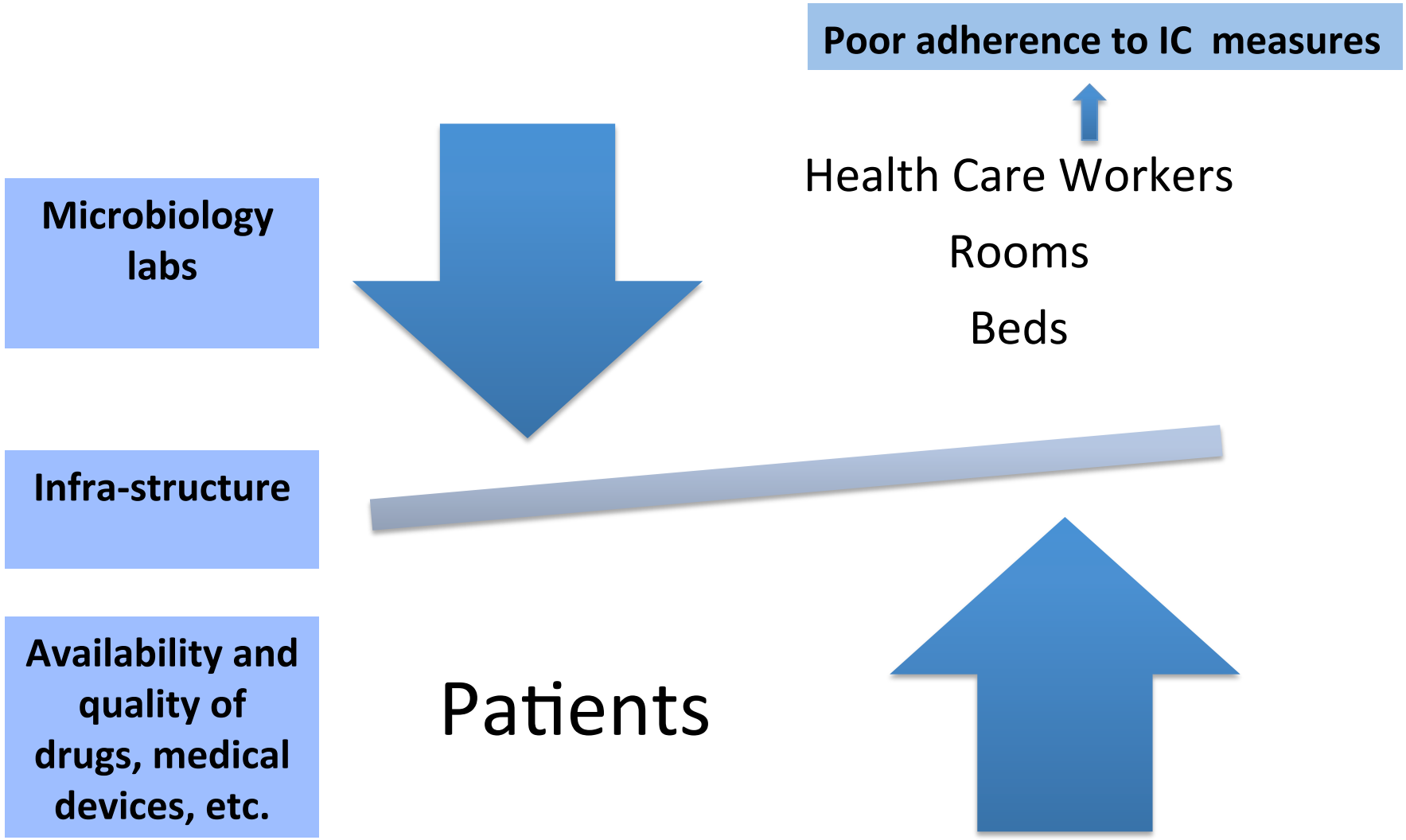
Peter Collignon[1,2]*, Prema-chandra Athukorala[3,4], Sanjaya Senanayake[5,6], Fahad Khan[3]



Note: Average antibiotic resistance is from EARS-Net database of the European Centre for Disease Prevention
The control of corruption indicator is from International Country Risk Guide

PloSOne, 10(3), 2015

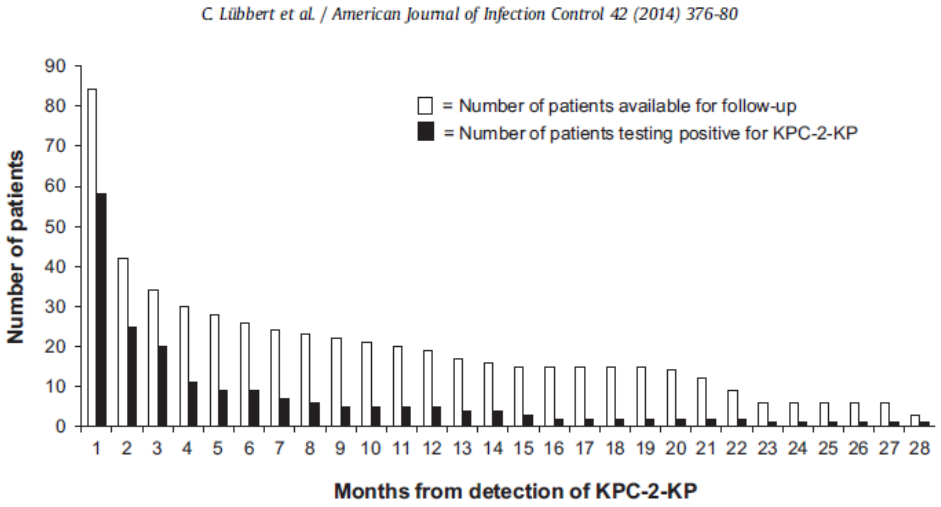
Spread of Antimicrobial Resistance



KPC Colonization for prolonged periods

Long-term carriage of KPC-2-producing *K.pneumoniae* in Germany

Acompanhou 86 pacientes após infecção ou colonização: 1m, 3m, 6m, 1 a e 2 anos
Swab retal ou fezes
Cultura e PCR
Resolução: min 3 PCR neg consecutivos com intervalo mínimo de 48 horas



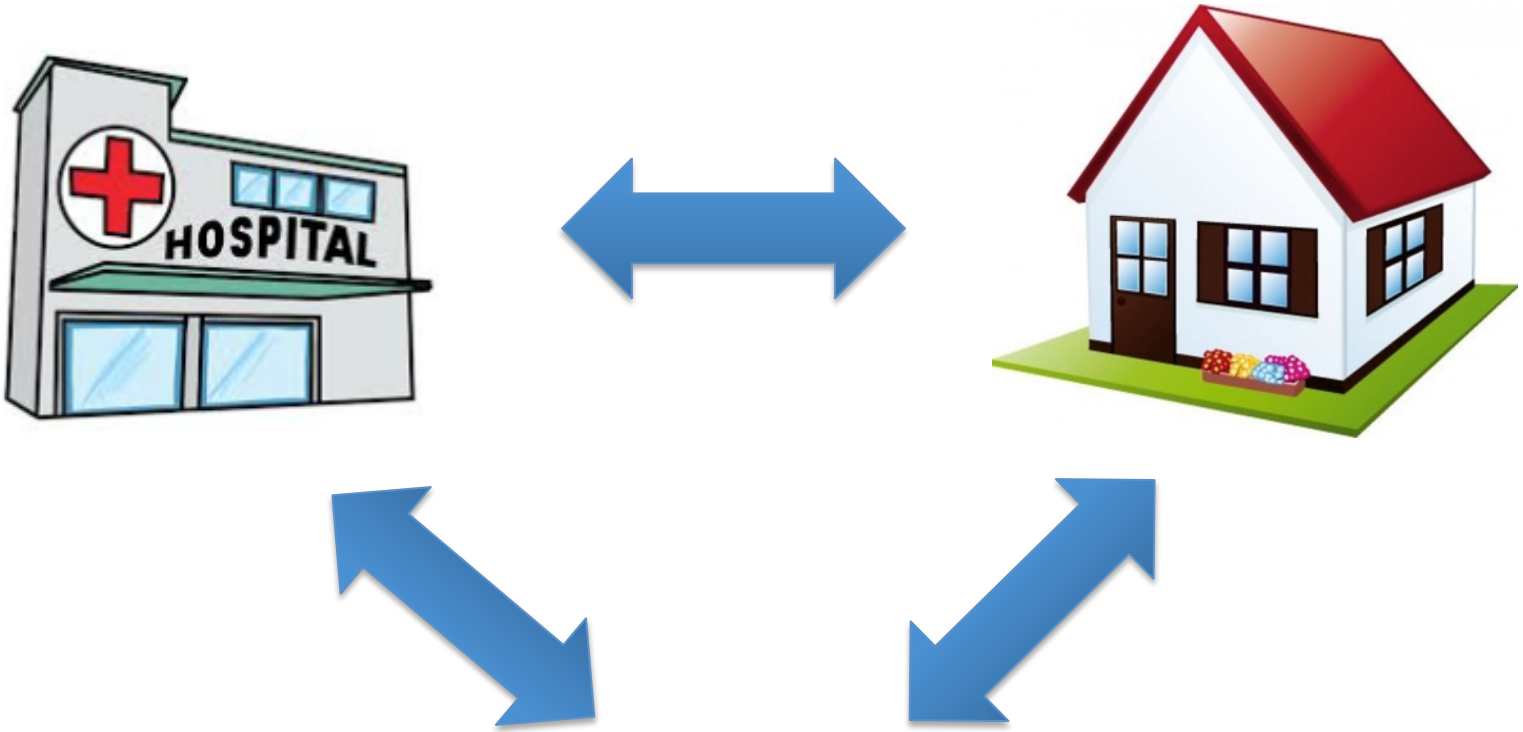
Aderência:
98% (84/86) 1 m
40% (34/86) 3 m
30% (26/86) 6 m
22% (19/86) 12 m
7% (6/86) 24 m

Table 1
Number and characteristics of patients along the 2 years of follow-up

Follow-up period from initial acquisition of KPC-2-KP	Patients available for follow-up	Patients testing KPC-positive
1 month	84 (98)	58 (69)
3 months	34 (40)	20 (59)
6 months	26 (30)	9 (35)
12 months	19 (22)	5 (26)
24 months	6 (7)	1 (17)

Lübbert et alAm J Infect Control. 2014 Apr;42(4):376-80.

MDR Spread



Environmental contamination

APPLIED AND ENVIRONMENTAL MICROBIOLOGY, May 2006, p. 3743–3745 Vol. 72, No. 5
0099-2240/06/$08.00+0 doi:10.1128/AEM.72.5.3743–3745.2006

Multiniche Screening Reveals the Clinically Relevant Metallo-β-Lactamase VIM-2 in *Pseudomonas aeruginosa* Far from the Hospital Setting: an Ongoing Dispersion Process?

Sandra Quinteira[1,2] and Luísa Peixe[1]*

REQUIMTE, Laboratório de Microbiologia, Faculdade de Farmácia, Universidade do Porto, Porto,[1] and Instituto Politécnico da Saúde do Norte-ESSVA, VN Famalicão,[2] Portugal

Received 9 September 2005/Accepted 8 February 2006

A screening study of the presence of metallo-β-lactamases (IMP and VIM types and SPM-1) in isolates from different nonhospital sources was conducted, and it revealed the presence of bla_{VIM-2}, associated with the In58 class 1 integron, in two unrelated *Pseudomonas aeruginosa* strains from aquatic habitats. The results suggest that the hospital setting was the possible origin of these bla_{VIM-2}-carrying strains.

Two *P. aeruginosa* isolates:

R2, obtained from a river,

E58, obtained from sewage downstream from the Hospital Porto

They were collected from geographically distant locations and that there was no physical link between the two aquatic ecosystems.

bla_{VIM-2} carried by In58

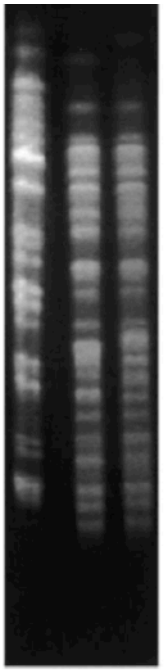


FIG. 1. PFGE patterns of SpeI-digested genomic DNA of bla_{VIM-2}-positive *P. aeruginosa* isolates. Lane A, isolate E58; lane B, hospital isolate IPO-3; lane C, isolate R2.

	Species	Minimal inhibitory concentration (mg/L)												Typical bla_{NDM-1} antibiogram	Genetic location	Plasmid		
		CTX	CTZ	IMP	MER	ATM	GEN	AMI	TOB	CIP	FOS	TIG	COL			Size	Stability*	Type
From waste seepage																		
B-3-2	*Pseudomonas putida*	64	4	0·5	2	64	0·25	1	0·25	0·125	256	4	0·125	No	Plasmid	ND	No	--
1-19	*Pseudomonas pseudoalcaligenes*	64	64	2	4	32	2	1	4	16	16	2	0·25	No	Plasmid	ND	No	--
3-1	*Escherichia coli*	512	256	16	32	64	8	4	16	32	16	4	0·5	Yes	Plasmid	140 kb	Yes	A/C
21-9	*Pseudomonas oryzihabitans*	16	4	2	2	16	0·25	2	0·25	0·25	4	4	0·25	No	Plasmid	ND	No	--
25-4	*Klebsiella pneumoniae*	512	256	32	128	64	32	64	16	32	256	8	0·25	Yes	Plasmid	140 kb	Yes	--
33-5	*Escherichia coli*	256	256	64	64	64	16	32	64	32	2	0·5	0·125	Yes	Plasmid	140 kb	Yes	A/C
65-4	*Escherichia coli*	256	128	8	64	32	16	2	32	16	16	0·5	0·125	Yes	Plasmid	140 kb	Yes	--
65-5	*Shigella boydii*	512	512	4	16	256	32	16	8	64	2	4	1	Yes	Plasmid	250 kb	Yes	--
72-28	*Sutonella indologenes*	32	4	2	4	32	1	2	0·5	0·25	>1024	8	2	No	Plasmid	--	No	--
79-6	*Pseudomonas pseudoalcaligenes*	128	16	2	4	32	4	2	2	8	16	8	0·25	No	Plasmid	280 kb	Yes	--
107-5	*Aeromonas caviae*	64	32	16	8	8	8	2	8	16	128	8	0·25	Yes	Chromo	--	Yes	--
107-7	*Pseudomonas putida*	64	1	32	4	0·25	16	16	32	16	256	16	0·25	No	Plasmid	250 kb	Yes	--
116-4	*Stenotrophomonas maltophilia*	256	256	128	64	64	32	64	16	64	256	16	0·5	Yes	Plasmid	250 kb	Yes	--
116-14	*Vibrio cholerae*	>256	>256	8	8	2	1	8	2	2	64	0·5	8	Yes	Plasmid and chromo	400 kb	Yes	--
116-17	*Vibrio cholerae*	>256	>256	16	1	2	1	0·5	2	2	64	0·5	8	Yes	Plasmid	170 kb	Yes	A/C
117-4	*Citrobacter freundii*	128	128	64	128	64	32	64	32	32	4	2	0·5	Yes	Plasmid	140 kb	Yes	A/C
From tap water																		
W32-17	*Achromobacter spp*	256	256	4	4	64	32	16	32	32	32	0·5	0·125	No	Plasmid	ND	No	--
W38-14	*Kingella denitrificans*	32	32	4	16	8	8	2	1	4	4	1	0·5	No	Plasmid	ND	No	--
W38-16	*Achromobacter spp*	128	128	4	2	32	32	16	4	16	32	0·5	0·25	No	Plasmid	ND	No	--
W38-17	*Pseudomonas aeruginosa*	256	256	32	32	16	32	64	32	16	256	8	0·5	Yes	Plasmid	ND	No	--

CTX=cefotaxime. CTZ=ceftazidime. IMP=imipenem. MER=meropenem. ATM=aztreonam. GEN=gentamicin. AMI=amikacin. TOB=tobramycin. CIP=ciprofloxacin. FOS=fosfomycin. TIG=tigecycline. COL=colistin. ND=not determined. Chromo=chromosome. *Plasmids were deemed unstable if lost within a 48-h period during subculturing without antibiotic selection.

Table 1: **Minimal inhibitory concentration of antimicrobials and genetic characteristics of NDM-1-positive bacteria**

Walsh et al. Lancet Infect Dis. 2011 May;11(5):355-62.

Warning: Bacterial Resistance

Sir Alexander Fleming

"The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant."

Selective Pressure Exerted by Antimicrobials

Excerpted from the 1945 Nobel Prize lecture by Alexander Fleming, the discoverer of Penicillin (accessible at http://www.nobelprize.org/nobel_prizes/medicine/laureates/1945/)

Large Nosocomial Outbreak of Colistin-Resistant, Carbapenemase-Producing *Klebsiella pneumoniae* Traced to Clonal Expansion of an *mgrB* Deletion Mutant

Tommaso Giani,[a] Fabio Arena,[a] Guendalina Vaggelli,[b] Viola Conte,[a] Adriana Chiarelli,[a] Lucia Henrici De Angelis,[a] Rossella Fornaini,[c] Maddalena Grazzini,[d] Fabrizio Niccolini,[d] Patrizia Pecile,[b] Gian Maria Rossolini[a,b,e,f]

Department of Medical Biotechnologies, University of Siena, Siena, Italy[a]; Clinical Microbiology and Virology Unit,[b] Hospital Pharmacy Unit,[c] and Hospital Medical Direction,[d] Florence Careggi University Hospital, Florence, Italy; Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy[e]; Don Carlo Gnocchi Foundation, Florence, Italy[f]

TABLE 1 Observed BSI caused by *K. pneumoniae* during the study period[a]

Yr	No. of *K. pneumoniae* BSI	No. (%) of *K. pneumoniae* isolates that were:			
		Carbapenemase sensitive	Carbapenemase resistant[b]	COL^r CRKP[b,c]	Colistin consumption[d]
2009	29	28 (97)	1 (3)	0 (0; 0)	0.004
2010	49	38 (78)	11 (22)*	1 (3; 9)	0.013
2011	76	44 (58)	32 (42)*	4 (5; 12)	0.018
2012	128	46 (36)	82 (64)*	53 (41; 65)*	0.014
2013	93	32 (34)	61 (66)	35 (38; 57)	0.015
Total	375	188 (50)	187 (50)	93 (25; 50)	

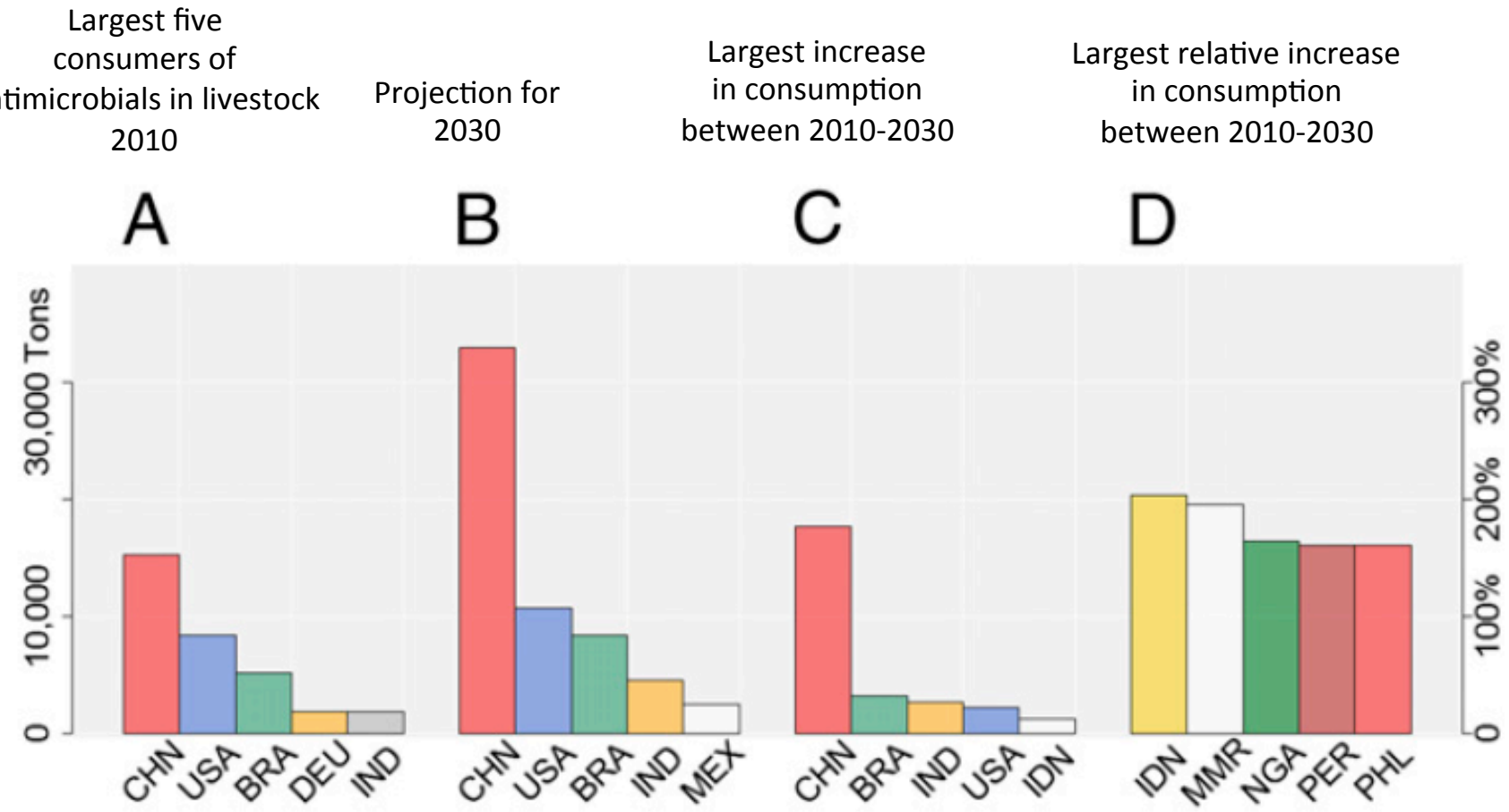
[a] Numbers and proportions of BSI cases caused by carbapenem-susceptible, carbapenem-resistant, and carbapenem- and colistin-resistant (COL^r CRKP) strains. For patients with recurrent BSI episodes, only the first episode was considered.

[b] An asterisk indicates that the difference in the proportion of resistant isolates was statistically significantly different ($P < 0.05$) from that for the previous year. For statistical analysis, the chi-squared test with Yates' correction or Fisher's exact test (as appropriate) was used.

[c] Proportions are reported in relation to both *K. pneumoniae* BSI and CRKP BSI. (Values are shown in parentheses and separated by semicolons.) COL^r *K. pneumoniae* was only observed among CRKP cases.

[d] Data on colistin consumption in the hospital during the study period, expressed as the defined daily dose per 1,000 inhabitants per day, are also reported.

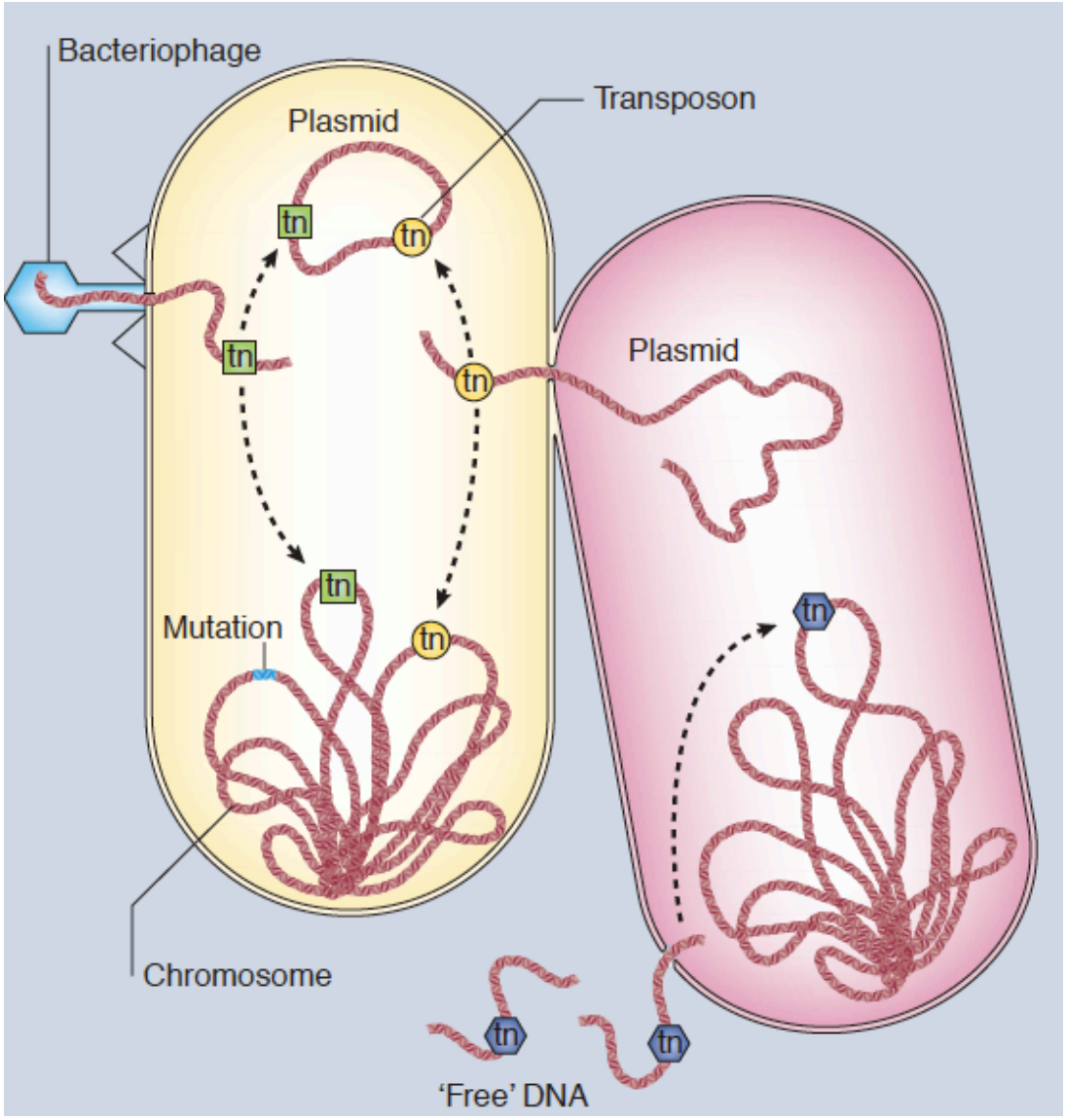
Global Trends in Antimicrobial Use in Food Animals



CHN, China; USA, United States; BRA, Brazil; DEU, Germany; IND, India; MEX, Mexico; IDN, Indonesia; MMR, Myanmar; NGA, Nigeria; PER, Peru;PHL, Philippines

Van Boeckel TP et al. Proc Natl Acad Sci U S A. 2015 May 5;112(18):5649-54.

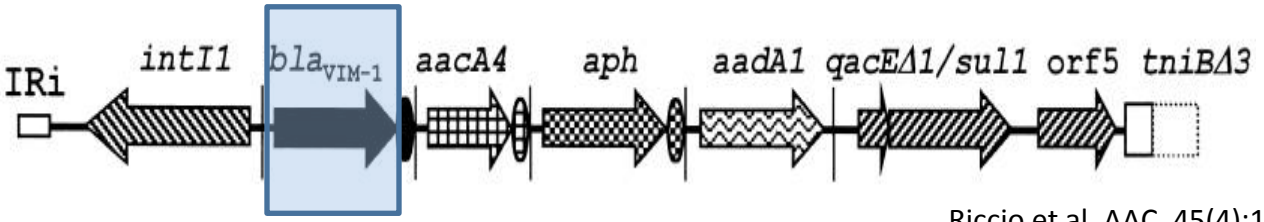
Spread of Genes Encoding for Resistance



Levy & Marshall. Nature Medicine 10, S122 - S129 (2004)

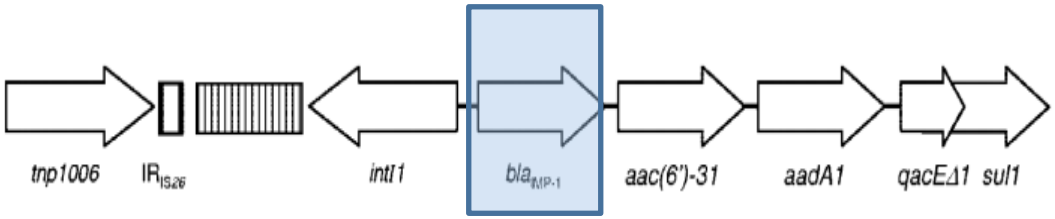
Metallo-β-Lactamases genes carried by mobile genetic elements like Integrons

VIM-1



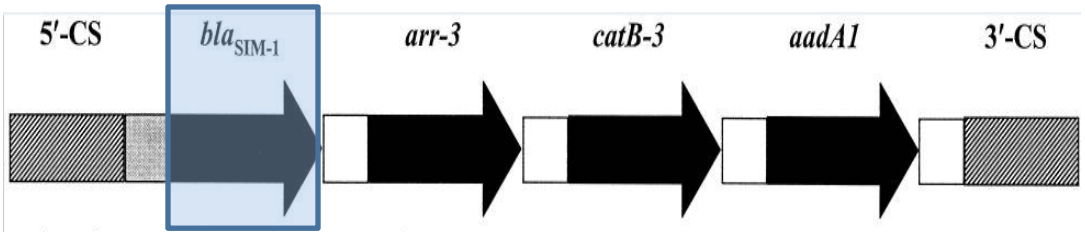
Riccio et al. AAC. 45(4):1249-53, 2001.

IMP-1



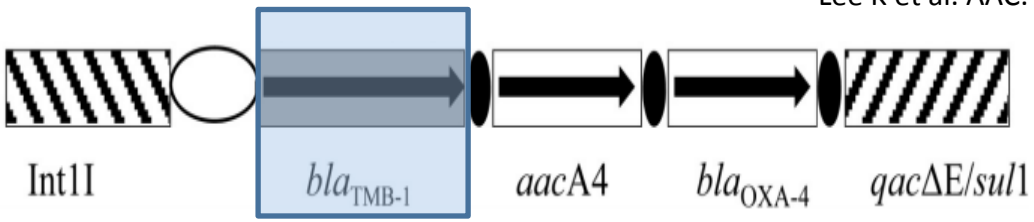
Mendes RE et al. AAC. 51(7): 2611-4, 2007.

SIM-1



Lee K et al. AAC. 49(11):4485-91, 2005.

TMB-1



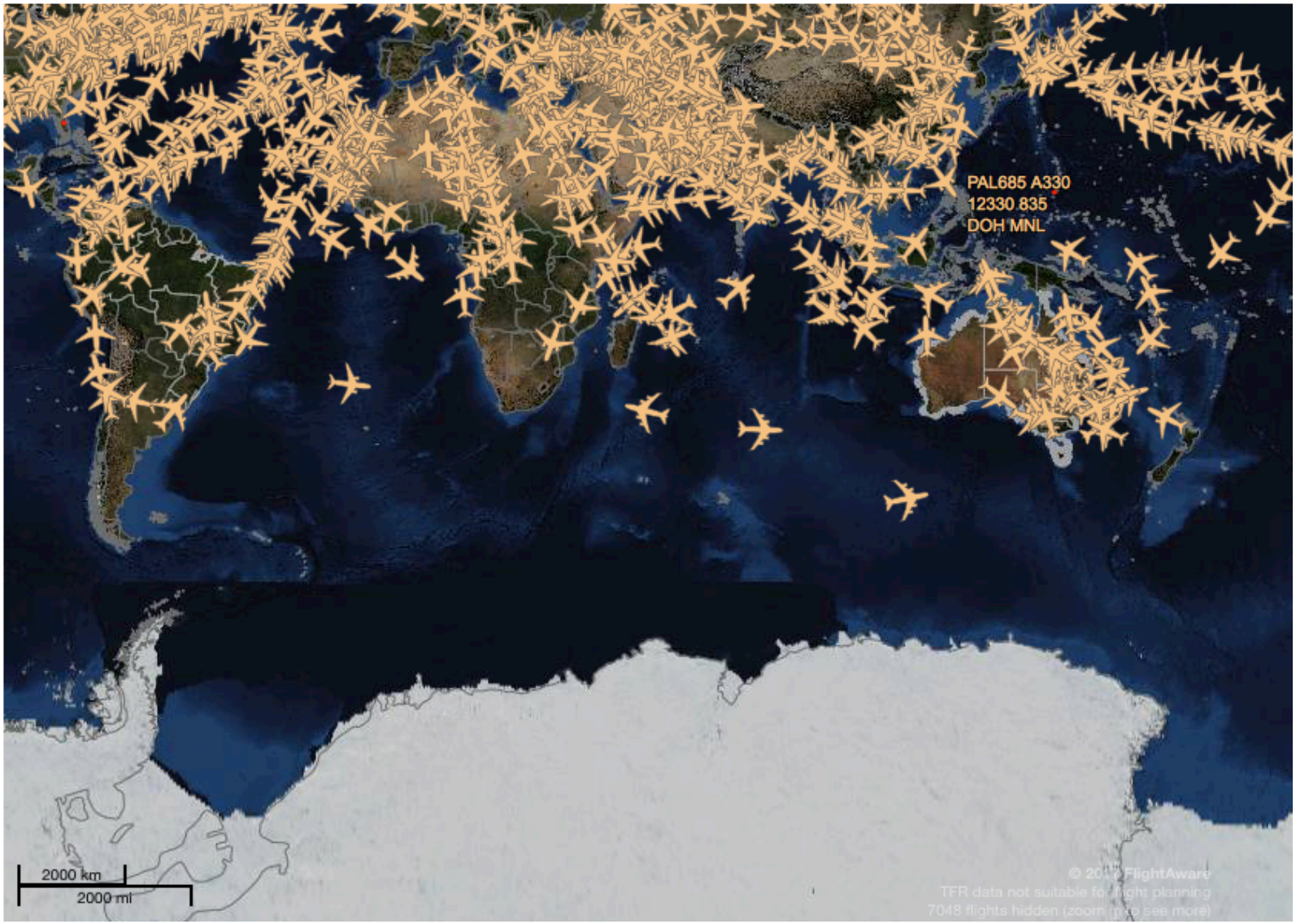
El Salabi et al. AAC. 56(5):2241-5, 2012.

Globalization

- **International travel – leisure or medical tourism;**
- **International trade (food);**
- **Immigration**

Is there any safe place?

Tráfego Aéreo



https://pt.flightaware.com/live/

10/Set/17 – 22:05h

Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study

Karthikeyan K Kumarasamy, Mark A Toleman, Timothy R Walsh, Jay Bagaria, Fafhana Butt, Ravikumar Balakrishnan, Uma Chaudhary, Michel Doumith, Christian G Giske, Seema Irfan, Padma Krishnan, Anil V Kumar, Sunil Maharjan, Shazad Mushtaq, Tabassum Noorie, David L Paterson, Andrew Pearson, Claire Perry, Rachel Pike, Bhargavi Rao, Ujjwayini Ray, Jayanta B Sarma, Madhu Sharma, Elizabeth Sheridan, Mandayam A Thirunarayan, Jane Turton, Supriya Upadhyay, Marina Warner, William Welfare, David M Livermore, Neil Woodford

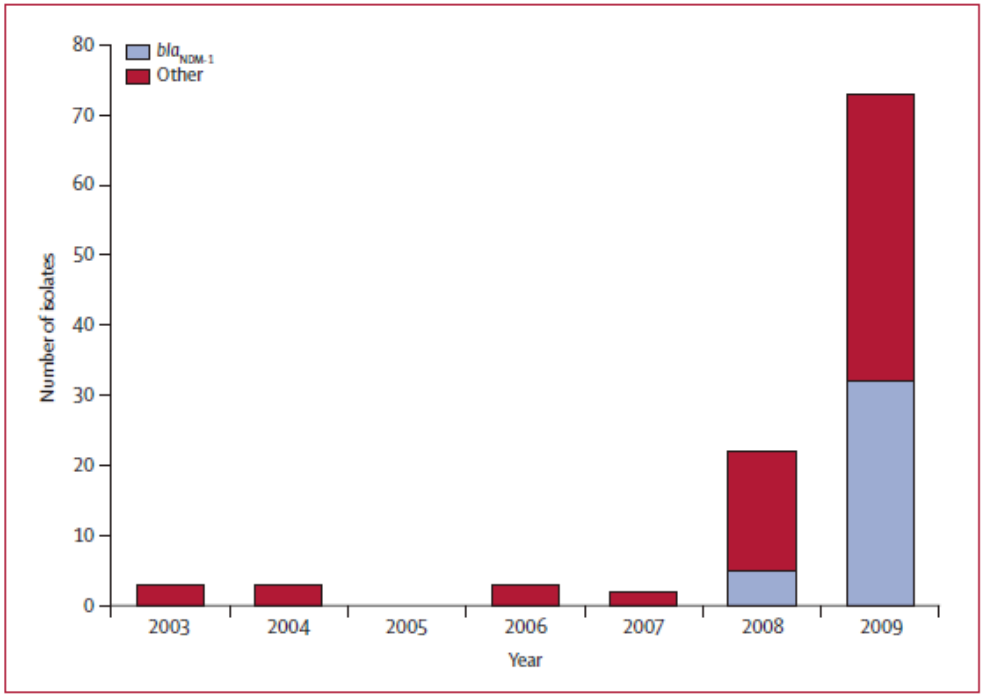


***Figure 1*: Numbers of carbapenemase-producing Enterobacteriaceae referred from UK laboratories to the UK Health Protection Agency's national reference laboratory from 2003 to 2009**
The predominant gene is bla_{NDM-1}, which was first identified in 2008. The other group includes diverse producers of KPC, OXA-48, IMP, and VIM enzymes.

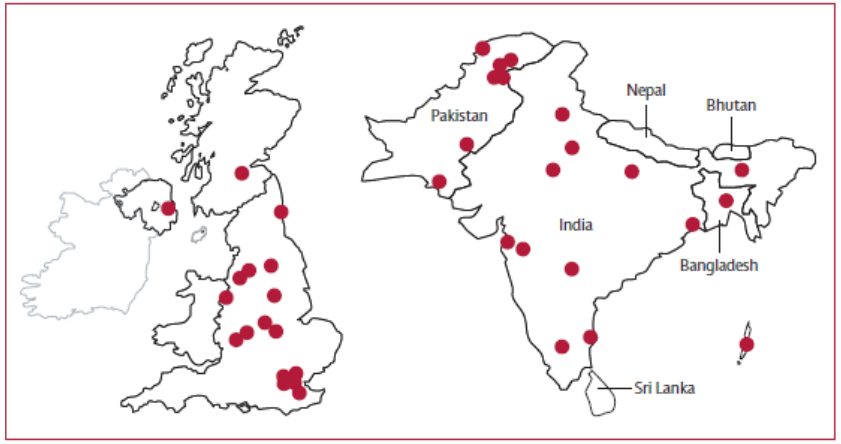


***Figure 5*: Distribution of NDM-1-producing Enterobacteriaceae strains in Bangladesh, Indian, Pakistan, and the UK**

International Travel
Medical Tourism

Lancet Infect Dis 2010;10:597-602.

OPEN ACCESS Freely available online

PLOS ONE

Risk Factors for Community-Acquired Urinary Tract Infections Caused by ESBL-Producing *Enterobacteriaceae* –A Case–Control Study in a Low Prevalence Country

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1 Department of Medical Microbiology, Vestre Viken Hospital Trust, Bærum, Norway, **2** Department of Microbiology and Infection Control, Reference Centre for Detection of Antimicrobial Resistance, University Hospital of North Norway, Tromsø, Norway, **3** Department of Medical Biology, Research Group for Host-Microbe Interactions, Faculty of Health Sciences, University of Tromsø, Tromsø, Norway, **4** Unit of Biostatistics and Epidemiology, Oslo University Hospital, Oslo, Norway

Table 4. Independent risk factors of ESBL positive community acquired urinary tract infection identified using multivariate logistic regression analysis.

Variable	Level	Adjusted OR	95% CI	P
Travelling to Asia, Middle East or Africa[a]				
- During the past 6 weeks	yes/no	21	4.5–97	<0.001
- Between the previous 6 weeks to 24 months	yes/no	2.3	1.2–4.4	0.017
Use of fluoroquinolones the past 90 days	yes/no	16	3.2–80	<0.001
Use of β-lactams except mecillinam in the past 90 days	yes/no	5.0	2.1–12	<0.001
Diabetes mellitus	yes/no	3.2	1.0–11	0.051
Recreational freshwater swim past year	yes/no	2.1	1.0–4.3	0.040
Age	5 year increase	0.89	0.82–0.97	0.014
Number of fish meals per week	1 meal increase	0.68	0.51–0.90	0.008

[a]Only trips lasting >24 hours are included.

doi:10.1371/journal.pone.0069581.t004

Carbapenemase-producing *P. fluorescens*-like in Lula, Canada - 2014

Loja chinesa em Saskatoon, Canadá, que importava alimentos da Coréia do Sul

Table. Antimicrobial drug susceptibility of a VIM-2 producing *Pseudomonas fluorescens*–like organism isolated from food (squid), Saskatoon, Canada, January 2014

Antimicrobial drug	MIC
Ampicilin	>32
Amoxicillin + clavulanic acid	>32
Cefoxitin	>32
Ceftiofur	>8
Ceftriaxone	>64
Azithromycin	16
Chloramphenicol	16
Tetracycline	≤4
Naladixic acid	16
Ciprofloxacin	0.06
Gentamicin	≤0.25
Kanamycin	16
Streptomycin	≤32
Sulfisoxazole	32
Trimethoprim + sulfamethoxazole	0.5
Ertapenem*	>32
Tigecycline*	0.125
Colistin*	3

*MICs determined by Etest; all others were determined by broth microdilution.

Rubin et al. Emerg Infect Dis. 2014 Jul;20(7):1264-5.

Immigration

2 Israeli hospitals (Poriya & Nahariya)

- 19/29 (66%) children were colonized by ESBL-producing Enterobacteriaceae (20) and MRSA (1);
- 28/60 (47%) adults were colonized by CRE (5; NDM:2); MRSA (11); ESBL (7), e MDR-*A. baumanni* (5).

Peretz et al. Clin Infect Dis 2014;59:753e4.

"we feel that contact isolation of Syrian patients, until carriage of MDR isolates is ruled out, is paramount to prevent further spread of these pathogens"

http://alternate-theories.blogspot.com.br/2011/12/upcoming-war-with-syria-russia-and-iran.html

Why is bacterial resistance a major threat to public health worldwide?

1. Present in all geographic regions
2. Worldwide Spread of MDR clones
3. Increase length of hospitalization, morbidity and mortality rates, and costs
4. Threat to global trade, tourism….

Global Health

A global, coordinated action must be taken to tackle bacterial resistance because the epidemiological context is complex.


Thank you!