



Resistência Microbiana

Epidemiologia

Carlos Magno Castelo Branco Fortaleza

Professor Livre-Docente, Departamento de Doenças Tropicais

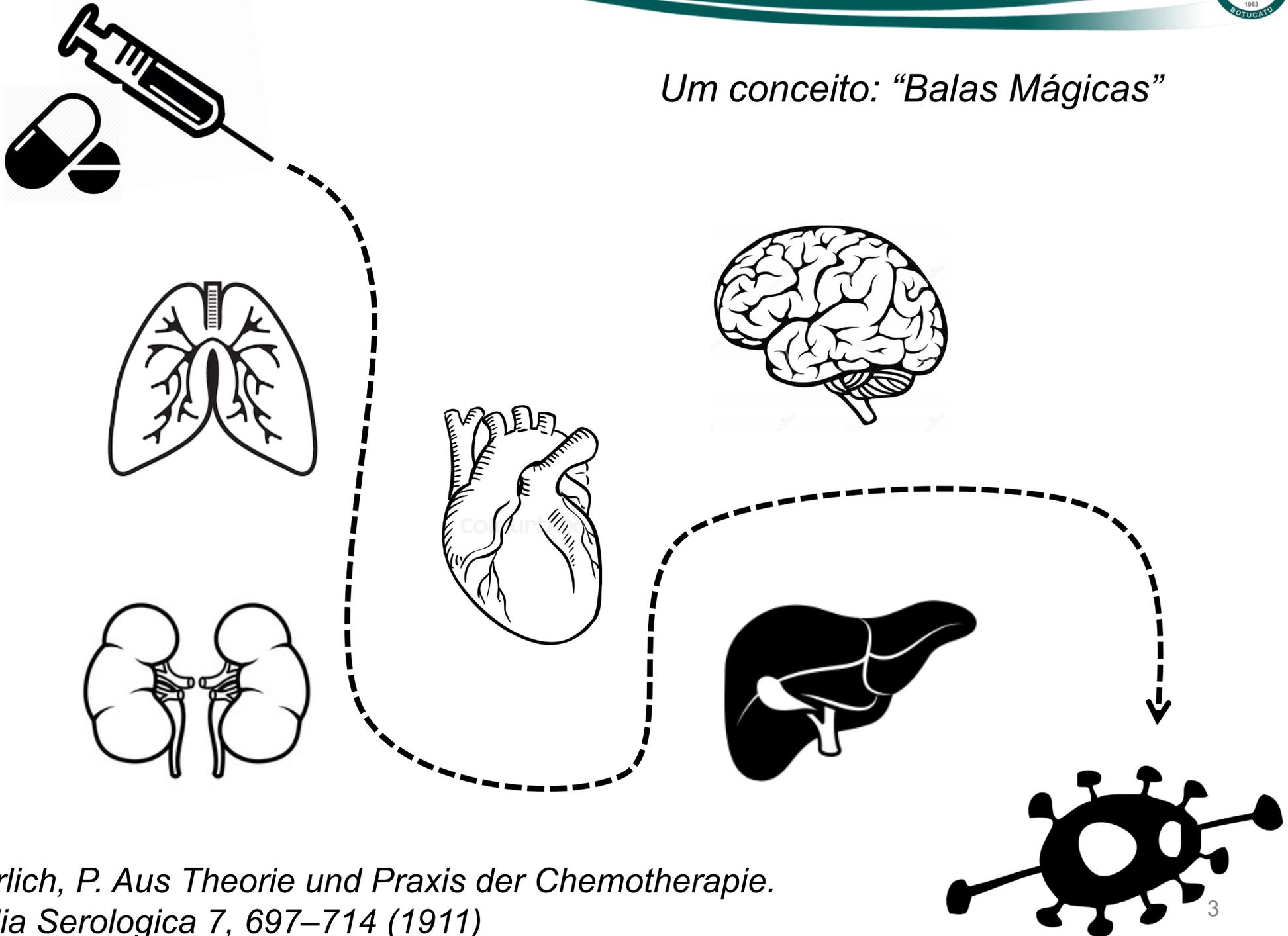
Faculdade de Medicina de Botucatu, Unesp

Presidente - Associação Paulista de Epidemiologia e Controle de Infecção Relacionada à Assistência à Saúde (APECIH)

- A crise da resistência microbiana.
- Microrganismos-problema em serviços de saúde.
- Uso de Antimicrobianos e resistência.
- Emergência e disseminação da resistência.
- Transmissão em ambientes de assistência.
- Resistência na comunidade e em hospitais.
- Medidas de prevenção e controle de resistência.

Plano de aula

Um conceito: “Balas Mágicas”



*Ehrlich, P. Aus Theorie und Praxis der Chemotherapie.
Folia Serologica 7, 697–714 (1911)*

Thanks to PENICILLIN
...He Will Come Home!



THRASH THE AXIS
BUY BONDS

**PENICILLIN
CURES
GONORRHEA**

THE GREAT CRIPPLER—STERILIZER

IN 4 HOURS

SEE YOUR DOCTOR TODAY

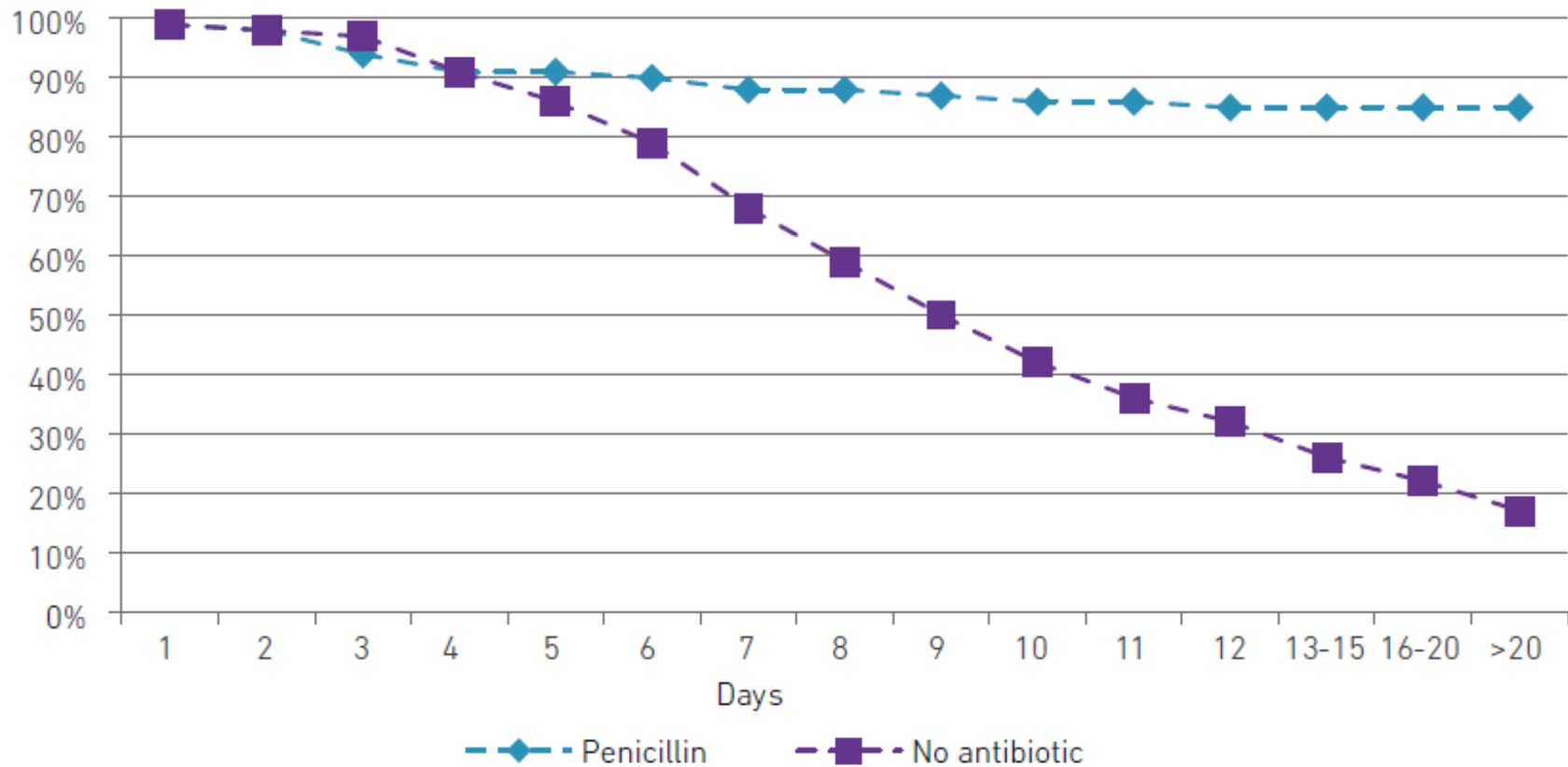
HE NOW HAS PENICILLIN
FOR YOUR TREATMENT

THE GREAT CRIPPLER IS FREE THROUGH APRIL 30, 1944
BY YOUR STATE AND CITY BUREAU OF HEALTH



Um conceito que salvou vidas

Figure 9 Survival after pneumococcal pneumonia with bloodstream infection before and after penicil treatment became available.





IDS

Bad Bugs, No Drugs: No ESKAPE!



Bad Bugs
Need Drugs



Ten new ANTIBIOTICS by 2020

“ESCAPE” the effects of
antibacterial drugs

Enterococcus faecium

Staphylococcus aureus

Klebsiella pneumoniae

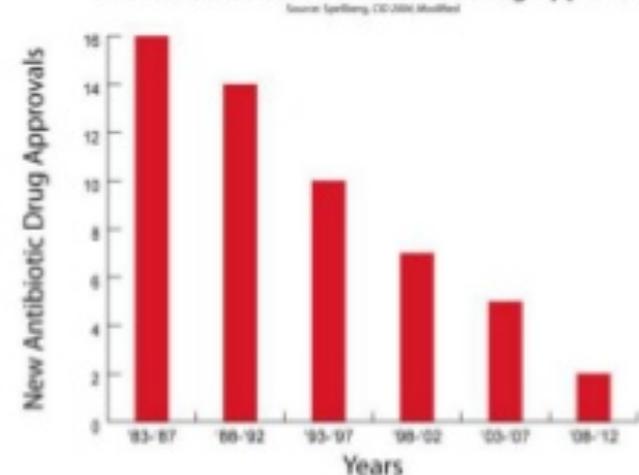
Acinetobacter baumannii

Pseudomonas aeruginosa

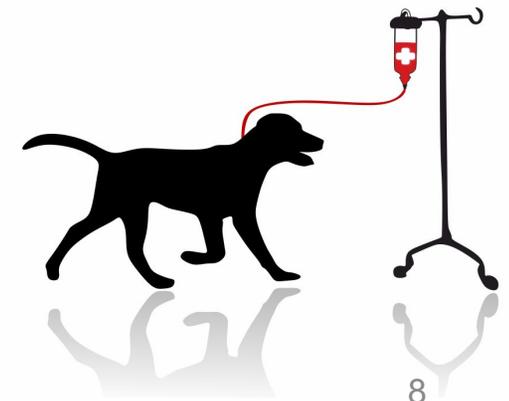
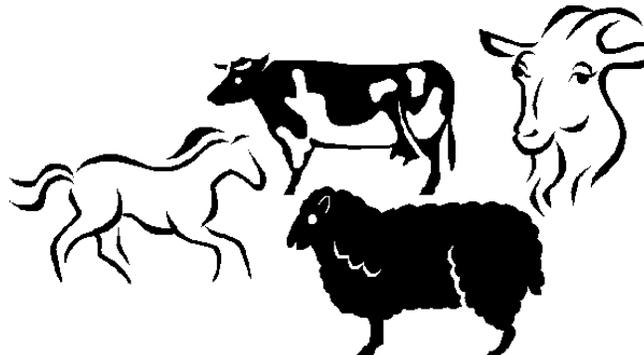
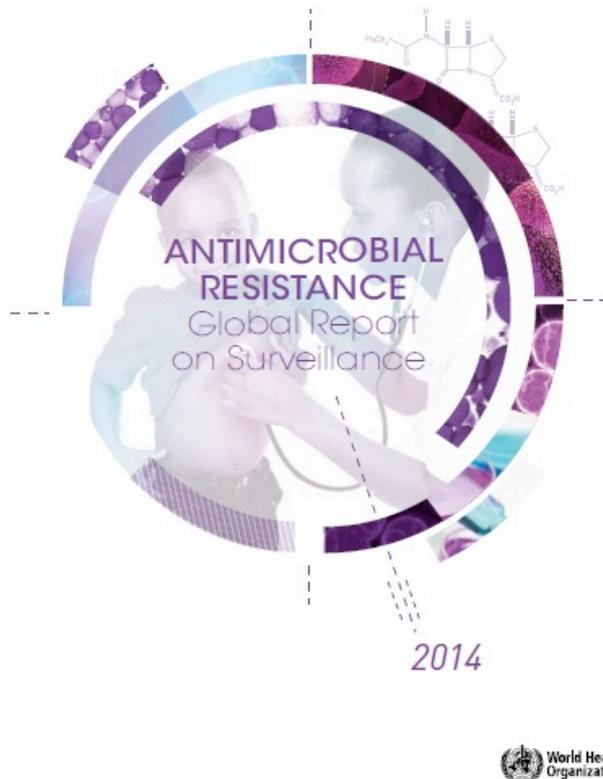
Enterobacter species

- Regulatory approvals for antibiotics have declined
- Clinically relevant resistance has increased

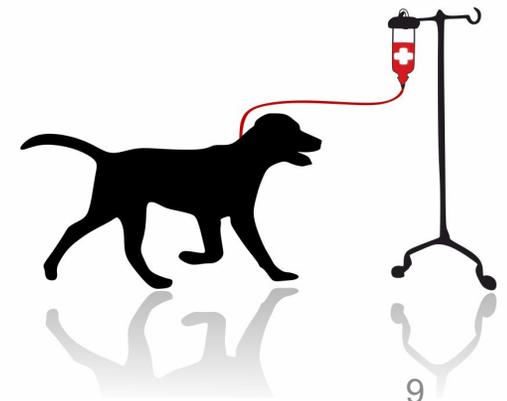
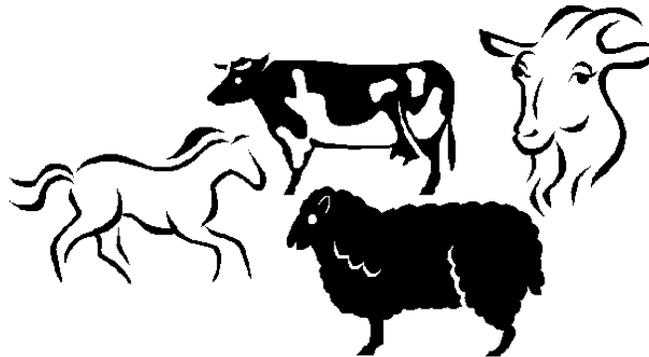
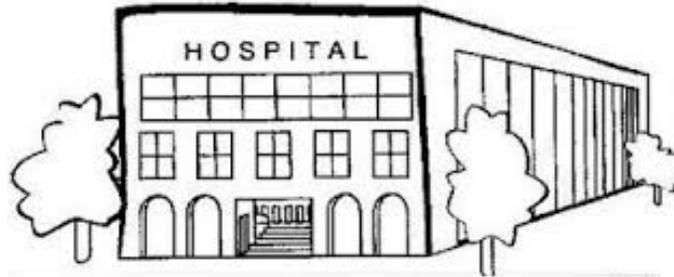
Dramatic Decrease in Antibiotic Drug Approvals



Um conceito em crise



Um conceito em crise



Antibiotic Resistance Is Prevalent in an Isolated Cave Microbiome

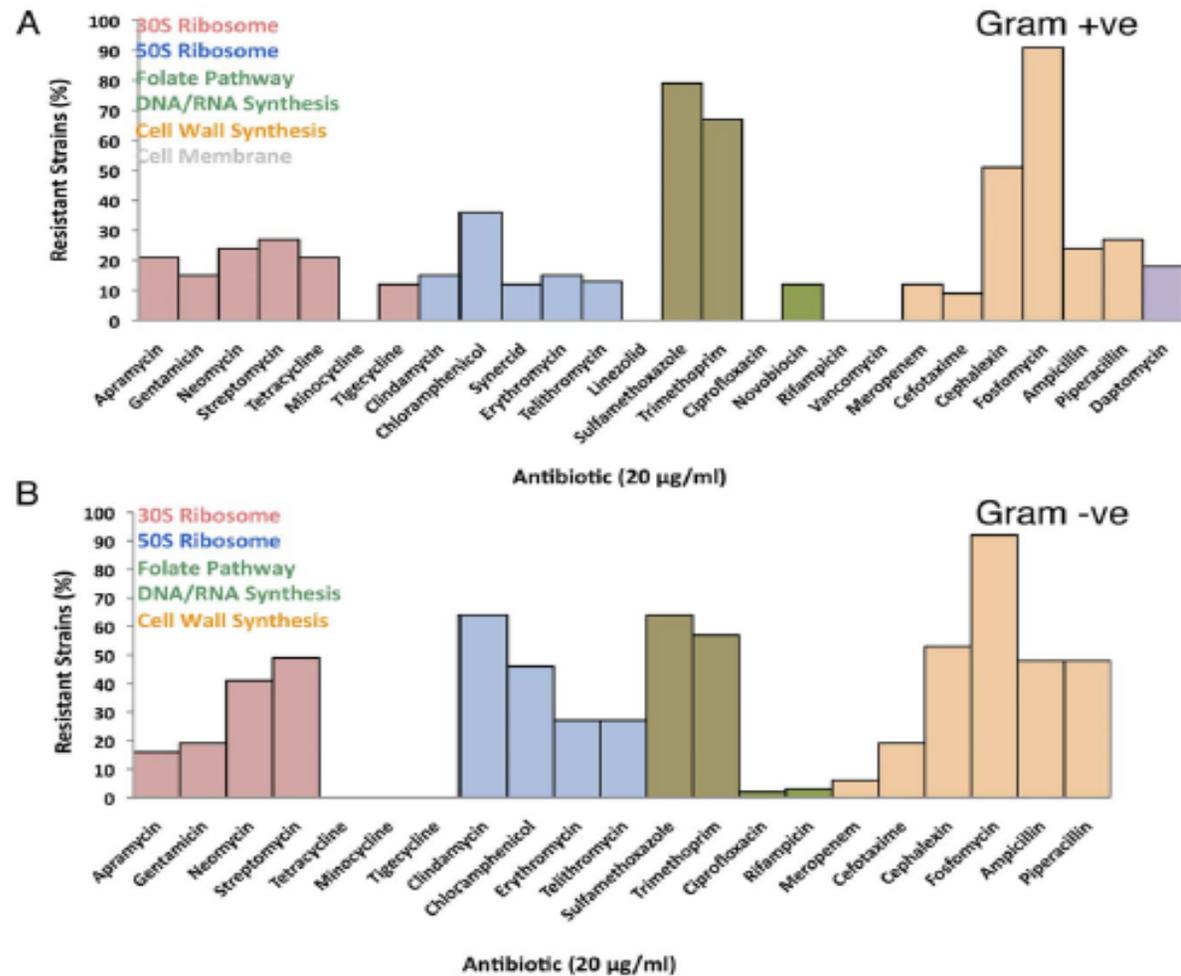
Kirandeep Bhullar¹, Nicholas Waglechner¹, Andrew Pawlowski¹, Kalinka Koteva¹, Eric D. Banks², Michael D. Johnston², Hazel A. Barton², Gerard D. Wright^{1*}

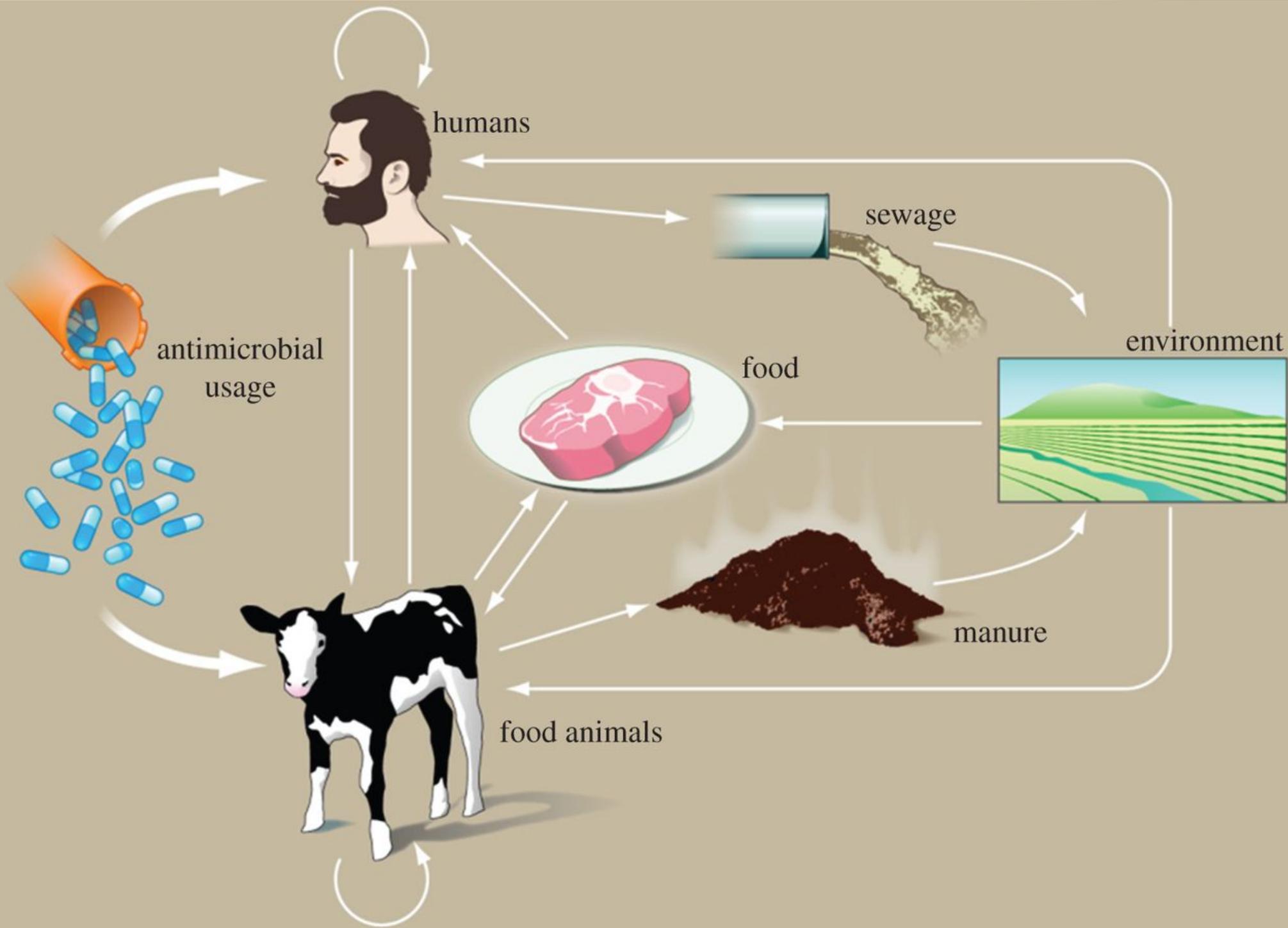


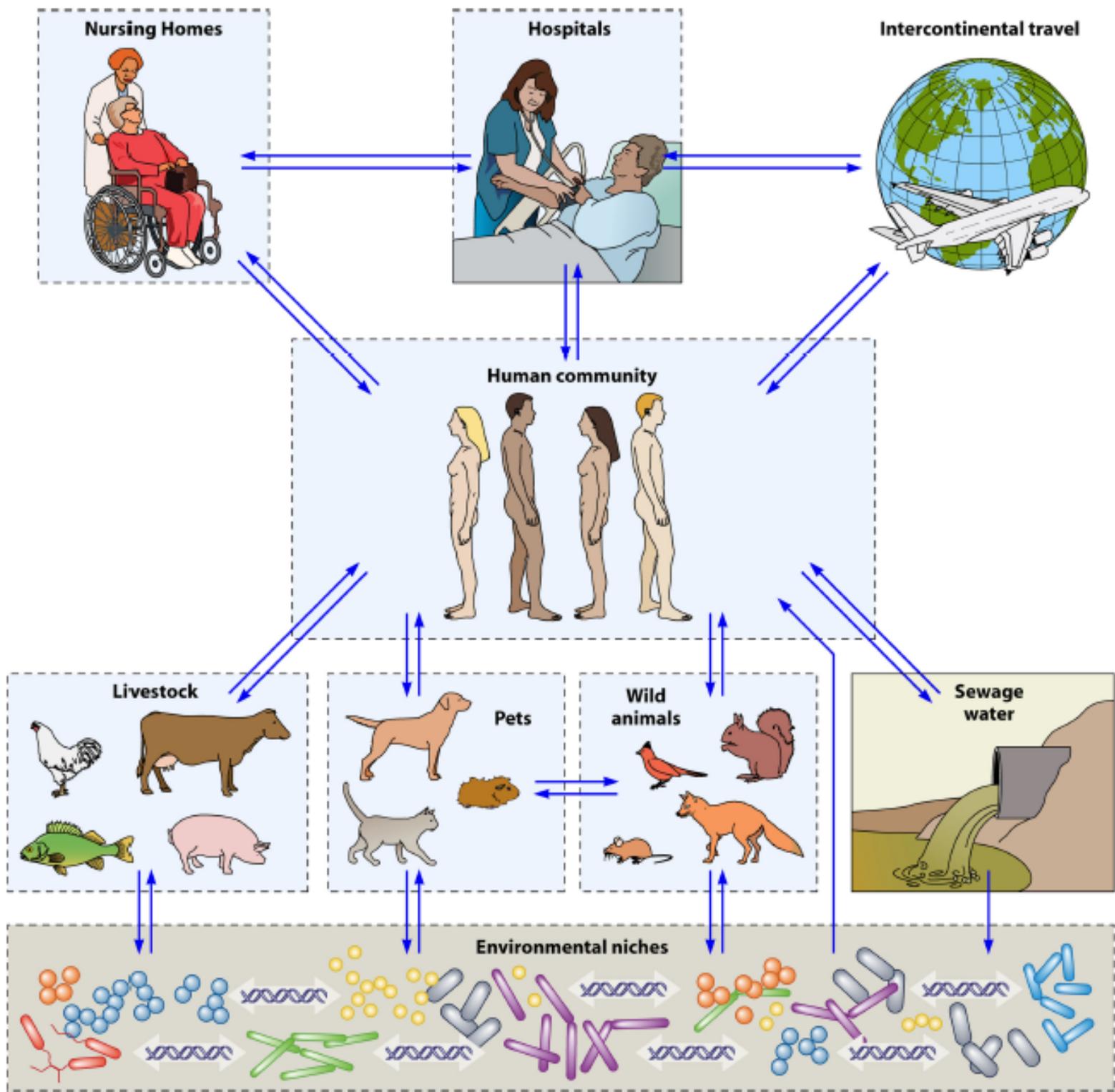
Lechuguilla Cave, New Mexico

Antibiotic Resistance Is Prevalent in an Isolated Cave Microbiome

Kirandeep Bhullar¹, Nicholas Waglechner¹, Andrew Pawlowski¹, Kalinka Koteva¹, Eric D. Banks², Michael D. Johnston², Hazel A. Barton², Gerard D. Wright^{1*}









Enterobactérias resistentes
aos carbapenêmicos (CRE)



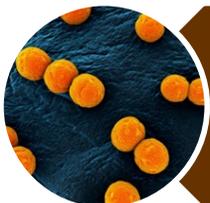
Acinetobacter baumannii resistente
aos carbapenêmicos (CRAB)



Pseudomonas aeruginosa resistente
aos carbapenêmicos (CRPsA)

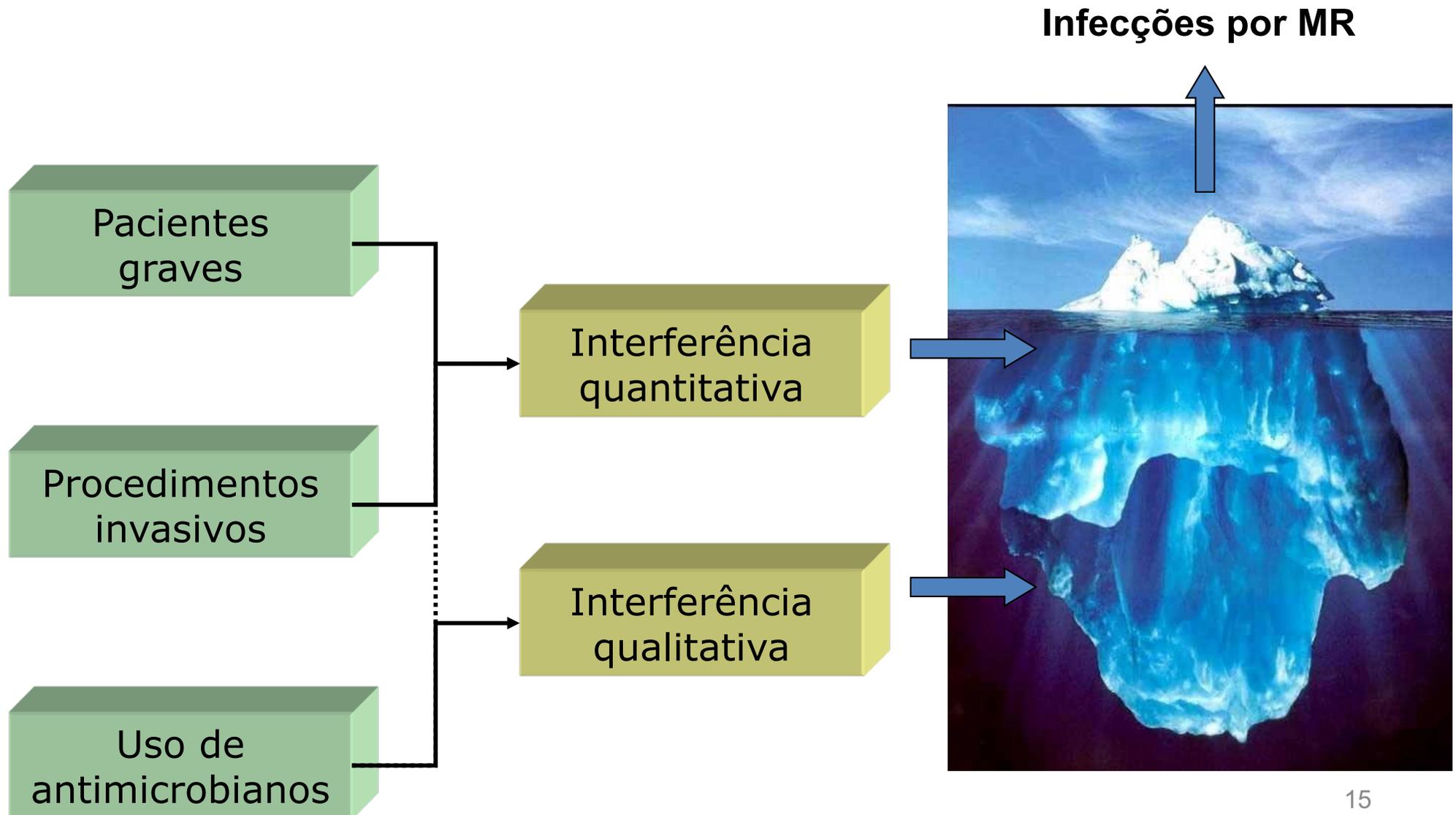


Staphylococcus aureus resistente
à Meticilina (MRSA)



Enterococcus spp. resistentes
à Vancomicina (VRE)

Ecologia da Resistência



The Commonality of Risk Factors for Nosocomial Colonization and Infection with Antimicrobial-Resistant *Staphylococcus aureus*, Enterococcus, Gram-Negative Bacilli, *Clostridium difficile*, and *Candida*

Nasia Safdar, MD, and Dennis G. Maki, MD

Idade

Dispositivos invasivos

Doença de base

Procedimentos

Internação prolongada

Uso de antimicrobianos

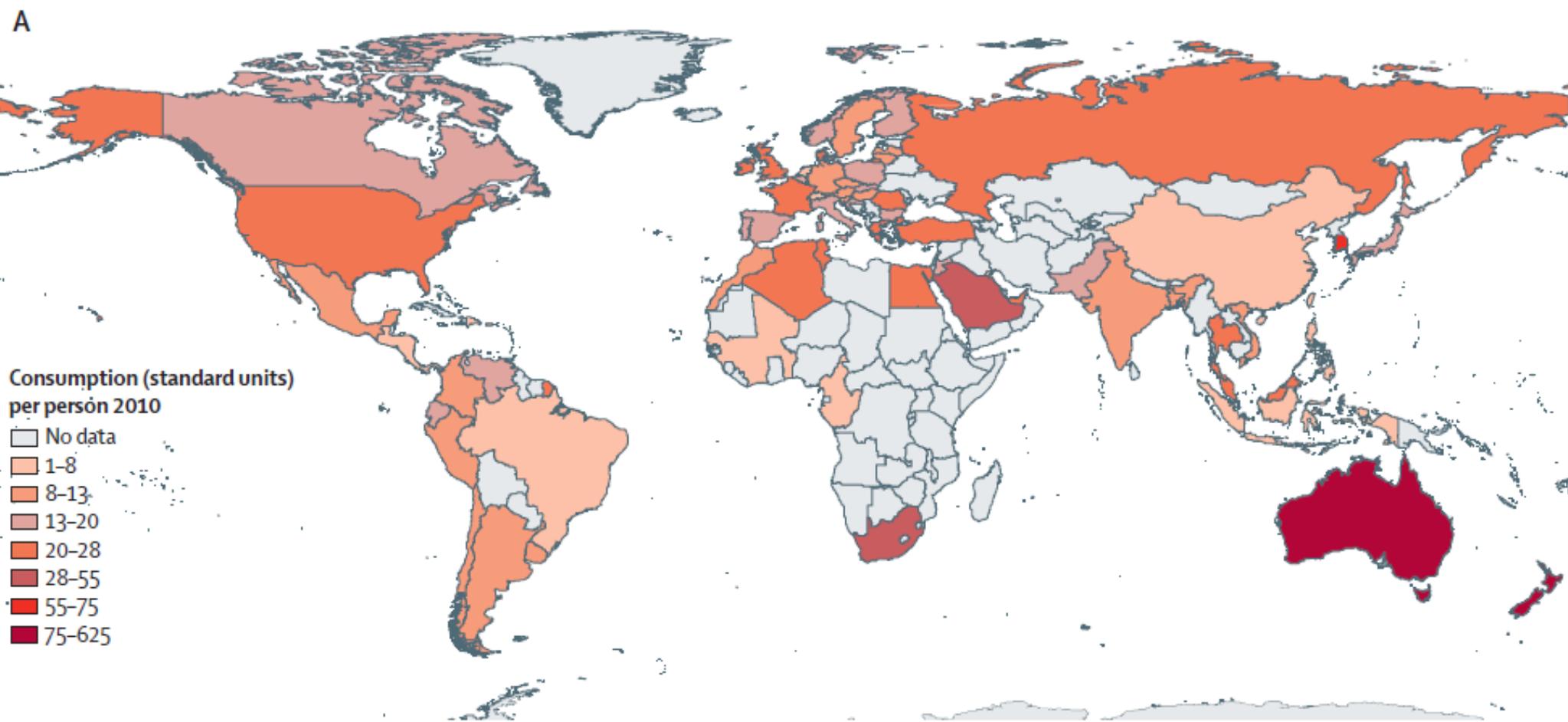
Transferência de outros hospitais

Imunossupressores

Uso de antimicrobianos

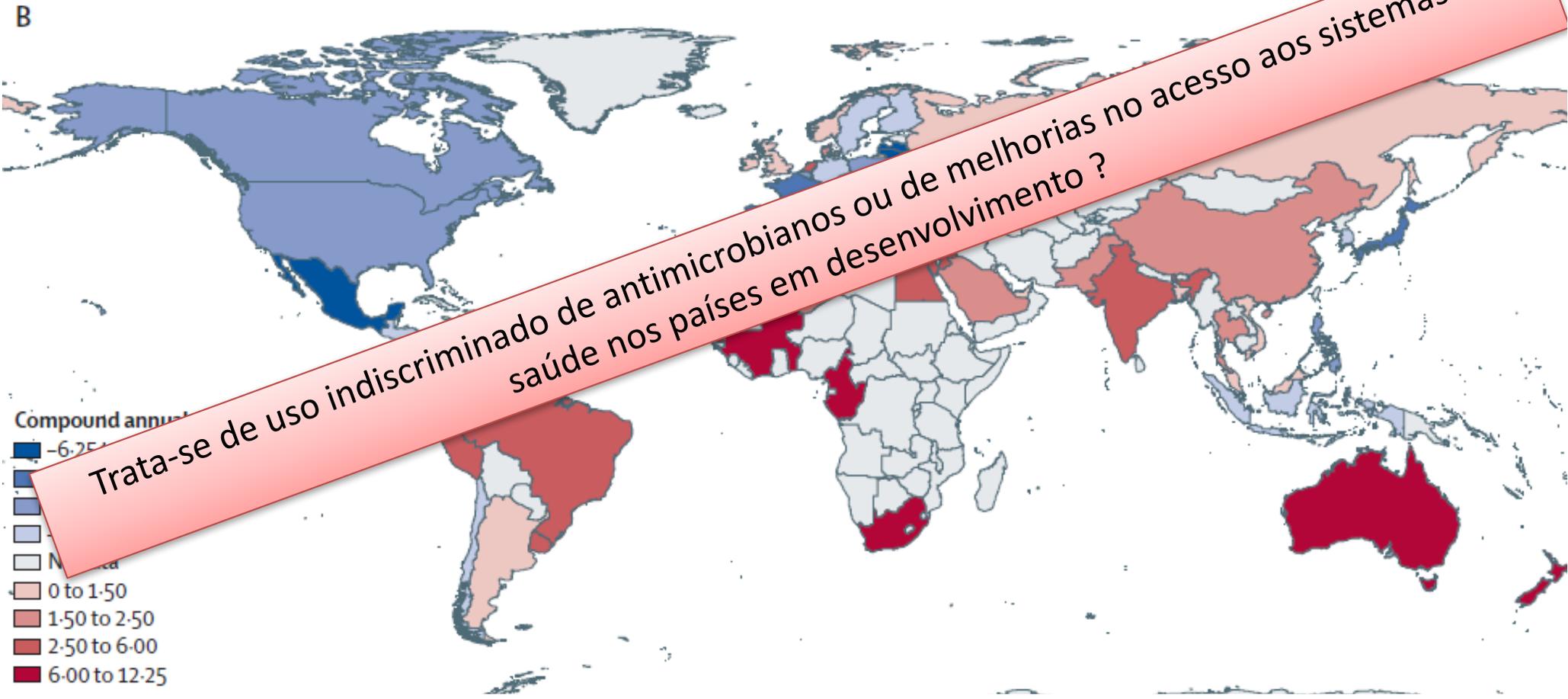
Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data

Thomas P Van Boeckel, Sumanth Gandra, Ashvin Ashok, Quentin Caudron, Bryan T Grenfell, Simon A Levin, Ramanan Laxminarayan



Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data

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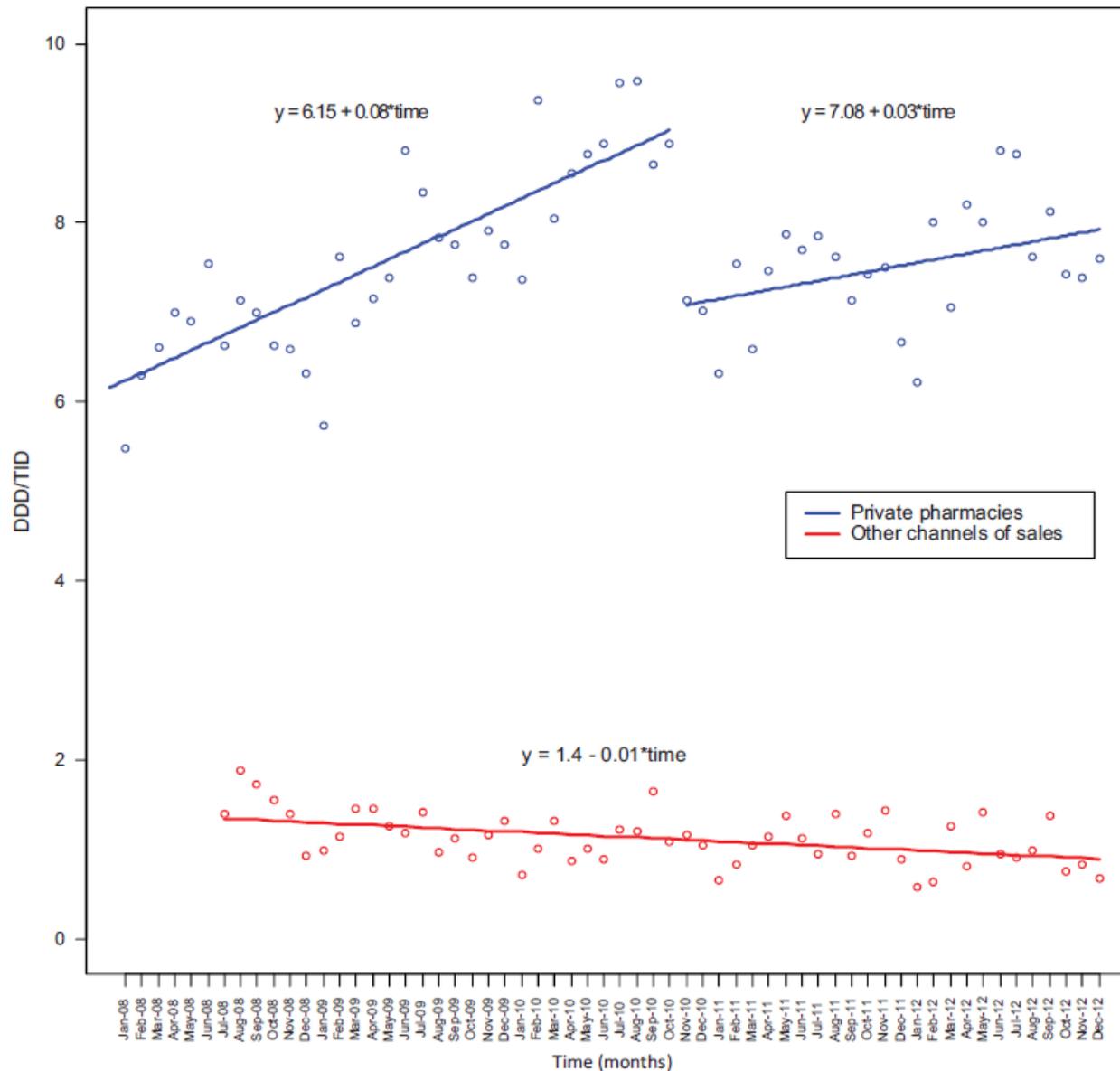
Brasil, Rússia, Índia, China e África do Sul respondem por 75% do aumento do consumo

The Impact of Restricting Over-the-Counter Sales of Antimicrobial Drugs

Preliminary Analysis of National Data

Medicine • Volume 94, Number 38, September 2015

Maria Luísa Moura, MD, Icaro Boszczowski, MD, Naíma Mortari, MD, Lígia Vizeu Barrozo, PhD,
Francisco Chiaravalloti Neto, PhD, Renata Desordi Lobo, PhD,
Antonio Carlos Pedroso de Lima, PhD, and Anna S. Levin, MD

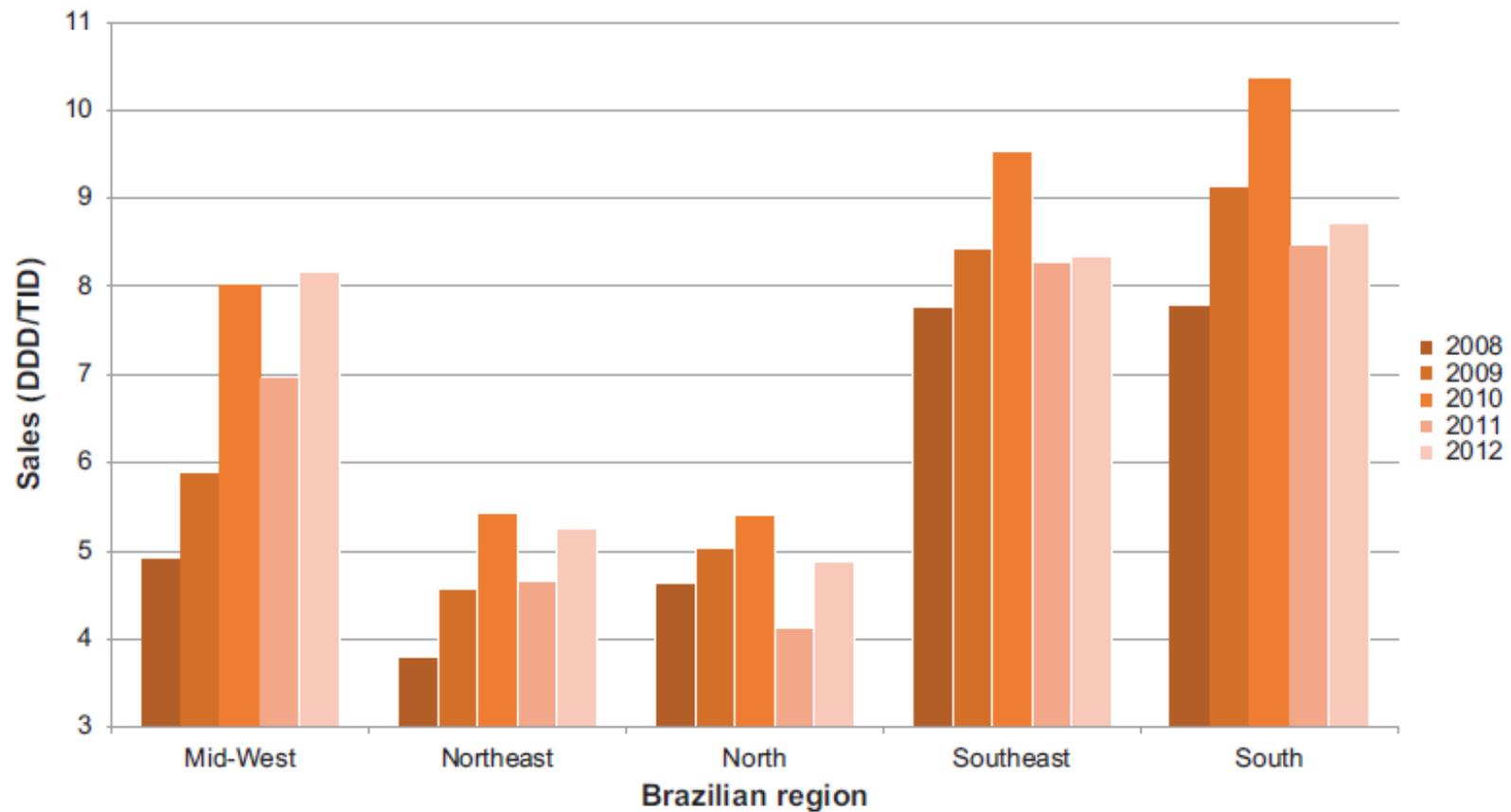


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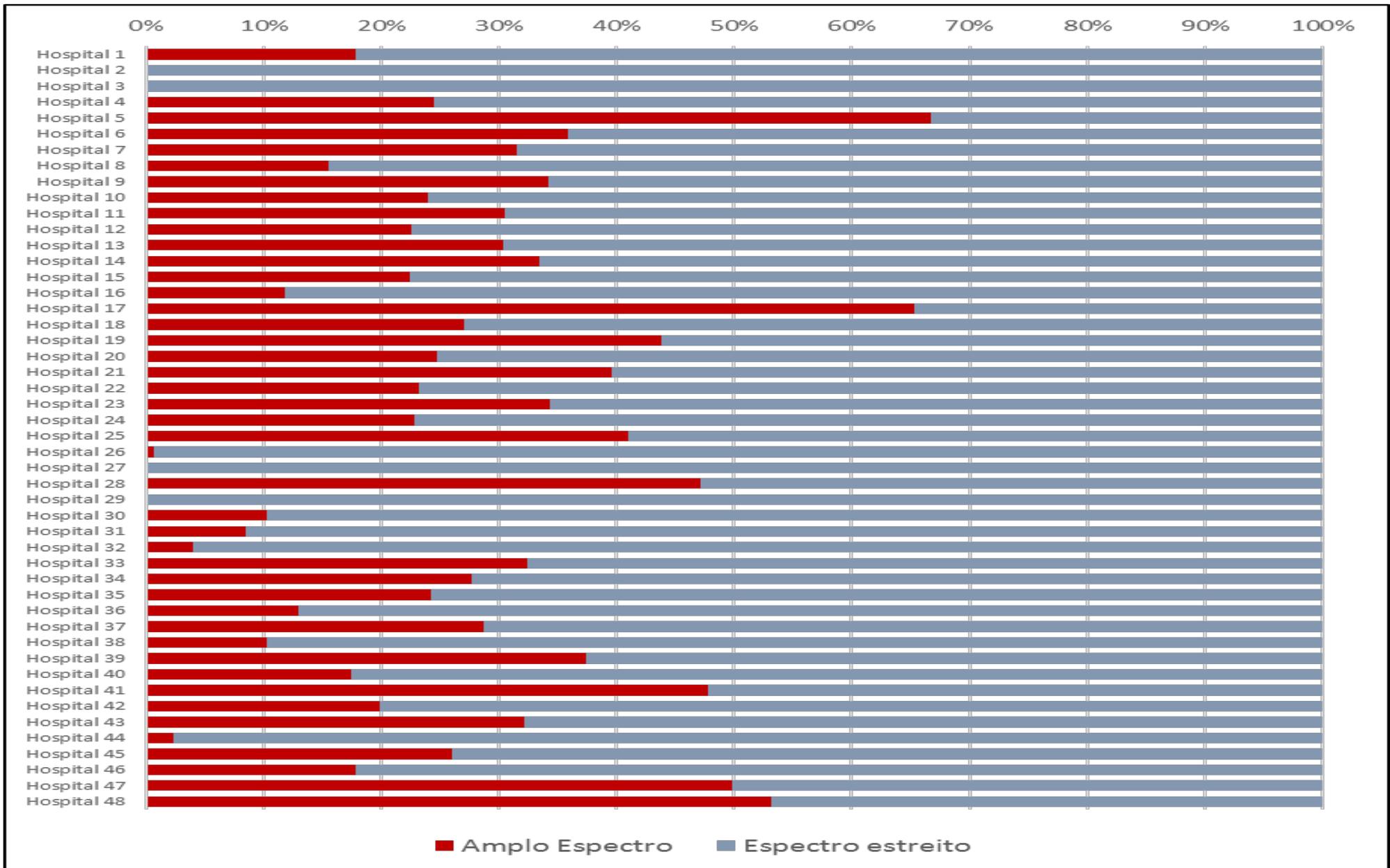


Inquérito de Prevalência (IRAS-Brasil)

153 hospitais – 10 estados

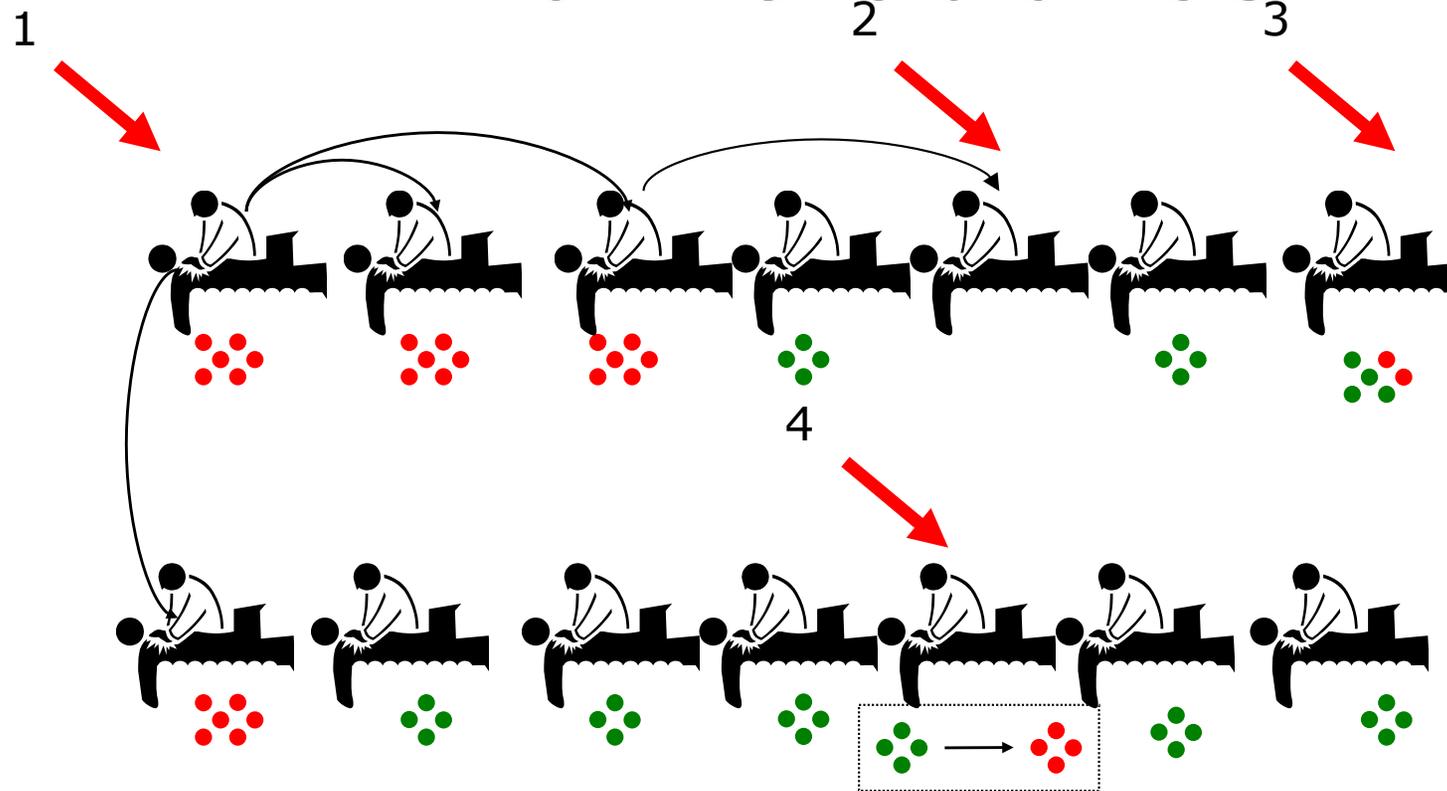
Categoria	0	1	2	3	4 ou mais	Qualquer ATB
Polos	60,5%	25,3%	11,6%	2,3%	0,3%	39,5%
>200 leitos	55,4%	25,4%	17,3%	1,8%	0,2%	44,7%
50-199 leitos	59,1%	30,5%	9,5%	0,8%	0,1%	40,9%
<50 leitos	56,0%	31,4%	11,7%	0,9%	0,0%	44,0%
<i>Total</i>	<i>58,9%</i>	<i>27,4%</i>	<i>11,9%</i>	<i>1,6%</i>	<i>0,2%</i>	<i>41,1%</i>

41% dos pacientes internados utilizavam pelo menos um antimicrobiano.





Efeitos populacionais dos Antimicrobianos



- 1) ↑ Circulação das cepas R
- 2) ↑ Suscetibilidade às cepas R

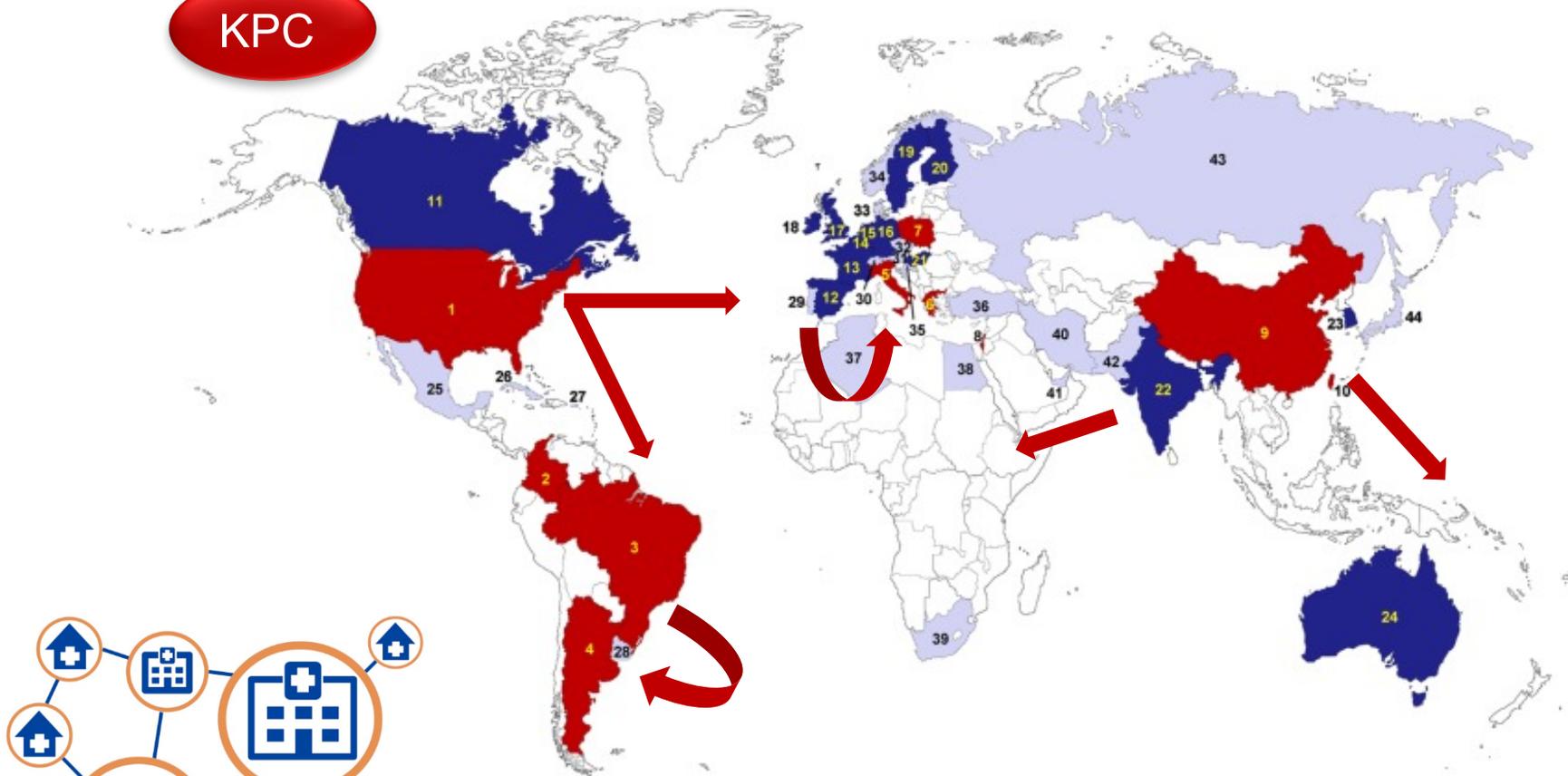
- 3) ↑ Expressão de cepas R já carreadas.
- 4) Indução da resistência.

Disseminação em redes

Introdução

Novos fenótipos de resistência microbiana emergem e sofrem disseminação global.

KPC



Redes de referência / contra-referência.

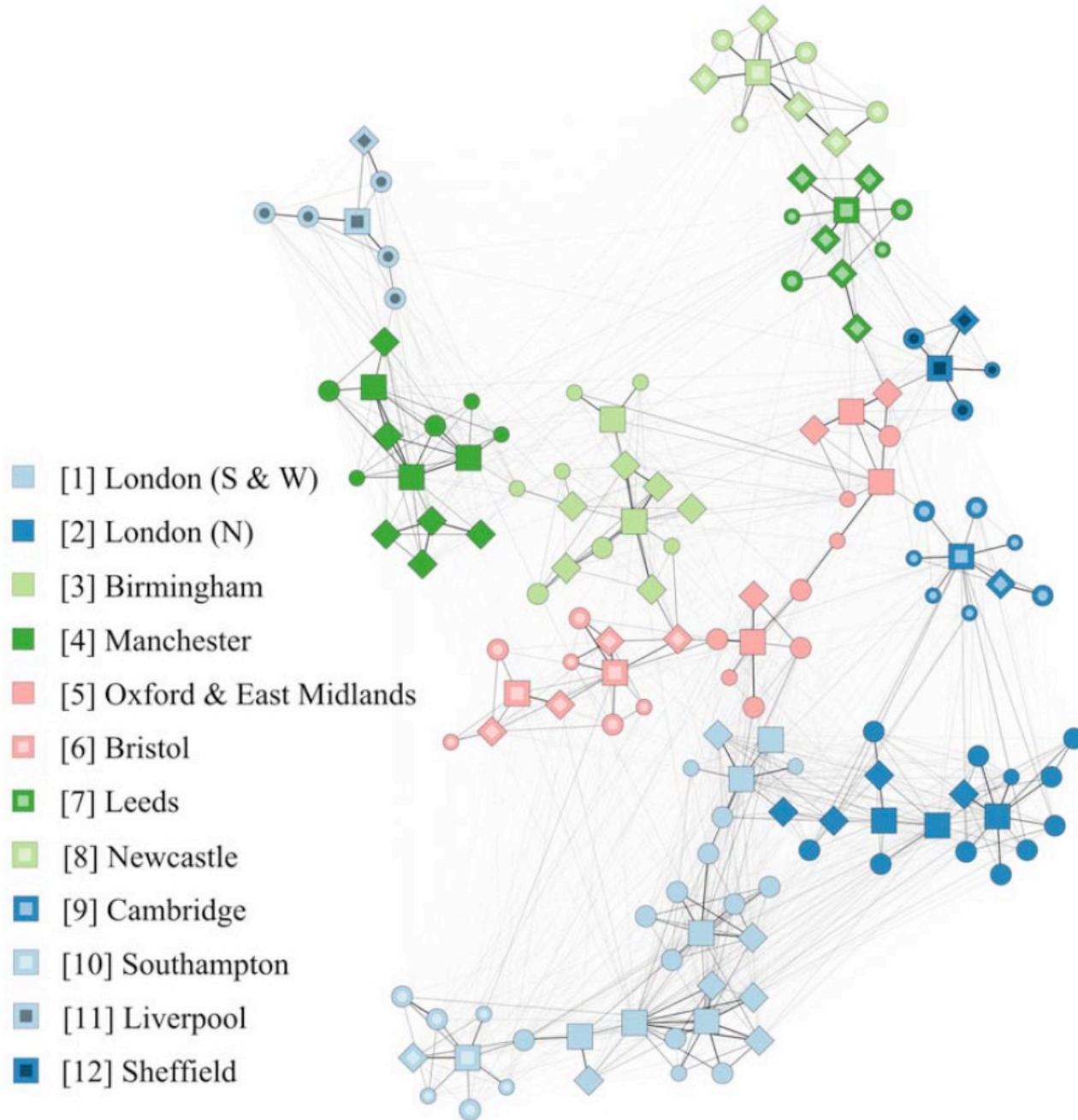
Lee CR et al. Front Microbiol. 2016; 7: 895.

Hospital Networks and the Dispersal of Hospital-Acquired Pathogens by Patient Transfer

Tjibbe Donker^{1,2}, Jacco Wallinga^{2,3}, Richard Slack⁴, Hajo Grundmann^{1,2*}

- As IRAS tem sido interpretadas como consequência de falhas de segurança e higiene precária em hospitais.
- **Isso no entanto ignora o fato de que (...) hospitais são conectados pelos pacientes que compartilham.**

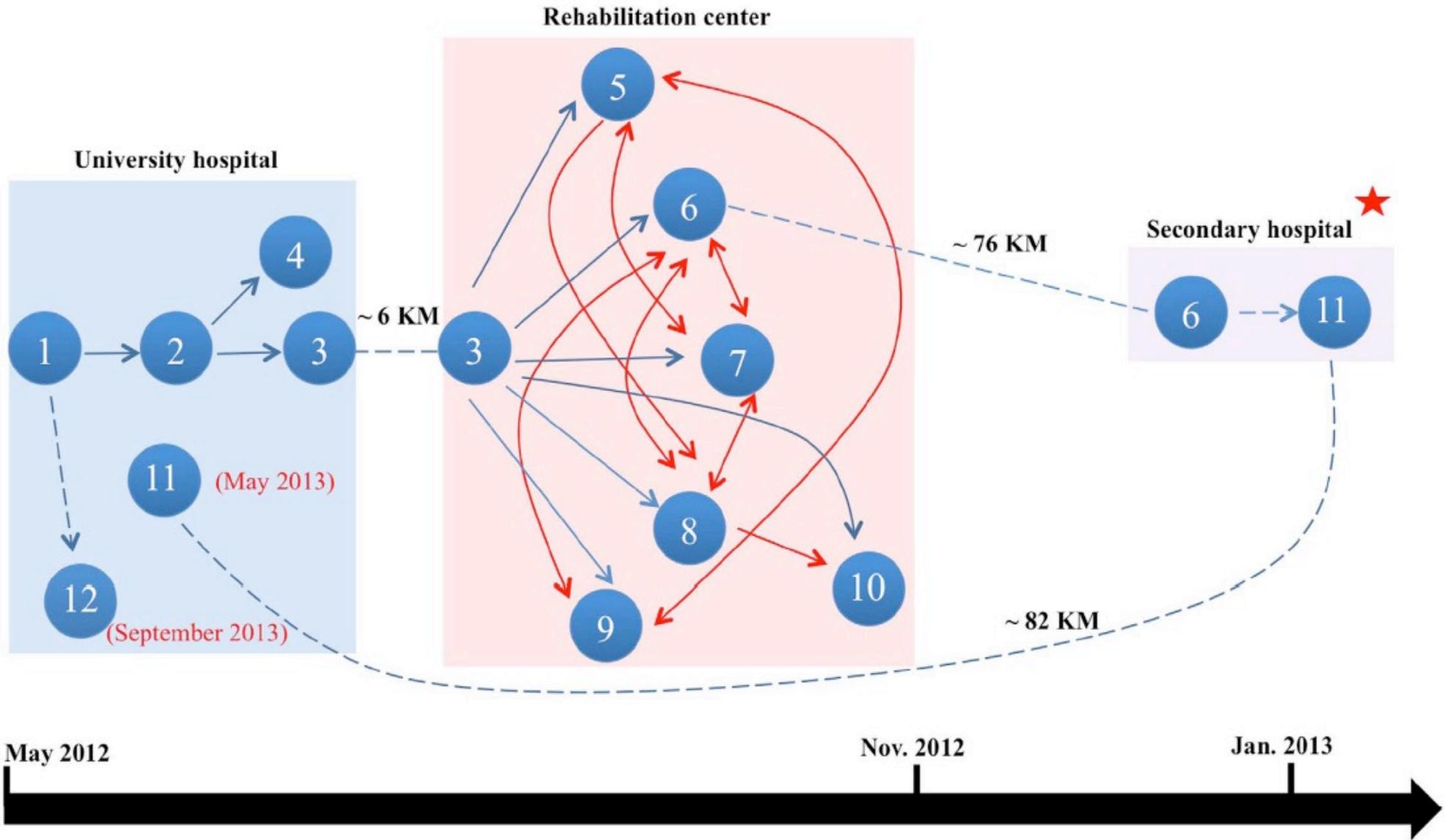




Use of whole-genome sequencing to trace, control and characterize the regional expansion of extended-spectrum β -lactamase producing ST15 *Klebsiella pneumoniae*

Kai Zhou^{1,3}, Mariette Lokate¹, Ruud H. Deurenberg¹, Marga Tepper², Jan P. Arends¹, Erwin G. C. Raangs¹, Jerome Lo-Ten-Foe¹, Hajo Grundmann¹, John W. A. Rossen^{1,*} & Alexander W. Friedrich^{1,*}

www.nature.com/scientificreports



Small hospitals matter: insights from the emergence and spread of vancomycin-resistant enterococci in 2 public hospitals in inner Brazil

Adriana Aparecida Feltrin Correa ^{a,b}, Antonio Carlos Campos Pignatari ^c, Monica da Silveira ^{a,b},
Roberta Cristina Cabral Mingone ^c, Vinicius Gomes de Sales Oliveira ^c, Carlos Magno Castelo Branco Fortaleza ^{a,*}

City of Bauru, Brazil
360.000 inhabitants

Hospital Estadual Bauru (HEB)
318 beds
High complexity



Hospital Estadual Manoel de Abreu (HEMA)
57 beds
Low complexity



VRE isolates
Surveillance cultures: 109
Clinical cultures: 13

VRE incidence

4 per 1,000 patients-day.



Previous admission to HEMA was a risk factor for VRE in HEB ($P < 0.001$)

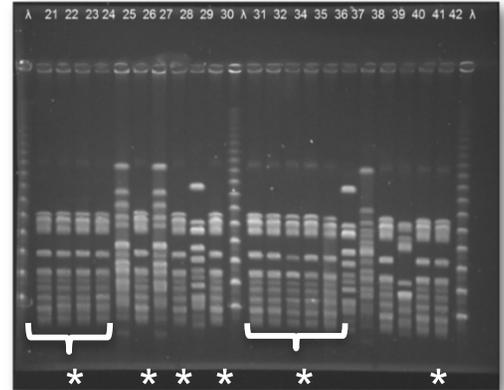
12 per 1,000 patients-day.

Multivariable analysis

Risk factors: Steroids, Mechanical ventilation, cefepime, imipenem

Risk factor: Oxacillin

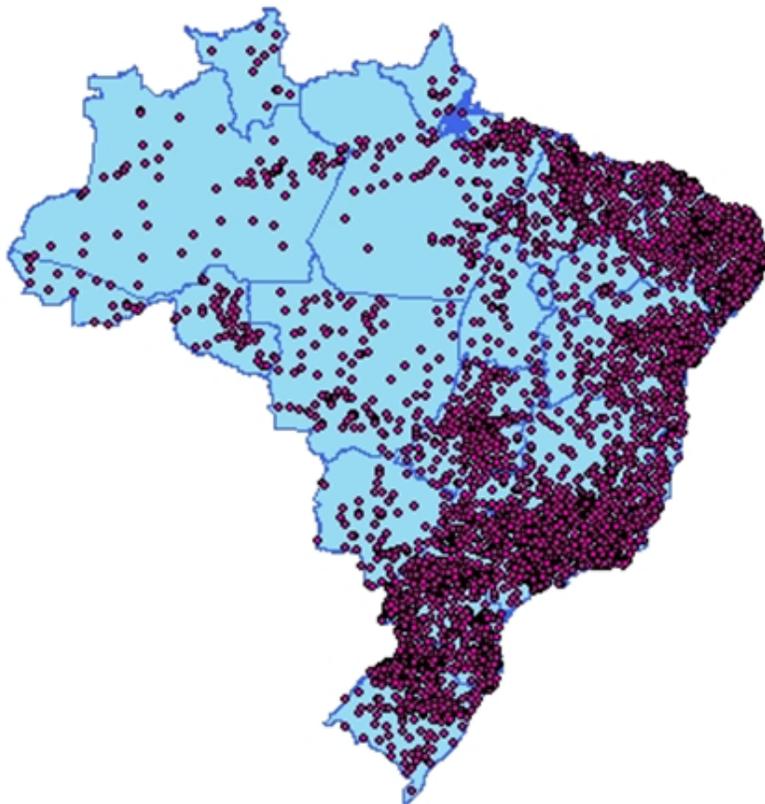
PFGE typing



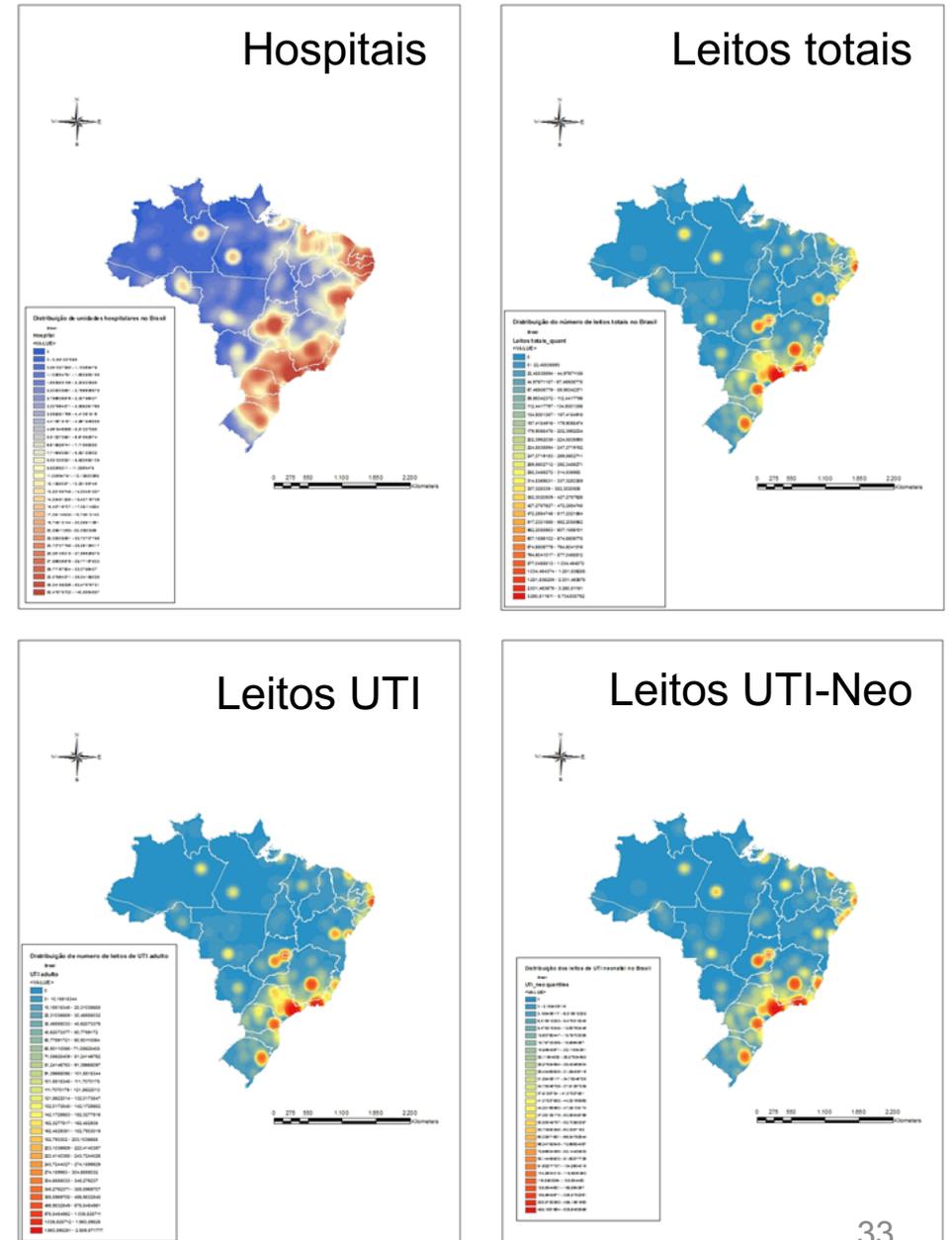
Most clones were spread in both hospitals.
106 isolates of *E. faecium*: 22 clones
Major clone (*): 40 patients
16 isolates of *E. faecalis*: 5 clones

Diagnostic Microbiology and Infectious Disease 82 (2015) 227–233

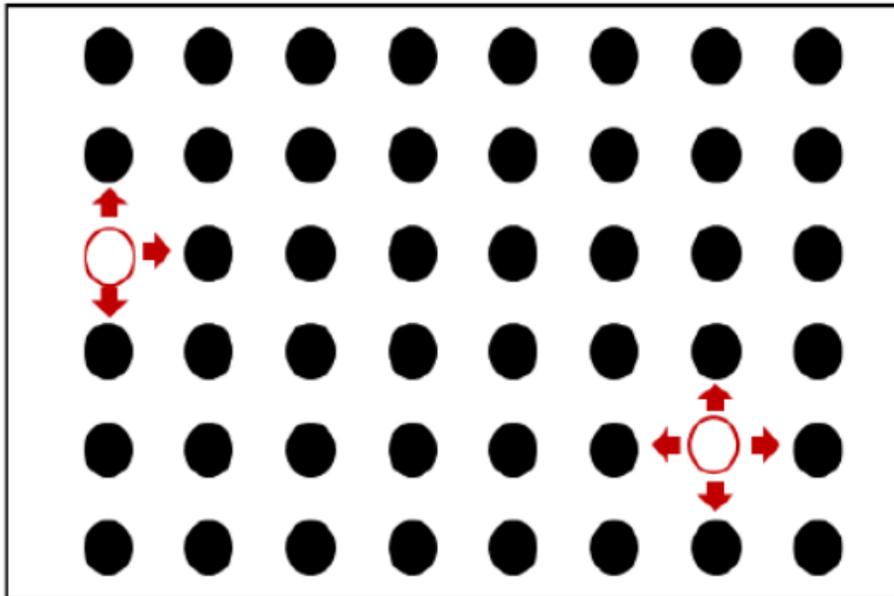
Brasil



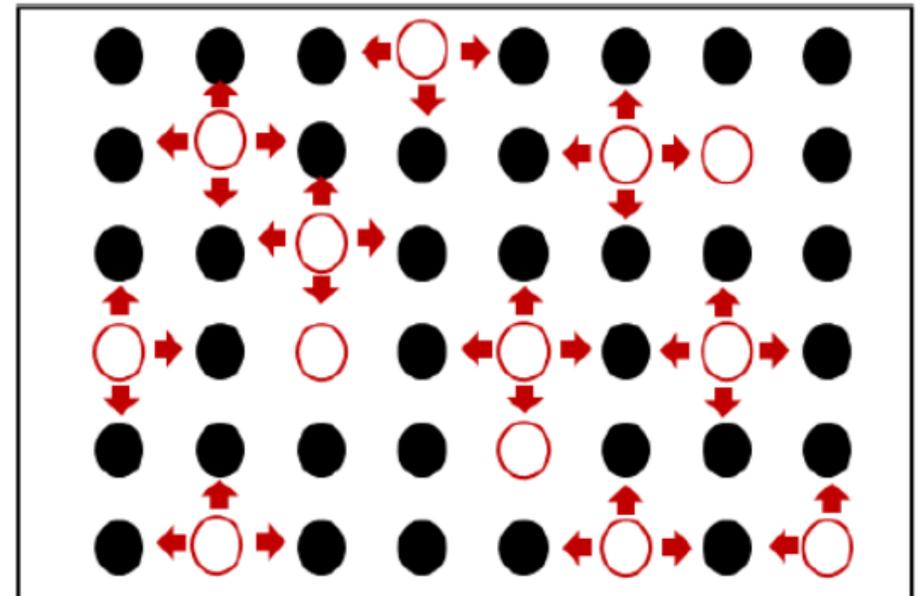
Kernel



Georreferenciamento (ArcGis 10)
dos hospitais brasileiros



Baixa pressão de colonização



Alta pressão de colonização

Pressão de colonização

Colonization pressure and risk factors for acquisition of imipenem-resistant *Acinetobacter baumannii* in a medical surgical intensive care unit in Brazil

Carlos Magno Castelo Branco Fortaleza MD, PhD *, Fernanda Moreira de Freitas MD, Gerhard da Paz Lauterbach MD

American Journal of Infection Control 41 (2013) 263-5

Table 1

Multivariable analysis of risk factors for acquisition of imipenem-resistant *Acinetobacter baumannii* for patients admitted to the intensive care unit in months with colonization pressure values below the median (8.7%)

Risk factors	OR (95% CI)	P value
Performance of tracheostomy	3.25 (1.09-9.67)	.03
Use of imipenem	10.96 (2.90-41.40)	<.001
Use of levofloxacin	0.24 (0.07-0.86)	.03
Use of metronidazole	5.34 (2.12-13.44)	<.001

Table 2

Multivariable analysis of risk factors for acquisition of imipenem-resistant *Acinetobacter baumannii* for patients admitted to the intensive care unit in months with colonization pressure values above the median (8.7%)

Risk factors	OR (95% CI)	P value
Charlson comorbidity index	1.24 (1.00-1.54)	.048
Performance of surgery	2.86 (1.11-7.33)	.03
Central venous catheter	3.95 (1.16-13.45)	.03
Parenteral nutrition	15.12 (3.97-57.66)	<.001

Quando as bactérias circulam muito (alta pressão de colonização) o uso de antibióticos não aparece como fator de risco para resistência.

Am J Infect Control 2010;38:173-81.

Exposure to hospital roommates as a risk factor for health care-associated infection

Meghan Hamel, MSc,^a Dick Zoutman, MD, FRCPC,^{a,b} and Chris O'Callaghan, DVM, MSc, PhD^a
Kingston, Ontario, Canada

From the Department of Community Health and Epidemiology, Queen's University, Kingston, Ontario, Canada^a; and Department of Pathology and Molecular Medicine Queen's University, Kingston, Ontario, Canada.^b

HR por “colegas-dia”

Variable	HR (95% CI)		
	<i>C difficile</i> model	MRSA model	VRE model
Univariate results			
Total roommates/day	1.06 (1.00 to 1.12)	1.12 (1.07 to 1.17)	1.13 (1.04 to 1.22)
Multivariate results			
Total roommates/day	1.11 (1.03 to 1.19)	1.10 (1.05 to 1.15)	1.11 (1.02 to 1.21)

HR por colegas individuais

Variable	HR (95% CI)		
	<i>C difficile</i> model	MRSA model	VRE model
Univariate results			
Unique roommates/day	1.03 (0.94 to 1.13)	1.10 (1.01 to 1.19)	1.17 (1.04 to 1.31)
Multivariate results			
Unique roommates/day	1.08 (0.94 to 1.24)	1.07 (0.99 to 1.17)	1.15 (1.02 to 1.28)

O risco de adquirir uma bactéria multidroga-resistente aumenta com o número de colegas de quarto no hospital, ou com o tempo de exposição a esses colegas.

Comunidade vs. Hospital

Dormindo com o inimigo...



Estudo NHANES (2001-2002): 9622 pessoas investigadas.

Resultado: 0,8% dos americanos estudados carregavam MRSA.

Kuehnert, 2006.

Inquérito de Prevalência em Botucatu (SP): 686 pessoas investigadas.

Resultado: 0,9% dos habitantes estudados carregavam MRSA (SCC*mec IV*)

Pires, 2012.



Systemic CA-MRSA infection following trauma during soccer match in inner Brazil: clinical and molecular characterization

Carlos Henrique Camargo ^a, Maria de Lourdes Ribeiro de Souza da Cunha ^{a,*}, Mariana Fávero Bonesso ^a, Fabiana Picoli da Cunha ^b, Alexandre Naime Barbosa ^b, Carlos Magno Castelo Branco Fortaleza ^b

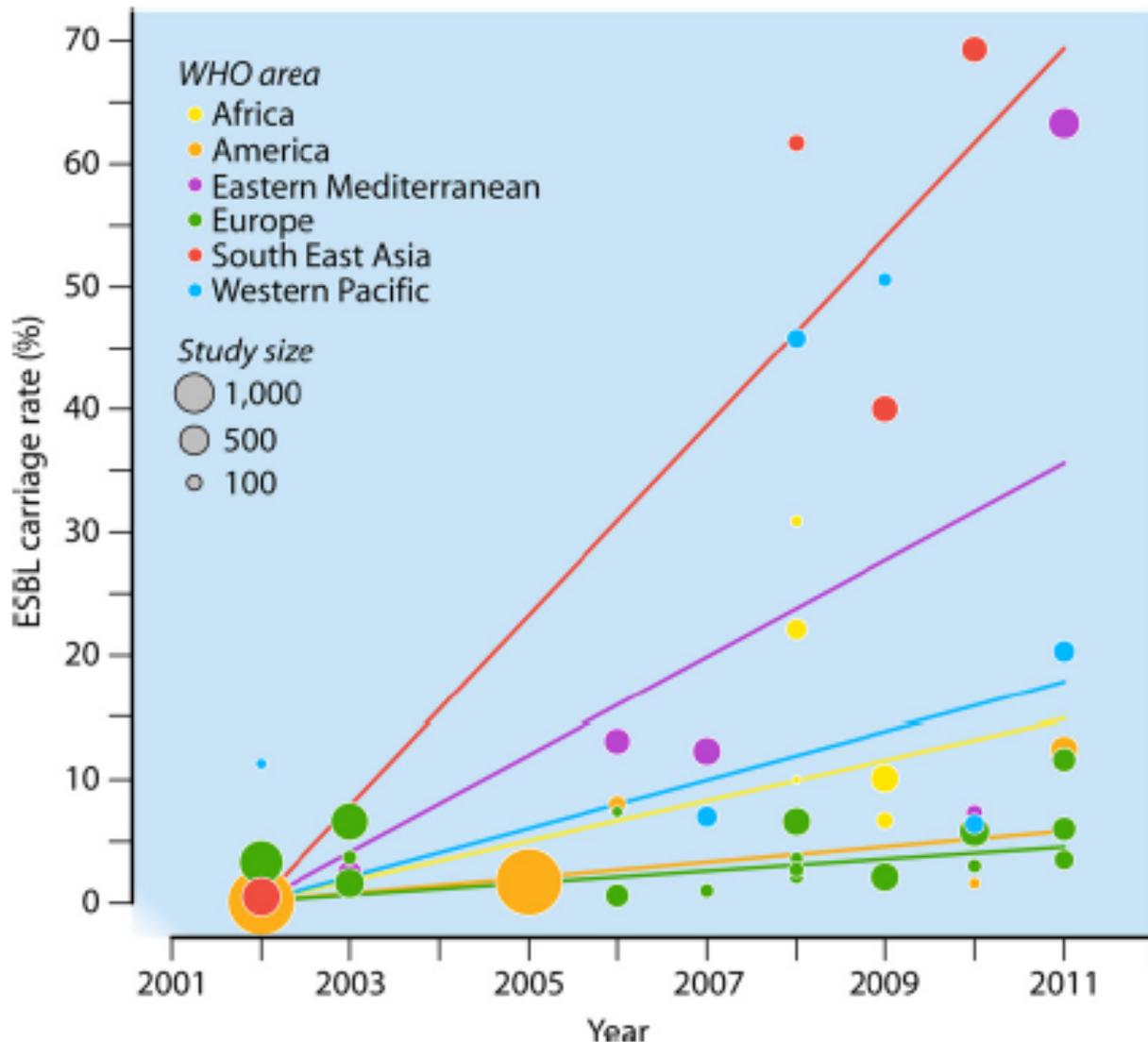
Infecção sistêmica por CA-MRSA após trauma durante partida de futebol (Bofete, SP)



- Adolescente sem internações ou viagem
- Celulite em coxa
- Pneumonia necrotizante
- Hemoculturas (+) para MRSA
- Cepa produtora de PVL
- Clone circulante na Argentina (spa type t311)

Trends in Human Fecal Carriage of Extended-Spectrum β -Lactamases in the Community: Toward the Globalization of CTX-M

Paul-Louis Woerther,^a Charles Burdet,^{b,c} Elisabeth Chachaty,^a Antoine Andremont^b

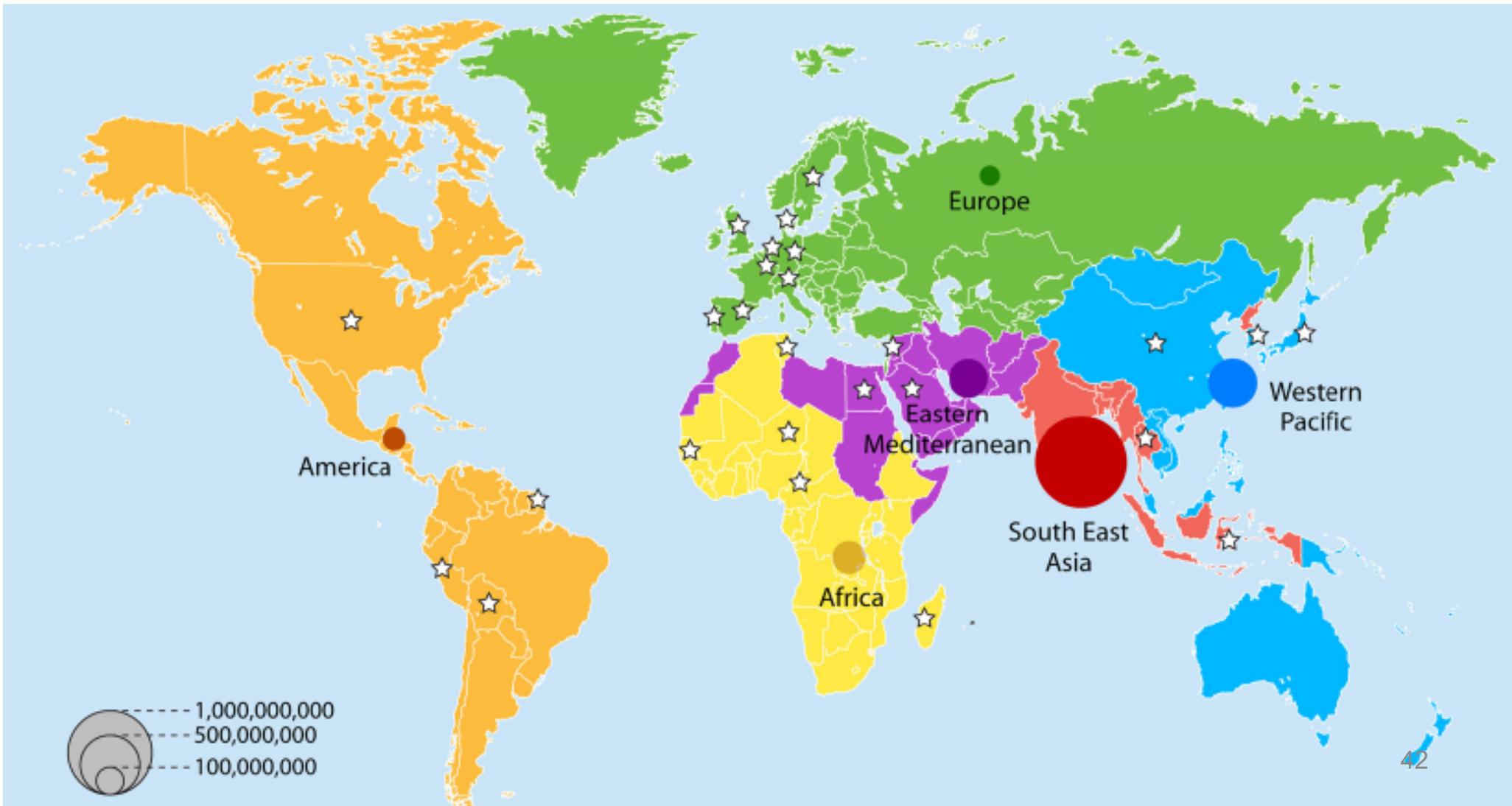


Bactérias multirresistentes encontradas na microbiota fecal de pessoas na comunidade.

Clin. Microbiol. Rev. 2013, 26(4):744. DOI: 10.1128/CMR.00023-13.

Trends in Human Fecal Carriage of Extended-Spectrum β -Lactamases in the Community: Toward the Globalization of CTX-M

Paul-Louis Woerther,^a Charles Burdet,^{b,c} Elisabeth Chachaty,^a Antoine Andremont^b



Prevenção e Controle

Em serviços de saúde

Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in health care facilities



Guidelines Prevention and control of multi-drug-resistant Gram-negative bacteria: recommendations from a Joint Working Party

A.P.R. Wilson^{a,*}, D.M. Livermore^b, J.A. Otter^c, R.E. Warren^d, P. Jenks^e, D.A. Enoch^f, W. Newsholme^g, B. Oppenheim^h, A. Leonardⁱ, C. McNulty^j, G. Tanner^k, S. Bennett^l, M. Cann^m, J. Bostockⁿ, E. Collins^o, S. Peckitt^p, L. Ritchie^q, C. Fry^r, P. Hawkey^s

^aConsultant Microbiologist, Department of Microbiology and Virology, University College London Hospitals, London, UK
^bProfessor of Medical Microbiology, Norwich Medical School, University of East Anglia, Norwich, UK
^cEpidemiologist, Infection Prevention and Control, Imperial College Healthcare NHS Trust, London, UK
^dRetired Consultant Microbiologist, Shrewsbury and Telford Hospital NHS Trust, Shrewsbury, UK
^eConsultant Microbiologist, Plymouth Hospitals NHS Trust, Plymouth, UK
^fConsultant Microbiologist, Public Health England, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK
^gConsultant in Infectious Diseases, Infection Control and General Medicine, Department of Infection, St Thomas' Hospital, London, UK
^hConsultant Microbiologist, University Hospitals Birmingham NHS Foundation Trust, Queen Elizabeth Hospital, Queen Elizabeth Medical Centre, Birmingham, UK
ⁱConsultant Microbiologist, Southern General Hospital, Glasgow, UK
^jHead of Primary Care Unit, Public Health England, and Honorary Visiting Professor Cardiff University, Microbiology Dept Gloucester Royal Hospital, Gloucester, UK
^kPatient Representative, Bristol, UK
^lPatient Representative, Member of Health Care Acquired Infections, Service Users Research Forum, Leicester, UK
^mTrustee, MRSA Action, Kirkham, UK
ⁿPatient Representative, Member of Health Care Acquired Infections, Service Users Research Forum, London, UK
^oClinical Lead Infection Prevention, University Hospitals of Leicester, Leicester Royal Infirmary, Leicester, UK
^pInfection Prevention and Control Lead for North Yorkshire and Humber Commissioning Support Unit, Hull, UK
^qNurse Consultant Infection Control, Infection Control Team HAI Group, Health Protection Scotland, Glasgow, UK
^rNursing Officer – Communicable Diseases Infectious Diseases and Blood Policy, Department of Health, London, UK
^sProfessor of Clinical and Public Health Bacteriology, Consultant Medical Microbiologist, Public Health Laboratory, Barns Heartlands Hospital, Bardeley Green East, Birmingham, UK



NICE has accredited the process used by the Healthcare Infection Society to produce its 'Prevention and control of multi-drug-resistant negative bacteria: recommendations from a Joint Working Party' guidelines. Accreditation is valid for 5 years from March 2015. More info on accreditation can be viewed at: <http://www.nice.org.uk/about/nhs-we-do/accreditation>
 * Corresponding author. Address: Department of Microbiology and Virology, University College London Hospitals, 60 Whitfield Street, London W1P 8LP, UK. Tel.: +44 (0) 2034 49515.
 E-mail address: peter.wilson@uclh.nhs.uk (A.P.R. Wilson).

<http://dx.doi.org/10.1016/j.jhin.2015.08.007>
 0195-6701/© 2015 The Healthcare Infection Society. Published by Elsevier Ltd. All rights reserved.

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY JULY 2014, VOL. 35, NO. 52
 SHEA/IDSA PRACTICE RECOMMENDATION

Strategies to Prevent Methicillin-Resistant *Staphylococcus aureus* Transmission and Infection in Acute Care Hospitals: 2014 Update

David P. Calfee, MD, MS;^{1,2} Cassandra D. Salgado, MD, MS;^{2,3} Aaron M. Milstone, MD;⁴ Anthony D. Harris, MD, MPH;⁵ David T. Kuhar, MD;⁶ Julia Moody, MS;⁷ Kathy Auredon, MS, MT, CIC;⁸ Susan S. Huang, MD, MPH;⁹ Lisa L. Maragakis, MD, MPH;⁷ Deborah S. Yokoe, MD, MPH¹⁰

PURPOSE

Previously published guidelines are available that provide comprehensive recommendations for detecting and preventing healthcare-associated infections (HAIs). The intent of this document is to highlight practical recommendations in a concise format designed to assist acute care hospitals in implementing and prioritizing their methicillin-resistant *Staphylococcus aureus* (MRSA) prevention efforts. This document updates "Strategies to Prevent Transmission of Methicillin-Resistant *Staphylococcus aureus* in Acute Care Hospitals,"¹ published in 2008. This expert guidance document is sponsored by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA), the American Hospital Association (AHA), the Association for Professionals in Infection Control and Epidemiology (APIC), and the Joint Commission, with major contributions from representatives of a number of organizations and societies with content expertise. The list of endorsing and supporting organizations is presented in the introduction to the 2014 updates.¹

SECTION 1: RATIONALE AND STATEMENTS OF CONCERN

1. HAIs caused by MRSA in acute-care facilities are common
 A. In the United States, the proportion of hospital-associated *S. aureus* infections resistant to methicillin remains high.
 1. The most recent data from the National Healthcare Safety Network (NHSN) reports that, from 2009 to

2010, 54.6% of *S. aureus* central line-associated bloodstream infections (CLABSI), 58.7% of *S. aureus* catheter-associated urinary tract infections, 48.4% of *S. aureus* ventilator-associated pneumonia (VAP) episodes, and 43.7% of *S. aureus* surgical site infections (SSIs) were caused by MRSA.^{1,2}

2. Compared with data from 2007 and 2008, the proportions caused by MRSA are lower for each of the HAIs, significantly so for VAP and SSI. Additionally, from 2005 through 2011, rates of hospital-onset invasive MRSA infections reportedly decreased 34.2%, with the greatest decreases for BSIs.^{3,4} In contrast, among pediatric populations, from 2005 to 2010, there were no significant reductions in healthcare-associated MRSA infections.⁵

3. Although these findings suggest some success in preventing healthcare-associated MRSA transmission and infection, many patient groups continue to be at risk.

II. Outcomes associated with MRSA HAIs

A. MRSA HAIs have been associated with significant morbidity and mortality.⁶⁻¹⁰ Although some investigators have found no difference in morbidity and mortality when comparing infections due to methicillin-susceptible *S. aureus* (MSSA) to those due to MRSA,^{11,12} some studies comparing patients with MSSA bacteremia to those with MRSA bacteremia have reported nearly twice the mortality rate, significantly longer hospital stays, and significantly higher median hospital costs for MRSA.^{8,13}

1. Compared with patients with an MSSA SSI, one study found that those with an MRSA SSI have a 3.4 times

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Recomendações



Estratégia multimodal PCI

Higiene das mãos

Vigilância da resistência

Precauções de contato

Controle ambiental

Prevenindo a transmissão em redes

- Mapear a complexidade da redes hospitalares.
- Identificar locais de alta vulnerabilidade para introdução e possíveis rotas de circulação de patógenos multidroga-resistentes (MDR) entre diferentes serviços.
- **Estimular vigilância e controle em hospitais estratégicos.**





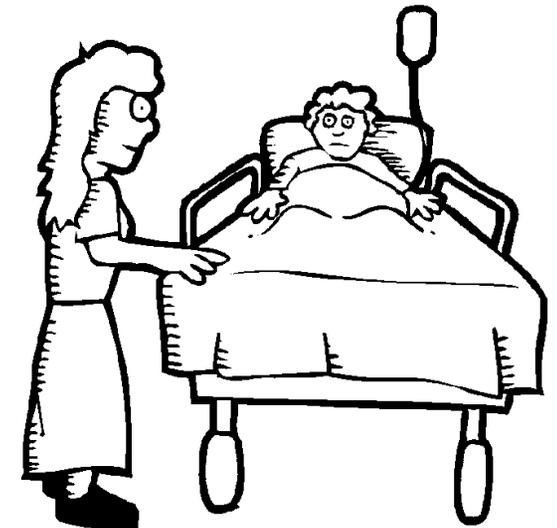
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Promotores





Obrigado