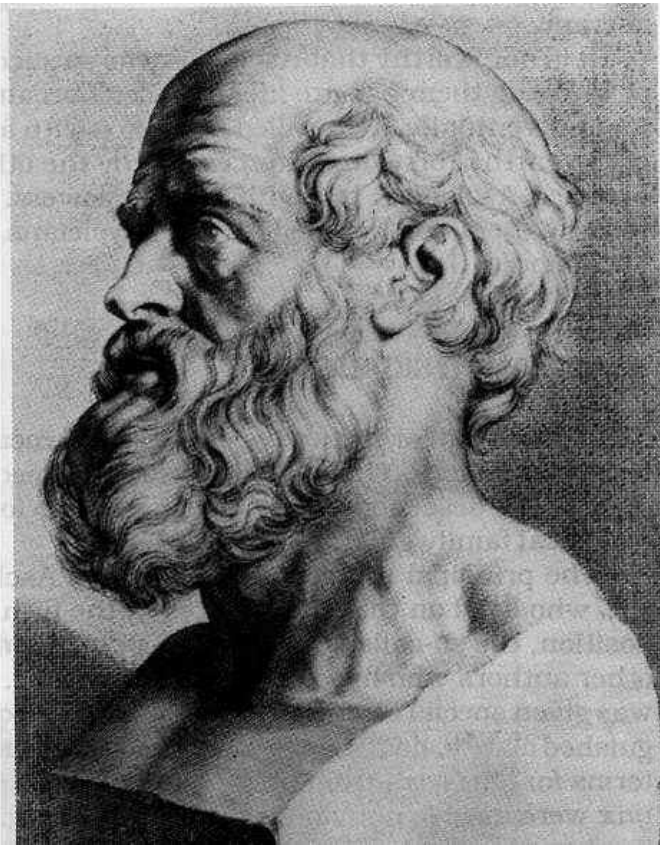


Fatores climáticos e IRAS (ênfase em Bacilos Gram Negativos)

Carlos Magno Castelo Branco Fortaleza

Faculdade de Medicina de Botucatu (UNESP)

Sazonalidade de Doenças

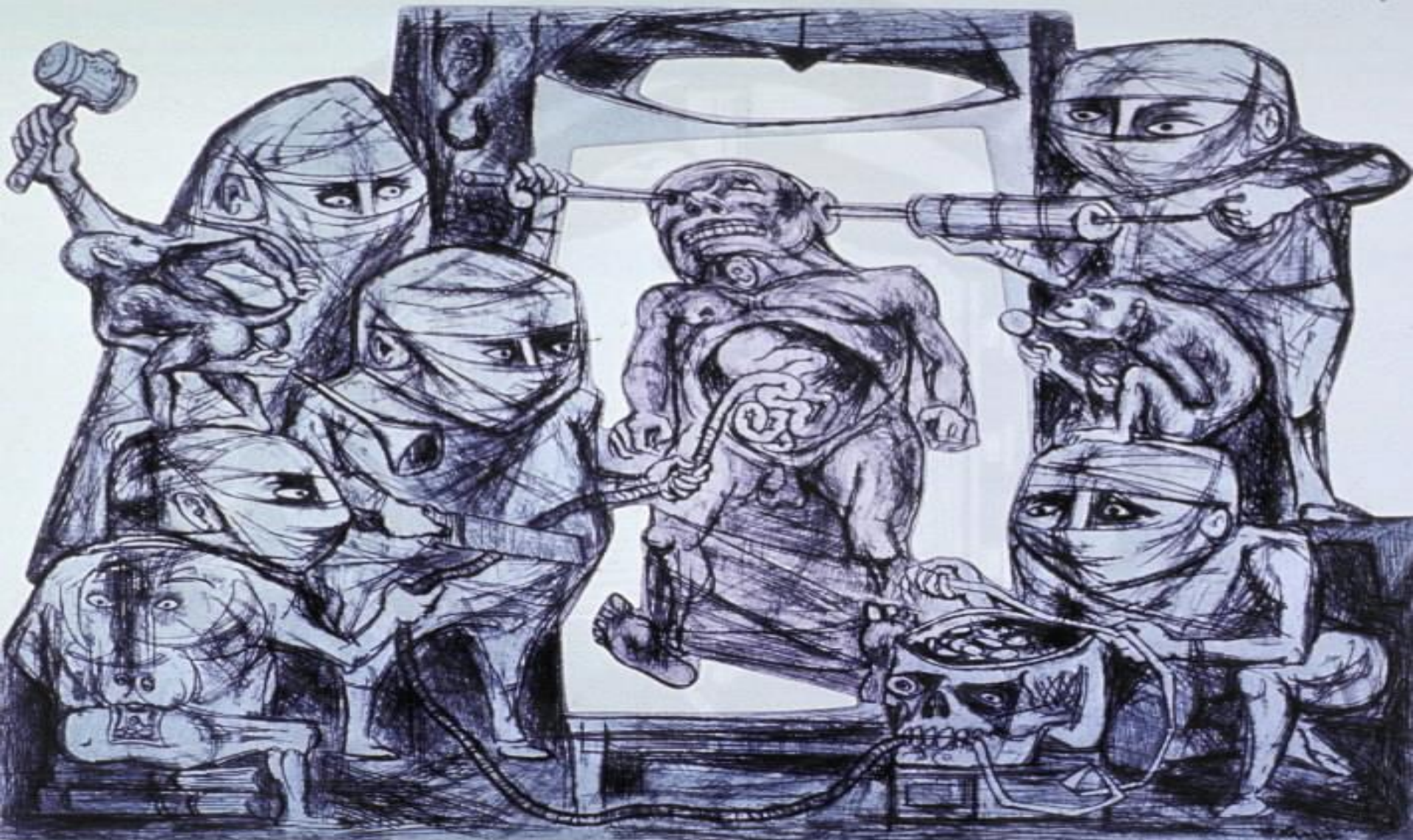


Hipócrates – Ares, águas, lugares.



Pneumonias, Varicela, Dengue, Diarréias

FATORES DETERMINANTES DE IRAS



Fatores associados à circulação de microrganismos



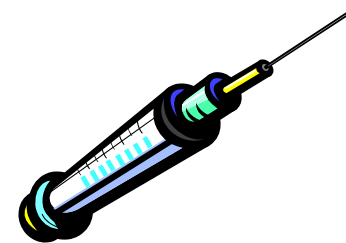
Gravidade do paciente



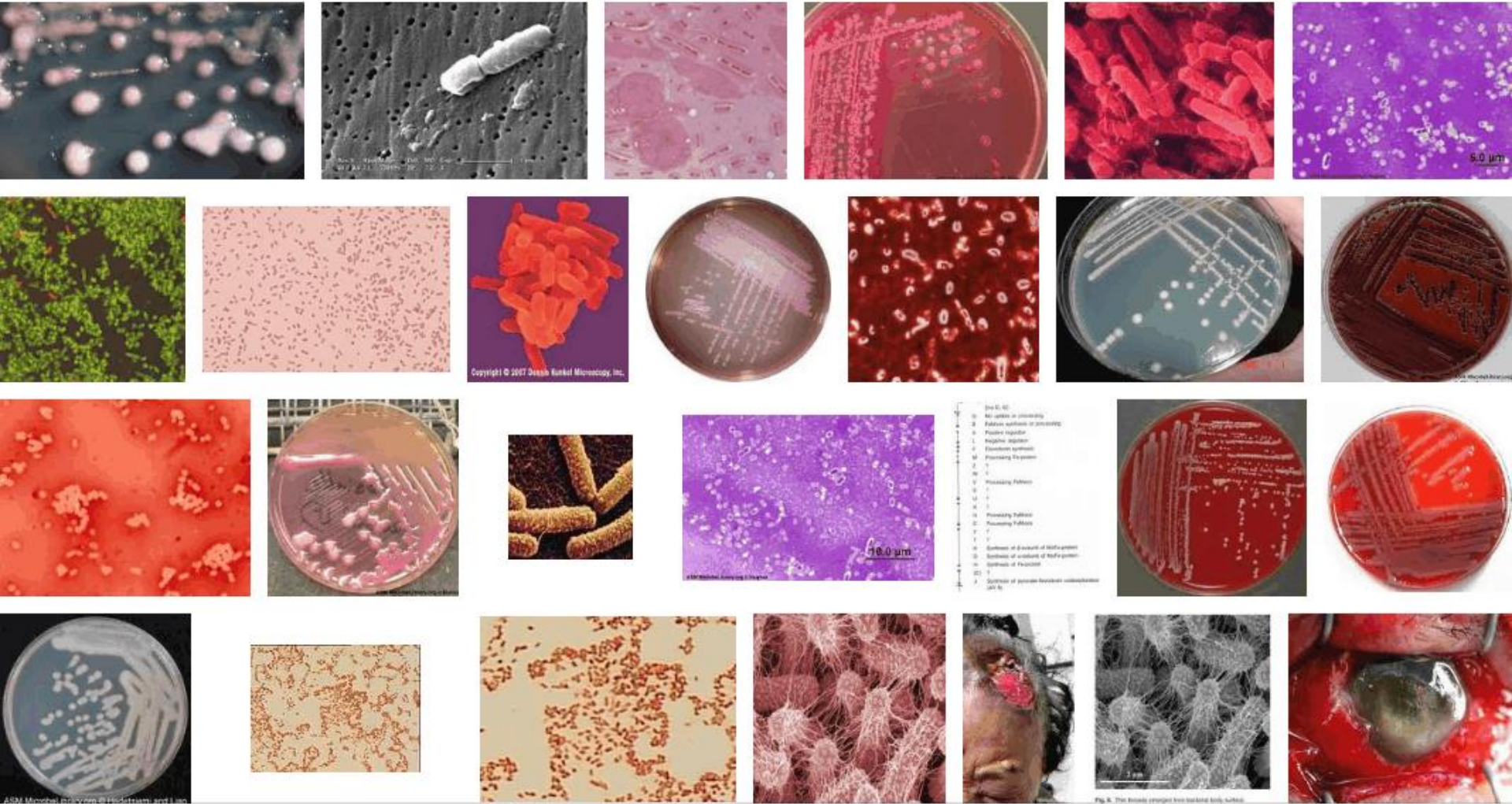
Procedimentos invasivos



“Understaffing”



Uso de antimicrobianos



Por que haveria sazonalidade de Infecções Relacionadas à Assistência à Saúde?

Richet H. Clin Microbiol Infect 2012; 18:934-40.

NO ENTANTO...

Seasonal Variation of *Acinetobacter* Infections: 1987–1996

L. Clifford McDonald,^a Shailen N. Banerjee,
William R. Jarvis, and the National Nosocomial
Infections Surveillance System

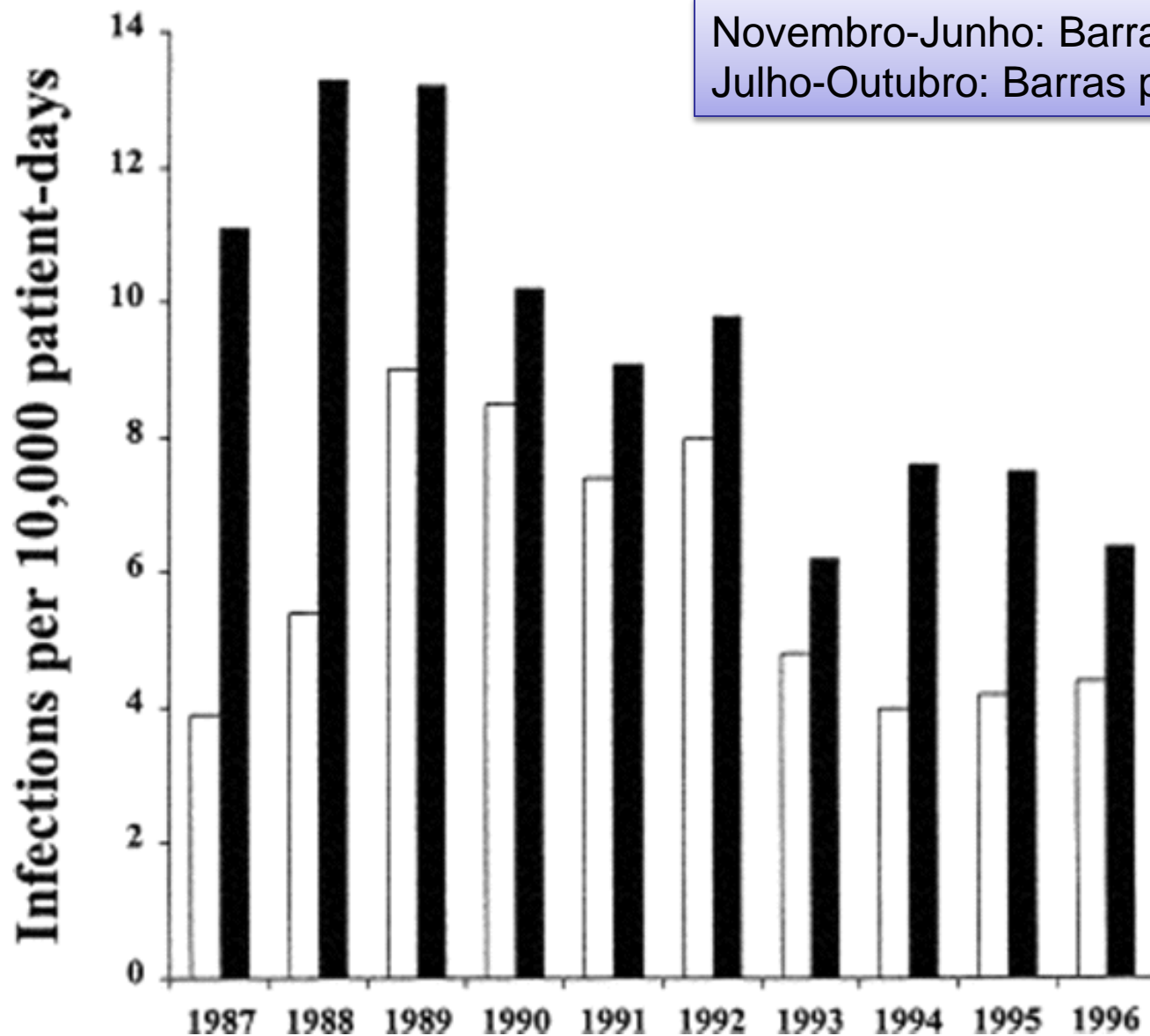
*From the Centers for Disease Control and Prevention, Public Health
Service, US Department of Health and Human Services,
Atlanta, Georgia*

Clinical Infectious Diseases 1999;29:1133–7

Infecções relatadas ao NNIS (atual NHSN) entre 1987 e 1996.

3.447 infecções por *Acinetobacter ssp.*

Incidência de 10,2 por 1000 pacientes-dia.



Novembro-Junho: Barras brancas
 Julho-Outubro: Barras pretas

Summer Peaks in the Incidences of Gram-Negative Bacterial Infection Among Hospitalized Patients

Eli N. Perencevich, MD, MS; Jessina C. McGregor, PhD; Michelle Shardell, PhD;
Jon P. Furuno, PhD; Anthony D. Harris, MD, MPH; J. Glenn Morris, Jr., MD, MPH&TM;
David N. Fisman, MD, MPH, FRCPC; Judith A. Johnson, PhD

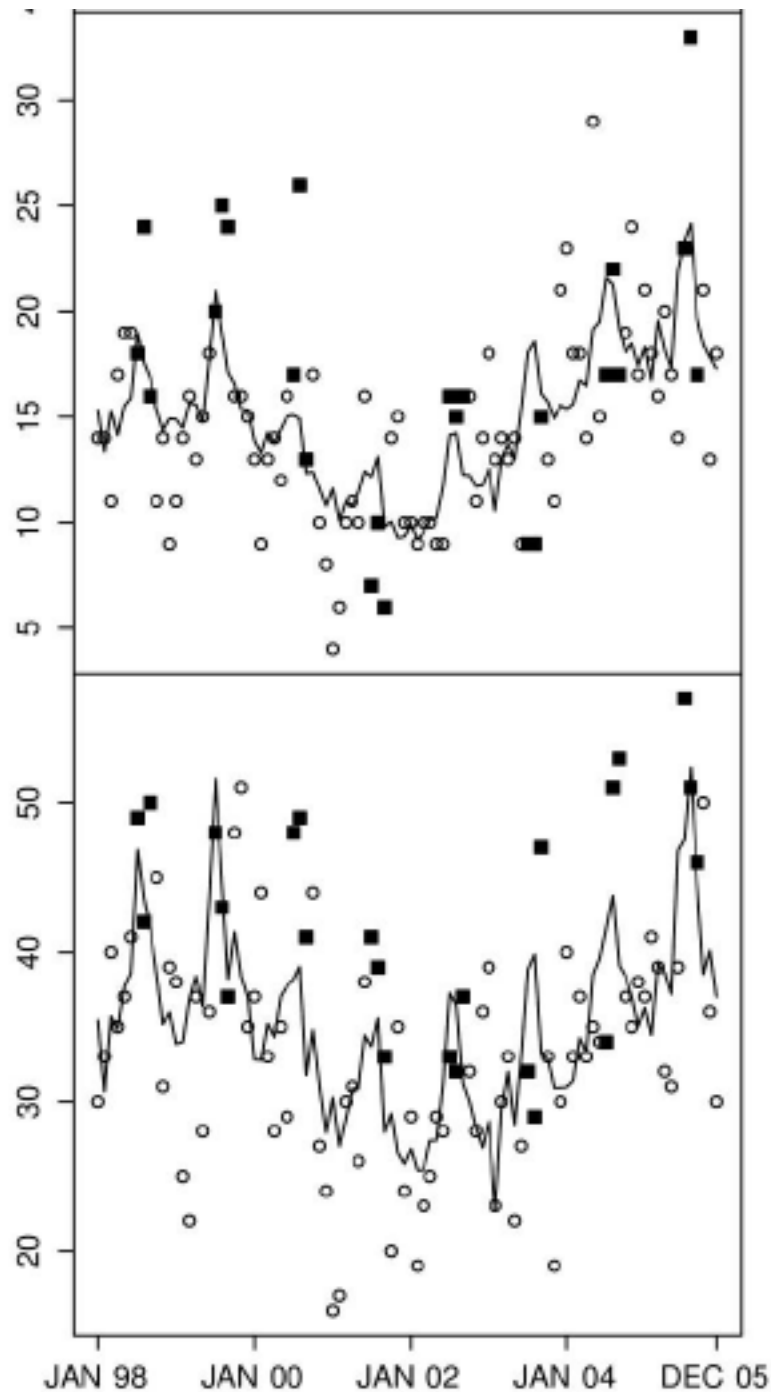
Infect Control Hosp Epidemiol 2008; 29:1124-1131

Hsopital da Universidade de Maryland

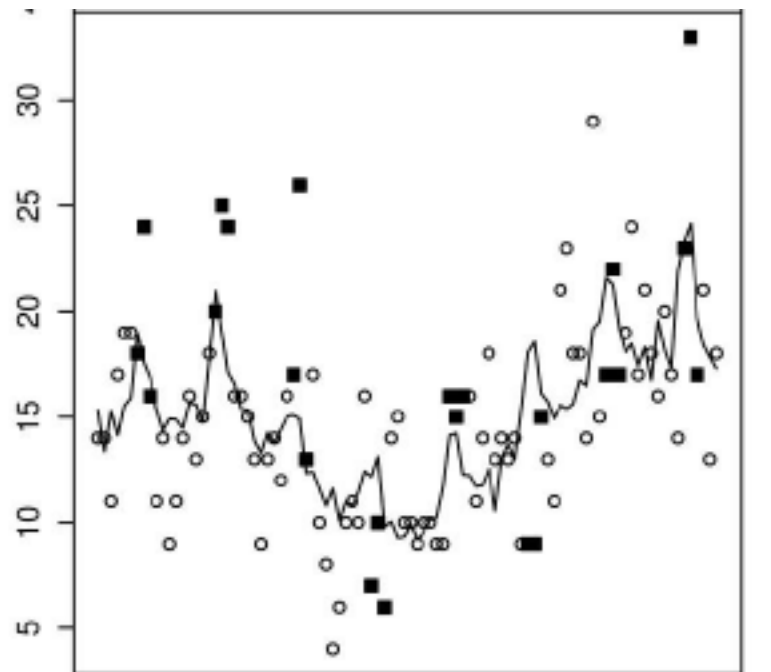
Período: 1998-2005

Infecções causadas por diversos agentes G-positivos e G-negativos

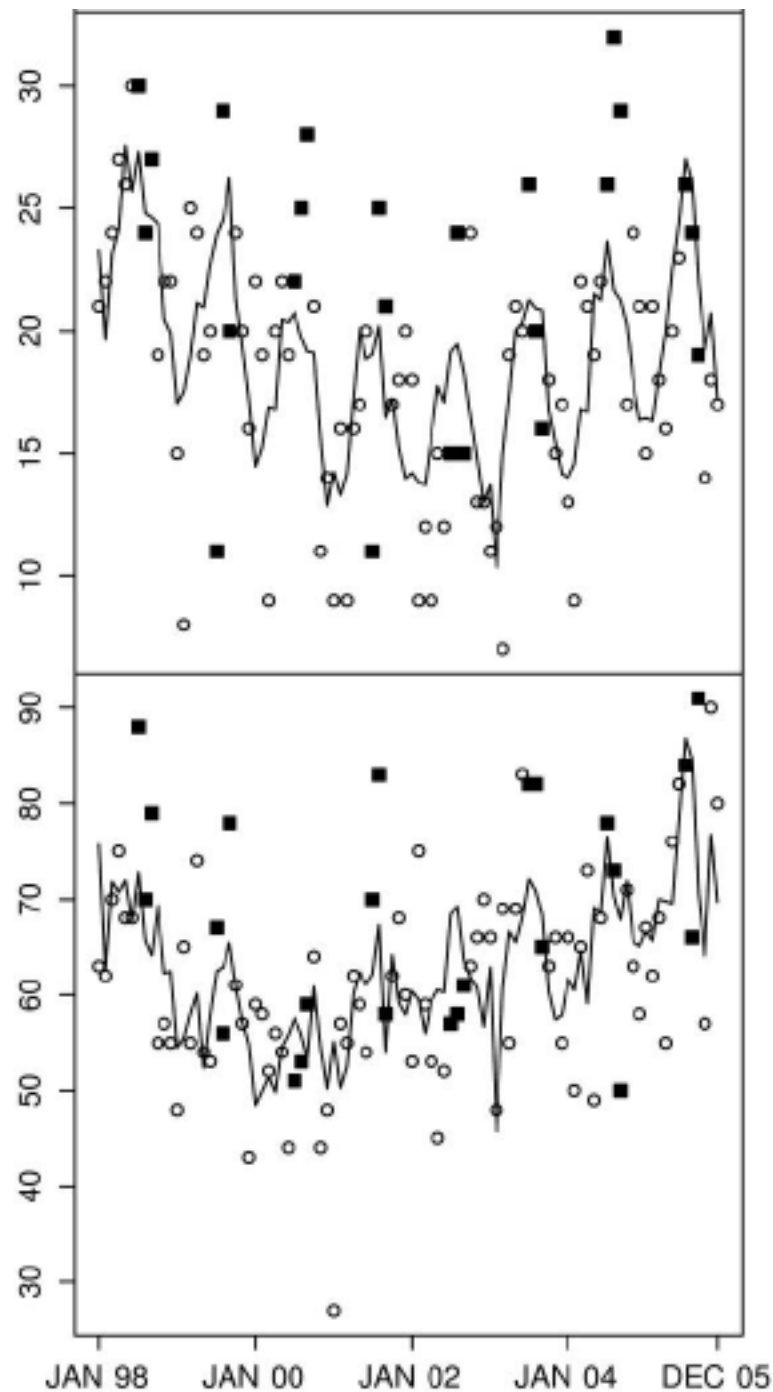
No. of *P. aeruginosa* infections



No. of *A. baumannii* infections



No. of *E. coli* infections



No. of *E. cloacae* infections

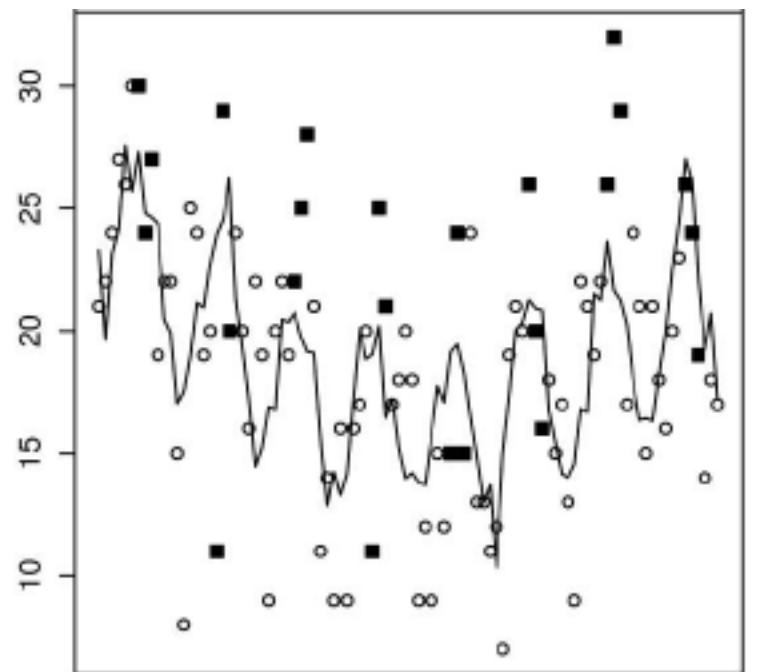


TABLE 1. Seasonal Incidences of Infection Among Hospitalized Patients at the University of Maryland Medical Center, 1998–2005, Compared With Winter

Infecting organism, by class	Incident Rate Ratio (95% CI)			P ^a
	Spring (N = 54,742 admissions)	Summer (N = 56,167 admissions)	Fall (N = 55,214 admissions)	
Gram-positive bacteria				
<i>Enterococcus</i> species	0.95 (0.88–1.03)	0.91 (0.84–0.98)	0.88 (0.81–0.95)	<.01
<i>Staphylococcus aureus</i>	0.99 (0.91–1.08)	1.04 (0.95–1.13)	1.02 (0.94–1.12)	.52
Gram-negative bacteria				
<i>Acinetobacter baumannii</i>	1.05 (0.90–1.23)	1.21 (1.04–1.41)	1.05 (0.89–1.23)	.06
<i>Pseudomonas aeruginosa</i>	0.98 (0.88–1.10)	1.28 (1.16–1.42)	1.06 (0.96–1.18)	<.01
<i>Enterobacter cloacae</i>	1.28 (1.12–1.48)	1.46 (1.27–1.67)	1.21 (1.04–1.39)	<.01
<i>Escherichia coli</i>	1.02 (0.93–1.11)	1.12 (1.03–1.22)	1.02 (0.93–1.12)	<.01

Seasonal Variation in *Klebsiella pneumoniae* Bloodstream Infection on 4 Continents

Deverick J. Anderson,¹ Hervé Richet,² Luke F. Chen,¹ Denis W. Spelman,³ Yi-Ju Hung,⁴ Andrew T. Huang,^{1,4} Daniel J. Sexton,¹ and Didier Raoult²

¹Duke University Medical Center, Durham, North Carolina; ²Faculté de Médecine, Université de la Méditerranée, UMR 6020, Marseille, France;

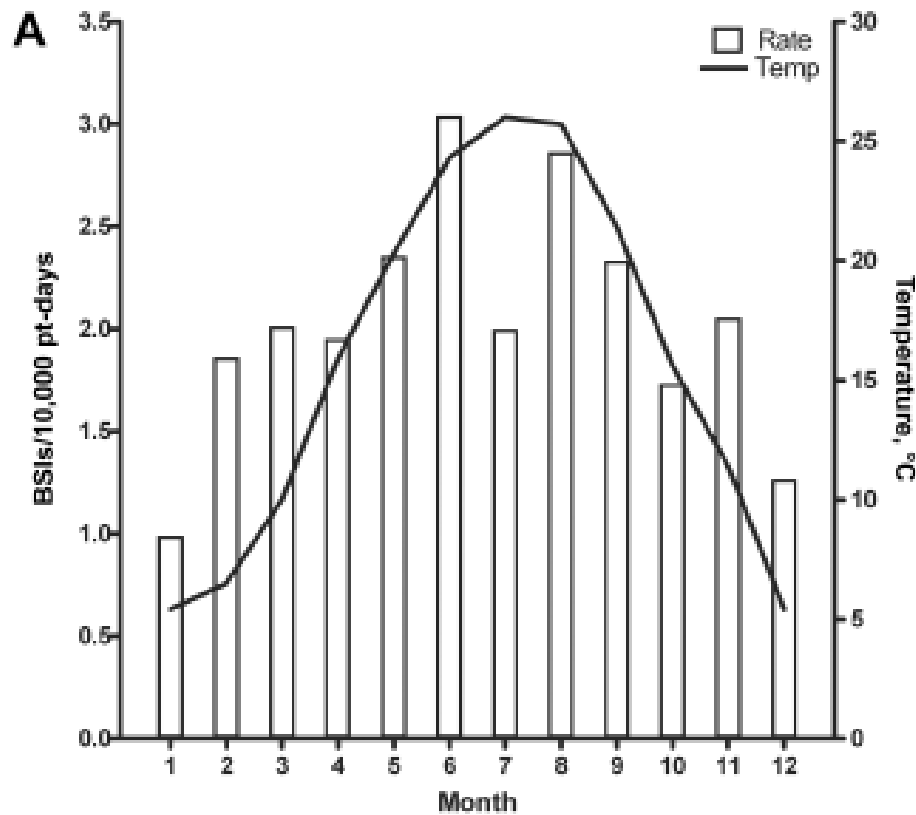
³The Alfred Hospital, Melbourne, Victoria, Australia; ⁴Koo Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan

The Journal of Infectious Diseases 2008; 197:752–6

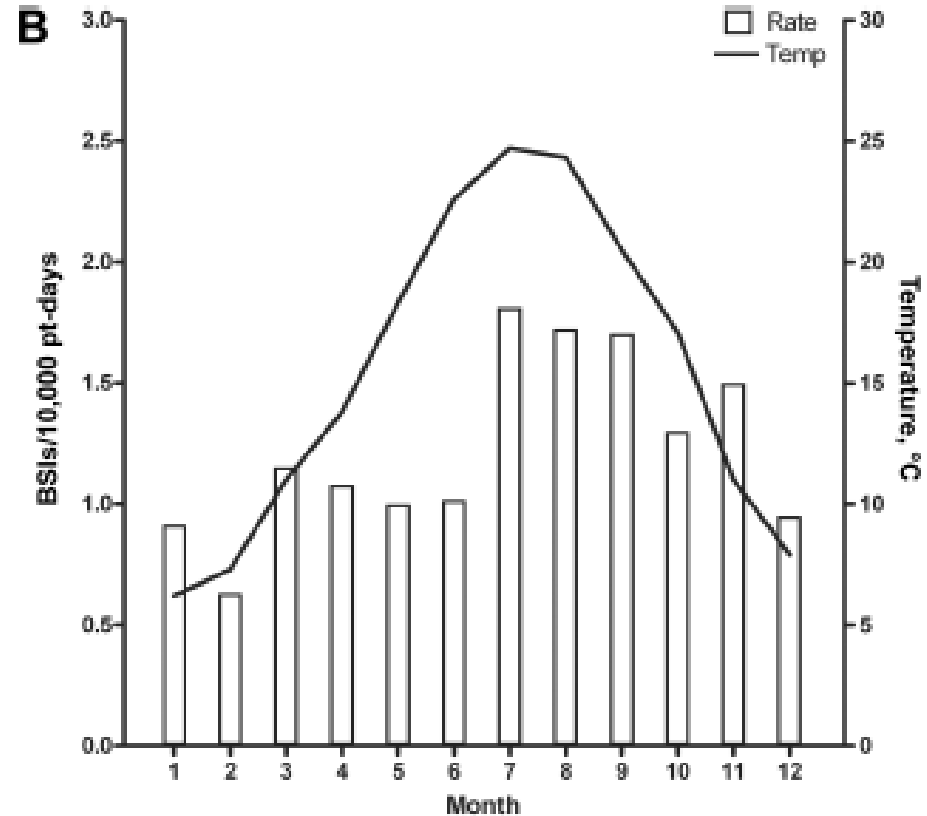
Hospitais de países em diferentes continentes

Estados Unidos, França, Austrália e Taiwan

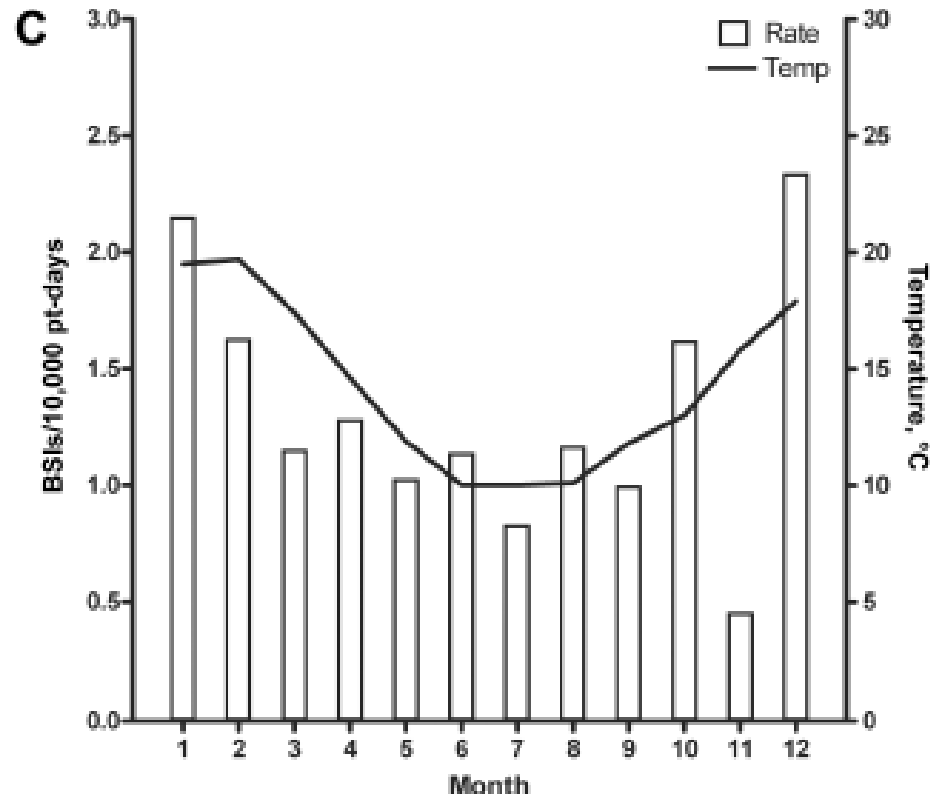
Infecções da corrente sanguínea em 2001-2006



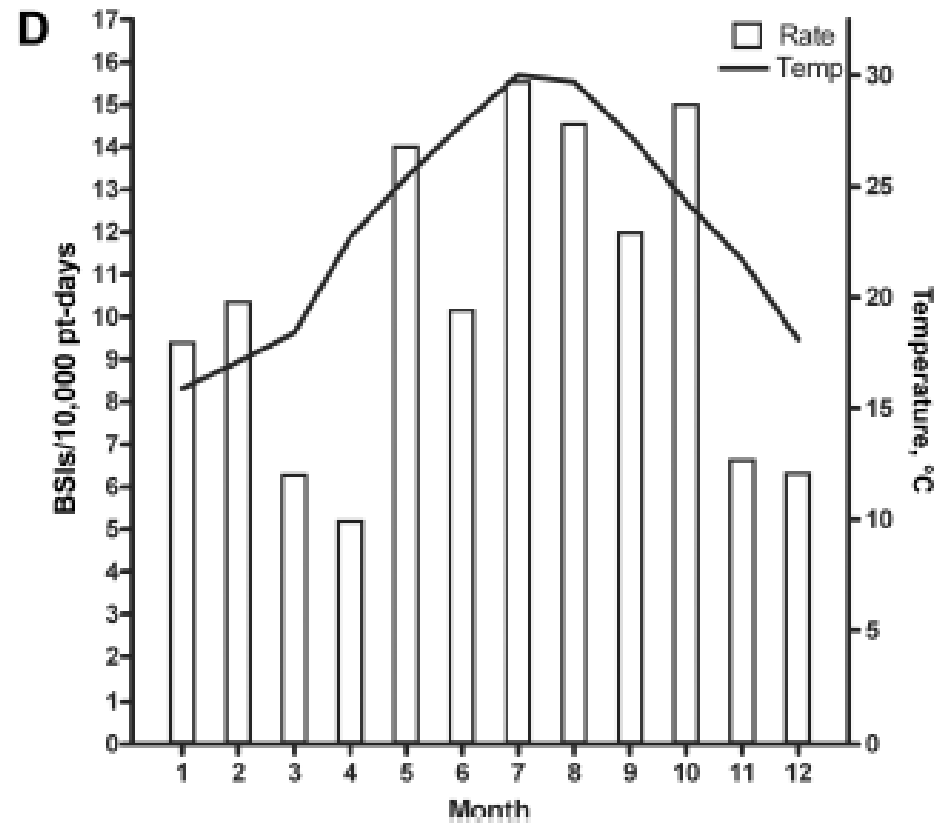
EUA



França



Austrália

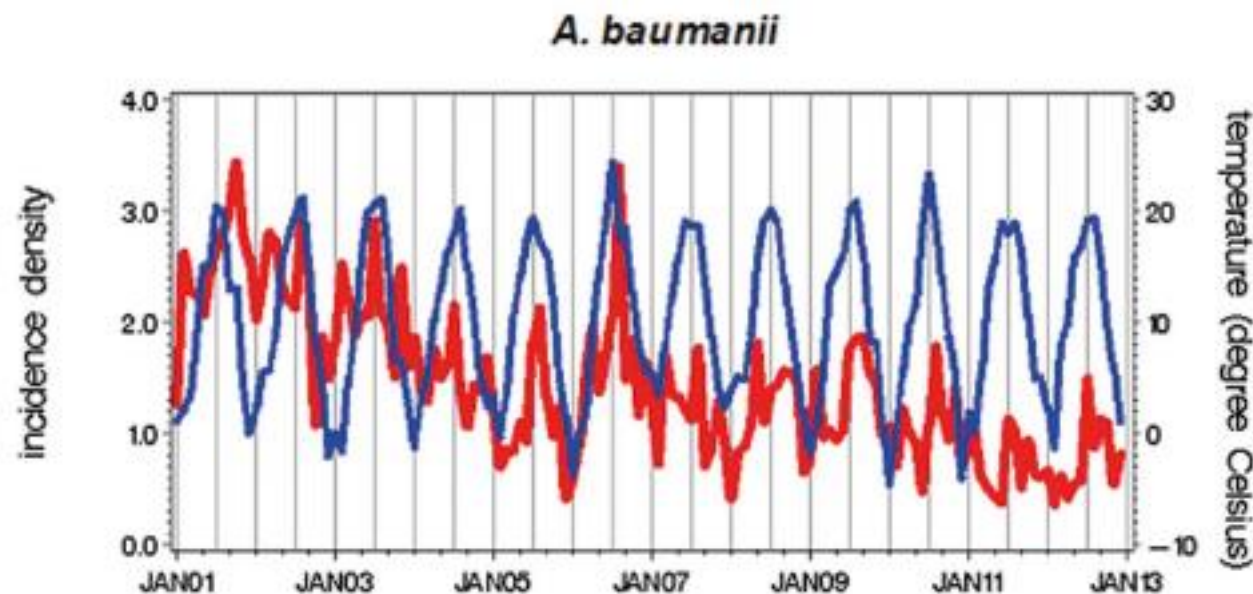


Taiwan

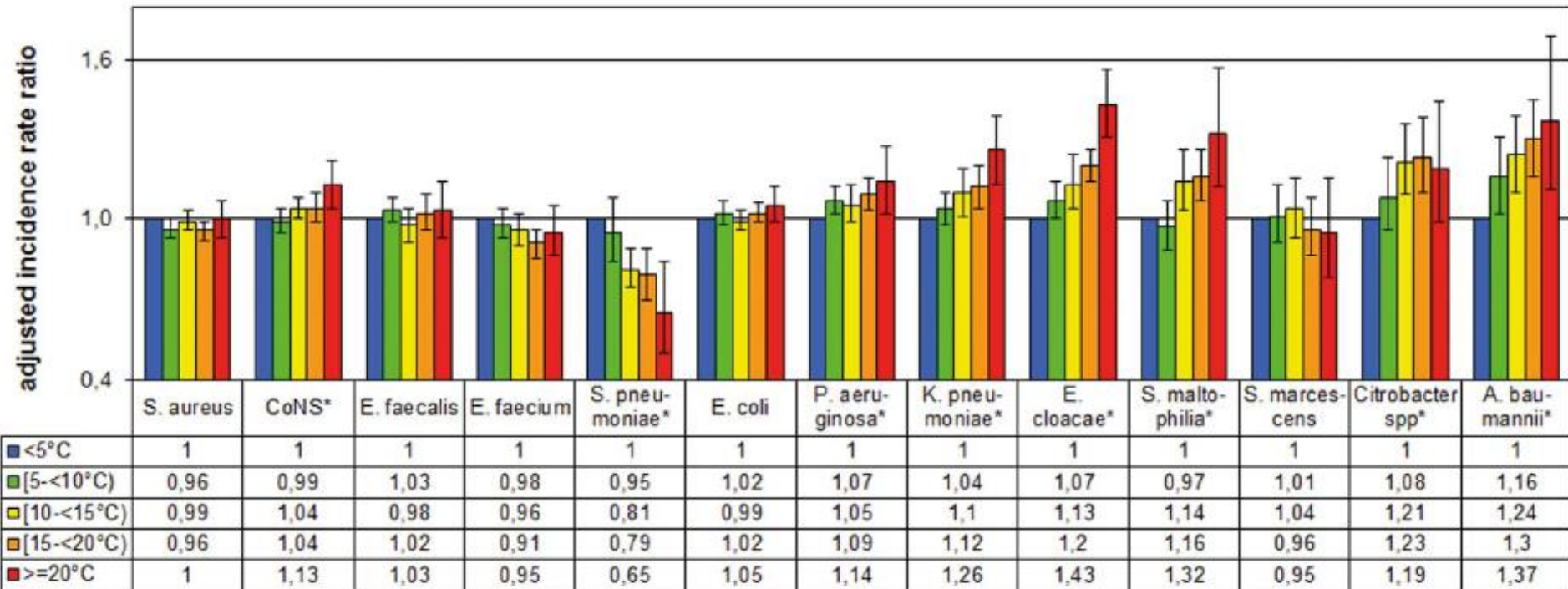
The Warmer the Weather, the More Gram-Negative Bacteria - Impact of Temperature on Clinical Isolates in Intensive Care Units

Frank Schwab^{1,2*}, Petra Gastmeier^{1,2}, Elisabeth Meyer^{1,2}

¹ Institute of Hygiene and Environmental Medicine, Charité - University Medicine Berlin, Berlin, Germany, ² National Reference Centre for Surveillance of Nosocomial Infections, Berlin, Germany



Citation: Schwab F, Gastmeier P, Meyer E (2014) The Warmer the Weather, the More Gram-Negative Bacteria - Impact of Temperature on Clinical Isolates in Intensive Care Units. PLoS ONE 9(3): e91105. doi:10.1371/journal.pone.0091105



CENÁRIO BRASILEIRO

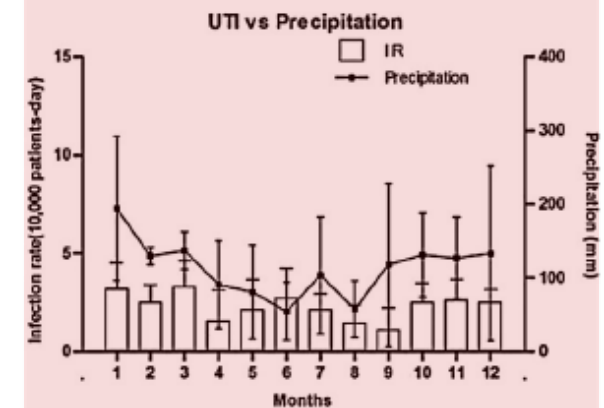
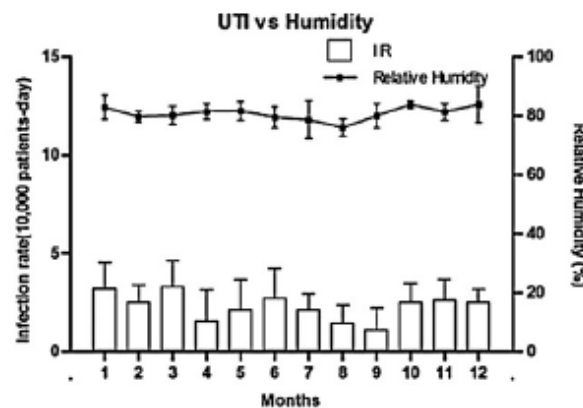
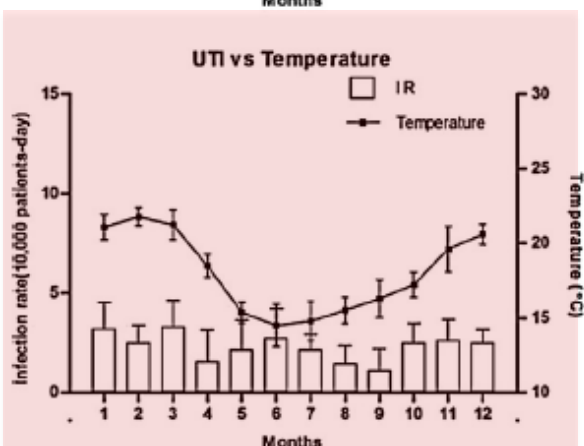
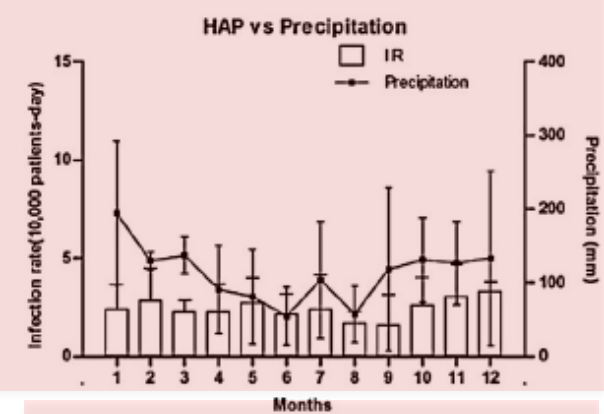
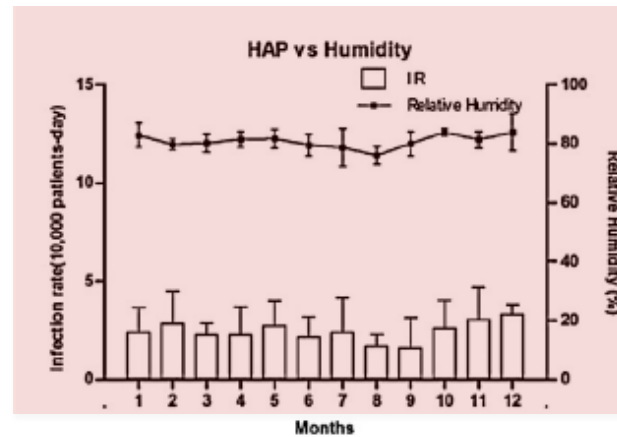
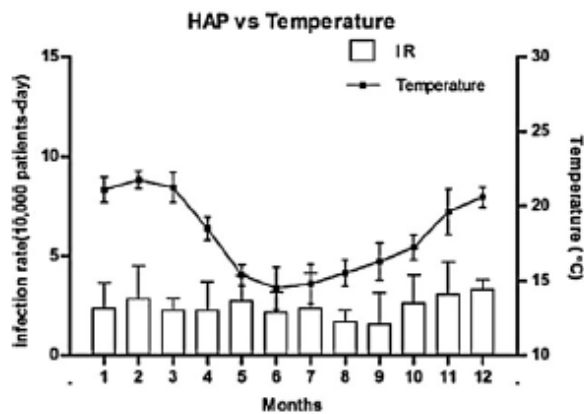
Seasonal humidity may influence *Pseudomonas aeruginosa* hospital-acquired infection rates

Guilherme P. Ramos^{a,*}, Jaime L. Rocha^b, Felipe F. Tuon^{a,c}

^a Division of Infectious and Parasitic Diseases, Hospital Universitário Evangélico de Curitiba, Al. Augusto Stella, 1908 (4o. Andar), Bigorrião, CEP 80730-150, Curitiba, Paraná, Brazil

^b Division of Microbiology, Frischmann Aisengart/DASA Medicina Diagnóstica, Curitiba, Paraná, Brazil

^c Division of Infectious Diseases, Hospital de Clínicas Universidade Federal do Paraná, Curitiba, Paraná, Brazil



Tropical Healthcare Epidemiology: Weather Determinants of the Etiology of Bloodstream Infections in a Brazilian Hospital

Carlos Magno Castelo Branco Fortaleza, MD, PhD;¹

Silvia Maria Caldeira, RN, MSc;¹

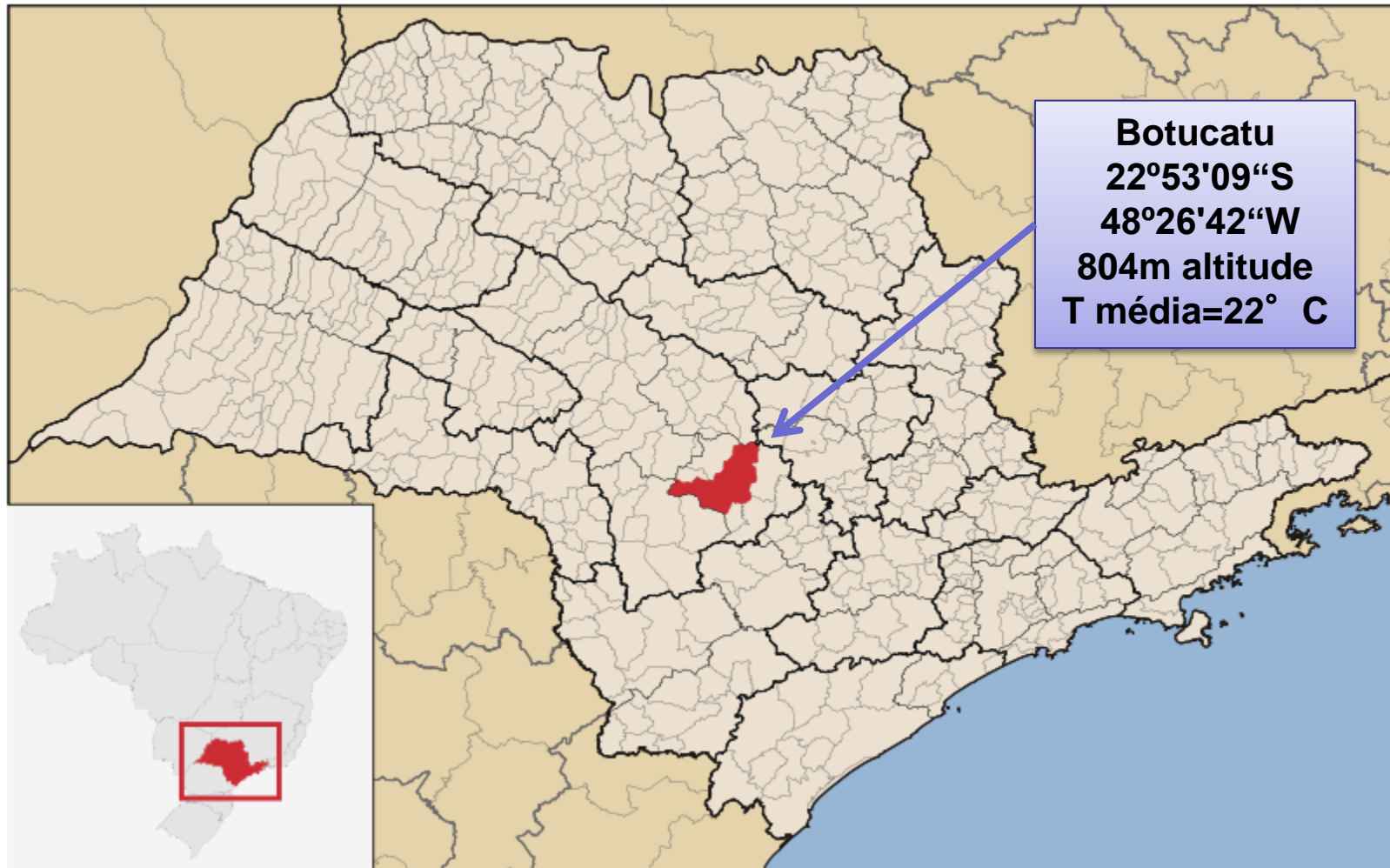
Rayana Gonçalves Moreira, MS;¹

Renata Tamie Akazawa, MS;¹

José Eduardo Corrente, PhD;²

Lenice do Rosário de Souza, MD, PhD;¹

Antônio Ribeiro da Cunha, PhD³



Hospital da Faculdade de Medicina de Botucatu (UNESP)



Estudo Ecológico



Unidade do Estudo: Mês.

Dados microbiológicos (mensais, 2005-2010)

- Hemoculturas colhidas após 3o. dia de internação.
- Eliminadas duplicidades: **1.672 culturas.**

Dados climáticos (mensais, 2005-2010)

- Temperatura média
- Umidade média

Análise

- Comparação taxas: “outubro-março” *versus* “abril-setembro”
- Modelo estocástico para avaliação de sazonalidade.
- Regressão linear multivariada (SPSS, v.19.0)

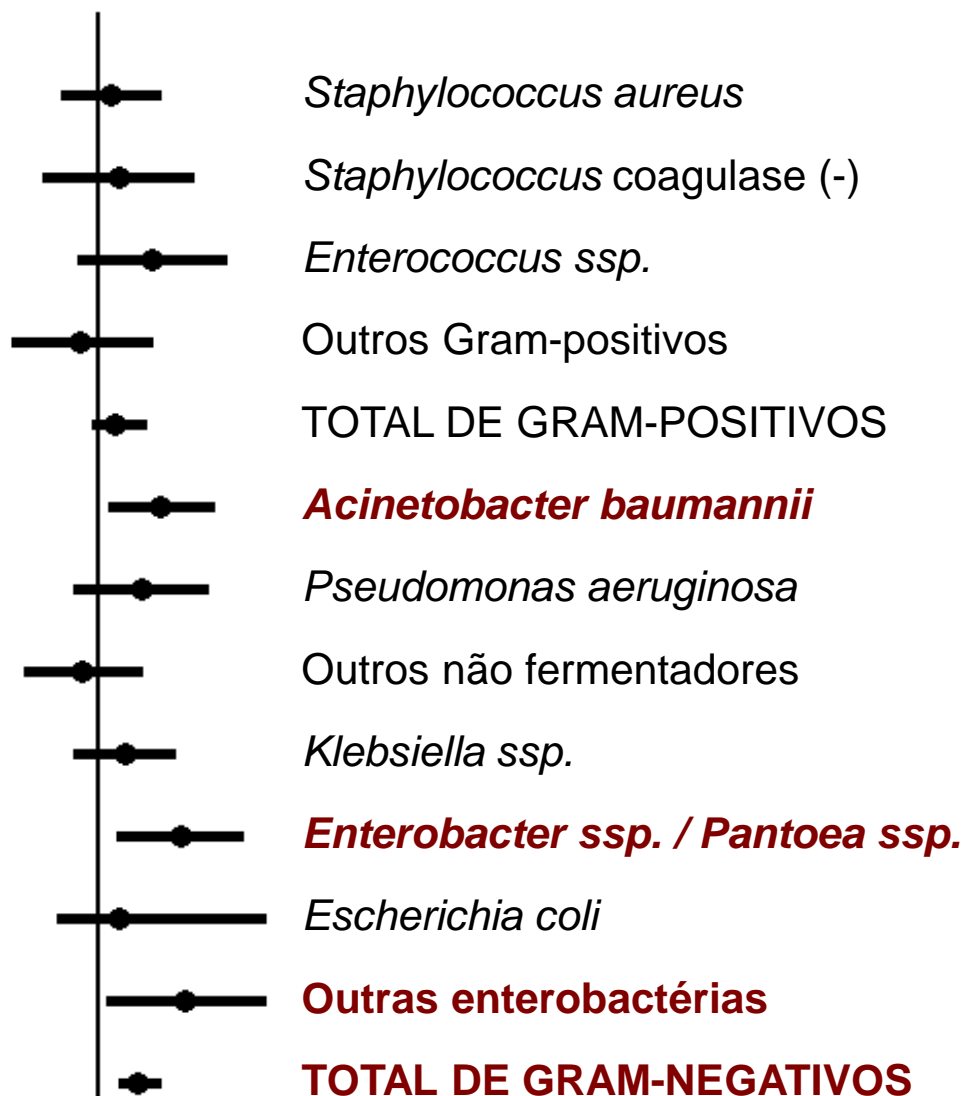
Resultados

TABLE 1. Comparison of Incidence Rates for Agents of Healthcare-Associated Bloodstream Infections during Warm (October–March) and Cold (April–September) Months

Pathogen	Incidence rate, per 10,000 patient-days			Rate ratio (95% CI)	P
	Overall	Oct–Mar	Apr–Sep		
Gram-positive cocci	6.72	7.01	6.45	1.09 (0.96–1.30)	.4
<i>Staphylococcus aureus</i>	2.79	2.89	2.70	1.07 (0.81–1.41)	.6
CoNS	1.22	1.29	1.16	1.11 (0.73–1.68)	.6
<i>Enterococcus</i> species	1.29	1.49	1.11	1.34 (0.89–2.02)	.2
Gram-negative bacilli	13.67	15.19	12.20	1.24 (1.11–1.41)	<.001
<i>Acinetobacter baumannii</i>	2.46	2.89	2.05	1.41 (1.05–1.90)	.02
<i>Pseudomonas aeruginosa</i>	1.61	1.80	1.43	1.26 (0.87–1.82)	.2
<i>Klebsiella</i> species	2.70	2.89	2.51	1.15 (0.87–1.53)	.3
<i>Enterobacter</i> species	1.79	2.20	1.40	1.57 (1.10–2.23)	.01
<i>Escherichia coli</i>	1.93	2.03	1.84	1.11 (0.79–2.53)	.6

NOTE. *Pantoea* species were grouped with *Enterobacter* species. Significant results are presented in boldface. CI, confidence interval; CoNS, coagulase-negative staphylococci.

RR (IC95%)



0.1 1 10
Forest Plot

Maior em meses frios

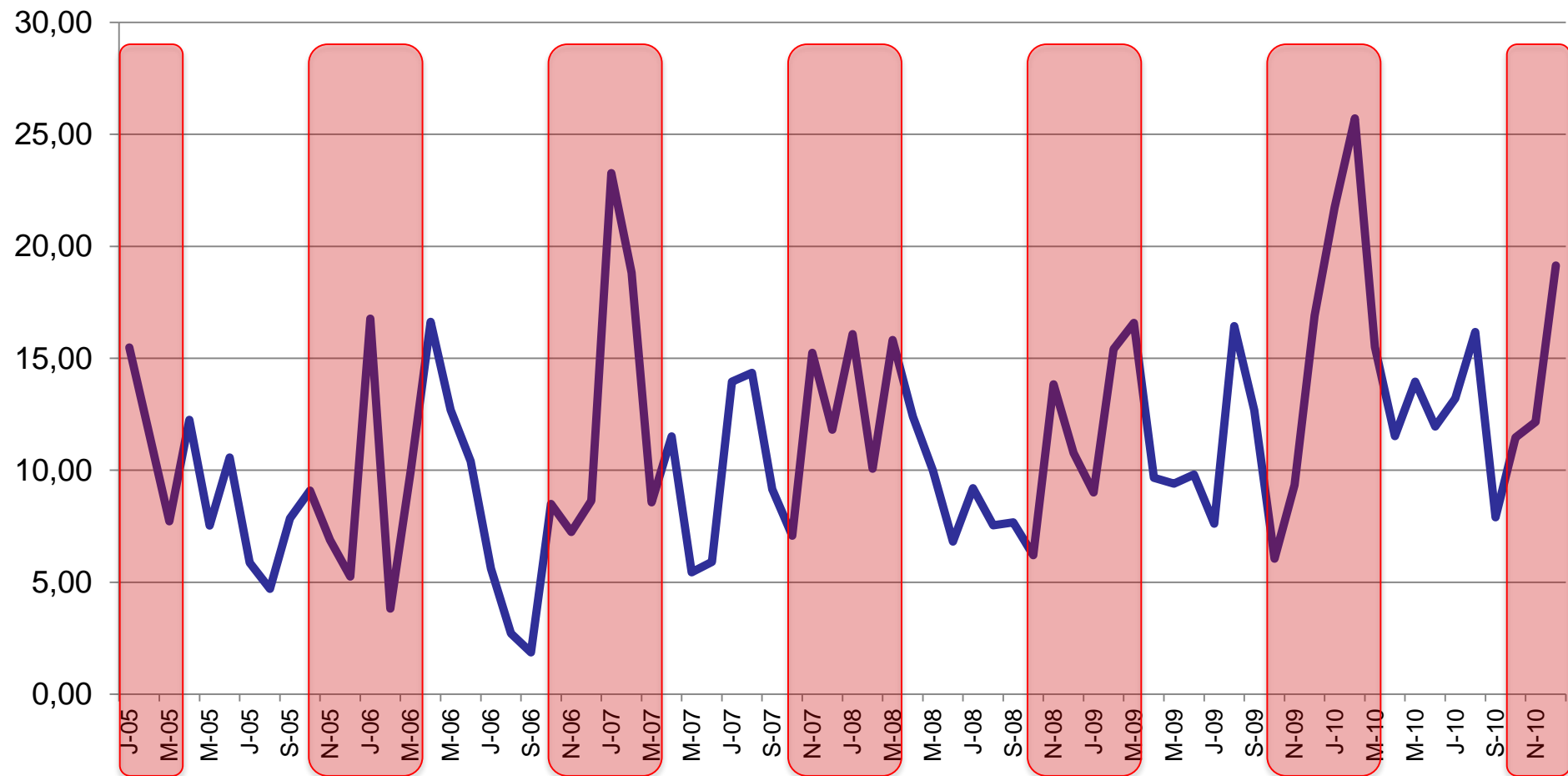
Maior em meses quentes

Pathogen, weather parameter	Adjusted rate ratio (95% CI)	P
Gram-positive cocci		
Temperature	0.99 (0.95–1.03)	.63
Relative humidity	1.01 (0.99–1.02)	.20
<i>Staphylococcus aureus</i>		
Temperature	0.99 (0.92–1.07)	.93
Relative humidity	0.99 (0.98–1.02)	.80
CoNS		
Temperature	0.95 (0.87–1.06)	.41
Relative humidity	1.02 (0.99–1.04)	.29
<i>Enterococcus</i> species		
Temperature	1.01 (0.92–1.12)	.75
Relative humidity	1.01 (0.99–1.04)	.32
Gram-negative bacilli		
Temperature	1.04 (1.01–1.08)	.005
Relative humidity	1.01 (1.00–1.02)	.06
<i>Acinetobacter baumannii</i>		
Temperature	1.13 (1.05–1.22)	.03
Relative humidity	1.00 (0.98–1.02)	.78
<i>Pseudomonas aeruginosa</i>		
Temperature	1.03 (0.95–1.14)	.41
Relative humidity	1.01 (0.99–1.03)	.24
<i>Klebsiella</i> species		
Temperature	1.01 (0.95–1.08)	.71
Relative humidity	1.01 (0.99–1.03)	.43
<i>Enterobacter</i> species		
Temperature	1.10 (1.01–1.19)	.03
Relative humidity	1.00 (0.98–1.02)	0.69
<i>Escherichia coli</i>		
Temperature	1.04 (0.96–1.12)	0.35
Relative humidity	1.00 (0.98–1.02)	0.99

Modelos Estocásticos

- Modelos ARIMA.
- Sazonalidade de ordem 12.
- Agentes sazonais ($p < 0,05$):
 - Gram-negativos como um todo.
 - *Acinetobacter baumannii*
 - *Enterobacter ssp.* / *Pantoea ssp.*

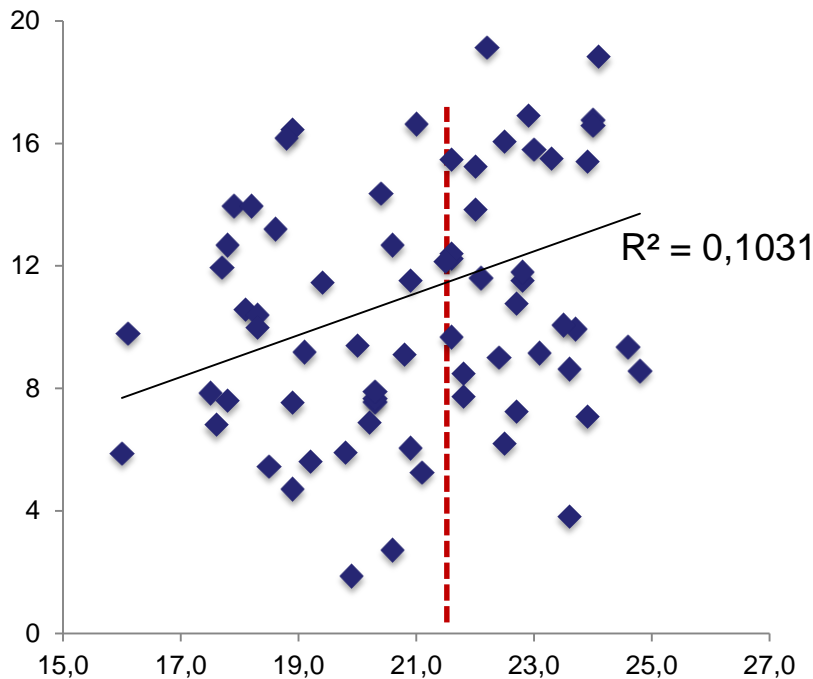
Bacilos Gram-negativos



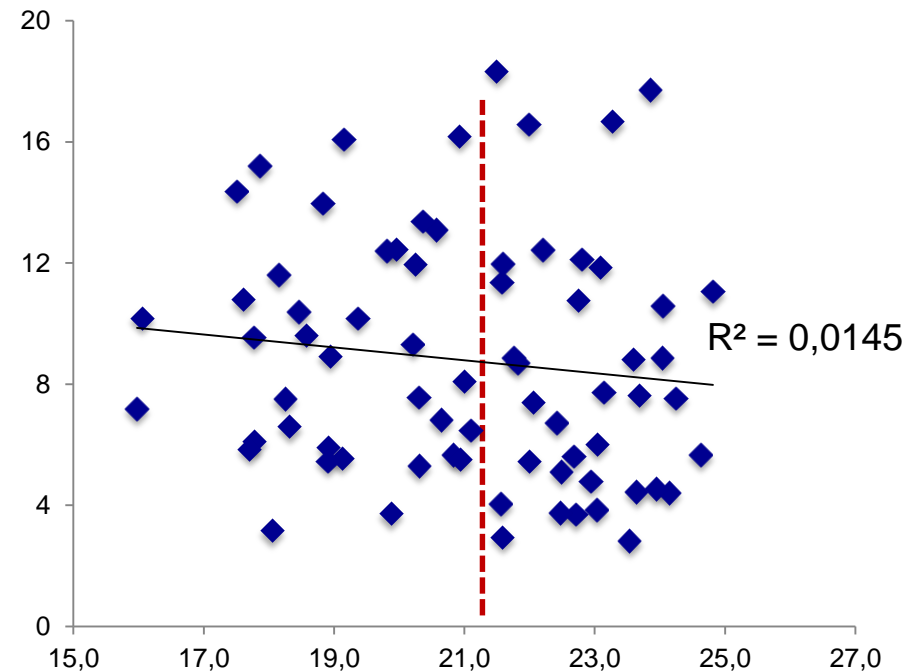
Regressão Linear Múltipla

(modelos incluindo **temperatura** e umidade)

Temperatura X Gram-negativos

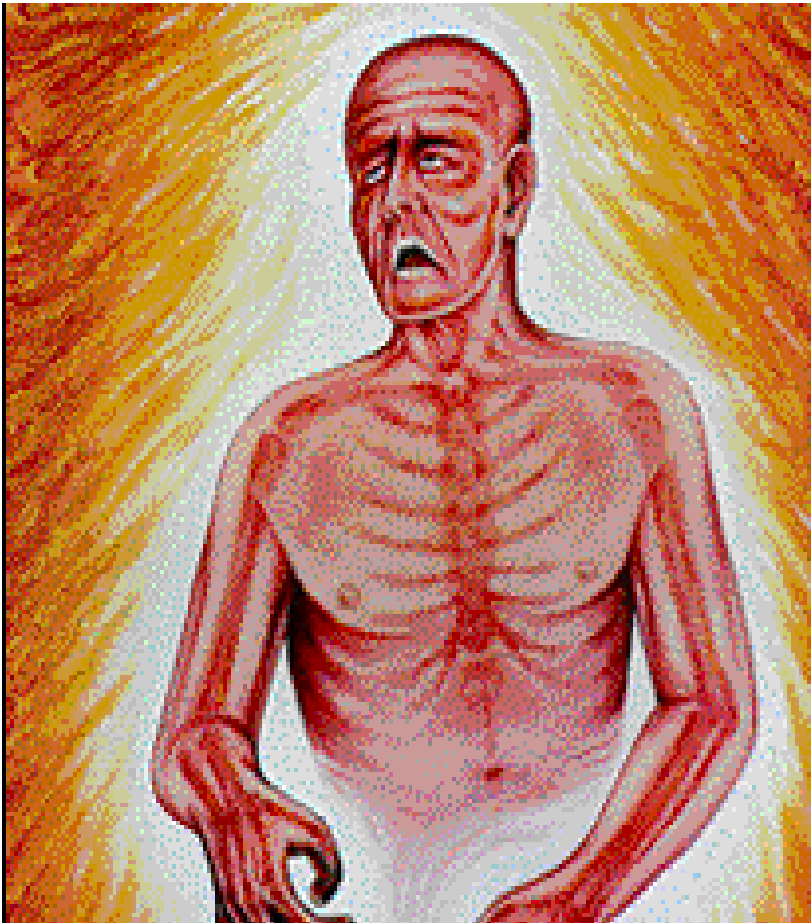


Temperatura X Gram-positivos



Temperatura → Gram-negativos ($p=0,04$), *A. baumannii* ($p=0,03$), *Enterobacter ssp/Pantoea ssp* ($p=0,04$) e outras enterobactérias minoritárias ($p=0,02$).

Estudo de Base Individual



- Caso-controle.
- 1.672 pacientes:
 - Hemoculturas (+) após D3 de internação.
- Análise: Regressão logística.
- Variáveis independentes:
 - Temperatura média dos 7 dias que precederam a coleta.
 - Umidade média dos 7 dias que precederam a coleta.
 - Internação em UTI (gravidade, climatização).

Table I. Comparison of the immediate meteorological parameters preceding the isolation of pathogens from blood cultures with overall data from the study period.

Category	No. of observations	Temperature (°C)	Relative Humidity (%)
<i>Overall data (reference)</i>	2815	20.99±2.66	70.20±10.76
Fungi	204	19.66±2.34	66.74±12.37
Bacteria	1417	21.84±2.74	71.29±10.27
Gram-positive cocci	627	20.93±2.83	73.40±8.55
Gram-negative bacilli	790	21.76±2.51	69.91±11.18
<i>Acinetobacter baumannii</i>	177	22.99±2.62	63.82±10.23

Predictive factors	Crude OR (95%CI)	Adjusted OR(1)	Adjusted OR(2)	Adjusted OR(3)
<i>Bacteria (1417) versus Fungi (204)</i>				
Temperature (°C)	1.25 (1.19-1.32)	1.25 (1.18-1.31)	1.25 (1.19-1.32)	1.26 (1.19-1.33)
Relative Humidity (%)	1.04 (1.02-1.05)	1.04 (1.02-1.05)	1.04 (1.02-1.05)	1.03 (1.02-1.05)
Intensive Care Unit	0.71 (0.52-0.99)	0.88 (0.63-1.24)
Time since admission	1.00 (0.99-1.01)	1.00 (0.99-1.01)
Age in years	1.02 (1.01-1.03)
Female gender	1.03 (0.75-1.40)
<i>GB (790) versus GPC (627)</i>				
Temperature (°C)	1.12 (1.08-1.17)	1.14 (1.10-1.19)	1.14 (1.10-1.19)	1.14 (1.10-1.19)
Relative Humidity (%)	0.96 (0.95-0.97)	0.96 (0.95-0.97)	0.96 (0.95-0.97)	0.96 (0.95-0.97)
Intensive Care Unit	0.79 (0.62-1.00)	0.75 (0.59-0.96)
Time since admission	1.00 (0.99-1.00)	1.00 (0.99-1.00)
Age in years	1.00 (0.99-1.00)
Female gender	1.21 (0.98-1.51)
<i>Acinetobacter baumannii (177) versus other GNB (613)</i>				
Temperature (°C)	1.23 (1.14-1.33)	1.26 (1.16-1.37)	1.26 (1.16-1.38)	1.26 (1.16-1.37)
Relative Humidity (%)	0.95 (0.93-0.96)	0.94 (0.93-0.96)	0.94 (0.93-0.96)	0.94 (0.93-0.96)
Intensive Care Unit	0.73 (0.49-1.11)	0.75 (0.49-1.13)
Time since admission	1.00 (0.99-1.00)	1.00 (0.99-1.00)
Age in years	1.00 (0.99-1.01)
Female gender	0.89 (0.62-1.28)

Seasonality in Gram-negative and healthcare-associated infections

H. Richet

IHU Méditerranée Infections, Aix-Marseille Université, Marseille, France

Clin Microbiol Infect 2012; 18: 934–940

TABLE 2. Seasonality in healthcare-associated infections and correlation with temperature

Microorganism	Author [reference]	Seasonality	Correlation with temperature
<i>Enterobacter cloacae</i>	Perencevich [15]	Yes	Yes
<i>Escherichia coli</i>	Perencevich [15]	Yes	Yes
<i>Acinetobacter baumannii</i>	Perencevich [15]	Yes	Yes
<i>Pseudomonas aeruginosa</i>	Perencevich [15]	Yes	Yes
<i>Acinetobacter</i> spp.	Retailliau [16]	Yes	–
	McDonald [17]	Yes	–
	Gales [18]	Yes	–
	Christie [19]	Yes	–

Sazonalidade e IH/IRAS

- Infecções do trato urinário.
 - Alta temperatura, baixa umidade.
- Infecções do sítio cirúrgico
 - Finlândia: Julho-Agosto.
- Gastreenterite por norovirus.
- Infecções da corrente sanguínea em pacientes hematológicos.
 - G-neg em meses quentes.
- Peritonite associada a diálise peritoneal domiciliar.
 - G-pos em meses quentes.

Smith TL et al. Infect Control Hosp Epidemiol 2002; 23: 239-43.

Koljonen V et al. Duodecim 2009; 125:1414-20.

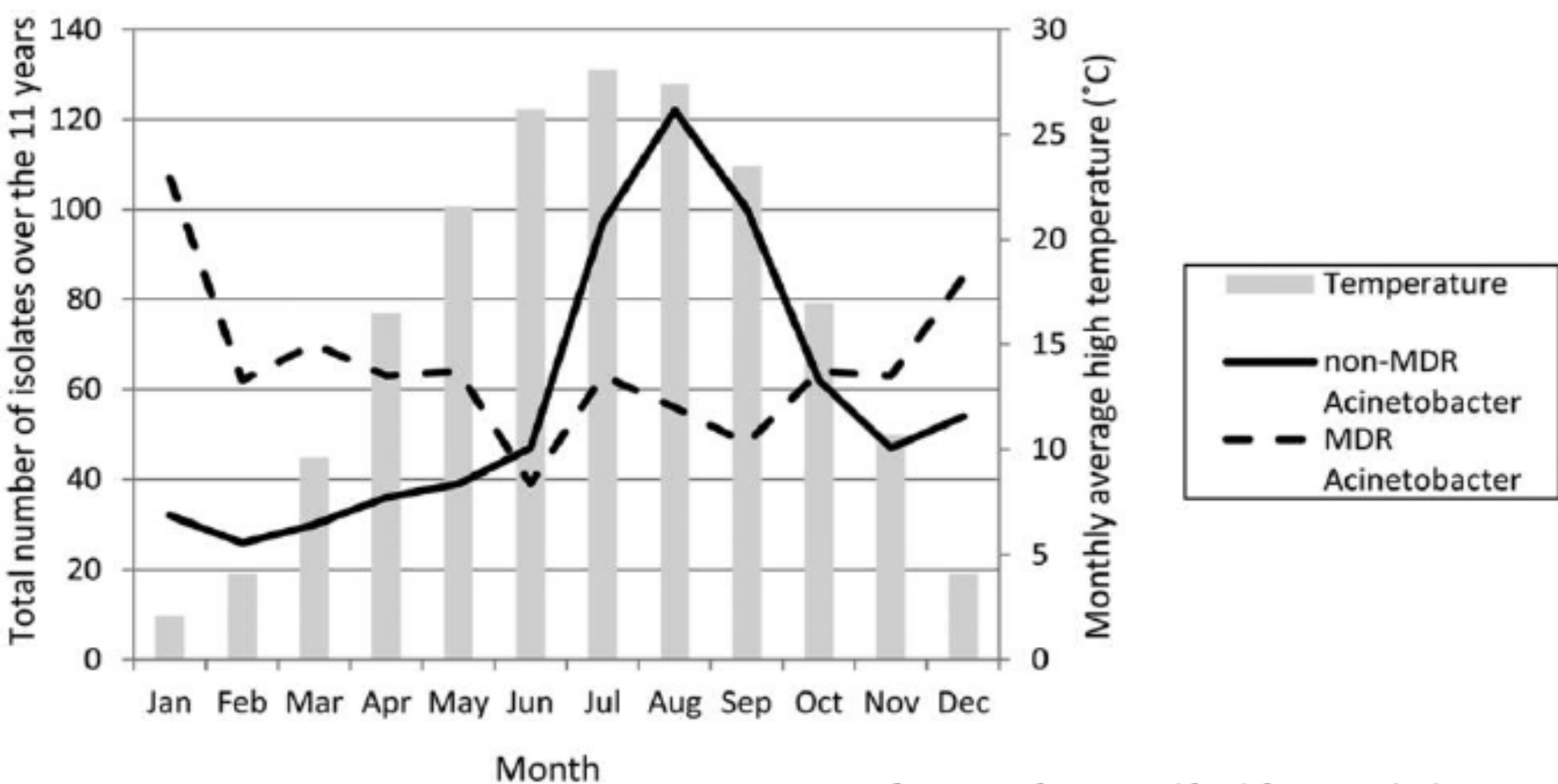
Cho Y et al. Nephrol Dial Transplant 2011; 4: 7-9.

Danial J et al. J Hosp Infect 2011; 79: 354-8.

SAZONALIDADE DA RESISTÊNCIA?

Lack of Seasonality in the Occurrence of Multidrug-Resistant *Acinetobacter baumannii* Complex

Yuriko Fukuta, MD;¹ Lloyd G. Clarke, MSc;²
Ryan K. Shields, PharmD;¹ Marilyn M. Wagener, MPH;³
A. William Pasculle, ScD;⁴ Yohei Doi, MD, PhD¹



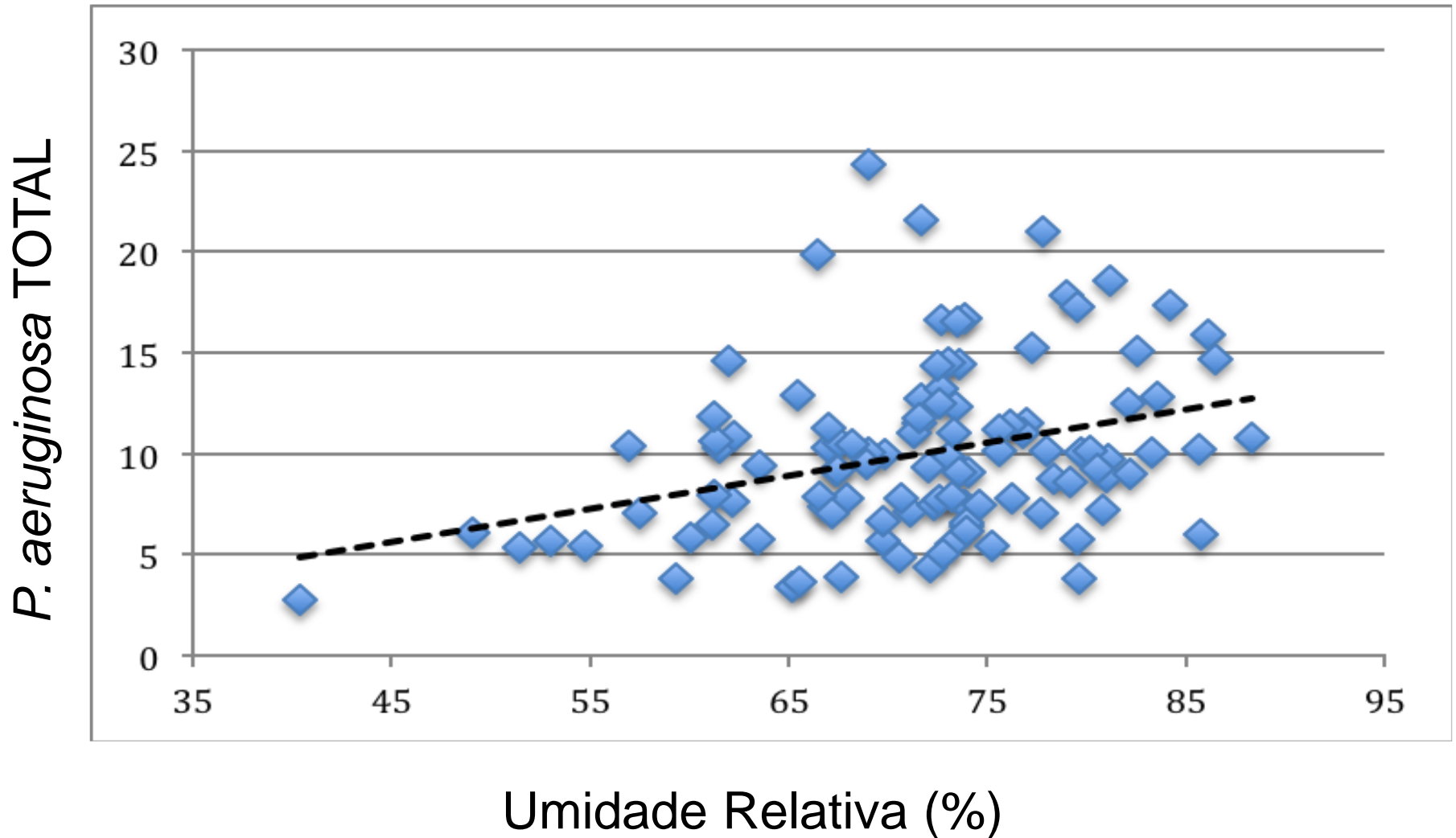
Definição arbitrária de Isolados Resistentes

Patógenos	Drogas definidoras de R
BGN não fermentadores	Imipenem
Enterobactérias	Cefalosporinas 3a G
Staphylococcus aureus	Oxacilina
Enterococcus spp.	Vancomicina

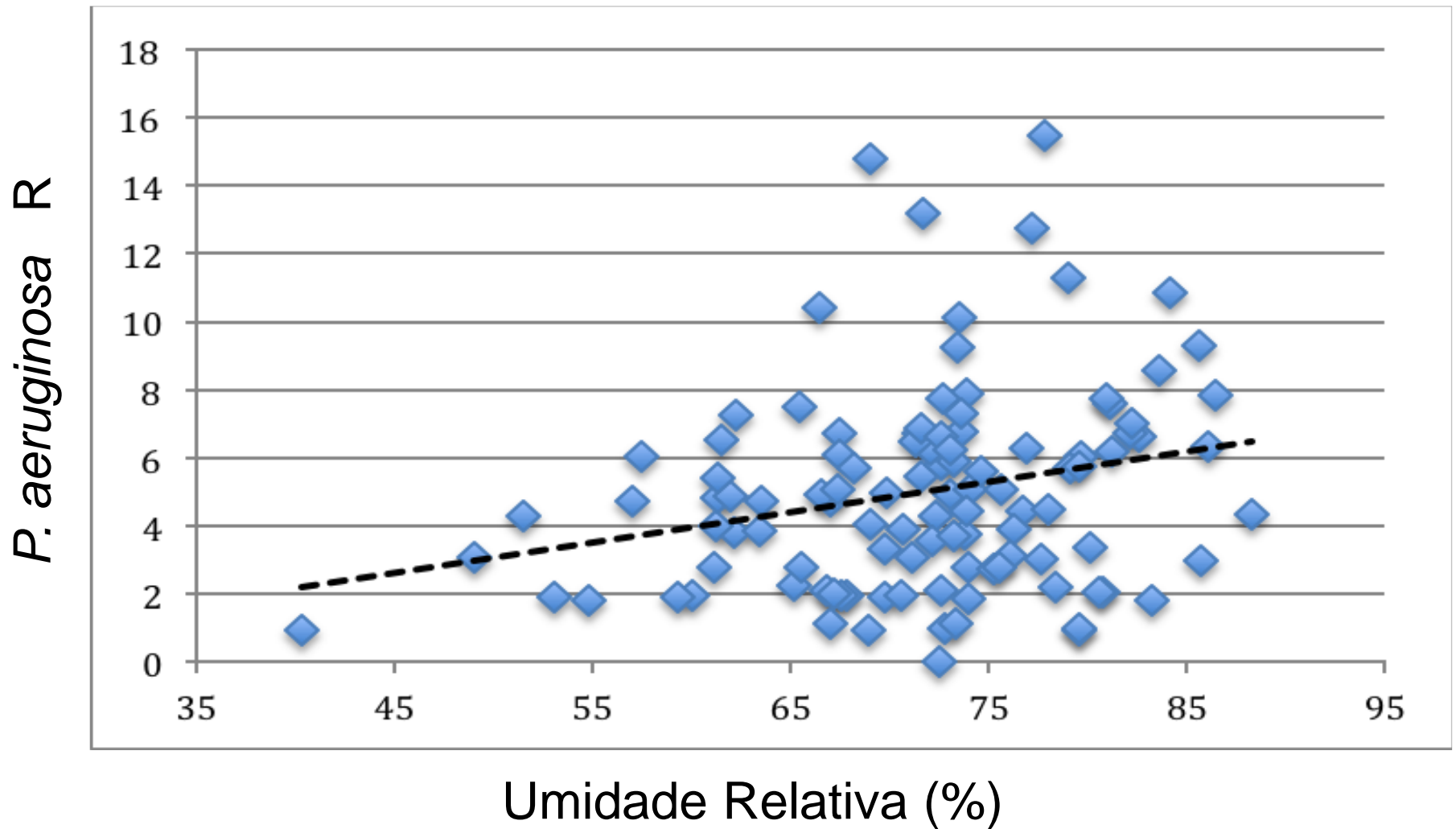
POISSON

Patógeno	RR (IC95%)	
	Temperatura (°C)	Umidade (%)
GRAM-NEGATIVOS		
<i>A baumannii</i>	1,04 (1,02-1,07)	1,00 (0,99-1,01)
<i>A baumannii</i> R	1,01 (0,97-1,04)	1,01 (1,002-1,02)
<i>P. aeruginosa</i>	0,99 (0,97-1,02)	1,02 (1,01-1,03)
<i>P. aeruginosa</i> R	1,00 (0,96-1,04)	1,02 (1,01-1,03)
<i>Enterobacter</i> spp	0,99 (0,97-1,02)	1,00 (0,99-1,01)
<i>Enterobacter</i> spp R	0,98 (0,94-1,01)	1,01 (1,001-1,02)
<i>Klebsiella</i> spp	1,01 (0,98-1,03)	1,00 (0,99-1,01)
<i>Klebsiella</i> R	1,02 (0,99-1,05)	1,00 (0,99-1,01)
GRAM-POSITIVOS		
<i>S. aureus</i>	0,98 (0,95-1,00)	1,00 (0,99-1,01)
<i>S. aureus</i> R	0,97 (0,95-1,01)	1,00 (0,99-1,01)
<i>Enterococcus</i> spp	0,99 (0,96-1,01)	1,00 (0,99-1,01)
<i>Enterococcus</i> spp R	0,95 (0,88-1,02)	1,00 (0,98-1,02)

CORRELAÇÃO



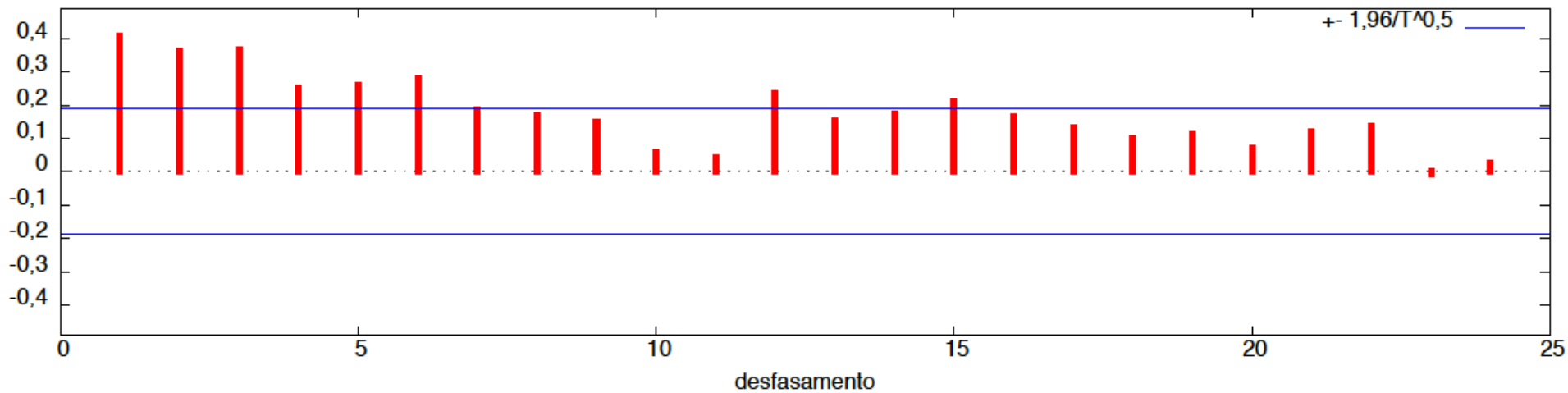
CORRELAÇÃO



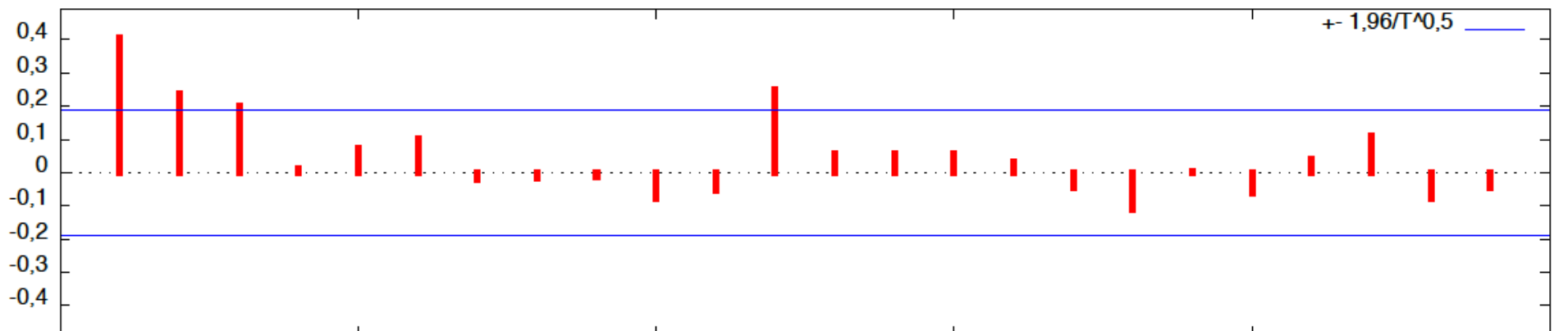
AUTOCORRELAÇÃO

A. baumannii TOTAL

ACF para TAXAACINETOTOTAL



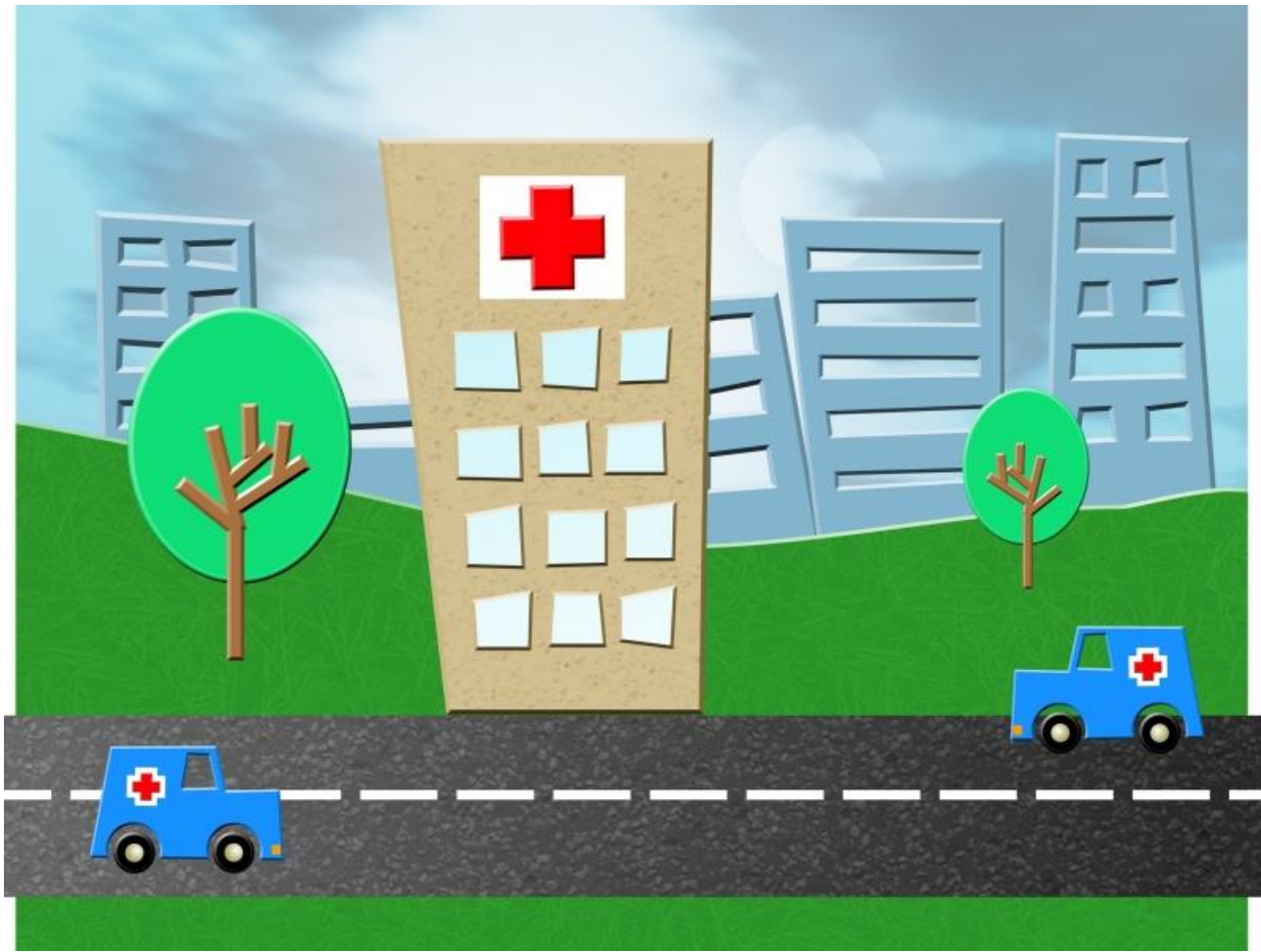
PACF para TAXAACINETOTOTAL



Embora sejam complexas, as variações periódicas e a influência do clima sobre a incidência de patógenos nosocomiais é consistente. Ao contrário do que foi sugerido em pesquisas anteriores, **esses fenômenos não são restritos a patógenos multidroga-suscetíveis.**

HIPÓTESES

PATÓGENOS TRAZIDOS DO AMBIENTE EXTERNO



UNDERSTAFFING EM FÉRIAS DE VERÃO



PATOGENICIDADE AUMENTADA



RESERVATÓRIOS AMBIENTAIS



Dúvidas e Problemas

- Quais os determinantes da sazonalidade de patógenos e síndromes infecciosas hospitalares?
 - Reservatórios ambientais?
 - Fatores comportamentais?
- Por que a sazonalidade hospitalar predomina em Gram negativos, se há clara sazonalidade de infecções por *S. aureus* na comunidade?
- Qual a relação entre IH/IRAS e alterações climáticas globais?
- Dificuldades na abordagem estatística apropriada
 - Métodos usuais (Chi-quadrado) não acurados (variáveis não são independentes).
 - Alternativas: modelos estocásticos, autocorrelação.

Fisman D. Annu Rev Public Health 2007; 28: 127-43.
Leekha S et al. Clin Microbiol Infect 2012: 927-33.
Chistiansen CF et al. Clin Microbiol Infect 2012; 18:963-9.

Comentários finais...

- Ainda há dúvidas quanto ao significado e determinantes da sazonalidade em IRAS.
- Há no entanto clara relação entre calor, BGN e alguns sítios de infecção.
- São necessários...
 - ... estudos multicêntricos.
 - ... esforços concentrados de controle de infecção.

Obrigado



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