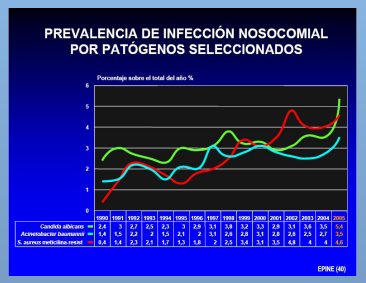
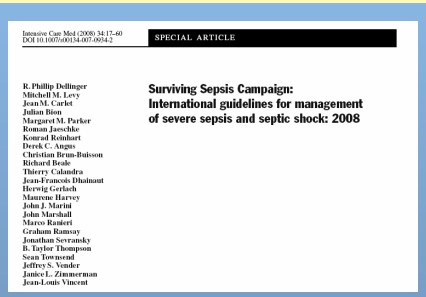
Manejo de la Sepsis por MRSA




Intensive Care Med (2008) 34:17–60
DOI 10.1007/s00134-007-0934-2

SPECIAL ARTICLE

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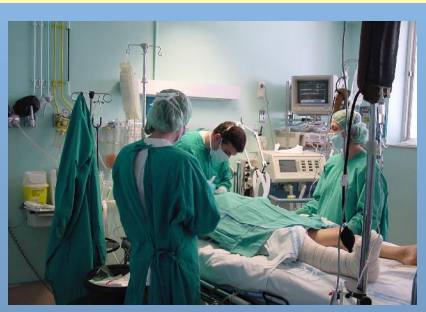
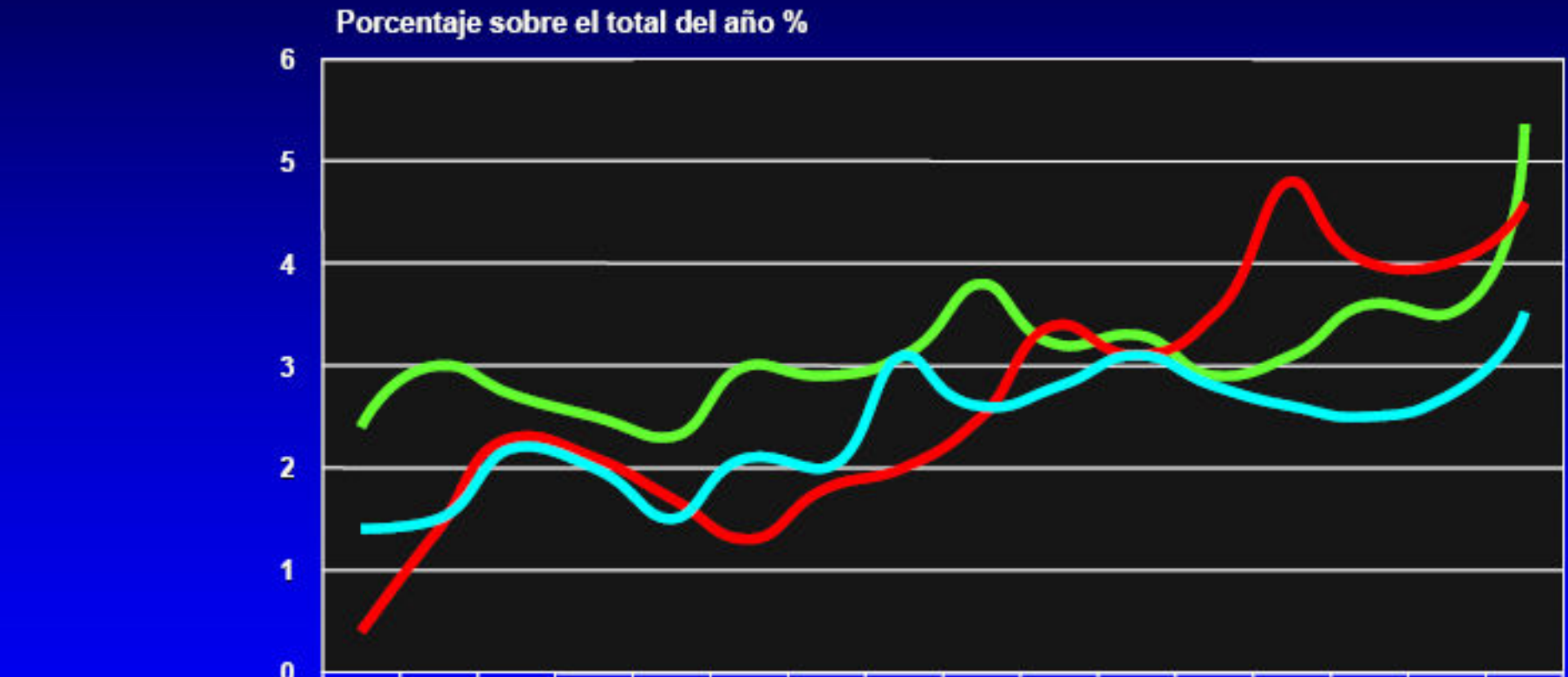
Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008



JI Ayestarán
UCI HSD

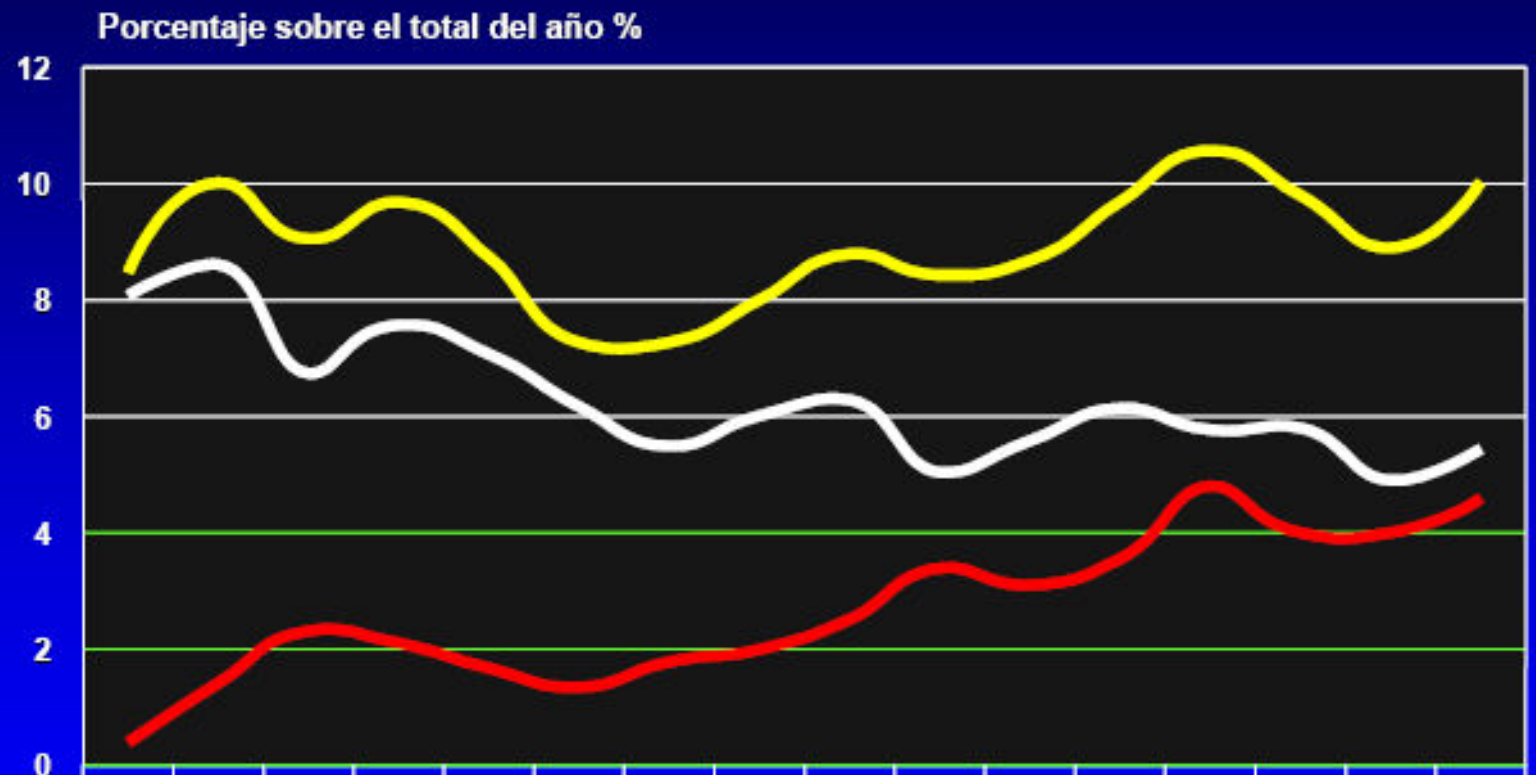
PREVALENCIA DE INFECCIÓN NOSOCOMIAL POR PATÓGENOS SELECCIONADOS



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Candida albicans	2,4	3	2,7	2,5	2,3	3	2,9	3,1	3,8	3,2	3,3	2,9	3,1	3,6	3,5	5,4
Acinetobacter baumannii	1,4	1,5	2,2	2	1,5	2,1	2	3,1	2,6	2,8	3,1	2,8	2,6	2,5	2,7	3,5
S. aureus meticilina-resist	0,4	1,4	2,3	2,1	1,7	1,3	1,8	2	2,5	3,4	3,1	3,5	4,8	4	4	4,6

EPINE (40)

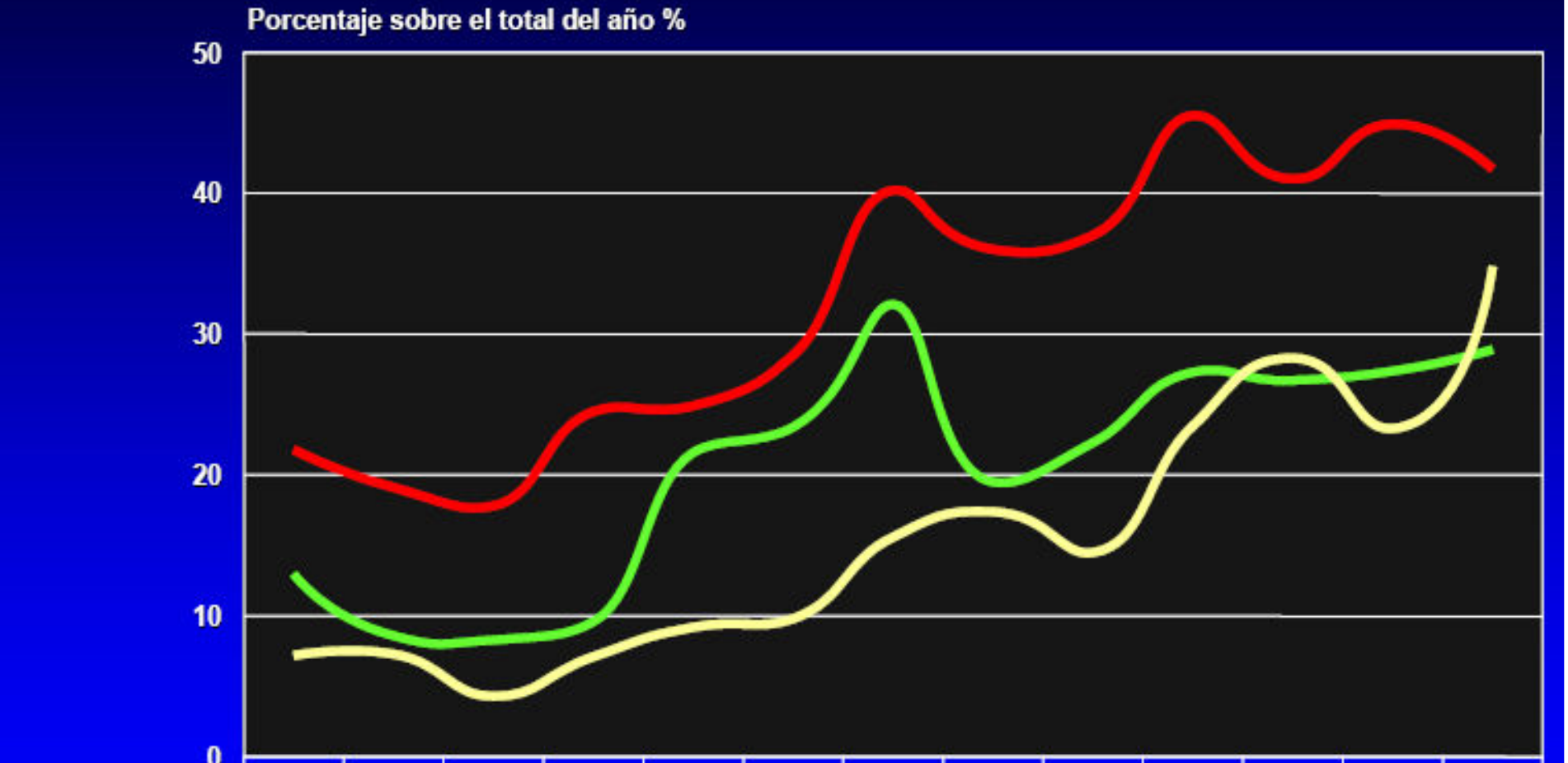
PREVALENCIA DE INFECCIÓN NOSOCOMIAL POR *STAPHYLOCOCCUS AUREUS*. EPINE 1990-2005



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
S. aureus (total)	8,5	10	9,1	9,7	8,7	7,3	7,3	8	8,8	8,4	8,7	9,7	10,6	9,8	8,9	10
S. a. meticilina sensibles	8,1	8,6	6,7	7,6	7,1	6,2	5,5	6	6,3	5	5,6	6,1	5,8	5,8	4,9	5,4
S. a. meticilina resistentes	0,4	1,4	2,3	2,1	1,7	1,3	1,8	2	2,5	3,4	3,1	3,6	4,8	4	4	4,6

EPINE (41)

PORCENTAJE DE *STAPHYLOCOCCUS AUREUS* RESISTENTES A METICILINA. EPINE 1993-2005



	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Inf. nosocomial	21,8	19,1	17,8	24,5	24,9	28,5	40,2	36,0	37,0	45,5	41,0	44,9	41,7
Inf. comunitaria	7,2	7,3	4,3	7,1	9,2	9,8	15,6	17,4	14,5	23,5	28,3	23,3	34,8
Bacteriemia	13,0	8,6	8,3	9,6	21,6	23,4	32,1	19,5	22,3	27,3	26,7	28,0	28,9

EPINE (43)

Methicillin-resistant *Staphylococcus aureus*: a new community-acquired pathogen?

Marin H. Kollef[a,b] and Scott T. Micek[c]

Current Opinion in Infectious Diseases 2006, 19:161–168

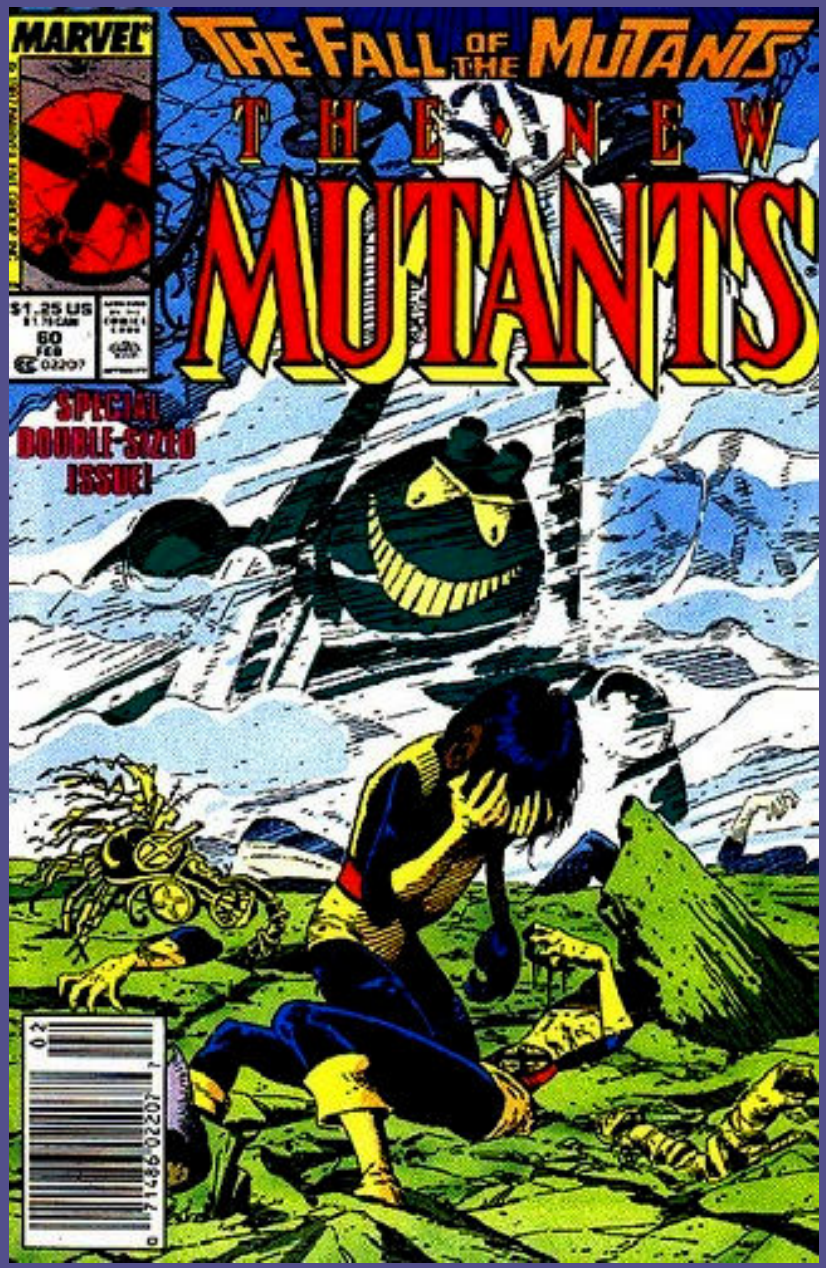
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Methicillin-Resistant *S. aureus* Infections among Patients in the Emergency Department

Gregory J. Moran, M.D., Anusha Krishnadasan, Ph.D., Rachel J. Gorwitz, M.D., M.P.H., Gregory E. Fosheim, M.P.H., Linda K. McDougal, M.S., Roberta B. Carey, Ph.D., and David A. Talan, M.D., for the *EMERGE*ncy ID Net Study Group*

N ENGL J MED 355;7 WWW.NEJM.ORG AUGUST 17, 2006


MARVEL
THE FALL OF THE MUTANTS
THE NEW
MUTANTS
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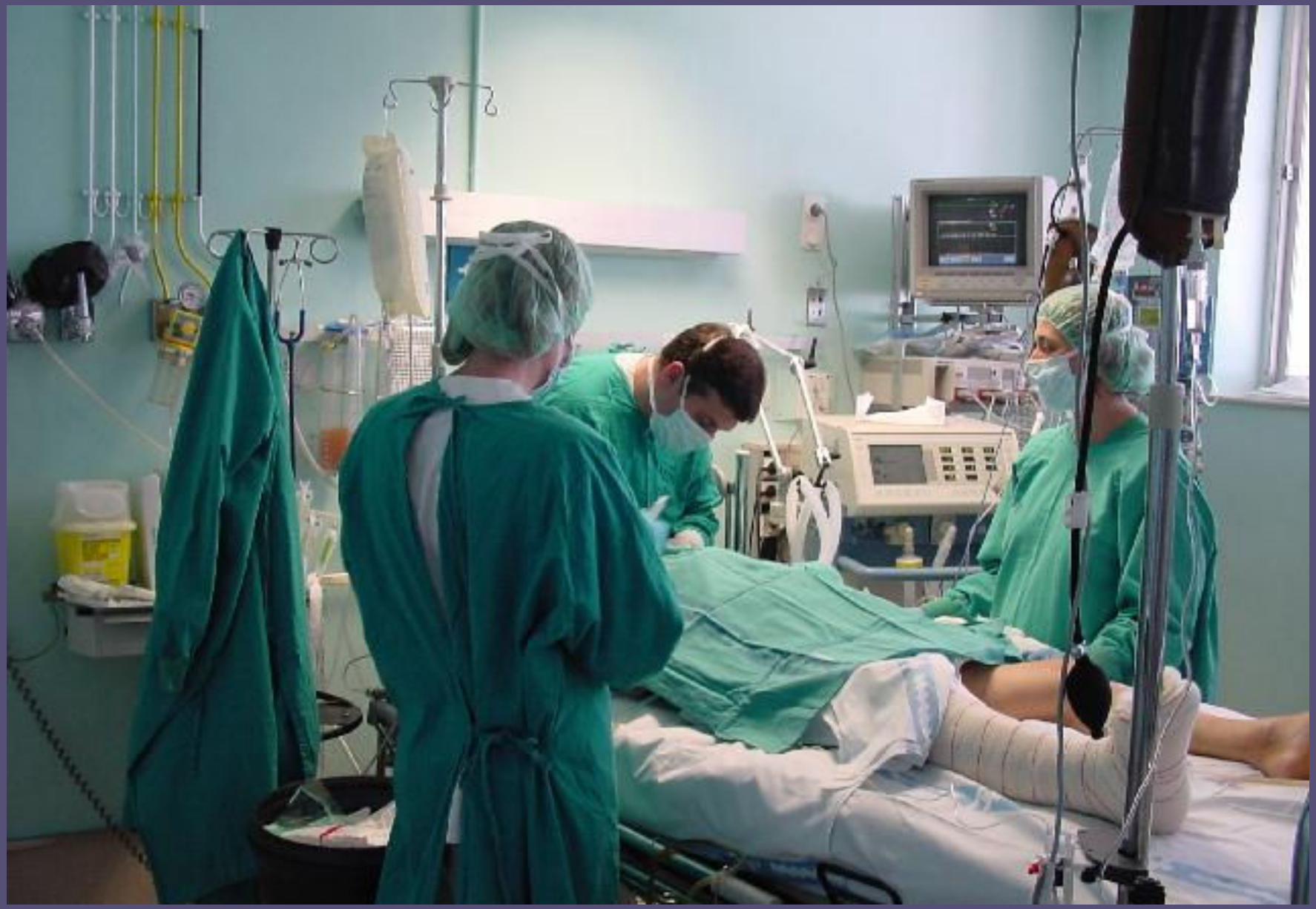
SPECIAL DOUBLE-SIZED ISSUE!



Staphylococcus aureus

A) Tendencias en la resistencia a meticilina (cepas MRSA)

	2006		2007	
	HSD	**Sólo UCI**	**HSD**	**Sólo UCI**
% cepas MRSA	27,7	22,4	32,6	32,1

- En 2006 se observó un estancamiento de la disminución progresiva desde el 2003 en la proporción de cepas MRSA sobre el total de cepas de *S. aureus*. En 2007 vuelve a aumentar ligeramente la proporción de MRSA. En 2007, la prevalencia de MRSA en la UCI fue similar a la del resto del hospital

Inadequate Antimicrobial Treatment of Infections: A Risk Factor for Hospital Mortality Among Critically Ill Patients

Marin H. Kollef, Glenda Sherman, Suzanne Ward and Victoria J. Fraser

Chest 1999;115;462-474

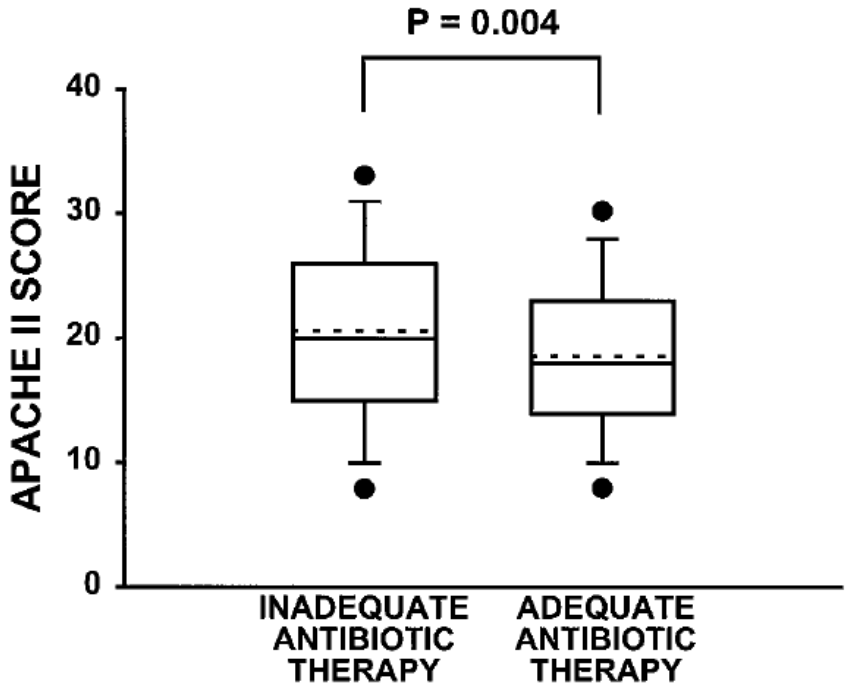


FIGURE 1. Box plots of APACHE II Scores for infected patients receiving either initially inadequate or adequate antimicrobial treatment. Boxes represent 25th to 75th percentiles with 50th percentile (solid line) and median (broken line) values shown with the boxes. The 10th and 90th percentiles are shown as capped bars, and symbols (solid circles) mark the 5th and 95th percentiles.

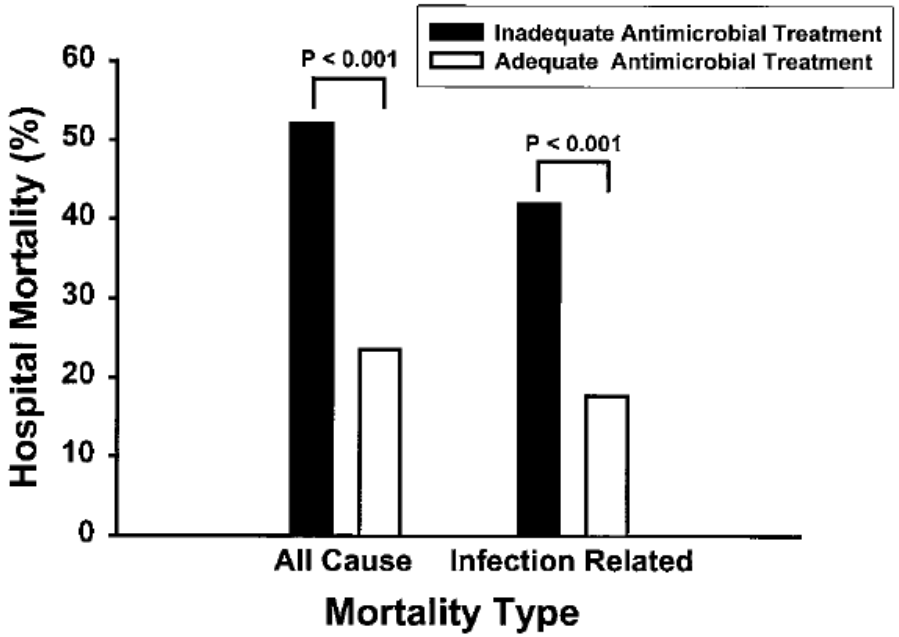


FIGURE 2. Hospital mortality and infection related mortality rates for infected patients from all causes (n = 655) receiving either initially inadequate or adequate antimicrobial treatment.

Outcome and Attributable Mortality in Critically Ill Patients With Bacteremia Involving Methicillin-Susceptible and Methicillin-Resistant *Staphylococcus aureus*

Stijn I. Blot, RN, MSc; Koenraad H. Vandewoude, MD; Eric A. Hoste, MD; Francis A. Colardyn, MD

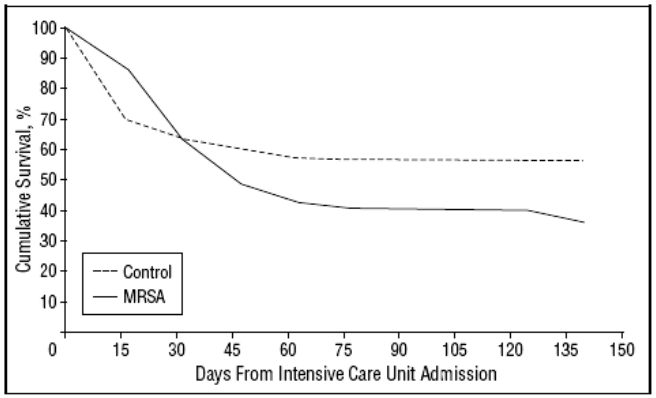


Figure 3. Survival curves for intensive care patients with methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia (n=47) and their matched control subjects (n=94) (log-rank test, *P*=.12; Wilcoxon test, *P*=.40).

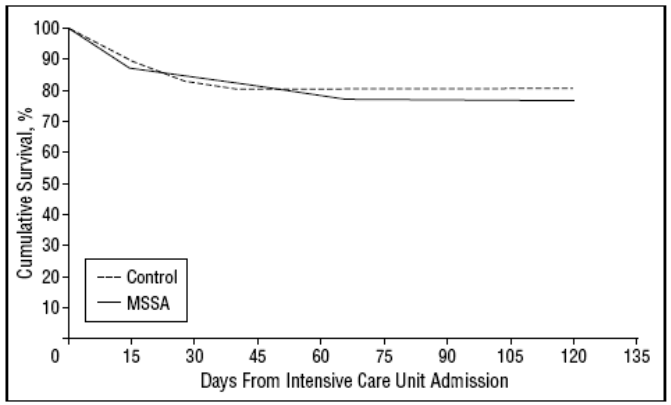


Figure 2. Survival curves for intensive care patients with methicillin-susceptible *Staphylococcus aureus* (MSSA) bacteremia (n=38) and their matched control subjects (n=76) (log-rank test, *P*=.435; Wilcoxon test, *P*=.44).

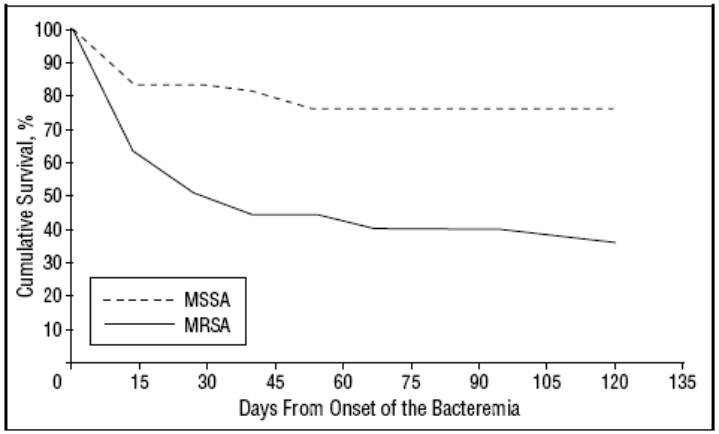


Figure 1. Survival curves for intensive care patients with bacteremia involving methicillin-susceptible *Staphylococcus aureus* (MSSA) (n=38) and methicillin-resistant *S aureus* (MRSA) (n=47) (log-rank test, *P*=.001; Wilcoxon test, *P*<.001).

Arch Intern Med. 2002;162:2229-2235

Comparison of Mortality Associated with Methicillin-Resistant and Methicillin-Susceptible *Staphylococcus aureus* Bacteremia: A Meta-analysis

Clinical Infectious Diseases 2003; 36:53–9

Sara E. Cosgrove,[1] George Sakoulas,[1] Eli N. Perencevich,[1] Mitchell J. Schwaber,[1] Adolf W. Karchmer,[1] and Yehuda Carmeli[1,2]

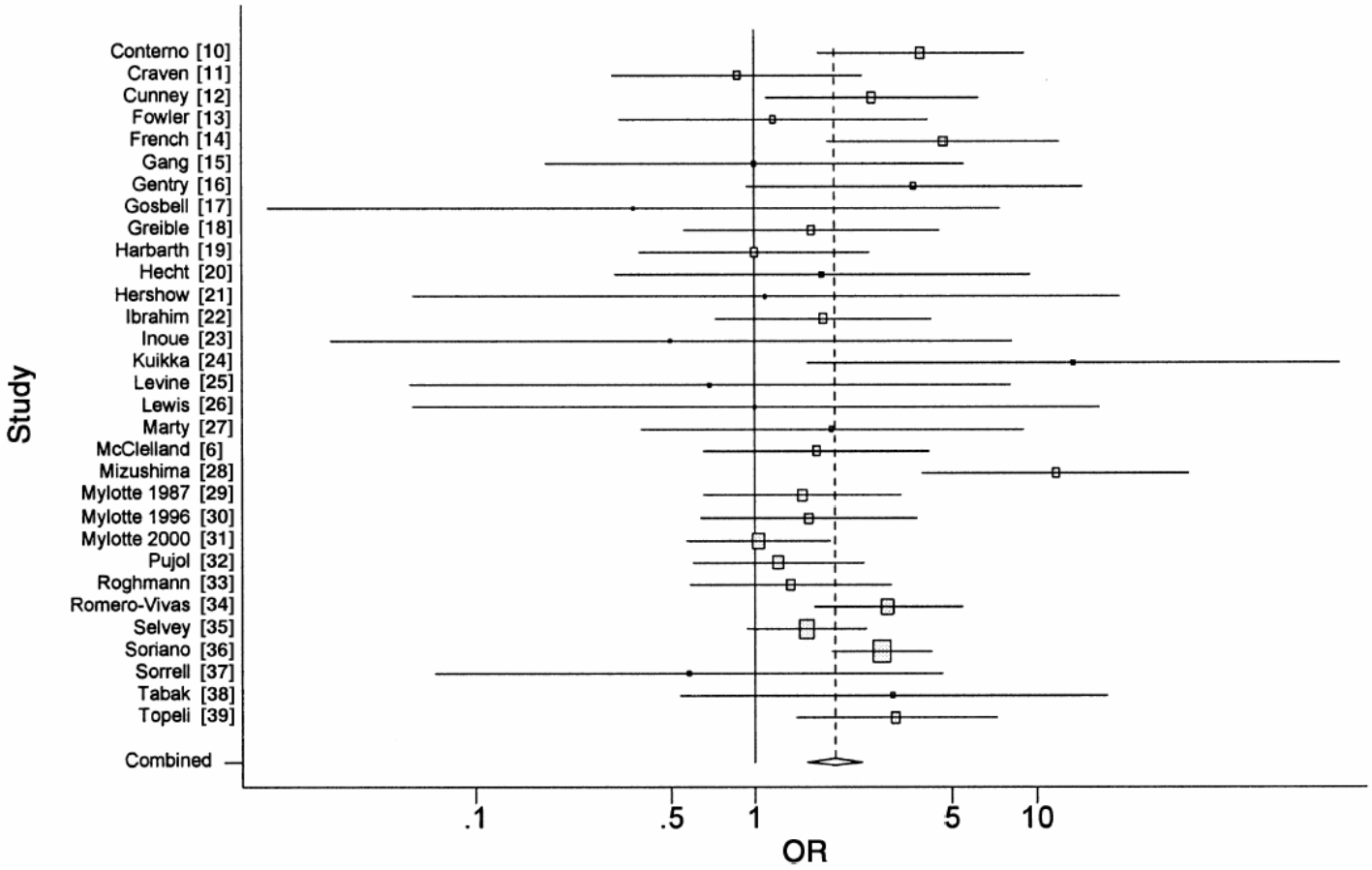


Figure 1. Forest plot summary of the unadjusted results of the 31 studies included in the meta-analysis. The OR and 95% CI are shown for each study. The pooled OR is 1.93 (95% CI, 1.54–2.42). There was significant heterogeneity among the studies' results ($P = .03$).

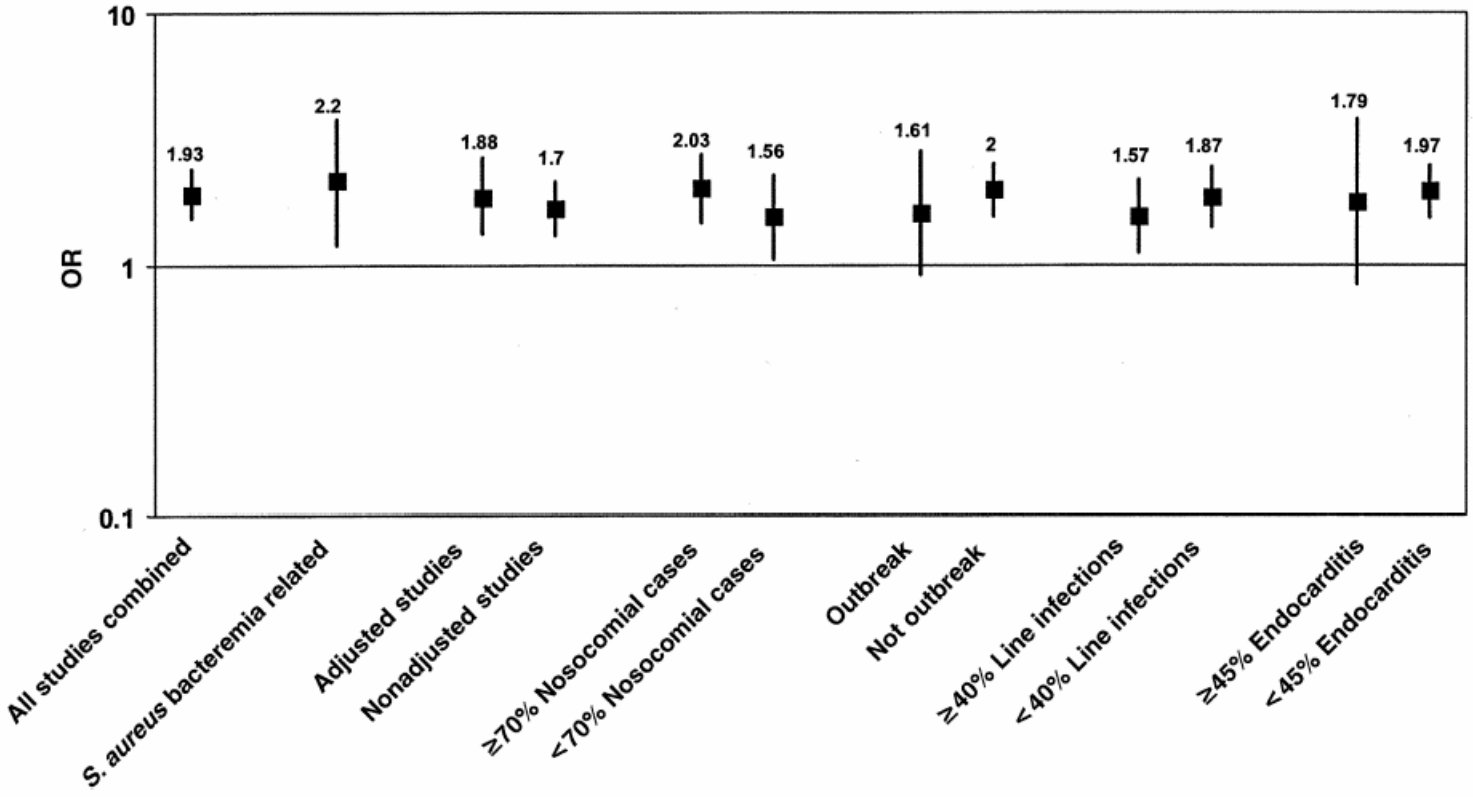
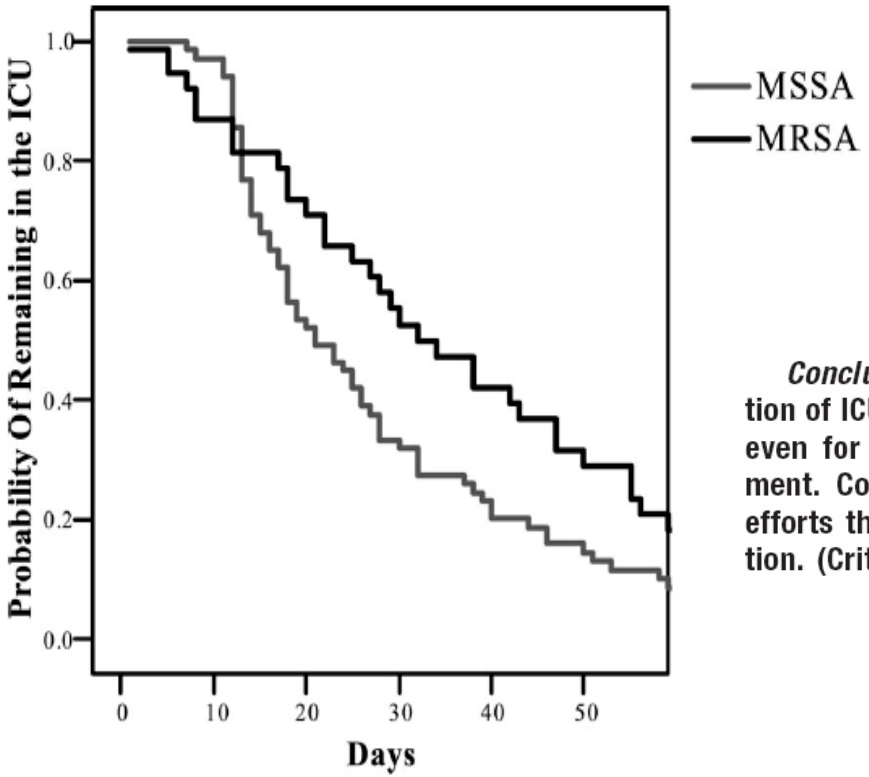


Figure 2. Summary of the subgroup analyses performed to explain the heterogeneity found in the pooled OR for all studies. The OR and 95% CI are shown for each subgroup. These analyses showed consistently increased rates of mortality associated with methicillin resistance, and there was minimal or no significant heterogeneity in each group.

Methicillin-resistant *Staphylococcus aureus* prolongs intensive care unit stay in ventilator-associated pneumonia, despite initially appropriate antibiotic therapy

Andrew F. Shorr, MD, MPH; Alain Combes, MD, PhD; Marin H. Kollef, MD; Jean Chastre, MD



Conclusions: **MRSA VAP independently prolongs the duration of ICU hospitalization, and in turn, increases overall costs, even for patients initially given appropriate antibiotic treatment. Confronting the adverse impact of MRSA will require efforts that address more than the initial antibiotic prescription. (Crit Care Med 2006; 34:700–706)**

Figure 3. Kaplan-Meier plot of probability of remaining in the ICU, on the basis of organism resistance (*ICU*, intensive care unit; *MRSA*, methicillin-resistant *Staphylococcus aureus*; *MSSA*, methicillin-

Pneumonia caused by oxacillin-resistant *Staphylococcus aureus* treated with glycopeptides*

Jordi Rello, MD, PhD; Jordi Sole-Violan, MD, PhD; Marcio Sa-Borges, MD; Jose Garnacho-Montero, MD, PhD; Emma Muñoz, MD; Gonzalo Sirgo, MD; Montserrat Olona, MD; Emili Diaz, MD, PhD

Crit Care Med 2005,33.1983

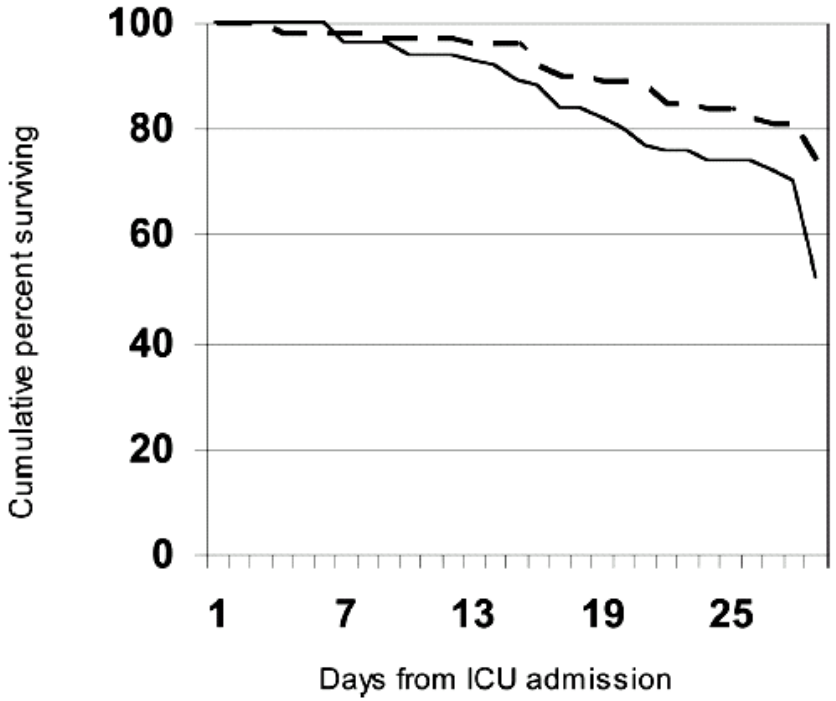


Figure 1. Twenty-eight-day cumulative survival curves for intensive care unit (*ICU*) patients with oxacillin-resistant *Staphylococcus aureus* ventilator-associated pneumonia (*solid line*, case patients; *dashed line*, control patients) (log-rank test $p < .05$).

Table 3. Odds ratios for intensive care unit (ICU) mortality in the multivariate analysis

	ICU Mortality	
Variable	Full Cohort (n = 150) OR (95% CI)	VAP-ORSA (n = 75) OR (95% CI)
VAP-ORSA	3.8[a] (1.05–14.1)	—
Bacteremia by ORSA	NS	4.4[a] (1.1–17.5)
Vancomycin in continuous infusion	—	0.22[a] (0.05–0.8)
Trauma	NS	NS

VAP, ventilator-associated pneumonia; ORSA, oxacillin-resistant *Staphylococcus aureus*; OR, odds ratio; CI, confidence interval; NS, not significant.

[a] $p < .05$.

Crit Care Med 2005,33.1983

Table 1. **Risk Factors for Nosocomial Colonization or Infection with Methicillin-Resistant *Staphylococcus aureus*, Vancomycin-Resistant Enterococcus, *Clostridium difficile*, Extended-Spectrum β-Lactamase–Producing Gram-Negative Bacilli, and *Candida**

Risk Factors	Odds Ratio or Relative Risk (References)				
	Methicillin-Resistant *Staphylococcus aureus* (11, 12, 16–26)	**Vancomycin-Resistant Enterococcus (27–48)**	**Extended-Spectrum β-Lactamase–Producing Gram-Negative Bacilli (49–57)**	***Clostridium difficile* (58–77)**	***Candida* (78–87)**
Advanced age	1.2 to 1.3 (17, 23)	2.6 (45)	NS (49, 51, 54, 56)	1.0 to 14.1 (60, 69, 74, 77)	1.5 (78)
Underlying disease			† (51), NS (49, 56, 57)		
Renal failure	† (12, 17, 18, 22, 23, 26)	4.4 to 6.98 (35, 42)		1.71 to 6.7 (66, 76)	1.4 to 22.1 (79, 84)
Hematologic cancer	† (12, 17, 23, 26), NS (22)	8.4 (33)			1.7 to 45.0 (82, 83)
Hepatic failure	† (12, 17, 23, 26)				7.3 to 42 (85, 86)
Severity of illness‡	1.9 (24)	2.3 to 6.1 (29, 30, 32, 47)	11.6 (53)	2.0 (63)	† (80–83, 85–87)
Interhospital transfer of a patient; patient from a nursing home	6.9 (24)	4.1 to 2.9 (32, 45)	3.6 (52)	3.1 (66)	21.3 (79)
Extended length of stay	1.7 to 17.5 (16–19, 21–23, 25, 26)	1.1 to 2.9 (28, 31–34, 38, 44)	1.1 to 9.0 (49, 50, 57)	1.3 to 3.6 (62, 67, 75)	(83)§
Invasive procedures or devices	(17)§				
Gastrointestinal surgery	(18, 45)§	3.3 to 6.93 (31, 48)	2.5 to 13 (49, 56)	1.6 to 6.0 (58, 60, 61, 74)	2.5 (84)
Transplantation	† (12, 18, 23, 25)	3.2 to 6.75 (44, 46)	† (51, 55, 56), NS (54, 57)	4.2 (66)	3.2 (84)
Central venous or arterial catheter	2.7 to 4.7 (12, 17, 22, 26)	2.7 (38)	1.8 (51, 52)	† (58–77)	5.8 to 26.4 (78–80, 87)
Urinary catheter	NS (11, 17, 18, 22, 26)	† (34, 36, 41, 44, 47, 48), NS (38, 40, 45)	2.5 to 12.8 (51, 54, 55)	† (58–62, 64–77), NS (63)	13.0 (79)
Intubation and mechanical ventilation	(18)§	† (34, 41, 44), NS (36, 38, 40, 45, 47)	1.2 to 2.8 (51, 54, 55)	† (58–77)	† (81, 85–87)
Tube feeding	5.5 (19)	1.3 to 6.1 (33, 36)	1.4 (56)	1.4 to 19.7 (63, 68, 73)	† (81, 85, 86), NS (87)
Anti-infective therapy					
Cephalosporins	3.1 (24)	1.6 to 13.8 (39, 41, 44)	NS (49, 52, 54–56), † (52, 56)	1.4 to 28.6 (64, 65, 69)	NS (81, 86, 87)
Penicillins	NS (22, 23), † (11, 12, 17, 18)	† (34, 36, 48), NS (37, 38, 40, 44)	NS (49, 55), † (51, 52, 54, 56)	3.4 to 4.9 (59, 68)	NS (81, 86, 87)
Clindamycin	† (12, 17, 18, 22, 26)	(37)§	NS (49, 55), † (51, 52, 54, 56)	15.6 to 42 (61, 62)	NS (81, 86, 87)
Vancomycin	† (11, 17, 18, 23), NS (22)	2.3 to 11.0 (27, 29, 32, 33, 40, 42, 44–46, 48)	† (49, 51, 52, 54, 55)	3.1 (59)	275 (81)
Fluoroquinolones		38 (29)	1.4 to 8.77 (49, 56, 57)		
Multiple antibiotics	1.7 to 11.3 (16, 19, 21, 24, 26)	1.6 to 14.5 (42, 43, 45, 47)	(49, 50, 53, 56)§	1.6 to 22.6 (63, 65, 70, 72, 74)	1.7 to 25.1 (79, 80)

* NS = not significant.

FACTORES DE RIESGO DE INFECCIÓN POR MRSA

Colonización previa por MRSA (contacto sociosanitario)

- Ingreso en el ultimo año
- Residencia en centros de dia, asilo, hospitalización domiciliaria
- Centros de diálisis
- Curas quirúrgicas domiciliarias

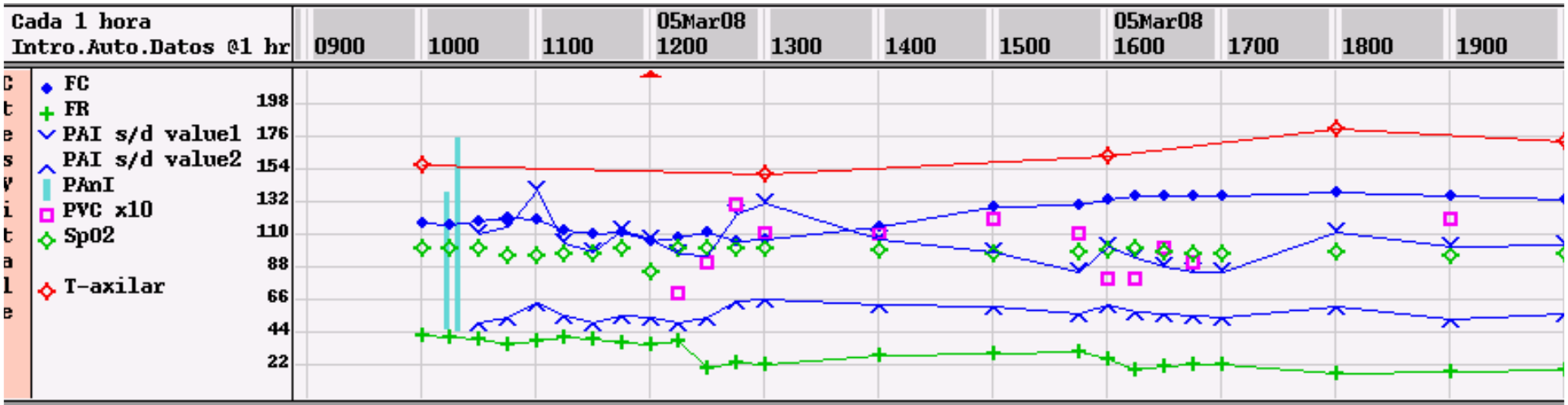
Factores relacionados con el paciente

- Edad
- Diabetes
- Insuficiencia renal crónica
- Tabaquismo
- Ulceras crónicas
- Sonda vesical permanente
- Dispositivos iv
- ADVP

Hospitalización actual

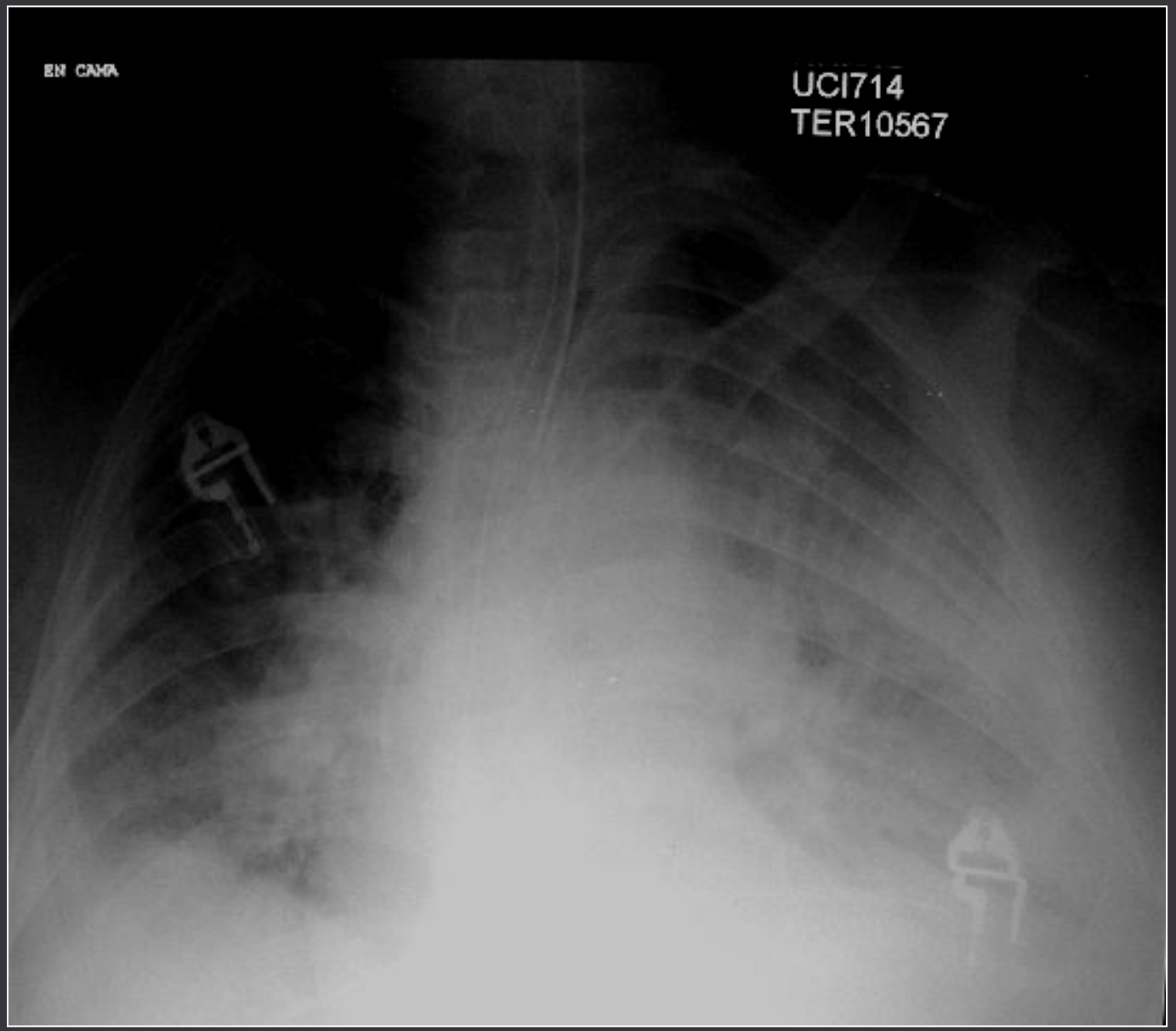
- Gravedad del proceso (APACHE, SAPS)
- Duración de la hospitalización
- Patología traumática o quirúrgica
- Ingreso en UCI
- Antibioterapia previa


scopulariosis
Porphyromonas
sedimentibacter
Neotestudina
Wangiella
dolosigranulum
¿MRSA?



C	FrecuenciaCardiaca			117		120		105	106	115		128		133	135	138	136	
o	FrecuenciaRespirator			42		38		36	23	28		30		26	22	17	18	
n	PrArterialInvasiva			110/ 51		139/ 64		106/ 54	131/ 66	106/ 62		98/ 61		101/ 63	84/ 54	111/ 61	102/ 53	
s	PresArterialNoInvasi			139/ 45														
t	PresiónArterialMedia			63,0		90,0		72,0	89,0	78,0		74,0		76,0	65,0	78,0	69,0	
a	PVC							46	11	11		12		8			12	
n	Temperatura Axilar			37,1					36,8					37,4		38,2		
t	SaturaciónPulxioxim			100		96		84	100	99		97		99	97	98	95	
B	BMtest(Glucosa/U)			146/					131/						191/ 5			
E	Electrocardiograma					hecho												
F	%FiO2			100		60			60			60			60	60		
M	Modo Ventilación											IPPV/A			IPPV/A	IPPV/A		
P	FR-VM											15						
a	Volumen Tidal Espir											610						
c	Volumen Minuto																	
á	PEEP											5						
m	Presión Pico																	
G	Tipo Muestra:			ART		ART			ART						ART	ART		
S	pH			7,34		7,34	!	7,01	7,34						7,29	7,39		
A	pO2			181		80			89						88	74		

P	Cisatrac mcg/kg/min																	3,00
e	Furosemida-250 mg/hr																	
r	Midazolam 105mg/kg/h								0,05					0,10				
f	Morfina 100 mg/kg/h								0,05					0,10				
u	Nora(16) mcg/kg/min													0,50			0,80	
s	Nora(16) mcg/kg/min							0,80	0,50					0,40			0,50	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Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

www.survivingsepsis.org

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- American College of Chest Physicians
- American College of Emergency Physicians
- American Thoracic Society
- Australian and New Zealand Intensive Care Society
- European Society of Clinical Microbiology and Infectious Diseases
- European Society of Intensive Care Medicine
- European Respiratory Society
- International Sepsis Forum
- Society of Critical Care Medicine
- Surgical Infection Society

IDENTIFICACIÓN DE LA SEPSIS GRAVE

A)¿Tiene el paciente historia clínica de **NUEVA INFECCIÓN**?

B)¿Presenta al menos 2 CRITERIOS de nueva infección y Síndrome de Respuesta Inflamatoria? *(SIRS)*

hipertermia > 38.3 ºC ó hipotermia < 36 ºC
taquicardia > 90 lpm
taquipnea > 20 rpm
alteración aguda del estado mental
leucocitosis > 12.000/mm3 ó leucopenia < 4.000/mm3
hiperglucemia > 120 mgr/dl (en ausencia de diabetes)

Si la respuesta a las preguntas A y B es SI, **existe la sospecha de SEPSIS**, y habrá que realizar pruebas complementarias que determinen la gravedad de la misma

ácido láctico
cultivos (2 hemocultivos, 1 de vía si < 48h)
analítica: leucocitos con recuento diferencial, hcto, hb, plaquetas, glucosa, creatinina, bilirrubina, INR, TTPa, gasometría arterial
otras (a criterio médico): sedimento orina, amilasa, lipasa, PCR, Rx Torax, ecografía, TAC…

C)¿Presenta algún criterio de **DISFUNCION ORGÁNICA**? (en un sitio diferente al de la localización de la infección y que no se considere disfunción crónica)

PAS < 90 mmHg (o descenso > 40 mmHg) o PAM < 65 mmHg
Necesidad de O2 para StO2 > 90% (o aumento de las necesidades basales de O2) o PO2/FiO2 < 300
Creatinina > 2 mgr/dl (o aumento > 0.5 mgr/gl) o Diuresis < 0,5 ml/h > 2 h
Bilirrubina > 2 mgr/dl
Plaquetas < 100.000/mm3
Coagulopatía (INR > 1.5 o TTPa > 60 seg)
Lactato > 2 mmol/l o 18 mgr/dl

Si la respuesta a A-B y C es sí, se cumplen **CRITERIOS DE SEPSIS GRAVE** y ha de iniciarse el protocolo de tratamiento para Sepsis Grave según las recomendaciones de la *"Surviving Sepsis Campaign"*

Valorar en cualquier momento el contacto con UCI

www.survivingsepsis.org

RECOMENDACIONES GEIP-SEIMC Y GTEI-SEMICYUC PARA EL TRATAMIENTO ANTIBIOTICO DE INFECCIONES POR COCOS GRAM POSITIVOS EN EL PACIENTE CRITICO

Madrid, 22 de Marzo de 2007
Hotel Melía Avenida de América
C/ Juan Ignacio Luca de Tena, Nº 36
MADRID

www.pfizer.es

Avda. Europa, 20 B. Parque Empresarial La Moraleja.
28108 Alcobendas. (Madrid)

Pfizer

Por un mundo más sano™

Staphylococcus aureus MRSA (cepas resistentes a la meticilina)

Antibiótico	Porcentaje de cepas sensibles		
	2005	2006	2007
Penicilina	0,0	0,0	0,0
Oxacilina	0,0	0,0	0,0
Gentamicina	68,2	79,5	79,5
Eritromicina	29,4	37,3	38,5
Clindamicina	31,7	54,2	56,0
Vancomicina	100,0	100,0	100,0
Teicoplanina	100,0	100,0	100,0
Cotrimoxazol	97,7	99,4	99,3
Ciprofloxacino	0,9	3,4	11,2
Rifampicina	79,9	98,9	98,6
Mupirocina	82,8	93,6	91,2
Ácido fusídico	92,2	98,2	98,2

Recomendaciones GEIPC-SEIMC y GTEI-SEMICYUC para el tratamiento antibiótico de infecciones por cocos grampositivos en el paciente crítico

P.M. OLAECHEA ASTIGARRAGA[a], J. GARNACHO MONTERO[b], S. GRAU CERRATO[c], O. RODRÍGUEZ COLOMO[d], M. PALOMAR MARTÍNEZ[e], R. ZARAGOZA CRESPO[f], P. MUÑOZ GARCÍA-PAREDES[g], E. CERDÁ CERDÁ[h] Y F. ÁLVAREZ LERMA[i]

Med Intensiva. 2007;31(6):294-317

Enferm Infecc Microbiol Clin 2007;25(7):446-66

Neumonia nosocomial

TABLA 6. **Recomendaciones de tratamiento de neumonía nosocomial y adquirida en la comunidad causadas por CGP**

Infección	Primera elección	G. Rec	Referencia	Alternativa	G. Rec	Referencia
Neumonía nosocomial						
T.E sin factores de riesgo de CGP resistente	Cefotaxima/ceftriaxona o amoxicilina-clavulánico	A-III	56,57	Levofloxacino	B-II	49,58,59
				Alergia a betalactámicos: levofloxacino	A-III	
TD *S. aureus* M. S	Cloxacilina	A-II	54	Alergia a betalactámicos: levofloxacino	A-III	
TE con factores de riesgo de CGP resistente o TD *S. aureus* M.R						
CMI de vancomicina ≤ 0, 5 mg/l	Linezolid o vancomicina	A-I	64,65	Linezolid primera elección	B-II	52,66
				Vancomicina en perfusión para alcanzar niveles de 15-20 mg/l	B-II	10
CMI de vancomincia ≥ 1 mg/l	Linezolid	A-III	69,71			

JOURNAL OF CLINICAL MICROBIOLOGY, June 2004, p. 2398–2402 Vol. 42, No. 6
0095-1137/04/$08.00+0 DOI: 10.1128/JCM.42.6.2398–2402.2004

Relationship of MIC and Bactericidal Activity to Efficacy of Vancomycin for Treatment of Methicillin-Resistant *Staphylococcus aureus* Bacteremia

George Sakoulas,[1]* Pamela A. Moise-Broder,[2] Jerome Schentag,[2] Alan Forrest,[2] Robert C. Moellering, Jr.,[3] and George M. Eliopoulos[3]

TABLE 3. Vancomycin treatment success rates and vancomycin bactericidal activity by sensitivity of the MRSA isolate to vancomycin

VAN[a] MIC (μg/ml)	*n*	Log_{10} (CFU/ml) of killing (mean ± SD [median])	Log_{10} (CFU/ml) of killing for group:			% VAN success[b]
			<4.71	4.71–6.26	≥6.27	
≤0.5 (5)	9	4.91 ± 2.26 (5.94)	3	3	3	55.6
1.0–2.0	21	5.32 ± 1.59 (5.40)	6	10	5	9.5

[a] VAN, vancomycin.
[b] $P = 0.01$ (Fisher's exact test).

TABLE 4. Multivariate analysis of factors associated with vancomycin treatment success

Factor	OR (95% CI)[a]	*P*
Increased VAN killing[b]	10.73 (1.24–92.95)	0.031
Decreased VAN MIC[c]	35.46 (1.76–715.95)	0.020

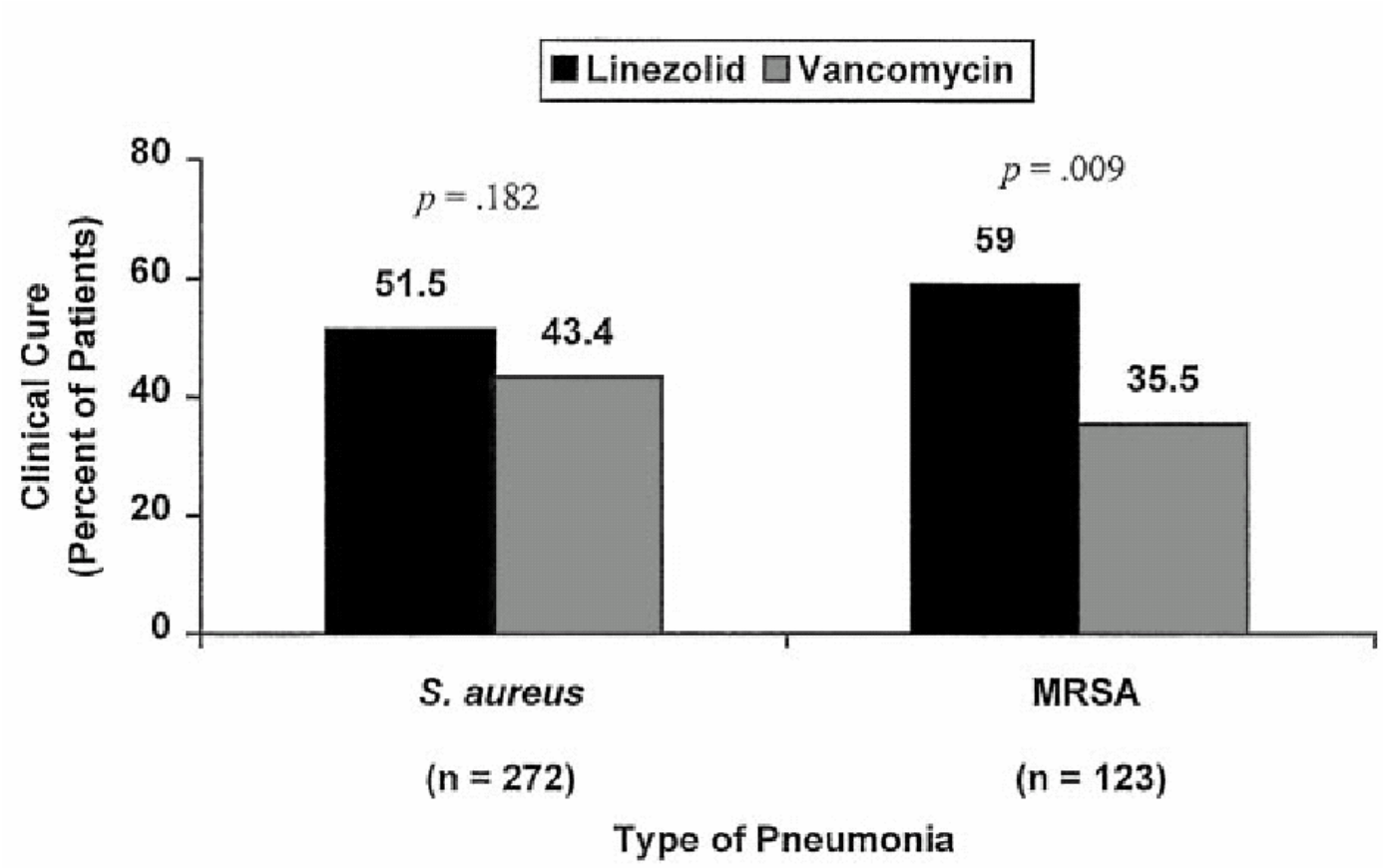
[a] OR, odds ratio; CI, confidence interval.
[b] The odds ratio for increased vancomycin killing represents the incremental increased chance of treatment success between the groups identified by regression tree modeling (log_{10} [CFU/ml] of killing at 72 h: group 1, <4.71; group 2, 4.71 to 6.26; group 3, ≥6.27). VAN, vancomycin.
[c] The odds ratio for decreased vancomycin MIC represents the increased chance of success for treatment of MRSA infection with vancomycin MIC ≤0.5 μg/ml versus MIC 1.0 to 2.0 μg/ml.

The vancomycin killing assay used in this investigation allowed us to demonstrate that increased bactericidal activity of vancomycin against MRSA may predict a higher probability of clinical success in the treatment of MRSA bacteremia. However, it should be pointed out that employing such methods in the clinical laboratory is impractical because they are too time consuming. In addition, although our data confirm a relationship between susceptibility to inhibition and killing by vancomycin in vitro and response to vancomycin treatment of MRSA bacteremia, the utility of these methods for testing individual isolates is doubtful.

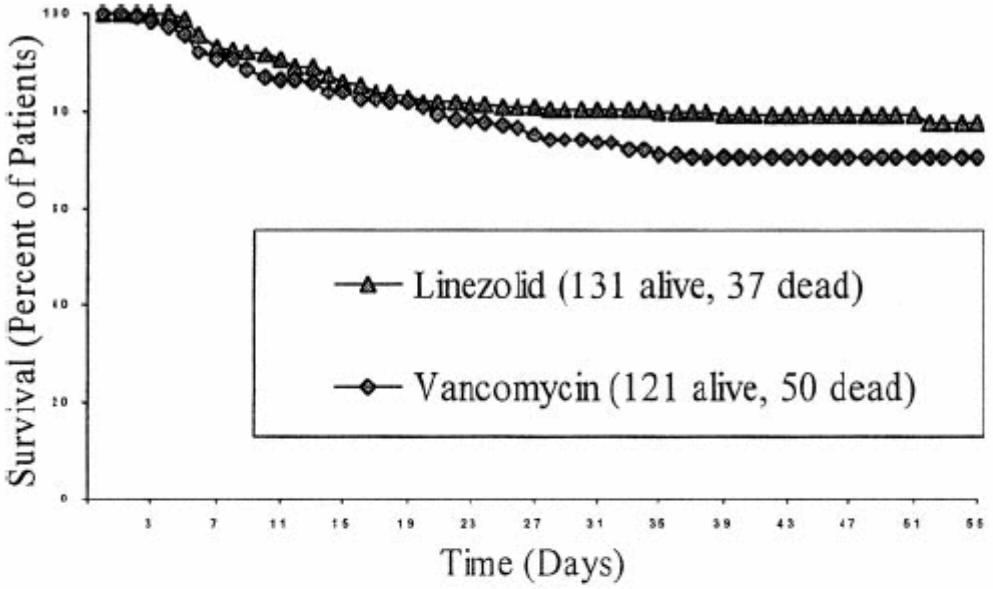
Linezolid vs Vancomycin: Analysis of Two Double-Blind Studies of Patients With Methicillin-Resistant Staphylococcus aureus Nosocomial Pneumonia

Richard G. Wunderink, Jordi Rello, Sue K. Cammarata, Rodney V. Croos-Dabrera and Marin H. Kollef

Chest 2003; 124: 1789

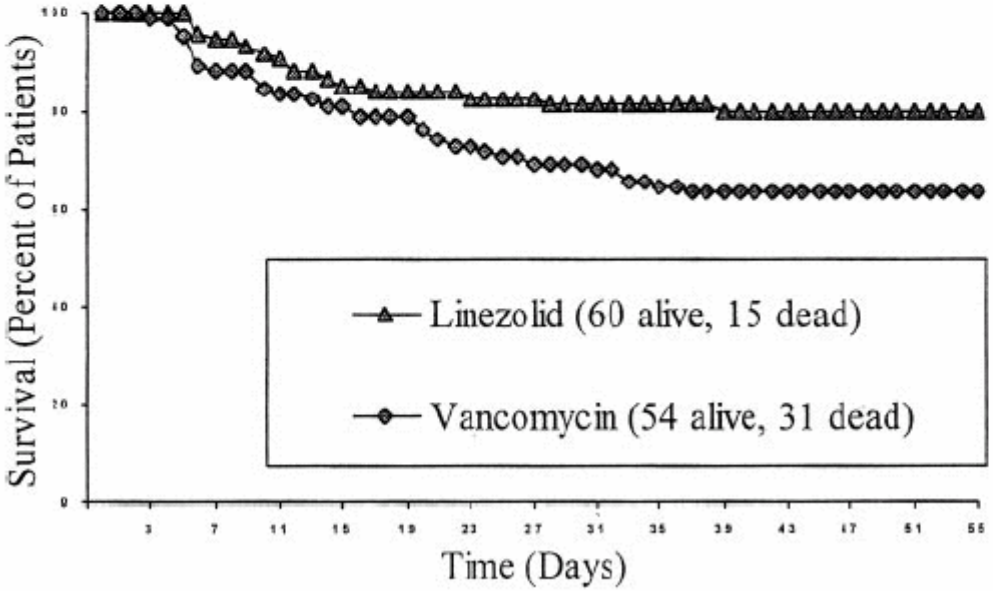


Tasa de curación clínica para pacientes con neumonía nosocomial por gram +



ITT *S. aureus* (n = 339)

$p = .131$



ITT MRSA (n = 160)

$p = .025$

Chest 2003; 124: 1789

FIGURE 2. Kaplan-Meier survival curves for uncensored data.

Linezolid vs Vancomycin: Analysis of Two Double-Blind Studies of Patients With Methicillin-Resistant Staphylococcus aureus Nosocomial Pneumonia

Richard G. Wunderink, Jordi Rello, Sue K. Cammarata, Rodney V. Croos-Dabrera and Marin H. Kollef

Table 2—*Results of Logistic Regression Analysis for Survival in Patients With Nosocomial Pneumonia*

Predictors	OR (95% CI)	p Value
ITT *S aureus* (n = 339)		
Linezolid therapy	1.7 (1.0–2.9)	0.068
Age < 65 yr	1.7 (0.9–3.0)	0.081
APACHE II score ≤ 20	3.7 (2.0–6.9)	< 0.001†
Single-lobe pneumonia	1.7 (1.0–2.9)	0.072
Presence of pleural effusion	1.6 (0.9–3.0)	0.127
Absence of cardiac comorbidities	2.3 (1.3–4.1)	0.005†
Absence of renal comorbidities	2.2 (1.0–4.8)	0.042†
ITT MRSA (n = 160)		
Linezolid therapy	2.2 (1.0–4.8)	0.050†
APACHE II score ≤ 20	2.1 (0.8–5.1)	0.116
Presence of pleural effusion	1.9 (0.8–4.6)	0.145
Creatinine ≤ 229.8 μmol/L*	11.9 (1.1–125.0)	0.038†
Absence of cardiac comorbidities	3.0 (1.4–6.6)	0.005†

*Less than or equal to 229.8 μmol/L (2.6 mg/dL) for men and ≤ 212.2 μmol/L (2.4 mg/dL) for women.
†Significant at 0.05 level.

Table 3—*Results of Logistic Regression Analysis for Clinical Cure in Patients With Nosocomial Pneumonia

Predictors	OR (95% CI)	p Value
S aureus pneumonia (n = 272)		
Linezolid therapy	1.6 (0.9–2.7)	0.090
APACHE II score ≤ 20	2.2 (1.0–4.6)	0.046†
Single-lobe pneumonia	2.0 (1.2–3.5)	0.014†
Absence of VAP	2.5 (1.4–4.6)	0.003†
Absence of cardiac comorbidities	2.1 (1.1–4.1)	0.034†
Absence of oncologic comorbidities	4.4 (1.4–13.5)	0.011†
Absence of renal comorbidities	13.5 (3.0–62.5)	< 0.001†
MRSA pneumonia (n = 123)		
Linezolid therapy	3.3 (1.3–8.3)	0.011†
Single-lobe pneumonia	3.7 (1.5–9.5)	0.006†
Absence of VAP	2.9 (1.1–7.5)	0.028†
Absence of oncologic comorbidities	21.7 (3.7–125.0)	< 0.001†
Absence of renal comorbidities	16.4 (3.2–83.3)	< 0.001†
Absence of hepatic comorbidities	4.2 (0.6–31.3)	0.154

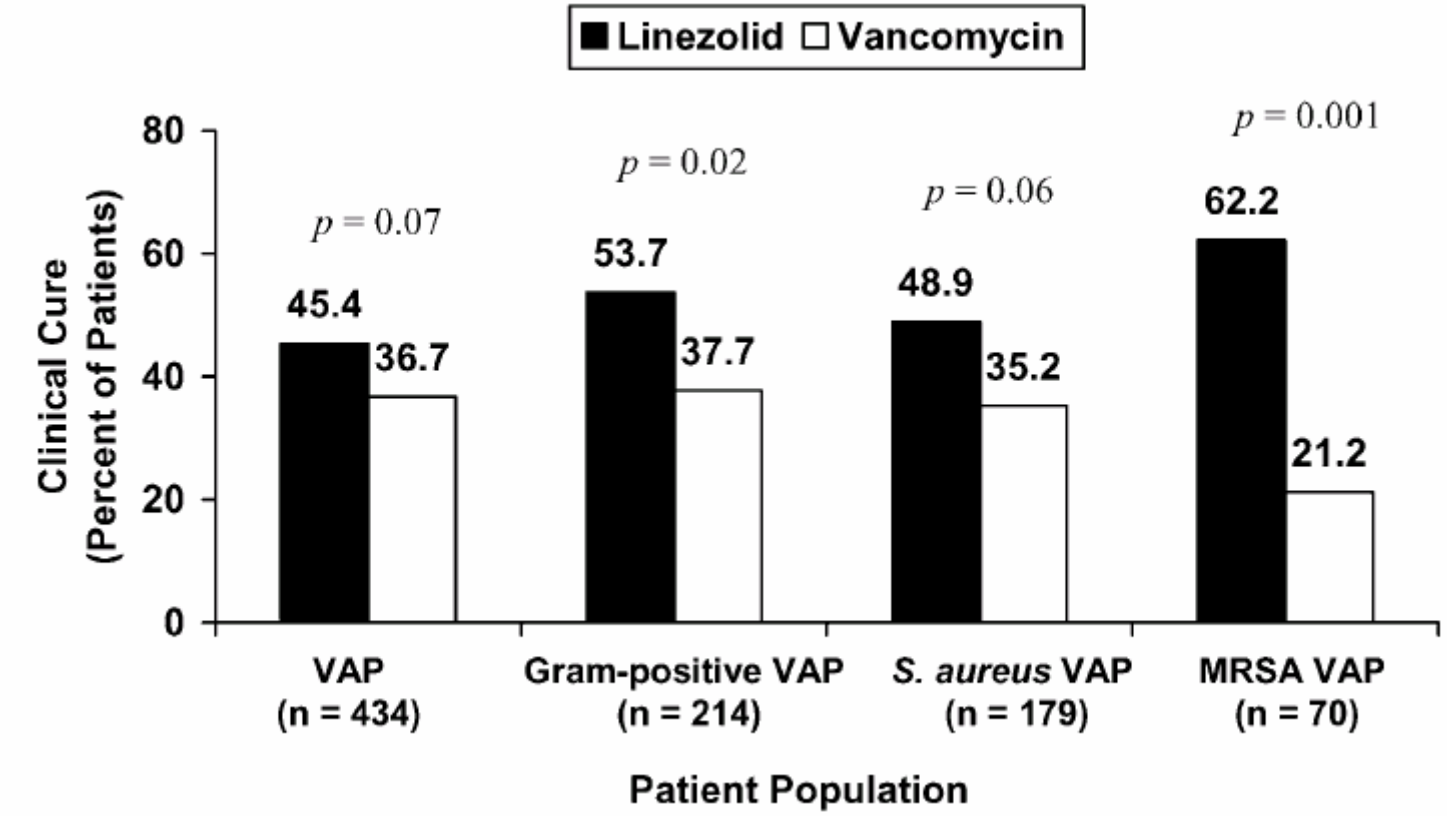
*Data from patients with clinical outcomes assessed as indeterminate or missing were excluded.
†Significant at 0.05 level.

Chest 2003; 124: 1789

Marin H. Kollef
Jordi Rello
Sue K. Cammarata
Rodney V. Croos-Dabrera
Richard G. Wunderink

Clinical cure and survival in Gram-positive ventilator-associated pneumonia: retrospective analysis of two double-blind studies comparing linezolid with vancomycin

Intensive Care Med 2004;30:388



Tasa de curación clínica para pacientes con NAVM por gram +

Table 2 Results of logistic regression analysis for clinical cure in patients (n=434) with ventilator-associated pneumonia (*VAP*); data from patients with clinical cure outcomes assessed as indeterminate or missing are excluded (*OR* odds ratio, *CI* confidence interval, *APACHE* Acute Physiology and Chronic Health Evaluation, *MRSA* methicillin-resistant *S. aureus*

Predictor	OR	95% CI	p
VAP n=434			
Linezolid therapy	1.8	1.2–2.7	0.008
APACHE II score ≤20	2.8	1.6–5.1	<0.001
Age <65 years	2.0	1.3–3.0	0.001
Single-lobe pneumonia	1.6	1.0–2.4	0.038
Mechanical ventilation ≤7 days	1.6	1.0–2.5	0.048
Creatinine ≤229.8 µmol/l[a]	5.6	1.3–25.0	0.024
ITT Gram-positive VAP n=214			
Linezolid therapy	2.4	1.3–4.3	0.005
APACHE II score ≤20	2.8	1.2–6.4	0.014
Absence of renal comorbidities	4.1	1.3–13.7	0.020
Absence of oncological comorbidities	3.5	1.1–11.8	0.039
S. aureus VAP n=179			
Linezolid therapy	2.1	1.1–4.0	0.031
APACHE II score ≤20	3.5	1.3–9.3	0.011
Mechanical ventilation ≤7 days	2.2	1.0–4.5	0.039
Absence of renal comorbidities	11.8	1.5–100.0	0.021
MRSA VAP n=70			
Linezolid therapy	20.0	4.3–92.0	<0.001
APACHE II score ≤20	18.2	2.8–125.0	0.003
Single-lobe pneumonia	4.0	1.1–15.4	0.041
Absence of hepatic comorbidities	31.3	2.1–500.0	0.013
Absence of vascular comorbidities	23.8	1.3–500.0	0.032

[a] ≤229.8 µmol/l (2.6 mg/dl) in men and 212.2 µmol/l (2.4 mg/dl) in women

Intensive Care Med 2004;30:388

Table 4 Results of logistic regression analysis for hospital survival in patients with ventilator-associated pneumonia (*OR* odds ratio, *CI* confidence interval, *ITT* intent to treat, *VAP* ventilator-associated pneumonia, *APACHE* Acute Physiology and Chronic Health Evaluation, *MRSA* methicillin-resistant *S. aureus*)

Predictor	OR	95% CI	*p*
ITT VAP (*n*=544)			
Linezolid therapy	1.6	1.0–2.4	0.040
APACHE II score ≤0	2.0	1.2–3.2	0.006
Age <65 years	2.2	1.4–3.5	<0.001
Single-lobe pneumonia	1.8	1.1–2.8	0.014
Creatinine ≤229.8 μmol/l[a]	3.8	1.7–8.4	<0.001
Absence of cardiac comorbidities	1.6	1.2–2.5	0.047
ITT Gram-positive VAP (*n*=264)			
Linezolid therapy	2.6	1.3–5.1	0.006
APACHE II score ≤20	3.3	1.5–7.0	0.002
Age <65 years	2.7	1.4–5.3	0.004
Presence of pleural effusion	2.3	1.1–5.0	0.030
Absence of cardiac morbidities	2.2	1.1–4.4	0.034
ITT *S. aureus* VAP (*n*=221)			
APACHE II score ≤20	2.9	1.4–5.9	0.005
Creatinine ≤229.8 μmol/l[a]	10.8	1.1–100.0	0.039
Absence of cardiac comorbidities	2.7	1.4–5.4	0.004
ITT MRSA VAP (*n*=91)			
Linezolid therapy	4.6	1.5–14.8	0.010
APACHE II score ≤20	7.2	2.0–26.3	0.003
Presence of pleural effusion	4.9	1.3–18.7	0.022
Absence of bacteremia	5.3	1.1–24.4	0.034

[a] ≤229.8 μmol/l (2.6 mg/dl) in men and 212.2 μmol/l (2.4 mg/dl) in women

?

Intensive Care Med 2004;30:388

Pneumonia caused by oxacillin-resistant *Staphylococcus aureus* treated with glycopeptides*

Jordi Rello, MD, PhD; Jordi Sole-Violan, MD, PhD; Marcio Sa-Borges, MD; Jose Garnacho-Montero, MD, PhD; Emma Muñoz, MD; Gonzalo Sirgo, MD; Montserrat Olona, MD; Emili Diaz, MD, PhD

Crit Care Med 2005,33.1983

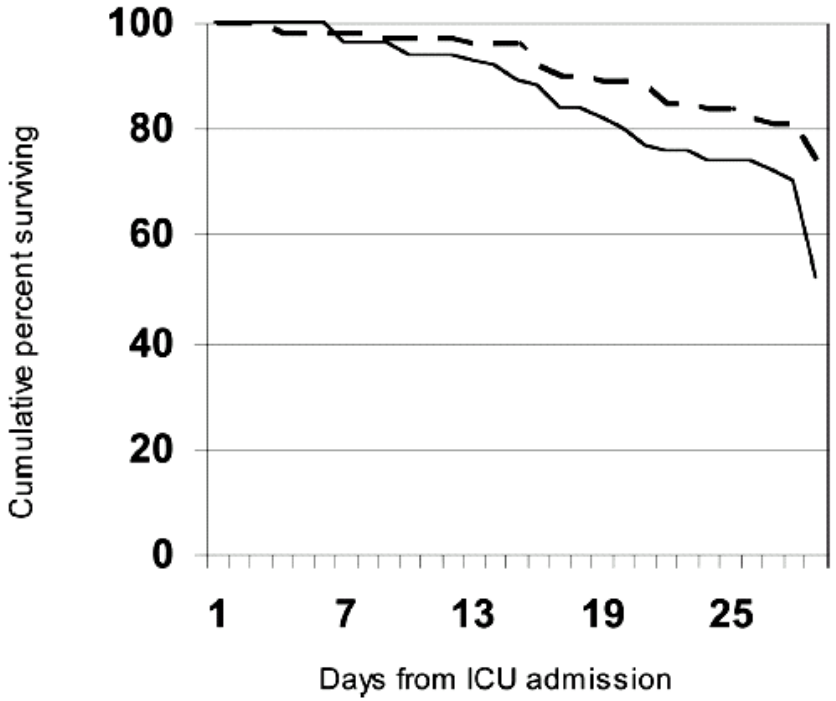


Figure 1. Twenty-eight-day cumulative survival curves for intensive care unit (*ICU*) patients with oxacillin-resistant *Staphylococcus aureus* ventilator-associated pneumonia (*solid line*, case patients; *dashed line*, control patients) (log-rank test $p < .05$).

Table 3. Odds ratios for intensive care unit (ICU) mortality in the multivariate analysis

	ICU Mortality	
Variable	Full Cohort (n = 150) OR (95% CI)	VAP-ORSA (n = 75) OR (95% CI)
VAP-ORSA	3.8[a] (1.05–14.1)	—
Bacteremia by ORSA	NS	4.4[a] (1.1–17.5)
Vancomycin in continuous infusion	—	0.22[a] (0.05–0.8)
Trauma	NS	NS

VAP, ventilator-associated pneumonia; ORSA, oxacillin-resistant *Staphylococcus aureus*; OR, odds ratio; CI, confidence interval; NS, not significant.

[a] $p < .05$.

Crit Care Med 2005,33.1983

One possible reason for the association between linezolid and improved survival is the poor penetration of vancomycin into the lungs seen in pharmacokinetic studies.

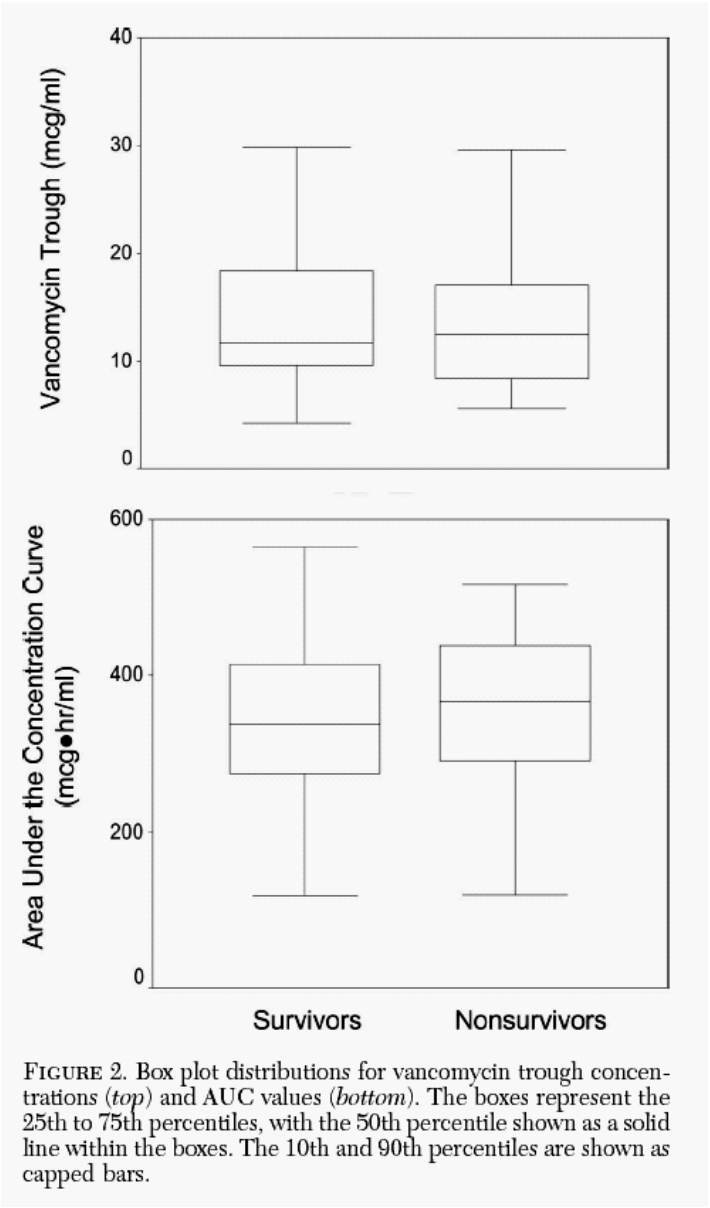


FIGURE 2. Box plot distributions for vancomycin trough concentrations (*top*) and AUC values (*bottom*). The boxes represent the 25th to 75th percentiles, with the 50th percentile shown as a solid line within the boxes. The 10th and 90th percentiles are shown as capped bars.

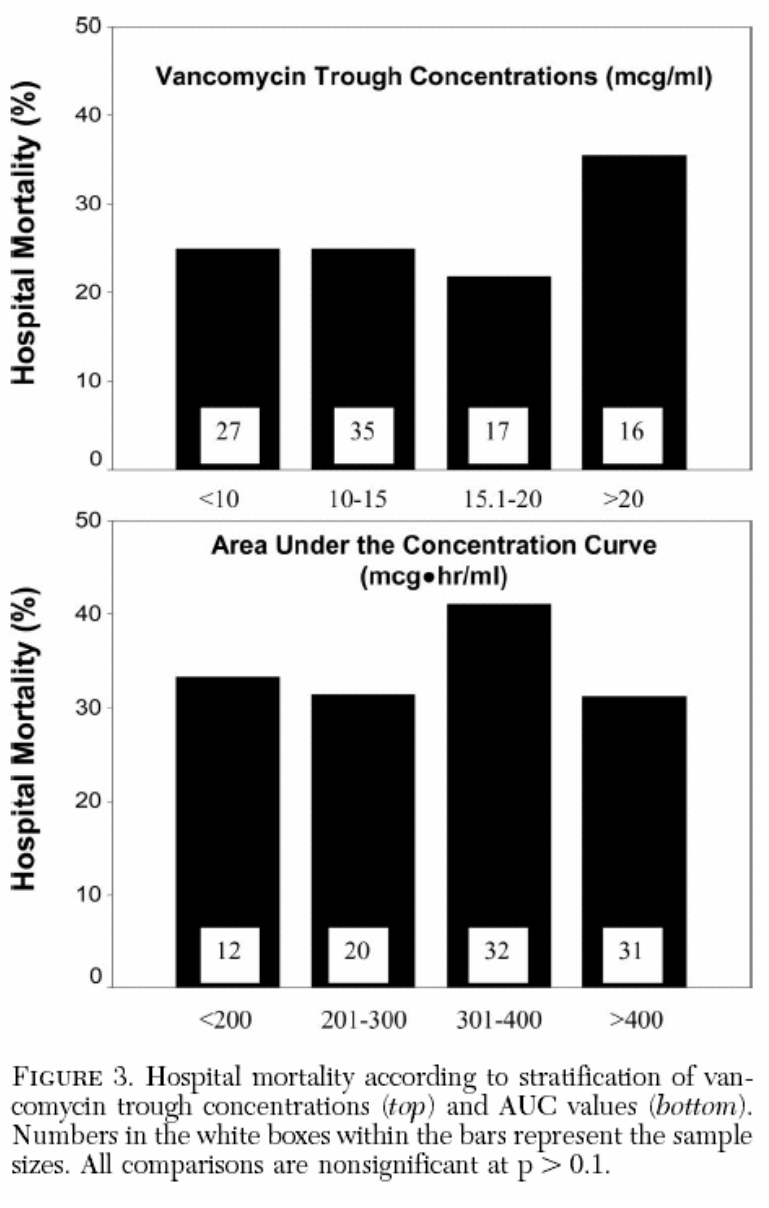


FIGURE 3. Hospital mortality according to stratification of vancomycin trough concentrations (*top*) and AUC values (*bottom*). Numbers in the white boxes within the bars represent the sample sizes. All comparisons are nonsignificant at $p > 0.1$.

Predictors of Mortality for Methicillin-Resistant *Staphylococcus aureus* Health-Care–Associated Pneumonia*

Chest 2006,130:947

Specific Evaluation of Vancomycin Pharmacokinetic Indices

Continuous versus Intermittent Infusion of Vancomycin in Severe Staphylococcal Infections: Prospective Multicenter Randomized Study

MARC WYSOCKI,[1]* FREDERIQUE DELATOUR,[2] FRANÇOIS FAURISSON,[2] ALAIN RAUSS, YVES PEAN,[4] BENOIT MISSET,[5] FRANK THOMAS,[6] JEAN-FRANÇOIS TIMSIT,[7] THOMAS SIMILOWSKI,[8] HERVE MENTEC,[9] LAURENCE MIER,[10] DIDIER DREYFUSS,[10] AND THE STUDY GROUP†

Antimicrob Agents Chemother 2001,45:2460

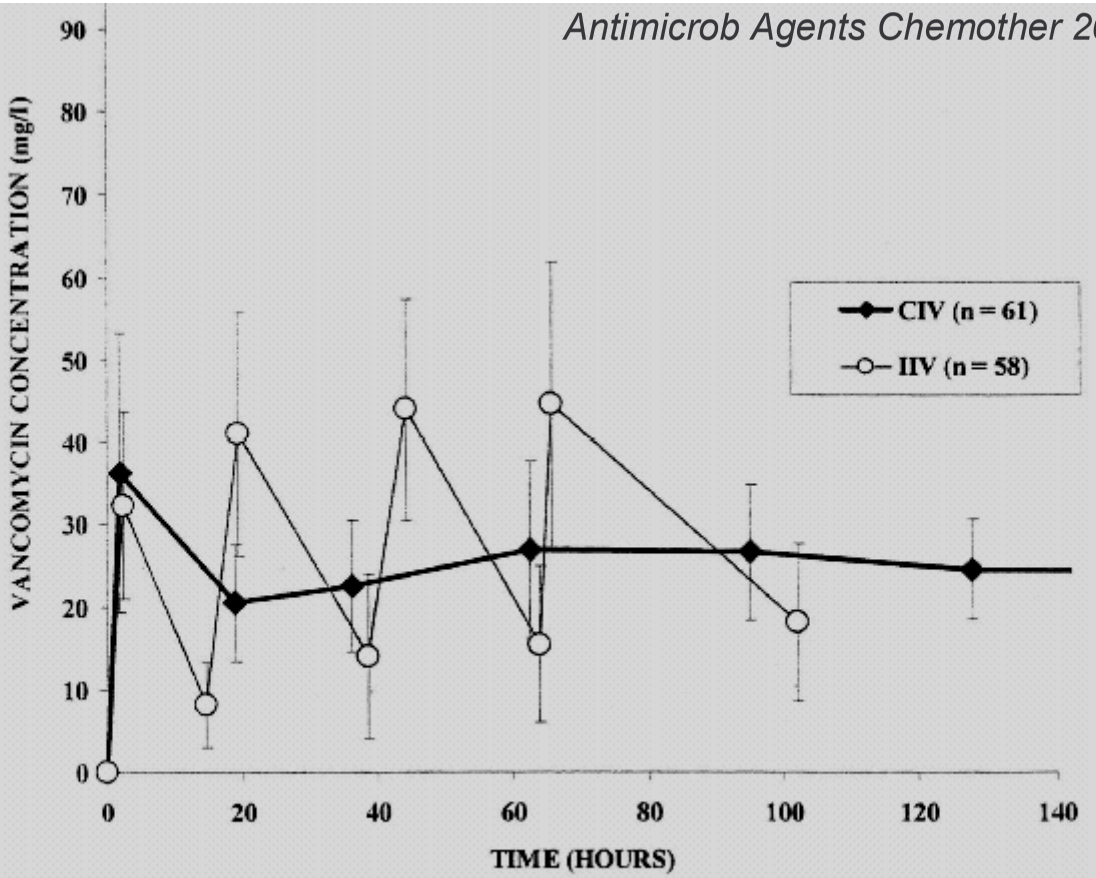


FIG. 3. Changes in serum vancomycin concentrations over time in the two treatment groups. The AUC_{24h} was 577 ± 120 in the CIV group and 653 ± 232 mg/liter/h in the IIV group. The AUC_{24h} and the daily dose given over 10 days of treatment have less variability between patients with CIV than with IIV (variance, 14,621 versus 53,975 $mg^2/liter^2/h^2$ [$P = 0.02$] and 414 versus 818 g^2 [$P = 0.05$], respectively).

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, June 2003, p. 2015–2017 Vol. 47, No. 6
0066-4804/03/$08.00+0 DOI: 10.1128/AAC.47.6.2015–2017.2003

Vancomycin Penetration of Uninfected Pleural Fluid Exudate after Continuous or Intermittent Infusion

Baudouin Byl,[1]* Frédérique Jacobs,[1] Pierre Wallemacq,[2] Camelia Rossi,[1] Philippe de Francquen,[3] Matteo Cappello,[3] Teresinha Leal,[2] and Jean-Pierre Thys[1]

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, May 2000, p. 1356–1358 Vol. 44, No. 5
0066-4804/00/$04.00+0

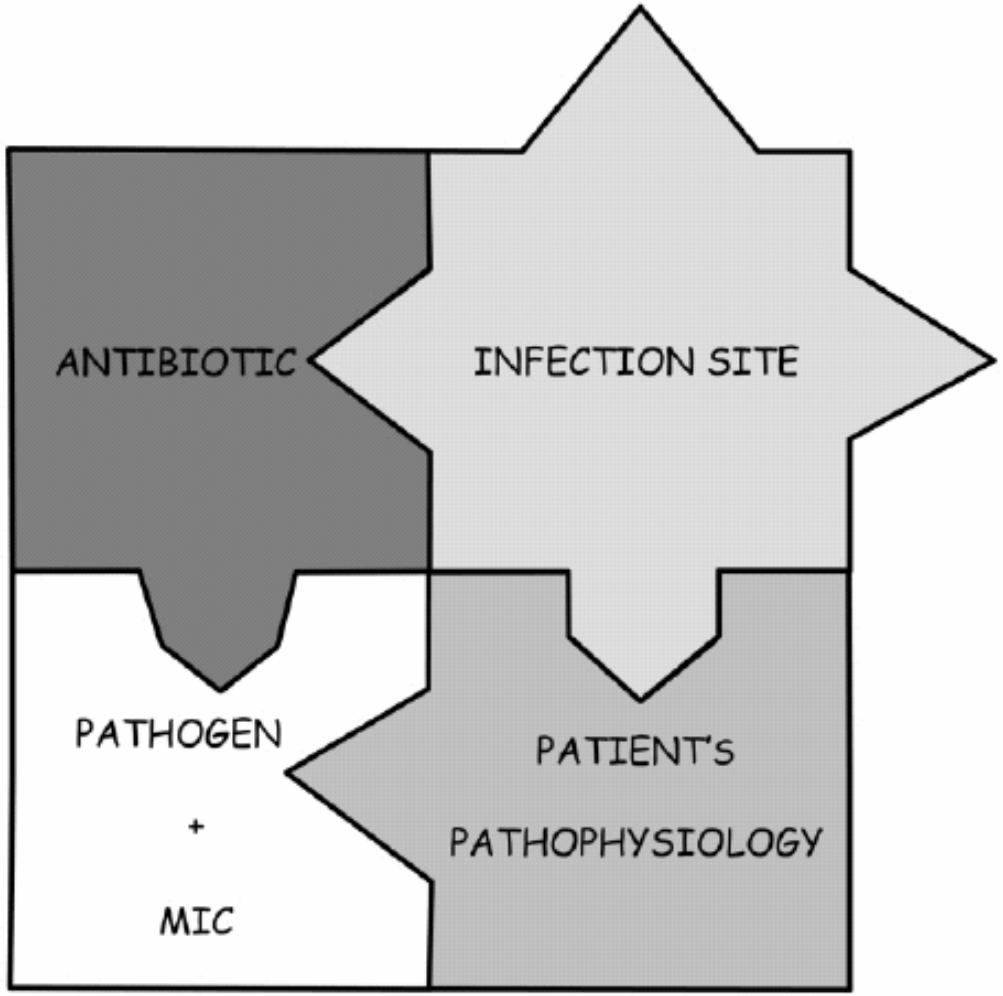
Cerebrospinal Fluid Penetration and Pharmacokinetics of Vancomycin Administered by Continuous Infusion to Mechanically Ventilated Patients in an Intensive Care Unit

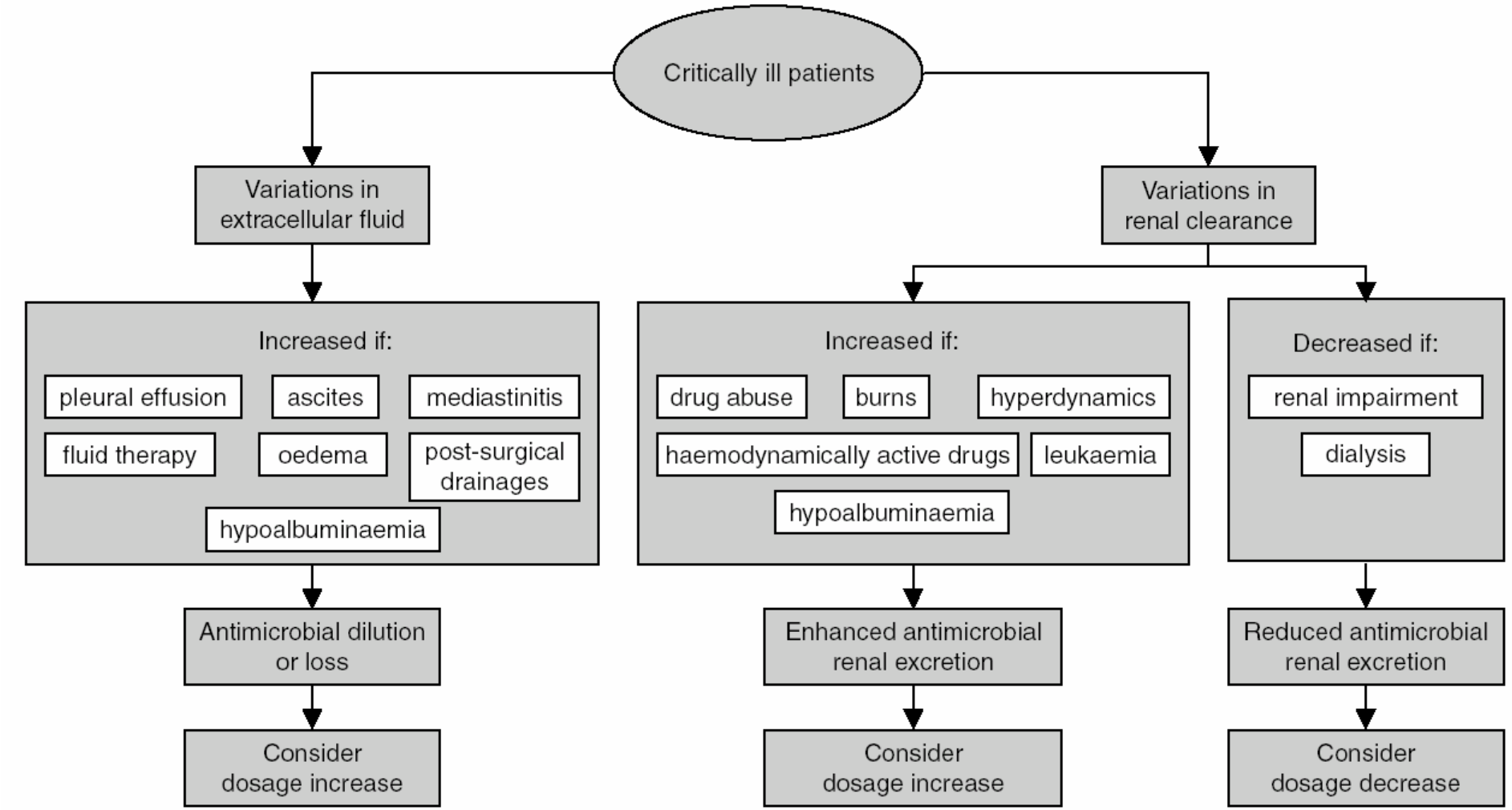
JACQUES ALBANÈSE,[1] MARC LÉONE,[1] BERNARD BRUGUEROLLE,[2] MARIE-LAURE AYEM,[1] BRUNO LACARELLE,[2] AND CLAUDE MARTIN[1]*

The Antimicrobial Therapy Puzzle: Could Pharmacokinetic-Pharmacodynamic Relationships Be Helpful in Addressing the Issue of Appropriate Pneumonia Treatment in Critically Ill Patients?

Federico Pea[1] and Pierluigi Viale[2]

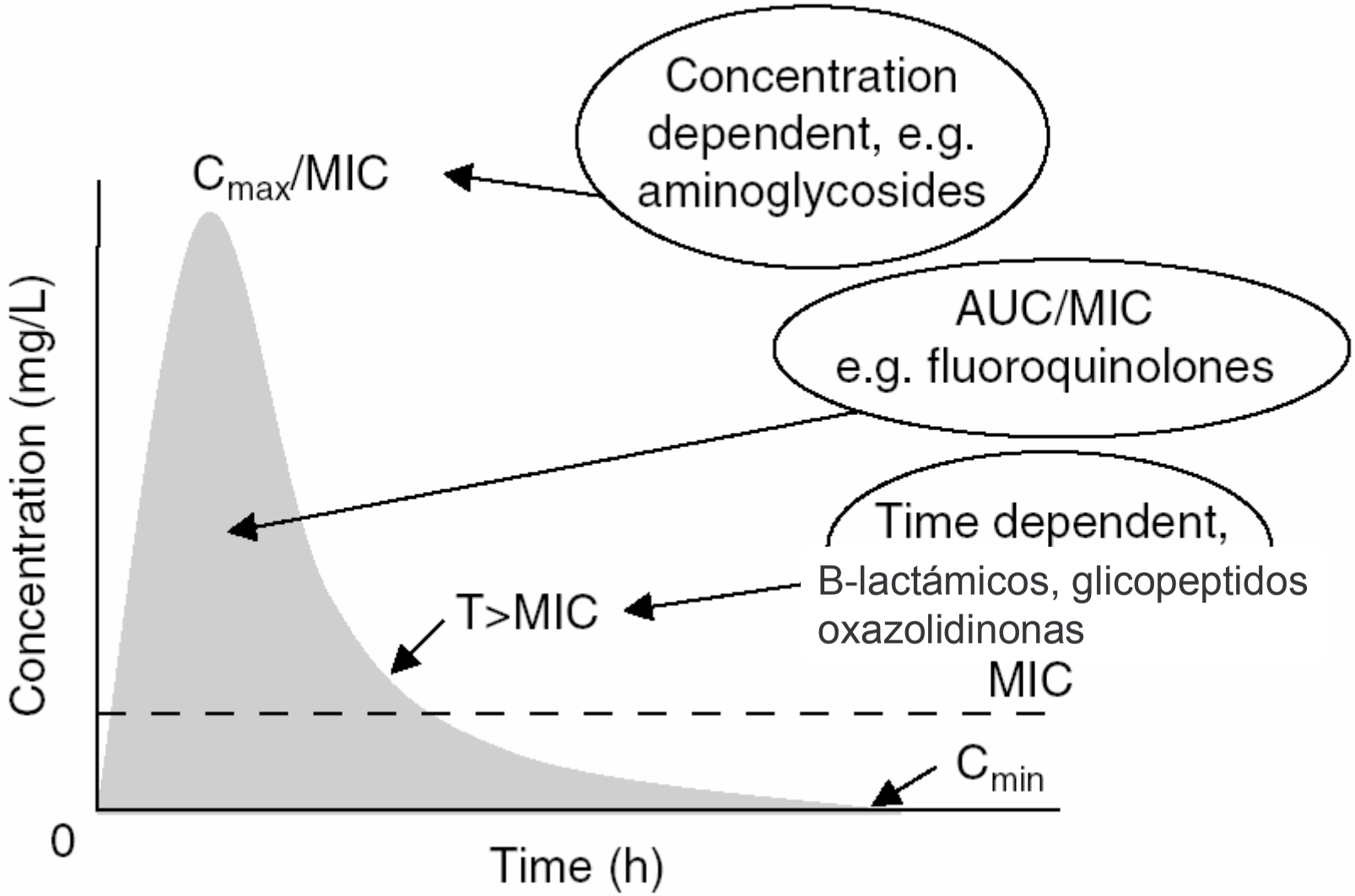
CID 2006;42.1764





Factores que afectan a la distribución y eliminación de los antimicrobianos

Clin Pharmacokinet 2005;44:1009

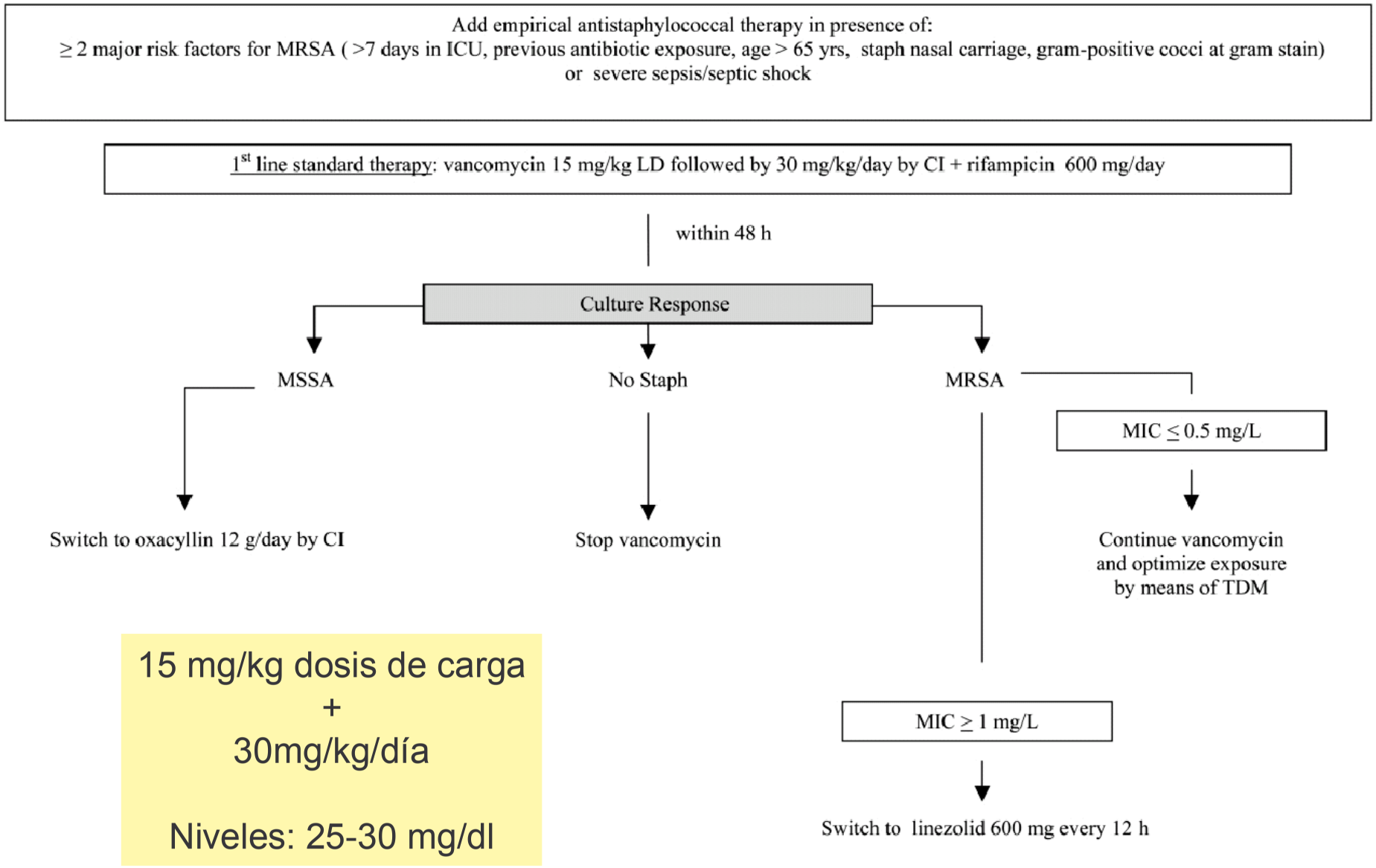


AUC: area bajo la concentración serica en relación al tº
Cmax: pico de concentración
Cmin: valle de concentración
MIC: concentración mínima inhibitoria
T>MIC: tiempo en que la concentración plasmatica es >MIC

Clin Pharmacokinet 2006;45:755

Table 1. Pulmonary disposition of some antimicrobial agents.

Antimicrobial agent (dosage)	Concentration levels at different time points, h																	
	ELF, mg/L									ELF-to-plasma ratio								
	0.5	1	2	4	6	8	12	24	48	0.5	1	2	4	6	8	12	24	48
Hydrophilic agents																		
Ceftazidime (4g/day CI)	8.2[a]	8.2	8.2	8.2	8.2	8.2	8.2	8.2	8.2	0.21[a]	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21
Meropenem (1g)	5.04	7.07	3.86	2.20	0.59	…	…	…	…	0.19	0.51	0.33	1.04	0.82	…	…	…	…
Vancomycin (15 mg/kg)[b]	4.5[a]	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	0.19[a]	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19
Lipophilic agents																		
Linezolid (600mg every 12 h)	…	…	…	64.3	…	31.4	24.3	7.60	0.7	…	…	…	4.15	…	3.53	2.38	4.22	3.5
Linezolid (600 mg every 12 h)	…	14.4	…	…	…	…	2.6	…	…	…	1.05	…	…	…	…	1.04	…	…



15 mg/kg dosis de carga
+
30mg/kg/día

Niveles: 25-30 mg/dl

The unstable hemodynamic and renal conditions and greater volume of distribution in critically ill patients may exacerbate the problem of lung penetration and explain the worse outcome with vancomycin in the ventilated population. The difficulties of achieving adequate local levels of vancomycin have led to the use of higher doses and pharmacokinetic monitoring to avoid toxicity and improve efficacy [13, 14]. Continuous infusion of vancomycin has also been studied [15]. However, none of these strategies has been demonstrated to improve clinical outcome, much less survival, compared with standard-dose vancomycin in a prospective study of patients with MRSA VAP.

Intensive Care Med 2004;30:388

TABLA 7. **Recomendaciones de tratamiento de la bacteriemia primaria y asociada a catéter por cocos grampositivos**

Infección	Primera elección	G. Rec	Referencia	Alternativa	G. Rec	Referencia
Bacteriemia primaria y relacionada con catéter						
Tratamiento empírico	Vancomicina	A-I	51,99-101	Si insuficiencia renal: linezolid o teicoplanina	A-II	51,102,103
TD *S.* coagulasa negativo						
Sensible a meticilina	Cloxacilina	B-III	99	Cefazolina	B-III	99
Resistente a meticilina	Vancomicina	A-I	99,100,104	Si insuficiencia renal: linezolid o teicoplanina	A-II	99,100,102-104
TD *S. aureus*						
Sensible a meticilina	Cloxacilina	A-I	105,106	Cefazolina	A-II	99
				Alergia a betalactámicos: vancomicina, linezolid o teicoplanina	A-II	
Resistente a meticilina	Vancomicina	A-I	101	Linezolid o teicoplanina	A-II	102,103

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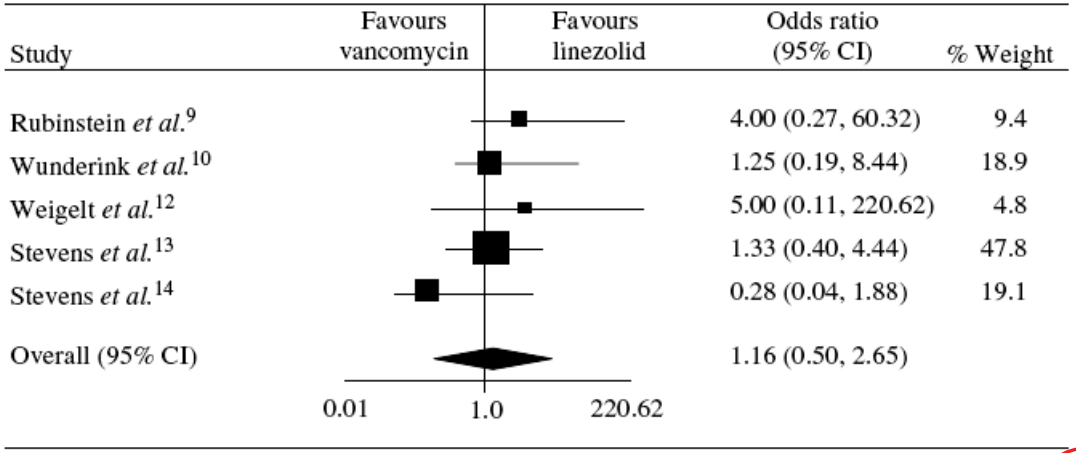
JAC

Linezolid versus vancomycin for *Staphylococcus aureus* bacteraemia: pooled analysis of randomized studies

Andrew F. Shorr[1]*, Mark J. Kunkel[2] and Marin Kollef[3]



*Random-effects model; test for heterogeneity, $P = 0.467$

Table 2. Safety in randomized studies comparing linezolid and vancomycin

Type of adverse event	Number of patients (%) linezolid (n = 74)	Number of patients (%) vancomycin (n = 70)	P value
Any adverse event, including those not related to study drug	59/74 (79.7)	48/69 (69.6)	0.16
Serious adverse event, as assessed by investigators	35/74 (47.3)	26/70 (37.1)	0.22
Discontinuation from treatment	27/74 (36.5)	27/70 (38.6)	0.80
New-onset thrombocytopenia[a]	5/36 (13.9)	0 (0)	0.02

[a]New-onset thrombocytopenia = decrease from baseline of ≥150 × 10^9 platelets/L to <150 × 10^9 platelets/L.

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JAC

Linezolid versus teicoplanin in the treatment of Gram-positive infections in the critically ill: a randomized, double-blind, multicentre study

Jorge A. Cepeda[1], Tony Whitehouse[2], Ben Cooper[1,3], Janeane Hails[2], Karen Jones[4], Felicia Kwaku[2], Lee Taylor[4], Samantha Hayman[1], Steven Shaw[4], Christopher Kibbler[3], Robert Shulman[5], Mervyn Singer[2] and A. Peter R. Wilson[1]*

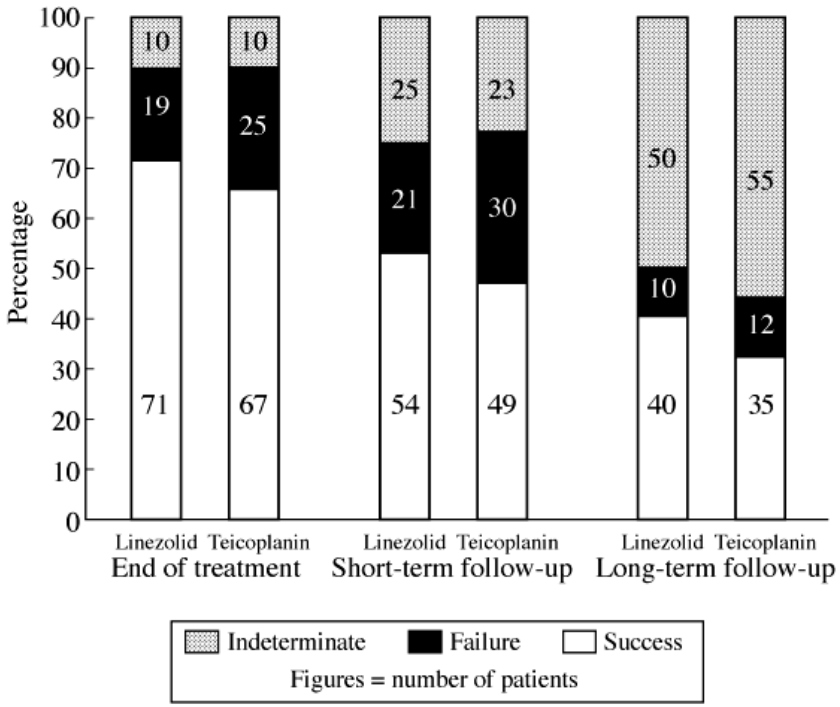

Figure 2. Clinical outcomes in intention-to-treat population (ITT).

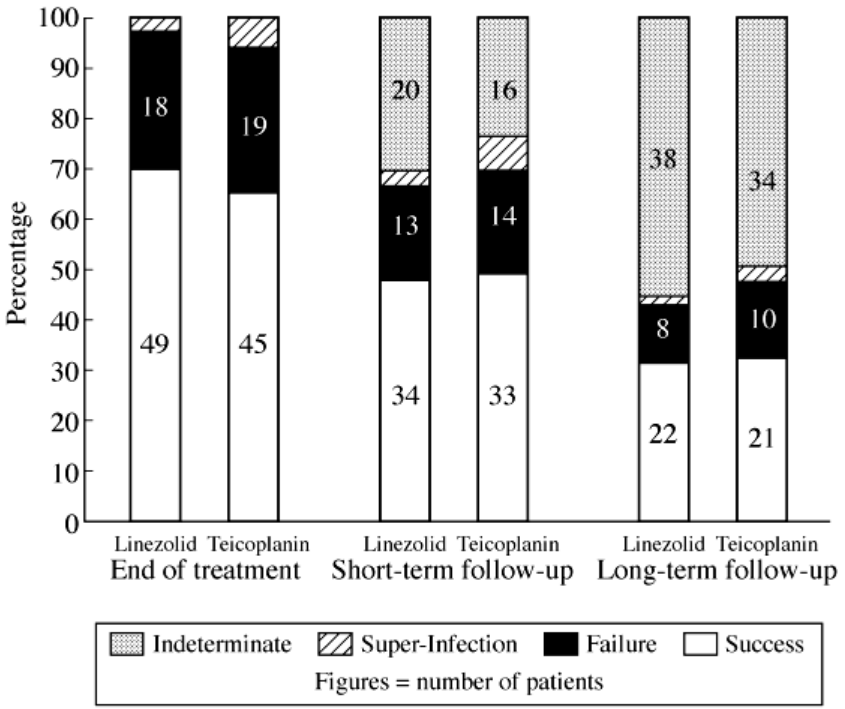

Figure 3. Microbiological outcomes in modified intention-to-treat population (MITT).

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JAC

Linezolid compared with teicoplanin for the treatment of suspected or proven Gram-positive infections

Mark Wilcox[1]*, Dilip Nathwani[2] and Matthew Dryden[3]

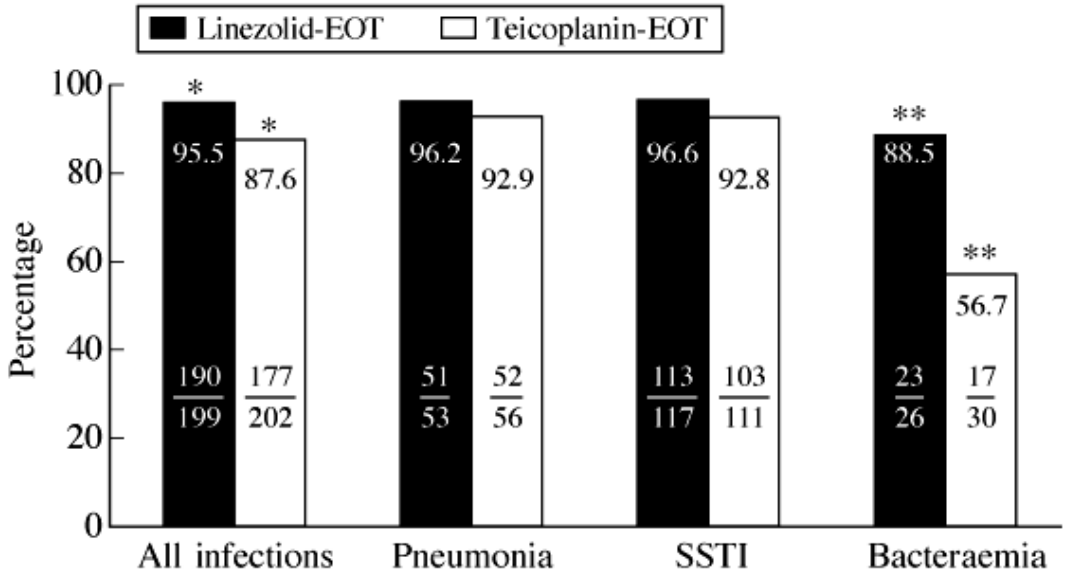

Figure 1. Rates of clinical success with linezolid and teicoplanin by site of infection at end-of-treatment visit: intent-to-treat population.*$P = 0.005$; **$P = 0.009$.

TABLA 8. **Recomendaciones para el tratamiento de infecciones del sistema nervioso central**

TD *S. aureus* y coagulasa negativa						
Sensible a meticilina	Cloxacilina	A-III	138,139	Meropenem	B-III	
				Alergia a betalactámicos: vancomicina o linezolid	C-III	
Resistente a meticilina	Vancomicina	A-III	138,147	Linezolid o vancomicina + rifampicina	B-III C-III	1

TABLA 9. **Recomendaciones para el tratamiento de la endocarditis infecciosa**

Estafilococos resistentes a meticilina	Vancomicina 4-6 semanas	A-II	Vancomicina ≥ 6 semanas + rifampicina		A-II
	o linezolid 4-6 semanas	B-III	≥ 6 semanas + gentamicina (3 dosis) 2 semanas		
	o trimetoprim-sulfametoxazol 4-6 semanas	B-II	(fluorquinolona si hay resistencia a gentamicina)		
	± rifampicina		o linezolid 4-6 semanas		B-III
	o doxicilina 4-6 semanas	C-III			

TIGECICLINA
DAPTOMICINA
MOXIFLOXACINO
DALVABACINA
CEFTOBIPROLE….

TIGECICLINA
DAPTOMICINA
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DALVABACINA
CEFTOBIPROLE….