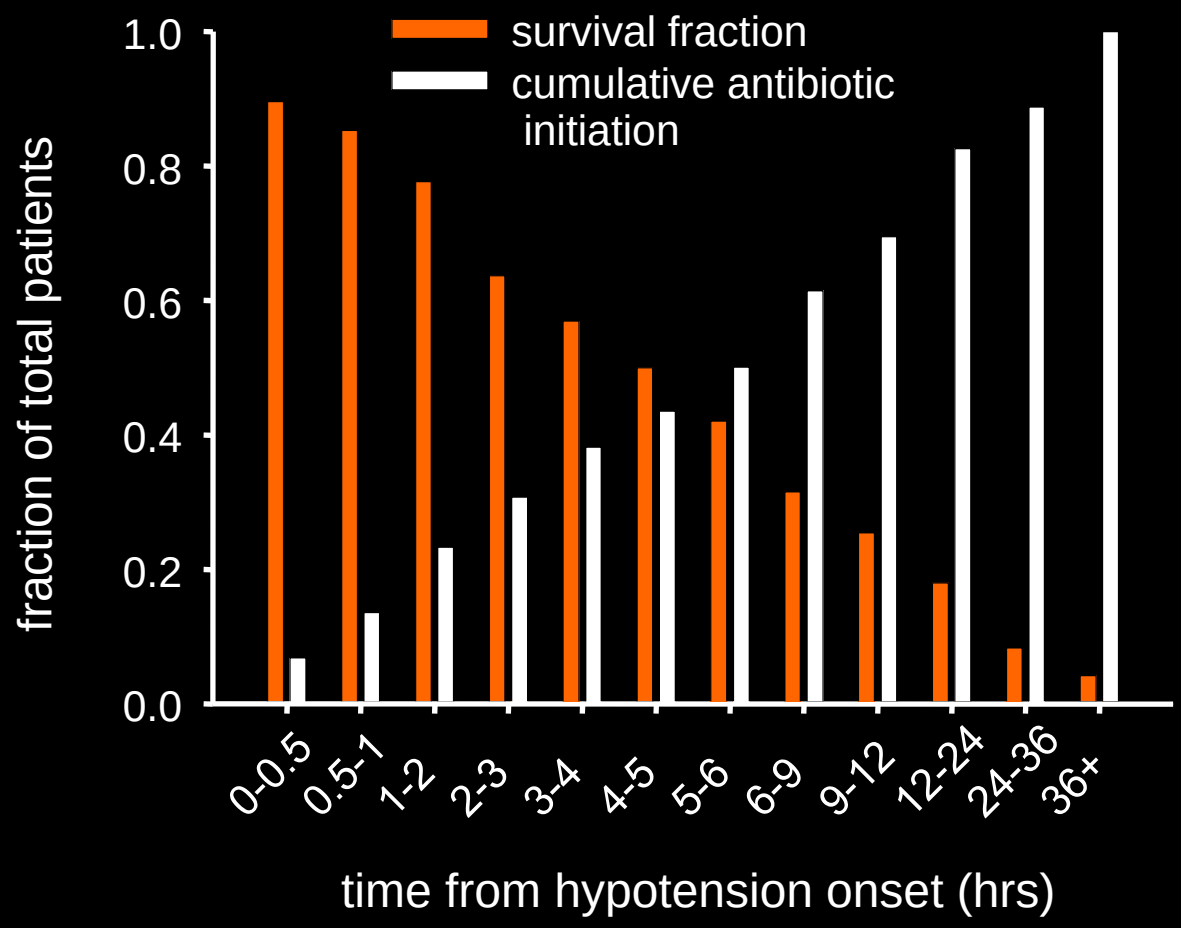
Anàlisis de la efectivitat d'una intervenció múltiple dirigida a millorar la antibioticoterapia empírica a la sepsis greu. Estudi ABISS-Edusepsis a Catalunya.

34 Reunió de la SOCMIC

Ricard Ferrer i grup de recerca Edusepsis
Critical Care Department
Mutua Terrassa University Hospital
Barcelona. SPAIN

Early antibiotic treatment



- Retrospective
- Only septic shock
- Adequate treatment

Kumar A et al. Crit Care Med 2006;34:1589-96

Surviving Sepsis Campaign

Institute for Healthcare Improvement

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

R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Jean M. Carlet, MD; Julian Bion, MD; Margaret M. Parker, MD; Roman Jaeschke, MD; Konrad Reinhart, MD; Derek C. Angus, MD, MPH; Christian Brun-Buisson, MD; Richard Beale, MD; Thierry Calandra, MD, PhD; Jean-Francois Dhainaut, MD; Herwig Gerlach, MD; Maurene Harvey, RN; John J. Marini, MD; John Marshall, MD; Marco Ranieri, MD; Graham Ramsay, MD; Jonathan Sevransky, MD; B. Taylor Thompson, MD; Sean Townsend, MD; Jeffrey S. Vender, MD; Janice L. Zimmerman, MD; Jean-Louis Vincent, MD, PhD; for the International Surviving Sepsis Campaign Guidelines Committee

SEPSIS RESUSCITATION BUNDLE

6H

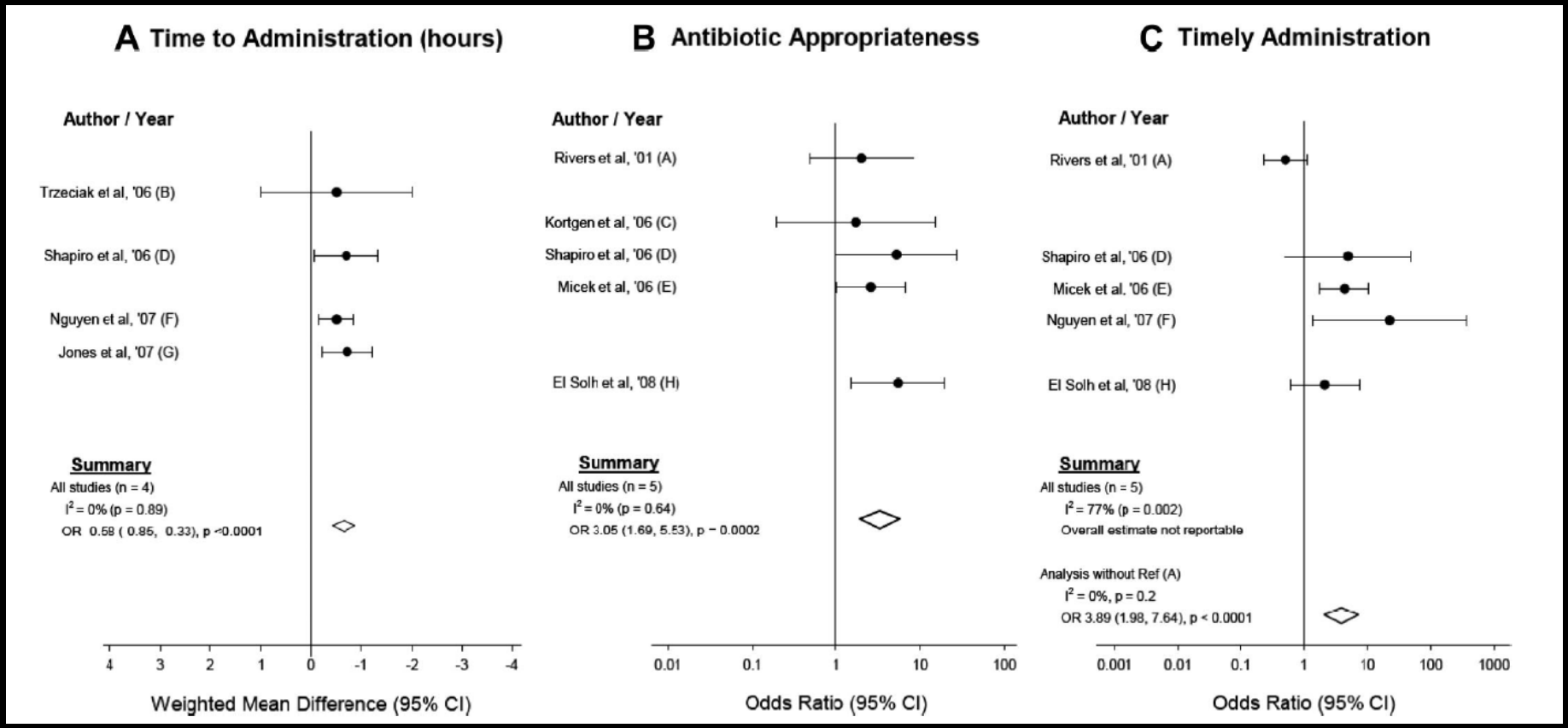
1. Measure serum lactate.
2. Obtain blood cultures prior to antibiotic administration.
3. Administer broad-spectrum antibiotics within 3 hours from time of presentation for ED admissions and 1 hour for non-ED ICU admissions.
4. In the event of hypotension and/or lactate > 4 mmol/L (36 mg/dL):
   a. Deliver an initial minimum of 20 ml/kg of crystalloid (or colloid equivalent).
   b. Apply vasopressors for hypotension not responding to initial fluid resuscitation to maintain mean arterial pressure (MAP) ≥ 65 mm Hg.
5. In the event of persistent hypotension despite fluid resuscitation (septic shock) and/or lactate > 4 mmol/L (36 mg/dL):
   a. Achieve central venous pressure (CVP) of ≥ 8 mm Hg.
   b. Achieve central venous oxygen saturation ($ScvO_2$) of ≥ 70%.*

Intensive Care Med 2008;34:17-60

Bundled care for septic shock: An analysis of clinical trials*

Amisha V. Barochia, MBBS; David Vitberg, MD; Xizhong Cui, MD, PhD; Anthony F. Suffredini, MD; Naomi P. O'Grady, MD; Steven M. Banks, PhD;† Peter Minneci, MD; Steven J. Kern, BS; Robert L. Danner, MD; Charles Natanson, MD; Peter Q. Eichacker, MD

Crit Care Med 2010



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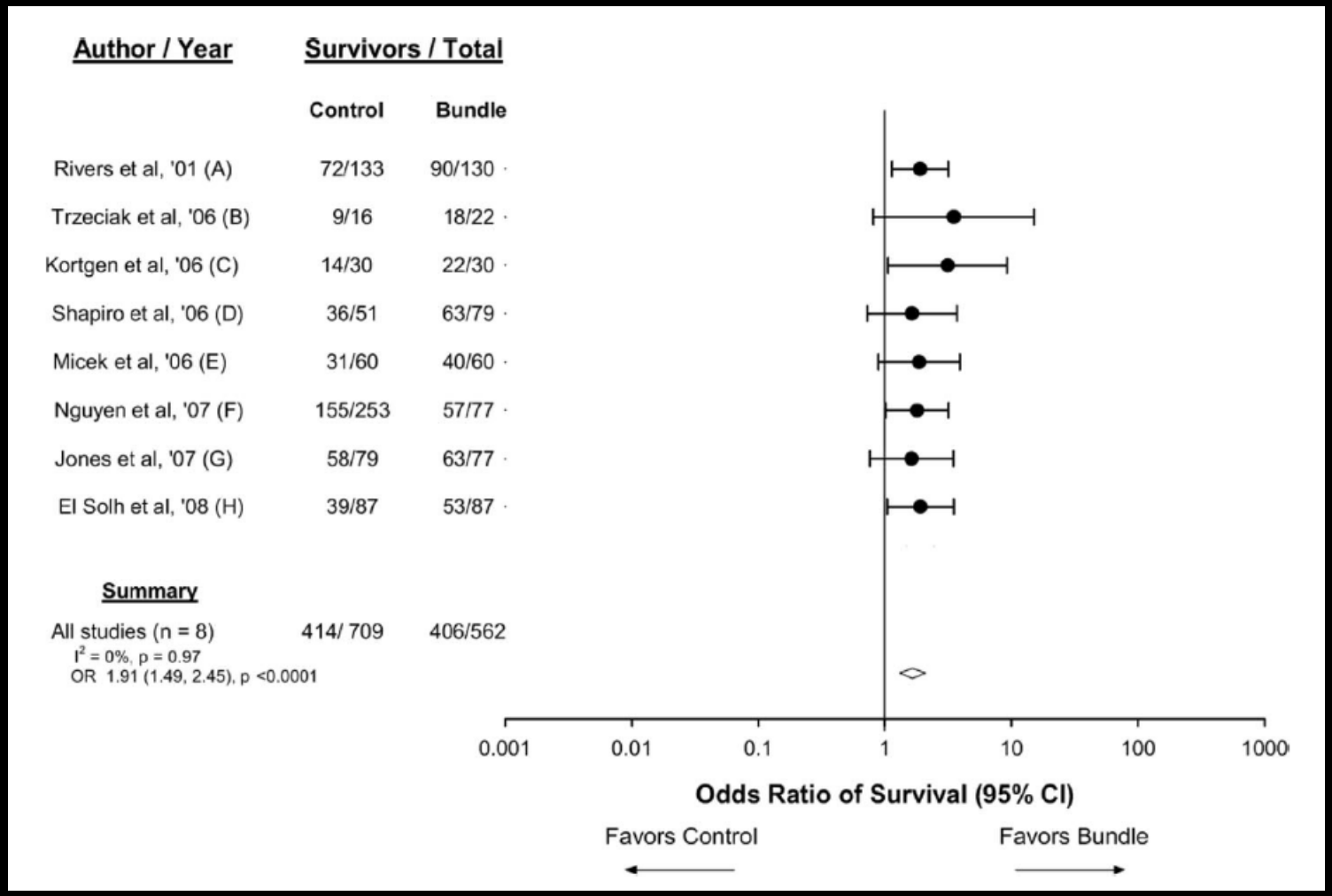
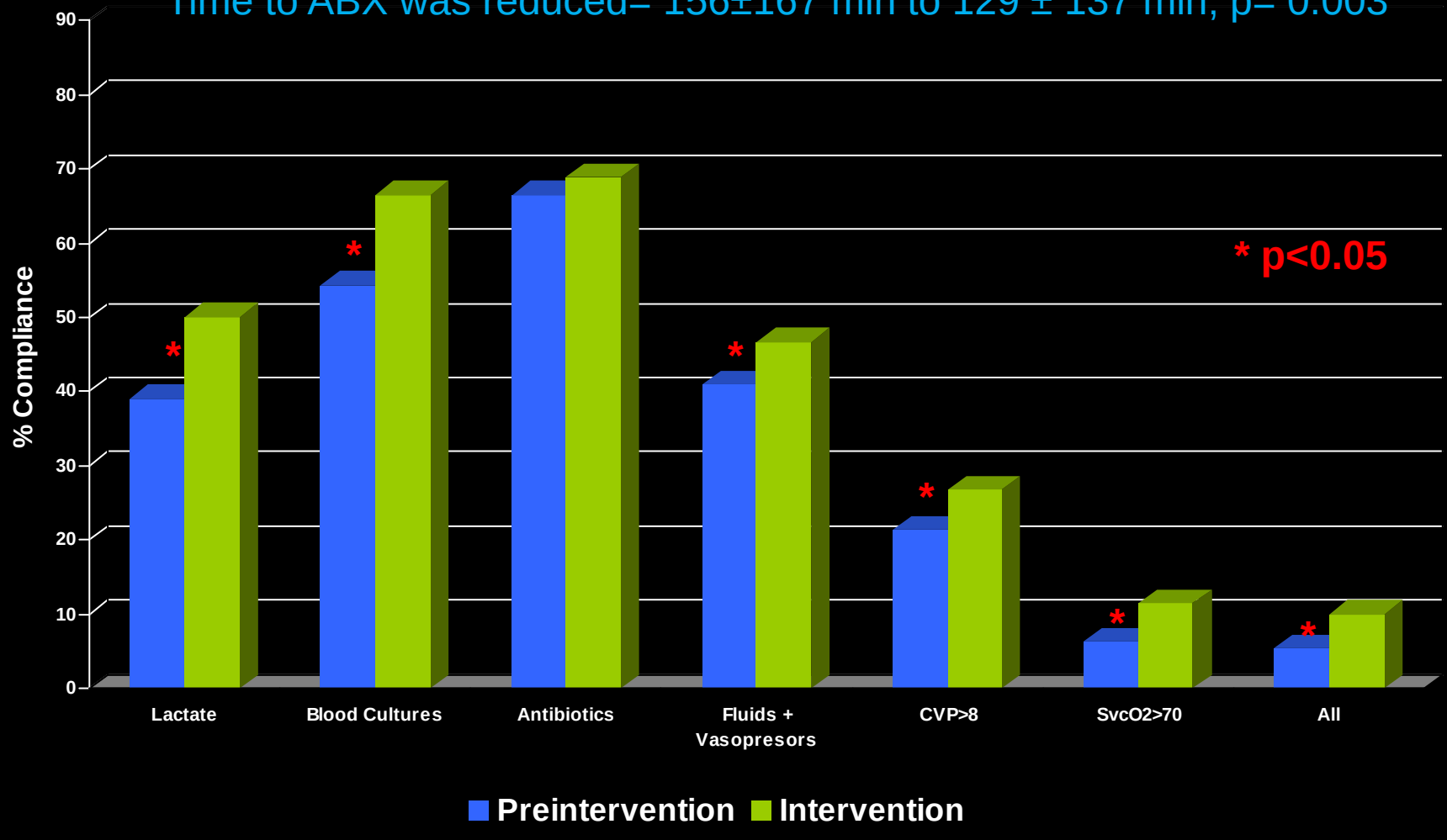
Crit Care Med 2010



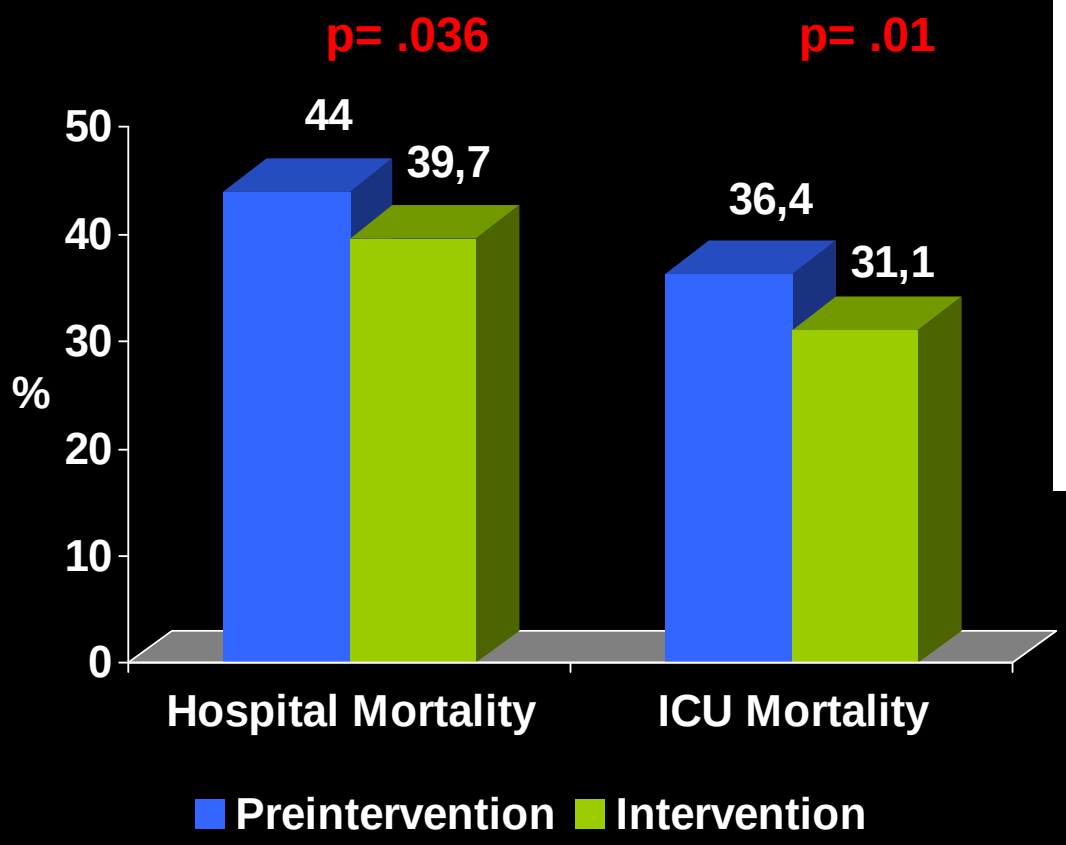
Edusepsis National Intervention

Time to ABX was reduced= 156±167 min to 129 ± 137 min; p= 0.003

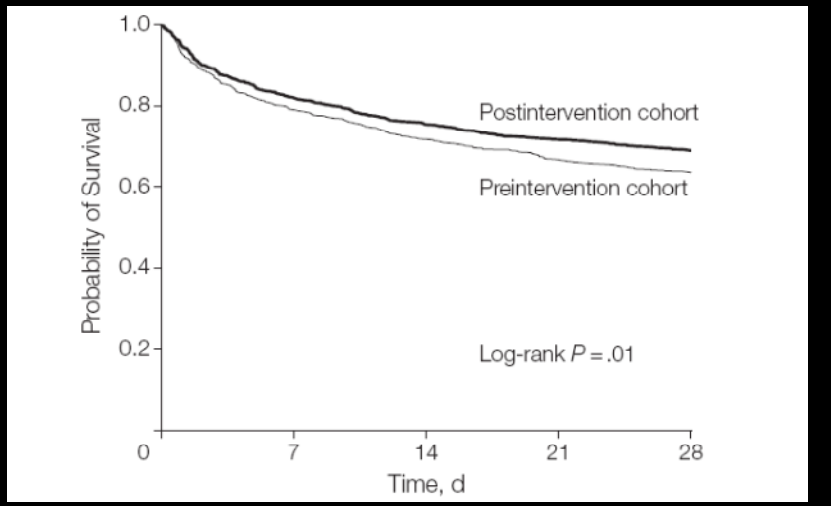


Ferrer R et al. JAMA 2008;299(19):2294-2303

Edusepsis National Intervention

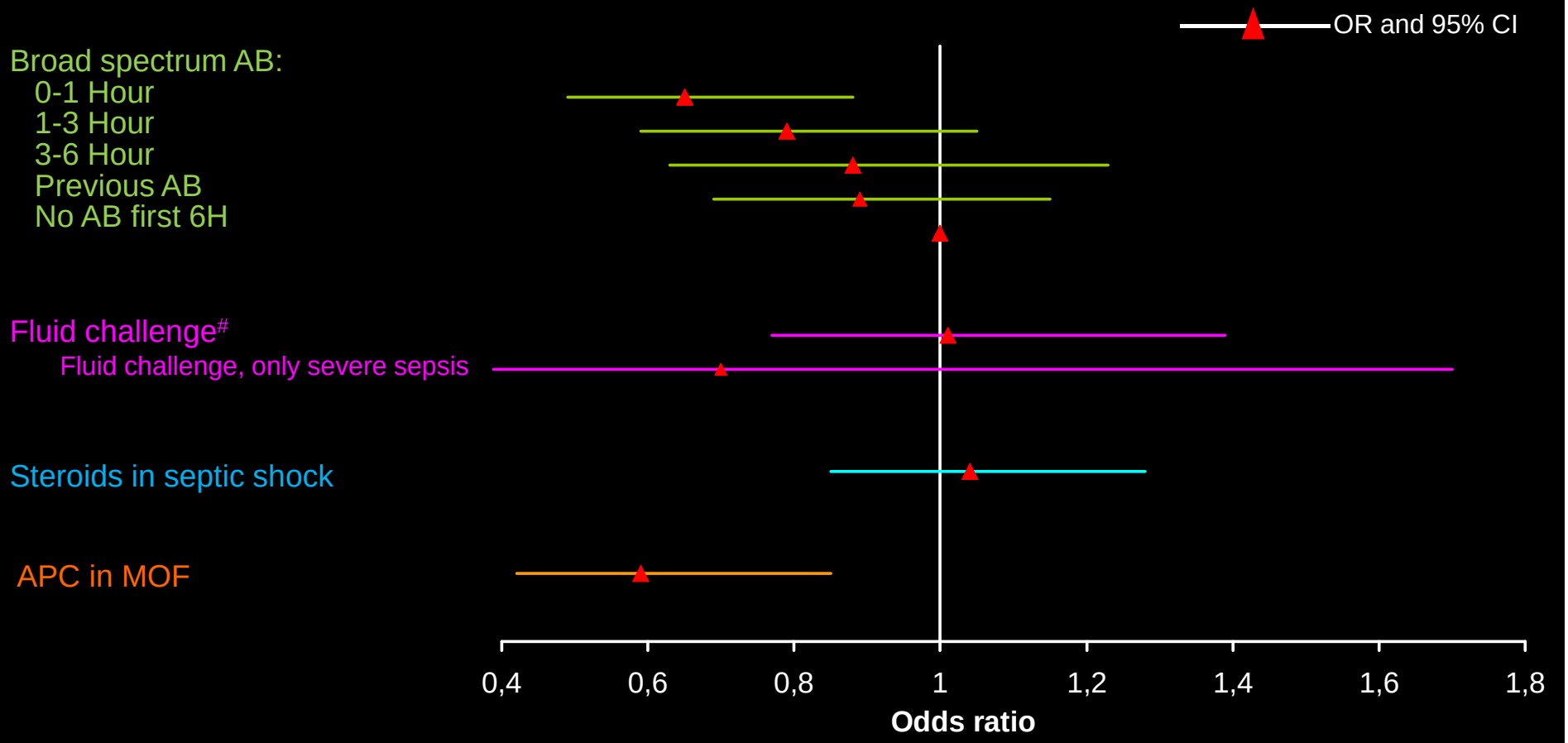


28d Mortality: Kaplan-Meier curve



Absolute reduction: 4.3%
Relative reduction 10%
SSC objective was 25%!

Effectiveness of APC in MOF
Final Model: All risk factors + Other TTMs + PS



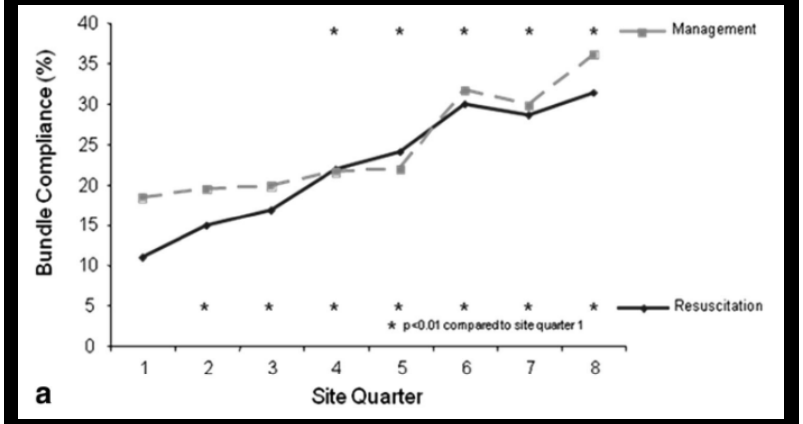
Ferrer R et al. AJRCCM 2009;180:861–866

The Surviving Sepsis Campaign: Results of an international guideline-based performance improvement program targeting severe sepsis

Mitchell M. Levy, MD; R. Phillip Dellinger, MD; Sean R. Townsend, MD; Walter T. Linde-Zwirble; John C. Marshall, MD; Julian Bion, MD; Christa Schorr, RN, MSN; Antonio Artigas, MD; Graham Ramsay, MD; Richard Beale, MD; Margaret M. Parker, MD; Herwig Gerlach, MD, PhD; Konrad Reinhart, MD; Eliezer Silva, MD; Maurene Harvey, RN, MPH; Susan Regan, PhD; Derek C. Angus, MD, MPH; on behalf of the Surviving Sepsis Campaign

n= 15.022

	Initial Quarter Achieved, %	Final Quarter Achieved, %[a]	*p* Value Compared With Initial
Initial care bundle (first 6 hrs of presentation)			
Measure lactate	61.0	78.7	≤.0001
Blood cultures before antibiotics	64.5	78.3	≤.0001
Broad-spectrum antibiotics	60.4	67.9	.0002
Fluids and vasopressors	59.8	77.0	≤.0001
CVP >8 mm Hg	26.3	38.0	≤.0001
Scv_{O_2} >70%	13.3	24.3	≤.0001
All resuscitative measures	10.9	21.5	≤.0001
Management bundle (first 24 hrs after presentation)			
Steroid policy	58.5	73.9	≤.0001
Administration of drotrecogin alfa policy	47.4	53.5	.003
Glucose control	51.4	56.8	.0009
Plateau pressure control	80.8	83.8	.24
All management measures	18.4	25.5	≤.0001



Crit Care Med 2010; 38(2):367-374

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n= 15.022

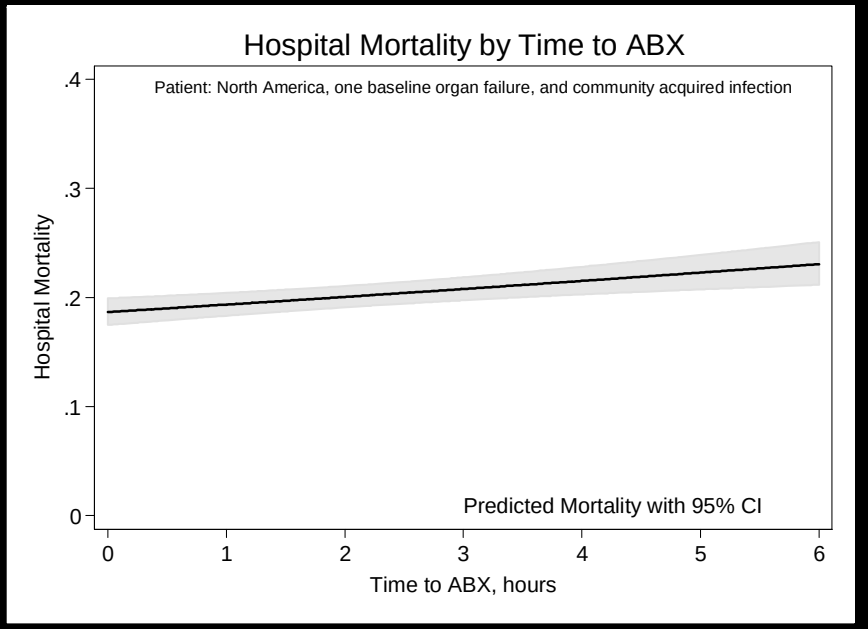
Bundle Target	Population	n	Unadjusted OR	Unadjusted *p*	Risk-Adjusted OR	Risk-Adjusted 95% CI	Risk-Adjusted *p*
Measure lactate	All[a]	15,022	0.86	<.0001	0.97	0.90, 1.05	.48
Obtain blood cultures before antibiotics	All[a]	15,022	0.70	<.0001	0.76	0.70, 0.83	<.0001
Commence broad-spectrum antibiotics	All[a]	15,022	0.78	<.0001	0.86	0.79, 0.93	<.0001
Achieve tight glucose control	All[a]	15,022	0.65	<.0001	0.67	0.62, 0.71	<.0001
Administer drotrecogin alfa	Multiorgan failure[b]	8733	0.90	.26	0.84	0.69, 1.02	.07
Administer drotrecogin alfa	Shock despite fluids[c]	7854	0.91	.30	0.81	0.68, 0.96	.02
Administer low-dose steroids	Shock despite fluids[c]	7854	1.06	.18	1.06	0.96, 1.17	.24
Demonstrate CVP ≥8 mm Hg	Shock despite fluids[c]	7854	1.08	.10	1.00	0.89, 1.12	.98
Demonstrate $Scvo_2$ ≥70%	Shock despite fluids[c]	7854	0.94	.24	0.98	0.86, 1.10	.69
Achieve low plateau pressure control	Mechanical ventilation[d]	7860	0.67	<.0001	0.70	0.62, 0.78	<.0001

Crit Care Med 2010; 38(2):367-374

Time to Treatment. Antibiotics

25.089 patients with severe sepsis or septic shock

Time to ABX, hrs	OR	95% CI		*p*-value
0 (ref)	1.00	---	---	---
1	1.05	1.02	1.07	< 0.001
2	1.09	1.04	1.15	< 0.001
3	1.14	1.06	1.23	< 0.001
4	1.19	1.08	1.32	< 0.001
5	1.25	1.11	1.41	< 0.001
6	1.31	1.13	1.51	< 0.001



Ferrer et al. ESICM 2011, Abstract 139; Annals Internal Medicine Submitted

Surviving Sepsis Campaign

D. Antimicrobial Therapy

1. Administration of effective intravenous antimicrobials within the first hour of recognition of septic shock (grade 1B) and severe sepsis without septic shock (grade 1C) as the goal of therapy.

2a. Initial empiric anti-infective therapy of one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into tissues presumed to be the source of sepsis (grade 1B).

2b. Antimicrobial regimen should be reassessed daily for potential deescalation (grade 1B).

Use of a protocolized approach to the management of sepsis can improve time to first dose of antibiotics ☆

Pamela S. Tipler DO, Jeremy Pamplin MD, Vincent Mysliwiec MD, David Anderson MD, Cristin A. Mount MD*

Madigan Army Medical Center, Tacoma, WA

Journal of Critical Care 2012

The sepsis protocol consisted of:

- a sepsis note in the electronic health record that supported clinical decision making.
- Guideline recommendations for empiric antibiotic therapies to treat the suspected source of infection.
- The note also includes calculations for the creatinine clearance and prompts to consider patient allergies and to record a measured lactate.
- The note is automatically sent to the pharmacist who then provides the requested antibiotics without initial ID approval.
- The ID consultant received automatically generated reports from the sepsis note to review the prescribing practices.

Use of a protocolized approach to the management of sepsis can improve time to first dose of antibiotics☆

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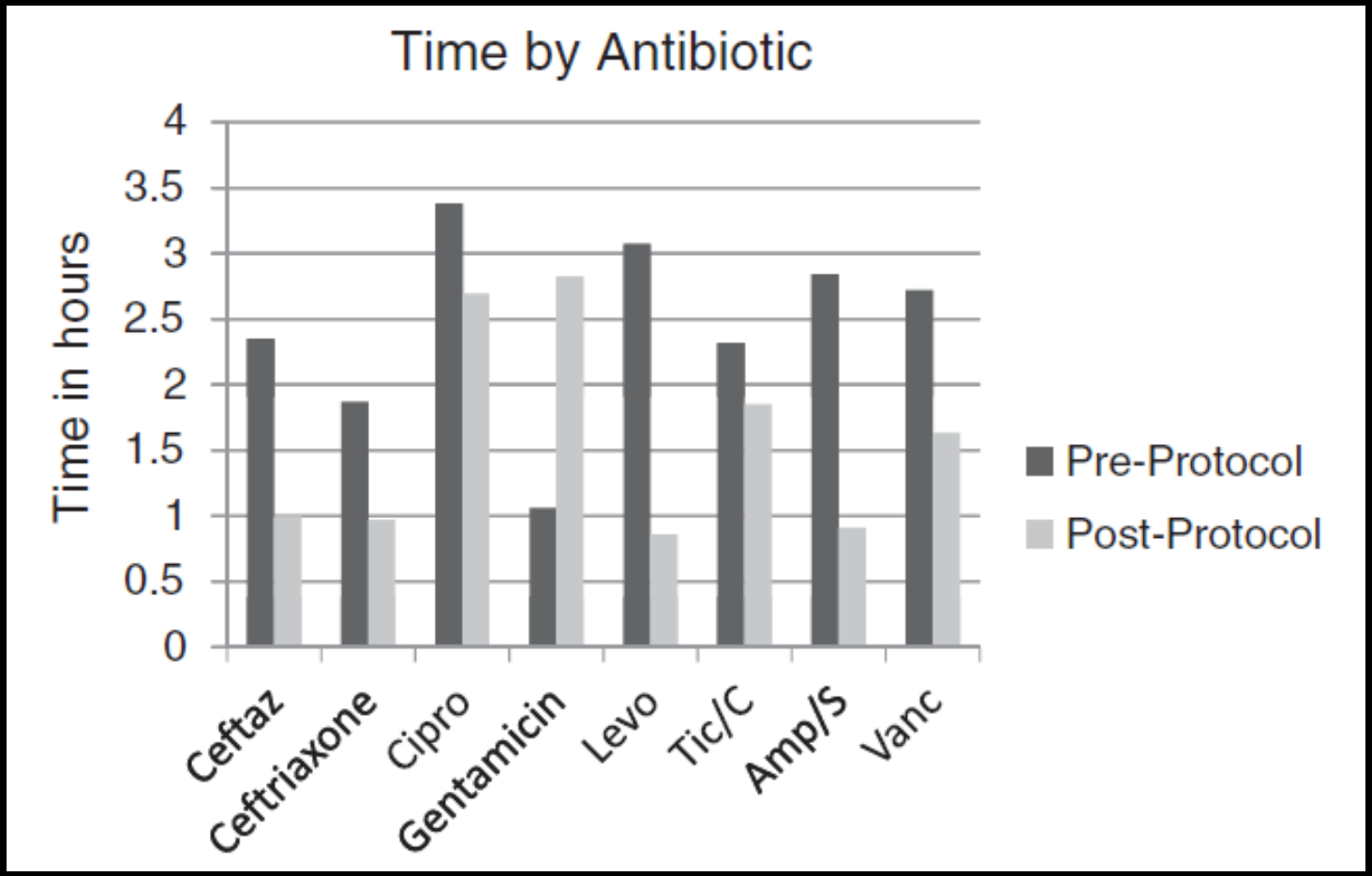


ABISS Edusepsis Study

Antibiotic Intervention in Severe Sepsis

edusepsis.org

Objectives

- Efficacy:
  - Reduce time to empiric antibiotic in severe sepsis.
  - Increase appropriateness of antibiotic treatment
  - Reduce hospital mortality.
- Safety:
  - Increase antibiotic deescalation.

By a multifaceted quality-improvement intervention in patients with severe sepsis/septic shock admitted to the Spanish ICUs.

Mètode

- Estudi Multicéntric, escala nacional.
- Diseny abans i després d'una intervenció.
- Criteris inclusió: Tots els episodis de sepsis greu o shock séptic que ingresin a UCI.
- Criteris d'exclusió: Pacients traslladats d'altres centres.

Cronograma

FIS

eCRD

SEMICYUC SUPPORT

CENTER SELECTION

AEMPS/CEICs

SURVEY	BASELINE DATA COLLECTION	INTERVENTION	POST-INTERVENTION DATA COLLECTION
JAN-MAY	APR-JUL	SEP-OCT	JAN-MAR

2011 2012

Mètode

- S'han comparat les variables clíniques, de tractament i mortalitat entre els dos grups.
- Les dades es presenten com percentatges o com mitja ± desviació estàndard.
- Anàlisis estadístic:
  - t de Student per variables continues.
  - chi quadrat per variables categòriques.

Centres Participants

- Centre Medic Delfos
- Hospital Parc Tauli de Sabadell
- Consorci Sanitari de Terrassa
- Hospital Mutua Terrassa
- Hospital Vall d'Hebron
- Hospital Josep Trueta de Girona
- General de Catalunya Capio
- Germans Trias Badalona
- Hospital Sant Pau
- Hospital de Mataró
- Hospital de Granollers
- Hospital del Mar.
- Hospital de Vic
- Hospital Moises Broggi
- Hospital General d'Hospitalet

Intervention

- Audit and Feed-back.
- Educational meetings: PP presentation.
- Interactive Sepsis simulation on-line.
- Posters and pocket material about initial TTM.
- Support for antibiotic prescription.
- Remainders by mail and SMS to all staff assisting to educational meetings.

Audit and Feed-Back

Apreciado investigador del estudio ABISS EDUSEPSIS,

Durante la fase preintervención del estudio hemos evaluado el tratamiento que reciben los pacientes con sepsis grave/shock séptico en tu centro y en más de 100 UCIs españolas.

Los resultados preliminares muestran:

	Tu Centro	**España**
Nº de pacientes incluidos		
Nº de pacientes sin tratamiento antibiótico previo		
Tiempo Sepsis Grave -Tratamiento antibiótico		
% Tratamiento antibiótico apropiado		
% Desescalamiento a las 72h		
Mortalidad		

Estos datos justifican plenamente una intervención dirigida a reducir el tiempo Sepsis Grave -Tratamiento antibiótico que incluye un programa educativo junto con material gráfico dirigido a médicos y enfermeras de los ámbitos que atienden pacientes sépticos.

Te ruego que hayas llegar esta información a tu Jefe de Servicio, Dirección Médica y Dirección de Enfermería. Asimismo, te pongas todo tu empeño en la implementación de la intervención del estudio ABISS-Edusepsis.

Un cordial saludo,

Ricard Ferrer

Coordinador del estudio ABISS-Edusepsis

ABISS EDUSEPSIS

Educational Material

PILARES DEL TRATAMIENTO DE LA SEPSIS

ANTIBIÓTICOS PRECOCES

- Tome 2 hemocultivos simultáneos en diferente localización lo antes posible.
- Adicionalmente tome las muestras pertinentes según la sospecha diagnóstica.
- PRESCRIBA ANTIBIÓTICOS INMEDIATAMENTE. Su administración precoz es fundamental y debe considerarse una EMERGENCIA!
- Utilice los protocolos de antibióticos de su centro.
- Reevalúe diariamente el tratamiento antibiótico para optimizar la eficacia, prevenir las resistencias, evitar toxicidad y minimizar costes.

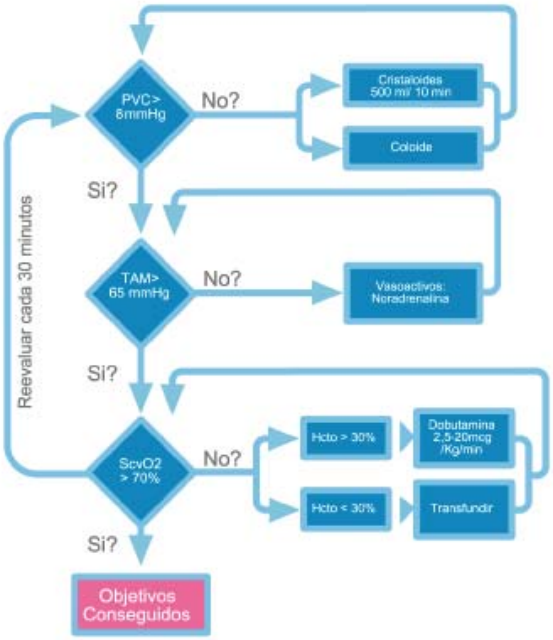
También están disponibles las siguientes pautas:

www.es.dgai-abx.de Usuario y Contraseña para cada centro.

Libro Rojo del GTEI-SEMICYUC: http://goo.gl/LEfai Socios SEMICYUC.

REANIMACIÓN HEMODINÁMICA

- Determine rápidamente lactato en sangre. Nos indicará el grado de hipoperfusión del enfermo.
- En caso de hipotensión o lactato elevado:
  - ADMINISTRE RÁPIDAMENTE FLUÍDOS! 20ml/Kg de suero salino en 1 hora.
  - Evalúe la respuesta de forma inmediata. Si persiste hipotensión o lactato elevado siga resucitando en función del algoritmo:



CONTROL DEL FOCO DE INFECCIÓN

- Se debe realizar la erradicación del foco causal ya sea drenaje de abscesos, desbridamiento de tejidos necróticos y retirada de dispositivos infectados.
- Las medidas de control del foco deben iniciarse inmediatamente tras la resucitación inicial.
- El proceso de sepsis no mejorará de no ser controlado y adecuadamente tratado el foco de origen.
- Deben realizarse TODAS las exploraciones complementarias pertinentes (Rx, TC, Eco, etc).

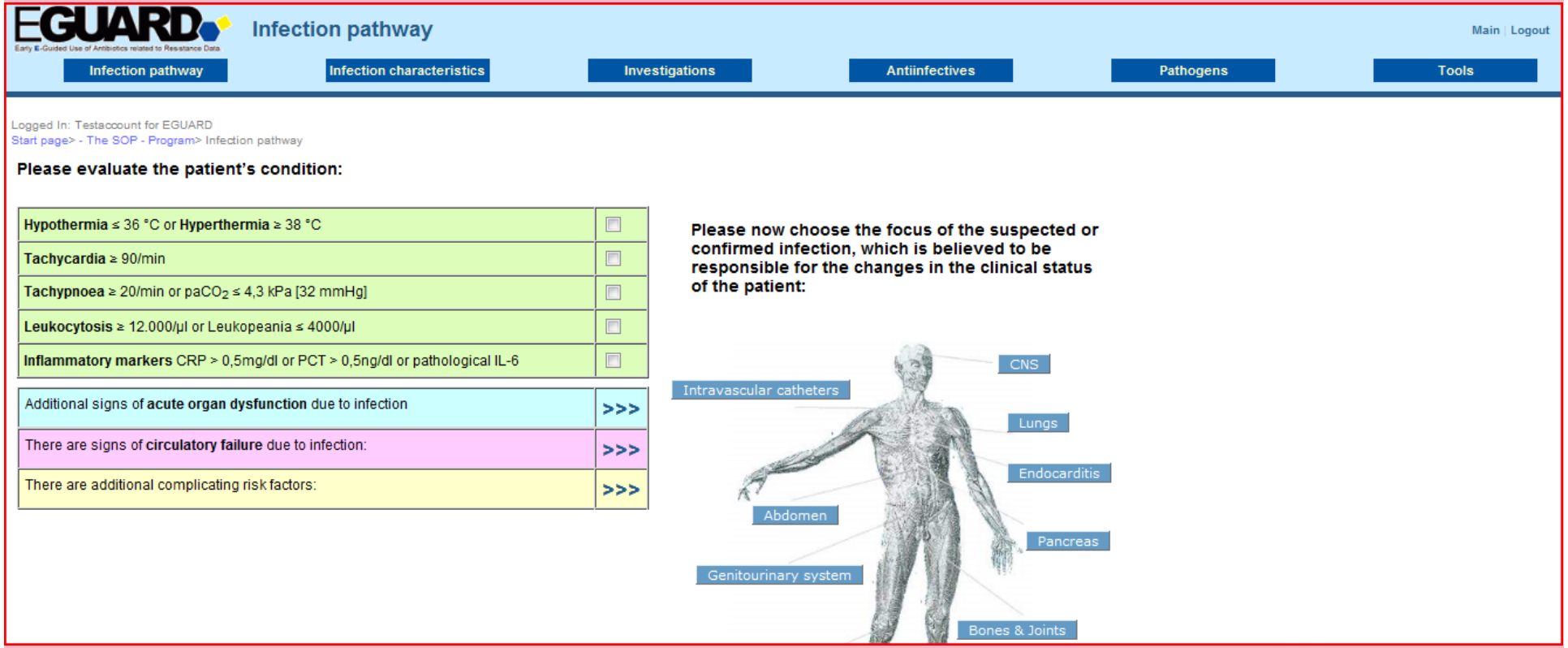
Ejemplos:

- Neumonía: Evalúe posible EMPIEMA.
- Si hay un absceso drénelo.
- Pielonefritis: Evalúe obstrucción y considere drenaje percutaneo.
- Colangitis: Evalúe obstrucción y considere drenaje
- Infección de piel y partes blandes: Considere desbridamiento.

Consulte con su equipo quirúrgico o de radiología intervencionista de referencia.

Prescription Support

- Local Guidelines of empiric antibiotic treatment
- Spanish Society of Intensive Care Guidelines of empiric antibiotic treatment



ABISS EDUSEPSIS

Gamification

Remainder. SMSs

- En sepsis la administración del antibiótico adecuado es una emergencia.Consulta tu guia local de tto antibiotico empirico.TU VELOCIDAD ES VIDA.
- Los pilares del tratamiento de la sepsis son:antibióticoterapia, control del foco y resucitación hemodinámica.¡COMPLETALOS RAPIDAMENTE!
- Tardamos 3 horas en administrar antibiótico empírico en sepsis con mortalidad 33%. Administrado en 1h la mortalidad sería inferior!.
- Antes del tto antibiótico, recuerda tomar hemocultivos + cultivos adicionales según foco de sepsis, después podrás ajustar tu tto empírico!.

Resultats

- 496 pacients: PRE 254, POST: 242
- Edat 63.9 ± 15.1 anys, 67.7% homes.
- CHARLSON 2.9 ± 2.4
- APACHE-II 21,3 ± 8,2.
- SOFA 8,4 ± 3,6
- PCT 32 ± 44
- Bacteriemia 34,3%

Resultats: Control del Focus

33% dels pacients precisen una tècnica de control del focus

Técnica
Colectomía parcial/total
Colecistectomía
Resección intestino delgado
Desbridamiento piel-partes blandas
Drenaje abdominal percutáneo
Nefrostomía
Cateterismo ureteral
Drenaje vía biliar
Drenaje torácico
Desbridamiento de absceso
Cirugía gástrica

Técnica
Apendicectomía
Pancreatectomía parcial
Sutura úlcera
Cirugía hepática
Nefrectomía
Esofaguectomía
Desbridamiento cuello/mediastino

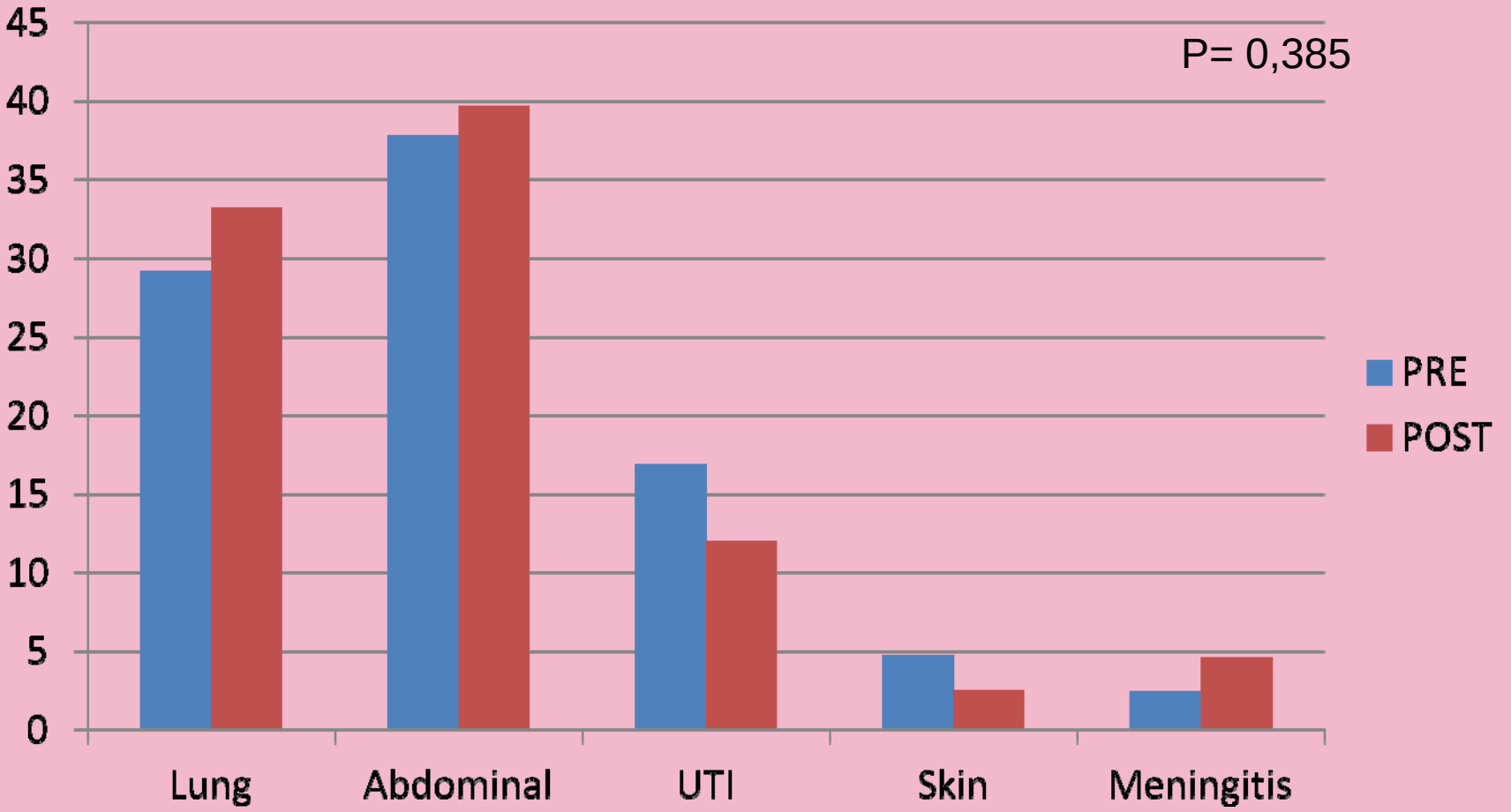
Resultats: Hemocultius

Microorganism	n
Escherichia coli	58
Streptococcus neumoniae	26
Staphylococcus aureus MS and MR	18
Klebsiella spp	14
Pseudomonas aeruginosa	11
Staphylococcus CN	6
Proteus mirabilis	6
Enterococcus spp	4
Streptococcus pyogenes	4
Enterobacter spp	3
Bacterioides fragillis	3
Acinetobacter baumanii	1
Clostridium	2
Neisseria meningitidis	1
Salmonella	2

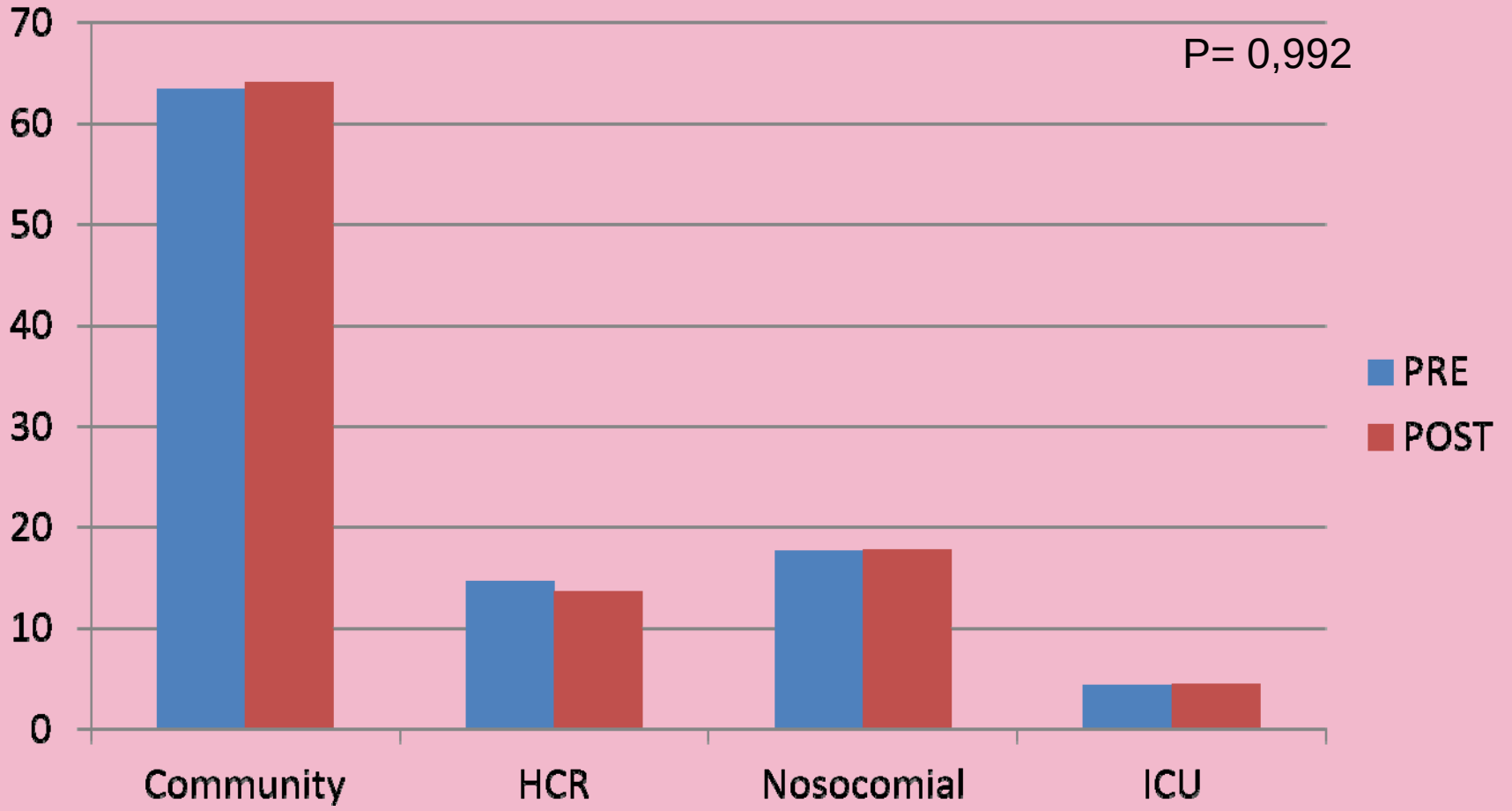
Resultats

	PRE	POST	P value
Age	64.3±15.3	63.9±15.0	0.480
Charlson	2.7±2.3	2.7±2.3	0.308
Leukocytes	16.5±13.5	15.2±10.4	0.234
CRP	26.8±22.9	24.3±12.7	0.164
PCT	31.0±46.6	33.1±41.2	0.790
Lactate (mmol/L)	3.7±3.1	3.7±2.8	0.972
APACHE II	21.7±7.7	20.9±8.7	0.257
Number OF	3.0±1.4	2.9±1.4	0.305
SOFA	8.6±3.5	8.2±3.5	0.305

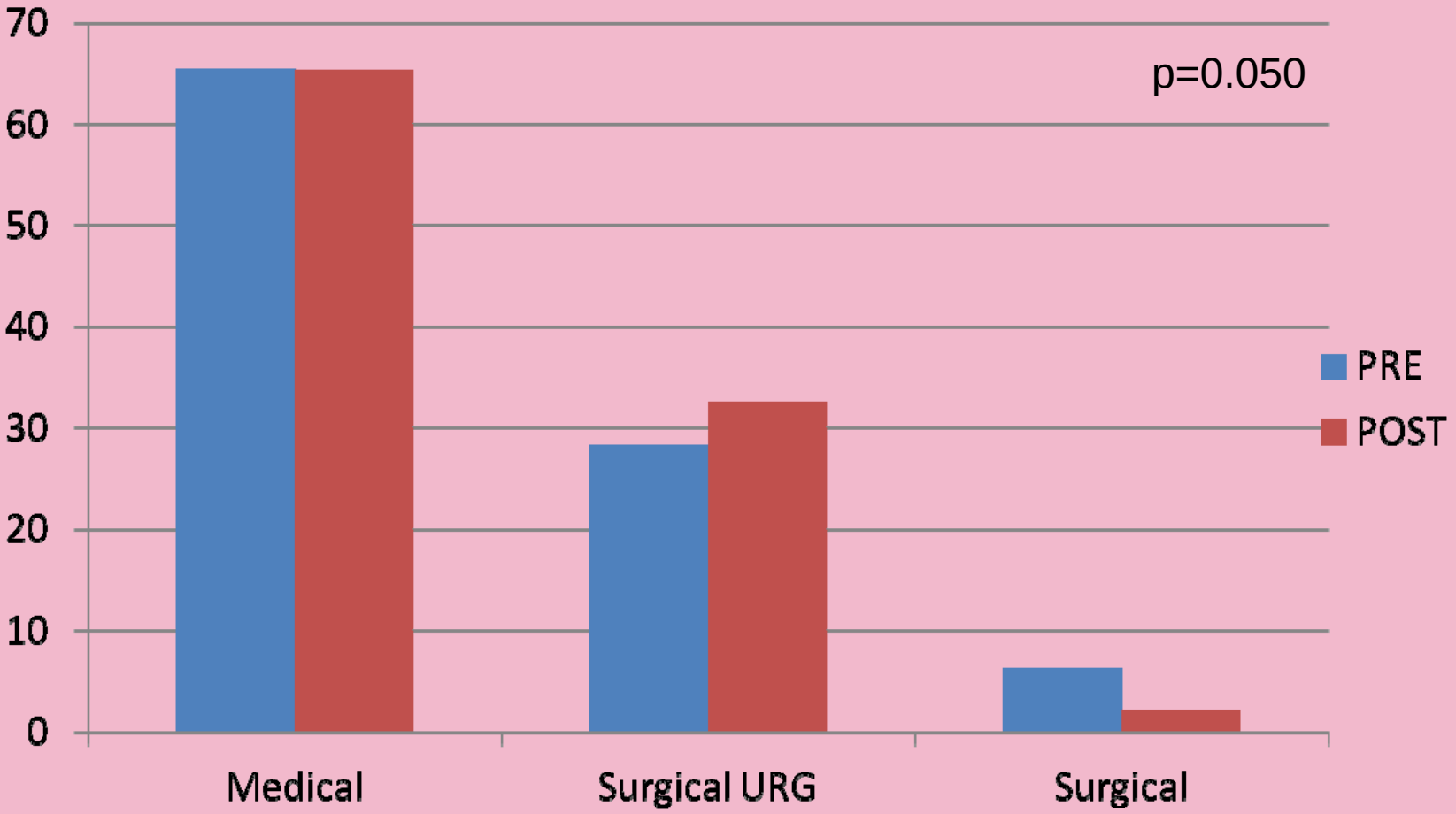
Resultats: Focus Infecció



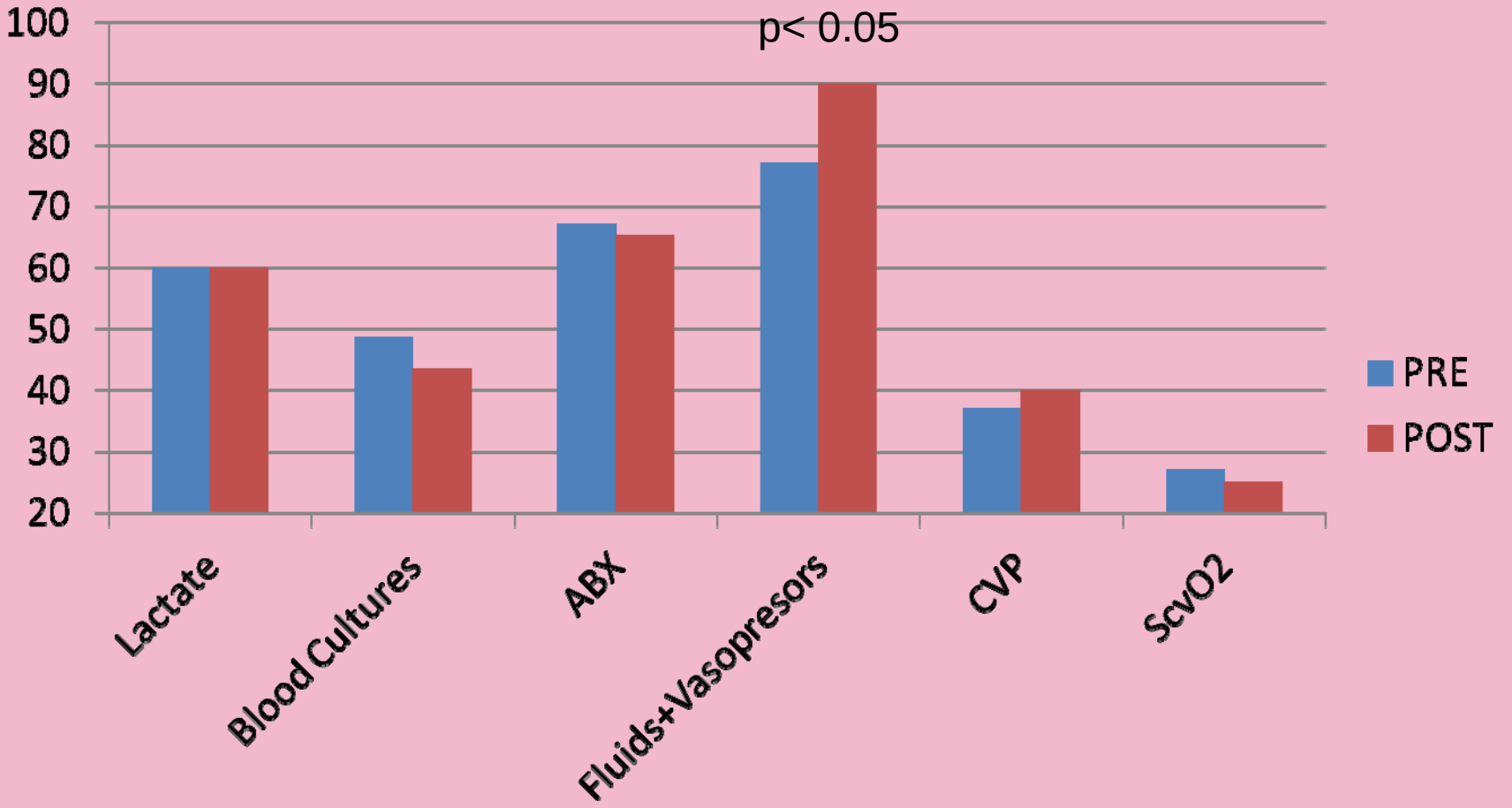
Resultats: Origen sepsis



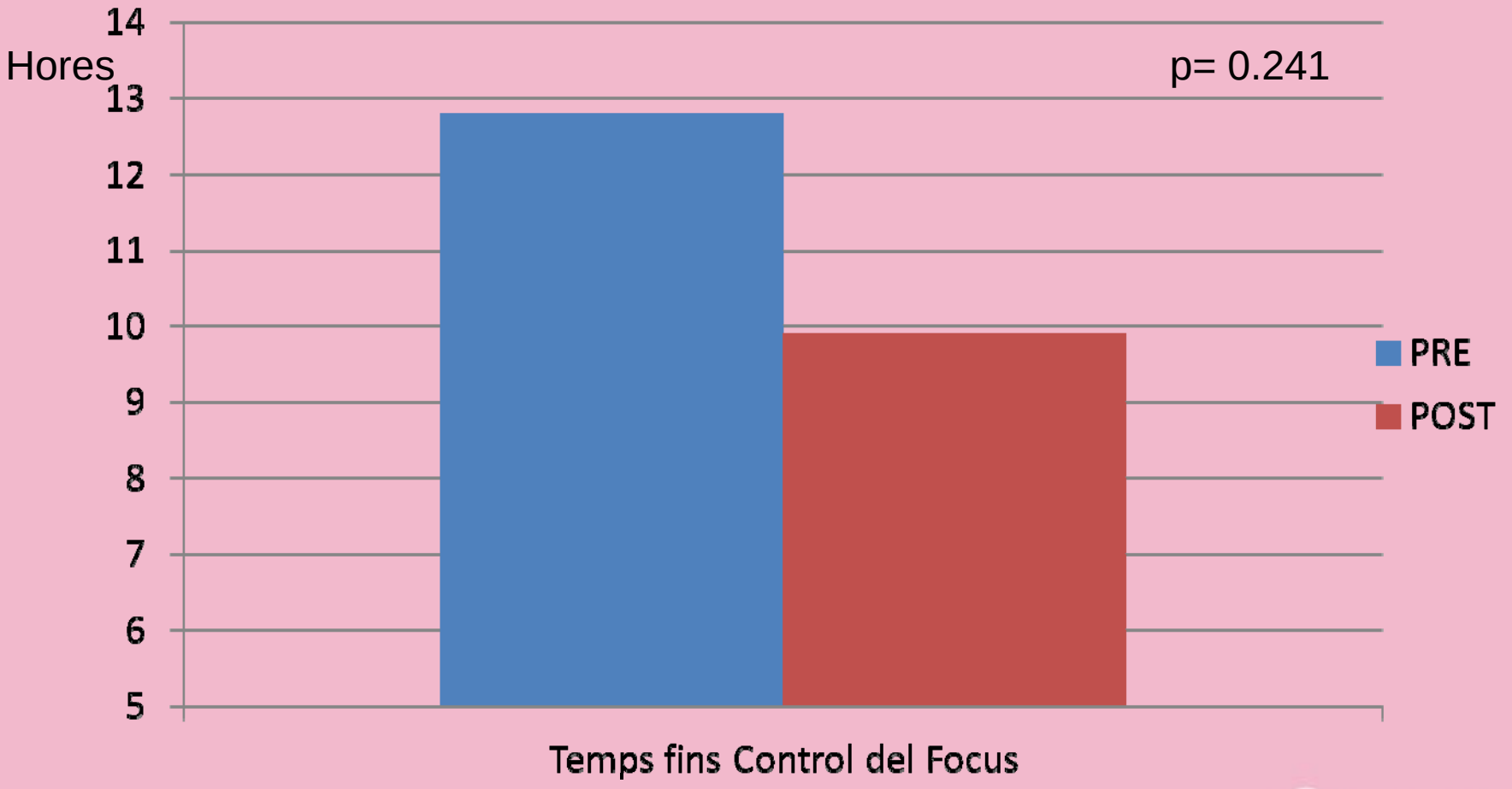
Resultat: Tipus de Patologia



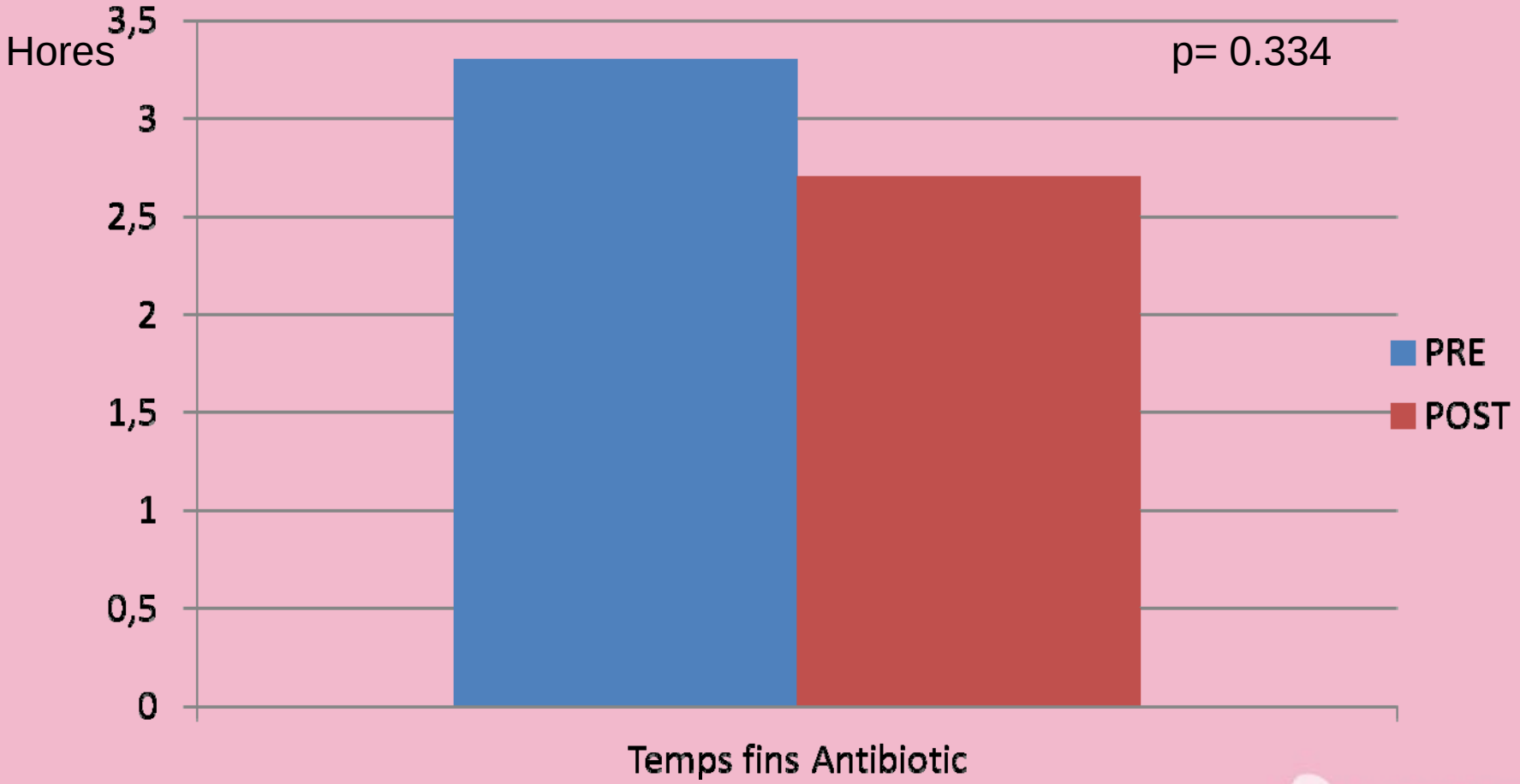
Results: Quality indicators



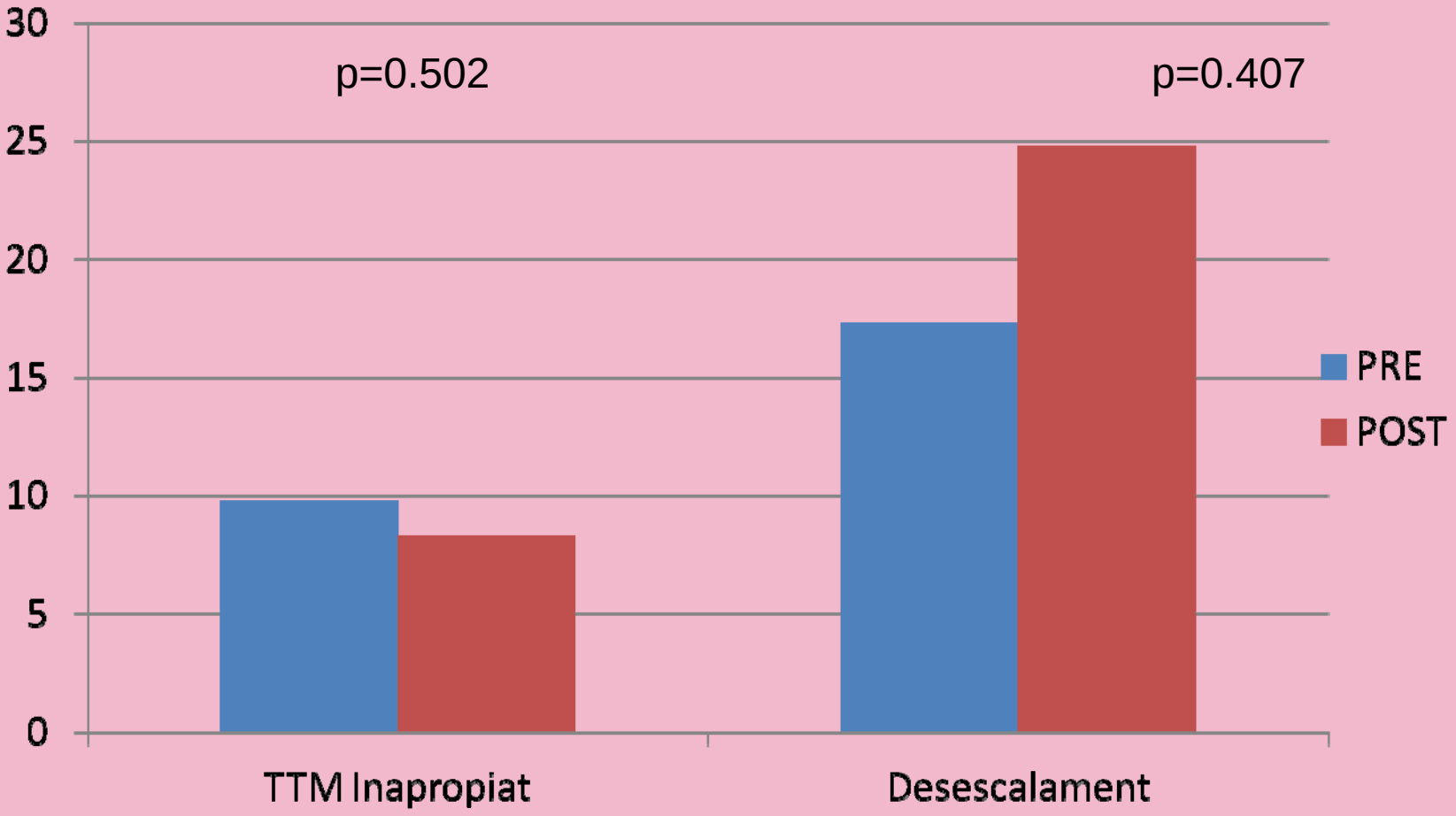
Resultats: Control del Focus



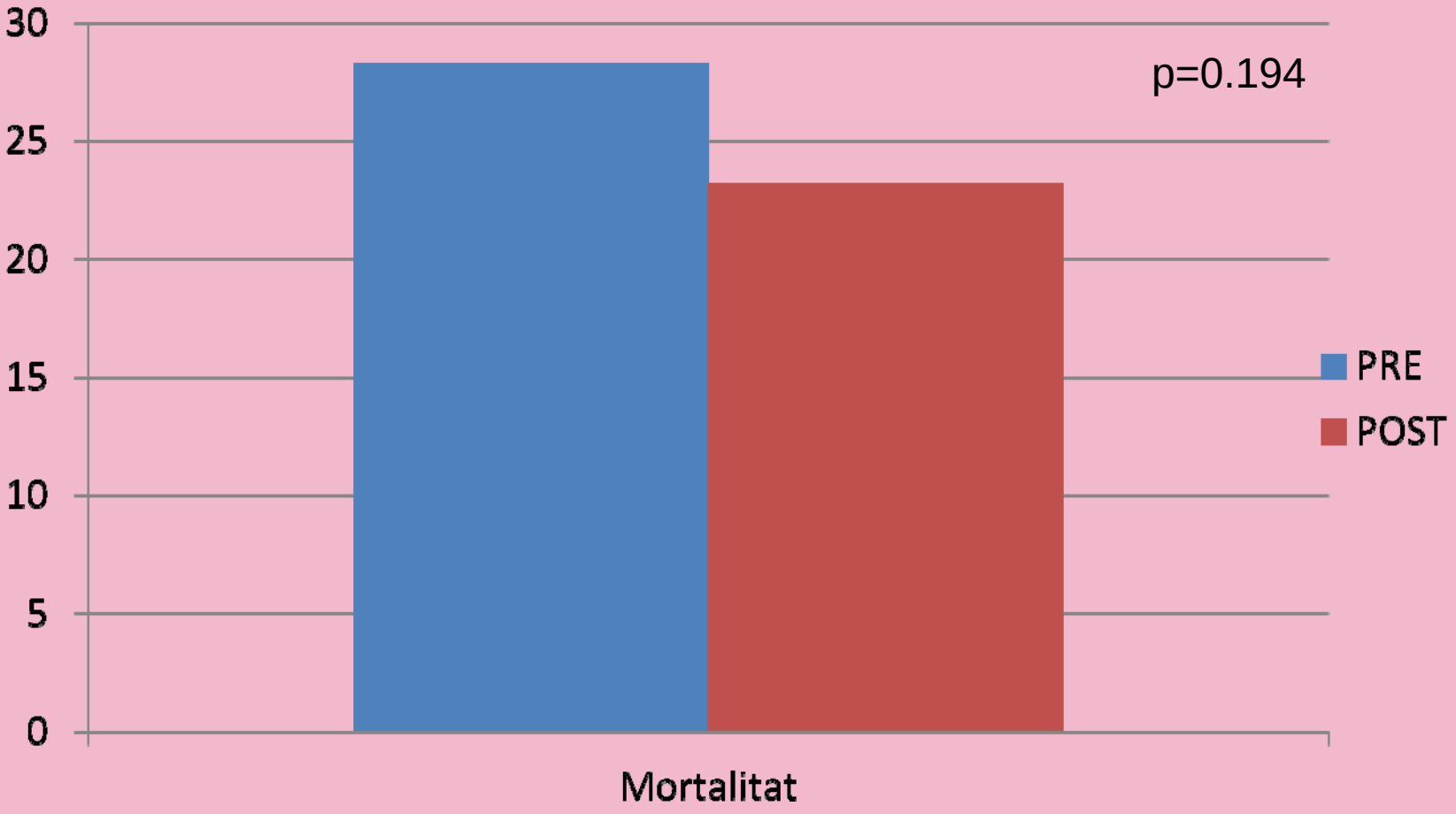
Resultats: Antibiòtic



Resultat: Antibiotics



Resultat: Mortalitat



Conclusió

- Malgrat les recents avanços, el tractament de la sepsis segueix sent susceptible de millora quan es realitzen intervencions amb potencia suficient.
- Aquestes millores en el tractament es poden traslladar en millores en la supervivència.

Agraïments

- Investigadors catalans Edusepsis.
- Unitat de Recerca Clínica del hospital de Sabadell
- Institut Carlos III.
- Astra-Zeneca pel suport logístic durant trobades d'investigadors.