

# Projecte Edusepsis

## 34 Reunió de la SOCMIC

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*ciberes*



Mútua Terrassa



UNIVERSITAT DE BARCELONA



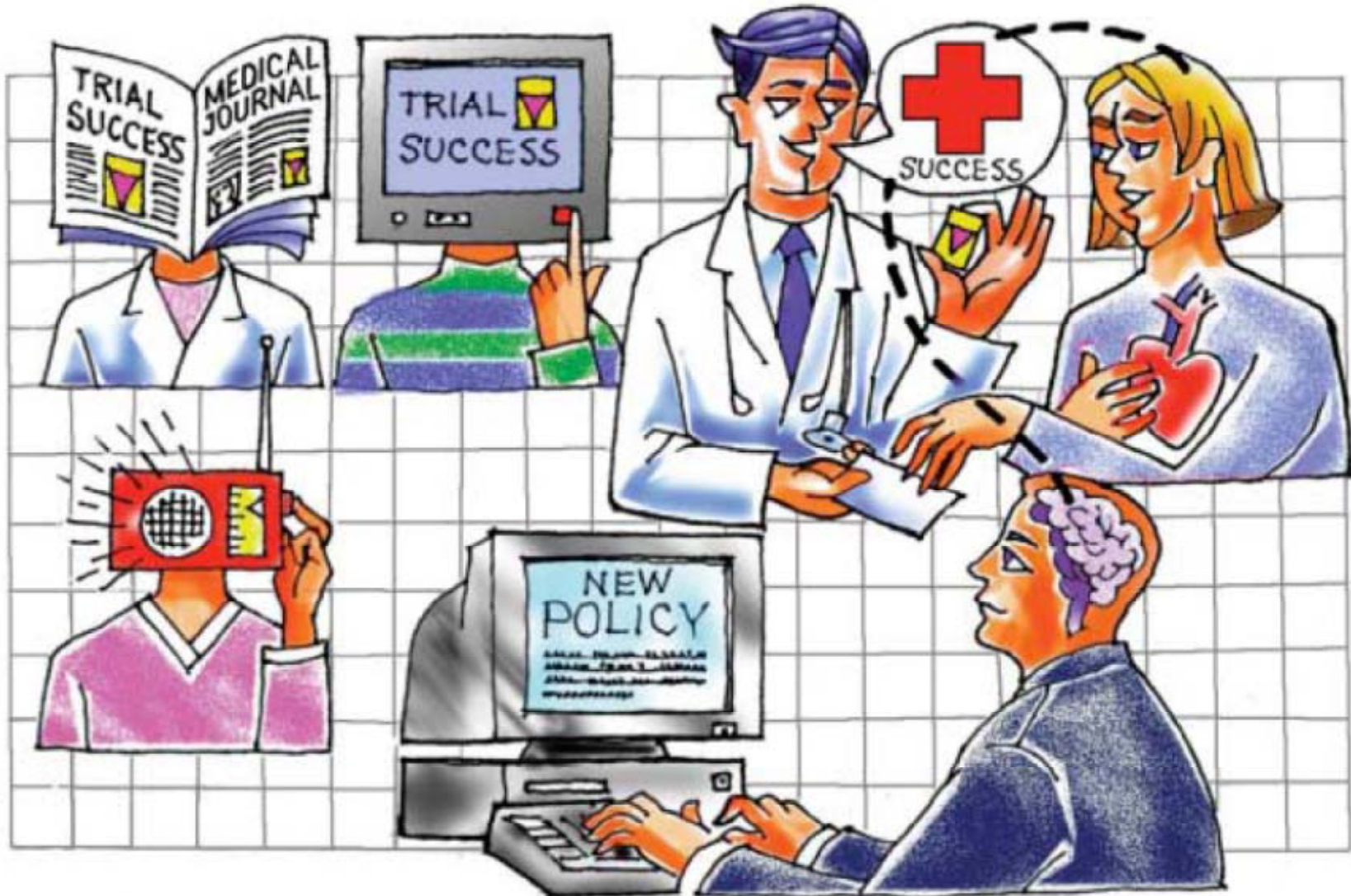
EDUSEPSIS



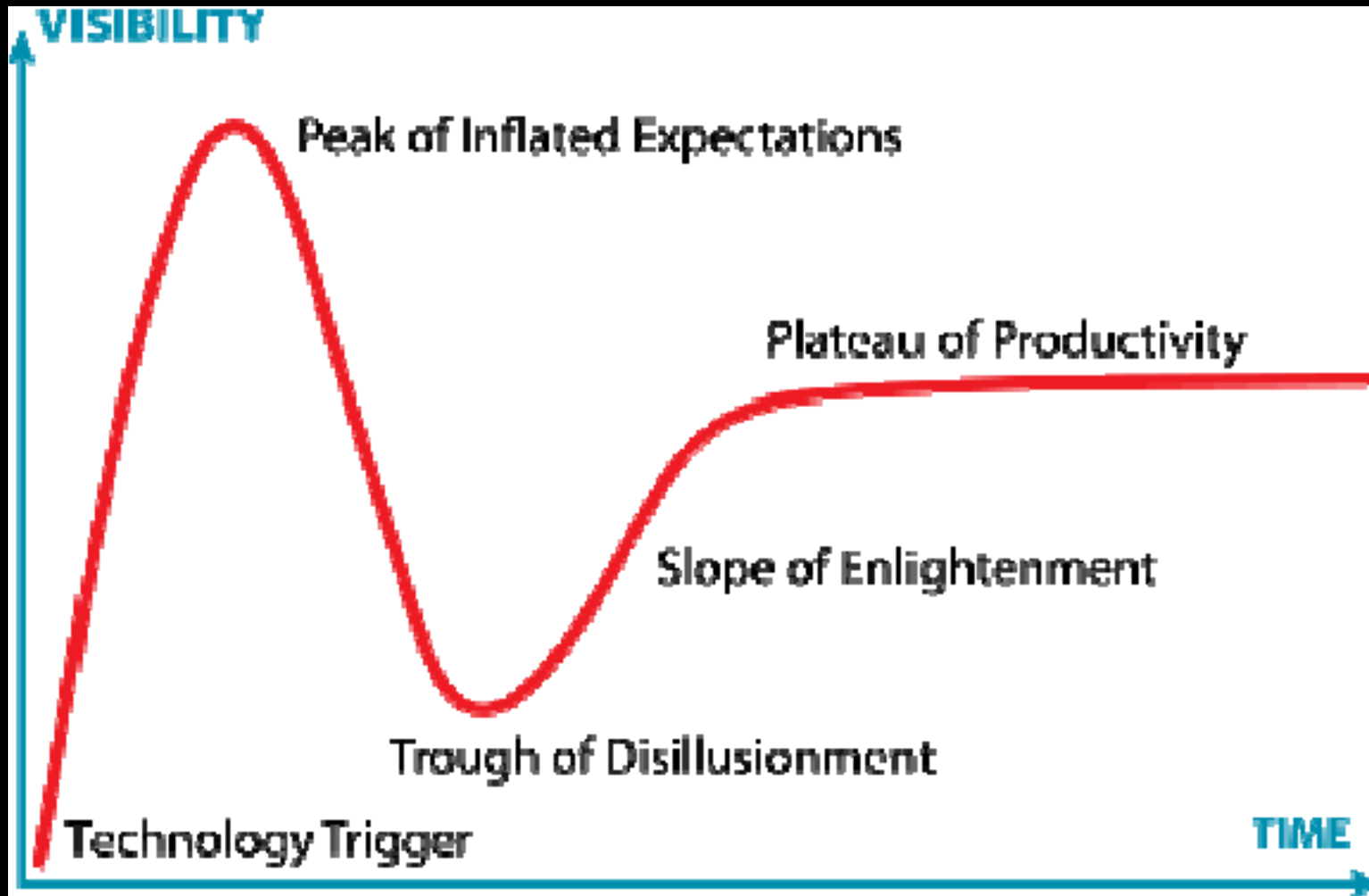
EDUSEPSIS es una organización independiente de profesionales que atienden al paciente crítico, tanto adulto como pediátrico, cuyo objetivo es reducir la mortalidad de la sepsis grave y el shock séptico mediante la evaluación de la eficacia y eficiencia de los tratamientos y la transferencia del conocimiento científico.

- Intervenciones de Transferencia del Conocimiento en Sepsis.
  - Adultos
  - Pediatría
- Evaluaciones de la efectividad de los tratamientos de la sepsis.
  - Nacional
  - Internacional: SSC
- Evaluaciones de costes y Coste-Efectividad.

# Transferencia del Conocimiento



# Knowledge Transfer: Hype cycle



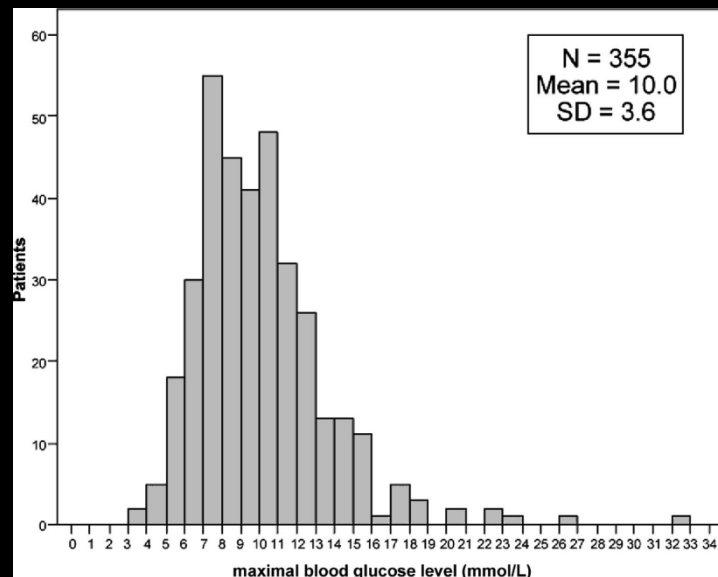
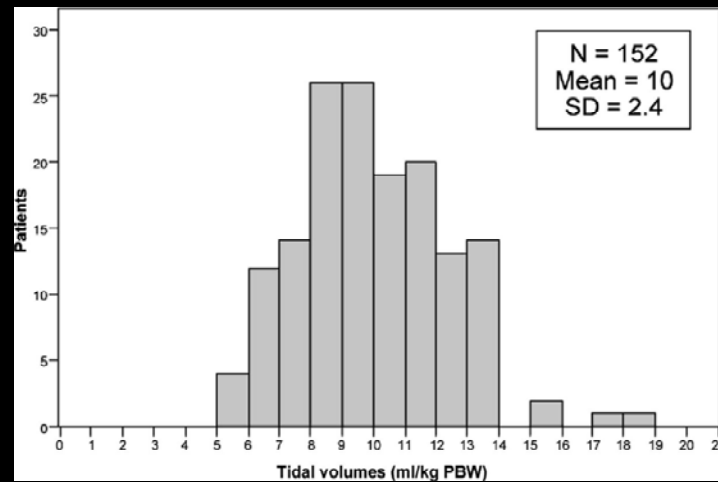
# Knowledge Transfer in Critical Care

Practice	Potentially Eligible Patients, %	Patients Without Contraindication, %	Patients Receiving Practice, % of Eligible Patients Without Contraindication (95% CI)
Thromboembolism prophylaxis	100	86	95.3 (88.5–98.7)
Antibiotic prophylaxis	51	51	94.1 (83.7–98.8)
Stress ulcer prophylaxis	68	68	89.7 (79.9–95.7)
Enteral nutrition	100	58	72.4 (59.1–83.3)
Insulin infusion	17	17	58.8 (32.9–81.5)
Low tidal volume ventilation	13	13	53.8 (25.1–80.8)
Perioperative $\beta$ -blockers	22	15	40.0 (16.3–67.7)
Steroids for septic shock	10	10	20 (2.5–55.6)
Specialty mattress	17	17	17.6 (3.8–43.4)
Interruption of sedation	68	48	8.3 (2.3–20.0)

# Practice and perception—A nationwide survey of therapy habits in sepsis\*

Crit Care Med 2008; 36:2719–2725

Frank M. Brunkhorst, MD; Christoph Engel, MD; Max Ragaller, MD; Tobias Welte, MD; Rolf Rossaint, MD; Herwig Gerlach, MD; Konstantin Mayer, MD; Stefan John, MD; Frank Stuber, MD; Norbert Weiler, MD; Michael Oppert, MD; Onnen Moerer, MD; Holger Bogatsch, MD; Konrad Reinhart, MD; Markus Loeffler, MD; Christiane Hartog, MD; for the German Sepsis Competence Network (SepNet)



## Perception

	All (N = 214)	S1 (n = 30)	S2 (n = 67)	S3 (n = 31)	S4 (n = 53)	S5 (n = 33)
Low-tidal volume ventilation						
Yes (%)	79.9	63.3	76.2	80.7	83.1	97.0
Not answered (%)	2.8	3.3	1.5	0.0	7.5	0.0
Glycemic control						
Yes (%)	65.9	63.3	59.7	71.0	66.1	75.8
Not answered (%)	0.5	0.0	0.0	0.0	1.9	0.0
Low-dose hydrocortisone						
Yes (%)	67.7	63.3	58.2	64.6	71.7	87.9
Not answered (%)	0.5	0.0	0.0	0.0	1.9	0.0
Activated protein C						
Yes (%)	1.4	0.0	0.0	6.5	1.9	0.0
Not answered (%)	1.4	0.0	1.5	0.0	1.9	3.0
Low-dose dopamine						
No (%)	79.0	46.7	73.2	80.6	92.5	97.0
Not answered (%)	0.5	0.0	0.0	0.0	1.9	0.0
Antithrombin						
No (%)	42.5	36.7	39.3	61.3	28.3	57.6
Not answered (%)	0.9	0.0	1.5	0.0	1.9	0.0

# Performance Improvement Interventions

PRE-INTERVENTION PROCESS-OF-CARE MEASURES

STRUCTURE AND  
ORGANIZATIONAL  
STRATEGIES

EDUCATIONAL  
STRATEGIES

IMPROVE KNOWLEDGE  
CHANGE BEHAVIOUR

POST-INTERVENTION PROCESS-OF-CARE MEASURES

IMPROVE OUTCOME





## 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)  $\geq$  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  $\geq$  8 mm Hg.
  - b. Achieve central venous oxygen saturation (ScvO<sub>2</sub>) of  $\geq$  70%.\*

### SEPSIS MANAGEMENT BUNDLE

#### 24H

1. Administer low-dose steroids\* for septic shock in accordance with a standardized ICU policy.
2. Administer drotrecogin alfa (activated) in accordance with a standardized ICU policy.
3. Maintain glucose control  $\geq$  lower limit of normal, but < 150 mg/dl (8.3 mmol/L).
4. Maintain inspiratory plateau pressures < 30 cm H<sub>2</sub>O for mechanically ventilated patients.

# Multifaceted Interventions

Intervention	Effect
Interventions incorporating educational outreach	Modest
Educational material + Educational meetings	Small-Modest
Educational material + Audit and Feedback	Modest
Educational material + Audit and Feedback + Educational meetings	Small-Modest
Educational material + Educational meetings + organizational interventions	Small-Modest
Reminders + Patient-directed interventions	Moderate-Large
Reminders have a summative effect with other interventions	

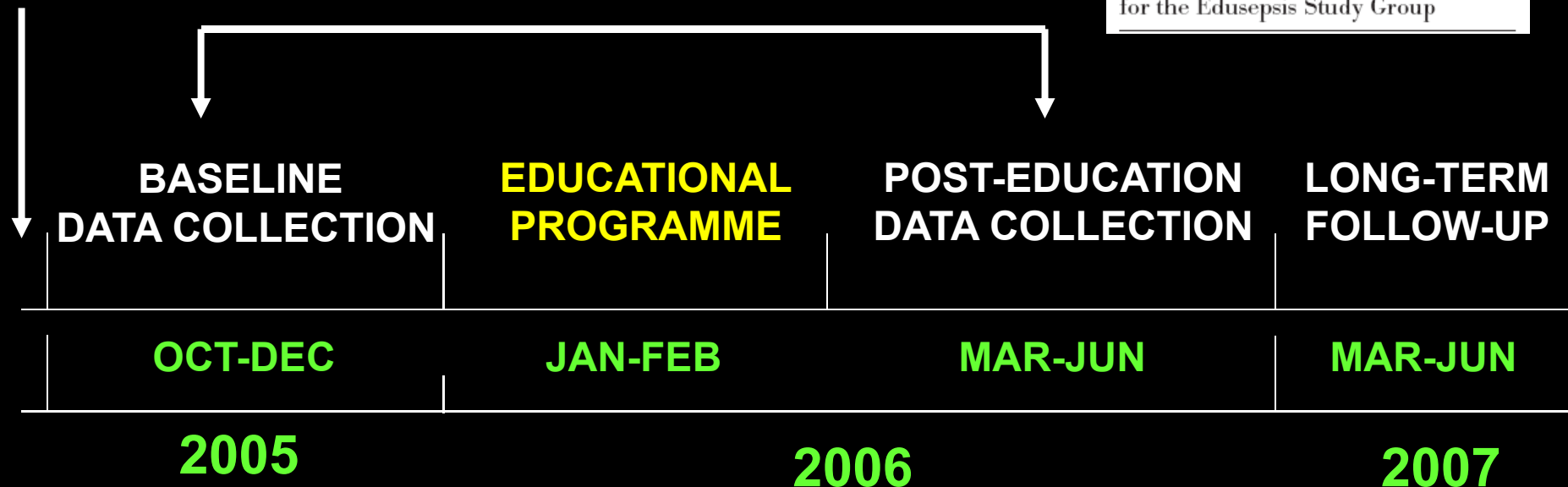
# Improvement in Process of Care and Outcome After a Multicenter Severe Sepsis Educational Program in Spain

JAMA 2008;299(19):2294-2303

## Study Timeline

PERCEPTION

a before-and-after intervention study



Ricard Ferrer, MD

Antonio Artigas, MD, PhD

Mitchell M. Levy, MD, FCCM

Jesús Blanco, MD, PhD

Gumersindo González-Díaz, MD, PhD

José Garnacho-Montero, MD, PhD

Jordi Ibáñez, MD, PhD

Eduardo Palencia, MD, PhD

Manuel Quintana, MD

María Victoria de la Torre-Prados, MD, PhD

for the Edusepsis Study Group

# Multifaceted Intervention

PI

Interview

Hospital Manager

Clinical training



Physicians

Nurses

ICU

ED

Medical Ward

Surgical Ward

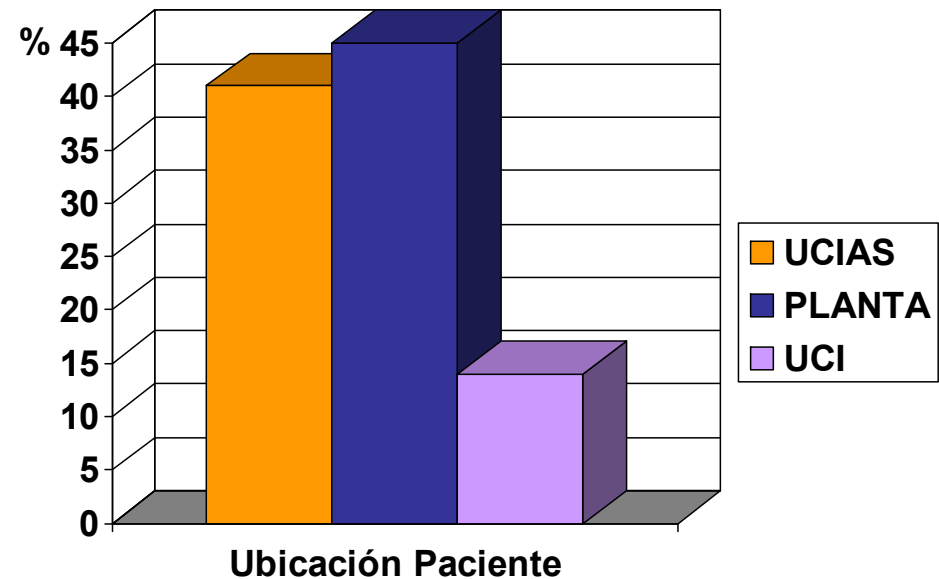
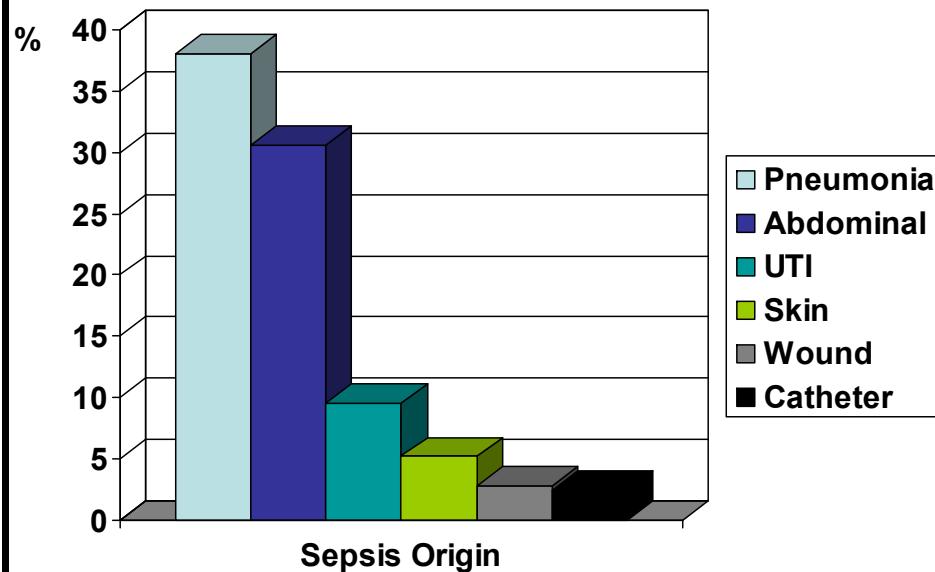
Graphic material:  
distribution and display



# Patient Characteristics

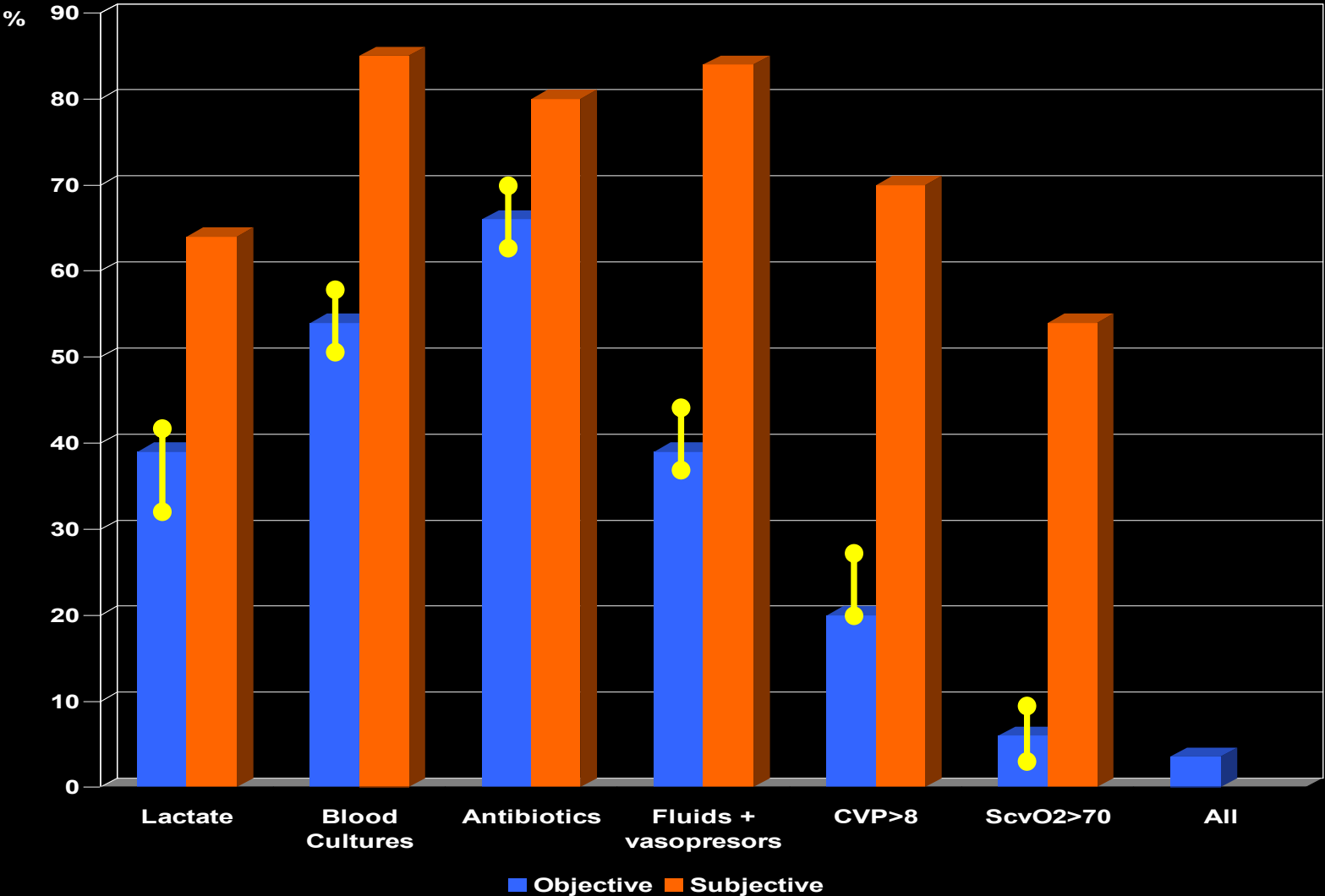
- Age  $62.2 \pm 16.3$  years
- APACHE II score  $21.1 \pm 7.7$
- 60.8% male
- Septic shock 79.6%
- Hospital mortality: 41.2%.

n= 2.796



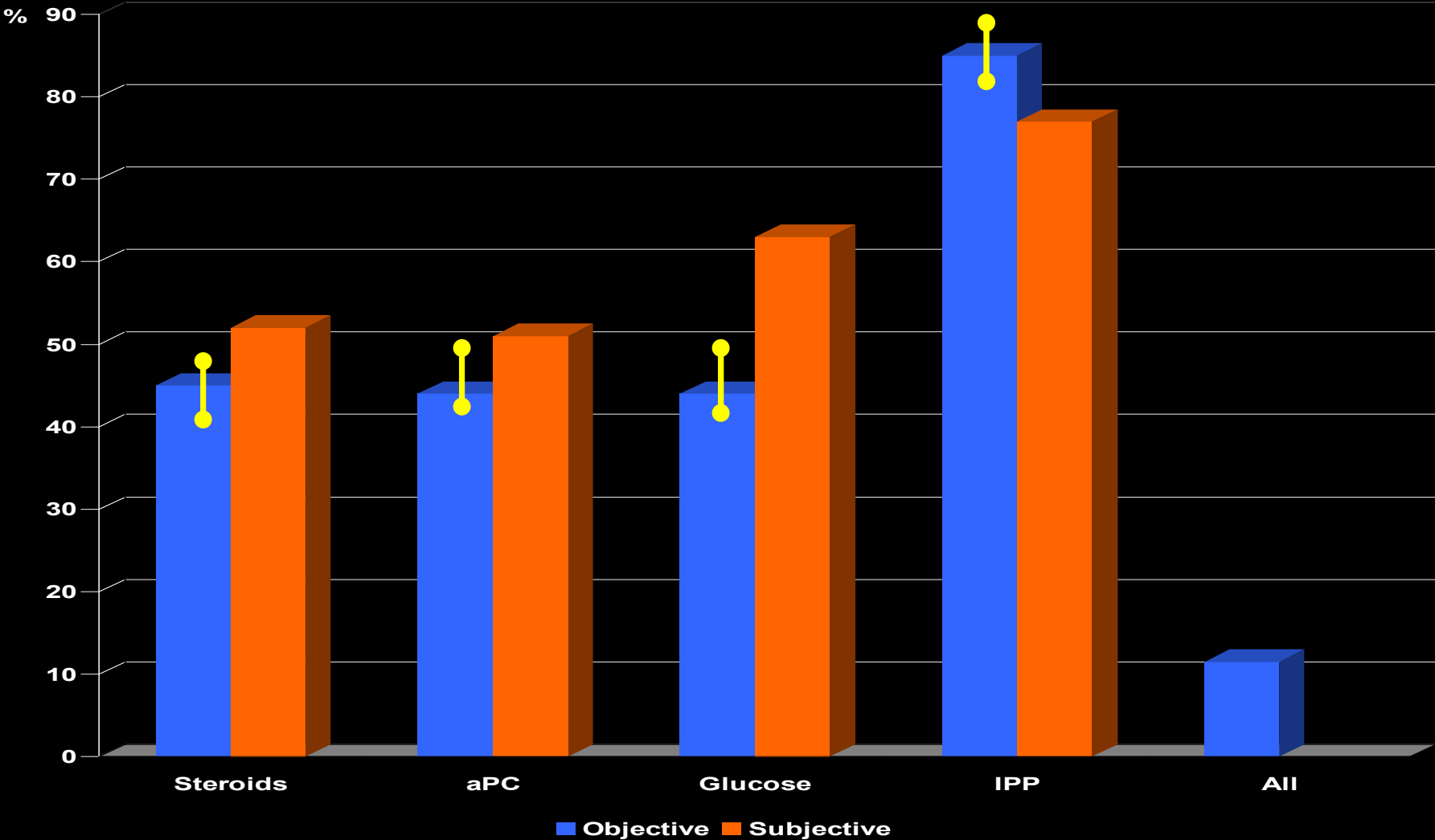
# Sepsis bundles: Audit vs Subjective Perception

RESUSCITATION BUNDLE COMPLIANCE

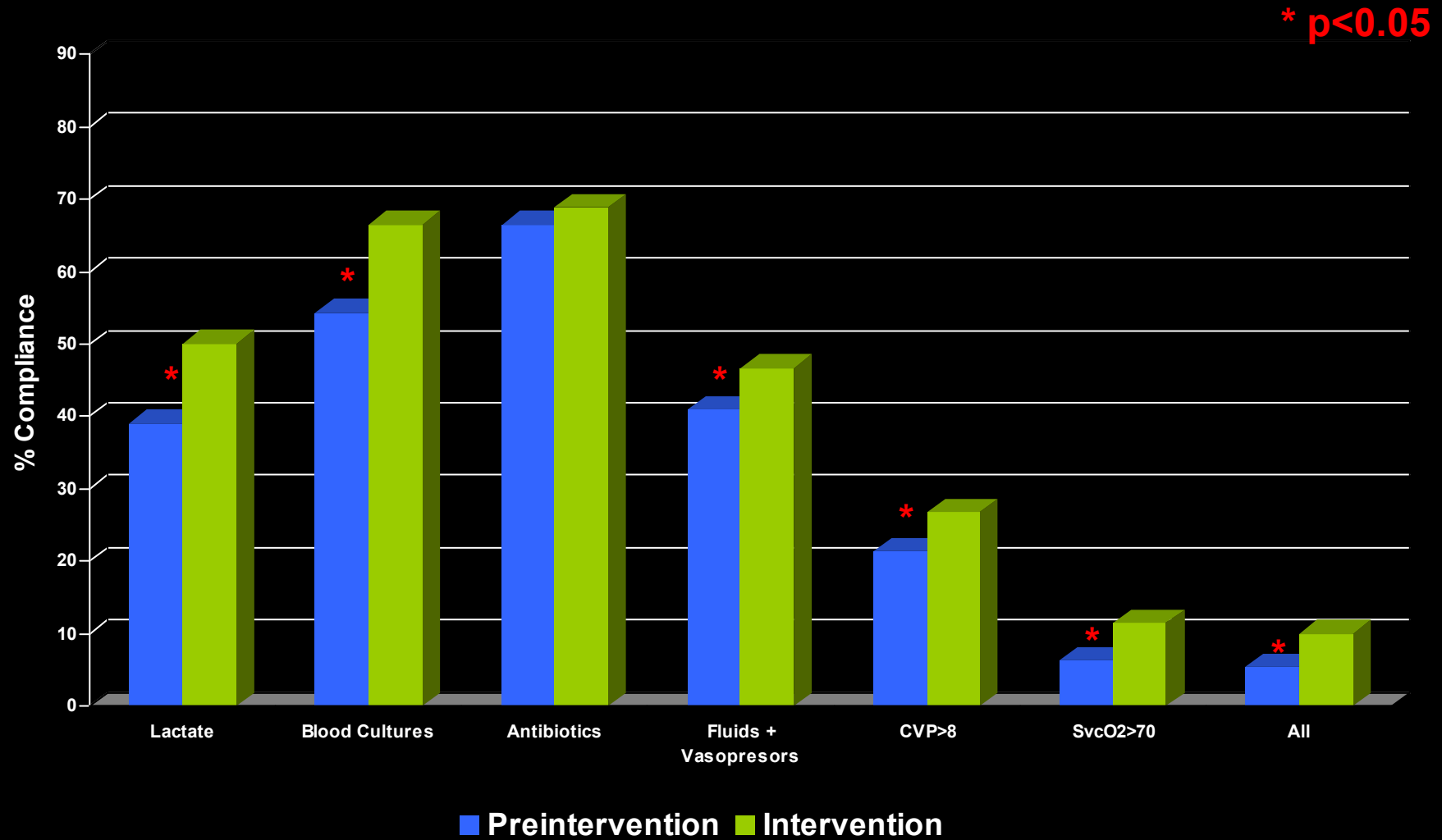


# Sepsis bundles: Audit vs Subjective Perception

MANAGEMENT BUNDLE COMPLIANCE

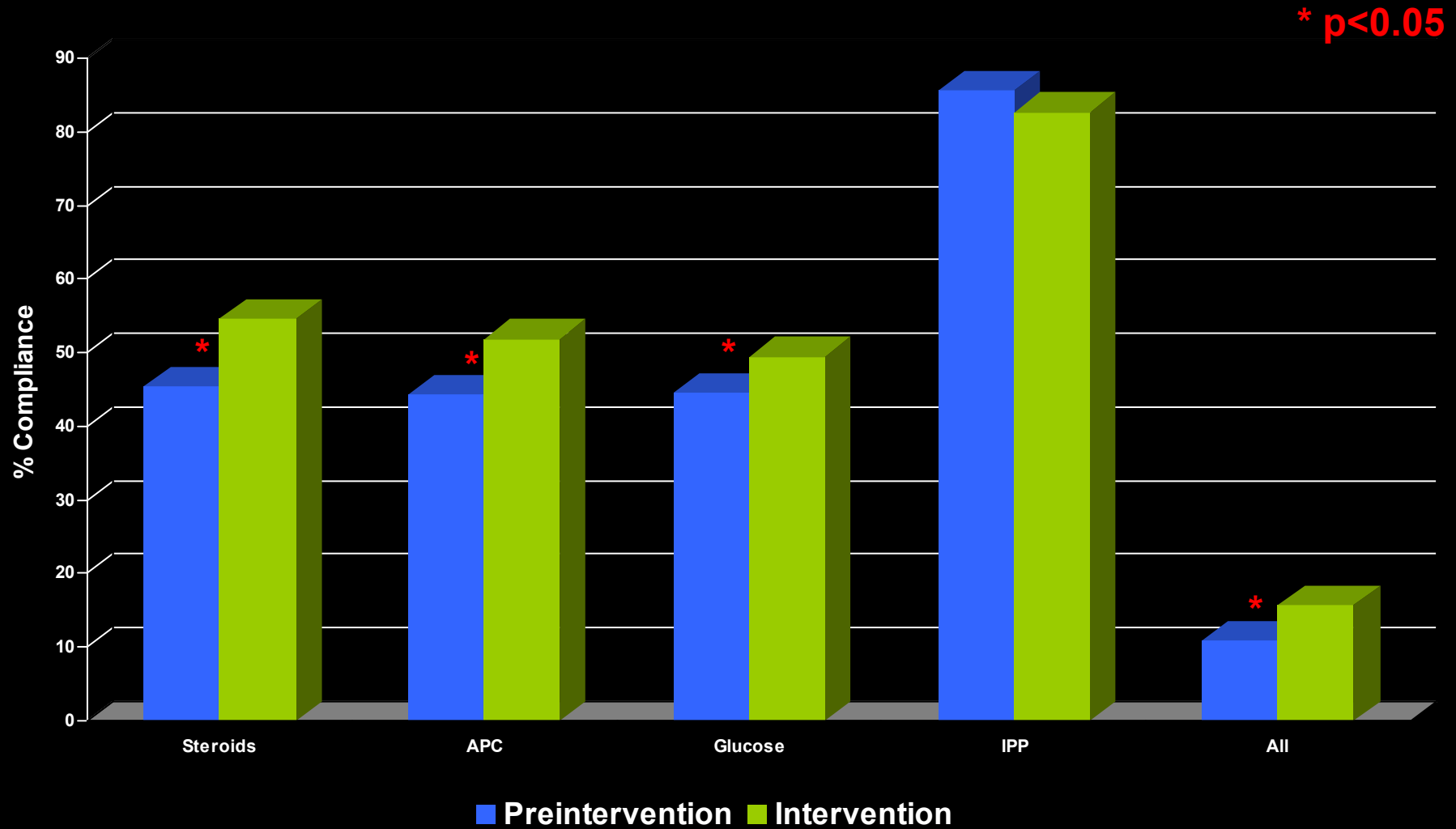


# Resuscitation Bundle (6H)

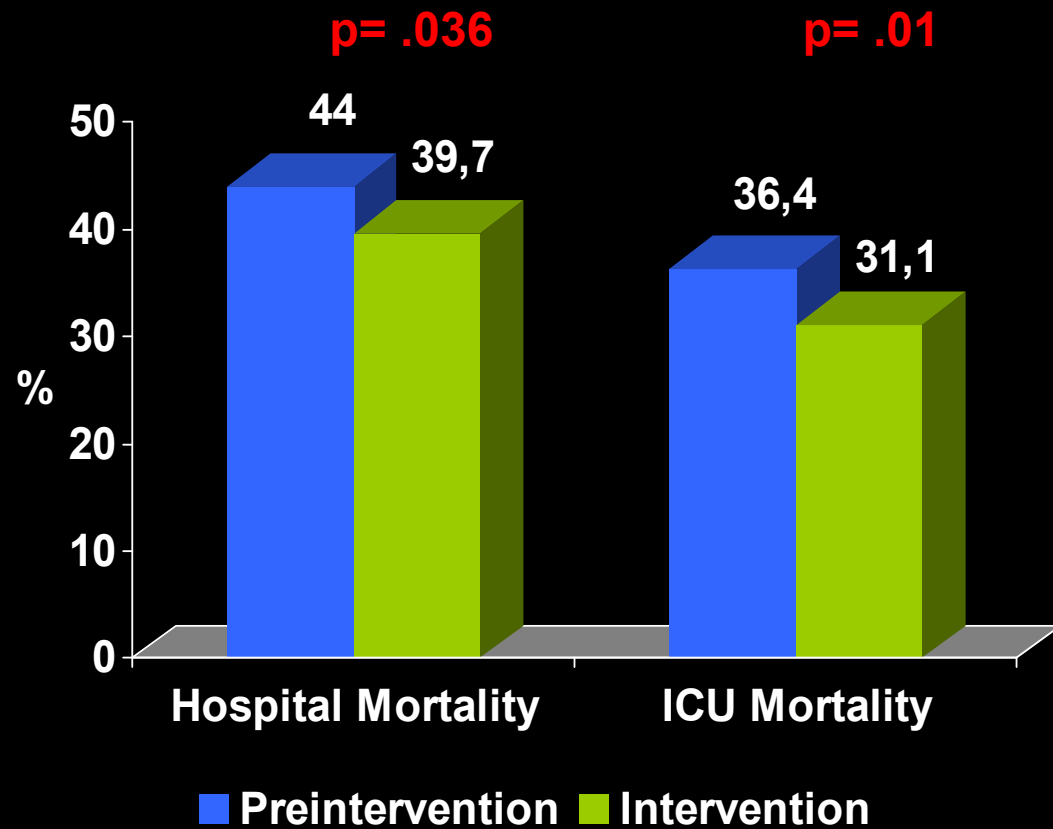




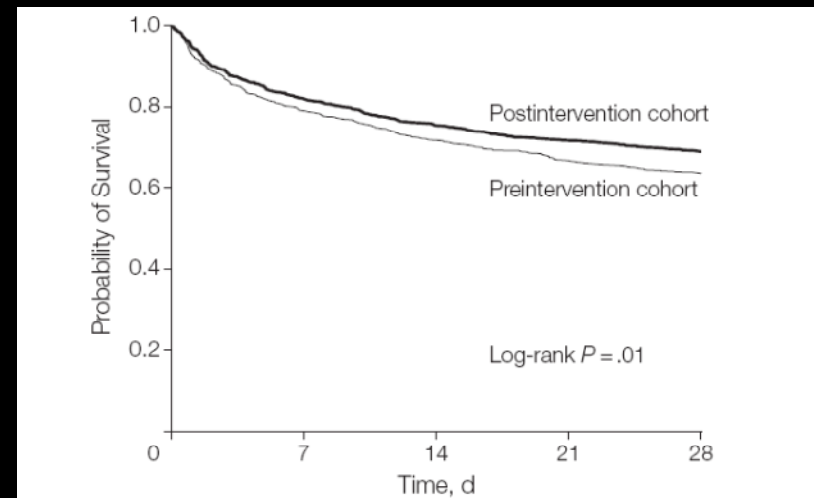
# Management Bundle (24h)



# Educational Program and Mortality

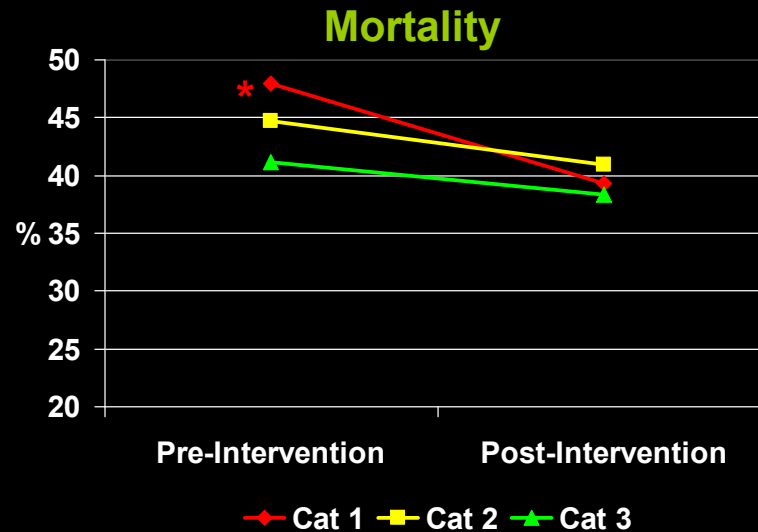
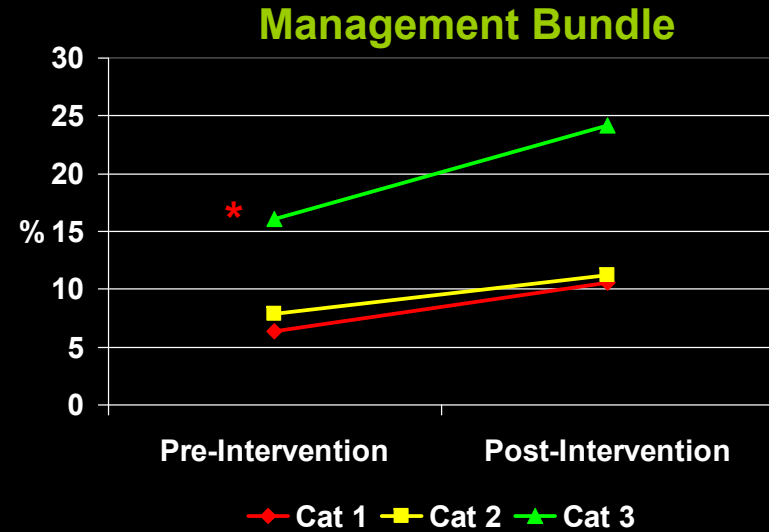
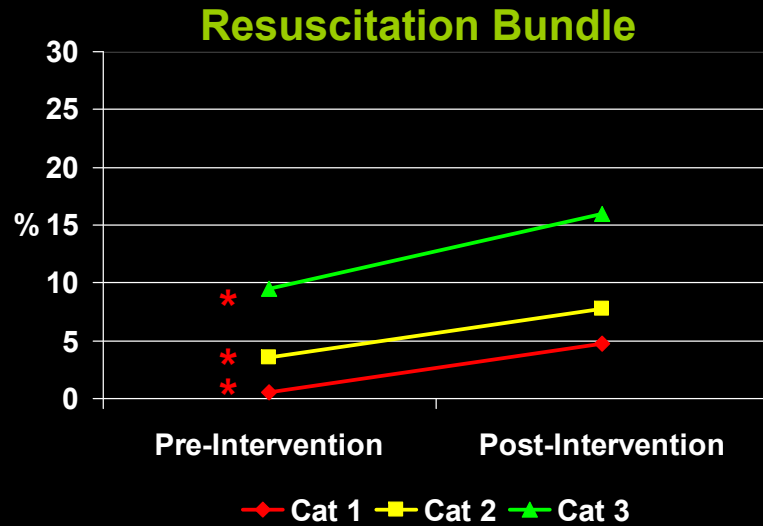


28d Mortality: Kaplan-Meier curve



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

# Impact of Baseline Compliance



\*  $p < 0.05$

Cat 1: < 4 tasks (n= 20)

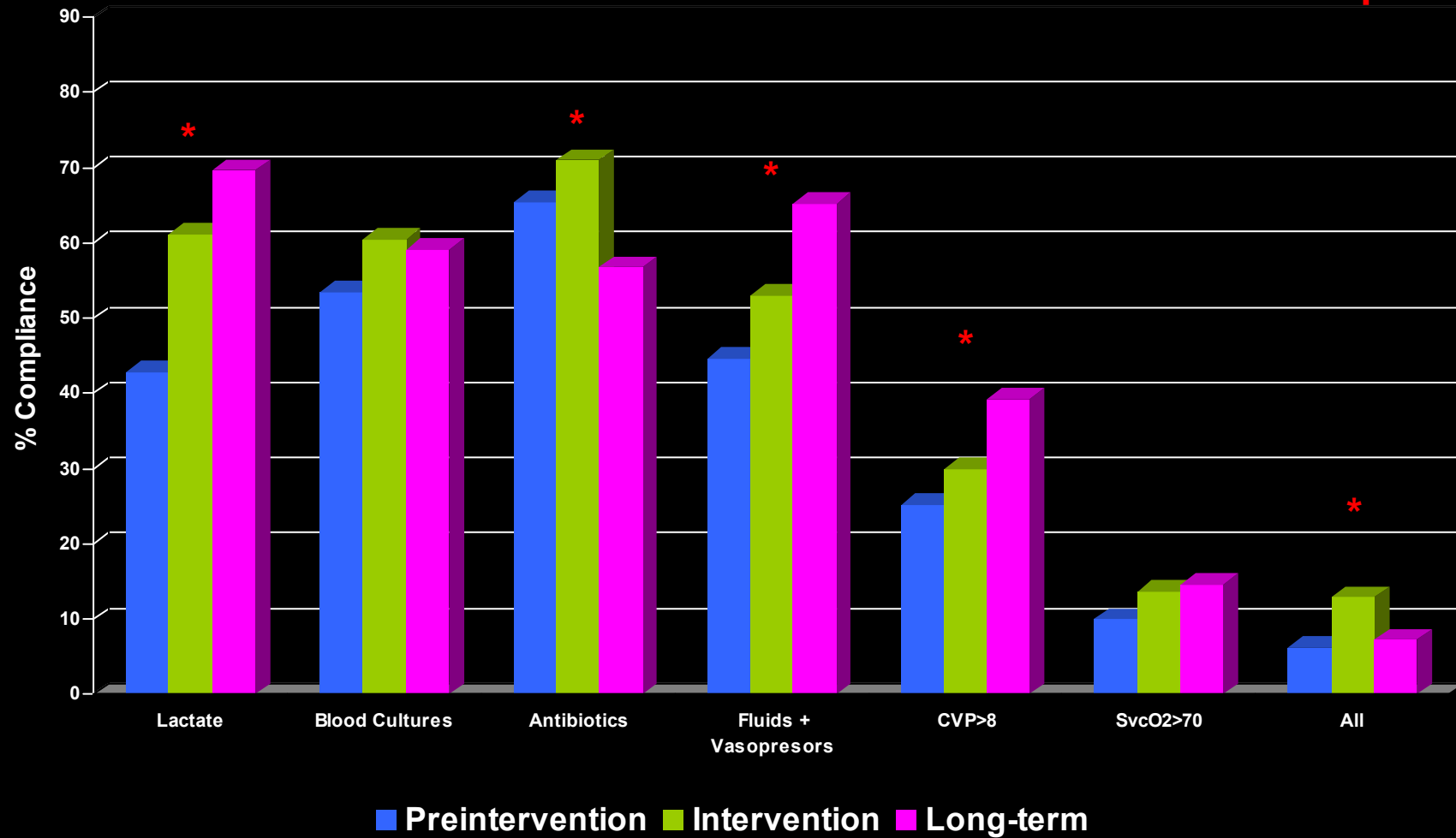
Cat 2: 4-5 tasks (n= 19)

Cat 3: > 5 tasks (n= 20)

# Resuscitation Bundle (6H)

Long-term follow up (23 centers)

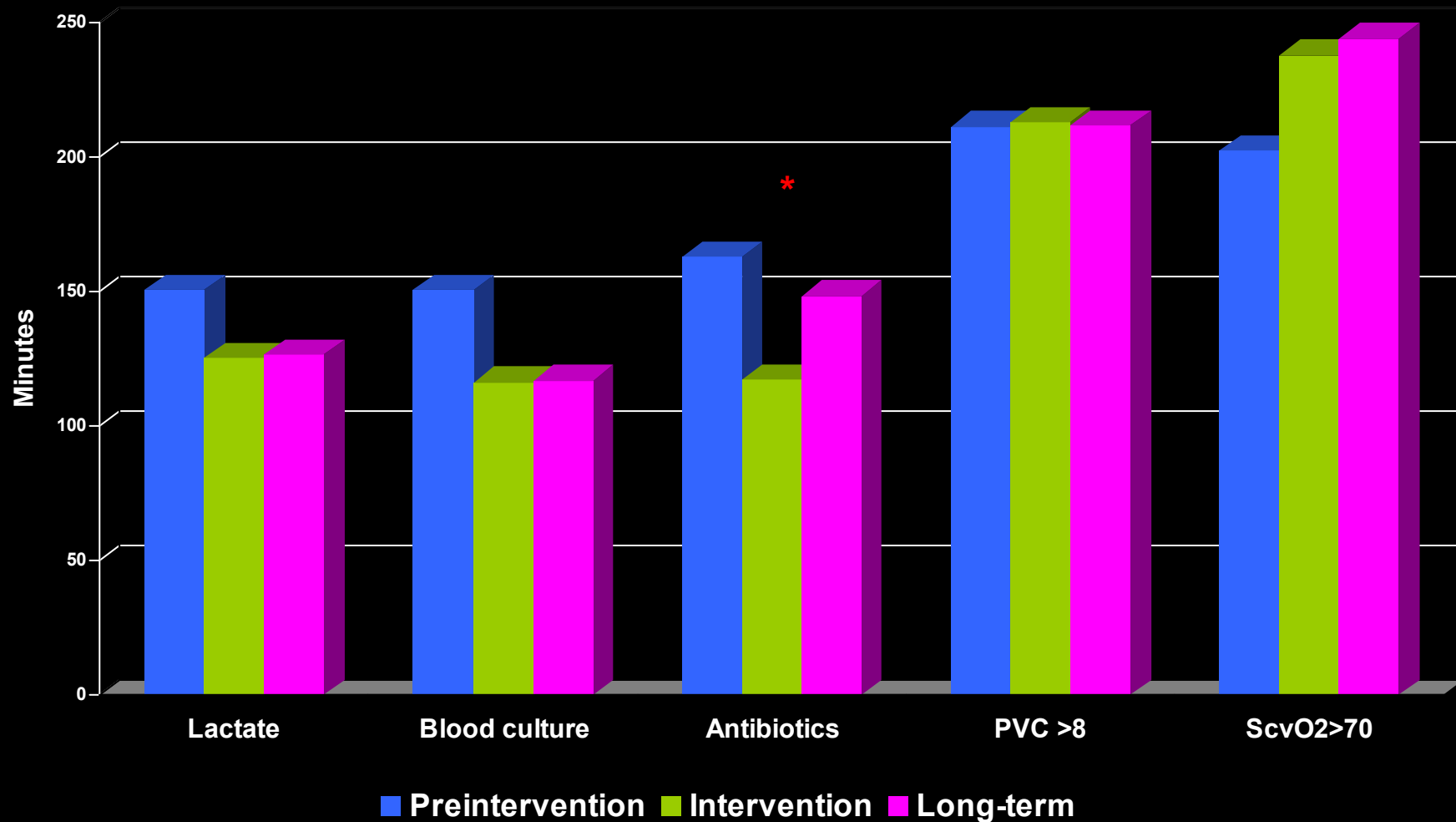
\* p<0.05



# Time to Treatment

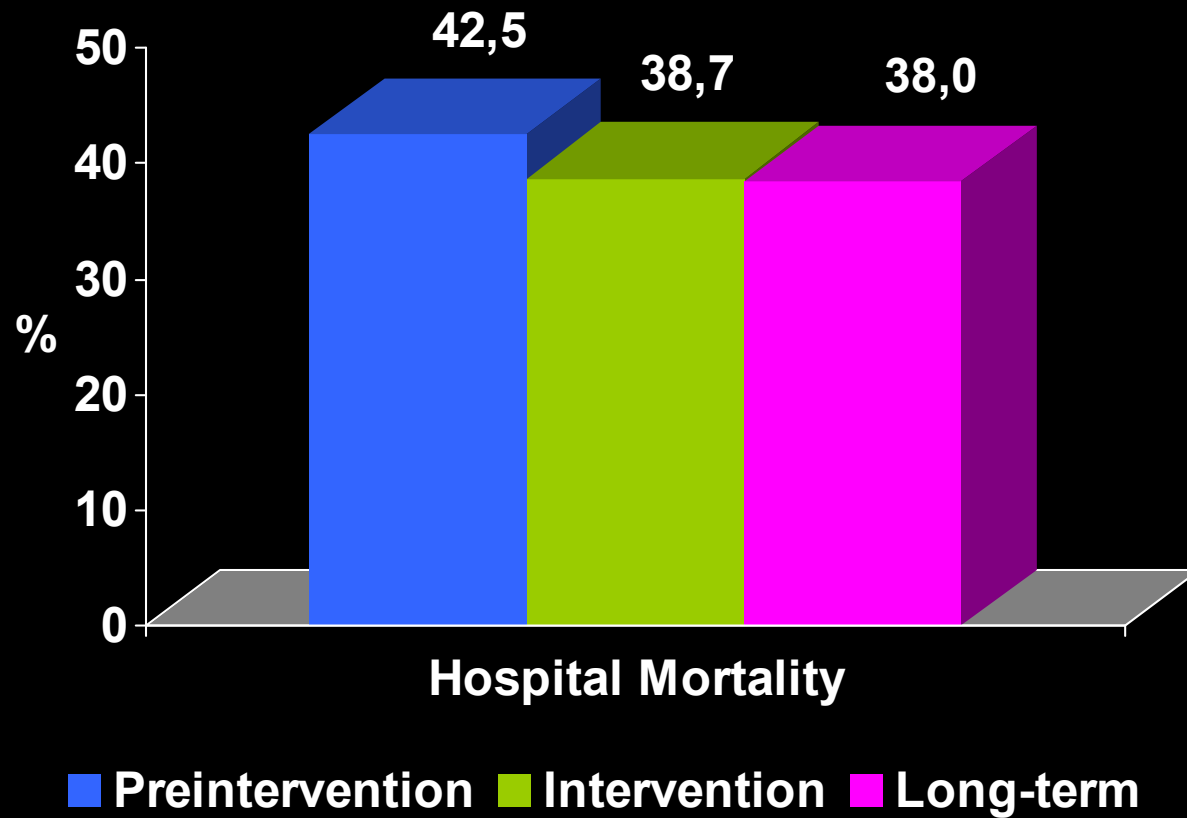
Long-term follow up (23 centers)

\* p<0.05



# Educational Program and Mortality

Long-term follow up (23 centers)



# Continuous Performance Improvement

PRE-INTERVENTION GUIDELINE IMPLEMENTATION



**EDUCATIONAL STRATEGIES**

IMPROVE KWONLEDGE



POST-INTERVENTION GUIDELINE IMPLEMENTATION



**IMPROVE OUTCOME**

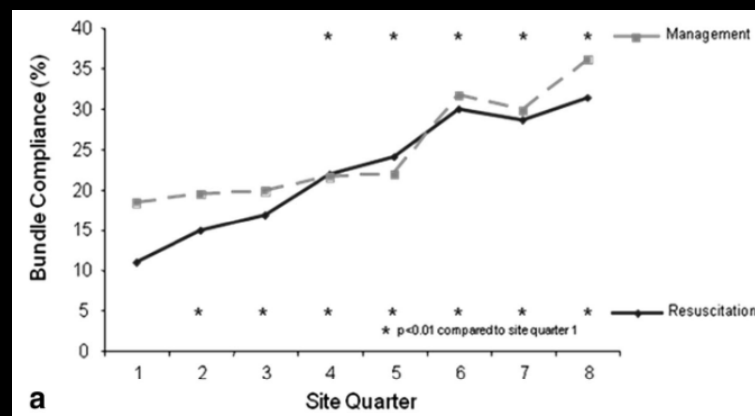


## The Surviving Sepsis Campaign: Results of an international guideline-based performance improvement program targeting severe sepsis

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

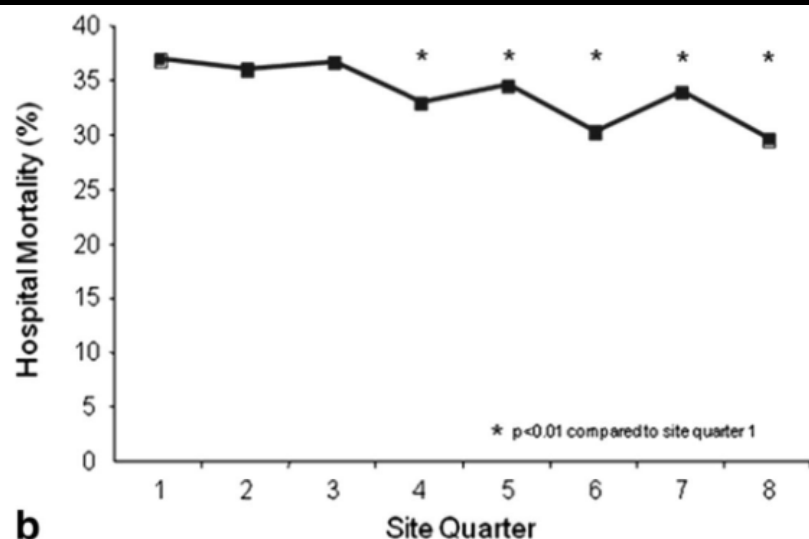
	Initial Quarter Achieved, %	Final Quarter Achieved, % <sup>a</sup>	p Value Compared With Initial
Initial care bundle (first 6 hrs of presentation)			
Measure lactate	61.0	78.7	≤.0001
Blood cultures before antibiotics	64.5	78.3	≤.0001
Broad-spectrum antibiotics	60.4	67.9	.0002
Fluids and vasopressors	59.8	77.0	≤.0001
CVP >8 mm Hg	26.3	38.0	≤.0001
Scvo <sub>2</sub> >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	47.4	53.5	.003
Alfa policy			
Glucose control	51.4	56.8	.0009
Plateau pressure control	80.8	83.8	.24
All management measures	18.4	25.5	≤.0001





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

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**b**

Variable	OR	95% CI	<i>p</i>
Admission source			
Ward compared to ED	1.87	1.73, 2.02	≤.0001
ICU compared to ED	2.25	2.02, 2.51	≤.0001
Pneumonia as source of sepsis compared to other infections	1.37	1.27, 1.48	≤.0001
Organ dysfunction at presentation			
Cardiovascular	1.39	1.26, 1.55	≤.0001
Respiratory	1.23	1.14, 1.34	≤.0001
Hematologic	1.61	1.48, 1.75	≤.0001
Hepatic	1.28	1.14, 1.75	≤.0001
Renal	1.40	1.30, 1.51	≤.0001
Site duration in Campaign			
Per quarter	0.97	0.96, 0.99	.0006

# ABISS Edusepsis Study

## Antibiotic Intervention in Severe Sepsis

# 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.

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

## The effect of mobile phone text-message reminders on Kenyan health workers' adherence to malaria treatment guidelines: a cluster randomised trial

*Lancet* 2011; 378: 795–803

*Dejan Zurovac, Raymond K Sudoj, Willis S Akhwale, Moses Ndiritu, Davidson H Hamer, Alexander K Rowe, Robert W Snow*

	Baseline		Follow-up one		Follow-up two		Effect size (difference of differences)			
	Control	Intervention	Control	Intervention	Control	Intervention	Immediately after end of intervention		6 months after end of intervention	
							% change (95% CI)	p value	% change (95% CI)	p value
<b>Composite performance</b>										
Correctly managed	422/47 (11.1%)	439/90 (20.5%)	358/59 (16.5%)	391/194 (49.6%)	332/58 (17.5%)	327/168 (51.4%)	23.7% (7.6 to 40.0)	0.0040	24.5% (8.1 to 41.0)	0.0034

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:

	<b>Tu Centro</b>	<b>España</b>
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

# Educational Meetings

120 hospitals were invited to participate and received the educational material:

- Poster “La Sepsis Mata”: 360
- Poster “Pilares del tratamiento de la Sepsis”: 360
- Poster “Juego interactivo”: 360
- Triptics “Pilares del tratamiento de la Sepsis”: 6000

## Educational intervention:

- 80 hospitals complete the educational intervention
- 4567 doctors and nurses attend to the meetings and provide a email address and/or mobile phone for remainders.

## PILARES DEL TRATAMIENTO DE LA SEPSIS

### ANTIBIÓTICOS PRECOSES

- 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.

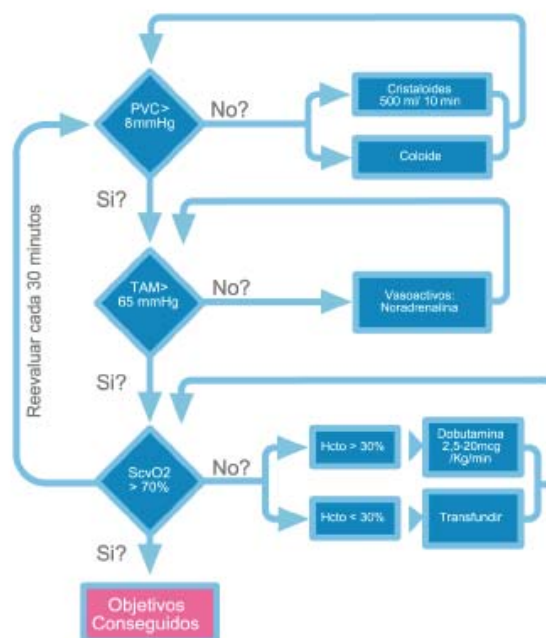
También están disponibles las siguientes pautas:

[www.es.dgai-abx.de](http://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 FLÚIDOS!** 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.



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



**Infection pathway**

Early & Guided Use of Antibiotics related to Resistance Data

Infection pathway

Infection characteristics

Investigations

Antiinfectives

Pathogens

Tools

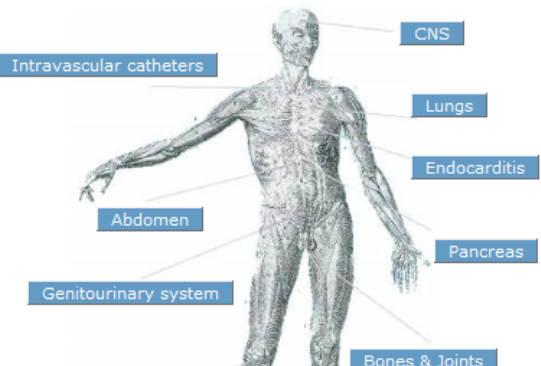
[Main](#) | [Logout](#)

Logged In: Testaccount for EGUARD  
[Start page](#) > - [The SOP - Program](#) > Infection pathway

**Please evaluate the patient's condition:**

Hypothermia $\leq 36$ °C or Hyperthermia $\geq 38$ °C	<input type="checkbox"/>
Tachycardia $\geq 90$ /min	<input type="checkbox"/>
Tachypnoea $\geq 20$ /min or $\text{paCO}_2 \leq 4,3$ kPa [32 mmHg]	<input type="checkbox"/>
Leukocytosis $\geq 12.000/\mu\text{l}$ or Leukopenia $\leq 4000/\mu\text{l}$	<input type="checkbox"/>
Inflammatory markers CRP $> 0,5\text{mg/dl}$ or PCT $> 0,5\text{ng/dl}$ or pathological IL-6	<input type="checkbox"/>
Additional signs of acute organ dysfunction due to infection	>>>
There are signs of circulatory failure due to infection:	>>>
There are additional complicating risk factors:	>>>

**Please now choose the focus of the suspected or confirmed infection, which is believed to be responsible for the changes in the clinical status of the patient:**



**EN SEPSIS,  
TU VELOCIDAD  
ES VIDA  
ACTÚA RÁPIDO**

PRACTICA CÓMO  
TRATAR LA SEPSIS  
EN NUESTRA WEB

[edusepsis.org/formacion](http://edusepsis.org/formacion)

AC SIMULATION.COM

EDUSEPSIS



- En sepsis la administración del antibiótico adecuado es una emergencia. Consulta tu guía 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!.

- 72 hospitals in Spain.
- 2576 patients: PRE 1,325, POST: 1,251
- Age  $64.1 \pm 15.1$  years, 54.1% male.
- CHARLSON  $2.7 \pm 2.2$
- Septic Shock 67.6%, 32.4% severe sepsis.
- Bacteriemia: 33%
- APACHE-II  $22 \pm 8$ .
- SOFA  $9 \pm 3$
- PCT  $25 \pm 35$

# Results: Blood Cultures

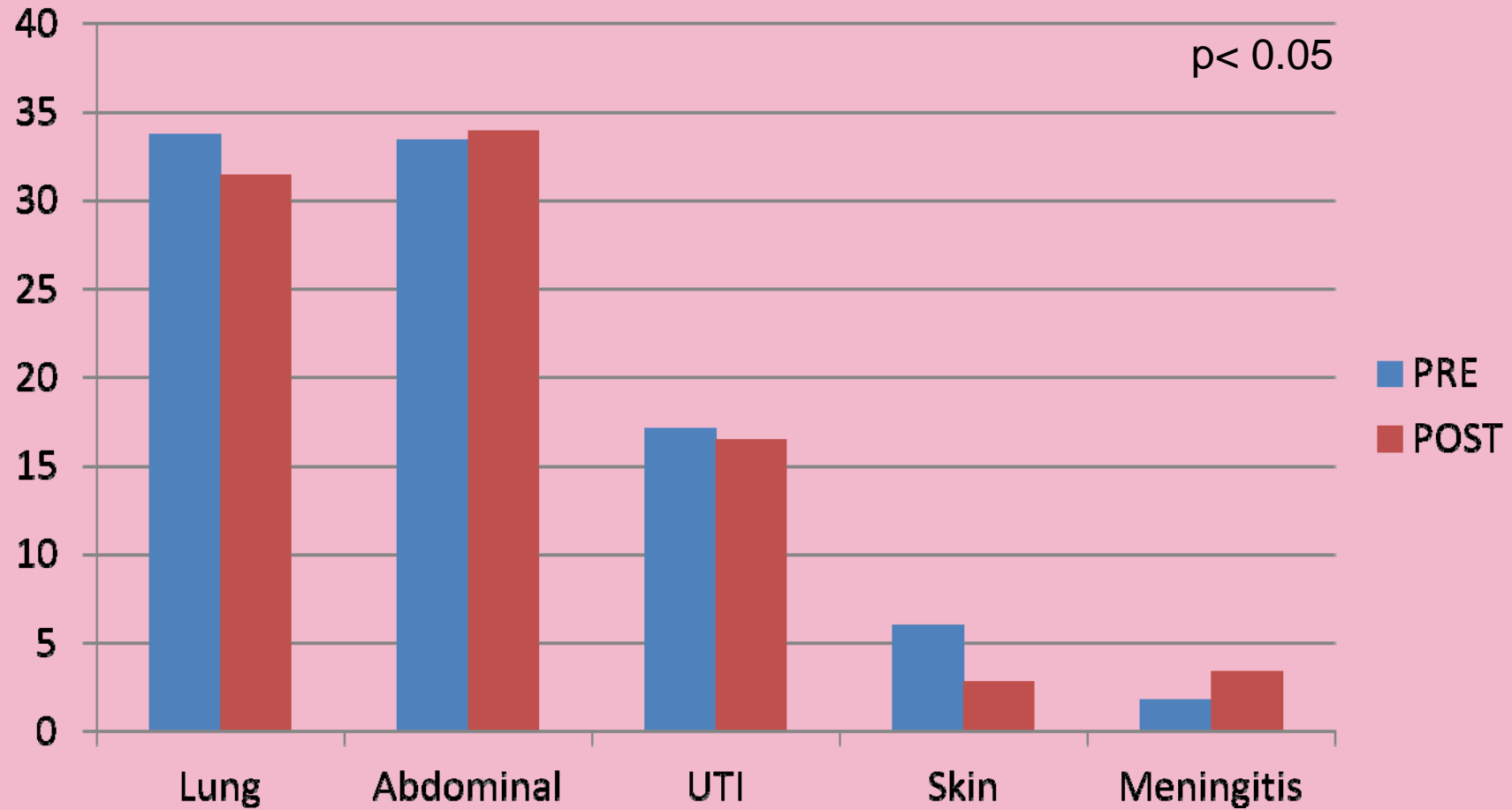
Microorganism	n
Escherichia coli	299
Staphylococcus aureus MS and MR	78
Streptococcus pneumoniae	75
Staphylococcus CN	60
Klebsiella spp	53
Pseudomonas aeruginosa	42
Enterococcus spp	35
Streptococcus pyogenes	28
Enterobacter spp	25
Streptococcus other	22
Candida spp	21
Multiple microorganisms	19
Proteus mirabilis	16
Bacterioides fragilis	14
Acinetobacter baumannii	11
Clostridium	6
Neisseria meningitidis	5
Salmonella	5
Listeria monocytogenes	4
Serratia marcescens	4

**28,3% de los pacientes precisan una técnica de control del foco**

Técnica	n	Técnica	n
Colectomía parcial/total	201	Apendicectomía	17
Colecistectomía	96	Pancreatectomía parcial	13
Resección intestino delgado	70	Sutura úlcera	17
Desbridamiento piel-partes blandas	77	Cirugía hepática	9
Drenaje abdominal percutáneo	48	Nefrectomía	7
Nefrostomía	41	Esofaguectomía	4
Cateterismo ureteral	37	Desbridamiento cuello/mediastino	6
Drenaje vía biliar	33	Histerectomía	3
Drenaje torácico	24	Cirugía craneal	2
Desbridamiento de absceso	19	Cirugía de pulmón y bronquio	1
Cirugía gástrica	19	Cirugía valvular cardiaca	1

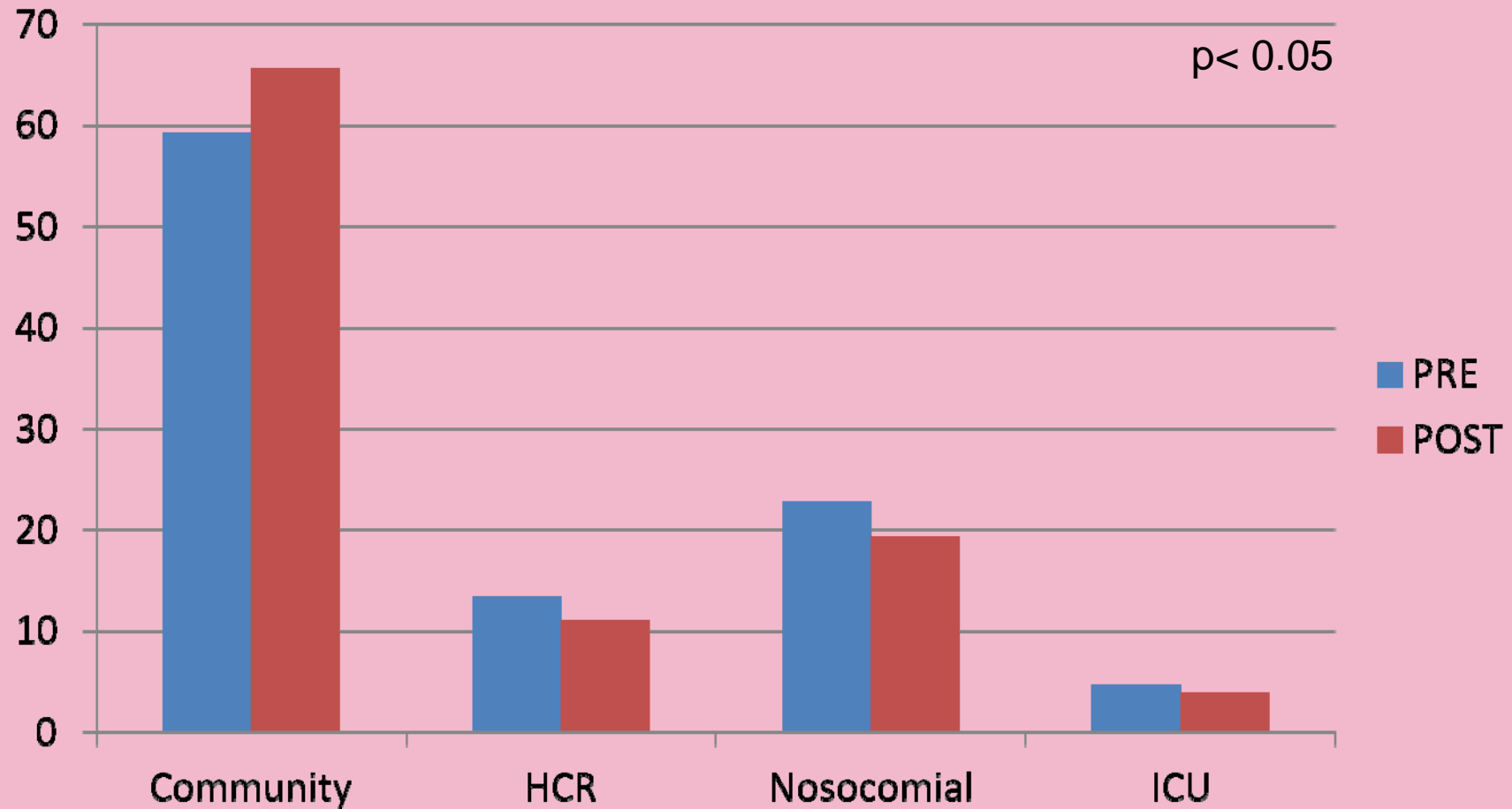
	PRE	POST	P value
Age	64.3±15.3	63.9±15.0	0.480
Charlson	2.7±2.3	2.7±2.3	0.308
Leukocytes	14.4±11.5	15.9±11.0	0.290
CRP	27.1±24.8	25.0±24.5	0.055
PCT	25.1±35.2	25.6±34.5	0.804
Lactate (mmol/L)	3.5±3.1	3.6±2.8	0.247
APACHE II	22.6±8.1	21.4±8.0	<0.001
Number OF	3.0±1.4	3.0±1.4	0.897
SOFA	8.7±3.5	8.5±3.4	0.073

# Results: Source Infection

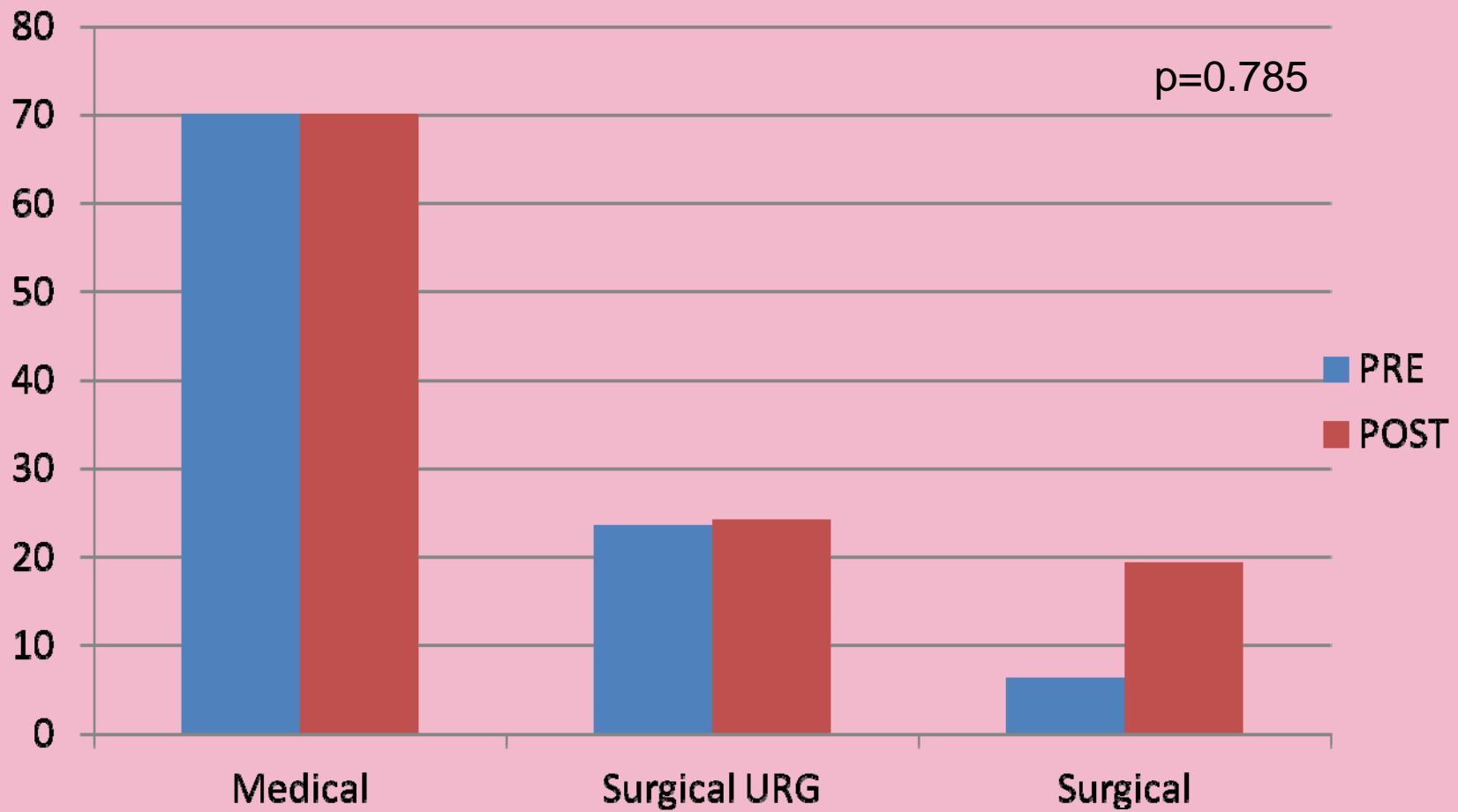




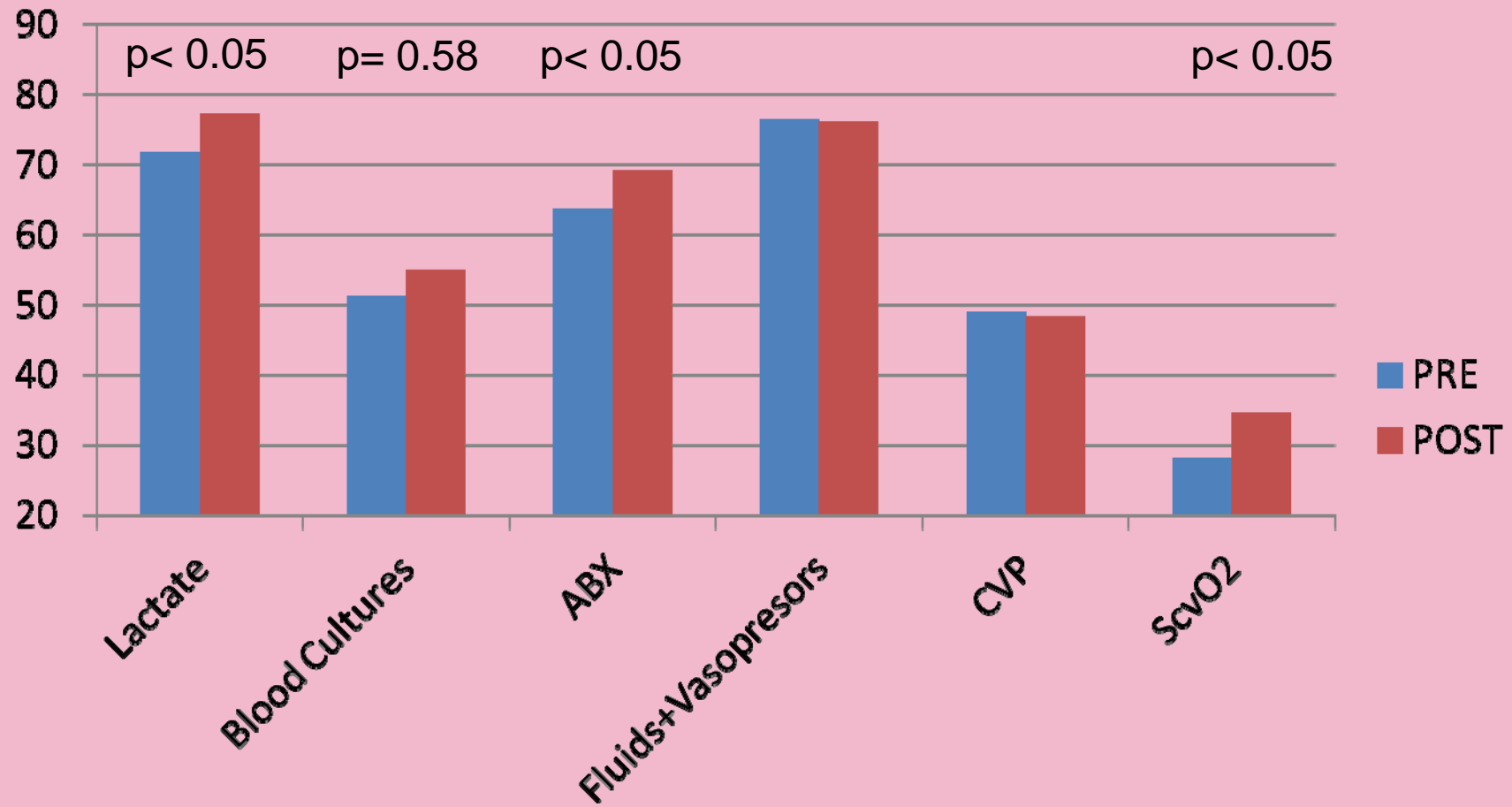
# Results: Acquisition



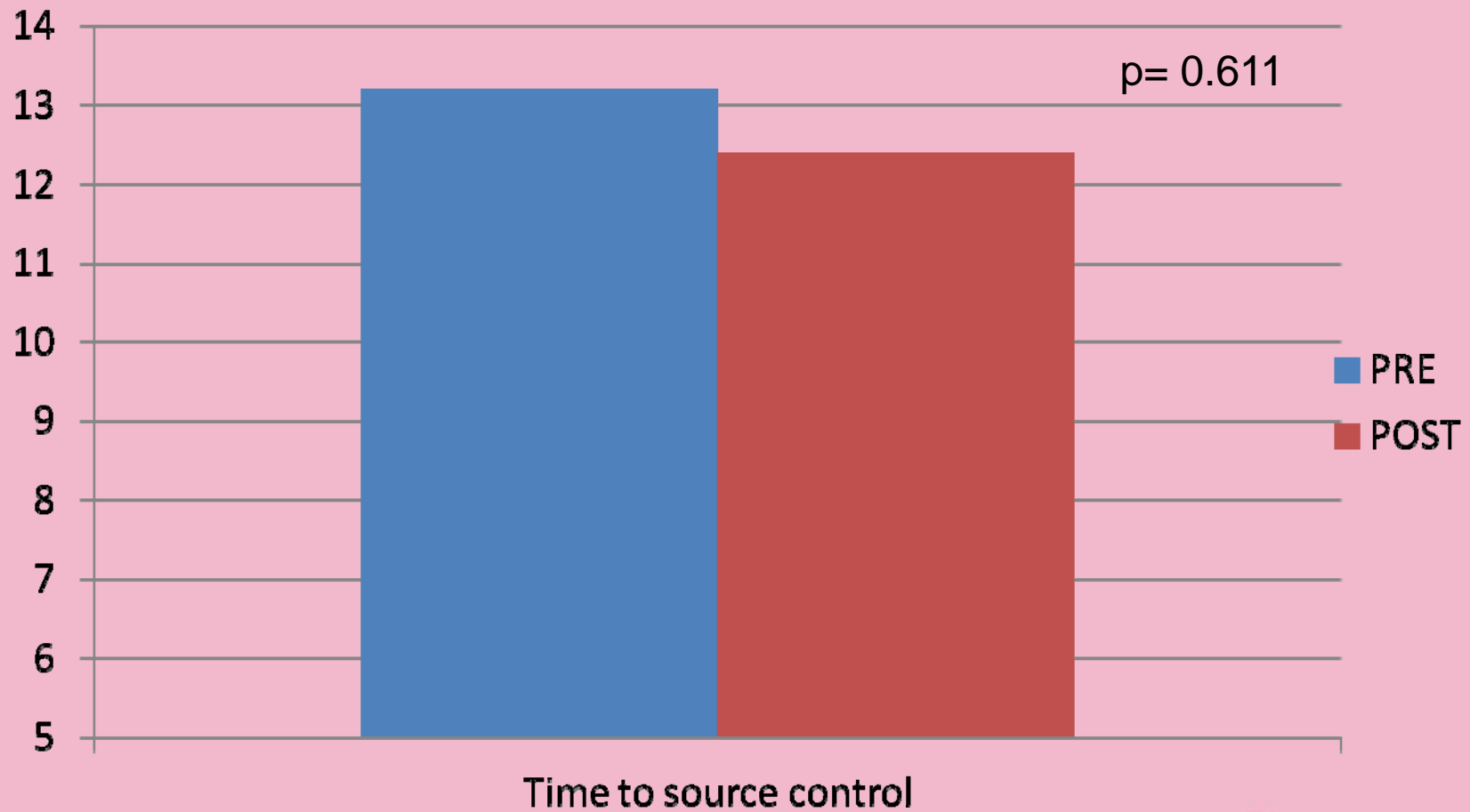
# Results: Type Pathology



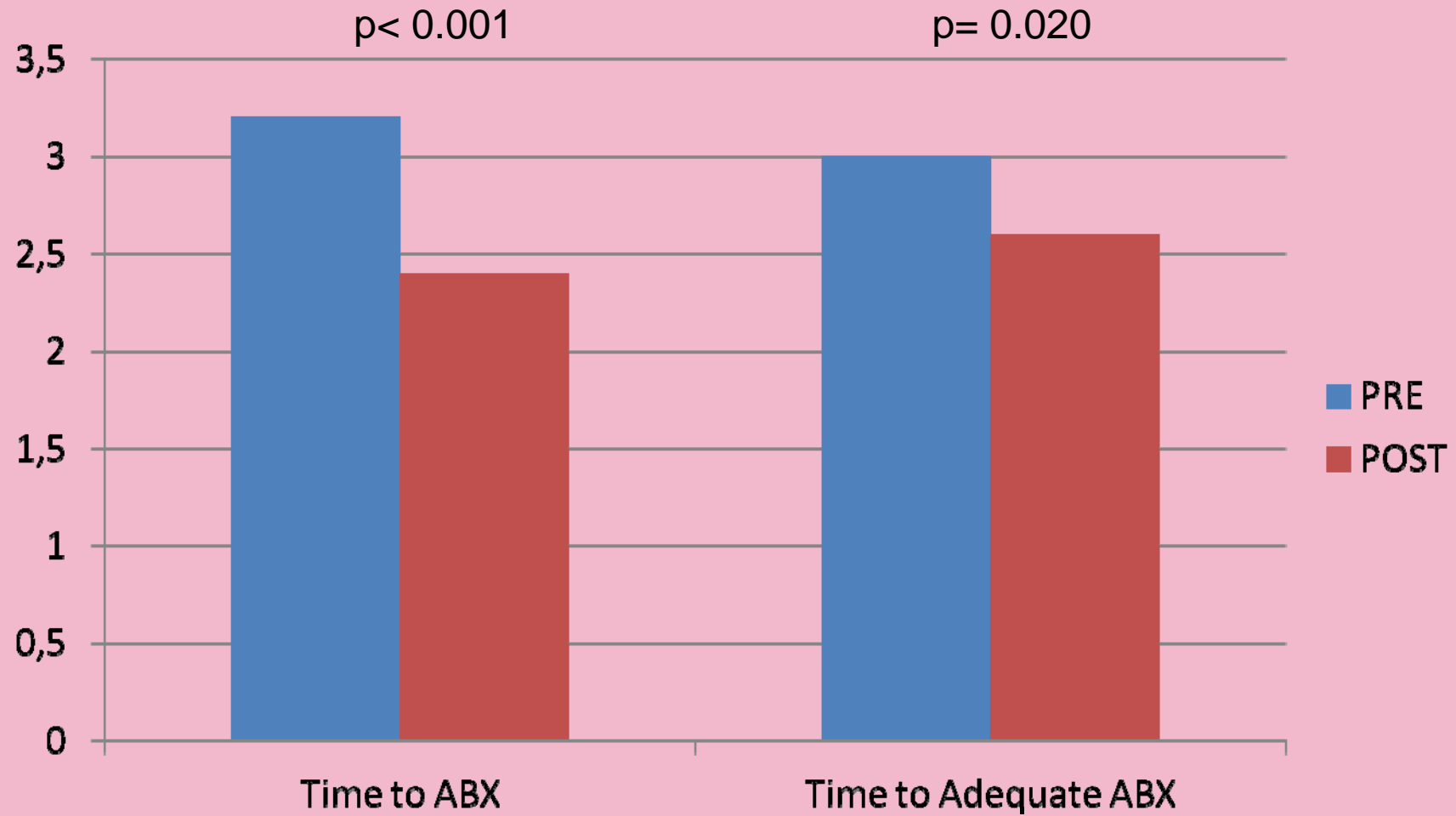
# Results: Quality indicators



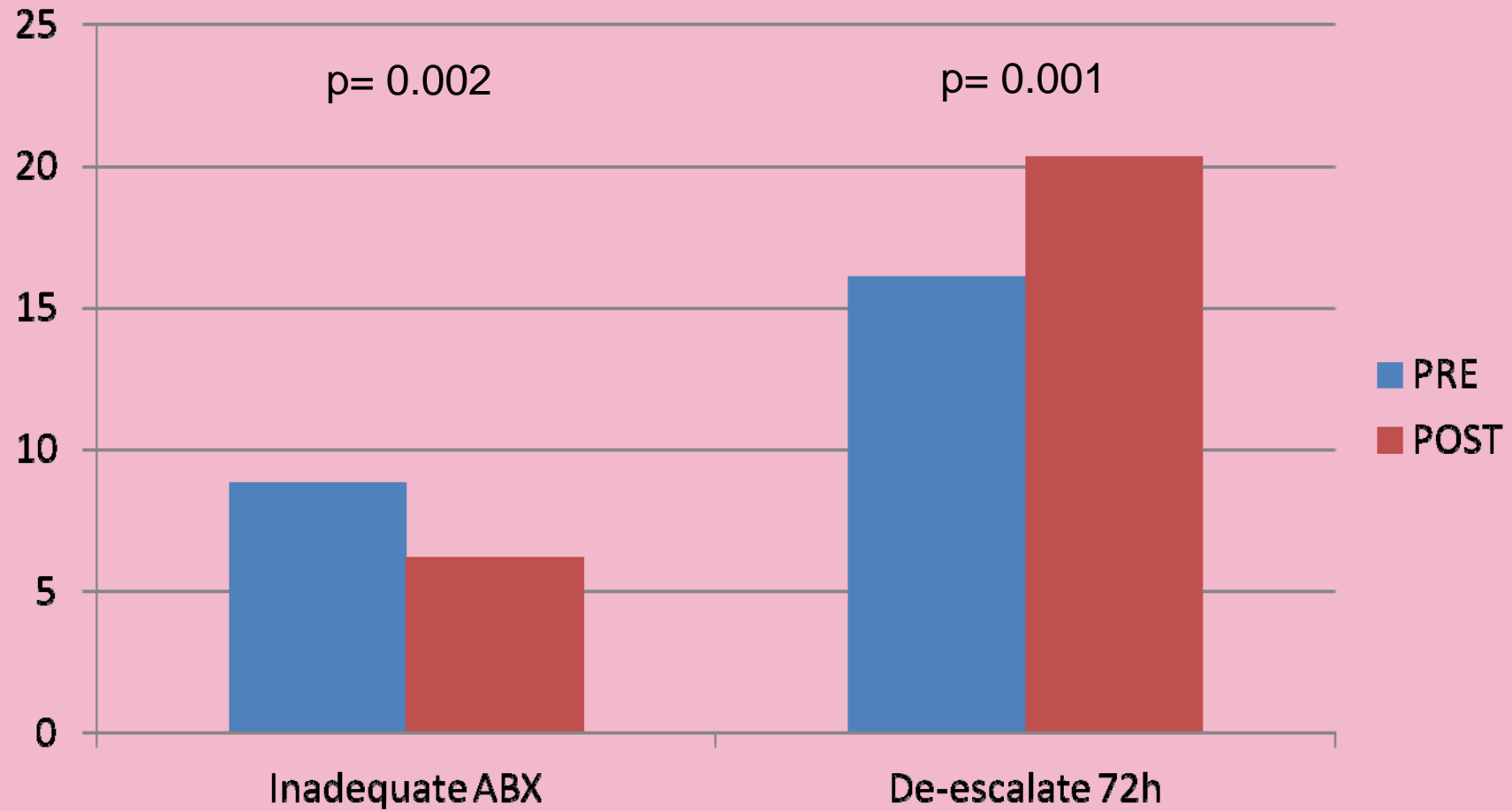
# Results: Source control



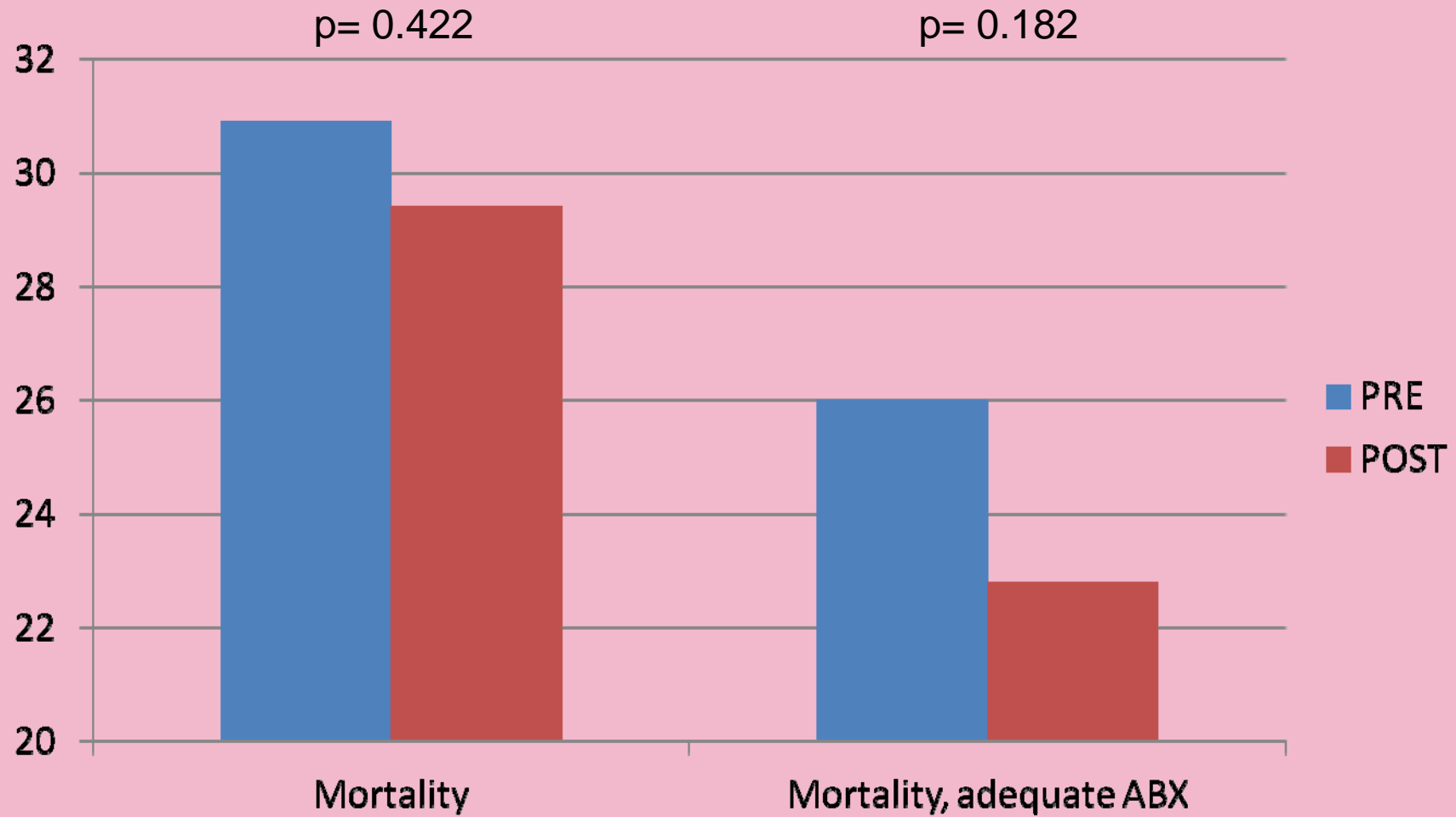
# Results: Antibiotics



# Results



# Results



# ABISS Edusepsis Pediatric

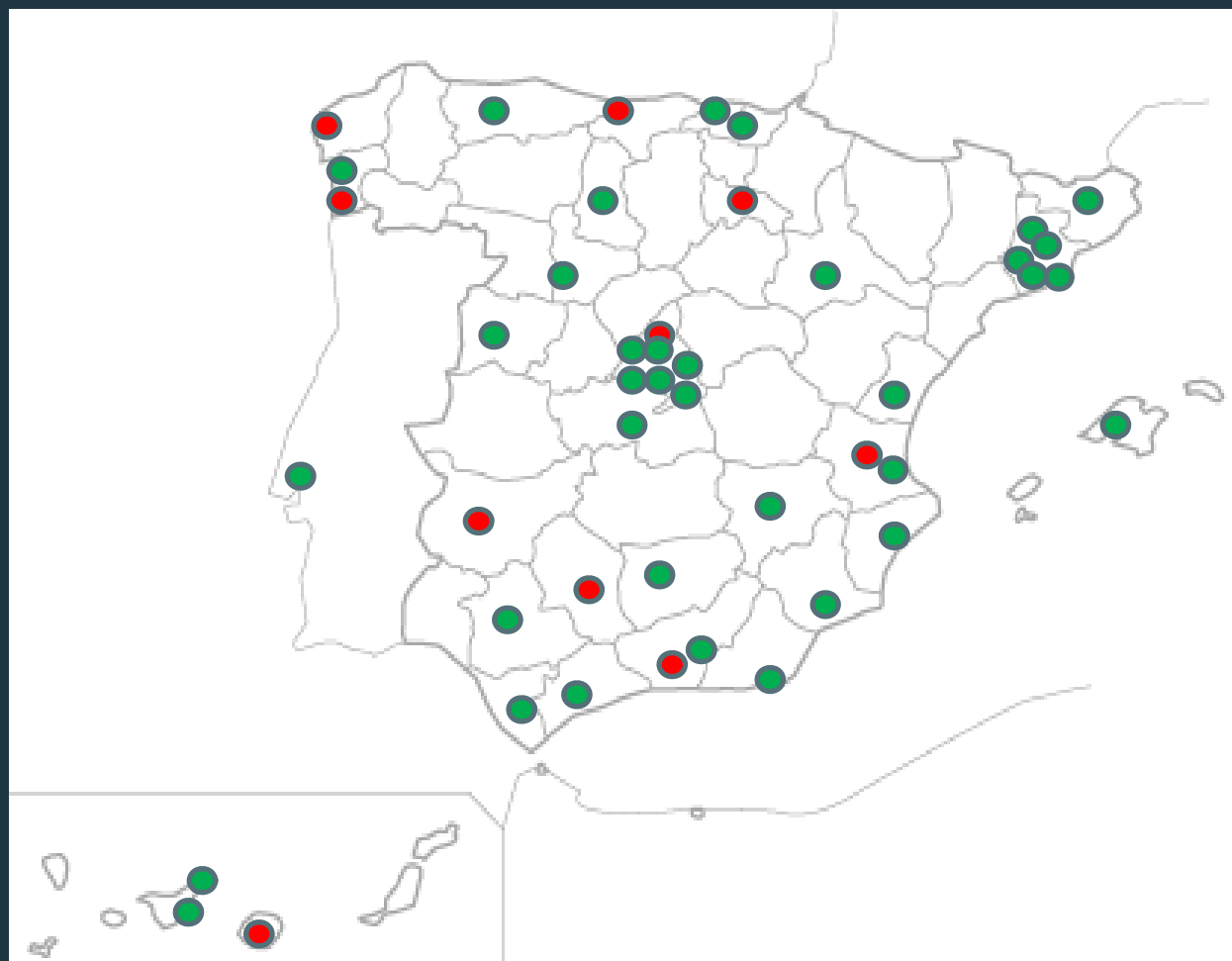




# ABISS pediatric net



PICUs ABISS: 33



# ABISS pediatric



## ABISS PICUs characteristics:

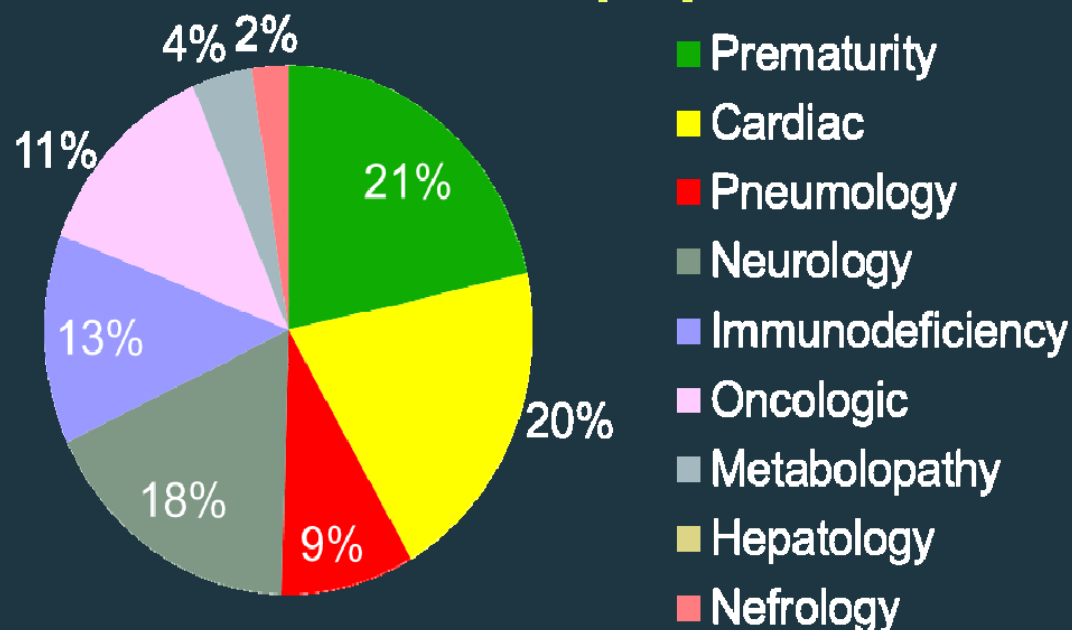
- Total: **380** PICU beds
- Total admissions/month: 1460
- 100% of PICU with residents
- 94% public
- **83.3%** medical and surgical, **25%** pediatrics-neonatal
- Protocols for sepsis management 100%
- Use of biomarkers: PCR 100%, PCT 64%
- Hemofiltration: 50%; ECMO: 20%

# Preintervention results



- **198 cases**
- 118 ♂ (59.6%)
- Median age (years)  $2.9 \pm 4.6$  ( 7 days-17.8 ys)
- Underlying diseases: 88 (44,4%)
- SOFA  $6,74 \pm 3.71$
- PRISM3  $10.71 \pm 7.21$
- Biomarkers:
  - PCT  $36.97 \pm 52.25$  ng/ml
  - CRP  $19.60 \pm 21.66$  mg/dl

## Underlying diseases



## Preintervention results

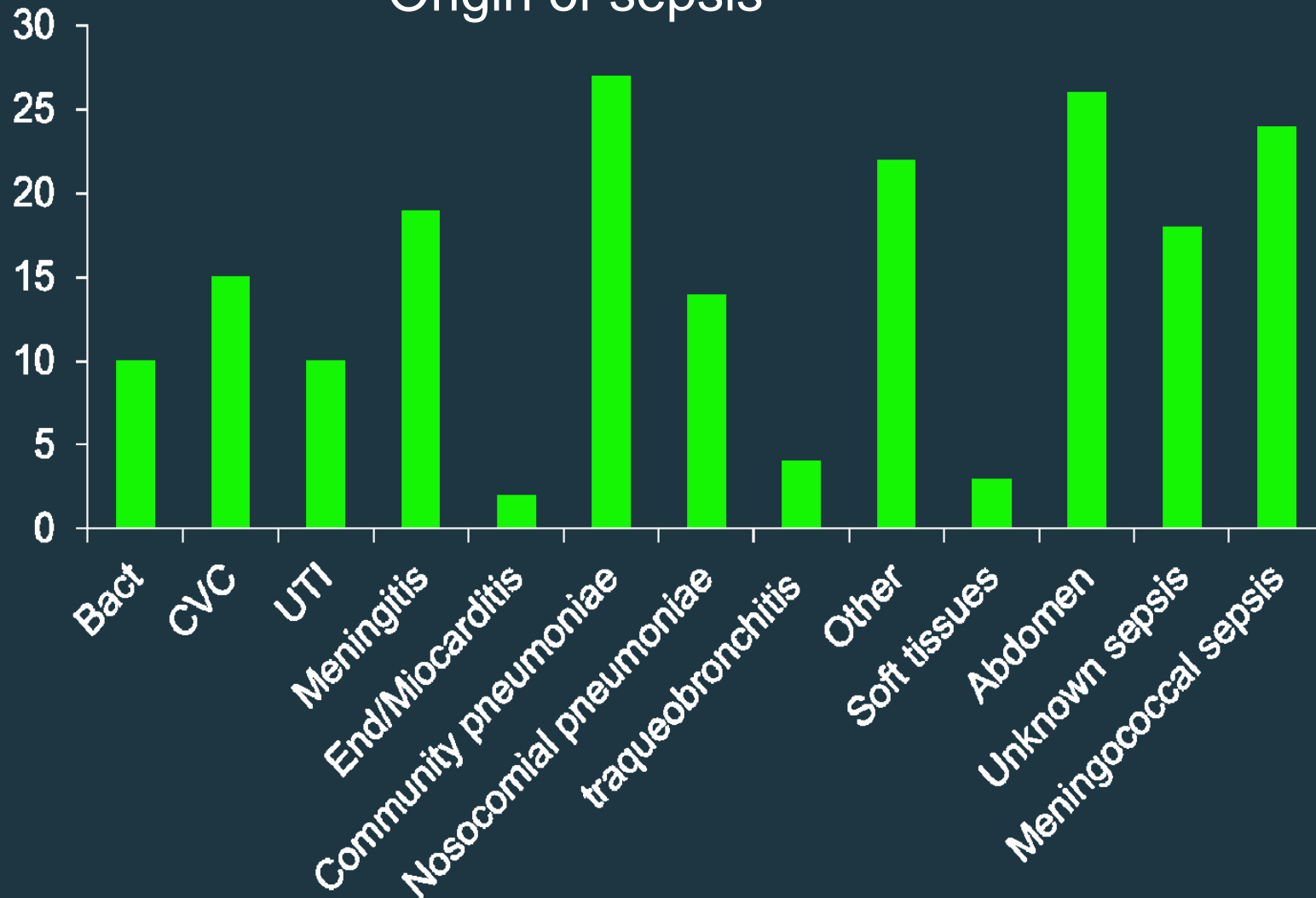


- Global Mortality **15.6%**
  - Mortality Septic shock **26.2%**
- Days of mechanical ventilation: 13.6±42.6
- Days of inotropic support: 5.77± 8.43
- PICU length of stay (days): 12.02±35.03
- Hospital length of stay (days): 26±45.09

# Preintervention results



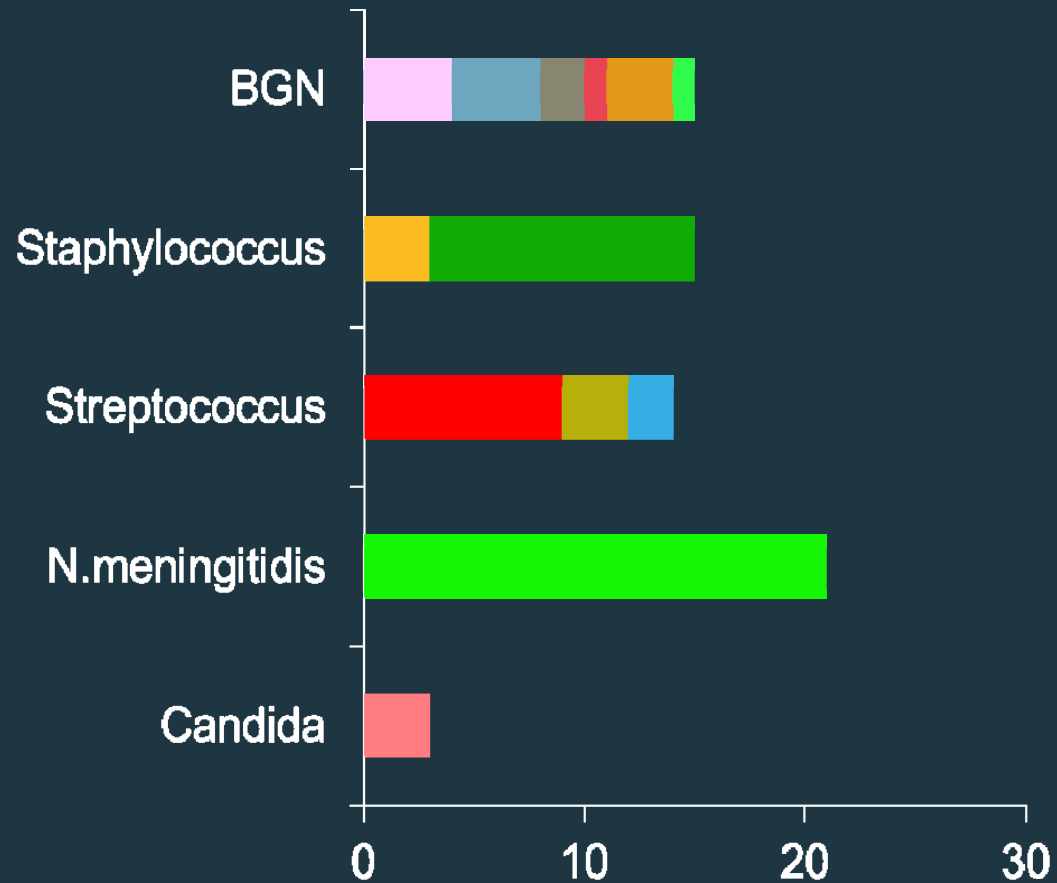
Origin of sepsis



# Preintervention results



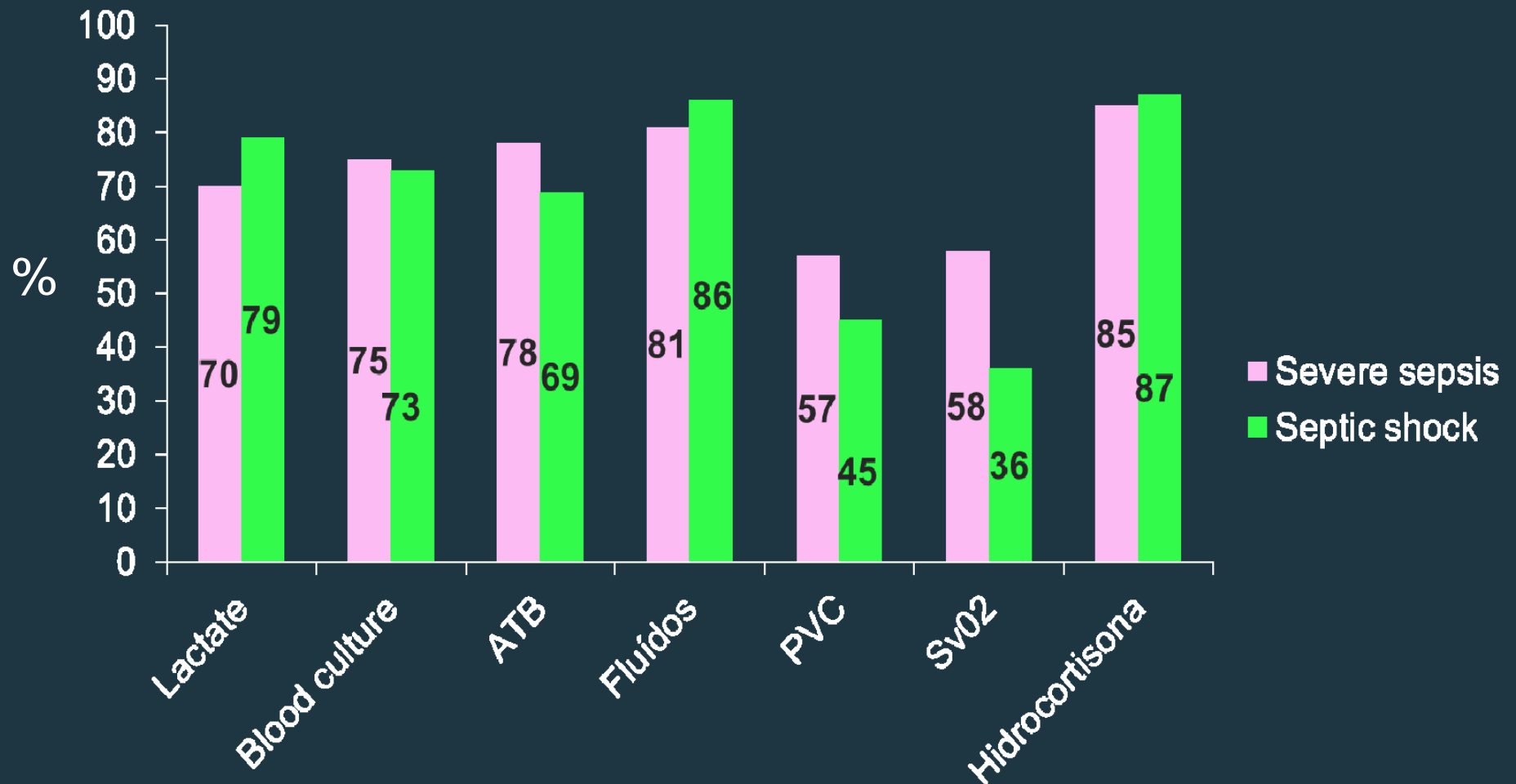
- Blood cultures:
  - 96.7% blood cultures
  - Bacteriemia: 40.4%



# Preintervention results



- % of Bundles compliance in severe sepsis and septic shock:



# Preintervention results



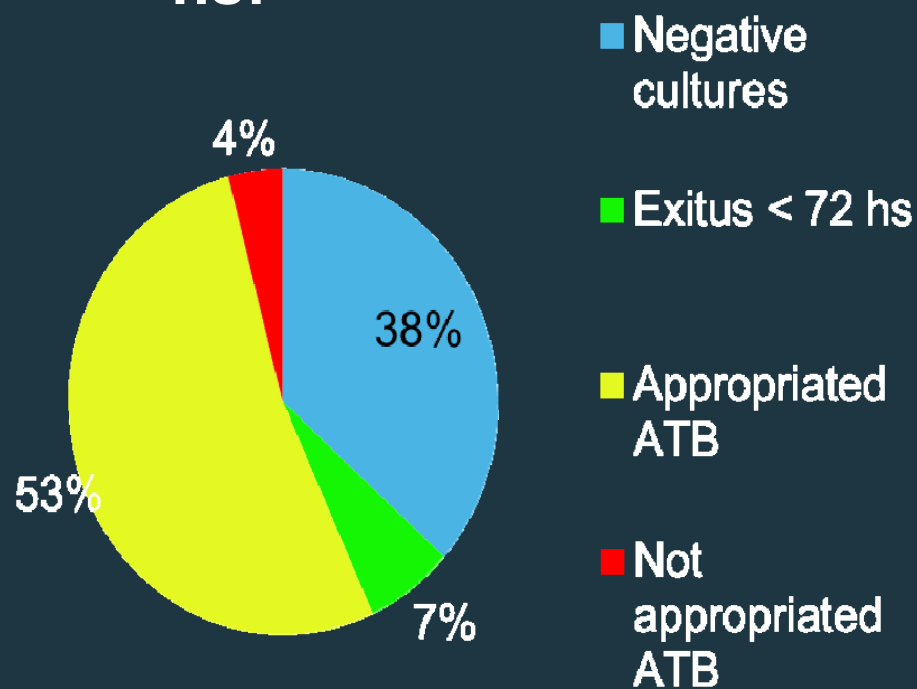
- Time to ATB from the diagnose of sepsis in patients without previous antibiotic treatment: mean **113.8±170.04 minutes**, median 60 minutes
  - In patients with septic shock 126.56±202.2 median 60
  - In patients with severe sepsis 101.53± 131.62, median 60



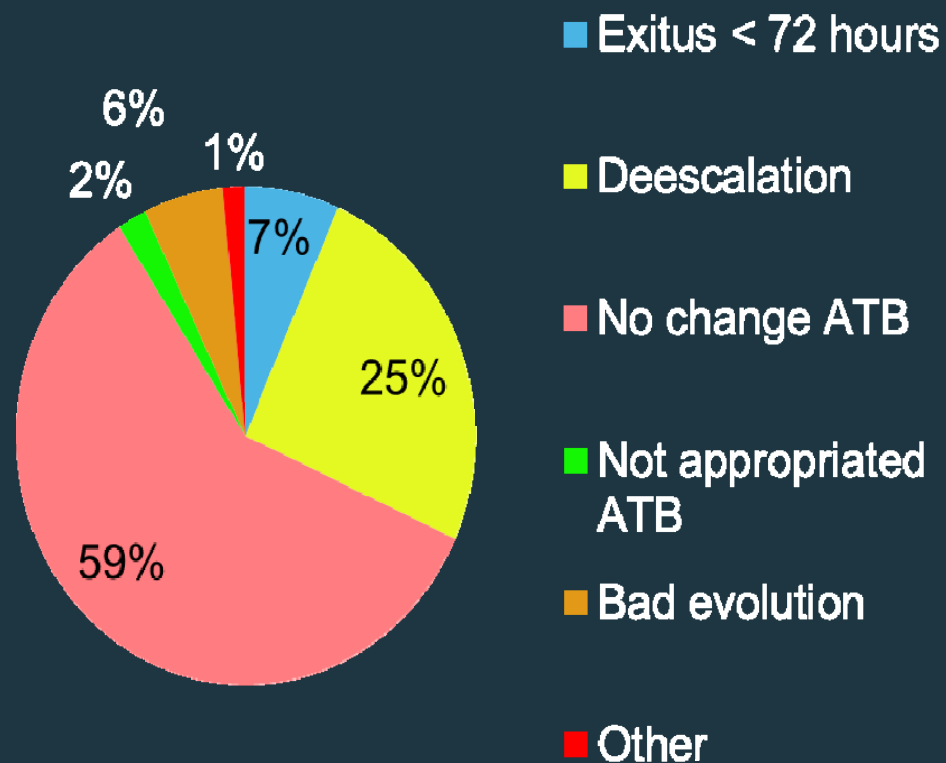
# Preintervention results



- Antibiotics previous to the onset of sepsis: **46 (23,2%)**
- Evaluation of treatment:  
hs:



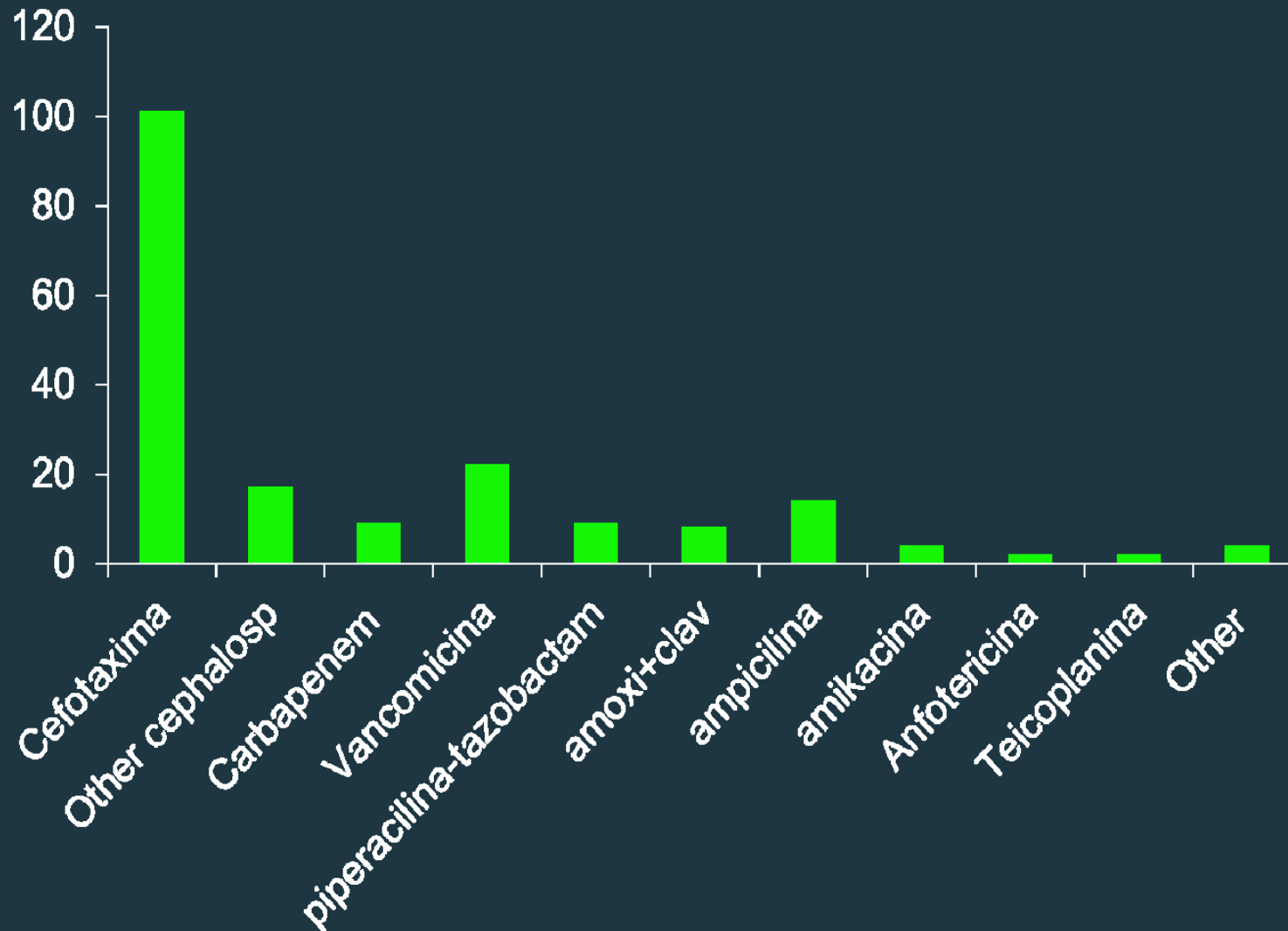
## Change of ATB at 72



# Preintervention results



## 1st ATB administered





# Evaluación Efectividad de los Tratamientos

Eficacia



Efectividad



# Assessment of the Effects of Treatments for Severe Sepsis on Mortality

---

Randomized  
Control Trials

Observational  
Studies

# Randomized Control Trials in CCM

---

## Pros:

- RCT is the standard for generating evidence.
- Bias are minimized.
- Confounders are limited.
- Data about efficacy and safety.

## Cons:

- Lack of biomarkers: Heterogeneous groups of patients.
- Stringent eligibility criteria.
- Difficult to homogenize treatments.
- Complex outcomes.
- Ethical constraints.

# Knowledge Generation

- **Consistency:**
  - Biological plausibility.
  - Confirmatory studies of single RCT.
  - Multicentric confirmation of unicentric studies.
- **Effectiveness** studies in “real world scenario”.
  - Patients excluded from RCT.
  - Effect of combining several treatment.
  - Feasibility of complex therapeutic interventions/algorithms.
- **Efficiency:** Cost-effectiveness studies.
- **Pharmacovigilance/Post-commercialization studies:** Safety

# Effectiveness of Treatments for Severe Sepsis

## A Prospective, Multicenter, Observational Study

Ricard Ferrer<sup>1</sup>, Antonio Artigas<sup>1</sup>, David Suarez<sup>2</sup>, Eduardo Palencia<sup>3</sup>, Mitchell M. Levy<sup>4</sup>, Angel Arenzana<sup>5</sup>, Xose Luis Pérez<sup>6</sup>, and Josep-Maria Sirvent<sup>7</sup> for the Edusepsis Study Group

**Objective:** To analyze the impact on hospital mortality of severe sepsis treatments included in the SSC guidelines in a prospective multicenter observational study (n= 2,796 adult patients with severe sepsis in 77 Spanish ICUs).

**Method:** The effectiveness of each sepsis treatment was estimated by using PS.

*AJRCCM 2009;180:861–866.*

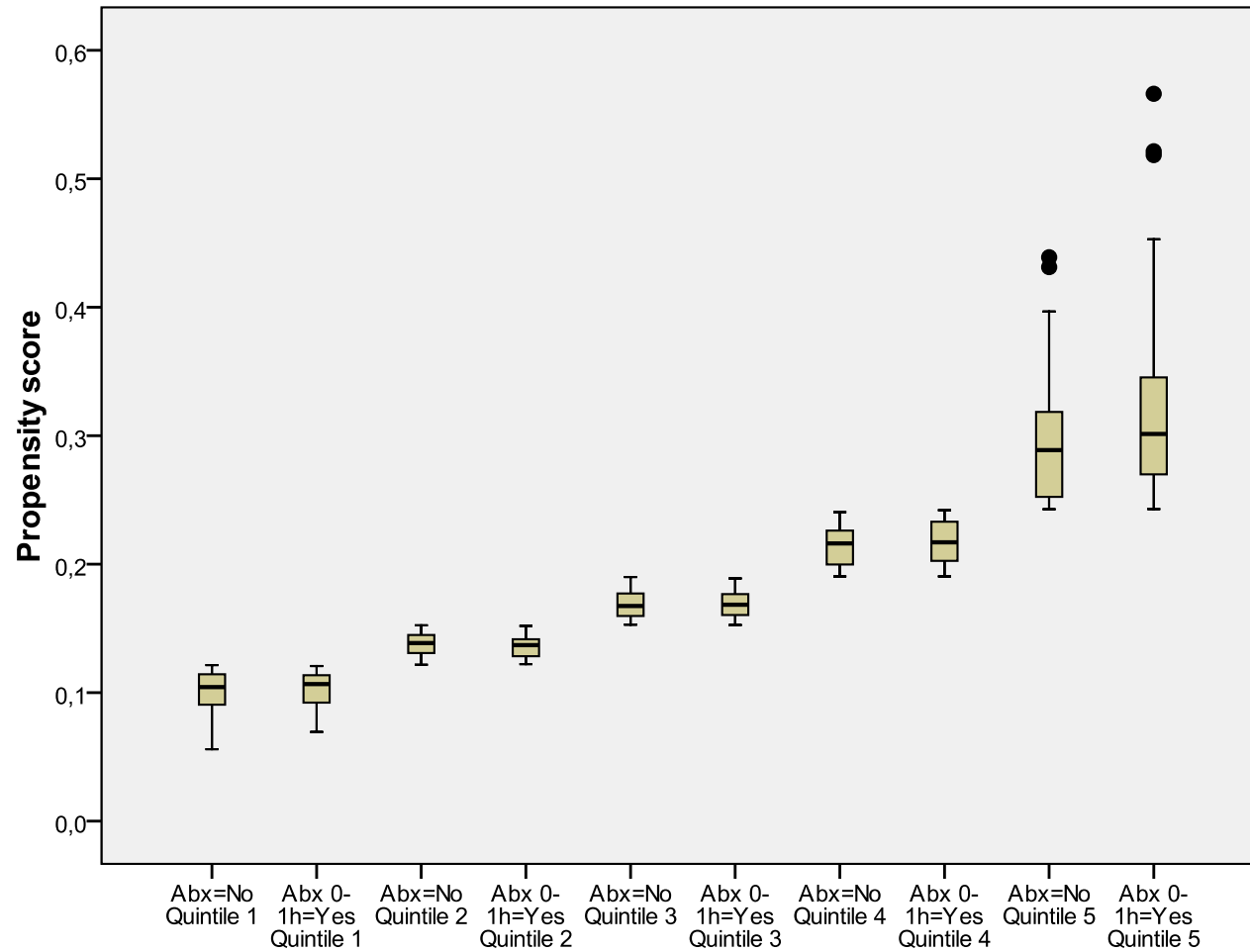


# TREATMENTS and MORTALITY

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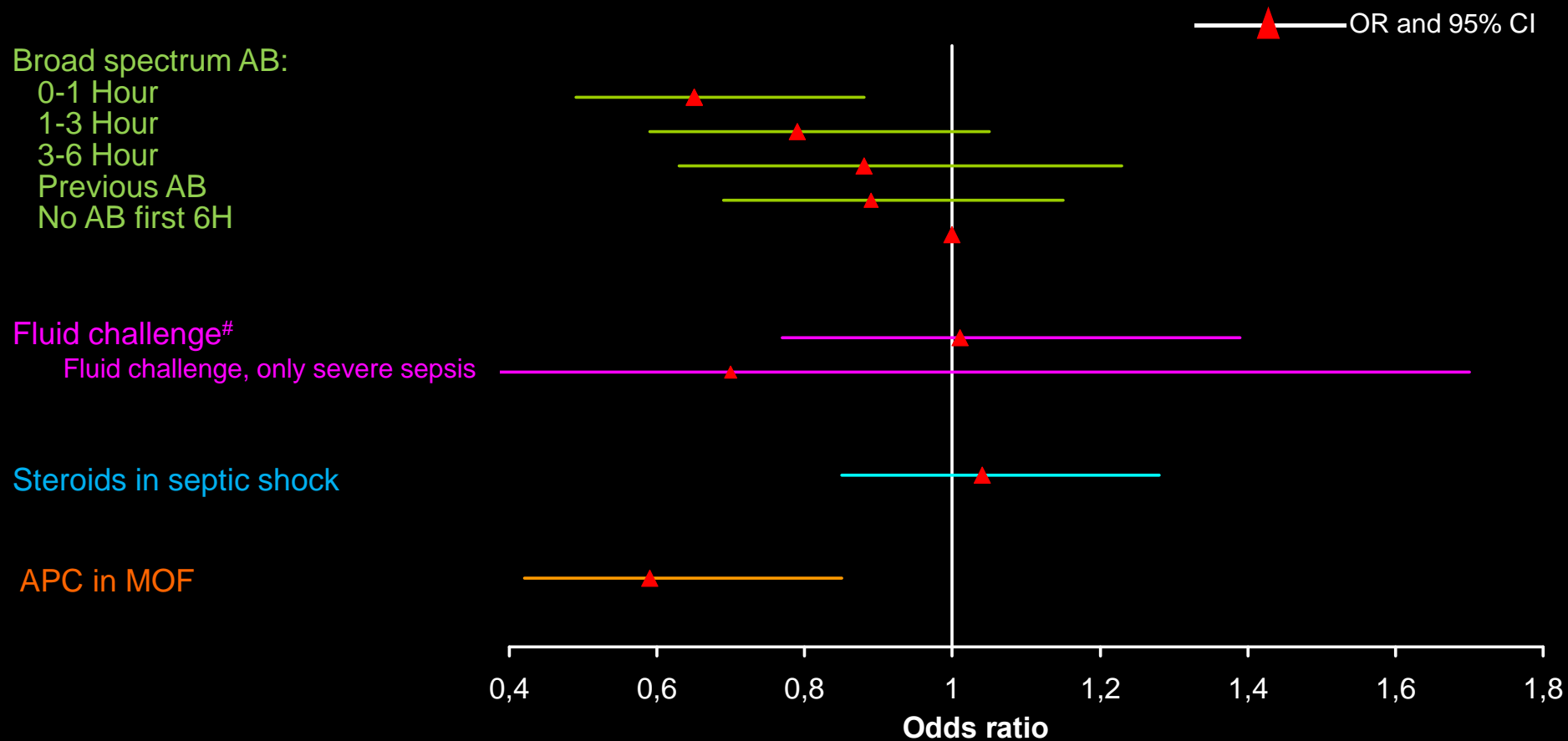
- Adjust for possible confounders:
  - Clinical risks factors for mortality
  - Other treatments and therapeutic goals
  - Propensity Score

# Propensity Score. **Antibiotics.**

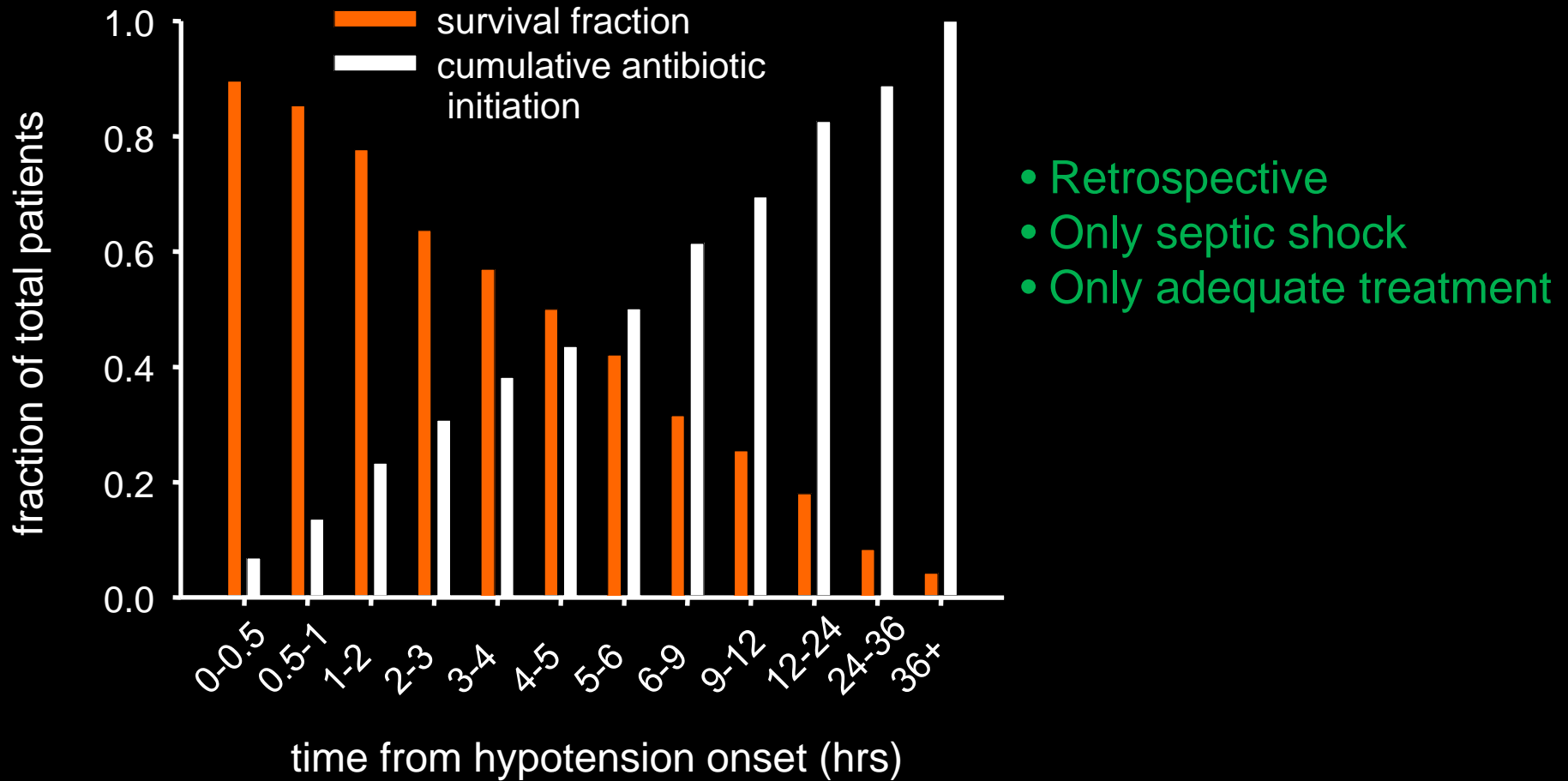


# Effectiveness of APC in MOF

## Final Model: All risk factors + Other TTMs + PS



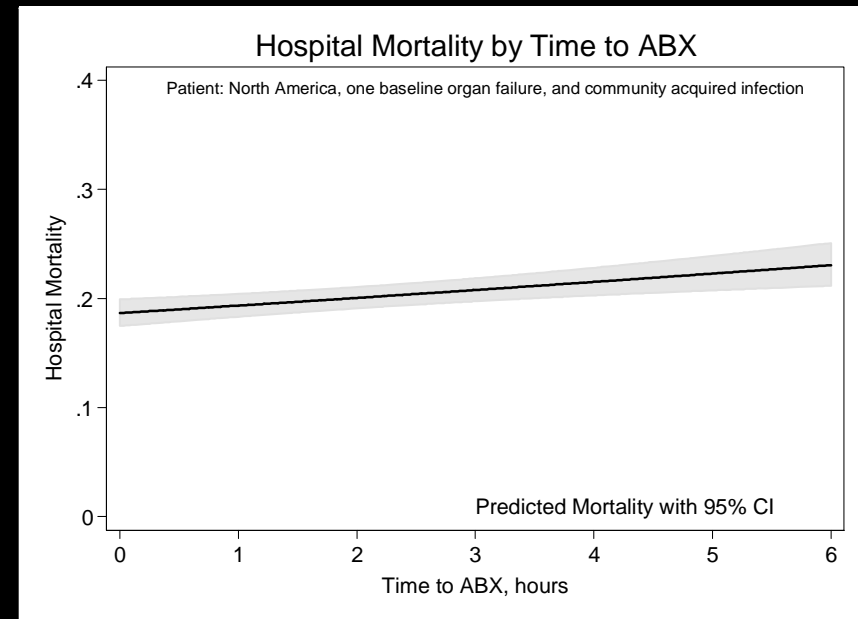
# Early antibiotic treatment



# Time to Treatment. Antibiotics

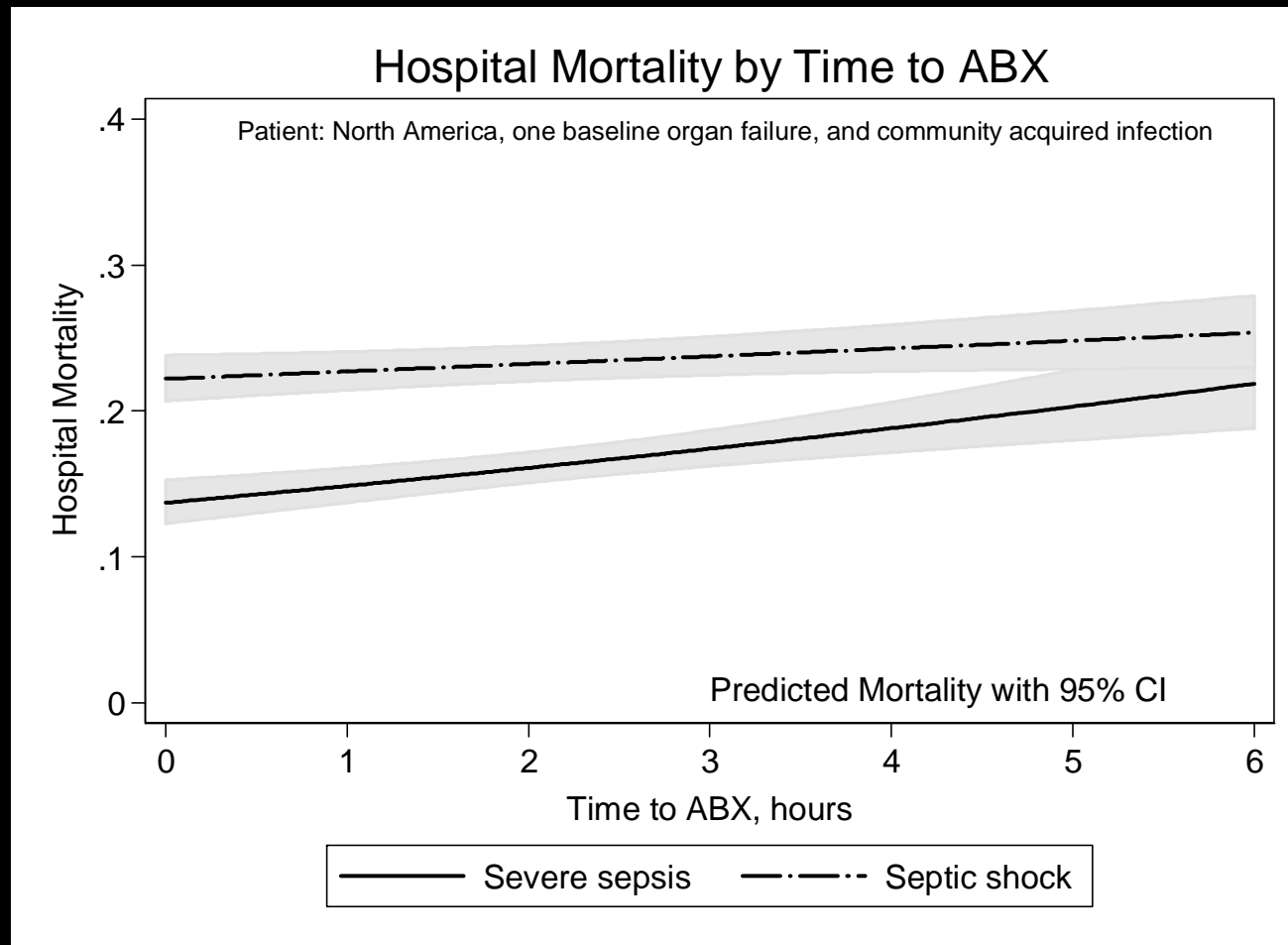
25.089 patients with severe sepsis or septic shock

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



# Time to Treatment. Antibiotics

25.089 patients with severe sepsis or septic shock



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

## Antibiotic prescription patterns in the empiric therapy of severe sepsis: combination of antimicrobials with different mechanisms of action reduces mortality

Antibiotics	Global <i>n</i> = 1,372	Community-acquired <i>n</i> = 1,022 (74.5%)	Nosocomial <i>n</i> = 350 (25.5%)	<i>P</i>
β-lactams	902 (65.7%)	708 (69.3%)	194 (55.4%)	<0.001
Carbapenems	345 (25.1%)	218 (21.3%)	127 (36.3%)	<0.001
Quinolones	282 (20.6%)	241 (23.6%)	41 (11.7%)	<0.001
Aminoglycosides	183 (13.3%)	114 (11.2%)	69 (19.7%)	<0.001
Macrolides	60 (4.4%)	54 (5.3%)	6 (1.7%)	0.004
Anti-gram-positive	161 (11.7%)	96 (9.4%)	65 (18.6%)	<0.001
Antifungals	38 (2.8%)	20 (2.0%)	18 (5.1%)	0.004
Others	151 (11.0%)	111 (10.9%)	40 (11.4%)	0.767

Antibiotics	Non-DCCT group <i>n</i> = 984 (71.7%)	DCCT group <i>n</i> = 388 (28.3%)	<i>P</i>
β-Lactams	582 (59.1%)	320 (82.5%)	<0.001
Carbapenems	269 (27.3%)	76 (19.6%)	0.003
Quinolones	96 (9.8%)	186 (47.9%)	<0.001
Aminoglycosides	25 (2.5%)	158 (40.7%)	<0.001
Macrolides	7 (0.7%)	53 (13.7%)	<0.001
Anti-gram-positive	120 (12.2%)	41 (10.6%)	0.456
Antifungals	21 (2.1%)	17 (4.4%)	0.028
Others	121 (12.3%)	30 (7.7%)	0.016

# Antibiotic prescription patterns in the empiric therapy of severe sepsis: combination of antimicrobials with different mechanisms of action reduces mortality

Ana Díaz-Martín<sup>1,2,3\*</sup>, María Luisa Martínez-González<sup>4</sup>, Ricard Ferrer<sup>5,6</sup>, Carlos Ortiz-Leyba<sup>1,2,3</sup>, Enrique Piacentini<sup>5</sup>, María Jesus Lopez-Pueyo<sup>7</sup>, Ignacio Martín-Loeches<sup>4,6</sup>, Mitchell M Levy<sup>8</sup>, Antoni Artigas<sup>4,6</sup>, José Garnacho-Montero<sup>1,2,3</sup> and for the Edusepsis Study Group

Factors	OR	CI (95%)	P
Age (years)	1.023	(1.014-1.032)	<0.001
Sex (male)	1.350	(1.041-1.750)	0.024
APACHE II	1.099	(1.099-1.141)	<0.001
Community-acquired	1.487	(1.119-1.974)	0.006
DCCT	0.699	(0.522-0.936)	0.016
Focus of infection			
Pneumonia	0.784	(0.358-1.718)	0.543
Abdominal	0.595	(0.269-1.317)	0.200
Urologic	0.241	(0.102-0.569)	0.001
Meningitis	0.357	(0.122-1.046)	0.060
Skin and soft-tissue	0.424	(0.157-1.141)	0.089
Catheter	0.441	(0.135-1.445)	0.177
Others	0.772	(0.330-1.806)	0.551
More than one focus	1		

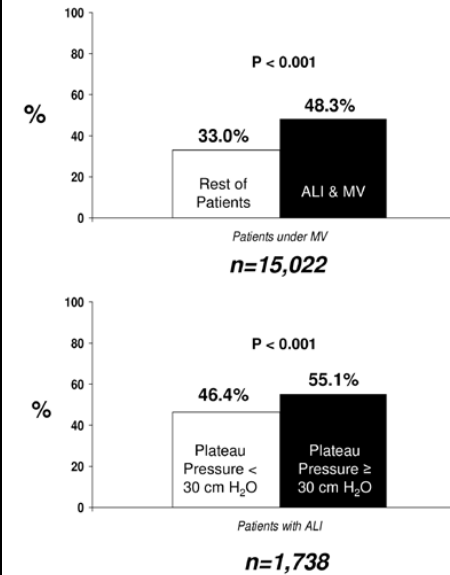




# Effectiveness of inspiratory pressure-limited approach to mechanical ventilation in septic patients

Ignacio Martin-Loeches<sup>\*↓</sup>, Candelaria de Haro<sup>\*</sup>, R. Phillip Dellinger<sup>#</sup>, Ricard Ferrer<sup>¶</sup>, Gary S. Phillips<sup>+</sup>, Mitchell M. Levy<sup>§</sup> and Antonio Artigas<sup>\*</sup>

ICU Mortality



## Cox proportional hazard regression of PP < 30 cm H<sub>2</sub>O in patients with ALI

Plateau pressure < 30 cm H <sub>2</sub> O	Observations	Mortality HR	95% CI	p-value
Unadjusted	1,737	0.88	0.75 – 1.03	0.111
Adjusted <sup>1</sup>	1,737	0.84	0.72 – 0.99	0.038

## Cox proportional hazard regression of PP < 30 cm H<sub>2</sub>O in patients without ALI

Plateau pressure < 30 cm H <sub>2</sub> O	Observations	Mortality HR	95% CI	p-value
Unadjusted	6,139	0.78	0.71 – 0.86	< 0.001
Adjusted <sup>1</sup>	6,139	0.77	0.70 – 0.85	< 0.001

# Factores de Riesgo de Muerte en Pacientes > 80 años

Hospital Mortality 48%  
Multivariate Analysis

	Very elderly N = 161 (54.2%) OR (95% CI)	<i>p</i>
Age (years) <sup>a</sup>	1.1 (0.9-1.2)	0.061
Sex(male)	1.1 (0.6-1.8)	0.710
APACHE II modified score <sup>b</sup>	1.1 (1.1-1.2)	0.000
ICU LOS	1.031 (1.0-1.0)	0.009
Patient location at sepsis diagnosis <sup>c</sup>		
-Ward	1.5 (0.8-2.7)	0.130
-ICU	0.6 (0.2-2.1)	0.507
Source of infection <sup>d</sup>		
-Peritonitis	0.9 (0.4-1.9)	0.856
-UTI	0.3 (0.1-1.0)	0.059
-SSTI	0.4 (0.1-2.1)	0.307
-Catheter-related bacteremia	0.9 (0.1-5.1)	0.243
-Other	1.1 (0.4-2.7)	0.864
Baseline acute organ dysfunction		
-Cardiovascular	0.6 (0.3-1.4)	0.316
-Pulmonary	1.1 (0.5-2.3)	0.621
-Renal	0.8 (0.4-1.7)	0.648
-Hepatic	0.7 (0.3-1.6)	0.466
-Trombopenia	0.9 (0.4-2.1)	0.955
-Coagulopathy	1.5 (0.8-2.6)	0.171
Resuscitation bundles	0.2 (0.1-0.9)	0.042
Treatment bundles	0.8 (0.3-1.8)	0.562





# Coste y Coste-Efectividad

**Efficacy**



Can it work?

**Effectiveness**



Does it work?

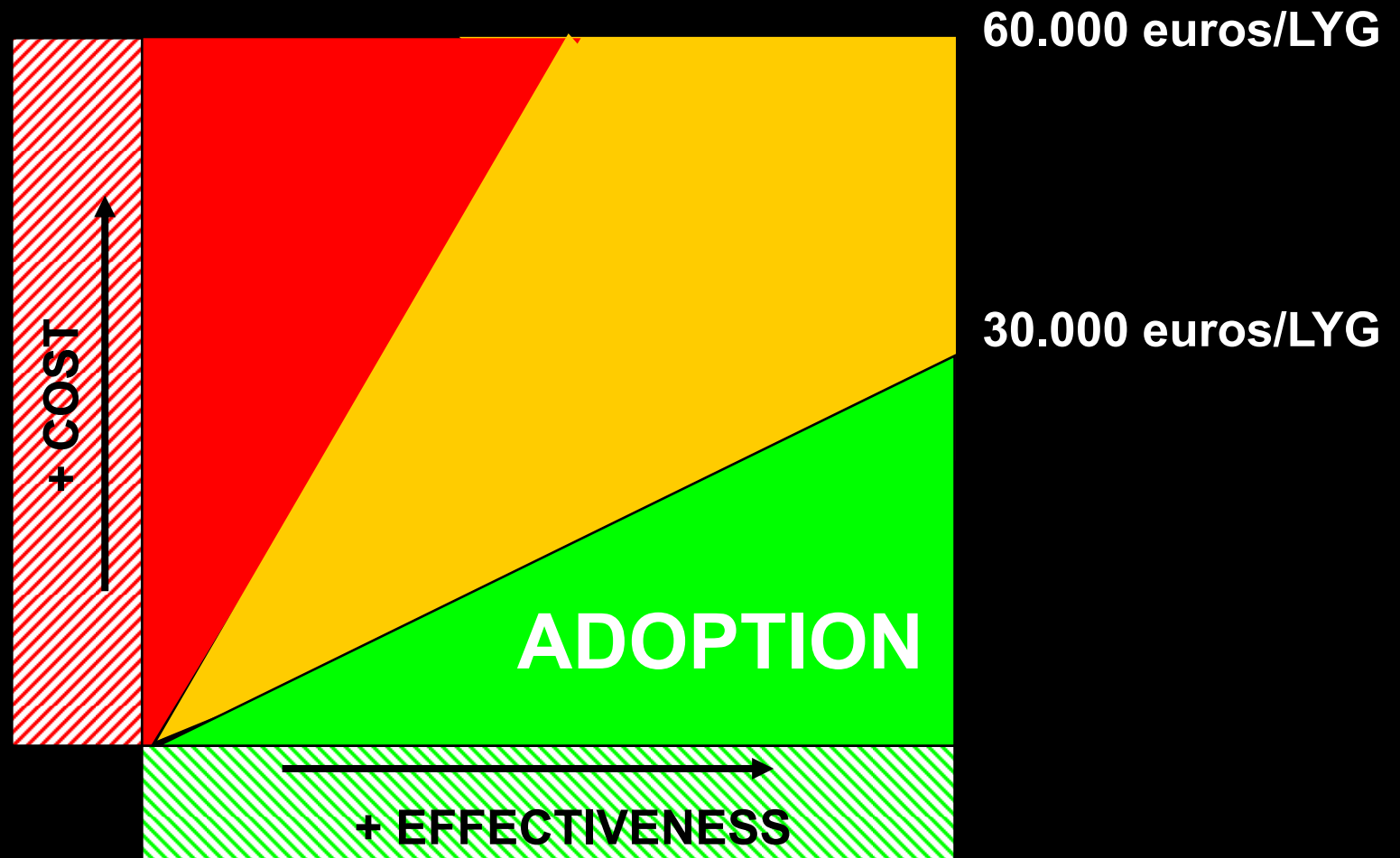
Life year gained (LYG)  
Quality adjusted life year (QALY)

**Efficiency**



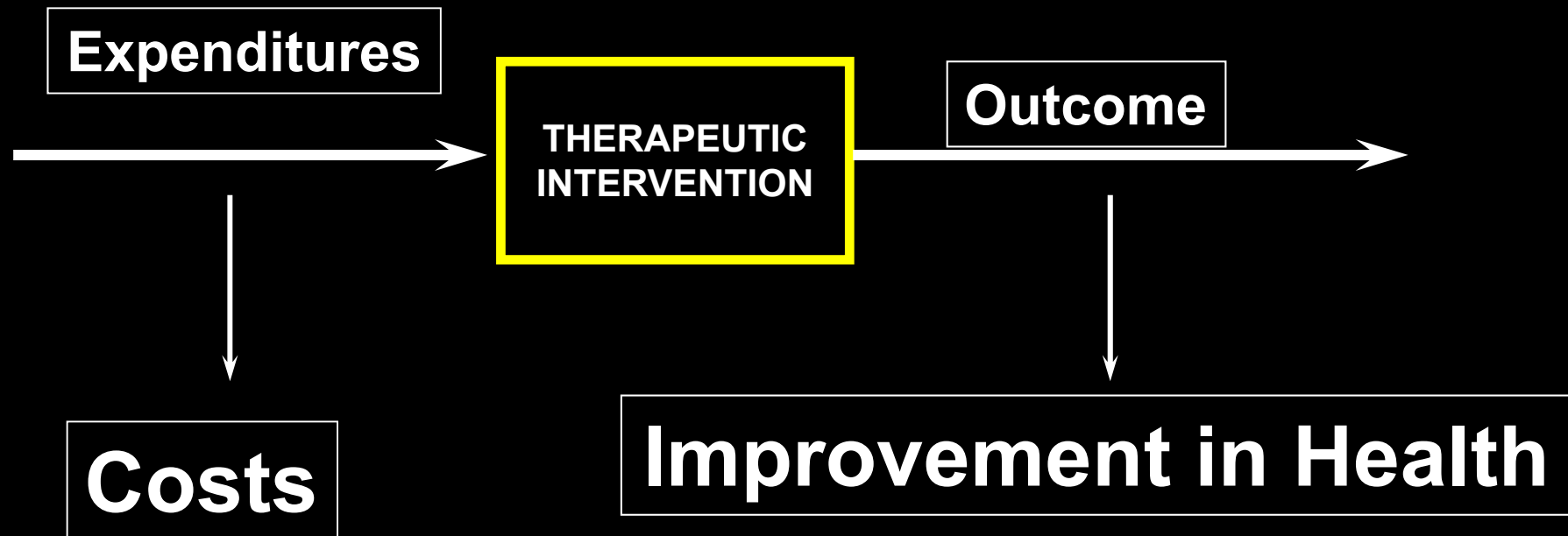
Is it worth it?

# Cost-Effectiveness



# Cost-Effectiveness Analysis

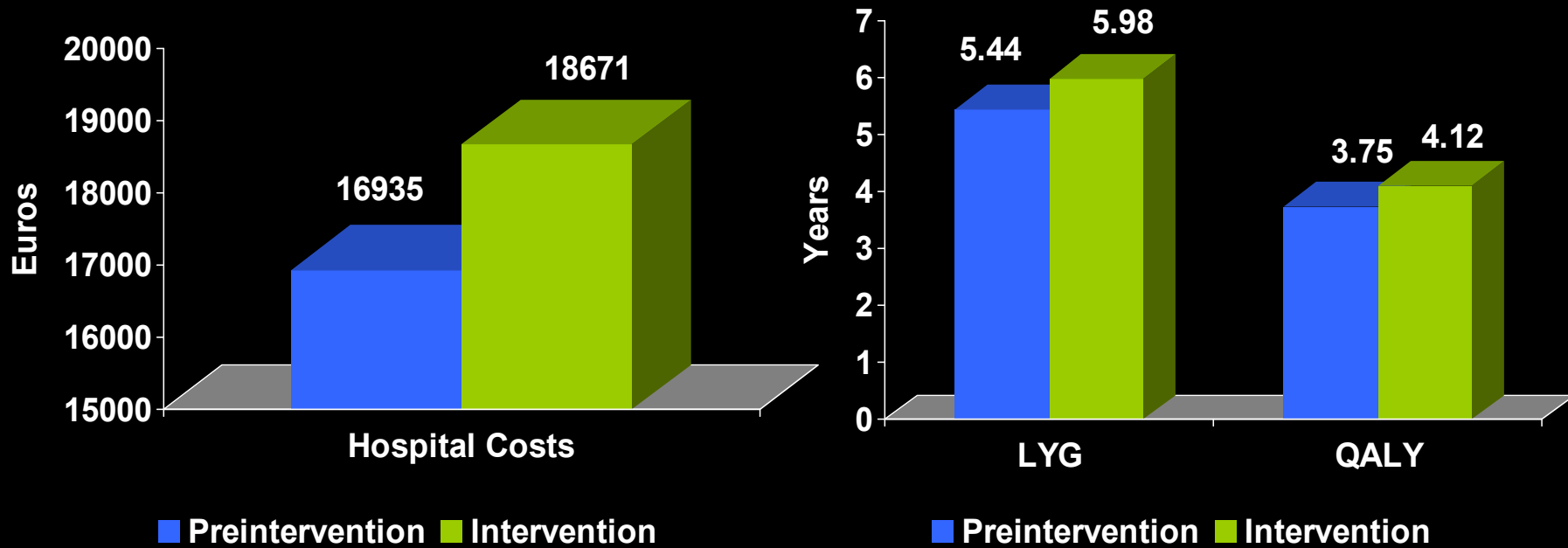
- Ratio of the cost of the intervention to a relevant measure of its effect.



**Incremental Cost-Effectiveness Ratio (ICER)**  
**Incremental Cost-Utility Ratio (ICUR)**

David Suarez  
Ricard Ferrer  
Antonio Artigas  
Izaskun Azkarate  
José Garnacho-Montero  
Gemma Gomà  
Mitchell M. Levy  
Juan Carlos Ruiz  
For the Edusepsis Study Group

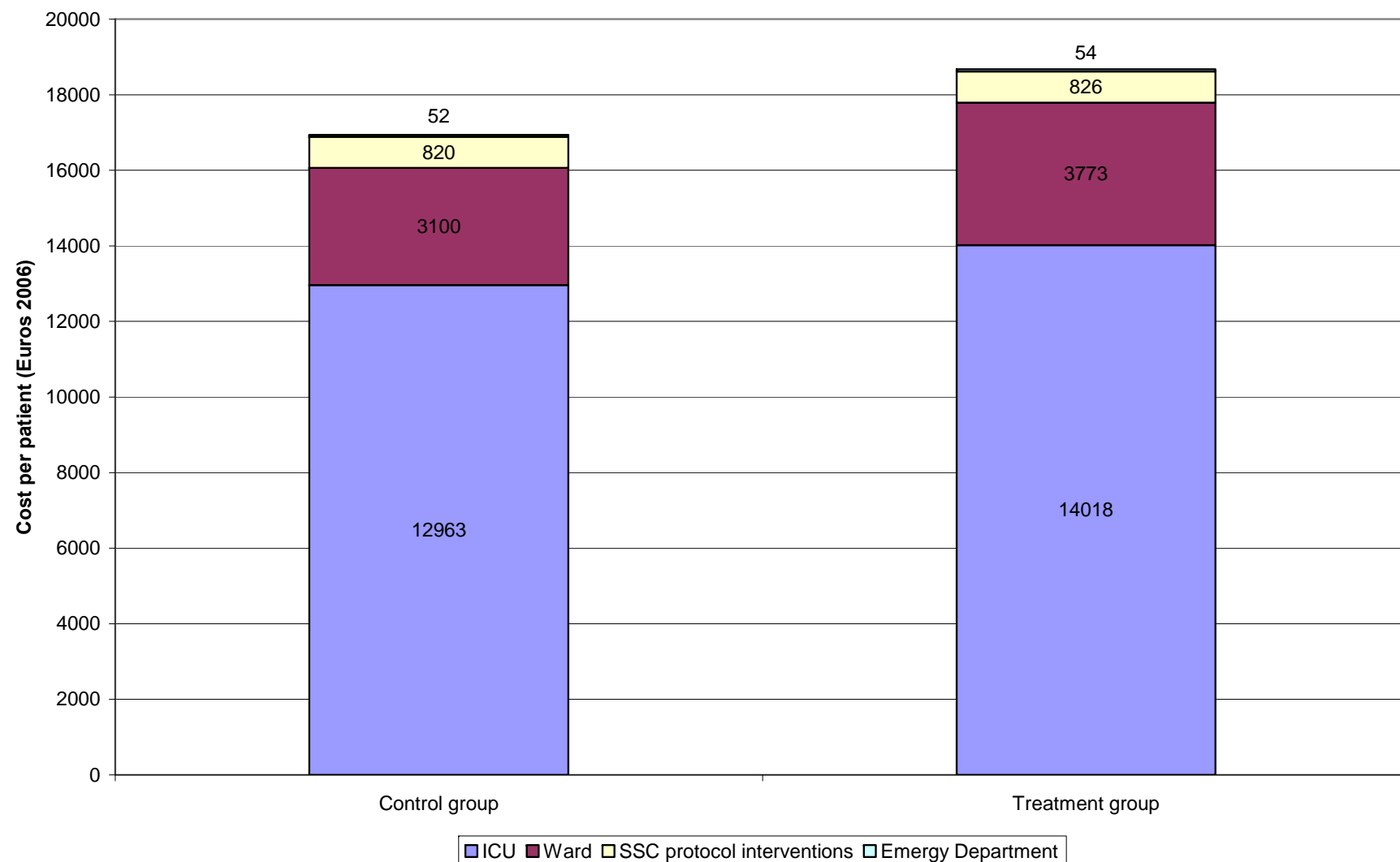
### Cost-effectiveness of the Surviving Sepsis Campaign protocol for severe sepsis: a prospective nation-wide study in Spain



**Adjusted ICER**  
**Adjusted ICUR**

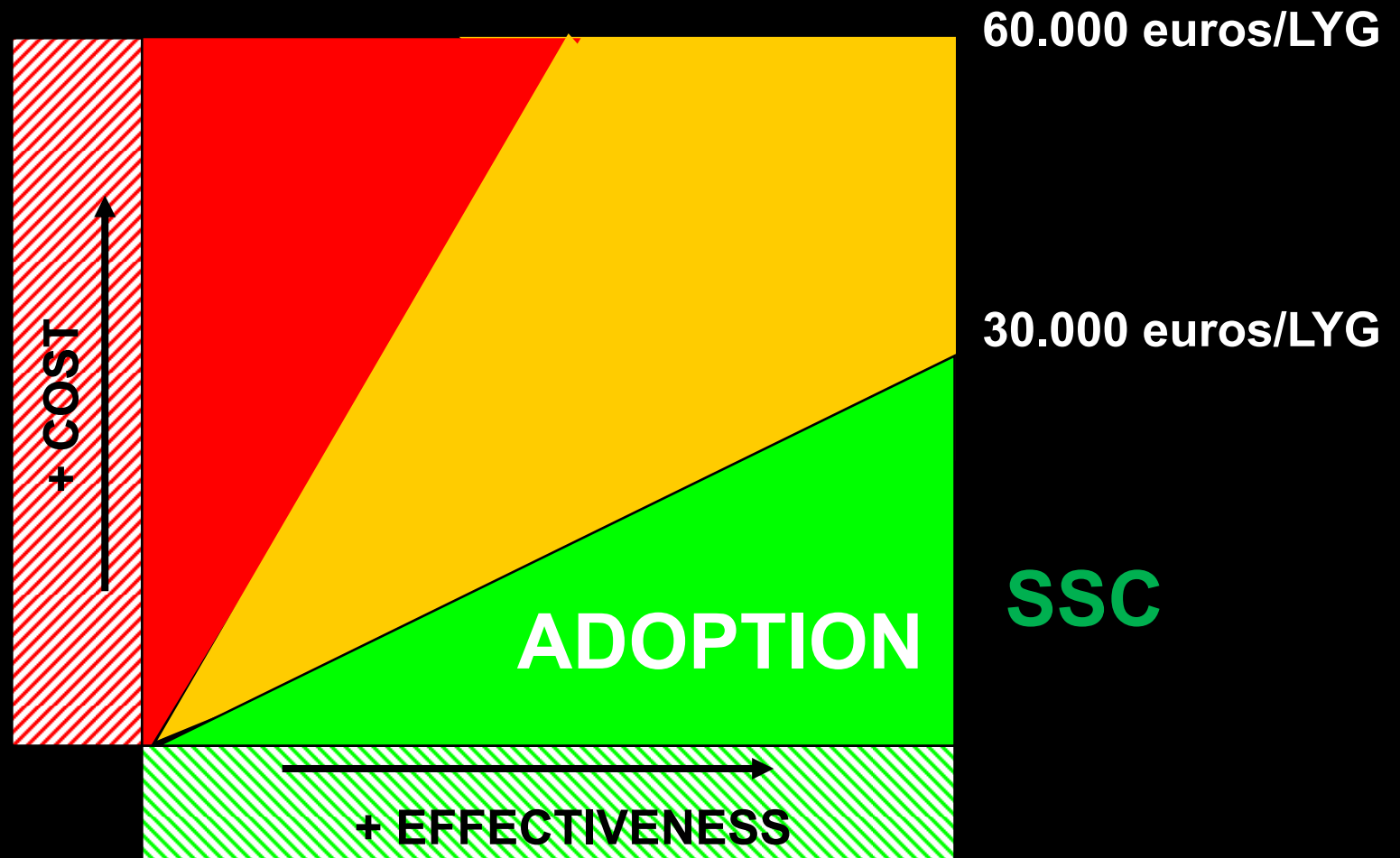
**4,435 euros per LYG**  
**6,428 euros per QALY**

# Distribution of mean costs per patient





# Cost-Effectiveness



1. **Premi a la millor comunicació** presentada a la SOCMIC 2008, Badalona.
2. **Mejores Ideas Diario Médico 2008** Política profesional por el Estudio Edusepsis.
3. **Accèsit a la millor comunicació mèdica presentada** SOCMIC 2009.
4. **Premi mutual mèdica Dr. Josep Font** millor article científic 2008.
5. **Award for the best abstract on sepsis** (International Sepsis Forum): Poster Award Winner 2009. 23rd Annual Congress ESICM.
6. **Millor Comunicació Publicada** SOCMIC 2010. AJRCCM.
7. **Millor comunicació mèdica presentada** SOCMIC 2010.
8. **Premis Científics Capiro – Hospital General de Catalunya, Edició 20.** Categoria Assistencial.
9. **Mejor Comunicación XLVII CONGRESO NACIONAL DE LA SEMICYUC**

# Conclusions

1. Els clínics identifiquen la sepsis com un problema i col·laboren en programes de transferència del coneixement i millora de la qualitat.
2. Lideratge
3. Metodologia.
4. Difusió de resultats. Subestudis. Publicacions i Abstracts.
5. Estructura centralitzada: Website, CRDe, monitorització, anàlisis.
6. Finançament:
  1. Beca FIS-Evaluación Tecnologías Sanitarias. Cost-Efectivitat.
  2. FIS PI10-01497. ABISS.
  3. Suport Logistic: Lilly, Astra-Zeneca.

[info@edusepsis.org](mailto:info@edusepsis.org)

