Importància del tractament precoç i adequat a la sèpsia greu

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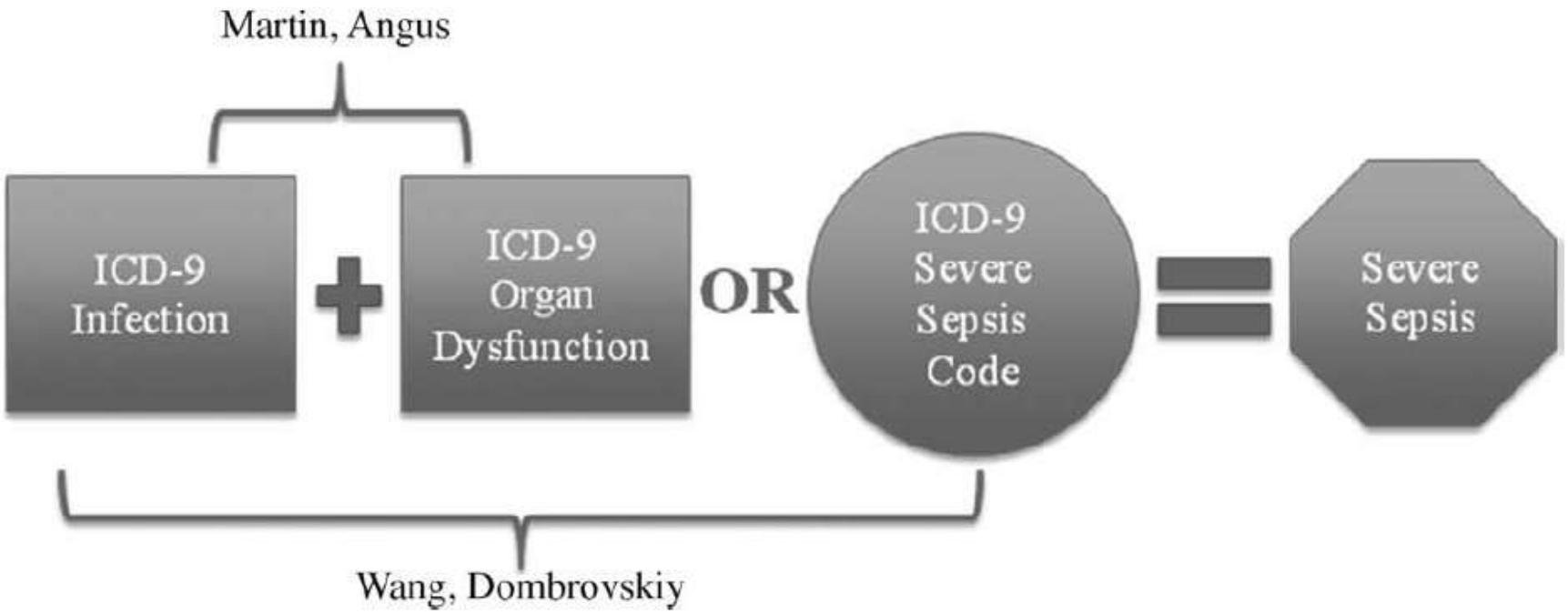
Barcelona. SPAIN

Outline

- Epidemiology of Sepsis.
- Time-to-treatment in Sepsis.
- Interventions. Sepsis Code.

Epidemiology of sepsis

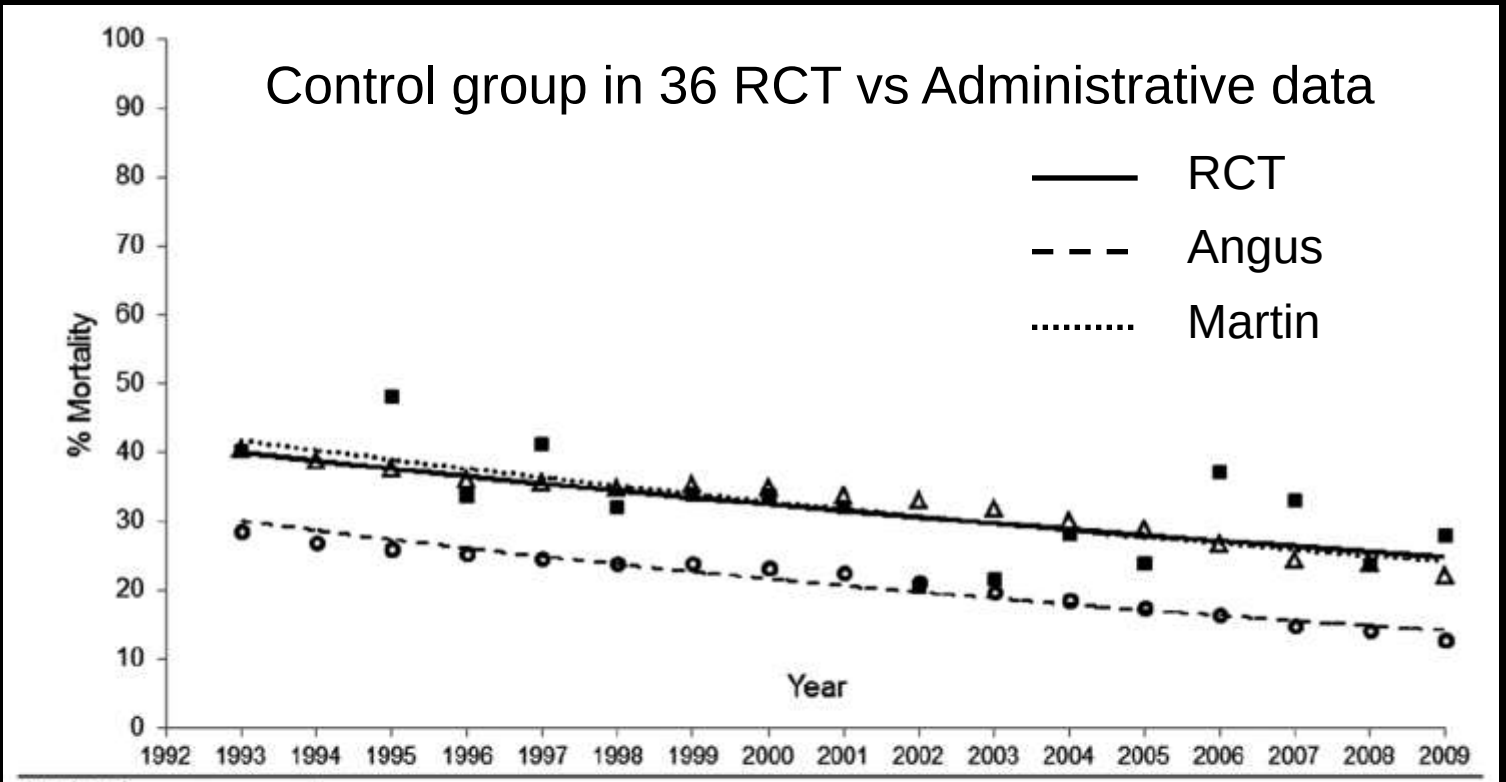
Use of Retrospective Administrative Data



Two Decades of Mortality Trends Among Patients With Severe Sepsis: A Comparative Meta-Analysis

DOI: 10.1097CCM.0000000000000026

Elizabeth K. Stevenson, MD, MS[1,2]; Amanda R. Rubenstein, MD[3]; Gregory T. Radin, MD[3]; Renda Soylemez Wiener, MD, MPH[1,2,4,5]; Allan J. Walkey, MD, MSc[1,2]



	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Number of Trial subjects	544	No trials	863	1682	1554	1148	97	882	1799	1670	537	648	91	509	545	834	400
Number of 'Angus' definition[a]	5.83	6.59	7.27	7.79	8.22	9.02	9.29	9.51	10.3	11.8	13.4	15.1	17.0	18.8	21.1	25.0	27.2
Number of 'Martin' definition[a]	2.07	2.33	2.59	2.90	3.12	3.36	3.48	3.55	3.94	4.49	5.13	6.09	6.90	7.91	8.89	10.2	10.8

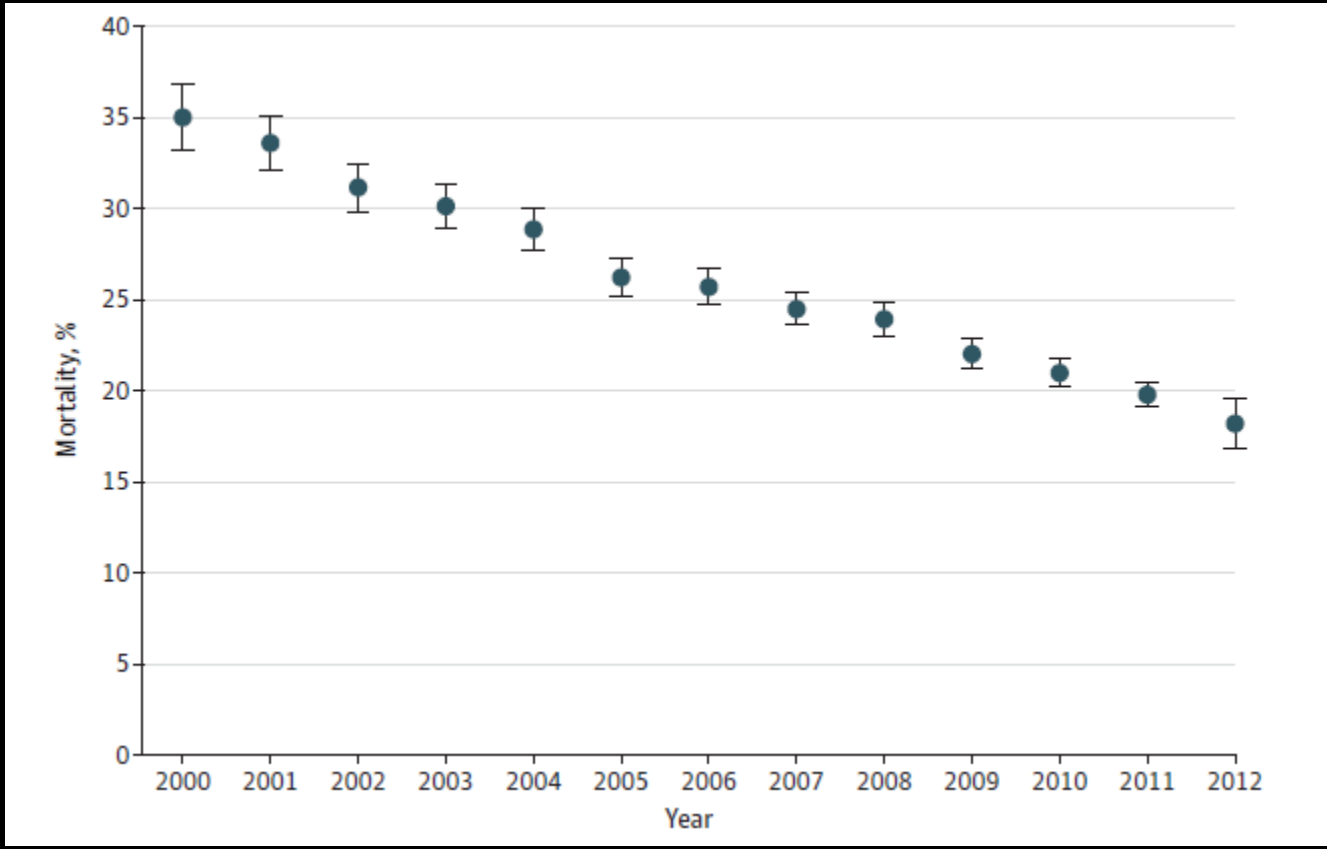
Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Mortality Related to Severe Sepsis and Septic Shock Among Critically Ill Patients in Australia and New Zealand, 2000-2012

Kirsi-Maija Kaukonen, MD, PhD, EDIC; Michael Bailey, PhD; Satoshi Suzuki, MD; David Pilcher, FCICM; Rinaldo Bellomo, MD, PhD

JAMA. doi:10.1001/jama.2014.2637
Published online March 18, 2014.

Australian and New Zealand Intensive Care Society adult ICU patient database



Mortality Reduction: 50%

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

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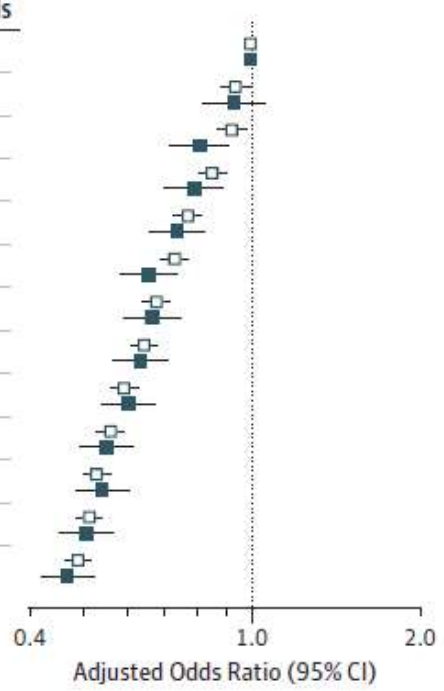
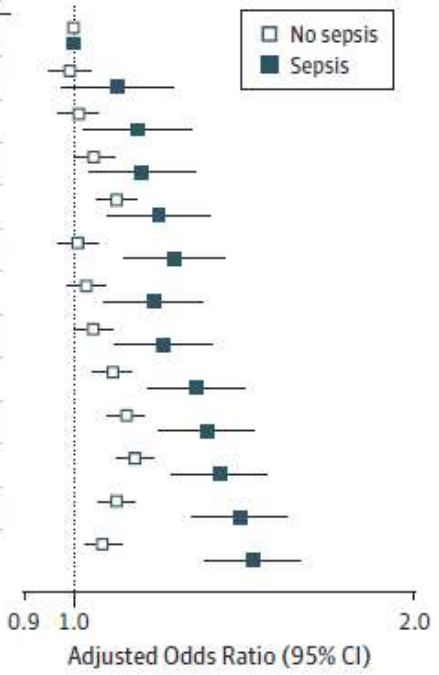
Australian and New Zealand Intensive Care Society adult ICU patient database

	2000			2012			Risk Reduction	
	No. of Events	No. of Patients	Mortality, % (95% CI)	No. of Events	No. of Patients	Mortality, % (95% CI)	Absolute	Relative
All patients with severe sepsis	949	2708	35.0 (33.2-36.8)	2300	12 512	18.4 (17.8-19.0)	16.7 (14.8-18.6)	47.5 (44.1-50.8)
Without comorbidities[b]	529	1800	29.4 (27.2-31.6)	1136	8110	14.0 (13.2-14.8)	15.4 (13.2-17.7)	52.3 (47.9-56.4)
With comorbidities[b]	420	908	46.3 (43.0-49.6)	1164	4402	26.4 (25.0-27.8)	19.8 (16.3-23.3)	42.8 (37.7-47.5)
Severe sepsis without shock	426	1411	30.2 (27.8-32.6)	815	5755	14.2 (13.2-15.2)	16.0 (13.5-18.6)	53.1 (48.1-57.6)
Septic shock	523	1297	40.3 (37.6-43.0)	1485	6757	22.0 (21.0-23.0)	18.3 (15.5-21.2)	45.5 (41.0-49.7)
Age, y								
≤44	98	443	22.1 (18.2-26.0)	130	1778	7.3 (6.1-8.5)	14.8 (11.0-19.1)	66.9 (58.0-74.0)
45-64	226	742	30.5 (27.2-33.8)	524	3660	14.3 (13.1-15.5)	16.1 (12.7-19.7)	53.0 (46.2-58.9)
65-84	537	1326	40.5 (38.0-43.0)	1260	5806	21.7 (20.7-22.7)	18.8 (16.0-21.7)	46.4 (41.9-50.6)
≥85	88	197	44.7 (37.6-51.8)	386	1268	30.4 (27.9-32.9)	14.2 (7.0-21.6)	31.9 (18.7-42.9)

Mortality Reduction > 50% in young and healthy

Year of ICU Admission	No. of Patients		A Mortality: No. of Events		B Discharged Home: No. of Events	
	Sepsis	No Sepsis	Sepsis	No Sepsis	Sepsis	No Sepsis
2000	2708	35014	949	4807	1371	26648
2001	3783	45000	1271	5855	1960	34223
2002	4668	51972	1455	6484	2486	39716
2003	5221	58393	1573	6996	2829	44674
2004	6375	65292	1841	7383	3462	49559
2005	6987	72220	1833	7825	3938	54588
2006	7627	75926	1961	7765	4238	57172
2007	8529	78297	2090	7844	4763	58521
2008	8797	77379	2106	7541	5003	57499
2009	10277	84842	2264	7943	5955	62986
2010	11367	93385	2386	8302	6743	69575
2011	12213	98045	2418	8535	7418	72459
2012	12512	100286	2300	8010	7699	74443



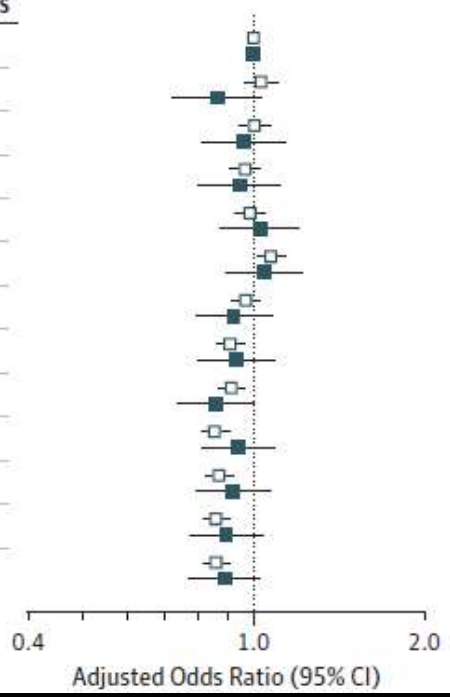


Mortality Reduction: +++

Discharged Home: ++

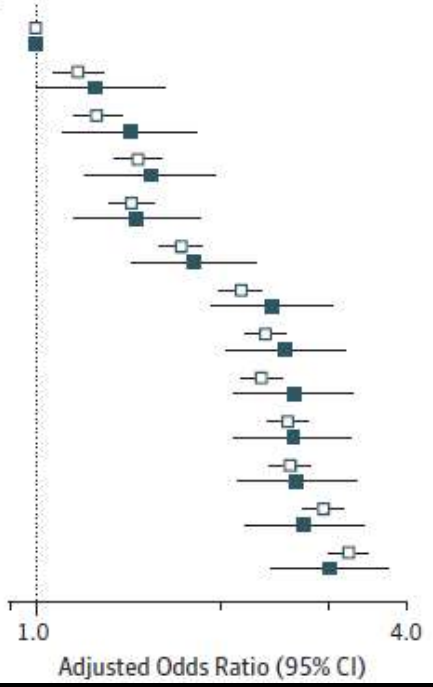
C Discharged to Another Hospital

Year of ICU Admission	No. of Patients		No. of Events	
	Sepsis	No Sepsis	Sepsis	No Sepsis
2000	2708	35014	278	2425
2001	3783	45000	374	3260
2002	4668	51972	479	3959
2003	5221	58393	537	4293
2004	6375	65292	706	5151
2005	6987	72220	800	6326
2006	7627	75926	841	6356
2007	8529	78297	1015	6731
2008	8797	77379	964	6940
2009	10277	84842	1236	7319
2010	11367	93385	1327	8186
2011	12213	98045	1401	8642
2012	12512	100286	1443	8733



D Discharged to Rehabilitation

No. of Events	
Sepsis	No Sepsis
110	1134
178	1662
248	1813
282	2430
366	3199
416	3481
587	4633
661	5201
724	5399
822	6594
911	7322
976	8409
1070	9100



Discharged to Another Hospital: -

Discharged to Rehabilitation: +++

Evolution of Sepsis care and mortality in Spain

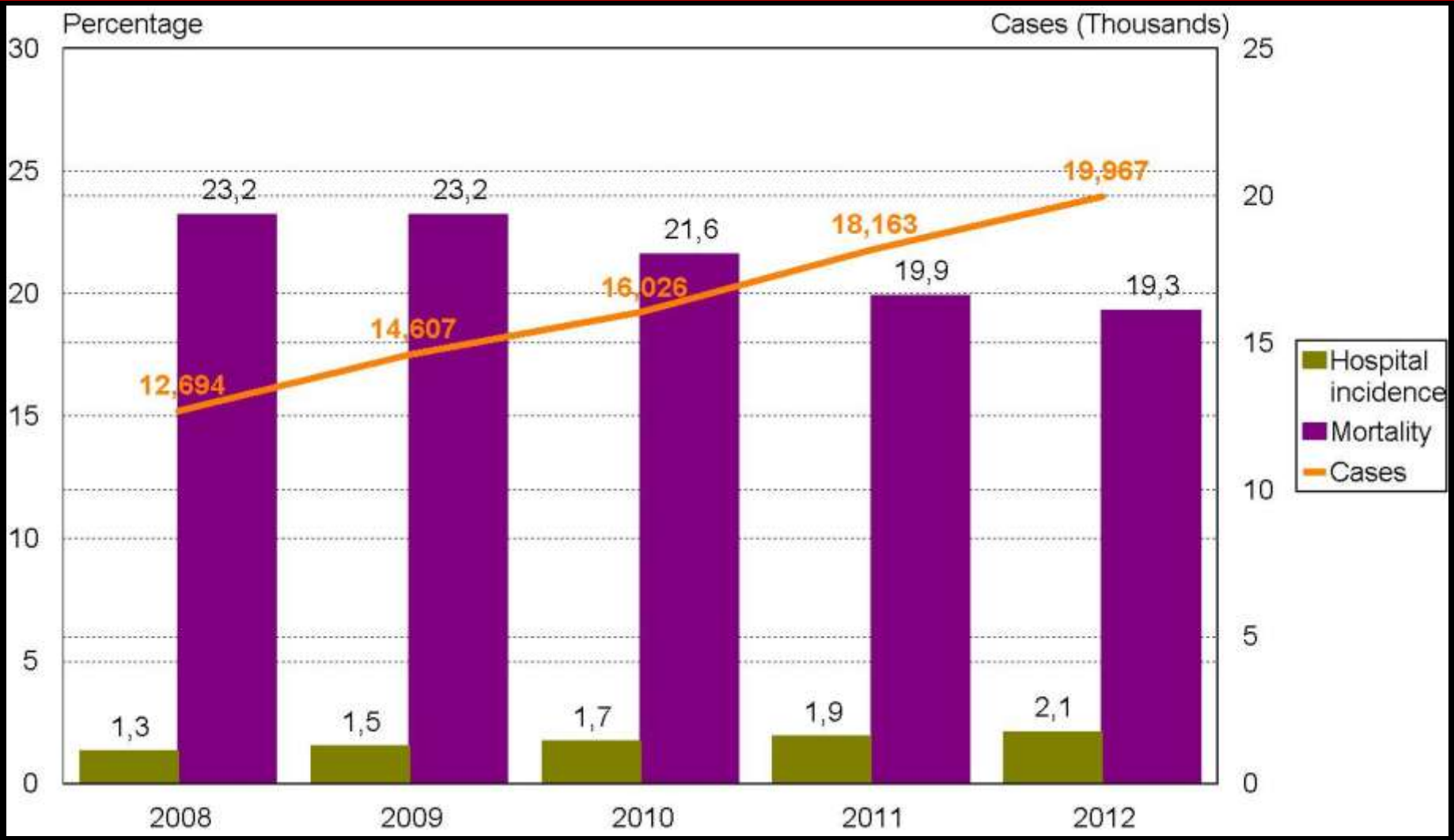
- 42 ICUs in Spain.
- All episodes of severe sepsis or septic shock in two periods of time.
  - 2 months in 2005, before EDUSEPSIS intervention.
  - 3 months in 2011, before ABISS intervention.
- 2011 patients were:
  - Older: 62.1±16.7 vs 64.9±14.9 years; p=0,023
  - More severe: APACHE II 20.7±7.2 vs 22.4±7.9; p=0,001

Evolution of Sepsis Mortality in Spain

Adjusted mortality: OR 0.638 (0.49-0.831); *p*=0,001

Evolución Mortalidad Sepsis Grave

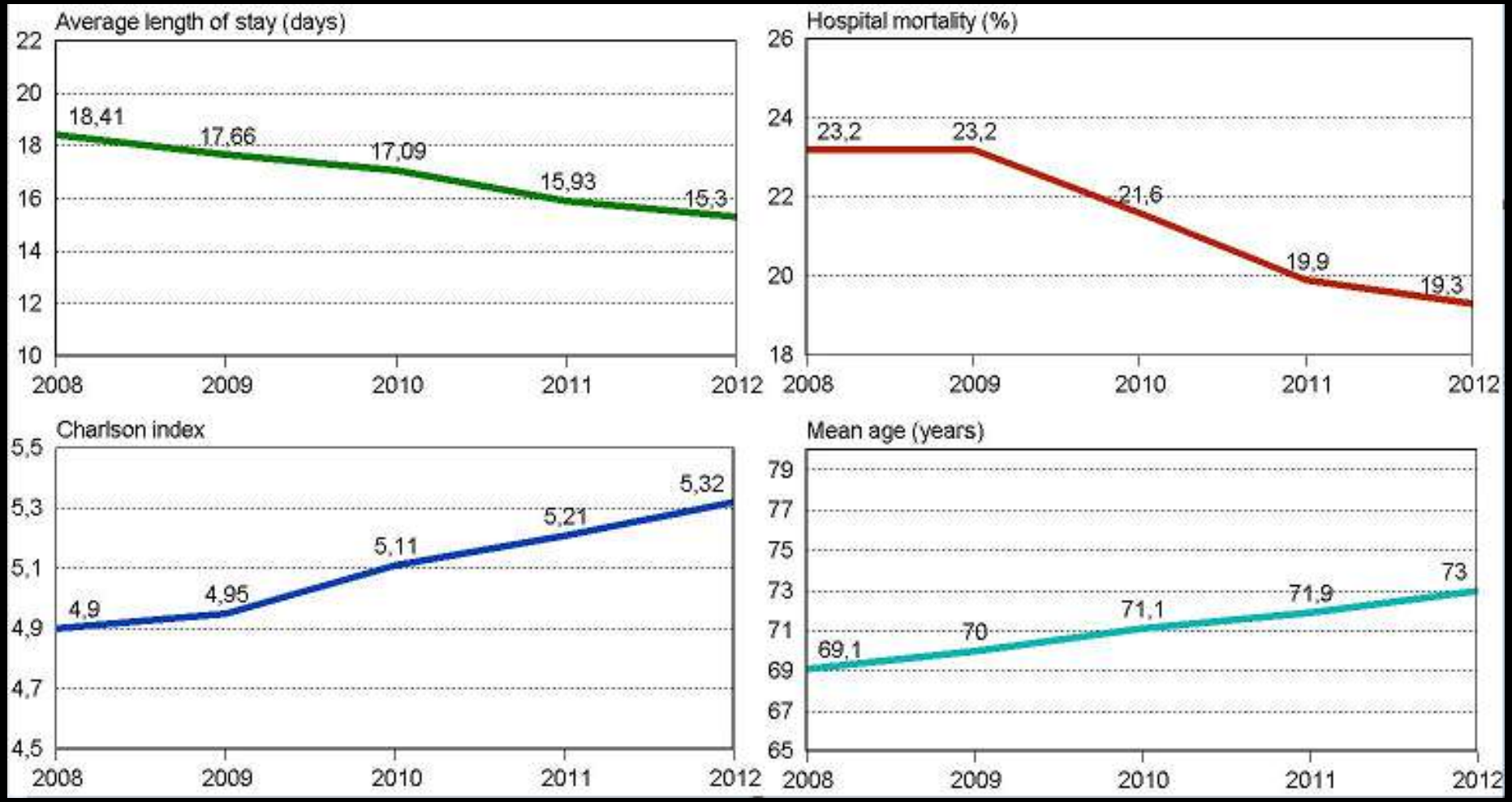
CMBD Cataluña



Ferrer R et al. SCCM Congress 2014

Evolución Mortalidad Sepsis Grave

CMBD Cataluña



Ferrer R et al. SCCM Congress 2014

Outline

- Epidemiology of Sepsis.
- Time-to-treatment in Sepsis.
- Sepsis Code.
- Cost-effectiveness.

SEVERE ANTI-INFLAMMATORY RESPONSE: HARMFUL

MODERATED ANTI-INFLAMMATORY RESPONSE:BENEFITIAL

Immuno-paralysis

ENDOTOXIN (PAMP)

MACROPHAGE

TLR-4 (PRR)

ANTI-INFLAMMATORY CYTOKINES IL-10, IL-11…

Apoptosis

TNFα

LYMPHOCYTES

↑ Treg %

LIPID MEDIATOR FACTORS PG, LEUCOTRIENS…

PAF

TISSUE FACTOR

PRO-INFLAMMATORY CYTOKINES (IL-1, IL-6, TNFα) HMGB1 COMPLEMENT ACTIVATION

CORTISOL CATECHOLAMINES VASOPRESSIN GLUCAGON

↑ VO_2

↑ DO_2

↑ PLATELET AGGREGATION

PAI-1 ↓ FIBRINOLISIS

THROMBIN ↑ COAGULATION

ENDOTHELIUM NEUTROPHILS

ANTINFECTIOUS RESPONSE

DIC COAGULOPATHY

NITRIC OXIDE

VASODILATATION HYPOTENSION MYOCARDIAL DYSFUNCTION

MICROVASCULAR DYSFUNCTION

CAPILARY LEAK INTERSTICIAL EDEMA

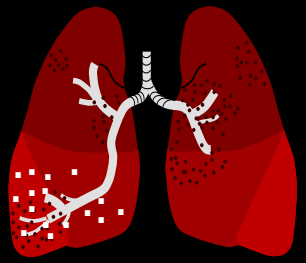
↓ DO_2

↓ VO_2, Cell Death, Multi-organ failure

MODERATED PRO-INFLAMMATORY RESPONSE: BENEFICIAL

SEVERE PRO-INFLAMMATORY RESPONSE: SEPTIC SHOCK

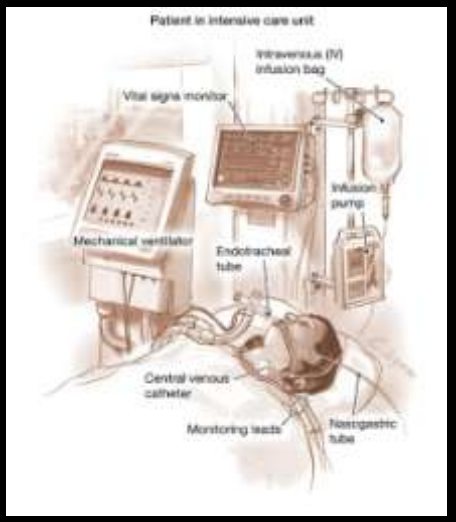
Stages of sepsis



Infection

↑ Microvascular Dysfunction

↑ Tissue dysoxia

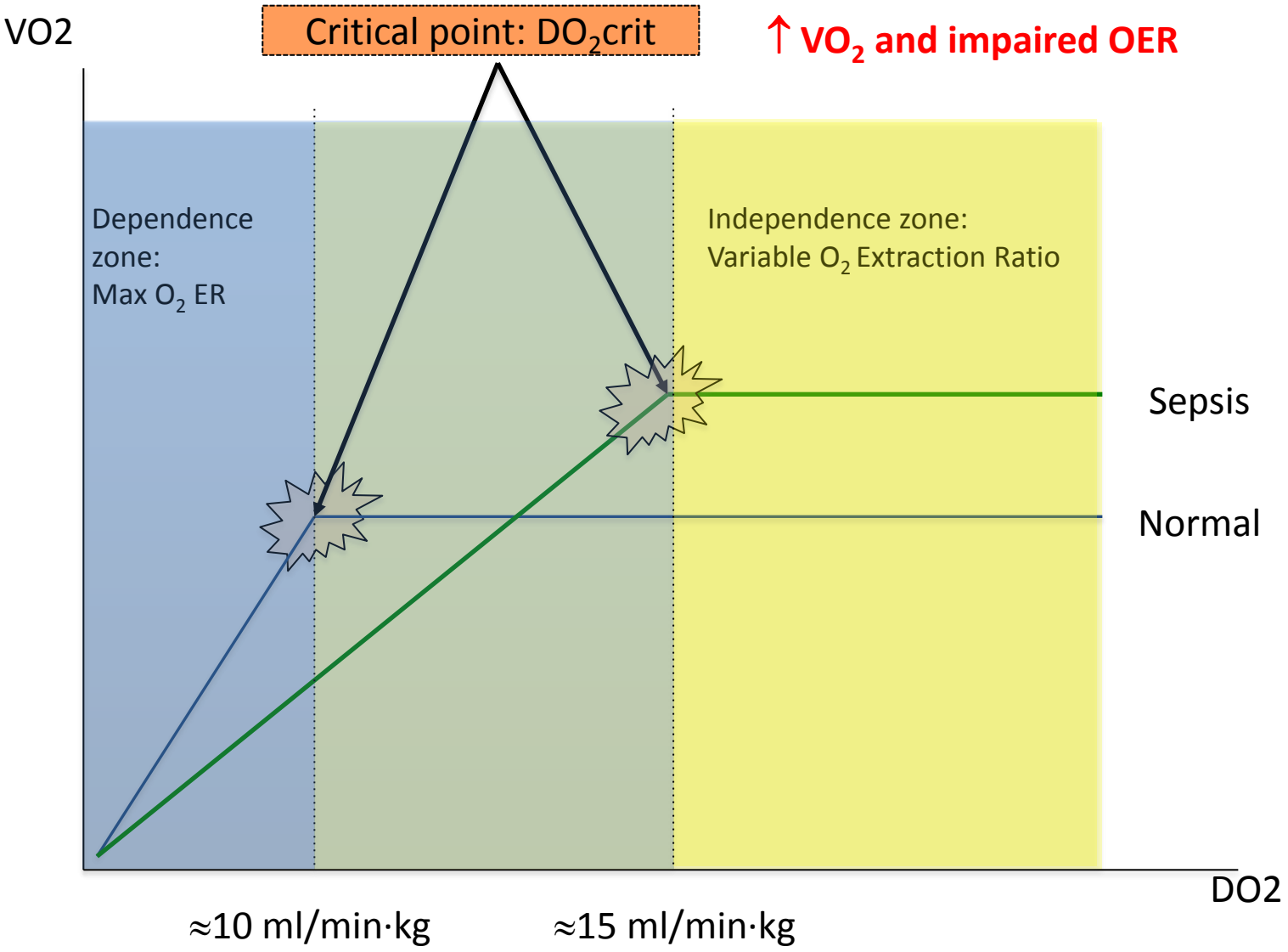


Infection → **SIRS: Sepsis** → **Severe Sepsis** → **Septic Shock** → **MODS**

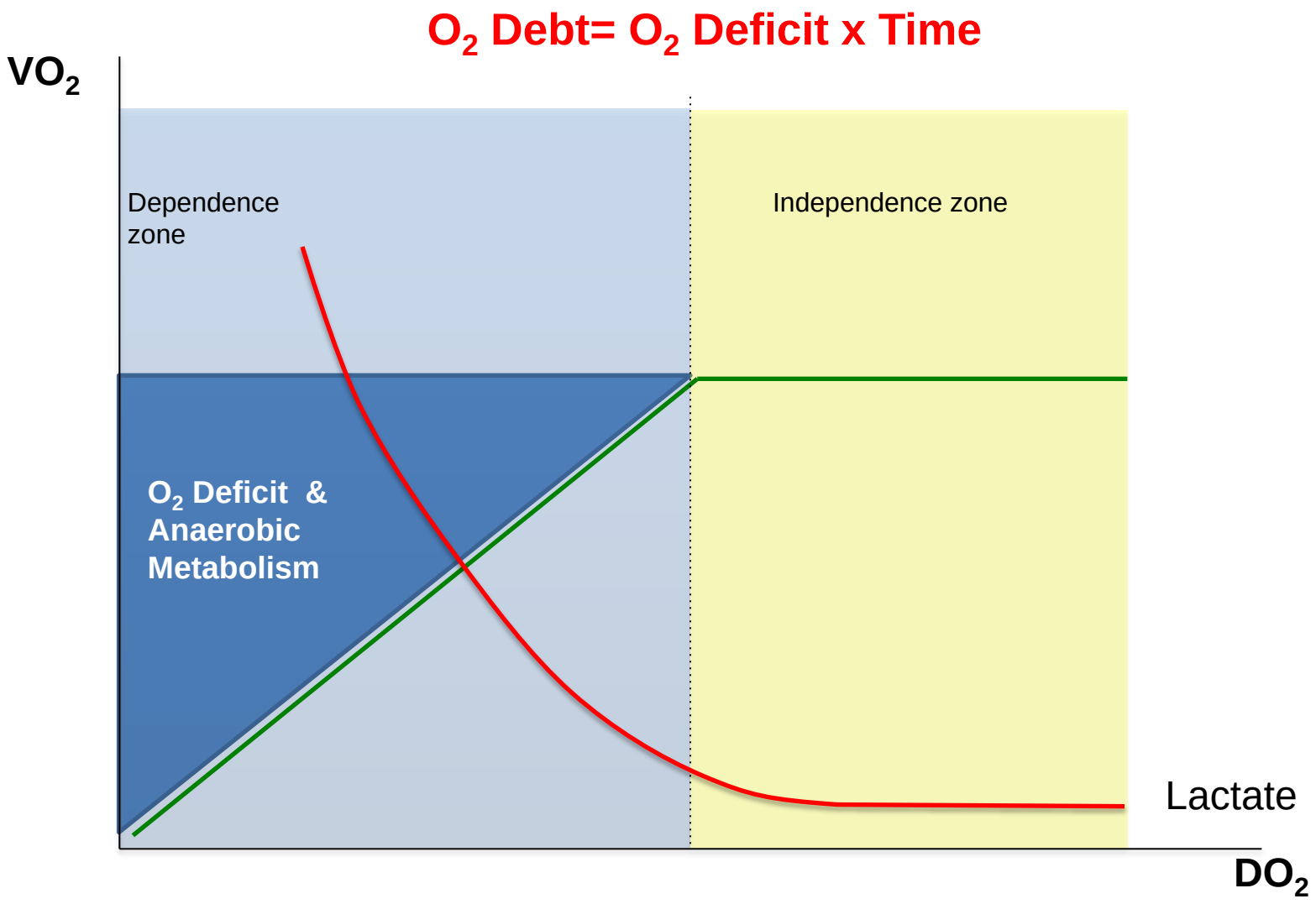
Time is Tissue

Adapted from Bone RC, Balk RA, Cerra FB et al. *Chest.* 1992;101:1644-55.

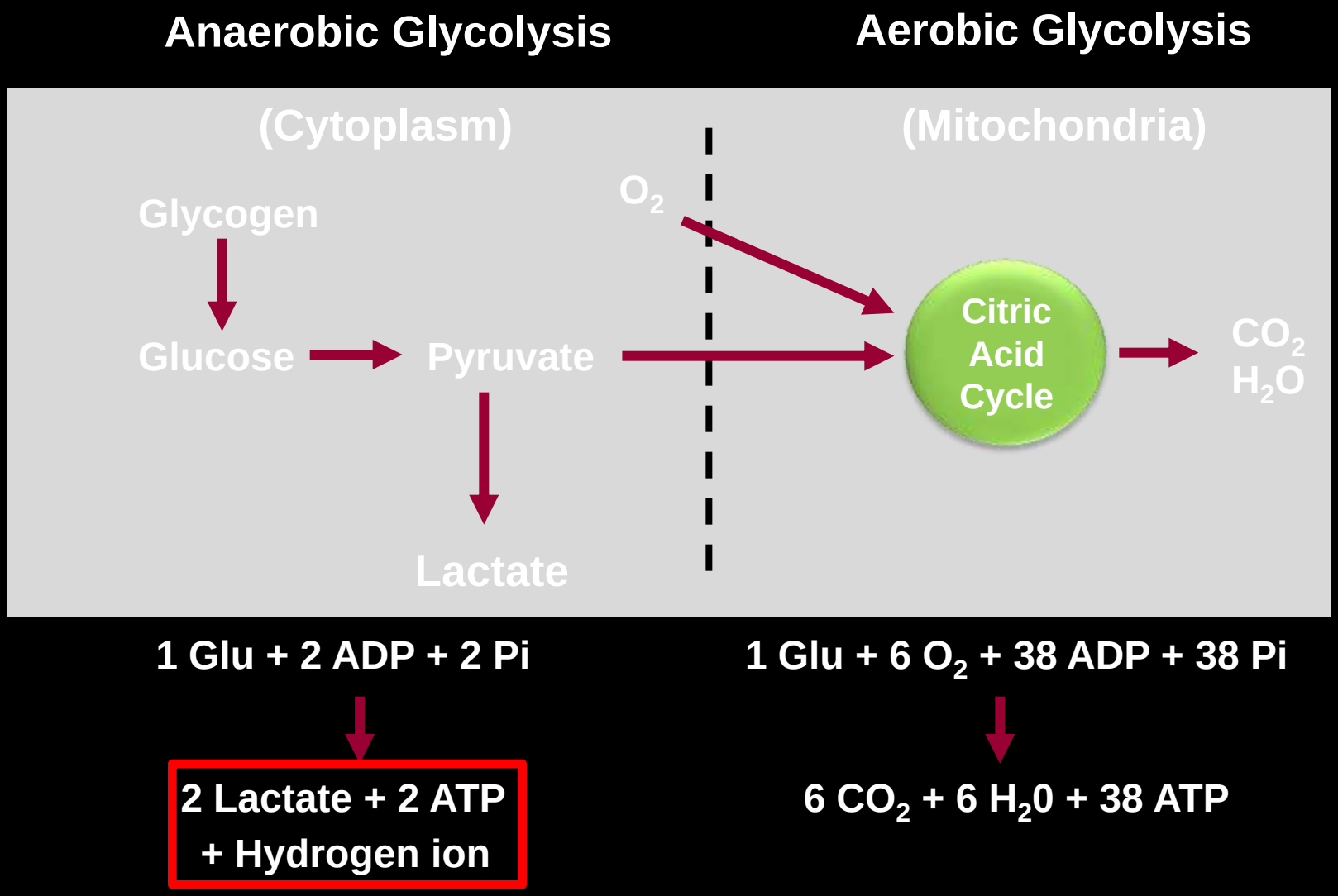
The biphasic VO_2 – DO_2 model



VO_2 – DO_2 model: O_2 Debt



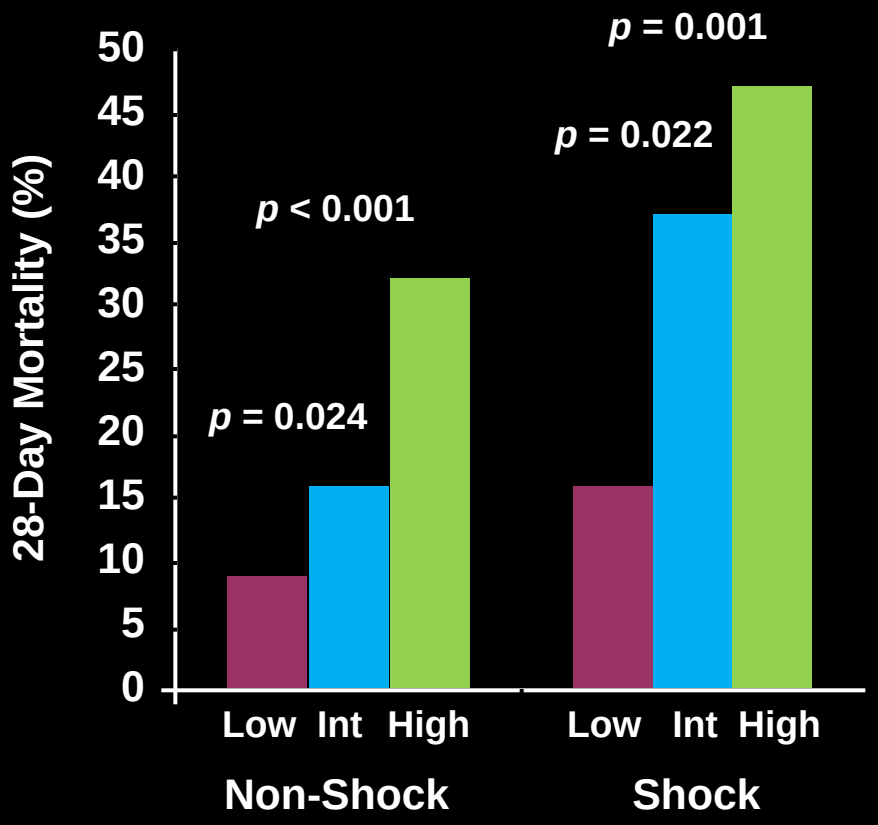
Markers of dysoxia: **Lactate**



Mizock BA, Falk JL. Crit Care Med. 1992;20:80-95.

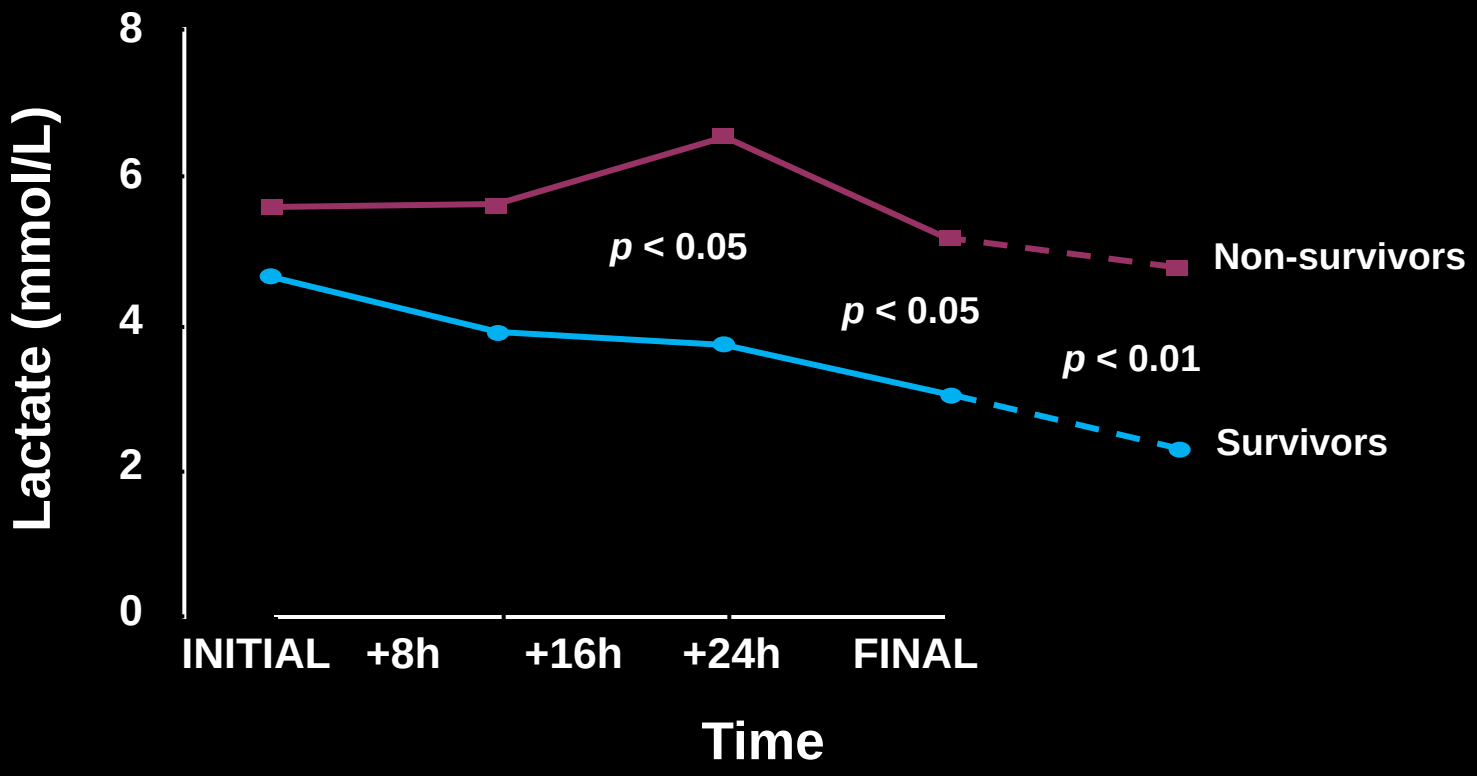
Serum Lactate and Mortality in Severe Sepsis

High initial serum lactate associated with ↑ mortality regardless of presence of shock (hypotension despite fluid resuscitation).



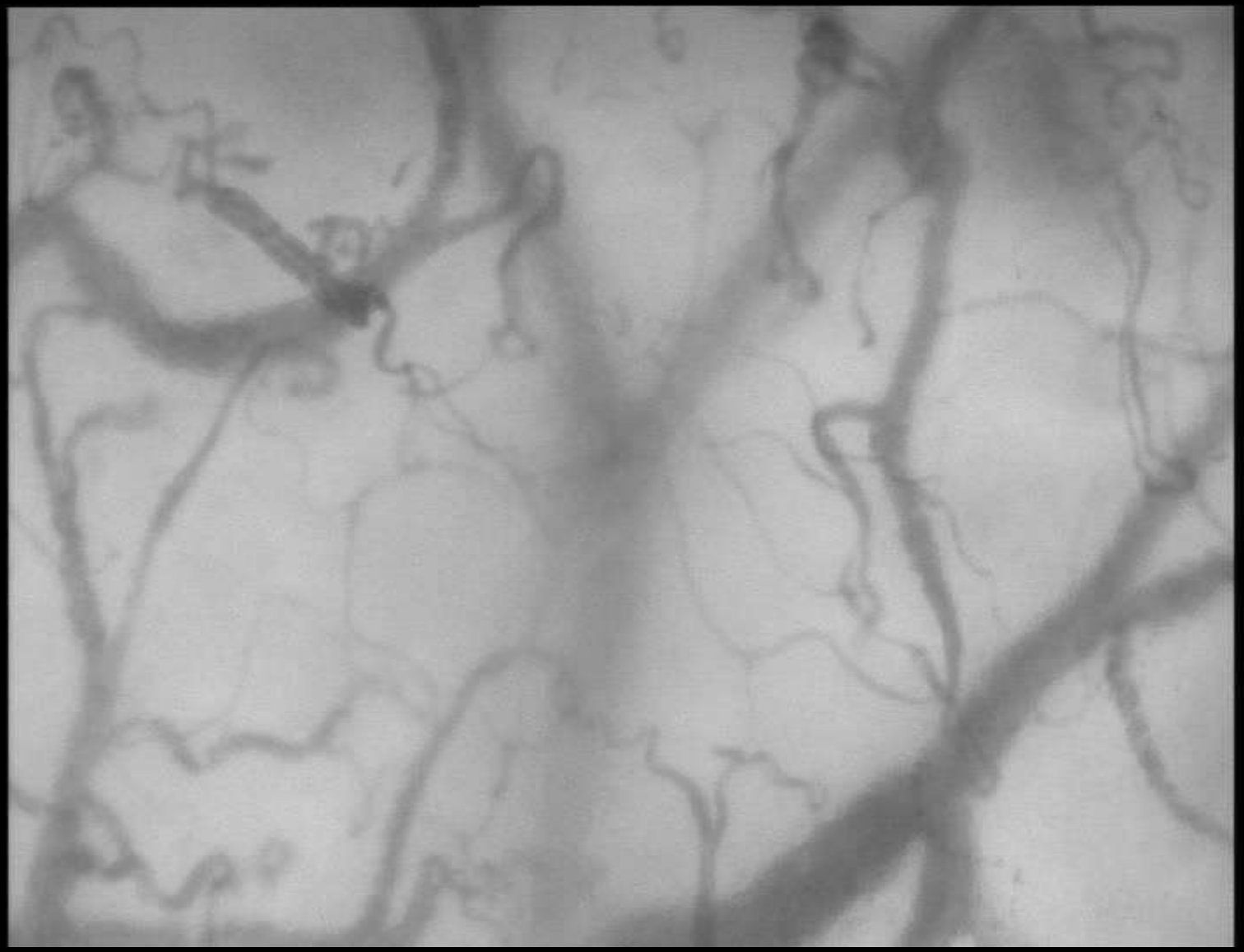
Mikkelsen ME, Miltiades AN, Gaieski DF et al. *Crit Care Med.* 2009;37:1670-7.

Improving Lactate: a Good Prognostic Sign



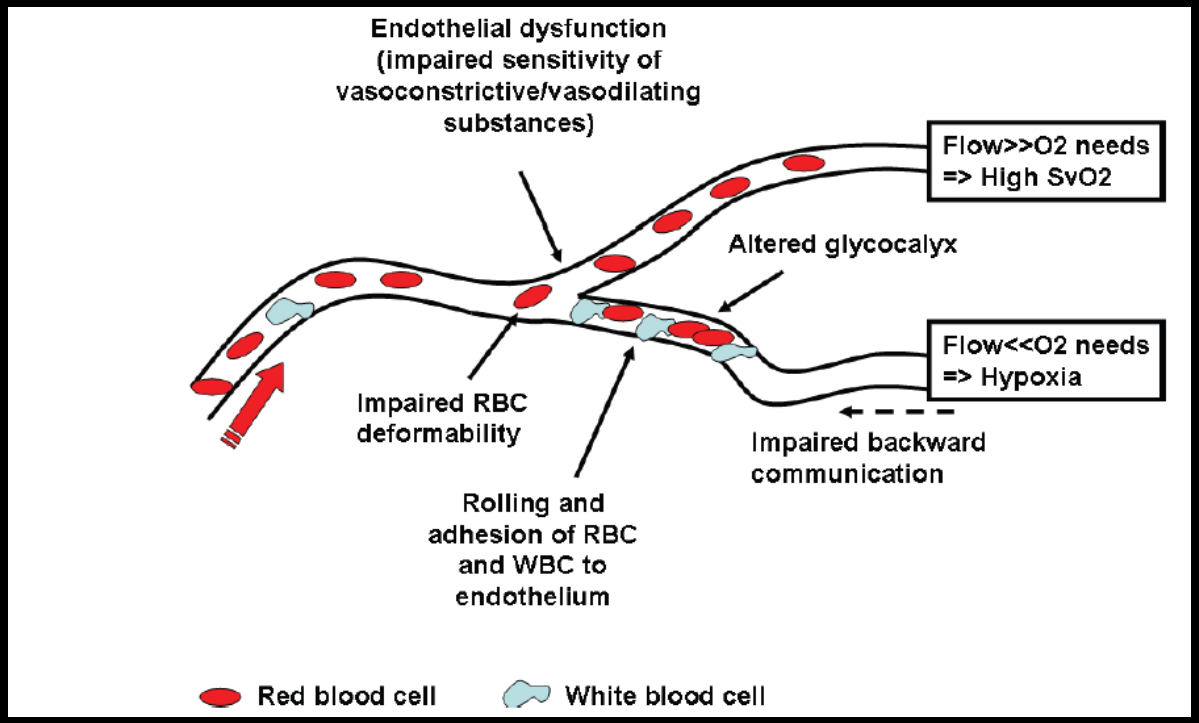
Bakker J, Gris P, Coffernils M et al. *Am J Surg*. 1996;171:221-6.

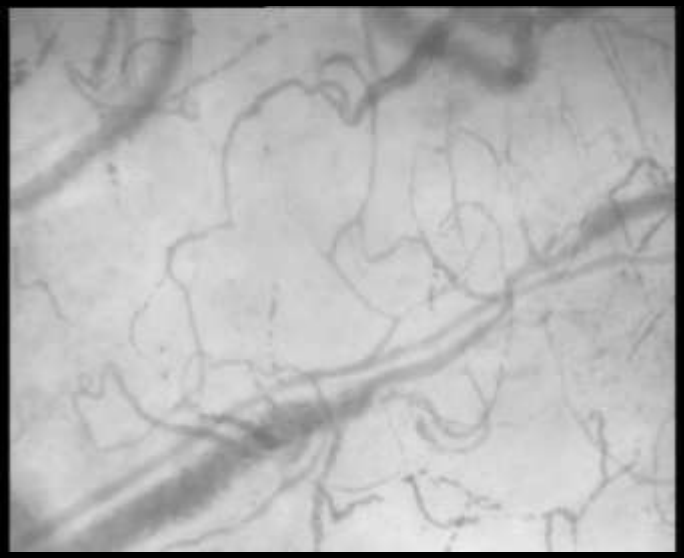
VO_2 and alteration of microvascular flow



VO_2 and alteration of microvascular flow

Principal mechanisms implicated in the development of microcirculatory alterations





↓ Capillary density
↑ number of stopped-flow and intermittent-flow capillaries

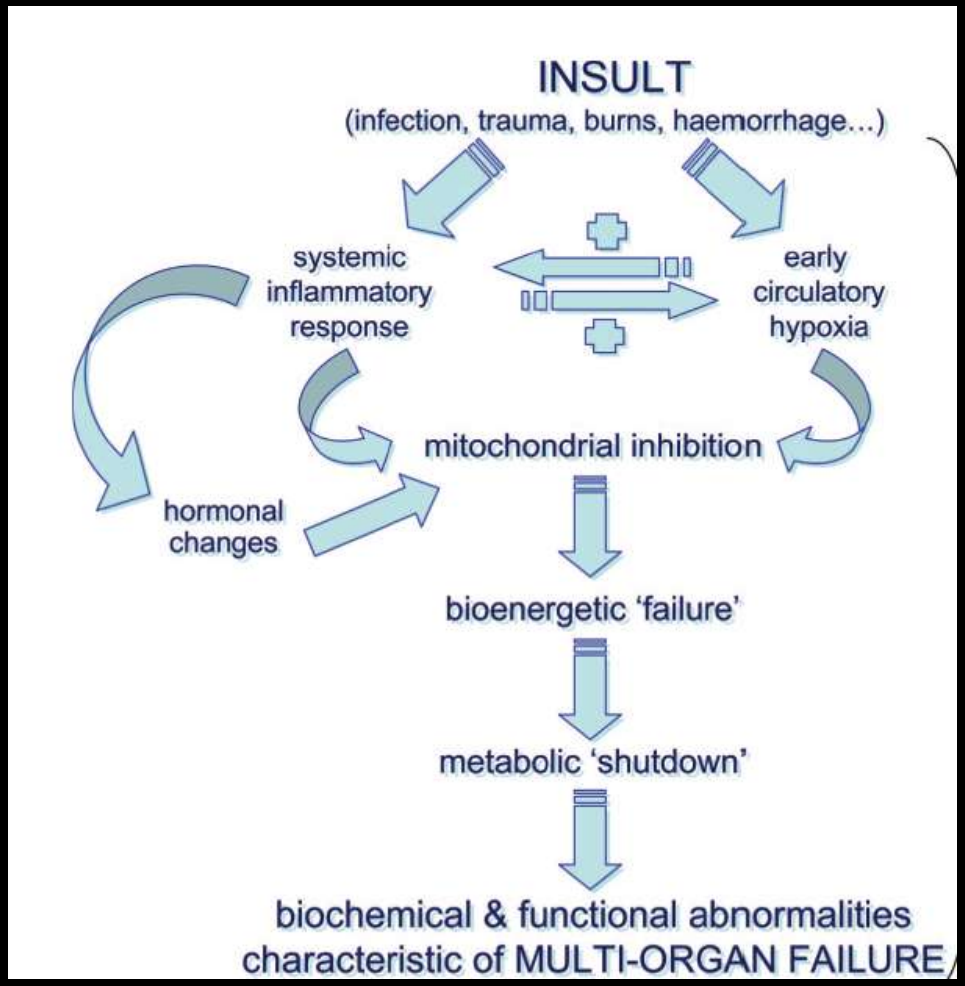
↓ surface for O_2 exchange

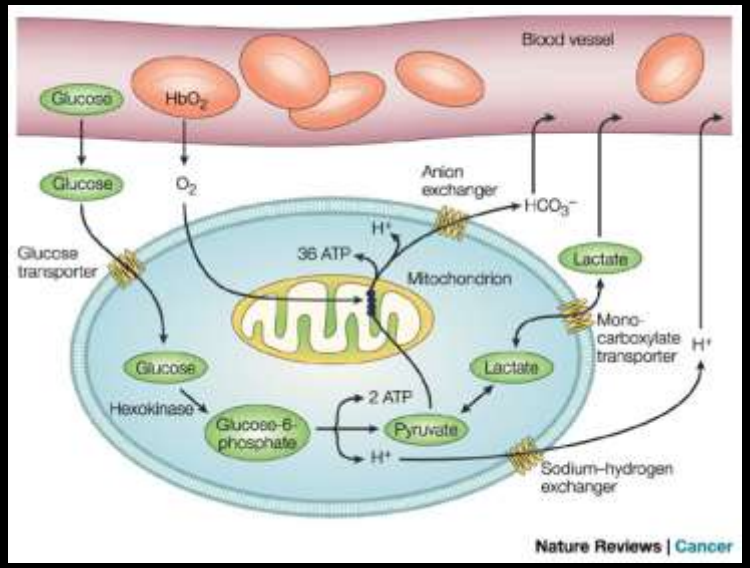
De Backer et al. Annals of Intensive Care 2011

Metabolic failure

Mervyn Singer, MD

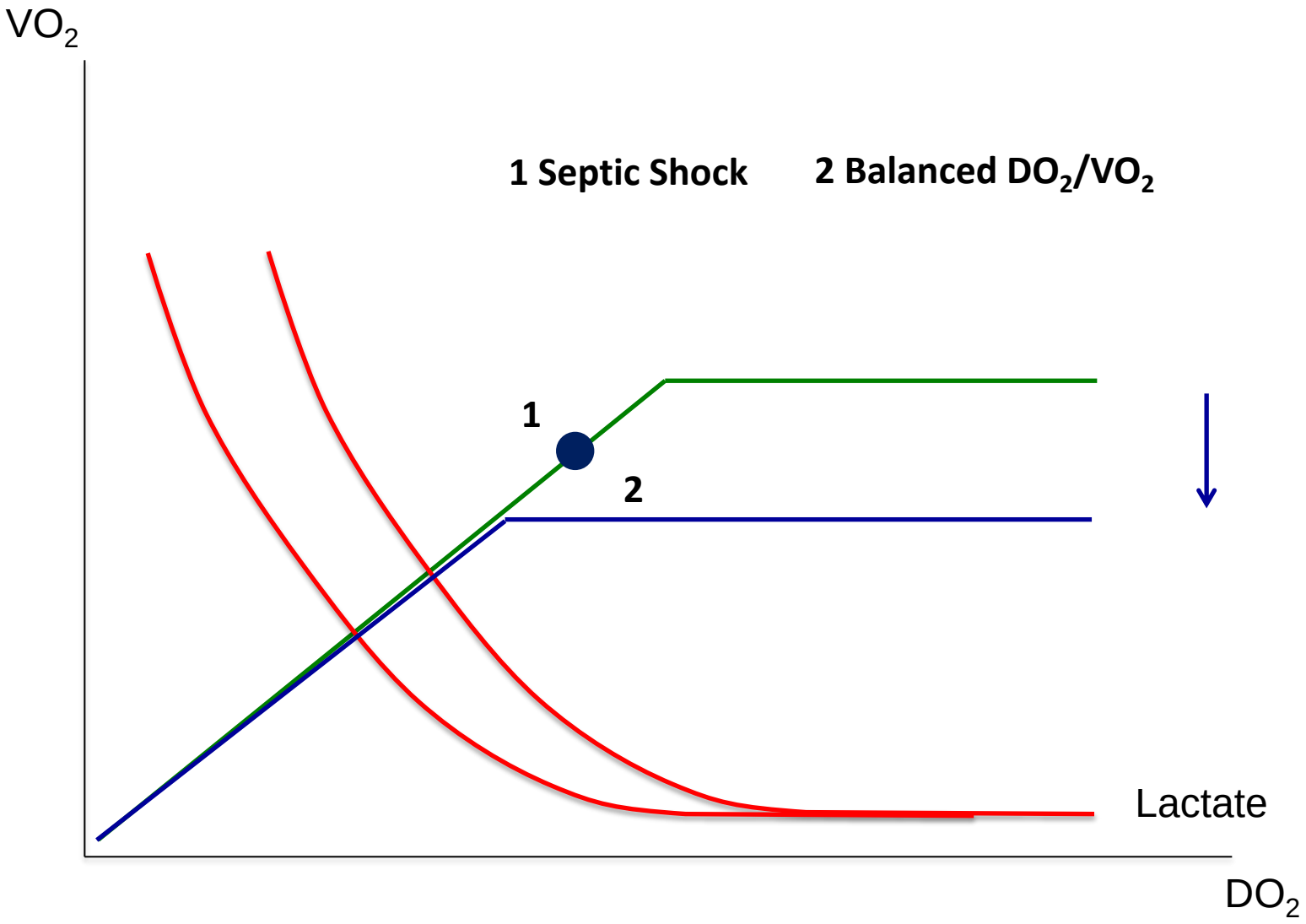
Crit Care Med 2005 Vol. 33, No. 12





Treatment strategies: balanced DO_2/VO_2

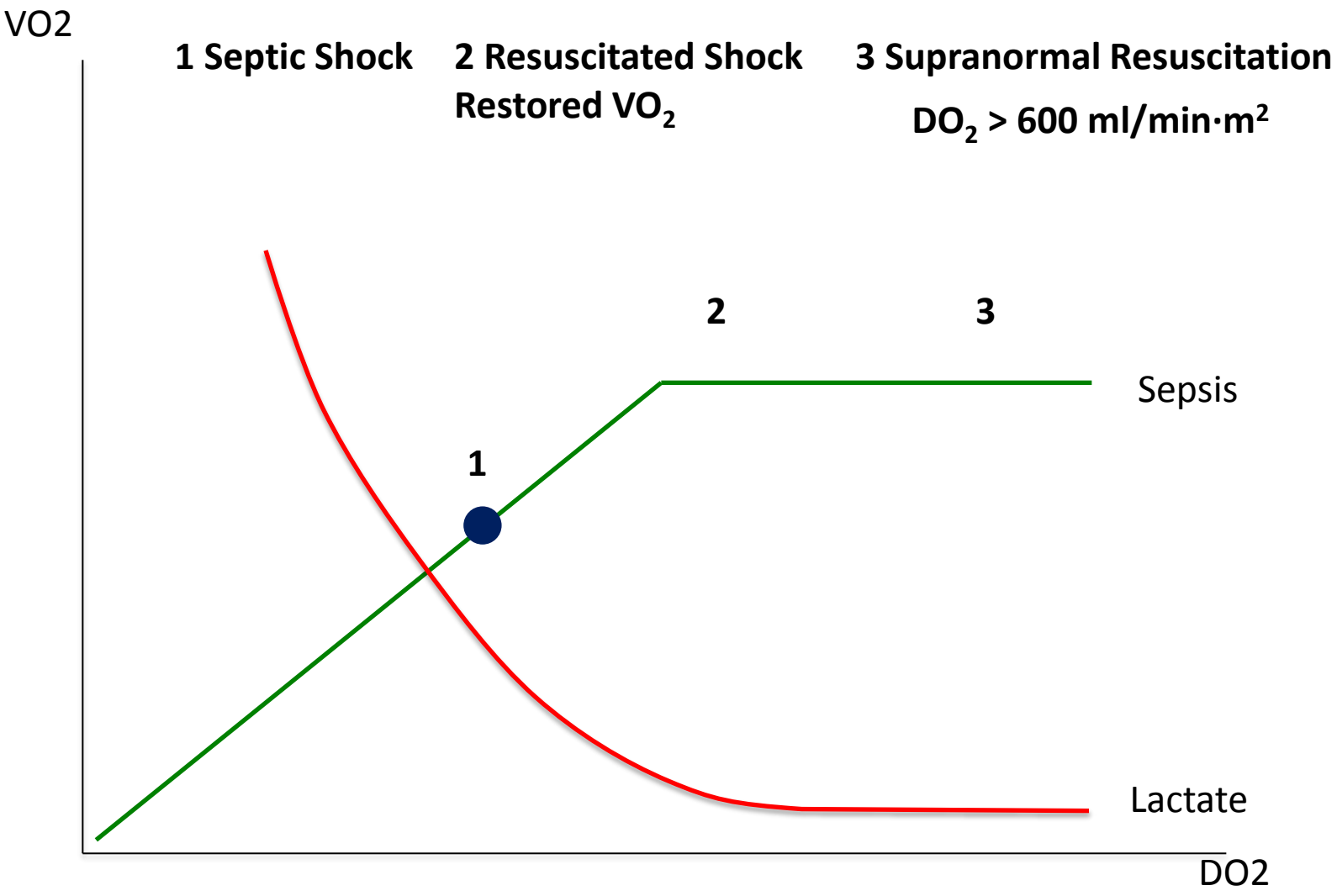
Decrease VO_2



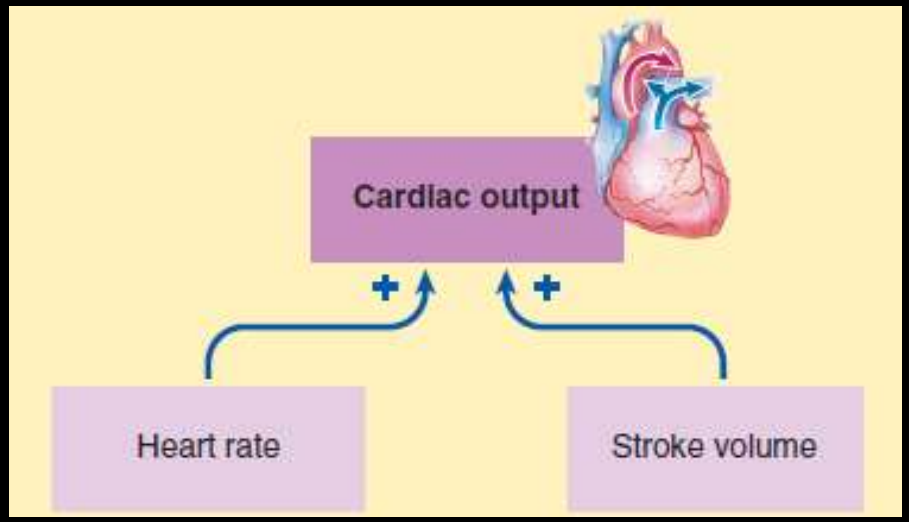
Decrease VO_2

- Infection control: Adequate empirical antibiotics and Source Control.
- Normotermia (or hipotermia)
- Analgesia
- Mechanical Ventilation.
- Titrate minimun dose of Termogenic drugs like inotropes.

Increase DO_2



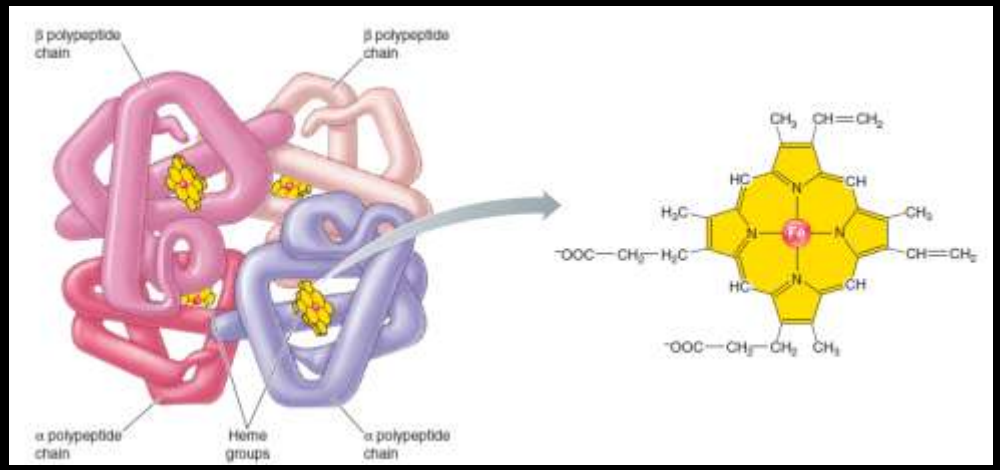
$DO_2 = CO \times CaO_2$



TREATMENTS

Fluids
Inotropes
Vasopressors

$CaO_2 \approx Hb \times 1.34 \times SaO_2/100$



O_2
PRBC

A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*

NEJM 2014

First 6H

RCT, 450 patients/group
Early Septic Shock

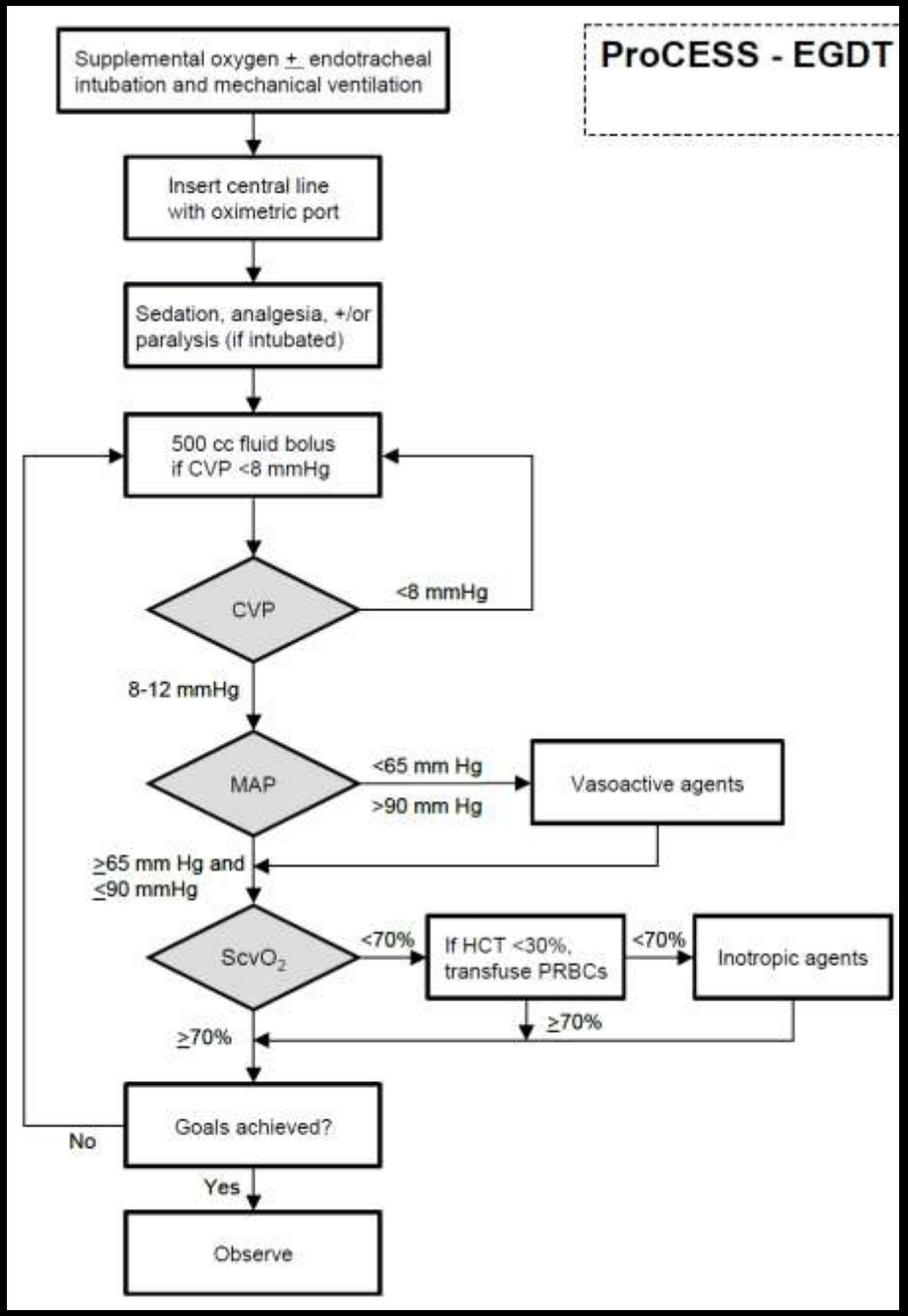
Protocol Based EGDT:

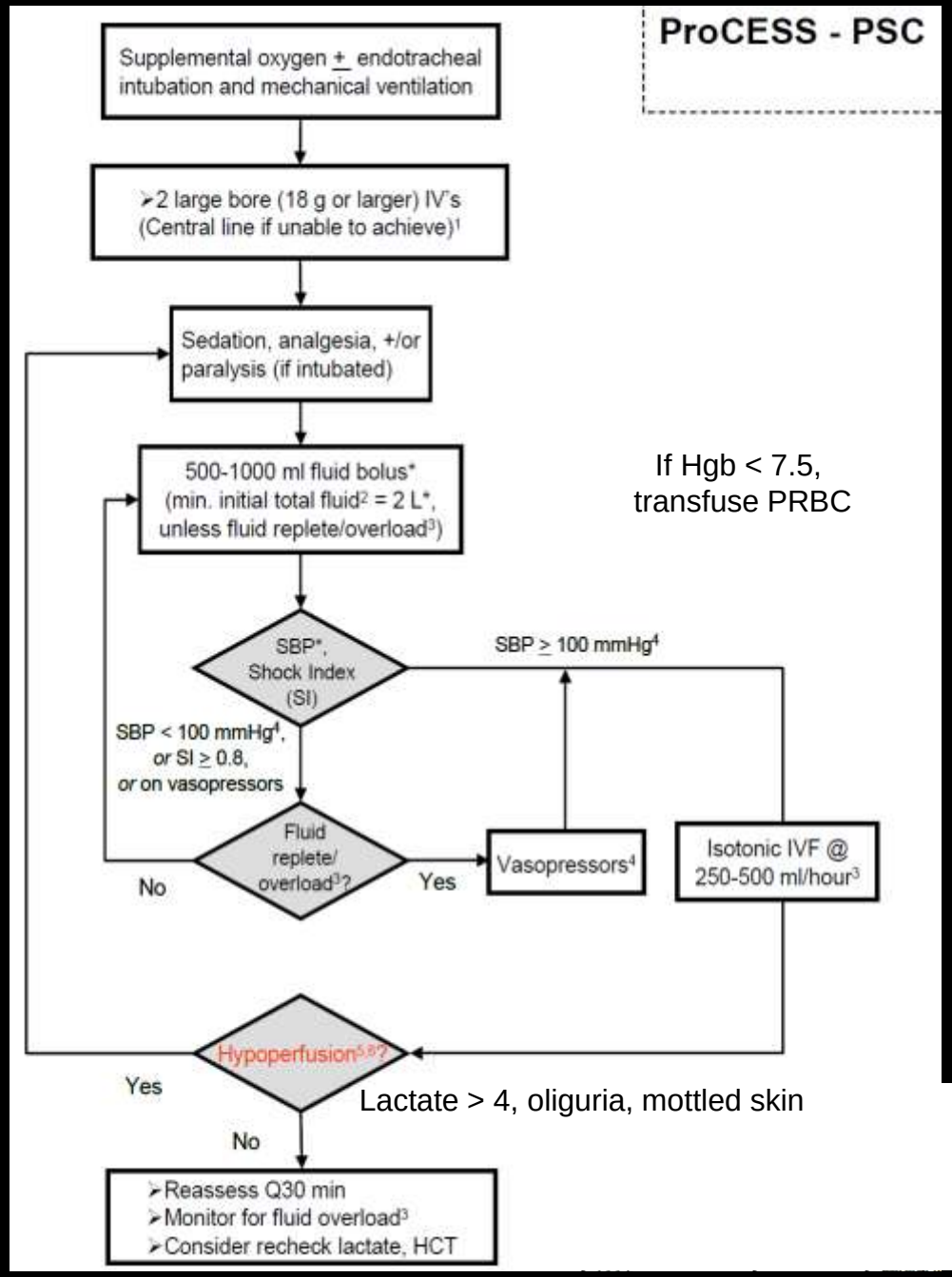
Requires Continous Central Venous Monitoring
Indications to ↑ DO_2 if $ScvO_2$ < 70%
Protocol similar to Rivers

Protocol Based Standard Therapy:

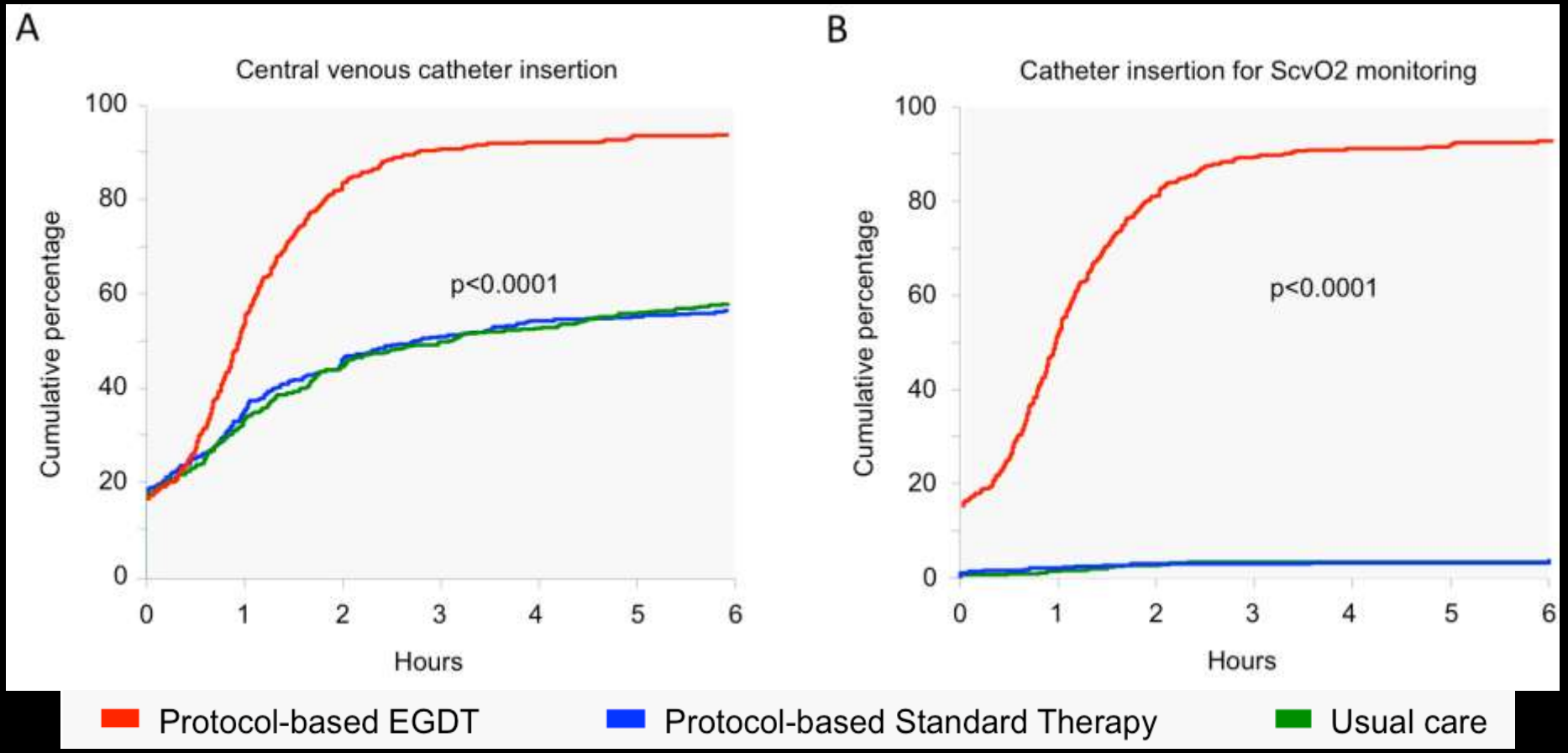
Protocolized resuscitation without CV monitoring
No special indications to ↑ DO_2

Usual care

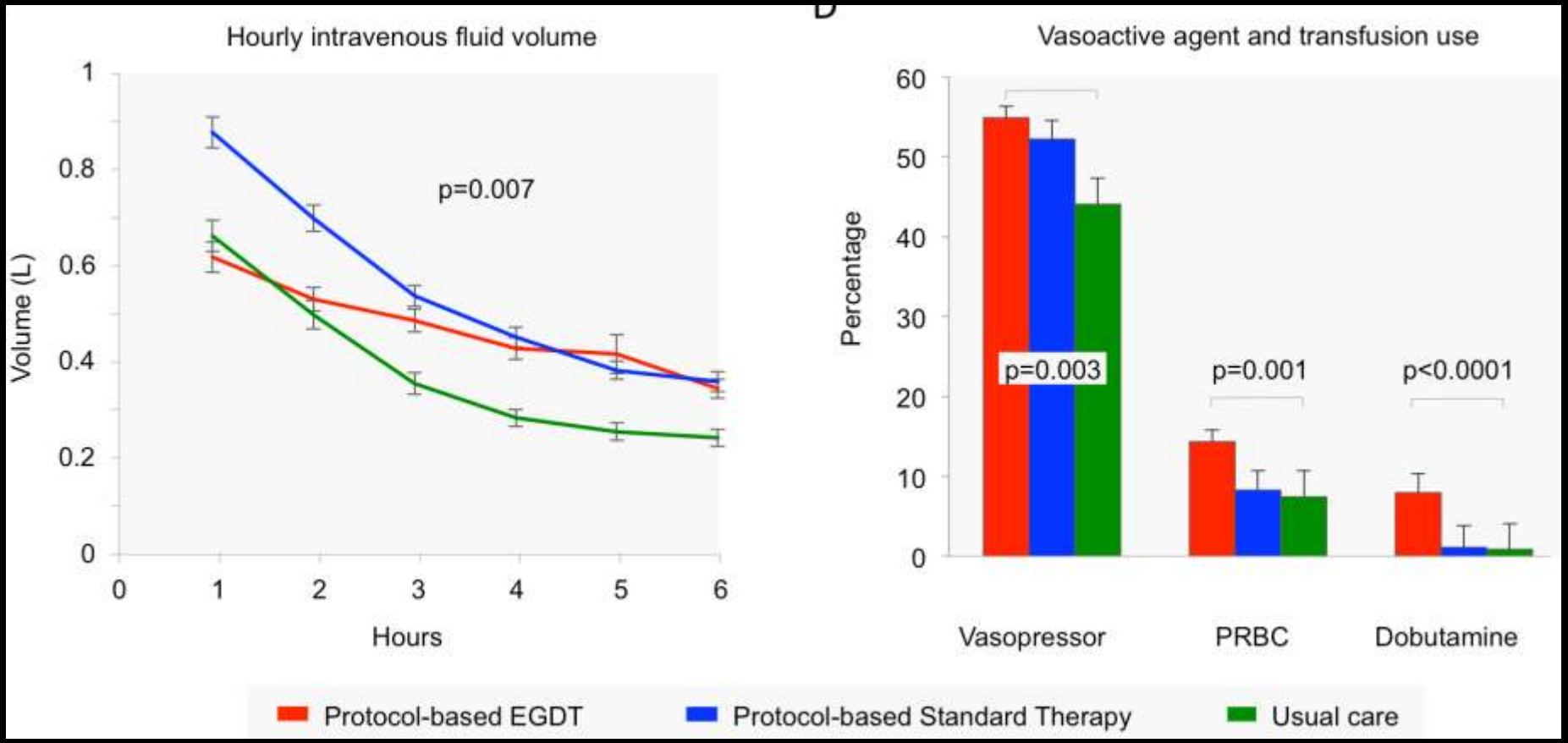

ProCESS - EGDT
Supplemental oxygen ± endotracheal intubation and mechanical ventilation
Insert central line with oximetric port
Sedation, analgesia, +/or paralysis (if intubated)
500 cc fluid bolus if CVP <8 mmHg
CVP
<8 mmHg
8-12 mmHg
MAP
<65 mm Hg
>90 mm Hg
Vasoactive agents
≥65 mm Hg and ≤90 mmHg
ScvO2
<70%
If HCT <30%, transfuse PRBCs
<70%
Inotropic agents
≥70%
≥70%
Goals achieved?
No
Yes
Observe


ProCESS - PSC
Supplemental oxygen ± endotracheal intubation and mechanical ventilation
➢2 large bore (18 g or larger) IV's (Central line if unable to achieve)[1]
Sedation, analgesia, +/or paralysis (if intubated)
500-1000 ml fluid bolus* (min. initial total fluid[2] = 2 L*, unless fluid replete/overload[3])
SBP*, Shock Index (SI)
SBP ≥ 100 mmHg[4]
SBP < 100 mmHg[4], or SI ≥ 0.8, or on vasopressors
Fluid replete/ overload[3]?
No
Yes
Vasopressors[4]
Isotonic IVF @ 250-500 ml/hour[3]
Hypoperfusion[5,6]?
Yes
No
➢Reassess Q30 min
➢Monitor for fluid overload[3]
➢Consider recheck lactate, HCT
If Hgb < 7.5, transfuse PRBC
Lactate > 4, oliguria, mottled skin

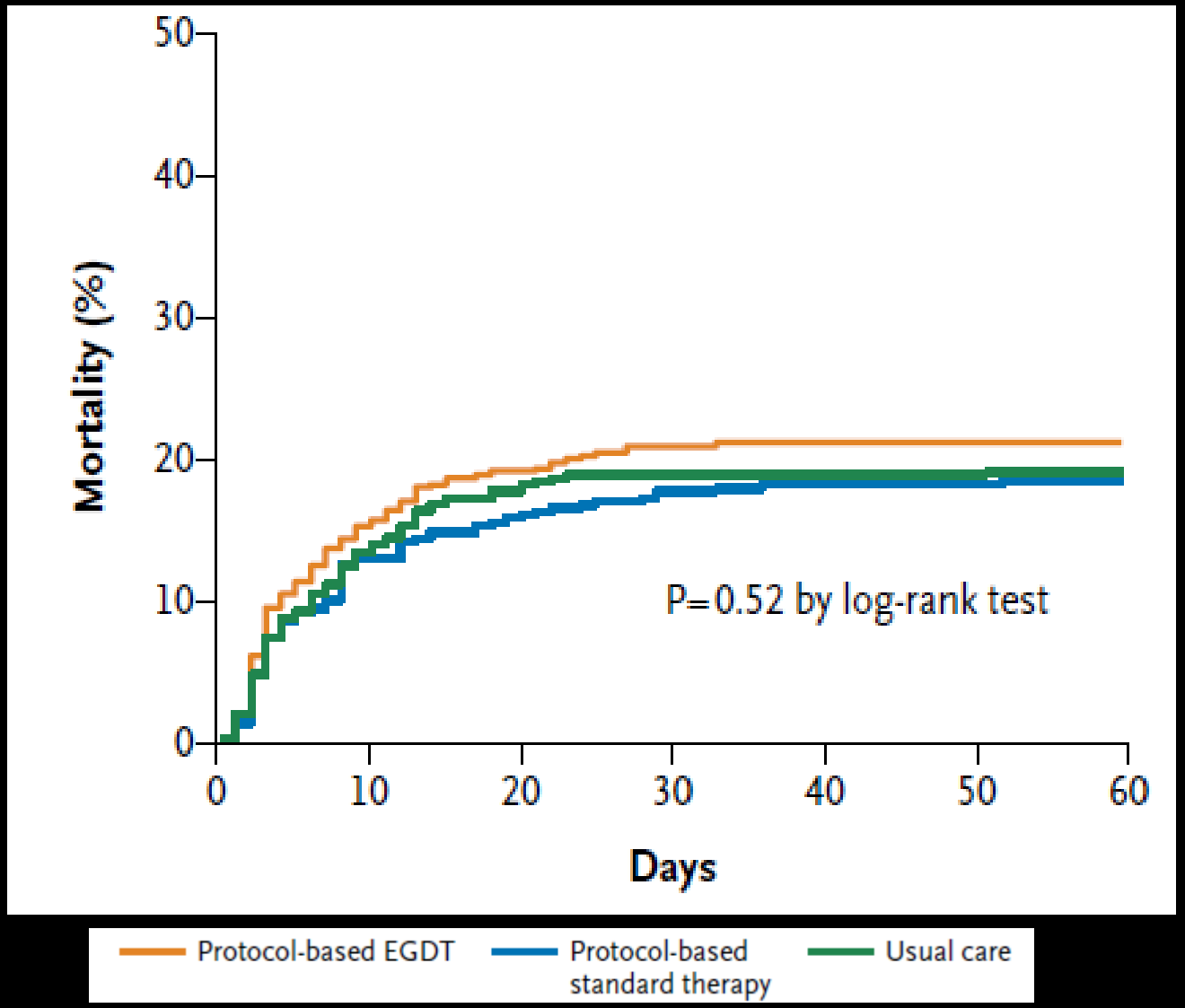
Monitorization



Treatments


Hourly intravenous fluid volume
Volume (L)
1
0.8
0.6
0.4
0.2
0
0
1
2
3
4
5
6
Hours
p=0.007
Vasoactive agent and transfusion use
Percentage
60
50
40
30
20
10
0
p=0.003
p=0.001
p<0.0001
Vasopressor
PRBC
Dobutamine
Protocol-based EGDT
Protocol-based Standard Therapy
Usual care

Outcome


Mortality (%)
50
40
30
20
10
0
0
10
20
30
40
50
60
Days
P=0.52 by log-rank test
Protocol-based EGDT
Protocol-based standard therapy
Usual care

Conclusions

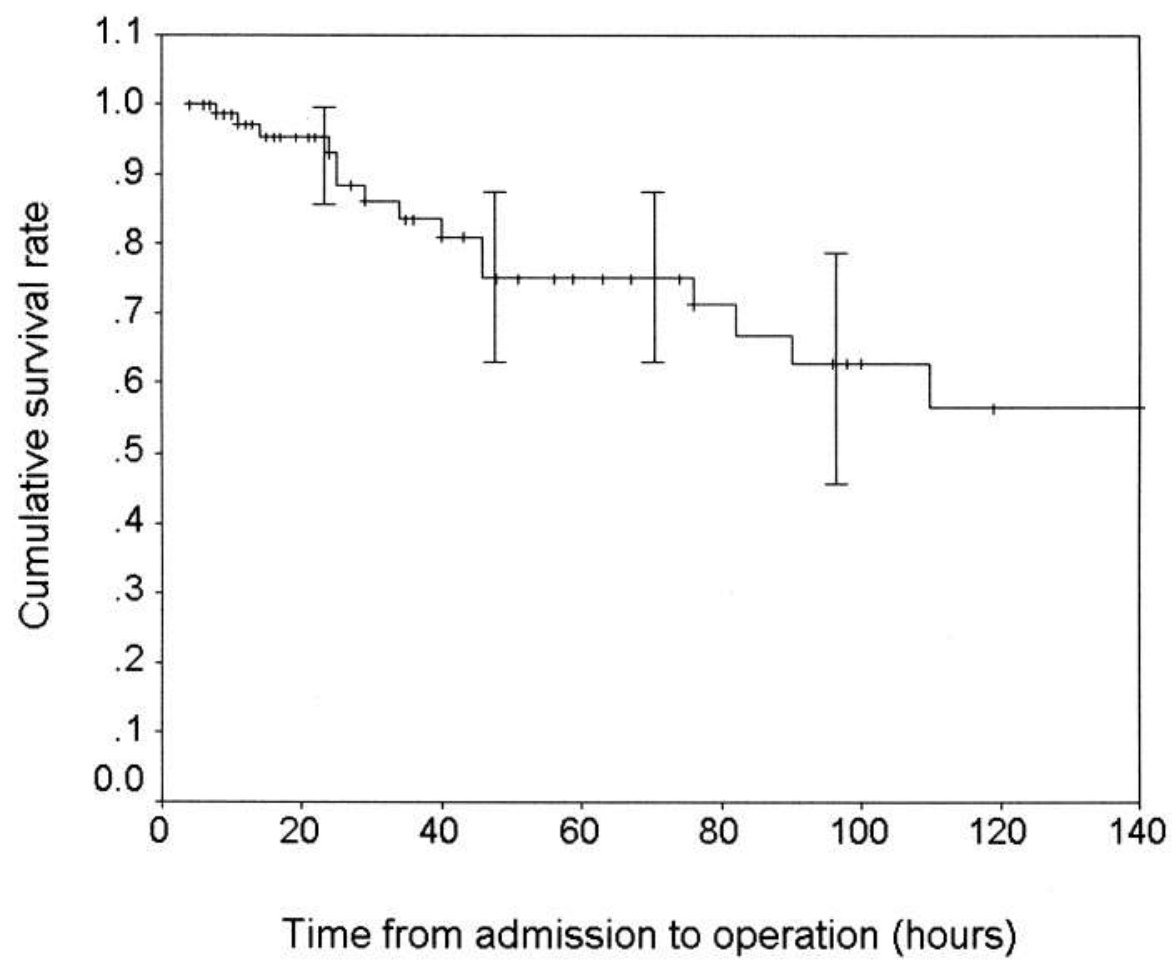
- Tissue dysoxia is playing an important role in the patho-physiology of sepsis:
  - Inadequate DO_2 to VO_2
  - Alterations in the microcirculation
  - Mitochondrial dysfunction.
- Early hemodynamic resuscitation based in a balanced DO_2/VO_2. The ideal protocol and goal are not well established.

Pillars of Sepsis Treatment

ABX Source Control HMDC Resusc.

YOUR speed is LIFE!

Timing of surgery in NSTI



Wong CH et al., J Bone Joint Surg Am 2003, 85-A: 1454-60.

SSC 2013 Guidelines

Surviving Sepsis Campaign
www.survivingsepsis.org

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

Remark: *Although the weight* of the evidence supports prompt administration of antibiotics following the recognition of severe sepsis and septic shock, the feasibility with which clinicians may achieve this ideal state has not been scientifically evaluated.

Selection of Antibiotic

Surviving Sepsis Campaign
www.survivingsepsis.org

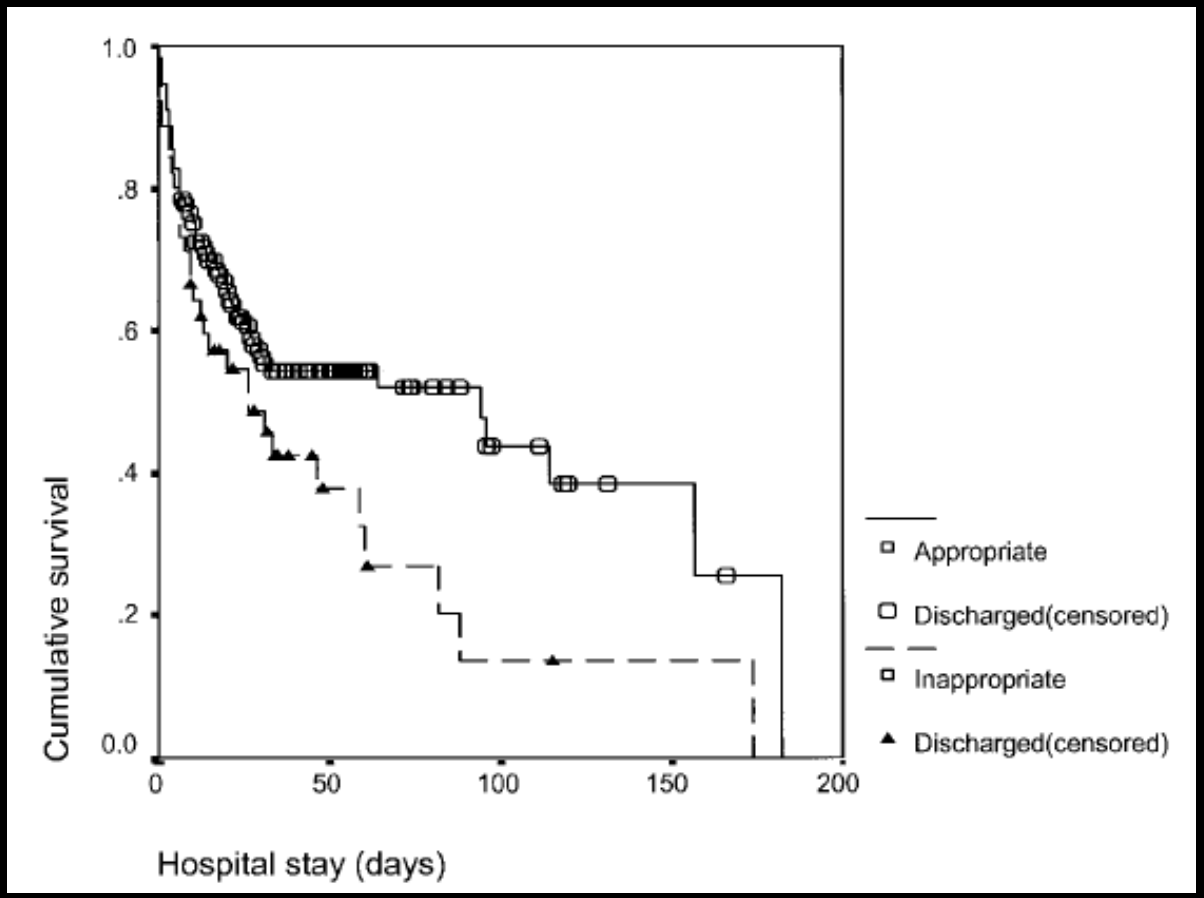
We recommend that initial empiric anti-infective therapy include one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into the tissues presumed to be the source of sepsis (grade 1B).

Effective empirical antibiotics

Impact of adequate empirical antibiotic therapy on the outcome of patients admitted to the intensive care unit with sepsis*

Crit Care Med 2003;31:2742–2751

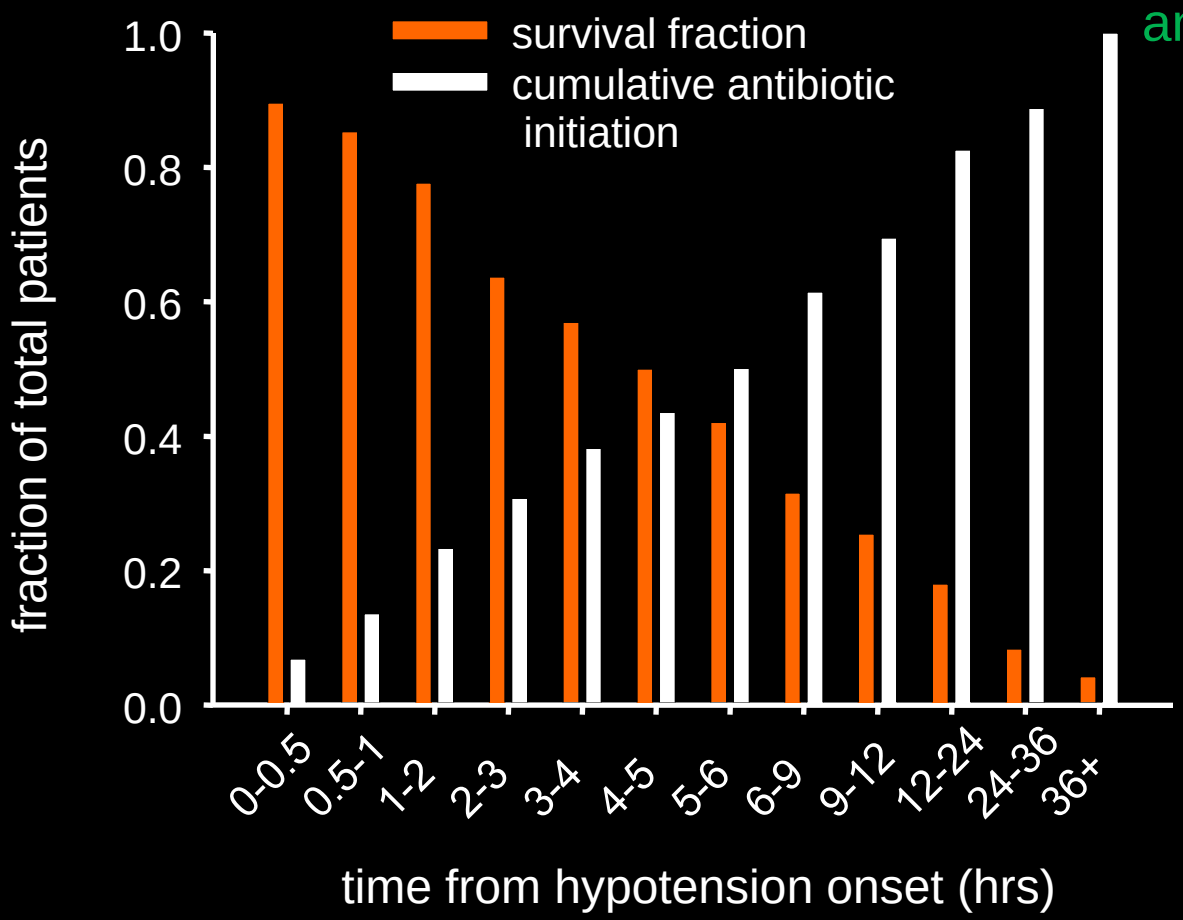
Jose Garnacho-Montero, MD, PhD; Jose Luis Garcia-Garmendia, MD, PhD; Ana Barrero-Almodovar, MD;



Risks:

- Mortality
- Morbidity
- Length of hospital stay
- Resistance selection
- Cost burden

Early antibiotic treatment

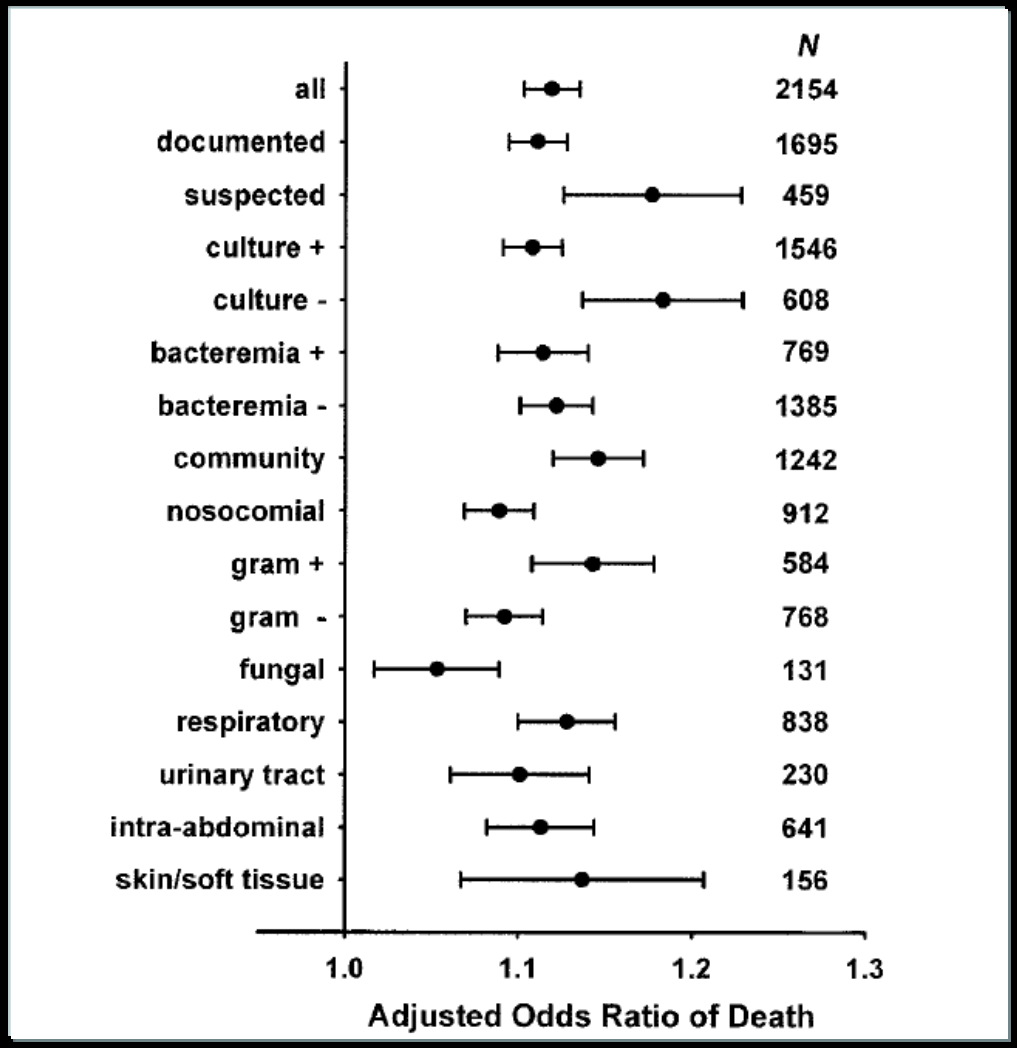


2.154 patients with septic shock and appropriate antibiotics

Median time to effective antimicrobial therapy was 6 hrs

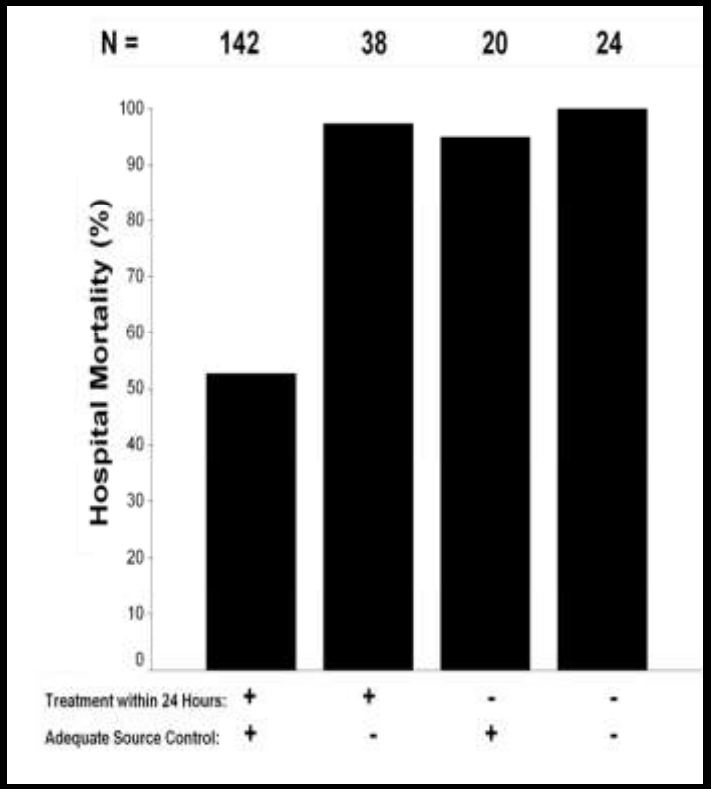
Kumar A et al. Crit Care Med 2006;34:1589-96

Mortality Risk with Increasing Delays in Initiation of Effective Antimicrobial Therapy



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

Septic shock secondary to *Candidemia*: importance of empiric therapy and source control



- 224 patients with septic shock and candidemia
- Multivariate logistic regression analysis showed as independently associated with hospital mortality
  - delayed antifungal therapy
    (AOR, 33.75; 95% CI, 9.65 – 118.04; p = 0.005)
  - failure to achieve timely source control
    (AOR, 77.40; 95% CI, 21.52 – 278.38; p = 0.001)

Kollef MH. Clin Infect Dis 2012; 54:1739-46

Effectiveness of Treatments for Severe Sepsis

A Prospective, Multicenter, Observational Study

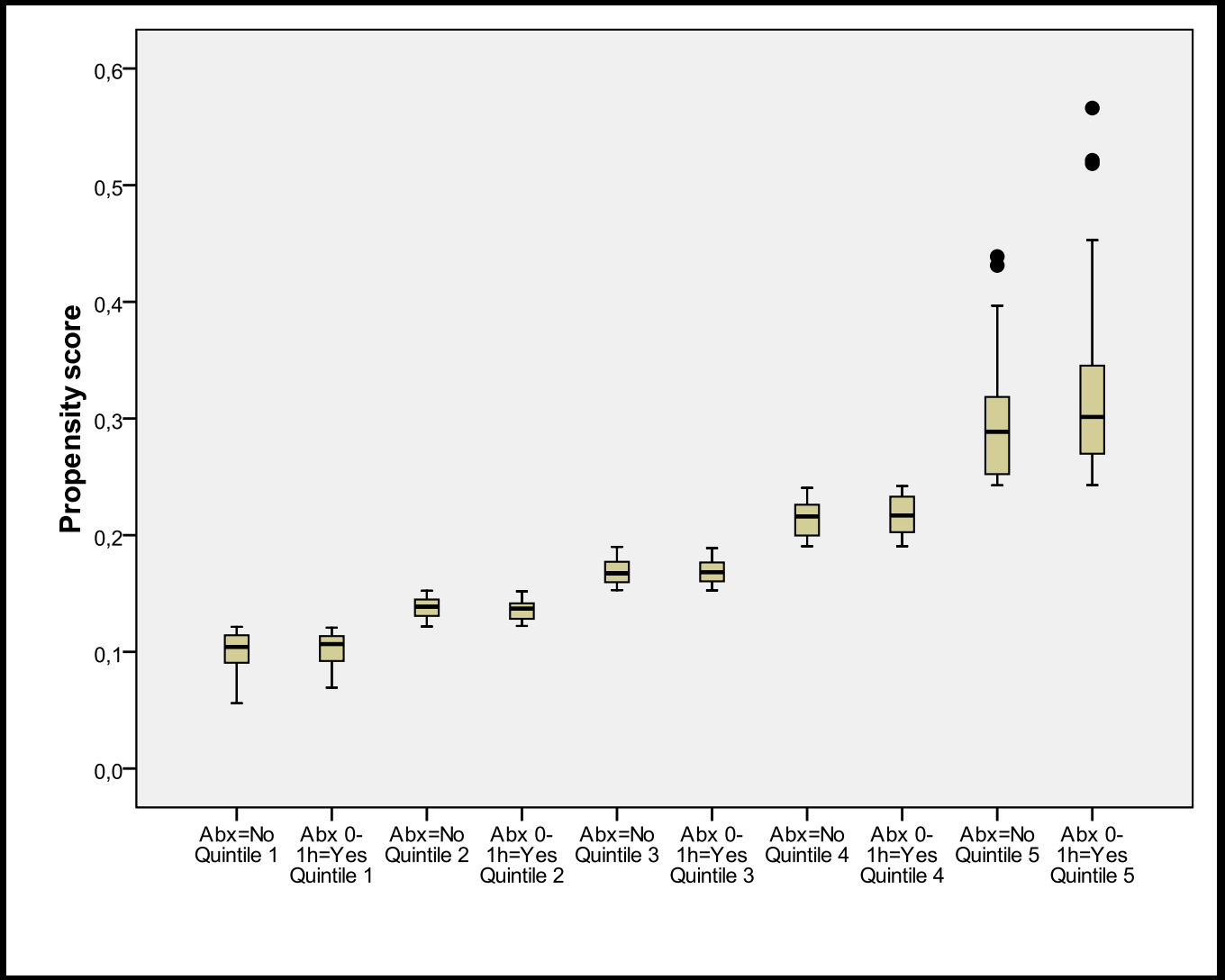
Ricard Ferrer[1], Antonio Artigas[1], David Suarez[2], Eduardo Palencia[3], Mitchell M. Levy[4], Angel Arenzana[5], Xose Luis Pérez[6], and Josep-Maria Sirvent[7] for the Edusepsis Study Group

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.

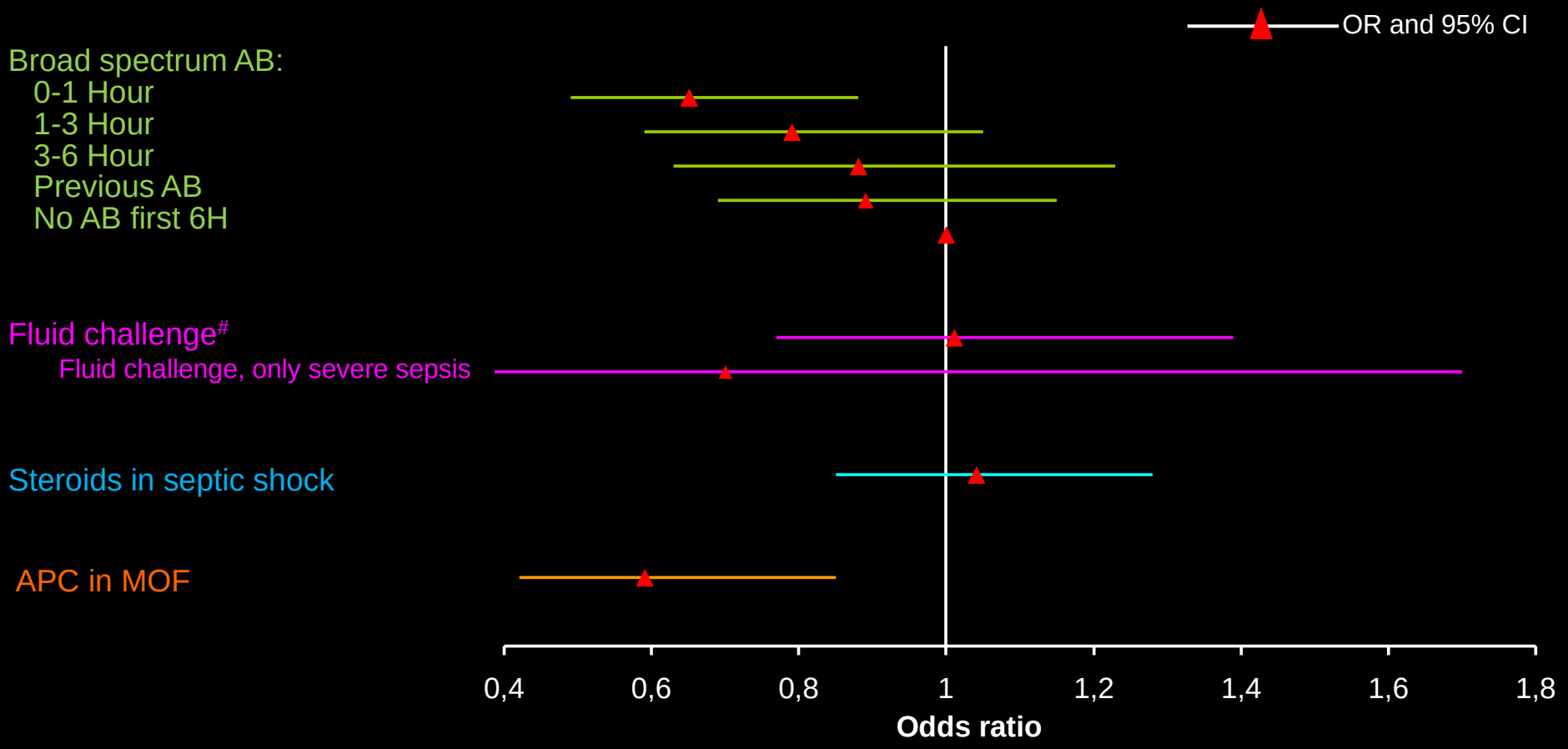
AJRCCM 2009;180:861–866.

Propensity Score. Antibiotics.



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

2.796 patients with severe sepsis or septic shock

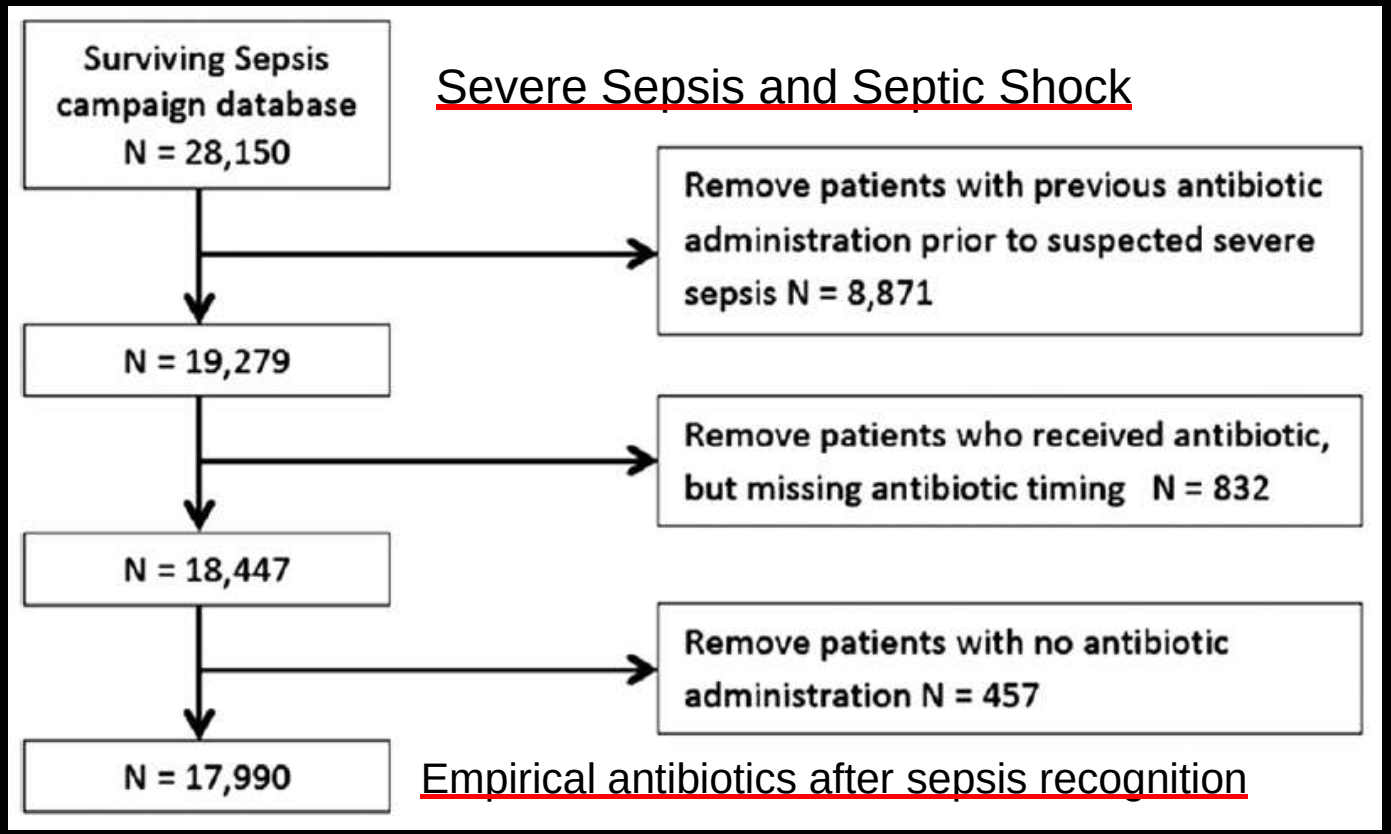


Ferrer R et al. AJRCCM 2009;180:861–866

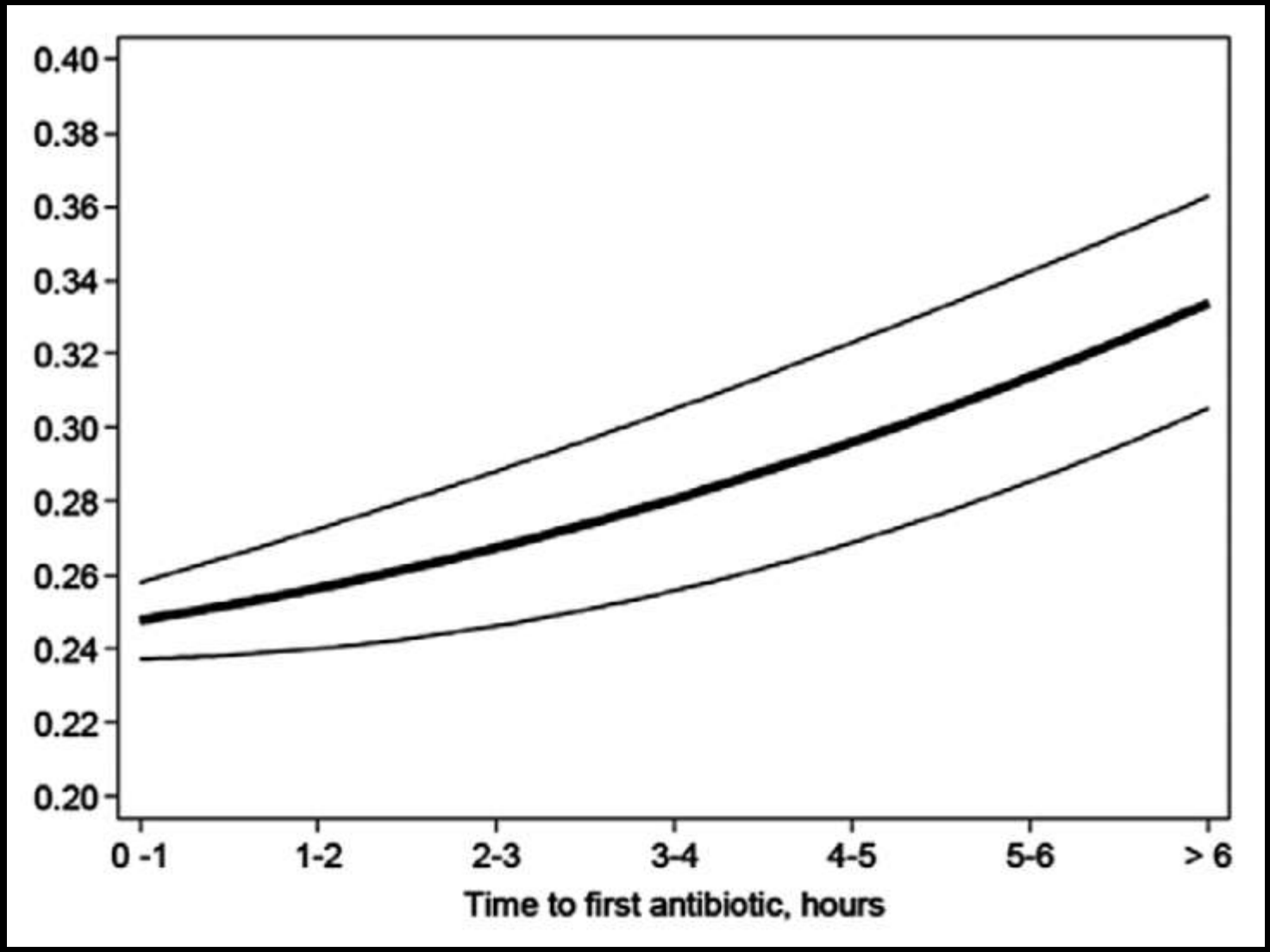
Empiric Antibiotic Treatment Reduces Mortality in Severe Sepsis and Septic Shock From the First Hour: Results From a Guideline-Based Performance Improvement Program

Ricard Ferrer, MD, PhD[1]; Ignacio Martin-Loeches, MD, PhD[2]; Gary Phillips, MAS[3]; Tiffany M. Osborn, MD, MPH[4]; Sean Townsend, MD[5]; R. Phillip Dellinger, MD, FCCP, FCCM[6]; Antonio Artigas, MD, PhD[2]; Christa Schorr, RN, MSN[7]; Mitchell M. Levy, MD, FCCP, FCCM[6]

Surviving Sepsis Campaign
www.survivingsepsis.org



CCM 2014;42:1749-55



Predicted hospital mortality and 95% CIs for time to first antibiotic administration

Results adjusted by the sepsis severity score, ICU admission source ([ED], ward, vs ICU), and geographic region (Europe, United States, and South America)

TABLE 1. Patient Characteristics by Timing in Hours to the First Antibiotic

Patient Characteristic, *n* (%)	Antibiotic Timing (Hr)							
	0.0–1.0	1.0–2.0	2.0–3.0	3.0–4.0	4.0–5.0	5.0–6.0	> 6.0	*p*[a]
n	4,728	4,595	3,020	1,734	1,037	640	2,239	
Hospital mortality	1,512 (32.0)	1,292 (28.1)	863 (28.6)	517 (29.8)	337 (32.5)	234 (36.6)	885 (39.6)	< 0.001
Severity sepsis score, median (IQR)	58 (42–73)	50 (36–66)	49 (35–64)	49 (35–66)	51 (37–68)	53 (38–69)	57 (40–71)	< 0.001
Nosocomial infection	812 (17.2)	357 (7.8)	229 (7.6)	173 (10.0)	128 (12.3)	89 (13.9)	403 (18.0)	< 0.001
Septic shock	3,289 (69.6)	2,880 (62.7)	1,847 (61.2)	1,047 (60.4)	684 (66.0)	441 (68.9)	1,370 (61.3)	< 0.001
Hospital LOS, median days (IQR)	13 (6.4–25)	10 (5.6–19)	10.0 (5.6–19)	11 (5.9–20)	12 (5.9–23)	12 (6.3–22)	14 (7.3–29)	< 0.001
ICU LOS, median days (IQR)	5.1 (2.4–11)	4.1 (2.1–8.9)	4.2 (2.1–8.8)	4.3 (2.0–9.5)	4.9 (2.4–11)	4.6 (2.1–10)	6.7 (2.8–15)	< 0.001
LOS prior to ICU, median days (IQR)	0.1 (0.0–0.8)	0.1 (0.0–0.3)	0.1 (0.0–0.3)	0.1 (0.0–0.4)	0.2 (0.0–0.5)	0.2 (0.0–0.7)	0.2 (0.0–1.4)	< 0.001

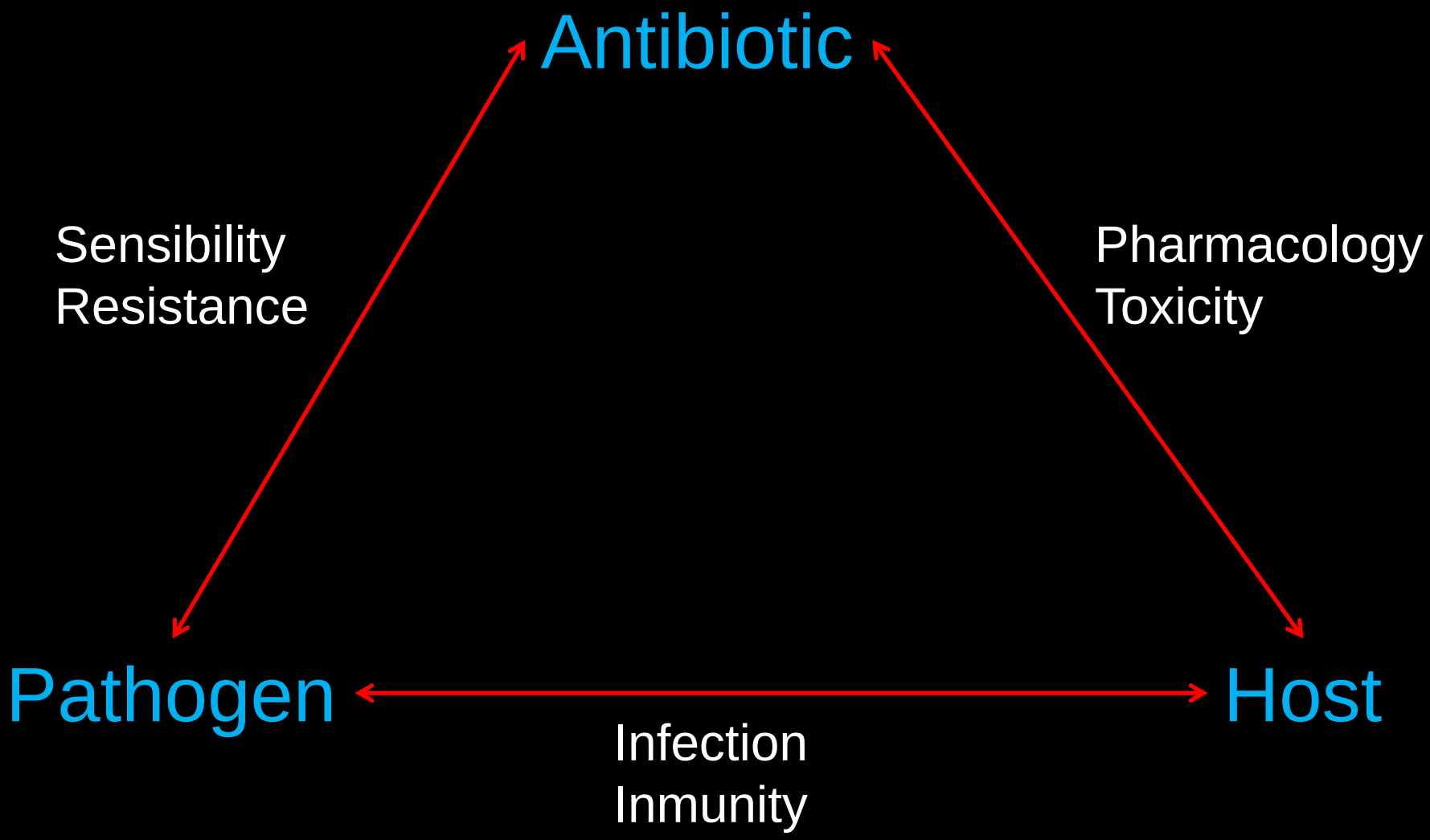
26.3% 51.8% 68.6% 78.2% 84.0% 87.5% 100%

Median time to empiric antibiotics

Adequate empirical antibiotics en less than 1H

Not so easy!

Selection of Antibiotics in Sepsis

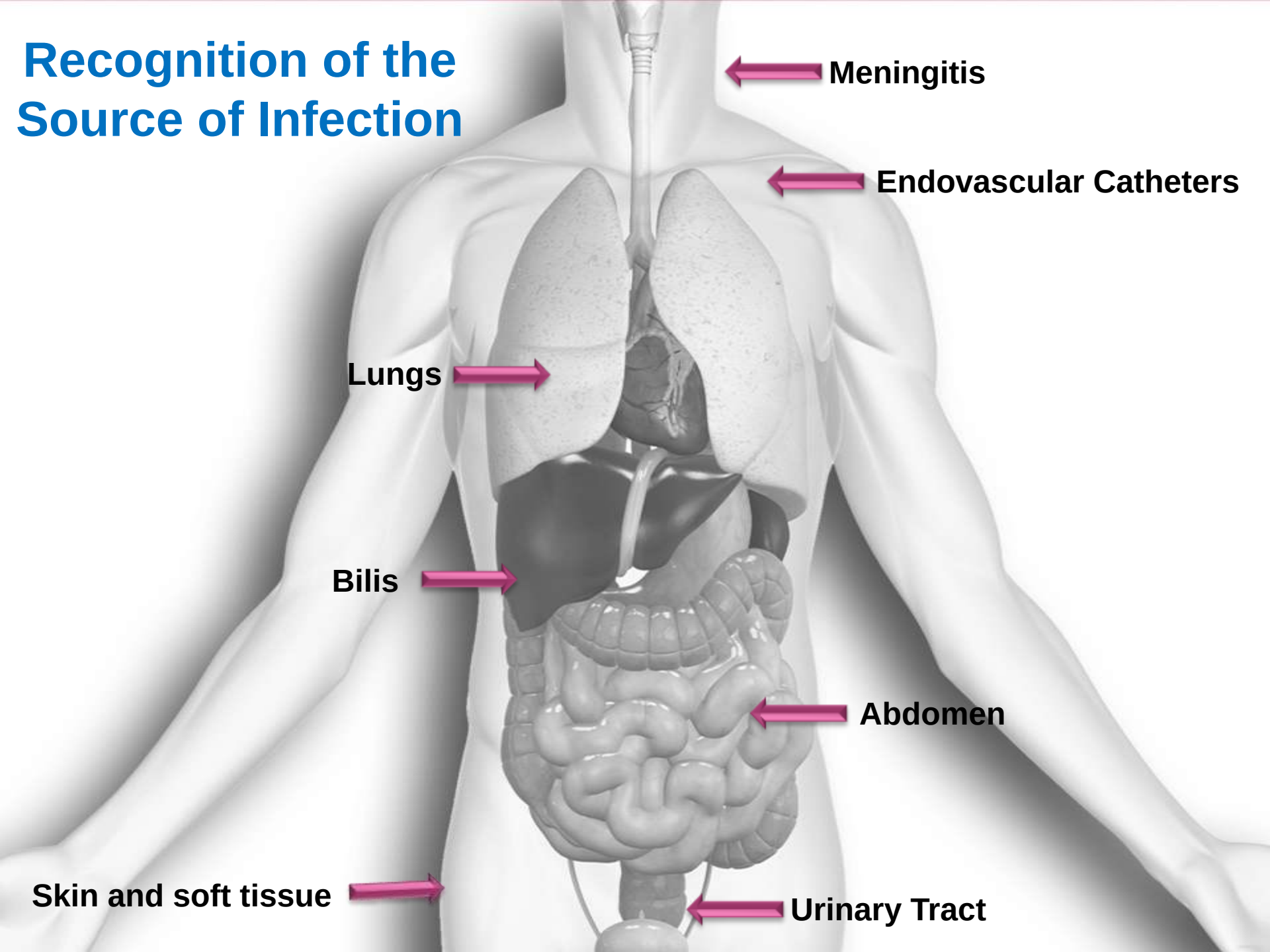


Selection of Antibiotics in Sepsis

Pathogen

Source

Recognition of the Source of Infection



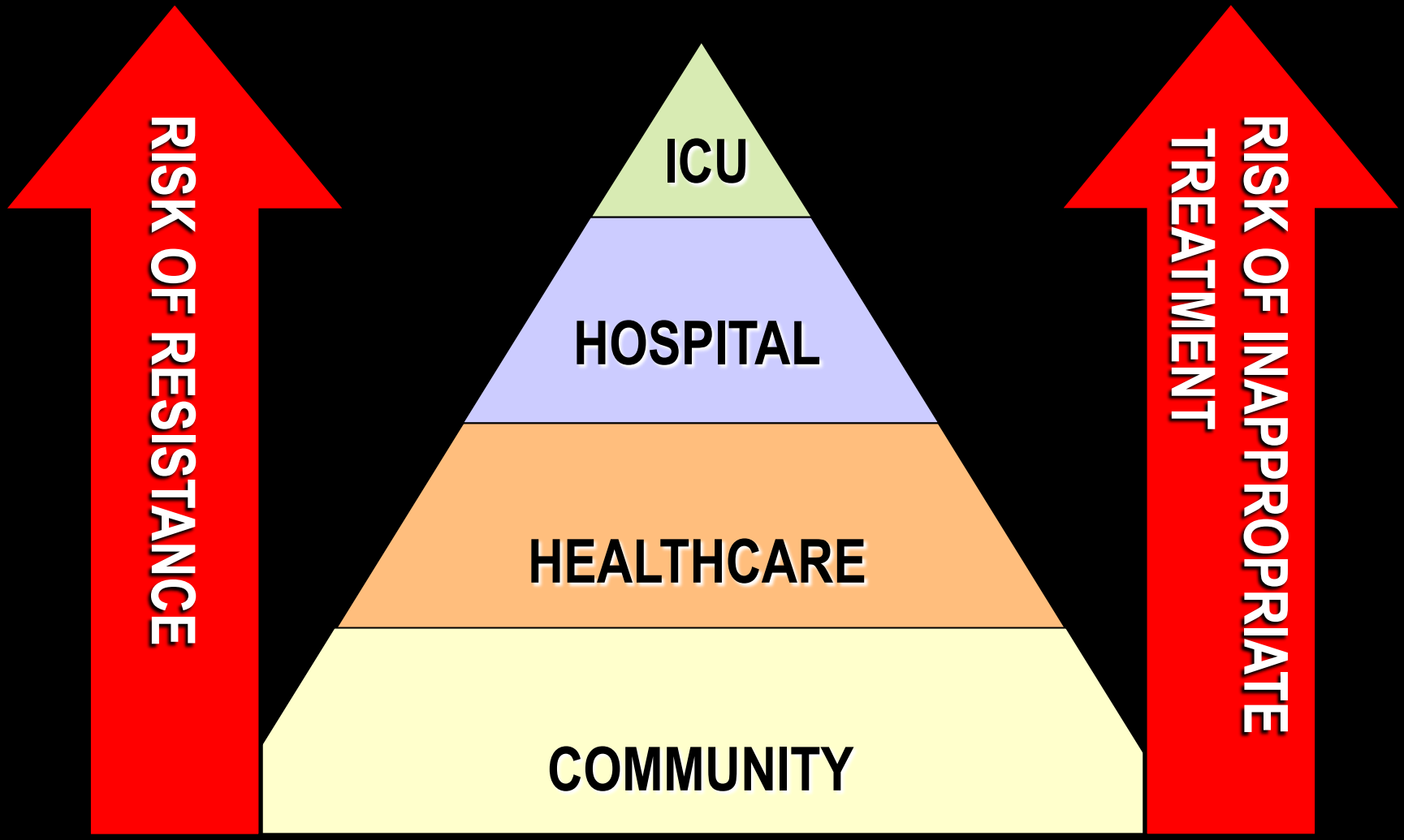
Selection of Antibiotics in Sepsis

Pathogen

Source

Setting: Community vs Nosocomial.

Setting and Adequate empiric antibiotics



HCAI: Risk factors

Health Care–Associated Bloodstream Infections in Adults: A Reason To Change the Accepted Definition of Community-Acquired Infections

N. Deborah Friedman, MBBS; Keith S. Kaye, MD, MPH; Jason E. Stout, MD, MHS; Sarah A. McGarry, MD; Sharon L. Trivette, RN; Jane P. Briggs, RN; Wanda Lamm, RN; Connie Clark, RN; Jennifer MacFarquhar, RN; Aaron L. Walton, MD; L. Barth Reller. MD: and Daniel J. Sexton, MD

Ann Intern Med. 2002;137:791-797.

- Received intravenous therapy at home; received wound care or specialized nursing care.
- Attended a hemodialysis clinic or received intravenous chemotherapy in the 30 days before the infection.
- Was hospitalized in an acute care hospital for 2 or more days in the 90 days before the infection.
- Resided in a nursing home or long-term care facility.

Selection of Antibiotics in Sepsis

Pathogen

Source

Setting: Community vs Nosocomial.

Biofilms

Local susceptibility patterns.

Outbreak?

Clinical syndrome: Shock

Initial microbiological information

Selection of Antibiotics in Sepsis

Pathogen

- Source
- Setting: Community vs Nosocomial.
- Biofilms
- Local susceptibility patterns.
- Outbreak?
- Clinical syndrome: Shock
- Initial microbiological information

Host

- Drug intolerances
- Previous colonization or infection.
- Recent antibiotics
- Comorbidities
- Immune Status

Selection of Antibiotics in Sepsis

Pathogen

- Source
- Setting: Community vs Nosocomial.
- Biofilms
- Local susceptibility patterns.
- Outbreak?
- Clinical syndrome: Shock
- Initial microbiological information

Host

- Drug intolerances
- Previous colonization or infection.
- Recent antibiotics
- Comorbidities
- Immune Status

Antibiotic

- Broad spectrum

Broad-/extended-spectrum antimicrobials available for monotherapy

Antibiotic	Gram-negative	Gram-positive	Resistant Gram-negative	Resistant Gram-positive	Anaerobe	*P. aeruginosa*
β-Lactam/ β-Lactamase inhibitor	■	■	■	■	■	■
3rd-Generation cephalosporins	■	■	■	■	■	■
Tigecycline	■ No Proteus	■	■	■	■	■
Glycopeptides	■	■	■	■	■	■
Carbapenems	■	■	■	■	■	■
Quinolones	■	■	■	■	■	■

■ Varies by product within class
■ *In vitro* activity
■ No *in vitro* activity

In vitro activity does not necessarily correlate with clinical efficacy

Selection of Antibiotics in Sepsis

Pathogen

- Source
- Setting: Community vs Nosocomial.
- Biofilms
- Local susceptibility patterns.
- Outbreak?
- Clinical syndrome: Shock
- Initial microbiological information

Host

- Drug intolerances
- Previous colonization or infection.
- Recent antibiotics
- Comorbidities
- Immune Status

Antibiotic

- Broad spectrum
- Bactericidal Activity
- Post-Antibiotic effect
- PK/PD. Tissue penetration
- Elimination by CRRT

Antifungals and CRRT

Treatment with echinocandins during continuous renal replacement therapy

González de Molina *et al. Critical Care* 2014, 18:218
http://ccforum.com/content/18/2/218

Francisco Javier González de Molina*, Maria de Los Ángeles Martínez-Alberici and Ricard Ferrer

- Fluconazol is removed by hemofiltration.
- All equinocandins are NOT removed by hemofiltration but can be adsorbed to filters.

- High dose of Fluconazol (800 mg/d).
- The removal of echinocandins by adsorption to the synthetic surfaces of hemofilters is unlikely to have clinical relevance. Same dose.

Selection of Antibiotics in Sepsis

Pathogen

- Source
- Setting: Community vs Nosocomial.
- Biofilms
- Local susceptibility patterns.
- Outbreak?
- Clinical syndrome: Shock
- Initial microbiological information

Host

- Drug intolerances
- Previous colonization or infection.
- Recent antibiotics
- Comorbidities
- Immune Status

Antibiotic

- Broad spectrum
- Bactericidal Activity
- Post-Antibiotic effect
- PK/PD. Tissue penetration
- Elimination by CRRT
- Toxicity
- Availability
- Cost

Antibiotic Combination Therapy

CRITICAL CARE

Díaz-Martín *et al. Critical Care* 2012, **16**:R223
http://ccforum.com/content/16/6/R223

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

Ana Díaz-Martín[1,2,3*], María Luisa Martínez-González[4], Ricard Ferrer[5,6], Carlos Ortiz-Leyba[1,2,3], Enrique Piacentini[5], María Jesús López-Pueyo[7], Ignacio Martín-Loeches[4,6], Mitchell M Levy[8], Antoni Artigas[4,6], José Garnacho-Montero[1,2,3] and for the Edusepsis Study Group

EDUSEPSIS

Antibiotics	Non-DCCT group *n* = 984 (71.7%)	DCCT group *n* = 388 (28.3%)	*P*
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

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		

Outline

- Epidemiology of Sepsis.
- Time-to-treatment in Sepsis.
- Interventions. Sepsis Code.

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.

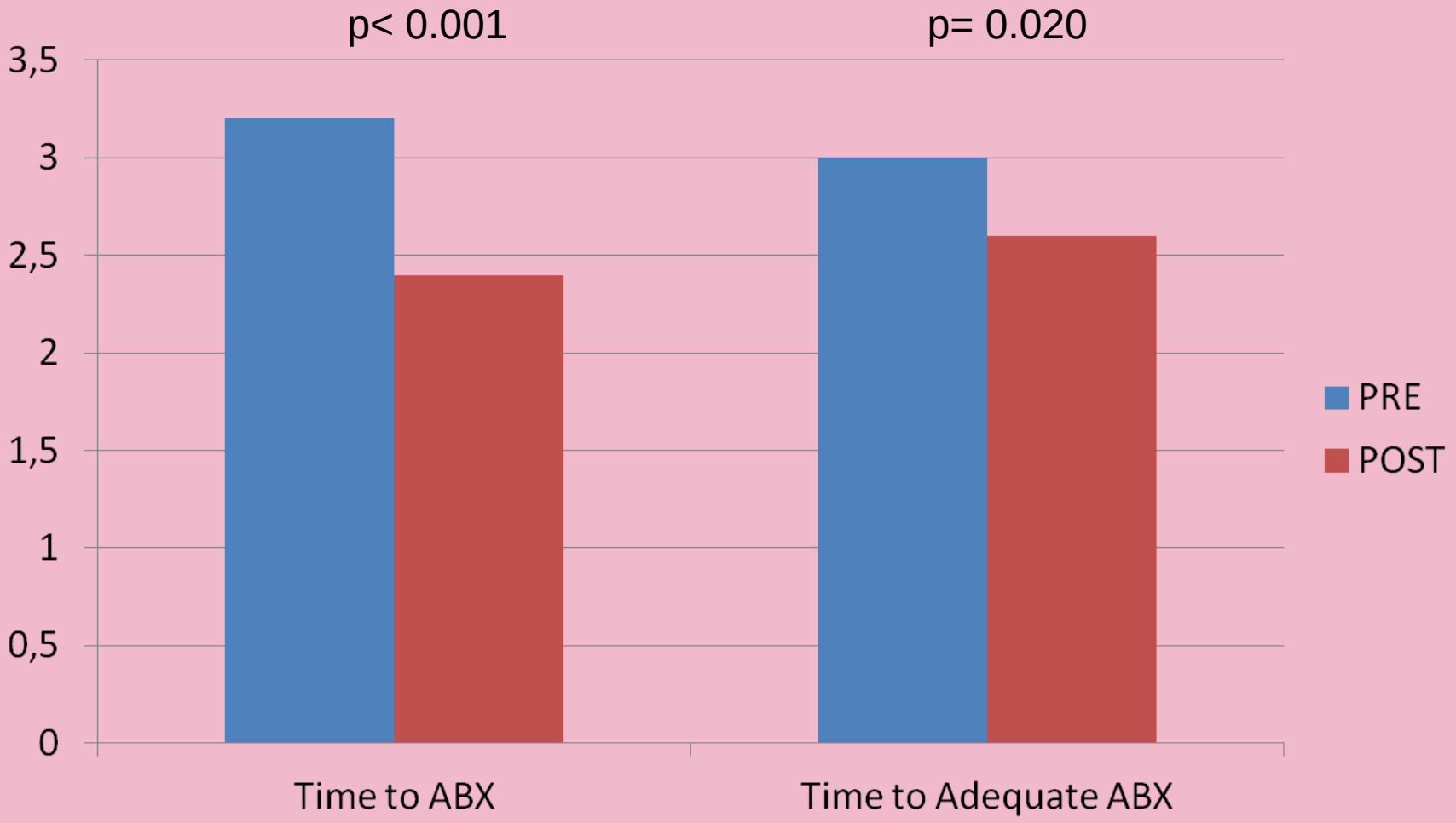
ABISS EDUSEPSIS

Gamification

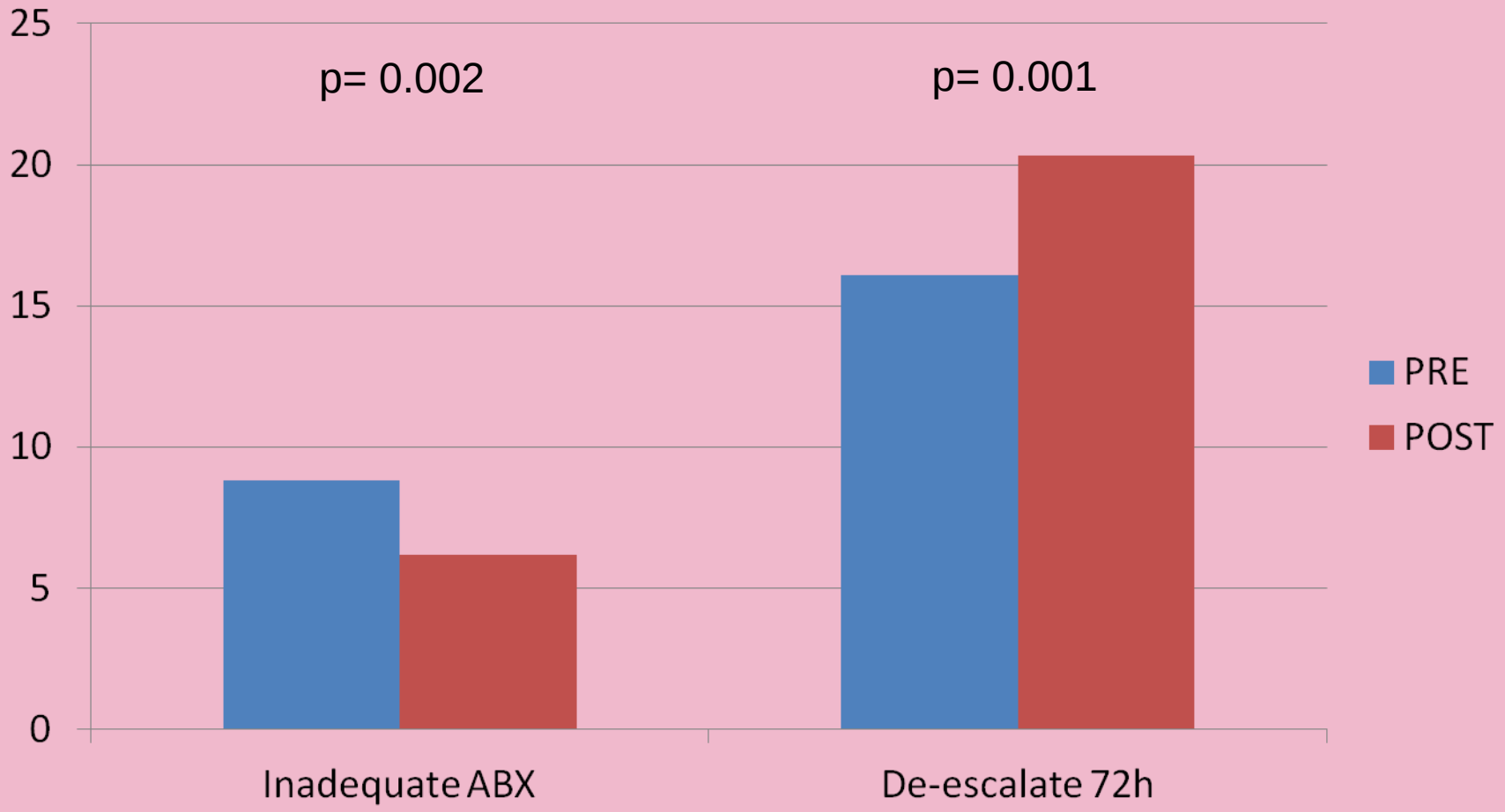
Results

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

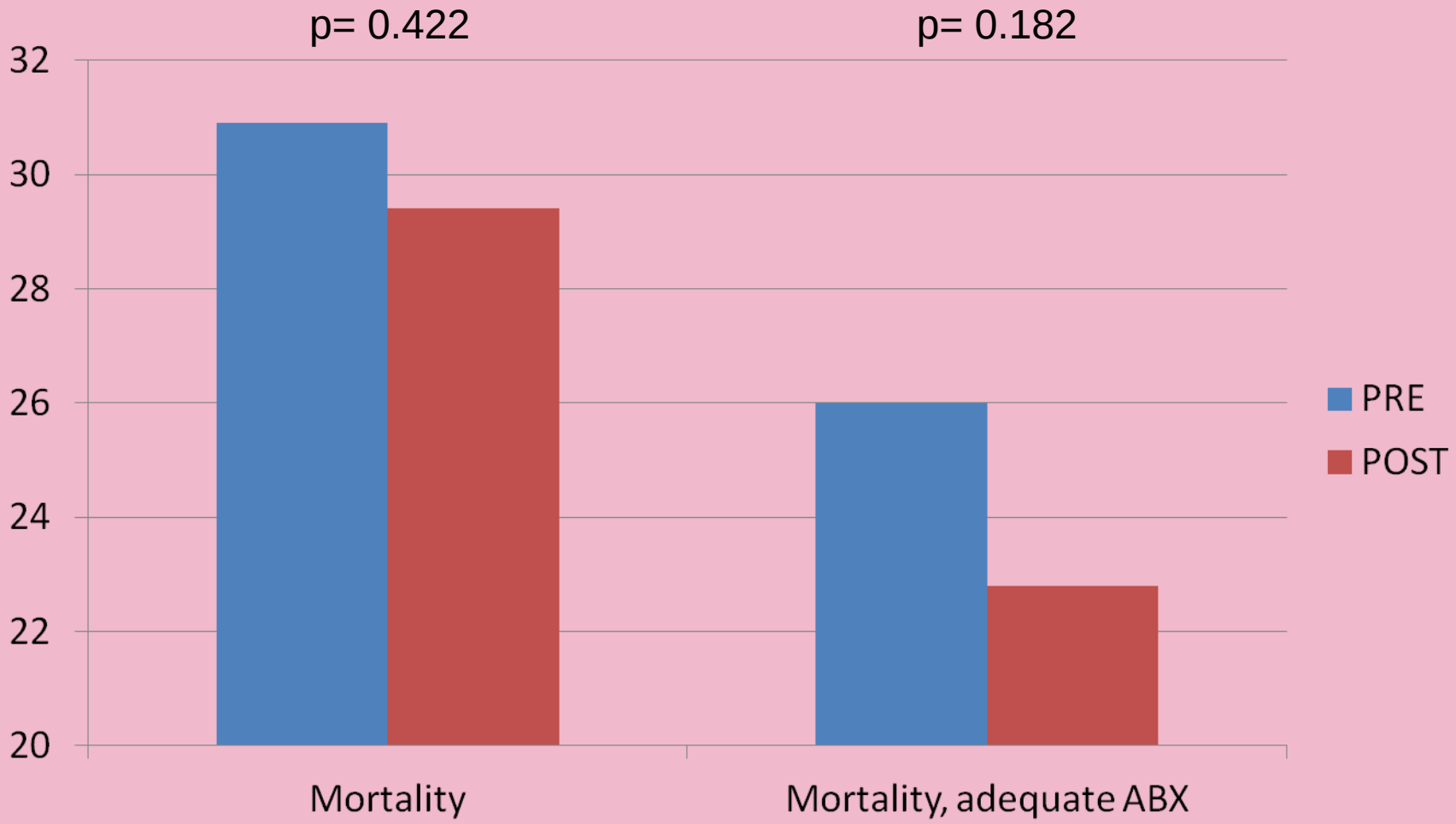
Results: Antibiotics



Results


25
20
15
10
5
0
p= 0.002
p= 0.001
PRE
POST
Inadequate ABX
De-escalate 72h

Results


p= 0.422
p= 0.182
32
30
28
26
24
22
20
PRE
POST
Mortality
Mortality, adequate ABX

Time-dependent Diseases

	AMI	STROKE	TRAUMA	SEPSIS
Clinical Recognition	Easy	Easy	Easy	Complex
Population	Homogeneous	Homogeneous	Heterogeneous	Heterogeneous
Biomarker	YES	NO	NO	YES/NO
Complex Treatment Algorithms	++	++	+++	+++
Multidisciplinary Approach	+	++	+++	+++
Well established guidelines	+++	+++	+++	++
Code	Yes	Yes	Yes	+/-

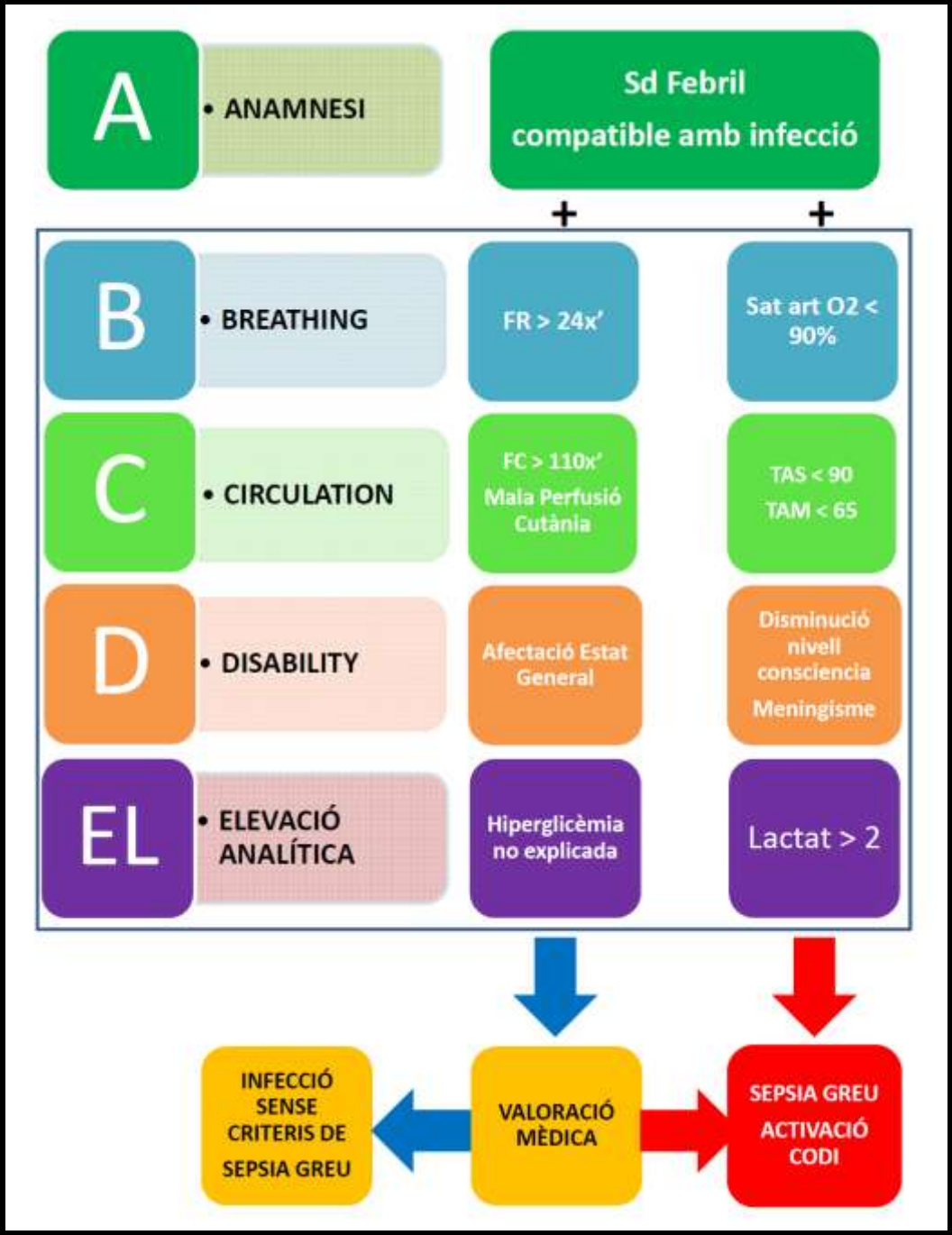
Other Strategies

- Sepsis Code: The health care system is organized to provide early treatment in all the area.
- Sepsis Unit, sepsis team: Hospitals are organized to warrant early delivery of treatments.
- Prescription support. Local guidelines.
- Innovation in the microbiology lab: early and precise information.

Ordenación Atención de la Sepsis Comunidad Autónoma

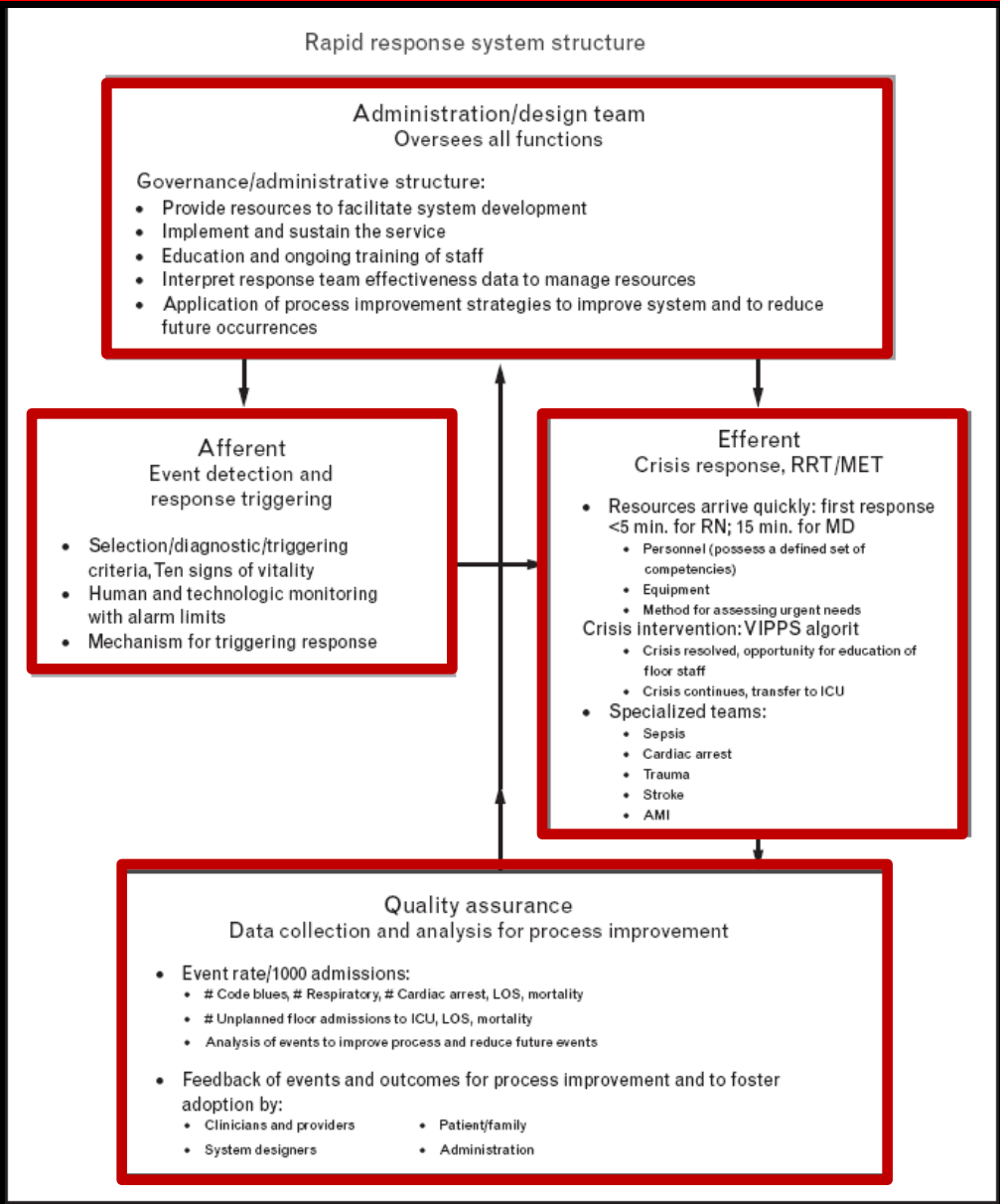
- Agentes implicados:
  - Primaria
  - Transporte
  - Hospitales

- Niveles asistenciales y requisitos: Quien pude hacer que.
- Sectorización: Donde
- Evaluación: Registro e Indicadores


A
• ANAMNESI
Sd Febril
compatible amb infecció
+
+
B
• BREATHING
FR > 24x'
Sat art O2 < 90%
C
• CIRCULATION
FC > 110x'
Mala Perfusió Cutània
TAS < 90
TAM < 65
D
• DISABILITY
Afectació Estat General
Disminució nivell consciencia
Meningisme
EL
• ELEVACIÓ ANALÍTICA
Hiperglicèmia no explicada
Lactat > 2
INFECCIÓ SENSE CRITERIS DE SEPSIA GREU
VALORACIÓ MÈDICA
SEPSIA GREU
ACTIVACIÓ CODI

Atención de la Sepsis en los Hospitales

- Early detection
- Rapid response teams
- Audit: Quality indicators
- Quality improvement interventions



Kumar A et al.
Current Opinion in Critical Care 2009, 15:301–307

Servei d'Urgències

Codi xoc sèptic

Etiqueta dades identificació

AQUESTA TRAJECTÒRIA SUBSTITUEIX LA GRÀFICA D'INFERMERIA

Trajectòria clínica

La trajectòria clínica no substitueix el judici clínic dels professionals. Aquesta trajectòria fa referència a l'evolució més habitual d'aquest procediment

AL·LÈRGIES: ☐ No conegudes ☐ Sí. Quines:_____

Hospital Universitari MútuaTerrassa

Aïllament:_____

Data: __/__/____

Criteris d'inclusió

A. Sospita d'infecció

B. Un o més signes:

- ❑ Tª <36ºC o Tª >38ºC
- ❑ FC >90bpm
- ❑ GCS <15
- ❑ FR >20 rpm

C. Disfunció cardiovascular:

- ❑ TA sist <90mmHg o TAM* <65mmHg
- ❑ ↓TA sist >40mmHg en HTA
- ❑ Lactat >3mmol/L

*TAM= TAD + (TAS-TAD/3)

Criteris d'exclusió

- ❑ Deteriorament cognitiu greu
- ❑ Deteriorament funcional important (Rankin >2)
- ❑ Malaltia onco/hematològica en tractament pal·liatiu
- ❑ Malaltia neurològica degenerativa avançada
- ❑ Malalt amb limitació de l'esforç terapèutic
- ❑ Cirrosi Child C

AVALUACIÓ DEL PACIENT

Criteris d'inclusió? (A + B +C)

Sí

Activar codi xoc sèptic
Avisar metge adjunt

Hora: .....
LLoc: .....

Criteris exclusió?

No

Sí

No continuar Trajectòria

BUNDLE DE RESUCITACIÓ

TAM ≥65 mmHg després d'administrar volum

No

Sí

Monitorització estricta

PVC >8 o signes de congestió pulmonar?

No

Sí

Cristal·loide 500ml/10 min o voluven 500 ml/10 min

- ❑ Avisar metge UCI (182710)
- ❑ Iniciar Noradrenalina 8 mg en 80 cc SG5% a 4 ml/h i revalorar en 10 minuts. Si persisteix doblar perfusió.

Tractament:

- ❑ Administració de volum: 1.500 cc de sèrum salí en una hora (mínim 20 ml / Kg)
- ❑ **ADMINISTRACIÓ PRECOÇ D'ANTIBIÒTIC EMPÍRIC** (PROA)
- ❑ Avaluar focus evacuable de sèpsia

Procediments:

- ❑ Realitzar hemocultius (2 extraccions simultànies, una de cada braç)
- ❑ Analítica (perfil codi sèpsia) + lactat + gasometria venosa central
- ❑ Canalitzar 2 vies perifèriques:

1) Calibre..... Lloc ..... 2) Calibre..... Lloc .....

- ❑ Col·locar drum amb control PVC. Lloc .....
- ❑ Radiografia de comprovació del drum
- ❑ Sonda vesical amb urimèter. Tipus.....

CODI METGE I I I I I

Anotacionsmèdiques......

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.....

.....

.....

.....

Impact of the Surviving Sepsis Campaign protocols on hospital length of stay and mortality in septic shock patients: Results of a three-year follow-up quasi-experimental study*

(Crit Care Med 2010; 38:1036–1043)

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Septic Shock

	Historical Group, n = 96 (20%)	Intervention Group, n = 384 (80%)	*p*
Patient characteristics			
Age, yr	62.2 ± 16.3	64.5 ± 15.1	.328
Male, n (%)	55 (57.3)	255 (66.4)	.097
Sequential Organ Failure Assessment score	10.2 ± 3.2	9.4 ± 3.2	.036
Acute Physiology and Chronic Health Evaluation II score	24.6 ± 7.8	23.2 ± 7.3	.136
Mechanical ventilation, n (%)	83 (86.4)	254 (66.1)	<.001
Central venous oxygen saturation (%) at ICU admission	67.1 ± 13.8	68.3 ± 13.7	.410
Location before ICU admission, n (%)			.007
Emergency department	19 (19.8)	126 (32.8)	
Medical ward	32 (33.3)	76 (19.8)	
Surgery department	26 (27.1)	123 (32.0)	
Another hospital	19 (19.8)	59 (15.4)	
Source of infection, n (%)			.850
Intra-abdominal infection	28 (29.2)	134 (35.3)	
Pneumonia	42 (43.8)	136 (35.8)	
Urinary tract infection	8 (8.3)	45 (11.8)	
Skin/soft tissue infection	5 (5.2)	15 (4.0)	
Other infections	7 (7.3)	25 (6.5)	
Unknown	6 (6.2)	25 (6.6)	
Hospital mortality, n (%)	55 (57.3)	144 (37.5)	.001

Septic shock: A multidisciplinary response team and weekly feedback to clinicians improve the process of care and mortality*

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Crit Care Med 2011; 39:252–258

The sepsis response team members

Multidisciplinary Member	Role
ICU attending physician	• Identifies patients who meet criteria for sepsis protocol • 24/7 bedside supervision of the ICU team in implementing the sepsis protocol
ICU fellow	• Identifies patients who meet criteria for sepsis protocol • Acts as team leader, allocating tasks to individual team members • Supervises ICU residents during the resuscitation, including placement of central venous catheter and implementation of the sepsis protocol
ICU resident	• Identifies patients who meet criteria for sepsis protocol • Responsible for the primary management of the patient in the ICU, including placement of central venous catheter and the implementation of the sepsis protocol
ICU nurse	• Identifies patients who meet criteria for sepsis protocol • Implements the sepsis protocol following the computerized physician standing orders, including fluid boluses triggered by central venous pressure measurement
ICU pharmacist	• Identifies patients who meet criteria for sepsis protocol • Responsible for timely order processing and administration of antibiotics, vasopressors, and inotropes
Respiratory therapist	• Assists in central venous catheter placement and calibration • Arterial line placement and calibration • Assists in the management of mechanical ventilation
Vascular access technician	• Timely bedside blood lactate measurements and drawing blood samples as ordered
Unit secretary	• Aids in activation of sepsis response team paging system • Notifies portable radiology technician if needed
Portable radiology technician	• Immediate chest radiograph performed when needed

Elements of the sepsis resuscitation bundle

Element	Definition
Lactate	Measured before or within 1 hr after blood culture
Blood culture	Drawn before antibiotics administered
Antibiotic	Administered within 1 hr of sepsis recognition and intensive care unit admission
Fluid resuscitation	In the event of hypotension and/or lactate >4 mmol/L, an initial bolus of 20 mL/kg (crystalloid or equivalent colloid) administered followed by subsequent fluid challenges until one of the following: • Central venous pressure ≥8 mm Hg (≥12 mm Hg if mechanical ventilation) • Mean arterial pressure ≥65 mm Hg without vasopressors and lactate <2.5 mmol/L and urine output >0.5 ml/kg/hr
Appropriate vasopressor use	Vasopressor administered for one of the following two: • Persistent MAP <65 mm Hg despite fluid challenge 20 mL/kg of crystalloid • Life-threatening hypotension with MAP <50 mm Hg for ≥15 mins Vasopressor not administered when one of the two not met
Red blood cell administration	Transfused if hematocrit <30% and $Scvo_2$ <70% or mixed venous O_2 <65% despite fluid resuscitation
Inotrope utilization	Started if Hct ≥30% and $Scvo_2$ <70% or mixed venous oxygen saturation <65% despite fluid resuscitation

Compliance with sepsis bundles

Bundle Element	Study Period: Baseline (n = 268)	Weekly Feedback (n = 284)	Sepsis Response Team Activation (n = 432)	p
Lactate measured	202 (75.4%)	259 (91.2%)	419 (97.0%)	<.001
Blood culture before antibiotics	235 (87.7%)	264 (93.0%)	422 (97.7%)	<.001
Timely antibiotics	207 (77.2%)	238 (83.8%)	393 (91.0%)	<.001
Adequate fluid	153 (57.1%)	182 (64.1%)	329 (76.2%)	<.001
Appropriate vasopressor	264 (93.0%)	252 (94.0%)	385 (89.1%)	.046
Appropriate red blood cell transfusion	221 (82.5%)	245 (86.3%)	370 (85.6%)	.397
Appropriate inotrope use	96 (35.8%)	158 (55.6%)	266 (61.6%)	<.001
All 7 elements	34 (12.7%)	107 (37.7%)	232 (53.7%)	<.001
Mortality	81 (30.3%)	78 (28.7%)	93 (22.0%)	.029

Independent predictors of mortality

Predictor Variable	Odds Ratio (95% Confidence Interval)	p
Female gender	1.329 (0.983–1.796)	.065
Acute Physiology and Chronic Health Evaluation comorbidities		
None	1	
Hepatic cirrhosis	3.313 (1.509–7.275)	.003
Hepatic failure	3.113 (1.598–6.066)	.001
Leukemia or multiple myeloma	1.677 (1.079–2.608)	.022
Lymphoma	1.486 (0.441–5.006)	.523
Immunocompromised	6.872 (0.556–84.961)	.133
Metastatic tumor	1.097 (0.564–2.134)	.784
Intensive care unit admission source		
Same hospital emergency department	1	
Same hospital ward	2.088 (1.476–2.953)	<.001
Other hospital emergency department	1.050 (0.666–1.654)	.835
Other hospital ward	1.241 (0.705–2.187)	.455
Do not resuscitate at recognition of severe sepsis or septic shock	1.492 (1.011–2.202)	.044
Lactate level	1.076 (1.012–1.144)	.019
Study period		
Baseline	1	
Weekly feedback	1.013 (0.685–1.497)	.950
Sepsis response team	0.657 (0.456–0.945)	.023

Crit Care Med 2011; 39:252–258

Help for Prescription: Guidelines

Clinical Practice Guidelines for the Management of Candidiasis: 2009 Update by the Infectious Diseas

Peter G. Pap
John E. Edw
Annette C. R

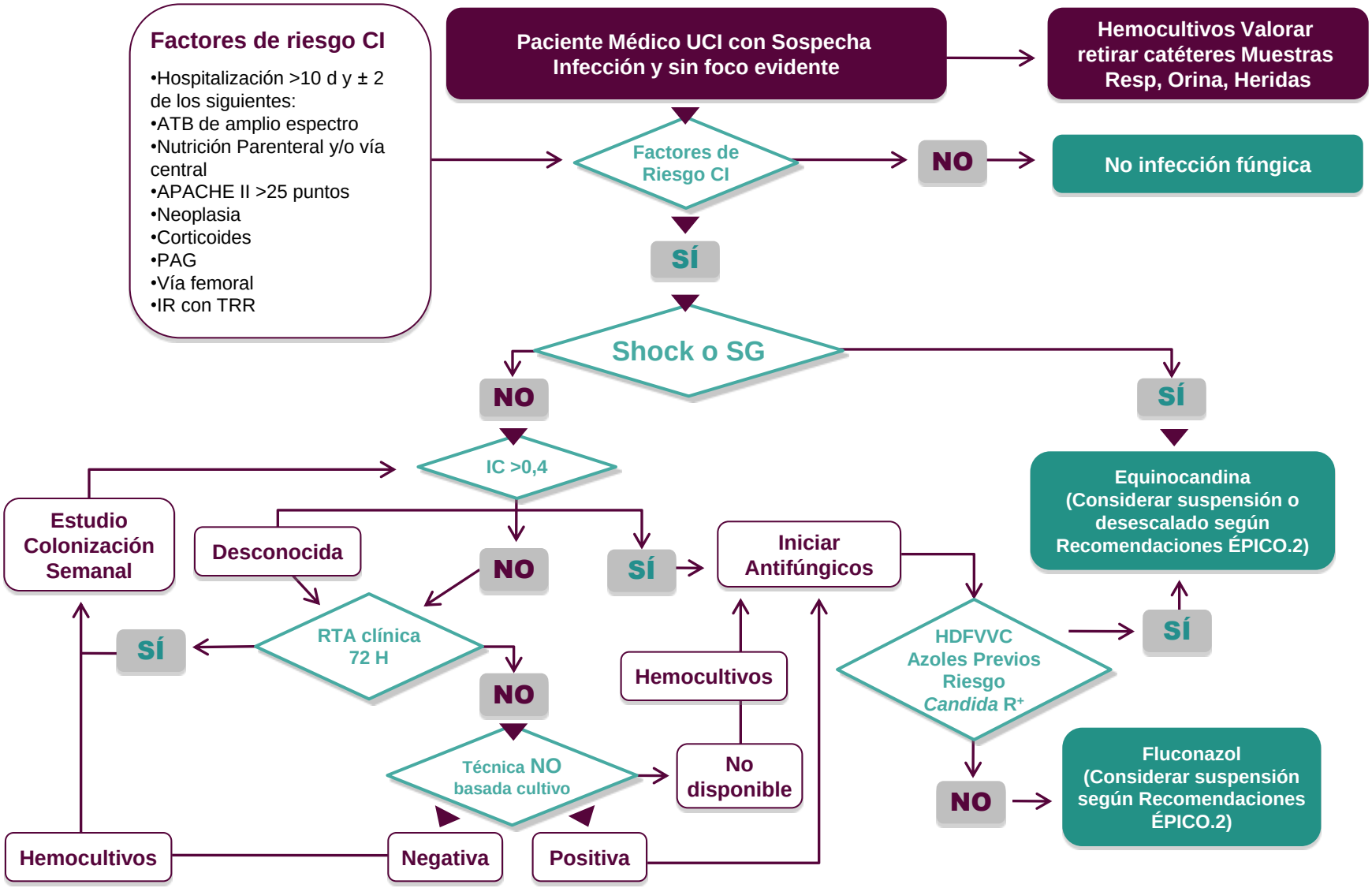
Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults

Lionel A. Mandell,[1,a]
Nathan C. Dean,[9,10] Sc
Antonio Torres,[16] and

European expert opinion on the management of invasive candidiasis in adults

B. J. Kullberg[1], P. E. Verweij[1], M. Akova[2], M. C. Arendrup[3], J. Bille[4], T. Calandra[4], M. Cuenca-Estrella[5], R. Herbrecht[6], F. Jacobs[7], M. Kalin[8], C. C. Kibbler[9], O. Lortholary[10,11], P. Martino[12†], J. F. Meis[13], P. Muñoz[14], F. C. Odds[15], B. E. De Pauw[1], J. H. Rex[16,17], E. Roilides[18], T. R. Rogers[19], M. Ruhnke[20], A. J. Ullmann[21], Ö. Uzun[2], K. Vandewoude[22], J.-L. Vincent[23] and J. P. Donnelly[1]

Help for Prescription: Algorithm



*Hospitalización >1 mes, colonización *Candida R*

Help for Prescription

Clinical Decision Support System

EGUARD
Early E-Guided Use of Antibiotics related to Resistance Data

Infection pathway

Main | Logout

Infection pathway | Infection characteristics | Investigations | Antiinfectives | Pathogens | Tools

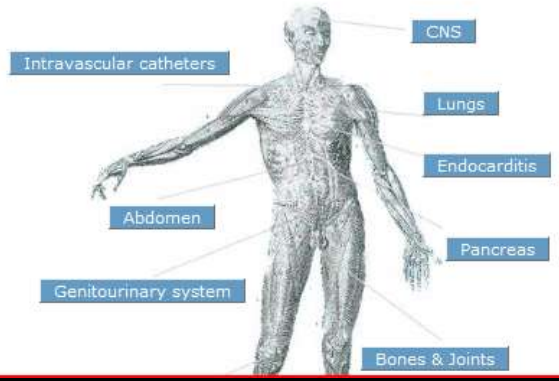
Logged In: Testaccount for EGUARD
Start page> - The SOP - Program> Infection pathway

Please evaluate the patient's condition:

Hypothermia ≤ 36 °C or **Hyperthermia** ≥ 38 °C	☐
Tachycardia ≥ 90/min	☐
Tachypnoea ≥ 20/min or $paCO_2$ ≤ 4,3 kPa [32 mmHg]	☐
Leukocytosis ≥ 12.000/µl or Leukopeania ≤ 4000/µl	☐
Inflammatory markers CRP > 0,5mg/dl or PCT > 0,5ng/dl or pathological IL-6	☐

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:



Help for Prescription: Local Guidelines
Catalan Sepsis Code

SOURCE	COMMUNITY	INTOLERANCE	RISK FACTORS FOR MULTIRESISTANT MO	INTOLERANCE
RESPIRATORY	3rd-Generation cephalosporins + macrolide	Levofloxacin	Antipseudomonal Beta-lactams + linezolid + levofloxacin	Aztreonam + Linezolid + levofloxacin
ABDOMINAL	3rd-Generation cephalosporins + amikacin + metronidazol	Ertapenem	Meropenem o Piperacillintazobactam +/- equinocandin	Aztreonam + metronidazol + Vancomycin +/- equinocandin
UTI	3rd-Generation cephalosporins + amikacin	Ertapenem	Meropenem +amikacina	Aztreonam + amikacina + Vancomycin
SKIN	Piperacilllin tazo bactam + clindamycin	Aztreonam + clindamycin	Piperacillin tazobactam + Vancomycin	tigecycline+ amikacina
MENINGITIS	Cefotaxima +/- Vancomycin+/- Ampicillin	Vancomycin+/- aztreonam +/- Cotrimoxazol	Meropenem + Vancomycin or linezolid	Aztreonam + Vancomycin or linezolid
UNKNOWN	meropenem + Vancomycin			

Local Antibiotic Guide

Hospital Universitari MútuaTerrassa

PROA: PROGRAMA D'OPTIMITZACIÓ DE L'ÚS D'ANTIBIÒTICS

TRACTAMENT EMPÍRIC DE LES MALALTIES INFECCIOSES EN ADULTS

Comissió d'Infeccions
Novembre 2011

Davant qualsevol dubte en quant a l'elecció de l'antimicrobià, durada del tractament o qualsevol altra qüestió revisar els protocols del PROA que es troben a la web. També podeu trucar als localitzadors **2513** o **2521**.

CISTITIS NO COMPLICADA:

- Cefuroxima 250mg/12h o Ciprofloxacino 250mg/12h (3-5 d) o Fosfomicina 3g/dosi única.

CISTITIS COMPLICADA:

- Cefuroxima 250mg/12h 7d, Fosfomicina 3g/48h (2 dosis)

PIELONEFRITIS AGUDA NO COMPLICADA (10-14d):

- Ceftriaxona 2g IV (dosis inicial) seguit de Cefuroxima 500mg/8h VO o Ceftriaxona 2g/d IM (si intolerància oral) 10-14d

PIELONEFRITIS COMPLICADA (14d)/ PROSTATITIS (4 setmanes):

- Amb criteris d'ingrés sense risc de microorganismes multiresistents o sepsis greu: Ceftriaxona 2g/24h o Cefotaxima 2g/8h IV
- Amb criteris d'ingrés i amb risc de microorganismes multiresistents o sepsis greu: Piperacil·lina-tazobactam 4 g/8 IV + Amikacina 1g/24h o Imipenem[1] 500mg/6h.

INFECCIÓ DEL TRACTA URINARI EN EL PACIENT SONDAT (7-14d)

- Ceftazidima 1g/8h + Ampicil·lina 1g/6h o Piperacil·lina-tazobactam 4g/6h o Imipenem[1] 500mg/6h IV

* En pacients al·lèrgics a B-lactàmics amb ITU (excepte en tractament ambulatori): Aztreonam 1g/8h + Vancomicina 1g/12h IV

PNEUMÒNIA NO GREU (FINE 1-2-3, CURB 0-2) (5-7d):

- Clínica típica: Amoxicil·lina 1g/8h o Amoxicil·lina-clavulànic 875/125 mg/8h si MPOC i risc d'infecció per *H. influenzae*. VO
- Clínica atípica o inespecífica: Levofloxacino 500mg/24h (5d) o Moxifloxacino 400mg/d (5d) Azitromicina 500mg/24h (3d) VO

PNEUMÒNIA GREU (FINE 4-5, CURB65 >2) 7-14d

- Ceftriaxona 2 g/d + levofloxacino 500 mg/12h IV (48 h de biteràpia).
- Si sospita de *P. aeruginosa*: Piperacil·lina-tazobactam 4g/8h + Amikacina 15mg/kg/24h o Meropenem 1g/8h IV

PNEUMÒNIA BRONCOASPIRATIVA:

- Amoxicil·lina-clavulànic 2g/8h IV
- En al·lèrgics: Clindamicina 600-900mg/8h IV

ABSCÉS PULMONAR (4-8 setmanes)

- Únic: Amoxicil·lina-clavulànic 2g/6h IV
- Múltiple: Cloxacil·lina 2g/4h + Gentamicina 3mg/kg/8h IV

PNEUMÒNIA NOSOCOMIAL* 7-14d

- Sense factors de risc de bacteris multirresistents i inici precoç (≤ 4 dies): Amoxicil·lina-clavulànic 1g/8h o Ceftriaxona 2g/24h IV.
- Inici tardà (> 4 dies), NAV o factors de risc de bacteris multirresistents: Piperacil·lina-tazobactam 4g/6h o Imipenem[1] 1g/6h IV

*Pacients greus afegir Levofloxacino 500mg/12h IV per cobrir *L.pneumophila*.

XOC SÈPTIC SENSE FOCUS

- Meropenem 1g/8h + Vancomicina[2] 15-20mg/8h

NEUTROPÈNIA FEBRIL:

- Sense sepsis greu: Piperacil·lina-tazobactam 4g/8h + Amikacina 15mg/kg/d o Meropenem 1g/8h IV
- Sepsis greu, shock sèptic o SDRA: Piperacil·lina-tazobactam 4g/6h (o meropenem 1g/8h) + Vancomicina[2] 1g/12h + Amikacina 15mg/kg/dia IV
- Al·lèrgics a B-lactàmics: Aztreonam 2g/8h + Vancomicina[2] 1g/12h + Amikacina 15mg/kg/dia IV

MENINGITIS (7-21 d en funció del patògen):

- Meningitis bacteriana comunitària:
  - Comunitària < 50 anys: Cefotaxima 300mg/kg/24h repartit en 6 dosis IV
  - Comunitària > 50 anys: Afegir Ampicil·lina 40-50 mg/kg/4h IV

1. Substituir per Meropenem 1g/8h en pacients amb ClCreat < 30, patologia estructural cerebral o epilepsia.
2. Administrar un bolus inicial de càrrega de 30mg/kg.

OPEN ACCESS Freely available online

PLOS ONE

Rapid Diagnosis of Bloodstream Infections with PCR Followed by Mass Spectrometry

Elena Jordana-Lluch[1], Heather E. Carolan[2], Montserrat Giménez[1], Rangarajan Sampath[2], David J. Ecker[2], M. Dolores Quesada[1], Josep M. Mòdol[3], Fernando Arméstar[4], Lawrence B. Blyn[2], Lendell L. Cummins[2], Vicente Ausina[1,5]*, Elisa Martró[1,6]

		Blood culture gold standard			Clinical infection criterion		
		Conventional methods			Conventional methods		
		Positive	Negative	Total	Positive	Negative	Total
A) PCR/ESI-MS in blood culture	Positive	78	11	**89**	83	6	**89**
	Negative	7	128	**135**	7	128	**135**
	Total	**85**	**139**	**224**	**90**	**134**	**224**
B) PCR/ESI-MS in whole blood	Positive	37	25	**62**	50*	12	**62**
	Negative	48	152	**200**	48	152	**200**
	Total	**85**	**177**	**262**	**98**	**164**	**262**

Better sensitivity

Better time-to-diagnosis

Take Home Messages

- Incidence of sepsis is increasing.
- Mortality is decreasing.
- Tissue dysoxia is playing an important role in the pathogenesis.
- Early identification is crucial.

Take Home Messages

Sepsis is time dependent: TEMPUS FUGIT

Take Home Messages

Early Treatment based on:

- Correct stratification
- Bundles and guidelines.
- Infection Setting and local resistance pattern.
- Source of infection
- Microbiological information.

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