

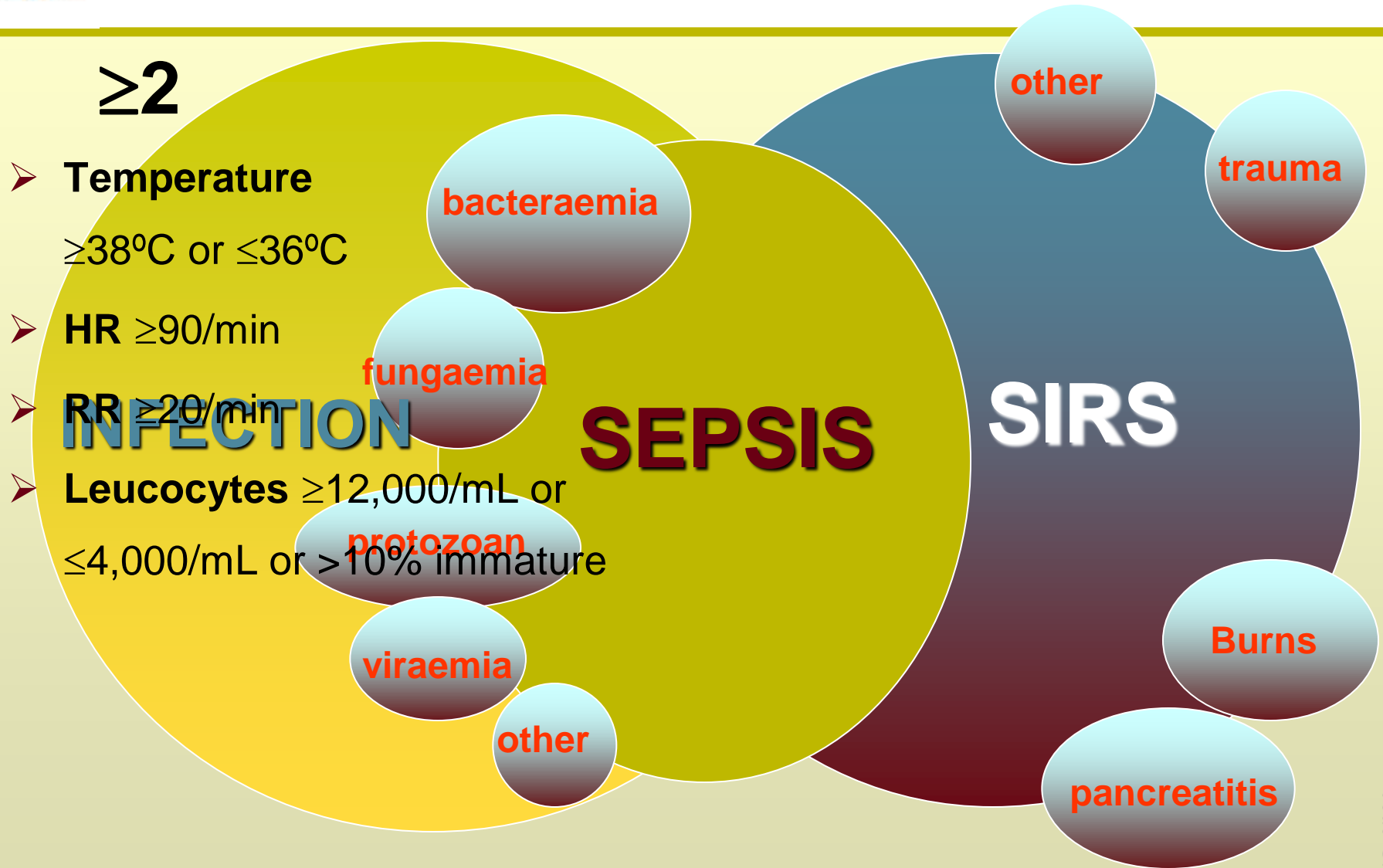
Sepsis

the clinical syndrome



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ICU director
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Systemic Inflammatory Response



Definitions (ACCP/SCCM)

- **Infection**

- A microbial phenomenon characterized by an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by those organisms.

- **Bacteremia**

The presence of viable bacteria in the blood.

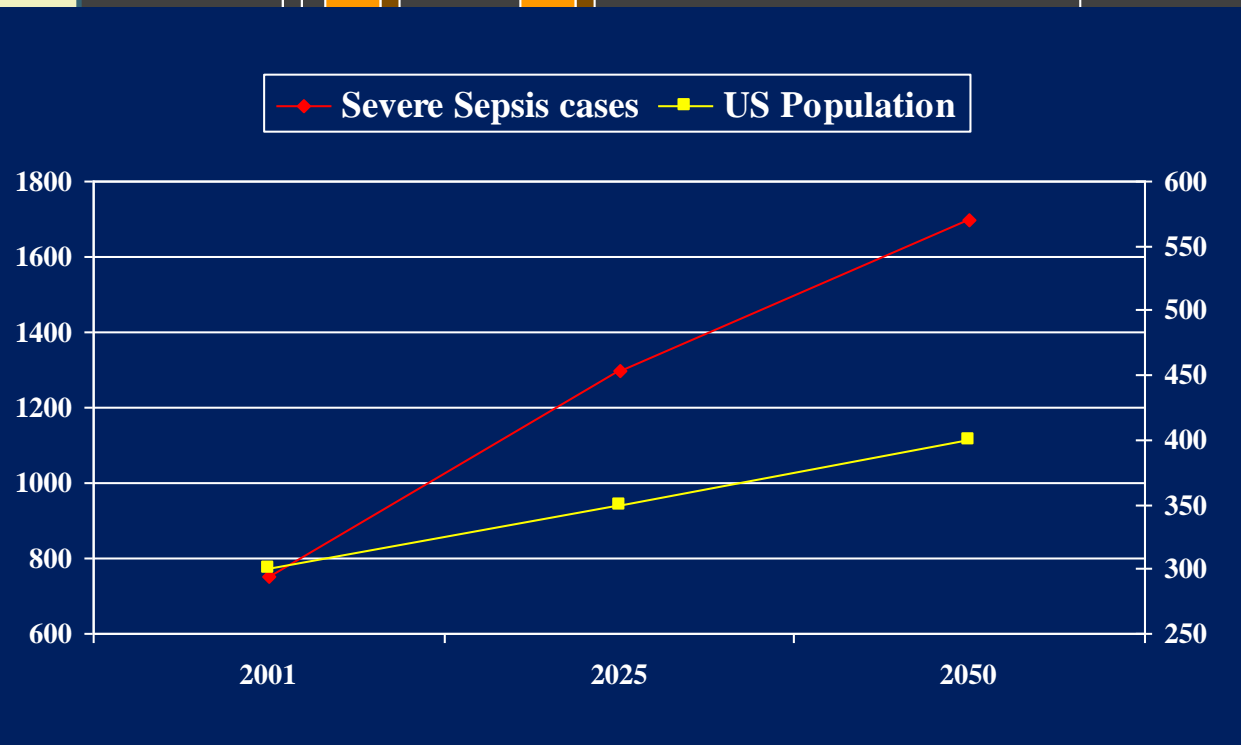
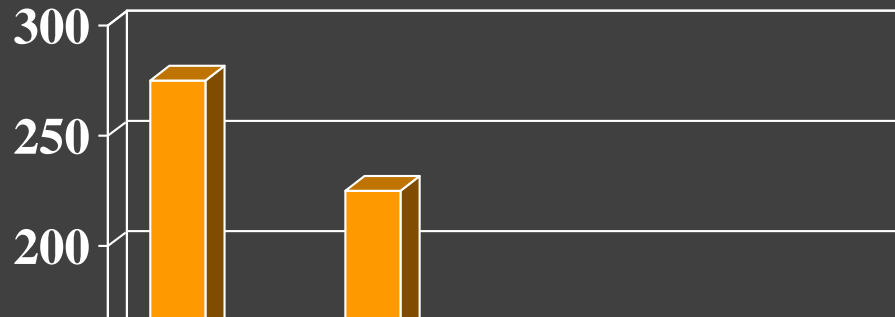
- **Sepsis**

Known or suspected infection, plus ≥ 2 SIRS Criteria

- **Severe Sepsis**

- Sepsis plus >1 organ dysfunction.

Severe Sepsis



Incidence
Mortality



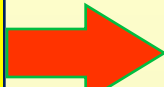
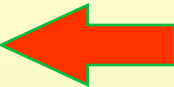
Infection



Vasodilation

Inflammatory Mediators

Endothelial Dysfunction



Hypotension

Microvascular Plugging

Vasoconstriction

Edema



Maldistribution of Microvascular Blood Flow



Ischemia



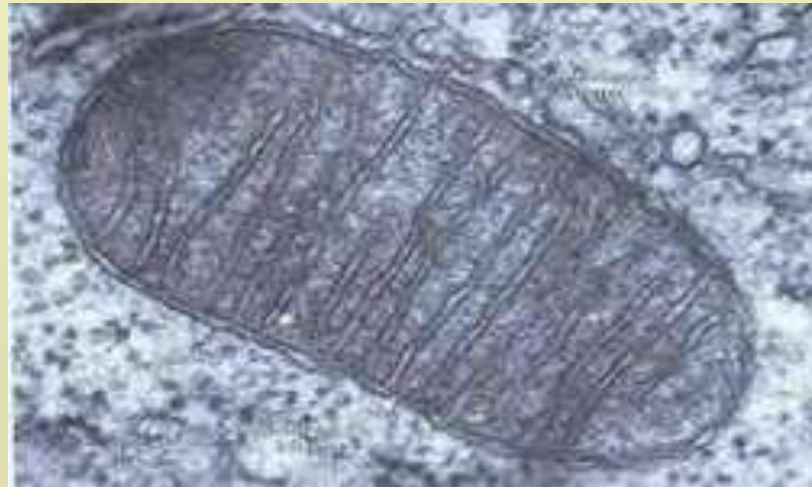
Cell Death



Organ Dysfunction

Clinical Signs of Severe Sepsis

- **Myocardial Depression.**
- **Altered Vasculature.**
- **Altered Organ Perfusion.**
- **Imbalance of O₂ delivery and Consumption.**
- **Metabolic (Lactic) Acidosis.**



Mythochondrial failure

Organ System Involvement

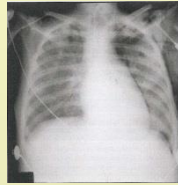
➤ Circulation

- Hypotension,
- increases in microvascular permeability
- Shock



➤ Lung

- Pulmonary Edema,
- hypoxemia,
- ARDS

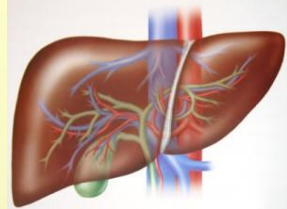


➤ Hematologic

- DIC, coagulopathy
- (DVT)



Organ System Involvement

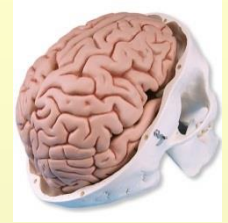


➤ GI tract

- Stress ulcer
- Translocation of bacteria,
- Liver Failure,
- Gastroparesis and ileus

➤ Nervous System

- Encephalopathy



▶ Skeletal Muscle

Table 4. Risk of death according to number of evolving organ dysfunctions after bacteremic sepsis

No. of Organ Dysfunctions	1984–1988			1994–1997		
	Hazard Ratio	95% CI	<i>p</i> Value	Hazard Ratio	95% CI	<i>p</i> Value
1	2.51	0.5–13.7	.28	1.46	0.3–8.0	.663
2	6.40	1.4–30.1	.019	3.05	0.7–14.2	.154
3	23.49	5.4–101.9	<.001	6.23	1.4–28.1	.017
≥4	36.04	8.7–150	<.001	11.07	2.5–48.2	.001

Definitions (ACCP/SCCM)

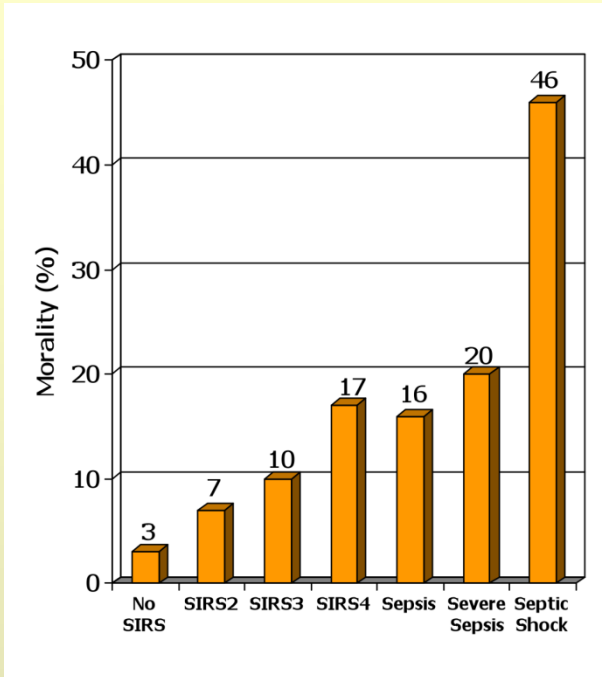
- **Septic Shock**

- **Sepsis induced with hypotension despite adequate resuscitation along with the presence of perfusion abnormalities which may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status.**

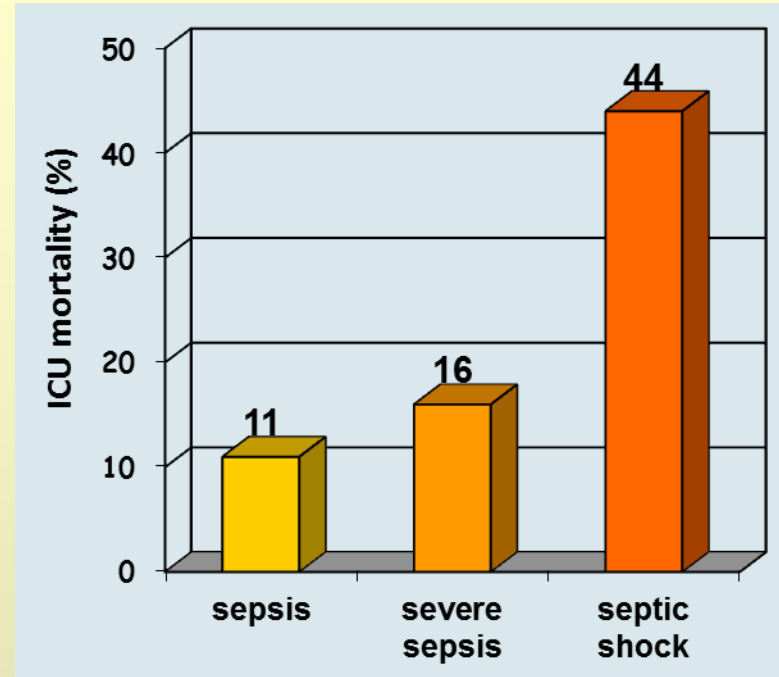


Sepsis & Mortality

Bone CCM 1992;20:864



Rangel-Frausto JAMA 1995;273:117



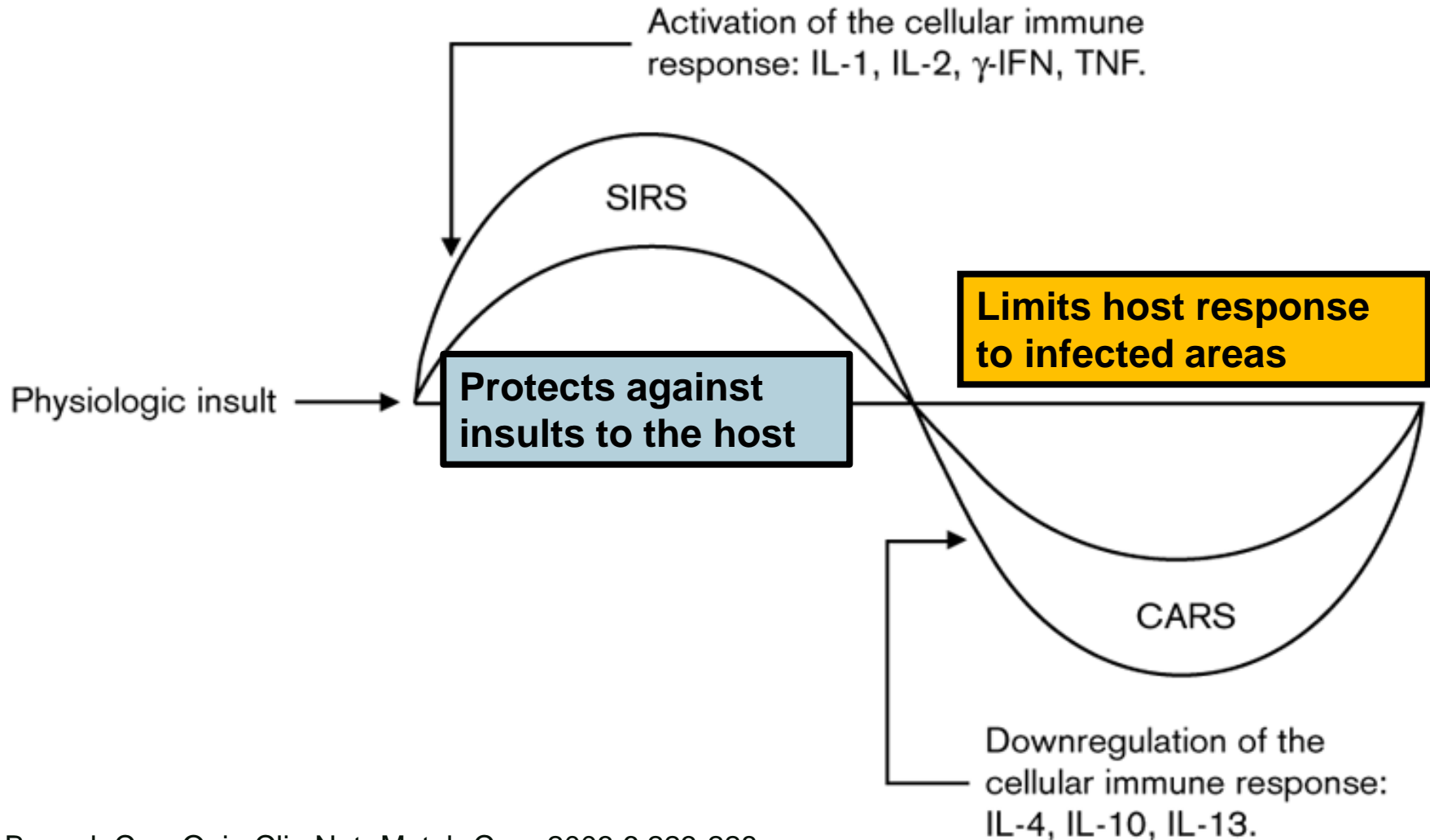
Povoa CCM 2009;37:410



Increasing of inflammatory activity and mortality!



Immune response in Sepsis



Therapeutic Strategies in Sepsis

➤ Early Detection

- Obtain serum lactate level.

➤ Early Blood Cx/Antibiotics

- within 3 hours of presentation.
- Source control

➤ Early EGDT:

- Hypotension (SBP < 90, MAP < 65) or lactate > 4 mmol/L:
- initial fluid bolus 20-40 ml of crystalloid (or colloid equivalent) per kg of body weight.

• Vasopressors:

- Hypotension not responding to fluid
- Titrate to MAP > 65 mmHg.

• Septic shock or lactate > 4 mmol/L:

- CVP and ScvO₂ measured.
- CVP maintained >8 mmHg.
- MAP maintain > 65 mmHg.

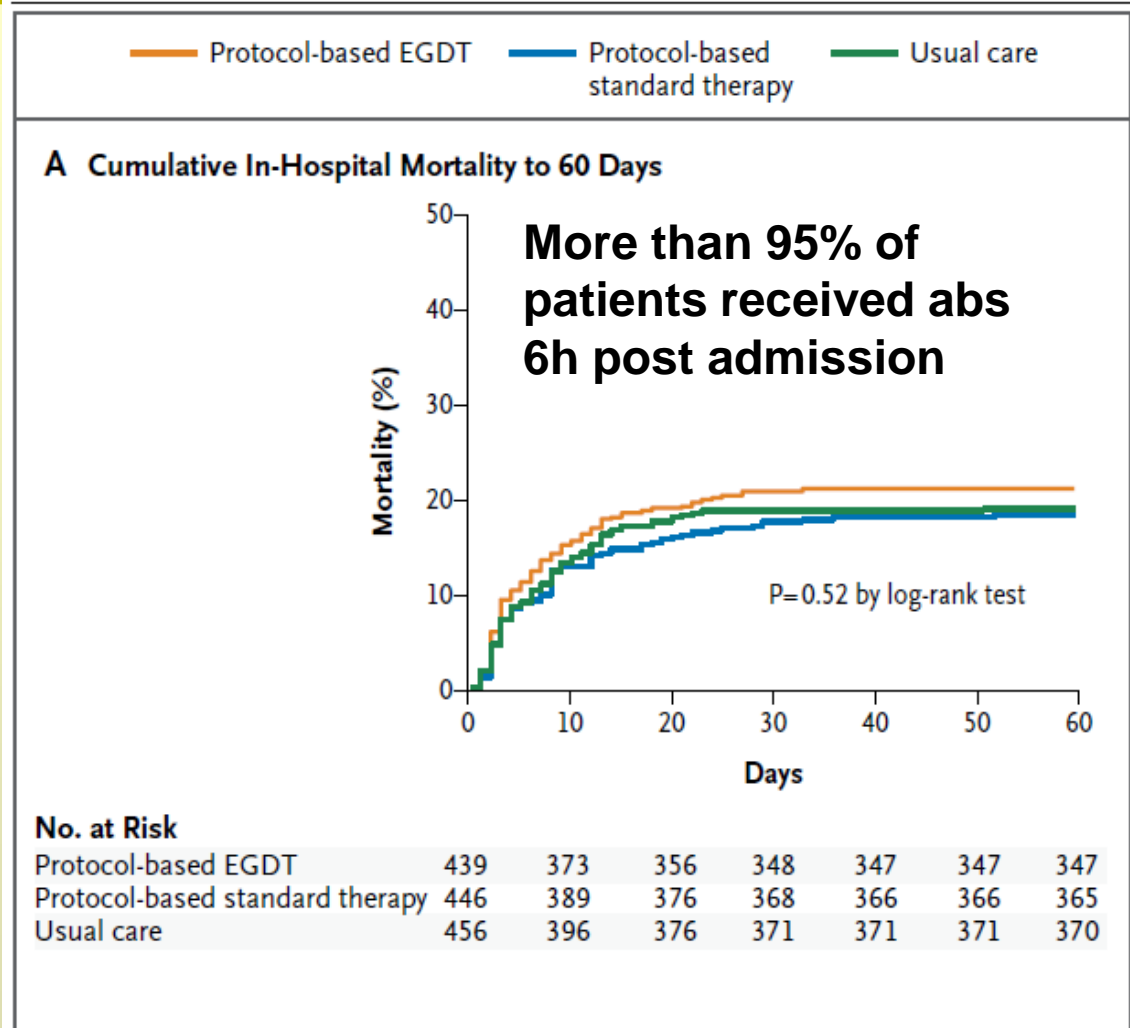
• ScvO₂ < 70% CVP > 8 mmHg, MAP > 65 mmHg:

- PRBCs if hematocrit < 30%.
- Inotropes.

Severe sepsis at the emergency department

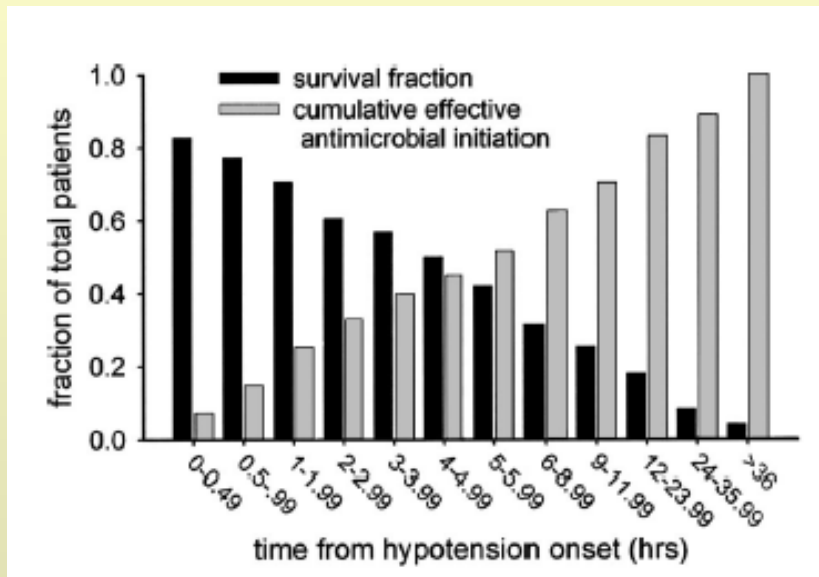
- Usual care

90 day mortality 18.9%



Diagnosis of infection

➤ AB delay → poor outcome ➤ **BUT**, AB are not benign!



Kumar CCM 2006;34:1589

↓AB → ↓ mortality
 → ↓ MDR
Singh AJRCCM 2000;162:505

↓AB → ↓ mortality
 → ↓ LOS
Weiss AJRCCM 2011;164:680

Only 50% receive ab until 6h after admission

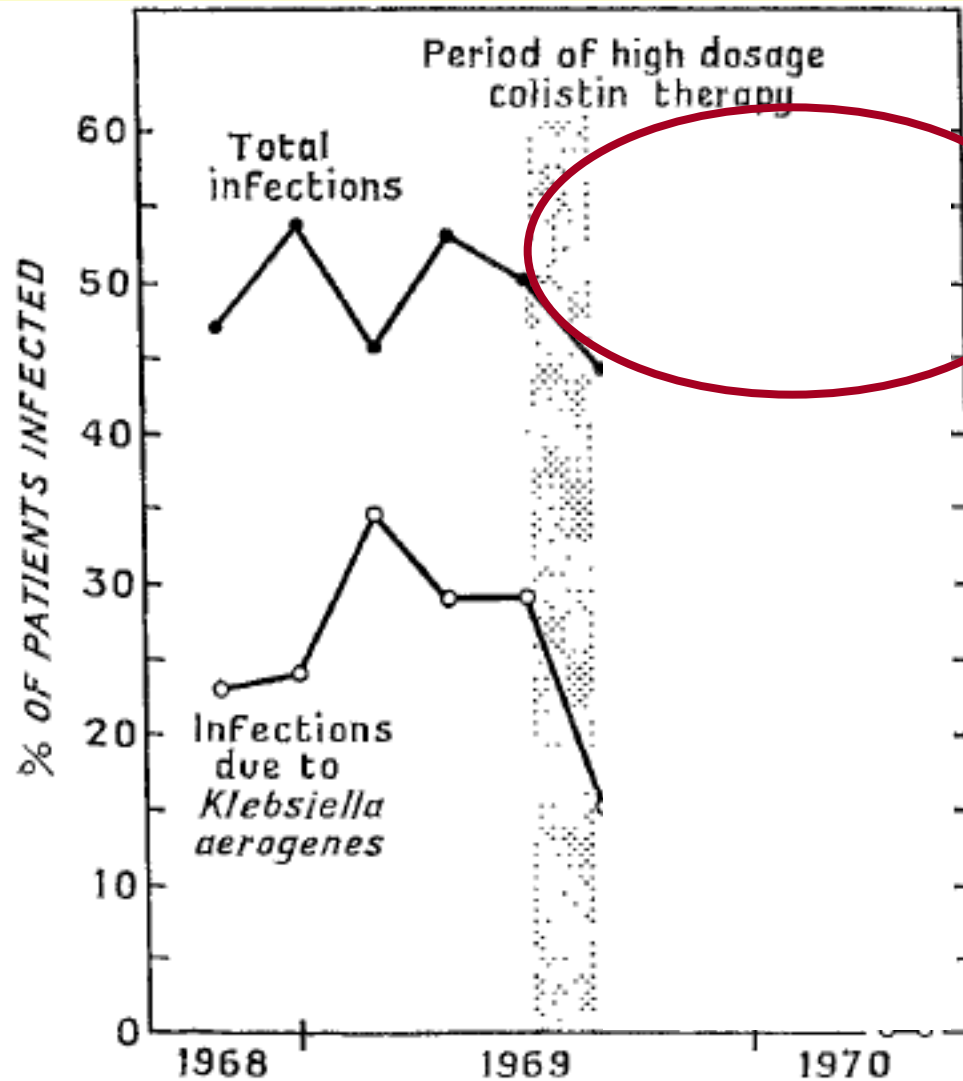
Antibiotic detrimental effects?

Neurosurgical patients

Klebsiella aerogens

High LOS

Increase Mortality





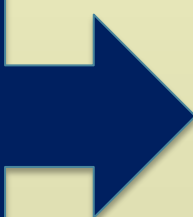
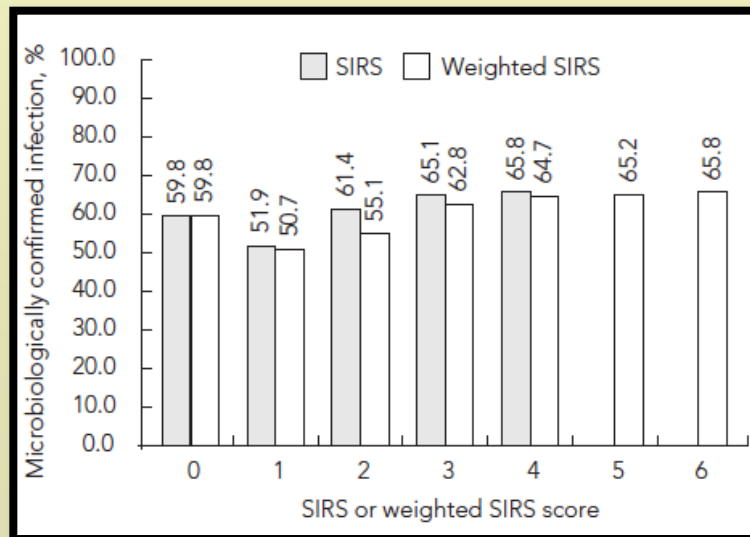
“as the physicians say it happens in hectic fever (*sepsis*), that **in the beginning of the malady it is easy to cure but difficult to detect**, but in the course of time, not having been either detected or treated in the beginning, **it becomes easy to detect but difficult to cure**”

SIRS criteria - criticisms

Table 1. SIRS criteria and weighted SIRS scores in predicting microbiologically confirmed infection

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Positive likelihood ratio	Negative likelihood ratio
WCC	52.5%	52.8%	63.3%	41.7%	1.11	0.90
Temperature	46.6%	59.0%	63.8%	41.6%	1.13	0.90
Tachycardia	65.2%	41.0%	63.2%	43.2%	1.11	0.85
Tachypnoea	49.4%	51.9%	61.5%	39.8%	1.03	0.97
Traditional (≥ 2) SIRS	70.6%	37.5%	63.7%	45.1%	1.13	0.79
Weighted SIRS ≥ 3	63.5%	45.7%	64.5%	44.6%	1.17	0.80
Both temp and WCC present	27.3%	77.5%	65.3%	40.7%	1.21	0.94

Number of SIRS criteria and the likelihood of documented infection

Identification of septic focus

- history and physical examination
- imaging
- cultures: Blood, urine, sputum, abscess.



- Lab results are poorly sensitive and have low specificity for the diagnosis of sepsis
- Microbiological cultures usually take 24-48h

Biomarkers and Diagnosis of Infection

	Sensitivity (%)	Specificity (%)	AUC
PCT	70-91	68-92	0.64-0.95
CRP	10-98	44-99	0.68-0.82

Simon CID 2004;39:206. Erratum: CID 2005;40:1386
 van der Meer BMJ 2005;331:26
 Uzzan CCM 2006;34:1996
 Tang Lancet Infect Dis 2007;7:210

Why use biomarkers?

From the PROBLEM Early diagnosis of infection, before clinical deterioration!

1. Heterogeneity assessment
2. ACCP/SCCM Consensus Conference criteria to define the absence of sepsis (assessing degrees of clinical severity)
3. **Gold standard, that is presence of documented infection and no antibiotic therapy (Cohen CCM 2000)**

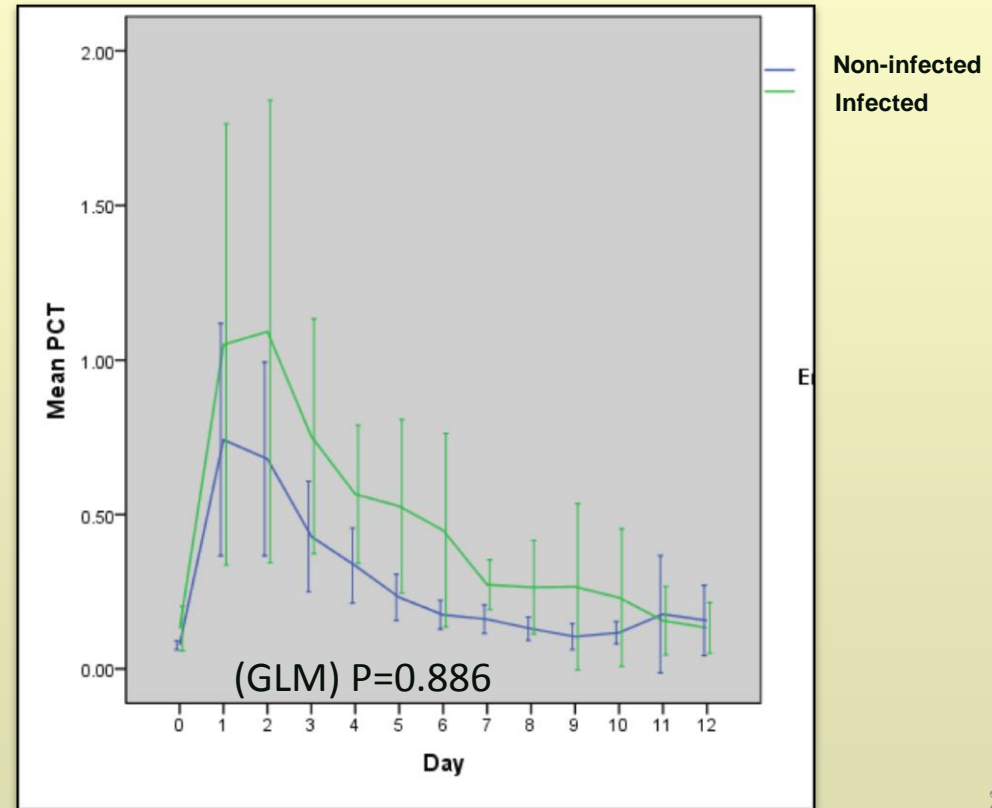
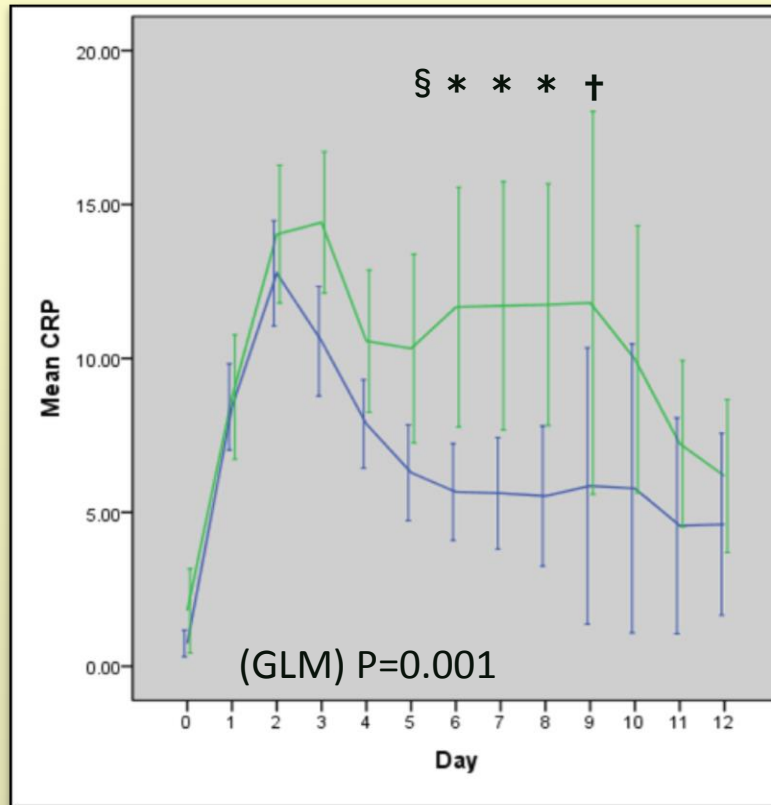


PCT and CRP Post operative infections in elective colonic surgery

N=50 pts

Infections 21 (16 surgical site infection)

Time of infection – day 7 (median)



*p<0.01 (Bonferroni correction)

§ - p=0.012

† - p=0.02



Sources of Sepsis

The International Cohort Study



	Severe Sepsis	Septic Shock
Respiratory	66	53
Abdomen	9	20
Bacteremia	14	16
Urinary	11	11
Multiple	-	-

35% mortality



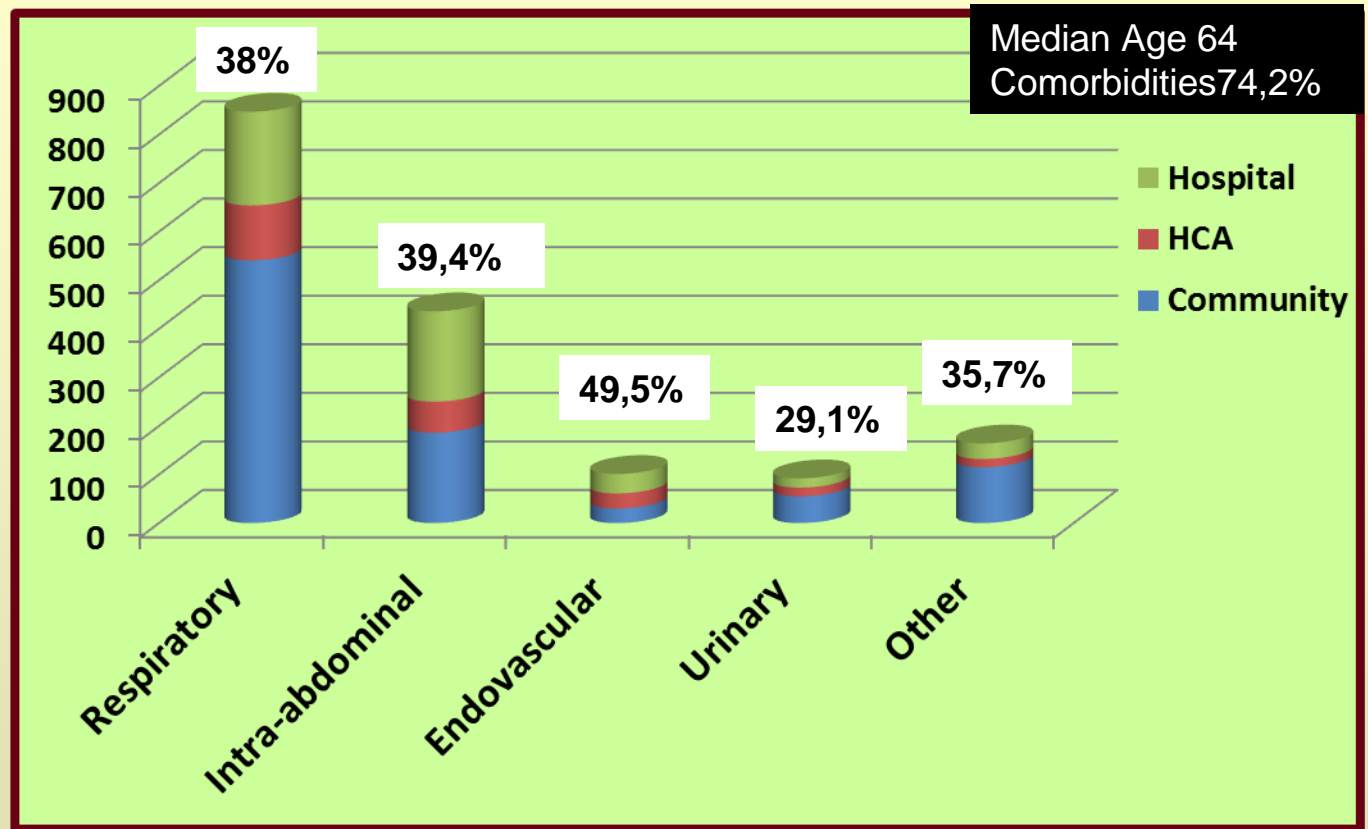
Sources of Sepsis

The INFAUCI study

INFAUCI

Infecção na
Admissão à UCI

- H Beja
- H Covões
- H Funchal
- H Gaia
- H Guimarães
- H L A
- H S F Xavier
- H S João
- H S Sebastião
- H Viseu
- HUC
- IPO PORTO



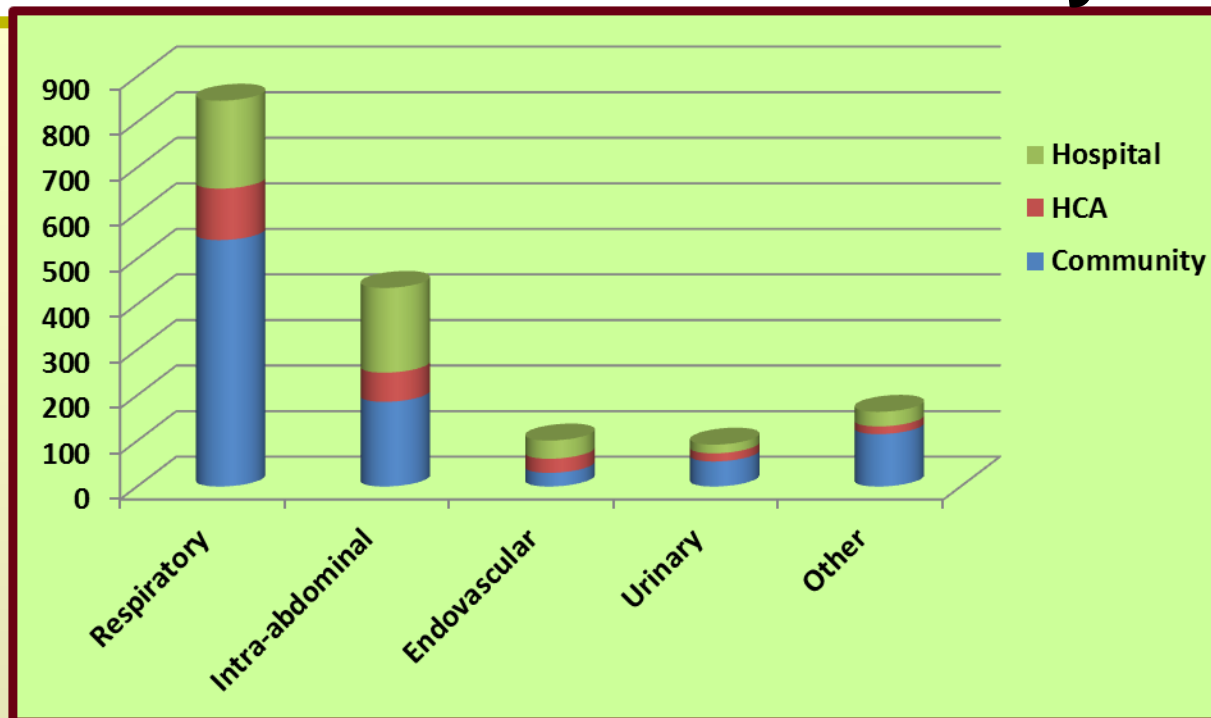
Hospital mortality 38,2%

Infection on admission to the ICU. Submitted



Sources of Sepsis

The INFAUCI study



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- IPO PORTO

Hospital mortality

38,2%

Septic Shock

51,8%

Positive Microbiology

48,3% (comm 39,9% vs H 57,5%)

Adequate antibiotics

74,4% (comm 83% vs H 62,8%)

Mortality after ICU discharge (inf 14,2% vs n inf 9,6%)

Late ICU admission (comm infections) 35,9% vs 35,1%

Infection on admission to the ICU. Submitted



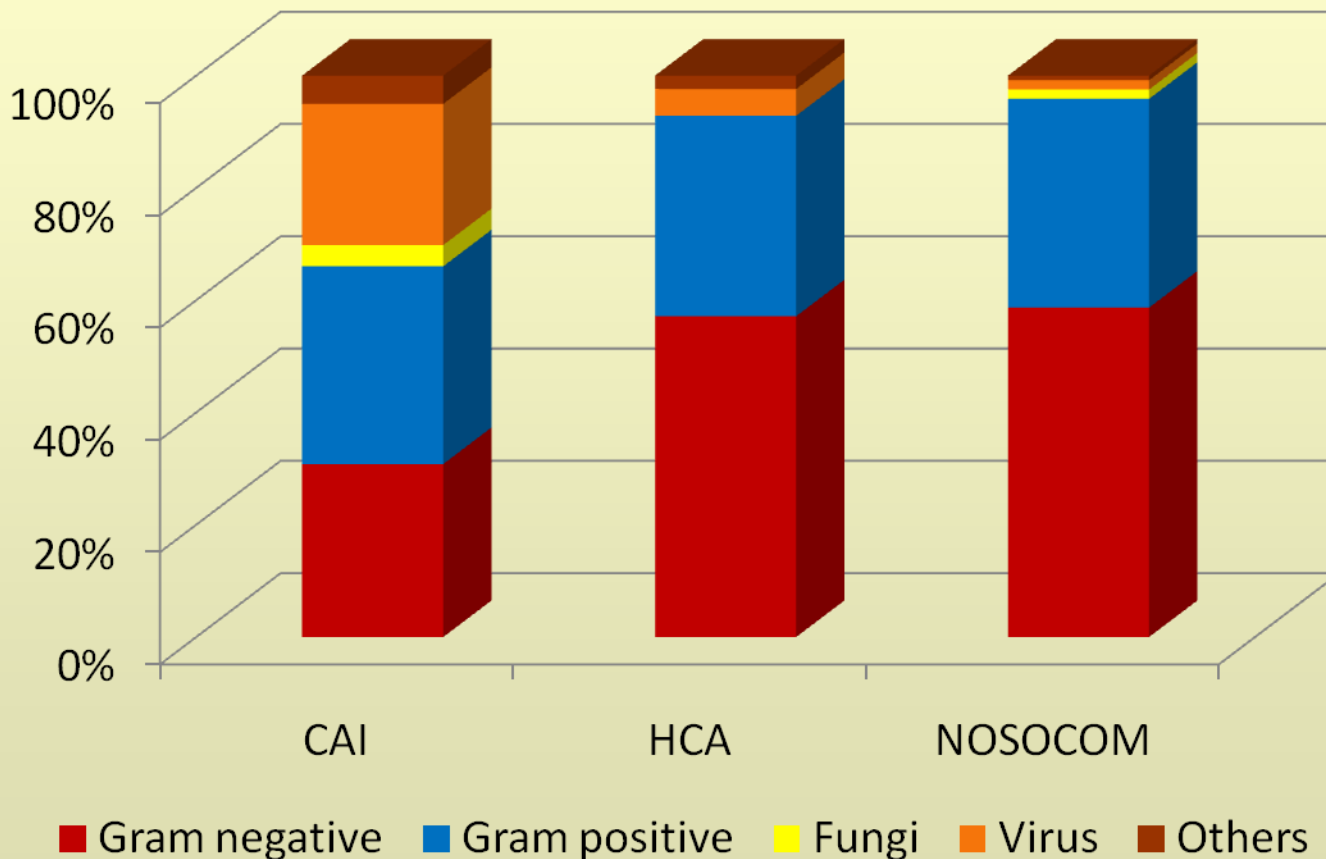


PNEUMONIA

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Infection on admission to the ICU. Submitted



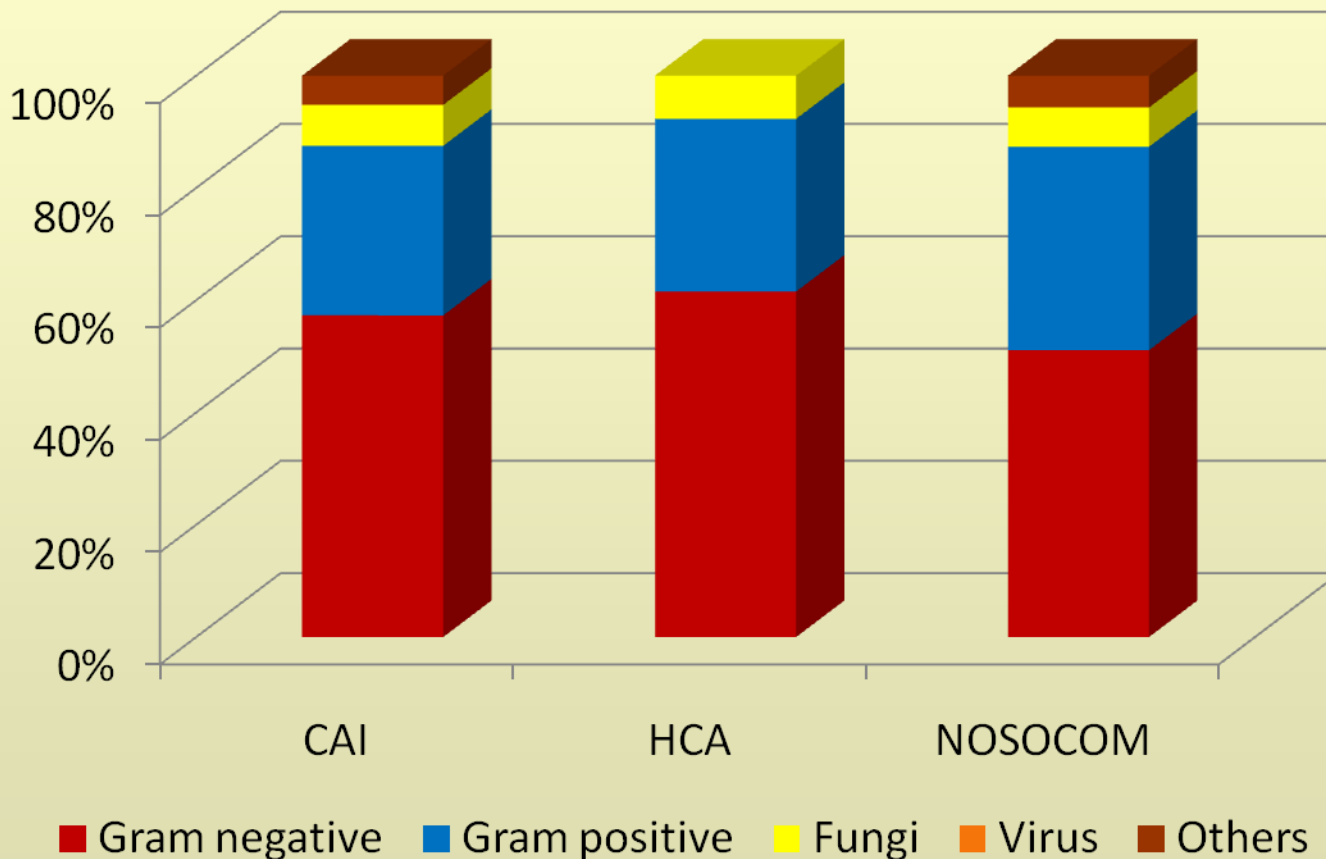


INTRA-ABDOMINAL

INFAUCI

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Infection on admission to the ICU. Submitted



Decrease in sepsis mortality in the XXIth century

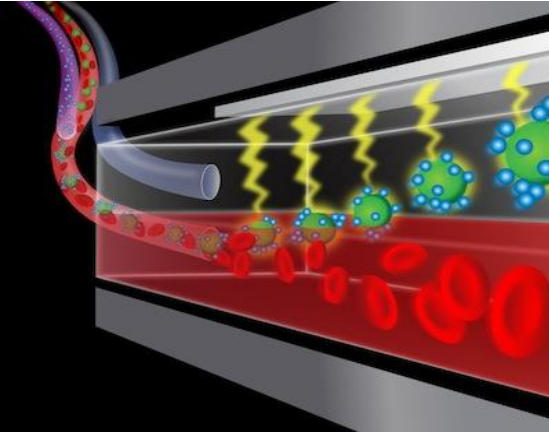
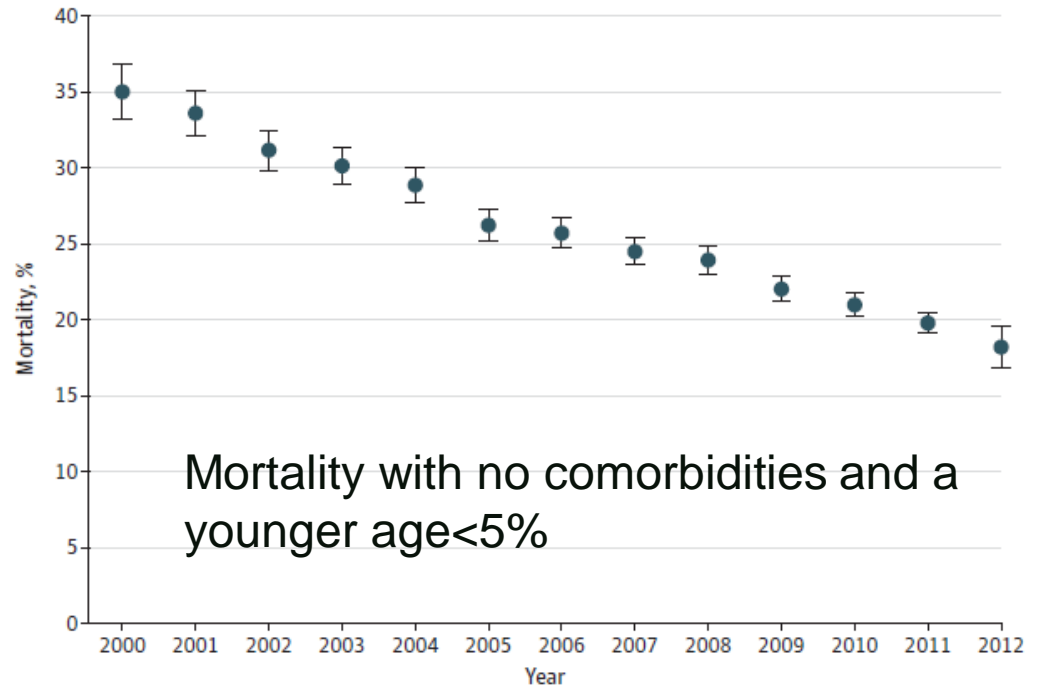


Figure 1. Mean Annual Mortality in Patients With Severe Sepsis

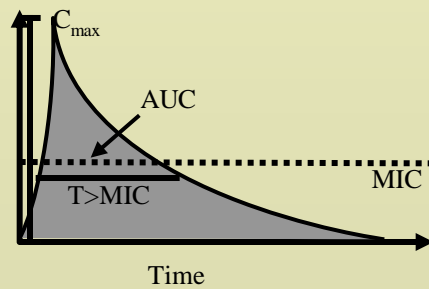
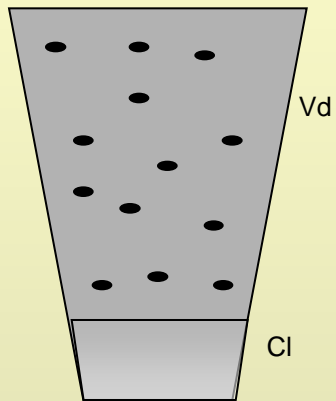


No. of patients 2708 3783 4668 5221 6375 6987 7627 8529 8797 10277 11367 12213 12512

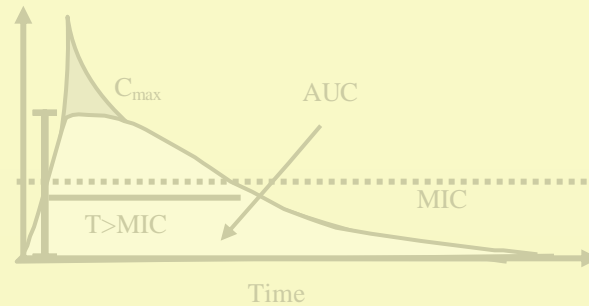
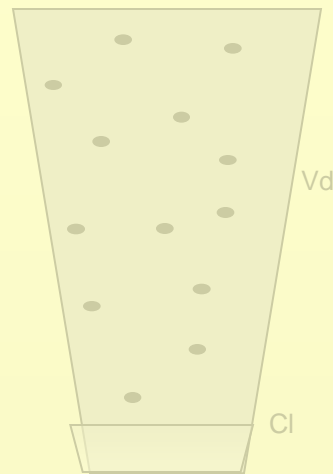
Kaukonen *JAMA*. doi:10.1001/jama.2014.2637

Antibiotics Pharmacokinetics

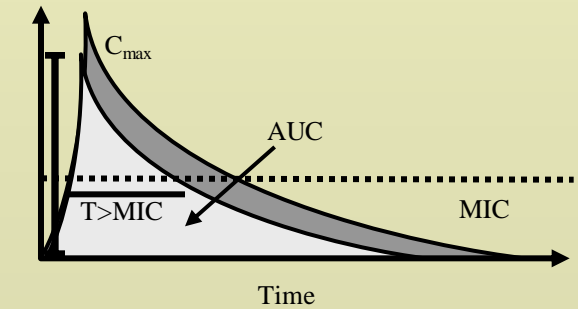
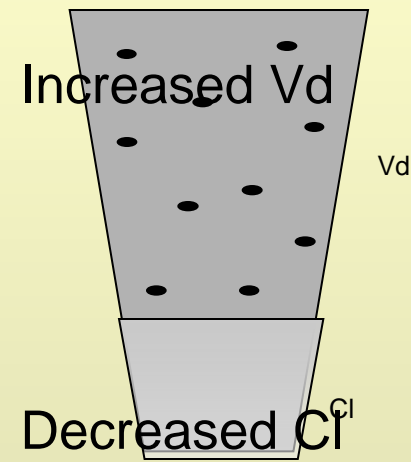
Healthy



Organ Failure



Sepsis



The Process of Care

Improvements in Sepsis outcome with careful process of care

- Early diagnosis (including adequate microbiological samples)
- Adequate and early referentiation to ICU or ward
- Early and adequate antibiotics

- Avoid nosocomial infections
- Careful post ICU care





SECOND OPINION

BY ROB ROGERS

