

# Qual o papel do médico no protocolo de sepse ?

*Danilo Teixeira Noritomi*  
*Coordenador da UTI do H. Paulistano*



# O Que é um médico?



# O Que é um medico?

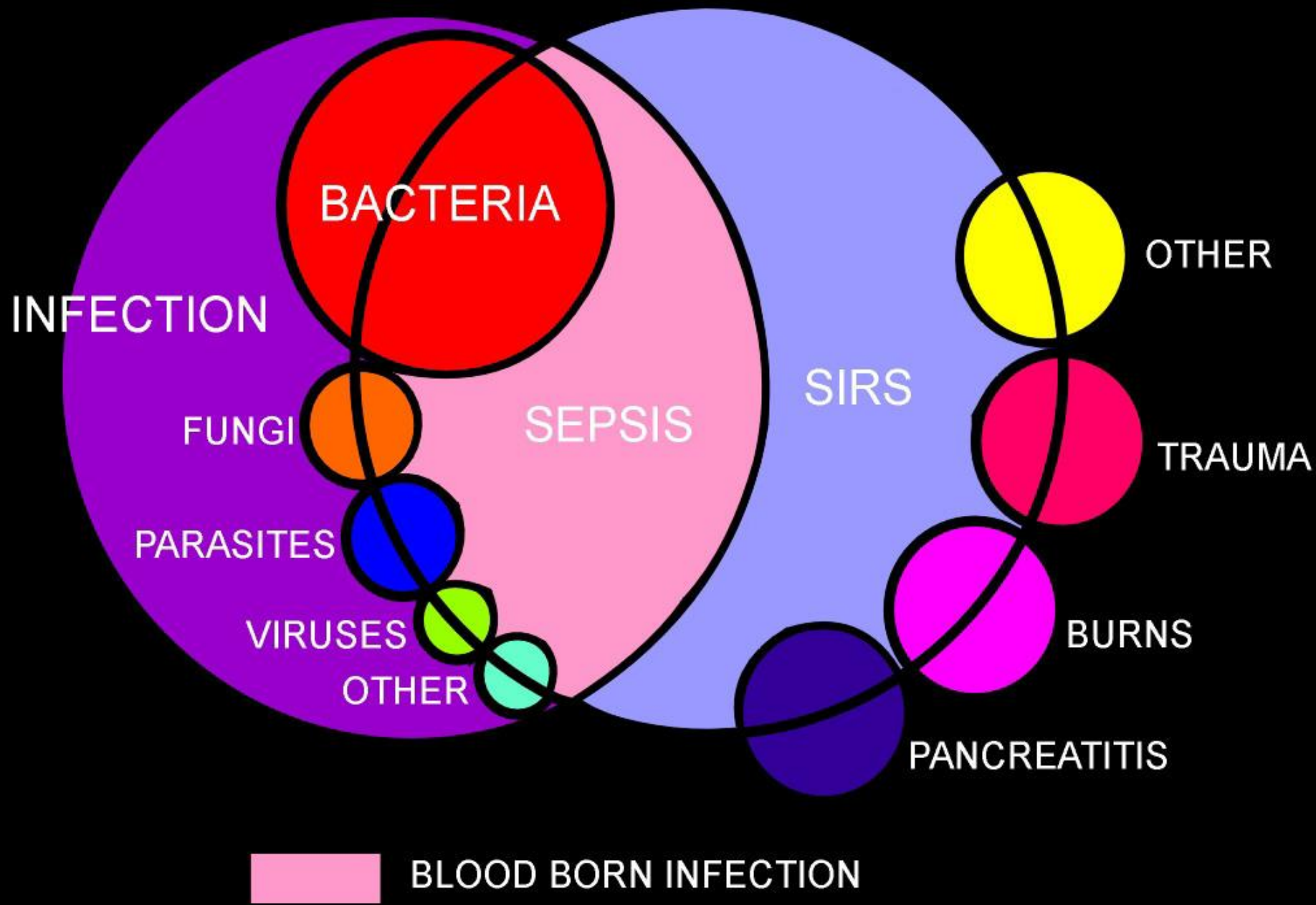
- Clínico
- Cientista
- Estudioso
- Líder
- Barreira
- Artista?



# O Clínico

- Apresentação
  - Cansaço, tosse
  - Sonolência
  - $T=38,2C$
  - Taquicardia
  - Roncos difusos







# Conduta

- Antitermico
- Repouso (atestado!)
- Vitamina C?



# Sepse é um problema?



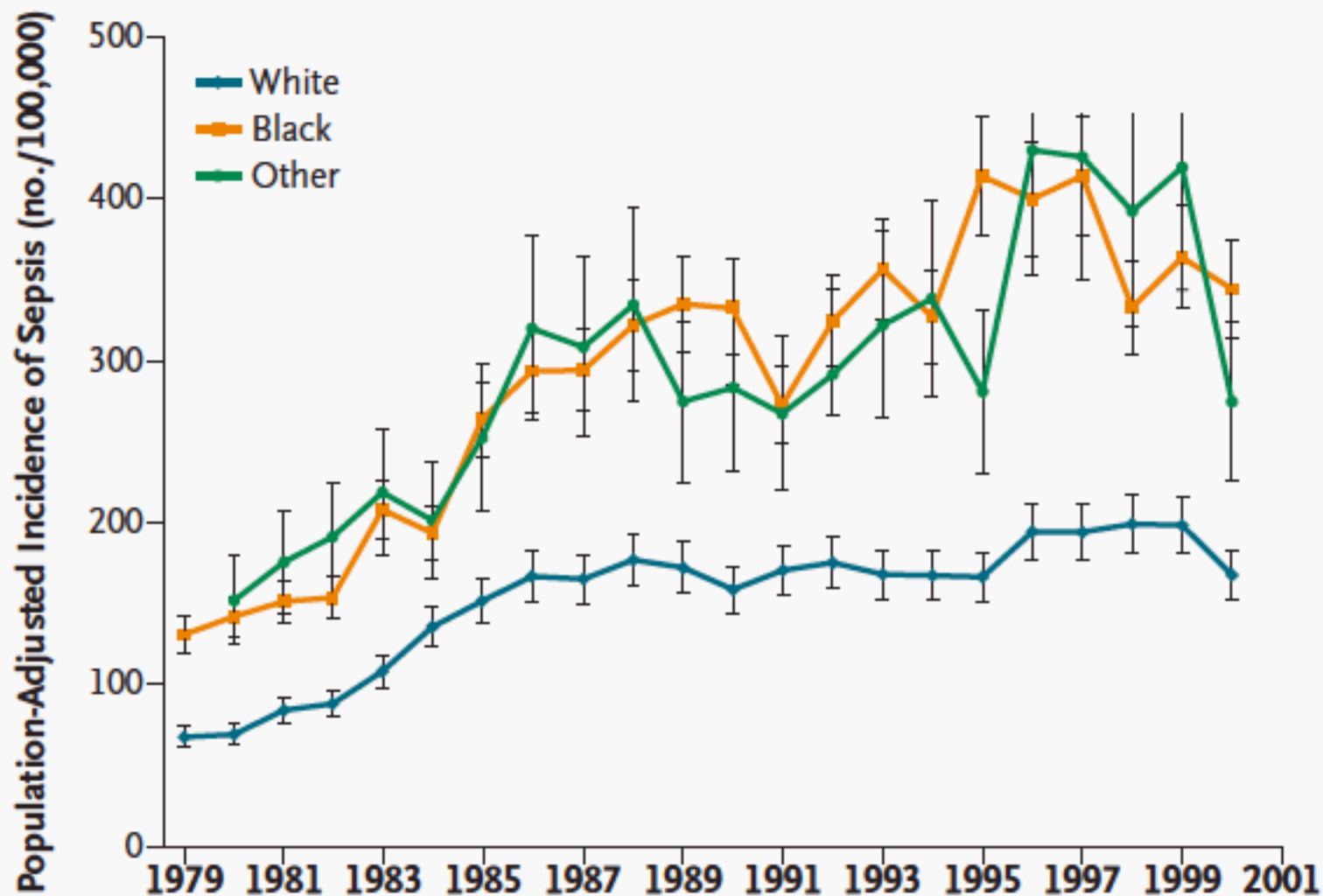
ORIGINAL ARTICLE

# The Epidemiology of Sepsis in the United States from 1979 through 2000

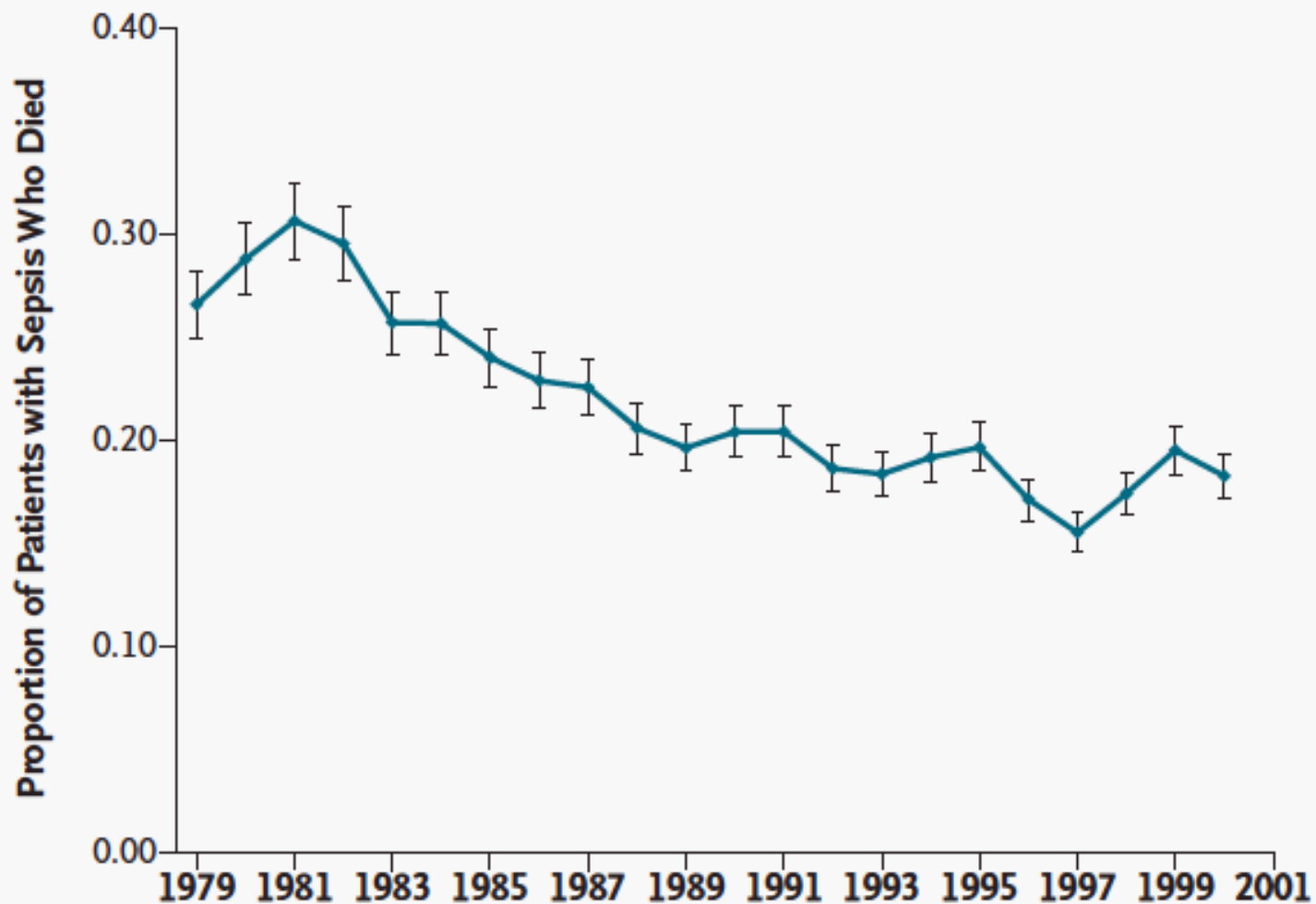
Greg S. Martin, M.D., David M. Mannino, M.D., Stephanie Eaton, M.D.,  
and Marc Moss, M.D.







**Figure 2. Population-Adjusted Incidence of Sepsis, According to Race, 1979–2000.** Points represent the annual incidence rate, and I bars the standard error.



**Figure 4.** Overall In-Hospital Mortality Rate among Patients Hospitalized for Sepsis, 1979–2000.

Mortality averaged 27.8 percent during the first six years of the study and 17.9 percent during the last six years. The I bars represent the standard error.

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

- Retrospectivo
- Banco de dados administrativo



## Severe sepsis admissions/All admissions (%)

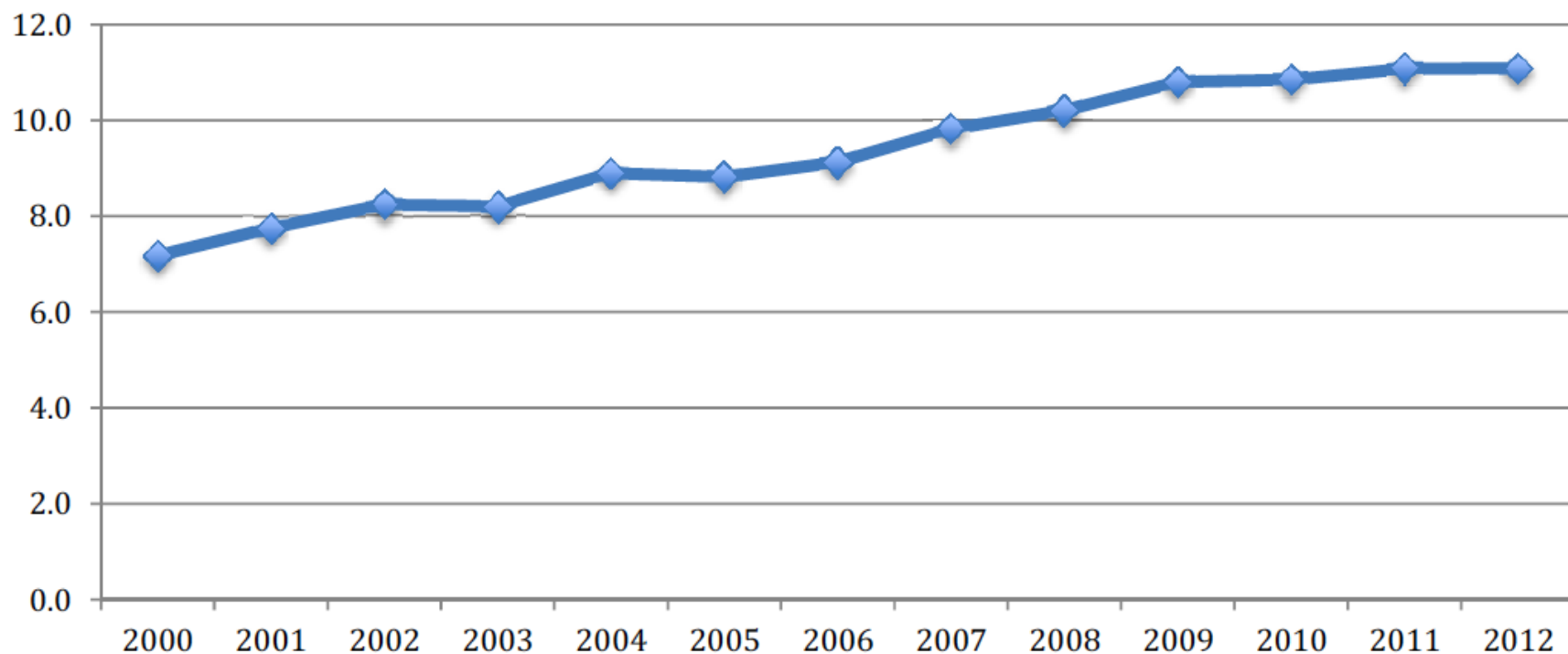
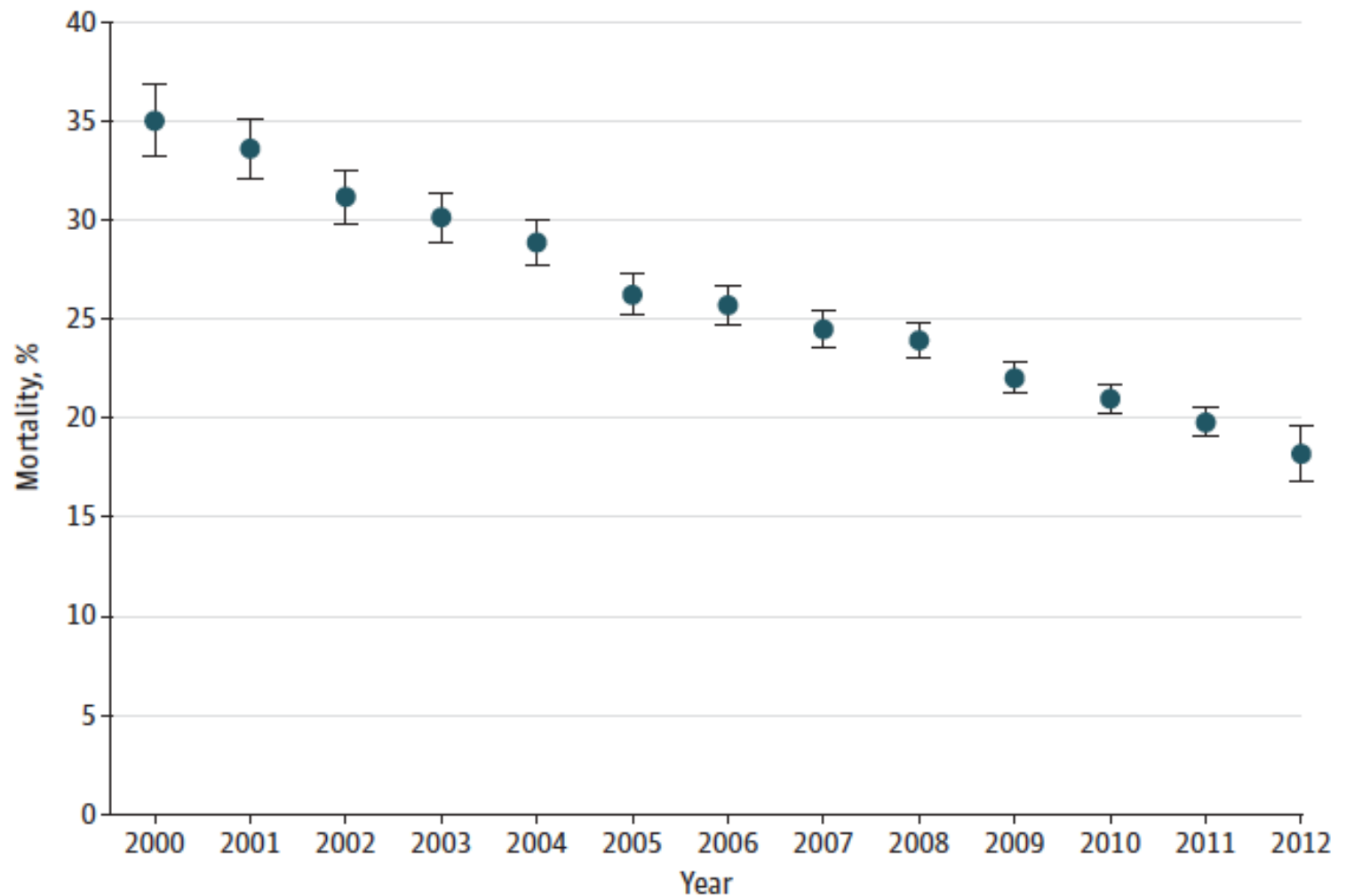


Figure 1. Mean Annual Mortality in Patients With Severe Sepsis



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



# Portanto

- P: Sepsé é um problema?
- R: Sim, sepsé é uma condição de incidencia crescente. A taxa de letalidade hospitalar é decrescente porem ainda significativa



# Próxima pergunta

- Temos uma solução?





What road do I take?

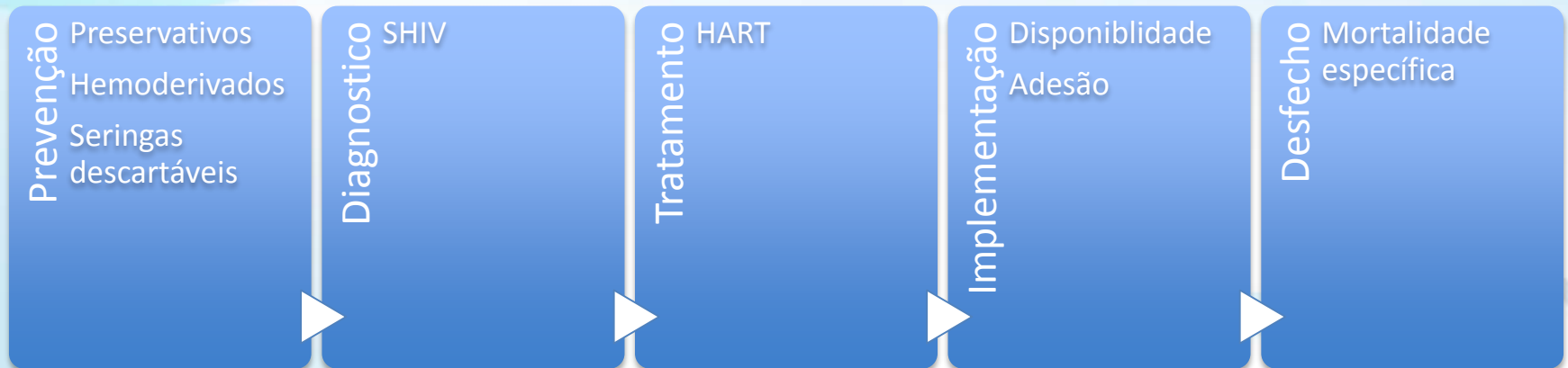
Well where are you going?

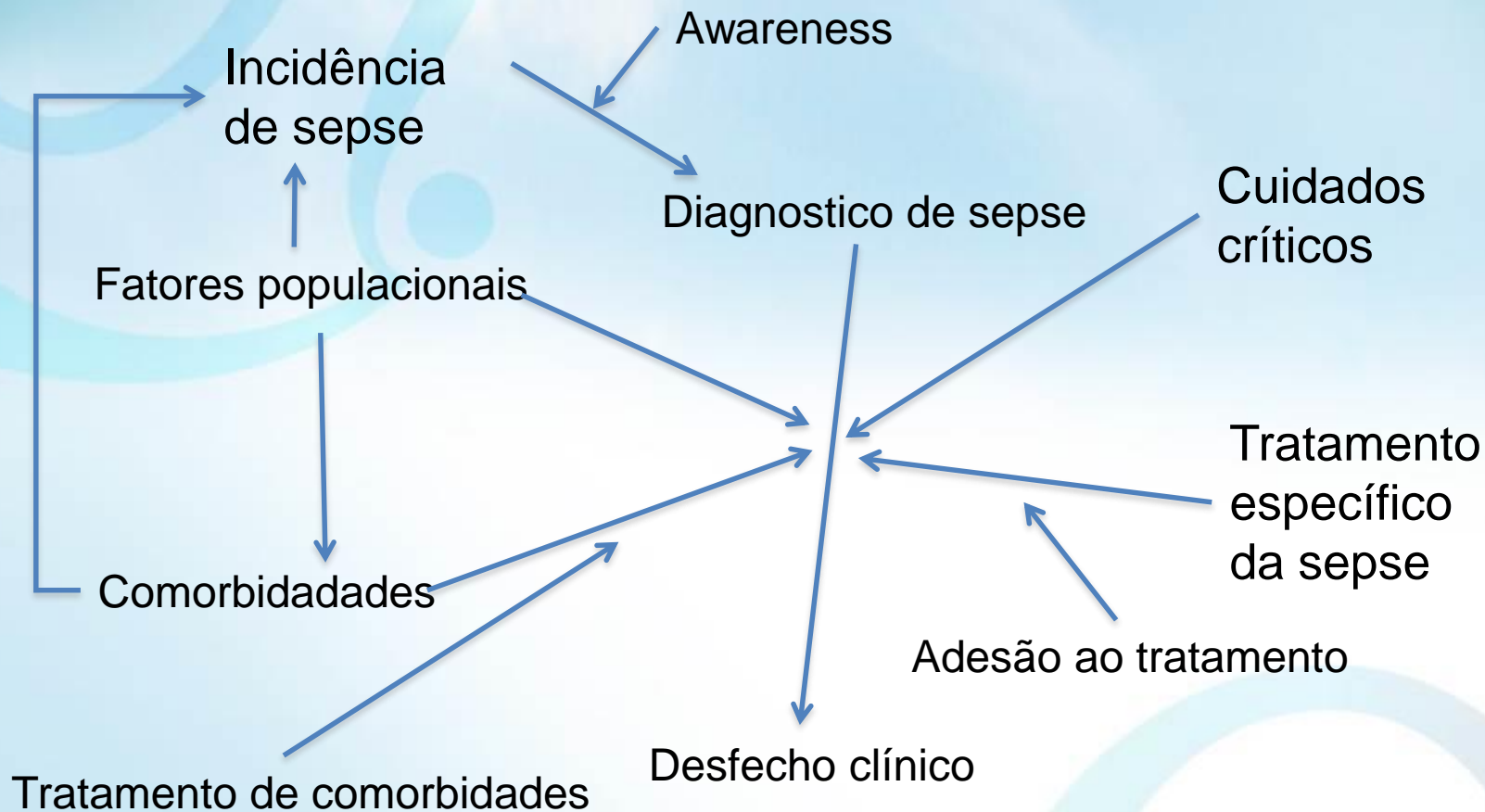
I don't know

Then it doesn't matter. If you  
don't know where you are going,  
any road will get you there.



# Se fosse assim...

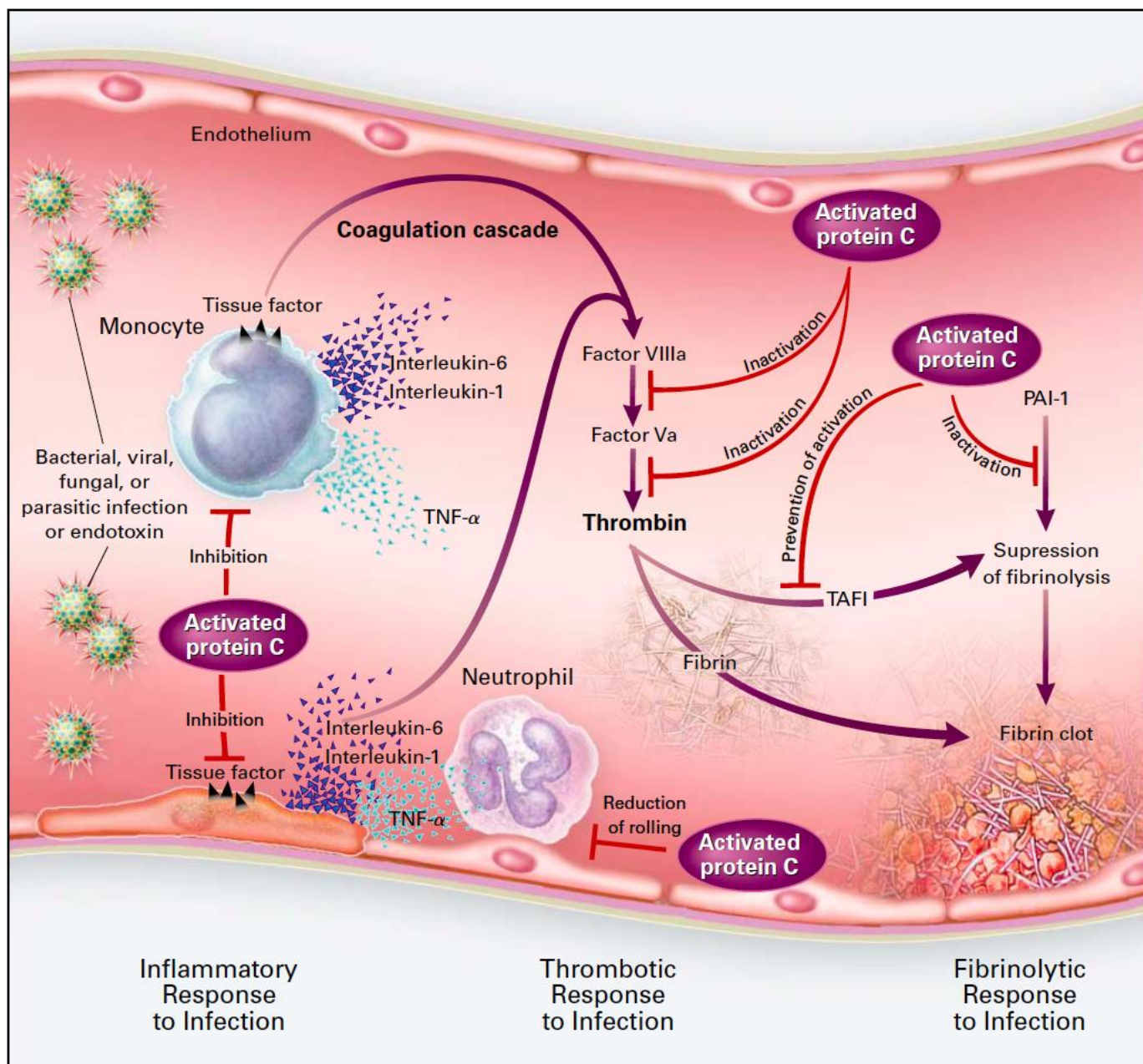




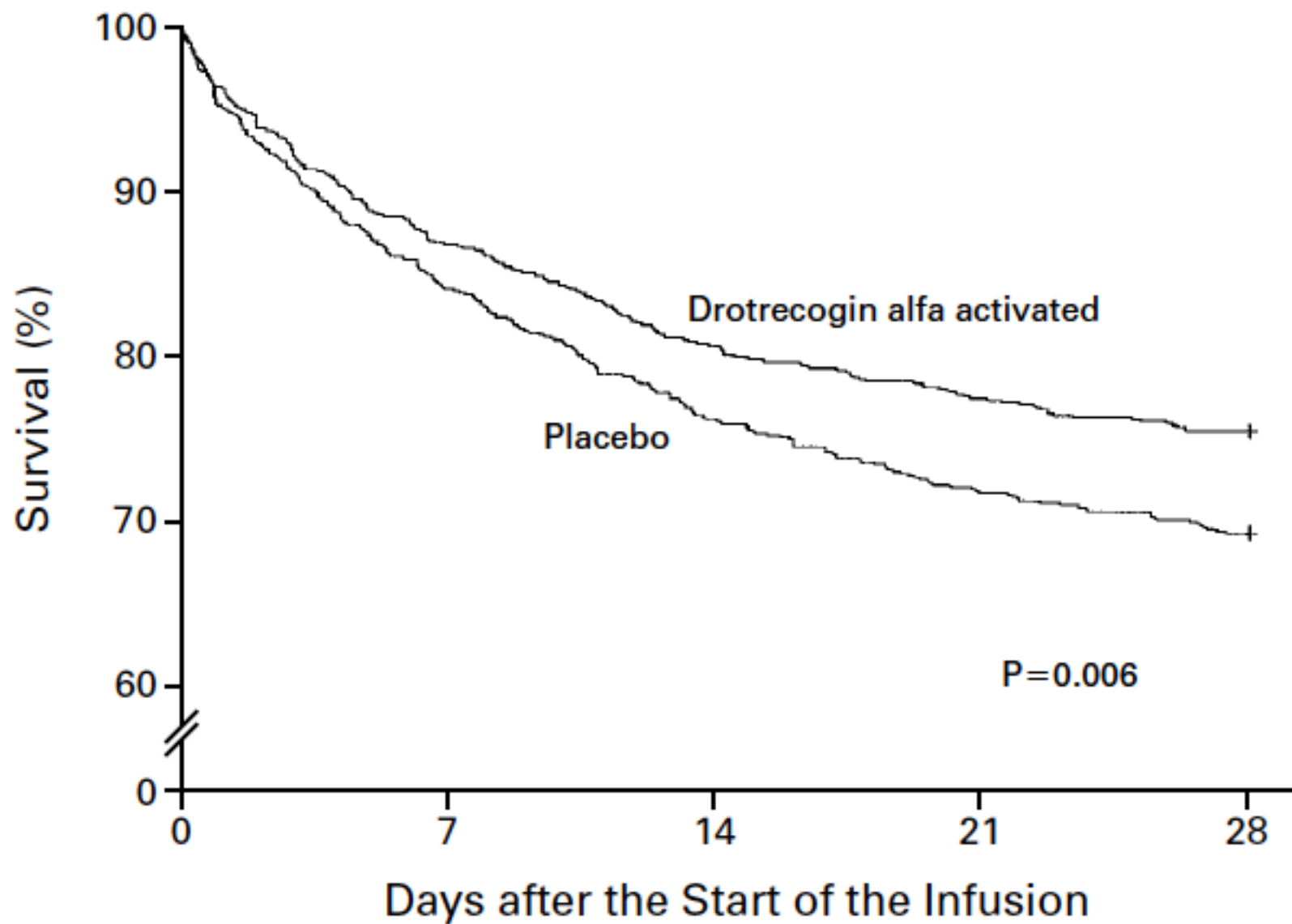


# Terapias específicas para sepse





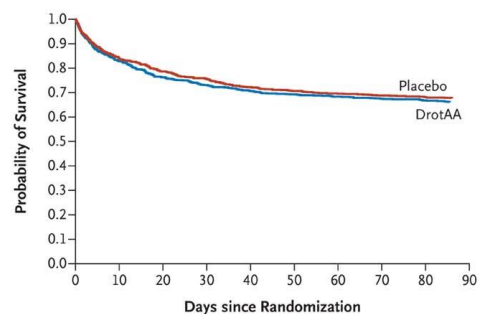
**Figure 1.** Proposed Actions of Activated Protein C in Modulating the Systemic Inflammatory, Procoagulant, and Fibrinolytic Host Responses to Infection.



# SEVERE SEPSIS — A NEW TREATMENT WITH BOTH ANTICOAGULANT AND ANTIINFLAMMATORY PROPERTIES

On the basis of the results of this trial, activated protein C should be given to patients who meet all the inclusion criteria, including evidence of end-organ dysfunction with shock, acidosis, oliguria, or hypox- emia... Because the cost of this new therapy will be substantial, ways to make this drug affordable throughout the world should be identified.

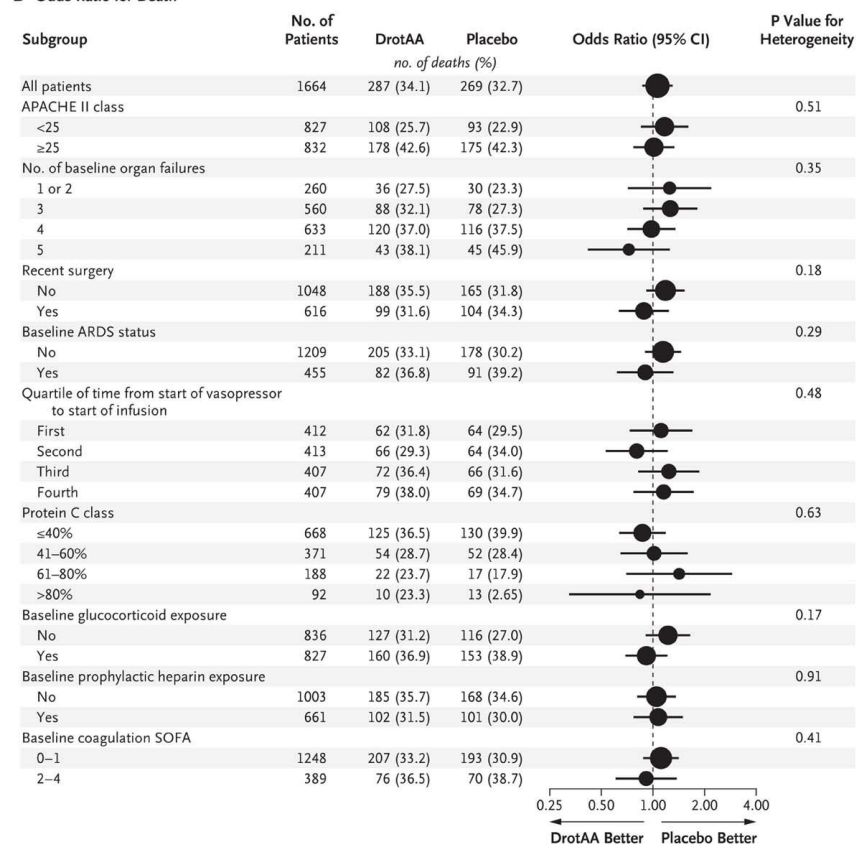
### A Probability of Survival



#### No. at Risk

Placebo	845	703	656	622	593	579	569	563	557	553
DrotAA	851	701	645	616	596	584	576	567	561	555

### B Odds Ratio for Death







## U.S. Food and Drug Administration

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## FDA Drug Safety Communication: Voluntary market withdrawal of Xigris [drotrecogin alfa (activated)] due to failure to show a survival benefit

### Safety Announcement

**[10-25-2011]** The U.S. Food and Drug Administration (FDA) is informing healthcare professionals and the public that on October 25, 2011, Eli Lilly and Company announced a worldwide voluntary market withdrawal of Xigris [drotrecogin alfa (activated)]. In a recent study, Xigris failed to show a survival benefit for patients with severe sepsis and septic shock.

**Xigris treatment should not be started in new patients. Xigris treatment should be stopped in patients being treated with Xigris.**

**All remaining Xigris product should be returned to the supplier from whom it was purchased.**

In a recently completed clinical trial (PROWESS-SHOCK trial), Xigris failed to show a survival benefit. In this trial of 1696 patients, 851 patients were enrolled in the Xigris arm and 845 patients were enrolled in the placebo arm. Results based on preliminary analyses done by Eli Lilly and Company, that were submitted to the FDA, showed a 28-day all cause mortality rate of 26.4% (223/846) in Xigris-treated patients compared to 24.2% (202/834) in placebo-treated patients, for a relative risk of 1.09; 95% CI (0.92, 1.28), and P-value = 0.31 (not statistically significant).



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# *The* NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

MAY 1, 2014

VOL. 370 NO. 18

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

The ProCESS Investigators\*

- RCT
- 3 braços
  - EGDT
  - Protocolo
  - Cuidados habituais

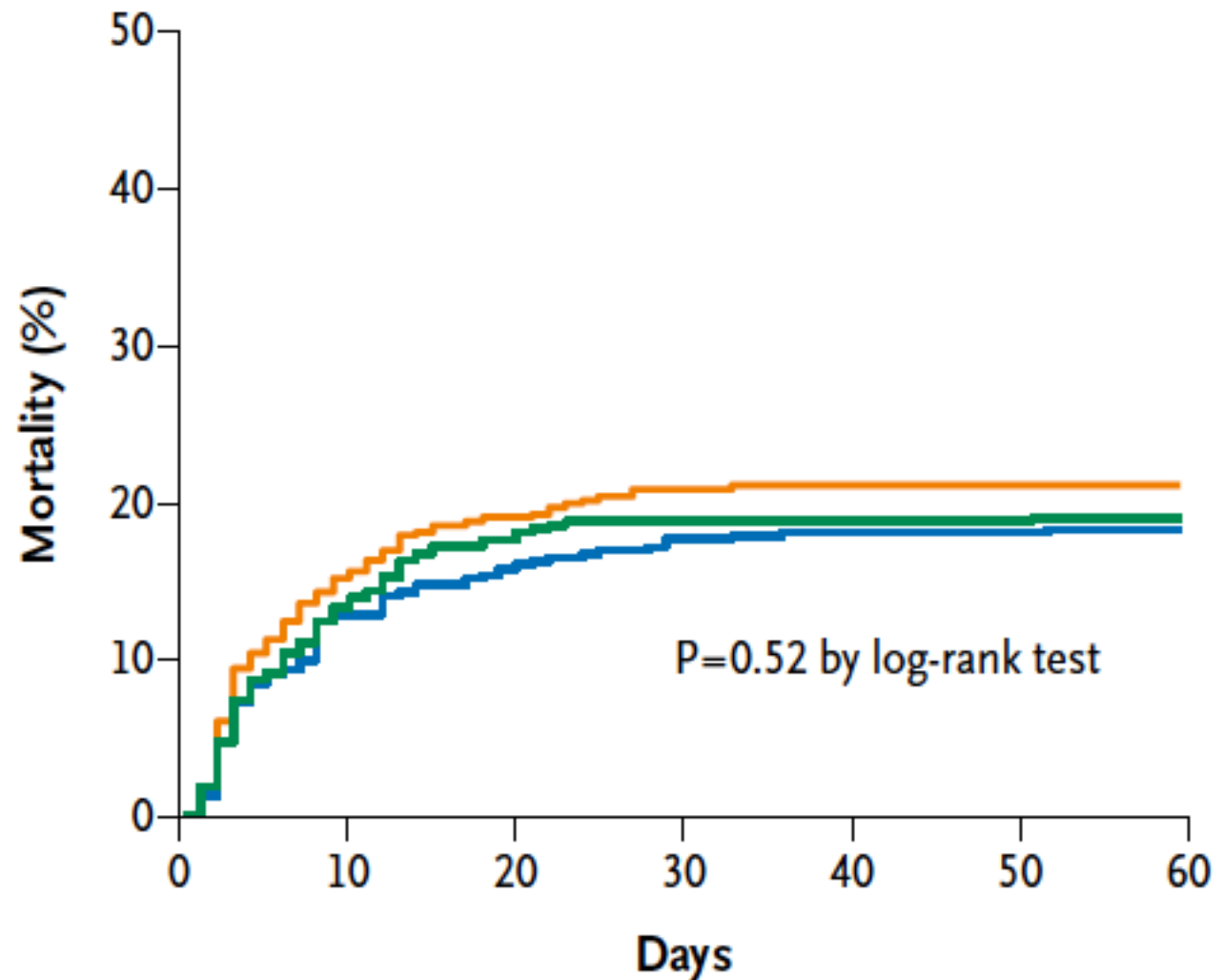


Protocol-based EGDT

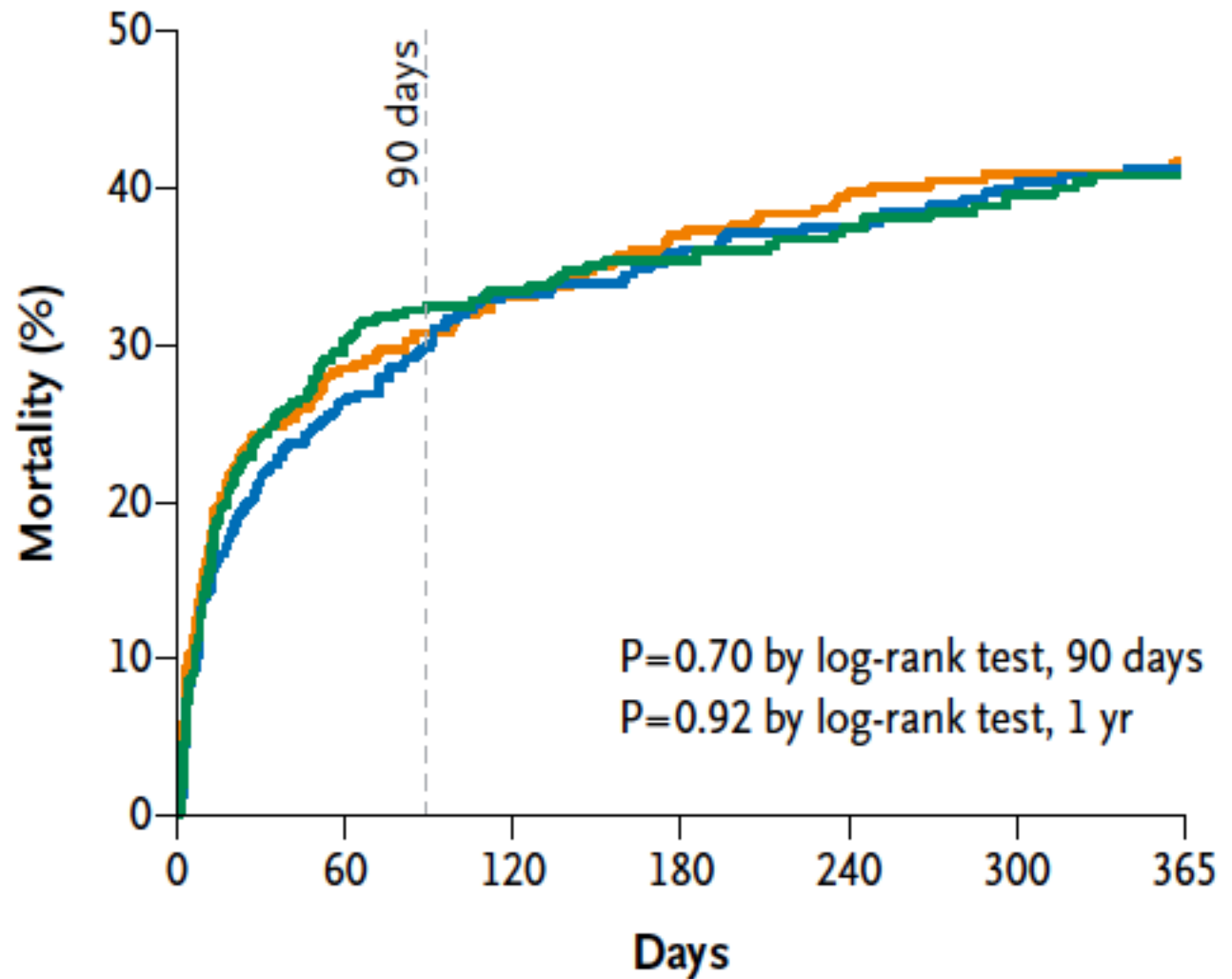
Protocol-based  
standard therapy

Usual care

## A Cumulative In-Hospital Mortality to 60 Days



## B Cumulative Mortality to 1 Yr

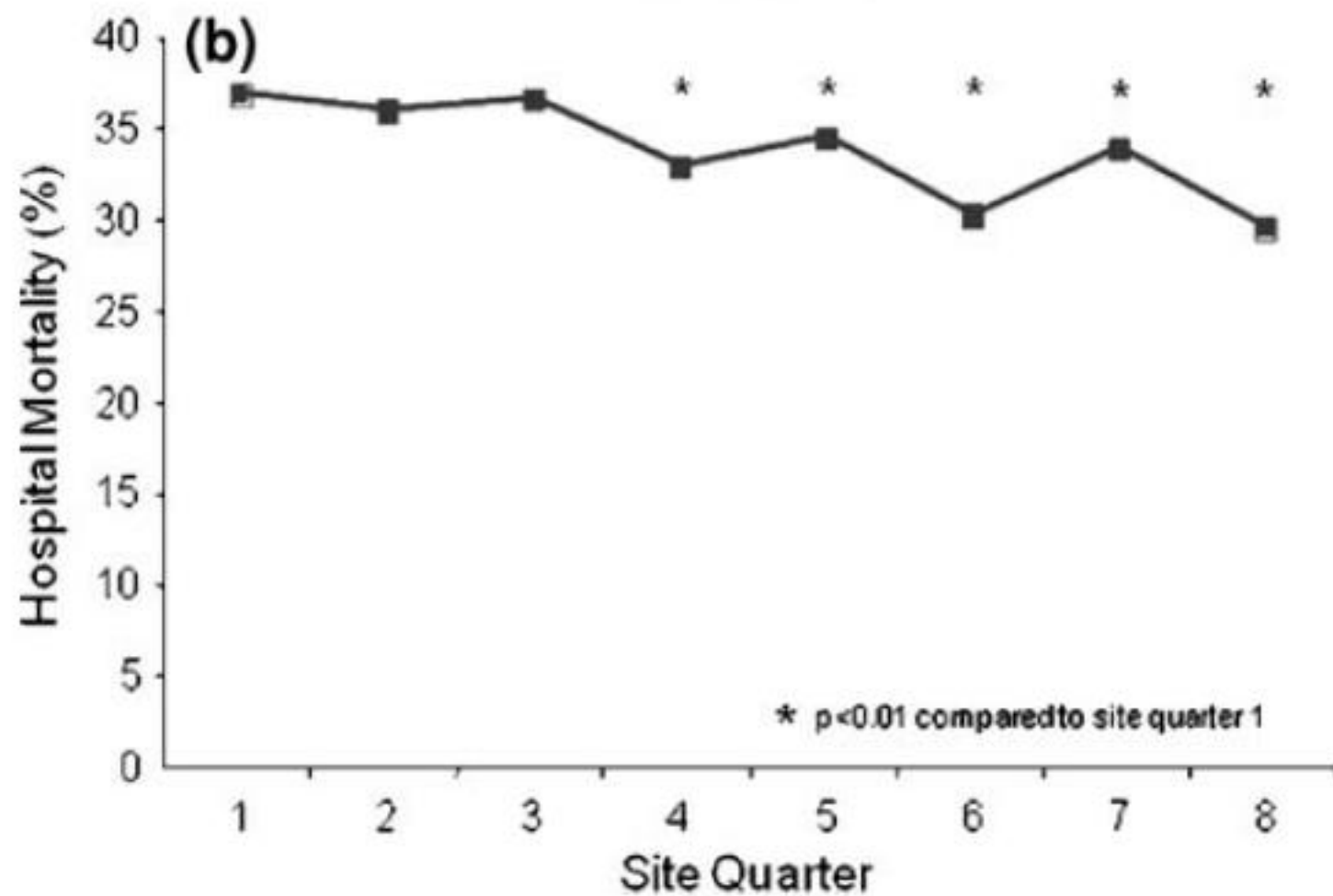


Mitchell M. Levy  
R. Phillip Dellinger  
Sean R. Townsend  
Walter T. Linde-Zwirble  
John C. Marshall  
Julian Bion  
Christa Schorr  
Antonio Artigas  
Graham Ramsay  
Richard Beale  
Margaret M. Parker  
Herwig Gerlach  
Konrad Reinhart  
Eliezer Silva  
Maurene Harvey  
Susan Regan  
Derek C. Angus

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







**Table 3** Propensity-weighted analysis of the impact of compliance with the components of the 6-h bundle on hospital mortality

Population		<i>n</i>	Bivariate analysis			Propensity-weighted analysis		
			cRR	95 % CI	<i>P</i>	cRR	95 % CI	<i>P</i>
Full compliance with the 6-h bundle	Whole	2,120	0.471	0.373–0.586	<0.001	0.736	0.557–0.941	0.02
Measure serum lactate	Whole	2,120	0.724	0.501–0.991	0.045	0.745	0.474–1.078	0.11
Obtain blood cultures prior to antibiotic administration	Whole	2,120	0.702	0.571–0.848	0.002	0.896	0.725–1.080	0.23
Promptly administer broad-spectrum antibiotic	Whole	2,120	0.646	0.525–0.781	<0.001	0.736	0.612–0.872	0.002
Fluid challenge/vasopressor	Hypotension or serum lactate >4 mmol/L	1,549	0.482	0.356–0.637	0.061	0.448	0.306–0.632	0.001
Achieving CVP >8 mm Hg	Septic shock or severe sepsis + lactate > 4 mmol/L	982	0.862	0.726–1.001	0.052	0.978	0.798–1.156	0.79
Achieving ScvO <sub>2</sub> > 70 %	Septic shock or severe sepsis + lactate > 4 mmol/L	982	0.953	0.773–1.134	0.57	1.052	0.881–1.217	0.51

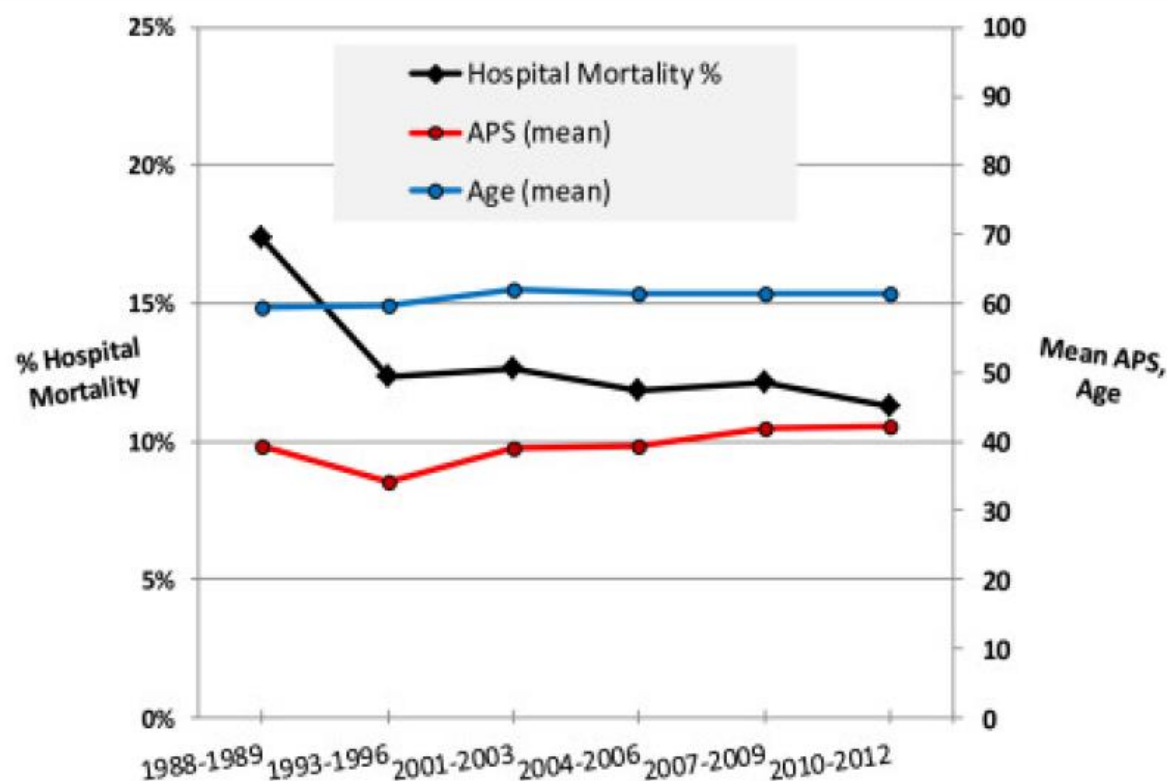
# Pausa para pensar

- A mortalidade cai...
- Mas não em todos os países...
- Nenhuma terapêutica nova...
- O que está acontecendo?

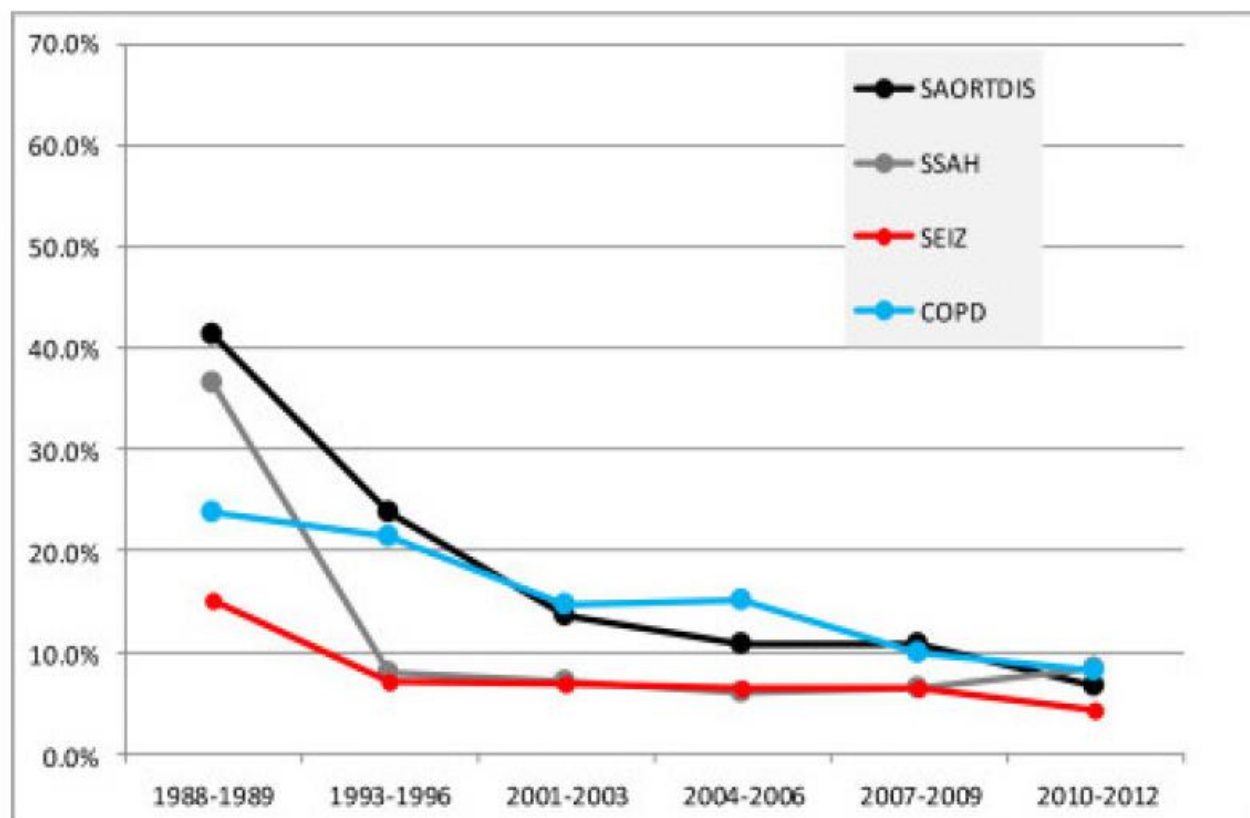


# Changes in hospital mortality for United States intensive care unit admissions from 1988 to 2012

Jack E Zimmerman<sup>1</sup>, Andrew A Kramer<sup>2\*</sup> and William A Knaus<sup>3</sup>

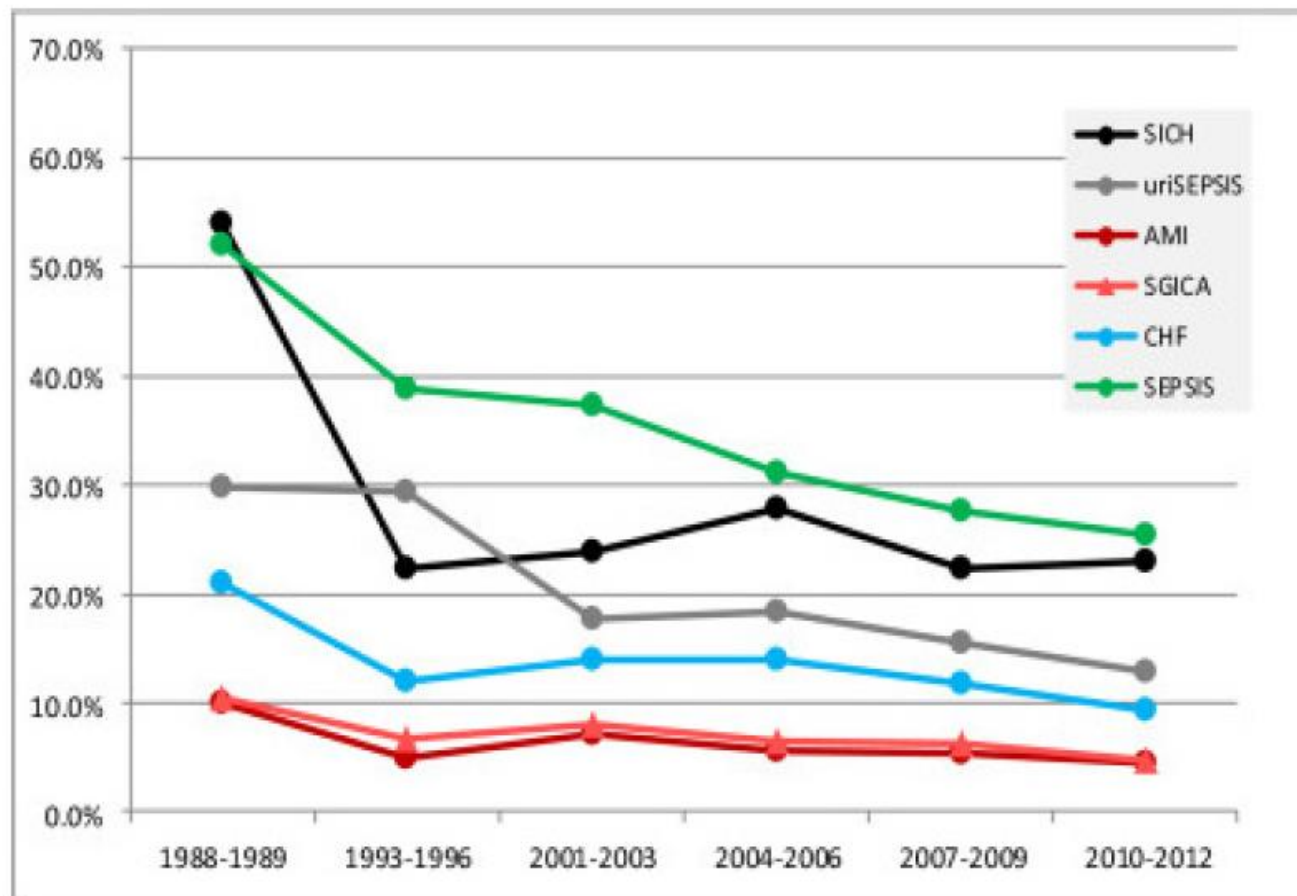


**Figure 1** Hospital mortality, age, and acute physiology score (APS) for 482,601 ICU admissions from 1988-1989 to 2010-2012.

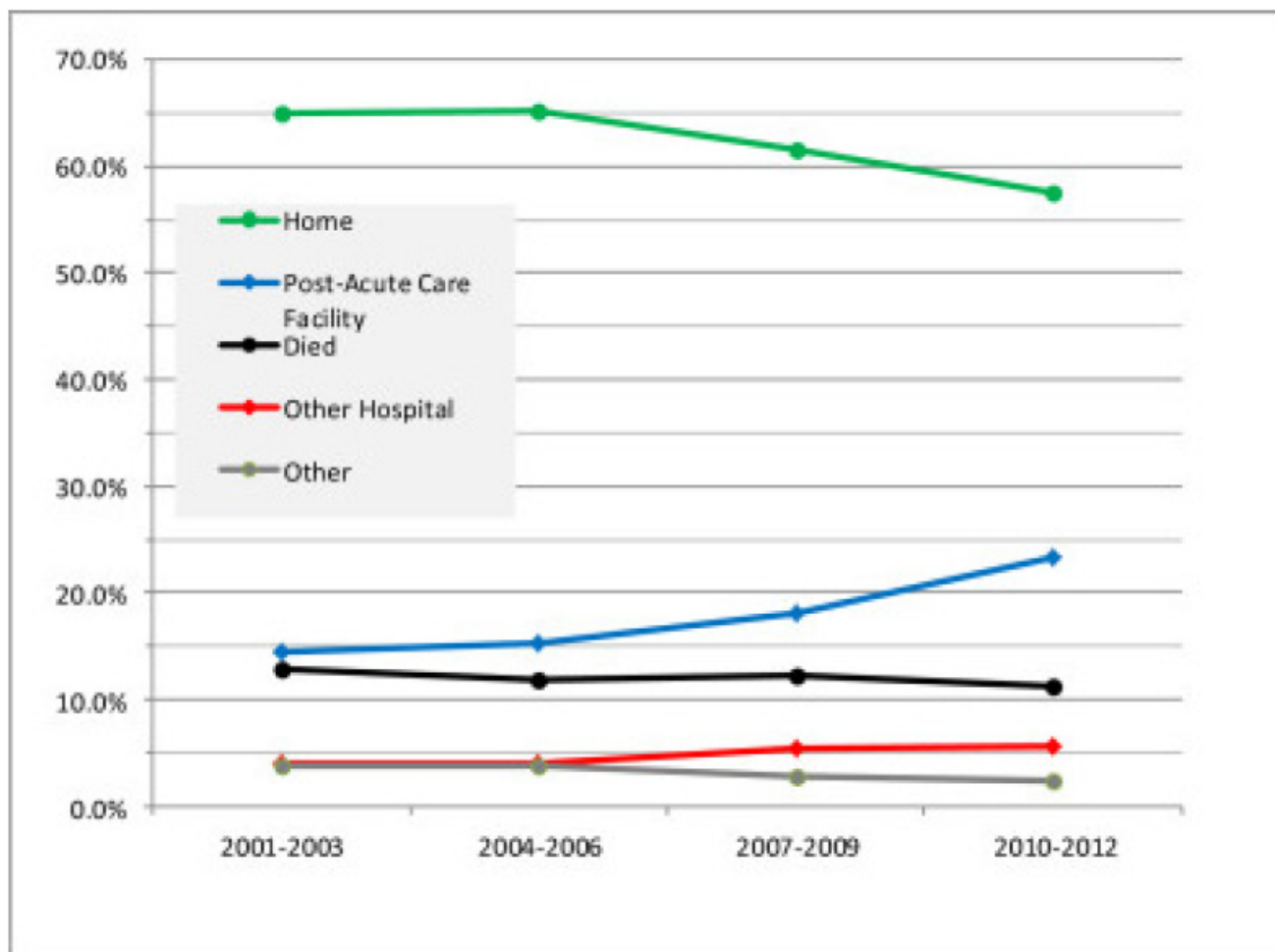


**Figure 2** Diagnostic groups with a >60% reduction in mortality from 1988-1989 to 2010-2012. Definition of abbreviations: COPD, chronic obstructive pulmonary disease; SAORTDIS, surgery for aortic dissection; SEIZ, seizures; SSAH, surgery for subarachnoid hemorrhage.





**Figure 3** Diagnostic groups with a 51% to 59% reduction in mortality from 1988-1989 to 2010-2012. Definition of abbreviations: AMI, acute myocardial infarction; CHF, congestive heart failure; SEPSIS, sepsis, non-urinary tract; SGICA, surgery for gastrointestinal malignancy; SICH, surgery for intracerebral hemorrhage; uriSEPSIS, sepsis, urinary tract.



**Figure 6** Hospital mortality and discharge destination for 422,294 ICU admissions from 2001 to 2012. Other hospital includes another acute care hospital or long term acute care facility.

# Portanto...

- P: Temos uma solução?
- R: A mortalidade por sepse cai devido a medidas terapêuticas gerais. A implementação de uma estratégia de reconhecimento precoce de pacientes e início de medidas simples (HMC e ATB) tem algum papel.



# Finalmente...

- Parcela significativa dos pacientes recebem tratamento diferente do ideal
- Novas modalidades terapêuticas levam aproximadamente 15 anos para se disseminarem
- Existem diversas barreiras para implementar mudanças



# The Meaning of Translational Research and Why It Matters

Woolf. JAMA 2008



- Biologia
- Genetica
- Outras ciências básicas

- epidemiologia
- síntese de evidencias
- teoria da comunicação
- Ciencia comportamental
- Políticas publicas
- Financiamento
- Teoria organizacional
- Reengenharia de sistemas
- Informatica
- Pesquisa qualitativa





# Why Don't Physicians Follow Clinical Practice Guidelines?

## A Framework for Improvement

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Michael D. Cabana, MD, MPH

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Cynthia S. Rand, PhD

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Neil R. Powe, MD, MPH, MBA

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Albert W. Wu, MD, MPH

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Modena H. Wilson, MD, MPH

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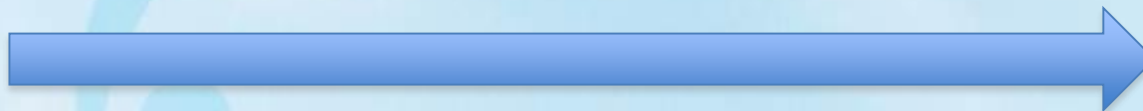
Paul-André C. Abboud, MD

---

Haya R. Rubin, MD, PhD

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# Barreiras



CONHECIMENTO	ATITUDE (MOTIVAÇÃO)	COMPORTAMENTO
<b>Desconhece a recomendação</b>	<b>Inercia</b>	<b>Fatores ambientais</b>
<i>acesso</i>	<b>Discorda da recomendação</b>	<i>tempo</i>
<i>tempo</i>	<b>Não se acha capaz</b>	<i>recursos</i>
<b>Desconhece o problema</b>	<b>Discorda de qualquer recomendação</b>	<b>Barreiras externas</b>
<i>acesso</i>		<i>preferências do paciente</i>
<i>tempo</i>		

# Toward Evidence-Based Quality Improvement

## Evidence (and its Limitations) of the Effectiveness of Guideline Dissemination and Implementation Strategies 1966–1998

Intervenção	Taxa de melhoria
Técnicas de lembrança	14.1 %
Material Educativo	8.1 %
Auditoria e feedback	7.0 %
Visitas educativas	6.0 %
Estratégias múltiplas	6.0 %

# NOSSA EXPERIÊNCIA



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# Nosso cenário inicial

- Incidência de sepse desconhecida
- Mortalidade desconhecida
- Conhecimento sobre os cuidados padronizados variável entre médicos





# Nossa estratégia

- Estratégia multifacetada tradicional
  - Case manager
  - Lider de opinião
  - Treinamento e visitas educativas
  - Auditoria e feedback
  - Lembretes
- “Novos” ingredientes
  - Benchmarking entre diversos hospitais
  - Remuneração variável



# Pay for performance in critical care: An executive summary of the position paper by the Society of Critical Care Medicine\*

The goal of a P4P program is to improve patient care

Physician participation is voluntary

Data collecting must be simple and valid

Confidentiality and public reporting

**EBM**

**Desenvolvimento**

**transparente**

***Accountability***

**Piloto**

**Resultados ajustados por  
risco**

**Demonstrar melhora no  
cuidado**

**Revisão ao menos a cada 2  
anos**

**Discussão e sugestões de  
melhorias**

**Avaliação em grupo**



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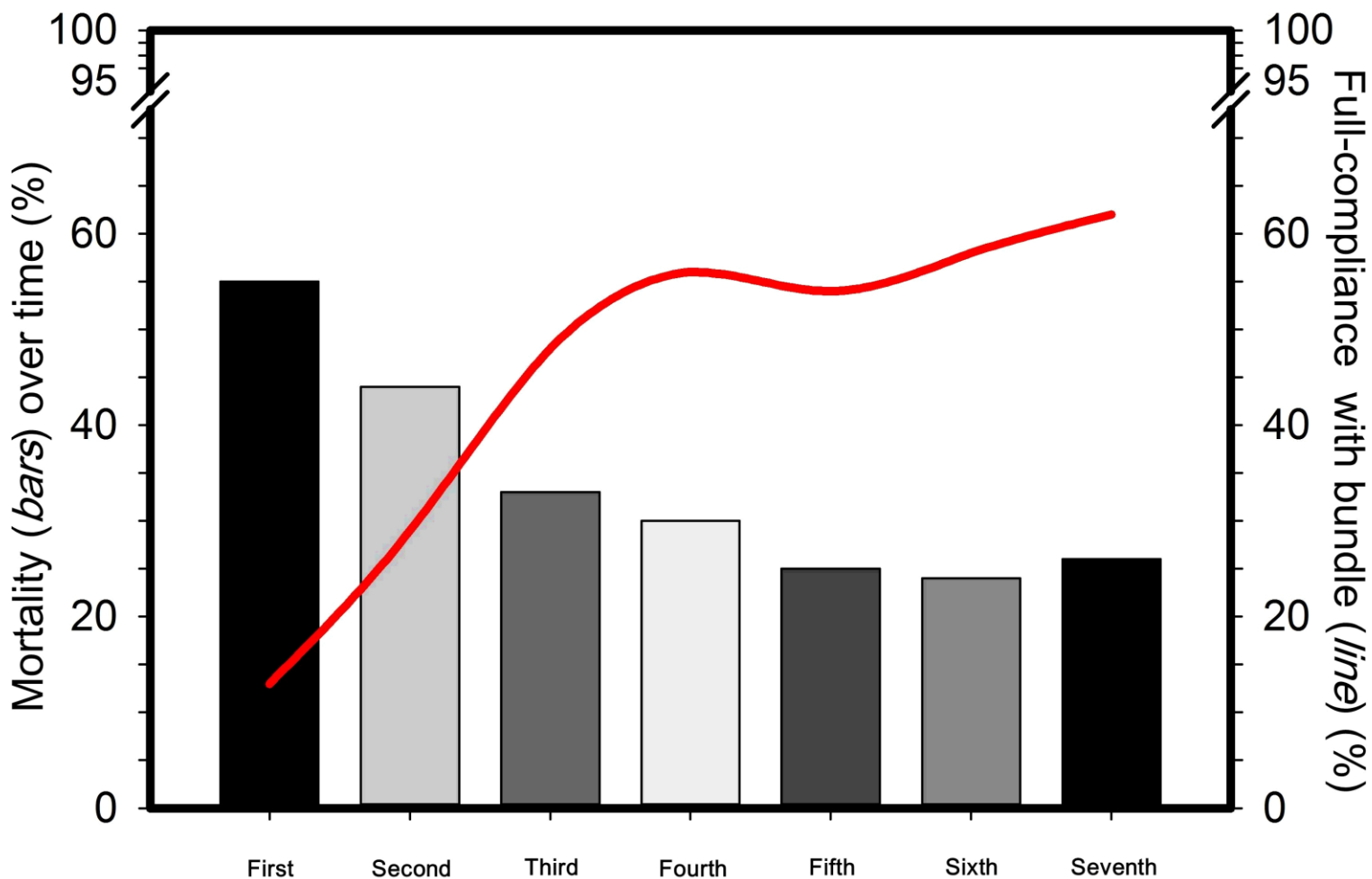
**Crit Care Med 2009**

# P4P Sepsis

- Baseada na adesão completa ao pacote de 6h
- Trimestral
- Gradual: faixas
- Pontuação máxima com adesão > 50%



# B



# Em resumo....

- P:Qual o papel do médico na sepse?
- R: ...



# Obrigado !

