



# Η ΑΝΑΠΝΕΥΣΤΙΚΗ ΑΝΕΠΑΡΚΕΙΑ ΑΠΟ ΤΗΝ ΠΦΥ ΕΩΣ ΤΗ ΜΕΘ

19-21 Νοεμβρίου 2021  
Πορταριά Μαγνησίας, PORTARIA HOTEL



## Αντιμετώπιση του σηπτικού ασθενούς: Sepsis 1 - 2 - 3... ή μια «επιστημολογική προσέγγιση»

### **A. ΑΡΜΑΓΑΝΙΔΗΣ**

Ομότιμος Καθηγητής Πνευμονολογίας  
και Εντατικής Θεραπείας  
Ιατρικής Σχολής ΕΚΠΑ



τ. Διευθυντής Β' Πανεπιστημιακής  
Κλινικής Εντατικής Θεραπείας  
(2003-2021) - Π.Γ.Ν. ΑΤΤΙΚΟΝ

# “Conflict” of interest (ενδια- ή συμ-φέρον)

Τίποτε που να αναφορά τη σημερινή  
παρουσίαση (μόνο interest χωρίς conflict)

# ***Presentation outline***

- The Guidelines for the management of septic patients and their application in a “Real Word setting”
  - Pathophysiologic «paradigms» of sepsis and septic shock
- AND
- *Evolution of scientific knowledge AND understanding* in relation with Definitions, Diagnostic approach and Treatment (= Real decision making)

**CME CREDIT** *EDUCATIONAL OBJECTIVE:* Readers will consider the recommendations of the Surviving Sepsis Campaign when ~~treating patients with sepsis~~

**R. PHILLIP DELLINGER, MD, MSc, MCCM**

Professor and Chair of Medicine, Cooper Medical School of Rowan University, Camden, NJ; Director, Adult Health Institute, and Senior Critical Care Attending, Cooper University Hospital, Camden, NJ; Steering Committee, Surviving Sepsis Campaign

**TAKE-HOME  
POINTS FROM  
LECTURES BY  
CLEVELAND  
CLINIC  
AND VISITING  
FACULTY**

\*\*\*\*\*

# The Surviving Sepsis Campaign: Where have we been and where are we going?

## Abstract

Chest. 1992 Jun;101(6):1644-55.

**Definitions for sepsis and organ failure and guidelines for the management of severe sepsis and septic shock: ACCP/SCCM Consensus Conference Committee Recommendations. Crit Care Medicine.**

Bone RC<sup>1</sup>, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, S

Emanuel P. Rivers, MD, MPH, IOM,

What a sepsis pilot must consider before taking flight with your next patient. *Crit Care Med* 2006; 34:1247

Patients are not airplanes and doctors  
are not pilots

Richard Rissmiller, MD, Internal Medicine, Carolinas Medical Center, Charlotte, NC

To the Editor:

While I do not claim to have the re-  
search experience of Drs. Kortgen and colleagues (1) and Dr. Rivers (2), I do have a fair amount of experience treating sepsis. I am tiring of the ongoing analogy of the airline industry or of a jet pilot in regard to

Emanuel P. Rivers, MD, MPH, IOM,

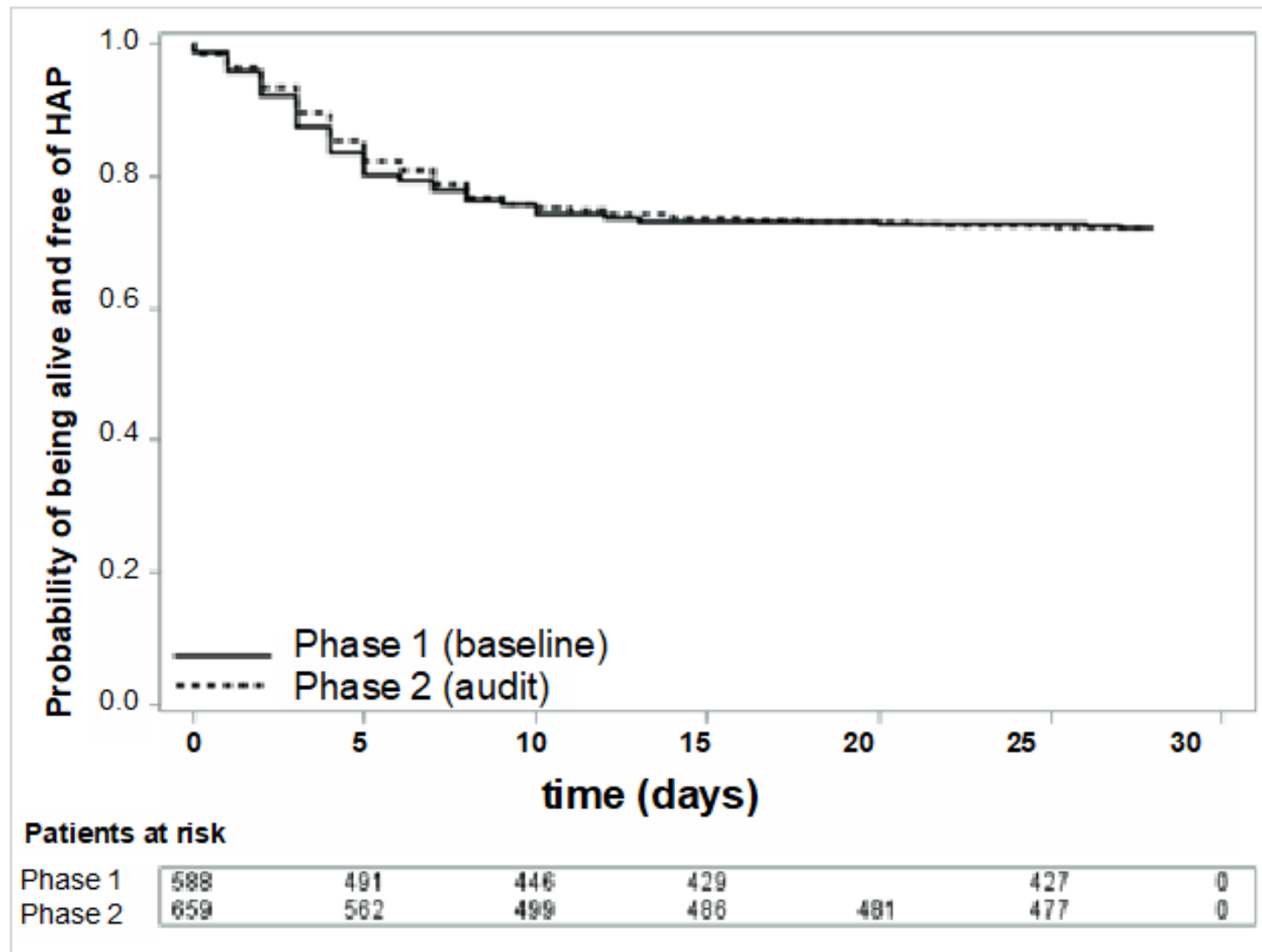
... sepsis management is less than optimal.

A recent survey has shown that:

- early goal directed therapy was performed in 17% of academic emergency departments, (2)
- protective lung strategies provided in 39% of patients on day 2 of acute lung injury (3), and
- aggressive glycemic control is provided 19% of the time with routine insulin protocols (4).
- the administration of recombinant human activated protein C ranged from 4% to 33% of patients in other studies examining the effectiveness of a sepsis protocol (5–7).

No matter what analogy is used,

the lack of compliance to base practice sepsis recommendations  
is associated with increased mortality (8, 9).



**Probability of HAP before (phase 1, n= 630 pts) or after (phase 2, n=650 pts) the application of the SFAR/SRLF recommendations**

*Roquilly et al Clin Infect Dis 2020*

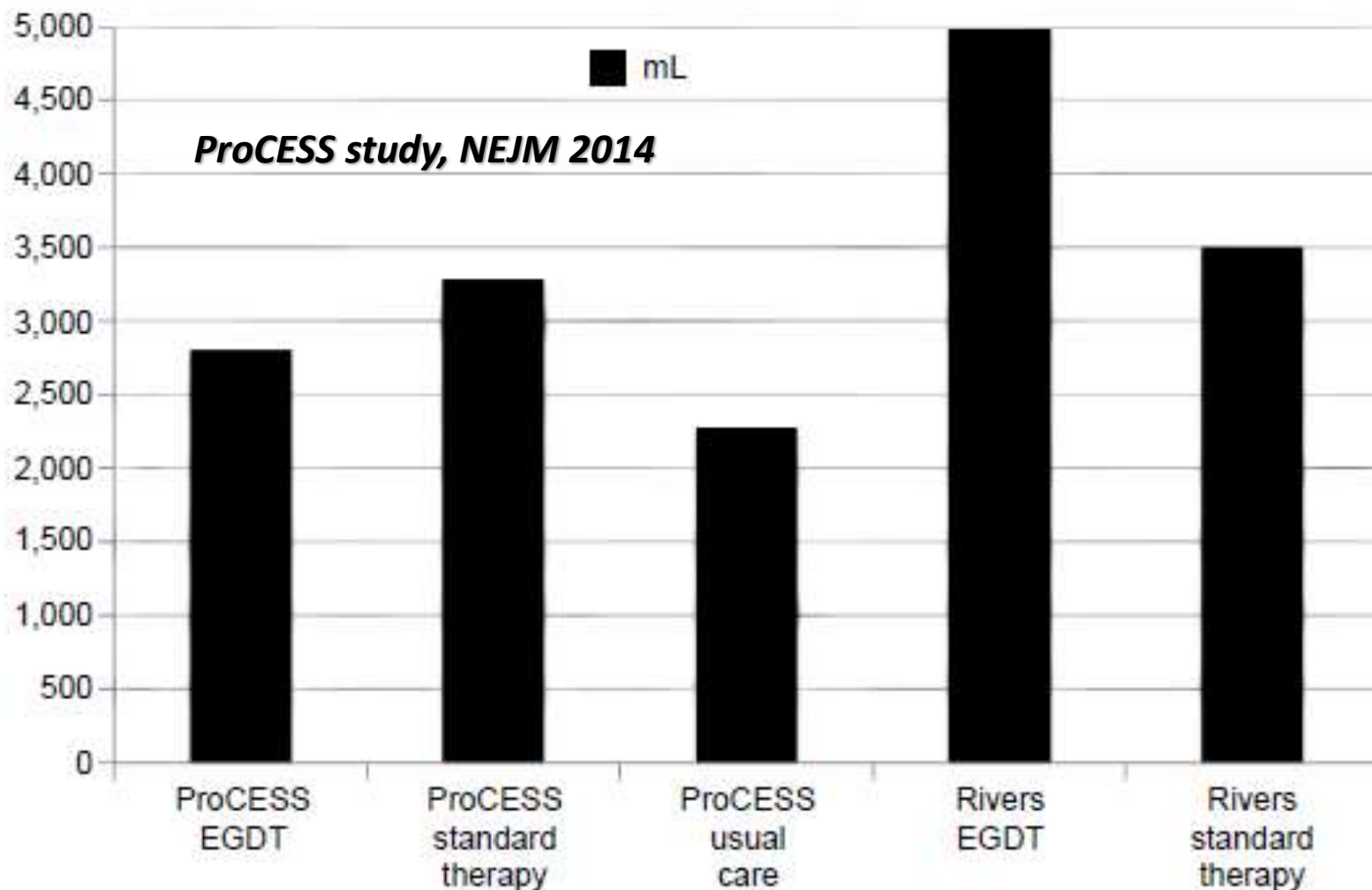


Figure 1 Fluid administration between 0 and 6 hours.

Abbreviations: ProCESS, Protocolized Care for Early Septic Shock; EGDT, Early Goal-Directed Therapy.



Modified from: Martin-Loeches I, Levy M., Artigas A

Drug Design, Development and Therapy 2015:9 2079–2088

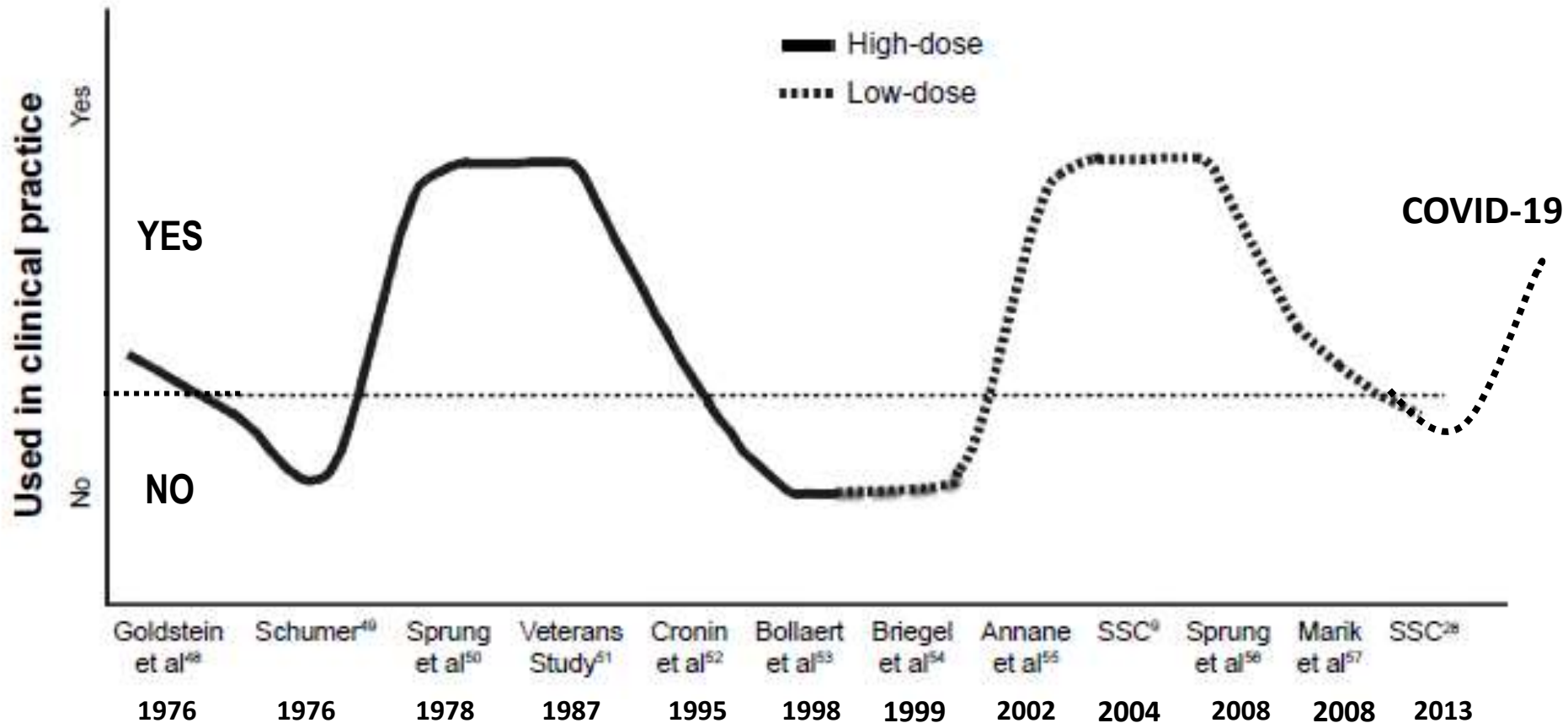
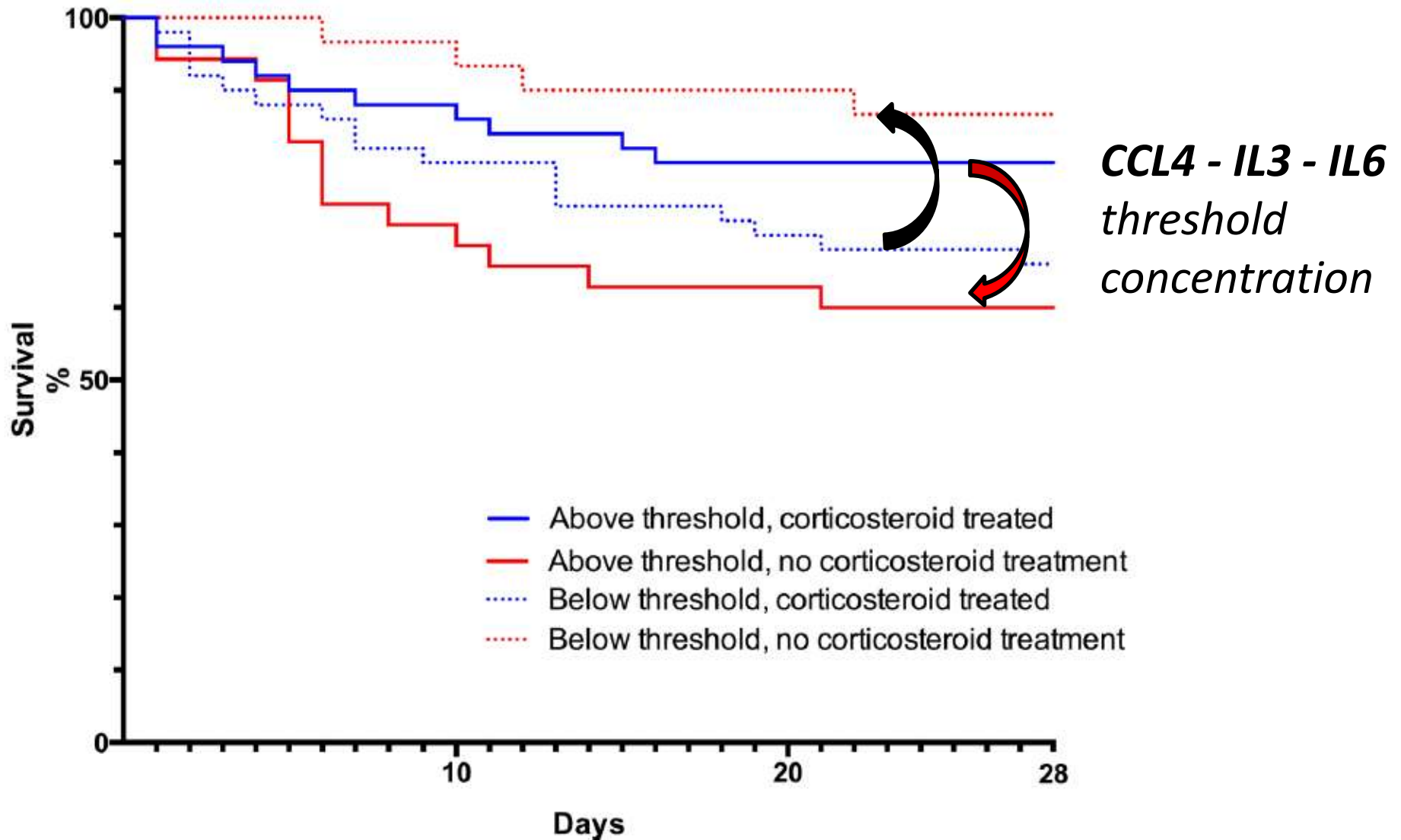


Figure 2 Steroids for treatment of infections, sepsis, and septic shock – ups and downs. Abbreviations: SSC, Surviving Sepsis Campaign.

# Plasma cytokine levels predict response to corticosteroids in septic shock

*Intensive Care Med* (2016) 42:1970–1979

Peter Bentzer<sup>1,2,3,4\*</sup>, Chris Fjell<sup>1,2</sup>, Keith R. Walley<sup>1,2</sup>, John Boyd<sup>1,2</sup> and James A. Russell<sup>1,2</sup>



# Key points (I)

- Σημασία του case-mix στις RCTs με βάση τις οποίες δημιουργούνται τα Guidelines (\*)

[Crit Care Med.](#) 1992 Jun;20(6):864-74.

**American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis.**

[No authors listed]

## **Abstract**

### **OBJECTIVE:**

To define the terms "sepsis" and "organ failure" in a precise manner.

### **DATA SOURCES:**

Review of the medical literature and the use of expert testimony at a consensus conference.

### **SETTING:**

American College of Chest Physicians (ACCP) headquarters in Northbrook, IL.

### **PARTICIPANTS:**

Leadership members of ACCP/Society of Critical Care Medicine (SCCM).

### **RESULTS:**

An ACCP/SCCM Consensus Conference was held in August of 1991 with the goal of agreeing on a set of definitions that could be applied to patients with sepsis and its sequelae. New definitions were offered for some terms, while others were discarded. Broad definitions of sepsis and the systemic inflammatory response syndrome were proposed, along with detailed physiologic variables by which a patient could be categorized. Definitions for severe sepsis, septic shock, hypotension, and multiple organ dysfunction syndrome were also offered. The use of severity scoring methods were recommended when dealing with septic patients as an adjunctive tool to assess mortality. Appropriate methods and applications for the use and testing of new therapies were recommended.

### **CONCLUSION:**

The use of these terms and techniques should assist clinicians and researchers who deal with sepsis and its sequelae.

Intensive Care Med. 2003 Apr;29(4):530-8. Epub 2003 Mar 28.

2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference.

Levy MM1, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, Cohen J, Opal SM, Vincent JL, Ramsay G; International Sepsis Definitions Conference.

Author information Mitchell\_Levy@brown.edu

Rhode Island Hospital, 593 Eddy Street, MICU Main 7, Providence RI 02903, USA. Abstract

#### OBJECTIVE:

In 1991, the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) convened a "Consensus Conference," the goals of which were to "provide a conceptual and a practical framework to define the systemic inflammatory response to infection, which is a progressive injurious process that falls under the generalized term 'sepsis' and includes sepsis-associated organ dysfunction as well. The general definitions introduced as a result of that conference have been widely used in practice, and have served as the foundation for inclusion criteria for numerous clinical trials of therapeutic interventions. Nevertheless, there has been an impetus from experts in the field to modify these definitions to reflect our current understanding of the pathophysiology of these syndromes.

#### DESIGN:

Several North American and European intensive care societies agreed to revisit the definitions for sepsis and related conditions. This conference was sponsored by the Society of Critical Care Medicine (SCCM), The European Society of Intensive Care Medicine (ESICM), The American College of Chest Physicians (ACCP), the American Thoracic Society (ATS), and the Surgical Infection Society (SIS).

#### METHODS:

29 participants attended the conference from Europe and North America. In advance of the conference, subgroups were formed to evaluate the following areas: signs and symptoms of sepsis, cell markers, cytokines, microbiologic data, and coagulation parameters. The present manuscript serves as the final report of the 2001 International Sepsis Definitions Conference.

## DESIGN:

Several North American and European intensive care societies agreed to revisit the definitions for sepsis and related conditions. This conference was sponsored by the Society of Critical Care Medicine (SCCM), The European Society of Intensive Care Medicine (ESICM), The American College of Chest Physicians (ACCP), the American Thoracic Society (ATS), and the Surgical Infection Society (SIS).

## METHODS:

29 participants attended the conference from Europe and North America. In advance of the conference, subgroups were formed to evaluate the following areas: signs and symptoms of sepsis, cell markers, cytokines, microbiologic data, and coagulation parameters. The present manuscript serves as the final report of the 2001 International Sepsis Definitions Conference.

## CONCLUSION:

1. Current concepts of sepsis, severe sepsis and septic shock remain useful to clinicians and researchers.
2. These definitions do not allow precise staging or prognostication of the host response to infection.
3. While SIRS remains a useful concept, the diagnostic criteria for SIRS published in 1992 are overly sensitive and non-specific.
4. An expanded list of signs and symptoms of sepsis may better reflect the clinical response to infection.
6. PIRO, a hypothetical model for staging sepsis is presented, which, in the future, may better characterize the syndrome on the basis of predisposing factors and premorbid conditions, the nature of the underlying infection, the characteristics of the host response, and the extent of the resultant organ dysfunction.

remain a useful concept

*Definitions for what purpose ??? Useful for whom ???*

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

# The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

JAMA. 2016;315(8):801-810.

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher W. Seymour, MD, PhD; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD, PhD; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom R. Van der Poll, MD, PhD

**Αναβάθμιση software ή  
ανώτερο επίπεδο  
επιστημονικής κατανόησης**

## Conclusions

These updated definitions and clinical criteria should clarify long-used descriptors and facilitate earlier recognition and more timely management of patients with sepsis or at risk of developing it. This process, however, remains a work in progress. As is done with software and other coding updates, the task force recommends that the new definition be designated Sepsis-3, with the 1991 and 2001 iterations being recognized as Sepsis-1 and Sepsis-2, respectively, to emphasize the need for future iterations.

## Key points (II)

- Σημασία του case-mix στις RCTs με βάση τις οποίες δημιουργούνται τα Guidelines (\*)
- Διαφορετικοί ορισμοί ανάλογα με το σκοπό για τον οποίο δημιουργούνται (\*) αλλά και το επίπεδο επιστημονικής κατανόησης



# ***Presentation outline***

- The Guidelines for the management of septic patients and their application in a “Real Word setting”
  - Pathophysiologic «paradigms» of sepsis and septic shock
- AND
- *Evolution of scientific knowledge AND understanding in relation with Definitions, Diagnostic approach and Treatment (= Real decision making)*

# An alternate pathophysiologic paradigm<sup>(\*)</sup> of sepsis and septic shock

Implications for optimizing antimicrobial therapy

---

Anand Kumar

- ***Current paradigm: Immunologic Model***
- ***The classic paradigm: Microbiologic Primacy***
- ***A new Composite Model: Integrating Shock***

# An alternate pathophysiologic paradigm of sepsis and septic shock

Implications for optimizing antimicrobial therapy

Anand Kumar

A key deficiency of this immunologic model of sepsis is that most pathogens cannot be eliminated quickly despite bactericidal antimicrobial therapy and likely persist during the period that immunomodulatory therapies (most of which are, in fact, immunosuppressive) might be initiated. A recent autopsy study of sepsis suggested that a persistent septic focus could be found in approximately 75% of 235 surgical ICU patients who died of sepsis/septic shock and in almost 90% of those succumbing in ICU after at least 7 days of treatment [26, 27, 28]

# An alternate pathophysiologic paradigm of sepsis and septic shock

Implications for optimizing antimicrobial therapy

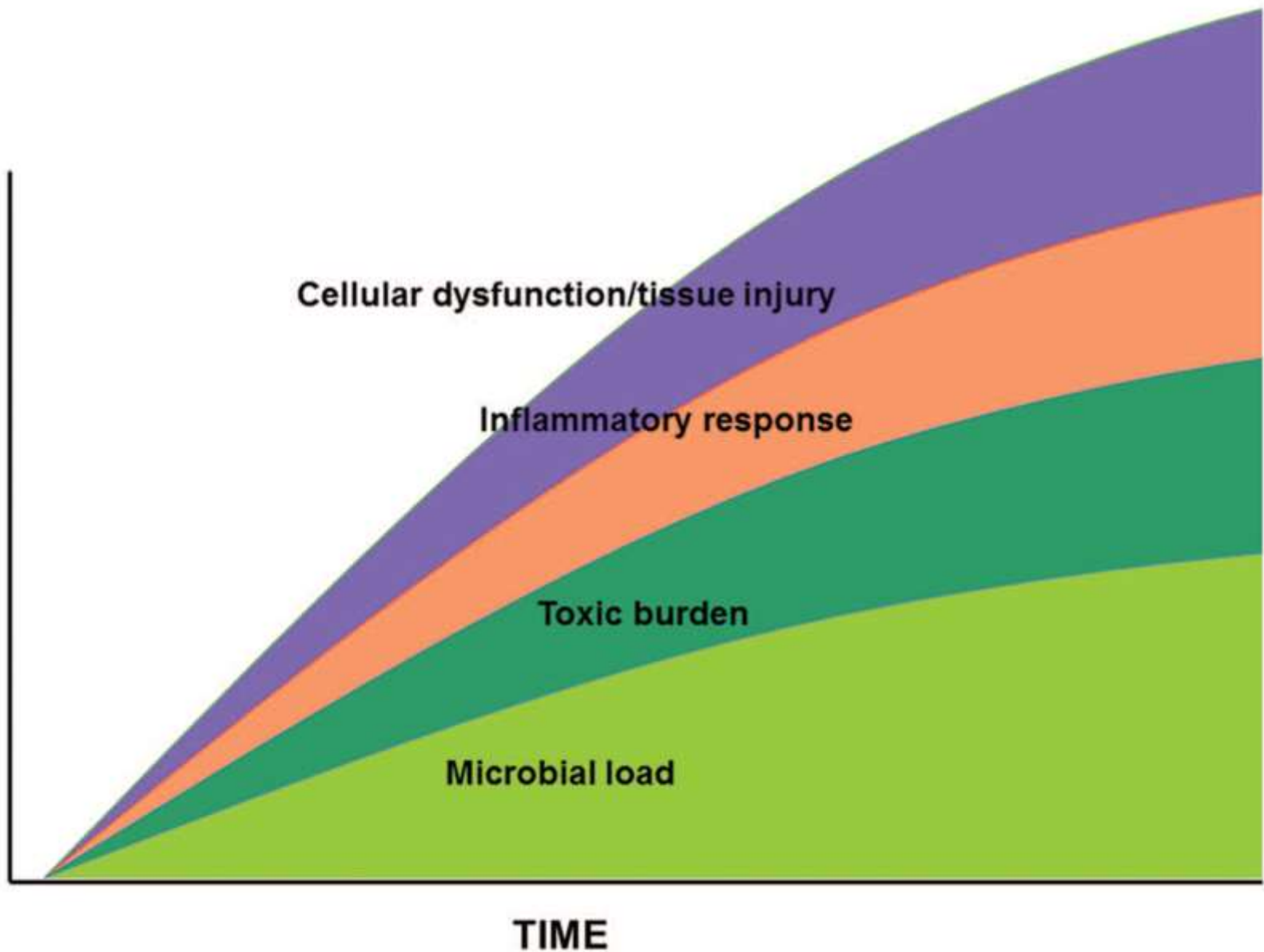
---

Anand Kumar

- *Current paradigm: Immunologic Model*
- *The classic paradigm: Microbiologic Primacy*
- *A new Composite Model: Integrating Shock*

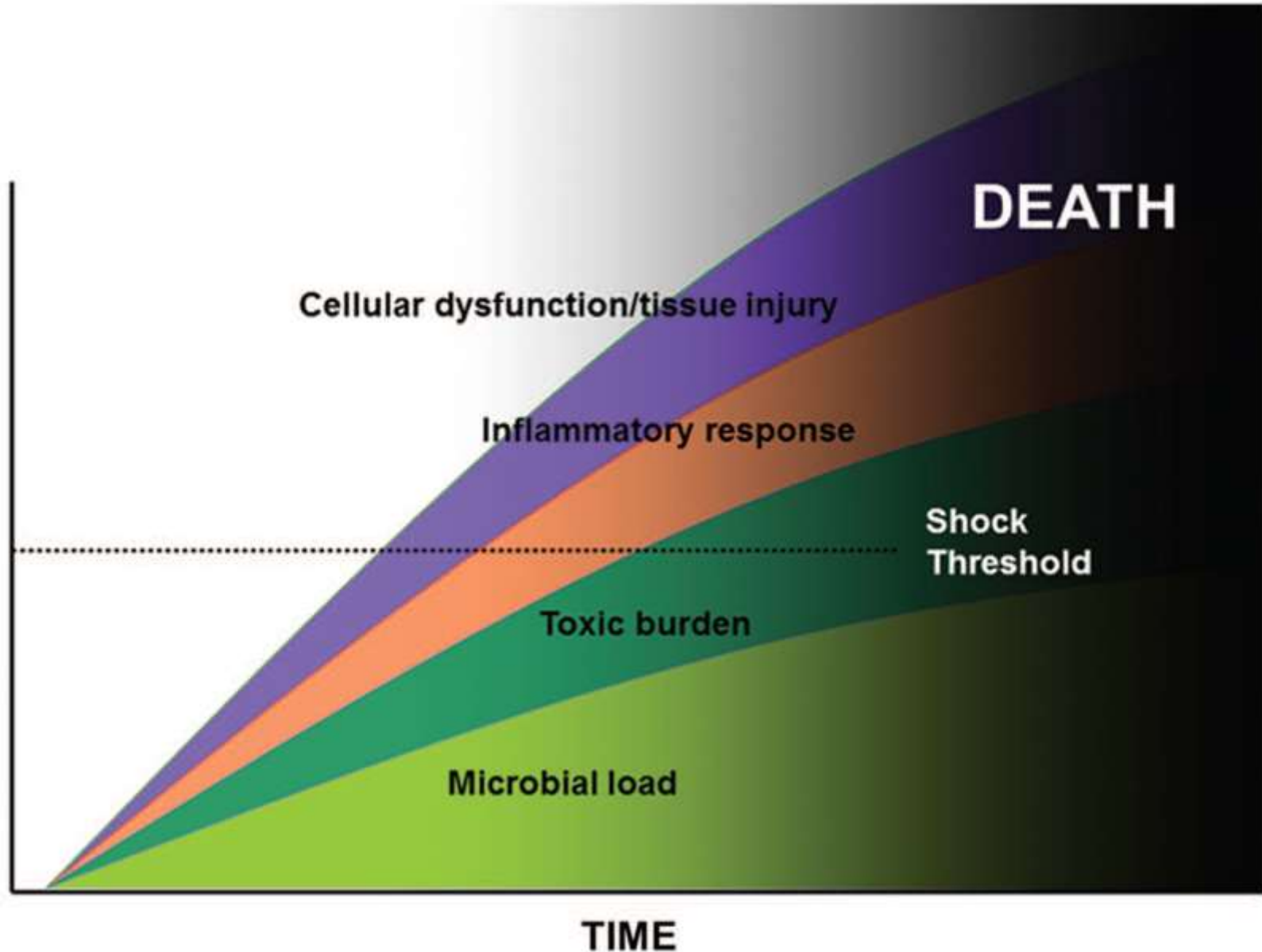
# Microbiologic view of sepsis and septic shock

Kumar A. 2014



# Composite Microbiologic view of sepsis and septic shock

Kumar A. 2014



# An alternate pathophysiologic paradigm of sepsis and septic shock

Implications for optimizing antimicrobial therapy

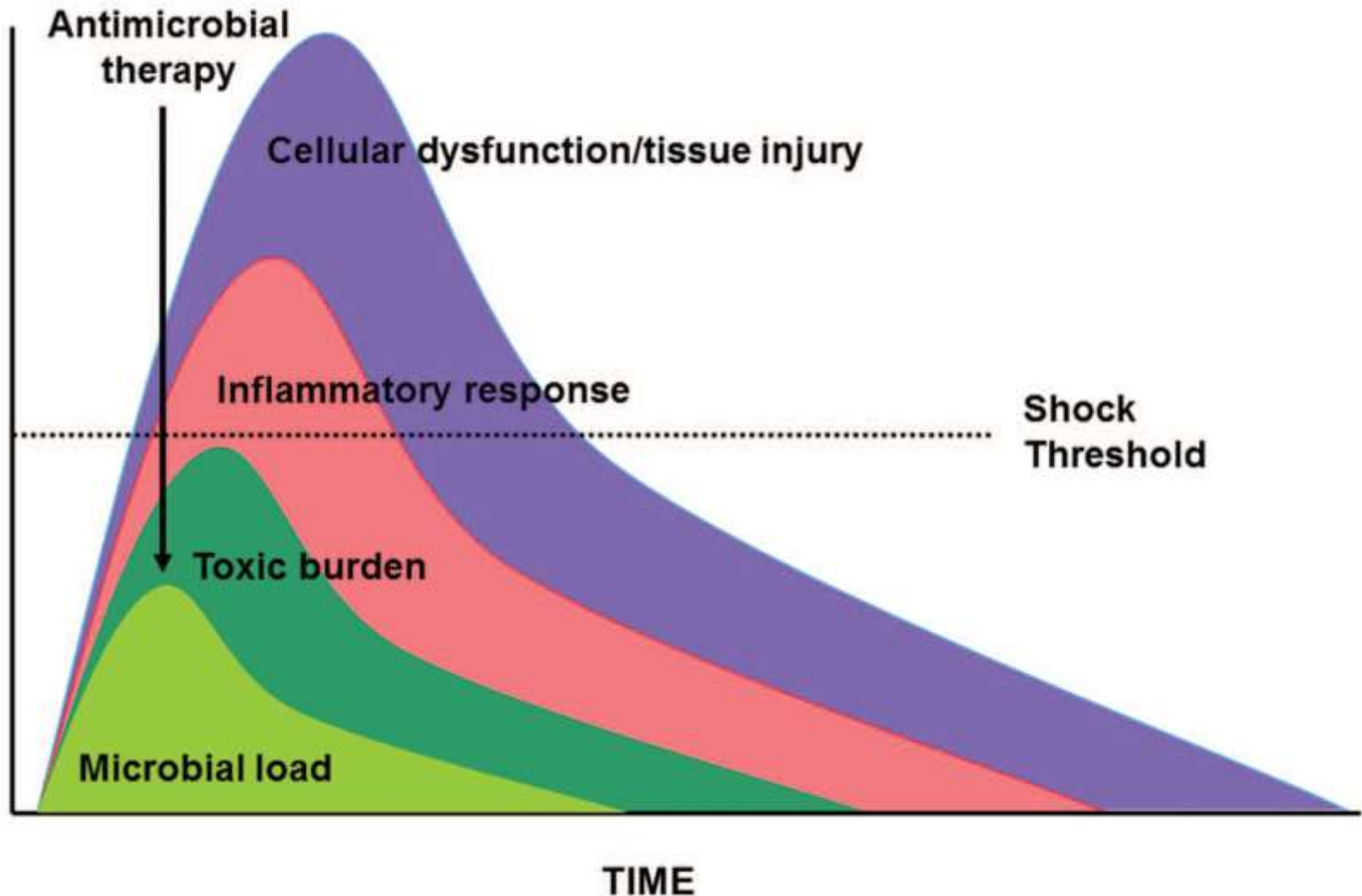
---

Anand Kumar

- *Current paradigm: Immunologic Model*
- *The classic paradigm: Microbiologic Primacy*
- ***A new Composite Model: Integrating Shock  
(a more and more complex multifactorial model)***

# Impact of appropriate antimicrobial therapy in sepsis and septic shock.

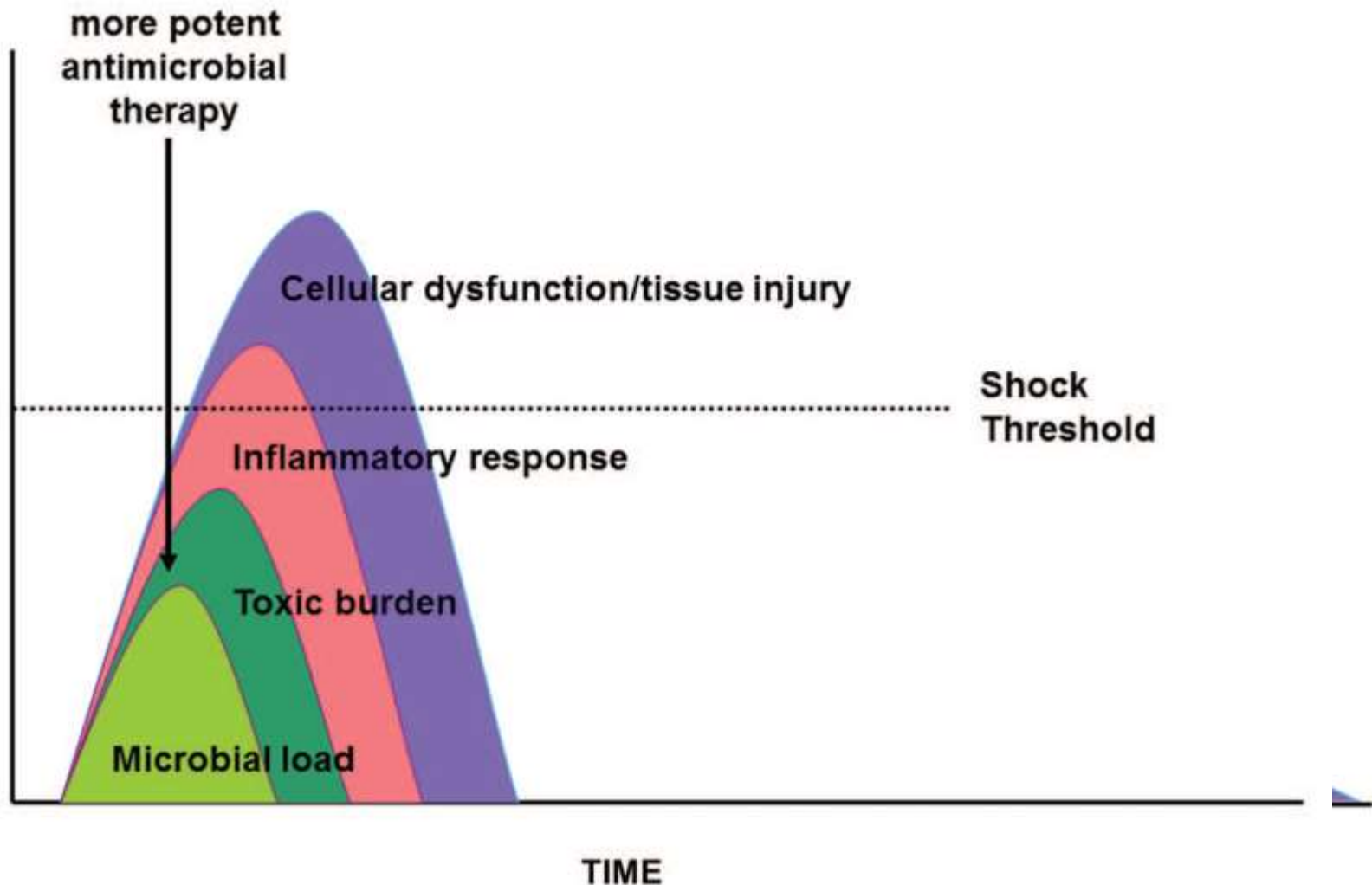
Kumar A. 2014





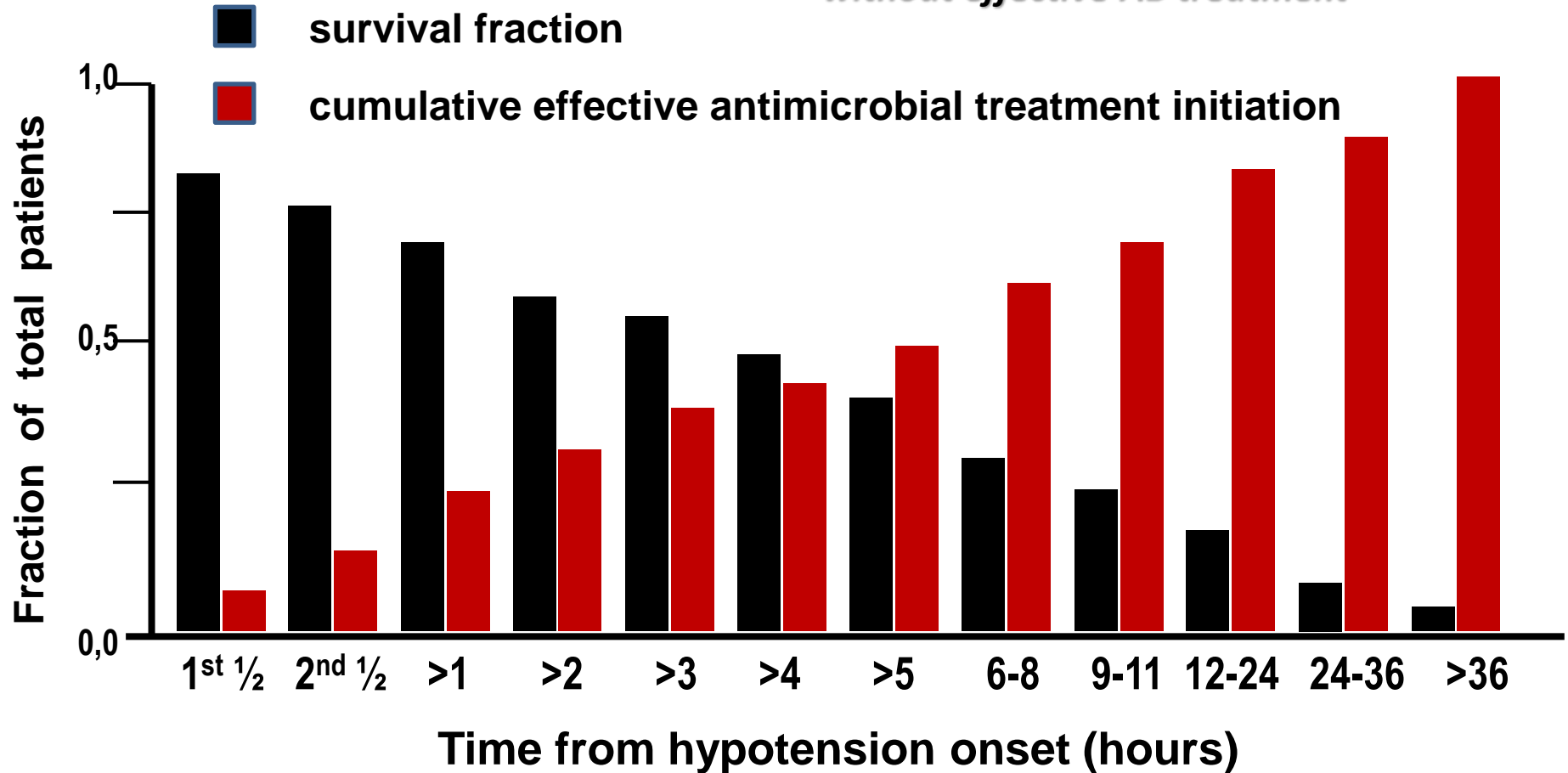
# Impact of more potent antimicrobial therapy in sepsis and septic shock.

Kumar A. 2014



# *In severe sepsis and septic shock, time is life*

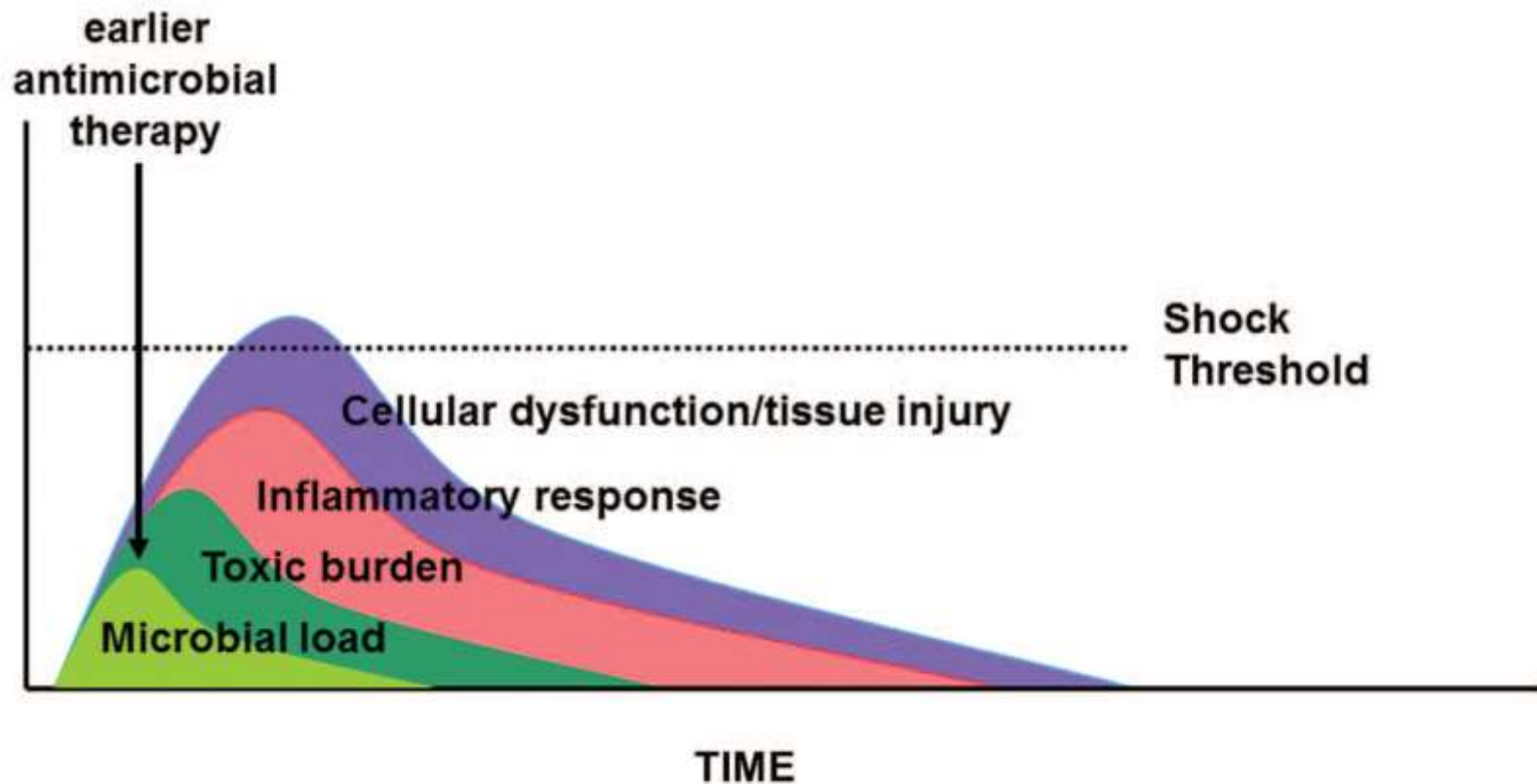
*7% decrease of survival every hour without effective AB treatment*



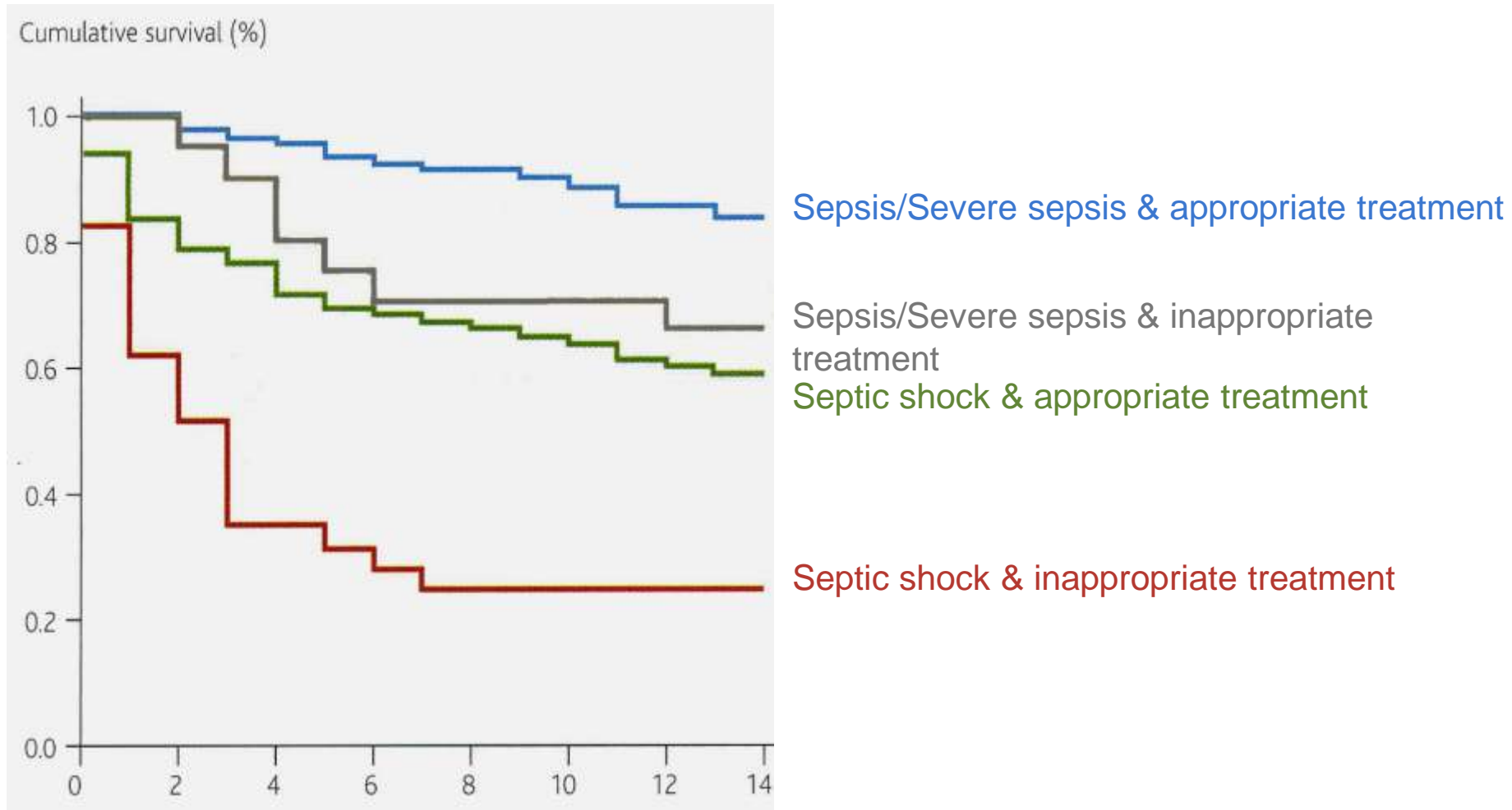
*Modified from: Kumar A, Robert D, Wood KE, Critical Care Med 2006; 34: 1589–1596*

# Impact of earlier appropriate antimicrobial therapy in sepsis and septic shock.

Kumar A. 2014



# Survival with appropriate OR inappropriate treatment



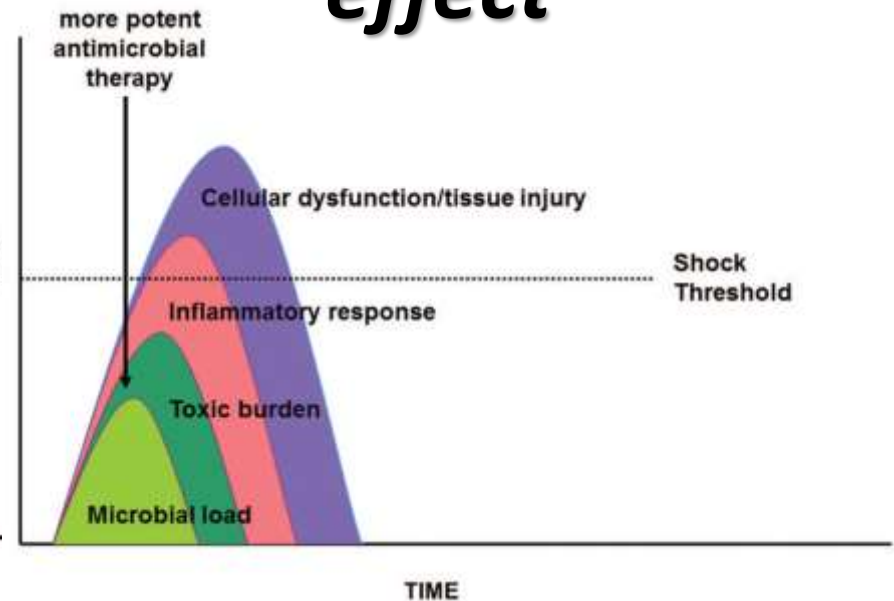
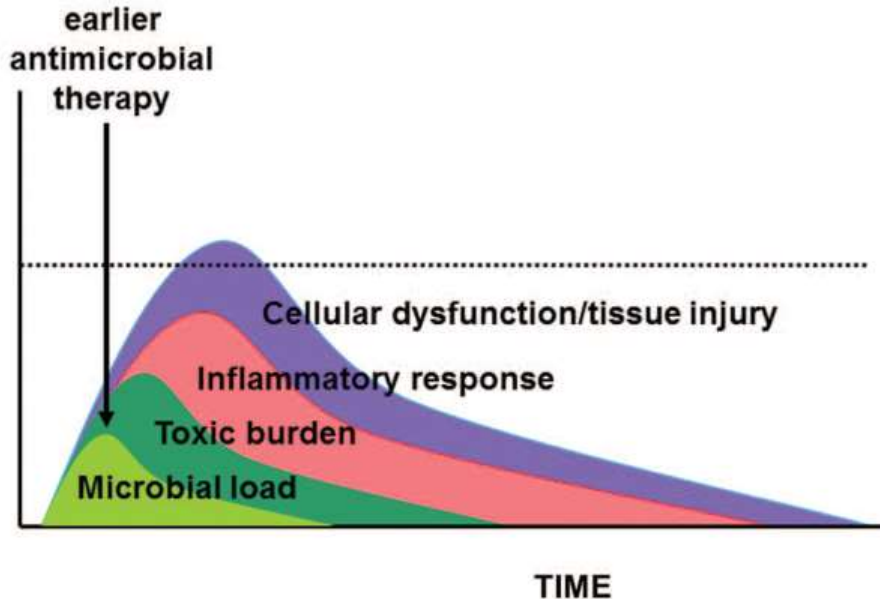
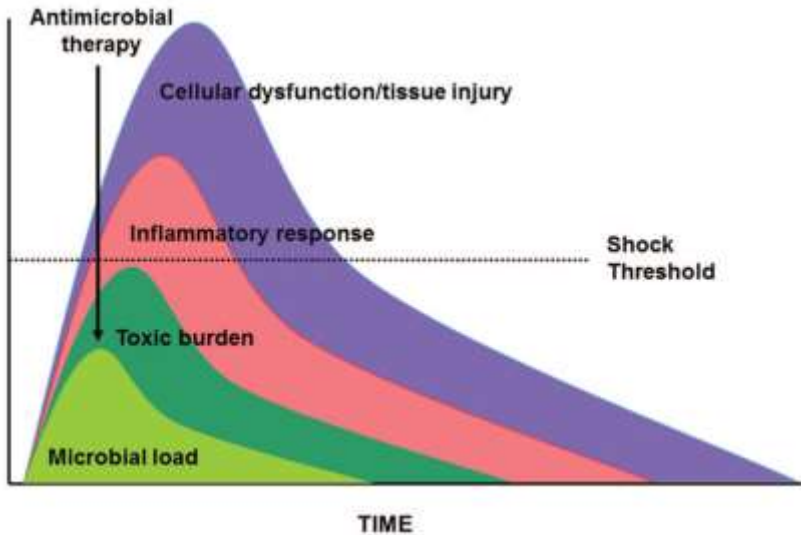
Days

Valles A, et al. Chest 2003; 123:1615-24

# Microbiologic view of sepsis and septic shock

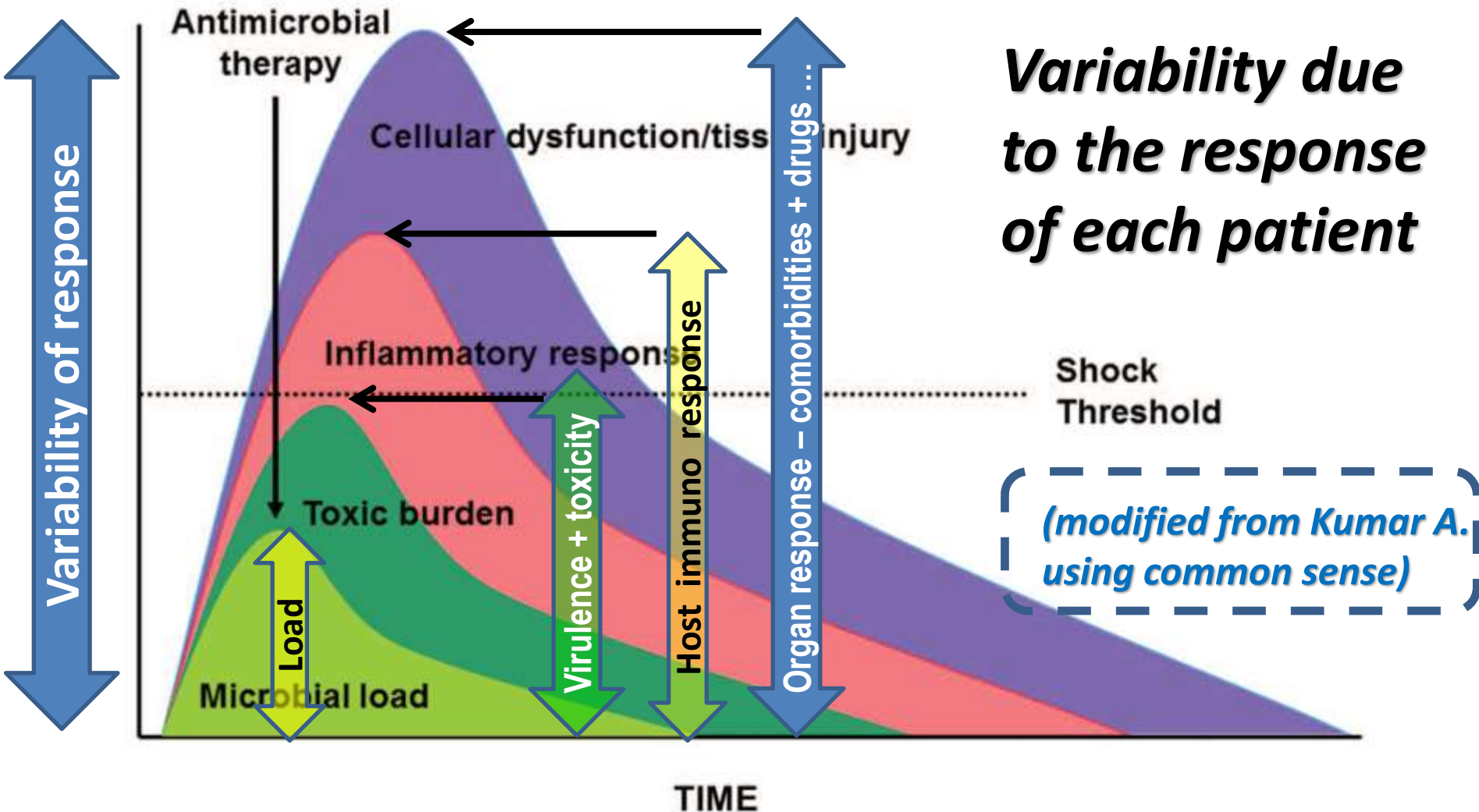
Kumar A. 2014

*Variability  
related to  
treatment  
effect*

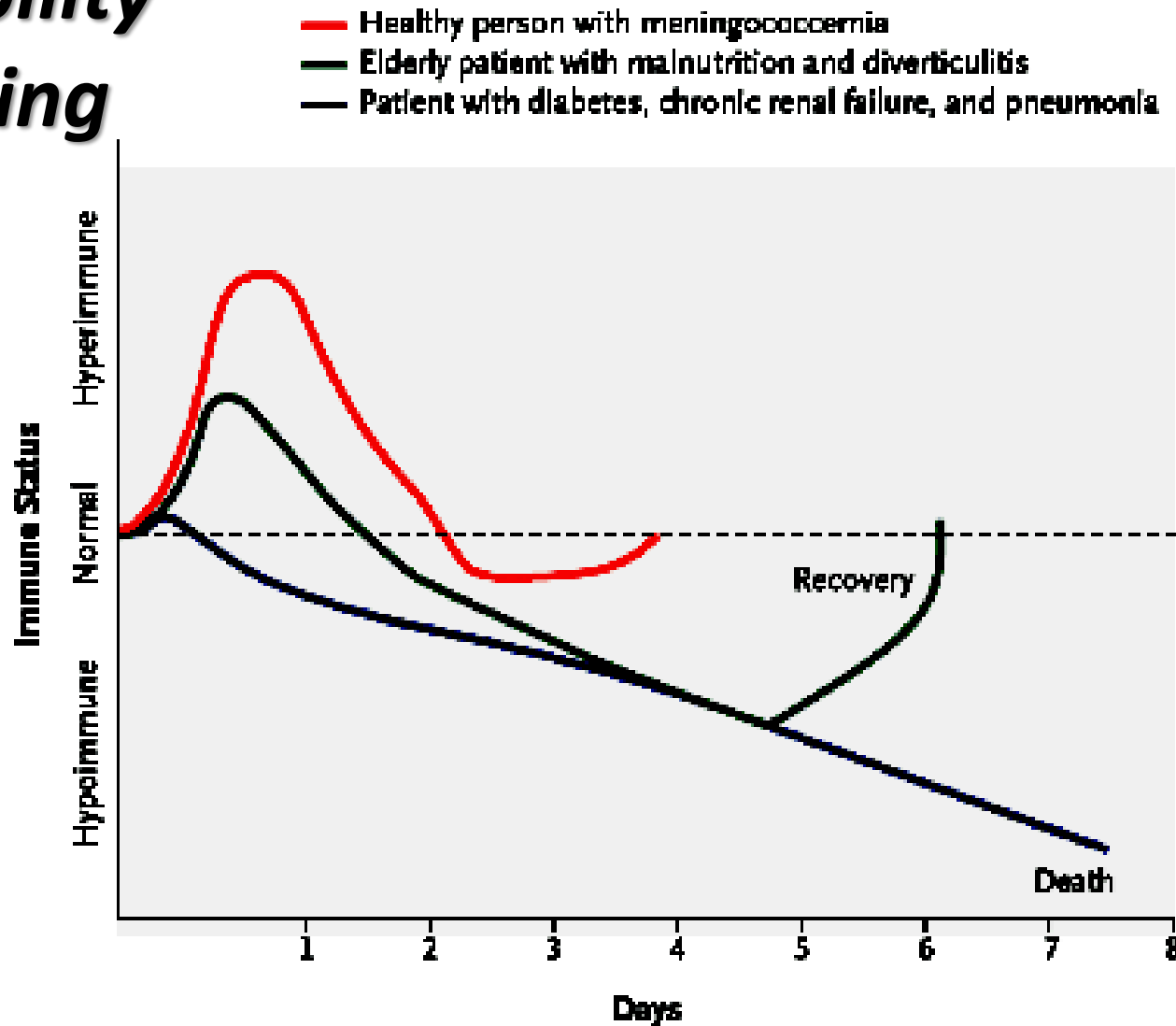


# Impact of appropriate antimicrobial therapy in patients with sepsis OR septic shock.

Kumar A. 2014



# Variability of timing (2003)



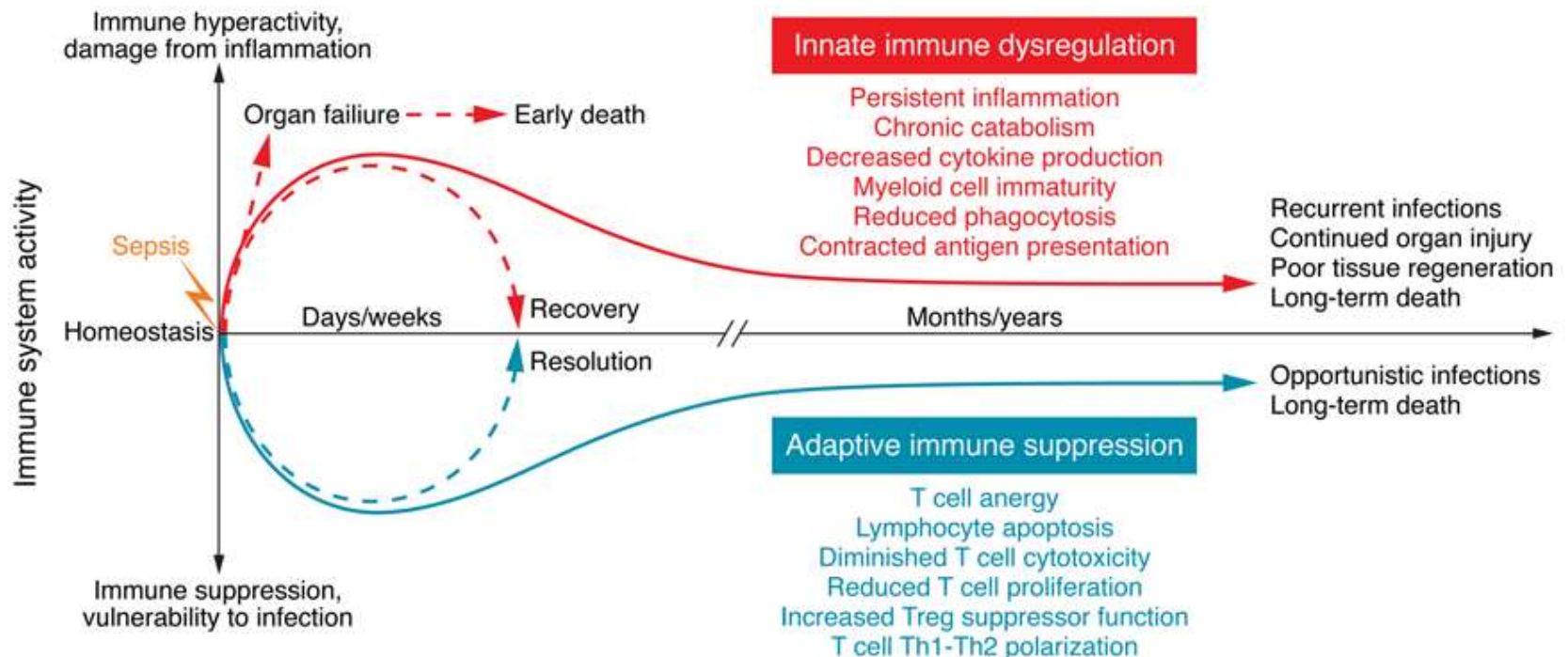
The pathophysiology and treatment of sepsis,  
Hotchkiss RS, Karl IE NEJM 2003; 348: 138-150.

# Variability of timing (2016 = 13yrs)

The Journal of Clinical Investigation 2016

## Sepsis-induced immune dysfunction: can immune therapies reduce mortality?

Matthew J. Delano<sup>1</sup> and Peter A. Ward<sup>2</sup>



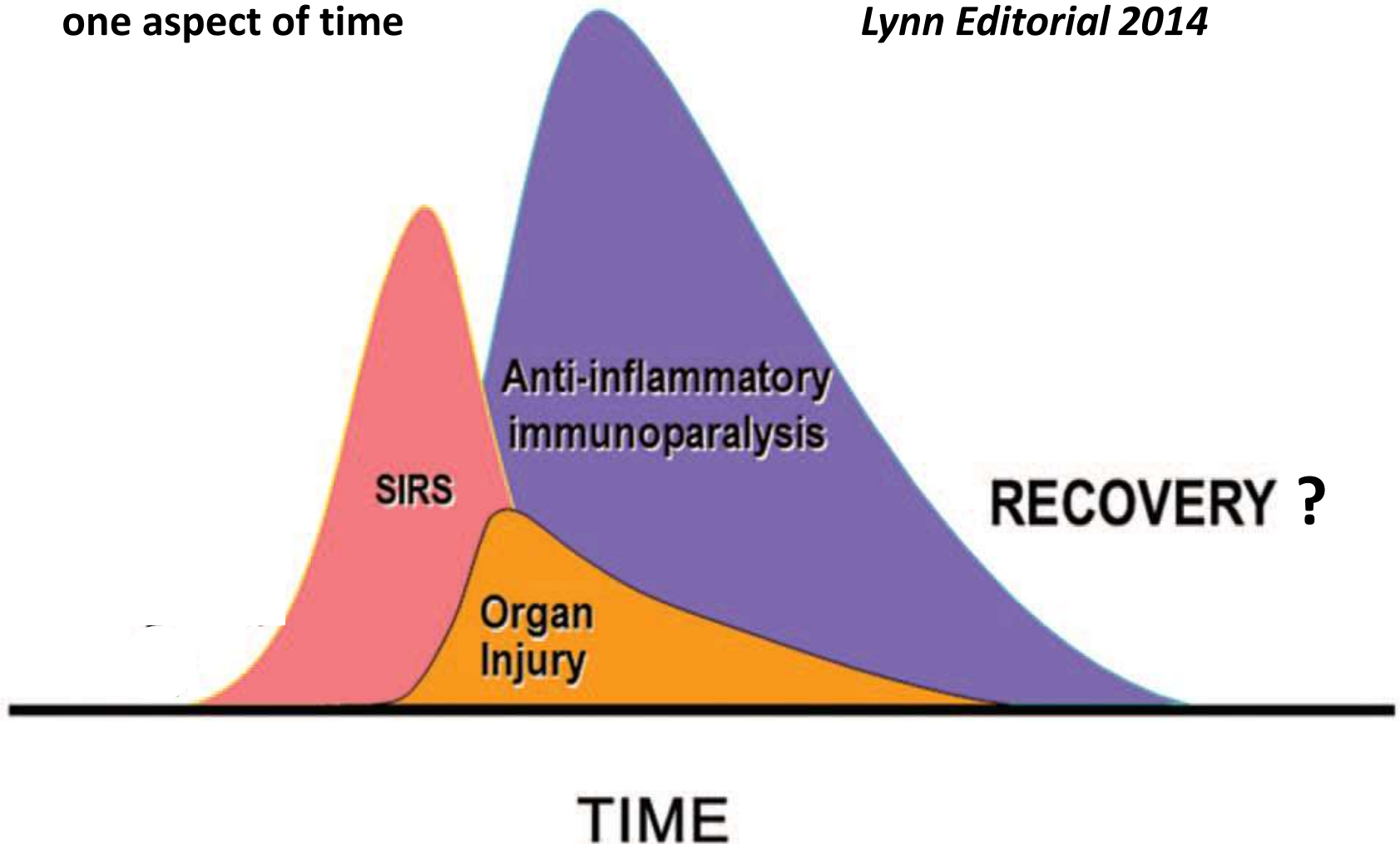


# Immunologic view of sepsis and septic shock

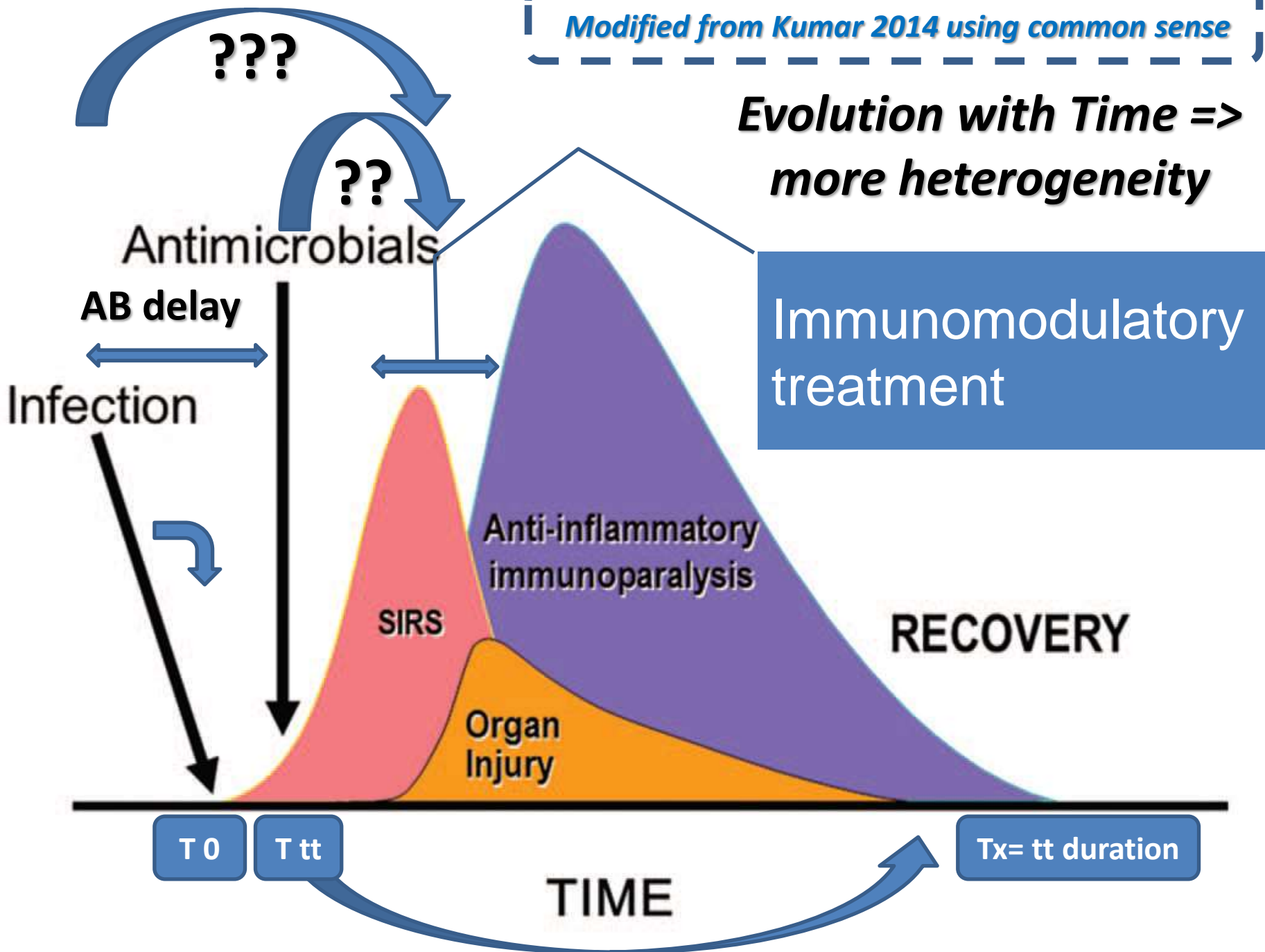
Modified from Kumar A. 2014

One needs no mathematical training to understand that a time critical process like sepsis should include at least one aspect of time

*Lynn Editorial 2014*

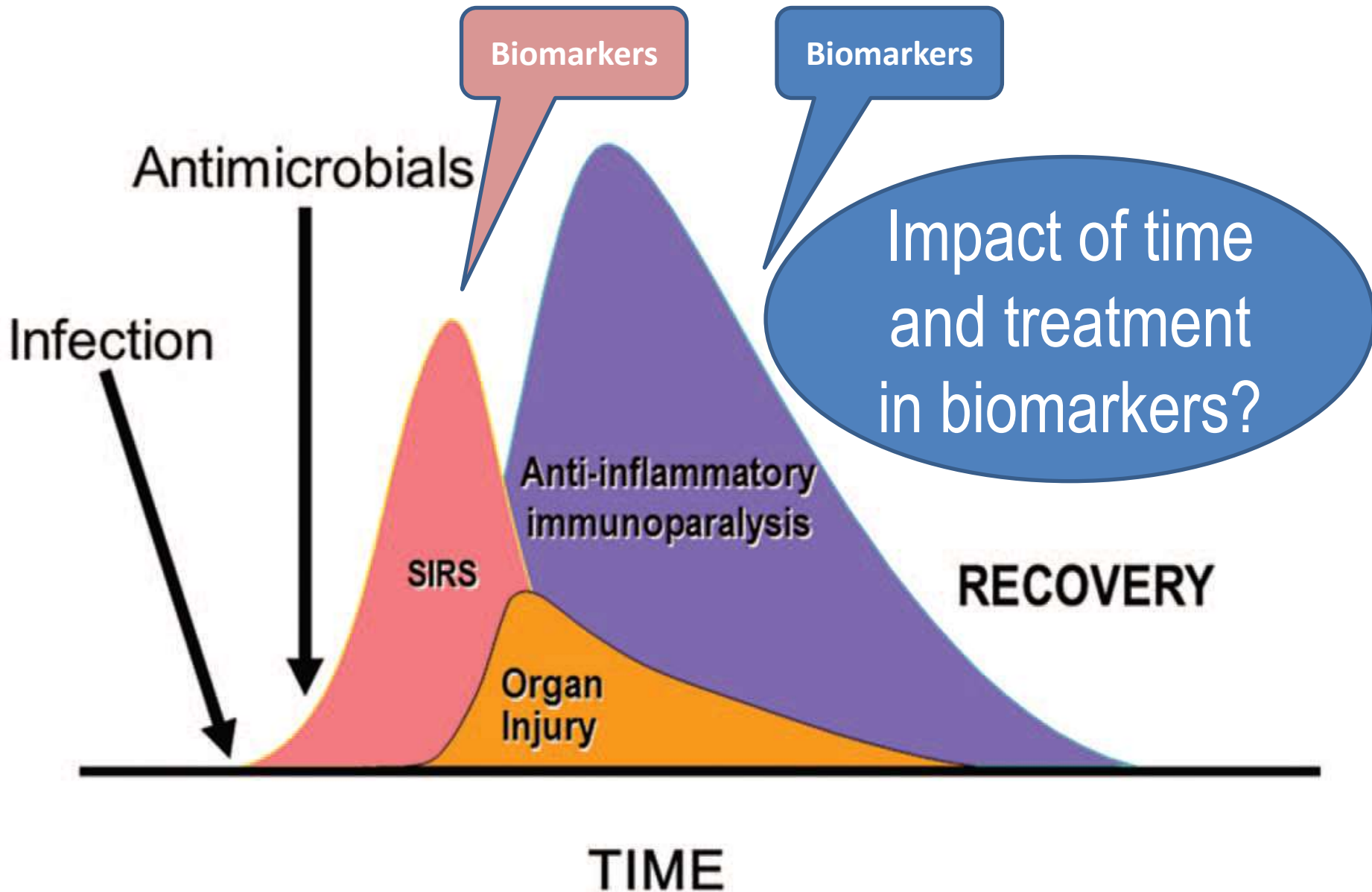


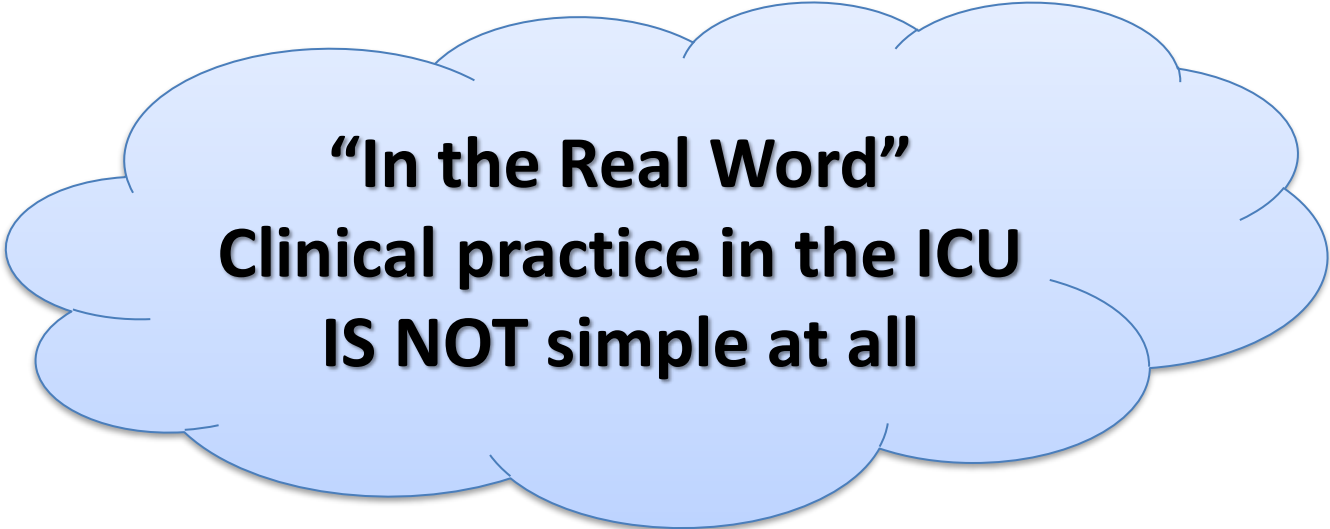
Modified from Kumar 2014 using common sense



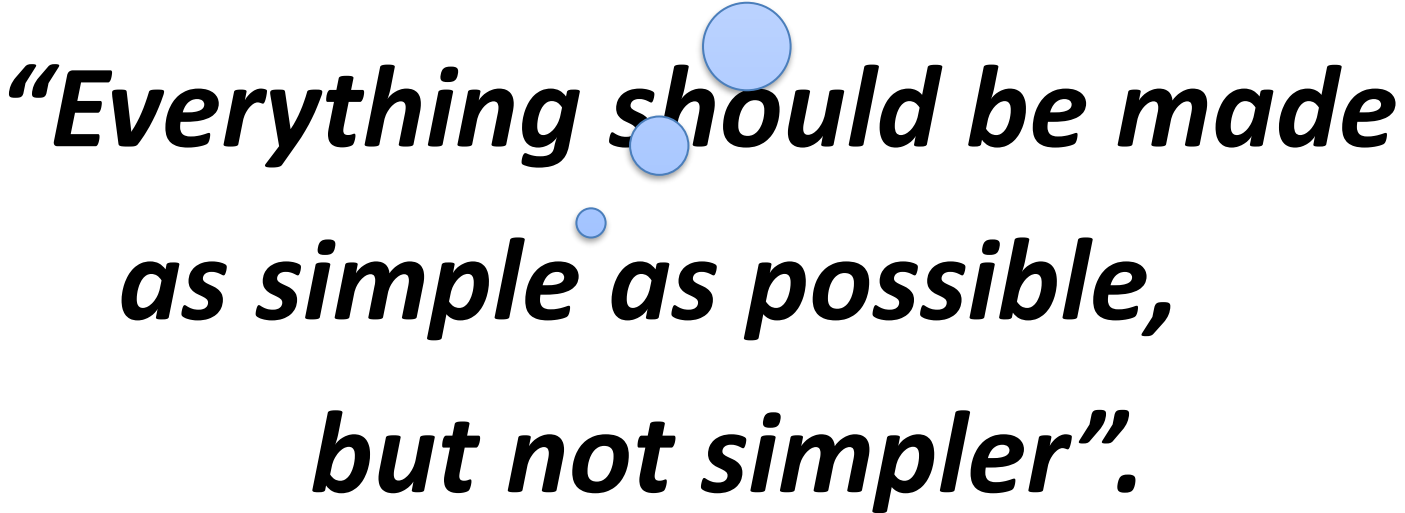
# Immunologic view of sepsis and septic shock

Modified from Kumar A. 2014





**“In the Real World”  
Clinical practice in the ICU  
IS NOT simple at all**



***“Everything should be made  
as simple as possible,  
but not simpler”.***

***Albert Einstein***

# Key points (III)

- Σημασία του case-mix στις RCTs με βάση τις οποίες δημιουργούνται τα Guidelines
- Διαφορετικοί ορισμοί ανάλογα με το σκοπό για τον οποίο δημιουργούνται αλλά και το επίπεδο επιστημονικής κατανόησης
- Πολυπλοκότητα των «μοντέλων» στον πραγματικό κόσμο (in the real world) => αναγκαιότητα της personalized medicine \*\*\*
- **ΕΠΙΣΤΗΜΟΛΟΓΙΚΗ ΠΡΟΣΕΓΓΙΣΗ =>**

# ***Presentation outline***

- The Guidelines for the management of septic patients and their application in a “Real Word setting”
- Pathophysiologic «paradigms» of sepsis and septic shock

**AND**

- *Evolution of scientific knowledge AND understanding* in relation with Definitions, Diagnostic approach and Treatment (= Real decision making)

# Philosophy / Epistemology (Part I)



Jean Piaget (1896-1980)

## STAGE 1

00500L5000L



Children from birth to 2 years learn through trial & error.

## STAGE 2

### Preoperational

Children develop language, memory, and intuitive intelligence through make believe play between 3 and 7 years of age.



## Piaget's 4 Stages of Cognitive Development

## STAGE 3

Logical thinking and concrete referencing develops from 7 to 11 years.



### Concrete Operational

## STAGE 4 Formal Operational

Adolescents and adults attain lifelong intellect through hypothetical and abstract thinking.



**ΠΑΡΑΔΕΙΓΜΑ = Ο πατέρας του παιδιού είναι και γιός του παππού ή ακόμα πιο απλό ο παππούς είναι και πατέρας (2 ιδιότητες)**

# *Philosophy / Epistemology (Part II)*

## *Theory of Ideas OR Theory of Forms*



428 – 348 before JC

Plato applies this concept to all things. According to Plato, there must be a form of the **tree itself** in somewhere. Trees that we can see in our lives share the property of the **Form of the tree itself**.

The reason why trees are trees is that they participate in the Form of the tree itself.

The reason why other things are not trees is that they don't participate in the Form of the tree itself.



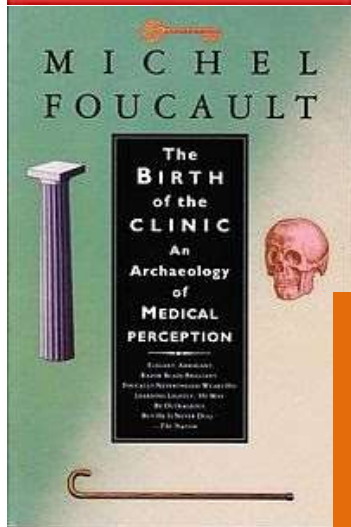
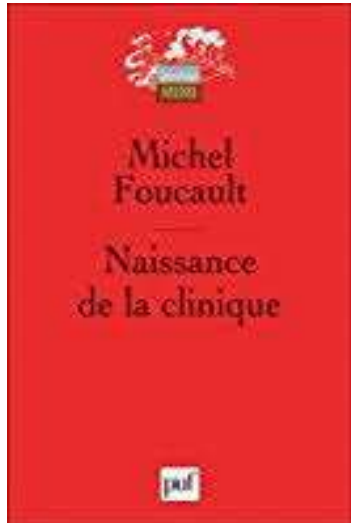
MICHEL  
FOUCAULT

1926-1984



## *Philosophy / Epistemology (III)*

What Foucault is telling us is that **the clinic** (the doctor's office) is built around the idea that the patient's body is doing the talking and the doctor is only an objective observer. The doctor uses his expert training to spot the signs of disease or disorder in the patient's body and then he objectively translates these signs into a diagnosis and a treatment plan.



*Diseases exist somewhere like Plato's "Ideas" or "Forms"  
"Know the name of the Evil Spirit to be able to face it"  
Diagnostic boxes=> automatically treatment instructions ?*

# Philosophy / Epistemology (Part I)



Jean Piaget (1896-1980)

## STAGE 1

00500-50001



Children from birth to 2 years learn through trial & error.

## STAGE 2

### Preoperational

Children develop language, memory, and intuitive intelligence through make believe play between 3 and 7 years of age.



## Piaget's 4 Stages of Cognitive Development

## STAGE 3

Logical thinking and concrete referencing develops from 7 to 11 years.



### Concrete Operational

## STAGE 4 Formal Operational

Adolescents and adults attain lifelong intellect through hypothetical and abstract thinking.



Adolescents begin to think more as a scientist thinks, devising plans to solve problems and systematically test opinions.[40] They use hypothetical-deductive reasoning, which means that they develop hypotheses or best guesses, and systematically deduce, or conclude, which is the best path to follow in solving the problem.[40]



## ***Philosophy / Epistemology (Part IVa)***

### ***Two forms of intelligence according to Piaget:***

#### **Figurative intelligence**

is the more or less static aspect of intelligence involving all means of representation used to retain in mind the states (i.e., successive forms, shapes, or locations) that intervene between transformations. Therefore, it involves perception, imitation, mental imagery, drawing, and language. [\[10\]](#)

#### **Operative intelligence**

is the active aspect of intelligence. It involves all actions, undertaken in order to follow, recover, or anticipate the transformations of the objects or persons of interest. [\[9\]](#)



## ***Philosophy / Epistemology (Part IVb)***

***Two forms of intelligence according to Piaget:***

Piaget stated that figurative aspects of intelligence are subservient to its operative and dynamic aspects, and therefore,

**understanding essentially derives from  
the operative aspect of intelligence.** [\[9\]](#)

***THINKING OUT OF THE "BOX" ???***

**SEPSIS = a 3 ticks disease**  
**SEVERE SEPSIS = a 4 ticks disease**  
**SEPTIC SHOCK = a 5 ticks disease**



**PARTICLE IDENTIFICATION**



**PCR**



**1300s**

**1950s**

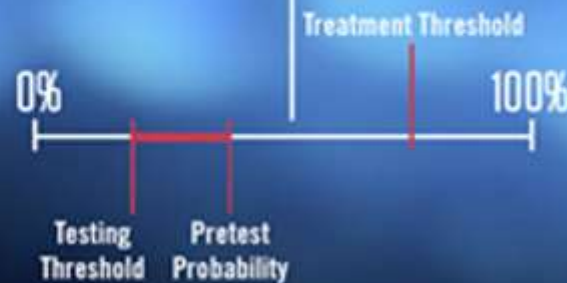
**1970s**

**1980s**

**1990s**

**2013**

**MEDICAL DIAGNOSIS**



**Lynn 2014**



Dellinger et al  
CCM 2004  
Vol. 32, No 11  
(Suppl)  
Introduction

**A clinician armed with a sepsis change bundle, attacks the three heads of sepsis (hypotension, hypoperfusion, and organ dysfunction).**

***Inspired by Hercules Kills Cerberus, Renato Pettinato***

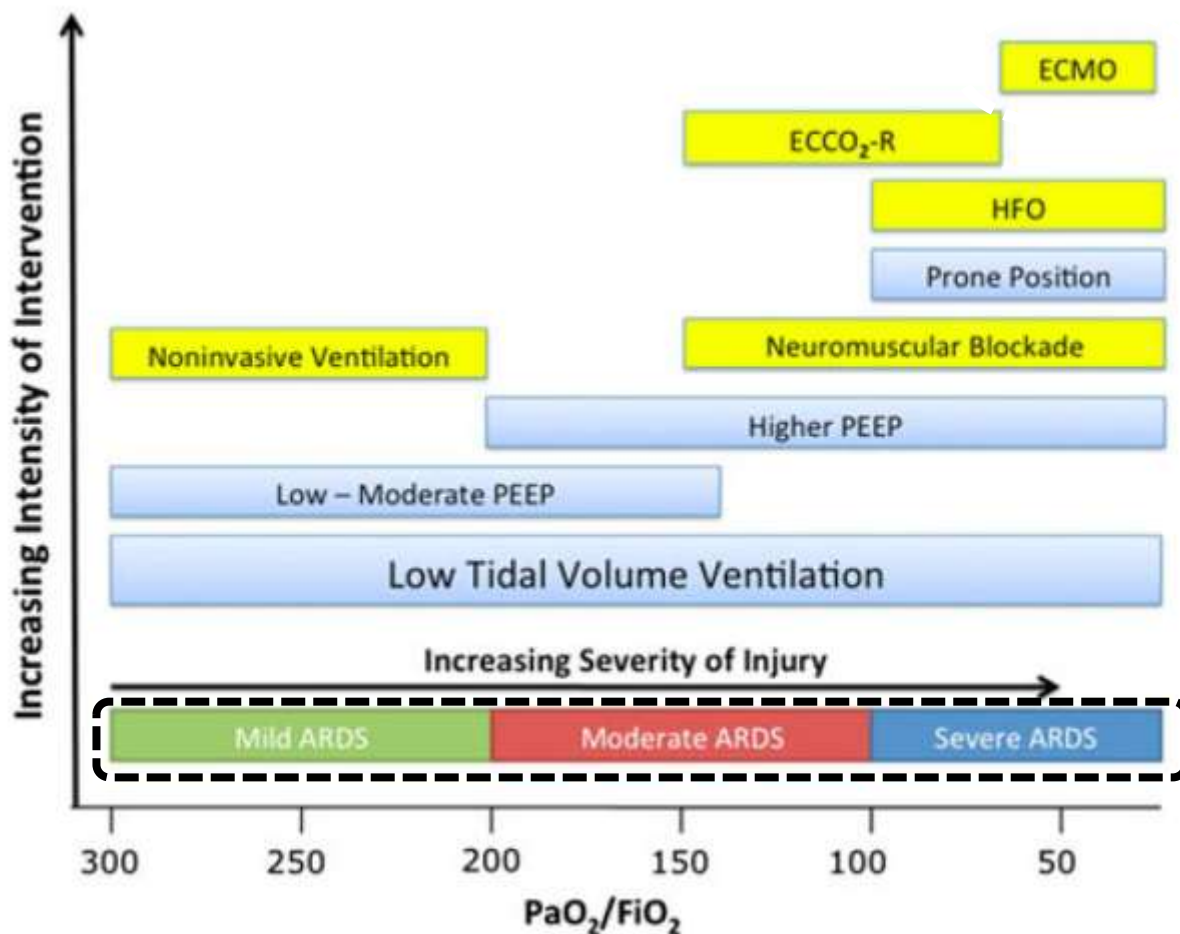
# American European Consensus Conference Criteria for ALI & ARDS

Clinical Variable	ALI	ARDS
Onset	Acute	Acute
Hypoxemia	PaO <sub>2</sub> /FiO <sub>2</sub> ≤300	PaO <sub>2</sub> /FiO <sub>2</sub> ≤200
Chest X-ray	B/L infiltrates Consistent with pul. Edema	B/L infiltrates Consistent with pul. Edema
Non-cardiac cause	No clinical e/o left atrial HTN or pulm artery occlusion pressure ≤18 mmHg	No clinical e/o left atrial HTN or pulm artery occlusion pressure ≤18 mmHg

**Bernard et al 1994**

Niall D. Ferguson  
Eddy Fan  
Luigi Camporota  
Massimo Antonelli  
Antonio Anzueto  
Richard Beale  
Laurent Brochard  
Roy Brower  
Andrés Esteban  
Luciano Gattinoni  
Andrew Rhodes  
Arthur S. Slutsky  
Jean-Louis Vincent  
Gordon D. Rubenfeld  
B. Taylor Thompson  
V. Marco Ranieri

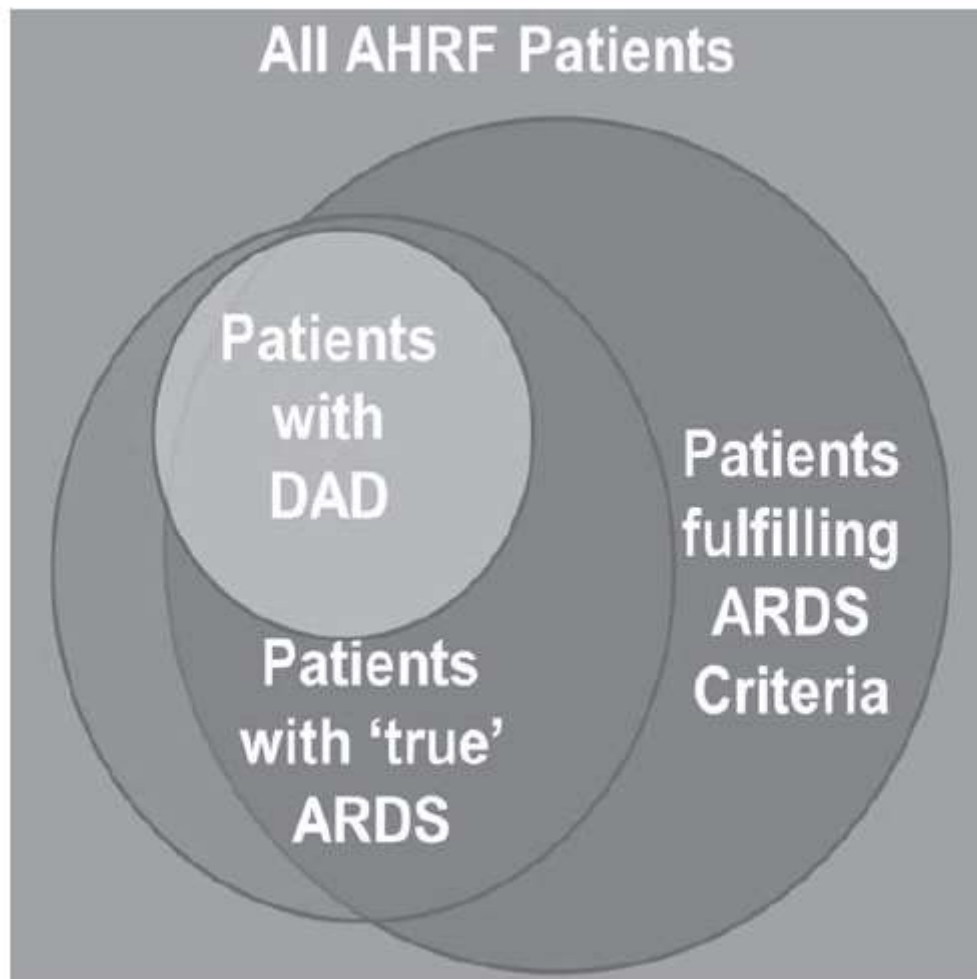
## The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material





# Continued under-recognition of acute respiratory distress syndrome after the Berlin definition: what is the solution?

John G. Laffey<sup>a,b</sup>, Tai Pham<sup>c</sup>, and Giacomo Bellani<sup>d,e</sup>



**Definitions  
follow  
Purposes  
Patients with  
the disease**

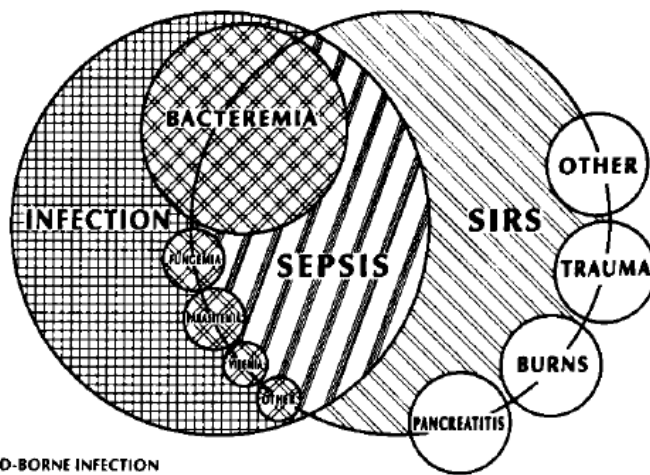
*Curr Opin Crit Care* 2017  
Feb; 23(1):10-17.

# An alternate pathophysiologic paradigm of sepsis and septic shock

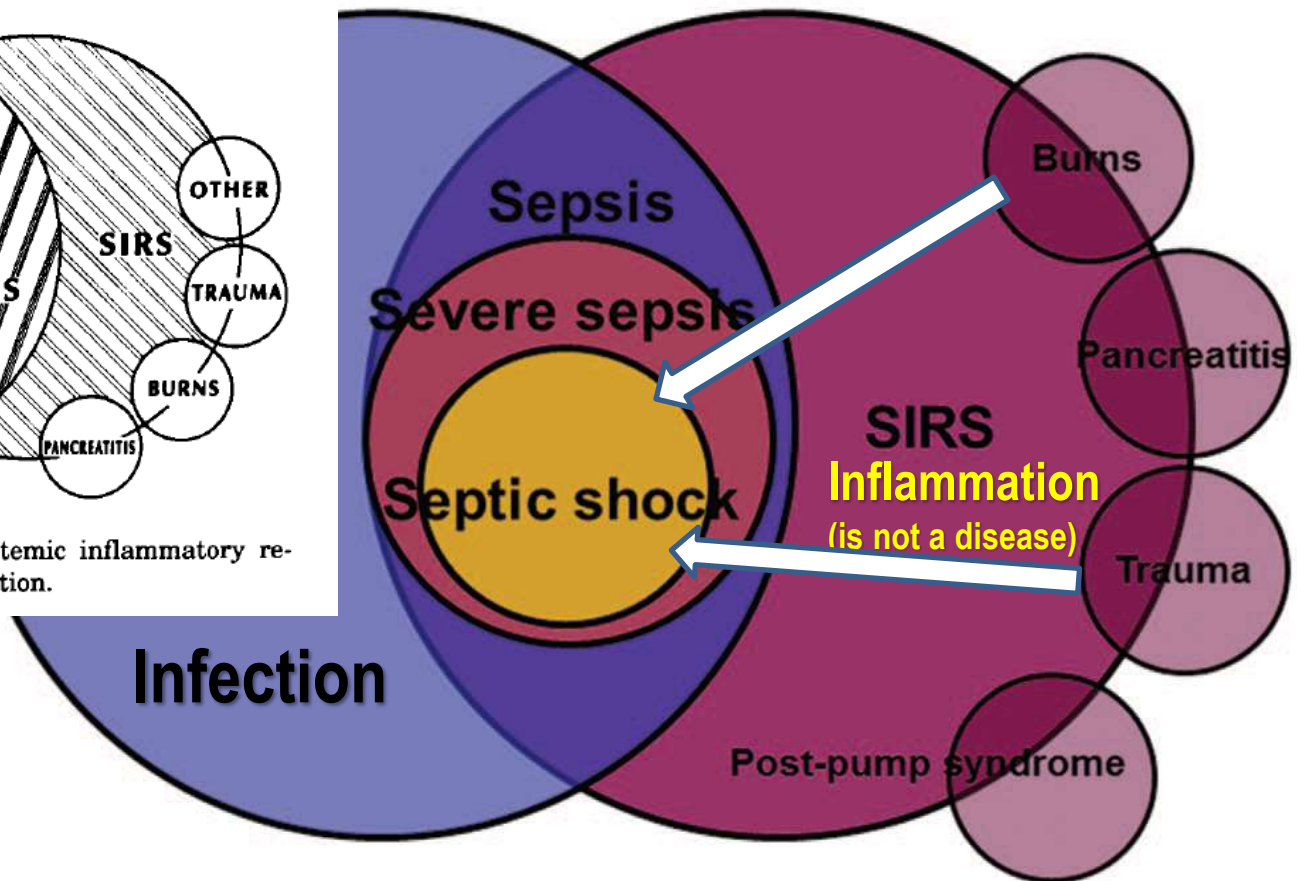
## Implications for optimizing antimicrobial therapy

Bone 1992

Anand Kumar 2014



**Figure 1.** Interrelationships among systemic inflammatory response syndrome (SIRS), sepsis, and infection.



# *Genotype-first approach (Wikipedia): “Genotypes” and “Phenotypes”*

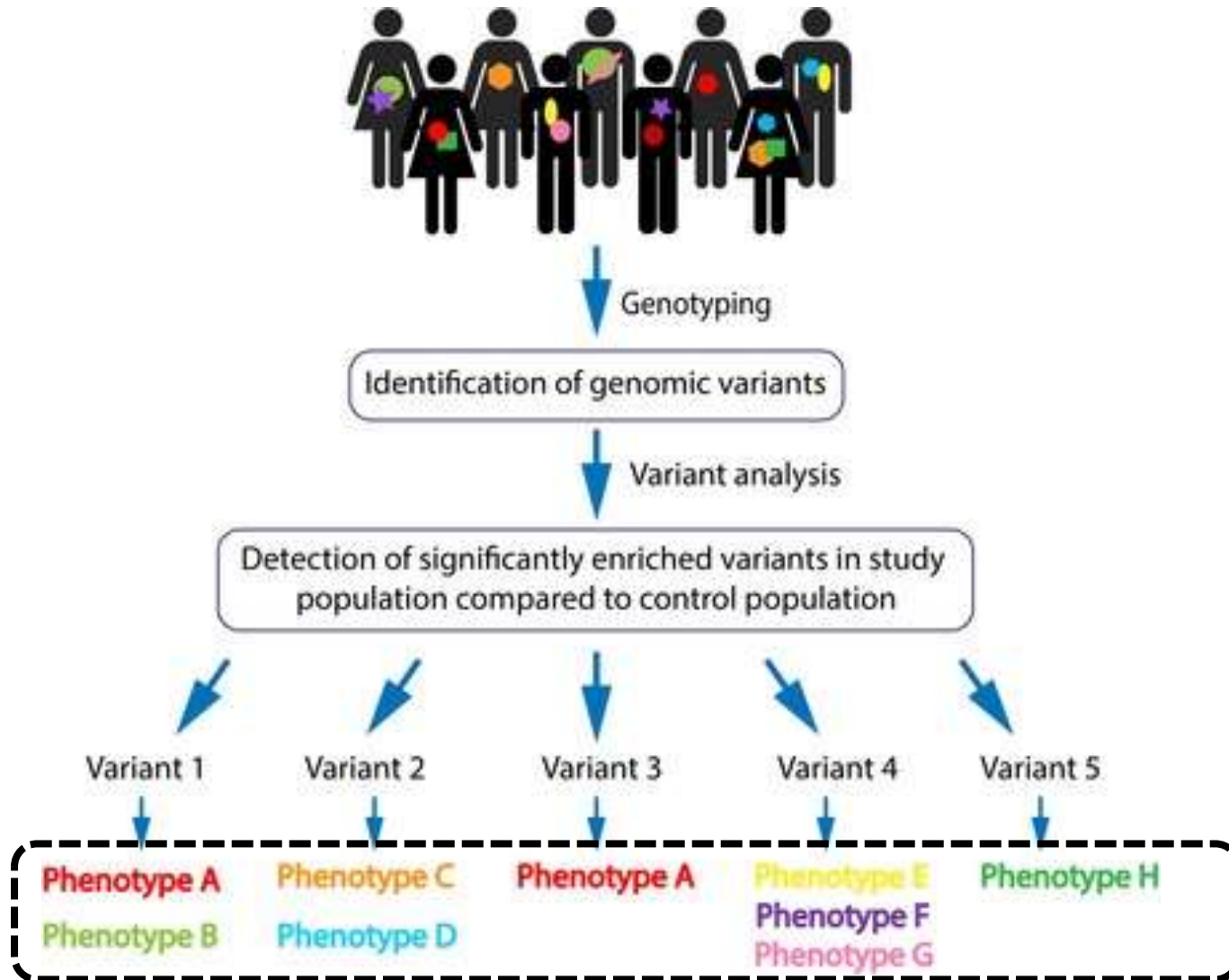


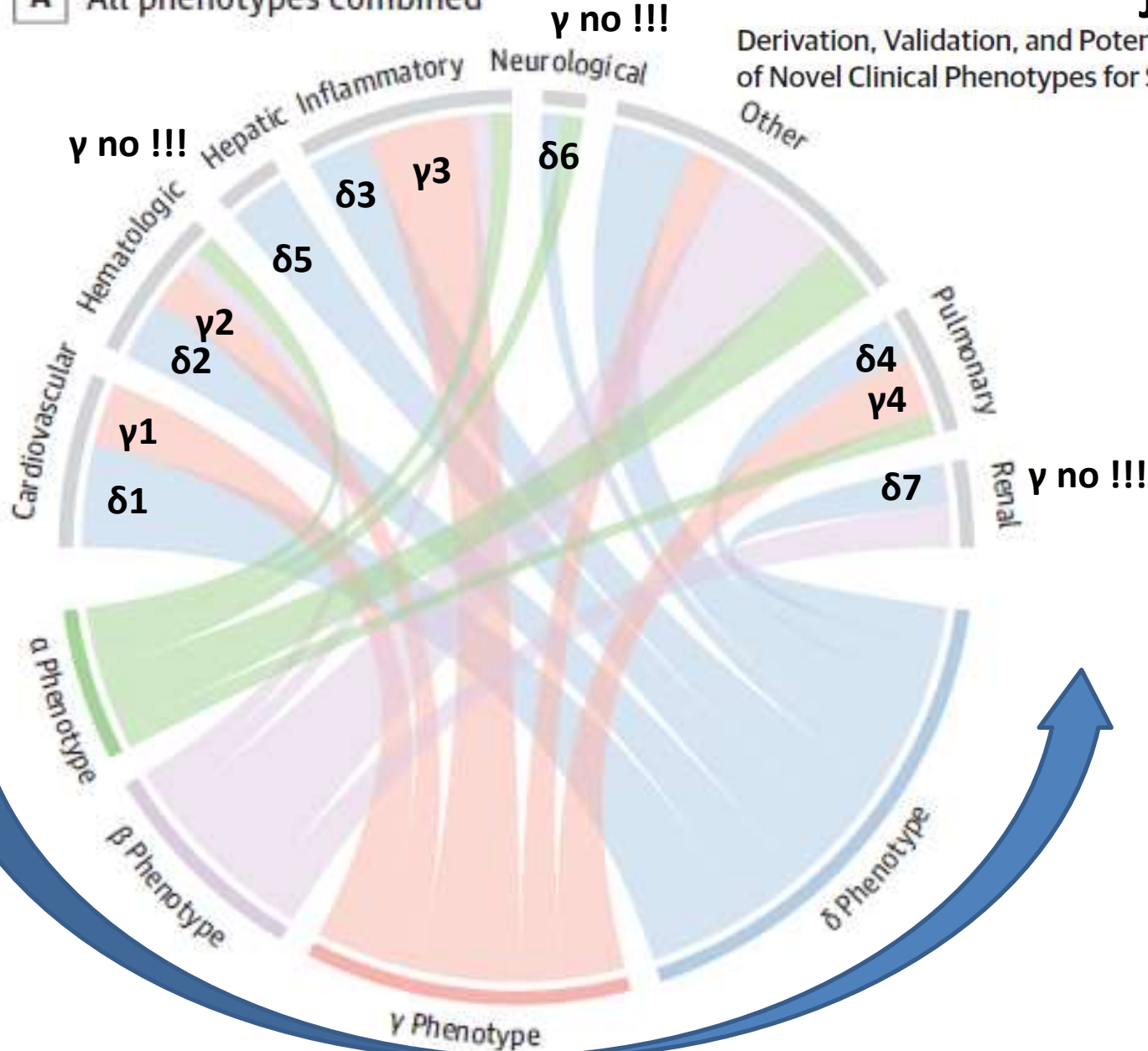
Figure 1. Chord Diagrams Showing Abnormal Clinical Variables by Phenotype

Seymour et al

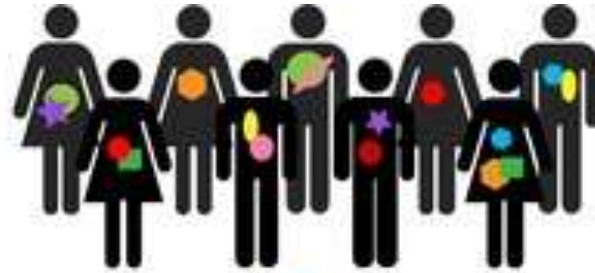
JAMA 2019

Derivation, Validation, and Potential Treatment Implications of Novel Clinical Phenotypes for Sepsis

**A** All phenotypes combined



# The usefulness of “phenotypes” in “medical cognitive development”



↓ Genotyping

Identification of genomic variants

↓ Variant analysis

Detection of significantly enriched variants in study population compared to control population

Variant 1

Variant 2

Variant 3

Variant 4

Variant 5

Phenotype A

Phenotype C

Phenotype A

Phenotype E

Phenotype H

Phenotype B

Phenotype D

Phenotype F

Phenotype G

*Comorbidities  
in each patient  
5 X ? variants*



# Validation of Inflammopathic, Adaptive, and Coagulopathic Sepsis Endotypes in Coronavirus Disease 2019

CCM 2021; 49 (2)

---

**OBJECTIVES:** Complex critical syndromes like sepsis and coronavirus disease 2019 may be composed of underlying “endotypes,” which may respond differently to treatment. The aim of this study was to test whether a previously defined bacterial sepsis endotypes classifier recapitulates the same clinical and immunological endotypes in coronavirus disease 2019.

Timothy E. Sweeney, MD, PhD<sup>1</sup>

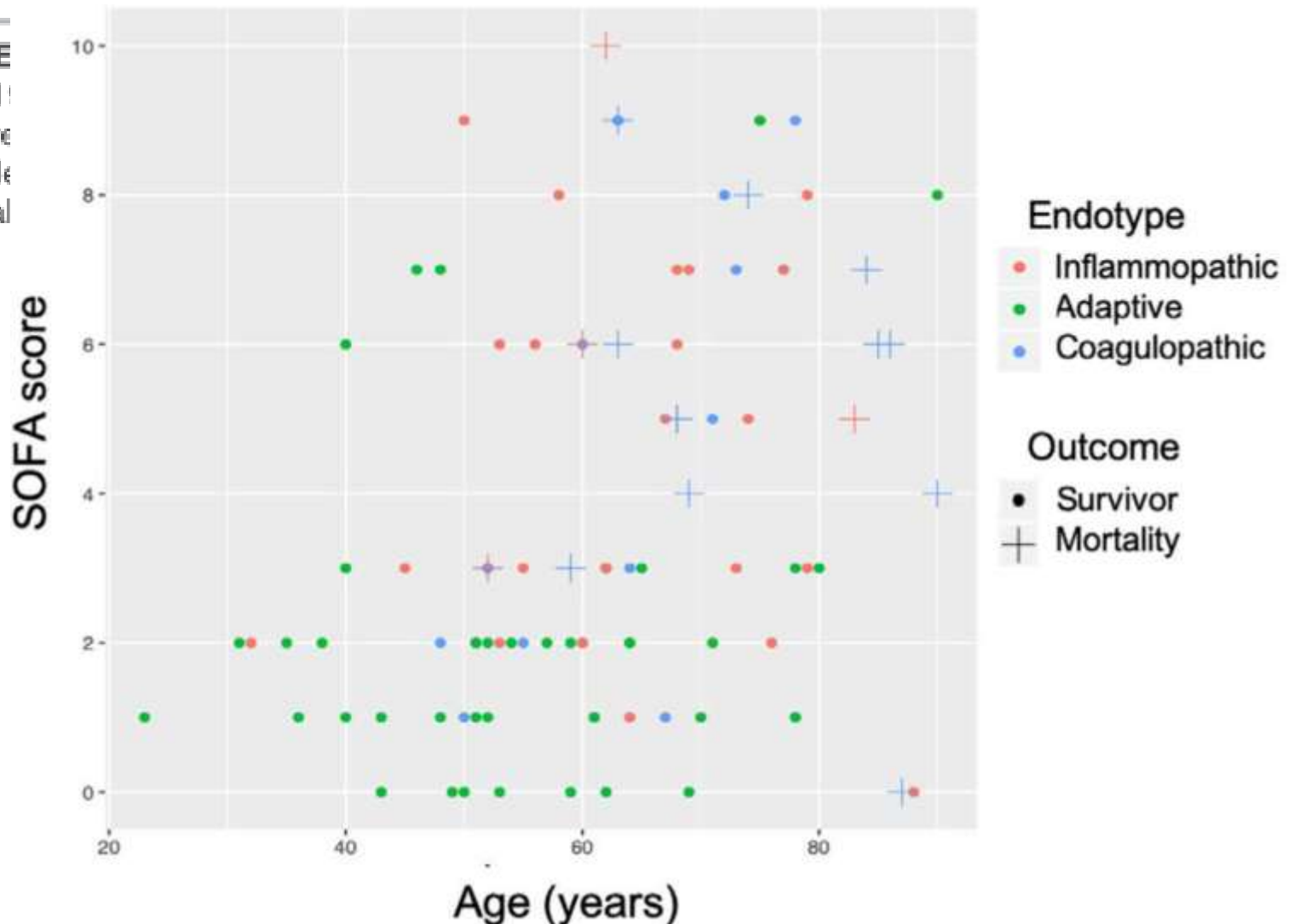
.....

Evangelos J. Giamarellos-Bourboulis, MD, PhD<sup>2</sup>

# Validation of Inflammopathic, Adaptive, and Coagulopathic Sepsis Endotypes in Coronavirus Disease 2019

CCM 2021; 49 (2)

**OBJECTIVE**  
disease 2019  
spond differ  
previously de  
same clinical



# The diagnosis of sepsis revisited - a challenge for young medical scientists in the 21st century

Lawrence A Lynn



Expert  
opinion

Lynn *Patient Safety in Surgery* 2014, **8**:1  
<http://www.pssjournal.com/content/8/1/1>

## Abstract

In 1991, a well-meaning consensus group of thought leaders derived a simple definition for sepsis which required the breach of only a few static thresholds. More than 20 years later, this simple definition has calcified to become the gold standard for sepsis protocols and research. Yet sepsis clearly comprises a complex, dynamic, and relational distortion of human life. Given the profound scope of the loss of life worldwide, there is a need to disengage from the simple concepts of the past. There is an acute need to develop 21st century approaches which engage sepsis in its true form, as a complex, dynamic, and relational pattern of death.

**There is a need  
to disengage from the simple concepts of the past  
and to develop 21<sup>st</sup> century approaches  
which engage sepsis in its true form,  
a complex-dynamic-relational pattern of death.**



# Key points (IV)

- Σημασία του case-mix στις RCTs με βάση τις οποίες δημιουργούνται τα Guidelines
- Διαφορετικοί ορισμοί ανάλογα με το σκοπό για τον οποίο δημιουργούνται
- Πολυπλοκότητα των «μοντέλων» στον πραγματικό κόσμο (in the real world) => αναγκαιότητα της personalized medicine \*\*\*
- Αναγκαιότητα για operational intelligence στην εξέλιξη της ιατρικής γνώσης- αντίληψης
- ***Decision making in the Real World =>***

# An alternate pathophysiologic paradigm of sepsis and septic shock

## Implications of individual response variability

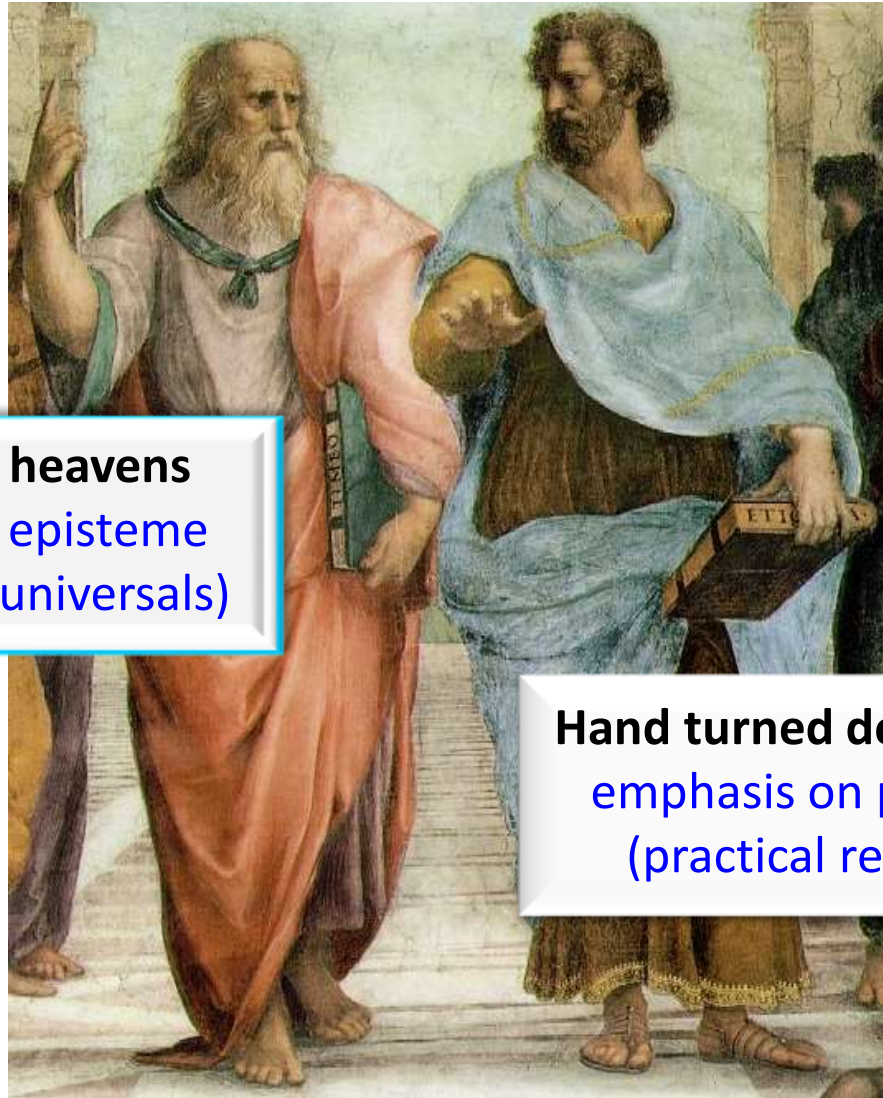
A new paradigm (modified from Anand Kumar )

- *Current paradigm: Immunologic Model*
- *The classic paradigm: Microbiologic Primacy*
- *A new Composite Model: Integrating Shock*
- *We need a more Composite Model = use a Dialectic Approach integrating:*
  - a) Time effect and variability in the real world*
  - b) risk /benefit analysis => risk of adverse effects in the individual patient (comorbidities ?)*
  - c) re-evaluation after response to treatment ?*



# Dialectic approach (Διαλεκτική προσέγγιση)

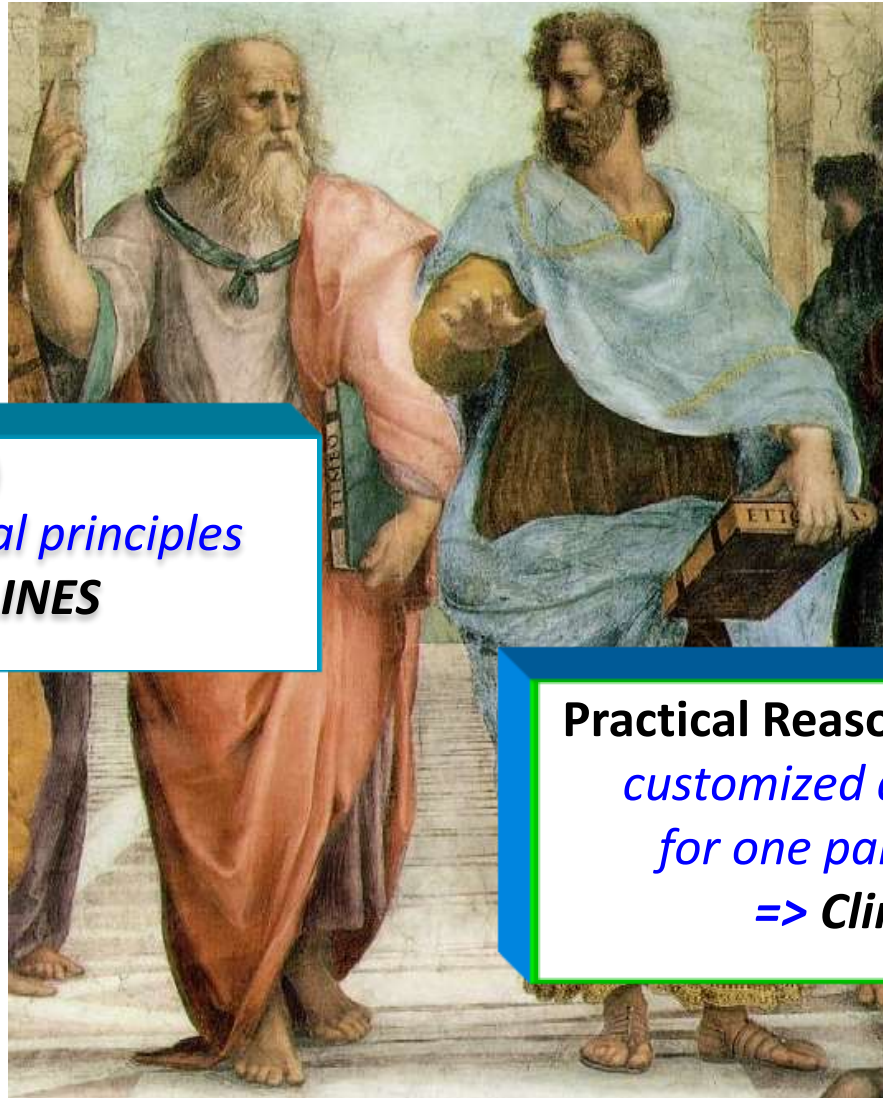
Raphael 1483-1520: The school of Athens 1510-11, Vaticano



**Pointing up to heavens**  
emphasis on episteme  
(theoretical universals)

**Hand turned down to earth**  
emphasis on phronesis  
(practical reasoning)

**Plato, 427-347 BC    Aristotle, 384– 322 BC**



**Science (*episteme*)**

*based on universal principles*

**=> GUIDELINES**

**Practical Reasoning (*phronesis*)**

*customized decision*

*for one particular patient*

**=> Clinical practice**

**Plato, 427-347 BC**

**Aristotle, 384– 322 BC**

*We need a dialectic approach  
using both Theory and Phronesis*

**“Clinical  
Practice  
Guidelines”**



**for a  
“customized”  
decision  
making  
in the  
individual  
patient**

**Plato, 427-347 BC      Aristotle, 384– 322 BC**

Patients are not airplanes and doctors  
are not pilots

Richard Rissmiller, MD, Internal Medicine, Carolinas Medical Center, Charlotte, NC

To the Editor:

While I do not claim to have the research experience of Drs. Kortgen and colleagues (1) and Dr. Rivers (2), I do have a fair amount of experience treating sepsis. I am tiring of the ongoing analogy of the

The authors reply:

Emanuel P. Rivers, MD, MPH, IOM,

Although co-morbidities make each patient unique, making the management of sepsis an art and a science, they also add a higher level of complexity requiring an orderly approach to patient care.

In the absence of order, chaos reigns, which benefits no one, including the patients we serve.

# EMERGENCY MEDICINE DECISION MAKING

*Critical Choices in  
Chaotic Environments*

SCOTT WEINGART  
PETER WYER



*One size  
DOES NOT  
fit all*





# **Expert (and my) Opinion**

*Russell Burck Rush University Medical Center, Chicago, IL*

*Editorial in Critical Care Medicine 2004*

***“Clearly, the reality of the science of critical care is that it is a messy.***

***That is not the problem in my view.***

***The problem would be if we did not notice, accept, and address that reality”***

# Expert (and my) Opinion

*Russell Burck Rush University Medical Center, Chicago, IL*

*Editorial in Critical Care Medicine 2004*

*“Clearly, the reality of the science of critical care is that it is a mess.*

*That*

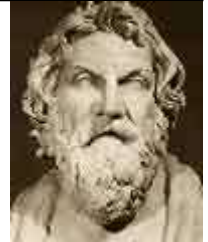
**In the ICU treatment  
must be “tailored”  
to pathophysiology**

*The p  
notice*

*... did not  
... and address that reality”*

# «Αρχή σοφίας η των ονομάτων επίσκεψις»

Αντισθένης (445 -360 π.Χ.)

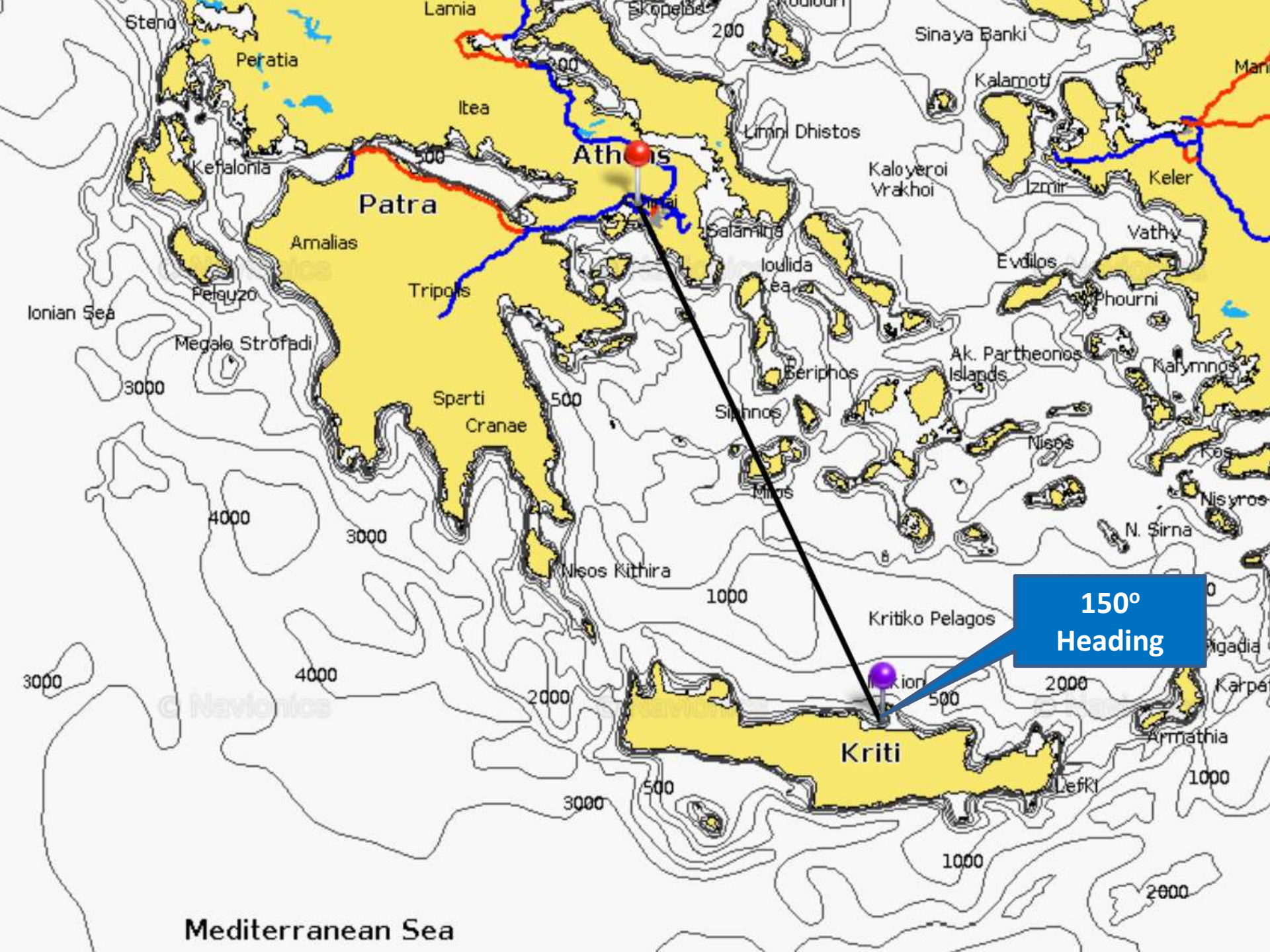


## Guidelines ΔΕΝ σημαίνει:

- Κανόνες ; (rules)
- Αρχές αντιμετώπισης ; (principles)
- Οδηγίες ; (instructions – manual ?)

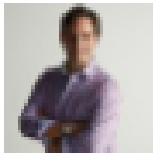
## Σημαίνει: ΚΑΤΕΥΘΥΝΤΗΡΙΕΣ ΓΡΑΜΜΕΣ

- Σημασία μετάφρασης: οικονομικά + νομικά θέματα αλλά και θέματα που έχουν σχέση με τη διδασκαλία, την κατανόηση των εννοιών «νόσος» και «σύνδρομο» και της παθοφυσιολογικής προσέγγισης και της διαλεκτικής αντιμετώπισης «ασθενών με νόσο X» και όχι «της νόσου X»
- Παράδειγμα πλοήγηση για Κρήτη=κατεύθυνση 150°



150°  
Heading

Mediterranean Sea



BY JOSH LINKNER

*Entrepreneur, author, VC, Jazz guitarist*



[@JoshLinkner](#)

<http://www.inc.com/josh-linkner/compasses-over-maps.html>



# Why You Need to Give Your Team a Compass, Not a Map

Shifting terrain, unexpected roadblocks, and surprise attacks can be conquered only by travelers who can think and act without detailed instructions.




BY JOSH LINKNER

*Entrepreneur, author, VC, Jazz guitarist*



[@JoshLinkner](#)

 WRITE A COMMENT

<http://www.inc.com/josh-linkner/compasses-over-maps.html>

# **Why You Need to Give Your Team a Compass, Not a Map**

Management-by-operating-manuals worked fine back in the days when markets were local, customers were homogenous, product cycles occurred over decades, and complexity was minimal. \*

Workers didn't need to think all that much on their own, as long as following the map would ensure their safe arrival.

# **Why You Need to Give Your Team a Compass, Not a Map**

When teams or organizations turn off their brains and simply follow the map, progress shrivels.

Shifting terrain, unexpected roadblocks, and surprise attacks can be conquered only by travelers who can think and act without detailed instructions.

# Evidence Based Medicine: the wolf in sheep's clothing [Cassiere et al 1998](#)

- “Decisions must be made by clinicians and not by reviewers, who combine experience, judgement and a thoughtful review of the literature”.





*It is more important to know the patient  
than the disease*      *Hippocrates*

The good physician      *The good clinician*  
treats the disease;      *follows Guidelines but...*  
the great physician      *The great clinician*  
treats the patient      *“translates” research to*  
who has the disease.      *“customize” treatment*

William Osler  
1849-1919



*for the patient who has  
the disease*  
*(personalized ≠ precision medicine)*

ΕΥΧΑΡΙΣΤΩ ΓΙΑ ΤΗΝ ΠΡΟΣΟΧΗ ΣΑΣ

PhD means

Doctor of Philosophy

