



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



A. ΑΡΜΑΓΑΝΙΔΗΣ

Καθηγητής Πνευμονολογίας
και Εντατικής Θεραπείας
Ιατρικής Σχολής ΕΚΠΑ



Διευθυντής Β' Πανεπιστημιακής
Κλινικής Εντατικής Θεραπείας
Π.Γ.Ν. ΑΤΤΙΚΟΝ

ΠΜΣ «Λοιμωξιολογία» 18/02/2020

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

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

Disclosures

- Honoraria for lectures - advisory boards:
Astellas, Bayer, Gilead, Janssen, MSD, Novartis, Pfizer, BIANEΞ, Polyphor
- Research Grands (μέσω ΕΛΚΕ):
Astellas, Gilead, MSD, Pfizer

Presentation outline

- RCTs and Guidelines usefulness mainly for the management of septic patients in a “Real World setting”
 - Pathophysiologic paradigms of sepsis and septic shock
- AND**
- Definitions, diagnostic approach and treatment (=decision making)

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

To the Editor:

While I do not claim to have the re-
search experience of Drs. Kortgen and col-
leagues (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

Richard Rissmiller, MD, Internal Med-
icine, Carolinas Medical Center, Char-
lotte, NC

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).

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

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

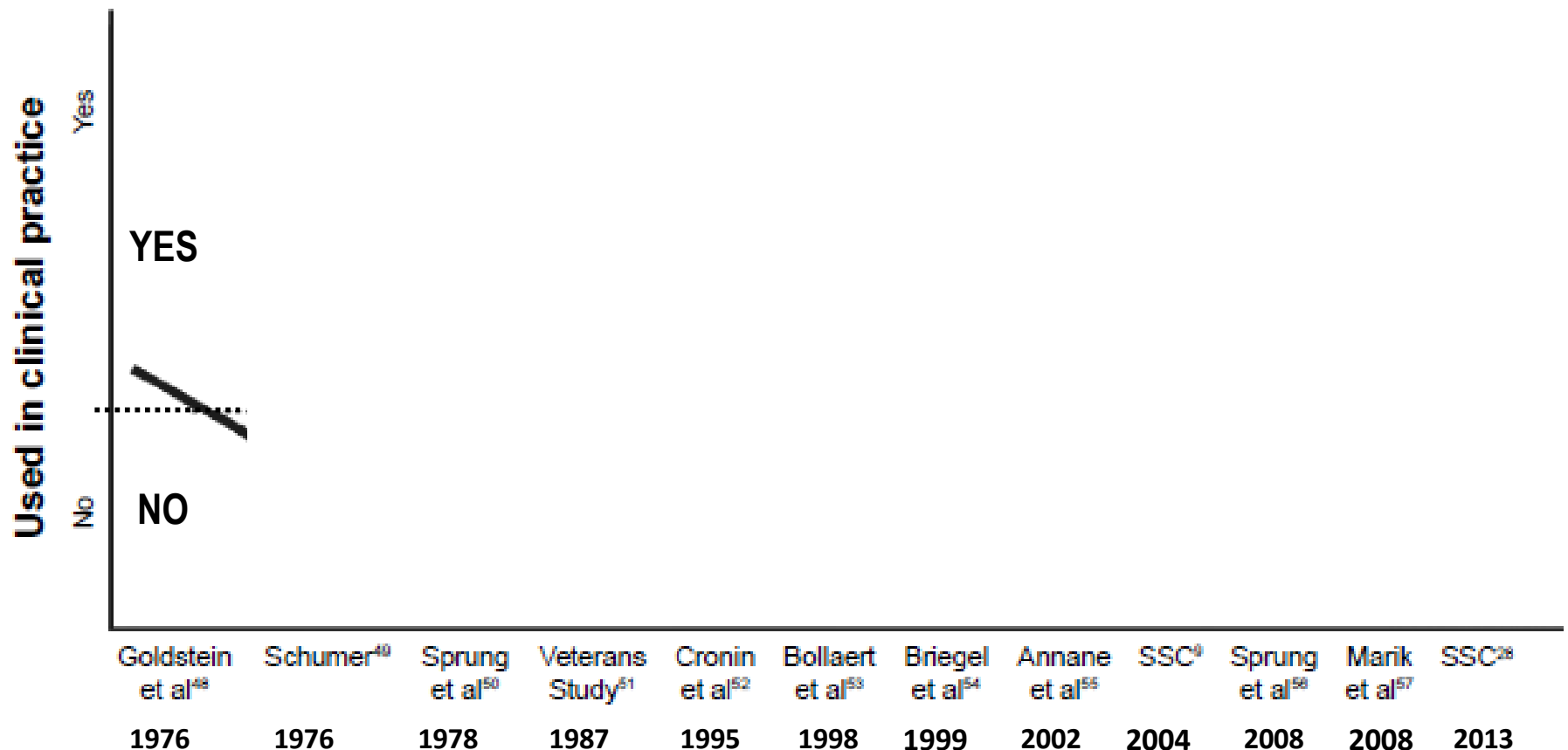


Figure 2 Steroids for treatment of infections, sepsis, and septic shock – ups and downs. Abbreviations: SSC, Surviving Sepsis Campaign.

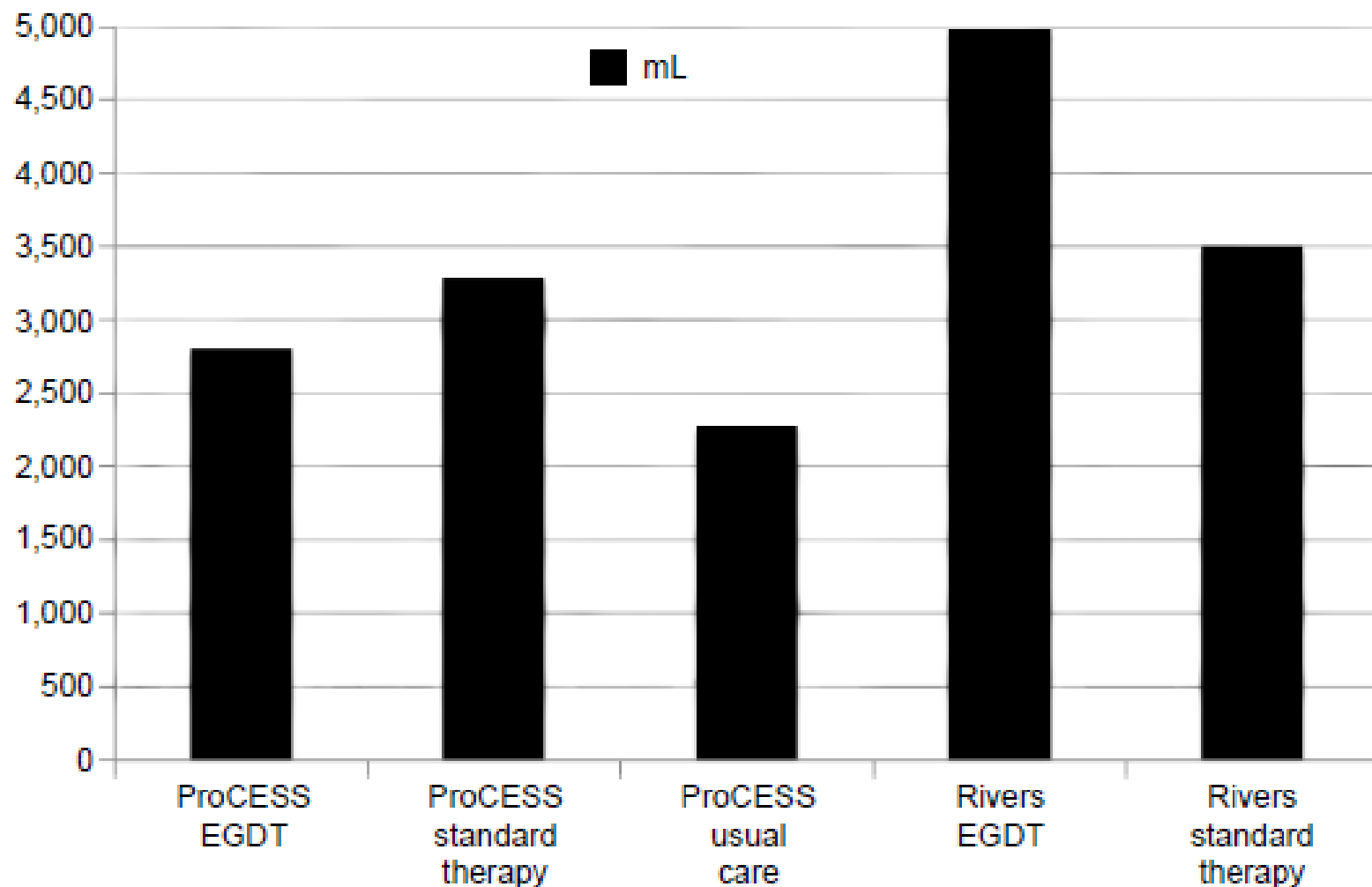
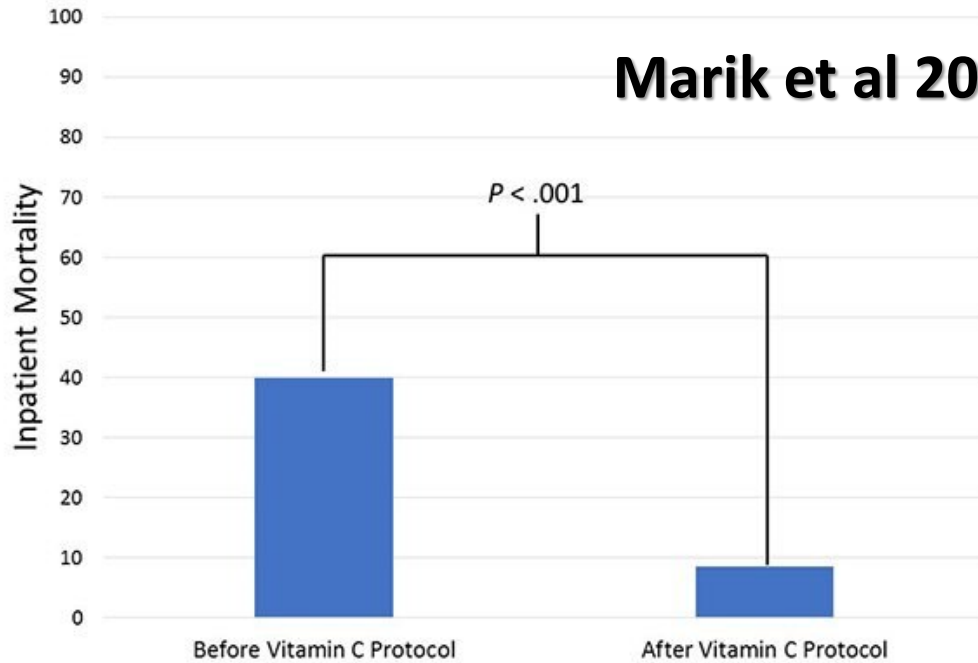


Figure 1 Fluid administration between 0 and 6 hours.

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

Vitamin C in "sepsis"

Marik et al 2017



Medscape

Fowler et al 2019

B mSOFA score

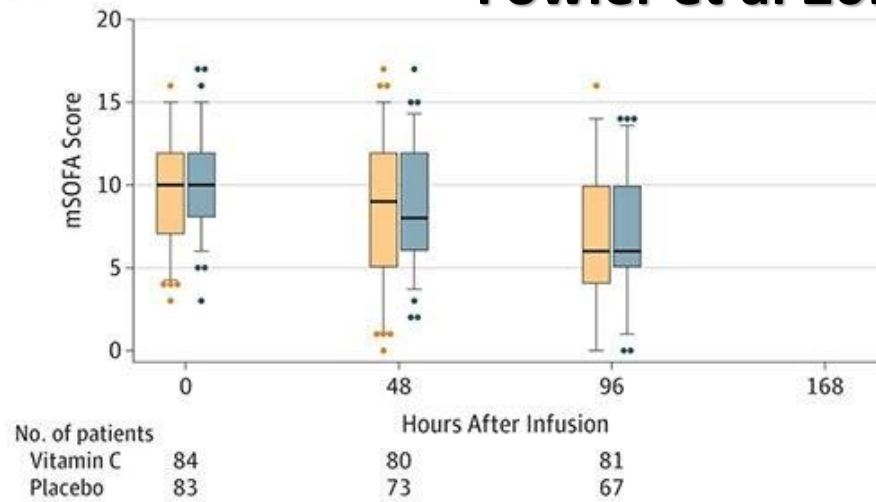
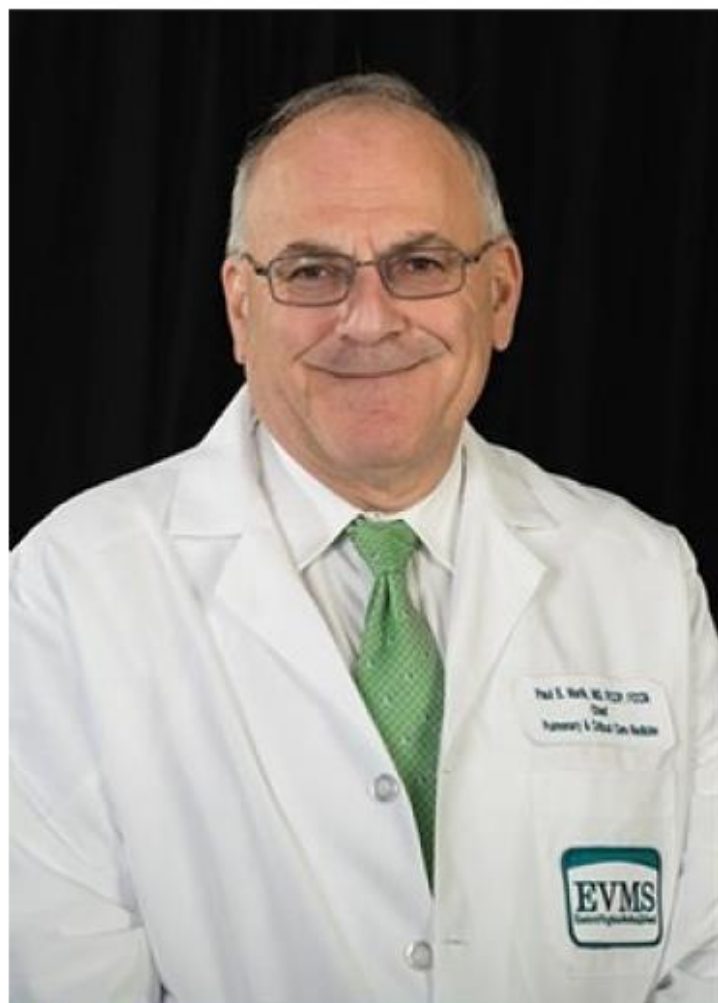


Image courtesy of JAMA Network®

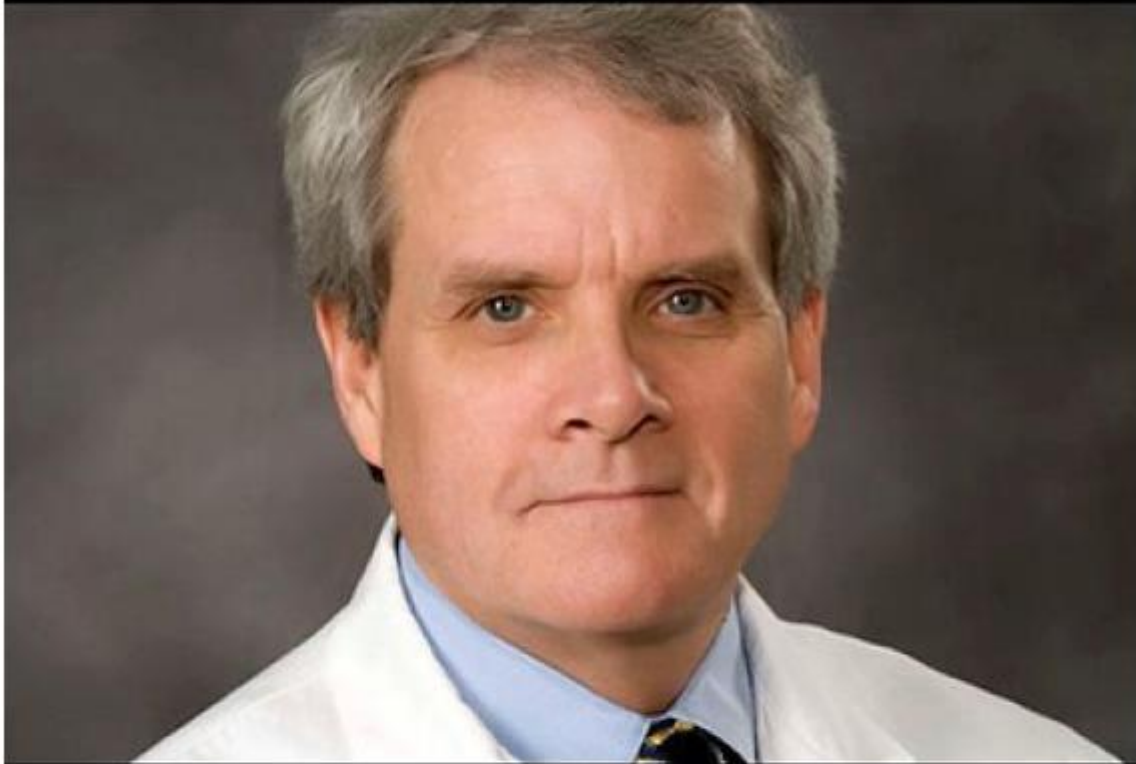
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Medscape



“Patients in our ICU do not die of sepsis. It just does not happen.”

-Paul E. Marik, MD
Chief, Pulmonary and Critical Care
Medicine
Eastern Virginia Medical School



“We were afraid to put mortality as a primary outcome when we designed it. And we were thinking, holy cow—if we put this as a primary outcome and it fails, you can kiss vitamin C goodbye.”

-Alpha “Berry” Fowler, MD
Chair, Pulmonary Disease and
Critical Care Medicine
Virginia Commonwealth University
School of Medicine

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 intensive care management of the patient with sepsis. ACCP/SCCM Consensus Conference Committee on Sepsis and Organ Failure. Crit Care Medicine.

Bone RC¹, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA

[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.

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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 useful concepts for what purpose ???

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 Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

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.

miology is assessed and reported, operationalization will necessarily involve proxies such as antibiotic commencement or a clinically determined probability of infection. Future epidemiology studies should consider reporting the proportion of microbiology-positive sepsis.

Greater clarity and consistency will also facilitate research and more accurate coding. Changes to ICD coding may take several years to enact, so the recommendations provided in Table 2 demonstrate how the new definitions can be applied in the interim within the current ICD system.

The debate and discussion that this work will inevitably generate are encouraged. Aspects of the new definitions do indeed rely on expert opinion; further understanding of the biology of sepsis, the availability of new diagnostic approaches, and

enhanced collection of data will fuel their continued reevaluation and revision.

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.

ARTICLE INFORMATION

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Author Contributions: Drs Singer and Deutschman had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design. All authors.

Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Singer, Deutschman, Seymour, Shankar-Hari, Angus.
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Statistical analysis: Shankar-Hari, Seymour.
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Study supervision: Singer, Deutschman.
 Drs Singer and Deutschman are joint first authors.

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his time spent in these roles. Dr Hotchkiss reports consulting on sepsis for GlaxoSmithKline, Merck, and Bristol-Myers Squibb and reports that his institution received grant support from Bristol-Myers Squibb and GlaxoSmithKline, as well as the NIH, for research on sepsis. Dr Marshall reports serving on the data and safety monitoring board (DSMB) of AKPA Pharma and Spectral Medical Steering Committee and receiving payment for speaking from Toray Ltd and Uni-Labs. Dr Martin reports serving on the board for SCCM and Project Help, serving on the DSMB for Cumberland Pharmaceuticals and Vanderbilt University, serving on the medical advisory board for Grifols and Pulsion Medical Systems, and grants to his institution from NIH, the Food and Drug Administration, Abbott, and Baxter. Dr Opal reports grants from GlaxoSmithKline, Amgen, Asahi-Kasei, Ferring, Cardax, and Anasnis outside the submitted work; personal fees from Anasnis, Ardis, Biocegis, Cyon, and Battelle; and serving on the DSMB for Achaogen, Spectral Diagnostics, and Paratek. No other disclosures were reported.

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Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Singer, Deutschman, Seymour, Shankar-Hari, Angus.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Shankar-Hari, Seymour.

Obtained funding: Deutschman, Chiche, Coopersmith.

Administrative, technical, or material support: Singer, Deutschman, Chiche, Coopersmith, Levy, Angus.

Study supervision: Singer, Deutschman.
 Drs Singer and Deutschman are joint first authors.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

Surviving Sepsis Campaign: *Intensive Care Med* (2017) 43:304–377 International Guidelines for Management of Sepsis and Septic Shock: 2016

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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***

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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

An alternate pathophysiologic paradigm of sepsis and septic shock

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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

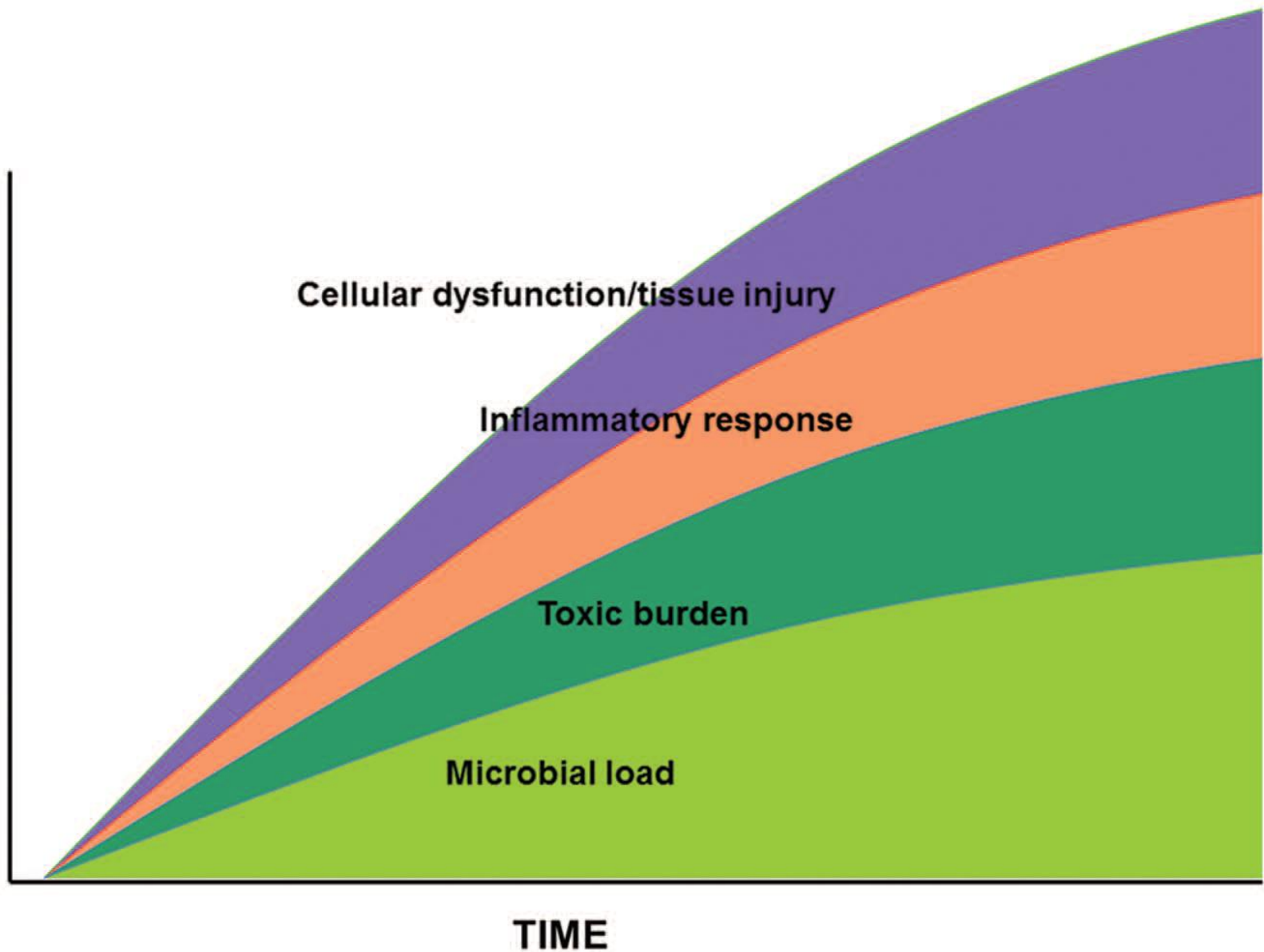
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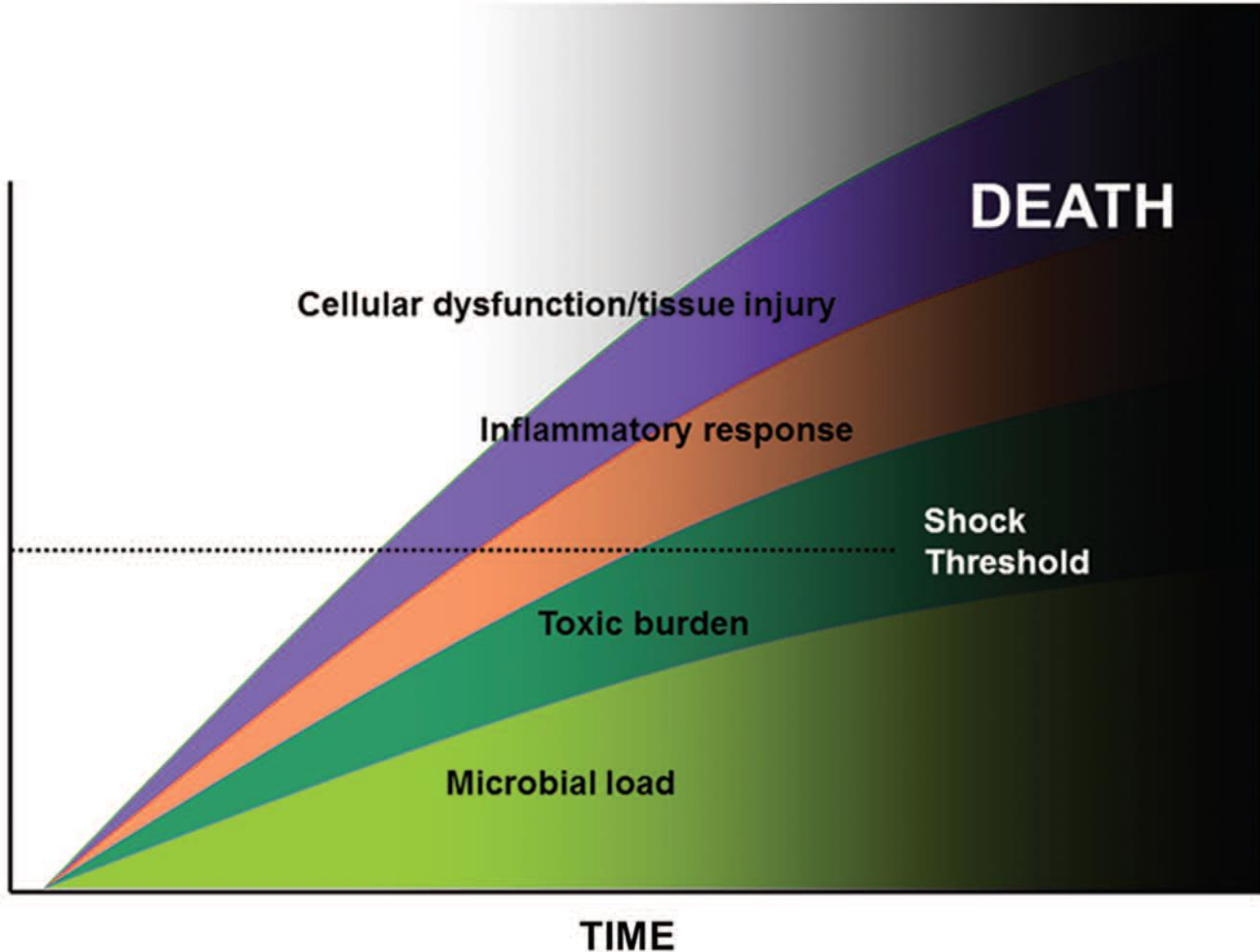
Microbiologic view of sepsis and septic shock

Kumar A. 2014



Composite Microbiologic view of sepsis and septic shock

Kumar A. 2014



An alternate pathophysiologic paradigm of sepsis and septic shock

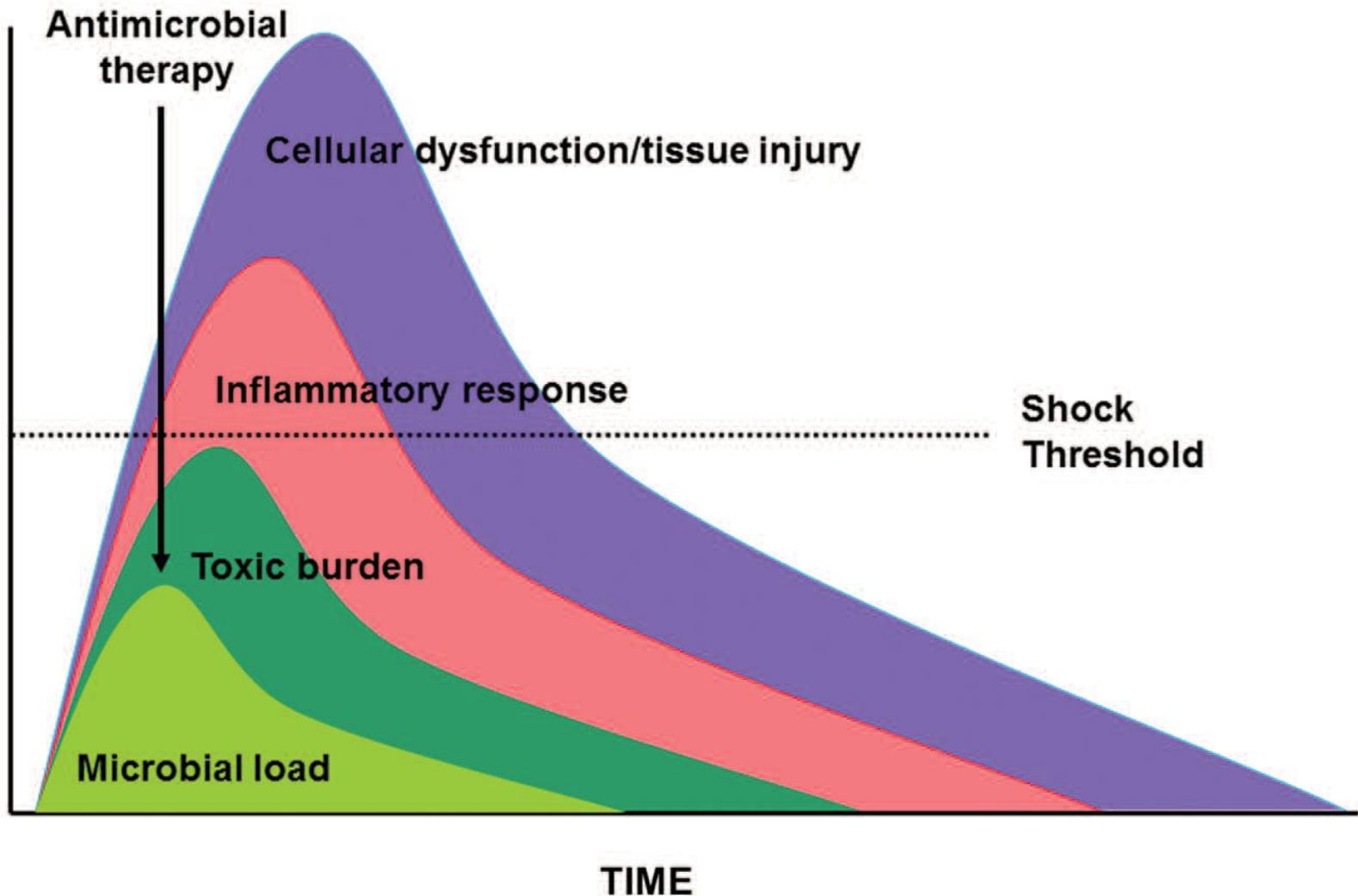
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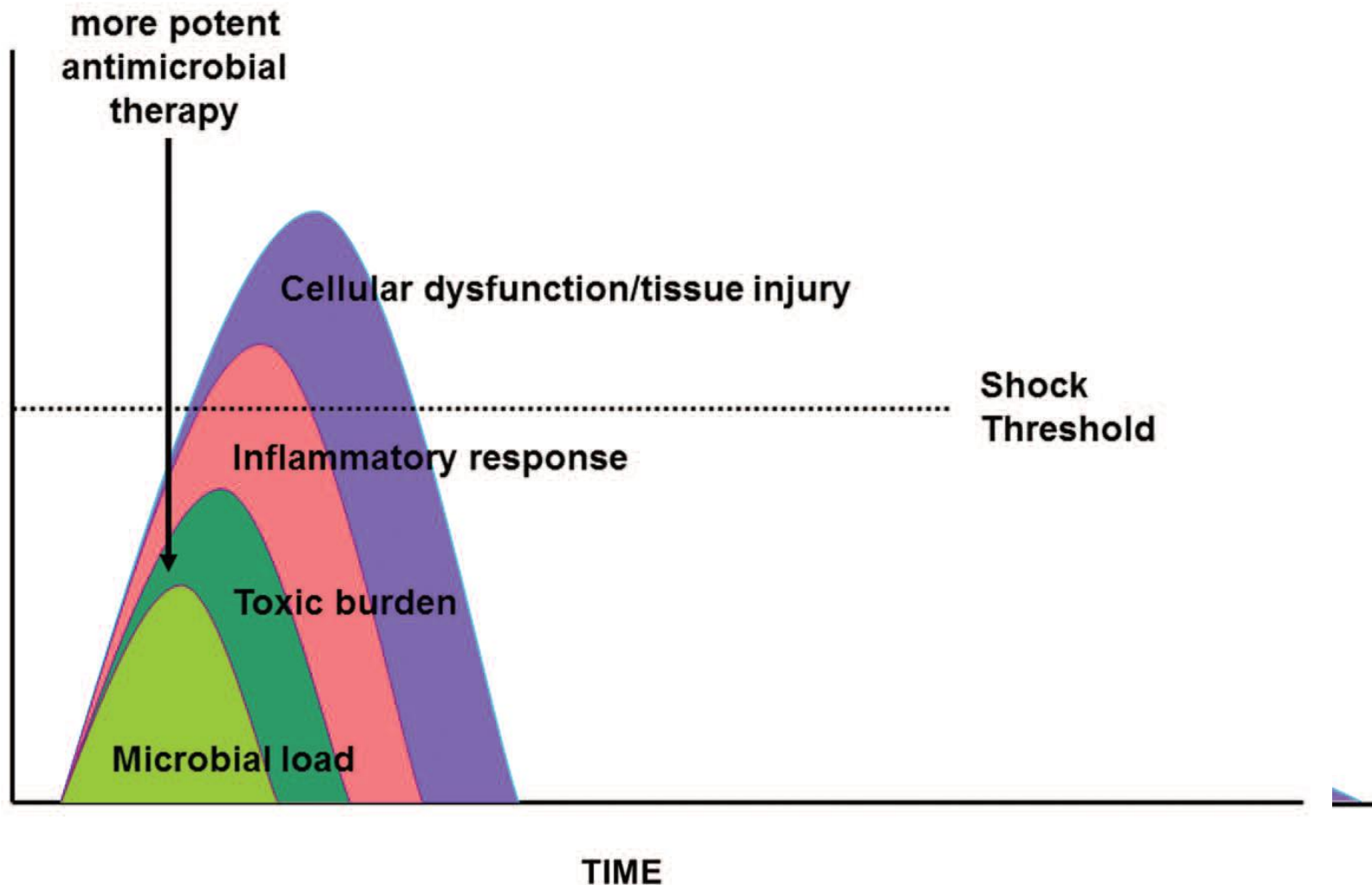
Impact of appropriate antimicrobial therapy in sepsis and septic shock.

Kumar A. 2014



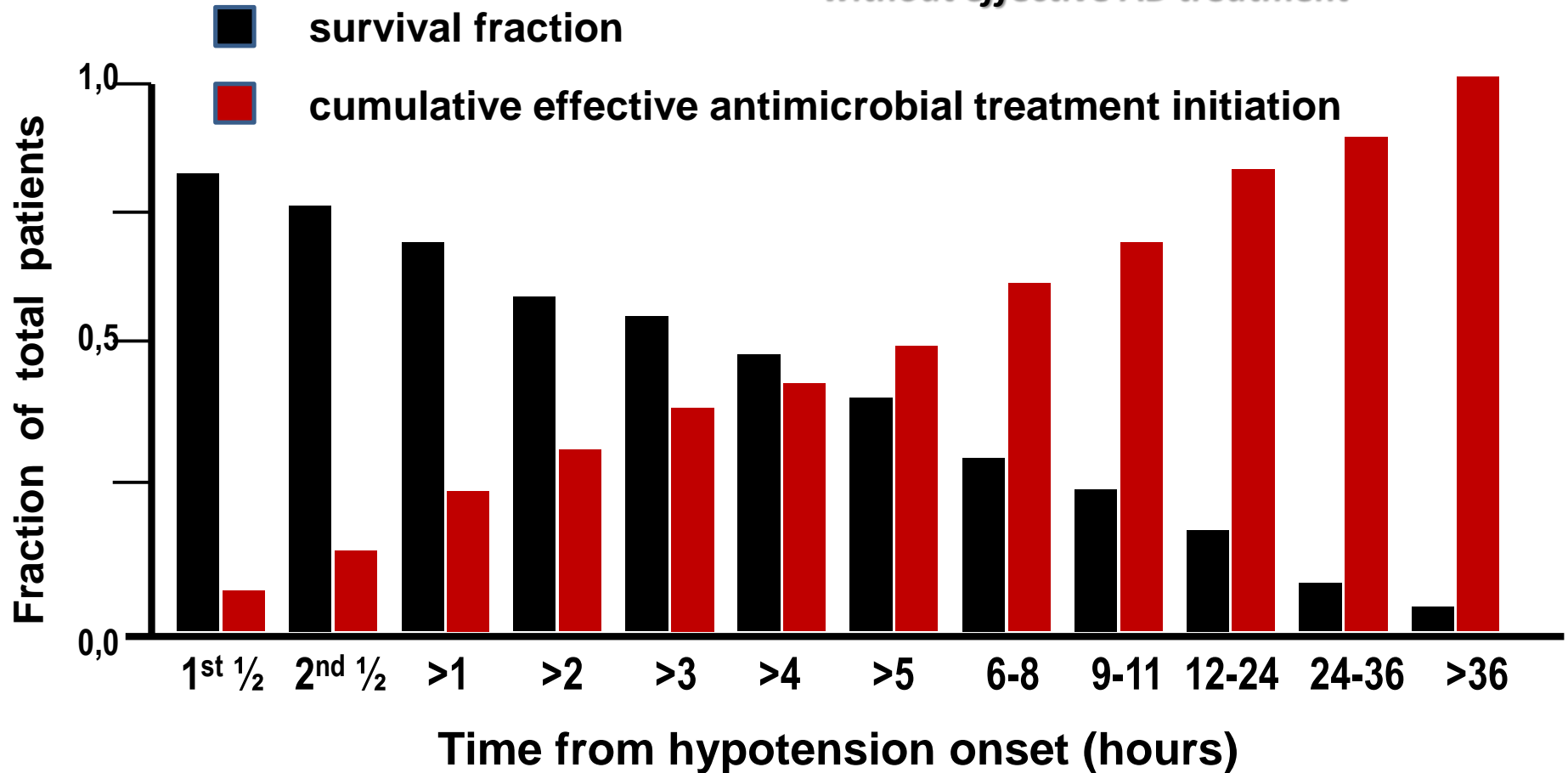
Impact of more potent antimicrobial therapy in sepsis and septic shock.

Kumar A. 2014



In severe sepsis and septic shock, time is life

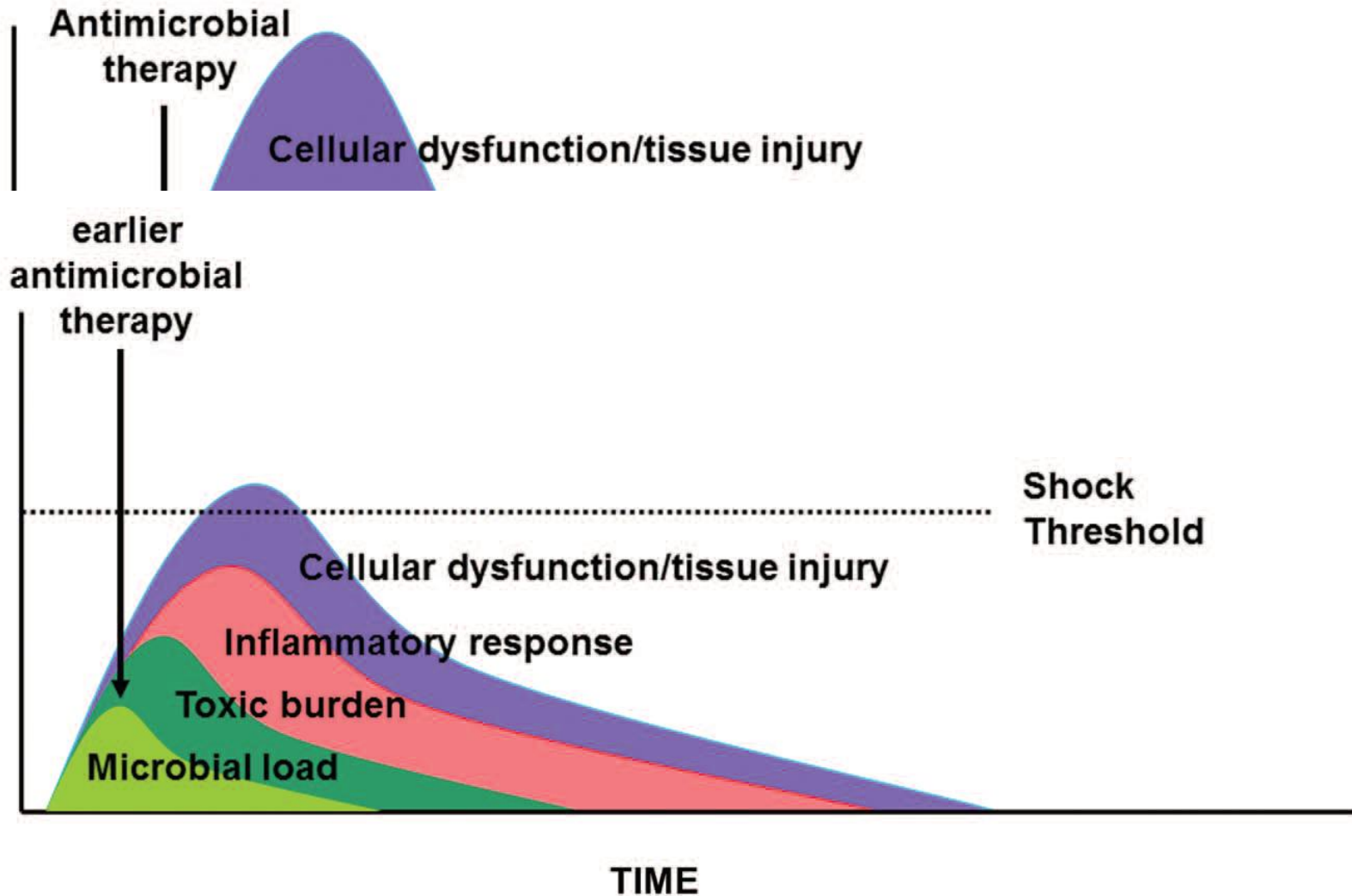
7% decrease of survival every hour without effective AB treatment



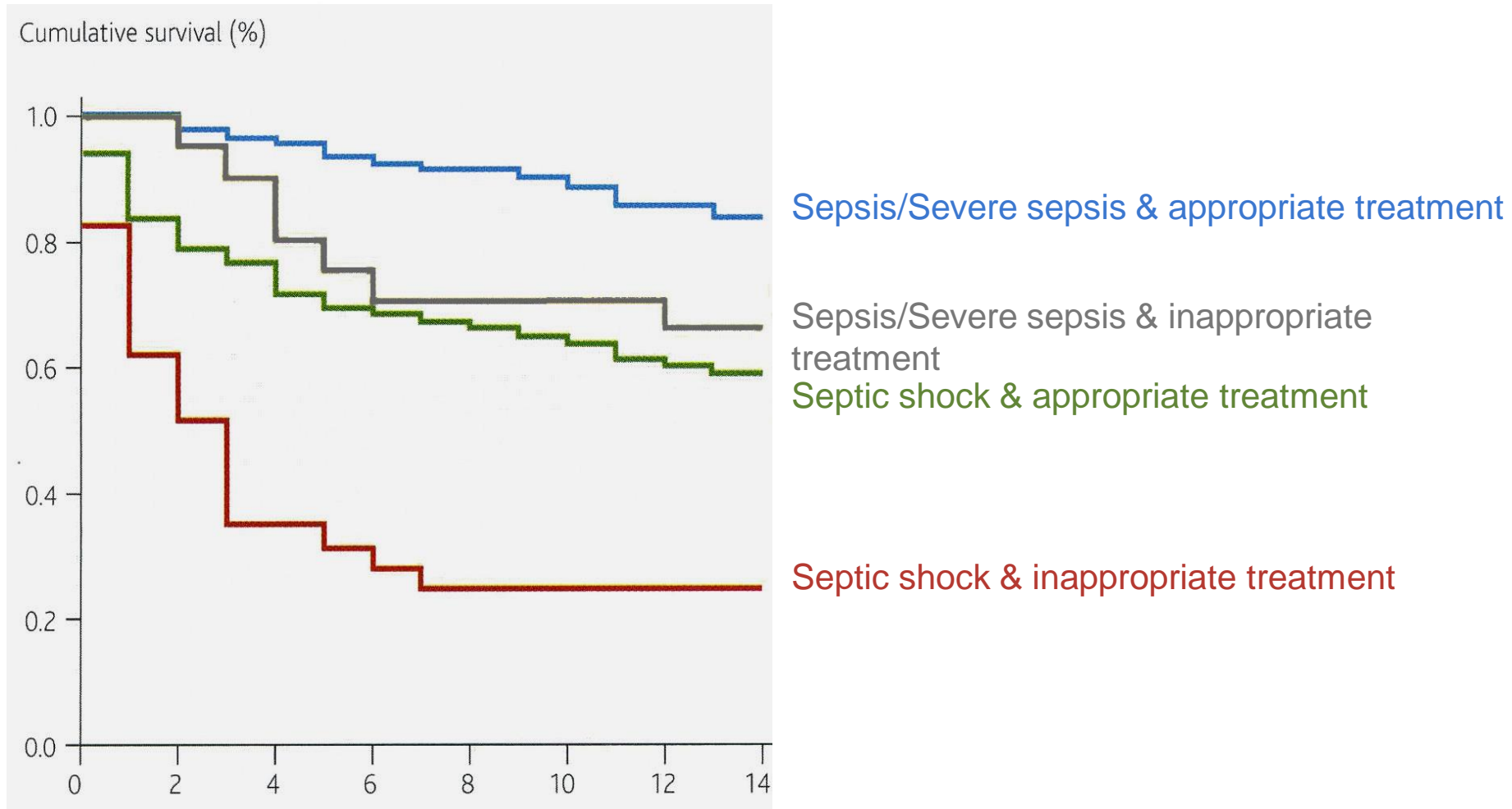
Modified from: Kumar A, Robert D, Wood KE, Critical Care Med 2006; 34: 1589–1596

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

Kumar A. 2014



Survival with appropriate OR inappropriate treatment



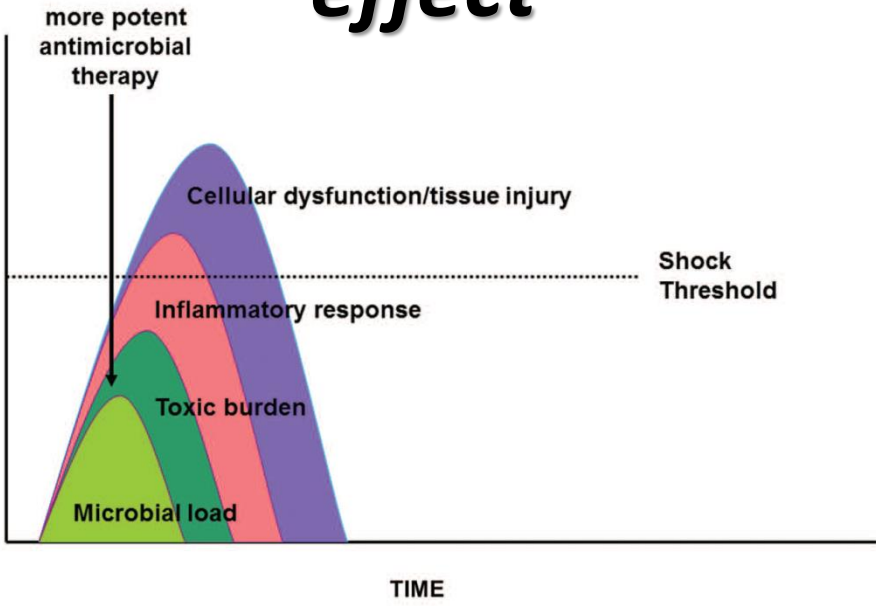
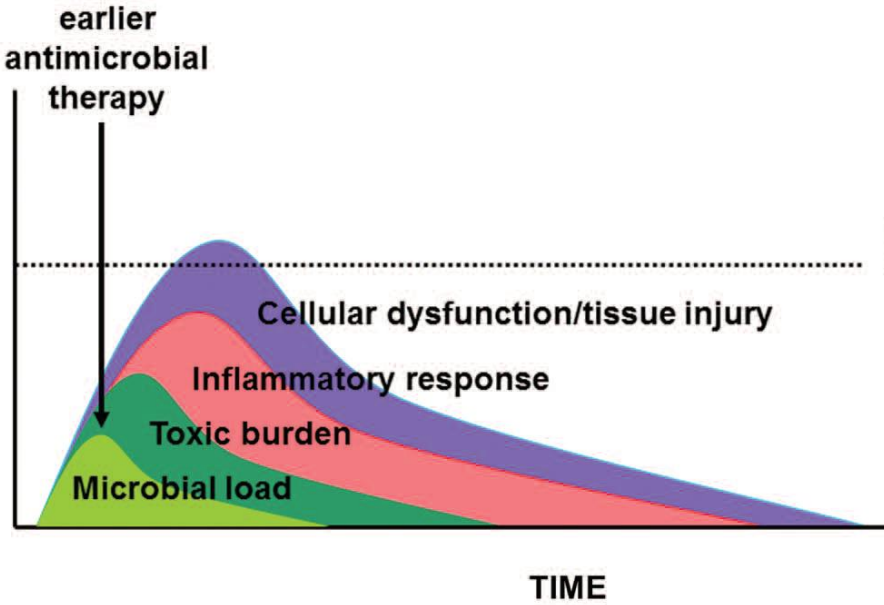
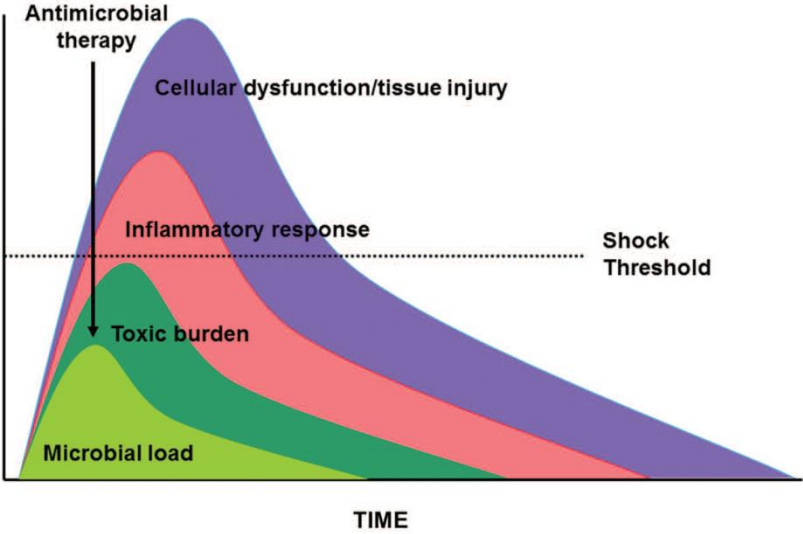
Days

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

Microbiologic view of sepsis and septic shock

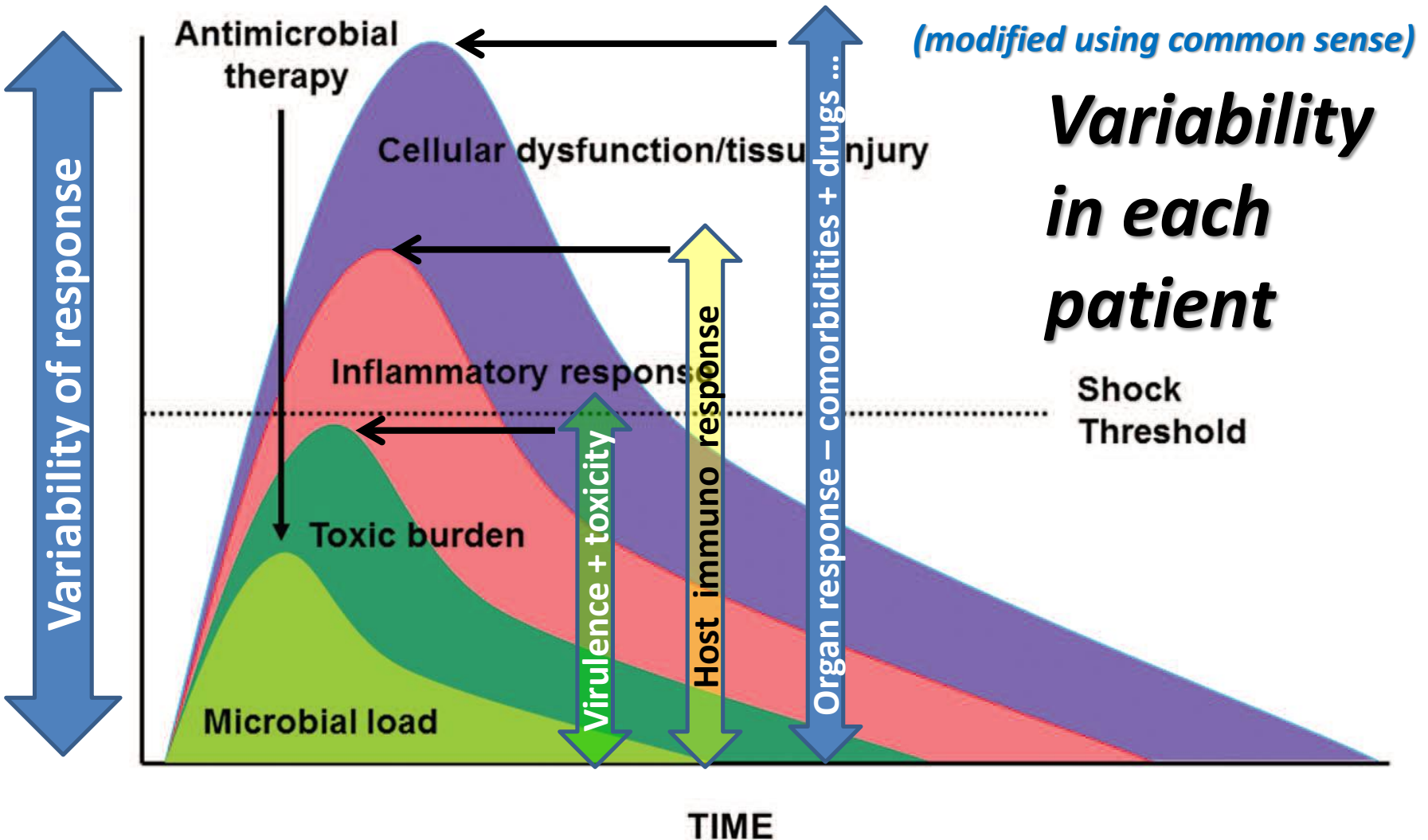
Kumar A. 2014

*Variability
related to
treatment
effect*

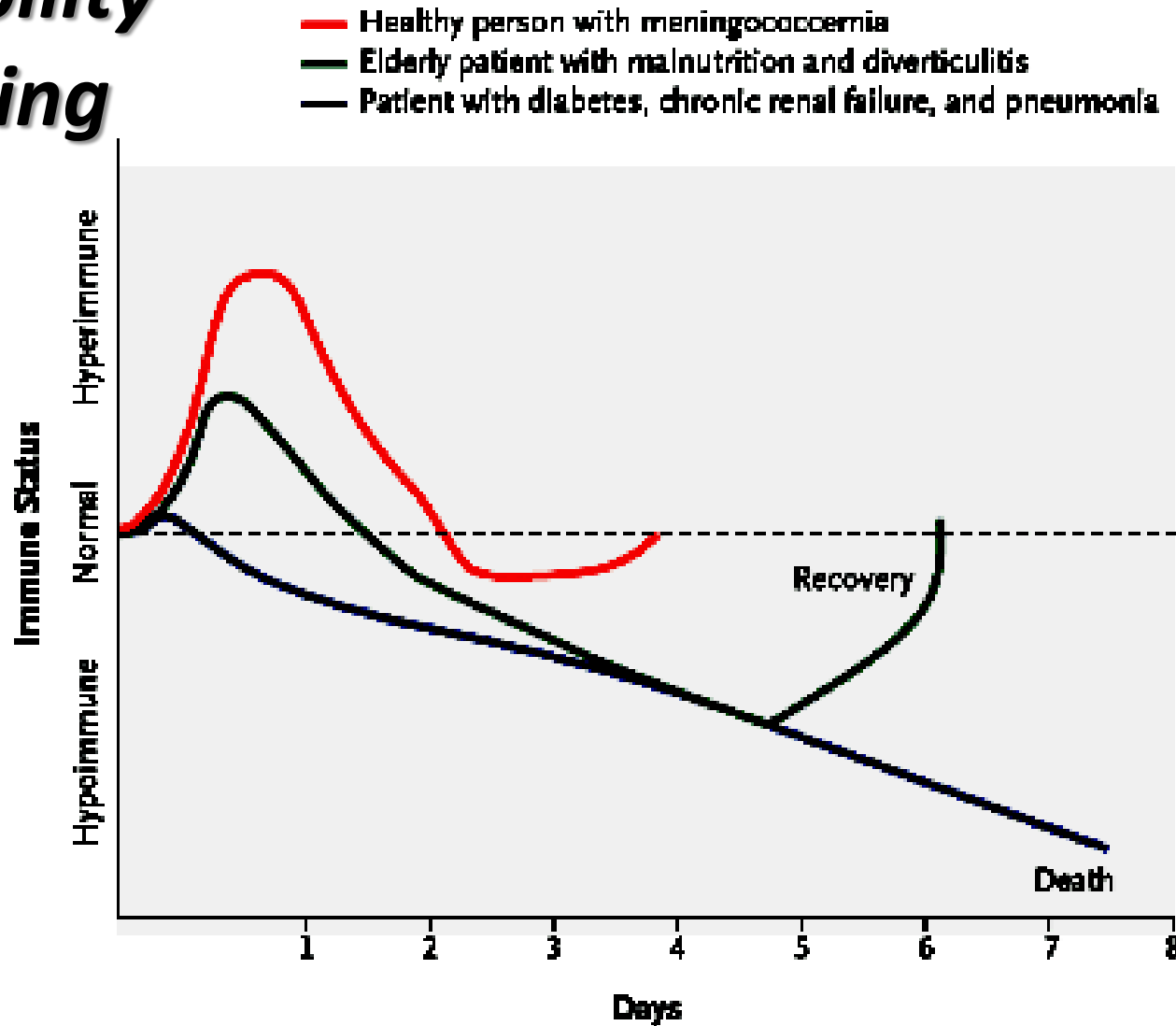


Impact of appropriate antimicrobial therapy in patients with sepsis OR septic shock.

Kumar A. 2014

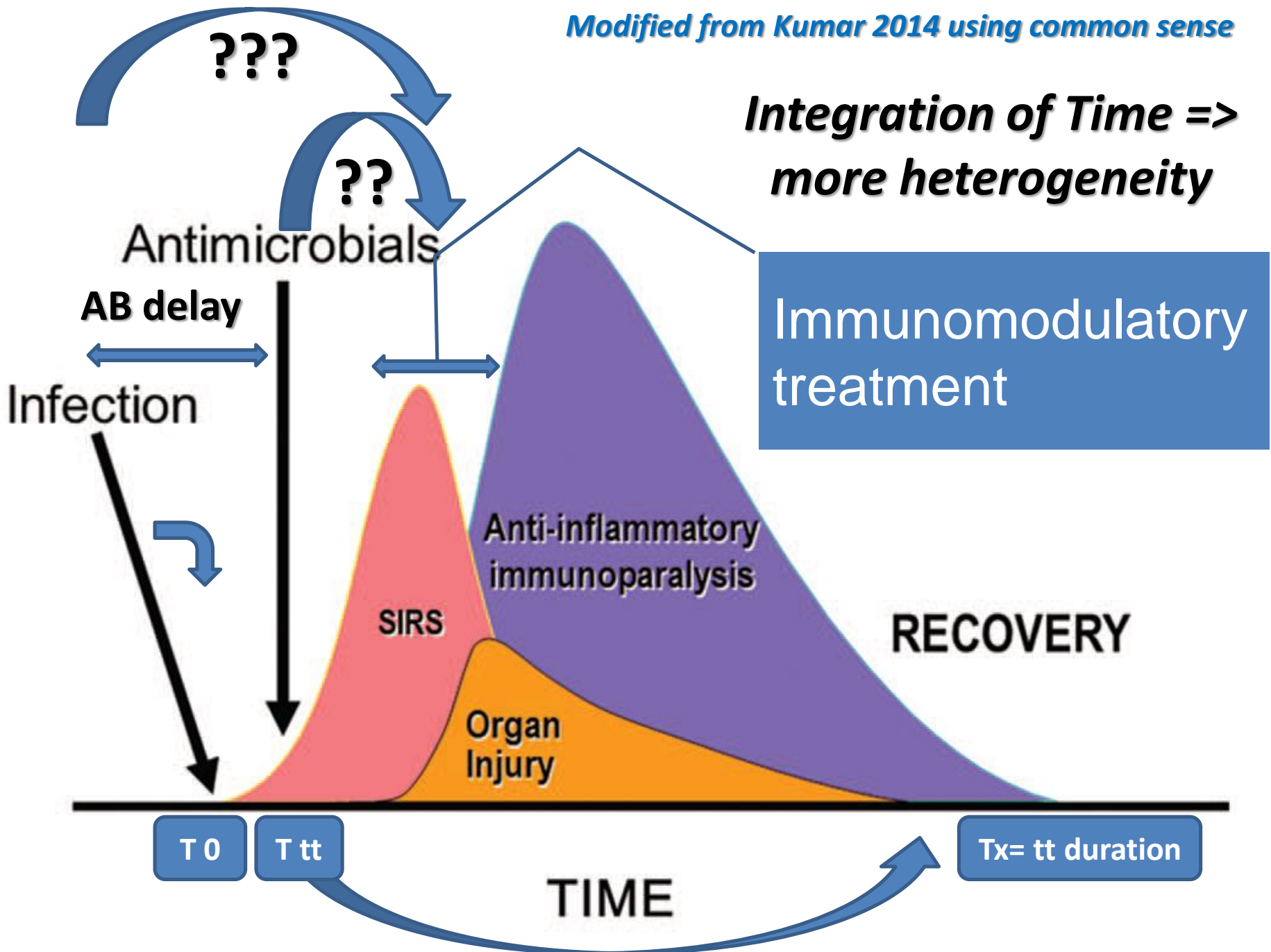


Variability of timing

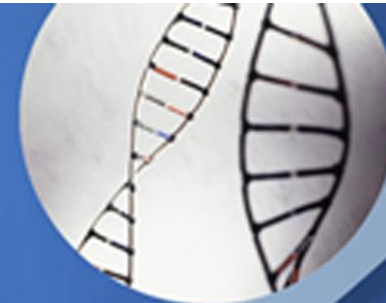


The pathophysiology and treatment of sepsis,
Hotchkiss RS, Karl IE NEJM 2003; 348: 138-150.

Modified from Kumar 2014 using common sense



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



PARTICLE IDENTIFICATION

1300s

1950s

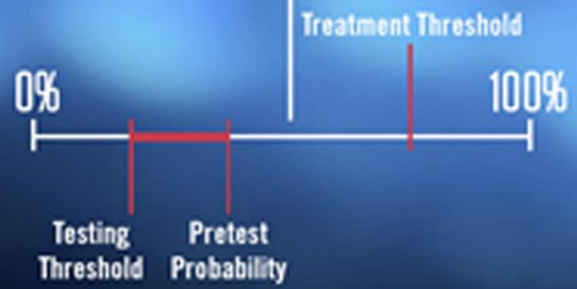
1970s

1980s

1990s

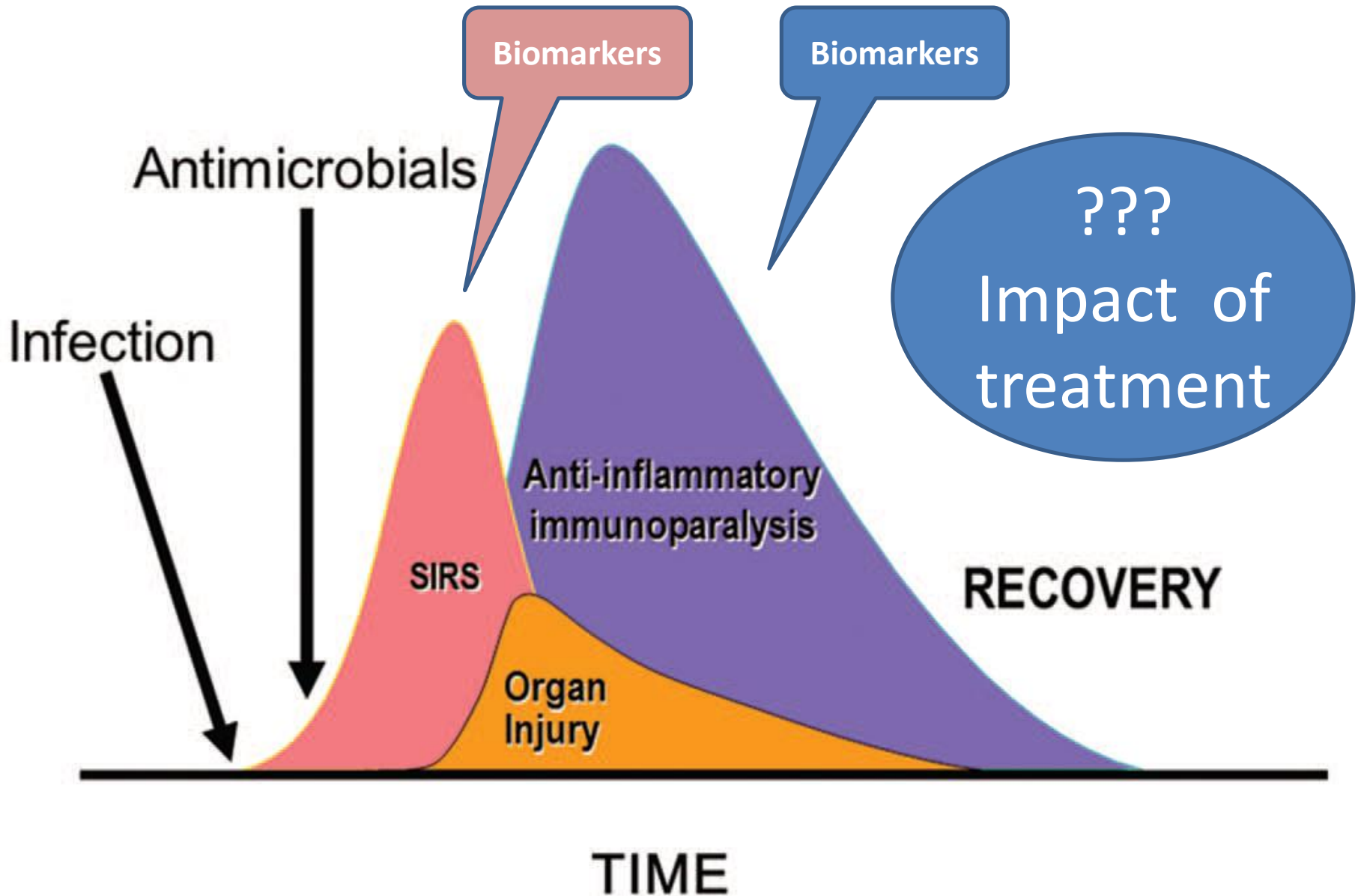
2013

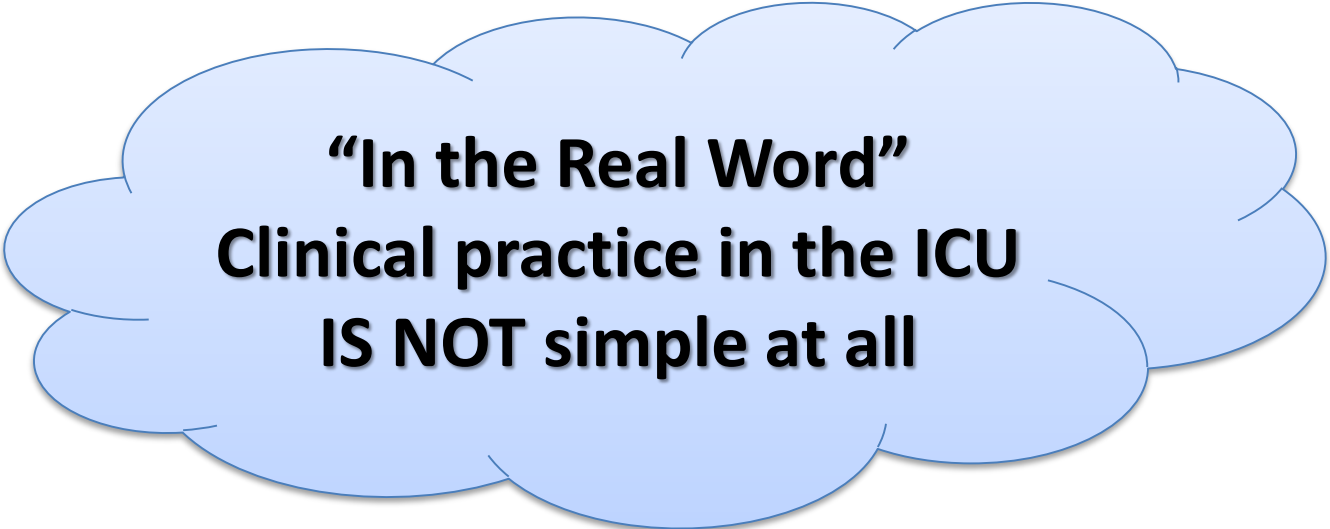
MEDICAL DIAGNOSIS




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

An alternate pathophysiologic paradigm of sepsis and septic shock

Implications for optimizing antimicrobial therapy

Bone 1992

Anand Kumar

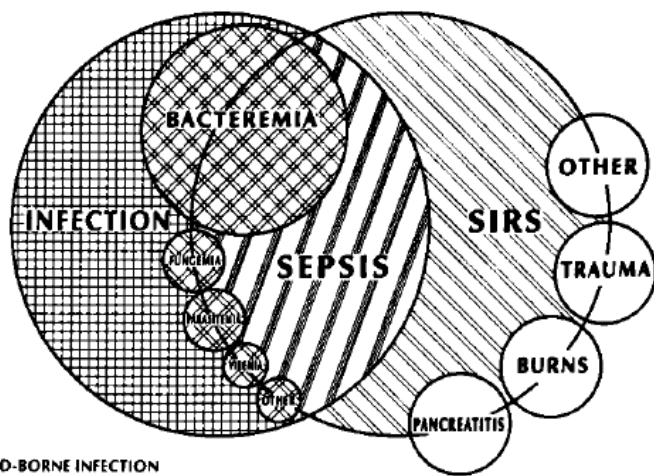
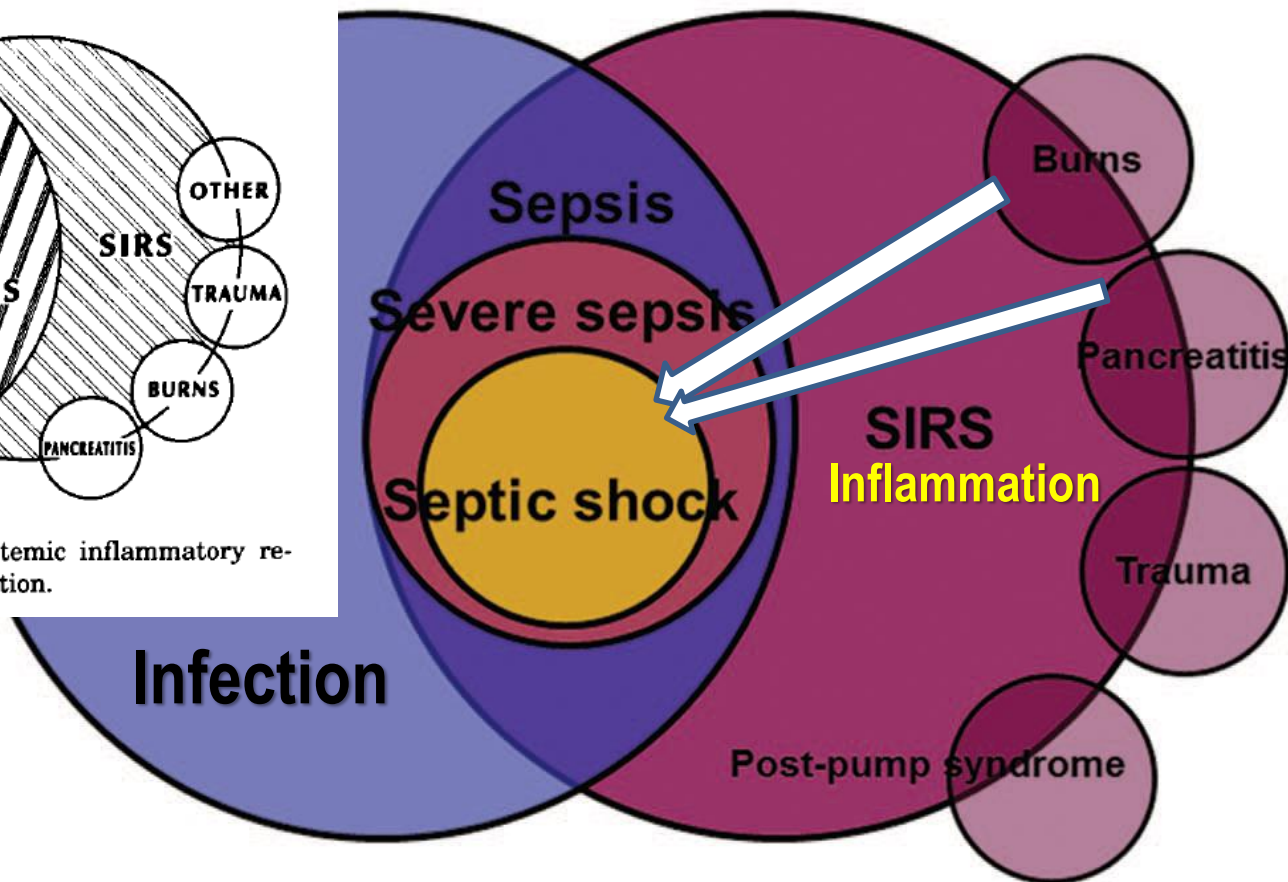
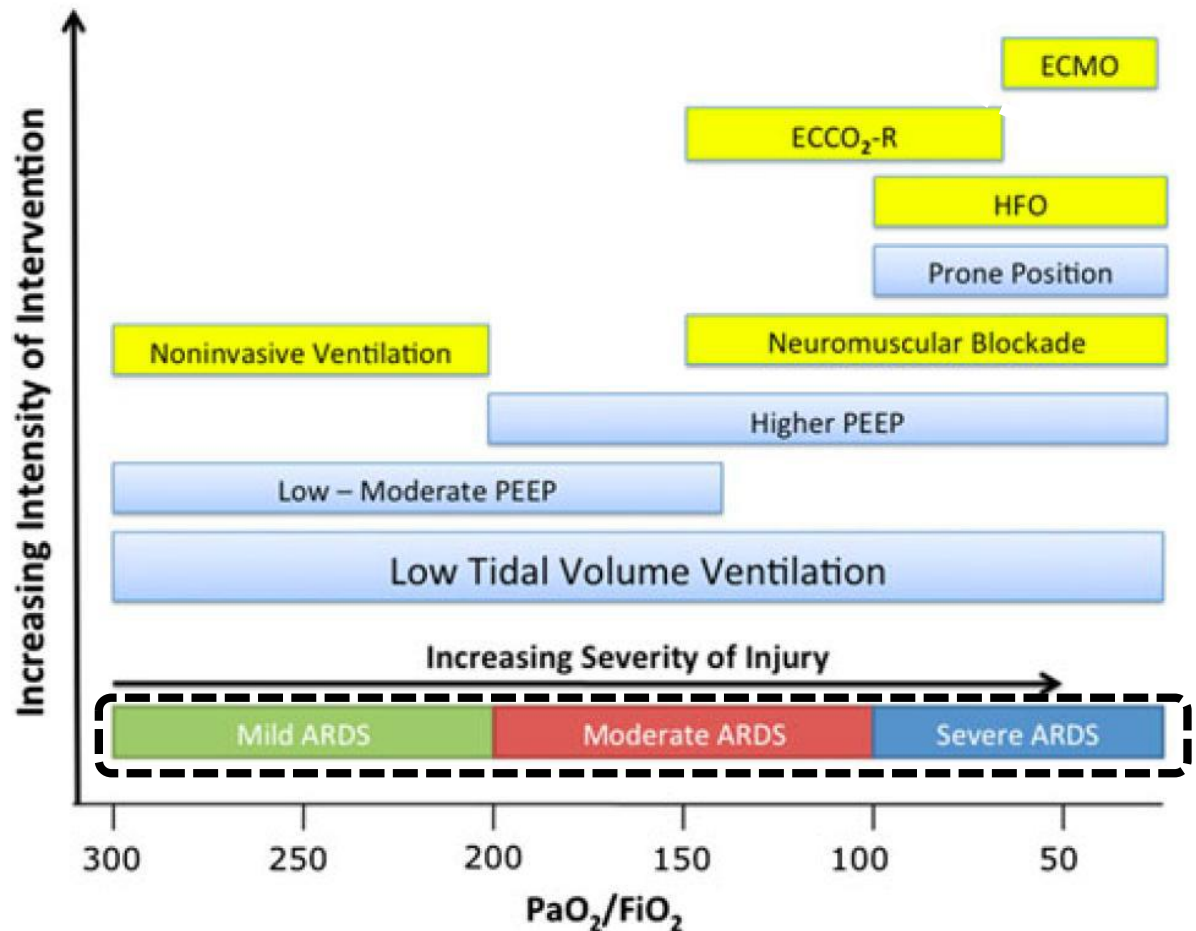


Figure 1. Interrelationships among systemic inflammatory response syndrome (SIRS), sepsis, and infection.



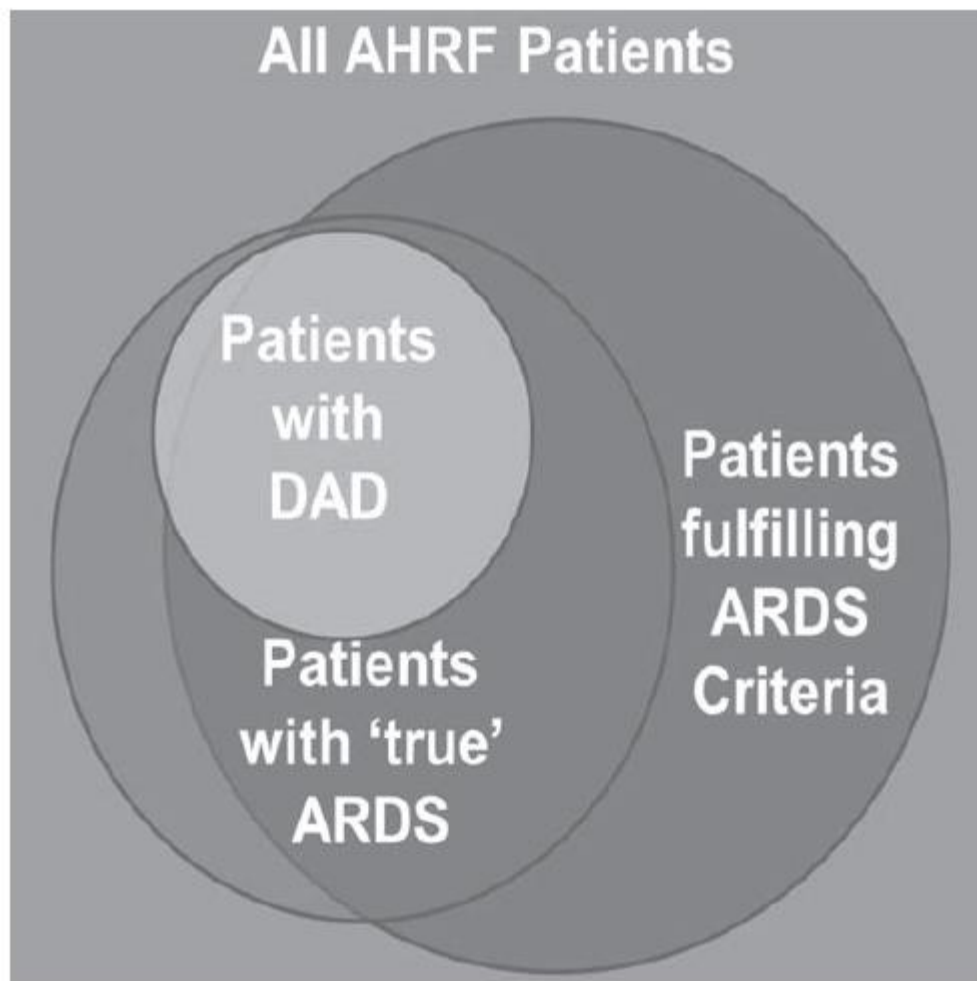
Niall D. Ferguson
Eddy Fan
Luigi Camporota
Massimo Antonelli
Antonio Anzueto
Richard Beale
Laurent Brochard
Roy Brower
Andrés Esteban
Luciano Gattinoni
Andrew Rhodes
Arthur S. Slutsky
Jean-Louis Vincent
Gordon D. Rubenfeld
B. Taylor Thompson
V. Marco Ranieri

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^{a,b}, Tài Pham^c, and Giacomo Bellani^{d,e}



***Definitions
follow
Purposes
Patients with
the disease***

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

Philosophy / Epistemology (Part I)

Theory of Ideas *OR* *Theory of Forms*



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.

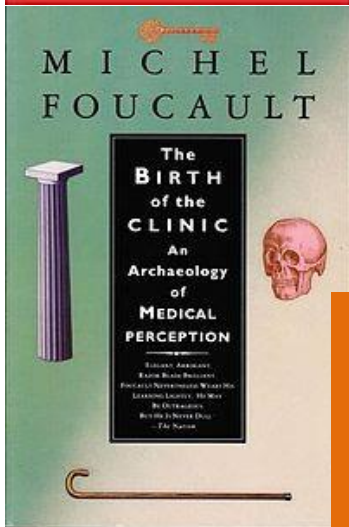
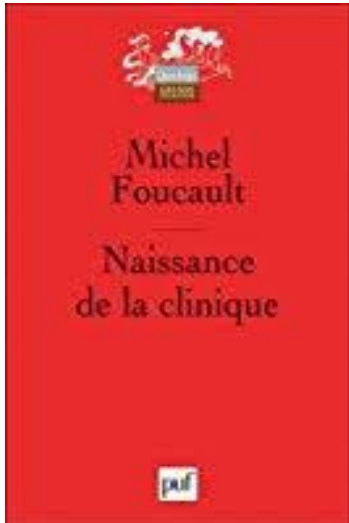
MICHEL
FOUCAULT



Philosophy / Epistemology (II)

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 ?*





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

Philosophy / Epistemology (Part IIIa)



Jean Piaget (1896-1980)

STAGE 1

00E00L00000



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 or representational 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" ???

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

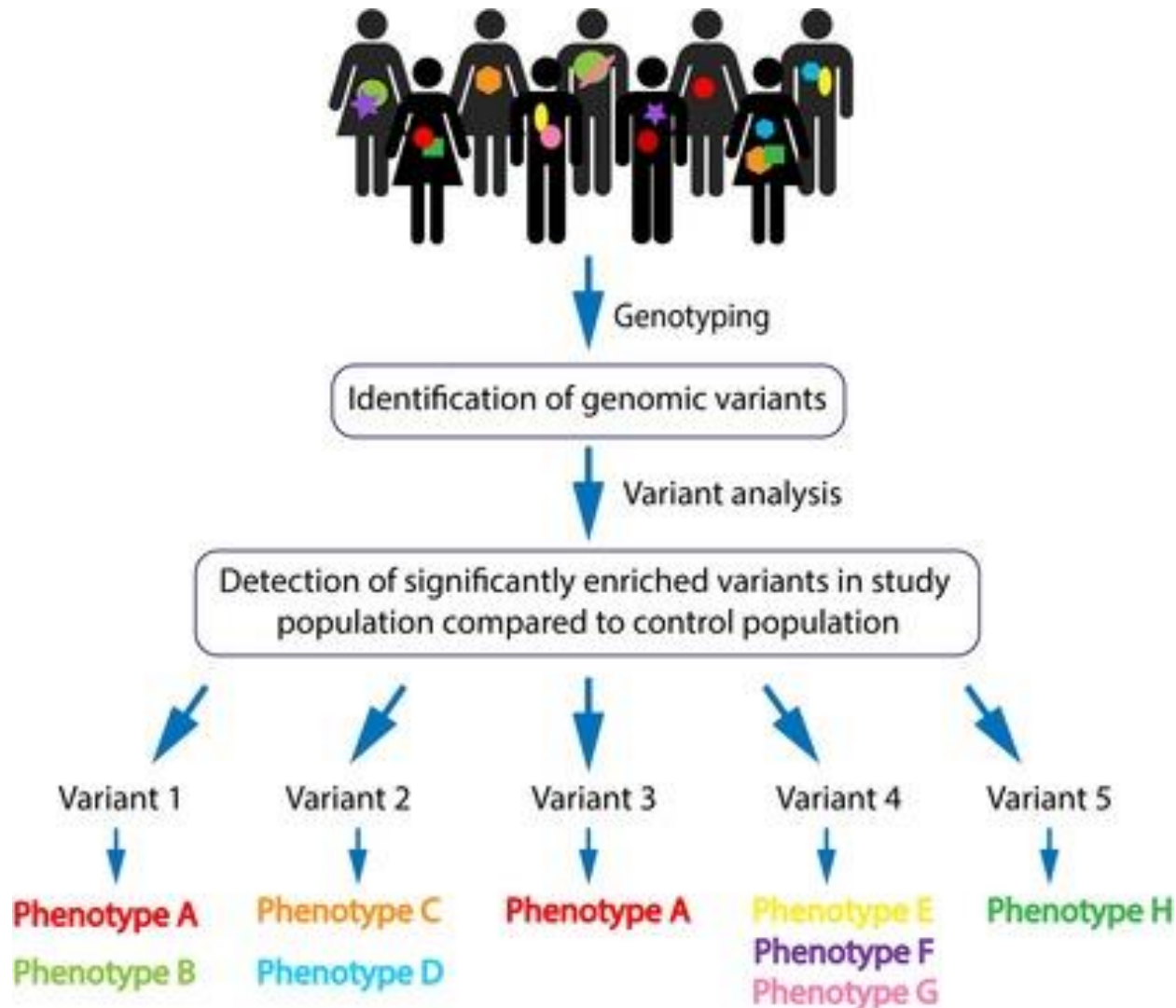


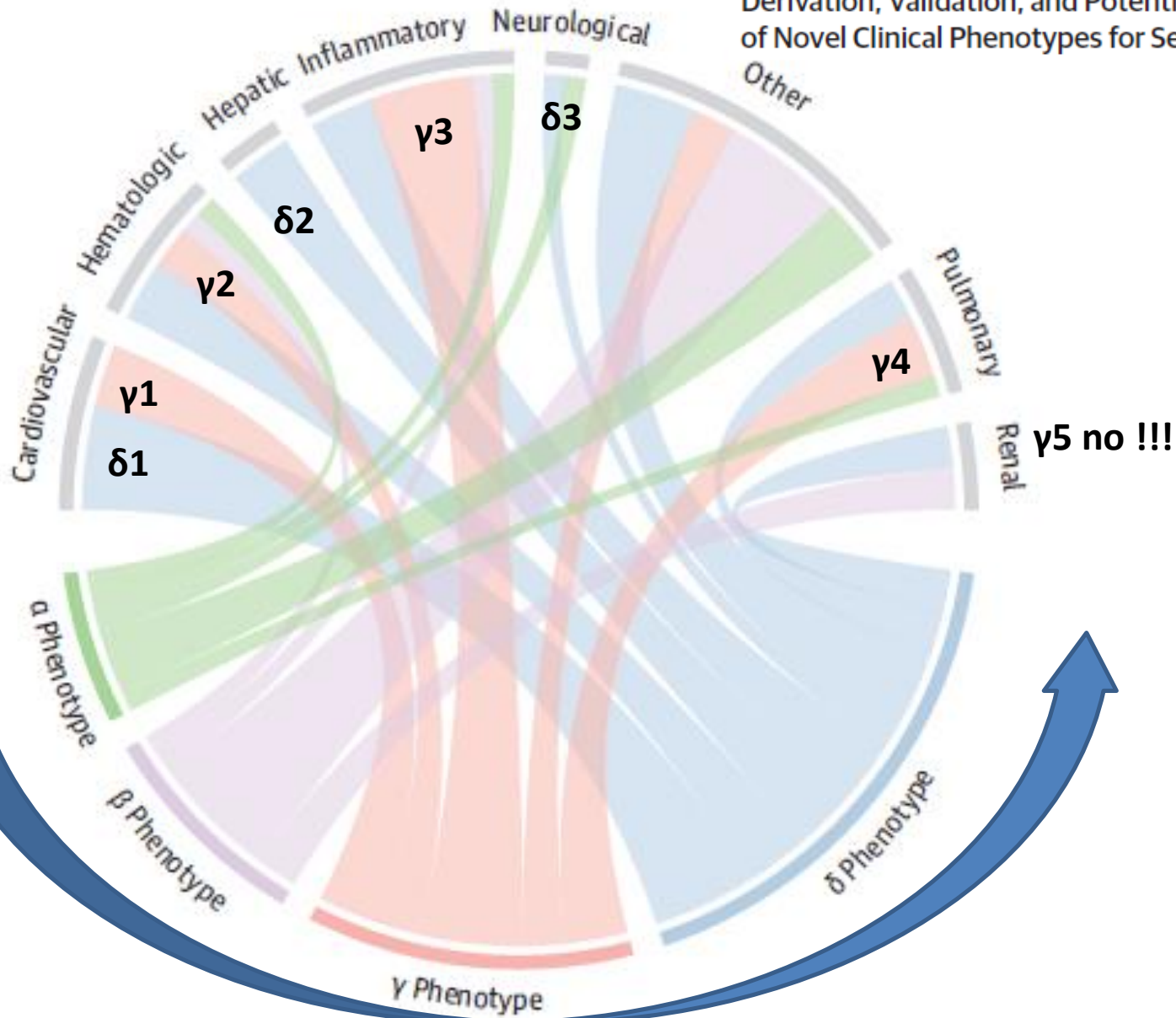
Figure 1. Chord Diagrams Showing Abnormal Clinical Variables by Phenotype

Seymour et al

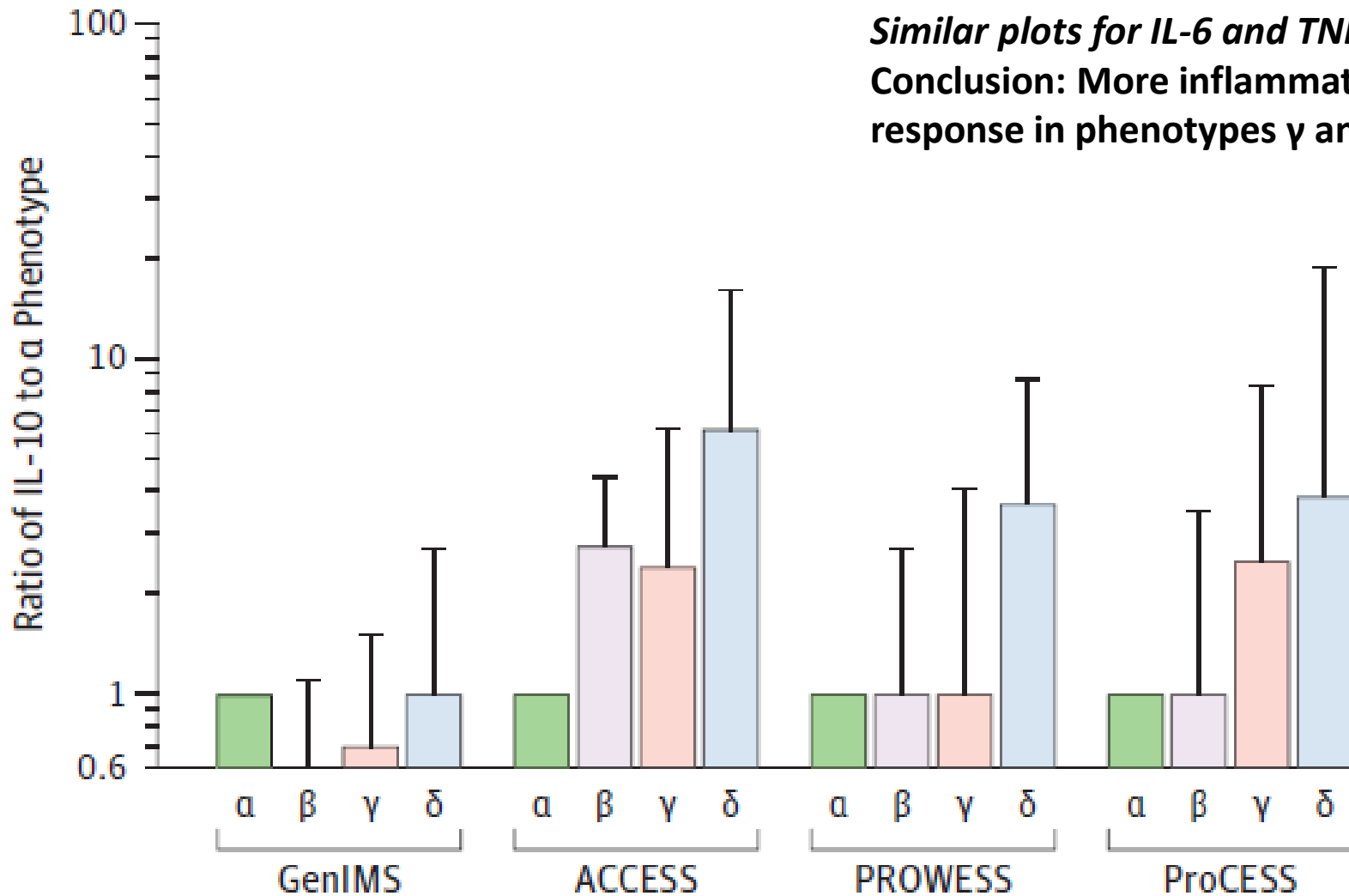
JAMA 2019

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

A All phenotypes combined

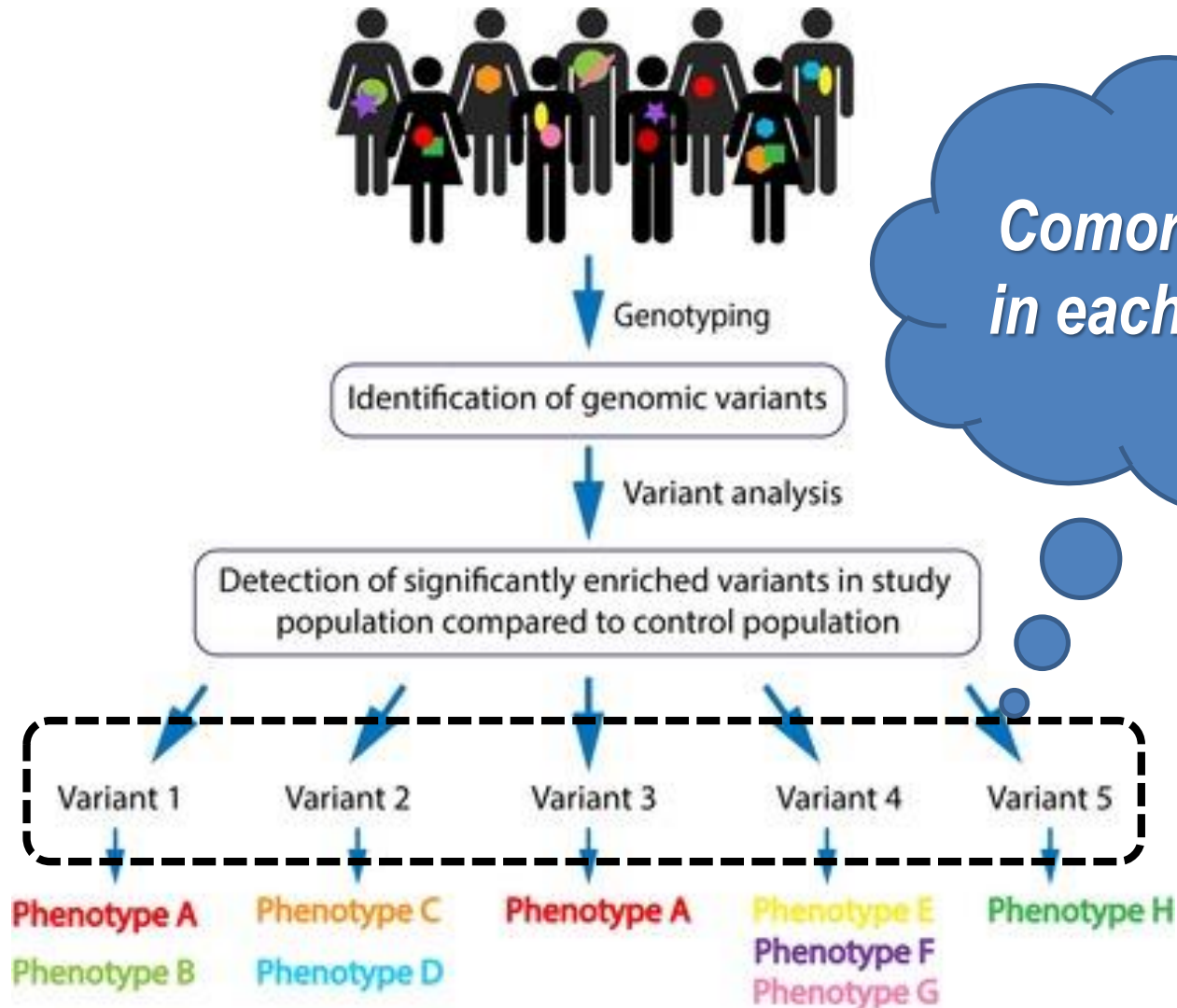


B Ratio of IL-10 to a phenotype



Similar plots for IL-6 and TNF
Conclusion: More inflammatory response in phenotypes γ and δ

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



*Comorbidities
in each patient*

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 21st century approaches
which engage sepsis in its true form,
a complex-dynamic-relational pattern of death.**

An alternate pathophysiologic paradigm of sepsis and septic shock

Implications of individual response variability

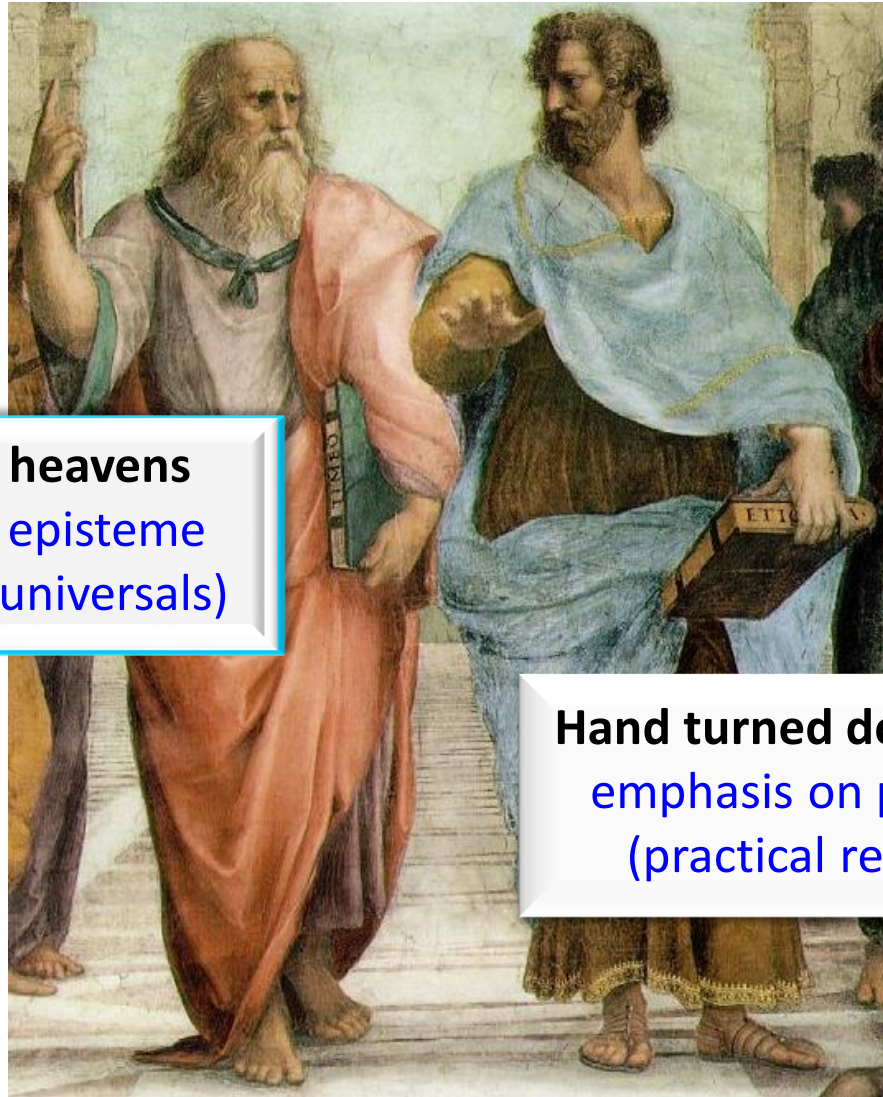
A new paradigm (modified from Anand Kumar)

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



Dialectic approach (Διαλεκτική προσέγγιση)

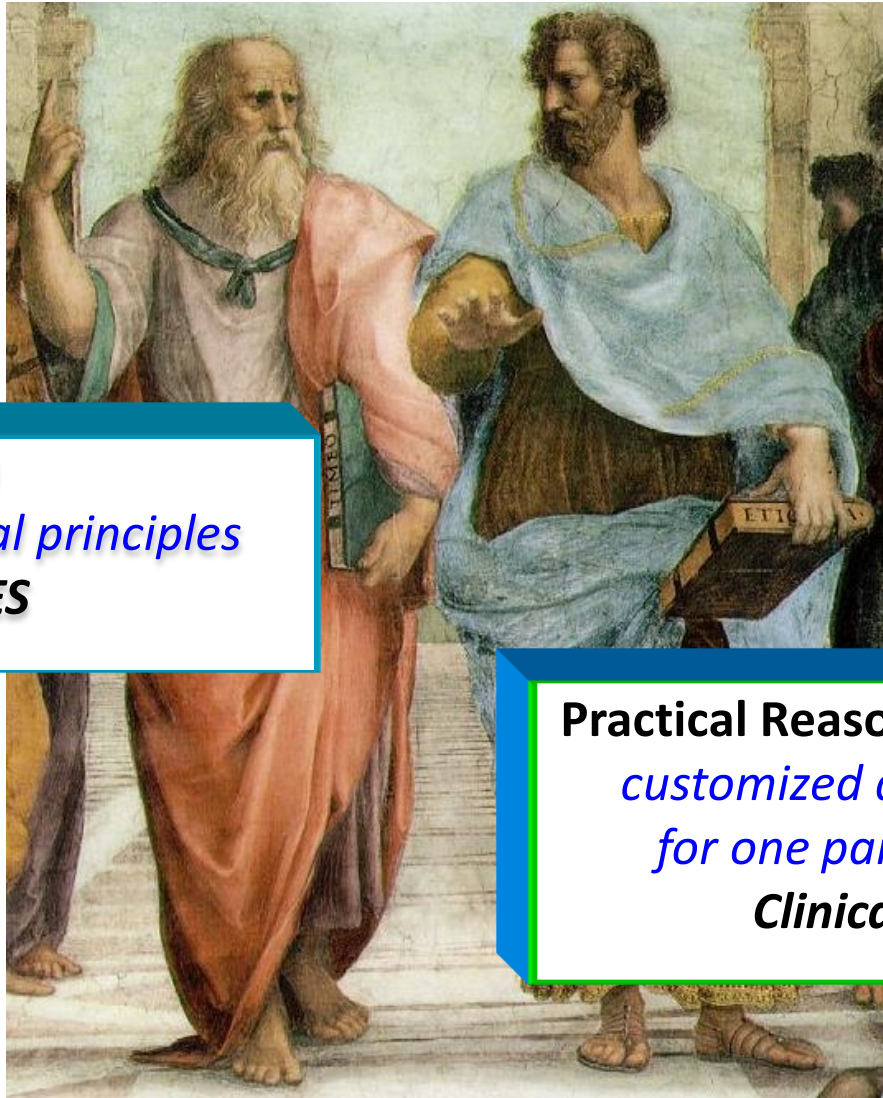
Raphael 1483-1520: The school of Athens 1510-11, Vaticano



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

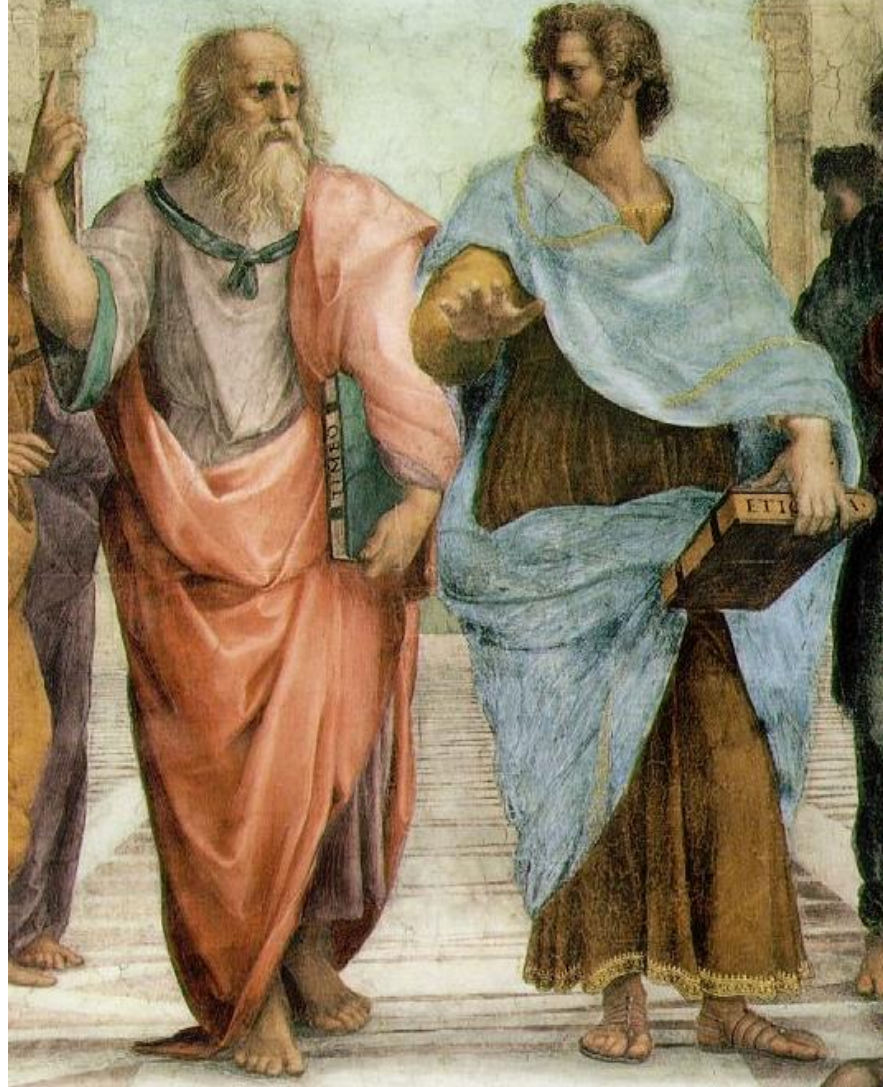
Clinical practice

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
for 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 airline industry or of a jet pilot in regard to

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 mess.

That

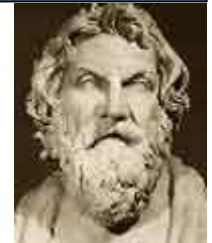
**In the ICU treatment
must be “tailored”
to pathophysiology**

*The p
notice*

*did not
address that reality”*

«Αρχή σοφίας η των ονομάτων επίσκεψις»

Αντισθένης (445 -360 π.Χ.)

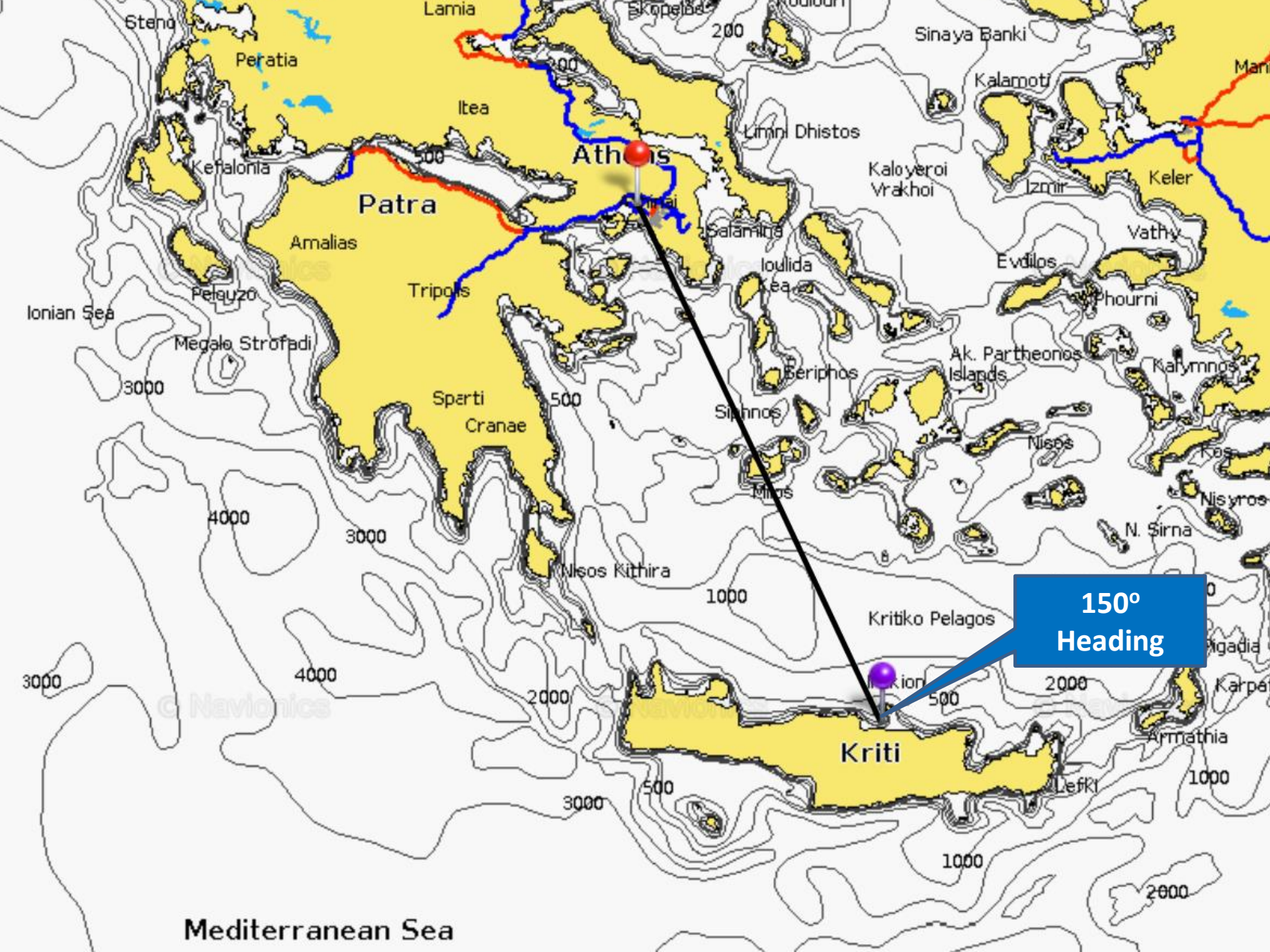


Guidelines ΔΕΝ σημαίνει:

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

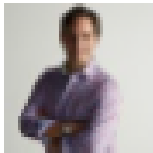
Σημαίνει: ΚΑΤΕΥΘΥΝΤΗΡΙΕΣ ΓΡΑΜΜΕΣ

- 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 και όχι «νόσων»
- Παράδειγμα πλοήγηση για Κρήτη=κατεύθυνση 150°



150°
Heading

Mediterranean Sea



BY JOSH LINKNER

Entrepreneur, author, VC, Jazz guitarist  [@JoshLinkner](https://twitter.com/JoshLinkner)

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




Why You Need to Give Your Team a Compass, Not a GPS

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](https://twitter.com/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 GPS

A map is certainly a handy tool to help you reach your destination. When the map is accurate, you can sit back and follow your course, no thinking required.

Your brain can really take a vacation if you're using the GPS guidance in your car or Google Map exactly how to navigate every twist and turn, you can focus elsewhere and simply comply. **Follow the Guidelines**

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.

To study the phenomenon of disease without books is to sail uncharted sea, while to study books without patients is not to go to sea at all.

William Osler



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”.

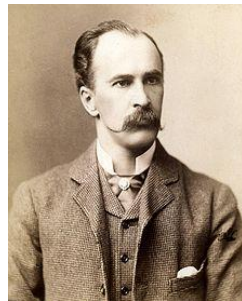


Είναι πολύ πιο σημαντικό να γνωρίζεις τον ασθενή, παρά την ασθένεια Ιπποκράτης

The good physician
treats the disease;
the great physician
treats the patient
who has the disease.

*The good researcher
studies the disease;
the great clinician
“translates” research to
“customize” treatment
for the patient who has
the disease*

William Osler



(personalized ≠ precision medicine)

ΕΥΧΑΡΙΣΤΩ ΓΙΑ ΤΗΝ ΠΡΟΣΟΧΗ ΣΑΣ

PhD means

Doctor of Philosophy

