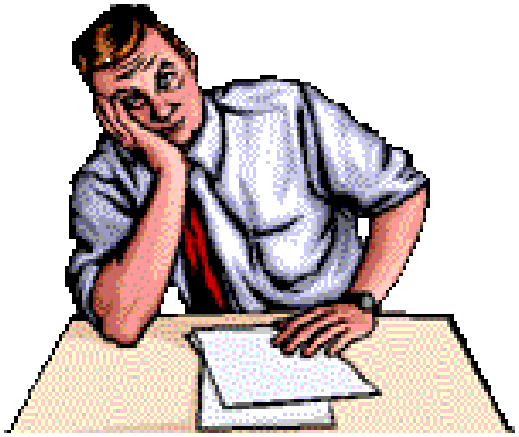
Evidence Based Medicine

Κατευθυντήριες γραμμές για την αντιμετώπιση ασθενών στην κλινική πράξη



Α. Αρμαγανίδης

Καθηγητής Πνευμονολογίας

– Εντατικής Θεραπείας

Ιατρικής Σχολής ΕΚΠΑ

ΠΜΣ «Λοιμωξιολογία» 12/10/2020

Κατευθυντήριες γραμμές/οδηγίες: Κριτική αξιολόγηση

“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
- Research Grands (μέσω ΕΛΚΕ):

  Astellas, Gilead, MSD, Pfizer

Διάγραμμα Παρουσίασης

- ***Σύγχρονη ιστορία των Guidelines (40 χρόνια)***
- ***Σύντομη παρουσίαση της μεθοδολογίας των Surviving Sepsis Campaign Guidelines***

  (αλλαγές στη μεθοδολογία διαμόρφωσης των Guidelines και επιπτώσεις για την κλινική πράξη)
- ***From "Grades of Evidence" to the "GRADE" SYSTEM (and modified "systems")***
- ***Clinical Practice Guidelines: αξιολόγηση και εφαρμογή στην κλινική πράξη***

Institute of Medicine
Guidelines for clinical practice:
From development to use
National Academy Press 1992

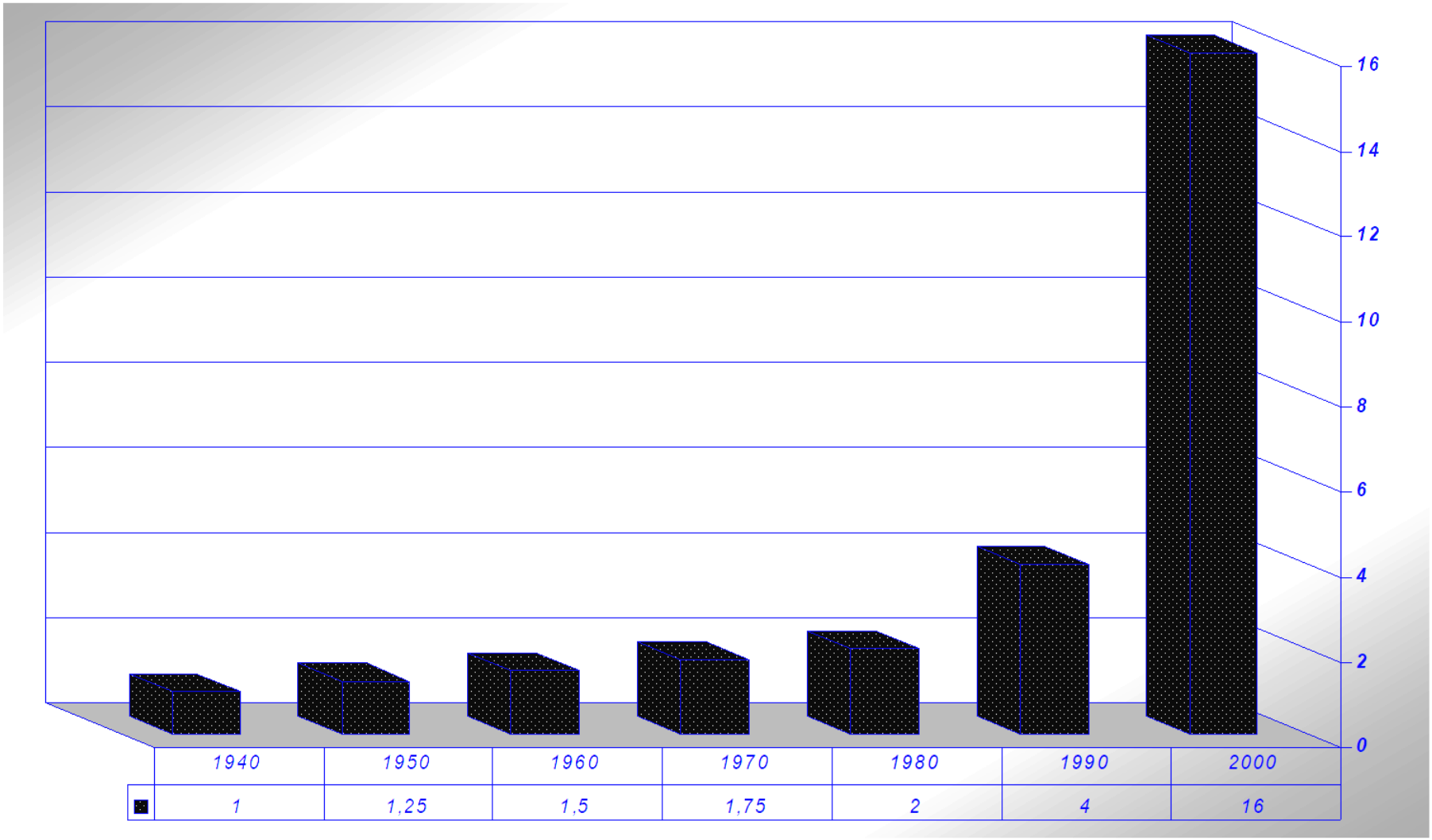
ΟΡΙΣΜΟΣ Clinical Practice Guidelines

«δηλώσεις» (statements) οι οποίες δημιουργούνται με συστηματικό τρόπο και βοηθούν τον κλινικό ιατρό να επιλέξει την κατάλληλη περίθαλψη-αντιμετώπιση σε συγκεκριμένες περιστάσεις (πχ CCS)

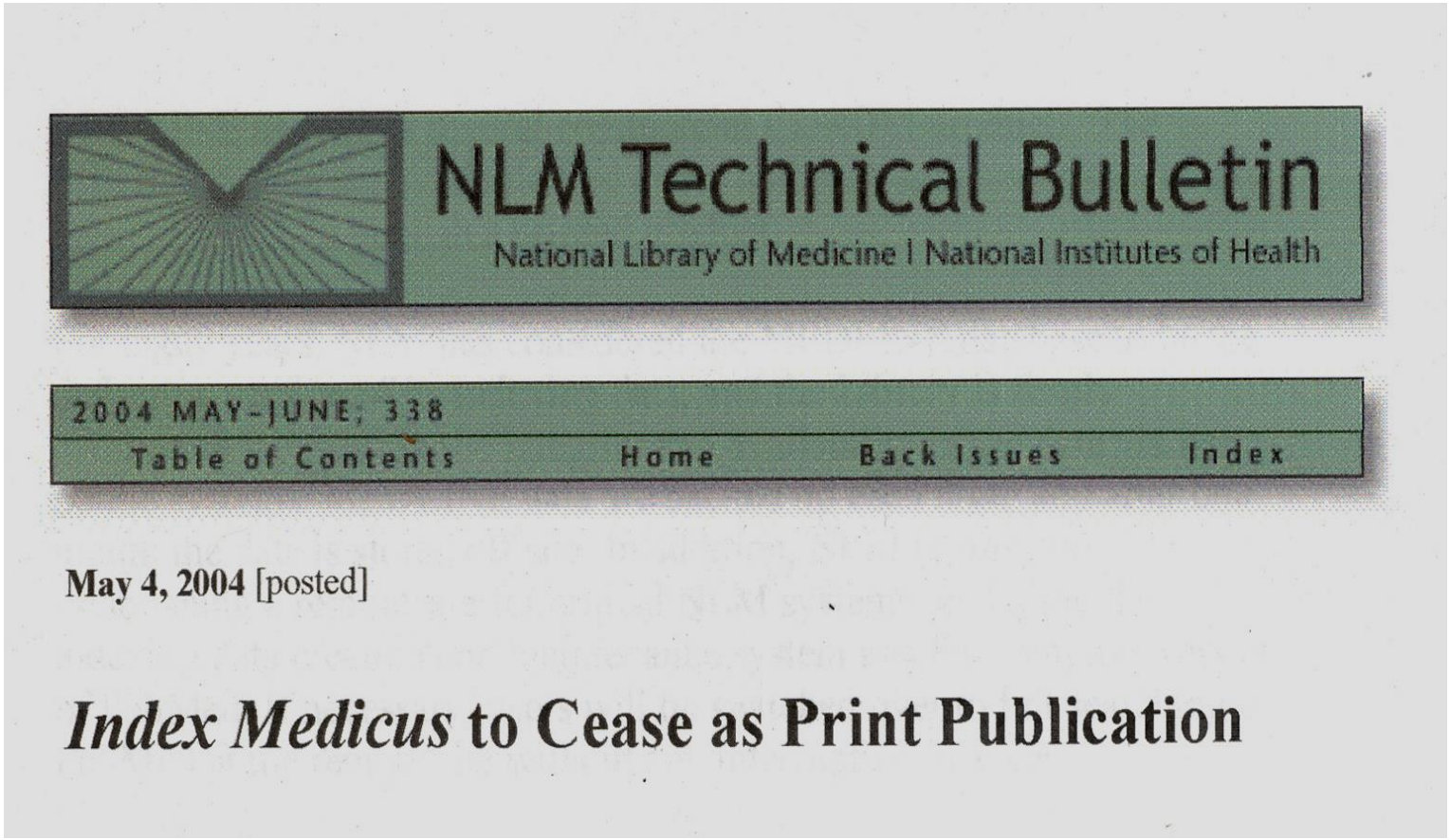
ΒΑΘΜΟΣ ΤΕΚΜΗΡΙΩΣΗΣ ???

Χρόνος διπλασιασμού ιατρικής γνώσης

ΕΒΜ - Α. Αρμαγανίδης



2004: “το τέλος του Index Medicus”



NLM Technical Bulletin

National Library of Medicine | National Institutes of Health

2004 MAY-JUNE; 338

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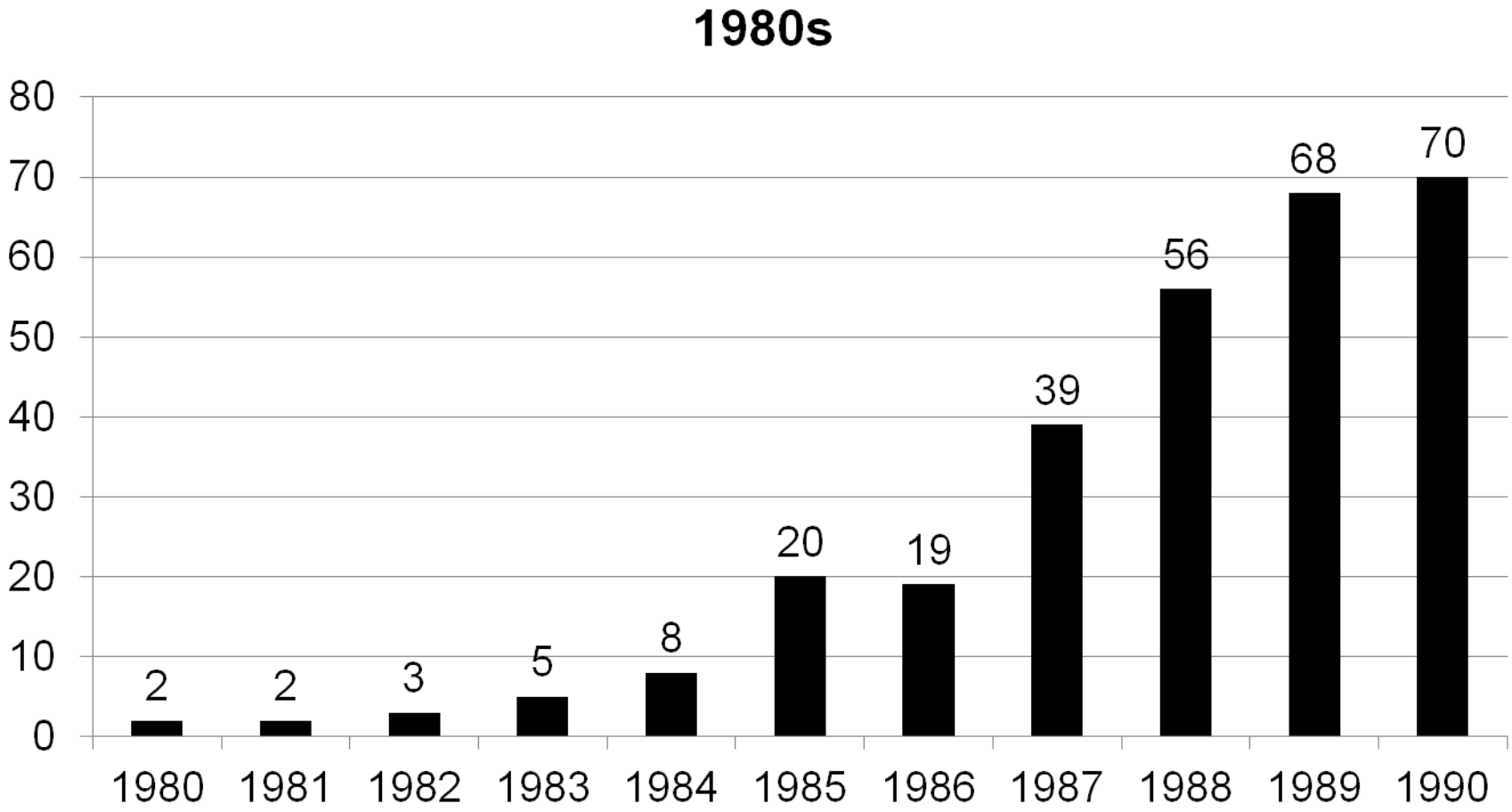
May 4, 2004 [posted]

Index Medicus **to Cease as Print Publication**

PubMed το νέο «πρόβλημα» =>

Evidence Based Medicine ?

Αριθμός δημοσιεύσεων «Clinical Practice Guidelines» (Pub Med)



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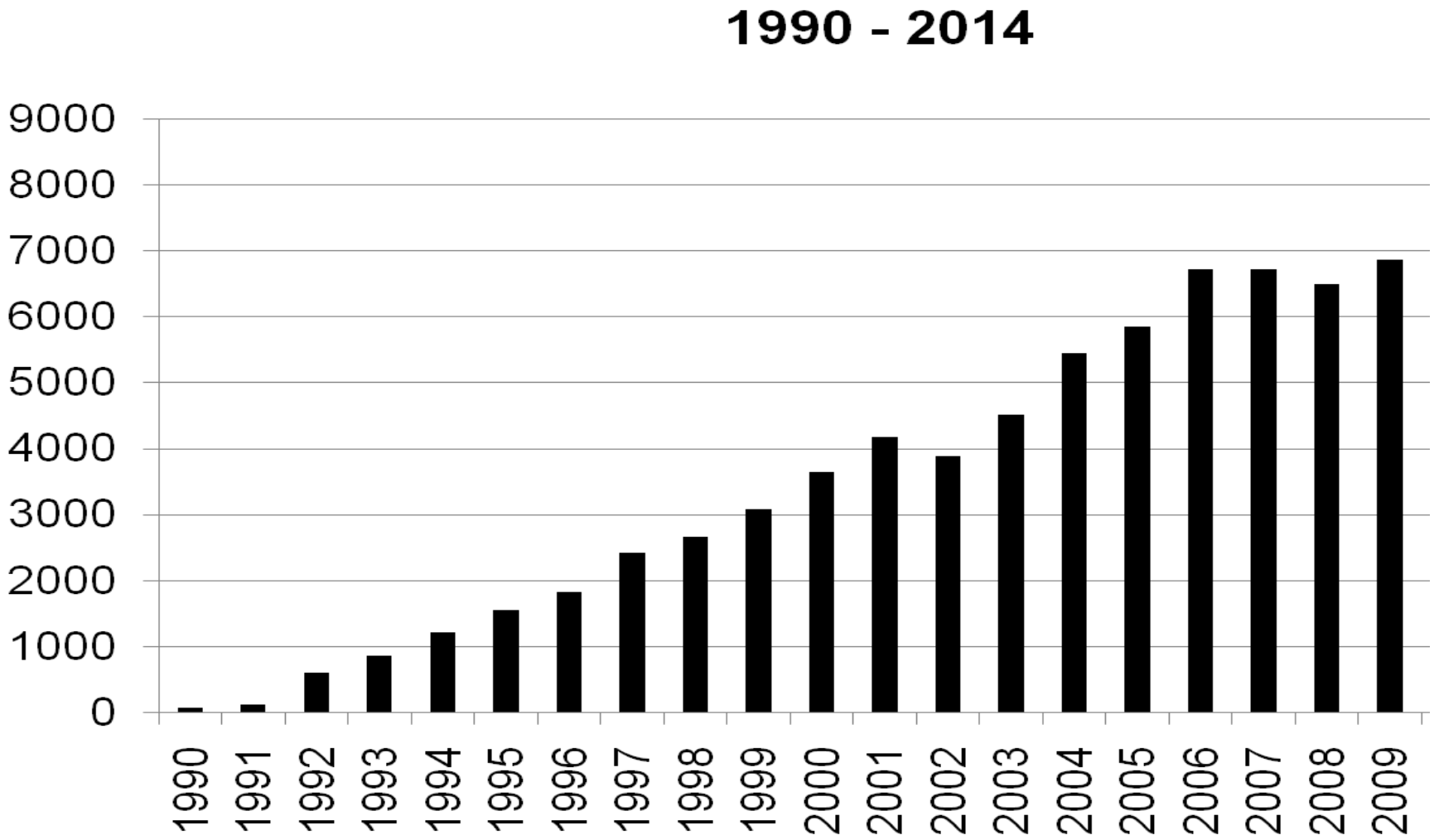
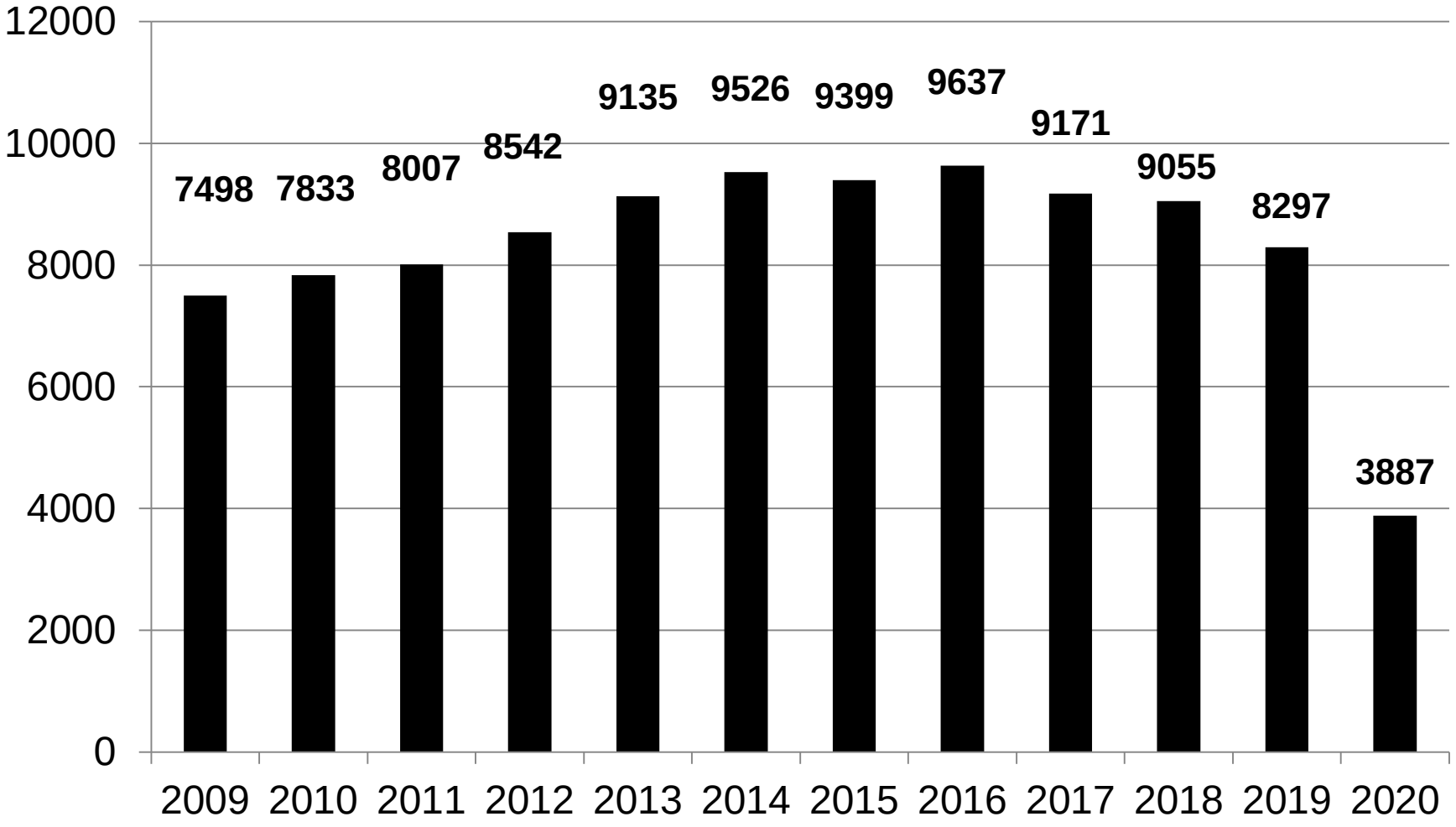
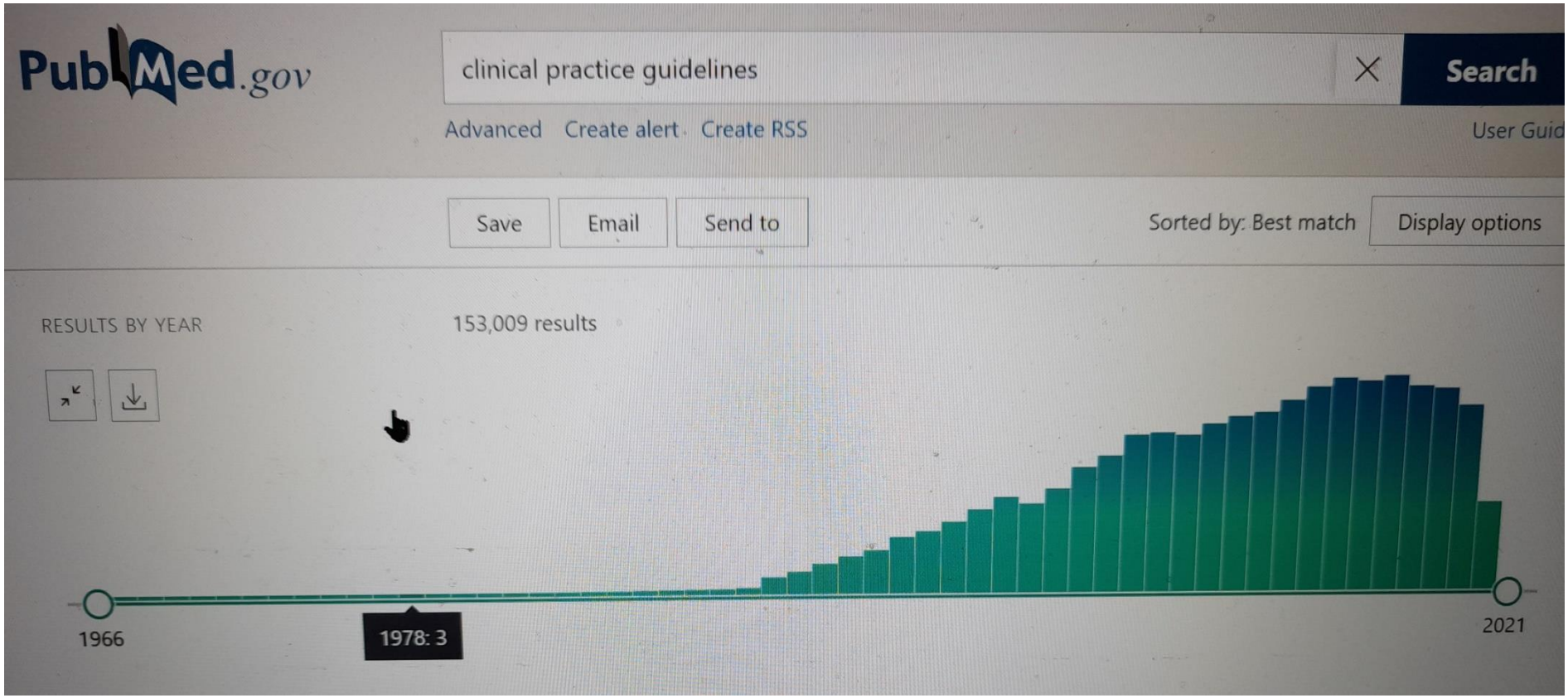


Αριθμός δημοσιεύσεων τελευταίας 10ετίας «Clinical Practice Guidelines» (Pub Med)



Αριθμός δημοσιεύσεων 1966 -2020 για «Clinical Practice Guidelines» (Pub Med)



Evidence Based Medicine:
(γιατί γενικά και ειδικά στην Εντατική?)

- **Πληθώρα βιβλιογραφικών αναφορών με διαφορετική βαρύτητα**
- **Πραγματική αδυναμία εξαγωγής συμπερασμάτων από τον θεράποντα**
- **«Αμυντική Ιατρική» στην εποχή των δικαστικών διεκδικήσεων**

  \+ ***της έμφασης στο κόστος***

Διάγραμμα Παρουσίασης

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- ***Σύντομη παρουσίαση της μεθοδολογίας των Surviving Sepsis Campaign Guidelines***

  (αλλαγές στη μεθοδολογία διαμόρφωσης των Guidelines και επιπτώσεις για την κλινική πράξη)
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- *Clinical Practice Guidelines: αξιολόγηση και εφαρμογή στην κλινική πράξη*

SSC Guidelines: evolution of methodological approach

Table 1 — Vincent and Marshall, Critical Care Vol 12 (3) 2008

Evolution of the sepsis guidelines

		Organizations involved	Number of participants	Process
2001	First	1 (ISF)	9[a]	EBM A to E
2004	Second	3 (ISF, ESICM, SCCM)[b]	24	EBM A to E
2008	Third	16	55	GRADE ?
	Dellinger et al, Crit Care Med Vol 41 (2) 2013			
2012	**Fourth**	**30**	**68**	**GRADE***

(?) "Significant education of committee members on the GRADE approach was performed via e-mail before the first committee meeting and at the first meeting".

(*) Modified approach of the GRADE SYSTEM

EBM: *"quality of studies" in 5 levels*

Quality control of the literature

- **Level I:** ***large, randomized trials with clear-cut results, low risk of (a) or (b) error***
- **Level II:** ***small, randomized trials with uncertain results, moderate or high risk of (a) or (b) error***
- **Level III:** ***non randomized, contemporary controls***
- **Level IV:** ***non randomized with historical controls***
- **Level V:** ***case series, uncontrolled studies and expert opinion***

Sackett DL: Chest 1989

Evidence Based Medicine

Levels of evidence => Grades of certainty

Grading of evidence based on the literature

Supported by:

- **Grade A: *at least two* Level I *investigations***
- **Grade B: *only one* Level I *investigation***
  - ***RCTs with low risk of error***
- **Grade C: *only* Level II *investigations***
  - ***RCTs with high risk of error***
- **Grade D: *at least one* Level III *investigation***
  - ***Controlled non randomized studies***
- **Grade E: *by* Level IV *or* Level V *evidence***
  - ***Uncontrolled studies and expert opinion***

Sackett DL: Chest 1989

Crit Care Med 2004 Vol. 32, No. 3

Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock

Θέσεις Ομοφωνίας

«… a scoring system was not used. The goal was total concensus, which was reached in all recommendations except two (sub-recommendations).

When there was difference in opinion about grading of a clinical trial, an outside epidemiologist was consulted (only once).

The french version of Concensus conference in the 80s

1. *BOGSAT technique*

Guidelines are created by a:

- ***B*** *unch*
- ***O*** *f*
- ***G*** *uys*
- ***S*** *itting*
- ***A*** *round a*
- ***T*** *able*

2. Delphi technique
Questions answered by experts (selection?) with agreement distribution from 1 to 9

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

The guidelines process included:

- **A modified Delphi method**
- **A concensus conference**
- **Several subsequent meetings of subgroups and key individuals**
- **Tele-conferences and electronic-based discussions**
- **Two follow-up nominal group meetings**

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

"The GRADE system"

is based on a sequential assessment of the quality of evidence,

followed by assessment of the balance between benefits vs. risks, burden and cost

(based on a pre-defined approach for the grading of recommendations)

BMJ 2004; 328:1490–1498

ΣΥΣΤΗΜΑ GRADE ΒΑΘΜΟΛΟΓΗΣΗΣ ΔΙΑΘΕΣΙΜΩΝ ΘΕΡΑΠΕΥΤΙΚΩΝ ΧΕΙΡΙΣΜΩΝ

Βαθμός σύστασης	Σχέση ωφέλειας/κινδύνου	Διαθέσιμες μελέτες	Σημασία βαθμολόγησης
1A	Ωφέλεια >>> Κίνδυνος (διάφορα outcomes vs. παρενέργειες, κόστος, φόρτος εργασίας) **A**	RCTs** χωρίς μεθοδολογικά προβλήματα και περιορισμούς ή αδιαμφισβήτητη τεκμηρίωση από μελέτες παρατήρησης	Ισχυρή ένδειξη για το σύνολο των ασθενών
1B **1**	Ωφέλεια >>> Κίνδυνος **B**	RCTs** με μεθοδολογικά προβλήματα και περιορισμούς ή ισχυρή τεκμηρίωση από μελέτες παρατήρησης	Επαρκής ένδειξη για το σύνολο των ασθενών
1C	Ωφέλεια >>> Κίνδυνος **C**	Μελέτες παρατήρησης	Επαρκής ένδειξη που δύναται να αλλάξει
2A	Ωφέλεια ≥ Κίνδυνος	RCTs** χωρίς μεθοδολογικά προβλήματα και περιορισμούς ή αδιαμφισβήτητη τεκμηρίωση από μελέτες παρατήρησης	Ασθενής ένδειξη
2B **2**	Ωφέλεια ≥ Κίνδυνος	RCTs** με μεθοδολογικά προβλήματα και περιορισμούς ή ισχυρή τεκμηρίωση από μελέτες παρατήρησης	Ασθενής ένδειξη
2C	Αμφίβολη σχέση ωφέλειας/κινδύνου	Μελέτες παρατήρησης	Πολύ ασθενής ένδειξη

*RCTs: τυχαιοποιημένες κλινικές μελέτες

ΣΥΣΤΗΜΑ GRADE ΒΑΘΜΟΛΟΓΗΣΗΣ ΔΙΑΘΕΣΙΜΩΝ ΘΕΡΑΠΕΥΤΙΚΩΝ ΧΕΙΡΙΣΜΩΝ

Βαθμός σύστασης	Σχέση ωφέλειας/κινδύνου	Διαθέσιμες μελέτες	Σημασία βαθμολόγησης
1A	Ωφέλεια >>> Κίνδυνος (διάφορα outcomes vs. παρενέργειες, κόστος, φόρτος εργασίας) **A**	RCTs** χωρίς μεθοδολογικά προβλήματα και περιορισμούς ή αδιαμφισβήτητη τεκμηρίωση από μελέτες παρατήρησης	Ισχυρή ένδειξη για το σύνολο των ασθενών
1B	Ωφέλεια >>> Κίνδυνος **B**	RCTs** με μεθοδολογικά προβλήματα και περιορισμούς ή ισχυρή τεκμηρίωση από μελέτες παρατήρησης	Επαρκής ένδειξη για το σύνολο των ασθενών
1C **1**	Ωφέλεια >>> Κίνδυνος **C**	Μελέτες παρατήρησης	Επαρκής ένδειξη που δύναται να αλλάξει
2A	Ωφέλεια ≥ Κίνδυνος	RCTs** χωρίς μεθοδολογικά προβλήματα και περιορισμούς ή αδιαμφισβήτητη τεκμηρίωση από μελέτες παρατήρησης	Ασθενής ένδειξη
2B	Ωφέλεια ≥ Κίνδυνος	RCTs** με μεθοδολογικά προβλήματα και περιορισμούς ή ισχυρή τεκμηρίωση από μελέτες παρατήρησης	Ασθενής ένδειξη
2C **2**	Αμφίβολη σχέση ωφέλειας/κινδύνου	Μελέτες παρατήρησης	Πολύ ασθενής ένδειξη

*RCTs: τυχαιοποιημένες κλινικές μελέτες

and D = very low GRADE in SSC

ΣΥΣΤΗΜΑ GRADE ΒΑΘΜΟΛΟΓΗΣΗΣ ΔΙΑΘΕΣΙΜΩΝ ΘΕΡΑΠΕΥΤΙΚΩΝ ΧΕΙΡΙΣΜΩΝ

Βαθμός σύστασης	Σχέση ωφέλειας/κινδύνου	Διαθέσιμες μελέτες	Σημασία βαθμολόγησης
1A	Ωφέλεια >>> Κίνδυνος (διάφορα outcomes vs. παρενέργειες, κόστος, φόρτος εργασίας) **A**	RCTs** χω… προβλήμ… αδιαμφ…	…α το σύνολο
1B	Ωφέλεια >>> Κίνδυνος **B**	προβ… ισχυρ…	
1C	Ωφέλεια >>> Κίνδυνος **C**	Μελέτες …	…η που δύναται …να αλλάξει
2A	Ωφέλεια ≥ Κίνδυνος	RCTs** χωρίς μεθοδ… προβλήματα κα… αδιαμφισβή… με…	…Ασθενής ένδειξη
2B	Ωφέλεια ≥ Κίνδυνος	προ… ισχυρ…	
2C	Αμφίβολη σχέση ωφέλειας/κινδύνου	Μελέτες πα…	…ενής ένδειξη

1 = 1A, 1B, 1C

2 = 2A, 2B, 2C

1 = STRONG we "recommend"

2 = WEAK we "suggest"

*RCTs: τυχαιοποιημένες κλινικές μελέτες

and D = very low GRADE in SSC

Differences in opinion about interpretation of evidence, wording of proposals, or strength of recommendations (in 2008) were resolved using a specifically developed set of rules

- Recommendation for direction was given if <20% against (neutral vote allowed)
- Strong (=1) or weak (=2) recommendation:
  > 70% of votes strong=> we recommend
  < 70% of votes => we suggest

Vincent and Marshall, Critical Care Vol 12 (3) 2008

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

R. Phillip Dellinger, ...eschke, MD;
Konrad Reinhart, M... PhD;
Jean-Francois Dhai... Ranieri, MD;
Graham Ramsay, M...
Janice L. Zimmerm... ...mittee

APPENDIX D

Recombinant Activated Protein C Nominal Group Vote

Strong for use, 6
Weak for use, 15
Neutral, 1
Weak for not using, 0
Strong for not using, 0

6/22 = 27%

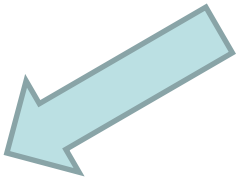
against

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

R. Phillip Dellinger, ... an Jaeschke, MD;
Konrad Reinhart, M ... , MD, PhD;
Jean-Francois Dhai ... larco Ranieri, MD;
Graham Ramsay, M ... MD;
Janice L. Zimmerm ... es Committee

I. Recombinant Human Activated Protein C (rhAPC)

1. We suggest that adult patients with sepsis-induced organ dysfunction associated with a clinical assessment of high risk of death, most of whom will have Acute Physiology and Chronic Health Evaluation (APACHE) II ≥25 or multiple organ failure, receive rhAPC if there are no contraindications (grade 2B except for patients within 30 days of surgery, for whom it is grade 2C). Relative contraindications should also be considered in decision making.



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Jean-Francois Dhai ... larco Ranieri, MD;
Graham Ramsay, M ... MD;
Janice L. Zimmerm ... ittee

I. Recombinant Human Activated Protein C (rhAPC)

2. We recommend that adult patients with severe sepsis and low risk of death, most of whom will have APACHE II <20 or one organ failure, do not receive rhAPC (grade 1A).

C. Glucose Control

We recommend that

1. pts with severe sepsis+hyperglycemia who are admitted to the ICU receive intravenous insulin therapy to reduce blood glucose levels (grade 1B).

2. all pts receiving IV insulin receive a glucose calorie source and that blood glucose values be monitored every 1–2 hrs until glucose values and insulin infusion rates are stable and then every 4 hrs (grade 1C).

3. low glucose levels obtained with point-of-care testing of capillary blood be interpreted with caution, as such measurements may overestimate arterial blood or plasma glucose values (grade 1B).

4. **We suggest** ***use of a validated protocol for insulin dose adjustments and targeting glucose levels to the 150 mg/dL range (grade 2C)***.

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

largaret M. Parker, MD; Roman Jaeschke, MD;
Beale, MD; Thierry Calandra, MD, PhD;
i, MD; John Marshall, MD; Marco Ranieri, MD;
end, MD; Jeffrey S. Vender, MD;
g Sepsis Campaign Guidelines Committee

APPENDIX G

Glycemic Control Committee Vote

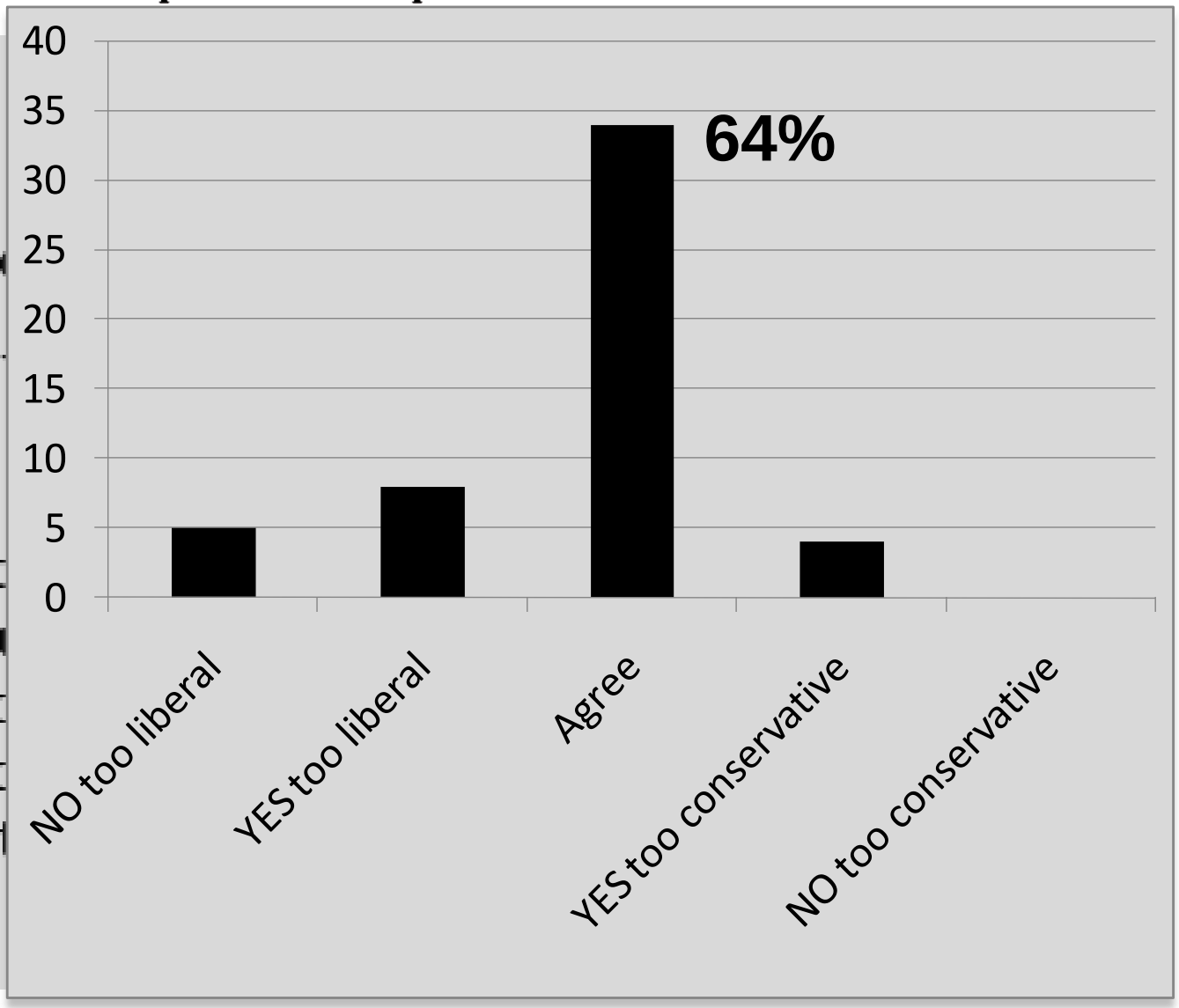
Glycemic control—90%
Total votes = 51
Agree—34
Too conservative, but accept—4
Too liberal, but accept—8
Disapprove, too conservative—0
Disapprove, too liberal—5
Disapprove, other—0

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

APPENDIX G

Glycemic Contr

Glycemic con
Total votes =
Agree—34
Too conservat
Too liberal, b
Disapprove, t
Disapprove, t
Disapprove, o



CLINICAL GUIDELINE

ACP Clinical Practice
American College of Physicians
GUIDELINES

Use of Intensive Insulin Therapy for the Management of Glycemic Control in Hospitalized Patients: A Clinical Practice Guideline From the American College of Physicians

Amir Qaseem, MD, PhD, MHA; Linda L. Humphrey, MD, MPH; Roger Chou, MD; Vincenza Snow, MD; and Paul Shekelle, MD, PhD, for the Clinical Guidelines Committee of the American College of Physicians*

Description: The American College of Physicians (ACP) developed this guideline to present the evidence for the link between the use of intensive insulin therapy to achieve different glycemic targets and health outcomes in hospitalized patients with or without diabetes mellitus.

Methods: Published literature on this topic was identified by using MEDLINE and the Cochrane Library. Additional articles were obtained from systematic reviews and the reference lists of pertinent studies, reviews, and editorials, as well as by consulting experts; unpublished studies on ClinicalTrials.gov were also identified. The literature search included studies published from 1950 through March 2009. Searches were limited to English-language publications. The primary outcomes of interest were short-term mortality and hypoglycemia. This guideline grades the evidence and recommendations by using the ACP clinical practice guidelines grading system.

Recommendation 1: ACP recommends not using intensive insulin therapy to strictly control blood glucose in non–surgical intensive care unit (SICU)/medical intensive care unit (MICU) patients with or without diabetes mellitus (Grade: strong recommendation, moderate-quality evidence).

Recommendation 2: ACP recommends not using intensive insulin therapy to normalize blood glucose in SICU/MICU patients with or without diabetes mellitus (Grade: strong recommendation, high-quality evidence).

Recommendation 3: ACP recommends a target blood glucose level of 7.8 to 11.1 mmol/L (140 to 200 mg/dL) if insulin therapy is used in SICU/MICU patients (Grade: weak recommendation, moderate-quality evidence).

Ann Intern Med. 2011;154:260-267. www.annals.org

For author affiliations, see end of text.

Critical Care Medicine

February 2013 • Volume 41 • Number 2

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4];

- Methodology and Grading – Conflict
- Initial resuscitation and Infection Issues and Surviving Sepsis Campaign Bundles
- Hemodynamic support and adjunctive tt
- Other supportive therapy of Severe Sepsis
- **Pediatrics**

58 pages, 636 references

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

The guidelines process included:

- ~~A modified Delphi method~~
- ~~A consensus conference~~

2012 guidelines

- Several subsequent meetings of subgroups and key individuals
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Διάγραμμα Παρουσίασης

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TABLE 1. CATEGORIES INDICATING THE STRENGTH OF EACH RECOMMENDATION FOR OR AGAINST ITS USE IN THE TREATMENT OF FUNGAL INFECTIONS

Limper et al 2010 ATS Guidelines for fungal infection

Category	
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation for or against use
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use

TABLE 2. GRADES OF EVIDENCE QUALITY ON WHICH RECOMMENDATIONS ARE BASED

Grade	Level	Definition
I		Evidence from at least 1 properly randomized, controlled trial
II		Evidence from at least 1 well-designed clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from > 1 center), from multiple patient series studies, or from dramatic results of uncontrolled experiments
III		Evidence from opinions of respected authorities, that is based on clinical experience, descriptive studies, or reports of expert committees.

erapy for the Management of Glycemic ients: A Clinical Practice Guideline From hysicians

D, MPH; Roger Chou, MD; Vincenza Snow, MD; and Paul Shekelle, MD, PhD, College of Physicians*

P) developed
en the use of
targets and
hout diabetes

fied by using
were obtained
tinent studies,
; unpublished
erature search
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ary outcomes
This guideline
e ACP clinical

care unit (SICU)/medical intensive care unit (MICU) patients with or without diabetes mellitus (Grade: strong recommendation, moderate-quality evidence).

Recommendation 2: ACP recommends not using intensive insulin therapy to normalize blood glucose in SICU/MICU patients with or without diabetes mellitus (Grade: strong recommendation, high-quality evidence).

Recommendation 3: ACP recommends a target blood glucose level of 7.8 to 11.1 mmol/L (140 to 200 mg/dL) if insulin therapy is used in SICU/MICU patients (Grade: weak recommendation, moderate-quality evidence).

Panel's Conclusion (?)

Quality

Πως αλλάζει το «Level» στο «Grade» με βάση την «Expert Opinion" ή Η εκδίκηση των Experts (βαθμός ≠ ποιότητα μελετών τεκμηρίωσης)

Strong

Conditional

We recommend/ We suggest

Grade

ΜΟΛΟΓΗΣΗΣ ΔΙΑ			
Βαθ	/κινδύνου ⟷	Διαθέσιμες μελέτες	
	ος	RCTs** χωρίς μεθοδολογικ προβλήματα και περιορισμού αδιαμφισβήτητη τεκμηρίωση μελέτες παρατήρησης	A
	>> Κίνδυνος	RCTs** με μεθοδολογικά προβλήματα και περιορισμούς ή ισχυρή τεκμηρίωση από μελέτες παρατήρησης	B — Επαρκής ένδειξη για το σύνολο των ασθενών
	Ωφέλεια >>> Κίνδυνος	Μελέτες παρατήρησης	C — Επαρκής ένδειξη που δύναται να αλλάξει
	Ωφέλεια ≥ Κίνδυνος	RCTs** χωρίς μεθοδολογικά προβλήματα και περιορισμούς ή αδιαμφισβήτητη τεκμηρίωση από μελέτες παρατήρησης	Ασθενής ένδειξη
2B	Ωφέλεια ≥ Κίνδυνος	RCTs** με μεθοδολογικά προβλήματα και περιορισμούς ή ισχυρή τεκμηρίωση από μελέτες παρατήρησης	Ασθενής ένδειξη
2C	Αμφίβολη σχέση ωφέλειας/κινδύνου	Μελέτες παρατήρησης	Πολύ ασθενής ένδειξη

2

*RCTs: τυχαιοποιημένες κλινικές μελέτες

and D = very low GRADE in SSC

SSC 2012 UG = non conducive for GRADE = Un Graded

SSC and the role of Guidelines

A **strong** recommendation in favor of an intervention **reflects the panel's evaluation or opinion** if:

the desirable effects

of adherence to a recommendation

will clearly outweigh the undesirable effects

beneficial	**Health Outcome**	harm
less	**Burden on staff and pts**	more
savings	**Cost**	greater

(In most but not in every individual patient OR in every environment or country)

Διάγραμμα Παρουσίασης

- *Σύγχρονη ιστορία των Guidelines (40 χρόνια)*
- *Σύντομη παρουσίαση της μεθοδολογίας των Surviving Sepsis Campaign Guidelines*

  (αλλαγές στη μεθοδολογία διαμόρφωσης των Guidelines και επιπτώσεις για την κλινική πράξη)
- *From "Grades of Evidence" to the "GRADE" SYSTEM (and modified "systems")*
- ***Clinical Practice Guidelines: αξιολόγηση και εφαρμογή στην κλινική πράξη***

Presentation Outline

- *Brief presentation of all 4 versions of Survival Sepsis Campaign Guidelines with emphasis on Methodological differences and their importance*
- *From Grades of Evidence to the "GRADE" SYSTEM (and modified or other "grading systems")*
- ***"Clinical Practice Guidelines" (in decision making): terminology, evaluation and usefulness for clinical practice in the "real ICU world"***

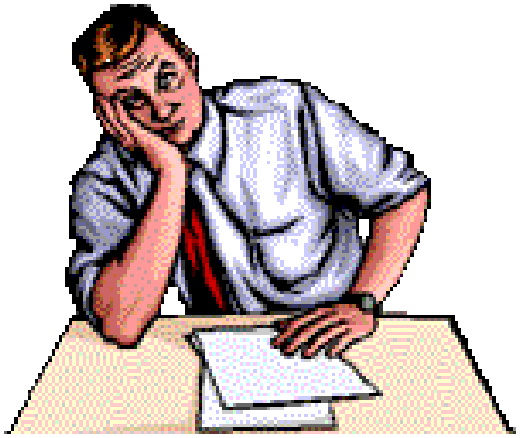
Evidence Based Medicine

Α. Αρμαγανίδης

Ιατρική Σχολή Πανεπιστημίου Αθηνών

Μεθοδολογία δημιουργίας και χρήση κατευθυντήριων γραμμών κλινικής πρακτικής

(Clinical Practice Guidelines)



9ο ΣΥΜΠΟΣΙΟ ΕΝΤΑΤΙΚΗΣ ΙΑΤΡΙΚΗΣ ΕΝΟΠΛΩΝ ΔΥΝΑΜΕΩΝ Αθήνα 26-27/5/2011

Guidelines: ΣΥΜΠΕΡΑΣΜΑ

- Οι κατευθυντήριες γραμμές ποικίλλουν ως προς τους στόχους και την προοπτική τους καθώς επίσης και ως προς τη μεθοδολογική ακρίβεια με την οποία συγκεντρώνονται.
- Επομένως πριν να εφαρμόσει τις όποιες κατευθυντήριες γραμμές, ο ιατρός πρέπει να αξιολογήσει την εγκυρότητά τους καθώς και τη δυνατότητα εφαρμογής τους σε κάθε ασθενή ξεχωριστά.

EVIDENCE-BASED MEDICINE
Friedland et al 1998

Οι υπεύθυνοι για ανάπτυξη Guidelines πρέπει να προσδιορίσουν:

- **την πηγή της χρηματοδότησής τους,**
- **τους επαγγελματικούς τους τίτλους και**
- **τις επαγγελματικές, ακαδημαϊκές ή εμπορικές διασυνδέσεις τους**

EVIDENCE-BASED MEDICINE
Friedland et al 1998

Αυτό βοηθά

- **να αξιολογήσουμε τους στόχους και την προοπτική των Guidelines**

  και

- **να εντοπίσουμε συστηματικά σφάλματα που ευνοούν την οργάνωση που χρηματοδοτεί ή υποστηρίζει γενικά τους συγγραφείς**

EVIDENCE-BASED MEDICINE
Friedland et al 1998

- **Ο προσδιορισμός του στόχου και της προοπτικής των Guidelines βοηθά να καθορίσουμε αν αυτά είναι σύμφωνα με τους δικούς μας στόχους.**
- **Για παράδειγμα τα Guidelines που προορίζονται να μειώσουν τις δαπάνες είναι πιθανό**

  να μην βελτιώνουν την ποιότητα της φροντίδας του ασθενή μας.

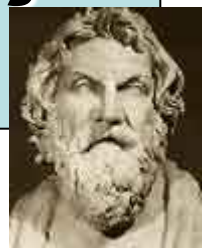
16 societies have endorsed the guidelines in 2008 but 2 societies elected not to

- The Australia and New Zealand Intensive Care Society was one of these, concluding that
- the guidelines do not represent current practice in Australasia
- some of the recommendations are the subject of ongoing clinical trials

While strongly supporting the guidelines process, the Society worry that guidelines might be used in local quality-improvement programmes, leading to imposition of practices that are inferior to current practices

Vincent and Marshall Crit Care 2008

«Αρχή σοφίας η των ονομάτων επίσκεψις»
Αντισθένης (445 -360 π.Χ.)



Guidelines ΔΕΝ σημαίνει:

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

2011

Σημαίνει: <u>ΚΑΤΕΥΘΥΝΤΗΡΙΕΣ ΓΡΑΜΜΕΣ</u>

- Παράδειγμα: πλοήγηση για Κρήτη
- *Σημασία μετάφρασης: οικονομικά αλλά και νομικά θέματα, π.χ. ασφαλιστικές εταιρείες (αρνητικά ή θετικά = πληρωμή και bonus!)*

Law Would Grant 'Safe Harbor' to Docs Who Follow Guidelines

Mark Crane | March 06, 2014

Physicians who are Medicare and Medicaid providers would be granted increased liability protection if they can de guidelines, according to a bill introduced in Congress this week.

The Saving Lives, Saving Costs Act, introduced by Reps. Andy Barr (R-KY) and Ami Bera (D-CA), would create a

«safe harbor» for physicians who follow best practice guidelines

B OME

In the era of PERSONALIZED MEDICINE should we believe that ONE SIZE FITS ALL?

The same approach could (or even more) must be used:

In all critically ill patients ?

In excluded from RCTs patients?

In the management of “syndromes”?

Τι να (μην) κάνουμε ;

(Γ)

The Guidelines
are NOT
Commendments

(Β)

ΣΤΑΤΙΣΤΙΚΗ ΚΑΙ ΥΓΕΙΑ
Γρηγόρης Χλουβεράκης
2009

ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

Hot Topics on Infections in the Critically Ill Patient

Organized by the ESG CIP In co-operation with the Hellenic Society of Chemotherapy National School of Public Health Athens- Greece

An appraisal of the usefulness of Guidelines in the management of severe infections

Apostolos ARMAGANIDIS
Professor of Intensive Care Medicine
Athens University Medical School
aarmag@med.uoa.gr

SSC and the role of Guidelines

Resource limitations in some institutions and countries may prevent physicians from accomplishing particular recommendations

.

Thus, these recommendations are intended to be best practice

(the committee considers this a goal for clinical practice and

not created to represent standard of care).

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4];

SSC and the role of Guidelines

The implications of calling a recommendation strong are that most well-informed patients would accept that intervention and that most clinicians should use it in most situations. Circumstances may exist in which a strong recommendation cannot or should not be followed for an individual because of that patient's preferences or clinical characteristics that make the recommendation less applicable. A strong recommendation does not automatically imply standard of care. For example, the strong recommendation

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4];

How to use these guidelines (Part I)

These ERS/ATS evidence-based guidelines for the use of NIV in critically ill patients provide the basis for stakeholders to make rational, informed decisions.

Clinicians, patients, third-party payers, institutional review committees, other stakeholders or the courts should never view these recommendations as dictates.

How to use these guidelines (Part II)

No recommendation can take into account all of the often-compelling unique individual clinical circumstances.

No one charged with evaluating a healthcare professional's actions should view these recommendations as absolute.

It is the individual responsibility of health professionals to consult other sources of relevant information, to make appropriate and accurate decisions in consideration of each patient's health condition and in consultation with the patient and the patient's caregiver.

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Andrew Rhodes[1*], Laura E. Evans[2], Waleed Alhazzani[3], Mitchell M. Levy[4], Massimo Antonelli[5], Ricard Ferrer[6],

Table 3 Comparison of 2016 grading terminology with previous alphanumeric descriptors

	2016 Descriptor	2012 Descriptor
Strength	Strong	1
	Weak	2
Quality	High	A
	Moderate	B
	Low	C
	Very Low	D
Ungraded strong recommendation	Best Practice Statement	Ungraded

Intensive Care Med (2017) 43:304–377

Appendix 2
Comparison of recommendations from 2012 to 2016

Intensive Care Med (2017) 43:304–377

2012 RECOMMENDATIONS	2016 RECOMMENDATIONS
A. INITIAL RESUSCITATION	**A. INITIAL RESUSCITATION**
1. Protocolized, quantitative resuscitation of patients with sepsisinduced tissue hypoperfusion (defined in this document ashypotension persisting after initial fluid challenge or blood lactate concentration ≥ 4 mmol/L). Goals during the first 6 hours of resuscitation: a. Central venous pressure 8–12 mm Hg b. Mean arterial pressure ≥ 65 mm Hg c. Urine output ≥ 0.5 mL/kg/hr d. Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively (grade 1C). 2. In patients with elevated lactate levels targeting resuscitation to normalize lactate (grade 2C).	1. Sepsis and septic shock are medicalemergencies, and we recommend that treatment and resuscitation begin immediately (BPS). 2. We recommend that, in the resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloid fluid be given within the first 3 hours (strong recommendation, low quality of evidence). 3. We recommend that, following initial fluid resuscitation, additional fluids be guided by frequent reassessment of hemodynamic status (BPS). Remarks: Reassessment should include a thorough clinical examination and evaluation of available physiologic variables (heart rate, blood pressure, arterial oxygen saturation, respiratory rate, temperature, urine output, and otherșas available) as well as other noninvasive or invasive monitoring,as available. 4. We recommend further hemodynamic assessment (such as assessing cardiac function) to determine the type of shock if the clinical examination does not lead to a clear diagnosis (BPS). 5. We suggest that dynamic over static variables be used to predict fluid responsiveness, where available (weak recommendation, low quality of evidence). 6. We recommend an initial target mean arterial pressure of 65 mmHg in patients with septic shock requiring vasopressors (strong recommendation, moderate quality of evidence). 7. We suggest guiding resuscitation to normalize lactate in patients with elevated lactate levels as a marker of tissue hypoperfusion (weak recommendation, low quality of evidence).

5. We suggest that dynamic over static variables be used to predict fluid responsiveness, where available (weak recommendation, low quality of evidence).

D. ANTIMICROBIAL THERAPY — 2012

1. Administration of effective IV antimicrobials within the first hour of recognition of septic shock (grade 1B) and severe sepsis without septic shock (grade 1C) as the goal of therapy.
2. Initial empiric antiinfective therapy of one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into tissues presumed to be the source of sepsis (grade 1B).
3. Antimicrobial regimen should be reassessed daily for potential de-escalation (grade 1B).
4. Use of low procalcitonin levels or similar biomarkers to assist the clinician in the discontinuation of empiric antibiotics in patients who initially appeared septic, but have no subsequent evidence of infection (grade 2C).
5. Combination empirical therapy for neutropenic patients with severe sepsis (grade 2B) and for patients with difficult-to-treat, multidrug-resistant bacterial pathogens such as *Acinetobacter* and *Pseudomonas* species (grade 2B). For patients with severe infections associated with respiratory failure and septic shock, combination therapy with an extended-spectrum ß-lactam and either an aminoglycoside or a fluoroquinolone for *Pseudomonas aeruginosa* bacteremia (grade 2B). A combination of ß-lactam and macrolide for patients with septic shock from bacteremic *Streptococcus pneumoniae* infections (grade 2B).
6. Empiric combination therapy should not be administered for more than 3 to 5 days. De-escalation to the most appropriate single therapy should be performed as soon as the susceptibility profile is known (grade 2B).
7. Duration of therapy typically 7 to 10 days; longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with *Staphylococcus aureus*, some fungal and viral infections, or immunologic deficiencies, including neutropenia (grade 2C).
8. Antiviral therapy initiated as early as possible in patients with severe sepsis or septic shock of viral origin (grade 2C).
9. Antimicrobial agents should not be used in patients with severe inflammatory states determined to be of noninfectious cause (UG).

1 *B = 2, 1C= 1* **2012**

2 *B = 2, 2C = 3, UG =1*

3 Strong + Moderate

7 Weak + Low quality

5 BPS =

Best Practice Statement **2016**

Intensive Care Med (2017) 43:304–377

D. ANTIMICROBIAL THERAPY — 2016

1. We recommend that administration of IV antimicrobials be initiated as soon as possible after recognition and within one hour for both sepsis and septic shock (strong recommendation, moderate quality of evidence).
2. We recommend empiric broad-spectrum therapy with one or more antimicrobials for patients presenting with sepsis or septic shock to cover all likely pathogens (including bacterial and potentially fungal or viral coverage) (strong recommendation, moderate quality of evidence).
3. We recommend that antimicrobial therapy is narrowed once pathogen identification and sensitivities are established and/or adequate clinical improvement is noted (BPS).
4. We recommend against sustained systemic antimicrobial prophylaxis in patients with severe inflammatory states of noninfectious origin (e.g., severe pancreatitis, burn injury) (BPS).
5. We recommend that dosing strategies of antimicrobials be optimized based on accepted pharmacokinetic/pharmacodynamic principles and specific drug properties in patients with sepsis or septic shock (BPS).
6. We suggest empiric combination therapy (using at least two antibiotics of different antimicrobial classes) aimed at the most likely bacterial pathogen(s) for the initial management of septic shock (weak recommendation, low quality of evidence).
   Remarks: Readers should review Table 6 for definitions of empiric, targeted/definitive, broad-spectrum, combination, and multidrug therapy before reading this section.
7. We suggest that combination therapy not be routinely used for ongoing treatment of most other serious infections, including bacteremia and sepsis without shock (weak recommendation, low quality of evidence).
   Remarks: This does not preclude the use of multidrug therapy to broaden antimicrobial activity.
8. We recommend against combination therapy for the routine treatment of neutropenic sepsis/bacteremia (strong recommendation, moderate quality of evidence).
   Remarks: This does not preclude the use of multidrug therapy to broaden antimicrobial activity.
9. If combination therapy is used for septic shock, we recommend de-escalation with discontinuation of combination therapy within the first few days in response to clinical improvement and/or evidence of infection resolution. This applies to both targeted (for culture-positive infections) and empiric (for culture-negative infections) combination therapy (BPS).
10. We suggest that an antimicrobial treatment duration of 7 to 10 days is adequate for most serious infections associated with sepsis and septic shock (weak recommendation, low quality of evidence).
11. We suggest that longer courses are appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with *Staphylococcus aureus*, some fungal and viral infections, or immunologic deficiencies, including neutropenia (Weak recommendation, low quality of evidence).
12. We suggest that shorter courses are appropriate in some patients, particularly those with rapid clinical resolution following effective source control of intra-abdominal or urinary sepsis and those with anatomically uncomplicated pyelonephritis (weak recommendation, low quality of evidence).
13. We recommend daily assessment for de-escalation of antimicrobial therapy in patients with sepsis and septic shock (BPS).
14. We suggest that measurement of procalcitonin levels can be used to support shortening the duration of antimicrobial therapy in sepsis patients (weak recommendation, low quality of evidence).
15. We suggest that procalcitonin levels can be used to support the discontinuation of empiric antibiotics in patients who initially appeared to have sepsis, but subsequently have limited clinical evidence of infection (weak recommendation, low quality of evidence).

1. Give AB early for all
2. + Broad spectrum
3. tt narrowed if ...*
4. Against prophylaxis*
5. Optimize dosing*
6. Empiric therapy
7. Combination therapy
8. Combination therapy
9. Combination therapy*
10. 7-10 days but …
11. Longer courses …
12. Shorter courses …
13. De-escalation (BPS)*
14. PCT for shortening
15. PCT+ discontinuation

Διάρκεια θεραπείας στην κλινική πράξη 2012 -2016

Surviving Sepsis Campaign Guidelines

SSC Guidelines 2012

Intensive Care Med (2017) 43:304–377

7. Duration of therapy typically 7 to 10 days; longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with *Staphylococcus aureus*, some fungal and viral infections, or immunologic deficiencies, including neutropenia (grade 2C).

SSC Guidelines 2016

10. We suggest that an antimicrobial treatment duration of 7 to 10 days is adequate for most serious infections associated with sepsis and septic shock (weak recommendation, low quality of evidence).
11. We suggest that longer courses are appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with *Staphylococcus aureus*, some fungal and viral infections, or immunologic deficiencies, including neutropenia (Weak recommendation, low quality of evidence).
12. We suggest that shorter courses are appropriate in some patients, particularly those with rapid clinical resolution following effective source control of intra-abdominal or urinary sepsis and those with anatomically uncomplicated pyelonephritis (weak recommendation, low quality of evidence).

Η PCT στην κλινική πράξη 2012 -2016

Intensive Care Med (2017) 43:304–377

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Andrew Rhodes[1*], Laura E. Evans[2], Waleed Alhazzani[3], Mitchell M. Levy[4], Massimo Antonelli[5], Ricard Ferrer[6],

SSC Guidelines 2012

4. Use of low procalcitonin levels or similar biomarkers to assist the clinician in the discontinuation of empiric antibiotics in patients who initially appeared septic, but have no subsequent evidence of infection (grade 2C).

SSC Guidelines 2016

14. We suggest that measurement of procalcitonin levels can be used to support shortening the duration of antimicrobial therapy in sepsis patients (weak recommendation, low quality of evidence).
15. We suggest that procalcitonin levels can be used to support the discontinuation of empiric antibiotics in patients who initially appeared to have sepsis, but subsequently have limited clinical evidence of infection (weak recommendation, low quality of evidence).

Surviving Sepsis Car
management of seve

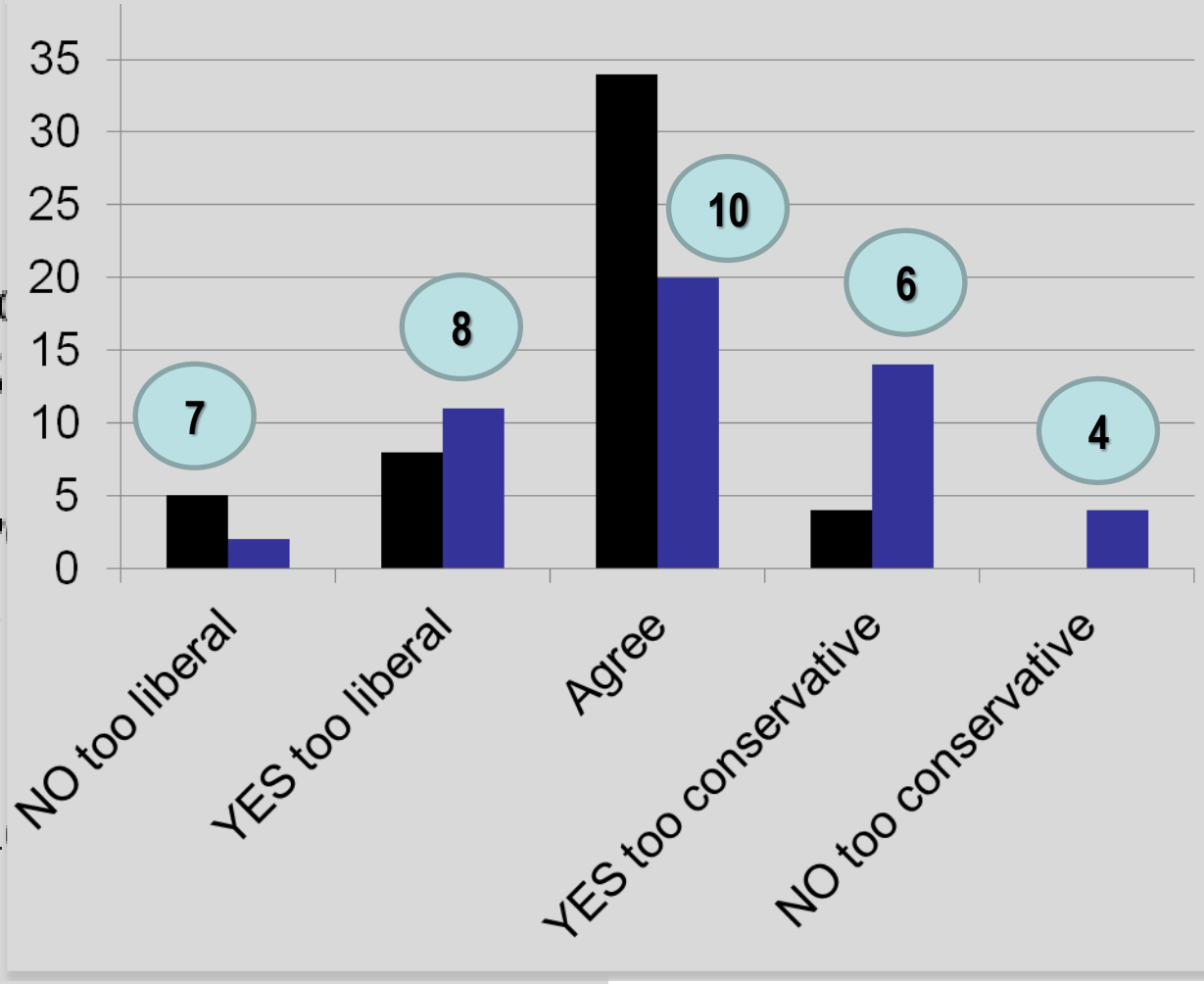
APPENDIX G

Glycemic Control

Glycemic contr
Total votes = 5
Agree—34
Too conservativ
Too liberal, but
Disapprove, too
Disapprove, too
Disapprove, oth

Προτεινόμενος τύπος εξετάσεων από το College des Enseignants de Reanimation

σε συγκεκριμένο ασθενή



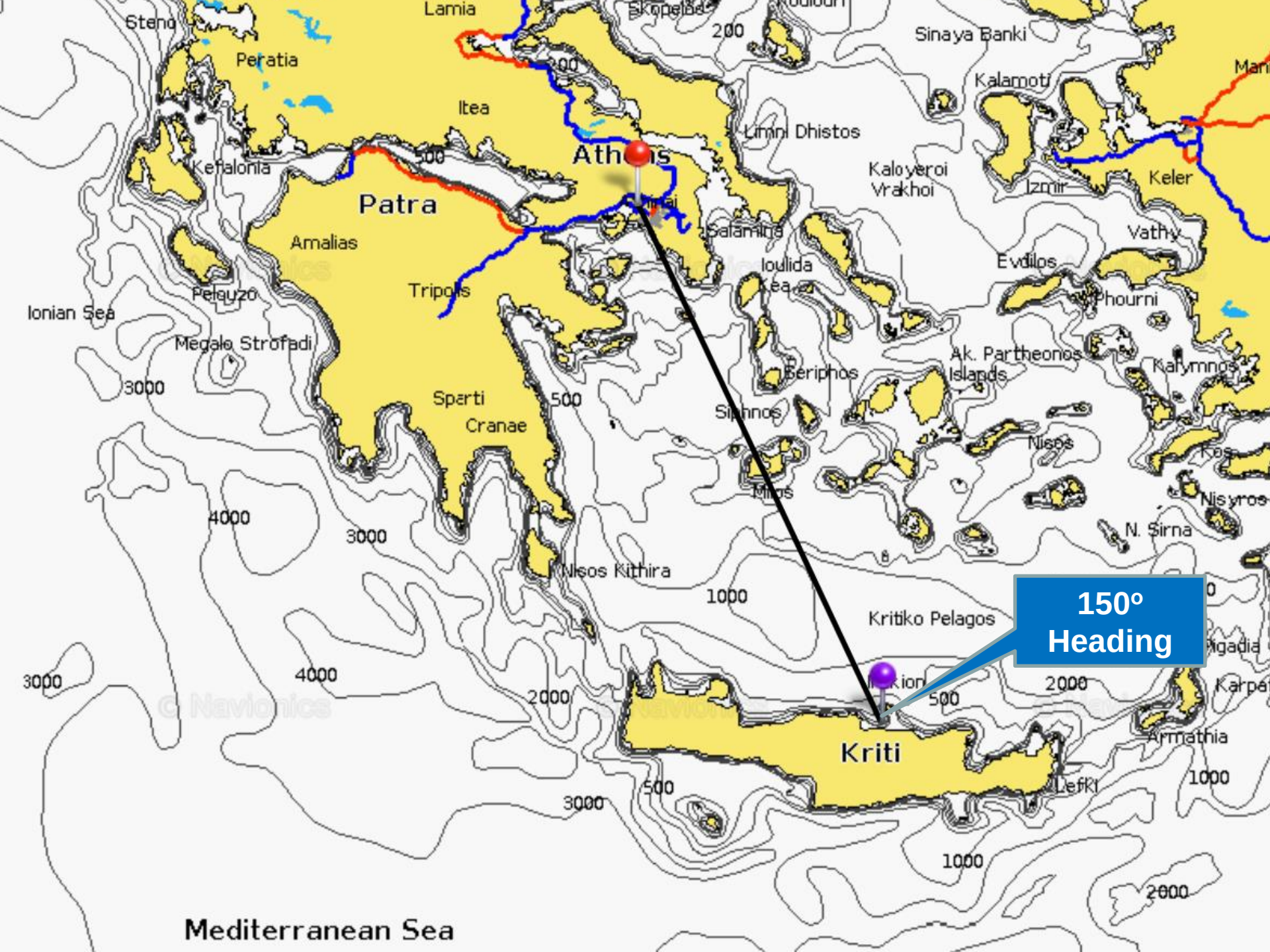
The role of Guidelines

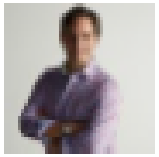
The recommendations in this document are intended to **provide guidance** for the clinician caring for a patient with severe sepsis or septic shock.

Recommendations from these guidelines **cannot replace the clinician's decision-making capability** when he is presented with a patient's unique set of clinical variables.

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4];


Sterea
Lamia
Peratia
Itea
Kefalonia
Patra
Amalias
Pelquzo
Ionian Sea
Megalo Strofadi
Tripolis
Sparti
Cranae
Athens
Salamina
Limni Dhistos
Kaloyeroi
Vrakhoi
Sinaya Banki
Kalamoti
Izmir
Keler
Vathy
Evdilos
Phourni
Ioulida
Kea
Ak. Partheonos
Islands
Kalymnos
Seriphos
Siphnos
Nisos
Kos
Nisyros
N. Sirna
Nisos Kithira
Kritiko Pelagos
Kriti
Armathia
Lefki
Karpa
150°
Heading
Mediterranean Sea
200
500
1000
2000
3000
4000



BY JOSH LINKNER *Entrepreneur, author, VC, Jazz guitarist* @JoshLinkner

Πλοήγηση από Πειραιά για Κρήτη

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

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 GPS 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.

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.

ΣΥΝΟΨΗ
ΒΑΣΙΚΑ ΣΗΜΕΙΑ
και
ΣΥΜΠΕΡΑΣΜΑΤΑ

(εικονογραφημένα)

BMJ

Grading quality of evidence and strength of recommendations

BMJ 2004;328;1490
doi:10.1136/bmj.328.7454.1490

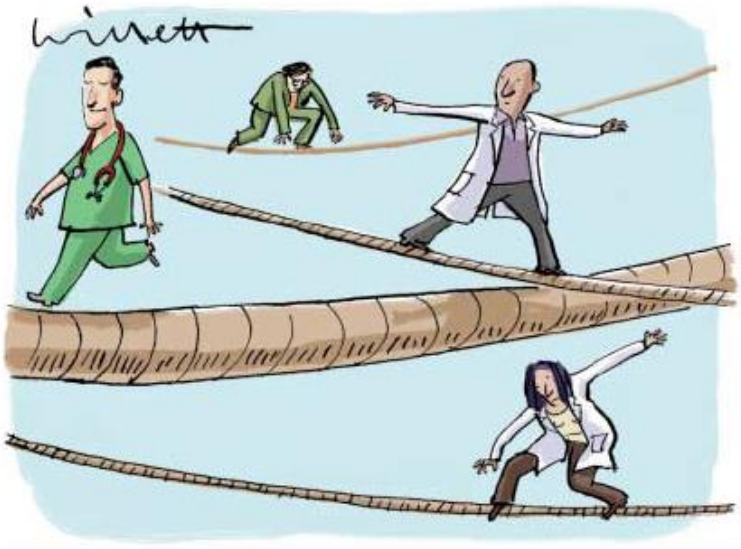
Grading quality of evidence and strength of recommendations

GRADE Working Group

Clinical guidelines are only as good as the evidence and judgments they are based on. The GRADE approach aims to make it easier for users to assess the judgments behind recommendations

Summary

Users of clinical practice guidelines and other recommendations need to know how much confidence they can place in the recommendations. Systematic and explicit methods of making judgments can reduce errors and improve communication. We have developed a system for grading the quality of evidence and the strength of recommendations that can be applied across a wide range of interventions and contexts. In this article we present a summary of our approach from the perspective of a guideline user. Judgments about the strength of a recommendation require consideration of the balance between benefits and harms, the quality of the evidence, translation of the evidence into specific circumstances, and the certainty of the baseline risk. It is also important to consider costs (resource utilisation) before making a recommendation. Inconsistencies among systems for



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

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

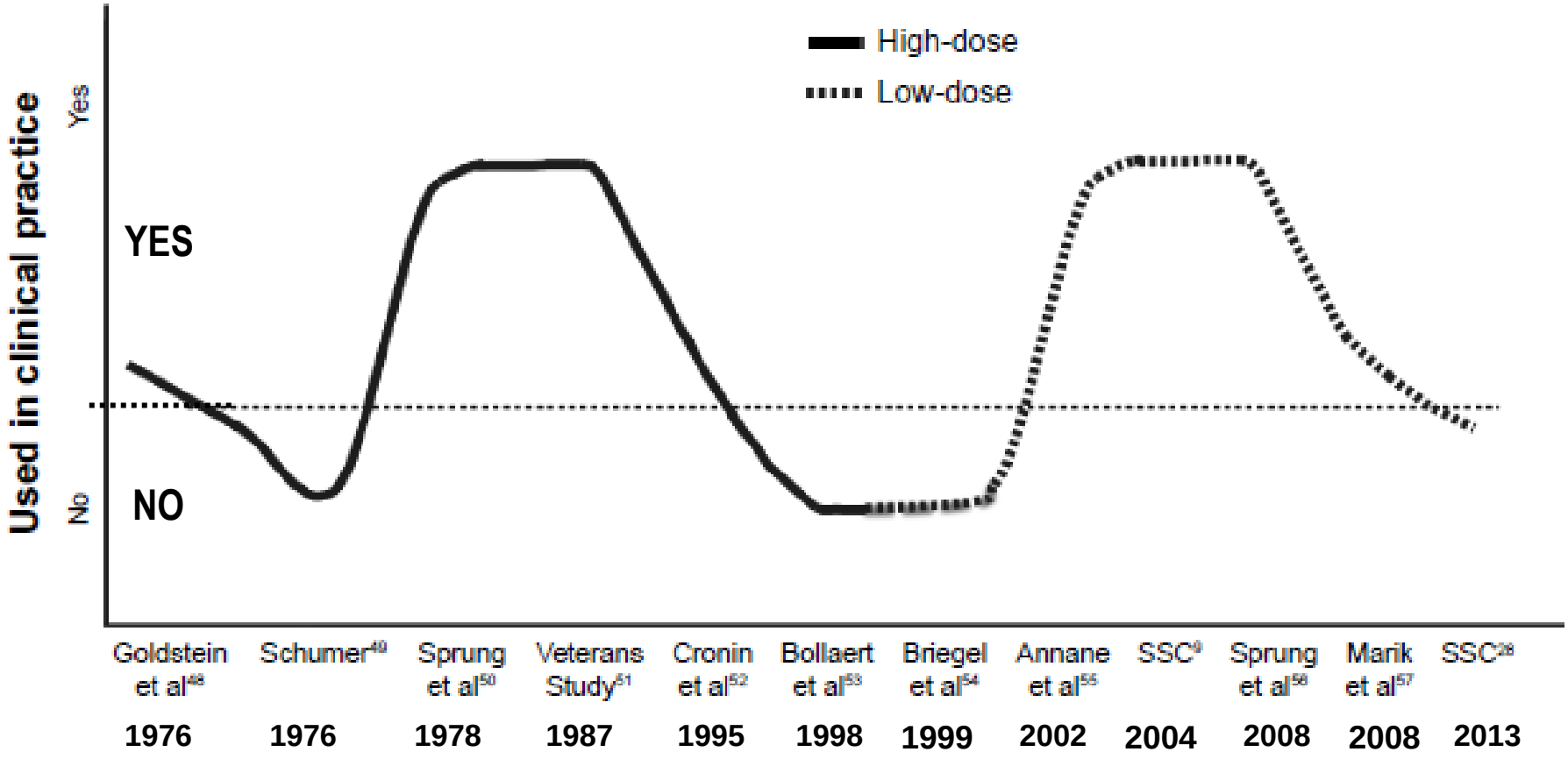


Figure 2 Steroids for treatment of infections, sepsis, and septic shock – ups and downs.
Abbreviations: SSC, Surviving Sepsis Campaign.

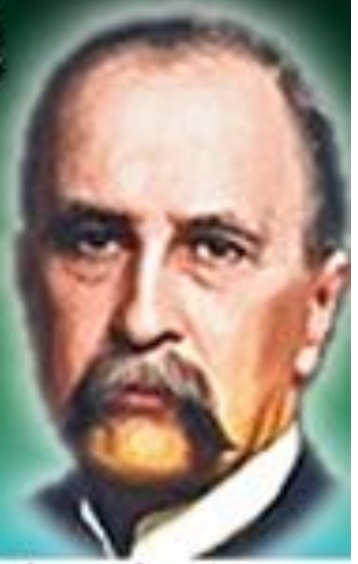
One size <u>DOES NOT</u> fits all

Luciano Gattinoni ???

Guidelines for Saturday night or for Monday morning ???

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

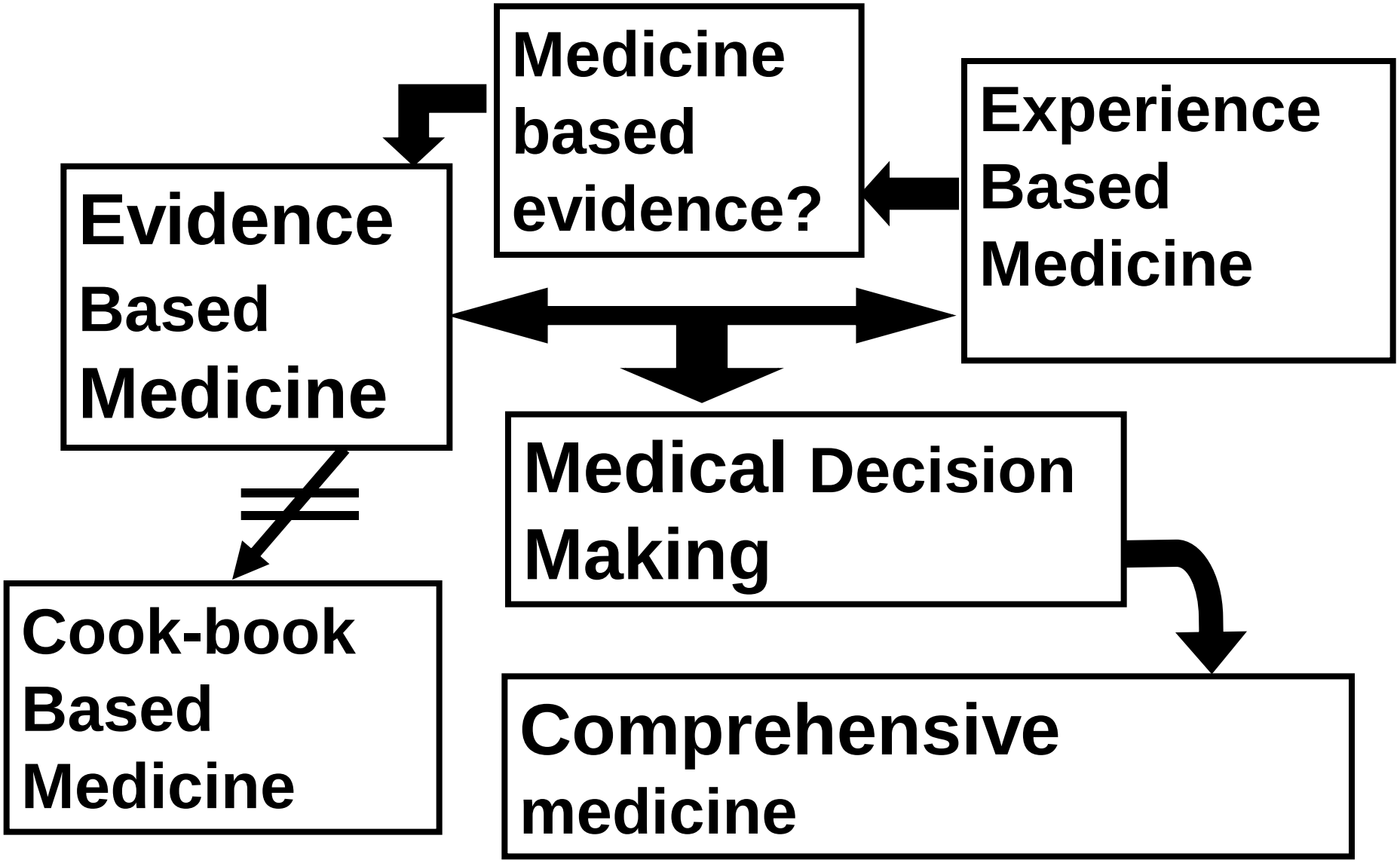


Evidence Based Medicine:
the wolf in sheep's clothing Cassiere et al 1998

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

Evidence-based medicine or fuzzy logic

Dreyffus and Salmon, Editorial in ICM 2002



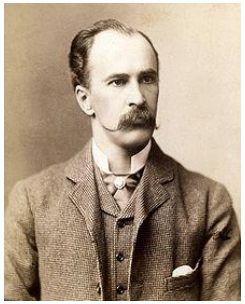
Είναι πολύ πιο σημαντικό να γνωρίζεις τον ασθενή, παρά την ασθένεια Ιπποκράτης

The good physician treats the disease;

the great physician treats the patient who has the disease

William Osler

1892



The good researcher studies the disease;

the great clinician *"translates" research* to "*customize treatment*" for the patient who has the disease

Conclusion: this is not a PRO – CON debate but a debate on "appropriate use" of EBM

Evidence Based Medicine must be used <u>as a tool for</u> and <u>not as a substitute of decision making</u>