Degrees of Recommendations and Levels of Evidence: What you Need to Know?

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Abstract

Clinical practice guidelines and other recommendations need to be used based on how much confidence can be placed in its recommendations. Systematic and explicit methods to make judgments can reduce errors and improve communication. In this article we present a summary of the practice approach to medicine based on evidence through the degrees of evidence and recommendation levels.

Keywords: Evidence based medicine; Degrees of recommendations; Levels of evidence

Introduction

We can define the practice of Evidence-Based Medicine (EBM) as the conscientious, explicit and judicious of the best available evidence in making decisions about care of a patient that requires integration of best evidence with clinical expertise and the values and circumstances of the patient (Figure 1). EBM requires new skills of the clinician, including efficient literature searching, and the application of formal rules of evidence in evaluating the clinical literature [1-16].

Figure 1: Define the practice of EBM.
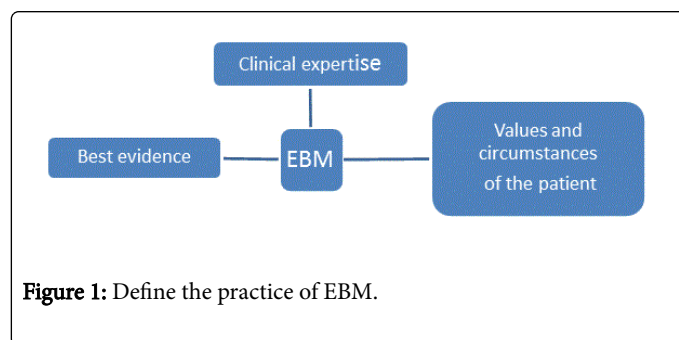
This practice basically comprises five steps: A1. Converting the need for information in a question structured; A2. Pursue the best clinical evidence to answer this question; A3. Critically evaluate this evidence with respect to its validity, importance and applicability; A4. Integrate critical appraisal with clinical expertise and with the values and circumstances of the patient; A5. Assess the effectiveness and efficiency in performing the steps above. Steps the EBM processes are presented in Table 1.

Table 1	Steps the EBM Process
ASSESS the patient	Start with the patient - a clinical problem or question arises from the care of the patient
ASK the question	Construct a well-built clinical question derived from the case
ACQUIRE the evidence	Select the appropriate resource(s) and conduct a search
APPRAISE the evidence	Appraise that evidence for its validity (closeness to the truth) and applicability (usefulness in clinical practice)
APPLY talk with the patient	Return to the patient - integrate that evidence with clinical expertise, patient preferences and apply it to practice

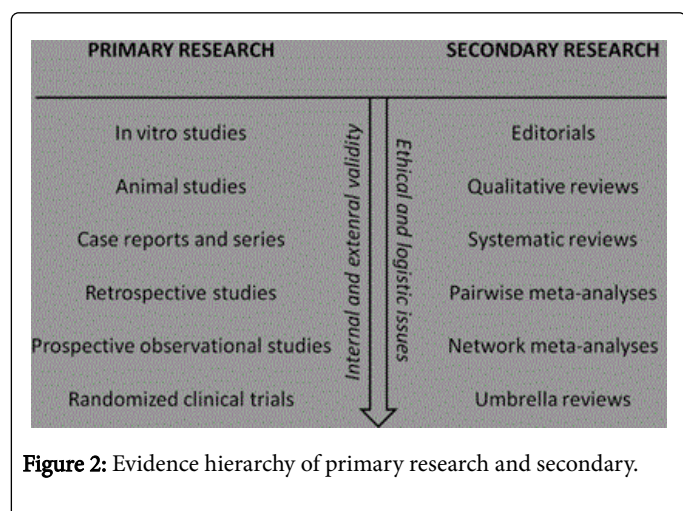**Table 1:** Steps in the EBM process.

The classification of the grade of recommendation corresponds to the strength of scientific evidence of the work and its main objectives: to provide transparency to the origin of the information, stimulate the search for scientific evidence of force majeure, introduce a didactic and simple way to help critical evaluation of the player, who bears the responsibility for making the decisions the patient being treated [2]. The degrees of recommendations are shown in Table 2.

Table 2	Grades of Recommendation
A	Directly based on Level I evidence
B	Directly based on Level II evidence or extrapolated recommendations from Level I evidence
C	Directly based on Level III evidence or extrapolated recommendations from Level I or II evidence
D	Directly based on Level IV evidence or extrapolated recommendations from Level I, II, or III evidence

Table 2: The degrees of recommendations. Data extrapolation can use in a situation that is potentially clinically important differences than the original study situation.

Levels of Evidence

Guidelines can deal with clinical issues such as diagnosis, prognosis, intervention, etiology and tracking. With this different research projects are developed, and consequently requires different hierarchies of evidence that recognize the importance of research designs relevant to the purpose of the guideline. Levels of evidence are presented in Figure 2 [2,16-22].

PRIMARY RESEARCH		SECONDARY RESEARCH
In vitro studies		Editorials
Animal studies		Qualitative reviews
Case reports and series		Systematic reviews
Retrospective studies	Internal and external validity / Ethical and logistic issues	Pairwise meta-analyses
Prospective observational studies		Network meta-analyses
Randomized clinical trials		Umbrella reviews

Figure 2: Evidence hierarchy of primary research and secondary.

Clinical trials are given to evaluate the safety and efficacy:

(1) A new product

(2) A new formulation of the same product or combination of products already in use

(3) A new clinical indication for a product already approved.

The assays can evaluate the therapeutic or prophylactic effect. *Studies* on *the etiology* are used in order to analyse the probable causes of the various types of diseases. When the perpetrators are discovered (or cause) of a specific disease, these are called "etiologic agents," precisely because they are the bodies responsible for development of a given pathology. Studies of harm are used to verify the effects of harmful agents on the important outcomes for patients [2].

Table 3	TPEH
IA	Systematic reviews (with homogeneity) of randomized controlled trials.
IB	Individual randomized controlled trials (with narrow confidence interval).
IC	All or none randomized controlled trials.
IIA	Systematic reviews (with homogeneity) of cohort studies
IIB	Individual cohort study or low quality randomized controlled trials (e.g. < 85% follow-up).
IIC	"Outcomes" Research; ecological studies.
IIIA	Systematic review (with homogeneity) of case-control studies.
IIIB	Case-control study.
IV	Case-series (and poor quality cohort and case-control studies)

V	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

Table 3: Levels of evidence for therapy, prevention, etiology and harm.

Diagnostic tests are invaluable tools used to distinguish between patients having a disease and those who have not. It is essential to be able to critically appraise published articles on a diagnostic test. The list of questions below can help you better appreciate and understand the diagnostic studies better [2]. Table 4 describes the levels of evidence for diagnosis.

Table 4	Diagnosis
IA	Systematic review (with homogeneity) of Level 1 diagnostic studies; or a clinical decision rule with 1b studies from different clinical centers.
IB	Validating cohort study with good reference standards; or clinical decision rule tested within one clinical center
IC	Absolute SpPins And SnNouts (An Absolute SpPin is a diagnostic finding whose Specificity is so high that a Positive result rules-in the diagnosis. An Absolute SnNout is a diagnostic finding whose Sensitivity is so high that a Negative result rules-out the diagnosis).
IIA	Systematic review (with homogeneity) of Level > 2 diagnostic studies
IIB	Exploratory cohort study with good reference standards; clinical decision rule after derivation, or validated only on split-sample or databases
IIIA	Systematic review (with homogeneity) of 3b and better studies
IIIB	Non-consecutive study; or without consistently applied reference standards
IV	Case-control study, poor or non-independent reference standard
V	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

Table 4: Levels of evidence.

Prognosis can be defined as the prediction of the future course of a disease after its installation. Patient groups are listed accompanied in time to measure their clinical outcomes [2]. Table 5 describes the levels of evidence for Prognosis.

Table 5	Prognosis
IA	Systematic review (with homogeneity) of inception cohort studies; or a clinical decision rule validated in different populations
IB	Individual inception cohort study with > 80% follow-up; or a clinical decision rule validated on a single population
IC	All or none case-series
IIA	Systematic review (with homogeneity) of either retrospective cohort studies or untreated control groups in randomized controlled trials.
IIB	Retrospective cohort study or follow-up of untreated control patients in a randomized controlled trial; or derivation of a clinical decision rule or validated on split-sample only
IV	"Outcomes" research

V	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

Table 5: Levels of evidence for prognosis.

Studies on the differential diagnosis are used in patients with a particular clinical presentation to set the frequency of adjacent disturbances [2]. Table 6 describes the levels of evidence for differential diagnosis / symptom prevalence study.

Table 6	Differential diagnosis / symptom prevalence study
IA	Systematic reviews (with homogeneity) of prospective cohort studies
IB	Prospective cohort study with good follow-up
IC	All or none randomized controlled trials.
IIA	Systematic reviews (with homogeneity) of 2b and better studies
IIB	Retrospective cohort study or poor follow-up.
IIC	Ecological studies.
IIIA	Systematic review (with homogeneity) of 3b and better studies
IIIB	Non-consecutive cohort study, or very limited population
IV	Case-series or superseded reference standards
V	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles".

Table 6: Levels of evidence for differential diagnosis / symptom prevalence study.

Economic analysis is a systematic and comparative assessment of the costs and consequences of two or more alternative treatments or programs of action for the promotion and health care. The basic function of an economic analysis is to identify, quantify, assess and compare the costs and consequences of alternatives considered for promotion and health care. The decision analysis to compare two or more decision options and this process involves identifying all available management options, and potential outcomes of each of a series of decisions that have to be made about patient care [2]. Table 7 describes the levels of evidence for Economic and decision analyses.

Table 7	Economic and Decision Analysis
IA	Systematic reviews (with homogeneity) of Level 1 economic studies
IB	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses
IC	Absolute better-value or worse-value analyses
IIA	Systematic reviews (with homogeneity) of Level > 2 economic
IIB	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses
IIC	Audit or outcomes research
IIIA	Systematic review (with homogeneity) of 3b and better studies

IIIB	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible
IV	Analysis with no sensitivity analysis
V	Expert opinion without explicit critical appraisal, or based on economic theory or "first principles"

Table 7: Levels of evidence for economic and decision analyses.

In conclusion, the conscious use of specific best evidence in making decisions, and the use of levels of evidence and grades of recommendations can benefit the patient and improve their clinical practice.

References

1. Evidence-Based Medicine Working Group (1992) Evidence-based medicine. A new approach to teaching the practice of medicine. JAMA 268: 2420-2425.
2. Guyatt G, Meade MO, Cook DJ, Rennie D (2014) Users' Guides to the Medical Literature: A Manual for Evidence-based Clinical Practice, Third edition. New York.
3. Sackett DL, Richardson WS, Rosemberg WS, Rosenberg W, Haynes BR (1997) Evidence-Based Medicine: how to practice and teach EBM. Churchill Livingstone.
4. Bligh J (1995) Problem-based learning in medicine: an introduction. Postgrad Med J 71: 323-326.
5. Guyatt GH, Sackett DL, Cook DJ (1993) Users' guides to the medical literature. II. How to use an article about therapy or prevention. A. Are the results of the study valid? Evidence-Based Medicine Working Group. JAMA 270: 2598-2601.
6. Guyatt GH, Sackett DL, Cook DJ (1994) Users' guides to the medical literature. II. How to use an article about therapy or prevention. B. What were the results and will they help me in caring for my patients? Evidence-Based Medicine Working Group. JAMA 271: 59-63.
7. Jaeschke R, Guyatt G, Sackett DL (1994) Users' guides to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid? JAMA 271: 389-391.
8. Jaeschke R, Guyatt GH, Sackett DL (1994) Users' guides to the medical literature. III. How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? The Evidence-Based Medicine Working Group. JAMA 271: 703-707.
9. Levine M, Walter S, Lee H, Haines T, Holbrook A, et al. (1994) Users' guides to the medical literature. IV. How to use an article about harm. Evidence-Based Medicine Working Group. JAMA 271: 1615-1619.
10. Laupacis A, Wells G, Richardson WS, Tugwell P (1994) Users' guides to the medical literature. V. How to use an article about prognosis. JAMA 272: 234-237
11. MI (1996) Epidemiologia Clínica: Elementos Essenciais. Porto Alegre, Artes Médicas.
12. Friedland DJ (1998) Evidence-Based Medicine: A Framework for Clinical Practice, Appleton & Lange, Stanford, CT.
13. Sackett DL, Richardson WS, Rosemberg WS, Rosenberg W, Haynes BR (2005) Evidence-Based Medicine: how to practice and teach EBM. Churchill Livingstone.
14. Garg AX, Adhikari NK, McDonald H, Rosas-Arellano MP, Devereaux PJ, et al. (2005) Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review. JAMA 293: 1223-1238.
15. Guyatt G, Rennie D, Meade MO, Cook DJ (2008) Users´Guides to the Medical Literature.
16. Wyer P, Hatala R, Guyatt G (2005) Challenges of teaching EBM. CMAJ. 172: 1424-1425.

17. Levels of Evidence (2010) Centre for Evidence-Based Medicine.

18. Burns PB, Rohrich RJ, Chung KC (2011) The levels of evidence and their role in evidence-based medicine. Plast Reconstr Surg. 128: 305-310.

19. Greco T, Biondi-Zoccai G, Saleh O, Pasin L, Cabrini L, et al. (2015) The attractiveness of network meta-analysis: a comprehensive systematic and narrative review. Heart Lung Vessel 7: 133-142.

20. Biondi-Zoccai G (2014) Network Meta-analysis: Evidence Synthesis with Mixed Treatment Comparison. Nova Science Publishers, Hauppauge, NY.

21. Biondi-Zoccai G, Abbate A , Benedetto U , Palmerini T , D'Ascenzo F, et al. (2015) Network meta-analysis for evidence synthesis: What is it and why is it posed to dominate cardiovascular decision making? International Journal of Cardiology 182: 309–314.