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REVIEW ARTICLE

Evidence based medicine

Anogianakis G[1], Ilonidis G[2]

[1]Dept of Physiology, Faculty of Medicine, Aristotle University of Thessaloniki, Greece
[2]Fourth Dept of Medicine, Aristotle University of Thessaloniki, Hippokratio General Hospital, Greece

Evidence based medicine (EBM) is the integration of best research evidence with clinical expertise and patient values, for the best possible patient management. It is the explicit and judicious use of current best evidence in making decisions about the treatment and care of individual patients. In practice, it means integrating the individual clinical skills of the doctor with the best available clinical evidence from systematic research. EBM is a "patient-centred" rather than "physician-centred" brand of medicine. It deals with clinical problems and questions that arise in the course of caring for individual patients. The practice of EBM is always triggered by a patient encounter which generates questions about the effects of therapy, the utility of diagnostic tests, the prognosis of disease or the etiology of a disorder. It always proceeds in five concrete steps that start from the construction of a clinical question; through the conduct the tracking down of the best evidence of outcomes that is presently available; onto the critical appraisal of the existing evidence and its application to the patient, ending with the physicians' self-evaluation of their performance.
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Corresponding author: Anogianakis G, Dept of Physiology, Faculty of Medicine, Aristotle University of Thessaloniki, 54124 Thessaloniki, Greece. Tel :+302310-999054 E-mail:anogian@auth.gr

What is EBM?

As in the case of any still developing field of medicine, there are many definitions of EBM. Each of them underlines some specific aspects of EBM practice (Table 1) and it reflects the reasons for which the user is practicing EBM.

For our present purposes we will define EBM as "the integration of best research evidence with clinical expertise and patient values, so as to achieve the best possible patient management". Since in clinical practice physicians make decisions, one can argue that EBM represents an attempt to make better decisions by improving the quality of information on which those decisions are based. Furthermore, the information that is relevant to EBM is empirical evidence about what works and what does not work when treating a disease; it has nothing to do with the pathophysiology of the disease.

This point is amply illustrated by the story of flecainide Glasziou et al[11]. Flecainide was used in the 80's to treat heart attacks. The idea was that since a heart attack, many times, leads to ventricular fibrillation and results in death, the administration of "a safe and long-acting antiarrhythmic drug that protects against ventricular fibrillation" to people at risk should save millions of lives. This "pathophysiologically sound" suggestion led to the widespread use of flecainide, which was an antiarrhythmic agent. Indeed, patients on flecainide had fewer preventricular contractions than patients on placebo. Since arrhythmias were the cause of death from heart attack, researchers concluded that people who had survived a heart attack should be given flecainide. Within 18 months of flecainade's introduction, however, it was clear that the death rate in the group of patients who were treated by flecainide was double than that in the placebo group. Eventually, the treatment had to be abandoned.

The moral of the flecainide story is twofold:

1. Despite our knowledge of the underlying mechanisms, other factors, not important in terms of pathophysiology but clearly important in terms of the intended outcome (i.e. patient survival and better quality of life), are at play. In the case of flecainide these factors made the drug toxic/dangerous.

2. More than information on the pathophysiology of the disease they treat, practicing physicians need information on the effectiveness of the treatment they prescribe, both in terms of patient survival and in terms of the possible improvements in the quality of their patients' lives.

EBM is a "patient-centred" rather than "physician-centred" brand of medicine. It deals with clinical problems and questions that arise in the course of caring for individual patients. The practice of EBM is always triggered by a patient encounter which generates questions about the effects of therapy, the utility of diagnostic tests, the prognosis of disease or the etiology of a disorder.

Table 1. *Definitions of EBM*

Origin	Definition/quote
Sackett DL, et al[1]	EBM is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of EBM means integrating individual clinical expertise with the best available external clinical evidence from systematic research. By individual clinical expertise we mean the proficiency and judgment that individual clinicians acquire through clinical experience and clinical practice. Increased expertise is reflected in many ways, but especially in more effective and efficient diagnosis and in the more thoughtful identification and compassionate use of individual patients' predicaments, rights, and preferences in making clinical decisions about their care. By best available external clinical evidence we mean clinically relevant research, often from the basic sciences of medicine, but especially from patient centered clinical research into the accuracy and precision of diagnostic tests (including the clinical examination), the power of prognostic markers, and the efficacy and safety of therapeutic, rehabilitative, and preventive regimens. External clinical evidence both invalidates previously accepted diagnostic tests and treatments and replaces them with new ones that are more powerful, more accurate, more efficacious, and safer.
McKibbon KA, et al[2]	EBM is an approach to health care that promotes the collection, interpretation, and integration of valid, important and applicable patient-reported, clinician-observed, and research-derived evidence. The best available evidence, moderated by patient circumstances and preferences, is applied to improve the quality of clinical judgments.
Appleby J, et al[3]	EBM involves evaluating rigorously the effectiveness of healthcare interventions, disseminating the results of evaluation and using those findings to influence clinical practice. It can be a complex task, in which the production of evidence, its dissemination to the right audiences, and the implementation of change can all present problems
Rosenberg W and Donald A[4]	EBM is the process of systematically finding, appraising, and using contemporaneous research findings as the basis for clinical decisions. EBM asks questions, finds and appraises the relevant data, and harnesses that information for everyday clinical practice. EBM follows four steps: formulate a clear clinical question from a patient's problem; search the literature for relevant clinical articles; evaluate (critically appraise) the evidence for its validity and usefulness; implement useful findings in clinical practice. The term "evidence based medicine" (no hyphen) was coined at McMaster Medical School in Canada in the 1980's to label this clinical learning strategy, which people at the school had been developing for over a decade
Cook DJ, Levy MM[5]	EBM involves caring for patients by explicitly integrating clinical research evidence with pathophysiologic reasoning, caregiver experience, and patient preferences. EBM is a style of practice and teaching which may also help plan future research
Geddes JR, Harrison PJ[6]	EBM is also a way of ensuring that clinical practice is based on the best available evidence through the use of strategies derived from clinical epidemiology and medical informatics
Muir Gray JA[7]	Evidence based clinical practice is an approach to decision making in which the clinician uses the best evidence available, in consultation with the patient, to decide upon the option which suits that patient best
First Annual Nordic Work-shop on how to critically appraise and use evidence in decisions about healthcare, National Institute of Public Health, Oslo, Norway[8]	Evidence-based healthcare is the conscientious use of current best evidence in making decisions about the care of individual patients or the delivery of health services. Current best evidence is up-to-date information from relevant, valid research about the effects of different forms of health care, the potential for harm from exposure to particular agents, the accuracy of diagnostic tests, and the predictive power of prognostic factors
Hicks N[9]	Evidence-based healthcare takes place when decisions that affect the care of patients are taken with due weight accorded to all valid, relevant information
Marwick C[10]	Evidence-based healthcare is a conscientious, explicit, and judicious use of the current best evidence to make a decision about the care of patients
Centre for Evidence Based Medicine Glossary http://www.cebm.net cited Sept 9, 2004	Evidence-Based Health Care extends the application of the principles of Evidence-Based Medicine (see above) to all professions associated with health care, including purchasing and management

Table 2. *Steps in EBM*

Step	Purpose
State the question	To construct a well built, i.e., answerable, clinical question derived from the case at hand.
Do the evaluation	To select the appropriate resource(s) and conduct the necessary search in order to track down the best evidence of outcomes that is presently available.
Judge the utility of the available resources	To critically appraise the evidence gathered for its validity (i.e., how close it is to the truth) and applicability (i.e., its usefulness) in the case at hand.
Get back to the patient	To apply the evidence in the case at hand, by using it to "hone" the physician's clinical expertise and by taking the patient preferences into account.
Perform a self-evaluation	To evaluate the physician's performance with each patient.

What Table 2 demonstrates is that, formally or informally, most of the activities that characterize EBM are used by clinicians ever since the early days of medicine. In fact, "western" medicine, as recently as 50 years ago, was EBM. Today's "alternative" and/or "traditional" types of medicine (e.g., herbal medicine, Ayurveda etc) are also EBM-like in the sense that their practitioners use their cumulative experience to formulate a clinical strategy for each case at hand rather than their knowledge of pathophysiology. In any case, such knowledge did not exist at least until the middle of the 17th century: William Harvey, e.g., described the circulation in 1628; Anthony van Leeuwenhoek invented the microscope in 1673, and Luigi Galvani described "animal electricity" in 1780. Finally, there are few practicing clinicians who do not use the literature, at least occasionally, to guide their decisions. What EBM adds to the traditional clinical approach is the formalization of the literature consultation process and the addition to it of the necessary filtering of the literature so that the decisions taken are always based on both the "strongest" and the "most relevant" evidence.

That being as it may, critics perceive an overt reliance of EBM on literature which has prompted them to call EBM "cook book medicine". They view EBM guided decisions as based solely on the evidence rather than on sound clinical judgment. The answer is that EBM does not supersede or annul individual clinical expertise but it represents a substantial part of clinical decision making (see /1; also http://www.hsl.unc.edu/lm/ebm/index.htm cited Sept 10, 2004). Evidence supports and supplements individual clinical expertise and helps the physician to satisfy patient preferences.

Another concern is that EBM relies on population studies to treat individuals (also at http://www.hsl.unc.edu/lm/ebm/index.htm cited Sept 10, 2004); that it takes the results of studies of large groups of people and tries to apply them to individuals who may have unique circumstances or characteristics, not found in the study groups. This is valid criticism insofar as it is not always possible to decide whether or not the information and results are applicable to the individual patient. In addition, discussing the results with the patient, as it is required by the EBM process, opens up the possibility for the patient to misunderstand the evidence and, as a result, to hinder the process of clinical decision making. In addition, some times there are no randomized controlled trials or "a gold standard" that applies to the clinical question at hand. In this case the clinician has the burden to decide how strong his evidence should be and to look for the best compromise as far as the strength of evidence is concerned.

The strength the different types of evidence can be thought of as a stepped pyramid (Figure 1). The stronger the evidence, the higher the level on the pyramid it occupies. The base of the "evidence pyramid" rests on the basic medical sciences (Anatomy, Biochemistry, Microbiology, Pathology, Pharmacology, Physiology, etc), the different clinical disciplines (Internal Medicine, Surgery, etc) and the different medical specialties. Clinical research most often starts from an observation or some compound suspected to have medicinal value or, finally, from a "raw" idea. All these have to be investigated at the level of pathophysiology, a process that starts with laboratory models, proceeds with animal testing, and finally ends with tests on humans. Human testing usually begins with volunteers and goes through several phases of clinical trials before the drug or diagnostic tool can be authorized for use within the general population. Randomized controlled trials are then done to further test the effectiveness and efficacy of a drug or therapy.

If the physician does not find the best level of evidence to answer his question, then he should consider moving down the pyramid and use other types of studies to supplant his clinical judgment. After all, in some cases there is no real evidence to support clinical judgment. In these cases the clinician should rely upon his knowledge of pathophysiology to guide him through. A simple definition for the type of evidence that forms each of the steps of the "evidence pyramid" is given in Table 3 along with indications as to the "strength" of each type of evidence. A guide as to how to "climb down" the pyramid steps in order to find the evidence best fitting a question is given in Table 4. Finally, one should be aware of Practice Guidelines. These are systematically developed statements that review, evaluate the evidence and make explicit recommendations. When available, they are of assistance to both practitioner and patient, helping to make decisions for specific clinical circumstances.

The ultimate application of EBM is at the level of the individual clinician's decisions about his patient. EBM, therefore, is an explicit approach to clinical problem solv-

Figure 1. *The "evidence pyramid" which is used to illustrate the evolution of the literature and indicate the strength of evidence available. As one moves up the pyramid the amount of available literature decreases while its relevance to the clinical setting increases. Adopted and adapted from http://www.hsl.unc.ed/lm/ebm/index.htm cited Sept 10, 2004*

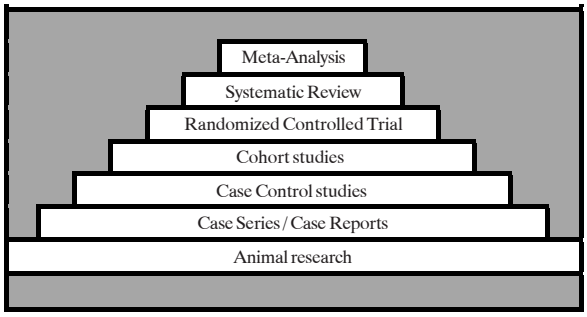

Table 3. *The constituting steps of the "evidence pyramid"*

Type of evidence	Informal Definition & Indications as to the evidence's "strength"
Meta-analysis	It uses statistical techniques to combine the results of several studies into one large study.
Systematic Reviews	They focus on a clinical topic and answer specific questions. They are based on extensive literature searches in order to identify studies with sound methodology. These studies are then reviewed, assessed, and summarized.
Randomized Controlled Trials (RCT)	They are carefully planned studies of the effect of a therapy or a test on patients. They attempt to reduce the potential for bias and allow for comparison between intervention and control groups.
Cohort Studies	They use large population samples and follow patients with a specific condition or patients , who receive a particular treatment over time and compare them with another group that is similar but has not been affected by the condition being studied.
Case Control Studies	They compare patients who have a specific condition with people who do not. They are less reliable than randomized controlled trials and cohort studies because statistical relationships do not imply causal links.
Case Series/ Case Reports	They are collections of reports on the treatment of individual patients (a report refers to a single patient). Since they cannot use controls with which to compare outcomes, they have no statistical validity.
Animal research	Delineation of the mechanisms of action of drugs and treatments and studies on the pathophysiology of disease.

Table 4. *Climbing down the "evidence pyramid"*

Therapy	RCT>cohort > case control > case series
Diagnosis	prospective, blind comparison to a gold standard
Etiology/Harm	RCT > cohort > case control > case series
Prognosis	cohort study > case control > case series
Prevention	RCT>cohort study > case control > case series
Clinical Exam	prospective, blind comparison to gold standard
Cost	economic analysis

ing, which requires the use of current best evidence in making medical decisions about each individual patient. It is also a way of professional development that relies on continual professional learning. Finally, EBM is based on the assessment by the physician of the validity of the information he gathers and his judgement as to its relevance to the individual patient.

It is clear that although EBM has been criticized for the fact that most of its actions or steps are in use by clinicians ever since the early days of medicine, in fact it would have been impossible for EBM to exist at any time prior to the 1980s. As late as the 1960s scientific (medical) information production was still manageable. Starting in the 1970s, however, it became large enough as to overwhelm the most studious and willing physician. Had the Internet and the associated databases and search engines not come of age, practicing EBM would not be what it is today. In 1979, for example, Professor Archie Cochrane /12 was complaining that "It is surely a great criticism of our profession that we have not organized a critical summary, by specialty or subspecialty, adapted periodically, of all relevant RCTs" .In other words, in 1979, even for a visionary like professor Cochrane, it was impossible to perceive that critical summaries "of all relevant RCTs" would be carried out by individual physicians, for each individual patient they treated; instead, the task seemed so huge that only a collective, slowly adapting effort to identifying "valid information" seemed to be the answer.

In order to achieve evidence-informed decisions, by searching secondary databases as well as the primary literature for relevant articles, by assessing the validity and usefulness of those articles and by judging the relevance of them to the individual patient, the health practitioner should be familiar with the precepts and IT tools available for practicing EBM. It is such a familiarity that makes it possible to bring the enormous relevant literature under control, and, as databases improve, to answer clinical questions at the point of care in real time.

Again, the Internet and its associated information handling technologies are the best place to start (and in most cases, end) the search. But this is not the end of the story: Again, EBM is the only way that a teleconsultant

can cope with such situations that tax the knowledge that an ordinary physician uses in his daily practice. Diseases that are characteristic of the so-called "western lifestyles," also appear in the less developed countries of the world. The treatment of cancer, cardiovascular diseases or pregnancy related problems is also of concern there, albeit in a different light and with respect to local population characteristics. The lifestyle related aggravating factors, for example, in the case of cardiovascular diseases, will definitely be different for a near-starvation reared patient in an African village than for a middle aged wealthy merchant from a neighboring city.

How are EBM services delivered?

Accessing the sources of evidence

Practicing EBM is synonymous to searching the published literature (Second step of the EBM process; Table 2) to find answers to clinical questions that were formulated during the first step ("State the question"; Table 2). In most cases, a well-built clinical question leads directly to a good search strategy. Always, the goal is to locate a randomized controlled trial; it would provide good evidence to help answer the clinical question. Since, at present, there are, roughly, approximately 15 million published reports, journal articles, correspondence and studies available to clinicians, choosing the best resource to search is an important decision. Large databases such as MEDLINE are good conduits to the primary literature. Secondary resources such as ACP Journal Club, POEMS and Clinical Evidence, provide assessments of the original studies. The Cochrane Library provides access to systematic reviews which help summarize the results from a number of studies. The main getaways to the EBM literature and practice guidelines are summarized in Table 5.

Starting from one of the getaways listed in Table 5,

Table 5.

No	Source	Content
1	Agency for Health Care Research and Policy (AHRQ) http://www.ahrq.gov cited Sept 9, 2004	Contains information about EBM including downloading of full text articles in .pdf. It also provides general knowledge concerning usual health problems and public health matters.
2	Bandolier http://www.jr2.ox.ac.uk/bandolier cited Sept 20, 2004	Monthly independent journal about Evidence based Healthcare. It contains reviews and analyses appearing in Pubmed and in the Cochrane Library.
3	BestBETS http://www.bestbets.org cited Sept 9, 2004	Developed by the Emergency Department of the Manchester Royal Infirmary in UK, it gives rapid answers to real life clinical questions. Focused on Emergency Medicine, it also contains a significant number of articles about cardiology, nursing, primary care and pediatrics. It links with other EBM websites.
4	Centre for Evidence Based Medicine http://www.cebm.net cited Sept 9, 2004	Developed by Oxford University, it contains information about EBM along with an EBM glossary, and FAQ about the practice of EBM
5	CINAHL http://www.urmc.rochester.edu/hslt/miner cited Sept 9, 2004	The Edward G. Miner Library is a digital library containing many databases, Medline, e-journals, e-books and is accessible from home. It contains resources for researchers, patients, students and professionals. In addition it contains an option for rare books and manuscripts in the area of medical, dental and nursing history.
6	Cochrane Library and Collaboration http://www.cochrane.org cited Sept 9, 2004	It has links to many sites concerning EBM. It contains over 350,000 controlled trials and 1500 systematic reviews. It is available both on CD-ROM and in the Internet (there are many databases included in the library). Search for words or for title is possible, while the on-line version of the library can be read in English, German, French, Chinese, Italian and Brazilian. Full text reviews can be downloaded.
7	EBM Tool Kit http://www.med.ualberta.ca/ebm/ebm.htm cited Sept 9, 2004	Developed at the University of Alberta, Canada, it contains an EBM glossary, links to other EBM sites, and strategies for more fruitful search such as a "basic search strategy", a "quick filter", and an "advanced search strategy"
8	Evidence- Based Medicine http://www.evidence-basedmedicine.com cited Sept 9, 2004	It is a bi-monthly journal , which includes articles concerning family practice, internal medicine, pediatrics, obstetrics, gynecology, psychiatry and surgery. It has many EBM Links and the ability to view the top 10 papers concerning EBM.
9	Evidence-Based Medicine Education Center of Excellence http://www.hsl.unc.edu/ahec/ebmcoe/pages/index.htm cited Sept 9, 2004	Developed by the University of North Carolina, it contains abstracts , links to the Cochrane Library and Pubmed databases, links to 2 e-journals and specific knowledge for learning and teaching EBM
10	http://healthweb.org cited Sept 9, 2004	Developed by the University of Illinois at Chicago, it links to EBM Websites, databases (like the Cochrane Library, the Pubmed, and the Trip Database), electronic journals and associations

No Source	Content
11 Health Information Research Unit - McMaster University http://hiru.hirunet.mcmaster.ca cited Sept 9, 2004	Developed by the McMaster University, it contains links to the Canadian Network and to Cancer Care Ontario
12 http://www.hsl.duke.edu/lm/ebm/ index.htm cited Sept 9, 2004	Contains an introduction to EBM along with an EBM glossary, a tutorial on the practice of EBM (including instruction on how to, e.g., conduct a literature search) and a presentation of a few cases for testing one's skills in using EBM.
13 MEDLINE http://www.uic.edu/depts/lib/lhsp/ resources/med.shtml cited Sept 9, 2004	This is the Premiere Biomedical Database. It was developed in the University of Illinois at Chicago and it provides information about other EBM Databases, EBM publications and internet resources. It contains over 4000 international biomedical journals and provides access to PubMed and Ovid Medline
14 National Guidelines Clearinghouse http://www.guideline.gov cited Sept 9, 2004	Developed by the US Department of Health and Human Services, it contains abstracts and links to full text guidelines. It permits the comparison of two or more guidelines and resources for themes such as bioterrorism, bibliographies, and glossary for terms used in abstracts and frequently asked questions.
15 Netting the Evidence http://www.shef.ac.uk/˜scharr/ir/netting cited Sept 9, 2004	Developed in Sheffield, UK, it contains journals, databases (including the Cochrane Database but not Pubmed), links to EBM Organizations and full text documents
16 POEMS (Patient Oriented Evidence That Matters) http://www.infopoems.com/	POEMS contains over 200 summaries of evidence based articles.
17 TRIPDatabase http://www.tripdatabase.com cited Sept 9, 2004	It is a monthly updated database which initially contained 1,100 links to EBM articles. It contains TripWire which is a way for users, to focus and specify their search.
18 University of Washington Pediatrics EBM CAT-Bank http://pedsccm.wustl.edu/EBS/ EB_Resources.html cited Sept 9, 2004	It provides a free access to full-text articles about EBM and links to EBM databases, groups in the web, journals and systematic reviews, along with a user's guide to medical literature.
19 University of Michigan Evidence-Based Pediatrics Critically Appraised Topics http://www.med.umich.edu/pediatrics/ ebm cited Sept 9, 2004	Developed by the Department of Pediatrics in the University of Michigan, it offers access to EBM links, a methodology for teaching EBM and a number of critically appraised topics in many medical specialties (cardiology, nephrology, neonatology, neurology, etc).
20 US Preventive Services http://odphp.osophs.dhhs.gov cited Sept 9, 2004	This page provides direct Internet access to the Guide to Clinical Preventive Services which is also available via the National Library of Medicine's HSTAT (Health Services/Technology Assessment Text) database at http://text.nlm.nih.gov/ and the Office of Disease Prevention and Health Promotion at http://odphp.osophs.dhhs.gov/pubs/guidecps. The latest information on the Guide is online at http://www.ahrq.gov/clinic/prevnew.htm
21 http://www.york.ac.uk/inst/crd/search.htm cited Sept 9, 2004	It is a center for review and dissemination that offers reviews on specific topics, links to three databases (DARE, NHS, HTA), publications, and a dissemination service able to accept enquiries via e-mail in the case of a question by the reader.
22 PUBMED http://www.ncbi.nlm.nih.gov/entrez/ query.fcgi	It is a database providing access mainly to MEDLINE and also to in-process citations and publisher supplied citations. MEDLINE contains bibliographic citations and author abstracts from more than 4,800 biomedical journals published in the United States and 70 other countries. The database contains over 12 million citations starting from the midcentury. A direct search is available from the home page, which may contain either the author's name or the journal titles and the title of the article. For more filtered and specific search the options of a)clinical queries b)the MESH database and the c)Journals database are available among others

or any other comparable source, one can collect and review both the titles and abstracts, that the search comes up with, and attempt to identify potentially relevant articles. What is fairly certain, is that at the end of a diligent search there will be a number of articles and other primary sources of current information , which can answer the clinical questions that were formulated during the first step of the EBM process. The next step is to read the article and evaluate the information keeping in mind that everything that will follow hinges upon three basic questions that need to be answered for every type of study:

1. Are the results of the study valid?
2. What are the results?
3. Will the results help in caring for the patient?

Normally, within a regular research paper or report,

the answers to these questions are found in the methodology section. It is here where the investigators normally address issues of statistical or systematic bias. Randomization, blinding and proper accounting for all patients and materials help insure that the study results are not overly influenced by the investigators, the patients or other external factors. However, apart from these general admonitions as to the design of a study that aspires to provide evidence, there are different requirements that an EBM user of a study's conclusions should insist upon, depending on the type of the study. Summaries of these requirements for the results of a therapy study to be valid, for a diagnostic study to be valid, for a prognosis study to be valid, and for the results of an Etiology/Harm study to be valid are presented in Tables 6 through 9, respectively.

The evaluation of medical literature is a complex undertaking. Answers to questions of validity are not al-

Table 6. *Conditions that should be met for the results of a therapy study to be valid*

No.	Requirement	Brief description
1	Randomized assignment of patients	Assignment of patients to either treatment or control groups must be done by a random allocation to ensure the creation of groups of patients, who will be similar in their risk of the events one wants to prevent. Randomization balances the groups for prognostic factors (such as disease severity) and eliminates over-representation of any one characteristic within the study group. Randomization should be concealed from the clinicians and researchers to help eliminate conscious or unconscious bias.
2	The patients who entered a trial must be properly accounted for at the trial's conclusion	The study should begin and end with the same number of patients and patients that dropped out of the study must be accounted for, otherwise the conclusions are invalid. In the case that patients drop out because of the adverse effects of the therapy being tested and are not accounted for, the conclusions reached may be over confident as far as the efficacy of the therapy is concerned.
3	Complete follow-up	Studies should have better than 80% follow-up for their patients, while lost patients should be assigned to the "worst-case" outcomes and still support the original conclusion of the study, if we want to be sure of a study's conclusions.
4	Patients should be analyzed in the groups to which they were originally assigned during randomization	Patients who forget or refuse their treatment should not be eliminated from the study analysis because excluding them leaves behind those that are more likely to have a positive outcome. This introduces biases in the study and annuls the effects of randomization
5	Blinding	To eliminate bias and preconceived notions as to how the treatments should be working, the people involved in a study should not know which treatments are given to which patients. In double blinding neither the patient nor the clinician knows which treatment is being administered. When it is difficult or even unethical to blind patients to a treatment, then the results should be interpreted by a "blinded" clinician.
6	Similarity of groups at the start of the trial	Treatment and control groups must be similar for all prognostic characteristics except one: whether or not they received the experimental treatment.
7	Groups should be treated equally	Study groups must be treated in exactly the same manner except for administration of the experimental treatment. If there are interventions, other than the study treatment, which are applied differently to each group, these must be clearly described.

Table 7. *Conditions that should be met for a diagnostic study to be valid*

No.	Requirement	Brief description
1	Independent, blind comparison with a "gold" standard	A "gold" standard (e.g., an autopsy or biopsy) either provides objective criteria (e.g., a laboratory test not requiring interpretation) or sets a current clinical standard (e.g., 3D sonohysterography) for diagnosis. Patients in the study should have undergone both the diagnostic test in question and "gold" standard test. Clinicians evaluating the tests should be blinded, i.e., the results of one test should not be known to the clinicians who are conducting or evaluating the other test.
2	The sample must include a wide spectrum of patients who will undergo the specific testing in clinical practice	The spectrum of patients must include those with mild and severe cases, early and late cases, and patients who were treated as well as patients who were untreated for the target disease. The test should also be applied to patients with disorders that are commonly confused with the target disease.
3	Replication	The study methodology should be presented in enough detail so that it can be repeated within the appropriate setting. This includes detailed specification of dosage levels, patient preparations, timing, etc.

Table 8. *Conditions that should be met for a prognosis study to be valid*

No.	Requirement	Brief description
1	Randomized assignment of patients, who are at a similar point in the course of the disease.	Patients must be included in the study at a uniformly early point in the disease, ideally, when the disease first manifests itself clinically.
2	Complete follow-up	Patients should be followed until they fully recover or one of the disease outcomes occurs. A long enough follow-up is necessary in order to develop a valid picture. Usually this means that at least 80% of participants are followed up until the occurrence of a major study end point.
3	Using objective and unbiased outcome criteria	If outcomes include a wide range of conditions between death and full recovery, these must be clearly defined, specific criteria should be proposed for each possible outcome of the disease and be used during patient follow-up. Investigators deciding on the clinical outcomes must be "blinded" to the patient characteristics and prognostic factors in order to eliminate possible bias in their observations.
4	Adjustment for important prognostic factors	Patients' clinical characteristics must be similar. This means that sometimes adjustments have to made based on age, gender, or sex to get a true picture of the clinical outcome.

Table 9. *Conditions that should be met for the results of an Etiology/Harm study to be valid*

No.	Requirement	Brief description
1	Clearly identified comparison groups.	The choice of comparison groups must ensure that they are similar with respect to important determinants of outcome, other than the one of interest. Comparability must be clearly demonstrated. Characteristics of the exposed and non exposed patients need to be carefully documented.
2	Exposures and outcomes must be measured in the same way in the groups being compared	The measurements should avoid any kind of bias, whether from recall bias (by patient motivation to help) or by interviewer bias (probing by interviewers for the "right" answer). Using objective data, such as medical records, can help eliminate bias.
3	Complete follow-up	Non-availability of patients for complete follow-up comprises the validity of the study since these patients may have very different outcomes than those that stayed with the study.
4	Correct temporal relationships must exist in terms of cause and effect	The intervention, whether therapeutic or harmful, must have happened before the adverse outcome occurred.
5	Existence of dose-response gradients	The utility of the results depends on whether it can be demonstrated that the adverse effect increases when the intensity or duration of the exposure to the harmful agent is increased. When the object of a study is to prove the beneficial effects of exposure to a therapeutic or prevention agent, then an increase in the intensity or duration of the exposure, should make it less likely for an adverse event to occur.

ways clearly stated in the literature and many times the clinicians have to decide on their own about the validity of the evidence that is turned up by their search.

However, assuming that the physician reaches a valid conclusion on the validity of the evidence he unearths, it is still necessary to examine the results of his search are applicable to his individual patient. This process is summarized in the following three questions that have to be answered:

1. Does the study represent people similar to the specific patient?

2. Does the study cover the aspect of the problem that is most important to the specific patient?

3. Does the study suggest a clear and useful plan of action?

Once the teleconsultant can answer all three of these questions affirmatively, then he can proceed to implement the plan of action he selected for his patient.

Evidence based medicine is flourishing in our days, as a different and more fruitful way to practice medicine, because it serves the need of the health professionals for valid information about diagnosis, prognosis, therapy and prevention , and fills the gap made from traditional sources for medical information e.g. medical journals. Its' advantages are now beginning to be validated and it will continue to prosper, changing the ,traditional and until now, way of medical practice . Due to Evidence based medicine the role of technology and in particular the internet into medicine is expected to grow, as a result the physicians will develop effective strategies for life-long learning and for improving their clinical performance.

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