Evidence-based medicine – an innovative approach to clinical medicine

***L. Spinei[1], N. Rotaru[2], O. Condrea[1,2]**

[1]School of Public Health, [2]Department of Radiology
Nicolae Testemitsanu State University of Medicine and Pharmacy, Chisinau, the Republic of Moldova
*Corresponding author: larisaspinei@gmail.com. Manuscript received April 30, 2015; accepted June 05, 2015

Abstract

Background: Evidence-based medicine (EBM) represents an approach that integrates clinical experience and patient's values with the best available research information. It involves a process of lifelong problem-based learning that requires a variety of new skills for medical practitioners such as efficient literature-searching, familiarity with the types of research evidence, clinical literature evaluation and evidence appraisal. The key elements of EBM such as common EBM steps that have been developed to provide an efficient framework for medical practitioners, the types of evidence and how the evidence is appraised for validity, the types of research studies and study designs as well as their corresponding levels of evidence and the "*evidence pyramid*". It is necessary to increase the awareness of EBM principles among medical practitioners and pave the way to an evidence-based clinical practice.
Conclusions: 1. EBM integrates the best available information with patient's values, clinical expertise and latest research evidence; 2. A significant progress in the practical implementation of EBM has been made by the increasing availability of EBM resources able to search, appraise and summarize the literature on a given topic; 3. An important element of external evidence and EBM are represented by the systematic reviews and meta-analyses, designed to provide relevant summaries about the best available evidence on a specific topic while minimizing the bias; 4. As a result of increasing demands for an evidence-based approach and a wider availability of information resources, EBM is gaining increasing support among the medical practitioners, optimizing their clinical decision-making, increasing their confidence and facilitating their clinical practice.

Key words: evidence-based medicine, evidence pyramid, research designs, level of evidence, patient's values.

Introduction

Evidence-Based Medicine (EBM) is a form of medicine aiming at transforming the delivery of healthcare based on a systematic and detailed approach that integrates patient's values with clinical expertise and current best research evidence. According to the definition given by David Sackett, who is considered the founding father of EBM, "*Evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research*"[1]. The concept of EBM was introduced in 1991 by Gordon Guyatt [2], even though many underlying principles have been developed earlier by the Scottish epidemiologist Archi Cochrane, who is also considered to be the originator of the idea of evidence-based medicine in our era [3, 4]. For his distinguished services towards EBM, Archi Cochrane has been honored through the naming of evidence-based medical research centers as Cochrane Centers and an international organization as the Cochrane Collaboration. Many programs have been developed lately to make EBM more accessible to medical practitioners. Among relevant EBM publications can be listed *EBM reviews* published by the Cochrane Center, the periodical *Clinical Evidence* launched by the BMJ Publishing Group, the *Journal of Evidence-Based Medicine* published by the Wiley Editing Services, etc. In many countries, EBM courses are also included in the standard curriculum of the medical schools. Furthermore, nowadays evidence-based practice is becoming a goal for health care institutions and often an accreditation requirement [5].

Evidence-Based Medicine – a six step approach

The practice of EBM provides a unique and enriching experience for medical practitioners, creating an environment of problem-based learning and identifying current information to support care decisions for individual patients. Such an approach based on identifying the best evidence with which to answer a clinical question correlated with a critical appraisal of the existing evidence for validity and clinical usefulness provides a foreground for effective evidence-based interventions that are responsive to patient's needs and priorities, avoiding uncritical acceptance of "usual practice". The integration of EBM into clinical practice is a complex process and several steps have been developed to provide an efficient framework for medical practitioners.

The *First Step* relates to converting the clinical information into focused questions. Thus, when a clinical problem arises during the care of a patient, it is very important to construct a well-built clinical question that can address such key points as identifying the problem, considering standard and alternative management strategies as well as potential outcomes. A commonly used mnemonic in this regard is PICO: P = Patient or Problem (identifying the most important characteristics, similarities and particularities compared to other patients), I = Intervention (i.e. what are the options, risks and benefits, etc.), C = Comparison (i.e. comparing the existing alternatives for the chosen intervention), O = Outcomes (i.e. what are we trying to reach with the chosen interventions, possible complications and prognostic factors).

The *Second Step* requires answering the focused questions based on "internal evidence", which includes acquired knowledge through formal education and professional training, personal experience accumulated from daily practice, specific experience gained from this particular patient, etc. [6]. Common questions that have to be answered during this step include, "How to proceed and what are the pros and cons based on the internal evidence?", "How much the expertise in the field has evolved since the internal evidence

was created?", "Are there any alternatives to reach this goal and is the internal evidence sufficient"?

The *Third Step* extends the search from internal evidence to "external evidence", which is represented by the available information from research studies performed on the topic of interest. This is frequently accomplished by searching medical literature databases created for this purpose. Selecting the appropriate resource and conducting a proper search represents an important step in the decision-making process and can be performed at several levels: *formal*, that involves searching the sources using formal terminology and key words; *cognitive*, that involves appraising the content; and *analytical*, when the practitioner understands the study design and potential implications on the presented data, being able to critically assess the available external resources. An important resource for external evidence can serve the Cochrane Library, which represents a collection of databases of systematic reviews and meta-analyses that summarize and interpret the results of medical research. The Cochrane Library is supported by the Cochrane Collaboration and a number of other organizations, representing a key resource in evidence-based medicine worldwide.

The *Fourth Step* involves appraising the evidence for validity and applicability to clinical practice. Examples of key issues requiring critical evaluation include randomization, blinding, concealed allocation, completed follow-up etc. The common questions that have to be answered during this step are as follows: "Are the results of the study and the available evidence valid?" and "Will the results help for answering the questions related to this patient?". Commonly used mnemonics in this step include DOE (Disease Oriented Evidence), POE (Patient Oriented Evidence) and POEM (Patient Oriented Evidence that Matters) [7-11]. DOEs are very common in the medical literature, being frequently brought to our attention by pharmaceutical representatives eager to promote their medication brands. This kind of evidence needs to be approached with caution as it may be misleading and should not be used to change practice, especially when other types of evidence such as POEM are available [10]. POEs use patient-oriented outcomes, however, most such studies confirm what we already do and the findings don't have the potential to change practice[11]. POEMs, on the other hand, use patient-oriented outcomes that have the potential to change our practice if the results are valid and applicable to our patient or clinical setting. The concept of "patient-oriented evidence that matters" was developed by David Slawson and Allen Shaughnessy in 1994 [8]. Apart from being patient-oriented and having the potential to change practice, the POEM approach allows medical practitioners to focus only on what's important for individual patients, significantly simplifying EBM. Today, about 30 to 40 POEMs in the form of short synopses of research focusing on patient-oriented evidence that matters are published monthly in such clinical journals as American Family Physician, the British Medical Journal, the Journal of Family Practice, etc. [9]. This helps physicians to find useful information and assists them in caring for their patients during their clinical practice.

The *Fifth Step* requires integrating "external evidence" that has been obtained through various resources into "internal evidence". As a whole, external and internal evidence may be mutually supportive, non-supportive, or even conflicting. When two sources of information (external and internal) are non-supportive or conflicting, medical practitioners may choose to use the external evidence to change their practice or to stick to their original opinion (i. e. to the "internal evidence"). As a third option, a practitioner may also decide to discuss the conflict between the internal and external evidence with the patient, offering him/her the possibility to take part in the decision-making process. Since by definition EBM integrates patient's values with clinical expertise and current best research evidence, the patient's preference is considered an essential part of EBM and, therefore, the last approach is recommended in this instance [6]. Because of this, some authors even call this stage as "returning to patient", when the acquired evidence is integrated with patient's preferences and clinical expertise before being applied to practice.

The *Sixth Step* relates to evaluating the decision-making process and final results. During this step the entire process is assessed, the outcome concerning the status of the patent is appreciated, the results are compared to those published in the literature as well as to the patient's expectations and potential options for improvement are identified. Furthermore, just because an intervention was effective in a rigorously controlled trial, it still doesn't mean it will show the same results in a clinical setting and potential negative consequences should be also identified. Familiarity with relevant parameters and a proper interpretation of the obtained results become indispensible for a valid evaluation.

The principles of EBM are not entirely new, as clinicians have always striven to combine their clinical expertise and their patients' values with the best available evidence. However, interest in EBM has grown tremendously after the term "evidence-based medicine" was introduced in the early 1990s and the subject was gradually included in the undergraduate and postgraduate curriculum in many schools [12, 13]. At the moment, the percentage of physicians who apply the EBM principles in their clinical practice remains largely unknown. Despite enlisted advantages of EBM, the actual implementation depends on many factors like institutional culture, lack of knowledge about EBM and familiarity with the basic skills, barriers to practicing high-quality medicine, busy schedule and lack of time, the need to develop new skills, lack of information resources in the spoken language, shortage of coherent, consistent scientific evidence, impediment of clinical freedom, difficulties in applying evidence to the care of individual patients, etc. [13-19]. Studies performed in Europe and Australia also indicate that textbooks are consulted more often than the Cochrane Library [17, 19, 20]. A lot of efforts have been directed to overcome these limitations and encountered difficulties at various levels. As a result of these efforts and a wider availability of information resources, EBM is gaining increasing support among the medical practitioners, facilitating their clinical activities in a variety of different ways such as:

- ✓ Keeping abreast with updated medical literature and the growing body of developments in the field;
- ✓ Active communication with specialty consultants and other medical practitioners;
- ✓ Effective use of available medical literature and information resources;
- ✓ Targeted and effective data collection and information processing related to patient's medical history, physical exam, laboratory and imaging findings;
- ✓ Optimized clinical decision-making and evidence-based clinical management;
- ✓ Helping clinicians to challenge dogma and to avoid uncritical acceptance of "usual practice";
- ✓ Teaching how to integrate the best available information with patient's values, clinical expertise and latest research evidence;
- ✓ Facilitating clinical judgment and allowing the physicians to individualize the information for every patient's situation;
- ✓ Stimulating a process of lifelong learning and an evidence-based up-to-date clinical practice.

It should be noted that EBM always begins (step 1) and ends (steps 5 and 6) with the patient, being usually triggered by a variety of patient's encounters that generate questions about the etiology of his/her condition, utility of diagnostic tests, the effects of therapy, expected outcome and overall prognosis. After identifying a problem, it is very important to formulate the question in such a way as to facilitate finding an answer applicable to patient's situation. At the same time, it is equally important at this stage to determine the most appropriate type of study able to provide a valid answer to our question. A brief summary of the main types of studies and study designs is provided by the so-called "*evidence pyramid*". The *evidence pyramid* also reflects the hierarchies of evidence that have been developed to help describe the quality of evidence that may be found to answer various questions. When viewed from its base to top, the pyramid consists of several main components such as *Animal Research °Case Reports °Case Control Studies °Cohort Studies °Randomized Control Trials °Systematic Reviews °Meta-Analysis*. Most information usually starts with an idea potentially leading to laboratory research, development of diagnostic tools or therapeutic interventions, which are subsequently tested in laboratory models, animals, and finally in humans.

Animal testing, or animal research, is the use of non-human animals in experiments, commonly being conducted inside universities, medical schools or pharmaceutical companies. It represents an initial step in the research hierarchy; therefore the range and reliability of research results obtained in animals are invariably restricted for being extended to clinical practice. Before a certain diagnostic tool or therapeutic agent can be authorized for use within general population, it should also undergo subsequent human testing on a limited number of volunteers, followed by extended testing within several phases of clinical trials according to the established standards.

Case reports and Case series represent published reports about the clinical features, diagnosis or treatment of individual patients. Because they report single cases and use no control groups with which to compare the outcome, case reports and case series have little statistical validity.

Case control studies represent studies in which patients who already have a certain condition are compared with people who do not have that condition. By definition, case-control studies are always retrospective since they start with patients who already have the outcome, while the researcher is trying to link the outcome with prior exposures and potential causative factors. Case control studies require fewer resources, but are often less reliable than cohort studies and randomized controlled trials because revealing a statistical relationship does not necessarily show a cause-and-effect relationship.

Cohort studies take a group of people who share a common characteristic or experience within a certain period (e. g., taking a particular treatment or have an exposure), follow them over time, and then compare the outcomes with a similar group that has not been affected by the treatment or exposed factor. Of note is that *Case control studies* and *Cohort studies* represent *Observational Studies*, where the researchers observe the effect of a risk factor, diagnostic test or treatment without trying to influence what happens. Observational studies are inherently not as reliable as experimental studies, since the studied groups may differ in ways other than in the variable under study. Sometimes, however, they may represent the only way to explore certain questions. For example, it would be unethical to design an experimental study to deliberately expose patients to certain harmful risk factors. Randomized controlled trials (RCTs) are carefully planned projects in which subjects are randomly assigned to two or more groups. One group receives the intervention (a certain drug or intervention) while the control group receives no intervention or placebo. This allows a formal comparison between intervention groups and control groups (no intervention), differences in the outcomes being directly linked to the intervention. Additional strengths include randomization and blinding that reduce the potential for bias. As a study design a randomized controlled trial represents an experiment and can provide scientific evidence related to the cause and effect. If the subjects are not randomly assigned to the treatment or control groups (i.e. the subject is allowed to choose which group to join or the investigator is assigning to a particular group for any other reason), the study is then called Controlled Clinical Trial (CCT) instead of Randomized Controlled Trial. Both *RCTs* and *CCTs* represent *Experimental Studies*, however, CCTs have a higher chance for "bias" compared to RCTs, since non-randomly assigned subjects have the potential to influence the final results. The RCTs are commonly considered the "gold standard" for producing reliable evidence because little is left to chance, even though such studies are usually time-consuming and expensive. A systematic review (also called systematic literature review or structured literature review) is a literature review focused on a research question that in-

volves a systematic search with a view to minimizing bias, followed by a formal appraisal and synthesis so that relevant conclusions can be drawn and decisions be made. The main difference from a traditional narrative review is that a narrative review is mainly descriptive and does not involve a systematic search of the literature for minimizing bias, while a systematic review typically involves a detailed plan and a search strategy derived as a priority, with the goal of reducing bias by identifying, appraising, and synthesizing all relevant studies on a particular topic [21, 22]. A systematic review may also include a quantitative statistical analysis of the collected data, called a meta-analysis. Thus, a meta-analysis will examine and select a number of valid studies on a topic and combine the results using formal statistical calculations. Many systematic reviews contain meta-analyses, but not all of them [22]. A well-known and respected international organization that promotes, supports, and disseminates systematic reviews and meta-analyses in the field of medicine is the Cochrane Collaboration (www.cochrane.org).

Familiarity with the hierarchy of study designs allows a practitioner to keep in mind the "*evidence pyramid*" when searching for the best evidence. However, the highest level of study to answer a particular question may not always be found or available. In such situation, a practitioner may consider moving down the pyramid. Furthermore, the highest ranked level of evidence might not always be applicable to a particular question. For example, although randomized clinical trials are considered the "gold standard" for establishing the effects of a treatment of intervention, they might not represent the best sources for answering questions about diagnosis, prognosis or harm [13]. Hence, familiarity with the types of study designs and their applicability to different clinical situations becomes indispensible when evaluating the evidence. Last, but not least, it should be also remembered that evidence, by itself, does not make a decision for a clinical practitioner, even though it represents an important variable in the process of EBM practicing. Therefore, the last two steps of EBM relate to integrating internal and external evidence with patient's preferences and clinical expertise before being applied to practice followed by a subsequent assessment of the decision-making process and final results. The integration of these EBM steps enables both the practitioner and patient to optimize their clinical decisions, so that optimal clinical outcomes can be achieved.

Conclusions

1. EBM integrates the best available information with patient's values, clinical expertise and latest research evidence.

2. A significant progress in the practical implementation of EBM has been made by the increasing availability of EBM resources able to search, appraise and summarize the literature on a given topic.

3. An important element of external evidence and EBM is represented by the systematic reviews and meta-analyses, designed to provide relevant summaries about the best available evidence on a specific topic while minimizing the bias.

4. As a result of increasing demands for an evidence-based approach and a wider availability of information resources, EBM is gaining increasing support among the medical practitioners, optimizing their clinical decision-making, increasing their confidence and facilitating their clinical practice.

References

1. Sackett DL, Rosenberg WM, Gray JA, et al. Evidence-based medicine: what it is and what it isn't. *BMJ.* 1996;312:71-72.
2. Guyatt G, Cairns J, Churchill D, et al. Evidence-based medicine. A new approach to teaching the practice of medicine. *JAMA.* 1992;268:2420-2425.
3. Cochrane AL. Archie Cochrane in his own words. Selections arranged from his 1972 introduction to "Effectiveness and Efficiency: Random Reflections on the Health Services" 1972. *Control Clin Trials.* 1989;10:428-433.
4. Stavrou A, Challoumas D, Dimitrakakis G. Archibald Cochrane (1909-1988): the father of evidence-based medicine. *Interact Cardiovasc Thorac Surg.* 2014;18:121-124.
5. Granger BB. Practical steps for evidence-based practice: putting one foot in front of the other. *AACN Adv Crit Care.* 2008;19:314-324.
6. Porzsolt F, Ohletz A, Thim A, et al. Evidence-based decision-making the 6-step approach. *ACP J Club.* 2003;139:A11-12.
7. Smith R. A POEM a week for the BMJ. *BMJ.* 2002;325:983.
8. Slawson DC, Shaughnessy AF, Bennett JH. Becoming a medical information master: feeling good about not knowing everything. *J Fam Pract.* 1994;38:505-513.
9. White B. Making evidence-based medicine doable in everyday practice. *Fam Pract Manag.* 2004;11:51-58.
10. van Rijswijk L, Gray M. Evidence, research, and clinical practice: a patient-centered framework for progress in wound care. *J Wound Ostomy Continence Nurs.* 2012;39:35-44.
11. Gimenez-Perez G, Caixas A, Gimenez-Palop O, et al. Dissemination of "patient-oriented evidence that matters" on the Internet: the case of Type 2 diabetes treatment. *Diabet Med.* 2005;22:688-692.
12. Evidence-Based Medicine Working Group. A new approach to teaching the practice of medicine. *JAMA.* 1992;268:2420-2425.
13. Straus SE, McAlister FA. Evidence-based medicine: a commentary on common criticisms. *CMAJ.* 2000;163:837-841.
14. Green ML, Ruff TR. Why do residents fail to answer their clinical questions? A qualitative study of barriers to practicing evidence-based medicine. *Acad Med.* 2005;80:176-182.
15. Lockwood D, Armstrong M, Grant A. Integrating evidence-based medicine into routine clinical practice: seven years' experience at the Hospital for Tropical Diseases, London. *BMJ.* 2004;329:1020-1023.
16. Hadley JA, Wall D, Khan KS. Learning needs analysis to guide teaching evidence-based medicine: knowledge and beliefs amongst trainees from various specialities. *BMC Med Educ.* 2007;7:11.
17. Oliveri RS, Gluud C, Wille-Jorgensen PA. Hospital doctors' self-rated skills in and use of evidence-based medicine - a questionnaire survey. *J Eval Clin Pract.* 2004;10:219-226.
18. McAlister FA, Graham I, Karr GW, Laupacis A. Evidence-based medicine and the practicing clinician. *J Gen Intern Med.* 1999;14:236-242.
19. Ulvenes LV, Aasland O, Nylenna M, Kristiansen IS. Norwegian physicians' knowledge of and opinions about evidence-based medicine: cross-sectional study. *PLoS One.* 2009;4:e7828. doi: 7810.1371/journal.pone.0007828.
20. Veness M, Rikard-Bell G, Ward J. Views of Australian and New Zealand radiation oncologists and registrars about evidence-based medicine and their access to Internet-based sources of evidence. *Australas Radiol.* 2003;47:409-415.
21. Uman LS. Systematic reviews and meta-analyses. *J Can Acad Child Adolesc Psychiatry.* 2011;20:57-59.
22. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med.* 2009;6:e1000100. doi: 1000110.1001371/ journal.pmed.1000100.