SQU JOURNAL FOR SCIENTIFIC RESEARCH:
MEDICAL SCIENCES 2001, VOL: 3, NO: 2, 105–112

Evidence-based Medicine:
An overview

*Kamlesh Bhargava[1], Roman Jaeschke[2]

الطب الدلائلي: نظرة عامة

كمليش بلغافا و رومان جيبشك

الملخص: رشح حقل الطب الدلائلي في العقد الماضي، أن يكون في طليعة التقدم الفكري بالنسبة إلى اتخاذ القرار السريري. يعجز الأطباء على التعامل مع أكثر من أربع ملايين مقالة علمية تنشر في أكثر من خمسة وعشرين ألف مجلة دورية طبية في السنة. إن مبادئ وممارسة الطب الدلائلي قد بينت الطريق لسد الفجوة بين البحث والممارسة، وأثارت ردود فعل مختلفة في المهنة الطبية تجاه هذا التخصص. تتراوح هذه الردود بين الرفض القاطع إلى القبول بحماس. إن الهدف من هذه الورقة هو تعريف القارئ بالمفاهيم المتعلقة بعبارة "الطب الدلائلي."

ABSTRACT. Evidence-based Medicine (EBM) has been proposed as the most significant intellectual advance in the process of clinical decision-making in the past decade. With more than 25,000 medical journals publishing 4 million articles a year, doctors are unable to cope with the information overload. The principles and practice of EBM show the way to bridge the gap between research and practice. Reactions evoked in the medical profession towards this new discipline have been in extremes, from outright rejection to enthusiastic acceptance. The goal of this paper is to familiarise the readers with the ideas and concepts associated with the phrase *Evidence-based Medicine*.

Key Words: Evidence-based Medicine, Review, Oman

The term evidence-based medicine (EBM) first appeared in an information document for prospective residents in internal medicine at McMaster University, Canada, in 1990. The relevant passage declared:

Residents are taught to develop an attitude of "enlightened scepticism" towards the application of diagnostic, therapeutic, and prognostic technologies in their day-to-day management of patients. This approach, which has been called "Evidence-Based Medicine," is based on principles outlined in the text Clinical Epidemiology.[1] The goal is to be aware of the evidence on which one's practice is based, the soundness of the evidence, and the strength of inference the evidence permits. The strategy employed requires a clear delineation of the relevant question(s); a thorough search for the relevant information (information in the form of primary evidence and/or in the form of synopsis or summary of such evidence, see further); a critical appraisal of the evidence, and its applicability to the clinical situation; a balanced application of the conclusions to the clinical problem.

The fact that the term EBM was coined in 1990 does not mean that its ideas were absent prior to that time. Some of EBM's proponents trace its origins to post-revolutionary Paris. The first step in modern clinical trials was the advent of the randomised trial as a methodology for resolving therapeutic dilemmas. Subsequent events included the development of the methodology of systematic overviews culminating in the Cochrane Collaboration, the introduction of informative abstracts specifying the key components of study design and results, and the advent of secondary journals that selectively present results of methodologically sound and clinically relevant articles previously published in primary journals. As practitioners realized that the principles of EBM are as applicable to nursing, podiatry, physiotherapy, occupational therapy and all other fields of healthcare as they are to medicine, the term Evidence-based Health Care (EBHC) has emerged.

In the remainder of this article we will address the need for EBM, the principles of evidence-based practice, and the electronic resources to practice EBM. Our comments will draw extensively from previous publications.

[1]Department of Family and Community Health, College of Medicine, Sultan Qaboos University, P.O.Box: 35, Postal Code: 123, Al-Khod, Sultanate of Oman. [2]Department of Medicine, McMaster University, Hamilton, Ontario, Canada.

*To whom correspondence should be addressed. E-mail: bhargava@squ.edu.om

IS THERE A NEED FOR EVIDENCE-BASED MEDICINE/HEALTH CARE?

Historically, physiological rationale is the basis for treatment recommendations, but it has repeatedly failed to predict the results of randomized trials as the following examples illustrate. In patients with heart failure, angiotensin-converting enzyme inhibitors have been proved to reduce mortality, whereas other promising vasodilators have had marginal or no effect[2] and some agents with vasodilator and ionotropic properties actually increase mortality.[3,4] While equally promising cerebrovascular surgical procedures have had no effect or have increased stroke morbidity,[5] others have proved dramatically effective in reducing stroke.[6] Antiarrhythmic agents can obliterate non-lethal cardiac arrhythmias while increasing mortality[7] and plasmapheresis confers benefit in some inflammatory conditions, but not others.[8,9] Chalmers and colleagues conducted meta-analyses of randomized trials of interventions in pregnancy and childbirth and found that 61 interventions should have been abandoned.[10]

A second impetus to the rise of evidence-based health care was provided by studies demonstrating that physicians manage similar patients very differently. In results unexplained by differences in patient characteristics or geographical variations, surgeons have chosen widely varying rates of breast-conserving surgical procedures in women with breast cancer,[11] the rates of common surgical procedures have varied up to seven-fold among countries,[12] the rates of coronary artery bypass surgery have varied more than three-fold among Canadian provinces,[13] the odds of tonsillectomy during childhood have ranged 8–70%, and those of hysterectomy, 20–80%.[14,15] A study of procedure rates for medicare patients in 13 large metropolitan areas in North America showed variations of more than 300% for more than half the procedures.[16]

Such wide variations raise questions about whether the differences might be reduced by appropriate application of research evidence. That some of these variations might lead to additional costs without additional benefit has made the dilemma more intense. This intensity has been further enhanced by the third major stimulus to evidence-based health care: reduced resources for health care delivery.

EBM VERSUS TRADITIONAL APPROACHES

How does EBM differ from the traditional approaches to health care? One can view these differences as fundamental or revolutionary, or evolutionary. The former view contends that evidence-based practice represents a shift in the underlying paradigm of healthcare delivery and notes changes in the associated assumptions, while the latter sees EBM as a fine-tuning of approaches and ideas already in wide use.

In the old paradigm, healthcare practitioners assumed that (i) observations from day-to-day clinical experience are a valid way of building and maintaining knowledge about patient prognosis, the value of diagnostic tests and the efficacy of treatment, (ii) the study and understanding of basic mechanisms of disease and pathophysiologic principles are an adequate guide for clinical practice, (iii) a combination of traditional medical training and common sense is sufficient to allow evaluation of new tests and treatments, and (iv) content expertise and clinical experience are a sufficient base from where to generate guidelines for clinical practice.

According to the old paradigm, clinicians sort out clinical problems by reflecting on their own clinical experience, reflecting on the underlying biology, referring to a textbook, or asking a local expert. Reading the introduction and discussion sections is considered adequate for gaining relevant information from a journal article. The old paradigm puts a high value on traditional scientific authority and adherence to standard approaches.[17]

The evidence-based healthcare paradigm also suggests that clinical experiences, and the development of clinical instincts (particularly with respect to diagnosis) are crucial parts of becoming a competent physician. Many aspects of clinical practice cannot be adequately tested because of ethical or practical considerations. Clinical experience is particularly important in these situations. In the absence of systematic observation, clinicians must be, however, cautious in interpreting information derived from clinical experience and intuition, for it may be misleading. Second, evidence-based healthcare practitioners believe that study and understanding of basic mechanisms of disease are necessary but insufficient guides for practice. Third, understanding rules of evidence is necessary to correctly interpret literature on prognosis, diagnostic tests, and treatment and potentially harmful exposures. Finally, when pronouncing their recommendations, clinical experts must refer to the evidence, whether from research studies in the published literature or other sources.

An alternative conceptualisation of evidence-based health care sees it as an evolutionary process. While clinicians have always used the healthcare literature to solve patient problems, evidence-based practitioners acknowledge an explicit hierarchy of evidence. For example, in making treatment decisions they may conduct an N of 1 randomised trial in determining the optimal treatment for an individual patient or seek a systematic review of randomised trials of treatment alternatives.[18] If a systematic

review is not available, they will look for individual randomised trials of relevant management strategies. Failing that, they will seek high quality observational studies. If unable to get the desired evidence from the above searches, they will fall back on the underlying biology, and on their own and their colleagues' clinical experience.

EBM emphasizes that the ultimate decision that clinicians make will not flow only from the evidence.[19] Since all clinical decisions involve tradeoffs, preference or value judgements about the alternatives will always be involved.[20] Ideally, the values and preferences for decisions about individual patient care will come from the patients themselves. Some patients may prefer the traditional parental model of care in which the health worker makes decisions, and the patient's role is to trust the practitioner and follow instructions. Others may insist on a more active role. Ideally, we should be striving for evidence-based patient choice; a concept that involves shared decision-making between clinician and patient.[21]

Whether one finds the revolutionary or evolutionary conceptualisation of Evidence-based Medicine more appealing, they both imply a number of steps in the development of clinical decisions, including clinical policies. These steps include identifying the relevant research, making an accurate assessment of the validity and the results, developing clinical policies with the best match between the research evidence and the clinical circumstances, and applying the research evidence to individual patients in the right way, place and time.[22] The ultimate goal is to provide the practice consistent with the current best evidence. Clinicians can achieve evidence based practice in a variety of ways, as we shall describe below.

EBM AND CLINICAL PRACTICE

The idea of clinical practice consistent with the current best evidence has become an important characteristic of high quality healthcare. Providing individual clinicians with the skills required to independently find from primary sources such as *Medline*, *Embase* or hand searching journals, appraise and apply the best evidence (i.e., training evidence-based practitioners), became one way of achieving this goal. A complementary approach creates a practice milieu that facilitates evidence-based care.

The skills that an evidence-based practitioner brings to resolving a clinical dilemma include all the above steps (defining the problem; searching for evidence; appraising it; considering that evidence and its implications in the context of patients, circumstances and values). Attaining this set of EBM skills requires intensive study and time-consuming application.

Thus, in a McMaster training program explicitly committed to creating evidence-based practitioners, we have found that only a minority of trainees are interested in attaining advanced EBM skills.[23] Our trainees' responses mirror those of UK general practitioners who, despite using evidence-based summaries generated by others (72%) and evidence-based practice guidelines or protocols (84%), overwhelmingly (95%) felt that learning the skills of evidence-based medicine was not the most appropriate method for moving from opinion-based to evidence-based medicine.[24] At the same time, our residency programme trainees all appear to develop a respect for, and ability to track down, recognise, and use evidence-based sources of information that provide immediately applicable conclusions. Having mastered this more restricted set of EBM skills, these trainees (whom we might call evidence users) could become highly competent, up-to-date practitioners capable of delivering evidence-based care.

The recognition that trying to train all clinicians to become evidence-based practitioners is not feasible, and that evidence-based practitioners require tools to optimise their efficiency, has led to the development of sources of pre-appraised evidence. These sources serve the needs of both evidence-based practitioners and clinicians who do not routinely read the methods and results sections of journal articles, yet seek and use evidence-based sources of information. These evidence-based users may also, when seeking expert advice, confine their attention to opinion leaders who undertake a systematic, explicit critical appraisal of the available evidence before making recommendations. As a result, evidence-using clinicians may achieve evidence-based care with nearly as much consistency, and considerably less effort, than those who spend time searching for and critiquing research evidence.

RESOURCES

New resources for practising EBM are developing every day; so are the individuals and organizations critically appraising and assimilating best evidence and developments in information technology. Brian Haines has proposed the *4S Resources* (Systems, Synopses, Syntheses and Studies), which redefine the earlier Primary and Secondary Resources.[25] These are available as paper journals, CD ROMs, and on websites. [Table 1.]

SYSTEMS (TERTIARY)

The ideal computerised decision support system (CDSS), now in development, would link the patients' problems to the best available evidence incorporating electronic medical records. Trials conducted with limited conditions

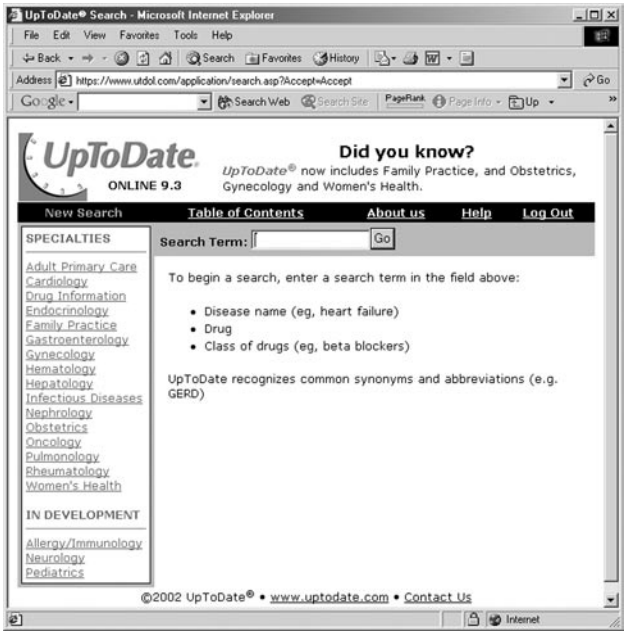
have shown that such systems may improve patient care. This, however, is mostly an issue for the future. Available at present are electronic textbooks such as *Clinical Evidence*, *UpToDate* and *Scientific American Medicine*. Though not integrated with the electronic medical records, these can be used on the same computer. These databases are focused more on internal medicine and subspecialties, and primary care.

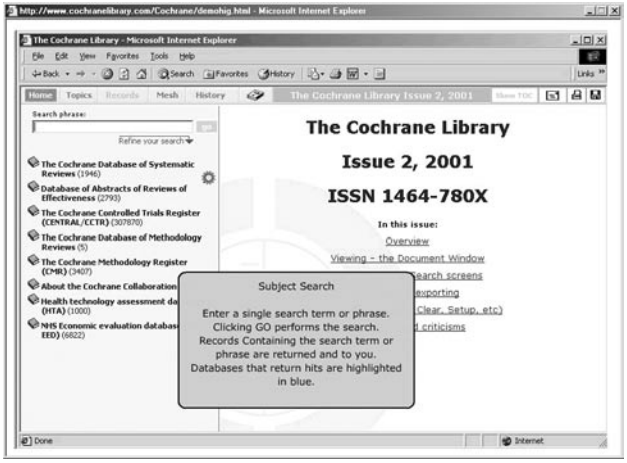
Clinical Evidence precise aims: to provide evidence to assist clinicians in answering the questions most relevant to clinical practice and to highlight areas where such evidence is lacking. The 'book' does not aim to make recommendations, nor does it judge effectiveness or cost-effectiveness. Both beneficial and harmful effects of therapy are presented, leaving clinicians to translate these effects into an estimate of effectiveness for the individual patient.[26]

UpToDate (www.uptodate.com) aims to provide information that is comprehensive, accurate, verifiable (well-referenced), easy to access, and updated regularly. It encompasses all areas of internal medicine, but the dermatology, oncology, and neurology sections are still under development. It describes most important studies briefly reviews quantitative data. Even though UpToDate does not give explicit criteria for seeking and appraising evidence, most clinicians have found it relevant and easy to use.

SYNOPSES (SECONDARY)

Resources for busy clinicians who do not have the time to read lengthy articles and digest them are available. One such resource for internal medicine and primary care is





Best Evidence, annually produced on CD-ROM by the American College of Physicians and American Society of Internal Medicine Best Evidence finds good studies from the top 150 journals, critically appraises them and gives a one-page synopsis for each, along with a commentary by an expert. The Best Evidence CD-ROM also features the entire contents of *ACP Journal Club (ACPJC), Evidence-Based Medicine (EBM),* and the textbook *Diagnostic Strategies for Common Medical Problems (DS)*. Most of its references are relevant to internal medicine: a reflection of the preponderance of ACPJC articles.[27]

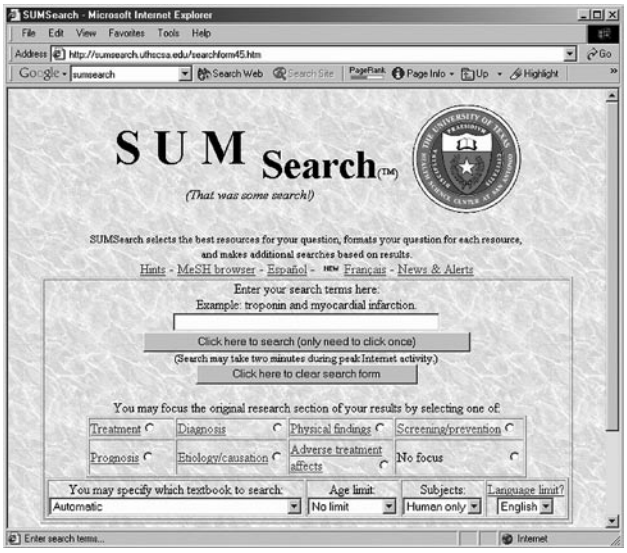
SYNTHESES (SECONDARY)

These resources include systematic reviews that are summaries of medical literature. They perform literature searches, critically appraise individual studies and statistically combine the studies, and are available as databases on CD-ROMs such as *Cochrane Library*. The Cochrane Collaboration (www.updateusa.com/clibip/clib.htm) was established in 1992 to facilitate systematic reviews of randomised controlled trials across all areas of health care.[28,29] This international organization aims to help people make well-informed decisions about health care by preparing, maintaining and ensuring the accessibility of systematic reviews of the effects of healthcare interventions. The Cochrane Library includes (i) *The Cochrane Database of Systematic Reviews*—regularly updated reviews of the effects of health care, (ii) *Database of Abstracts of Reviews of Effectiveness*—critical assessments and structured abstracts of good systematic reviews published elsewhere; (iii) *The Cochrane Controlled Trials Register* —bibliographic information on controlled trials and (iv) Other sources of information—the science of reviewing, research and evidence-based health care. The abstracts of the Cochrane Reviews can be browsed free at www.update-software.com/abstracts/titlelist.htm.

Practice guidelines are also being developed by various organizations, some based on the principles of EBM, others not so explicit. These can be found on the web at sites such as the National Guideline Clearinghouse and Medline.

STUDIES (PRIMARY)

Original studies form the last resource for finding evidence. These can be accessed in several ways. For the beginner, *SUMSearch* might be a good starting point. SUMSearch is a 'meta-searching service' that searches the following resources: (i) *Merck Manual* (which it uses as the default textbook), (ii) *Medline* (for original research, review articles and editorials from general journals), (iii) *National Guideline Clearinghouse* from the Agency for Health Care Policy and Research (AHCPR), and (iv) *Database of Abstract of Reviews of Effectiveness* (DARE). Depending of the focus requested, SUMSearch will search PubMed with the highest sensitivity filters developed by Haynes et al. For example, if the search were about physical examination, SUMSearch would search the database Bedside Diagnosis.[30]

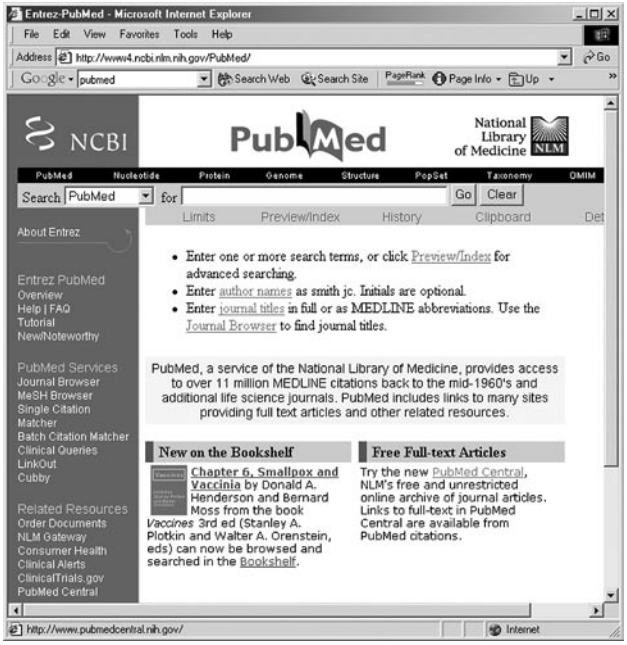


Another option is to use 'clinical queries' in PubMed followed by searching the Medline through PubMed. Medline, the database maintained by the National Library of Medicine in Bethesda, Maryland, USA, is the electronic equivalent of Index Medicus. It includes more than 11 million citations dating from 1966, from over 4,000 journals. The strength of this database is its relatively comprehensive coverage of medical journals and free accessibility via the Internet at www.ncbi.nlm.nih.gov/entrez/query.fcgi.[31] The downside is that Medline's sheer size calls for skills and time to retrieve information, and it mostly provides only abstracts with links to full-text sites (2,588 as on January 2002) that often need paid subscription. Again, the studies thus found need to be critically appraised by the clinician be applying them for patient care. Thus the utility of Medline searches are limited to rare conditions and where the more dedicated resources are unsuccessful.

Over the last several years the concepts and ideas

Table 1. *Useful EBM resources*

Source	Site	Yearly cost (US $)
Best Evidence	www.acponline.org/catalog/electronic/best_evidence.htm	85
Cochrane Library	www.updateusa.com/clibip/clib.htm	235
Medline	clinical.updateusa.edu/pubmed.htm	Free
UpToDate	www.uptodate.com	530
SumSearch	SUMsearch.UTHSCSA.edu	Free
TRIP	www.Tripdatabase.com	Free
Scientific American Medicine	www.samed.com	299
Clinical Evidence	www.evidence.org/index-welcome.htm	110
eMedicine	www.emedicine.com	Free
ScHARR Netting the Evidence	www.shef.ac.uk/~scharr/ir/netting/	Free
ACP Journal Club	www.acponline.org/journals/acpjc/jcmenu.htm/wni	Free
BMJ	www.bmj.com	Free
JAMA	jama.ama-assn.org	125
Lancet	www.thelancet.com	50
Evidence-Based Medicine: How to practice and teach EBM	www.churchillmed.com	31
MD Consult	www.mdconsult.com	219
Bandolier	www.jr2.ox.ac.uk/Bandolier	Free
Centre for Evidence-Based Medicine	cebm.jr2.ox.ac.uk	Free
McMaster Health Information	hiru.mcmaster.ca	Free



attributed to and labelled collectively as EBM became part of daily clinical lives. Clinicians hear about evidence-based medicine, EB healthcare, EB guidelines, EB care paths, and EB questions and solutions. The controversy has shifted from whether to implement the new concepts to how to do so sensibly and efficiently while avoiding numerous potential problems on the way.

There are many reasons why EBM-related skills and solutions would allow us to function more rationally, and with more satisfaction and fun, in our daily practice. Even though original literature keeps spewing forth new evidences that should influence the way we practice, our access to such information is limited, and thereby we risk obsolescence. EBM provides solutions here.[32] However, while adopting EBM strategies, clinicians must avoid a series of misconceptions about EBM. Some critics have mistakenly suggested that EBM equates evidence with results of randomised trials, statistical significance with clinical relevance, evidence (of whatever kind) with decisions, and lack of evidence of efficacy with the evidence for the lack of efficacy. A final mistaken notion is that EBM is a cost-containment tool, rather than a tool for providing optimal patient care[33].

Each healthcare practitioner needs to decide to what extent she would like to become an EBM practitioner. Learning the advanced skills of locating and assessing evidence from the original literature gives the practitioners the skills to judge competing recommendations and alternative courses of action while making healthcare practice more intellectually stimulating and rewarding. EBM skills are very much essential for anyone whose goal is to provide recommendations for optimal practice to others by authoring reviews, editorials or practice guidelines, or as clinical teacher. The advent of EBM has meant that traditional sources of authority such as age and experience must be supplemented by explicit reference to the available valid and clinically relevant literature. Awareness of such literature, and of rules that allow one to integrate evidence from multiple sources to draw valid conclusions, are rapidly becoming essential for all teachers. Those without such skills risk missing an important tool for communicating with their learners.Becoming an accomplished EBM practitioner comes at the cost of time, effort, and sacrificing other priorities. As pointed out earlier, an equally legitimate alternative for clinicians is to actively seek information from sources that explicitly use EBM tools in their selection and presentation of evidence. Even here the clinician requires specific EBM skills to be able to apply the gleaned information to individual patients. For instance, in helping patients weigh the risks and benefits of a treatment they are considering, the clinician must understand the best estimate of the magnitude of the treatment effect, and the precision of that estimate.

For the policy decision makers, including regulators and payers, the evolution of EBM provides new opportunities and challenges. The opportunities lie in the fact that, when properly used, EBM tools help generate data to inform and rationalize healthcare decisions. The challenges, even dangers, lie in the superficial use of EBM concepts, hijacking EBM labels to support preconceived ideas and using labels of EBM without actually applying the concepts. For example, in the recent assessment of the methodological quality of 279 practice guidelines, Shaneyfelt et al found that authors described the method of identifying evidence in only 17%, indicated the methods of grading the evidence in 15%, described the role and use of expert opinion in 8%, indicated the role of value judgement in making recommendations in 6%, and graded the strength of recommendations according to the quality of evidence behind them in 13%. Even more surprisingly, the purpose of the guideline was specified in only 75% of the publications, the background and expertise of authors described in only 25%, and the process of external review revealed in only 32%.[38] Not surprisingly, one can find practice guidelines or care paths supporting all kinds of questionable practices. The findings of this survey are particularly distressing when one considers that practice guidelines may, in some institutions and organizations, acquire the status of practice directives. Generating policies or recommendations intended for wide use requires a detailed understanding of the way such

policies should be constructed, what constitutes 'admissible' evidence, how research evidence can be integrated with patients and societal values, and how the strength of a recommendation relates to the quality of underlying evidence and the tradeoffs between risks and benefits.

EBM IN OMAN

During 1999–2000, a survey of 227 doctors was conducted in Oman to assess their knowledge, attitudes and practices of EBM (unpublished data). It showed that 87% doctors felt that the practice of EBM would improve the standards of care, and help put research findings into practice. Even though 87% had access to computers, the Internet, and were aware of Medline searches, they never used critically appraised databases like Cochrane, Best Evidence, UpToDate, Bandolier, Clinical evidence or National Guideline Clearing House. The participants had limited understanding of the basic EBM terms such as Numbers Needed to Treat (NNT), Likelihood Ratios, Odds Ratio and Relative Risk.

Table 2. *Steps to practise EBM*

1. Ask answerable questions
2. Translate them to effective searches for the best evidence
3. Critically appraise
4. Apply the evidence
5. Evaluate performance

To promote the understanding and practice of EBM, yearly workshops are being conducted in Oman. The three-day workshop held in April 2000 involved small group (10–12) teaching, with two facilitators in each group. The participants were from various specialties and levels of experience. The facilitators represented the major centres of EBM including the McMaster, Canada, the Centre of Evidence-based Medicine in Oxford, and a reviewer for the Cochrane Collaboration. A manual was developed for self-study. The focus was on covering the 5 steps of EBM [Table 2]. There were three plenary sessions, two hands-on computer lab sessions, one for Medline searches, the other for non-Medline searches using databases on CD ROMs such as Best Evidence, Cochrane and UpToDate. Questionnaire surveys before and after the workshop showed that the participants had gained an understanding of EBM and demonstrated that workshops are effective ways to learn the practice of EBM. After the workshop the participants have been trying to practice themselves and introduce the concepts of EBM in their organizations.

CONCLUSION

The purpose of EBM is to provide healthcare practitioners and decision-makers (physicians, nurses, administrators, regulators) with tools that allow them to gather, access, interpret, and summarize evidence required to buttress their decisions and to explicitly integrate this evidence with patients' and providers' values. In this sense, EBM is not an end in itself, but rather a set of principles and tools that helps us distinguish evidence from unsubstantiated opinions, ignorance of evidence from real scientific uncertainty, and ultimately, serves to provide better patient care.

REFERENCES

1. **Sackett DL, Haynes RD, Guyatt GH, Tugwell P**. In: *Clinical Epidemiology Basic Science for Clinical Medicine*. Boston, Little Brown, 1991.
2. **Mulrow CD, Mulrow JP, Linn WD, et. al**. Relative efficacy of vasodilator therapy in chronic congestive heart failure. *JAMA* 1988, **259,** 3422–6.
3. **Packer M, Carver JR, Rodeheffer RJ, Ivanhoe RJ, DiBianco R, Zeldis SM et a**l. Effect of oral milrinone on mortality in severe chronic heart failure. *N Engl J Med* 1991, **325**, 1468–75.
4. **Yusuf S, Teo KK**. Inotropic agents increase mortality in patients with congestive heart failure. *Circulation* 1990, **82**, 673.
5. **The EC/IC Bypass Study Group**. Failure of extracranial-intracranial arterial bypass to reduce the risk of ischemic stroke. *N Engl J Med* 1985, **313**, 1191–200.
6. **North American Symptomatic Carotid Endarterectomy Trial Collaborators**. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 1991, **325**, 445–53.
7. **Echt DS, Liebson PR, Mitchell LB, Peters RW, Obias-Manno D, Barker AH, et al.** Mortality and morbidity in patients receiving encainide, flecainide, or placebo. The Cardiac Arrhythmia Suppression Trial. *N Engl J Med* 1991, **324**, 781–8.
8. **Miller FW, Leitman SF, Cronin ME, Hicks JE, Leff RL, Wesley R, et al.** Controlled trial of plasma exchange and leukapheresis in polymyositis and dermatomyositis. *New Engl J Med* 1992, **326**, 1380–4.
9. **Lewis EJ, Hunsicker LG, Lan S, Rohde RD, Lachin JM**. A controlled trial of plasmapheresis therapy in severe lupus nephritis. *N Engl J Med* 1992, **326**, 1373–9.
10. **Chalmers I, Enkin M, Keirse NJNC**. *Effective Care in Pregnancy and Childbirth*. Oxford University Press, Oxford, 1989, 39–65.
11. **Iscoe NA, Goel V, Wu K, Fehringer G, Holowaty EJ, Naylor CD**. Variation in breast cancer surgery in Ontario. *Can Med Assoc J* 1994, **150**, 345–52.
12. **McPherson K**. Why do variations occur? In: Anderson TF, Mooney G (eds.). *The Challenges of Medical Practice Variations*. Macmillan, London: 1990, 16–35.
13. **Anderson GM, Lomas J**. Regionalization of coronary artery bypass surgery: effects on access. *Med Care* 1989, **27**, 288–96.
14. **Wennberg J.** Dealing with medical practice variations: a proposal for action. *Health Aff Millwood* 1984, **3,** 6–32.
15. **Eddy DM**. *Clinical Decision Making: From Theory to Practice: A Collection of Essays From JAMA*. Boston: Jones & Bartlett Publishers, 1996.

16. **Chassin MR, Brook RH, Park RE, Keesey J, Fink A, Kosecoff J, et al.** Variations in the use of medical and surgical services by the medicare population. N Engl J Med 1986, **314**, 285–90.
17. **Light DW**. Uncertainty and control in professional training. *J Health Social Behav* 1979, **20**, 310–22.
18. **Chalmers I**. Scientific inquiry and authoritarianism in perinatal care and education. *Birth* 1983, **10**, 151–64.
19. **Hayward R, Wilson MC, Tunis SR, Bass EB, Guyatt GH.** How to use clinical practice guidelines. A. Are the Recommendations Valid?The Evidence-Based Medicine Working Group. *JAMA* 1995, **274**, 570–4.
20. **Guyatt GH, Sackett DL, Sinclair J, Hayward RS, Cook DJ, Cook RJ**. Users' guides to the medical literature. IX. A method for grading health care recommendations. *JAMA* 1995, **274**, 1800–4.
21. **Hope T**. *Evidence based patient choice.* Report to the Anglia and Oxford Health Authority into the use of evidence based information for enhancing patient choice. Old Road, Headington, Oxford: Anglia and Oxford Regional Health Authority, 1995.
22. **Haynes RB, Lomas J, Hayward RSA**. Bridges between healthcare research evidence and clinical practice. *J Amer Med Inform Assoc* 1995, **2**, 342–50.
23. **Evidence-based Medicine Working Group**. Evidence-based medicine: a new approach to teaching the practice of medicine. *JAMA* 1992, **268**, 2420–5.
24. **McColl A, Smith H, White P, Field J**. General practitioners' perceptions of the route to evidence based medicine: a questionnaire survey. *BMJ* 1998, **316**, 361–5.
25. **Haynes R B.** Of studies,syntheses, synopses, and systems: the "4S" evolution of services for finding current best evidence. *Evidence Based Medicine* 2001 March-April. 6, 36–38.
26. **Haynes B, Glasziou P, Straus S.** Advances in evidence-based information resources for clinical practice, *ACP Journal Club* 2000, **132**, A-11-A-13.
27. **Straus SE, Sackett DL.** Getting research findings into practice. Using research findings in clinical practice *BMJ* 1998, **317**, 339–42.
28. **Kenneth AL.** Resource Corner Best Evidence 5. *ACP Journal Club*. 2000 **133**, A-15.
Chalmers I, Dickersin K, Chalmers TC. Getting to grips with Archie Cochrane's agenda. *BMJ* 1992, **305**, 786–8.
30. **Editorial**. Cochrane's Legacy. *Lancet* 1992, **340**, 1131–2.
31. **Booth A. O'Rourke A**. Resource Corner, SUMSearch and PubMed: 2 Internet-Based Evidence-Based Medicine Tools, *ACP Journal Club*. 2000, **132**, A-16.
32. **Sackett DL, Richardson WS, Rosnberg W, Haynes RB**. *Evidence-based Medicine. How to Practice and Teach EBM.* Churchill Livingstone, 1997.
33. **Sackett DL, Rosenberg WMC, Gray JAM, Haynes RB, Richardson WS.** Evidence-based Medicine: what it is and what it isn't. *BMJ* 1996, **312**, 71–2.
34. **Shaneyfelt TM, Mayo-Smith MF, Rothwangl JR.** Are guidelines following guidelines? The methodological quality of clinical practice guidelines in the peer-reviewed medical literature. *JAMA* 1999, **281**, 1900–5.