Malaysian Family Physician 2009; Volume 4, Number 1
ISSN: 1985-207X (print), 1985-2274 (electronic)

Online version: http://www.ejournal.afpm.org.my/

Review Article

Evidence Based Medicine Series

EVIDENCE BASED MEDICINE: AN OVERVIEW

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Lai NM. Evidence based medicine: an overview. Malaysian Family Physician. 2009;4(1):19-22

Less than 20 years after making its entrance, Evidence Based Medicine (EBM) is now one of the most-quoted terms in health care. Today, EBM is a central theme in clinical practice, health care policy-making, and medical training at postgraduate and undergraduate levels. In an online poll hosted by the *British Medical Journal* in January 2007, EBM was ranked seventh, ahead of computer and medical imaging, among 15 most important milestones that shape modern medicine.[1]

THE NEED FOR EBM

EBM was introduced as a way to help clinicians decide what is best for their patients, making use of the current medical information.[2] One might argue that this is how medicine has been practiced since the beginning of time, and there is nothing new in EBM. A look at the traditional yardstick of a clinician will help us understand why EBM, as described in the late 20th century, is necessarily different. Traditionally, a clinician is seen as competent if he is well-equipped with comprehensive knowledge on human body and medical treatment including anatomy, physiology and pharmacology. Such knowledge, acquired chiefly from venerated, voluminous texts, forms the foundation to all clinical decisions. When faced with clinical uncertainties, the clinician uses an additional attribute, termed clinical acumen, which encompasses among others, the power of observation, reasoning, deduction and intuition. This attribute is acquired chiefly through role modelling of established clinicians, or as some would argue, comes naturally in those gifted in this field. Through repeated use of clinical acumen with trial-and-errors, experience accumulates, and better clinical decisions ensue, or at least many had believed so.

We have come to know that such model in clinical practice although gratifying and awe-inspiring when one gets it right, is no longer sufficient on its own to withstand the pace of change in the realms of clinical diagnosis and management. This is a result of an explosion in medical information, delivered mainly through the fast-advancing information technologies. Today, we have a staggering size of medical knowledge from numerous sources. For example, the Mesh Thesaurus of the PubMed database has over 25,000 concepts and 160,000 concept names.[3] Diagnosis Pro, a database dedicated for diagnosis of diseases, houses over 15,000 disease entries, many of which can be confused with others, and each may have several possible ways of care.[4] A rough estimate a few years ago showed that each day, over 5,000 journal articles were published, with 1,800 indexed in MEDLINE and over 50 randomized controlled trial.[5] As of May 2009, ClinicalTrials.gov has registered over 73,000 trials from 167 countries, which will become evidence in the near future.[6] It is inconceivable that one can keep a complete and current knowledge on human body. In our practice as clinicians, we need to constantly refer, and know how best to do so.

We need to know how best to refer, as new evidence worthy of changing clinical practice is likely to be there before we see it in textbooks or practice guidelines. Striking examples of evidence-practice lag abound in recent history of medicine, some of which have probably cost many lives. For example, until late last century, prone was the recommended sleep position of infants to reduce the chance of choking on vomitus.[7] In early 90s, the "back-to-sleep" campaign was introduced to reduce sudden infant death syndrome (SIDS), based on evidence from a collection of observational studies. A closer look reveals that evidence on the association between infant prone sleeping and death, should someone put them together, would have been obvious in the 70s. Had the "back to sleep" campaign been implemented a decade earlier, over 60,000 lives worldwide could have been saved.[8] The widespread use of sulficoxazole in the 50s, an antibiotics as prophylaxis for premature neonates and subsequent awareness of its association with kernicterus, a disabling brain disorder, and the liberal use of oxygen and its association with retinopathy of prematurity (ROP), a blinding eye problem,[9] are other painful lessons embedded in the history of neonatal medicine as a result of blind acceptance of medical tradition. A landmark paper in the early 90s provides perhaps the strongest evidence to date on how far expert recommendations trail behind evidence. In this paper, the authors tracked the appearance of new evidence on treatment for myocardial infarct, and examined the content of textbooks or review articles published in the same period. They noted that recommendations on some potential life-saving therapies have been delayed for more than a decade, while potentially harmful treatments continued to be recommended despite evidence of their adverse effects.[10] In the midst of a changing medical world, knowledge

contained within a fixed volume of textbook or the advocacy by authority can no longer assure us of the best patient care.

Merely keeping pace with new evidence is not good enough, as many sources of evidence are either useless or even harmful,[11] although most are well-disguised and tend to escape the uncritical eyes. Some examples where flawed evidence was blindly adopted include the once popular electronic foetal monitoring, the routine practice of episiotomy,[12] and the misguided enthusiasm on hormone replacement therapy for menopausal women based on the belief of its cardiovascular benefits.[13,14] A critical assessment of new evidence as it arrives could probably have avoided such mishaps in the recent history of medicine. Wisdom acquired as we age does not seem to give us any reassurance of better clinical decisions, at least according to a recent systematic review of 62 studies. In this paper, 58 studies found decreasing competence for at least some tasks with increasing physician age.[15] Recognising the limitations of our personal belief and experiences in guiding clinical decisions, we need to know how best to refer, and how to identify the most useful evidence for our practice and filter out the less useful. EBM gives us an organised approach in doing so.

THE BIRTH OF EBM

The concept of seeking validation to our clinical decisions exists as far back as the 10th century CE.[16] However, the ways evidence was sought and applied at that time were often non-scientific. People relied on intuition and guess work, and evidence was subjected to widely varied interpretations from person to person. As a result, the "right evidence" might only emerge after generations of painstaking searches, reflections and endurance with flaws and failures. It was not until the 20th century that a pressing need for an efficient and systematic approach in dealing with clinical evidence arose, as a result of the explosion in medical information. Several key figures helped shape what is to be EBM today. Archie Cochrane (1909-1988), whose experience as a physician for the prisoners of war in Greece and Germany during the Nazi occupation has led him to advocate for an organised summary of clinical evidence based on high quality research such as randomized controlled trials.[17] Alvin Feinstein (1926-2001) made epidemiology relevant to the bedside care of the patients, and introduced clinical epidemiology as an additional dimension required of a competent clinician. In honour of Archie Cochrane for his vision, the Cochrane Collaboration was founded in 1993 under the leadership of Sir Iain Chalmers. Through its major product, the *Cochrane Database Of Systematic Reviews*, it has become the main torch-bearer of EBM.[18] In 1992, EBM was formally introduced by the McMaster EBM Working Group,[2] led by Professor Gordon Guyatt and David Sackett, who is widely known for championing EBM through action by demonstrating the relevance of EBM at the bedside using his "evidence cart".[19] The concepts and approach of EBM were then widened to health care as a whole by Sir Muir Gray, who introduced Evidence Based Health Care and Policy Making.[20]

DEFINITION

The term "Evidence Based Medicine" first appeared in 1992 in an article by a McMaster working Group.[2] The article introduced a new approach in teaching the practice of medicine, and highlighted major barriers to such approach, all of which are still relevant today. A widely quoted definition appeared in a *BMJ* editorial in 1996, as "the conscientious, judicious and explicit use of best available evidence, integrating with clinical judgment and patient values to provide the best individual care for the patient".[21] This definition puts research evidence in its rightful place in the overall care of a patient.

APPROACH

There are five major steps in the practice of EBM,[22] namely:

1. Asking answerable clinical questions
2. Accessing clinical information resources to find possible answers
3. Appraising our possible answers
4. Applying what we have appraised to our patient care
5. Assessing our performance in the first four steps

The following is a scenario of the EBM process:

Mr K, a healthy 50 year old man comes to your practice with common cold. You check him thoroughly, reassure him that there is no complication like pneumonia, and give him some paracetamol with advice to rest. Before he leaves, he asks whether taking a large amount of vitamin C is useful in making his symptoms better, as his boss has recommended it as a remedy, but he is skeptical. You tell him that you are not exactly sure what the current state of evidence is. You promise to look it up and get back to him.

Based on Mr K's query, you set yourself a clinical question to answer: "In otherwise healthy adult, does vitamin C, compared to not taking vitamin C, reduces the duration of symptoms related to the common cold?" (Step 1).

You then set aside 20 minutes, open the PubMed database on your office computer, and type the following keywords in your search: "vitamin C" AND "common cold". You limit the search by checking only randomized controlled trial and meta-analysis. You saw 19 hits. First caught your eyes is an Australian paper, a randomized controlled trial published in 2001, that seems to answer your question.[23] (Step 2).

You open the full text article, which happens to be free, and look through the key passages to decide whether the results are believable. You find that this is a randomized, "double-blind, placebo controlled" trial. Healthy volunteers from an Australian university were recruited for the trial. However, how randomisation was performed, and whether there was allocation concealment were not clear. You checked that the "placebo" was actually a sub-therapeutic dose of vitamin C, which was used to provide comparable taste to the treatment (high-dose vitamin C). This measure was taken to ensure blinding of the participants as well as the investigators, hence the "double-blinding". However, you are concerned about the drop-out rate. Out of 323 volunteers initially recruited for the study, only 149 completed the study, a nearly 54% drop-out rate. In addition, the group that received the high-dose vitamin C was significantly older than the placebo group, although you are not sure whether the difference in age by itself could have influenced the results. Overall, the study found no difference in the mean duration of cold symptoms and severity score between the intervention and the placebo groups at days 7, 14 and 28.

With some reservation about the validity of the findings, as highlighted above, you start looking for more similar studies among the 19 hits of your search. You happen to find a Cochrane systematic review that examines vitamin C as prevention and treatment for common cold.[24] The review on vitamin C as a treatment, combining the results of seven randomized controlled trials including the study that you first assessed, shows no overall benefit. (Step 3).

Looking through the inclusion criteria of the studies in the Cochrane review, you decide that the result is indeed applicable to Mr K, as he is a healthy adult, similar to the population included. You pick up the phone and tell Mr K that his suspicion is right, that currently vitamin c on its own has not shown to be an effective treatment for common cold. (Step 4).

You assess your performance in the previous four steps, and found that you would have come across the Cochrane review first and saved some time had you look through the two reviews that are displayed in the next browser window alongside your total search yields. (Step 5).

PERSPECTIVE

EBM emphasizes a balanced consideration of external evidence, clinical circumstances and patient values in guiding our day-to-day clinical decisions.[21] Recognising the limit of personal belief, intuition, experiences and pathophysiological reasoning in guiding clinical decisions should not be seen as devaluing human judgment,[2] as good clinical judgment is needed to integrate the three elements of EBM. However, it has been proven difficult to conceive the term "EBM" without being intuitively swayed towards the word "evidence". The perception that research evidence is the main thing in EBM has led to many misconceptions.[25,26] In a recent survey of medical students across four South East Asian countries, over 80% inappropriately regarded research evidence as the singular element of importance in EBM, and only 3.5% defined EBM with consideration of all three elements (Ho J, Lai NM and MacDonald S, unpublished). To avoid such misperceptions, we should constantly refer to the definition of EBM.[21]

Some understanding on the types of evidence that match our clinical questions will probably help in clearing our misconceptions on EBM. Randomized controlled trials (RCT), although considered gold standard of clinical studies, cannot answer all our clinical questions. They are suitable to answer only questions on therapy. To answer questions on prognosis of disease, we should look for inception cohort studies, and for questions on diagnostic value of a test, studies involving the use of the test in question in comparison to a gold standard.[22] Regardless of whether we can find the best research design in the hierarchy of evidence, there will always be evidence to answer our clinical questions, be it other forms of research, anecdotal notes or opinions of experienced colleagues. We use the best available evidence we can get to guide our clinical decisions, and bear in mind the increasing risk of bias further down the level of evidence.[28] To blindly revere RCT in all situations, and to dismiss all treatment decisions taken without the support of RCT is to defy the judicious use of evidence, hence an abuse of EBM.

EBM: A YOUNG SCIENCE

In only its second decade, EBM faces many barriers to practice. The lack of technological support at the point-of-care, the lack of time to learn and apply EBM skills and poor awareness are the major barriers that have been highlighted consistently over two decades.[2,29-31] While the introduction of pre-appraised resources, evidence-based short summaries and specialized EBM-oriented search engines have greatly improved the efficiency of evidence based practice,[18,32-36] EBM will only reach its full maturity when the medical community as a whole realize its importance in patient care, and incorporate the essential attributes of an EBM practitioner into the armoury of our core clinical skills. These attributes include the willingness to recognize and admit our own uncertainties, the ability to identify critical information needs in our daily encounters with patients, convert these needs into specific answerable questions, and apply the evidence with genuine regards of each patient as unique individuals with values and preferences. When such time comes, EBM shall no longer be seen as a separate skill, but an integral part of good clinical practice.

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