American Journal of Gastroenterology

Published by Blackwell Publishing

ISSN 0002-9270
doi: 10.1111/j.1572-0241.2008.02193.x

DEBATE

EBM: Savior or Scourge of Clinical Practice

(Am J Gastroenterol 2008;103:2965–2971)

PRO: EBM: An Invaluable Tool for Medical Practice

WHAT IS EVIDENCE-BASED MEDICINE (EBM)?

David Sackett, the "father" of evidence-based medicine (EBM), stated that EBM is "the conscientious and judicious use of current best evidence from clinical care research in the management of individual patients" (1). In this definition:

> *Conscientious use* implies that physicians review articles about clinical research and apply this information to clinical decision making.
>
> *Current best evidence from clinical care research* implies that physicians systematically appraise the methods and results of clinical research articles using EBM tools. With these tools, physicians can separate the "wheat from the chaff" when reading medical journals and identify poorly designed studies that will produce biased results and should be "tossed out" before being applied to patient care.
>
> *Judicious use* implies that a physician's experience and patient's preferences are crucial components of decision making and these judgments must be balanced with the data from "best evidence."

DOES EBM = "COOKBOOK" MEDICINE?

"*Judicious use*" of "*best evidence*" is a particularly important concept to understand (2). Many critics state that the practice of EBM is "cookbook" medicine where the results of a randomized controlled trial are routinely applied to all patients with a specific disorder. This type of criticism says that EBM devalues the judgment of a clinician and the values of an individual patient. Nothing could be farther from the truth. First, adequate evidence is lacking to answer more than 50% of clinical questions, so physicians must rely on their clinical experience and judgment to make decisions when evidence is lacking. When evidence is available to guide decision making, physicians must consider a patient's preferences about the potential benefits and side effects and costs of a medication when deciding upon a specific treatment. Also, a specific patient may not fit the criteria for enrollment of patients into a randomized controlled trial. For example, a randomized controlled trial (RCT) demonstrated that rifaximin, a nonabsorbable antibiotic, improved bloating in Lebanese patients with bloating (3). Most of these patients met symptom-based criteria for irritable bowel syndrome (IBS). Will bloating, abdominal cramping and altered bowel habits improve if rifaximin is used in IBS patients in the United States? If we assume that these results are applicable to IBS patients in the United States, then is it worthwhile to use a treatment that may only produce a temporary relief of symptoms? What if the patient had a past history of *Clostridium difficile* colitis after a course of ciprofloxacin? Would the patient be willing to risk another case of *C. difficile* colitis? What if the patient does not have insurance and would pay $200 for this prescription? These questions are qualitative questions that require clinical judgments on the part of the patient and the physician (4). Although the "best evidence" from a RCT (3) may identify an effective treatment for bloating, physician judgment and patient preferences must be utilized, too, for effective clinical decision making. Thus, EBM and a reliance on "best evidence" is not intended to be "cookbook" medicine (4).

WHY IS EBM HELPFUL?

Nevertheless, EBM is an invaluable tool for the practice of medicine because it facilitates a systematic examination of study methodology and results (5). The medical literature is expanding at an exponential rate (5), and the time available for reading is hurried and fragmented. Physicians need tools to rapidly evaluate the methods and results of published studies, and EBM provides these frameworks (6, 7). With these frameworks, physicians can rapidly identify well-designed studies that produce accurate and unbiased results, which should be applied to patient care. Studies using improper methodology and biased results are quickly identified and ignored. The implementation of EBM is crucial to prevent us from slipping back to "those ancient and primordial days [1970s] of medical science [when] case reports, observational studies of a few dozen patients and physiologic experiments ruled journal pages... studies that have intermediate endpoints rather than meaningful clinical outcomes" (8).

EBM HELPS INSURE THAT WE AVOID INEFFECTIVE THERAPIES

Some physicians argue that EBM is too time-consuming, but we put our patients in peril with useless and ineffective diagnostic tests and treatments if we ignore the tenets of EBM.

There are numerous examples where clinical practice is at odds with clear-cut evidence. Consider the following example. Assume that it is 1999 and we are treating a 70-year-old NSAID-using man who presents with melena and hematemesis. His naso-gastric lavage produces "coffee grounds" which clear with 200 cc of lavage, suggesting that active upper gastrointestinal (UGI) bleeding has stopped. Hemodynamic stabilization is begun with infusion of normal saline while transfusions of packed red blood cells are prepared. What other treatments is this patient likely to get? In 1999, the standard of care would be an infusion of H2 receptor antagonists (H2RA), and most UGI bleeding patients that I evaluated in the emergency department had an H2RA infusion running. What is the point of this treatment? A careful application of EBM principles would demonstrate that this was a useless intervention, although it might have made physicians feel better because they were doing something! More importantly, truly effective treatments were available in 1999 and were routinely ignored in favor of H2RA infusions.

EBM is predicated on several principles. First, a clear question must be developed: among patients with bleeding peptic ulcers (patient population), do H2RA infusions (treatment) reduce recurrent peptic ulcer bleeding (outcome)? Second, medical literature can be searched to find studies that address this question. In our scenario, this search would produce a meta-analysis of multiple placebo-controlled RCTs (9) and a report of a single very large (>1000 patients) placebo-controlled RCT on this topic (10). Third, frameworks for the systematic assessment of study methodology and results are applied (6). Application of these frameworks would demonstrate that these were well-designed RCTs that are likely to produce accurate results. H2RA-treated patients and placebo-treated patients had very similar rates of recurrent peptic ulcer bleeding in the meta-analysis (23% *vs*. 26%) and the single large RCT of over 1000 patients (24% *vs*. 25%), demonstrating that IV H2RAs had no impact on preventing recurrent peptic ulcer bleeding. These data were published in 1985 in the *New England Journal of Medicine* (9) and in 1992 in *Lancet* (10), so physicians cannot argue that these were new findings or that they were published in obscure journals while they continued to prescribe ineffective IV H2RA infusions for patients with peptic ulcer bleeding. The continued use of this ineffective medication became even more problematic in 1997 when Khuroo *et al*. (11) demonstrated that high doses of oral proton pump inhibitors (40 mg omeprazole po bid) did reduce recurrent peptic ulcer bleeding compared to placebo (9% *vs.* 35%, $P < 0.01$). Again, these data were published in the *New England Journal of Medicine*, so it is difficult for physicians to argue that they were unaware of these data. Eventually, IV proton pump inhibitors became available and they became the standard of care for initial treatment of patients with peptic ulcer bleeding. Nevertheless, how many patients suffered recurrent peptic ulcer bleeding that led to prolonged hospitalizations, surgical therapy of bleeding ulcers, or even death because we failed to simply start patients on high-dose oral proton pump inhibitors and continued to use ineffective IV H2RAs. We may never have evidence to answer the last question, but this case scenario provides a prime example where we ignored "the evidence" at the detriment of our patients.

CONCLUSION

In conclusion, EBM is not a "cure-all" nor is it "cookbook medicine." Physicians must use their clinical judgment when evidence is lacking or when deciding how to balance the risks and benefits of treatment for an individual patient whose medical problem may not fit exactly into the question assessed in a research study. Nevertheless, we ignore EBM at our own peril. If we do not systematically assess the methods and results of well-designed research studies, then we risk collapsing into destructive patterns of practice variation and substandard care.

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CONFLICT OF INTEREST

Guarantors of the article: Philip Schoenfeld.
Specific author contributions: Philip Schoenfeld is the sole contributor to this manuscript. He is responsible for all aspects of manuscript preparation.
Financial support: None.
Potential competing interests: None.

CON: Evidence-Based Medicine—The Emperor's New Clothes?

INTRODUCTION

Since the term was coined over 15 years ago (1) evidence-based medicine (EBM) has taken the medical community by storm. As a measure of how successful the movement has become, when the Red Journal approached some authors who had previously written criticizing EBM to take part in a debate on the subject none were willing to take an opposing view. It has therefore fallen to me to write this article and play the devil's advocate despite being a proponent of EBM.

Archie Cochrane argued in the 1970s that the effectiveness of most investigations and interventions had not been demonstrated and indeed may be doing more harm than good (2). He advocated the expansion of randomized controlled trials (RCTs) as the best evidence for the effectiveness of interventions and proposed systematically reviewing all RCT evidence and, when appropriate, synthesizing the results as a meta-analysis. This led to the formation of the Cochrane Collaboration, an international not-for-profit organization that has developed the methodology of systematic reviews and "prepares, maintains, and promotes the accessibility of systematic reviews of the effects of health care," in the Cochrane Library (3). These ideas were also taken up by David Sackett and others at McMaster University and epidemiological principles were applied to assessing diagnostic tests and health-care interventions. This further crystallized thinking on how health care should be evaluated and this led to a paradigm shift where clinical decisions were made on the basis of the best available evidence rather than clinical intuition or blindly following medical tradition.

Initially there were detractors to the EBM movement (4) and whilst there are some valid concerns regarding the application of these principles (5) the number of clinicians opposing EBM have dwindled over the years and it is now an accepted part of medical practice. Indeed, it is almost impossible to argue that applying interventions that have been shown to work in clinical trials is not good practice. Of course even the most ardent EBM exponent would accept that sometimes evidence is simply not there and a clinician must do the best they can for the individual patient. When evidence is available the clinician should apply sound scientific principles in evaluating these data to give the most cost-effective care for their patients. The aim of this paper is to highlight that there are serious concerns over EBM and that perhaps the whole movement is hiding deeper problems that the medical community is facing.

EBM View of "Science" Is Too Restrictive

RCTs are the gold standard for assessing the efficacy of health-care intervention as confounding and bias are eliminated if studies are large, appropriately randomized with concealment of allocation, double blind, and have complete follow-up. This type of RCT is rare and usually there are one or more methodological flaws that may influence the outcome. There are many research questions that can't be answered by RCTs and EBM proponents have expanded the definition (6) to include other epidemiological designs such as cross-sectional and cohort studies that are appropriate to other important information such as prognostic factors.

The aim of EBM is to apply scientific methodology to the evaluation of the health care. There are many philosophical theses that try and define scientific evidence. These range from Karl Popper's falsification theories, Kuhn's paradigm shifts and Lakatos' positive and negative heuristics (7). There is no philosophical view of science, however, that highlights the randomized controlled trial or other epidemiological designs. Whatever their view of science all philosophers would agree that it is much broader than this (7). If science is more extensive than this shouldn't we use all kinds of scientific evidence rather than the restrictive EBM definition?

EBM Does Not Adhere to Its Own Principles

One of the main tenets of EBM is that we should not accept conventional medical practice as "self evident" but should look for rigorous evidence that a test is diagnostically useful or that a therapy is efficacious and also that this technology is an efficient use of health-care resources. Surely this principle should apply to EBM itself. A review of the literature, however, could not identify any evidence that would meet the standards of EBM sets for other health-care interventions (8). Clinicians need to devote a considerable amount of time learning EBM methods and also keeping up to date with all the relevant evidence. EBM therefore indirectly consumes considerable health-care resources in attempting to improve care for patients and the movement should encourage research that justifies that expenditure. Proponents of EBM argue that it is impossible to conduct standard double blind RCTs that would evaluate the practice. This is true but it is still possible to evaluate EBM using a cluster-randomized

design. This approach has been taken to evaluate guidelines that are grounded in EBM but not been used to evaluate the methodology itself as far as I am aware.

There is a Problem of Applying Mean Results to Individual Patients

RCTs are extremely valuable in deciding whether a treatment is efficacious. They also quantify the efficacy of therapy using outcome measures such as number needed to treat (NNT). The problem is that all trials have exclusion criteria for potential participants to increase the internal validity of the study. Eligible patients are given the choice of whether to take part in a clinical trial and some refuse to participate. Researchers may also not enroll all potential patients into a trial for a variety of reasons including time pressures, lack of equipoise, or lack of engagement with the study. Those included in studies are therefore usually not representative of all patients that might be treated with a given intervention. The NNT described in the study may therefore bear little relation to the patient in front of you in the office. Researchers recognize this problem and often perform subgroup analyses to try and identify patient characteristics that predict better or poorer responses to treatment. This is a laudable aim from a clinical point of view but statistically this approach is fraught with problems as any difference between subgroups may have occurred by chance as there are usually hundreds of subgroups that could be created and therefore it is likely that a few will obtain statistically significant *P* values.

There is also the issue of patient values, which need to be considered when suggesting treatment options. For example, a patient may have a strong aversion to risk and though treatment is more likely to result in benefit than harm, the small possibility of a serious adverse event may dissuade individual patients from accepting therapy. Measures such as NNT may be useful to clinicians but they are often not met with overwhelming enthusiasm by patients who prefer less scientific approaches to the presentation of benefit such as listening to other personal experiences and anecdotes (9).

Supporters of EBM recognize this and one of the steps involved in practicing EBM is to "integrate EBM appraisal with clinical expertise and patient values to apply the results in clinical practice" (5). The problem is that there is little in the way of concrete guidance as to exactly how to incorporate clinical expertise and patient values with EBM. At the one extreme, data from RCTs will dictate what intervention is given and at the other extreme clinical expertise and patient values will be given absolute priority, which is essentially the situation we were in before EBM was espoused. Clearly a compromise between these two poles is sensible but how this is achieved in practice is far from clear.

How Do We Synthesize All the Evidence?

A well-conducted systematic review is considered the highest level of evidence in EBM. It seems intuitive that the best guidance on how to manage a given disorder will be achieved by identifying all the available evidence, before extracting and synthesizing this evidence in a reproducible manner. Even if we ignore the concern about what constitutes "evidence" there is still the problem of combining results of RCTs or epidemiological data. Usually data from different studies are heterogeneous and so it can be difficult to interpret the overall result. Statistically it is possible to pool the results but the models that do this tend to increase the weight of smaller studies that are often of poorer quality (10). It is important therefore to explore reasons for heterogeneity rather than accepting the overall pooled result (10). Nevertheless there are often situations where there is no apparent reason for the differences between studies and then it can be difficult to reach any definitive conclusions.

The Problem of Conflicts of Interest

EBM assumes that evidence for health-care interventions will be assessed objectively. Indeed processes such as the modified Delphi technique have been developed for improving the reproducibility of decision-making. The problem is that all parties making these decisions will have conflicts of interest. Clinicians may have financial ties to pharmaceutical companies and have a vested interest in promoting their specialty, Food and Drug Administrators are government funded, patients are more likely to favor therapies directed at their problem rather than taking a societal perspective. In general decision makers will do their best to reach an objective decision despite these conflicts of interest but the very fact they are present will mean that there will be occasions where evidence is not interpreted correctly. There are of course no easy solutions to this issue and conflicts of interest are not peculiar to EBM and will impact on any approach to health-care decision making. It is highlighted here as some EBM advocated gloss over the fact that the appraisal of evidence is usually far from scientific and this can undermine the whole process.

The other problem related to this is the influence the pharmaceutical industry has on research. Studies sponsored by the drug industry are more likely to reach a positive conclusion and are more likely to recommend the intervention as the treatment of choice. The pharmaceutical industry also often sets the research agenda as funding agencies rarely support RCTs of medical therapy (11). For example, there have been 225 RCTs of pharmacological therapies for gastroesophageal reflux disease involving 55,540 participants (11) and yet there have been only a handful of RCTs involving a few hundred participants assessing antacids and lifestyle measures. It is no surprise that guidelines following EBM principles have focused on drug therapy. If the foundations on which EBM is built are heavily influenced by the pharmaceutical industry this calls into question the objectivity of the conclusions reached.

Conclusions

This article has outlined some concerns with EBM. These are serious issues that represent enormous challenges to EBM.

There are also areas where EBM is not that helpful and clinical experience or "common sense" should prevail. We do not have RCT evidence that parachutes are effective in reducing mortality after jumping out of an airplane (12). Nevertheless most rational people would want this intervention to continue and would not want to take part in an RCT or have this practice scrutinized by EBM.

My major concern with EBM, however, is the focus on the RCT. Great discoveries in medicine are not achieved through RCTs. It is true that the RCT is a great tool for evaluating whether an intervention discovered by science really results in health benefit. It is also likely that careful scrutiny of RCTs and epidemiological research can help us treat our patients better. The problem is that fewer clinicians in developed countries are choosing a career in research and pharmaceutical companies are merging for commercial gain. This will stifle innovation and thus the building blocks for future progress in medicine will dwindle.

In the fable by Hans Christian Andersen the crowd was initially too afraid to point out that the Emperor was not wearing any clothes as two dishonest tailors had convinced everyone that if they could not see the clothes they were stupid. My fear is that too many clinicians are focusing on EBM, which is hiding the paucity of really innovative research going on in medicine today.

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CONFLICT OF INTEREST

Guarantor of the article: Paul Moayyedi.
Specific author contribution: Paul Moayyedi has conceived, collected data, analyzed, and written the paper.
Financial support: There was no financial support given to this project.
Potential competing interest: Paul Moayyedi has acted as an independent medical consultant for AstraZeneca and Janssen Ortho. He is on the speaker's bureau for AstraZeneca, Janssen Ortho, Nycomed, and Esai and holds a Chair that is funded partly through an unrestricted donation from AstraZeneca Canada to McMaster University.

A BALANCING VIEW: Evidence-Based Medicine: Neither Savior Nor Scourge but a Practical Tool for Clinical Practice

INTRODUCTION

Before the term evidence-based medicine (EBM) was coined, physicians had for centuries observed the response to different treatments and applied the results of their observations as "evidence" in their practice (1). However, such evidence was usually observational, subject to bias, and often found to be wrong. Nevertheless, this form of "evidence" made substantial contributions to the evolution of modern medicine. Physicians were essentially trained within a framework of "evidence," but today's concepts of EBM are based on well-documented, validated, rigorous approaches to the evidence.

The practice of EBM requires the integration of the current best evidence together with the physician's experience and patient's preferences (2). EBM replaces invalidated diagnostic tests, prevents patients from continuing to receive ineffective or potentially harmful treatments, and draws on the conclusions from systematic reviews/meta-analyses, which avoids the need for further unnecessary, small clinical trials.

At face value, the definition of EBM seems equivalent to the wise use of the best available evidence, and so it is

puzzling to see the practice of EBM being questioned: "Who could possibly be opposed to using the best evidence wisely?" (3). While many criticisms of EBM are misinterpretations or misperceptions or lack conceptual clarity about EBM, the evidence-based approach does have limitations. In this issue of the journal, two acknowledged experts present some of their pros and cons of practicing EBM.

FOUNDATIONS OF EBM

Dr. Schoenfeld has summarized the foundations of EBM and given us a road map with practical steps for the practice of EBM, none of which is controversial.

This approach makes EBM sound rather laborious and impractical, but it should be neither a "cook-book" approach nor a panacea. The majority of clinical questions are not readily answered by available evidence, and patients included in randomized controlled trials (RCTs) are selectively different from those seen in daily clinical practice. Thus, the results of a trial may only apply to low-risk, uncomplicated patients making the application of EBM difficult in the real world, and in practice we must avoid applying the "mean results" to individual patients, as suggested by Dr. Moayyedi.

A further concern expressed by Dr. Moayyedi that is really a misconception of EBM for many general practitioners is that EBM is focused on meta-analyses and RCTs. Both are considered as the "best" sources of medical evidence but the principles of EBM emphasize the importance of seeking the best available evidence with which to answer a clinical question. Furthermore, evidence from basic science has a fundamental role in understanding the biology of disease and mechanisms of treatment. So, we should not ignore other such sources of evidence including observational studies, case reports and expert opinion, as well as clinical experience.

It is also important to remember that systematic reviews and meta-analyses are retrospective in study design, and their quality is directly related to that of the original studies and all are subject to some kind of bias. Many so-called meta-analyses are often flawed because they lack a protocol or adherence to it or the techniques are inappropriately applied. Systematic evaluation of the study methodology and patient characteristics is very important rather than interpretation of the overall pooled result. Although subgroup analyses are important for interpreting statistical heterogeneity, we do not always have results for the subset in which we are interested. Clinical heterogeneity is also important but it is common for physicians searching for a meta-analysis to apply the conclusions without considering the possible differences between their patients and those enrolled in the studies, especially when the meta-analysis presents a convincing Forest plot with a strong conclusion!

In reality, most busy physicians do not practice the full approach to EBM starting from systematic collection and analysis of clinical trials, which is very time consuming and requires methodological training. Thus, most busy physicians draw on the "products" of EBM, such as disease-driven regional or global guidelines, which usually combine evidence with expert opinion and use approaches such as the Delphi method in their in the development. Guidelines ask broad questions and some consensus reports are worded to fit the available evidence, rather than providing conclusions based on a comprehensive search of the evidence to answer the important clinical questions. Moreover, only when a large body of respected opinion accepts the findings of a trial are they generally accepted into clinical practice, and this often takes a long time. The extent to which guidelines are based on opinion rather than evidence is often overlooked. In addition, global guidelines do not apply to all regions of the world, and "change" is not necessarily always the best thing in clinical practice. If it is difficult to implement a guideline in a developing region, especially when the benefit to be gained is marginal, or the physicians do not have the skill to apply the new technique, it is probably better not to implement it, even when the current practice falls short of the "highest standard of care." Thus, EBM should not become or be seen as a barrier to the practice of high-quality medicine.

CURRENT ISSUES CONCERNING EBM

Some unresolved concerns are raised by Dr. Moayyedi, which might exaggerate these problems, such as "how to incorporate clinical expertise, patient values, and EBM?" The importance of this is not denied, but often, there are no simple answers to apparently simple questions. EBM, opinion-based medicine, and real world medicine are not equivalent and there is a considerable overlap (4). It is appropriate to practice medicine within the framework of EBM, but physicians should always continue to think clinically based on clinical experience. There is no rule of thumb for the individual weighting of these three components in final decision making and the solution is usually personal: physicians make their own judgment putting all three components together based on the patient's circumstance, and "common sense."

We agree that the EBM view of science might be too restrictive, but this has little relevance to most general physicians who prefer to apply summarized/synthesized evidence. EBM is no longer considered to be a "paradigm shift," but rather an approach to medical practice that is importantly different from the alternatives (3). Moreover, EBM is still open to study, evaluation, and evolution for how to apply the best "scientific methodology and scientific evidence to EBM." The impact of "practicing EBM" in developing countries when the evidence is coming only from western countries requires further study. Should the practice in less developed regions be based on local experience even when that lacks the rigor of western studies and until high-quality local evidence becomes available? It has been suggested that

sometimes it is more important to do things the "same" than to do it "right," and not make changes for change's sake; error rates fall (fewer mistakes), costs fall (staff is more efficient) and you can apply the scientific methods systematically, which ends up with best demonstrated care in practice (5).

We also agree that the "cluster randomized trial design" is one new concept, which offers the opportunity to determine the usefulness of an intervention directed at groups of patients or practices. It is not difficult to conduct but requires physicians who are willing to contribute to clinical research and are from different centers to participate.

We agree with Dr. Moayyedi that conflicts of interest, including the role of pharmaceutical companies in establishing evidence, are a current topic of discussion. This is an issue that may not be easily resolved since all those involved in a trial are conflicted in one way or the other. For high-quality trials there will always be a sponsor. Even without a pharmaceutical industry support, there may be government, insurance companies, or payors providing support. All parties have their own agenda and interests that may impact the study conclusions. Thus, the ethics of research are critical and require that we place the patients' interest above all others; results should be evaluated independently and should be available to public scrutiny; the role of each party should be transparent and the interest should be declared. EBM should not be applied as a cost-cutting approach and should be used for the identification and application of the most effective interventions to maximize and prolong the quality of an individual patient's life.

EBM AS A PRACTICAL TOOL

There are many challenges to practicing EBM in gastroenterology (6). EBM is neither a savior nor a scourge for clinical practice but is an ideal practical tool, which allows the best evaluated methods of health care to be identified and enables physicians to make better-informed clinical decisions. Evidence, physician experience, and patient values are three core elements and none can replace the others. However, there are limitations in the implementation of EBM and sometimes the evidence we need is just not available. We should always bear in mind that applying the results of RCTs or meta-analyses may disadvantage some patients. EBM provides an excellent broad direction for clinical practice but the individual patient care still requires expert knowledge and clinical experience.

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Specific author contributions: Equal contributions of authors.
Financial support: None.
Potential competing interests: None.