

# Evidence-Based Medicine: An Introduction for Medical Students

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## ABSTRACT

Despite its recent development, *evidence-based medicine* (EBM) is increasingly being implemented in clinical practice, taught in medical schools, and relied upon in government policy-making. Although the principles guiding EBM may seem simple, the translation of scientific and clinical evidence into medical practice has inherent challenges. This review of EBM provides an overview of the history and development of EBM. In addition, we discuss some of the current academic groups that provide EBM resources, specifically the Cochrane Collaboration and the Therapeutics Initiative. We also present several challenges that face the practice of EBM and the barriers that persist in the medical curricula as educators strive to teach these concepts.

**KEYWORDS:** *Evidence-based, systematic, Cochrane, Therapeutics Initiative*

## HISTORY AND BACKGROUND

**E**vidence-based medicine (EBM) is a relatively new idea in clinical practice and has been defined as “the conscientious, explicit, and judicious use of the best current evidence in making decisions about the care of individual patients”.<sup>1</sup> EBM acts as an important link between current scientific research and clinical practice and aims to provide patients with the best possible care.<sup>2</sup> Although the concept of testing various interventions for efficacy has existed for many centuries, EBM has only started to gain prominence in the late twentieth century. First developed through the work of the Scottish epidemiologist and physician Archie Cochrane in the 1970s, EBM was later introduced into medical practice and education by David Sackett and Gordon Guyatt of McMaster University in the 1990s.<sup>3</sup> A recent online poll conducted by the British Medical Journal named EBM the eighth most important medical breakthrough since 1840, illustrating its increasing significance.<sup>4</sup>

The use of EBM in clinical practice is a process that requires the application of five steps.<sup>5</sup> These steps, outlined in Table 1<sup>1</sup>, should be followed in a rigorous manner in order to maximize benefits to patient care.

When evaluating studies for EBM, it is essential to use the best available evidence. In most cases, randomized controlled trials (RCTs) are considered to be the best evidence, while non-controlled trials, observational studies, and medical opinions that are not based on scientific research are considered weaker sources (Table 2).<sup>2</sup> The strength of RCTs lies in the process of

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randomization. This process balances both known and unknown confounding and biasing factors across the comparison groups, and thus makes the conclusions more reliable. However, while RCTs are considered the gold standard for evidence, they may not always be practical or ethical. For example, if one wanted to evaluate the effect of smoking on lung cancer, it would be unethical to assign one group of patients to smoke every day, while at the same time, assigning another group to refrain from smoking. In situations like these, observational or case-control studies are necessary. Similarly, lower levels of evidence are acceptable for the study of rare conditions where it is more difficult to perform large RCTs.

Several fundamental concepts underlie the proper application of the EBM process and the appropriate appraisal of evidence. The first is the use of suitable study outcomes. A clinical endpoint may or may not be perceived by the patient, but is clinically relevant. Morbidity and mortality are two clinical endpoints commonly used in clinical trials. Conversely, surrogate markers are those that act as surrogates for a disease process and are typically thought to be important in the pathophysiology of the disease. For example, medications for diabetes mellitus are often selected based on their ability to lower levels of hemoglobin A1C levels.<sup>6</sup> However, even if the drug is able to lower this surrogate marker of diabetes, it may not improve the quality of life or decrease the mortality and morbidity associated with the disease. In fact, in some instances, drugs that have been shown to act beneficially on surrogate markers have actually increased mortality and morbidity.<sup>7</sup> Evidently, to the patient, the quantity and quality of life are more important than blood levels of hemoglobin A1C. Thus, when evaluating trials, it is preferable to look at clinical outcomes as opposed to surrogate outcomes.

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**Table 1.** Steps Involved in the Use of Evidence-Based Medicine

1. Defined and focused clinical question
2. Thorough search of the appropriate literature for all relevant clinical trials
3. Critical appraisal of the collected evidence
4. Patient-centred decision making
5. Monitoring of clinical outcomes

## EBM IN PRACTICE

One of the central, but arguably most challenging, aspects of modern medicine is keeping informed of the latest research. In order to assist physicians with this task, systematic reviews have become an important component of the practice of EBM. A systematic review is the process whereby all available clinical trials that seek to answer a clinical question and meet predefined inclusion criteria are aggregated into an analysis in order to create an overall conclusion. Once a systematic review has been performed, updates with new relevant research are expected. Some groups, such as the Cochrane Collaboration, require such updates be performed at least every two years. These reviews are especially useful to practicing clinicians as they are designed to provide a summary of the relevant clinical points that can be applied in medical practice.

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There are several independent organizations around the world that are involved in producing systematic reviews. The largest and most comprehensive is the Cochrane Collaboration, which was founded in 1992 and named in honour of Archie Cochrane, a pioneer in the use of randomized controlled trials.<sup>8</sup> It is a non-profit organization with centers distributed internationally. At each centre, experts in EBM produce systematic reviews that appraise and summarize evidence from many trials on a particular topic. This type of evidence arguably ranks the highest because it critically appraises and interprets the evidence and then provides both the clinical implications and future research directions.

Another major organization involved in producing evidence-based reports is the Therapeutics Initiative (TI), which was established in 1994 in the Department of Pharmacology and Therapeutics at the University of British Columbia.<sup>9</sup> The TI addresses controversial topics in medicine through short “Therapeutic Letters”, which are published every two months. The goal of these letters is to provide evidence-based prescription drug therapy after an extensive review of the most current literature by the Drug Assessment Working Group of the TI.

Before the letters are published, drafts are reviewed by all the members of the TI, including experts in a particular therapeutic area. As a member of the International Society of Drug Bulletins and of the Cochrane Collaboration, the TI has both international and local impact through the dissemination of its Therapeutic Letters and other evidence-based reports on its website.

As an example, in letter 62, the TI provides a case scenario to investigate the benefit gained from treating a patient with mild hypertension, defined as a blood pressure (BP) in the range of 140-160/90-100 mmHg.<sup>10</sup> They conducted a best-evidence search and concluded that treating patients within this BP range for five years achieves, on average, a 0.8% absolute risk reduction for total cardiovascular events. These results indicate that 125 patients must be treated with anti-hypertensive medications for five years in order to prevent one heart attack or stroke; in other words, the number needed to treat (NNT) would be 125 patients for five years. In addition, no significant reduction in total mortality was demonstrated. Should the patient therefore be treated? It is important that the patient understands the probability of benefit and participates in the decisions regarding treatment. This scenario demonstrates the complexity and difficulty of using EBM in practice. The fundamental message is that even the best evidence should not be blindly applied based on well-memorized cut-offs without placing the patient in context.

## EBM IN THE MEDICAL CURRICULUM

Careful practice of EBM by physicians and residents can help improve patient outcomes in the clinical setting, but will the use of EBM in teaching help medical students become better clinicians? Over the past decade, EBM has become increasingly integrated into the curricula of many medical schools. This change has been shown to improve students' ability to develop clinical questions and perform effective literature searches.<sup>11</sup> Evaluation of a longitudinal EBM curriculum has also shown an association with an increased breadth of knowledge of EBM that was sustained throughout the entire curriculum.<sup>12</sup> However, much work remains to be done in developing an effective curriculum for teaching EBM. One study evaluated perceived competence and actual performance in EBM techniques among medical graduates and found that, although many felt competent, the average score of the students was only 55% correct.<sup>13</sup>

In shaping their EBM curricula, many medical schools are moving away from teaching methods of critical appraisal, which form the basis of EBM, and instead simply emphasizing the implementation of evidence.<sup>14</sup> It is crucial that critical appraisal

**Table 2.** Levels of Evidence by Study Design

Level	Investigation Design
Ia	Meta-analysis of many RCTs
Ib	At least one large RCT
IIa	One controlled trial, without randomization
IIb	Controlled cohort or case-control studies
III	Non-experimental observational studies
IV	Case reports and clinical opinions

of evidence be applied at all levels of EBM. The term “evidence-based” may be used incorrectly or out of context, and it is important to consider factors such as for-profit funding, inappropriate controls, use of surrogate outcomes, publication and reporting biases and misleading reporting, when assessing the validity of individual studies or reviews.<sup>14</sup> This is the rationale behind the need to teach principles of EBM in addition to applying it in practice. Although systematic reviews are deemed to be the strongest form of medical evidence, not all systemic reviews follow the same set of standardized methodology or are of equal quality and reliability. A poorly conducted systematic review may not be immediately obvious to the reader. Additionally, many systematic reviews are not current; only Cochrane reviews are reliably updated every two years. Thus, simply reading the conclusion of a systematic review is seldom sufficient.

### CHALLENGES FACING EBM

While EBM may seem to be the calling of medicine in the twenty-first century, there are many barriers that EBM faces before it can become completely accepted as the standard in patient care. While some arguments against EBM are based on misunderstandings, other concerns are legitimate and must be addressed. A common criticism is that EBM is a clinical cookbook for physicians to apply to every patient with a certain illness. However, it is important to understand that EBM is only one component of clinical practice: the goal of EBM is to allow the physician to integrate patient preferences with clinical judgment and appropriate evidence.<sup>14</sup> Another misconception is that only the results of RCTs should be used as a basis for clinical recommendations. While RCTs may be desirable, they are not, as discussed earlier, suitable for all situations and outcomes.<sup>14</sup> EBM strives to use the best available evidence, which may not always be the best form of evidence (i.e., when RCTs are not available). Finally, a lack of evidence in the literature is not equivalent proof that a certain intervention lacks effectiveness.<sup>14</sup> EBM serves to identify knowledge gaps in the literature, acting as an important stimulus for additional RCTs.

There exist other genuine concerns that need to be addressed before EBM becomes more widely accepted. The greatest challenge now is identifying ways to modify clinical behaviour so that EBM is used routinely by practicing physicians.<sup>15</sup> As in any professional field, there is often resistance to change. Barriers to the adoption of EBM often cited by physicians include feasibility, time constraints, and inadequate resources.<sup>15</sup> In a study of surgical residents, challenges faced in the application of EBM were categorized as 1) at the institutional level, where the availability of resources and time needed to obtain them is limited; 2) at the resident level, where the motivation and desire to apply literature to practice is lacking and resistance from attending staff is sensed; and 3) at the attending level, where there is inadequate EBM knowledge and practice. All three factors impeded the use of EBM.<sup>15</sup>

Finally, the private sector constitutes another substantial barrier to the proper implementation of EBM. Several of these issues have been raised previously, including for-profit funding of research trials and the marketing of medications based on surrogate outcomes. Pharmaceutical companies may oppose

EBM when it conflicts with their marketing strategies and when certain medications, which may be more costly than older-generation drugs, are not shown to be any better in terms of clinical outcomes. It is also imperative to consider the influence that the pharmaceutical industry has on the development of clinical guidelines. Unfortunately, many current guidelines do not follow EBM principles as they are funded by groups with a vested interest. It is therefore vital that clinicians view recommended guidelines critically and be aware of biases when applying them in practice.

### SUMMARY

Although EBM continues to evolve and play a key role in providing systematic reviews to answer crucial questions in medical practice, there remain numerous challenges in the dissemination, acceptance, and application of that evidence. The principles of EBM are rooted in the use of the best-possible study designs, large sample sizes, and the careful and unbiased interpretation of the best available evidence to support or oppose given medical treatments or interventions. However, although EBM may help provide a fundamental framework for practitioners in the delivery of health care, it must be applied appropriately and be sensitive to the needs of individual patients. ☺

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