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A MANUAL FOR EVIDENCE-BASED CLINICAL PRACTICE

SECOND EDITION

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2 THE PHILOSOPHY OF EVIDENCE-BASED MEDICINE

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IN THIS CHAPTER:

Evidence-based medicine (*EBM*) is about solving clinical problems.[1] In 1992, we described EBM as a shift in medical paradigms.[1] In contrast to the traditional paradigm of medical practice, EBM places lower value on unsystematic clinical experience and pathophysiologic rationale, stresses the examination of *evidence* from clinical research, suggests that interpreting the results of clinical research requires a formal set of rules, and places a lower value on authority than the traditional medical paradigm. Although we continue to find this paradigm shift a valid way of conceptualizing EBM, the world is often complex enough to invite more than 1 useful way of thinking about an idea or a phenomenon. In this chapter, we describe another conceptualization that emphasizes how EBM complements and enhances the traditional skills of clinical practice.

TWO FUNDAMENTAL PRINCIPLES OF EBM

As a distinctive approach to patient care, EBM involves 2 fundamental principles. First, EBM posits a *hierarchy of evidence* to guide clinical decision making. Second, evidence alone is never sufficient to make a clinical decision. Decision makers must always trade off the benefits and *risks*, inconvenience, and costs associated with alternative management strategies and, in doing so, consider their patients' values and preferences.[1]

A Hierarchy of Evidence

What is the nature of the *evidence* in EBM? We suggest a broad definition: any empirical observation constitutes potential evidence, whether systematically collected or not. Thus, the unsystematic observations of the individual clinician constitute one source of evidence; physiologic experiments constitute another source. Unsystematic observations can lead to profound insights, and wise clinicians develop a healthy respect for the insights of their senior colleagues in issues of clinical observation, diagnosis, and relations with patients and colleagues.

At the same time, our personal clinical observations are often limited by small sample size and by deficiencies in human processes of making inferences.[3] Predictions about *intervention effects* on patient-important outcomes based on physiologic experiments usually are right but occasionally are disastrously wrong. Numerous factors can lead clinicians astray as they try to interpret the results of conventional open trials of therapy. These include *natural history*, *placebo effects*, patient and health worker expectations, and the patient's desire to please. We provide a number of examples of just how wrong predictions based on physiologic rationale can be in Chapter 9.2, Surprising Results of Randomized Trials.

Given the limitations of unsystematic clinical observations and physiologic rationale, EBM suggests a number of hierarchies of evidence, one of which relates to issues of *prevention* and treatment (Table 2-1).

TABLE 2-1

Hierarchy of Strength of Evidence for Prevention and Treatment Decisions

- N-of-1 randomized trial
- Systematic reviews of randomized trials
- Single randomized trial
- Systematic review of observational studies addressing patient-important outcomes
- Single observational study addressing patient-important outcomes
- Physiologic studies (studies of blood pressure, cardiac output, exercise capacity, bone density, and so forth)
- Unsystematic clinical observations

Issues of diagnosis or *prognosis* require different hierarchies. For instance, *randomization* is not relevant to sorting out how well a test is able to distinguish individuals with a *target condition* or disease from those who are healthy or have a competing condition or disease. For diagnosis, the top of the hierarchy would include studies that enrolled patients about whom clinicians had diagnostic uncertainty and that undertook a *blind* comparison between the candidate test and a *criterion standard* (see Chapter 16, Diagnostic Tests).

Clinical research goes beyond unsystematic clinical observation in providing strategies that avoid or attenuate spurious results. The same strategies that minimize *bias* in conventional therapeutic trials involving multiple patients can guard against misleading results in studies involving single patients.[4] In the *n-of-1 randomized controlled trial* (*n-of-1 RCT*), a patient and clinician are *blind* to whether that patient is receiving active or placebo medication. The patient makes quantitative ratings of troublesome symptoms during each period, and the n-of-1 RCT continues until both the patient and the clinician conclude that the patient is or is not obtaining benefit from the target intervention. N-of-1 RCTs can provide definitive evidence of treatment effectiveness in individual patients[5,6] and may lead to long-term differences in treatment administration (see Chapter 9.5, N-of-1 Randomized Controlled Trials).[7] Unfortunately, n-of-1 RCTs are restricted to chronic conditions with treatments that act and cease acting quickly and are subject to considerable logistic challenges. We must therefore usually rely on studies of other patients to make inferences regarding the patient before us.

The requirement that clinicians generalize from results in other people to their patients inevitably weakens inferences about treatment impact and introduces complex issues of how trial results apply to individual patients. Inferences may nevertheless be strong if results come from a *systematic review* of methodologically strong RCTs with consistent results. Inferences generally will be somewhat weaker if only a single RCT is being considered, unless it is large and has enrolled patients much like the patient under consideration (Table 2-1). Because *observational studies* may underestimate or, more typically, overestimate *treatment effects* in an unpredictable fashion,[8,9] their results are far less trustworthy than those of RCTs.

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