

to determine for themselves whether medical interventions alter the disease course and improve the length or quality of life. The meaning of practicing EBM becomes clearer through an examination of its four key steps:

1. Formulating the management question to be answered
2. Searching the literature and online databases for applicable research data
3. Appraising the evidence gathered with regard to its validity and relevance
4. Integrating this appraisal with knowledge about the unique aspects of the patient (including the patient's preferences about the possible outcomes)

The process of searching the world's research literature and appraising the quality and relevance of studies thus identified can be quite time-consuming and requires skills and training that most clinicians do not possess. Thus, identifying recent systematic overviews of the problem in question (Table 3-3) may offer the best starting point for most EBM searches.

Generally, the EBM tools listed in Table 3-3 provide access to research information in one of two forms. The first, primary research reports, is the original peer-reviewed research work that is published in medical journals and accessible through MEDLINE in abstract form. However, without training in using MEDLINE, quickly and efficiently locating reports that are on point in a huge sea of irrelevant or unhelpful citations may be difficult, and important studies could also be missed. The second form, systematic reviews, is the highest level of evidence in the hierarchy because it comprehensively summarizes the available evidence on a particular topic up to a certain date. To avoid the potential biases in review articles, predefined explicit search strategies and inclusion and exclusion criteria are used to find all of the relevant scientific research and grade its quality. The prototype for this kind of resource is the Cochrane Database of Systematic Reviews. When appropriate, a meta-analysis quantitatively summarizes the systematic review findings. The next two sections explicate the major types of clinical research reports available in the literature and the process of aggregating those data into meta-analyses.

SOURCES OF EVIDENCE: CLINICAL TRIALS AND REGISTRIES

The notion of learning from observation of patients is as old as medicine itself. Over the last 50 years, physicians' understanding of how best to turn raw observation into useful evidence has evolved considerably. Case reports, personal anecdotal experience, and small single-center case series are now recognized as having severe limitations in validity and generalizability, and although they may generate hypotheses or be the first reports of adverse events, they have no role

in formulating modern standards of practice. The major tools used to develop reliable evidence consist of the randomized clinical trial and the large observational registry. A registry or database typically is focused on a disease or syndrome (e.g., cancer, CAD, heart failure), a clinical procedure (e.g., bone marrow transplantation, coronary revascularization), or an administrative process (e.g., claims data used for billing and reimbursement).

By definition, in observational data, the investigator does not control patient care. Carefully collected *prospective* observational data, however, can achieve a level of evidence quality approaching that of major clinical trial data. At the other end of the spectrum, data collected retrospectively (e.g., chart review) are limited in form and content to what previous observers recorded, which may not include the specific research data being sought, e.g., claims data. Advantages of observational data include the inclusion of a broader population as encountered in practice than is typically represented in clinical trials because of their restrictive inclusion and exclusion criteria. In addition, observational data provide primary evidence for research questions when a randomized trial cannot be performed. For example, it would be difficult to randomize patients to test diagnostic or therapeutic strategies that are unproven but widely accepted in practice, and it would be unethical to randomize based on sex, racial/ethnic group, socioeconomic status, or country of residence or to randomize patients to a potentially harmful intervention, such as smoking or deliberately overeating to develop obesity.

A well-done prospective observational study of a particular management strategy differs from a well-done randomized clinical trial most importantly by its lack of protection from treatment selection bias. The use of observational data to compare diagnostic or therapeutic strategies assumes that sufficient uncertainty exists in clinical practice to ensure that similar patients will be managed differently by different physicians. In short, the analysis assumes that a sufficient element of randomness (in the sense of disorder rather than in the formal statistical sense) exists in clinical management. In such cases, statistical models attempt to adjust for important imbalances to "level the playing field" so that a fair comparison among treatment options can be made. When management is clearly not random (e.g., all eligible left main CAD patients are referred for coronary bypass surgery), the problem may be too confounded (biased) for statistical correction, and observational data may not provide reliable evidence.

In general, the use of concurrent controls is vastly preferable to that of historical controls. For example, comparison of current surgical management of left main CAD with left main CAD patients treated medically during the 1970s (the last time these patients were routinely treated with medicine alone) would be extremely misleading because "medical therapy" has substantially improved in the interim.

TABLE 3-3 SELECTED TOOLS FOR FINDING THE EVIDENCE IN EVIDENCE-BASED MEDICINE (EBM)

Name	Description	Web Address	Availability
Evidence-Based Medicine Reviews	Comprehensive electronic database that combines and integrates: 1. The Cochrane Database of Systematic Reviews 2. ACP Journal Club 3. The Database of Abstracts of Reviews of Effectiveness	www.ovid.com	Subscription required. Available through medical center libraries and other institutions.
Cochrane Library	Collection of EBM databases, including The Cochrane Database of Systematic Reviews—full text articles reviewing specific health care topics.	www.cochrane.org	Subscription required. Abstracts of systematic reviews available free online. Some countries have funding to provide free access to all residents.
ACP Journal Club	Collection of summaries of original studies and systematic reviews. Published bimonthly. All data since 1991 available on website, updated yearly.	www.acpj.org	Subscription required.
Clinical Evidence	Monthly updated directory of concise overviews of common clinical interventions.	www.clinicalevidence.com	Subscription required. Free access for United Kingdom and developing countries.
MEDLINE	National Library of Medicine database with citations back to 1966.	www.nlm.nih.gov	Free via Internet.