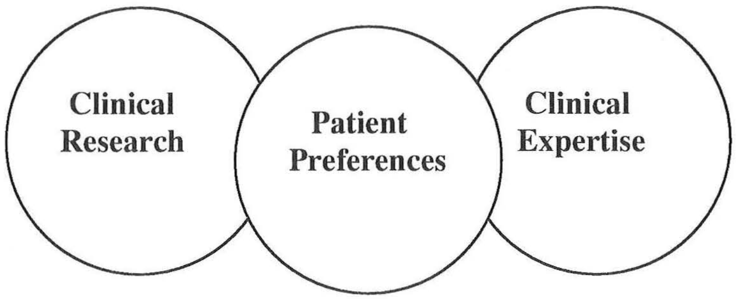
Ask and Ye Shall Retrieve: Bringing Evidence to the Point of Care



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> **"There is a science to the art of intervening in the health of persons and populations. It has its basis in the successful quest for interventions that produce huge changes in the structure and functions of cells, tissues, organs and entire organisms, including humans and their societies (1)."**

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THE CLINICIAN'S NEED FOR INFORMATION

Generating the Information Need: The Clinical Scenario

Consider the following day practicing medicine on the general medicine inpatient service and in the general medicine primary care clinic.

- Patient One: A 67-year-old man with a history of atrial fibrillation for several years presents for a routine clinic visit. He is usually seen by one of the other clinicians in the clinic but today he is scheduled with you. He reports no symptoms or limitations, but you notice that he is on any anticoagulation medication. You perform an ECG which reveals atrial fibrillation with a controlled ventricular response of 80. Upon reviewing the patient's chart, you cannot locate any prior study of his systolic function or left atrial size, but he has no history of clinical CHF, prior stroke or TIA, diabetes mellitus or hypertension. Would anticoagulation with warfarin be more effective in reducing this patient's risk of stroke than aspirin; and would the benefits of warfarin outweigh the associated risks of bleeding? What is the likelihood that cardioversion would be successful in reverting this man to NSR and his rhythm remaining in sinus? What factors influence his prognosis and how will you answer his question: "What can I expect?"
- Patient Two: a 34 year-old woman with a history of migraine headaches walks in to the primary care clinic. She reports a severe migraine headache over the last several days that has precipitated outbursts of rage and physical violence. However, her history is complicated by substance abuse, including narcotic dependence. She also has a complicated psychiatric profile. A phone call to her neurologist reveals that she has already violated her pain contract ii having used a 3 month supply of intranasal Staydol in 2 weeks. He recommends avoidance of narcotics. She states that NSAIDS, sumatriptin and dihydroergotamine are ineffective for her. What other options are available to treat her acute headache?
- Patient Three: a 28 year-old man with Type I diabetes mellitus presents for a routine visit. You have previously requested a 24-hour urine for creatinine and protein but it has not been returned. When questioned, the patient relates that he works long hours as an accountant and found it very difficult and embarrassing to be collecting his urine at work. You wonder how a spot urine for microalbumin measurement would compare as a diagnostic test for significant albuminuria in this patient.
- Patient Four: a 49 year-old woman with bilateral silicone breast implants presents to clinic with records from a rheumatologist who practices outside your health care system. She sought his opinion regarding whether her implants were causing her symptoms of fatigue, myalgia and arthralgia. She has undergone extensive evaluation by a rheumatologist at your institution which has been unrevealing for any objective findings of connective tissue disease. The outside rheumatologist disagrees and has concluded that she is manifesting the latter and that it is likely due to her implants. The patient is preparing to file suit against the manufacturer of the implants and she asks that, as her primary care physician, you testify on her behalf. Could this woman be experiencing adverse side effects from her silicone breast implants?

These are just a sample of the patients seen and the questions generated by the residents, and myself, who saw them. Most clinicians will not find this experience unusual for a typical day in clinical practice. Just how often do questions arise in clinical practice? Investigators have observed and interviewed physicians while they practice, counting the questions. The rate of question asking in these studies ranged widely, from as few as 1 question every 15 patients in outpatient family practices (2) to 1 question every 1 or 2 patients in mixed specialty practices (3,4) and up to 5 questions per patient on an inpatient medicine teaching service (5). This discussion will cover how we as clinicians might pose better questions and answer them more efficiently and effectively.

How have Information Needs been Met?

What do we as clinicians do with all these questions that clinical practice generates and are needed to provide care for our patients? In a detailed study of office-based physicians, of all the questions formulated by clinicians only approximately 30% were pursued. (3) And of the questions asked, how do clinicians decide what to pursue? Physicians are most likely to pursue questions that they consider urgent and likely to have a definitive answer but still, even with this priority, only 50 to 60% of these were pursued (4). In this study it was notable that out of 295 questions, literature searches were performed for only two questions.

What do clinicians use to answer clinical questions? Most frequently, they report using medical textbooks and colleagues, either peers or subspecialty consultants. One of the largest and best performed studies of how office-based clinicians obtain information utilized a standardized telephone survey of a random sample of the American Medical Association's "Masterlist of Physicians". The use of textbooks and consultation with specialists and peers were the most common methods for meeting immediate needs for information to solve a clinical problem (6). Although this study is older and the response rate was only about 50%, other studies have confirmed its findings (3,7). Although physicians say they use journals, textbooks and other print material, in one study in which clinicians were directly observed these resources were actually used for less than 20% of the questions for which an answer was pursued. Most questions in an ambulatory care practice go unanswered and the remainder are usually answered by a colleague (3).

What are the Consequences of How Information Needs are Met?

The methods by which clinicians keep up to date and pursue answers to clinical questions have obvious practical implications for how they practice medicine. It is concerning that for many clinical interventions that have been adopted before their evaluation was complete, they were later found to be harmful for patients (8). For example, at one time flecanide and encainide were used quite commonly for ventricular arrhythmia prophylaxis but it wasn't until later that it was appreciated that, although they suppressed premature ventricular contractions, their use was associated with an increase in mortality (9).

It is also concerning that several studies have demonstrated that for many important innovations in medicine, clinical practice lags behind the evidence. Williamson and colleagues found that practitioners were often unaware of several common and recommended procedures for patient management (7). For example, about 40% were not aware of the established role of glycosolated hemoglobin for assessing diabetic control. Stross found delays in the implementation of results from the Hypertension Detection and Follow-Up Program into clinical management of hypertension that correlated strongly with the time since training was completed (10). Despite the fact that ACE inhibitors have consistently been shown to improve the symptoms of heart failure, increase survival with this condition and reduce its economic burden, the best overall treatment is 50-60% (11). Antman and colleagues compared the recommendations of experts with cumulative meta-analyses of randomized controlled trials of the effectiveness of various treatments for myocardial infarction and found significant delays in experts' recommendation of the therapies (12). Most significantly, it took over half of the experts 13 years to begin recommending thrombolytic therapy when compared with the time at which post hoc cumulative meta-analysis demonstrated efficacy for this treatment. So, however clinicians are addressing their information needs, there appears to be a problem getting the research evidence into clinical practice.

What are Barriers to Meeting Information Needs?

1) Information explosion in biomedicine

Why do clinicians pursue so few of the clinical questions they ask? And why does clinical practice lag behind the research evidence? There are likely many reasons. First of all, there has been an information explosion in biomedicine over the last decade. There are now more than 20,000 biomedical journals and more than 17,000 new biomedical books (13) and six million new articles published annually (14). If you read two articles per day by the end of a year you'll be 55 centuries behind in reading, and that was in 1979 (15). No wonder 2/3 of physicians feel the current volume of scientific literature is unmanageable (7).

Not only has there been an increase in the overall volume of knowledge, but also astonishing advances in the quality of clinical care interventions. Consider a brief time interval in clinical medicine and the advancements in the many different fields of medicine. Over the interval from 1994 to 1996, reports were published that established inhaled corticosteroids as the cornerstone treatment for asthma, metformin as a useful adjunct therapy to glyburide in Type I diabetes mellitus, the role of serotonin reuptake inhibitors in the treatment of depression, and demonstrated that ACE inhibitors combined with more intensive insulin therapy have more favorable effects on long-term outcomes in patients with Type I diabetes mellitus, that ACE inhibitors have life-prolonging efficacy in the management of CHF, that eradication of *Helicobacter pylori* leads to cure approximately 90% of the time and that this organism is the most common cause of ulcer disease, and that famcyclovir reduces the duration of postherpetic neuralgia in patients over 50 years (16). In reviewing this list, the enormous impact of these interventions on the quality of clinical care is obvious.

2) Finding information is difficult

But for all the information that is 'out there' to help our patients, it has become increasingly difficult to get at the information that is usable and ready for application to our patients. This difficulty is partly due to the sheer volume, but there are other reasons as well. In order to achieve innovations in biomedicine, many more preliminary studies are performed than those that finally establish a successful role for an intervention. Usually thousands of studies are must be done to find and verify one clinically useful truth (17). For example, the number of original studies and systematic review articles in the most prestigious medical journals that provide reasonable strong evidence and are ready for application into clinical practice has been assessed to be less than one in every two issues, which represents only 10% of the total (18). These thousands of studies are dispersed among all the biomedical and clinical journals and as clinicians, we must sort among them somehow to find what is valid and clinically useful recognizing that many of these preliminary findings turn out to be invalid or represent false leads.

Not only are the definitive studies for clinical medicine difficult to find due to the sheer volume, but they may also be difficult to find because the clinically useful information is often not in places that clinicians routinely read to keep up with their field. Most medical journals serve archival and organizational objectives so clinicians are often not well served by what is published in them (17).

3) The quality of evidence cannot be inferred from a journal's reputation

Surveys of physicians have found that they place great importance on the reputation of the journal in deciding what to read and the overall merit of the studies published. In a study by Williamson, almost 60% of physicians responded that for an evaluation of the material they read, they rely on the peer-review process (7). But the quality of a study cannot be reliably inferred from the reputation of the medical journal in which it is published. There are a number of reports regarding the suboptimal methodologic quality of studies published in peer-reviewed journals (19-22). In a representative cross-sectional survey of biomedical journals having either the highest impact based on the number of times articles from a journal were cited in other scientific journals and medical librarians' recommendations, only one third of biomedical journals had policies mandating statistical review and half sent reports to a statistician only at discretion of the editor (19). Editors judged, however, that statistical review resulted in an important change in a manuscript about half of the time. This represents an improvement, albeit less than ideal methodologic review, in the 10 years that have elapsed since a previous study using the same design (20). Other studies assessing the methodologic quality of published articles from various highly reputable journals of high circulation using standardized criteria have demonstrated serious deficiencies as well (7, 21, 22). In general, these deficiencies tend to bias towards an exaggeration of treatment differences (22).

Some journals have now begun to employ methodologic review as a component of the review process. These include *The Lancet*, *British Medical Journal*, the *Journal of the American Medical Association* and the *Annals of Internal Medicine*. However, Gore reported the impact of implementing statistical review of submitted papers that were considered candidates for publication after conventional review in *Lancet* (23) Biostatisticians evaluated various methodological aspects of 191 reports according to well-accepted, standardized methodologic criteria. Only 8% of the reports were recommended for publication, while the majority received the recommendation to accept with revision or revise and review. Of the 14% that received a recommendation to reject due to methodologic problems that were considered insurmountable, a third were still published.

The finding of methodologic problems in many reported studies does not necessarily imply a purposive intent to ignore the scientific validity and applicability of studies in what is published. There are many factors that are considered in the editorial process of biomedical journals that influence what is finally published. An important factor is that these journals serve multiple communication purposes: that of scientist to scientist, scientist to clinician, clinician to clinician and clinician to scientist (14). However, given the lack of understanding of basic statistical concepts demonstrated by most clinicians, they are clearly at a disadvantage in evaluating the scientific merit of the articles they read (24, 25).

4) The way clinicians currently obtain and seek information doesn't work

Information acquisition can be understood as that directed to maintain "current awareness" and that directed towards " look-up sources" for clinical problem-solving (26). The former type of information seeking keeps clinicians up to date on innovations and advancements in medicine in general. The latter type is used by clinicians when faced with a specific patient's clinical problem since information acquired for general use often fails to come or is insufficient to address the information needs generated by a specific patient at a particular time.

As previously mentioned, the predominant means that clinicians use to answer clinical questions that arise in encounters with patients are textbooks or consultation with peers or subspecialists. Most textbooks of medicine are published on a two to four year cycle. In addition, it takes about a year for a chapter to be published once the author finishes writing it (27). For example, four years after the publication of a review of 33 randomized trials (28) clearly showing the value of thrombolytic therapy a new version of a prominent textbook claimed that the benefits of thrombolytic therapy were not established (29). Textbooks are valuable and convenient sources for some information that remains fairly stable but may not be sufficiently reliable for something as rapidly advancing as therapeutics. However, evidence demonstrating the effectiveness of consultations with peers or specialists in keeping physicians up to date is lacking (30).

In addition to textbooks and their colleagues, clinicians also rely heavily on biomedical journals, and informal and formal continuing medical education conferences (CME) primarily to meet ongoing, general information needs (6). The problems clinicians have accessing relevant information in journals and the difficulty in assessing the methodologic stengths of the articles they contain have already been discussed. Despite the ubiquitous offerings of CME, its effectiveness has been poorly studied. In one systematic review of the effectiveness of CME interventions, only 13% were randomized trials and an even smaller proportion assessed impact on patient outcomes (31).

In general, mailed CME materials and formal CME in the form of didactic programs have not been demonstrated to have an appreciable effect on performance (31-34). Of interest, in one study evaluating the efficacy of didactic CME, although little change in performance was demonstrated for topics selected by participants, some change was observed for those topics to which the participants were assigned (33). However, CME programs that involve a pretest assessment of knowledge or practice needs, which provide the opportunity to practice or rehearse new techniques or skills and provide postcourse activities that facilitate change in physician's practice setting have been found to have some efficacy (34).

5) The limiting factor of time

Most older studies indicate that the average clinicians spend between three and five hours per week reading (35, 36). A more recent study of UK houseofficers and clinicians revealed only about one hour of average reading time per week (37). Clearly, in the midst of a busy practice finding time to keep up with the literature and pursue answers to clinical questions is difficult, particularly with the additional demand to increase the volume of patients seen inherent to managed care. In one survey of clinicians, the barrier the clinicians themselves offered most frequently to their keeping up and pursuing clinical questions was lack of time, but they also cited the cost, poor organization and nonexistance of sources (3). Clinicians are obviously challenged to meet their needs for information in the most efficient and effective means possible.

EVIDENCE-BASED MEDICINE: A PARADIGM FOR ASKING AND ANSWERING CLINICAL QUESTIONS (AND MORE...)

What Evidence-Based Medicine Is

How can asking and answering questions in clinical medicine be conceptualized so that we can become more effective as clinicians in caring for patients? An emerging paradigm is that of evidence-based medicine (EBM) which has largely been developed by the Evidence-Based Medicine Working Group at McMaster University in Canada (38, 39). "EBM is the conscientious and judicious use of current best evidence from the clinical care research in the management of individual patients" (38).

EBM can be conceptualized as a model for evidence-based clinical decisions. In a simplified form, clinical decisions can be represented as encompassing three components that interface in deciding on the care for an individual patient's problem: 1) clinical research evidence, 2) patient preferences and 3) clinical expertise (8). Sound evidence from research must be an integral part of clinical decision-making. The basic question is not whether research evidence should play a role but how to establish this role effectively and efficiently. Patient preferences encompass the choice of treatments, seeking care from other providers and compliance with recommended therapy. The impact of patient preferences can be expected to grow in importance as patients gain increasingly greater and independent access to medical information. The clinical expertise needed to assess patient's problem draws from knowledge of basic disease mechanisms and pathophysiology, skills in history taking, physical diagnosis, diagnostic testing, and prescribing treatment. In plain terms, EBM involves being able to discern current best evidence from the full spectrum of studies and for clinicians to provide themselves with quick access to dependable, up-to-date sources of information in which the link with research evidence is honest and explicit.

What Evidence-Based Medicine Isn't

Understanding what EBM is helps one understand what it isn't (37, 38), especially since much has been written about EBM and the perceptions of what it embodies may no longer be directly linked to its original conceptual model.

1) For the most part, it is not already in practice

The previous discussion regarding how clinicians meet their needs for information highlighted the ample "evidence" that their approach to taking care of patients does not routinely encompass explicitly formulating questions regarding their patients, looking for relevant literature and judging its scientific merit prior to integrating the information into clinical practice: in short, it does not constitute practicing evidence-based medicine. This conclusion is most convincingly borne out by the disparity between clinical practice and the evidence for many newer interventions.

2) It doesn't compete with or replace the role of basic science in our understanding of medicine

An important symbiosis exists between clinical care research and evidence from research into the basic nature of health disorders. Studies in the laboratory form the foundation of our knowledge about clinical problems and the groundwork for most diagnostic procedures and clinical interventions. But systematic studies of their application in clinical settings are needed. EBM focuses on these systematic studies because they represent the most advanced stages of testing to ascertain whether the innovations of basic science work, how well they work, and for whom they work when applied in the clinical setting. EBM depends on and builds on basic science.

3) It is not synonymous with cookbook medicine

Some clinical decisions are straightforward. Others are very sophisticated and cannot be replicated by even the most advanced computer software programs. EBM involves the judicious use of research evidence and requires clinical expertise in balancing the risks and benefits of diagnostic tests and alternative treatments for each patient. It takes into account his or her unique clinical circumstances, such as baseline risk , comorbid conditions, and preferences and must inform the physician where evidence is lacking, is poorly done or doesn't apply. Although "evidence" is often incorporated into clinical guidelines, the conceptual basis of EBM does not promote a reflexive application to patients.

4) It is not the privileged tool of managed care to lower costs and inappropriately restrain the practice of medicine.

Some of the "products" of EBM have inevitably, and not always inappropriately, been used to support decisions of managed care organizations to limit services in an attempt to reduce the cost of health care. Although some studies may well not support the scientific merit of an intervention overall or for a more limited group of patients, nothing inherent to EBM guarantees that the cost of providing clinical care will be less. If a new intervention is found to be effective, its dissemination could well lead to an overall increase in costs and this is not incompatible with practicing EBM. It is a misperception of the full scope and intent of what EBM embodies to use it in a selective manner without regard for improving the quality care, and life, of patients.

5) It is not impossible

Many clinicians facing the barriers to keeping up with and integrating research evidence into practice are of the opinion that evidence-based medicine, if it is possible, is so only in the protected environment of the academic center where the "luxury" of spending the time needed to acquire skills in literature searching and critical appraisal, and the time to perform them, uniquely exist. But many studies have already demonstrated that students and clinicians can learn these skills, and that an evidence-based approach to clinical care is workable within our usual clinical environments (40, 41, 42). One study has found that McMaster medical school graduates who have been trained in EBM were more knowledgeable with respect to current therapeutic guidelines in the treatment of hypertension than were graduate of a traditional medical school (41). The McMaster Group have also successfully piloted the use of an "evidence cart" on the general medicine ward service that facilitated an evidence-based foundation for the majority of its clinical questions (42). The purpose of my discussion is to demonstrate that practicing evidence-based medicine isn't impossible; it is an acquired skill like many others we use as clinicians to care for patients. It is my intent to show how possible it is.

Steps in EBM

On a practical level, EBM can be conceptualized as a five-step process that most importantly BEGINS and ENDS with the PATIENT:

1) formulating a focused question
2) find the best evidence to answer the question
3) determine whether this evidence is valid and applicable to your patient
4) apply the evidence appropriately to your patient
5) evaluate your performance

FORMULATING THE CLINICAL QUESTION

The remainder of this discussion will focus on the first two steps involved in practicing evidence-based medicine: asking the question and retrieving the literature. The protocol will also a provide brief overview of critically appraising the literature and resources to assist in carrying out that step.

What comprises a well-built clinical question?

First, a well-built clinical question should be directly relevant to the problem at hand (43). Second, the question should be phrased to facilitate searching for a precise answer. A good question therefore needs to be focused and well articulated for all parts of its "anatomy". Questions can be understood as being comprised of four elements: the question is usually about a patient or a problem, seeks to know what intervention or exposure is associated with harm or will lead to helping the patient, seeks to compare this intervention with an alternative intervention, and asks what is the outcome of interest (44). Table 1 presents the elements of a good clinical question and tips for building them. The example illustrates building a clinical question for case one.

Table 1: Elements of a Well-Built Clinical Question

	1. Patient or problem	2. Intervention (a cause, a prognostic factor, a treatment, etc.)	3. Comparison intervention or exposure (when relevant)	4. Outcome(s)
Tips for building	Starting with your patient, ask 'How would I describe a group of patients similar to mine?' Balance brevity with precision.	Ask 'Which main intervention am I considering?' Be specific.	Ask 'What is the main alternative to compare with the intervention?' Again, be specific.	Ask 'What can I hope to accomplish or 'What could this really affect?' Again, be specific.
Example	'In patients with atrial fibrillation who over 67, but do not have DM, HTN, recent CHF or prior CVA…'	'…would adding anticoagulation with warfarin,…'	'…when compared with aspirin,…'	'…lead to lower rate of stroke from thromboembolism? Is this enough to be worth the increased risk of bleeding?'

Adapted from Sackett, 1997 (44).

Types of Clinical Questions

A vast spectrum of questions can be asked regarding clinical care, but the majority of questions that clinicians ask about stem from the central tasks of clinical work: clinical findings, etiology, differential diagnosis, diagnostic tests, prognosis, therapy, prevention, and self-improvement. Table 2 summarizes where questions arise from and provides descriptions for these clinical tasks (44). A more comprehensive grid can be constructed which serves as an explicit and systematic framework within which to ask questions about our patients. Table 3 presents the application of this framework to Patient One. It serves to illustrate the full spectrum of questions that can be generated for a single clinical problem. This framework is also helpful to refer to when you find that you're stuck in generating questions about your patient. What do you do if too many questions arise? Answer the question that is related to the most important issue for the patient. Which question, when answered, will help the patient the most? Keep in mind that different clinicians will ask different questions, depending on how a clinician perceives a patient's illness, his/her role in caring for a patient, what he/she recognizes as her knowledge deficits and how questions are prioritized and selected for pursuit based on urgency, feasibility, most frequent encountered, etc.

Table 2: Where Clinical Questions Arise

Clinical findings: how to properly gather and interpret findings from the history and physical exam
Etiology: how to identify causes for diseases
Differential diagnosis: when considering the possible causes of a patient's clinical problem, how to rank them by likelihood, seriousness and treatability.
Diagnostic tests: how to select and interpret diagnostic tests, in order to confirm or exclude a diagnosis, based on considering their precision, accuracy, acceptability, expense, safety, etc.
Prognosis : how to estimate the patient's likely clinical course over time and anticipate likely complications of the disease
Therapy: how to select treatments to offer patients that do more good than harm and that are worth the efforts and costs of using them.
Prevention: how to reduce the chance of disease by identifying and modifying risk factors and how to diagnose disease early by screening.
Self-improvement: how to keep up to date, improve your clinical skills and run a better, more efficient clinical practice.

Taken from Sackett, 1997 (44).

Table 3: Summary of Clinical Questions Formulated for a Clinical Encounter

Clinical tasks	1. Patient Or problem	2. Intervention	1. Comparison (if relevant)	4. Outcome(s)
1. Clinical examination	Heart failure	3rd heart sound	Echocardiogram	Sensitivity and specificity
2. Determining etiology	Atrial fibrillation	Alcohol	Other risk factors	Likelihood of different causes
3. Making a differential diagnosis	Atrial fibrillation	Age, hypertension,	Other causes	Likelihood of different causes
4. Selecting diagnostic tests	Systolic dysfunction	Echocardiogram	MUGA	Accuracy
5. Predicting prognosis	Atrial fibrillation	Duration of atrial fibrillation /left atrial size	Other prognostic factors	Resumption of NSR
6. Selecting therapy	Maintenance of NSR	Procainamide or quinidine	No antiarhythmic drug	All-cause mortality
7. Attempting prevention	Atrial fibrillation	Warfarin	Aspirin	Thromboembolic and bleeding events
8. Seeking self-improvement	Warfarin/aspirin	To the CD-ROM	To the library	Better understanding

Adapted from Sackett, 1997 (44)

Why bother to focus on building better questions?

Why should busy clinicians bother to build their skills in spotting their knowledge gaps and asking answerable questions? Many more-experienced clinicians may feel they are already adequately skilled in identifying information gaps that stem from a patient encounter and in formulating these gaps as clinical questions. In fact, when asked, this is the response of most clinicians. However, clinicians tend to ask predominantly therapy and diagnosis questions, and do not routinely sample from the full spectrum of the types of questions that can be asked. One might presume that these are, " in truth", the most common questions but these are not the questions that are of most interest to patients. Making a diagnosis and defining treatment are no doubt important in the clinical care of patients but what patients most want to know is "what's going to happen to them" (27). This question is one of prognosis. But even if clinicians are adept in identifying their information gaps, they often are not skilled in formulating a question in such a way as to make it more searchable. The formulation of a question to facilitate searching involves appropriately identifying the study question type so that the optimal type of study design to answer the question can be recognized, so that abbreviated search strategies can be utilized and so that the question is precise enough to narrow the search to what will be most relevant to your patient's care and save time.

Table 4: A Comparison of the Type of Question and the Best Study Type to Answer It

Type of Question	Type of Study
Clinical examination	Prospective, blind comparison to gold standard
Diagnostic Test	Prospective, blind comparison to gold standard
Prognosis	Cohort study > case-control study > case series
Therapy	Randomized controlled trial is strongly preferred
Etiology / Harm	Randomized, controlled trial > cohort study > case-control study > case series
Prevention	Randomized, controlled trial > cohort study > case-control study > case series
Cost	Economic analysis

Asking questions takes curiosity, humility, practice, and some coaching. Even though no clinical trial as yet has demonstrated that explicitly and systematically building good clinical questions provides better outcomes for patients, this process may help (45):

- to suggest questions that might otherwise be overlooked
- make the best use of scarce reading time in a manner most directly relevant to out patients
- keep reading time focused on our own learning needs
- suggest the forms answers will take so we'll recognize them more quickly when we find them
- lead directly to planning efficient search strategies
- reawaken the power of our curiosity and delight in learning and reinforce the self-directness of our own learning
- communication with other physicians when developed in the context of referrals or consultation
- facilitate teaching clinical medicine by making questions more explicit for learners.

CLINICAL EVIDENCE SOURCES: FINDING AND FILTERING THE EVIDENCE

Once a clinical question is asked, the hurdle of answering it is presented. Never before have there been such vast amounts of valid information and such rapid, powerful ways of finding it. The key is finding it and knowing what to do with it. To manage information needs, Fletcher describes a sequence where clinicians must find potentially relevant information, filter out the best from the much larger volume of less credible information, and judge whether to believe the information that remains (14). My discussion of clinical evidence sources will begin with those sources clinicians typically begin with, then move on to the expanded possibilities of resources now available, and finally consider some overall strategies for meeting information needs.

Electronic textbooks

Although textbooks are especially good for topics that have not changed much in recent years, they are limited sources of information in fields that are rapidly changing. Many electronic textbooks on CD-ROM are now available but most textbooks offered in this form are usually updated no more frequently than the parent, paper-based book. However, some electronic textbooks are unique in undergoing regular updates (usually quarterly) so that evidence is more current and for citing of evidence, often in some detail so as to facilitate an abbreviated critical appraisal. This type of textbook is more expensive, but you get so much more. The CD-ROM versions of these electronic textbooks are recommended so that adding new pages isn't cumbersome.

The most familiar resource of this type is SAM (Scientific American Medicine) (Rubenstein E, Federman DD, eds. Scientific American Medicine. New York: Scientific American Inc). A new addition to offerings in electronic textbooks is Current Practice of Medicine (Gotto AM ed. Current Medicine Inc. Philadelphia, PA). The paper-based version consists of 12 soft-cover issues, each addressing subspecialties in medicine but it does not address primary care. It is updated only annually and costs $239. A CD-ROM version is also available (at a cost of $125) which also includes MEDLINE, GenRx drug information, and major society practice guidelines.

UpToDate (Adult Primary Care and Internal Medicine. Fletcher SW, Fletcher RH, Aronson MD. eds) is another updated electronic textbook that reviews 130 medical journals every month and is updated quarterly. It addresses subspecialty areas in medicine as well as offering the newly added Adult Primary Care and Internal Medicine. It also includes an extensive drug information database and is fully referenced, which facilitates database searching, with instant access to MEDLINE abstracts for cited references. A demo of Up-To-Date can be downloaded from their web site: www.uptodate.com.

Full-Text On-line Journals

Increasingly, the full-text of several leading journals such as the *Annals of Internal Medicine*, the *British Medical Journal*, the *Journal of the American Medical Association*, the *Lancet*, and the *New England Journal of Medicine* are available on-line and on CD-ROM. Although the electronic version facilitates searching, this type of evidence source still provides inadequate exposure to the literature. Even if a clinician read 11 journals regularly she would still have only seen 80% of the scientifically strong, clinically relevant articles (18).

The MEDLINE Database

Most clinicians will have some familiarity with MEDLINE. This premiere biomedical database is prepared by the National Library of Medicine (NLM) and covers all areas of medicine beginning in 1966. It now indexes over 4000 journals, contains over nine million citations and is updated weekly (46).

1) The structure of MEDLINE

The NLM indexes each new MEDLINE citation with a number of terms (usually 10-12) which represent the contents of the article. These terms comprise a vocabulary, referred to as Medical Subject Headings (MeSH), which function as a controlled thesaurus in which each MeSH term represents a single concept appearing in the biomedical literature. A few terms attached to each citation are judged as representing the major concepts of the article, referred to as "Major Concept" headings, which comprise the Index Medicus. The other MeSH terms are considered secondary. The major concept terms are organized into a complex set of 15 hierarchies, called the MeSH Tree Structure, within which the MeSH terms are arranged into a set of branching, tree-like structures. Each hierarchy begins with a category that forms the root of the tree, and then progresses from more general to more specific as one moves from the root to the branches of the tree. New MeSH terms are added, modified or removed on an annual basis to reflect important changes in biomedical concepts appearing in the literature.

2) Searching MEDLINE: the Fundamentals

MeSH terms can be used to rapidly retrieve a citation or others indexed with the same term. In addition, MeSH subheadings are a group of 80 terms that are used to qualify MeSH terms and limit retrieval to a specific aspect of a biomedical concept. These subheadings are explained in MEDLINE "Scope Notes" that help the searcher select appropriate subheadings to aid in searching. MeSH contains some types of terms not designated as major concept headings but which can also be used for searching. The most useful of these are the MeSH "Publication Types" which characterize the type of publication rather than what the article is about. Some examples of these include "clinical trial", "randomized controlled trial", "consensus development conference", "meta-analysis", and "review". The indexing of some aspects of research methodology in "publication types" facilitates not only rapid retrieval, but also retrieval of citations that are the most relevant and scientifically sound.

The greatest challenge in using MEDLINE to search the literature is how to represent the topic or question to be searched. Free-text terms in the title or abstract can be used to search for citations but since the language used by the author does not necessarily conform to any standard or conventional vocabulary, there is no assurance of a match between words selected for the search and the concept conveyed by the author. For example, a clinician searching MEDLINE using the text word "hypercholesterolemia" may miss citations for which the author used the term "hyperlipidemia" to convey the same concept. Therefore, it is usually best to start with the MeSH indexing term as a good first approach. Studies have demonstrated that MeSH-based searching of the literature is more sensitive than free-test searching. However, using title and abstract searching (called text word searching) can be helpful for new concepts that indexers have not yet assigned MeSH terms to. However, 90% of clinicians report having at least moderate difficulty with inadequacies of terms in Index Medicus (7). The MeSH vocabulary is large, complex and difficult to master. Fortunately, extensive cross-referencing and the use of MeSH entry terms that link commonly used terms to MeSH terms (often called mapping) have been developed and are now aided by increasingly sophisticated software programs.

How well a search strategy performs depends on the goals for the search and these should be kept in mind when developing search strategies (46). Sensitivity, or recall, can be understood as the ability of the search to identify all relevant citations in the database. The average sensitivity of MeSH-based searching is about 50%. Some strategies that can be used to increase the sensitivity of a search are provided in Table 5. However, information needs are not always best satisfied by a comprehensive retrieval of a large volume of <u>all</u> the relevant citations. The specificity, or precision, of the search reflects its ability to exclude irrelevant citations. Often, the timely and effective application of information requires that only a few of the <u>most</u> relevant citations be retrieved and that time is not wasted in excluding irrelevant citations. The specificity of MeSH-based searches averages about 65%. In general, the specificity of free-text searches is usually better than their sensitivity. Some strategies that can be used to enhance the specificity of a search are presented in Table 6. The relationship between sensitivity and specificity of a search is related to a number of variables, but in general, strategies to optimize one usually compromise the other. A searcher must learn to effectively balance the sensitivity and specificity of searching.

Table 5: Strategies for Increasing the Sensitivity of a Search

1) Broaden the question
2) Use the "Explode" feature of MEDLINE
3) Locate a known relevant article in MEDLINE, then search with the relevant article's MeSH terms
4) Identify a specific MeSH term by browsing the appropriate MeSH tree
5) Try different combinations of terms
6) Add in and combine terms of related meaning
7) Use truncation (* or $) or wildcard (?) in free text/text word or thesaurus/subject

Table 6: Strategies to Enhance the Specificity of a Search

1) Narrow the question using MeSH terms, adding in terms (using AND) to represent other aspects of the question
2) Limiting to language of article, to human or animal subjects, to publication types, to country or year of publication.

3) What do you need to search MEDLINE?

MEDLINE can be found in most medical libraries, many of which will have the full database dating back to 1966. MEDLINE can also be accessed electronically on CD-ROM or through the Internet. To search MEDLINE, you need a personal computer (preferably 485 or equivalent) and either a modem or a CD-ROM drive. (27). Searching MEDLINE requires a specialized interface called a search engine. Several relatively user-friendly search engines are available for MEDLINE which include Ovid, Grateful Med, PubMed and Paperchase. Numerous CD-ROM products containing MEDLINE are available, of which SilverPlatter is probably the best known. On-line free searching of MEDLINE is now offered by the NLM using its GratefulMed and PubMed . The NLM maintains a list of commercial organizations which offer document delivery of journal articles. Other free sites for searching MEDLINE include the following:

- Dr Felix's Free MEDLINE page: http://www.docnet.org.uk/drfelix/
- OMNI's MEDLINE Resource Centre: http://omni.ac.uk/general-info/internet_medline.html
- NLM: see section on Internet

Unfortunately, most physicians' are poorly skilled in information-seeking including the use of computers. In older studies, less than 10% of physicians in full-time clinical practice reported the use of computer-assisted literature searching (7). In another study, about 50% of the clinicians surveyed owned a computer, but the majority rated their computer skills as low. (6). In a more recent randomized cross-sectional study of 250 Michigan family practice physicians, 10% did not use computers for any purpose, about 15% used them for CD-ROM medical references, and even less used computers for clinician decision-support software or to access the databases of the NLM (47). However, even in the study where participants received limited training, MEDLINE searching averaged only once per week (48).

All MEDLINE systems come with basic instructions for searching and most medical libraries and MEDLINE vendors, including the NLM, also offer training courses (27). More recent studies have demonstrated that medical students, residents and practicing physicians can be successfully trained, increase their utilization and report moderate to high satisfaction with searching (49, 50). In one study just a two-hour introduction to on-line searching of MEDLINE was enough to develop sufficient skill to obtain relevant citations on most occasions when searching was compared with that of a medical librarian. Most searches were also perceived by the clinicians as leading to at least some improvement in clinical care

(48).

4) MEDLINE search filters

Performing a MEDLINE search can be a highly effective way to locate current literature on a topic. No other method currently can reproduce the same depth and scope of (26, 27). However, these advantages also lead to its drawback: it can also be quite messy. Fletcher has suggested that this inefficiency limits the use of MEDLINE to a more specialized role in meeting information needs: for comprehensive searching for clinical presentations, side effects or treatments of uncommon conditions (14). However, the efficiency and effectiveness of searching can be improved by using methodologic search filters for searching MEDLINE with the OVID system developed by Brian Haynes and Ann McKibbon from McMaster University. These filters are designed to retrieve high quality evidence from published studies appropriate to decision-making. They were developed by evaluating various search terms for their ability to retrieve articles compared with a "gold standard" based on manual searching of 10 medical journals over a 5 year period (51-57).

The best single-term search strategies, which maximize efficiency, are presented in Table 7 (58). The most effective, although more complex, search strategies are presented in Appendix 1. It is important to realize that these strategies are to be used in combination with a comprehensive (i.e. sensitive) subject search strategy which has first been used to retrieve as much information as possible relevant to the subject. Methodologic search filters are especially helpful for studies of prognosis and diagnosis due to the lack of MeSH terms for effective capture. Studies of prognosis are the most uncommon types in the literature and yet questions of prognosis are the most commonly asked and valued questions by patients (59). Textbooks are even more unlikely to provide concise summaries of prognosis as they do for therapy and diagnosis which are afforded considerable emphasis.

Note that ":" indicates all possible endings of a search term. "(tw)" indicates text word, "exp" indicates explode, "(mh)" indicates MeSH, and "(sh)' indicates subheading. Further enhancements in indexing and search strategies and the creation of specialized literature files that are tailored to the needs of the user should continue to improve efficiency and effectiveness of literature searching. More information on efficient searching and search strategies for systems for MEDLINE and other systems can be found at the following web sites:

- McMaster University: (http://hiru.hirunet.mcmaster.ca/ebm/userguid/1_lit.htm
- The Centre for Evidence-Based Medicine: (http://cebm.jr2.ox.ac.uk/docs/searching.html)
- The NLM's PubMed search engine for MEDLINE with built-in methodologic filters: (http://www3.ncbi.nlm.gov/PubMed/clinical.html)

Table 7: The Best Single Word Search Terms for Different Question Types

Type of Question	Single Word Search Term
Therapy	clinical trial (pt)
Diagnostic tests	sensitivity (tw)
Etiology	risk (tw)
Prognosis	explode cohort studies for prognosis
Systematic reviews	meta-analysis (pt) or [review (pt) and MEDLINE (tw)]

Taken from Sackett, 1997 (58)

5) Other Databases Available Through the National Library of Medicine

A number of other databases are available through the National Library of Medicine (27). These include:

- AIDSLINE contains references taken from MEDLINE, HEALTH and CANCERLIT databases from 1980 forward with some additional unique citations. AIDSLINE, AIDSDRUGS and AIDSTRIALS are available free of charge.
- CANCERLIT provides citations to cancer literature dating back to 1963.
- CATLINE contains citations to printed books and journals in the collection at NLM.
- CHEMLINE is a combined dictionary and database containing data that can be helpful in selecting strategies for other NLM databases. Once a substance of interest is identified, its Chemical Abstracts Registry number can be used to cross-reference it with other databases which may contain information about the substance.
- DIRLINE contains information on over 15,000 organizations that act as information resource centers. The references in this database include names, addresses, telephone numbers, and descriptions of each organization, including primary interests and services.
- HEALTH Planning and Administration database provides references back to 1975 on nonclinical aspects of health care delivery including administration and planning of health facilities, services, health insurance and health aspects of financial management, regulation, personnel, quality assurance, licensure and accreditation.
- SDILINE (Selective Dissemination of Information) is a database that contains references from the current month of MEDLINE and permits you to "store" searches for automatic updating each month.
- TOXLINE and TOXLINE65 contain references to the pharmacologic, physiologic, biochemical and toxicologic effects of drugs and other chemicals. TOXLIT and TOXLIT65. These latter databases overlap the former to a large extent and are more expensive to search due to royalty charges but do contain some unique citations which may be important.

The Cochrane Database of Systematic Reviews

The Cochrane Database of Systematic Reviews is part of the Cochrane Library, the premier compendium of systematic summaries of evidence about health care interventions (1). The Cochrane Library consists of systematic reviews prepared by Cochrane review groups, other systematic reviews published in the medical literature and a large database of clinical trials. The Cochrane Library is supported by the Cochrane Collaboration, an organization of health care providers, consumers, and scientists that collaborate to carry out exhaustive searches for all relevant trials, scrutinize them for relevance and quality, assemble and analyze them, draw conclusions about how the net result should be applied in health care, and prepare structured reports for widespread dissemination to health care providers and planners. The Cochrane Collaboration is organized into Health Problem Review Groups and coordinated by a worldwide network of Cochrane Centers. Each group may be provided with extensive citations and a "tool kit" of scientific strategies and tactics for carrying out their reviews and with a wide array of multiple, coordinated approaches to the electronic and paper-based dissemination of their reports. The Cochrane Library can be accessed through the Internet and is also available on CD-ROM which can be purchased or accessed through medical school libraries. Cochrane Library is also now available in an electronic form of the same name which includes the latest additions to the databases. The latest issue, Issue 2, added 55 systematic reviews to the database.

Clinical Evidence Processing and Synthesis Services

Several services that review a large spectrum of literature and process and synthesize evidence have emerged in recent years (26). Each article in these publications is summarized with enhanced structured abstracts that provide key details so that clinical readers can decide for themselves whether the findings ought to be applied in their own clinical practice. Brief commentaries by content experts accompany each article that facilitate putting the individual article in context. These services employ explicit quality filters, using well-established techniques of clinical epidemiology and critical appraisal and select articles for publication with information that is highly relevant to clinical practice. These services now often provide better answers to clinical questions that come up in daily practices because of their selection, search filters, and indexing.

ACP Journal Club was the first of these evidence processing and synthesizing publications (26). Its editors review more than 30 journals to encompass the content areas of internal medicine and its subspecialties. The quality and clinical relevance filtering functions to reduce the 6 million articles published annually to approximately 300 key articles, which is more reasonably within the reading capacity of clinicians. The paper-based version is published bimonthly but *ACP Journal Club* became available on CD-ROM in 1995. This version is complimentary to the print version since print is easier to browse and read and because the CD-ROM version is not updated bimonthly. The CD-ROM version allows for access to all citations on a specific clinical topic and individual items can be printed out, and incorporated into computerized notes.

Evidence-Based Medicine is another publication that uses the same approach as ACP Journal Club but has a broader clinical coverage, covering internal medicine, family medicine, pediatrics, psychiatry, surgery, obstetrics, and gynecology (26). Of special interest, the editors of EBM have begun including study questions in the structured abstracts under a heading "Questions". Having study questions more explicitly stated should make it easier for readers to match their questions to the study questions (45).

Best Evidence (formerly *ACP Journal Club* on Disc) is the electronic presentation of all issues of ACP Journal Club (1991-current) and Evidence-based Medicine (1995-current) (60). It is available on CD-ROM and became available on the Internet in 1998 through OVID technologies (www.ovid.com) as part of its new service, Evidence Based Medicine Reviews. The electronic version compiles evidence on an annual basis, weeding out outdated items to provide a database of current evidence. The most important use of *Best Evidence* is for solving clinical problems in "real time". *Best Evidence* is indexed and can be searched in this manner or by full-text. The database is relatively small compared with MEDLINE so single terms are usually sufficient for searching, but on occasion multiple terms are needed. An important additional features is its capacity to copy all or part of an item to a disc or paper. Best Evidence can be subscribed to by contacting the ACP web site (www.acponline.org) or the BMJ Publishing Group web site (www.bmjpg.com/data sjindex.htm).

Other information synthesizing journals of a similar quality exist for other disciplines. However, other abstract services exist that do not specify the criteria for evaluating the validity of the articles published. It is important to be able to discern which publications are truly evidence-based and to do so each issue must provide its explicit rules for critical appraisal and article selection from a list of specified journals.

Critically Appraised Topics (CAT) and CAT Banks

Critically appraised topics (CAT) are one-page summaries of the critical appraisal of clinical questions (61, 44). For common clinical problems, or those that at least share some component that is common, CAT's serve to summarize, store and share the product of a clinician's inquiry into a patient's problem. The steps in creating a CAT emulate the steps in EBM that have already been outlined, albeit in a very concise manner. The final CAT product begins with a declarative answer to the clinical question that was generated and with a one-sentence concise summary of the clinical problem. It then quickly moves on to its most distinctive feature, the clinical bottom line, which summarizes the application of the information critiqued to the patient. Following the clinical bottom line, a table summarizing the key evidence is provided. Relevant notes regarding pertinent issues in critical appraisal and the citation for the reference used to answer the clinical question are also provided. The use of CAT's facilitate easy and rapid digestion of critically appraised studies for application. Evidence-Based medicine: How to teach and practice EBM, Sackett). Evidence-Based Medicine:

A software program called CATmaker has been developed by the NHS R&D Centre for Evidence-Based Medicine at Oxford and is now on its World-Wide Web page. This program was developed from a paper prototype process by fellows at McMaster University. CATmaker walks the learner through the steps in creating a CAT, including offering separate screens comprised of tables that summarize, but also function to cue the user, for the following information: 1) the first screen is used to describe the clinical problem, develop the related three-part question and display search terms, 2) the second screen is used to summarize the study patients of the article selected to apply to the patient, 3) the third screen summarizes the evidence of this study, 4) the fourth screen displays the clinical bottom line and 5) the fifth screen summarizes pertinent information.

CATmaker offers several very useful functions. The time, effort and knowledge to perform the calculations for many of the summary measures for therapy (absolute risk and relative risk reduction and number needed to treat) and diagnosis (sensitivity, specificity, likelihood ratios) are often barriers to EBM but the screens that are used to summarize the study evidence automatically perform these calculations for the user, including calculating confidence intervals. CATmaker is also capable of storing CAT's, either in the unfinished form called a KITTY, or in its final form, as a CAT. A file containing the CAT can be generated and then downloaded into a word processing program for print-out or used to transfer the CAT to other CAT Banks. A number of CAT banks which store collections of CAT's are now available at various sites on the Word-Wide Web. The web site for McMaster University contains links for the most important CAT banks. Creating CAT's as a part of the experience of a residency journal club is gaining popularity and some CAT banks have been created to offer the cumulative product of such forum. The McMaster web site also contains a demo of CATmaker which can be downloaded for trial use and its own CAT bank. As yet, negotiations are in progress to make CATmaker commercially available.

CAT's clearly have many advantages: they are evidence-based, concise and portable. But as useful as CAT's are in clinical practice, there are several caveats to keep in mind when using them. CAT's are generally answers to clinical questions that are based on a single reference and as such are not comprehensive literature searches and syntheses. Since they are only as current as the piece of evidence they summarize, they also become obsolete with the passage of time. Since they are developed and used in "real time", they also lack peer-review, and thus may be inaccurate or misapplied. Due to this short "shelf life", expiration dates beyond which the CAT should be considered obsolete are recommended for inclusion in the summary.

Internet Sites

The Internet has given rise to an unprecedented information revolution and the expanding volume of information we have access to is astounding. The case of EBM sources is no different. The following are EBM resources that have been suggested by a number of "expert" EBM reviewers.

EBM links and bibliographic services:

- Netting the Evidence: a guide to sources of evidence on the Internet, compiled by Andrew Booth, Director of Information Resources at the School of Public Health and Related Research (ScHARR) at the University of Shefield. This is the most comprehensive listing that exists. (http://www.shef.ac.uk/~scharr/ir/netting.html)
- Evidence-Based Medicine Links: contains links for the Centre for Evidence-Based Medicine at Oxford, for Best Evidence at McMaster, British Medical Journal online, the ACP, MEDLINE advanced search mode at the National Library of Medicine, and others. It contains other resources as well which include an evidence-based medicine resource center. It recently added a feature that provides a regularly updated search of MEDLINE for evidence-based medicine citations, the full citations of which can be downloaded. (http://www.paracelsus-heute.ch/ebmlinks.htm)
- Evidence-Based Medicine and Evidence-Based medicine Practice Resources: reviewed by Medicine on the Net, this list offers connections to EBM sites throughout the world. (http://www.ogh.on.ca/library/evidence.htm)

Organizations:

- Centre for Evidence-Based Medicine at Oxford: (http://cebm.jr2.ox.ac.uk/docs/adminpage.html)
- McMaster Web site for EBM: also contains full-text of User's Guides to the Medical Literature. (http://hiru.hirunet.mcmaster.ca/ebm.userguid/overview.htm)
- National Institutes of Health: go to the Health Information link. Contains links to excellent evidence-based practice guidelines, consumer information and more. http://www.nih.gov
- American College of Physicians, has ACP Journal Club on-line for members only. (http://www.acponline.org)
- CDC Web site: www.cdc.gov, see Traveler's health section.

Databases:

- National Library of Medicine MEDLINE database: available on the Internet free of charge. Features two MEDLINE search tools: Internet Grateful Med and PubMed using built-in methodologic search filters (www.nlm.gov/databases/freemedl.html).
  Additional NLM databases, including U.S. Preventive Services Task Force Guidelines and the Agency for Health Care Policy and Research Clinical Practice Guidelines, accessed at http://text.nml.nih.gov/
- Best Evidence: (http://www.bmjpg.com/data/ebm.htm)
- Cochrane's Database of Systematic reviews: contains titles of reviews, reviews themselves only available by subscription. (http://hirumcmaster.ca/cochrane/cochrane/revabstr/abidx.htm)
- EBM Reviews: contains Cochrane's Database of Systematic Reviews and Best Evidence, available through OVID Technologies. (www.ovid.com)
- PubMed Clinical Queries with Methodologic Filters. Free from NLM. (http://www3.ncbi.nml.nih.gov/PunMed/clinical.html)

Guidelines

- Agency for Health Care Policy and Research (AHCPR): select "AHCPR Supported Guidelines". Contains evidence-based health care information resources, many designed for primary care providers. (http://text.nlm.nih.gov/)
- National Guidelines Clearinghouse: contains pre-approved (by the AHCPR) practice guidelines on a broad array of topics, among others. http://www.guideline.gov
- NHS Centre for Reviews and Dissemination (CRD) at York. Contains the Database of Abstracts of Reviews of Effectiveness (DARE), which includes structured abstracts of reviews identified and appraised by CRD http://nhscrd.york.ac.uk
- Guide to Clinical Preventive Services (1996 edition): (http://text.nml.nih.gov)

Journals and newsletters and other:

- Evidence-Based Medicine: (http://www.acponline.org/journals/ebm/ebmmenu.htm)
- ACP Journal Club: (http://www.acponline,org/journals/acpjc/jcmenu.htm)
- Bandolier Evidence-Based Health Care: an online EBM journal focusing on EBM "bullets" of evidence related to outpatient practice. (http://www.jr2.ox.ac.uk/Bandolier/index.html)
- British Medical Journal: (http://www.bmj.org)
- New England Journal of Medicine: full text for subscribers available online for no additional fee. http://www.nejm.org
- InfoRetriever: (http://www.familypractice.msu.edu/retriever.htm)

Learning EBM:

- McMaster University web site: see above
- Centre for Evidence-Based Medicine web site: see above
- SUNY Health Sciences Evidence-Based Medicine Course: (http://courses.hscbklyn.edu/ebm/)
- Information Mastery: An Introduction. (http://www.family practice.msu.edu/InfoMastery/)

The Internet, and especially the World Wide Web , is a "vast mountain of gems and junk". The challenge is not just finding information but also judging the applicability and credibility of the information. Internet users may rely on a number of Internet resources that review and rate Web sites that provide health information that function like the Consumer Reports of Internet resources. For ourselves and our patients the Internet "has the potential to become the world's largest vanity press" (62). The following core standards have been suggested as a means of judging the credibility of an Internet site:

1) authorship: who, their affiliations and credentials.
2) attribution: references and sources for all content listed clearly
3) disclosure: web site ownership should be prominently and fully disclosed and any sponsorship, advertising, underwriting, commercial funding arrangement, potential conflicts of interest.
4) currency: dates that content posted and updated should be indicated.

Web sites and other Internet-based sources of medical information that fail to meet these criteria should be suspect. The best will make this process explicit as a part of the editorial process. With these criteria in mind, one study that identified and rated instruments used to rate Web sites providing health information on the Internet found the majority failed to meet even these basic criteria (63). None of the instruments provided information on interobserver reliability and construct validity of the rating measurements used. The dynamic and complex nature of information on the Internet make it a challenging area in which to regulate quality so "user beware".

Computer Software programs

Computer software programs that facilitate locating resources for and tools to assist in the practice of EBM have now emerged. Currently, the most promising is a software program developed by investigators from Michigan State University, called InfoRetriever, which brings a variety of evidence-based reference materials to the bedside. It contains the following: 1) abstracts of every completed systematic review from the Cochrane Database of Systematic Reviews, 2) a large number of POEMs (patient-oriented evidence that matters), 3) a diagnostic test calculator that contains the sensitivity, specificity and likelihood rations for a large number of commonly used imaging and laboratory tests, 4) summaries and evidence tables from key evidence-based practice guidelines, including those of the US Preventive Services Task Force, 5) clinical prediction rules, 6) prescribing information and relative costs for over 1000 medications and 7) critical appraisals from the Evidence-Based Practice newsletter. The advantages of InfoRetriever include regular updates at least every three months and full indexing. Searching is extremely flexible and can be accomplished by using the symptom or diagnosis, using ICD-9 keywords or numeric codes, by any word in the title or text or by the type of information. Requirements for the use of InfoRetriever include a PC with Windows '95 or '98 or NT 4.0 operating systems and a 486 or higher processor (although a Pentium or higher is recommended), a minimum of 20 mB hard drive space,a CD-ROM and a minimum of 16 mB (but 32 mB is recommended). InfoRetriever costs $99 ($79 for residents, and $49 for students), which includes free updates for at least the first year. To subscribe to InforRetriever, or to download a demo for trial basis, contact its Web site at http://www.familypractice.msu.edu/retriever.htm.

In general, clinicians would like to see computerized decision-support hardware and software be available for handheld as well as networked and desktop computers, include drug information (particularly interactions, warnings and side effects), include overviews of treatment recommendations, patient education materials and have a uniform user interface and be updated at least annually. (47). InfoRetriever has been available for Newton handheld computers and is undergoing further modifications for other handheld computers

BRINGING EVIDENCE SOURCES TO BEAR ON CLINICAL PROBLEMS: EXAMPLES

Let's return to Patient One, the 67 year-old man with atrial fibrillation for whom the question arose regarding the efficacy of warfarin compared to aspirin for the prevention of thromboembolic stroke. Table 8 provides the results of searching MEDLINE (1996 –1999) using various strategies. Searching without methodologic search filters yields an unmanageable number of citations. Even combining searches for all components of the clinical question yielded 46 articles. However, using the simplest filtering strategy available for a question regarding an overview (steps 1 and 2 representing the comprehensive subject search, steps 3-7 representing the methodologic filter, and step 8 representing their combination) quickly limits the search to a very reasonable 13 citations. In reviewing these citations, there are several references that address the question and provide quantitative estimates of the benefit of warfarin versus aspirin, although the quality of the evidence is not ensured.

However, in general, the most efficient and effective strategy for answering clinical questions, especially those regarding therapy, is to begin with Cochrane's Database of Systematic Reviews (CDSR). Although a search using the text word "atrial fibrillation" retrieved 11 citations, none were relevant to the question regarding this patient. The next best step is then to move to searching *Best Evidence.* The approach using these two sources serve to abbreviate the search and yet ensures an assessment of quality of the retrieved articles. A search of *Best Evidence* using the text word "atrial fibrillation" produced 46 citations. When this search was combined with a search for warfarin. tw. , the number of citations was reduced to 23. Limiting the search to the same years as the MEDLINE database used (since review articles can become outdated after a couple years), further limited the number of citations to 10, which were then reduced to 2 when limited to articles pertaining to therapeutics (an option with *Best Evidence*). One of these citations was for a systematic review of warfarin and aspirin in preventing stroke in patient with atrial fibrillation that expanded on an earlier meta-analysis (64). It indicated with for patients within the age range of 65-75 years without additional risk factors, warfarin and aspirin were comparable in reducing the risk for stroke. The patient should have an echocardiogram to assess the structural integrity of his heart but if this is normal, aspirin would be a reasonable therapeutic choice for him.

Table 8: Results of MEDLINE Searching for Anticoagulation in Atrial Fibrillation Case

#	Search History	Results
1	exp Atrial fibrillation/	2184
2	limit 1 to (human and english language)	1708
3	meta-analysis.pt.	1904
4	review.pt.	174,578
5	MEDLINE.tw.	2345
6	4 AND 5	1531
7	3 OR 6	3435
8	2 AND 7	13
9	exp warfarin	1044
10	exp aspirin	2572
11	exp Cerebrovascular Disorders/	20771
12	2 AND 9 AND 10 AND 11	46
13	limit 12 to (human, english)	46

Now turning to Patient Two, the woman with a severe migraine headache complicated by narcotic dependence and psychiatric overlay who refused dihydroergotamine, NSAIDS and sumatriptin, a brief search of CDSR using the text word "migraine headache" did not yield any citations. However, a search of *Best Evidence* produces 7 citations, but only one systematic review of the diagnosis and treatment of migraine headache which was reviewed in Evidence-Based Medicine. A link to the full text article is even provided. This article recommends chlorpromazine and prochlorperazine as back-up treatment when first-line agents for severe migraines, sumatripin and dihydroergotamine are not options. Another option would be dexamethazone (65).

Turning to Patient Three, to address the question of the accuracy of a spot urine for microalbumin measurement as compared to a 24-hour urine collection for the same, you begin searching with *Best Evidence* since this question has to do with diagnosis (although, to reassure you a search of CDSR did not yield any citations relevant to this question). Searching using the text word diabetes mellitus yields 214 citations, which is reduced to 14 when limited to diagnosis. One of these addresses the question and indicates, using ROC curves, that the spot urine test compares favorably to the gold standard (66).

Finally, turning to patient four to address whether her silicone breast implants could be causing some symptoms of connective tissue disease, you again turn to *Best Evidence*, and searching with the text words "breast implants" you retrieve 2 citations. One is a cohort study, the best type of study to address a question regarding etiology and the other is a systematic review. Both articles conclude that there is no demonstrated increased risk for connective tissue disorders in women with silicone breast implants (67, 68).

RECOMMENDED STRATEGIES FOR KEEPING UP-TO-DATE WITH THE MEDICAL LITERATURE

Given all these resources, what strategies can be recommended to meet the information needs of clinicians? The Fletchers point out that a strong research base for how physicians should keep up with medical literature is not available. However, they recommend the strategy in Table 9 to support general awareness of the literature (14). David Sackett's book, Clinical Epidemiology: A Basic Science for Clinical Medicine, devotes an entire chapter to keeping up with and how to read the medical literature (69). Approaches for seeking answers for clinical problems related to specific patients have also been presented (26, 70, 71). In general, these involve a sequence of searching Cochrane's Database of Systematic Reviews, then *Best Evidence*, followed by CAT banks, then MEDLINE using single-term search strategies and then more complex search filters if these are unsuccessful. This sequence may be modified somewhat depending on the specific goals of your search.

Table 9: Elements of an Information Plan

1) Browse at least one general journal regularly
2) Maintain surveillance on new information
3) Establish reliable ways of looking up common facts.
4) Identify a set of ways to look up obscure facts.
5) Develop critical appraisal skills
6) Set aside high-quality time regularly to deal with information needs
7) Invest time to discover new sources of useful information

Judging the evidence: Critically Appraising the Literature

Since usually thousands of studies are must be done to find and verify one clinically useful truth, the process of separating good from bad, noise from signal, is very messy. Practitioners must be able to determine for themselves that research is ready for clinical application, since only a few information services use explicit criteria for selecting scientifically strong, clinically sound studies. During the past two decades, various guides to critical appraisal of research evidence have been published and have subsequently undergone evolution (26). Critical appraisal guides are explicit criteria for use in determining whether a study is scientifically valid and clinical sound of a study. These guides were developed from methodologic rules of evidence obtained from reviewing this body of literature. Much of this effort has been spearheaded by the Evidence-Based Working Group at McMaster University. The most recent series published by this group appeared in JAMA under the running title "Users' Guides to the Medical Literature" (59, 72-79). Versions are also available on pocket cards that accompany texts on evidence-based medicine.

When critically appraising any study, the same three general questions are asked regardless of the type of study being evaluated: is the study valid, what were the results, can the results be applied to my patient(s)? The specific guides for each type of study question vary, depending on the influence of such factors as the optimal study design that addresses that study question type and its methodologic characteristics. Some of these guides are considered "primary" since they address the fundamental features of study design and validity; others are considered secondary but still influential. Table 10 summarizes the primary guides to assess the validity of a study for questions relating to therapy/prevention, diagnosis, prognosis, etiology/harm and overview (26).

A detailed discussion of critical appraisal is beyond the scope of this presentation. Increasingly, these skills are being taught in medical schools and residency programs. Unfortunately, most physicians in practice trained at a time when these skills were not included in formal medical school curriculum, and thus are disadvantaged in applying them to their current practice. However, many resources in a multitude of formats are available to assist physicians in the attainment of critical appraisal skills. The JAMA "Users' Guides" are an excellent place to start. More in-depth knowledge can be gained from textbooks such as *Evidence-Based Medicine: How to Practice and Teach EBM (80)* , *Clinical Epidemiology: A Basic Science for Clinical Medicine* (81), and *Clinical Epidemiology (82)* by Robert and Suzanne Fletcher.

Table 10: Bare-Bones Users' Guides for Appraisal of the Validity of Medical Studies.

Purpose of Study	Guides		
Therapy	Concealed random allocation of patients to comparison groups	Outcome measure of known or probable clinical importance	Few lost to follow-up compared with number of bad outcomes
Diagnosis	Patients to whom you would want to apply the test in practice	Objective or reproducible diagnostic standard, applied to all participants	Blinded assessment of test and diagnostic standards
Prognosis	Inception cohort, early in the course of the disorder and initially free of the outcome of interest	Objective or reproducible assessment of clinically important outcomes	Few lost to follow-up compared with number of bad outcomes
Etiology	Clearly identified comparison group or those at risk for, or having, the outcome of interest	Blinding of observers of outcome to exposure; blinding of observers of exposure to outcome	
Reviews	Explicit criteria for selecting articles and rating validity	Comprehensive search for all relevant articles	

The need to remain up-to-date with advancements in medicine and answer questions that arise in caring for our patients is not a new phenomenon. William Osler pointed out that "a physician who does not use books and journals, who does not need a library, who does not read one or two of the best weeklies and monthlies, soon sinks to the level of the cross-counter prescriber..." (83). We are fortunate to have witnessed the remarkable advances in medicine over the last several decades. Rather than being overwhelmed by all this potential we need to find ways to manage and utilize this information on behalf of our patients. In 1989, Huth looked ahead to a time when clinicians would have the kinds of information they needed: 1) expertly selected, 2) carefully assessed, 3) thoroughly digestable, and 4) highly relevant information drawn from the current literature (84). He also envisioned developing the means of gathering and saving others' critical judgments about current literature for future reference. Information resources such as Cochrane's database of Systematic Reviews, Best Evidence, CAT banks and the many others that have been reviewed go a long way to having what we were lacking just ten years ago.

Appendix 1: Most Effective Searching Strategies According to Clinical Problem Type

Clinical Problem Type	Search Strategy	
Therapy	Use to favor comprehensive retrieval: 1 random$.ti,ab,sh. 2 tu.fs. 3 dt.fs. 4 randomized controlled trial .pt.	Use to enhance relevance: 1 (double and blind$).ti,ab,sh. 2 placebo$.ti,ab,sh. 3 1 or 2
Randomized Controlled Trials	1 exp clinical trials/ 2 (clinical trial or controlled clinical trial).pt. 3 (meta analysis or multicenter study).pt. 4 randomized controlled trial.pt. 5 1 or 2 or 3 or 4	
Diagnostic test	Use to favor comprehensive retrieval: 1 "sensitivity and specificity"/ 2 sensitivity.ti,ab,sh. 3 di.fs 4 ri.fs. 5 du.fs 6 specificity.ti,ab,sh. 7 1 or 2 or 3 or 4 or 5 or 6	Use to emphacize relevance: 1 exp sensitivity-and-specificity/ 2 (predictive and value$) .tw. 3 1 or 2
Etiology	Use to favor comprehensive retrieval: 1 exp cohort -studies/ 2 exp risk/ 3 (odds and ratio$).ti,ab,sh. 4 (relative and risk).ti,ab,sh. 5 (case and control$).ti,ab,sh. 6 1 or 2 or 3 or 4 or 5	Use to emphacize relevance: 1 case-control studies/ 2 cohort studies/ 3 1 or 2
Prognosis	Use to favor comprehensive retrieval: 1 incidence.ti,ab,sh. 2 prognos$.ti,ab,sh. 3 predict$.ti,ab,sh. 4 course.ti,ab,sh. 5 exp mortality/ 6 follow-up studies/ 7 mo.fs. 8 1 or 2 or 3 or 4 or 5 or 6 or 7	Use to emphacize relevance: 1 survival analysis/ 2 prognosis.ti.ab,sh. 3 1 or 2
Systematic Reviews (and meta-analyses	1 review-academic (pt) 2 review-tutorial (pt) 3 (systematic$ and (review$ or overview$)).ti,ab,sh. 4 (meta-anal$ or metaanaly$ or meta analy$).ti,ab,sh. 5 1 or 2 or 3 or 4	

Appendix 1 (continued): Most Effective Searching Strategies According to Clinical Problem Type

Clinical Problem Type		Search Strategy
Randomized Controlled Trials And Controlled Trials	1	randomized-controlled-trial (pt)
	2	meta-analysis (pt)
	3	controlled-clinical –trial (pt)
	4	clinical-trial (pt)
	5	random$.ti,ab,sh.
	6	(meta-anal$ or metaanaly$ or meta analy$).ti,ab,sh.
	7	((doubl$ or singl$) and blind$).ti,ab,sh.
	8	Exp clinical trials/
	9	crossover.ti,ab,sh.
	10	1 o 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9

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