

Closing the Gaps Between Evidence and Practice*

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ABSTRACT

Evidence-based medicine (EBM) is the modern approach to scientific medical practice. EBM is based on the premise that the results of experiments (e.g. randomised clinical trials) should guide clinical care rather than theory, opinion or tradition. There are both practical and fundamental limits to the EBM approach. High quality, adequately powered clinical trials are not feasible to answer every clinical question, leaving gaps in evidence. The empirical data may not provide enough detail, especially about the absolute level of benefit attainable among various patient subgroups. Effective dissemination of high quality evidence to decision-makers requires effort and skill. The development of guidelines by professional societies and establishing a consensus among professionals that the guidelines should be adopted is an important step in translation to practice. Economic assessment has not been a major component of EBM to date. Effective evidence-based therapy usually costs more money, and interested parties who would lose money by changing practice will resist that change. Finally, effective delivery of therapy may require institutional changes within the healthcare system, including acceptance by many different professional groups. Setting goals and holding healthcare organisations accountable in meeting those goals may speed adoption of effective evidence-based therapies. Evidence is necessary, but not sufficient to improve practice; dissemination requires numerous steps to establish new practice patterns.

Keywords: evidence-based medicine, guideline adherence, practice guidelines, quality of health care

INTRODUCTION

Evidence-based medicine (EBM) is a new term for the old idea that medical practice should be grounded in science. Medicine began its link to science in the 19th century by embracing microbiology, chemistry, pathology and physiology. Medical education in the United States was revolutionised when the famous Flexner Report of 1910 pushed medical schools to join universities and required study of the basic laboratory sciences. Despite greater insights into pathophysiology, medical practice was not terribly scientific until the experimental method was applied to therapeutics. The randomised clinical trial was introduced to medicine in the late 1940s, and grew in importance as regulatory authorities required evidence from clinical trials before registering new drugs for

use. This rise of clinical trials was fostered in large part by advances in the new basic sciences of biostatistics and epidemiology. The power and sophistication of clinical trials has grown enormously in the past 25 years. Trials are now conducted collaboratively across multiple continents, and enroll thousands and even tens of thousands of patients.

EBM is predicated on the belief that data from randomised clinical trials are the soundest basis for the practice of medicine. EBM is the culmination of the movement for a scientific and empirical basis of medical practice that began over 100 years ago. EBM has made enormous strides, and has drawn physicians from all clinical disciplines and all parts of the world.

Despite the successes of EBM, there are many gaps between evidence and practice.¹⁻⁴ Some of these gaps involve simple lack of evidence — no clinical trials have been done. Other gaps are due to the type and quality of the available trials — have the right questions

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been asked? Have the data been analysed and presented in ways that are needed to support the practice of medicine? Still other gaps have to do with how the evidence is digested by the practising physicians, and whether the medical care system has the capability to apply evidence-based therapies.^{5,6}

GAPS IN EVIDENCE

Lack of Trials

The ideal situation is for the practitioner of EBM to have results from multiple large randomised trials on a clinical question. Randomised trials are not, however, available for all clinical questions, in large part because trials are expensive, time consuming, and difficult to perform.⁷ Most clinical trials are sponsored by the pharmaceutical industry to obtain approval of new products. While this system harnesses the profit motive of the industry to provide a public good, it has inherent limitations. Phase III clinical studies are generally performed in ideal patient populations and compare active drug with placebo. The main endpoints may be physiologic markers — surrogate endpoints for patient-centered outcomes. The trials do not compare the new drug with likely competitors, nor apply it in more general and realistic patient populations and practice settings. Naturally, older drugs are not studied, nor are interventions such as surgery, devices, diets, behavioral therapies, and novel clinical management tools. Newer strategies are needed to support clinical trials that address the actual needs of medical practice, and not just the narrower interests of the pharmaceutical industry. Additional sources of financial support for clinical trials are clearly needed — perhaps provided by health insurers as “Research and Development” investments in better medical care.

Issues with Clinical Studies

The results of multiple randomised trials are often combined in a quantitative overview, or meta-analysis, to provide the best summary measure of the efficacy of therapy. The results of this analysis are conventionally expressed as the relative risk reduction from the new therapy as compared with the old therapy. Relative risk reduction is a very useful number, as it highlights the specific contribution of therapy to outcome — it is essentially a measure of the strength of a mechanism of action. Despite its great usefulness, the relative risk reduction has several important limitations as a guide to clinical decision-making.

The relative risk reduction is not a constant, fixed quantity, but rather should be regarded as a function of patient-related factors, clinician-related factors, or

both. All clinical trials use inclusion and exclusion criteria to limit the population studied, even “large simple trials”. There will always be questions of how much the trial results can be generalised to broader populations of patients. Trials often examine clinical subgroups to see whether the therapeutic effect is homogenous across the patient population. This exercise is limited by the narrow range of eligible patients and the low statistical power to detect differences in therapeutic efficacy across subgroups. Meta-analysis is not much help with subgroups, as individual patient level data are really needed to test variability in therapeutic efficacy according to clinical characteristics. The trialists may pool their data, but not the reader of journal reports. A more subtle problem is that results of therapy may depend on the skill of the clinician and the quality of the healthcare system in which the care is provided. Trials of devices and procedures are conducted in the “best hospitals” by the “top doctors”. Even if the trial shows efficacy in these ideal circumstances, can the results be applied to average hospitals and average doctors?

Even if the relative risk reduction is indeed the same across all types of patients and in all practice settings, it is not the number most relevant to clinical decisions. The absolute risk reduction — the number of lives saved or the number of symptoms relieved — is the figure of merit. A therapy with a 50% relative risk reduction may be widely accepted when it cuts mortality from 10 to 5%, but not if the risk is cut from 0.001 to 0.0005%. The key point is that even when relative risk reduction is the same across clinical subgroups defined by age or disease severity, the absolute benefit may vary by factors of 10 or more. Rational clinical decisions should be made on the absolute risk reduction, since the risks and costs of therapy are usually similar across patient subgroups, so risk-benefit and cost-benefit comparisons will be quite different across patient groups. The challenge for EBM is to provide the information needed at the point of decision.

Varieties of Evidence

What sorts of data are to be considered admissible “evidence”? Randomised trial results are the best evidence, but are they the only evidence? Trials are clearly performed within a context of medical knowledge from pathophysiology, observational data, and understandings drawn from other fields. This qualitative information affects how we interpret the results of a trial, yet there is no simple way to combine information from disparate sources — different kinds of evidence — in quantitative overviews.

For a given condition, many types of interventions may have been tried, and knowing which have worked and which have not is helpful information (e.g. if anticoagulants are effective in unstable angina, we are more inclined to believe that antiplatelet agents will also be effective). However, it is difficult to incorporate this type of expert knowledge into a systematic overview. Similarly, the intervention under study may have been tested for a related condition (e.g. might drugs effective for transient ischaemic attacks also be useful for unstable angina, since both conditions have similar pathophysiology?). Perhaps Bayesian methods or decision analysis could be helpful techniques to combine disparate types of evidence and improve treatment assessments.

FROM EVIDENCE TO PRACTICE

Completion of randomised trials and a quantitative overview of their results provides solid evidence about the efficacy of therapy. Simply publishing a journal article or posting information on a website is insufficient to change clinical practice, however. There are many additional steps, including achieving a professional consensus on the value of the therapy, developing clinical guidelines, disseminating guidelines to the practicing community, and changing the system of care to deliver the therapy. We must not forget that the payors also have to be willing to foot the bill, and patients have to be willing to accept the recommended therapy. While these factors are ultimately beyond the control of the EBM community, all of these factors can be influenced by how the data are analysed, presented and disseminated. Simply having a product is not enough — it has to be a good product that meets the needs of the public, is affordable, and is readily available.

How convincing is the evidence? Clinical trial results are interpreted in the context of other available knowledge about a disease, pathogenesis, and therapy. A therapy that fits well within the accepted paradigm will have swifter acceptance than one that runs counter to it. Reperfusion therapy for acute myocardial infarction was more readily accepted once the pathophysiology of the disease was understood and animal models showed the potential value of therapy. Newer methods of reperfusion therapy build on this generally accepted model. By contrast, beta-blocker therapy for congestive heart failure has been received more skeptically, as cardiologists found it counter-intuitive to use beta-blockade when beta-adrenergic stimulation has been used to treat decompensated heart failure.

The burden of proof is higher when there is a controversy in a field. The same evidence can convince one side in the controversy while leaving the other side skeptical. Interestingly, each side is acting rationally in a Bayesian framework. The strength of evidence must be much higher to move a skeptic (prior trial belief of <10%) to a believer (post-trial belief >90%) than to change an agnostic (prior belief of 50%) into a believer. Change in practice is more readily achieved when there is a broad professional consensus about a therapy's value.

Development of Guidelines

Professional organisations have embraced clinical practice guidelines as a means to promote quality of care. In theory, a practice guideline should rest on the evidence, the best of which is provided by an overview of randomised trials. In reality, guidelines are written by committees of experts named by the professional societies. Members of the committee may not have EBM training, making it harder for them to develop evidence-based guidelines. Guideline committee members may have professional biases (surgeons think surgery is a good thing), or even conflicts of interest. The composition of the committee may therefore affect the resulting guideline. In this light, it is not surprising that different professional societies interpret the evidence differently — the American Cancer Society, for instance, recommends more cancer screening than the US Preventive Services Task Force recommends.

Guideline committees have little time to do their work, and lack the resources to thoroughly gather, sift, weigh and synthesise all the pertinent evidence for every recommendation. While the Evidence-Based Practice Centers in the United States have supported many guidelines committees, even then the scope of work is too broad and often the evidence is insufficient to answer key questions. Clinical guidelines are thus a mixture of evidence and expert opinion; at least the better guidelines grade the quality of evidence behind each recommendation. As the quality of evidence improves over time, one hopes that guidelines will be increasingly evidence-based.

Adoption of Guidelines

There are many barriers to the widespread adoption of clinical guidelines and their evidence-based recommendations.⁴ Cabana et al classified these under the general headings of “knowledge”, “attitudes” and “behaviours”.⁸ One major barrier to evidence-based practice is that clinicians are often unaware of

guidelines because they are simply too busy, have too much to keep up with, and the information is not readily accessible. Even if clinicians know about a guideline, they may not be sufficiently familiar with it to use it in practice.

Lack of agreement with guidelines is commonly cited by physicians as a reason not to follow them. This may be an issue of psychology more than science. Physicians are independent by nature and resent infringements on their professional autonomy. They may object to the whole concept of clinical guidelines as “cookbook medicine”. I suspect that younger physicians who have been trained in EBM will be more comfortable with recommendations based on evidence (although they may resist those based simply on expert opinion).

Even if physicians are aware of a clinical guideline, they may still not change their practice patterns. Dissemination of guidelines by traditional means such as journal articles, grand rounds, and conferences may increase agreement and acceptance, yet still not alter habits.³ Active intervention, such as academic detailing (a one-on-one meeting with a respected opinion leader), have been more effective in changing behaviour. Standardised orders, reminders on charts or in computer systems, and other cues in the environment will help prompt a busy clinician to use evidence-based therapies. Involvement of the entire hospital care team using measures such as critical pathways will also make it easier for physicians to change their prescribing behaviours.

Cost and Cost-Effectiveness

A bigger barrier to using evidence-based therapies in practice is that the economic implications of recommendations have been generally ignored.⁵ At a time when healthcare budgets are constrained and most new therapies are expensive, recommendations to adopt new treatments will meet resistance from those who pay the bills. Indeed, new technology is the main driver of rising healthcare costs around the world. The EBM community should not ignore the cost of therapy.

One solution is to measure economic outcomes as well as clinical outcomes in randomised trials. This approach has been widely adopted in cardiovascular medicine, where cost and cost-effectiveness are often analysed as endpoints. While economic analyses face methodologic challenges, these studies will become more common as the importance of having cost data is appreciated.

The results of a medical and economic study fall into several categories. The most favourable finding is when the new therapy has better clinical outcomes and also has lower costs. In this situation, the new treatment is readily accepted, but this happy combination is rather rare. Most commonly, the more effective therapy costs more than the alternative. Cost-effectiveness analyses provides a method to assess quantitatively whether the added cost is worth the added benefit. It is critical to note that even if a therapy is clearly “cost-effective”, it costs more money and thus may be unaffordable to a healthcare system strapped for funds. In the United States, for instance, the Center for Medicine and Medicaid Services was asked to pay for implantable cardioverter defibrillators (ICDs), at a cost of over USD30,000 each, for the hundreds of thousands of patients who met the criteria for the MADIT-II trial.⁹ Even though use of the ICD for this indication appears to be “cost-effective”, the added cost to the US government would be several billion dollars.¹⁰ The evidence-base needs to be very strong indeed to justify expenditures of this magnitude.

A more subtle issue in the economics of new therapies is the issue of winners and losers. A new device may save many to the healthcare system in general over a period of a few years, but would not be accepted by hospitals that face large losses on each patient treated because reimbursements would not cover their higher costs. A new medical treatment may be better than surgery, but surgeons would not be pleased with doing fewer cases and having lower incomes as a result. The economic barriers to adoption of therapy may be formidable, and acceptance in practice has less to do with evidence than with finance.

Individual Change or Systems Change?

The target audience of EBM was the individual, scholarly physician who would carefully weigh the evidence and advise patients in his office. Needless to say, the contemporary audience differs considerably from this early ideal, as today’s physician is time pressured and is likely to work in a large group practice or integrated healthcare system with other professionals, and is under numerous constraints. In this environment, there are many barriers to full implementation of evidence-based therapies. In a ten-minute visit with a typical patient who has several chronic medical conditions, how can a physician do all the right things according to the evidence? Perhaps it is not surprising that simply telling doctors about guidelines does not have a tremendous effect.

Many observers suggest that we should redesign the system of healthcare delivery to improve the quality of care, especially the use of evidence-based therapies. Management of chronic conditions such as heart failure, diabetes, and asthma, or of medications such as coumadin, might be better handled by an integrated system of care that includes nurses and pharmacists, makes liberal use of information and communications technologies, and is designed to ensure use of the best therapies in an integrated system. Use of therapies can be tracked, reminders generated, and goals met.

Evidence-based management of acute illnesses may also require changes at the healthcare system level. The effective delivery of reperfusion therapy for acute myocardial infarction required enormous changes in the healthcare system — from ambulances to emergency departments to pharmacies to cardiac catheterisation laboratories and to coronary care units. Emergency medical technicians, nurses, doctors, and pharmacists all needed to contribute to a redesign of the system of care. Simply publishing a few papers in the *New England Journal of Medicine* about the value of reperfusion therapy was not enough to effect changes of this magnitude. Translating evidence into practice requires more, and sometimes a lot more.

Substantial changes in the healthcare delivery may also require changes in the healthcare financing system. In the United States, physicians are often paid for office visits but not for having a nurse practitioner keep in touch with patients over the phone. Hospitals are paid separately, and on an episode of care basis. Fragmented payments lead to fragmented care and perverse incentives. System redesign will be very difficult but progress can be made, even without a major overhaul of the healthcare system.

One concept is that healthcare providers will be more likely to adopt changes when they are publicly accountable for the care they deliver and the outcomes they achieve. This idea has led to the development of quality indicators and performance measures by a variety of organisations.^{5,11} An institution may be judged by how many patients with acute myocardial infarction receive reperfusion therapy and how quickly it is delivered. The number of patients discharged on evidence-based therapies, such as beta-blockers, can be counted and compared against “best practice” benchmarks. EBM is critical to the development of these quality indicators. Indeed, in cardiovascular medicine, virtually every such indicator is based on solid evidence from multiple randomised trials, recognised by professional societies and established in guidelines.

There is evidence that measuring performance and providing feedback improves the rate of use of evidence-based therapies. Rates of use of 20 of 22 indicators improved among US Medicare beneficiaries between 1999 and 2001.¹² General acceptance of the value of therapies helps to push their use. Nevertheless, rates are still well below 100%.

CONCLUSION

EBM is scientifically based medicine, but founded upon using clinical and population science rather than basic science. There are many gaps, however, between evidence and practice. We do not always have the evidence we need, and much of this problem is due to gaps in funding and incentives for clinical trials. When we do have trials, they may focus on tangential questions, or provide less pertinent evidence than is really needed. Often, the evidence is about how therapy works for ideal patients under ideal circumstances, and we need more robust data pertinent to usual practice. Translation of evidence to guidelines is imperfect, but improving. Implementing evidence-based therapy requires more than simply providing information. Often, very active steps are needed to convince clinicians and change the healthcare system to provide optimal care. And the best care often costs more money, so in the end we must convince the public to provide the financial wherewithal for quality care.

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