

The Evidence-Based Transformation of American Medicine

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In American medicine today, the patient-physician relationship is being largely replaced by “expert” protocols or “best practices.” Although these may be called “guidelines,” the physician may be required to justify any “deviation.” Adherence to the guideline may protect him from liability for a bad outcome, but deviance may be punished by a malpractice judgment, licensure board sanction, civil monetary penalties from Medicare, or dismissal from a hospital staff or insurance panel. The guidelines are created with and justified by “evidence-based medicine” (EBM).

Compliance

The concept of compliance originally comes from physical science: the change in volume per unit change in pressure (dV/dP)—a measure of the ease with which a structure may be deformed. In common usage, it means: 1) a tendency to give in to others; 2) obedience to a dictate given by an authority; or 3) in a vulgar medical parlance, doing what the doctor wants.¹

The issue of “compliance” was “discovered” in the 1960s, and a professional discourse was created around this subject in the 1970s by Sackett and Haynes.² Initially, thousands of studies have sought to identify causes and design “corrective” interventions on the basis of the assumption that in the age of “evidence-based medicine,” patients always ought to follow their doctors’ orders and that those who do not are “deviant.”³

This approach, not surprisingly, has been met with the substantial criticism by general public. In response to many critical voices, the new so called “patient centered approach” was proposed.⁴ One could argue that the pendulum started to shift dangerously too far in the other direction, since under this approach patients started to be perceived as “consumers” who are clients of “medical providers.” Consequently, patients’ subjective satisfaction with “providers” became more important than objective results of treatment. Interestingly, however, the blame for any potential malpractice was still left with “providers.”

This situation was complicated further by the steadily declining prestige of the medical profession. The former high societal respect for physicians has been replaced by anti-doctor bias. The leaders of the EBM movement tried to remedy the drawbacks of this “medical consumerism” by introducing the concept of “shared medical decision making.”⁵ In theory, this concept was supposed to introduce balance into the patient-physician relationship. Instead of assigning the full decision-making authority to either a physician or a patient, the emphasis was put on the process of negotiating the decisions about treatment. In those negotiations, both physician and patient were to be given a status of equally important partners. However, this lofty theory has failed miserably in practice.

Unfortunately, government and third parties in today’s

world demand that physicians be in “compliance” with large volumes of convoluted and frequently contradictory rules. “Noncompliance” may be the cause for punitive sanctions. Thus, external regulations are likely to trump any negotiations between the physician and his patient. In such a setting, the traditionally sacrosanct patient-physician relationship has been broken. Clearly, when the term “compliance” is used, it denotes that the subject is in a subordinate position and is very likely to have signed an agreement in which he is called a “provider.” The role of the “provider” is apparently not to heal, but somehow to keep both his “consumers/clients” and corporate/governmental masters happy.

In summary, there were three distinct eras in the history of medical compliance. During the first era, patients were supposed to be fully compliant with physicians’ orders. In the second era, physicians were supposed to strive to fulfill patients’ (consumers’) wishes. Now, both physicians and patients are told to be fully compliant with rules and regulations set forth by third parties: either insurance companies or governmental agencies.

Evidence-Based Medicine: a Response to 21st Century Challenges

The practice of medicine has never been easy; however, the beginning of 21st century has brought numerous new challenges to the medical profession. These include information overload, a changed societal perception of medicine, and calls for cost containment.

In the age of the Internet, both information and misinformation became easily accessible for physicians and their patients. Before this high-tech digital era, physicians had to rely on printed materials (textbooks and journals) for their professional education. For most patients, their physicians served as the main source of medical information. The proliferation of hand-held information technologies has put the access to virtually unlimited amount of medical knowledge at everyone’s fingertips.

This easy accessibility has been accompanied by the exponential growth of scientific publications—including medical papers. Ultimately, this sheer volume of medical information available on the Internet became an unmanageable problem.⁶ In contrast to the past, in order to follow recent advances in medicine it is not enough to simply subscribe to a few leading medical journals. Clinicians have to master the use of electronic resources, allowing them to sift through the ocean of redundant medical research, in order to identify and synthesize the most relevant information for their work.

Societal views of the medical profession have changed significantly during the last 50 years. The past unfettered

respect and gratitude toward physicians have been replaced by distrust and unlimited demands. The truth that in medicine there are frequently many right answers to the very same clinical question has been lost. Instead, lay people and even some medical leaders demand near-robotic uniformity in medical diagnosis and treatment. Emphasis is placed on compliance with the newest medical theories. This attitude is based upon the false premise that newness *per se* guarantees the correctness of the medical paradigm. Perfect positive outcomes of treatment are not just expected, but demanded by patients, payers, and various “quality assurance” agencies. Obviously, due to the very nature of medicine, nothing can ever guarantee the positive outcome of every single medical intervention. Biology is simply too complex for that. This is another inconvenient truth, which seems to be widely disregarded. In such an atmosphere, the public is repetitively told that many clinicians, even if highly respected, may not practice medicine up to the most current “best of standards”⁷ and “something” has to be done about it. Our society’s increased litigiousness means that malpractice lawsuits and other punitive actions directed against such “outliers” have become the preferred way of medical quality control and assurance.

Medicine has transformed from a cottage industry into the strictly managed industrial complex in which profitability trumps anything else. Physicians became virtual factory workers, managed by the ruling class of business administrators. Those powerful bureaucrats constantly instruct physicians that their patients have to be treated as “clients” who have to be satisfied with the “services rendered,” rather than objectively healed from their maladies. In reality however, third-party payers are the actual customers in this system. Their willingness to pay (or not) for the medical services has much bigger significance for the managers than either objective outcomes or subjective patient satisfaction.

To solve this convoluted conundrum of obstacles facing medicine, a concept known as evidence-based medicine (EBM) has been invented and vigorously promoted. The term EBM was originally coined to denote a novel paradigm for teaching and decision-making by individual clinicians treating individual patients.⁸ This paradigm has de-emphasized the role of intuition, personal clinical experience, and theory-driven conclusions in diagnosis and treatment. Instead, it proposes that medical practice be guided by the evidence classified from the epistemological perspective. Such a classification assigns the highest value (or grade) to the evidence considered to be free from potential biases.⁹ Consequently, randomized controlled trials are assigned the highest grade, while theory-driven conclusions, expert opinions, and anecdotal evidence receive the lowest ratings.

Due to its emphasis on applied epidemiology, the EBM concept has naturally expanded to include creation of clinical guidelines aimed at management of whole populations of patients, rather than individual cases.¹⁰ In this context, while EBM was traditionally defined as the care of patients using the best available research evidence to guide clinical decision making,¹¹ perhaps the most balanced definition now is that EBM constitutes “methods of incorporating epidemiologic evidence into clinical practice.”¹²

What Is “Evidence”?

Although EBM is supposed to replace authority-based medicine, it may effectively just replace the clinical professor with a committee, which is vested with the authority to rule on what constitutes evidence, what type of evidence gathering will be permitted and funded, and how such evidence will be used in formulation of clinical recommendations.

Of the proposed hierarchical grading schemes, the system known as GRADE (Grading of Recommendations, Assessment, Development, and Evaluation)¹³ has been most widely accepted.^{14,15} GRADE establishes three-to-four levels of quality of evidence: High, moderate, low, and very low. Low and very low-quality evidence are sometimes combined into one category: low. High-quality evidence has to be derived from well-designed randomized controlled trials. Moderate-quality evidence is obtained from randomized trials with some limitations in design. Low-quality evidence consists of results of observational studies, or controlled trials with substantial limitations. Finally, non-systematic observations (“anecdotes”), theory-driven reasoning, experts’ opinions, or seriously limited observational studies are considered to constitute very low-quality evidence. The established level of quality of evidence is subsequently used in the process of assessing the strength of recommendations, which are made upon this evidence. The recommendation is said to be “strong” if the benefits of intervention definitively outweigh the risks for nearly all patients. In a contrast, a recommendation of action for which risks and benefits are either closely balanced or uncertain, is considered to be “weak.”

The very low level of quality assigned to anecdotal evidence in this system requires a brief comment. In keeping with the mantra that “the plural of anecdote is not evidence,”¹⁶ any usefulness of “anecdotes” in clinical practice is dismissed outright by EBM. However, as one wise professor observed, “Every epidemic starts with a single case report” (R.L. Kimber, personal communication, 2000). Serendipitous breakthroughs are made by individuals who make careful observations of patients from close range, seldom or never by a team encumbered by a rigid experimental protocol and the huge number of subjects needed to reach statistical significance. Single observations may be extremely important, even if not statistically significant in the context of a large trial. Say, for example, a rare, otherwise unexplained event follows a medical intervention: a patient takes a drug and inexplicably goes blind. It might be a coincidence, or it might be a side effect of the drug. One cannot rule out a causal relationship based on lack of a statistically significant difference in this occurrence between the drug and placebo groups in a trial of insufficient power to detect a rare event. One is obligated to investigate further.¹

Another important aspect of potential value of anecdotes should be considered. Theoretically, the plural of anecdote may not be as strong evidence as systematically collected data. Nevertheless, the paucity (or absence) of anecdotes consistent with the accepted theory may provide the impetus for re-examination of its validity. This would be especially true for the theories which have been constructed based upon data collected from the limited population samples and under reductionist conditions. As a matter of course, many

EBM conclusions are derived under such circumstances. In this context, EBM's reflexive dismissal of any anecdotal evidence may appear to be quite ironic.

The initial enthusiasm about the EBM model is decreasing, and even its past ardent promoters are willing to admit that this movement is in crisis.¹⁷ Numerous problems of EBM are being discussed in major medical journals. These include:

- Distortion of the EBM approach by its misappropriation by vested interests (pharmaceutical industry, payers and administrators);
- Tenuous nature of "evidence" touted by EBM;
- Focus on marginal gains, and interest shift from disease to risk;
- Over-emphasis on following algorithmic rules over sound clinical judgment;
- Poor fit for multi-morbidity;
- Disregard for genetic differences between patients.

Evidence-based medicine is distilled into practice guidelines, which have been filtered through the opinions of experts and journal editors. Opinion about the evidence, as opposed to the evidence itself, has a much greater importance than is usually acknowledged.¹ In fact, "opinion-based medicine" might be a more appropriate term than "evidence-based medicine."¹⁸ One should remember Frank Lloyd Wright's definition of expert: "a man who has stopped thinking—he knows!"¹⁹

Number Needed to Treat

Primum non nocere (first, do no harm) is the most basic tenet of medicine. The harm can be done through action or inaction. One does not need to perform epidemiological studies to know that medical intervention (such as pharmacotherapy or surgery) does not necessarily help every patient. Some patients will benefit from it, some will be harmed, and others may be unaffected by it. The same can be said about withholding of treatment.

Obviously, the proper diagnosis has to be made before the decision about starting the treatment. Diagnostic process is extremely complex and time-consuming. In a real world, even without the constraints imposed by industrialized medicine, physicians do not have time to perform a textbook-grade, comprehensive head-to-toe examination, nor they are able to order every single available test on every patient. Diagnostic tasks have to be prioritized.

All this leads to a dilemma on which specific issues it is best to concentrate during the diagnostic work-up, and after the diagnosis is made whether to proceed with a treatment. An EBM concept that offers a quantitative way to help with these questions is the Number Needed to Treat (NNT).

The patient is harmed if a readily treatable condition is overlooked while searching for trendy risk factors, especially if he is then subjected to interventions with a very high NNT (and often, a low "number needed to harm"). The NNT is the inverse of the absolute risk reduction rate (ARR), which, for prophylactic interventions, is the control event rate (CER) minus the experimental event rate (EER):

$$\text{NNT} = 1/\text{ARR}$$

For treatments, the ARR is the proportion improved in the treatment group minus the proportion improved in the control group.

One benefit of the NNT approach is to emphasize the importance of the absolute improvement rate, which might look much less favorable than the relative improvement rate. The latter is likely to be highlighted in presentations touting the benefit of an expensive drug or procedure.

Analogously, the number needed to harm would be the reciprocal of the difference between the proportion of the experimental group suffering a specified adverse outcome and the proportion of the control group having that outcome.¹

NNT was initially developed as a clinically useful epidemiological concept. However, it became also a very important parameter in pharmaco-economics,²⁰ mainly as a tool used by third-party payers in cost-effectiveness analyses (CEAs). Such CEAs are used by payers to justify their decisions about payment for medical interventions.

EBM and Personalized Medicine

Strict application of EBM implies a mechanistic algorithm-driven approach, similar to primitive pre-artificial-intelligence computer programs of the past. In such an approach, the doctor sees the patient as a statistic rather than an individual. This sort of medicine could be practiced by administrators. In the real world, however, clinical trials may tell which treatments are effective, but not necessarily which patients should receive them.¹⁸

Modern studies of the human genome and proteome have deepened our understanding of the importance and vast extent of biochemical individuality. The patient could be in a subset of patients whose excellent response to an intervention was diluted out in the large number of randomized subjects. It is recognized, for example, that two genes affect how patients process 25 percent of drugs now on the market.²¹ In fact, advances in pharmacogenetics may render the EBM model obsolete and replace it with "Genomic Medicine."^{22,23} One of the major promises of pharmacogenomics is the ability to precisely predict the individual patient's response to medical intervention, without the need to indirectly draw such conclusion from the large epidemiology-based studies.

Additionally, patients seen in real-world practice are likely to be older than the experimental subjects and to suffer from multiple diseases requiring multiple treatments, which would have excluded them from the trial. A large number of prospective subjects are generally screened in order to select suitable subjects, and still more will probably have been eliminated, say, for failing to keep an appointment, during the run-in period. Thus, study subjects may be quite atypical.¹

Conclusions

Modern trends, including evidence-based medicine, are eroding the patient-physician relationship and threatening to turn medical practice into a depersonalized, industrial process. However, the flaws in EBM are becoming apparent. Ironically, advances in our scientific knowledge are showing the importance of the focus on the individual. The science is validating the art.

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