

EVIDENCE-BASED MEDICINE AND CLINICAL RESEARCH—AN UNEASY PARTNERSHIP

The treatments we offer patients should be based on good scientific evidence—a fact that surely is obvious. Evidence-based medicine (EBM) is an exciting and a helpful concept, but there is a risk of it being interpreted with a narrow focus on the synthesis of clinical trials and systematic reviews. This was not the intention when the term was coined some 15 years ago at McMaster University, and it is a potentially harmful interpretation.

For some, the idea of synthesizing evidence and making it widely available held the promise to potentially demystify medicine. Everyone would be able to “look it up” and see which treatments worked and which did not. Journals appeared that promoted review articles that were “evidenced-based” and made us feel good because of their perceived purity. Here was the real stuff, unadulterated by questionable science—a detoxification experience.

Although the analysis of evidence is important, it must be seen as part of a wider picture and become better integrated with everyday clinical practice, evolving alongside a range of other ways of supporting clinical decision-making.

What are the problems? EBM is seducing some into believing that evidence does not count for much unless it is of the highest quality, such as that obtained from well-

conducted meta-analyses of randomized clinical trials. This has led to meta-analyses being conducted as soon as more than one trial emerges and to a lack of clarity around the implications of subtle differences in trial protocols and around the use of subanalyses in individual trials. As one doctor recently remarked somewhat cynically, “it takes just two randomized controlled trials to generate three different meta-analyses.”

Less seasoned physicians, and even some who are quite experienced, may respond with uncertainty and despair on rounds when they realize that the treatments offered do not meet the highest evidence-based standards. Often, the appropriate research studies have simply not been done, or the research has failed to demonstrate a strong conclusion. This will continue to be the case as new treatments emerge, and this is especially true in our own specialty of neonatology.

When confidence is undermined, it can result in therapeutic nihilism and a loss of direction in our approach toward patients. In some cases, the notion of equipoise is being used to encourage patient choice, in a way that amounts to the devolution of responsibility for treatments to patients. In the UK, this comes at a time when informed consent for treatments and the idea of patient choice have achieved a high profile in the National Health Service (NHS).

Raising this subject requires us to be circumspect because some would say that a bit more therapeutic nihilism might be a good thing. The history of neonatology and other specialties is punctuated by therapeutic disasters, where the risks of treatments were not

fully appreciated at the time they were administered. However, there are broad implications here concerning the way we train doctors for the sharp end of clinical practice and concerning professional and public expectations from research.

When the highest level of evidence exists for or against a given treatment, it is easy to practice evidence-based medicine. Perinatal-neonatal medicine provides some examples of a few therapies that are based on the highest quality of evidence—and which have made an important difference to outcomes—such as the use of antenatal steroids in preterm labor and surfactant therapy for RDS in preterm newborns.

However, there are a huge number of clinical problems for which there is no strong evidence base for their best management. The real challenge, therefore, is how we should be training and preparing doctors to practice medicine in these circumstances, without despair and without walking away from the problem. To put it starkly, how should we practice non-evidenced-based medicine?

We need to acknowledge the limitations as well as the strengths of EBM in everyday clinical practice. Central to this training are the reading and critical interpretation of individual scientific papers that may not have been addressed in meta-analyses. When treatments are conventionally offered without the highest level of evidence, an understanding of the balance of risks is crucial, and this balance includes the risks of therapeutic nihilism or a delay in initiating treatments.

Some degree uniformity of practice is important on wards and in departments, even if there is uncertainty that such policies are based on a high level of scientific evidence. Working to policies, while acknowledging at the same time that what we do may not turn out to be the best approach, is an important element of training for doctors. This attitude encourages and makes it easier for them to become involved in quality assessment of local outcomes. It is an approach that deserves the same high profile as conventional research, and it is a way of structuring training to address some of the despair and anxiety felt by young doctors who expect too much from EBM.

Where does clinical research fit in this challenge? Curiously, clinical research has come under threat in many advanced countries for a number of complex reasons. This is paradoxical because it seems to have coincided with the development of EBM.

It has become difficult for aspiring researchers to gain proper training in clinical research. This happens partly because training in the UK for a career as a consultant in the NHS has become highly competitive, and many fear that taking time out for a formal research project may nudge them off the ladder to no advantage. Although there are arrangements for taking a year out during specialist training, this plan rarely provides sufficient background for a future research career.

Junior doctors in the NHS often make important contributions to multicenter randomized, controlled trials in terms of enrolling patients and keeping data. Although this work may receive formal recognition when their training is being assessed, it often is not valued by

seniors in university research departments. The university agenda is heavily weighted toward importing established researchers with strong research output because this powerfully influences central funding for the universities.

The precarious state of clinical research also owes much to the difficulty at present in getting projects off the ground. Leaving aside the issue of funding, which has always been a challenge, there is a huge bureaucratic mountain to climb. The demands of many research ethics committees have increased, and some have been accused of being unreasonably obstructive rather than fulfilling a primary role of protecting participants in research.

To some extent, the defensive role of research ethics committees is understandable because of the media attention given to a small number of doctors who have taken liberties with informed consent of patients, especially in matters of organ or tissue retention. There clearly has to be a balance between protecting potential participants and positively discouraging them from consenting to research. Some patient research information leaflets are so positively discouraging it is a wonder that anyone is recruited into trials.

The threat to clinical research has been recognized in the UK, and some of these issues have started to be addressed. The Government now has NHS research high on its agenda with a commitment to reduce unnecessary bureaucracy and to target research that will

potentially improve patient care. A career structure has now been proposed to improve the training of doctors who may wish to embark on a research career.

It is too early to know how these proposals will develop. In the meantime, we need to keep the public on board not only for their potential contribution to safe clinical trials but also to encourage funding for medical science. An unreasonably negative attitude toward treatments by a narrow interpretation of EBM as the output of meta-analyses is unhelpful. The public can be forgiven for wondering, with all this equipoise around, where has all the research money been spent?

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