

Evidence based medicine and meta-analysis: in search of the Holy Graal

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Abstract

The authors reflect on the evolution of medical education and feel that the emphasis given to evidence-based medicine and meta-analysis is excessive. Based on an analysis of the methodological problems of randomised controlled trials and meta-analysis, the

use of such methods in clinical practice is further discussed.

Key words: evidence-based medicine, meta-analysis, randomised controlled trials, medical education.

Medical training

Medical training has undergone massive changes in recent years. Traditionally, medical training was done at the patient's bedside. The increasing difficulties involved in collecting the clinical history and carrying out a careful objective examination were the building blocks that led to the gradual differentiation of clinical practice. Direct contact with older, more experienced colleagues was fundamental. There were few specialized journals and books, and in most cases, these were doctrinal, transmitting only well-founded, consensual information.

Around the middle of this century, the explosion of the written Press, including in the field of Medicine, led to what we can call the first revolution in medical training. The proliferation and specialization of medical journals gave direct access to the results of research, for those who were interested. It also broke the direct link between student and teacher, the latter being replaced, in part, by well-respected and prolific authors.

In this decade, we have seen the start of a new revolution. Although the first computerized databases made their appearance among us more than a decade ago, it was the increasing availability of Internet access that led to the real revolution. The immediate availability of research in databases like MEDLINE

and EMBASE has given physicians rapid and low-cost access to abstracts of the biomedical publications.¹

Today, we are paying the price for this youth. Cases of physicians trained through the reading of abstracts, who rarely read a complete book or article, are becoming more and more common. Careful study of an investigation work, with special emphasis on the methodology, which is essential for determining the validity and application of the study in our patients, is being replaced by an immediate, and often hurried reading of the results and conclusions. This immediacy, based on the absence of references and the relativity of beliefs, which some are now calling post-modern Medicine, is clearly exemplified in a recent editorial by Paul Hodgkin:² "Do enough research on MEDLINE and you fill the answers to your prayers".

A simultaneous phenomenon was the proliferation of the available information. Today, there are more than 30,000 biomedical journals, and the number of original articles published each year is exceeding the capacity of physicians to read the publications in their area of specialization. For example, in the field of intensive Medicine, a study on MEDLINE with the keywords "intensive-care" or "critical-care" results in 2238 articles in the last year, and 24,165 in the last ten years.

Finally, the quality of the information published is often debatable, and the same results are often published several times with just minor differences to the text, with revisions or revisions of revisions becoming ever more frequent.

Evidence based medicine

Evidence based medicine (EBM) emerged as a result of these problems. EBM is an approach to the teaching of Medicine based on knowledge of the evidence, in

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which the medical practice is based on the strength of this evidence. It emphasizes the idea that clinical decisions must be based on results of controlled investigations, warning of the need for extreme caution whenever the clinical practice is based exclusively on the results of animal studies, or non-controlled observations.³ The practice of EBM seeks to integrate individual clinical experience with the best external evidence available.⁴ It is hailed as the way of the future for the teaching of Medicine. This approach has seen an exponential growth, and today, there is even a journal dedicated exclusively to it.⁵

The methods on which EBM are based are not new or incorrect. For a long time now, clinical and biostatistical epidemiology have been fundamental pillars of modern Medicine. But while its basic principles may be correct, the application of EBM in clinical practice is a different matter altogether. Its almost exclusive concentration on randomized controlled clinical trials (RCT) and meta-analyses of those trials, advocated by the defenders of this movement,⁶ makes it restrictive. Therefore, the question that should be asked is: on what evidence is EBM based?

Controlled randomized clinical trials

In recent decades, CRCTs have emerged as a paradigm of good clinical investigation. Carried out on large groups, they paradoxically include a restricted population of patients which, it is hoped, will respond positively to the therapy, with an intermediate degree of severity and with relatively few co-morbidities. The study of these trials is undeniably important, but it leaves physicians with the dilemma of how to apply their conclusions to individual patients in their own clinics, given that the conclusions are only applicable to average patients, who meet the criteria for inclusion in the study. Often, there are doubts as to the methods used, and the correction of execution.^{7,8}

In many areas of Medicine, clinical trials cannot be carried out due to a lack of financial support or ethical opposition. Thus, areas are left out in which there is no evidence, or the evidence is incomplete, or in which there are contradictory results, so-called "grey areas" of medical practice, known among us as "black holes of medicine"⁹ which unfortunately, are extremely vast.¹⁰ To resolve the latter problem, practitioners of EBM frequently use techniques of combining data, such as meta-analyses,^{11,13} although other techniques have also been described.¹⁴ They also

seek to combine the information obtained from various CRCTs, to obtain greater precision in the results.¹⁵

Meta-analysis

Meta-analysis can be defined as the combination, using statistical methods, of a high number of analyses resulting from individual studies with the aim of integrating the results.¹⁶ Since its appearance, it has raised disparate reactions among researchers, ranging from complete aversion^{17,18} and skepticism^{19,20} to enthusiasm.^{13,21,22}

The main goal of this technique is to carry out a literature review, through the combined use of statistical methods and a systematic qualitative review; as such, it is a method of presenting and systematizing the data, and combining the results of various studies. Furthermore, it enables increased power in the estimation of measurements, assuming that the calculation of these measurement is appropriate for a given situation. It is logical that combining the data from various studies, the scale of the sample, and therefore the statistical power, will increase. However, this affirmation is only true if the studies are capable of being combined, i.e. if the heterogeneity is low. But this is not the case, as there are always major differences between studies. The practice of rejecting heterogeneity is also restrictive, as we probably have much more to learn from the causes underlying the apparently contradictory results, among the various studies.²³

Additional problems in the practice of meta-analysis are the selection and the quality of the studies analyzed, their statistical bases, and the applicability of the results.^{18,24} It is hardly surprising, therefore that in some cases, the results of a meta-analysis and a subsequent CRCT are contradictory.²⁵ However, what Alvin Feinstein calls statistical alchemy for the 21st century appears to be here to stay.¹⁸

Thus, a new paradigm and a new paraclinical specialist is created: the meta-analyst. Based on the results of the CRCTs, and given their in-depth knowledge in the techniques of literature searching, the meta-analyst appears as the saviour of the clinic. This individual does not investigate, but analyzes the investigations of others; does not apply the results, but publishes truths. However, this approach has been supported by a strange alliance of hospital managers, academics and doctors, who have been away from the clinical practice for a long time. More than a means of

improving the medical practice, EBM has been seen as a means of limiting healthcare costs and imposing administrative control on the medical practices. It is, perhaps, no mere coincidence that this movement is occurring at a time when attempts are being made to minimize the importance of clinical practice, and the choice of those responsible for the Services is being increasingly based on administrative, i.e. political factors.

Final note

Although it requires experience in the precise definition of patients' problems, bibliographic research, critical evaluation and the application of relevant information from the literature,³ the practice of EBM fails to take into consideration the etiological and physiopathological approach to disease.

Derived almost exclusively from CRCT and meta-analyses, the data do not include many types of treatments or patients observed in daily practice; the results that demonstrate the comparative effectiveness in the treatment of an "average" patient in the trial are not relevant for the majority of cases seen in the clinic, and the analyses generally omit important events that have occurred after the patient's inclusion in the trial. Information based on RCTs is rarely available on matters of etiology, physiopathology, diagnosis and prognosis. The commendable objective of making clinical decisions based on evidence can therefore be compromised by the restricted quality, and the scope of what is the "best evidence available". The authoritative air given to the collection can, however, lead to abuses that result in incorrect protocols or doctrinal dogmas, which are unfortunately very frequent in academic circles, where the motivating factor seems to more fashion than science.^{26,27}

Today, like the crusades that traveled the World in search of the Holy Graal, we set off on a pilgrimage to the world of journals to find the answer to our doubts and prayers. But, both yesterday and today, we are more likely to find it there among us. Applied to Medicine, this means finding the answer in a rational clinical practice, based on a careful semiology and on in-depth knowledge of the etiological and physiopathological mechanisms of disease, rather than - sacred though it may be - on evidence.

In other words, that which J. André Knottnerus said to us when he affirmed that medicine-based evidence is a pre-requisite for evidence-based medicine.²⁸ ■

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