ABSTRACT | INTRODUCTION: Evidence-based medicine is one of the most widespread trends in contemporaneous medical education. It proposes a scientific framework not only for medical training, but also for medical research and practice. However, knowledge about EBM roots and historical developments is not usual within Brazilian medical community. Indeed most common publications for non specialists medical readers, like handbooks and tutorials papers on EBM, are not sufficiently rich for providing historical knowledge.

OBJECTIVES: To present a brief narrative of the historical development of evidence-based medicine.

METHODS: Historiographical review essay.

MATERIALS: Primary and secondary sources on the history of EBM.

RESULTS: As EBM founder, David Sackett stated against clinical decisions based solely on physicians authority and intuition achieved by long term clinical experience and pathophysiological knowledge. Paradoxically, in his retiring letter, Sackett alleged that his own prestige and authority could retard the scientific advance of EBM.

CONCLUSION: Since the early 2000’s, critical appraisal, systematic reviews and clinical practice guidelines has merged in a unified approach that characterizes current practice in EBM.

KEYWORDS: Evidence-Based Medicine. History of Medicine. Medical Education
In 1964, a report from the Canadian government recommended the creation of a new medical school at McMaster University, Ontario, that should introduce a new approach to medical education, current medical school programs were evaluated out-of-date. This new approach was based in the introduction of clinical epidemiology and biostatistics in the medical program also the medical curriculum would be based on valid outcomes of medical research. David Sackett was the first director of the Department of Clinical Epidemiology and Biostatistics at the Medical School established in 1967. He claimed that clinicians should be trained to develop skills needed to ask epidemiological questions relevant to solve practical clinical problems. Since then, debates about Sackett’s proposal have target the meaning and relevance of epidemiological knowledge in clinical practice, as well as the uncertainty of medical judgments based on medical authority.

David Sackett were influenced by Alvan Feinstein’s ideas questioning the authority of medical knowledge and the individual judgment arising from clinical experience. Feinstein, Professor of the Yale University School of Medicine, one of the founders of Clinical Epidemiology, proposed a method for applying scientific criteria to clinical judgments and solving the problem of uncertainty in medical practice, anticipating the proposals for Evidence-Based Medicine (EBM) that would later be launched by Sackett.

The other side of Atlantic, in the 1970’s, Archibald Cochrane advocated the use of randomized controlled trials (RCT) to ensure effectiveness and efficiency in prevention and treatment procedures undertaken by the National Health System (NHS) of the United Kingdom, disseminating and systematizing the pioneering studies of medical statistics conducted by Austin Bradford Hill from 1937.

According to Cochrane, clinical opinions were the worst type of evidence for scientifically test a hypothesis:

Two of the most striking changes in word usage in the last twenty years are the upgrading of “opinion” in comparison with other types of evidence, and the downgrading of the word “experiment”. (...)

The general scientific problem with which we are primarily concerned is that of testing a hypothesis that a certain treatment alters the natural history of a disease for the better. The particular problem is the value of various types of evidence in testing the hypothesis. The oldest, and probably still the commonest form of evidence proffered, is clinical opinion. This varies in value with the ability of the clinician and the width of his experience, but it value must be rated low, because there is no quantitative measurement, no attempt to discover what would have happened if the patients had had no treatment, and ever possibility of bias affecting the assessment of the result. It could be described as the simplest (worst) type of observational evidence.

At that time a dilemma emerged: What are the rules of evidence that should be adopted as the basis for the clinical management of patients? Should only RCT - validated evidence be used to prevent or minimize the use of therapeutic resources innocuous or harmful to patients? Or should clinicians experiences also be admitted as a basis for maximizing the potential patients health benefits?

Yet in 1976, at Copenhagen, Hendrik Wulff had detailed the logical and probabilistic aspects involved in the application of RCT outcomes in clinical practice. He drew attention to the difference between therapeutic efficacy as measured by the statistical likelihood obtained from RCT and clinical effectiveness as measured by the subjective likelihood of the physician’s belief in the cure of a particular patient, calculated by applying the Bayes theorem. Even patients with the same disease differ in a number of ways, so that it is not always rationally certain that the physician will base his belief (subjective probability) on the overall experience of a group of patients (statistical probability). In addition, the physician should assess to what extent it is appropriate to apply group experience to the individual.

In the 1980s, clinical epidemiology spread internationally in medical education curricula, despite the difficulties faced due to the required mathematical and statistical knowledge and skills. The initial stimulus for this diffusion came from the Rockefeller Foundation, which in 1978 funded the establishment of the International Clinical
Epidemiology Network (INCLEN) to train medical professors in clinical epidemiology methods to promote curriculum changes and health policies in “third countries world”.

In 1989, Iain Chalmers published the first systematic RCT review involving an international collaboration that gave rise to the Cochrane Collaborations and Oxford University's Cochrane Center in 1992, with NHS resources, directed by Muir Gray. They invited David Sackett to move to the University of Oxford, United Kingdom, where he founded and directed the Center for Evidence-Based Medicine from 1995 to 2010. Simultaneously, in Copenhagen, Peter C. Gøtzsche, co-author of the new editions of Wulff's book and co-founder of Cochrane Collaboration, founded the Nordic Cochrane Center. In Brazil, under the leadership of Alvaro Nagib Atallah, the Cochrane Brazil Center was founded in 1996.

The McMaster University Evidence-Based Medicine Group, featured by previous Sackett's students Brian Haynes, Gordon Guyatt and Peter Tugwell, presented itself to the international public in 1991 and 1992, respectively, in an editorial from the American College of Physicians Journal Club, and a paper in the Journal of the American Medical Association (JAMA). Evidence-Based Medicine (EBM) has been presented as a new paradigm for medical practice and a new approach to medical education, which requires physicians to seek new skills and evaluate clinical evidence in the literature. On the other hand, they rejected intuition, unsystematic clinical experience, and pathophysiologic rationale as sufficient basis for clinical decision making. They highlighted the importance of RCT for assuring the efficacy of diagnoses and therapeutics; systematic reviews and meta-analyses as methods for summarizing and evaluating RCT outcomes; and the crucial roles played by both in defining treatment protocols.

In 1995, David Sackett and Brian Haynes wrote for the first issue of the British Medical Journal - Evidence Based Medicine, which was being released:

(...)(EBM), the emerging clinical discipline that brings the best evidence from clinical and health care research to the bedside, to the surgery or clinic, and to the community. The practice of EBM is a process of life-long, problem-based learning in which caring for our own patients creates the need for evidence about diagnosis, prognosis, therapy, and other clinical and health care issues. In the EBM, process, we 1) convert these information needs into answerable questions; 2) track down, with maximum efficiency, the best evidence with which to answer them (whether from the clinical examination, the diagnostic laboratory, the published literature, or other sources); 3) critically appraise that evidence for its validity (closeness to the truth) and usefulness (clinical applicability); 4) apply the results of this appraisal in our clinical practice; and 5) evaluate our performance.

However, according to David Eddy, there were actually two “evidence-based” approaches: one aimed at developing guidelines (EBG) and another directed at the individual development of physicians (EBID). The latter was designed, developed, and disseminated by Sackett and his partners, while the other was his own work, following a line of research on health care costs that began in the 1980s with RAND Corporation: “In the 1980s a group at RAND began publishing studies showing that large proportions of procedures being performed by physicians were considered inappropriate even by the standards of their own experts.”

The RAND corporation was a center of health services expertise by the late 1970s, when neoliberal policies was introduced by Ronald Reagan in the United States. This time, the focus of the political debate on health had shifted from poor people's access to health services to managing the costs of health services:

In the Medicare program, as in American health care more generally, the concerns of policymakers soon shifted from access to cost (...) In time, then, the field of health services research turned its attention to the technical issues and quality concerns related to cost containment. An important point in this process was the RAND health insurance experiment.
An important point in this process was the Rand health insurance experiment\(^{20}\). RAND had developed an institutional expertise in the application of quantitative methods to the education and health. The impetus for the health insurance experiment came not so much from clinicians concerned about health outcomes, as from economists who focused their attention on the relationship between the cost of medical care and its consumption. By the time, the experiment was intended to anticipate the creation of a national health insurance, but it failed in its purpose. Nonetheless, outcomes of the experiment contributed to the big increase of cost sharing that occurred in the 1980s, and this tended to reduce services in an indiscriminate fashion with adverse effects on the health of vulnerable:

(...) it tended to reduce services in an indiscriminate fashion — the good along with the bad. Furthermore, the experiment showed that cost-sharing had adverse effects on the health of vulnerable groups, such as low-income children, "just a catastrophic drop in the use of services, clearly services that were needed as well as services that weren't that you didn't see so much for kids with a higher income\(^{20}\)."

David Eddy himself has been linked to the private health insurance industry from 1984 to 2005, as chief scientist for the Technology and Coverage Program and the Medical Advisory Panel of Blue Cross Blue Shield, a federation of health insurers, which serves more than 100 million Americans\(^ {21,22}\). In this context that Eddy wrote the first evidence-based guidelines for the American Cancer Society:

*First, there must be good evidence that each test or procedure recommended is medically effective in reducing morbidity or mortality; second, the medical benefits must outweigh the risks; third, the cost of each test or procedure must be reasonable compared to its expected benefits; and finally, the recommended actions must be practical and feasible\(^ {23}\).*

At that time there was indeed a concern with the relationship between the search for good evidence for the clinical effectiveness of the procedures with their cost and benefit efficiency. In his 2005 paper, David Eddy asked that, since the current definition of EBM includes EBID but not EBG, whether the definition of EBM should be expanded to include evidence-based guidelines and its related branches, instead of focusing only on physicians and their individual decisions, comprising a set of principles and methods to ensure that medical decisions, protocols, guidelines and other types of health policy would be based and consistent with good evidence of effectiveness and benefit\(^ {19}\).

Indeed, in 1997, in the same year that David Sackett published his EBM handbook\(^ {24}\), Muir Gray also published another EBM handbook by the same publisher, Churchill Livingstone, of the Elsevier (Elsevier Science) group\(^ {25}\) the first focused on individualized clinical practice and the second on health policies. In his book, Muir Gray includes rising costs and “delayed implementation of research results in practice” in the list of major convergent and common problems to the delivery of healthcare world-wide, so that the same solutions should be adopted, either in the post-industrial northern countries or in the “third world” countries, whose health systems should be restructured. In short, the solutions highlighted by Muir Gray focused on aspects such as cost control, healthcare purchasing, and clinical practice management:

* (...) a growing appreciation of the need for the purchasers of healthcare to manage the evolution and development of clinical practice in partnership with clinical professions;*  

* increasing public and political interest in the evidence on which decisions about the effectiveness and safety of healthcare are based\(^ {25}\).*

In 2000, David Sackett wrote a letter to the BMJ announcing his retirement from EBM. Sackett alleged that:

* (...) experts like me commit two sins that retard the advance of science and harm the young. Firstly, adding our prestige to our opinions gives the lattes far greater persuasive powers than they deserve on scientific grounds alone (... others tend not to challenge them and progress toward the truth is impaired in the presence of an expert. The second sin of expertness is committed on
grant applications and manuscripts that challenge the current expert consensus. Reviewer face the unavoidable temptation to accept or reject new evidence or ideas, not on the basis of their scientific merit, but on the extent to which they agree or disagree with the public positions taken by experts on these matters26.

Based on his self-criticism, Sackett repeated what he had done almost twenty years earlier, when he had voluntarily retired from research on patient compliance in therapeutic regimens, saying that he would leave the field open for younger people. Since this, David Sackett would only devote himself to “thinking, teaching, and writing about randomized trials.”

However, in an article devoted to David Sackett, a year after his death in 2016, Gordon Guyatt stated: “Dave created an ethos that to this day characterizes what has become the world of evidence-based medicine (EBM) science and evangelism”27. Paradoxically, Guyatt seemed to admit that Sackett’s authority remained influencing EBM beyond his physical presence.

In 2017, in his commemorative paper on EBM’s 25th Anniversary, Gordon Guyatt acknowledged the seminal roles played by David Sackett, Archie Chocrane and David Eddy in the early days of EBM, when they argued for critical appraisal, development of systematic reviews, and clinical practice guidelines, three domains that merged in the 2000s to characterize the current practice of EBM28.

Author contributions

Lapa TG is the first author of the article which is an extract from her thesis. Rocha MD supervised the research. Almeida N was co-advisor of the thesis, contributing mainly, but not exclusively, to the aspects of work related to Evidence-Based Medicine, including his vision as a model of contemporary education in the health sciences field. Mattedi A contributed to the methodological aspects related to the history of scientific controversies.

Conflicts of interests

No financial, legal or political competing interests with third parties (government, commercial, private foundation, etc.) were disclosed for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.).

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