

Evidence Based Complementary and Alternative Medicine: Promises and Problems

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Key Words

Evidence-based medicine · Complementary and Alternative Medicine

Summary

Objective: The present paper examines the experience of establishing a center for evidence-based complementary and alternative medicine (EBCAM) practice. It examines both the difficulties and the challenges of doing research to establish EBCAM. The paper also examines the political context of the demand for evidence-based practice (EBP) for CAM. **Implementation:** A center for EBCAM was funded for 3 years within the Southern California Evidence-Based Practice Center by the National Center for CAM and administered by the Agency for Health Research Quality. This experience provides the basis for this paper. **Results:** While the experience of creating an EBM Center for CAM has shown that much work can be accomplished by applying standard methods of EBP medicine, it also highlights the weaknesses of such an agenda. Many standard research methods are simply not applicable to CAM, and even where they are, effectiveness is a much more important means of assessing CAM than simply efficacy. Researchers however, must be conscious of the political motivations behind much of the demand for EBCAM. Where such demands are coming from allopathic medicine, they clearly form a continuing part of medical opposition to CAM and may be intended to perpetuate the dominance of the biomedical paradigm in healthcare. The challenge for CAM is to recognize the limitations of EBP but not to throw the 'baby out with the bathwater'. There is much in EBP that clearly should be emulated by the CAM community but only where it is appropriate.

Schlüsselwörter

Evidenzbasierte Medizin · Komplementär- und Alternativmedizin

Zusammenfassung

Ziel: In der vorliegenden Arbeit werden unsere Erfahrungen bei der Gründung eines Zentrums für praktische evidenzbasierte Komplementär- und Alternativmedizin (EBCAM) erläutert. Es werden sowohl Schwierigkeiten als auch Herausforderungen in der zur Etablierung von EBCAM erforderlichen Forschung diskutiert. Darüber hinaus untersucht diese Arbeit den politischen Kontext der Forderung nach einer evidenzbasierten Praxis (EBP) in der Komplementär- und Alternativmedizin. **Implementierung:** Grundlage dieses Aufsatzes sind die Erfahrungen, die mit einem EBCAM-Zentrum innerhalb des Southern California Evidence-Based Practice Center gemacht wurden. Dieses wurde 3 Jahre lang vom National Centre for Complementary- and Alternative Medicine finanziert und von der Agency for Health Research Quality verwaltet. **Ergebnisse:** Während die Erfahrungen bei der Gründung eines evidenzbasierten Zentrums für Komplementär- und Alternativmedizin zeigen, dass vieles bereits durch die Anwendung von Standardverfahren der evidenzbasierten medizinischen Praxis erreicht werden kann, machen sie auch die Schwierigkeiten eines solchen Vorhabens deutlich. Viele Standard-Forschungsmethoden sind in der Komplementär- und Alternativmedizin nicht anwendbar, und selbst wenn sie es sind – Effektivität und Brauchbarkeit (effectiveness) sind weitaus wichtigere Kriterien zur Beurteilung von Komplementär- und Alternativmedizin als lediglich Wirksamkeit (efficacy). Forscher müssen sich jedoch bewusst sein, dass viele Forderungen nach EBCAM politisch motiviert sind. Kommen solche Forderungen aus der allopathischen Medizin, sind sie offensichtlicher Ausdruck anhaltender medizinischer Vorbehalte gegenüber der Komplementär- und Alternativmedizin mit dem Ziel, die Vorherrschaft des biomedizinischen Paradigmas im Gesundheitssystem zu erhalten. Die Herausforderung für die Komplementär- und Alternativmedizin ist es, die Grenzen evidenzbasierter medizinischer Praxis zu erkennen, ohne jedoch das «Kind mit dem Bade auszuschütten». Eindeutig sollte vieles von der evidenzbasierten medizinischen Praxis in die Komplementär- und Alternativmedizin übernommen werden, aber nur, wenn dies auch angemessen ist.

Introduction

While there have been previous attempts by sociologists to discuss complementary and alternative medicine (CAM) and evidence-based medicine (EBM) [1], none has been from the insider's perspective of doing research in evidence-based complementary and alternative medicine, EBCAM. This partly reflects lack of opportunity, in that firstly there have been very few evidence-based practice (EBP) centers for CAM, and secondly, because in the author's experience few sociologists have participated in such centers or in fact in EBM in general. This article will focus on the process of establishing a U.S. Center for EBM, reflecting some of the methodological challenges involved in such a project. The author was the Principal Investigator for a grant to investigate CAM in this center.

Setting up an EBM center of CAM

In 1997, the Agency for Health Care Policy and Research (AHCPR, later called the Agency for Health Research Quality or AHRQ) established 12 evidence-based practice centers (EPCs) throughout the U.S. and Canada. This has since been increased to 13. One of these is located at RAND, a major not-for-profit center for health policy/health services research located in Santa Monica, California (RAND historically stood for research and development). This is the Southern California Evidence-Based Practice Center (SCEPC). This center involves several major institutions in addition to RAND including the University of California Los Angeles (UCLA), the University of California San Diego (UCSD), the University of Southern California (USC), the Cedars Sinai Medical Center, and three of the Veterans Administration Centers (Sepulveda, West Los Angeles and San Diego).

Each EPC is constructed a little differently and each must compete annually for contracts to produce evidence reports for the government agency, or on occasions, for third party organizations. The topics may be the result of the need to hold a NIH Consensus Conference (such as the treatment and management of caries) or may be the result of political concerns such as the one on Ephedra (a drug taken by young athletes some of whom had collapsed and died). They may also simply reflect a topic of interest to an agency. The topics are selected in a process of discussion with the EPC and AHRQ and in the case of CAM with the National Center for CAM who funded the project.

The major method used by the EPCs is that of systematic literature reviews. The centers usually include experts in epidemiology, health services research, biostatistics, economics, decision analysis and cost-effectiveness analysis. They produce systematic reviews of benefits, risks, harms and costs of medical interventions (called 'evidence reports'); provide technical assistance to third parties interested in developing practice guidelines, medical review criteria, or other products from ev-

idence reports; and perform research on the science of systematic review or guideline development. In this particular project, 25% of the grant was allocated for the development of methods to support EBP research.

The work can be organized around a condition, a topic proposed by a third party or involve a national group of technical experts to determine 3–5 most important clinical questions followed by an exhaustive review of evidence for those 3–5 questions. One of the centers' main use is to provide a standardized 'evidence base' for other groups to use when developing practice guidelines or review criteria.

In some instances, the AHRQ administers grants awarded by other NIH agencies, particularly if they lack the experience with EPCs. The primary NIH agency responsible for research into CAM is the National Center for Complementary and Alternative Medicine (NCCAM). In 2001, the NCCAM through AHRQ released a request for proposals to establish an EPC for Complementary and Alternative Medicine (CAM). Only the existing EPCs already established by AHRQ were eligible to compete for this contract. The SCEPC was successful in obtaining this grant and from 2000 to 2003 was involved in several major studies in EBP for CAM. Prior to being awarded this contract, RAND had been involved in examining the evidence for the basis of chiropractic manipulation and the appropriateness of manipulation for low back pain and the appropriateness of cervical manipulation. This paper is based on the experience gained from this work.

What Is Evidence-Based Practice?

In most discussions, EBP is viewed as defined within biomedical circles as; 'the conscientious, explicit and judicious use of the current best evidence in making decisions about the care of individual patients' [2]. In practice, 'evidence-based medicine constitutes the integration of individual clinical expertise with the best available external clinical evidence from systematic research' [3]. Further 'the practice of EBM, then, is the process of life-long, self directed learning in which caring for our own patients creates the need for clinically important information about diagnosis, prognosis, therapy, and other clinical and health issues' [4]. This is contrasted with tradition-based care [5], which is characterized as 'practical, prudent, and personal.' In traditional care, emphasis is placed on the accumulated knowledge and experience, adherence to accepted standards, and the opinion of experts and peers. EBP in contrast places a premium on using current evidence to solve clinical questions [6]. At the very minimum, it involves reading current literature, being able to critically appraise the literature [7], being able to synthesize the literature or appraise syntheses, drawing conclusions that are relevant to clinical practice, and applying the results of these processes to individual patients [8–9].

Despite the great expectations held by some groups for EBP, there is little evidence to suggest that it results in better out-

comes for patients or that those who are educated in EBP, in fact, practice better medicine [10, 11].

There is considerable debate about how much of clinical practice is actually evidence based. Initial estimates by the Office of Technology Assessment in 1979 [12] and 1983 [13] held that only about 10–20% of medicine could claim to be evidence based. As noted by Imrie and Ramey [14], this figure was simply an estimate [15]. They further note that other commentators have given figures as low as 15%. In 2001, an editorial in the 'British Medical Journal' quoted a figure of 15% for solid scientific interventions for medical interventions [16].

The problem of establishing this figure is you first need to define what will constitute 'evidence'. How you do that has a significant impact on the result. If, for example, you demand only one good single randomized controlled trial (RCT), the figure will be much higher than if you require repeated RCTs. The use of a single RCT, no matter how good the study, does pose methodological problems, as single studies can be (and have been) contradicted by later studies. To overcome the problem of a single study, studies are pooled if they are homogeneous enough to permit a meta-analysis. This also greatly increases the sample sizes on which analyses can be done [17, 18]. Examples of misleading meta-analyses have already been documented in the literature [19].

By its nature, an RCT tests a procedure or therapy under ideal conditions and feasibility of applying the practice in a real setting and therefore may have limited relevance for actual practice. This deals with efficacy not effectiveness [20, 21].

Towards Evidence-Based CAM

Because of the ideological nature over much of the debate about the evidence basis of CAM it is necessary and prudent to acknowledge this context.

Although the increasing popularity of CAM in Western societies has been well documented [22], it should be noted that there have also been negative reactions amongst certain groups. This has led to the creation of one journal, the 'Scientific Review of Alternative Medicine', whose purpose is to examine the claims of CAM [23]. On the other hand, there is a suspicion among alternative health care providers [24] that only those studies with negative results about CAM will be published in mainstream journals in stark contrast to medicine where there is a suspected bias against publishing negative results [25].

Many commentators have argued that CAM should be subjected to the same rules of evidence that are assumed to be held for medicine [26–29], and for the same methods of evaluation such as, assessment of clinical skills, and safety evaluations [30–32].

Astin et al. [33] note there are three major physician objections to CAM. The first is that CAM providers lack extensive knowledge particularly with regard to diagnosis. A second is

that there is a lack of evidence for efficacy. A third is that there is a risk for patients because they delay getting appropriate medical care by using CAM. A more radical position is that there is only one kind of medicine, that which has empirical support and that until CAM can demonstrate this support, it should not be considered complementary or alternative [34]. The position that EBP is the basis for integrating CAM and conventional medicine is fraught with difficulties and assumes that modern medicine is itself evidence based. Allopathic medicine itself could not meet such a strict criterion [35].

However for some writers, CAM is portrayed as having a 'free ride' by not having been subjected to the demands of science in the way medicine is [34]. One has to wonder in what sense CAM has been given a free ride. For the most part, science has ignored investigating CAM. If it is meant as a criticism of the CAM community, then again one might question the fairness of the comment. The great research endeavors that are presumed to make biomedicine scientific have not been paid for by the medical profession, nor in large part, conducted by the medical profession.

In the U.S., the CAM community can hardly be blamed given the historical resistance (and current resistance in some quarters) to having a single NIH agency to support research in CAM. Though the current budget for the NCCAM is over USD 120 million, that is a tiny fraction of the money spent by the NIH on research in biomedicine and furthermore, such monies have only been available for a very short time (about 10 years). The CAM budget for 2006 was only 0.42% of the total NIH budget [36].

The experience at RAND has been, and the increasing publications about efficacy of CAM would suggest, that the CAM community is only too willing to cooperate with researchers whose agenda is research and not political.

Practical Work of the SCEPC

The Southern California Evidence-Based Practice Center (SCEPC) held a contract from the AHRQ Agency for 3 years to conduct systematic literature reviews for CAM therapies. We completed 9 systematic reviews in CAM. Prior to the SCEPC, RAND had completed 2 systematic reviews in chiropractic manipulation. The completed topics include manipulation for low back pain, cervical manipulation, mind-body therapy for gastro-intestinal (GI) problems; Ayurvedic medicine for diabetes; S-Adenosyl-L-Methionine (S-AMe) for depression, osteoarthritis, and chronic liver problems; Coenzyme Q10, vitamin E and vitamin C for treating or preventing cardiovascular disease and Coenzyme Q10, vitamin E and vitamin C for treating or preventing cancer.

A search of MEDLINE, HealthSTAR, EMBASE, Allied and Complementary Medicine, MANTIS, BIOSIS previews, PsycINFO, Social Science Citation Index, two files of Science Citation Index, CAB HEALTH and CINAHL was conducted

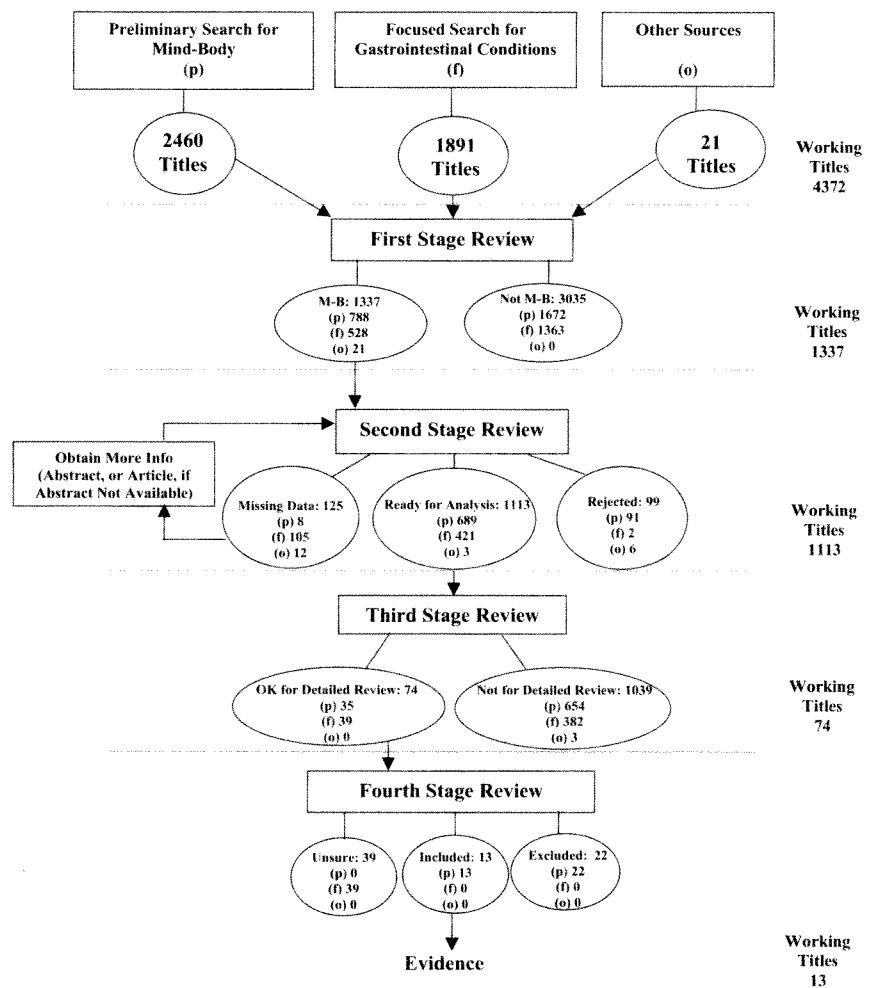


Fig. 1. Literature Search and Review Strategy.

for the CAM therapies. For manipulation, a chiropractic database, CHIROLARS, was also accessed. Languages other than English were included. Two independent reviewers reviewed all titles, abstracts, or articles. The studies were scored for quality. The systematic reviews were performed according to the principles of the Cochrane Collaboration and the EBP Center Program. There was no language restriction in the searches. An example of a search strategy is shown in figure 1. There are some differences between the Cochrane Collaboration Reviews and the ones conducted in this Center. Most of the differences ultimately have to do with the resources available. In the EBP Centers funded in the U.S., the staff and the project is fully funded. This enables the project to conduct a more rigorous and more extensive search. This shows up in the number of databases searched, the number of search terms used, in accessing all languages and in a much more vigorous attempt to access the grey literature. This can be seen most vividly in the review of Ayurvedic medicine and diabetes which is outlined in the following section.

The Ayurvedic Study

For the review of Ayurvedic medicine, we sent an investigator who had an Indian medical degree and spoke local languages to India in order to retrieve literature. He administered interviews to a sample of key informants that included librarians from biomedical universities, librarians from Ayurvedic medical schools, Ayurvedic researchers and clinicians, faculty at Ayurvedic research institutes and pharmaceutical company researchers using a snowball sampling technique. Notes and recordings were made during all of these interviews. The notes and recordings were transcribed by our investigator, and based on an analysis of these transcripts, institutions that potentially held research databases were identified.

The investigator then visited two of these research institutions, CCRAS (Central Council for Research on Ayurveda and Siddha) and Gujarat Ayurveda University, which were the two most prominently mentioned institutions in the interviews. An important book, 'Researches in Ayurveda: A Classified Direc-

tory of All India P.G. and Ph.D. Theses of Ayurveda' by Baghel (1997), was also identified. This work lists all post-graduate theses in Ayurveda from 1980 to 1997. A convenience sample of selected post-graduate medical theses from Gujarat Ayurveda University in Jamnagar was screened for quality by our reviewer. Lastly, our reviewer evaluated a subset of abstracts published by the CCRAS in Hindi.

We not only reviewed the literature in the language in which they were written, we also purchased their research journals and examined theses. In the final systematic review, 35 studies came from the Western literature and 27 came from the Indian literature.

Systematic Reviews of CAM: What Do the Results Show About the Method?

While the results are too extensive to be reported fully here, the following brief discussion indicates the amount of literature that can be accessed even within CAM and the potential for producing systematic data on the effectiveness of particular CAMs. Its focus is on the methods and the issues associated with this type of research. The publications of the evidence reports discussed here are available from AHRQ (www.ahrq.gov/clinic/evrptpdfs.htm) and from RAND (<http://intranet.rand.org/cgi-bin/Abstracts/abdb.pl>) for the reports on manipulation.

Manipulation for Low Back Pain

We identified 1,600 articles that focused on manipulation for low back pain [37–40]. Of these, we were able to conduct a meta-analysis on 29 RCTs, 9 trials with other therapy [37, 41–43].

For cervical manipulation, we identified 1,100 articles and conducted a systematic review on 67 articles on efficacy and 14 RCTs. No meta-analysis was possible because of the heterogeneity in the studies [39–40, 44].

Mind-Body Therapy for GI Problems

We identified 4,397 titles from which 1,362 articles were selected for further review. There were 52 studies where there was a control or comparison group: biofeedback, hypnosis, relaxation, behavioral therapy, multimodal therapy, cognitive therapy, imagery, and placebo. Because of the clinical heterogeneity it was not possible to conduct a meta-analysis. Most of the studies in the field of mind-body therapy have substantial methodological problems [45, 46].

Ayurvedic Medicine for Diabetes

A total of 1,311 potentially relevant titles were identified from all sources. 54 articles reported on the results of 62 studies in diabetes. As previously noted, 35 studies came from the Western literature and 27 came from the Indian literature. The designs of the 62 studies were varied. There were 7 RCTs and 10

controlled clinical trials (CCTs). There were 38 case series – the most frequently used clinical design – and 7 cohort studies. The report demonstrates the existence of a body of evidence evaluating Ayurvedic herbal interventions for diabetes. Further, significant amounts of English language literature relevant to this topic were available in India. Overall, the literature consisted of a few RCTs and CCTs with relatively low quality scores as well as a larger number of case series [47].

S-Adenosyl-L-Methionine

An initial broad search of the literature found 1,553 titles, of which 258 were judged to be RCTs, CCTs or systematic reviews (including meta-analyses). 89 articles met the criteria for inclusion (they were focused on SAME treatment for depression, osteoarthritis, or liver disease and presented data from a clinical trial in humans). Of these, 38 focused on depression, 38 on liver disease and 13 on osteoarthritis. Interventions using SAME were heterogeneous both for route of administration and dosage and the study populations also displayed considerable variability. The majority of the studies enrolled small numbers of patients and the quality of the studies varied widely. However, a sufficient range of studies with homogeneous enough outcomes and disease states existed to perform meta-analyses of data on depression, osteoarthritis and cholestasis of pregnancy [48].

Coenzyme Q10, Vitamin E and Vitamin C for Treating or Preventing Cardiovascular Disease

Our literature search process identified 8,173 titles from which we found 144 unique trials (i.e. those reporting data not duplicated in another publication) for cardiovascular disease. Of the reports, one-third were judged to be of high quality [49]. Studies reporting on the outcomes of death, myocardial infarction, and/or blood lipid levels were selected for further analysis. For the interventions of vitamin E alone and in combination with other antioxidants, sufficient numbers of studies existed to perform pooled analyses.

We identified 1 meta-analysis of the effect of coenzyme Q10 and 4 studies were identified that assessed the effect of vitamin C (mostly in combination with other antioxidants) on clinical outcomes in patients with or at high risk for cardiovascular disease.

Coenzyme Q10, Vitamin E and Vitamin C for Treating or Preventing Cancer

From the 8,173 titles, we identified 432 articles for screening of which 35 articles met the criteria for inclusion in the analysis for cancer [50]. The identified studies varied greatly in quality. Sufficient numbers of homogeneous studies did not exist to permit a meta-analysis of the efficacy of vitamin C or E or coenzyme Q10 for the outcomes of death or new tumors. A meta-analysis was possible for polyps as an outcome. Additional qualitative reviews were done for studies that could not be pooled and for studies with intermediate outcomes [50].

Discussion

We have been able to identify some common problems across the CAM studies.

1. the small number of good RCTs;
2. the large number of observational studies;
3. heterogeneity in study designs;
4. heterogeneity in the clinical intervention in the trials;
5. few trials receiving good quality scores. This was due to (a) lack of randomization, (b) small sample sizes, (c) being underpowered, (d) inappropriate statistical methods;
6. the large number of studies in languages other than English;
7. accessing studies in non-traditional databases and in countries lacking the library infrastructures of developed countries;
8. lack of studies testing a system of care as opposed to individual therapies within that system;
9. the lack of studies of effectiveness.

It is the last two issues that pose challenges for the advancement of EBCAM, but they are methodological challenges and not insurmountable ones. Although beyond the focus of this paper, they are being addressed in studies looking at observation studies and reviews [51–54], whole systems research [55–57], on new forms of evidence such as non-hierarchical forms of evidence [58–59], and on studies looking at effectiveness as opposed to efficacy studies [2, 60–62].

We are now entering an important period in EBP. On the one side are those who see it as a process of privileging certain types of evidence over other forms [63] and look for reconciliation. On the other hand, there are those critics who see in it a form of intellectual fascism [64] and who would reject it entirely. The challenge for CAM is to recognize the limitations of

EBP but not to throw the ‘baby out with the bathwater’. There is much in EBP that clearly should be emulated by the CAM community but only where it is appropriate. The challenge will be to establish where the boundaries are to be drawn.

Conclusion

In conclusion, the results of the Center indicate that a lot more ‘evidence’ exists for CAM than one might expect. In fact in many cases, such as low back pain and manipulation, the number of RCTs now exceeds that found for many medical interventions. Where that evidence does exist, a good case can be made that they should be subjected to systematic reviews in the same way as mainstream medicine. This is both politically smart for those involved in CAM but also academically smart in that it assembles the best kind of evidence. As the searches demonstrated there are quite large bodies of literature that can be accessed and that are available. This does require considerable effort and resources.

What role do systematic reviews of CAM play? This can be seen in the review of manipulation of low back pain. Prior to the RAND study, the general stance among many medical commentators was that manipulation had no role, had no efficacy. After the study, the question became for what conditions, for what type of patients and in whose hands does it have the best outcomes? This does not mean the debate about manipulation has been resolved but it does mean the debate has moved in its focus. In that sense, the reviews function to clear ‘the undergrowth’ so the real plants can be seen. It allows the debate and the research to move to a new level of questions and more clinically significant questions.

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