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Can CAM treatments be evidence-based?

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Abstract

In this article, we first take a critical look at the definitions of evidence-based medicine (EBM) and complementary and alternative medicine (CAM). We then explore the question of whether there can be evidence-based forms of CAM. With the help of three examples, we show that EBM and CAM are not opposites, but rather concepts pointing at different dimensions. Each of the three examples is an evidence-based treatment according to three to five randomised, double-blind placebo controlled trials with consistent findings and narrow pooled confidence intervals. The most reasonable interpretation for the existence of evidence-based CAM treatments seems to be that the opposite of CAM is 'mainstream medicine', and the demarcation line between CAM and mainstream medicine is not simply defined by the question of whether a treatment works or not. Some effective treatments may belong to the CAM domain for historical reasons and because of preconceptions within mainstream medicine. Therefore, some treatments that currently lie outside mainstream medicine can be evidence-based.

Keywords

Alternative medicine • ascorbic acid • common cold • complementary therapies • evidence-based medicine

In 2004, the journal *Evidence-Based Complementary and Alternative Medicine* (*eCAM*) was launched. According to the *eCAM* website, the journal 'seeks to understand the sources and to encourage rigorous research in this new, yet ancient world of complementary and alternative medicine.'[1] In 2013, this open-access journal had published over 1000 papers.

This new combination of 'evidence-based medicine' (EBM) and 'complementary and alternative medicine' (CAM) is interesting, but we find it strange that the journal does not provide any definition or explanation of the two terms. Both terms have many meanings, and their combination can also be understood in numerous ways. The aim of this paper is to look at the definitions of EBM and CAM, and to explore the question of whether there can be evidence-based forms of CAM.

What is EBM?

The term EBM appeared initially in an information document aimed at prospective or new students at the McMaster University in Canada in the autumn of 1990.[2] McMaster was the home of a group of physicians who demanded that clinical decisions be based on 'best evidence'.

The concept of EBM was introduced to the wider medical community in the *Journal of the American Medical Association* (*JAMA*) in 1992.[3] Evidence-based medicine was promoted as 'a new approach to teaching the practice of medicine' and 'a new paradigm for medical practice'. No specific definition was given in the article, but the authors did indicate that EBM 'de-emphasizes intuition, unsystematic clinical experience, and pathophysiologic rationale as sufficient grounds for clinical decision making and stresses the examination of evidence from clinical research'. In particular, the 1992 paper instructed clinicians to search for studies with the question 'Was the assignment of patients to treatments randomized?' The article was a bold programme statement that divided the medical world into the old-fashioned pre-EBM and the revolutionary new EBM types of medicine.

A rather general definition of EBM was formulated 4 years later:

'Evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.'[4]

This has remained the most widely cited definition of EBM. Nevertheless, it is not a surprise that the medical world did not unanimously welcome this new programme. In 1998, Tonelli, a critic of EBM, noted that there is not a physician alive who would not claim to practise EBM when it is defined as the 'conscientious, explicit and judicious use of current best evidence in making decisions'.[5] In the same year, Charlton and Miles published a paper titled 'The Rise and Fall of EBM', in which they sharply criticised the EBM approach.[6] The above definition of EBM is so vague that it does not provide any demarcation line between EBM and non-EBM.

Since then, other definitions of EBM have been proposed such as:

'EBM is currently understood to incorporate clinical epidemiological data, meaningful deliberations of professionals' pathophysiological knowledge and clinical experience, together with patient preferences.'[7]

'the evidence to which EBM refers to ought to comprise six dimensions: scientific evidence, theoretic evidence, practical evidence, expert evidence, judicial evidence and ethics-based evidence.'[8]

These definitions highlight the various interpretations of EBM. They also raise the question of whether there is any actual difference between EBM and pre-EBM, since all six dimensions were important issues in mainstream medicine before 1992. In 2005, Timmermans and Mauck sarcastically wrote:

'The term [EBM] is loosely used and can refer to anything from conducting a statistical meta-analysis of accumulated research, to promoting randomized clinical trials, to supporting uniform reporting styles for research, to a personal orientation toward critical self-evaluation.'[9]

Despite the disagreements and confusions about the basic definitions of EBM, one aspect of the EBM programme has been particularly essential since the introduction of the term in 1992, namely, the view of valid evidence: 'comparative clinical studies, preferably from randomized trials [RCTs], are deemed to provide better evidence than mechanistic reasoning and clinical experience.'[2,3]

What is CAM?

The acronym CAM combines two terms: 'complementary medicine' and 'alternative medicine', neither of which is ancient. According to PubMed, 'alternative medicine' first appeared in medical journals in 1975 and 'complementary medicine' in 1985.[10] The former term dates back to the alternative lifestyle movement that originated in the USA in the late 1960s.[10,11] The latter term was adopted in Britain with the political objective of raising the question of whether medicine could include some of the alternative healing practices in its tool kit.[10] A further related term, 'integrative medicine', was introduced in the 1990s in order to suggest a deeper marriage between alternative treatments and medicine.[10]

The meanings of 'alternative' in 'alternative medicine' or 'complementary' in 'complementary medicine' have not been properly explained, but it is common that their supporters present 'official' medicine as a rigid and closed system that is full of prejudices. 'Alternative' and 'complementary' are often used as buzzwords, important-sounding phrases 'of little meaning used chiefly to impress laymen'.[12] Some proponents of CAM often use other buzzwords such as 'natural' or 'holistic', meanings of which are also vague.[11,13]

Wolpe has suggested that CAM is best understood as a 'residual category', which means that it is defined by its exclusion from 'official' or 'medical school' medicine, which we refer to as 'mainstream medicine' in this paper.[14]

The Committee on the Use of Complementary and Alternative Medicine of the American Public Board on Health Promotion and Disease Prevention define CAM as:

'a broad domain of resources that encompasses health systems, modalities, and practices and their accompanying theories and beliefs, other than those intrinsic to the dominant health system of a particular society or culture in a given historical period. CAM includes such resources perceived by their users as associated with positive health outcomes. Boundaries within CAM and between the CAM domain and the domain of the dominant system are not always sharp or fixed.'[15]

Like the definitions of EBM, the preceding definition is too vague to provide even a rough demarcation line between CAM and the 'dominant system'. It is, however, an important description in pointing out the diversity of the phenomena behind the concept. This complexity also explains why the boundaries between the CAM domain and mainstream medicine are not sharp or constant.

The meanings of CAM and 'alternative medicine' largely overlap, and, for the purposes of this paper, we use the short and pragmatic definition of the latter, which was used in 1998 in a study investigating

national trends in alternative medicine use in the USA:

'Alternative medical therapies, functionally defined as interventions neither taught widely in medical schools nor generally available in US hospitals . . .'[16]

Although such a sociological definition has its own problems, we consider it to be the most useful definition for the purpose of this paper.

Are there EBM treatments in the CAM domain?

The terms EBM and CAM are both rather vague, escaping rigorous definition. Here we take a pragmatic approach and consider CAM to mean therapies that lie outside mainstream medicine. We also consider the most fundamental principle of EBM to be the requirement that treatments be based on the findings of RCTs. Thus, various treatments can be arranged simultaneously into a 2×2 table on the basis of both concepts, as shown in Table 1.

Cell 1 in Table 1 covers treatments in mainstream medicine that are based on numerous large RCTs (e.g. treatments of hypertension and myocardial infarction).

Cell 2 covers mainstream medicine treatments that are not based on RCTs. It not only includes potentially ineffective treatments that are used for historical reasons, but also treatments that cannot be examined with RCTs because of practical or ethical reasons (e.g. antibiotics for severe bacterial infections, volume replacement therapy in severe bleeding). Such treatments are justified on the basis of 'mechanistic reasoning and clinical experience', which are discouraged by proponents of EBM.[2,3] Thus, cell 2 is a mixed collection of valid treatments (though not based on RCTs) and potentially ineffective treatments.

For this paper, the most interesting part of Table 1 is cell 3: are there treatments based on RCTs that lie outside mainstream medicine? If we argue that a treatment falls into cell 3, we must first show that the treatment belongs to the CAM domain, and, second, there must be consistently positive findings from RCTs that justify the conclusion that the treatment is effective.

Table 1 Treatments according to the EBM and CAM concepts

	Mainstream medicine	CAM
Evidence-based medicine (treatments based on RCTs)	Cell 1	Cell 3
Not evidence-based medicine (treatments not based on RCTs)	Cell 2	Cell 4

Vitamins and minerals are commonly classified as a form of CAM. For example, the National Center for Complementary and Alternative Medicine (NCCAM), which is part of the NIH in the USA, states on its website that 'Natural [CAM] Products' include 'vitamins and minerals . . . They are widely marketed, readily available to consumers, and often sold as dietary supplements.'[17] Specifically, according to the NCCAM, the use of vitamin C and zinc for the common cold falls into the CAM domain,[18] as does vitamin C for asthma.[19] The Cochrane Library also classifies these three interventions as CAM treatments.[20,21] We suggest that there is strong evidence for the efficacy of these three treatments. In our view, they are examples of treatments that fall into cell 3 in Table 1.

In three RCTs, high-dose zinc acetate lozenges shortened the duration of colds by 42% (95% CI: 35% to 48%).[22] In five RCTs, vitamin C administration reduced the incidence of cold symptoms in people under short-term physical stress by 48% (95% CI: 35% to 64%).[23] Finally, in three RCTs, vitamin C administration was beneficial for patients with exercise-induced asthma since it reduced the post-exercise decline in forced expiratory flow in 1s (FEV_1) by 48% (95% CI: 33% to 64%).[24] Thus, according to the NCCAM and The Cochrane Library, these treatments fall into the CAM domain, and, on the basis of consistent positive findings from RCTs, they are evidence-based treatments.

Why are the three preceding examples part of CAM and not part of current mainstream medicine?

In the preceding discussion, we showed that EBM and CAM are not opposites, but rather they are concepts pointing at different dimensions (Table 1). In our view, the opposite of CAM is 'mainstream medicine', which is not the same as EBM. For example, 'mechanistic reasoning' (i.e. theoretical argumentation) has been an essential part of mainstream medicine for two millennia, and, in many time periods, theory has been much more important than empiricism.[25–27] However, mechanistic reasoning is explicitly de-emphasised by EBM, which strongly favours RCTs.[2,3]

Evidence-based medicine originated from the concern that numerous ineffective treatments had been adopted by mainstream medicine, and the RCT was viewed as the most reliable method with which to identify treatments that actually work. However, there is an opposite problem 'when an efficacious treatment for a certain disease is ignored or rejected because it does not make sense in the light of accepted theories of disease mechanism and drug action'.[26] Goodwin and Goodwin (1984)[26] named this phenomenon 'the tomato effect'. With this name,

they were referring to the historical background of the USA, where tomatoes were considered poisonous for a few centuries after they had been widely adopted in European kitchens. The idea of tomatoes being poisonous was based on theoretical argumentation: the tomato belongs to the *Solanaceae* family, which includes several deadly poisonous plants; therefore tomatoes must also be poisonous.[26]

Goodwin and Goodwin[25,26] gave several examples of medical 'tomatoes': treatments that were rejected because they did not fit prevailing theories. Furthermore, in some cases, the effective treatment had been used for a long time, but changes in the theories of pathogenesis led to the rejection of the treatments because they no longer made any sense, even though the clinical effects did not disappear with the changes in theories.

With the recent explosion in the molecular level understanding of the origin of diseases, the importance of theoretical explanations has not been decreasing in mainstream medicine. However, if the emphasis on theory is too strong, the evaluation of treatments focuses on mechanistic reasoning, and not on the empirical question of whether a treatment works or not.[25–27]

In mainstream medicine the dominant theory of vitamins is that their purpose in the body is to prevent deficiency diseases, and therefore, other uses belong to the CAM domain.[17,27,28] Nevertheless, there are biological rationalisations to explain some effects of vitamins unrelated to treating deficiencies. For example, exercise causes oxidative stress, and vitamin C, as an antioxidant, could protect against such stress. Consequently, the effects of vitamin C may be particularly pronounced during exercise, which is the factor common in two of the aforementioned effects.[23,24] However, such an explanation is rather vague when compared with the explanations of the effects of modern drugs that bind to well-defined specific receptors.

In addition to the inconsistencies with theories, Goodwin and Goodwin mentioned another reason for the 'tomatoes' in medicine: 'if a treatment bypasses the medical establishment and is sold directly to the public . . . the temptation in the medical community is to accept uncritically the first bad news that comes along'.[26,27] This seems to be a problem also with the three examples given in the preceding discussion.

Two influential reviews on vitamin C and the common cold in the 1970s concluded that vitamin C is useless for colds, and the reviews were extensively cited. However, the reviews were shown to be flawed over a decade ago.[28–30] Apparently, the conclusions of the reviews fitted so well with the theory in mainstream medicine that the validity of the reviews was not considered when they were published. Cochrane reviews are usually restricted to RCTs, but that does not imply that they are always trustworthy. Those on zinc and the common cold, and vitamin C and asthma, were shown to have severe errors in the extraction of data and in the data analysis, and these errors invalidated the conclusions of the reviews.[31–33]

Little commonality in diversity of CAM treatments, except for being outside mainstream medicine

There is no unifying theory behind all of the diverse CAM treatments. We agree with Wolpe[14] (see the preceding discussion), who views CAM as a 'residual category'; that is, a category of treatments outside mainstream medicine. In our view, many CAM treatments are not credible from a scientific point of view, and there are good reasons for them to be outside mainstream medicine. Nevertheless, as shown in the preceding discussion, the fact that a specific treatment falls into the CAM domain does not prove that the treatment is ineffective.

Some CAM treatments, such as homeopathy, are fundamentally incompatible with science. We do not believe that such treatments will ever become part of mainstream medicine, even if some RCT findings have been positive. Publication bias and methodological flaws are far more plausible explanations for the positive RCT results related to homeopathy than are errors in basic theories of chemistry. When there is a very strong theory, empiricism is secondary. This statement not only applies to the rejection of homeopathy but also, for example, to the use of antibiotics for severe infections, irrespective of whether RCTs have been carried out or not.

Some treatments, such as the three aforementioned examples, may belong to the CAM domain for historical reasons and because of preconceptions within mainstream medicine. The Cochrane Collaboration, for instance, defines CAM as a category of 'therapies that are self-care', which implies that these therapies are not delivered by credentialed medical personnel.[21] We assume that, sooner or later, effective CAM treatments will be included in mainstream medicine. The borderline between mainstream medicine and CAM is not constant.

As noted in the beginning of this paper, the journal *eCAM* has announced that it 'seeks to understand the sources and to encourage rigorous research in this new, yet ancient world of complementary and alternative medicine'.[1] To explore the meaning of the term 'evidence-based' in the journal title, we reviewed 100 consecutive papers that were published in *eCAM* in Autumn 2013. We found only 10% of the published papers reported the results of RCTs, and about 50% reported the results of animal or *in vitro* experiments. In this respect, the term 'evidence-based' seems to be more of a marketing term to

increase the credibility of the journal than a signal of adherence to EBM reasoning.

Conclusions

The purpose of this paper is not to provide general support to CAM treatments. Instead, the purpose is to point out that the demarcation line between CAM and mainstream medicine is not simply defined by the question of whether a treatment works or not. The demarcation line is also defined by historical and political grounds and by the theories of disease aetiologies and treatment mechanisms. Mainstream medicine does not equal EBM, which emphasises RCTs as the source of valid information on treatment efficacy. Consequently, some treatments that currently lie outside mainstream medicine can therefore be evidence-based.

Conflict of interest None declared.

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