



Assessing the Effectiveness of Complementary & Alternative Medicine

**The Convergence
of Complementary,
Alternative &
Conventional
Health Care:**

**Educational Resources
for Health
Professionals**

This publication is one in a series of educational resource materials on complementary and alternative health care issues published by the Program on Integrative Medicine, University of North Carolina at Chapel Hill, entitled:

The Convergence of Complementary, Alternative & Conventional Health Care: Educational Resources for Health Professionals

Titles in the series include:

Understanding the Convergence of Complementary, Alternative & Conventional Care in the United States

Concepts of Healing & Models of Care

Evidence-Based Medicine & Complementary & Alternative Therapies

Assessing the Effectiveness of Complementary & Alternative Medicine

Safety Issues in Complementary & Alternative Medicine

Evaluating Information Sources for Complementary & Alternative Health Care

Information Sources for Complementary & Alternative Therapies

Integrating Complementary & Alternative Therapies With Conventional Care

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The Program on Integrative Medicine, Department of Physical Medicine & Rehabilitation
of the School of Medicine of the University of North Carolina at Chapel Hill

With support from the National Center for Complementary and Alternative Medicine (NCCAM),
National Institutes of Health, U.S. Department of Health & Human Services Grant No. 5-R25-AT00540-01

This publication was funded by the National Center for Complementary and Alternative Medicine (NCCAM)
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Curtis, PC. *Assessing the Effectiveness of Complementary & Alternative Medicine*. In S. Gaylord, S. Norton, P. Curtis (Eds.), *The Convergence of Complementary, Alternative & Conventional Health Care: Educational Resources for Health Professionals*. University of North Carolina at Chapel Hill, Program on Integrative Medicine, 2004.

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Assessing the Effectiveness of Complementary & Alternative Medicine

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THE CONVERGENCE OF COMPLEMENTARY, ALTERNATIVE & CONVENTIONAL HEALTH CARE

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Assessing the Effectiveness of Complementary & Alternative Medicine is one publication in a series entitled *The Convergence of Complementary, Alternative & Conventional Health Care*, developed as an educational resource for health professionals by the Program on Integrative Medicine, University of North Carolina at Chapel Hill, with support from the National Center for Complementary and Alternative Medicine (NCCAM), National Institutes of Health.

This series responds to the many questions raised as conventional health care practitioners encounter widespread and increasing use of complementary and alternative therapies. Each publication in the series highlights one or more of the key issues facing health professionals today—including assessing information, safety, effectiveness, and the integration of conventional, complementary, and alternative health care.

Assessing the Effectiveness of Complementary & Alternative Medicine examines the issues raised when conventional health care practitioners seek to answer the deceptively simple question: “Do complementary and alternative therapies work?” Responding to that question requires an understanding of different healing paradigms, measurement techniques, and sources of information.

Assessing the Effectiveness of Complementary & Alternative Medicine

foreword

The widespread use of complementary and alternative medicine by over 40 percent of the U.S. population (Eisenberg, et al., 1998) presents the conventional health care practitioner with a considerable challenge: How to assess the effectiveness of a wide variety of therapies and treatments that are largely unfamiliar. The difficulty arises because the simple question—Does it work?—often does not have a simple answer.

To fully answer that question, it is first necessary to appreciate the different healing approaches of conventional medicine and many complementary and alternative therapies, and to understand how these differences affect treatment approaches and measurement of outcomes. Additionally, one must understand how conventional research methodologies and evidence reporting limit or conflict with the ability to accurately assess complementary and alternative therapies' effectiveness. Finally, one must know where to find reliable information about the effectiveness of such therapies.

This publication explores the issues raised when techniques for measuring efficacy in conventional medicine are applied to the measurement of effectiveness in the clinical setting of a complementary/alternative medical practice. In particular, readers are invited to:

- Distinguish between “effectiveness” and “effi-

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cacy,” and to understand how these terms apply to conventional, complementary, and alternative medicine;

- Understand the problems that exist in measuring the effectiveness of complementary and alternative therapies, and the limitations of conventional measurement tools;
- Understand where to look for and how to evaluate evidence for CAM effectiveness.

Finally, a note about the terminology used in this publication. In recent years, the term “CAM” has come into common usage to describe, in the words of the National Center for Complementary and Alternative Medicine, “a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine.” Despite its convenient brevity, the acronym CAM has some unfortunate implications. It suggests, for example, a homogeneity among the practices included under the umbrella term—something that is not at all true. It also implies a clear and complete distinction between conventional and CAM systems of care. That also is inaccurate.

The term CAM is therefore used sparingly here. When used, it is shorthand for that “group of diverse medical and health care systems. . .” where the emphasis is on the word “diverse.”

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Assessing the Effectiveness Of Complementary & Alternative Medicine

Effectiveness of care—the positive outcome of treatment—is the result of a combination of factors, including: the *efficacy* of an intervention, the *approach to the patient*, the *response of the patient*, and the *setting* in which the care is given. Effectiveness also may reflect certain aspects of the placebo or “expectancy” effect (Flay, 1986). By contrast, efficacy offers a more limited assessment (*see box, right*)—describing whether a technology, procedure, or treatment is helpful or harmful under optimum conditions. Tests of efficacy are necessary steps in the development of new technologies or pharmaceuticals, but do not necessarily demonstrate effectiveness in the real world.

Because of costs, safety issues, and the dominance of pharmaceutical interventions, demonstrating efficacy has relied heavily on a single tool for the measurement of a biological therapeutic effect—the randomized controlled clinical trial (RCT). This research technique:

- tests a well-specified and standardized treatment;
- is delivered uniformly in a standard setting to specified subjects;
- is designed for those who ideally have only the target condition being treated; and
- includes agreements with subjects to comply and adhere to the protocol, usually for a reward (Flay, 1986).

Because of this design, efficacy studies specifically *exclude* multiple, “real world” clinical factors, such

EFFICACY VS EFFECTIVENESS

It is important to distinguish between the terms “efficacy” and “effectiveness” when evaluating outcomes of treatment. Efficacy means that the treatment or substance (surgery, medication, herbal remedy) clearly produces a change in biological or psychosocial function under optimum conditions—after excluding other possible causes for the change. That biological change may be beneficial or deleterious. Effectiveness, on the other hand, refers to the treatment’s success in day-to-day clinical practice.

Efficacy is most usefully demonstrated under rigorous experimental conditions and has been described as “fastidious efficacy” (Kaptchuk, 2002a). Such studies seek to optimize the **internal validity** of a research study—the certainty with which conclusions can be drawn from the study because of its rigor and design. But, the more complex, controlled, and rigorous the study, the less one can generalize the results to day-to-day practice (**external validity**).

Effectiveness describes the **external validity** of a study—often called “performative efficacy” (Kaptchuk, 2002a). This means that the treatment works for patients in the routine practice setting (the real world), in which many other factors—such as the placebo effect and the style of the clinician—may also contribute to the patient’s outcomes. An effective treatment must not only be efficacious, but also must be available and acceptable to the patient in normal day-to-day life.

Thus, a drug shown to be efficacious in a research setting might not actually be effective in practice, for example, because patients cannot tolerate its side effects, or because it must be taken eight times a day and no patient is likely to adhere to this regimen. Another example of reduced effectiveness of an efficacious drug is when a health professional administers it suboptimally or inappropriately. Furthermore, the effectiveness seen in day-to-day practice might be due more to the placebo or caring effect than to the drug.

Outcomes of complementary and alternative medicine can be studied by using both efficacy and effectiveness research.

as the approach to the patient, treatment setting, adherence to medication protocols, and lifestyle issues.

The model of single-intervention clinical trials may be more useful for studying pharmaceutical treatments than for assessing outcomes of most complementary and alternative therapies where treatment protocols usually are tailored to individuals rather than a standard group of subjects. For example, clinical trial results are reported as means, medians, or likelihood ratios for the large numbers of subjects studied (populations). These results offer generalized data that guide clinicians' decisions about specific therapies and diseases. However, they do not offer the detailed information (individual response and susceptibility to adverse effects) that might apply to the individual patient sitting opposite the clinician (Welch & Lurie, 2000). Indeed, the limits of the RCT approach to determining the clinical merits of complementary and alternative interventions are important, given the highly individualized and multi-faceted treatment protocols typically employed. Assessment of complementary and alternative therapy effectiveness may require a different approach to gathering and interpreting evidence.

Similar challenges have been found in other therapies that, while recognized as "conventional medicine," have complex interactive factors or cannot be measured by hard biological data. For example, the disciplines of psychotherapy, health behavior, and psychiatry faced the challenge of how to measure program and therapeutic outcomes, finally discarding or modifying efficacy studies in favor of effectiveness studies (Flay, 1986; Carroll & Rounsaville, 2003).

The simple question—*Does it work?*—is appropriate when asked about a pharmaceutical product in a conventional clinical setting, because its answer can be obtained from standardized clinical trials. It is also an appropriate question when asked about a specific, isolated complementary treatment such as the use of a single nutritional supplement—for example, alpha lipoic acid for painful peripheral neuropathy.

However, in the clinical world of many complementary and alternative practices, "it"—the treatment—is not typically a single drug or intervention, but a complex therapeutic modality that also may involve physical and emotional interaction with the therapist.

TABLE 1
DRUG EFFICACY RATES FOR
COMMON HEALTH CONDITIONS

| CONDITION | % PATIENTS REPORTING |
|----------------------|----------------------|
| Asthma | 60% |
| Cardiac arrhythmia | 62% |
| Depression (SSRI) | 62% |
| Diabetes | 57% |
| Migraine | 52% |
| Rheumatoid arthritis | 50% |
| Cancer | 25% |

(Roses, 2003)

rethinking assumptions about efficacy

Clinicians have long assumed that pharmaceutical research and the FDA approval process ensure that medications are demonstrably effective for patients. That assumption is now suspect. A report of a speech by Allen Roses, a pharmacogeneticist at Duke University and Vice President at Glaxo Wellcome, cited research (The *Independent* newspaper, UK, Monday, December 8, 2003) revealing that most pharmaceuticals are efficacious for only 30-50 percent of patients, because of individual genetic characteristics. An example of pharmaceutical response rates is seen in Table 1.

Despite enormous effort and investment, the reality of clinical medicine is that it falls well below our assumptions and expectations regarding efficacy. It may well be that attention to the individual rather than the group response to therapy may produce more information about how to target treatment and follow-up, and improve outcomes.

assessing effectiveness in clinical practice

Not only is treatment effectiveness influenced by multiple factors, but its assessment may depend on the clinician's healing paradigm, such as biomedical, homeopathic, or naturopathic. Long proposes three effects that play a role in the assessment of a CAM treatment's effectiveness; the dominance of each of these may vary, depending on the type of complementary approach (Long, 2002). They are:

- The effect of the philosophy of healing (self-healing, balance, systems approach, and holism);
- The effect of the clinician-patient relationship; and
- The set of therapeutic methods used to enhance the healing process.

Homeopathy offers an example of the effect of healing philosophy on the evaluation of outcomes. Despite evidence from randomized studies and meta-analyses of some homeopathic treatments—which show a significant beneficial effect—many conventional clinicians strongly reject scientific conclusions of effectiveness of homeopathy therapy because the “non-material” nature of homeopathic remedies is outside the conventional scientific paradigm and is dismissed as placebo (Linde, et al., 1997; Feder & Katz, 2002).

explaining effectiveness: reflecting on different approaches to healing

A question the conventional clinician is likely to ask about a complementary and alternative therapy—such as mindfulness, homeopathy, or acupuncture—is whether CAM practitioners are simply harnessing the placebo effect to meet the deep ‘human’ needs of patients, or are actually giving effective care (Kaptchuk, 2002a). The question is asked with the expectation that these therapies should be assessed by the same methods used for a conventional medical treatment or drug. The response of the CAM practitioner to that question is likely to be, “Yes, we believe our approach/modality/remedy really works, beyond the placebo effect.” Often, that conviction emanates from a wholly different view on evidence of effectiveness.

Conventional medicine generally takes a material and reductionist approach to treatment. An assessment of constellations of symptoms or test results leads to the application of a diagnostic label, followed by a specific treatment program targeted at the diagnosis, not the patient. Typically, the primary focus of the treatment program is management of clinical markers (such as platelet counts) or symptoms. Ideally, treatment decisions are based on evidence from research studies.

In contrast, many therapies under the rubric of “CAM” tend to a more holistic, individualized approach to symptoms within a broad context of the patient's life. The context may be more important than the symptoms, or at least may provide insight into the interpretation of the symptom pattern. For example, homeopathic remedies, particularly for chronic conditions, are commonly selected based on the totality of symptoms and personal constitutional characteristics of the patient. This contrasts with the conventional medical approach, which is to assign a diagnosis to a group of symptoms and then apply a specific treatment protocol with little or no individualization relative to constitutional variation. In homeopathy, the diagnosis is believed to fully describe the patient and the patient's medical needs also define the course of treatment.

Rather than just managing a disease process, holistic treatment also focuses on rebalancing and supporting the body's systems as an aggregate whole, rather than correcting specific symp-

toms or confirming diagnoses. Symptoms can be a signal for the CAM clinician of some form of emotional or biological dysfunction or dysregulation, rather than a well-defined pattern that always represents the same disease entity. Moreover, a disease state may be understood to have a non-material (e.g., energy, spiritual) source and solution.

different perspective on effectiveness

These differences in perspective have a profound impact on the assessment of effectiveness. In conventional medical practice, for example, the focus is usually on a standard of care applicable to a large number of people and the desired outcome is a certain percentage of success with a single medication or other treatment. Elimination or reduction of symptoms is also considered an indicator of effective treatment, so effectiveness is also often defined in terms of short-term clinical outcomes defined by researchers, not necessarily the patient's goal. On the other hand, holistic practitioners, with their focus on individual treatment, are unlikely to measure effectiveness in terms of a percentage of success with large numbers of patients. They will tend, instead, to evaluate a treatment's outcomes for an individual patient. Further, since many CAM therapies are designed to stimulate self-healing, their effectiveness may be measured over a longer time period, and short-term outcomes are less relevant.

Defining "effectiveness" for a given therapy is further complicated by the nature of many complementary and alternative treatments, which involve multiple components whose benefits are derived, at least in part, from their interaction with each other. Similarly, many holistic care plans combine specific treatments (such as acupuncture) with complementary therapies such as diet and exercise. In Traditional Chinese Medicine, for example, remedies containing a number of herbal preparations will often be given in conjunction with acupuncture, meditation, exercises, and dietary guidance. While it may be difficult to determine the precise role each component plays in healing, it seems clear that the *combination* of elements contributes to the success of a CAM care plan (Vickers & Zollman, 1999; Spinella, 2002).

Compared to conventional medicine, it is also more challenging to measure outcomes of CAM treatments by the presence, absence, or change of symptoms. This is because different healing systems regard the relevance of symptoms differently. In homeopathy, for example, treatment may at first intensify symptoms (Leckridge, 1997). The transient worsening of symptoms is considered to be a sign of the remedy's impact and ideally will be followed by a healing response. In the process of healing, particularly from chronic conditions, there may be a temporary return of old symptoms. It is also considered a good sign when returning symptoms shift the focus of illness from more vital to less vital organ systems.

the power of beliefs in determining effectiveness

There are no research data to suggest that, overall, the role of placebo is different for complementary and alternative therapies than for conventional medicine. Patients' beliefs about treatments and medicines play an important role in any healing setting (Peters, 2001). However, CAM practitioners' more leisurely and patient-centered approach fits the model described by Benson (1997) for obtaining a non-specific placebo effect. The non-specific placebo effect is that produced by the clinical setting and health professionals' style, rather than the specific placebo or chemical effect of the intervention (such as manual therapy or acupuncture needling). It is likely, therefore, that practitioners of complementary and alternative therapies may achieve some of their success by maximizing the non-specific placebo response (Kaptchuk, 2002b). To the extent that

conventional practitioners also engage in a patient-centered model of care, their treatment will be influenced by such non-specific positive effects.

The relationship between the placebo or “expectancy” effect and many complementary and alternative modalities presents a challenge to those attempting to measure treatment effectiveness. For many CAM practitioners, it is a goal of the therapy to engage the patient (including the patient’s emotional and physical expectations) in the healing process. This can make it more difficult, if not impossible, to control for the placebo effect in study design.

Other beliefs also influence the success of a treatment or therapy. In the United States, cultural bias may include lower expectations for CAM treatments. This may be especially true when a patient comes to a CAM practitioner as a last resort after conventional medicine has failed to help (Kaptchuk, 2002b).

evaluating evidence for complementary & alternative medicine effectiveness

Clinicians are faced with five basic questions about the effectiveness of a given CAM therapy or healing system:

1. To what extent is it proven to be efficacious and effective?
2. Is its effectiveness also dependent on the placebo effect?
3. For which patients and conditions would this treatment be beneficial?
4. If it is effective, should it be incorporated into routine medical care?
5. If it is effective, is it cost-effective?

In general, current research on effectiveness of CAM is directed towards answering the first three questions. As with conventional medicine, incorporation into routine practice and cost-effectiveness take many years to be well demonstrated.

Studies of effectiveness usually consist of clinical trials comparing treatments (as well as comparing treatment with no treatment) in real-world health care settings (Lewith, Walach & Jonas, 2002). The amount of such research in the field of complementary and alternative medicine is substantial. In 1998, it was reported that over 690 scientific journals published CAM articles throughout the world (Ezzo, Berman, Vickers, & Linde, 1998). A substantial proportion of this research has been conducted and published in other countries (such as Germany and France), where complementary/alternative medicine has been incorporated for some time into the health care system and medical education. Similarly, countries such as India and China that still consider their traditional healing systems to be a key element in health care have long-established institutions of research for natural substances at the laboratory, pharmacological, and clinical levels. There are over 10,000 published basic science and clinical studies (of efficacy and effectiveness) involving many styles or traditions of acupuncture techniques, of which over 500 were randomized controlled trials. Additionally, meta-analysis (the pooling of data from many studies) is a useful tool that has, for example, strongly supported the benefit of acupuncture for the treatment of nausea and various pain syndromes (Kaptchuk, 2002a).

Despite the international volume of research on alternative and complementary therapies, conventional practitioners in the United States may have difficulty finding evidence of CAM outcomes. Although there are numerous published studies on some CAM therapies, such as acupuncture and chiropractic, there are many other complementary and alternative therapies, such as

TABLE 2
SUMMARY OF CAM EFFECTIVENESS FOR SELECTED MEDICAL CONDITIONS

| problem | therapies | evidence strength | evidence direction |
|------------------------------|--|-------------------|--------------------|
| Alzheimer's Disease | Ginkgo | low to moderate | uncertain |
| Anxiety | Kava, relaxation, aromatherapy | moderate | positive |
| Asthma | Hypnosis, homeopathy, yoga | low to moderate | positive |
| Eczema | Primrose oil, Chinese herbs | moderate | uncertain |
| Back Pain | Acupuncture, massage, manual therapy | moderate | positive |
| Chronic Fatigue | Exercise, herbals, homeopathy | low to moderate | positive |
| Constipation | Biofeedback, massage, herbals | low to high | positive |
| Depression | St. John's wort, relaxation, music | low to high | positive |
| Fibromyalgia | Exercise, homeopathy, biofeedback | low to moderate | positive |
| Hypercholesterolemia | Diet, garlic, guar gum, red yeast rice | high | positive |
| Insomnia | Kava, valerian, relaxation, melatonin | moderate | positive |
| Migraine | Acupuncture, biofeedback, feverfew | moderate | positive |
| Osteoarthritis | Acupuncture, devil's claw, glucosamine | moderate | positive |
| Palliative Care | Acupuncture, healing touch | low | positive |
| Prostatic Hyperplasia | Palmetto, African plum, nettle | moderate | positive |

(Adapted from Ernst, 2001)

craniosacral and magnet therapy, with only a few small studies (Green, Martin, Bassett, & Kazanjian, 1999; Alfano, et al., 2001) on which little research has been done.

Given that only a few of the 690 journals publishing complementary and alternative medicine articles are published in English and considered "mainstream" in the United States, relevant data may be out of reach for the practicing clinician (Ezzo, et al., 1998). Although the clinician interested in researching evidence for a particular therapy can access such databases as AMED, Med-line (PubMed), EMBASE, ASCOM, and the Cochrane Database of Systematic Reviews, search strategies for clinical evidence of complementary and alternative therapies' efficacy and effectiveness may still be limited in scope (Ezzo, et al., 1998; Sigouin & Jadad, 2002). For example, only 50 percent of the actual number of RCTs in conventional medicine find their way onto Medline, and the percentage is much lower for studies of non-conventional therapies (Ezzo, et al., 1998). Clinicians might best seek out integrative medicine conferences for accessing the most pertinent continuing medical education.

In the United States, the major initiative promoting research on the effectiveness on the outcomes of CAM has come from the National Center for Complementary and Alternative Medicine (www.nccam.nih.gov). NCCAM has steadily increased its capacity to fund scientifically based projects, including setting up a variety of CAM centers of excellence in academic institutions to study specific modalities, clinical problems, or integrative services in collaboration with complementary and alternative practitioners.

examples of assessing the effectiveness of CAM

There is evidence supporting the efficacy and effectiveness of a number of complementary and alternative therapies for different health conditions. Table 2, for example, summarizes research on the efficacy and effectiveness of selected therapies for common clinical problems for which some evidence has accumulated. (A positive direction of evidence indicates that the treatment provides benefit; a negative direction indicates no benefit for the clinical problem.) Nonetheless, there remains considerable variability in the amount and quality of effectiveness data available.

An example of an analysis of the weight of evidence in complementary and alternative medicine is the article published in the journal *Rheumatology*, “Herbal Medicines for the Treatment of Osteoarthritis: A Systematic Review” (Long, Soeken, & Ernst, 2001). In this article, the authors (from Exeter University, UK, and the University of Maryland School of Medicine, US) indicate that current conventional treatment of osteoarthritis with NSAIDs causes about 2,000 deaths a year. They also conclude that there is still a need for safe and effective drugs for patients who don’t respond well to conventional therapy. They searched the literature for RCTs of herbal remedies for osteoarthritis, and found 12 trials and 2 systematic reviews. (Some of these were unrepeated studies.) Eleven remedies were studied: articulin-F (an Ayurvedic herbal-mineral formulation); avocado/soybean unsaponifiables (ASU); capsaicin (derived from hot chili peppers, applied topically); devil’s claw (African plant, active agent: iridoid glycoside); eazmov (Ayurvedic herbal mixture); ginger; gitadyl (combination of feverfew, aspen, and milfoil); phytodolor (three herb combination); reumalex (white willow bark, guaiacum, black cohosh, sarsaparilla, and poplar bark); stinging nettle; and willow bark. After reviewing the weight of evidence they made the following recommendations:

- Moderately strong (3+ favorable trials) evidence for: phytodolor, capsaicin.
- Promising evidence (2 trials with favorable outcomes) for: ASU, devil’s claw.
- Weak evidence (1 trial with favorable outcome) for: reumalex, willow bark, stinging nettle, articulin-F.
- No evidence (no positive trials) for eazmov, gitadyl, ginger extract.

The authors indicate that there were some generally promising complementary and alternative options for clinical care, but compared to conventional treatments these were still substantially under-researched.

problems in measuring efficacy & effectiveness in CAM

Research into the outcomes of complementary and alternative therapies must account for a number of factors incompatible with conventional research methodologies. These include:

- the role of individualized treatment for the patient;
- the variability of products as well as the expected variability in clinical approach, as in Traditional Chinese Medicine (Zhang, Bausell, Lao, Handwerker, & Berman, 2003);
- the use of simultaneous, synergistic, multiple interventions (e.g., exercise, relaxation, herbs, diet);
- the therapeutic interaction between herbs and nutritional supplements; and
- the role of the skilled practitioner (who cannot be blinded) as an element of treatment.

All these factors complicate the process of designing efficacy studies because conventional research design consciously excludes them. In most complementary/alternative practices, individualized diagnosis and treatment and multiple, synergistic interventions are essential components of the treatment program and cannot be excluded. Thus, many CAM treatment modalities used are not easily standardized. Thus, rather than attempting to evaluate them with standardized research designs and techniques, different assessment methods are needed.

design challenges

From the perspective of conventional medicine and federal funding, only large, blinded, randomized clinical trials (RCTs) using strictly defined interventions are seen as the ideal solution to separate the real from the apparent clinical effects of a treatment. However, as previously discussed, research design challenges are presented by *both* conventional and complementary treatments that employ complex, individualized therapies in which the therapist is part of the treatment. Research designs of studies of these therapies often are labeled as “flawed” by the conventional research establishment. Many earlier RCTs were of poor methodological quality (De Smet, 2002; Taylor, Reilly, Llewellyn-Jones, McSharry, & Aitchison, 2000). Now, well-designed, large clinical trials and meta-analyses of some complementary/alternative therapies have recently begun to appear in major medical journals (for example: St. John’s Wort to treat depression; ginkgo for Alzheimer’s; saw palmetto for benign prostatic hyperplasia; homeopathy for rhinitis). Many of these are pharmacologically active therapies that can be isolated as a single intervention and prescribed in the form of a pill.

Although the RCT is regarded as the “best science” research method with strong internal validity, the results often do not represent the real world of clinical practice because of the highly controlled conditions and sometimes unrealistic settings of the studies (Eskinazi & Muehsam, 2000; Nahin & Straus, 2001). Many believe that other research methodologies are more applicable to CAM studies (Lewith, Jonas, & Walach, 2002). Alternative approaches, such as crossover, qualitative, and N-of-1 studies (intermittent crossover measures for a single patient over an extended period of time) may offer more relevant data for assessing therapeutic effectiveness.

varied clinical approaches

In CAM, as in some conventional therapeutics, diagnosis and treatment protocols are not always the same among clinicians in the same discipline. For example, not all chiropractors practice in like ways—they are a diverse profession trained in schools with different philosophies and techniques. Similarly, there are several styles of acupuncture using different techniques, and the location of specific recommended acupuncture points by students and experts can be highly variable (Aird, Cobbin, & Rogers, 2002; Kaptchuk, 2002a). Likewise, homeopaths can be “unicists” (one remedy at a time) or “pluralists” (several remedies at a time).

Despite these variabilities, reliability of clinical assessment can be achieved. In an observational study, for example, nine Traditional Chinese Medicine practitioners agreed on a specific TCM diagnosis in just over 80 percent of visits made by 23 women with menopausal symptoms (Zell, et al., 2000).

synergistic interventions

Complementary and alternative therapies are usually administered multiply, involving combined herbs or the serial or combined use of several remedies or modalities; they also often

involve a particular, holistically oriented way of caring for and advising the patient. The question then is, “Which specific activity provides the benefit or do the different modalities interact with each other in some way?”

The answer appears to be that the synergy of multiple remedies is a key part of the healing process. In the area of herbal remedies, for example, there is evidence that “buffering” (reducing toxicity) and synergy of whole plant products may have more useful treatment effects than processed biological extracts. Treatment with a single type of ginseng is less efficacious in producing vasodilation than a combination of types of ginseng; berberine’s effect (antibacterial) is enhanced six-fold by another 5MHC compound (Vickers & Zollman, 1999; Spinella, 2002). Similar enhancing combinations are found in conventional medicine, as with amoxicillin/clavulanic acid (McCormack & Keating, 2005) and combined anti-cancer protocols (Hayes, 2004; Nagourney, Link, Blitzer, Forsthoff, & Evans, 2000).

This synergy is found in foods as well, which are also often a part of conventional therapeutics. For example, whole grains, in combination, have an independent effect in preventing cardiac disease compared to the use of separate elements of the grains (Anderson, 2003; Slavin, 2003). In another instance, the LDL cholesterol-lowering effect increases from processed olive oil, to virgin olive oil (first cold pressing), to the whole olive (Faine, et al., 2004; Ramirez-Tortosa, et al., 1999).

product variability in CAM studies

Another complicating factor in studying outcomes of herbal medicine is the bioavailability of herbs and nutritional supplements used in clinical trials. For example, ratios of therapeutic fractions vary from one product to another (fish oil EPA:DHA ratios is one example). Comparisons of outcome studies may be unreliable because the herb differed in some qualitative way—perhaps it was harvested at a different time. The variability of product quality is substantial. For example, one survey found the following variations: ephedra 0-154 percent of label claim; ginseng 10-fold variation in ginsenosides; yohimbine, none of 26 products contained an effective dose (“Herbal Roulette,” 1995). Any valid study of efficacy or effectiveness of herbals must use a well standardized product with a clear indication of its processing, purity, and bioavailability.

control groups in CAM studies

It often is difficult to design a study using the conventional model of a blind “control” group that receives a sham or placebo remedy. How does one administer “fake” acupuncture, “non-massage,” or a fake magnet? The patient expectancy bias towards the alternative therapy also may be a problem in recruiting subjects (Kirsch, 1999). Those interested in participating may already be strongly biased toward the CAM modality under investigation and may not accept the possibility of a sham treatment. Many also will have tried conventional care with little improvement and may not want to participate in a trial comparing conventional therapy with an alternative if it means the chance of receiving conventional care again (Lewith, Walach, et al., 2002).

Finally, if the placebo effect is very substantial, it may dominate the effect of an active treatment. This phenomenon may occur in modalities where the clinician’s approach or relationship to the patient is a key element of treatment. Attempting to exclude this factor from the design of the research may negate what may be an essential part of providing care. It is not always the modality that makes this placebo effect important. Patients may respond better to treatments ad-

PRINCIPLES OF HEALING EMPHASIZED IN MANY COMPLEMENTARY AND ALTERNATIVE THERAPIES

While a disparate array of alternative therapies and healing systems fall under the umbrella term “CAM,” what they typically have in common are fundamental principles of health and healing. These principles are not unique to CAM (conventional medicine subscribes to some), nor do all CAM therapies embrace them equally. Taken together, however, they provide a framework for understanding CAM approaches to healing that contrast with the biomedical model of care. Many CAM therapeutic systems emphasize some or all of the following principles to a greater degree than conventional medicine. Effective integration of CAM and conventional care must rest on acknowledgment, appreciation, and application of these principles in a patient-centered context.

- **Promote the body’s self-healing abilities** (This is perhaps the most important principle, influencing all others.)
- **Emphasize effective communication between patient and healer**, which builds trust and promotes integration.
- **Emphasize self-care** and empowerment of the patient in the healing process.
- **Recognize mind, body, and spirit** as interactive and inseparable.
- **Address underlying causes of illness**—including emotional, environmental, and spiritual factors—rather than just its clinical manifestations.
- **Prevent ill health** by remaining in balance and harmony with the psychosocial and physical environment.
- **Enhance wellness** with optimal diet, exercise, and a reduced-stress lifestyle.
- **Individualize treatment** to the particular patient, rather than focusing on the disease condition.
- **Emphasize the use of natural non-pharmaceutical substances** or non-surgical techniques in the care of the patient.
- **Appreciate the electromagnetic and energetic nature of the human organism** and the importance of vitality in healing.
- **Appreciate the importance of intuitive awareness** and the individual’s unique experiences in determining pathways to healing.
- **Acknowledge the healing journey** and that the return to wholeness can be a gentle and gradual, developmental process.

(adapted from Gaylord & Coeytaux, 2002)

serum cholesterol) used in conventional medicine. Examples of measurement instruments that can assist in providing a more realistic assessment of the efficacy or effectiveness of complementary and alternative medicine are: global improvement scales (Streiner & Norman, 1995; Paterson & Britten, 2000), the Empathy Scale (Burns & Auerbach, 1996); and the Holistic Practice Questionnaire (Long, Mercer, & Hughes, 2000).

ministered by people with whom they feel safe or otherwise share a meaningful connection.

desired outcomes & “un-measurable” factors

Many complementary and alternative medical practitioners share similar beliefs about health and healing (*see box, left*). These principles form the foundation for the various therapies and techniques employed, and are fundamental to healing. They concern desired outcomes and the processes of health and healing rather than specific therapies or protocols. Despite their central importance to CAM treatments, there currently are almost no testable measures of these principles (Long, 2002).

Often in complementary and alternative medicine, desired outcomes involve coping, adaptation, functioning, and feeling at ease. These factors have meaning for patients and are currently measurable only subjectively, although new tools—such as the measurement of heart rate variability—may be useful in confirming subjective self-reported data. There are few measures that simultaneously address the self-healing effect, the therapeutic relationship effect, and the complementary modality. Therefore, to fully assess efficacy or effectiveness, additional measurements are necessary beyond the usual physiological indicators (e.g., range of motion or serum

the economics of studying efficacy and effectiveness

The production of new knowledge in contemporary society is driven by many factors, of which the most important may be economic and political. Ideally we would seek to prevent illness, promote health, and reduce health costs. Economically, the medical-industrial complex seeks innovation and clinical effectiveness that is tied to financial rewards for industry. CAM, by use of natural products and low-cost approaches, does not attract the kind of investment and resources that would deliver substantial research into effectiveness.

attitudes about the effectiveness of CAM

Perceptions of efficacy are also an issue in the debate over the effectiveness of complementary and alternative therapies. Conventional practitioners' opinions can be based not only on research findings (of variable quality), but also on numerous cultural, emotional, and personal influences and on professional bias and experience. These additional factors may either minimize or promote research findings. For example, a meta-analysis of 12 studies of attitudes toward complementary and alternative medicine showed that, despite a paucity of studies of the efficacy of complementary medicine, conventional practitioners believed that many of these therapies were indeed moderately effective (Ernst, Resch, & White, 1995).

People working in complementary medicine quite reasonably suggest that long experience by clinicians and patients using certain therapies or healing systems—often over hundreds of years—provides valid historical evidence of effectiveness. Conventional medicine's expectation is that this long clinical experience would translate into a few well-honed therapies for a particular problem. In actuality, the extensive historical experience of many complementary and alternative healing practices has produced not a few but a great variety of treatments for specific problems. A review of several CAM textbooks, for example, identified 65 different therapies for asthma (Ernst, 2001). For the study's authors, this range of therapies suggests that many years of experience have not necessarily clarified clinical efficacy and that historical evidence may not be relied upon to demonstrate effectiveness. A contrasting perspective is that there are many different scientifically unproven therapies that do work for "asthma," perhaps operating through different mechanisms. For example, therapies may differ in their effect on patients with asthma because of individual genetic differences in responding to the therapy or because of individual differences in the causation of the asthma.

efficacy & effectiveness of complementary medical modalities: systematic reviews & meta-analyses

Demonstrating the outcomes of complementary and alternative therapies from the perspective of mainstream medicine usually centers around five questions:

- Is there biological evidence to support the mechanism of action of the modality under study?
- Does the diagnostic approach of the modality coincide with the biomedical diagnostic process?
- Are the data obtained in studying a complementary/alternative modality free of bias?
- Is the study designed, implemented, and interpreted in a rigorous fashion?
- Can the therapy be effective in real world populations?

Following are three examples of different research approaches to effectiveness in complementary and alternative therapies that relate to the above questions and will give the reader a taste of the challenges facing this new field of medical care.

**EXAMPLE 1:
a review of the rationale , mechanism, efficacy, and effectiveness of
craniosacral therapy for various clinical problems
(Green, et al., 1999)**

Craniosacral therapy (CST), a modality developed in the 20th century, is used by chiropractic, osteopathic, and naturopathic physicians, massage therapists, and dentists for headaches, migraines, insomnia, injury, sinusitis, learning difficulties, and the results of birth trauma. The rationale supporting craniosacral therapy is that there is some dysfunction in the flow of cerebrospinal fluid (CSF) that causes or contributes to specific clinical problems, and that the restriction of cranial bone movement may be responsible. Furthermore, rhythmic movement of the cranial bones and the vertical spine by the therapist can help restore normal CSF flow and relieve symptoms.

The review, by the Office of Health Technology Assessment in British Columbia, Canada, covered a series of questions about the effectiveness of craniosacral therapy (CSF). The questions and conclusions are shown below.

QUESTIONS & CONCLUSIONS

PATHOPHYSIOLOGY

questions

- Does the CSF actually flow in rhythmic fashion? (10 studies reviewed)
- Does movement between cranial bones occur? (9 studies reviewed)
- Is there a link between cranial bone restriction and clinical symptoms? (3 studies reviewed)

conclusions

- CSF clearly has a rhythmic flow of 8-15 cycles per minute.
- Movement of cranial bones occurs but is slight (contrary to conventional teaching that there is no motion).
- No evidence has been established that different cranial bone positions produce changes in CSF flow or that changed CSF flow leads to symptoms.

DIAGNOSIS

question: Can clinicians agree on findings in craniosacral evaluation? (5 studies reviewed)

conclusions

- No tools exist to measure craniosacral motion or dysfunction.
- Inter-observer agreement between practitioners of craniosacral therapy is weak and unreliable.

TREATMENT

question: Is craniosacral treatment effective? (7 studies reviewed) These studies were mostly case reports, retrospective case series, pre- and post-intervention studies, all of poor quality. None showed convincing evidence of the benefit of craniosacral therapy.

conclusions

- Craniosacral therapy is currently not supported by evidence of efficacy. Once there is more clarity regarding standards of diagnosis, and different measures of craniosacral motion have been established, well-designed, randomized controlled studies might confirm effectiveness. But is RCT design a good fit for CST? It would be difficult to avoid quality problems inherent to RCT. As noted before, other methodologies, such as case series, may be better suited.

EXAMPLE 2:
do certain countries produce only positive results?
a systematic review of controlled trials
(Vickers, Goyal, Harland & Rees, 1998; Bandolier, 2000)

This study addressed the issue of possible national bias in publishing results of efficacy studies on complementary and alternative therapies, since a majority have been done outside the US and UK.

QUESTIONS & CONCLUSIONS

QUESTION: Is there variability among different countries in the positive outcomes reported for acupuncture?

A search was performed for randomized controlled trials of acupuncture vs control or placebo interventions in the previous 30 years. For each of the over 160 studies, reviewers were blinded to the country of origin. The outcome assessed was the superiority of acupuncture over the control/placebo. When the countries with 100 percent of their acupuncture trials showing superiority over control/placebo were compared to the United Kingdom in terms of conventional medical RCTs not involving acupuncture, the following data were obtained:

RESULTS

| region | % of trials showing superiority of acupuncture over control/placebo |
|----------------|--|
| Australasia | 30 % |
| North America | 44 % |
| Western Europe | 63 % |
| Eastern Europe | 85 % |
| East Asia | 100 % |

| country | # of RCT studies (non- acupuncture) | % showing superiority over placebo | # of acupuncture studies | % showing superiority over placebo |
|---------|--|---|--------------------------------|---|
| England | 107 | 75% | 20 | 60% |
| Russia | 29 | 97% | 11 | 91% |
| China | 109 | 99% | 36 | 100% |
| Japan | 120 | 89% | 5 | 100% |
| Taiwan | 40 | 95% | 6 | 100% |

CONCLUSION

- There seems to be a clear pattern of consistently positive results for all RCTs in certain countries, which suggests that substantial bias or error in study design or reporting exists. In general, one would expect the outcomes of acupuncture treatment to be very similar across countries. The authors of the two reviews mentioned at the beginning point out that one high-quality study was far more useful in establishing efficacy or effectiveness than large numbers of poorly designed clinical trials, implying that most were of questionable quality.

EXAMPLE 3:
the efficacy and effectiveness of a specific herbal preparation for a specific illness: the use of *ginkgo biloba* extract for peripheral vascular disease (Pittler & Ernst, 2000)

Intermittent claudication describes ischemic pain felt in the legs as a result of reduced blood flow. It is a chronic problem, limiting function, and is caused by narrowing of the arteries to the legs, usually atherosclerosis. Ginkgo extract has a biological activity on platelets and clotting factors that improves blood flow.

QUESTIONS & CONCLUSIONS

QUESTION

- Is Ginkgo biloba effective in treating intermittent claudication in patients with peripheral vascular disease?

RESULTS

- This meta-analysis (pooling of all data) identified eight good-quality clinical trials (385 patients), comparing ginkgo extracts to placebos. In each study, the outcome was improved walking distance and freedom from pain. All studies demonstrated significant improvement with ginkgo extract—with decreased pain and increased walking distance by about 100 feet.

CONCLUSION

- Despite the relatively small numbers of subjects (about 40 per study), the rigorous design and high quality of the studies support the evidence that ginkgo extract is effective for intermittent claudication.

summary

In conventional as well as complementary and alternative medicine, the effectiveness of a treatment protocol is determined by multiple factors, not limited to the efficacy of a specific intervention. Nonetheless, despite the multi-dimensional nature of effectiveness assessments, conventional medical practice relies primarily on evidence of efficacy from highly focused, randomized controlled clinical trials to inform clinical decisions.

Today's health care system includes a wide variety of complementary and alternative healing modalities that are employed by nearly half the population. The conventional practitioner is challenged to make informed clinical decisions about the use of complementary and alternative therapies and to provide information and counsel to his or her patients about these therapies.

The overwhelming reliance on a single research methodology to inform the clinician poses significant problems in testing the outcomes of CAM. RCT study designs do not serve well in evaluating healing systems that are individualized, multi-faceted, and synergistic. Additionally, the numbers of good studies available—while growing—are still small.

The challenge to researchers is to find more varied and appropriate ways of studying the effectiveness of complementary and alternative therapies, and to make this information readily accessible to clinicians despite economic, cultural, and political obstacles. The challenge to practitioners is to broaden their clinical decision-making processes by accessing appropriate information about complementary therapies and not relying only on RCT data in making treatment decisions.

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