Principles for Prioritizing Commission Recommendations

With such diversity of topics and motivations in integrated medicine how can the Commission identify and prioritize recommendations so that they best serve the public. The following principles may help in developing guidelines for prioritizing recommendations. The Commission is primarily interested in facilitating programs, practices and activities that have the following characteristics.

Safe and Long-term. All effective treatments are not equal.

A. Induction of salutogenesis, self-healing processes. Interventions that work by stimulating repair and recovery are more likely to be safe than interventions that inhibit or remove specific biological or psychological functions.
B. Support systems for maintaining healing processes. Long-term improvement requires that common causes of chronic disease be addressed by using comprehensive approaches.
C. Minimally invasive. In diagnosis, minimally invasive methods are safer than highly invasive methods.
D. Low-impact. Once a practice is "standard of care," it becomes difficult to access alternative methods. Since profitable and rapidly acting, short-term, high-impact procedures are the easiest to bring to the public and so the first to become established, more slow and comprehensively acting, long-term, low-impact methods are then not discovered, even if they may be cheaper, safer, and more effective.
E. The Commission will preferentially support: 1) the integration of minimally invasive approaches, 2) comprehensive therapeutic systems of CAM that support natural healing processes; 3) specific modalities that induce normal, rather than inhibit abnormal, physiological and molecular processes; 4) practices that tend to have multisystem, non-specific health promoting effects rather than singular and specific effects.

Low Cost_ Medical care costs are high and rising rapidly.

A. Early detection and intervention. High costs largely due to the use of expensive methods that intervene late in the disease process. Cost reduction requires access to methods that focus on: 1) early and functional aspects of illnesses and, 2) health promotion and prevention in support of long-term improvement.
B. Low-cost technology. The top activities cannot rely on expensive equipment and procedures if they are to reduce costs.
C. Non-patentability/profitability. Methods that are not patentable or profitable provide little incentive for research and development. Incentives for profit from self-healing practices should be explored
D. Self-care. Practices that involve self-care, behavioral medicine, self-treatment, lifestyle change are some of the most useful and neglected areas of medicine and in need of better integration.
E. The Commission, therefore, will seek out and support the integration of: 1) early

detection methods; 2) low-cost technology based approaches; 3) low-cost CAM approaches; 4) methods with low-profit potential such as possible over-the counter, self-care a methods.

Person-centered and Comprehensive. "Effectiveness" must be defined in the context of the patient who gets the therapy.

A. Patient preferences. Patient preferences and the subjective experience of medical care, should be considered when defining integration strategies.
B. Comprehensive outcomes. Integration approaches are needed that facilitate comprehensive and long-term outcomes of the patient with the illness. Desired outcomes should consist of a minimum representative set of physical, functional, behavioral, quality of life, mental and spiritual domains tailored to the population and condition being studied.
C. Ecological (systems) models. Integration should focus on comprehensive systems of healing that include the patient's experience of the health care system.

Scientifically Rigorous and Contextually Sensitive_ Most current medical practices are determined more by specialty influence, economic motives, and habit, than by adequate scientific evidence.

A. Claims vs. reality. Patients, physicians, and policy makers looking for alternatives to current care are faced with an undifferentiated smorgasbord of claims. These claims are often exaggerated or minimized in a manner that is disproportional to the evidence available on their effectiveness. Often implications and judgments are made about claims out of context of their application and use.
B. High quality science. Poor evidence is worse that no evidence as it leads to false assumptions and mistakes in care. Weak methodology is a major problem in all of medicine. Powerful principles for gaining and clarifying cause and effect through scientific methodology are continually developing and we currently have a diversity of rigorous research tools to help us sort out value and reality in medicine. Access to knowledge and expertise is essential to the full range of these tools if diverse CAM practices are to be identified and provided.
C. Contextually sensitive. Science must be delivered in a way that is sensitive to the context and the assumptions of the cultural model in which it is used. Research and practice must be both scientifically rigorous and contextually sensitive
D. Explicit scientific methodology. The Commission will work to develop, validate, and apply pre-determined criteria for evaluating the scientific and contextual validity of alternative and orthodox medical claims. An Evidence House should be created for all programs and practices that follow explicit scientific criteria and provide the results of those evaluations for use by the public, patients, therapists, policymakers, organizations, and researchers.

Education and Training

Ongoing public and professional education and training is needed if useful CAM

practices are to be integrated into the current health care system. Few individuals understand and are well educated in both conventional and alternative practices. Didactic, and especially experiential education is required in order to understand and use therapeutic and healing modalities.

Information Access and Technology

The opportunity to understand and enhance healing is unprecedented at this time in history. Access to information and methods about healing throughout the world are more and more available.. The ability to access and influence matter and energy through with technology allows greater precision and flexibility in the application of healing practices to the promotion of wellness.

The Management of Judgement Processes in Alternative Medicine Research

"Most people admit the limitations of their memory but few the limitations of their judgement, yet both are often equally flawed." - JRC Joyce.

Science is inherently a social process in which judgements are made about the validity and value of information in the context of the inherent human bias. While the tools of rigorous scientific methodology are designed to minimize judgement errors and bias, scientists themselves are not more rational or objective than any other human group. (Collins, Lakotas, Hufford, Starr, etc.) Trust, a common world view, the ability to communicate, a cooperative intention and a willingness to change based on agreed upon rules are all necessary for the proper application of scientific methods. When these common values are shared groups of scientists can apply research methods in a highly effective and rational manner. This is called "normal science" and operates within a common "paradigm" or worldview. (Kuhn, Tarnas) Under the conditions of "normal" science, research methods increase objectivity and reduce bias.

When a common "paradigm" or worldview is not shared, or when distrust and miscommunication exist between groups, then the value of scientific methodology for managing judgement errors and bias is ineffective. (Berger, Feyerabend) Under these conditions, research methods often become tools whereby political power, social bias and judgement error confound and decrease objectivity. In the later environment processes for the management of social judgement, communication and distrust are required before scientific methods can be effectively applied. Research into alternative medicine frequently involves groups who operate from different worldviews, with different assumptions, or in a climate of distrust and miscommunication. Thus, the management of judgement processes becomes an essential component for the proper application of scientific methods.

In 1995 the Office of Alternative Medicine (OAM) and the National Cancer Institute (NCI) at the National Institutes of Health (NIH) shut down a $600,000 research project on an alternative cancer therapy because of disagreements over methodological issues while conducting the project. Each party communicated negative information about the other party's judgement errors through their own avenues. To help understand the social processes that led to this study's failure the OAM commissioned an expert group in conflict resolution to examine the social dynamics of this project. Interviews with all parties were done and detailed analysis of these processes completed. Following this report a conference was held with experts on conflict management and resolution who presented several models for the possible management of such situations in the future. (Hammer, 1996).

A year later, the OAM and NCI jointly sponsored a meeting bringing together oncology researchers, alternative medicine cancer practitioners and the public. The purpose of the meeting was to discuss a plan for managing social and judgement processes when conducting research on cancer in situations of distrust or differing "world views". This resulted in the Practice Outcomes Monitoring and Evaluation System (POMES) report.

(POMES, 1997) At the POMES meeting an example of a alternative cancer research project that involved the explicit development of trust, the enhancement of communication and the management of conflict issues around research methods was presented. This project was brokered by the late Ernst Wynder, M.D. and is now being sponsored by the NIH, including the NCI at Colombia University. Despite some disagreements about research design and some outside attempts to derail it this project it has adapted and adjusted its methodology in way close to what happens in normal science.

In order to help facilitate the management of social judgement processes on a on going basis, the NIH set up a Cancer Advisory Panel for CAM (CAPCAM). The purpose of the CAPCAM is to assist the NIH in evaluating claims of efficacy relating to complementary and alternative medicine for cancer. The Panel is to: 1) review and evaluate summaries of evidence for CAM cancer claims submitted by practitioners; 2) make recommendations to the Office of Alternative Medicine (OAM) and the National Cancer Institutes (NCI) on whether and how these evaluations should be followed up; and, 3) be available to observe and provide advice about ongoing studies supported by the OAM and NCI, and about communication of the results of those studies to the public.

The CAPCAM does not replace the functions of existing review and oversight groups such as Institutional Review Boards (IRB), Data Safety and Monitoring Boards (DSMB), or Investigational New Drug (IND) or grant application procedures that operate effectively under normal conditions. It is to advise and oversee the social and judgement processes in CAM cancer research so that these processes facilitate rather than interfere with good scientific methodology. Its purpose is not to develop research methodology; rather it is to advise the NIH on how to create a "normal" environment for doing so. Its focus in on facilitation of trust building, communication between parties and fairness in the execution of cancer research projects.

Membership on the CAPCAM is selected from specific categories of groups involved cancer research to help maximize fair representation and communication of all parties involved. This includes:

- Chair: member of both conventional and CAM communities
- oncology research community (2 members)
- complementary and alternative cancer community (2 members)
- patient advocate with experience in cancer and CAM (2 members)
- clinical imaging community (1 member)
- expert in clinical trials with experience in CAM research
- statistician
- representative from the OAM Advisory Board
- representative from the NCI
- oncology nurse
- communication and conflict expert
- a facilitator (advisory only)

With this charge and membership, the CAPCAM should develop more solid models and a process of social and judgement management from those proposed. In addition, it should use what has been learned from past projects (both those that have failed and succeeded) to produce an efficient process for "normalization" of the scientific process in cancer research in alternative medicine. It can do this by advising the NIH on how to build trust, improve communication, manage conflict, bridge worldviews and develop fair judgement processes in alternative medicine research.

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The Evidence House: A Place We All Can Live

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We all want good evidence when making medical decisions. Evidence, however, comes in a variety of forms and purposes and what may be good for one purpose may not be good for another. The term "evidence-based medicine" (EBM) has become almost cliché in recent years being used as a synonym for "good" or "scientific" both to support and deny the value of complementary medicine practices. (1) The usual approach to EBM is to use the "hierarchy of evidence" (Figure 1A). In this arrangement information from systematic reviews (SR) of randomized controlled trials are seen as the "best" evidence, followed by individual randomized controlled trials (RCT), then by non-randomized trials, observational studies and case-series. (2) In such a "hierarchy" all efforts are focused on approximating the type of evidence at the top of the pyramid and lower levels are considered inferior. Clinical experiments that isolate additive, casual links between selected aspects of an intervention and selected outcomes of an illness become the "gold standard" when the hierarchy model is used.

As every clinician knows patients recover for complex, synergistic reasons many of which are not additive and cannot be isolated in controlled environments. The best evidence under these circumstances may be observational data from clinical practice that can estimate the probability of a patient's recovery in a realistic context. (3) In addition, patient's illnesses are complex physical, psychological and social experiences that cannot be reduced to single, objective measures. (4) In some cases the most valuable information for a clinical decision is a highly subjective judgment about life quality. The personal experience of illness might only be captured with qualitative research, not questionnaires or blood tests. (5) The "best" evidence under these circumstances may be the meaning a patient has of their illness and recovery. At other times the "best" evidence comes from laboratory studies. The discovery that St. John's Wort can accelerate the metabolism of immunosuppressive drugs, for example, is the most crucial evidence for its management in patients on such medications. (6) Controlled trials often do not discover such interactions. By arranging types of evidence in a "hierarchy" we obscure the fact that sometimes the best evidence is not attributional, not objective, not additive and not clinical. (7)

Instead of an evidence hierarchy, I suggest we build an evidence "house" with rooms for different types of information and purposes (Figure 1B). On the left side of this Evidence House are types of information that seek out causal attributions and mechanisms of action. Laboratory research (room I) forms a foundation of understanding of mechanisms and causal links on which controlled clinical research can build. In the case of homeopathy or prayer, for example, randomized controlled trial data seem to point us in an illogical direction that can only be resolved with basic science research. (8)

Randomized controlled trials (room III) and systematic reviews of randomized controlled trials (room V) attempt to verify suspected causal links of specific interventions. However, if we confine ourselves to the left side of the Evidence House we will never obtain information about the relevance of medicine for patients (room II) or what happens in the actual world of clinical practice (room IV) or the generalizability of an intervention in our health care delivery system (room VI). The "rooms" on the right side of the Evidence House provide information about relevance and utility of practices, both proven and unproven.

Whether we construct an evidence hierarchy or an evidence house also has ethical implications for medicine. (9) Different groups tend to prefer different types of evidence. Regulatory authorities and those interested in the approval of new treatments are most interested in RCT (room III) or SR (room V) data rather than observational research although the need for alternative strategies for many treatments is evident. (10) Health care practitioners frequently want to know the probability of effects in populations in clinical practice (room VI). Those paying for care are generally more interested in health services research (room VI). Patients are intensely interested in stories and detailed descriptions of patients similar to them (room II). (11) Rationalists want to know how things work and some will accept only their conceptual plausibility (room I). (12) If resources are disproportionately invested into one room of the house (say for the regulatory goals of rooms III and V) to the neglect of others, science will not obtain the evidence needed for full public participation in clinical decisions. A livable house should not have an elaborate kitchen and no bathroom. Each has different functions and all need to be high quality.

Complementary and alternative medicine helps us think about who will live in the Evidence House and how it should be constructed. The public is the architect, driving the interest in complementary medicine. They are seeking more holistic and preventive care, safer treatments for chronic illness and more participation in health care decisions. (11) As patient advocates we must help them find a seat at the research table so we can build an Evidence House where all can live.

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Table 7. Identifying CAM Practices

Areas usually considered CAM include:

- Chiropractic Medicine
- Acupuncture
- Traditional and indigenous systems (e.g. Ayurvedic medicine, Qi gong, Kampo, etc.)
- Naturopathy
- Homeopathy
- Massage
- Therapeutic Touch
- Spirituality and prayer

Areas considered CAM only if explained and applied in unconventional ways include:

- Mind/body methods
  (when explained with unorthdox theories or used in unconventional ways)
- Diet/lifestyle therapies
  (extreme or unusually diets or unusual uses of diets for therapeutic and preventive purposes)
- Herbal therapies
  (when investigating therapeutic effects of whole plants or plant combinations rather than "active ingredients" for drug development)
- Nutritional supplements
  (when used by CAM practitioners in unorthodox ways or in "mega" doses)
- Pharmacological therapies
  (when used by CAM practitioners or in unorthodox ways)

Table 8. Identifying Research Priorities and Funding Opportunities in Complementary And Alternative Medicine

Identifying potential research areas: Potential research topics arise because of either:

- extensive public use,
- accumulating supportive data or
- an evolving theoretical rationale.

The following criteria for funding research on CAM follows those established by the NIH for biomedical research in general and strives to identify those areas where CAM may provide unique contributions to science, medicine and public health. (from "Setting Research Priorities at the National Institutes of Health", NIH Publication No. 97-4265, September, 1997, pp. __.)
These criteria fall into four categories.

- assessing health care needs,
- funding the continuum of research from basic inquiries to clinical applications,
- assessing scientific opportunities, and
- identifying potential contributions from research on CAM.

***Assessing health care needs*:** There are many possible ways of measuring health needs and distributing research funds. One approach used for assessing health care needs for biomedical research involves the simultaneous evaluation of several criteria that look at the burden of illness and the balance of research approaches.
Criteria for addressing burden of the illness include:

- prevalence: the number of people with a particular problem;
- mortality: the number of deaths caused by a disease;
- morbidity: the degree of disability and suffering produced by a disease
- loss of productive years: the degree to which a disease cuts short a normal, productive, comfortable lifetime;
- costs: the economic and social costs of a disease, and
- urgency: the need to act rapidly to control the spread of a disease.

***Funding the continuum of research*:** By supporting a balance along disease-related and basic research projects, both:

- near-term improvements in the diagnosis, treatment and prevention of specific diseases, and
- long-term discoveries in basic science that in time will produce advances in our ability to understand, treat, and prevent disease or delay its onset can be achieved.

A variety of research methods may be needed in investigating CAM but the appropriate balance may be achieved in a particular CAM area by emphasizing certain methods at a particular time. These methods may include:

- controlled clinical trials,
- systematic review and meta-analysis,
- laboratory research,
- epidemiological and outcomes research,
- qualitative and descriptive methods and
- health service research.

***Accessing scientific opportunities*:** Assessing scientific opportunities is complex and requires expertise in various scientific and medical fields, breadth of vision across many disciplines, and judgment to determine the likely yield from making investments in particular areas of research. Special scientific panels, review processes and advisory inputs from a variety of groups are needed to help make these decisions. Experts with experience

in research methods and content experts in CAM and clinical topics are required on review panels and advisory groups.

Scientific review includes the following criteria.

- the importance of the problem or question,
- the innovation and creativity employed in approaching the problem,
- the adequacy of the methodology proposed,
- the qualifications and experience of the investigators,
- the adequacy of the environment in which the work will be done, and
- the likelihood that valuable information will be produced with the resources available.

Identifying potential contributions from research on CAM: Areas where complementary and alternative medical practices are thought to offer particular contributions to health care are in:

- improved management or prevention chronic disease, especially in the areas of:
  a) symptom reduction,
  b) improved function,
  c) improved quality of life and wellness;
- reducing side effects of current treatments,
- reducing costs of current treatments,
- improving out understanding of whole or integrated prevention and treatment approaches that incorporate a biopsychosocial perspective;
- filling gaps in knowledge, especially by:
  a) contributing to our understanding of the mechanisms by which CAM practices may stimulate auto-regulatory or self-healing processes, and
  b) addressing anomalous findings that seem to call for an expanded conceptual model for investigating the natural world than is used currently in conventional science.

Table 9. Knowledge Domains

A strategic approach to science in such diverse areas that CAM encompasses requires evidence from a variety of knowledge domains.

1. **Attribution or "safety and efficacy":** In clinical research, this is termed "efficacy" and is best obtained through research methods such as the randomized controlled trial. This domain looks for cause and effect evidence of proof and is useful when information is needed to make claims about how parts of a therapeutic system effects certain outcomes in a clinical condition.

2. **Confidence or "proof":** This knowledge domain is done through peer-review, systematic reviews, and meta-analysis of scientific literature. Its purpose is to refine and determine whether definitive proof for a phenomena exists. It is part of, but not the whole, validation process, and requires intimate involvement of a wide peer-review process. This area, like all others, requires an objective, systematic, explicit, and comprehensive approach for valid conclusions.

3. **Basic biological effects or "Mechanisms"**: This is investigated through basic science and laboratory techniques and asks the questions, "what happens and why?" Basic research can provide us with explanations for biological processes that are required to refine and advance our knowledge in any therapeutic field.

4. **Patient relevance or "Meaning"**: This information comes through stories, anecdotes, and descriptions of case reports. Quality research in this area, however, requires detailed qualitative evaluation methods which were outlined in the Qualitative evaluation section of the OAM Methodology Conference. This knowledge domain provides information about whether our efforts are taking the correct focus by incorporating patient-centered outcomes, patient preferences which then reduces the risk of outcomes substitution when a therapy is applied.

5. **Associations or "clinical effectiveness":** When the identification of cause and effect links is impractical, unethical, unreasonable, or impossible the fourth domain of information -- looking for associations -- is needed. In clinical medicine this is known as "effectiveness" and involves such research methods as epidemiological and outcomes research strategies. This is best applied when one is evaluating complex, long-term, or chronic conditions. Complex systems evaluation is needed for traditional medicine and the utility of specific therapies when applied in the clinical situation. This type of knowledge is useful when indications are the desired outcome and when one is seeking knowledge about possible adverse effects that have not been previously expected.

6. **Utility and Generalizability**: This area involves an even wider public review process and is desirable when the goal of that information is the acceptance and adoption of particular practices. This area deals with the evaluation of external validity aspects such as access, feasibility, use, etc. It primarily involves public use. The type of research that provides information in this knowledge domain is health services research.

Goals of Research.

- From the clinical perspective, the main goal of research is the identification of optimal medical management approaches and the selection of diagnostic or therapeutic strategies.
- From the clinical research and public policy perspective, the main goal of research is identification of practices that warrant randomized controlled trials and evaluation of those trials.
- From the basic science perspective, the main goal of research is the understanding and control of the fundamental processes of life.
- Clearly, all these goals are worthy of research investment.

Table 10. Research methods and strategies

*1. **Research Methods.*** The OAM has uses the following research methods. The initial method in a research strategy for a specific CAM areas may include either exploratory, developmental or confirmatory approaches.

Methods often used as exploratory and developmental approaches

- Laboratory research to investigate mechanisms of action of emerging areas such as herbal products, and proof-of-principle experiments in frontier areas such as homeopathy and direct mental influence on living systems.
- Epidemiological and outcomes research is used to gain preliminary information (such as practice standardization, outcome measures, safety and risk assessment, effect size information for power calculations, etc.) for more controlled trials and to gather longitudinal data on cumulative safety and chronic disease effectiveness. An example of an area evaluated using this approach is the effects of religion on health.
- Qualitative methods can inform us about the reasons for CAM use and to identify patient relevant outcomes to address in research. The development of instruments for the measurement of spiritual outcomes are an example of research using qualitative methods.

Methods often used as confirmatory approaches

- Randomized controlled clinical trials for isolation of the specific effects of clearly defined medicinal products or nutritional supplements such as the NIMH/ODS/OAM trial of hypericum and depression.
- Consensus conferences, systematic reviews and meta-analyses can obtain information on the quality of research literature and can help guide future research and practice.
- Health service research to can obtain information about the outcomes of clinical decisions and provide information on costs, access and treatment variations.

*2. **Research Strategies.*** In general, frontier and some emerging CAM topics are initially approached using exploratory and developmental methods, whereas other CAM-related topics that are already integrating into conventional medicine are best addressed using confirmatory methods.

The following are some example strategies currently being used.

- For complex practices that are not well described, observational data and outcomes research or pilot trials may be the best initial approach. Field investigations of naturopathy for AIDS and complex CAM cancer therapies are being investigated in this way.
- For CAM practices that are well described, pilot trials or outcomes data coupled with decision analysis followed by selective application of randomized controlled trials may provide the best strategic approach. Acupuncture for the investigation of depression, osteoarthitis and alcoholism are being investigated in this manner.
- For CAM products whose constituents are unknown, basic laboratory characterization may be needed before clinical research is undertaken.
- For CAM products that are well charaterized, randomized controlled trials are appropriate. The efficacy of the herb St. John's Wort is being investigated in this manner.

Table 11. The audience and the evidence

When deciding whether or not to use a therapy, everyone wants to know if there is evidence that the therapy is safe and will work. Different groups often look for different types of evidence to make these decisions, however.

Patients. Patients who are ill or for their family members may want to hear details about other individuals with similar illnesses who have used a treatment and recovered. If the treatment appears to be safe and there is little risk of harm from it, evidence from these stories may convince them to use the treatment. This type of evidence is called anecdotal, or case reports.

Practitioners. Doctors, who see many patients may want a different type of evidence. They realize that what works in one case may not work in another and need more than a few patient recovery stories to recommend a therapy. They often want to know what the likelihood or probability is that a patient will recover or have an adverse effect based on a whole series of similar patients who have received the treatment in actual practice. For example, out of 100 patients with the condition who received a treatment did 20% or 80% improve and how many had side effects? They also want to know about the complexity of using the therapy, including its cost and inconvenience? This type of evidence comes from observational or clinical outcomes data.

Clinical Researchers. Scientists doing patient-oriented research may want a different type of evidence. They often want to know how much improvement occurred in a group who received the treatment compared to another group who did not receive the treatment. If 80% of patients who received a treatment got better, do 75% of similar patients get better just from coming to the doctor and getting any treatment. It this case only 5% of the improvement would be attributed to the treatment? This is comparative clinical trial evidence. Some scientists will only accept comparative evidence for a treatment if it has come from an experiment in which blinding and randomization have been followed. This is clinical experimental or randomized controlled trial evidence.

Basic Scientists. Basic science investigators may want objective evidence supporting a mechanism of action from laboratory experiments that can explain the effects observed in clinical research or guide better clinical research. This is basic science evidence.

Policy Makers. Those in charge of determining public laws and policy often need definitive "proof" that a practice is safe and effective. They required evidence in which a high degree of confidence can be placed since errors made in policy can adversely effect millions of people and cost billions of dollars. This type of evidence comes from extensive evaluation and synthesis of several research reports through systematic reviews, meta-analyses and consenus evaluations from experts in the field.

The Evaluation of Complementary and Alternative Medicine

For the Macy Conference on

Complementary and Alternative Medicine and Medical Education

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The views, opinions and assertions expressed in this article are those of the authors and do not reflect official policy of the Department of the Army, Department of Defense, or the U.S. Government.

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Introduction

Complementary and alternative medicine (CAM) is a set of medical practices that not part of conventional care but still used by patients in their health care management. These practices have recently increased in popularity in recent years emerging as an area of great public interest and activity, both nationally and globally. [1] The current definition of CAM creates a category of health care and medical practices that is wide and variable, ranging from nutritional and behavioral interventions, to ancient and comprehensive systems such as Ayurvedic and Traditional Chinese Medicine. As the use of CAM practices rises obtaining reliable information about the safety, effectiveness and mechanisms of these practices requires rigorous investigation. This chapter discusses the issues important for evaluating these practices.

Conventional physicians often refer for CAM and, to a lesser extent, provide CAM services. In a review of 25 survey's of conventional physician referral and use of CAM in the United States Astin found that 43% of physicians referred patients for acupuncture, 40% for chiropractic and 21% for massage. The majority believed in the efficacy of these three practices. Use of CAM practices by physicians was much lower ranging from 9% (homeopathy) to 19% (chiropractic and massage). [2] Organizations such as the British and American Medical Associations and the Federation of State Medical Boards in the United States have called on physicians to learn about CAM, discuss these practices with their patients and incorporate them into proper clinical management. [3, 4]

The Potential Risks and Benefits of CAM

Many CAM practices, such as acupuncture, chiropractic manipulation, homeopathy, and meditation, are low risk but still need to be used by competently trained practitioners in order to avoid misuse. [3] Some CAM practices, such as acupuncture, require extensive

training and skill to properly deliver yet conventional physicians are legally allowed to use such practices even if they may not have received adequate training or certification in them. The adequacy of training of CAM practitioners also varies - many having no certification or state licensing and overview procedures at all.

Herbal preparations are readily available over the counter and contain powerful pharmacological substances, which can be toxic and produce herb-drug interaction. [5] These drug-herb interactions may be quite significant and hard to detect without concerted basic and clinical investigation. For example, St. John's Wort, an herb considered quite safe and commonly used for the treatment of depression and dysthymia has recently been reported to accelerate drug metabolism of anti-retroviral and cytotoxic agents resulting in increased viral load in HIV infected patients and organ rejection in transplant patients. [6, 7] Herbs need the same phase I and II clinical testing as pharmaceuticals to assess pharmacodynamics and drug-herb interactions before moving into large scale clinical trials or marketing. This testing is complicated by the fact that many herbs have multiple or unknown active ingredients making such testing difficult. Thus, systematic post-marketing surveillance is especially important. Adulteration, contamination and poor quality control are also possibilities with these products, especially if shipped from Asia and India. [8] Safety monitoring and product quality seems to be the minimum evidence necessary for marketing. Evaluation of efficacy with large randomized trials is difficult in herbalism due to the modest effect sizes, paucity of funding and their use in mostly chronic, non-life-threatening conditions.

Some CAM practices have clear value for the treatment and prevention of disease. In botanical medicine, for example, there is research showing benefit of herbal products such as *ginkgo biloba* for improving multi-infarct dementia [9] and possibly Alzheimer's; [10] benign prostatic hypertrophy with saw palmetto and other herbal preparations; [11, 12]

and the prevention of heart disease with garlic. [13, 14] It appears that St. John's Wort is effective in the treatment of depression and produces less side effects and costs less than some conventional anti-depressants. [15] The quality of many of these trials is poor, however, with small sample sizes, variable outcome measures and lengths of follow-up and differing product standards.

The Scientific Method in Medicine

Clinical research in CAM needs the same rigorous research methods developed for conventional medicine. Sometimes more rigor is required because of the complexities and implausibility of CAM practices. Figure 1 illustrates six types of research frequently used in the investigation of medicine and the type of information these approaches provide.

These are:

1) Qualitative research methods. This includes detailed case studies and patient interviews that describe diagnostic and treatment approaches and investigate patient preferences and relevance. Qualitative approaches have been developed in anthropology and are becoming increasingly common in nursing and primary care.
2) Laboratory and basic science approaches. These methods investigate the basic mechanisms and biological plausibility of medical practices. *In vitro* (cell culture, intra-cellular such as with probe technology) and *in vivo* (testing in normal, disease prone or genetically altered animals) are now extensively used and expanding into molecular realms.
3) Observational studies. These methods include practice audit and epidemiological research, outcomes research, surveys and other types of observational research. These studies may not have a comparison group or they may attempt to create comparison groups by sampling patients not treated with the intervention.

4) Randomized controlled trials. This method attempts to isolate the specific contribution of different interventions on selected outcomes. Such studies usually involve the assignment of patients to one treatment group or another using a random method. Various approaches are used to make group assignments such as randomly selected numbers or computer-generated random assignment. The best approach involves concealing knowledge of which patients will get which treatment at the time of assignment (allocation concealment).

5) Meta-analysis, systematic reviews. These approaches and less rigorous approaches such as expert review and evaluation are methods for assessing the accuracy and precision of clinical research. Criteria-based systematic reviews are increasingly being used in place of subjective reviews.

6) Health technology assessment and health services research. These are a collection of approaches for examining the utility and impact of interventions in the light of treatment delivery factors such as access, feasibility, costs, practitioner competence, patient compliance, etc. This may take the form of survey's or sampling from groups already getting an intervention to evaluating quality of care, costs and other factors. Random sampling may or may not be used.

Differential Goals of Research Types

Certain groups may preferentially seek out one or more of these research methods and the type of information they provide. For example, basic scientists may have more interest in the results of laboratory research, clinicians more interest in the results of clinical trials, etc. Note that the methods on each side of figure 1 have different general goals. Laboratory research randomized controlled trials and systematic reviews or meta-analyses (left side of figure 1) are testing for the existence of a specific effect from an intervention or are used to support a theory about mechanisms. Qualitative research, observational trials or health technology assessment (right side of figure 1) are testing for the

probability, magnitude and relevance of an effect in clinical practices or health care delivery systems. There may be tension between research that tries to isolate specific effects (laboratory, RCTs, meta-analyses, etc., left side of figure 1) and research that tries to define the utility, public impact and relevance of a practice in the real world (qualitative, observational and health services, etc., right side of figure 1). Since one can rarely address more than one question in a single research project designing research that attempts to address both specific (left sided) and pragmatic (right sided) questions simultaneously is problematic. To address both specificity and utility carefully developed research and evaluation strategies are needed to prevent each method from being interpreted in isolation. Consistent decision rules for the evaluation of research is an important step in the continued development of science-based medicine. [16] To understand the relationship between different types of research methods we must be able to judge the quality of research from within each of the domains in figure 1. [17]

Quality Criteria for Research on CAM

Evaluation of complementary and alternative medicine is fundamentally no different from evaluating conventional medicine. [18, 19] There are, however, certain conceptual and contextual issues that investigators should be aware of when evaluating research on CAM topics. [20] The validity of randomized controlled trials, for example, involves a set of quality criteria that test "internal validity" or the likelihood that observed effects are biased. The applicability of information from clinical research, including RCTs and observational trials, criteria for "external validity" or the likelihood that the observed effects will occur in varied situations are used. The CONSORT group have produced a widely adopted set of reporting guidelines for RCTs. [21, 22] These guidelines emphasize the importance of allocation concealment, randomization method, blinding, proper statistical methods, attention to drops-out and other factors. [23, 24]

Model Validity

In addition to internal and external validity, research on CAM requires additional criteria that address what I call "model validity" or the likelihood that the research has adequately addressed the diagnostic taxonomy and therapeutic context of the CAM system. [25] Many complementary medicine practices come from systems of medicine developed outside these standard assumptions of Western medicine. Therefore, it is important to consider the interaction of research methods with the conceptual systems being investigated. For example, some CAM treatments are investigated in populations for which the practice is integral to the culture and may produce variation in responses even when standardized. [26] Individual expectations within a culture and the nature of the information given to patients (including the informed consent procedure) can also impact outcomes significantly. [27, 28] "Model validity" in the evaluation of CAM research involves addressing these factors. Table 1 lists the main criteria for internal, external and model validity when evaluating clinical research on CAM. These criteria are summarized in an evaluation approach called the "Likelihood of Validity Evaluation" (LOVE) system that has been applied to the evaluation of several different areas of CAM clinical research. (Table 1).

Diagnostic Taxonomy

In a clinical trial, an investigator first collects a "homogeneous" group of patients with a common diagnosis. When this "homogenous" group is evaluated from the perspective of another medical tradition, however, these patients may not be homogenous. Research not incorporating these variations in patient classification can be problematic.

For example, a homogenous group of osteoarthritis patients from the Western perspective may represent over a dozen treatment groups when evaluated by traditional Chinese medicine (TCM). A "standardized" treatment can approximate the "average" syndrome and is the way many investigators handle this situation. Standardization has advantages

in that it simplifies the treatment strategy, may allow for blinding and may prevent treatment confounding. It has the disadvantage of providing suboptimal treatment and so produce "false negative" results. This is a problem of model validity. For example, Bensoussan conducted a study of patients with irritable bowel syndrome. One third of the patients were treated with individualized traditional Chinese medicine, one third were treated with a standardized Chinese medicine approach and one third served a controls, receiving placebo. Subjects treated with the TCM model improved for longer than those given the standardized approach. Both groups did better than the placebo control group. [29]

Double Classification

Another approach to the different diagnostic taxonomies in alternative medical systems is by double classification and selection in clinical trials. Initial selection criteria are according to standard Western medicine then additional criteria are applied according to the alternative system. This double classification approach is possible in many situations but adds considerable complexity to the study and increases the likelihood that the trial will produce ambiguous results. For example, Shipley, conducted a placebo-controlled trial of the homeopathic remedy *Rhus toxicum* on a "homogenous" group of osteoarthritis patients without careful classification according to the homoepathic "model" and reported no effect of *Rhus toxicum* over placebo. [30] Fisher, in a follow-up investigation used a "double selection" approach for testing *Rhus toxicum* that provided both good internal validity and model validity. Patients had to meet strict criteria for fibromyalgia and *Rhus toxicum* producing a group of subjects "homogenous" for both systems of medicine. In this study patients treated with homeopathy did better than those given placebo. [31] Such studies are more complicated and may require more resources than the average drug study.

Adequacy of Treatment

A standardized approach can lead to inadequate treatment. For example, in a study of acupuncture of HIV associated peripheral neuropathy a "standardized" approach to treatment was used. To do this, the investigators had to markedly altered what most TCM acupuncturists do in such cases. The study reported the results as negative while many acupuncturists report good results with when using TCM principles in this condition. [32] Considerable time, collaboration and testing are needed in order to work out the best balance between internal, external and model validity factors when evaluating CAM. How to determine when adequate treatment has occurred may not be simple. For example, acupuncture is more like physical therapy or surgery than drug therapy and is applied in very different ways with different skills. If one treatment style is interpreted as *the* acupuncture treatment, it must be optimal or at least *representative*, for a defined group of providers. This has implications for the design and strategy of acupuncture research. For example, in a review of 15 randomized trials of acupuncture for asthma we found very different treatment approaches [33]. Only two trials used the same points and these were by the same author.

Placebo and non-specific effects.

The observed benefits of many alternative medical practices are often attributed to "placebo" or "non-specific" effects. It is not unusual to see 70-80% effectiveness from many practices both conventional and alternative. [34, 35] Traditional Chinese Medicine, Ayurveda, Native American medicine and various mind/body and spiritual healing approaches induce self-healing partly by manipulating the context, meaning and interpretation of illness and outcomes. Manipulation of "meaning" (the placebo aspect of treatment) can interact with specific therapies in complex ways. [26, 27, 36] Many traditional medical practices provide sophisticated ways of producing these "meaning effects". Arthur Klieman's classic studies of why traditional healers provide relief

illustrated the importance of contextual issues for all medicine. [37] The interaction of these specific and contextual or "placebo" effects is an important area for focused research. [38]

Smoking cessation is of particular interest in regard to the placebo problem and some CAM therapies. For example, research on smoking cessation shows that there is clear evidence that acupuncture acts like "placebo" acupuncture [39, 40]. While there is no difference in smoking cessation rates between acupuncture and "placebo"-acupuncture there is also no difference between acupuncture and proven effective smoking cessation treatments [40]. Thus, acupuncture, in spite of being a placebo, appears to be equally effective as an effective conventional intervention! How can we deal with this paradox? The rationale that we are simply fooling patients with placebo is too simplistic an interpretation to be useful. Certainly an important part of the solution is to ask patients if they care if they stop smoking because of a "placebo" effect or a "specific" effect by an otherwise safe and inexpensive procedure.

The introduction of placebo controls and blinding enhances and confuses the conclusions of clinical research in acupuncture. What is an adequate placebo control for acupuncture? Should we use stimulation of non-acupuncture points, or points thought not to be indicated, or superficial needling, or the use of devices using ultra-sound, electrical or laser stimulation, which are switched off for the placebo condition? Deep needling techniques are unlikely to be inert. Procedures without needling are likely to be distinguishable. The question that matters most to patients (and most physicians) is not its specific effects but whether acupuncture benefits patients. Patient oriented acupuncture research would include careful, multidimensional measurement of outcomes, inclusion of independent, and if possible blinded evaluators and rigorous monitoring.

This type of research approach might be better for many conditions rather than to use questionable placebo controls.

Selecting Patient or Theory Relevant Outcomes and Designs

An outcome that is easy to measure may be substituted for or used to represent other outcomes that may me more important for patients or groups of patients. Eric Cassel and others have pointed out that may occur because of an over emphasis on trying to find a "cure" distracting us from healing the illness, one of the core goals of medicine. [41] This occurs when there is an overemphasis on conducting efficacy studies that maximize "internal validity" using objective measures at the expense of "external" and "model" validity. Selection of outcomes that are irrelevant to patients is more likely to occur when researchers select the study outcome without adequate patient input. For example, Cassidy did interviews with over 400 patients who visited acupuncturists and explored the reported benefits. [42, 43] Most patients did not have major improvement of their Western diagnosis, however, they continued to return for acupuncture treatment because of an improved ability to "manage" their illness and a sense of wellbeing after acupuncture. This type of outcome is not easy to measure "objectively" in clinical trials and so is rarely incorporated into research. Clinical researchers investigating CAM need to pay special attention to selecting outcomes that address the most important patient concerns for their illness. This may require adding a person and process (such as qualitative research methods) for identifying such outcomes when designing the trial.

Finding the balance between rigorous *evidence* and patient *relevance* is illustrated with two examples from acupuncture. Because of its simplicity, more than 30 trials have investigated this P6 acupuncture in the study of nausea and vomiting with positive results [44]. It is a simple intervention, easily standardized and also studies a condition where outcomes are straightforward and follow-up short. It is the most studied area in

acupuncture because it is easy to study. The findings are not very useful for the acupuncturist, however, who rarely uses P6 only when treating this condition. More important for the public than nausea are conditions such as chronic pain, stroke rehabilitation and drug addiction where placebo controlled evidence is much less convincing [45, 46], but these are more difficult to study in independently repeated rigorous clinical trials.

A similar dilemma exists when evaluating homeopathy, another CAM systems in which research has narrowly focused on the placebo question. However, placebo in clinical trials of homeopathy has different meaning than in conventional medicine. For example, if a specific chemical drug is tested in a placebo-controlled trial there is usually no question about its biological activity regardless of its clinical usefulness. Homeopathic remedies in high dilutions, however, are usually assumed, *a priori,* to be inactive. Thus, clinical trials in homeopathy are only partly true clinical trials in a conventional sense. This is because they try to simultaneously answer not only the question of clinical efficacy but also what would usually be considered a basic science question addressed in laboratory research. Mixing these questions into a single trial is not a reasonable strategy because it produces ambiguous answers for both questions. Not only do these studies not answer the placebo question they are largely irrelevant for improving the practice of homeopathy. The most investigated clinical models in homeopathy are of *Galphimia glauca* for hay fever [47], Opium, Raphanus, Arnica or China for postoperative ileus (see [48] for review), and homeopathic immunotherapy (HIT) for allergic rhinitis. [49] The remedy *Galphimia* and the HIT approach are rarely used by homeopaths. To use either alone would be considered a suboptimal application of the therapy. Likewise, postoperative ileus is hardly ever treated with homeopathy. As in acupuncture, these conditions are studied because they are easy to study not because they are relevant to patients or practice. The pressure to answer the question of placebo with rigor in all clinical research

results in neglect of research most relevant for practice. In addition, it also fails to definitively answer the placebo question. [48]

Hypothesis Testing

Hypothesis generated research is the method by which we identify cause and effect relationships in medicine. It is a powerful method for studying and confirming pre-identified therapy-outcome links. A down side of hypothesis generated research is that by focusing on a priori theoretical associations that explore particular theory driven outcome links we run the risk of prematurely establishing conclusions about the ultimate value of a therapy and restrict exploration of other possibly better therapies. [50] Once treatments are established using hypotheses generated from a single perspective they become "standard of care" and alternative treatments are then more difficult to explore. For example, coronary artery by-pass grafting (CABG) is an established treatment of coronary artery disease (CAD). This treatment assumes an anatomically based hypotheses about the etiology of CAD. An extensive industry has developed around this procedure. Lifestyle therapy can also treat CAD but is based on a non-anatomical hypotheses of CAD etiology. Lifestyle therapy might be superior to CABG in the treatment of CAD given its low cost, preventive potential, reduction in fatigue and improvement in wellbeing. [51-54] However, adequate comparison of lifestyle therapy vs. CABG is problematic largely because perceptions and resources are already committed to CABG. We do not know if either hypothesis about the etiology of CAD is correct because neither approach can be tested in placebo controlled trials. In the early 1960s sham surgery of internal mammary ligation produced positive effect rates similar to what CABG produces today. [55] Sham testing cannot be done for CABG today even though the contribution from placebo effects in surgery may be large. [56, 57] Thus, hypothesis formation and testing in clinical research can be a double-edged sword by revealing partial causes and running the risk of obscuring more fundamental knowledge and exploring more beneficial therapies for

chronic disease. Clinical research for disease with complex and multi-factorial causes should provide for research strategies that test multiple hypotheses [58-60]

The Value of Randomization

Randomization has value in science and medicine for many, but not all, interventions. In some clinical situations, randomization may assist in revealing true effect sizes. In other cases, for example, in behavioral medicine, it may obscure or have no effect on outcome. [61] Some alternative systems assume that randomization can interfere with important aspects of the therapy and obscure our awareness of how bias is occurring. For example, traditional Chinese medicine (TCM) is based on an assumption that "correspondences" occur across system levels (biological, social, cosmic, etc.). [62, 63] These traditional medical systems view extensive efforts to establish precise the causal links of an intervention and outcome within a level (as done in RCTs) is less valuable than is assumed in Western medicine. [64]

In some CAM systems practitioner and investigator intention is assumed to have influences on outcomes and experimental results. They assume that the effects of intention are inherent at all levels of the therapeutic and experimental process and can alter and even create apparent chance phenomena. [65] If these assumptions are correct the interaction of bias and randomization is more complex than medical science and statistics currently assume. [66, 67] The extent to which investigator intention is relevant to medical research is unknown. These issues are probably only significant when contradictory information from high quality trials arises. Thus, examining the influence of intentionality can only be done with rigorous research methods and cannot be evaluated if the quality of research is poor. Unfortunately, the quality of research in CAM is rarely this good. [68]

Blinding/Masking and Expectancy Control

While we currently have no completely acceptable way to check for successful blinding, it is still considered an important part of quality research design. [21] Many alternative treatments, such as herbal therapies and acupuncture can be blinded or at least partially blinded. In herbal studies care must be taken to match smell and taste. In acupuncture, usually the practitioner cannot be blinded while homeopathy is easily double blinded. Studies of complex behavioral and lifestyle programs will find blinding impossible. In these cases, however, control for time and attention and blinding of the outcome assessment and analysis is possible. For example, in trials of therapeutic touch, providing equal time for relaxation and a sham therapist can be incorporated into the study design. [69] Blinding the evaluation is accomplished by having an individual or group separate from the therapists do the outcome measurements. Analysis can be done blind by having results coded in a way that does not reveal the intervention to the statistician.

Equipoise and Patient/Practitioner Preferences

Patient and practitioner beliefs also have important consequences for clinical research, especially in CAM. Randomization can be ethically done only when there is true equipoise between treatment groups, that is, when the question of efficacy is truly ambiguous and there is no strong belief about the value of the therapy. Equipoise is usually present when new drugs are tested. This situation rarely exists in alternative medicine, however. Most patients and therapist have been using or avoiding CAM therapies because of strong preferences. [70] This makes recruitment to problematic. Several clinical trials of CAM have been stopped either because conventional practitioners would not refer patients to a CAM study or because patients refused to be randomized to the conventional control group. [71] It is known that randomization schemes have been subverted by well-meaning health care practitioners in conventional medicine, a problem that may be even more extensive in trails on CAM. [72] In addition,

clinical research may be significantly contaminated when subjects are using other alternative therapies that interact with the treatments being tested. For example, over 16% of patients enrolled in clinical trials at the NIH Clinical Center are using herbal therapies. This herbal use is usually not reported to investigators. [73] Patient and practitioner preferences must be carefully considered when designing and managing clinical research on CAM.

Summarizing Research

We live in the information age. Keeping up with the literature even in a small subspecialty is a daunting task. There are currently at least 80 major databases and over 400 journals publishing alternative medical literature around the world. It is not surprising that various research summaries may come to markedly different conclusions. Contributing to differences in interpretation of the literature are publication bias, incomplete access to the literature, poor quality original research, varying standards of evaluation, inaccuracies and disagreements when applying evaluation criteria, failure to use consistent research goals and objectives when selecting and evaluating studies and differing beliefs about CAM in general. [24, 74, 75] State-of-the-art review methods, such as those developed by the Cochrane Collaboration, should be used as they provide the best current approach to clinical research summary. [76] Other methods, such as those used to establish practice guidelines and the NIH Consensus Conference methods, are usually less systematic and less rigorous for evaluating clinical research.

Risk Stratification and the Level of Scientific Proof

Many therapies, both conventional or alternative, become accepted before convincing evidence from randomized trials is collected. [77] Acupuncture provides a current example of this in CAM. Even in the absence of proof for acupuncture's effectiveness for most conditions for which it is used, positive experiences by patients and a growing number of

physicians are contributing to a growing acceptance of acupuncture in general. The safety of acupuncture made the NIH acupuncture consensus panel willing to recommend it with less evidence than other interventions with a higher risk. Thus, risk stratification may be a good initial step before deciding on the kind of evidence required for acceptance in CAM. Risk stratification is a key element to balancing rigor and relevance when evaluating research strategies and practicing evidence-based medicine. [78] While more and better randomized clinical trials are clearly important there are a number of preconditions for such trials. This includes:

- The investigated treatment should be representative of actual practice for at least a defined group of practitioners. Representativeness should be demonstrated empirically in observational and outcomes studies. An alternative is to use treatment approaches and qualification standards officially recommended by professional societies.
- Pilot studies are mandatory before starting randomized trials.
- The use of placebo control conditions as a requirement for determining what is adopted in practice is questionable. C
- Clinical studies comparing CAM to or in addition to standard therapies of proven effectiveness should be used more often. For example, a direct comparison of acupuncture to standard therapy or as an addition to standard therapy is useful if we believe that acupuncture might produce fewer side effects or alter costs than standard therapy alone.

There is a growing need for observational studies before extensive, broadly based, controlled trial research is conducted. Practice audit and outcome studies may identify areas of strength and weakness in these practices and so help guide both practice and research. [71]

Matching Goals and Methods in Clinical Research

A recurrent theme in research is the importance of clearly defining the questions being asked, the goals those questions seek to fulfill, and applying the appropriate methods used to answer those questions. [79] As presented in figure 1 there are many types of research methods, each with its own purpose, value and limitations. The quality of these methods should not be judged in isolation rather in relationship to the research goals and questions being explored. Figure 2 illustrates these goal-method relationships. The decision to pursue a particular approach depends on a number of factors including:

- The simplicity or complexity of the condition and therapy being investigated;
- The type of information sought (causal, descriptive, associative, etc.);
- The purpose for which a particular audience will use the information; and,
- The methods of investigation that are available, ethical and affordable.

For example, a physician considering a patient referral for acupuncture might want to know what kind of patients the local acupuncturists see, how they are treated, whether patients are satisfied with treatment and the outcomes. This type of information comes from practice audit (observational or outcomes research). Thus, observational designs may be of more value than relying on the results of small-scale, placebo-controlled trials done in another country with practitioners and populations quite different than those in the community. Observational studies must be as rigorously performed as experimental studies. For CAM theories and data that do not fit into our current assumptions about the nature of reality (e.g. prayer, "energy" healing, homeopathy, etc.) a multi-domain and carefully thought out research strategy is needed. Given the public interest in and the implications for science of these areas it is irresponsible for the scientific community to completely ignore them. [25]

General guidelines for matching goals and methods are as follows:

1. When defining problems and definitions of terms, and when assessing the relevance of outcome measures across diverse populations, qualitative methods with in-depth interviews and content analysis are necessary.
2. When assessing the incidence, prevalence and associations of variables, surveys, or cross-sectional and longitudinal studies with methods for construct development and factor analysis are the most useful.
3. When identifying the comprehensive impact of complex interventions delivered in the clinical context is the goal, pragmatic trials and outcomes approaches should be applied.
4. When attempting to isolate specific effects of treatment on selected outcomes, randomized controlled trials are the method of choice.
5. When exploring mechanisms of action or attempting to determine optimal timing, dosage and combinations for use in clinical trials, laboratory research is needed.

An important part of research evaluation is checking to see that the questions asked and the methods selected are appropriate for each other. [71] Of course, once selected each method must be executed in a rigorous and quality manner.

Assuring Research Quality

For each of these evidence domains (figure 1), criteria for scientific rigor should be defined in relationship to the particular goals pursued. A number of quality criteria have been described in this chapter. These methods cannot function in isolation nor do they always stand in a particular fixed hierarchy as is often suggested. [80, 81] Both experimental and observational designs are needed to explore the validity and value of CAM practices and assumptions. Interdisciplinary research, involving experts in both conventional and CAM fields are needed. For example, the field of psychoneuroimmunology (PNI) arose because psychologists and immunologists began to conduct collaborative projects bringing together their laboratory and clinical research

expertise. Development of other interdisciplinary fields are likely if scientists design projects that cut across research domains without violating quality criteria within each domain. Such exploration would allow us to develop a scientific basis for therapeutic diversity in chronic disease management.

Rigor, Relevance and Realism

Evaluating the safety, effectiveness and mechanisms of CAM practices is complex and a handful of large-scale randomized trials will not answer even the main questions needed. The resources required for extensive, systematic, cross-domain research will not be available in the next several years even for the most prevalent interventions. Yet, the use of CAM continues to increase. Given this situation, we cannot afford to fix *a priori* on a single research method but must balance our research strategies between a) relevance; b) scientific rigor; and c) feasibility. In addition, studies should address the interests of different audiences that research serves. As a minimum input on research priorities should be balanced with the interests of 1) patients; 2) providers; 3) the scientific community; and 4) policy makers. These groups are each interested in overlapping types of information but they may have differing priorities. This will require different types of research approaches and strategies. (Figure 2)

CAM and the Evolution of the Scientific Method

In the past, the interaction of conventional and unconventional medicine has resulted in improvements in the scientific method. For example, fifty years ago methods of blinding and randomization became accepted into orthodox medical research only after they were first applied to unorthodox practices such as mesmerism, psychic healing and homeopathy. [82] Today traditional and cross-cultural medicine challenges us to make explicit the meaning of quality in biomedical science and show the evidence upon which those quality criteria are based. Thus, research in CAM may help us develop decision

rules for improving research rigor and for developing a better strategic approach for science in the age of global medicine.

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a) See article from Trib 9/12/2001
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Q&A

Dr. James Gordon

Commission studies what's not covered in medical schools

By Quynh-Giang Tran
Tribune staff reporter

Dr. James Gordon is chairman of the White House Commission on Complementary and Alternative Medicine Policy, which will be releasing an interim report soon. A graduate of Harvard Medical School, Gordon is also a clinical professor in psychiatry and family medicine at Georgetown University School of Medicine.

Q What is the purpose of the commission?

A It was created to bring the benefits of complementary and alternative medicine, what we call CAM, to the American people. We were charged to examine four major areas: what kind of research should be done, what kind of services should be made available, what kind of education should health-care professionals have about CAM and how can the public best get the authoritative info about these therapies. We expanded from the four areas to include how CAM can contribute to health promotion and wellness. We are not here to ratify any particular kind of alternative therapy but to set the ground rules by which Americans will have available those things that are useful and know those things that are not. The commission's final recommendations will be coming out in March 2002.

Q What power will the report have?

A We will have a blueprint for some of the ways to integrate these approaches into health care for everybody. We hope to have specific suggestions for federal agencies and the basis for Congress for a legislative agenda. Whether that agenda will be enacted will depend on what the American people want. I suspect there will be significant legislation. There is tremendous bipartisan support and from the Bush administration.

Q What is CAM?

A CAM is everything not taught in medical schools. We can divide them into mind-body practices: relaxation, yoga, qigong; nutritional therapies: supplements, diets; manual therapies: massage, chiropractic, osteopathy; energy therapies: acupuncture, light or magnet therapy; herbal therapies; and traditional systems: Chinese, Ayurvedic, Orisha.

Q What types of therapies are best for what illnesses?

A Start with therapies you can use for yourself and integrate them into your life on an ongoing basis. For example, mind-body therapies, physical exercise and good nutrition should be part of everybody's care. Realize you can do something for yourself no matter the illness and take responsibility for your health. Another is group support, which is very powerful for chronic pain, cancer and heart disease. Massage is great for premature infants and for people with serious illnesses. It increases blood flow and improves joint function, relaxation and mood. In cancer, use of traditional Chinese herbal therapies with chemotherapy and radiation in some studies seemed to show improved quality of life and has helped people to live longer. Herbal therapies enhance the body's capacity for self-healing; conventional cancer therapy destroys the cancer cells. They work in different ways, which can be complementary.

For most acute emergencies, conventional medicine is great. If you have a broken bone, you need someone who can set the bone. If you've been hit by a car, you'd better have a good surgeon. For most chronic illnesses, we don't have successful treatments, and that's where CAM has been used more and more. The most fundamental principle is that we have to individualize treatment. It may be different at different times.

Listening to people has opened up our perspective on what medicine is and can be. One day medicine will have a bigger definition, but enlarging medicine is not an easy process.

Q What is the reaction from the American Medical Association and established traditional medical practitioners?

A Much of the concerns revolved around making sure that the information provided to the public is authoritative and accurate. The medical

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establishment recognizes the importance of these approaches and the huge numbers of Americans using these therapies, especially people with serious illness, such as cancer.

Q What are the misconceptions about CAM?

A Some physicians feel none of these therapies should be used together with conventional treatment, which is based on a lack of understanding. Some people feel these therapies are harmless and they don't interfere with conventional therapies. For one, just because it's natural, it's safe. That's not true because there are natural poisons as well.

Q What types of CAM users should we be concerned about in this regard?

A Whether 2 out of 10 or 4 out of 10 Americans use it, we should be concerned about everybody. People need to know what they are putting into their mouths, and what they are doing with their bodies and their minds, whether they are using CAM once or daily. The most important thing is that there be good and accurate information.

Q Are you trying to regulate the products or services or the people dispensing them?

A There needs to be a guarantee and periodic monitoring of manufacturing. The FDA already has the authority to enforce good manufacturing practices but it's not happening yet. Providers supplying inferior products will have to be made accountable. There needs to be better reporting of adverse events such as bad reactions to a substance. It's up to the state to license service providers. We are talking about whether there should be national guidelines about licensing the different professions and certifications.

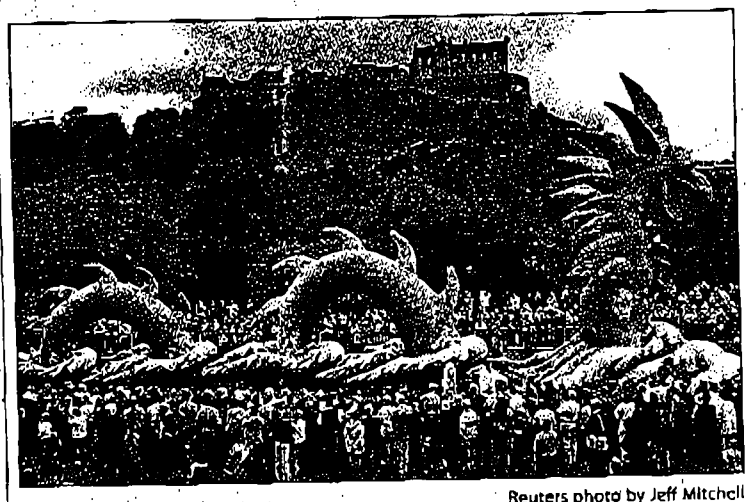
Q Who is going to have the authority to enforce the legislation?

A The Food & Drug Administration has some authority. The Federal Trade Commission has authority on advertising claims. In some cases, they need the funds to do the enforcement. In other cases, they may need new positions.

This is an edited transcript.

NEWS QUIZ

By Susanne Fowler



Reuters photo by Jeff Mitchell

Dragon and all, this lively cavalcade celebrated: A. China's entry into the World Trade Organization B. China's entry into NATO C. China's entry into the Society for Professional Journalists D. The start of the Edinburgh Festival

1. President Bush said stem cell research should:
   A. Proceed at all costs
   B. Be stopped at all costs
   C. Continue, but with restrictions
   D. Be studied exclusively at the University of Chicago

2. The biggest study of its kind said diet and exercise may stave off:
   A. Hernias
   B. Herniated disks
   C. Disk errors
   D. Diabetes

3. This shut down the Dan Ryan at morning rush:
   A. Running of the Bulls
   B. Flooding
   C. Hazardous materials
   D. An oil spill

4. Illinois officials say Chicago has one too many:
   A. Neighborhood festivals
   B. Charter schools
   C. Wrought-iron fences
   D. Baseball teams

5. At first, Mayor Daley said Millennium Park is costing so much because:
   A. His friends charge too much
   B. The architect charges too much
   C. It will be such a great cultural attraction
   D. Parks are darned expensive.

6. Norma "Duffy" Lyon is getting a pat on the back for:
   A. Founding the Lyons Club
   B. Sculpting the butter cow
   C. Heading the Peace Corps
   D. Directing the Lincoln Park Zoo

7. Gov. George Ryan announced that he:
   A. Will seek re-election
   B. Will not seek re-election
   C. Will seek re-election as an independent
   D. Is hiding from the licensing scandal

Who are they?

8. Dorothy and Gwen Hennessey

The answers:

Photo: In the shadow of a famed Scottish castle, the parade launched the annual Edinburgh festival.

1. Continue, but with restrictions, and be studied by a panel led by a U. of C. expert. 2. Diabetes. 3. A spill of toxic chemicals that released a vapor cloud and closed the expressway. 4. The Illinois State Board of Education says Chicago exceeds its quota of two charter schools. 5. Acknowledging the cost overruns, Daley at first blamed the architect. 6. She is being honored for having sculpted a cow out of butter for 80 Illinois State Fairs. 7. Ryan said he will not seek re-election, and did not mention the driver's license scandal. 8. Sibling nuns, ages 68 and 88, imprisoned in Pekin, Ill., for protesting at a military school.

Readers may send NewsQuiz e-mail to sufowler@tribune.com

Bill Fletcher contributed.

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■ AUGUST 2001 VOLUME 3, NUMBER 8 ■

ONCOLOGY

Black Cohosh and Hot Flashes in Breast Cancer Survivors

by Catherine Downey, ND

Jacobson et al recently studied the effect of *Cimicifuga racemosa* (black cohosh), a plant native to the eastern United States and Canada, on the frequency and intensity of hot flashes in women with a history of breast cancer. A substantial proportion of these women report experiencing hot flashes, but many are reluctant to take hormone replacement therapy. Black cohosh was recently included in the American College of Obstetricians and Gynecologists guidelines for botanical management of menopause (see p. 64). This study, a two-arm randomized, double blind, placebo-controlled trial, was intended to review whether the benefits seen by members of the general population when consuming therapeutic doses of black cohosh would also be seen in women with a history of breast cancer. The study looked at the effects of black cohosh or placebo on 85 women, 59

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BUSINESS/POLICY

White House Commission on CAM Policy

Understanding Coverage and Reimbursement: May 14, 15
Research Challenges: May 15, 16

The final hearing of the White House Commission on CAM Policy (WHC-CAMP) focused on topics of reimbursement and research.

Reimbursement

Financing of CAM is a central issue for insurance and managed care plans, as well as for state and federal healthcare policy-makers. Testimony opened with presentations from a number of groups including HCFA, the National Conference of State Legislatures, the American Association of Health Plans, various insurers and health plans, and several foundations and healthcare policy groups. Five key issues related to reimbursement of CAM products and services were identified:

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Cost Issues

Documentation of the cost effectiveness of CAM and resultant cost offsets in increased worker productivity and reduced use of conventional medical services is the most effective tool in convincing insurance and managed care to offer CAM services. The "cost neutral" policy of healthcare decision-makers will be more pronounced in the coming year as substantial increases in core insurance premiums are predicted.

A central tenet of insurance premium setting is that about 80 percent of those insured will not use services for which coverage is offered or directly provided. With an estimated 40 percent of consumers using CAM, the complexity of estimating premiums is heightened beyond the capacity of most insurance actuary groups.

Policy Issues

Added to the barrier of cost are reimbursement problems related to the question of collective vs. individual responsibility in healthcare; generalized individual and institutional resistance to change; potential conflicts of interest among benefit policymakers who also practice conventional medicine; the lack of CAM expertise on public and private insurance policy boards; and regulatory barriers to classes of practitioners.

Coding Issues

A central concern of several presenters was the lack of appropriate coding for CAM procedures. The larger problem is an inability to capture the nature of CAM practitioner-patient interactions using codes. There is no agreed-upon mechanism for developing codes to reflect even the mechanics of CAM services. Without this basic component of reimbursement, implementation of CAM coverage policy is certain to be difficult.

Political Issues

CAM practices and services cut across the entire system and are therefore affected by complex social and financial considerations within the healthcare system itself. Private reimbursement policy makers must, in the words of Alan Korn of Blue Cross Blue Shield Association of America, "maintain open, consistent, and defensible business practices." At the same time, they need to be concerned about potential problems of liability.

Issues of Consumer Demand

It was reported that 70 percent of consumers want health insurance coverage for CAM and 78 percent want more research on CAM. Twelve states are currently working to develop "health freedom laws" that would allow greater access to CAM providers; this could significantly expand demand for CAM services and reimbursement. Federal tax and social program policy, now in development, will also affect the potential for CAM services reimbursement.

Given this interest and the related issues, the Commissioners made a number of proposals, as shown in Table 1 below.

Table 1: Commission Proposals on Reimbursement

1. Require NIH and/or the AHRQ to develop a web-site focused on the scientific evidence for CAM and promote site to insurers and other healthcare financing policy groups.
2. Develop publicly financed demonstration projects that evaluate different strategies for reimbursement for CAM products and services.
3. Instruct the Health Care Financing Administration to evaluate CAM for clinical outcomes and its impact on use of other medical services.
4. Offer tax credits to businesses that provide services to employees that reduce health risks and increase wellness.
5. Encourage large employers, perhaps through grants, to collect utilization and outcome data on CAM and to undertake demonstration projects equivalent to those done by the public sector (see #2 and #3 above).
6. Support inclusion of CAM experts on reimbursement policy advisory boards.
7. Require broad-based public education on CAM services and practices.

Research

The May meeting continued with presentations from several foundations active in CAM research including the Robert Wood Johnson Foundation, followed by speakers representing the Agency for Healthcare Research and Quality (AHRQ), the National Library of Medicine, and NCCAM. These were joined by representatives from CAM programs at several conventional and CAM academic medical centers, the Cochrane Collaboration, and a number of medical journals such as the *New England Journal of Medicine, JAMA, Alternative Therapies in Health and Medicine,* and the *Journal of Alternative and Complementary Medicine*. Three key areas identified were:

Infrastructure. The current state of CAM research requires creation of basic infrastructure support, both public and private, for institutions and individual researchers.

Collaboration. Researchers need to seek collaboration with CAM providers and/or educators. Funding administrators and established researchers need to have both didactic and experiential exposure to CAM practices.

Attitude. A major issue for most research institutions vis a vis CAM has to do with attitudes, which can range from excess enthusiasm to significant hostility.

While the October 2000 WHC-CAMP research meeting was retrospective, focusing on descriptive reports from institutions that had developed CAM clinical and/or research initiatives, the May meeting was forward-looking, highlighting areas of concern and requirements for further development of CAM research. Some of the major research issues discussed were the need to:

- Establish acceptable levels of evidence for CAM practices.
- Ensure that available research methodologies are adequate for the investigation of CAM.
- Invest in basic science research in the field of CAM. The mechanism of action for many CAM practices is not well-understood, as exemplified by the case of homeopathy.
- Address safety issues related to herbs. Specific topics included lack of adverse event reporting, product labeling inaccuracies, herb-drug interactions, and deficiencies in FDA oversight. There were calls for repeal of DSHEA, with others suggesting that the law should stand but with amendments.

In terms of recent developments in

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Stroke

continued from previous page

dence is "probably rare," such events may include severe neurological complications of the sort mentioned in the Rothwell et al and Stevinson et al studies.

Discussion

Strokes are tragic events; no analysis of data can minimize their impact on the affected individuals. In exceedingly rare instances, SMT can trigger a stroke. Incidents of apparent post-SMT stroke often receive substantial attention in both professional and lay media. The Rothwell et al study, the first to utilize a control group in its analysis of post-SMT stroke, has generated such publicity. The appropriately cautious conclusions of the authors have been overshadowed by stories reporting that the Rothwell et al study demonstrates an incidence of post-SMT stroke much higher than previous estimates. Even the editorial (Bousser) accompanying the Rothwell et al article asserts that VBA incidence in the Ontario study "is far more than the one case per million generally believed."

In fact, it is about the same: The million in the commonly cited "one in a million" figure refers to the number of cervical manipulations (estimated at 10 per case), not the number of persons treated. Rothwell et al's conclusion that the incidence of VBA in Ontario is 1 per 100,000 persons treated with SMT actually turns out to be the same as 1 per 1 million manipulations. So in fact, Rothwell is confirming previous estimates.

Moreover, the inference that strokes may be associated with neck manipulation within the previous week (using a methodology comparing patients with post-SMT strokes with a control group) is drawn from a total of five individual cases, occurring over a 6-year period.

Although the data from this small number of incidents does indicate a fivefold increase in likelihood of stroke for those younger than age 45 who visited a chiropractor in the week preceding the stroke, direct causation cannot be inferred from this data. The correlation may indicate that certain patients on the verge of a stroke visited a chiropractic practitioner because they were experiencing symptoms such as neck pain or headaches. Until a study evaluates the Ontario data to determine the number of stroke patients who visited other types of practitioners in the week before their VBAs, it is premature to conclude that chiropractic treatment was the causal factor. For example, if the rate of stroke among those who visited a neurologist and did not receive spinal manipulation was equal to or higher than the rate of stroke among those who visited a chiropractor, assumptions about manipulation causing the strokes would be seriously weakened.

Dan Redwood, Consult advisory board member, has written extensively on chiropractic.

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CAM Policy

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CAM research, the most significant were those described by the NCCAM and AHRQ. NCCAM program officers reviewed the substantial investment being made in research training for both institutions and individuals. The AHRQ's CAM representative described the basic survey reports and outcome studies the agency has supported, as well as recently released and planned evidence reports. These publications are frequently used by medical specialty societies as the basis for practice guidelines, and thus may influence large numbers of conventional practitioners' perspectives on CAM.

Table 2: Recommendations for Research

1. In the short term, conventionally trained researchers should be sent to CAM schools to teach research methodology.
2. NCCAM should be directed to develop technical and financial research methodology curriculum support for faculty of CAM colleges.
3. For projects that focus on evaluation of research literature in CAM, collaboration with CAM practitioners should be encouraged.
4. Peer-reviewed journals should enlist CAM practitioners or experts for their review boards.
5. NCCAM should publish an electronic or print journal similar to the Office of Dietary Supplement at NIH's "Year's Best" research.
6. All federal healthcare agencies should put CAM research information on their websites.
7. The NCCAM website should list contact names for foundations with interests in CAM.
8. A federal group should be developed to coordinate public-private research.
9. Foundations should pool their resources to fund one or more large CAM project.
10. Resources should be devoted to informing the public about research findings.

At the conclusion of testimony, the Commissioners outlined a number of recommendations to address research challenges, as shown in Table 2.

The testimony received during the public comment period at the end of the 3-day meeting largely focused on support for the Commission's recommendations. It included presentations from CAM practitioners, dietary supplement manufacturers, and several CAM specialty societies, associations, and colleges. *Visit the Commission at:* **www.whccamp.hhs.gov**

This article was adapted from a longer report prepared by Hannah V. Bradford, CAM Communications and Reports. She can be contacted by email at **hvbradford@cs.com**