# Complementary and alternative medicine: the convergence of public interest and science in the United States

*CAM research is leading to changes in the vitamin cabinet and the clinic*

Many Americans use one or more health promotion, illness prevention or healing practices that are considered as complementary and alternative medicine (CAM).[1] In recognition of this, the United States Congress legislated in 1991 to establish the Office of Alternative Medicine to "investigate and evaluate promising unconventional medical practices". In 1998, Congress expanded this mandate by enacting legislation that created the National Center for Complementary and Alternative Medicine (NCCAM), endowing it with the resources and authority to fund research, train researchers, and disseminate information to the public and healthcare professionals.

A number of factors contributed to the creation of NCCAM. First was the popularity of unproven medical practices, with users of one or more CAM modalities tending to be women, people with higher education, those with an interest in the role of the mind in health, or those with some chronic illness.[2] Second was an increasing recognition of the importance of traditional healing practices among an ethnically diverse American population. Third, in 1994, the US Congress passed legislation that permitted wide access to dietary supplements without confirmation of their composition, safety or efficacy, and a concomitant loosening of legal restraints on alternative practices such as chiropractic medicine and acupuncture.

## Setting priorities — science first

Given the diversity of CAM approaches and questions about their safety and efficacy, setting research priorities for NCCAM is a significant challenge. The US$117.7 million allocated to NCCAM in 2004, while generous by most standards, permits only a limited sampling of possible CAM approaches. To develop its approach, NCCAM sought input from diverse communities of stakeholders. The resulting first strategic plan stressed investment in basic and clinical research, training, dissemination of findings, and integration of safe and effective practices.[3] NCCAM made a commitment to aspire to the same rigorous standards that characterise National Institutes of Health (NIH) research in general, while its research priorities would focus on the most promising scientific opportunities. As NCCAM celebrates its fifth anniversary, it is possible to list its not inconsiderable achievements to date (see Box 1), and to reflect on some of the lessons learned for current and future directions.

### Investing in research centres

To create a sustainable research infrastructure, NCCAM funded a first generation of research centres spanning a range of health disorders and disciplines. Based on formal reviews, a second generation of more focused centres is being developed. Some of these are involved in elucidating mechanisms of action of CAM therapies. Others promote collaborations between CAM and conventional institutions. Still others represent new initiatives to forge scientific partnerships between investigators at US and foreign institutions.

**1 Activities of the National Center for Complementary and Alternative Medicine in its first 5 years**

- It built a centre responsive to its mission and integrated into the other institutes at the United States National Institutes of Health
- It funded over 780 projects at 123 institutions, resulting in over 700 scientific publications
- It awarded more than 100 individual doctoral and postdoctoral training and career awards
- It enrolled nearly 40 000 participants in clinical protocols
- It received over 1.5 million visitors to the website <www.nccam.nih.gov> each year who search for information about CAM, clinical trials, and research opportunities
- It developed a database known as "CAM on PubMED" that lists nearly 400 000 articles on CAM-related subjects published in 45 languages from 70 countries
- It informed public policy, patient choice, and clinical practice through outreach activities, including public town meetings, public media, and scientific and professional conferences

### Botanical trials — overcoming obstacles

When NCCAM was created, it was assumed that existing literature on herbal supplements would be sufficient to justify and design major studies of their safety and efficacy. It quickly became apparent that many botanical preparations are not standardised, and may be contaminated with heavy metals or drugs,[4] precluding the conduct of meaningful and ethical studies.

As a result, NCCAM is now working with academic and industrial partners to identify more optimal research-grade materials, and requires evidence of product quality for all its sponsored research. These approaches raise the quality of the studies, but consume time and resources.

### Phase III clinical trials — balancing pressure for progress

The results of NCCAM's very first large clinical trial dictated a more deliberate and phased approach for future studies, even when high quality products are available. The three-arm randomised controlled trial failed to show that *Hypericum perforatum* (St John's wort) ameliorates major depression.[5] Advocates for the product faulted the study for having addressed too serious a form of depression. While the target population, the product, its dose, and endpoints had been thoroughly discussed, it was ultimately clear that more preliminary research and consensus development was needed to determine the optimal design of other large trials.

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**2 Status of National Center for Complementary and Alternative Medicine Phase III Clinical Trials**

| Complementary and alternative medicine modality | Target disease | Sample size | Status | National Institutes of Health Partner |
|---|---|---|---|---|
| Acupuncture | Osteoarthritis | 570 | Trial complete; analysis underway | NIAMS |
| Glucosamine/chondroitin | Osteoarthritis | 1 588 | Enrolment complete; ongoing | NIAMS |
| Ginkgo biloba | Dementia | 3 073 | Enrolment complete; ongoing | NINDS, NIA, NIMH |
| Shark cartilage | Lung cancer | 756 | Patients enrolling; ongoing | NCI |
| Vitamin E | Prostate cancer | 32 400 | Enrolment complete; ongoing | NCI |
| St John's wort | Minor depression | 300 | Patients enrolling; ongoing | NIMH, ODS |
| EDTA chelation therapy | Coronary artery disease | 2 372 | Patients enrolling; ongoing | NHLBI |
| Saw palmetto | Benign prostatic hyperplasia | 2 860 | Final protocol under development | NIDDK, ODS |

NIAMS = National Institute of Arthritis and Musculoskeletal and Skin Diseases; NINDS = National Institute of Neurological Disorders and Stroke; NIA = National Institute on Aging; NIMH = National Institute of Mental Health; NCI = National Cancer Institute; ODS = Office of Dietary Supplements; NHLBI = National Heart, Lung, and Blood Institute; NIDDK = National Institute of Diabetes and Digestive and Kidney Diseases.

Such efforts are being made now in trials of *Ginkgo biloba* for cognitive decline in the elderly, and glucosamine for osteoarthritis. Each of these, and other ongoing trials (Box 2), are being conducted with input from relevant communities of patients, practitioners and scientists, and cofunded by other NIH institutes.

### Brain–mind–body medicine — an emerging science

The capacity of the brain and mind to affect health is a CAM domain that is receiving more attention at NCCAM. Surveys indicate that about one in five adults use at least one mind–body therapy.[6] Functional neuroimaging provides powerful new tools to identify changes in brain structures involved in generating emotional responses, interaction of distress and pain, and response to treatment. With this and other new laboratory and ambulatory methods, NCCAM is funding investigators to identify pathways of influence, and to test interventions, such as meditation in preventing illness, slowing disease progression and promoting well-being.

## Planning for the future

Lessons learned at NCCAM forecast a future with a greater emphasis on preclinical and early-phase clinical studies that are designed to elucidate mechanisms, identify optimal dosing and schedules, and select appropriate target populations and control conditions before launching clinical trials. Clinical studies at all levels are increasingly being conducted as collaborative efforts between funded investigators and NCCAM staff, who provide technical guidance, from sophisticated design and statistical consultation, to advice on recruitment and retention. Research on natural products is being conducted within a framework in which NCCAM either provides well-characterised and standardised clinical trial materials for investigators to use, or tests products being used by investigators to assure characterisation and standardisation. Finally, NCCAM is taking full advantage of new technologies, from genomics to brain imaging, and applying them to new areas, such as the capacity of the mind to affect health, in its multidisciplinary research.

While NCCAM first built a domestic scientific constituency, it seeks to engender and strengthen relationships with other countries that have both established research in conventional medicine, and a tradition that is rich in indigenous practices. We invite scientific leaders in these countries to join the global CAM research effort.

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