

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CENTER FOR COMPLEMENTARY
AND ALTERNATIVE MEDICINE**

**NATIONAL ADVISORY COUNCIL FOR COMPLEMENTARY
AND ALTERNATIVE MEDICINE
MINUTES OF THE FORTY-FIRST MEETING
February 4, 2011**

NACCAM Members Present

*Dr. Brian Berman, Baltimore, MD
Dr. Gert Bronfort, Bloomington, MN
Dr. Adam Burke, San Francisco, CA
Dr. Lupo Carlota, Memphis, TN
*Dr. Daniel Cherkin, Seattle, WA
Dr. Gary Curhan, Boston, MA
Dr. Steven DeKosky, Charlottesville, VA
Dr. Stephen Ezeji-Okoye, Palo Alto, CA
Dr. Susan Folkman, San Francisco, CA
Dr. Janet Kahn, Burlington, VT
*Dr. David Kingston, Blacksburg, VA
Dr. Shin Lin, Irvine, CA
*Dr. James Michener, Durham, NC
Dr. Richard Niemtzw, Clinton, MD
Dr. Katherine Shear, New York, NY
Dr. Herman Taylor, Jackson, MS
Dr. Xiaoming Tian, Bethesda, MD

*Ad-hoc

NACCAM Members Not Present

Dr. Timothy Birdsall, Goodyear, AZ

NIH Staff Present

Mirian Alkliddar, OCCAM, NCI
Francis Collins, NIH
Judy Dulovich, OHR, OD, NIH
Seymour Garte, DPPS, CSR, NIH
Robert Kaplan, OBSSR, NIH
Linda Southworth, CM, NCI
Anne Tatem, OLPA, OD, NIH
Dan Xi, OCCAM, NCI

Members of the Public

Tyler Cymet
Steven Dentali
Anthony Dinoto
Jeffery Dusek
Shin Hyoung Joo
Michelle Keown
Annette Kornblum
Colleen McEachern
Bilinda Straight
Evelyn Williams
Samuel Williams

I. Open Session—Call to Order

The open session of the National Advisory Council for Complementary and Alternative Medicine (NACCAM) meeting convened at 8:30 a.m. Dr. Martin Goldrosen, NACCAM Executive Secretary, called the meeting to order. After Council members introduced themselves, Dr. Josephine Briggs, Director of the National Center for Complementary and Alternative Medicine (NCCAM), introduced Dr. Francis Collins, Director of the National Institutes of Health (NIH).

II. Report From the NIH Director

Dr. Collins thanked Council members for the opportunity to address them and expressed his support for NCCAM's work. With 40 percent of Americans using complementary and alternative medicine (CAM), it is critical to determine which forms of CAM have the greatest value and to protect the public against unanticipated side effects. Dr. Collins cited two examples of situations in which science has learned from traditional medicine: the drug artemisinin, which was derived from a Chinese herb, *Artemisia annua* and is now a mainstay of malaria treatment, and silymarin, an extract of the herb milk thistle, which NCCAM is currently studying as a possible treatment for hepatitis C. He also expressed interest in the recent randomized trial of tai chi for fibromyalgia, which would be discussed in detail later in the day.

NIH is devoted to both the pursuit of fundamental knowledge and the application of that knowledge to benefit human health. Discoveries related to the molecular basis of diseases have proliferated in recent years, but more needs to be done to optimize the translation of these discoveries into clinical practice.

NIH contributes to the translational pipeline in multiple ways, including the Molecular Libraries Initiative, the Therapeutics for Rare and Neglected Diseases program, the Clinical and Translational Science Awards network, clinical trials at the NIH Clinical Center, and cooperative regulatory science efforts with the U.S. Food and Drug Administration (FDA). In October 2011, NIH will launch the National Center for Advancing Translational Sciences (NCATS), which will bring together existing and new programs to facilitate translational research across NIH.

NIH is increasingly emphasizing another part of the translational agenda, comparative effectiveness research (CER), because of the interest in health care reform. In 2009, the Institute of Medicine identified 100 priority topics for CER; NIH is now conducting research on all of

them. The Patient-Centered Outcomes Research Institute (PCORI), a new nonprofit corporation to organize and fund CER, is expected to become a major contributor to CER. CAM was explicitly included in the design of PCORI's mission.

NIH currently faces difficult challenges in terms of funding. The temporary boost from the American Recovery and Reinvestment Act has ended; funding has reached a plateau and may decrease, limiting NIH's ability to support new research. Therefore, everything NIH does must be subjected to closer scrutiny, and some of the investments that NIH would like to make may not be possible. The tight funding situation puts particular pressure on advisory councils such as NACCAM to identify exceptional opportunities that might not otherwise be funded.

Discussion. Dr. Briggs commented that many of Dr. Collins' points are especially relevant as NCCAM rolls out its new strategic plan. She highlighted CAM approaches to symptom management and the contributions of CAM to Americans' search for wellness. Dr. Collins agreed that enthusiasm for wellness is growing and expressed the hope that NIH can help pull together work in this area. Dr. Briggs noted the interest among those in military settings in CAM approaches to symptom management and wellness and explained that NCCAM is working with military partners to incorporate science into their real-world experience. Dr. Collins thanked Dr. Briggs for her leadership of NCCAM and other contributions to NIH and thanked NCCAM Deputy Director Dr. Jack Killen and the NCCAM staff for their work.

III. Closed Session

The second portion of the 41st meeting of NACCAM was closed to the public, in accordance with the provisions set forth in Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S.C., and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

A total of 197 applications were assigned to NCCAM. Of these, 50 were reviewed by NCCAM, 147 by Center for Scientific Review. Applications that were noncompetitive, not discussed, or were not recommended for further consideration by the scientific review groups were not considered by Council.

Council agreed with staff recommendations on 108 applications, requesting \$55,965,823 in total costs.

IV. Reconvened Open Session

The open session of the NACCAM meeting reconvened at 11:05 a.m.

Minutes from the September 3, 2010, Council meeting were unanimously approved.

Dr. Goldrosen explained the procedures for public comment and announced that the next NACCAM meeting would be held on June 3, 2011.

V. Report From the NCCAM Director

The Third Strategic Plan

Dr. Briggs and Dr. Killen presented highlights of NCCAM's new strategic plan, which was released that day, and explained how the plan was developed. The starting point was NCCAM's legislative mandate, which calls for the study of the integration of complementary methods into health care delivery systems in the United States but allows much discretion in choosing priorities for investigation, thus making strategic planning critical. In the early years of NCCAM, the focus was on bringing rigorous methodology to the evaluation of CAM practices. However, the current emphasis on the importance of outcomes and effectiveness research has prompted new priorities in strategic thinking.

The development of the strategic plan took 15 months and involved workshops or think tanks on a wide variety of topics, high-level review of the intramural research program, publication of white papers, and opportunities for public comment. Council played a key role in creating the strategic vision outlined in the plan. Public interest was high; almost 3,600 comments were received in response to position papers and the draft plan posted on the NCCAM Web site.

Key elements of the plan include new mission and vision statements and three broad goals: (1) to advance the science and practice of symptom management; (2) to develop effective, practical, personalized strategies for promoting health and well-being; and (3) to enable better evidence-based decisionmaking regarding CAM use and its integration into health care and health promotion.

NCCAM hopes to leverage real-world situations as natural experiments by, for example, collaborating with military partners to explore the utility of CAM approaches as complements to conventional strategies for pain management and treatment of posttraumatic stress disorder. The intent is to learn as much as possible about what is happening in the real world while maintaining scientific rigor and using good methodology.

As has been discussed with Council, NCCAM plans to further increase its focus on outcomes and effectiveness research and translational research. Clinical trials will remain important, but before they are conducted, it is necessary to have sufficient understanding of biological mechanisms, thus making it possible to incorporate biomarkers or other objective measures into the trials.

The new strategic plan sets a structure for priority setting, with an activist Advisory Council and energetic debate about how NCCAM can best use the taxpayer's dollars. Criteria for priority setting, for both investigator-initiated projects and major initiatives, will include the following:

- *Scientific promise.* Is the scientific evidence sufficient to support the scope and direction of the proposed research? Does reasonable evidence support the potential of the proposed research to benefit human health?
- *Amenability to rigorous scientific inquiry.* Are the key research goals achievable? Are the potential research approaches feasible and scientifically plausible, and do they lend themselves to rigorous quality control?
- *Potential to change health practices.* Is it reasonably likely that the results of the research could lead to changes in the health practices of consumers or health care providers? Could the results lead to changes in the decisions made by health policymakers?

- *Relationship to use and practice.* Does the proposed project address an important public health concern or scientific information need regarding the efficacy, safety, or public use of CAM?

Discussion. Discussion of the strategic plan focused on the broader concept of healing and the importance of patient-practitioner interaction, the use of CAM modalities as probes to elucidate biology, the potential value of electronic health records for research, and the issue of cultural competency and its relationship to health disparities. Dr. Briggs clarified that NCCAM collaborates extensively with other NIH institutes and centers (ICs) and that all major NCCAM clinical trials are cosponsored with the IC that specializes in the condition under investigation.

NACCAM, NCCAM, and NIH News

Dr. Briggs introduced four new ad hoc Council members: Drs. Brian Berman, Daniel Cherkin, David Kingston, and J. Lloyd Michener.

Dr. Jeremy Berg is departing as Director of the National Institute of General Medical Sciences. Dr. Amy Patterson has been appointed Associate Director for Science Policy, NIH.

The NIH Scientific Management Review Board has recommended (1) creating NCATS and (2) merging the overlapping portfolios of the National Institute on Drug Abuse and the National Institute on Alcohol Abuse and Alcoholism.

Dr. Briggs introduced six new NCCAM staff members to Council: Dr. Kristen Huntley, program officer in the Division of Extramural Research (DER); Richard Kotz, biostatistician in the Office of Clinical and Regulatory Affairs (OCRA); Jean Bérubé, legislative liaison in the Office of Policy, Planning, and Evaluation (OPPE); Dr. Nilesh Kalyanaraman, AAAS fellow in OPPE; Dawn Wayman, program analyst in DER; and Marcella Canada, lead administrative officer in the Office of Administrative Operations. Two staff members have recently left NCCAM: Dr. Michael Quon, Division of Intramural Research, and Dr. Sheila Caldwell, DER.

FY 2011 Budget

NCCAM is operating at 2010 budget levels under a continuing resolution until March 4, 2011. Dr. Briggs presented information on the fiscal year (FY) 2010 budget and on appropriations planned for FY 2011 but noted that the budget for FY 2011 could be significantly lower than indicated. NIH has tried to honor all commitments made to existing grant awards, but in situations of flat or decreasing budgets, inflationary adjustments will not be made. NCCAM's commitment to ongoing (noncompeting) projects has risen this year, and as a consequence, funds available for new awards have decreased. In response to a question from a Council member, Dr. Briggs clarified that collaborations with other ICs can result in funds either coming into NCCAM or going out, depending on which IC is administering the project. There is some funding flexibility for intramural projects, as well as possible opportunities for collaboration in intramural research, and NCCAM anticipates funding two or three intramural pilot projects.

Legislative Update

Dr. Briggs recently briefed Senator Tom Udall (D-NM) on NCCAM activities and was the keynote speaker at a town hall-style Complementary and Alternative Health Care Conference sponsored by Senator Bernie Sanders (I-VT).

Research and Outreach Updates

NCCAM is working closely with the HMO Research Network to enhance the potential of this organization to perform large-scale CER, cluster randomization, and biospecimen collection studies in addition to its current research portfolio.

A recent study showed lower vaccination rates of children in families with heavy use of CAM; this finding is an important cause for concern. NCCAM is working with colleagues across NIH to address vaccine safety issues, discussing these issues with CAM professional groups, and developing Web site materials on this topic.

Dr. Briggs briefly highlighted recent research on the benefits of various types of support for cancer patients, the use of echinacea to treat the common cold, and the use of placebos without deception. A recent study of red yeast rice prompted safety concerns about this supplement; NCCAM prominently featured information about the study findings on its Web site. The Agency for Healthcare Research and Quality just completed an NCCAM-commissioned report on the use of CAM for back pain, which provided an assessment of current knowledge and confirmed that the evidence is incomplete. A full bibliography of NCCAM's research portfolio will be provided at the June 2011 Council meeting.

Dr. Briggs reviewed her recent outreach efforts, including presentations to the Association of American Medical Colleges Annual Meeting, the American Heart Association Scientific Sessions, the Defense Health Board, the Leonard P. Zakim Center for Integrative Therapies of the Dana-Farber Cancer Institute, the Research Centers in Minority Institutions International Symposium on Health Disparities, and a conference on integrated health care reform at Georgetown University. Dr. Vikas Sukhatme of Harvard Medical School presented the Second Annual Stephen E. Straus Distinguished Lecture, focusing on metabolic hypotheses for the mechanisms of action of traditional therapies. NCCAM will be the lead IC for a conference on omega-3 fatty acids later in February 2011 and will cosponsor a conference on vitamin E in May 2011.

Discussion. Members noted the increasing prominence of NCCAM in national forums. Dr. Briggs commented that NCCAM is articulating problem areas that are attracting public attention, such as the inadequacy of current approaches to pain management. In response to a question about whether public opinion of the value of NCCAM has changed, Dr. Killen expressed the view that NCCAM and the Council should focus on being responsible stewards and promoting rigorous science, rather than devoting too much attention to criticisms from NCCAM's very diverse constituency. Members observed that NCCAM's increasing ability to develop partnerships, both with other ICs and with organizations outside NIH, is encouraging.

VI. Council Operating Procedures

Dr. Goldrosen reviewed Council operating procedures, including processes for NCCAM reports to Council, secondary review of grant applications, approval of concepts for research initiatives, and handling of appeals from applicants.

Council unanimously passed a motion approving the operating procedures as presented.

VII. Oversight of Clinical Research

Dr. Catherine Meyers, Director of OCRA, presented the 2011 biennial report certifying compliance with NIH policy on inclusion guidelines for women and members of minority groups and reviewed NCCAM oversight of the clinical research portfolio. In FY 2009, women and minorities represented 52 and 17 percent, respectively, of enrollees in all NCCAM-funded clinical research and 46 and 5 percent, respectively, of enrollees in Phase III trials. In FY 2010, women represented 48 percent and minorities 19 percent of enrollees in all NCCAM-funded clinical research; NCCAM did not fund any Phase III trials in FY 2010.

NCCAM oversees clinical grants at both the pre-award and post-award stages. The pre-award oversight process focuses on maximizing scientific rigor and impact, as well as study feasibility, and engages NCCAM staff in careful dialogue with investigators. Post-award oversight includes regular assessment of enrollment and monitoring plans, annual progress reports, and a proactive approach to problems that develop as a study is conducted. The goals for NCCAM oversight are to minimize risk to participants; maximize the success, scientific potential, and impact of funded work; and maximize the productivity and relevance of NCCAM programs.

Council unanimously passed a motion approving the biennial report as presented.

Discussion. Dr. Meyers clarified that targets for female and minority enrollment are addressed individually for each project and that if enrollment goals are not met, remediation efforts are undertaken. NCCAM has not analyzed the geographic dispersion of participants in the studies it funds but could do so for studies that are currently enrolling participants. Dr. Briggs commented that a very high proportion of NCCAM-funded projects involve human subjects, and careful oversight of these projects is extremely important.

VIII. A Randomized Trial of Tai Chi for Fibromyalgia

Dr. Chenchen Wang, Associate Professor of Medicine at Tufts University School of Medicine, presented the results of her research group's NCCAM-funded randomized trial of tai chi for fibromyalgia. Fibromyalgia syndrome is a complex chronic illness affecting 2 percent of the total population, with women more likely to be affected than men. It is the second most common condition seen in rheumatologic practice in the United States. Fibromyalgia causes numerous physical and psychological changes, including widespread pain, functional impairment, fatigue, sleep disturbance, depression/anxiety/stress, poor self-efficacy, and poor quality of life, and it is a very difficult condition to treat.

Tai chi, a mind-body practice that originated in China as a martial art, combines slow, gentle, graceful movements with meditation, deep breathing, and relaxation. It is a complex, multicomponent intervention that integrates physical, psychosocial, emotional, spiritual, and behavioral elements. Tai chi was investigated as a possible treatment for fibromyalgia because systematic reviews of the scientific literature had indicated that tai chi may have both physical and psychological benefits for patients with a variety of chronic conditions.

The trial, which used a single-blind, randomized design and included 66 participants with fibromyalgia (diagnosed according to American College of Rheumatology criteria), compared classic Yang-style tai chi with a control intervention consisting of wellness education and stretching. Both interventions were delivered for 12 weeks in twice-weekly sessions, and 92 percent of participants completed the study. The tai chi group had clinically important improvements in scores on the Fibromyalgia Impact Questionnaire (a global assessment of

symptoms) sleep quality, depression and quality of life, with statistically significant differences between the tai chi group and the control group. Some participants experienced dramatic improvement and felt that tai chi had changed their lives. Improvements were maintained at 24 weeks (12 weeks after the intervention ended).

Dr. Wang and her colleagues concluded that tai chi may be a useful treatment for fibromyalgia and warrants longer term study in larger groups of people, both to assess the generalizability of the findings and to deepen understanding of this therapeutic modality. Limitations of the study included the participation of only one tai chi master and the lack of a double-blind study design. The researchers' future plans include developing appropriate controls for large trials, conducting comparative effectiveness and cost-effectiveness research, exploring brain and central nervous system mechanisms, and, eventually, establishing a multidisciplinary mind-body clinical research program.

Discussion. Dr. Wang clarified that during the 12 weeks of active intervention, participants were asked to practice tai chi (or, for the control group, stretching) for 20 minutes daily at home. Almost all continued to do so between weeks 12 and 24. Most participants in the tai chi group showed week-by-week improvement during the active intervention, but a few did not respond. In future studies, it would be desirable to learn what distinguishes responders from nonresponders. Other important subjects for future investigation include the importance of the practitioner and how best to assess the long-term effects of the intervention. Council members commented that this was an impressive study with remarkable and very encouraging results and noted the importance of studying mind-body medicine and self-care. Dr. Briggs commented that more studies that focus on symptom management (like this one) are needed.

IX. Interpreting the Evidence Supporting Intervention

Dr. Robert Kaplan, the newly appointed director of NIH's Office of Behavioral and Social Sciences Research, presented some personal insights on the application of clinical trial results, particularly from trials that focus on intermediate endpoints, to clinical practice. This topic is especially relevant now because revisions of practice guidelines on high blood pressure and high blood cholesterol are expected in 2011. Each new edition of these guidelines has tended to be more aggressive with regard to thresholds for initiation of treatment, with larger portions of the population being identified as candidates for surveillance each time the guidelines are updated. Not everyone agrees with this trend, however. Notably, guidelines in the European Union are more conservative than those in the United States, even though both are based on the same body of scientific evidence.

Pressure exists to generalize the results of clinical trials to populations who were not evaluated (for example, to use statin drugs in people without risk factors). At the same time, the definitions of "disease" keep changing to include larger numbers of people. Criteria are now so stringent that 97.2 percent of Americans qualify as abnormal in terms of blood glucose, blood pressure, and/or low-density lipoprotein cholesterol.

Mathematical models are widely used to predict the results of interventions, but models usually assume linearity, and the human body rarely responds in a linear way. Physiologists know that the human body is complex, with interacting systems, and that intervening on one system affects others. Modification of risk factors, such as blood pressure or blood cholesterol levels, may not produce predicted outcomes, such as reductions of the number of heart attacks and strokes. In

fact, changes in risk factors may have no effect on the outcomes of greatest importance: length of life and quality of life.

Many clinical trials have produced unexpected results. In most of these instances, an intermediate endpoint (such as blood pressure or blood cholesterol) indicated that aggressive treatment was beneficial. However, aggressive treatment either failed to increase the length or quality of life or produced poorer outcomes than those seen with less aggressive treatment (such as an increased rate of complications in the aggressive treatment group). A well-known example of a trial in which overall outcomes showed no benefit of intervention is the Physicians' Health Study. In this randomized, controlled trial, the use of aspirin by healthy men dramatically reduced heart attack deaths but had no effect on overall mortality. An example of a situation in which aggressive treatment led to improvement in an intermediate endpoint but poorer overall outcomes involves the management of anemia in patients with cancer or severe kidney disease. In these patients, aggressive treatment of anemia raised hemoglobin levels but led to an increased risk of serious complications, such as the need for dialysis.

Dr. Kaplan concluded his presentation by pointing out that aggressive care may not necessarily be the best care. There is still a place for randomized, controlled trials, but overall outcomes need to be considered, and the costs (including opportunity costs) of treating mild abnormalities should be taken into account.

Discussion. Dr. Briggs thanked Dr. Kaplan for his stimulating and provocative presentation and commented that she is struck by how often we do not know what we think we know. In response to Council members' questions, Dr. Kaplan clarified that when he described results for mortality in clinical trials, all of the deaths were premature deaths that occurred during the defined study period. One reason aggressive treatment may lead to poorer results is that treating only one abnormality may break down regulatory systems.

Electronic medical records may offer opportunities for new types of research that previously were impossible. Appropriate new statistical methodologies need to be developed for these studies.

The application of results of clinical trials to populations not included in the trials raises difficult ethical issues. For example, clinical trials have not shown statistically significant benefits of statins in women, although the trends are similar to those in men, and the lack of significance may reflect the smaller number of female participants in the trials. Some people have argued that it is unethical to give statins to women because confidence intervals for women cross 1.0, and therefore the scientific justification for the use of these drugs is inadequate. Others argue that it is unethical to not give statins to women because the trends are the same as those for men and women should not be denied this intervention because trials were underpowered. Similar dilemmas arise when applying results to other less-studied populations such as elderly people and members of minority groups.

X. Public Comment Session and Closing

Dr. Briggs opened the floor for public comment.

Dr. Jeffrey Dusek expressed approval of the new NCCAM strategic plan's emphasis on concepts, such as wellness, effectiveness, and outcomes, that relate to what happens in the real

world rather than what happens in randomized clinical trials. He also noted that the costs of CAM interventions need to be considered when decisions are made about their use.

The Reverend Samuel Williams of the House of David Ministries noted that he has been a minister for 25 years and has experience with exorcism. He recommended that exorcism should be studied scientifically and proposed a collaboration with NCCAM to investigate exorcism as part of a holistic approach to health care.

Dr. Briggs thanked Council members and adjourned the meeting at 4:00 p.m.

We hereby certify that, to be the best of our knowledge, the foregoing minutes are accurate and complete.

Martin Goldrosen, Ph.D.
Executive Secretary
National Advisory Council for
Complementary and Alternative
Medicine

Josephine Briggs, M.D.
Chairperson
National Advisory Council for
Complementary and Alternative
Medicine