Review for NCCAM Is Overdue

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he U.S. National Institutes of Health (NIH) were created by Congress to conduct research on the causes and treatment of common diseases. In contrast, the National Center for Complementary and Alternative Medicine (NCCAM) was created by pressure from a few advocates in Congress (1–3). The NCCAM budget for 2005 was $123.1 million. At a time when NIH support of biomedical research is decreasing (4) and many excellent grant proposals are not being funded, NCCAM’s expenditure of funds deserves scrutiny.

History of OAM and NCCAM

NCCAM began as the Office of Alternative Medicine (OAM) in 1992 (1–3). It was created within the office of the NIH director with a budget of $2 million by a directive from the Senate Appropriations Committee. The driving force behind the directive was Senator Tom Harkin (D–IA), chairman of the Appropriations Committee, a long-time supporter of NIH research and advocate for alternative medicine.

In 1997, Senator Harkin proposed that OAM become an independent center with direct authority to appoint peer-review panels and to award grants. Despite opposition to this proposal from prominent scientists, including former presidential science adviser D. Allen Bromley and Nobel laureates Paul Berg and Jerome Friedman (5, 6), NCCAM was created in 1998 with an initial budget of $50 million. In response to Harkin’s complaints that alternative medicine specialists were excluded from previous review panels, the new NCCAM charter stipulated that 12 of the 18 members of the NCCAM Advisory Council “shall be selected from among the leading representatives of the health and scientific disciplines ... in the area of complementary and alternative medicine. Nine of the members shall be practitioners licensed in one or more of the major systems with which the Center is involved” (7).

In 1999, Stephen Straus, a respected virologist and immunologist, and chief of the Laboratory of Clinical Investigation of the National Institute of Allergy and Infectious Diseases, was appointed director of NCCAM. He has stated frequently that alternative therapies can and should be evaluated by the same methodology used in clinical trials of conventional treatments (8). What kinds of studies has NCCAM funded?

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Clinical Trials Funded by NCCAM

A major emphasis of NCCAM’s first 5-year strategic plan was to perform phase III clinical trials of popular herbal medicines and other supplements to inform the public about their efficacy (9). Accordingly, the fraction of funds allocated to clinical research by NCCAM has been high, ranging from 80% in fiscal 2000 to 68% in 2004, compared with ~33% by the rest of NIH. The results of clinical trials of St. John’s wort, echinacea, and saw palmetto have been published (10–12), and none of these herbal medicines was more effective than the placebo controls. Although Straus has commented that “he for one is satisfied that echinacea is not an effective cold remedy” (13), spokesmen for the herbal and nutraceutical industries predictably responded that the studies were flawed and that more research is needed. It appears doubtful that these negative trials will change the practices of many people who use herbal remedies, given their belief in the healing power of natural products and their distrust of physicians, scientists, and the pharmaceutical industry. When regular users of dietary supplements were asked, “If a government agency said that the dietary supplement is ineffective, what would you do?,” 71% responded that they would keep using the supplement (14).

NCCAM’s strategic plan for 2005–09 (9) recognizes the lack of quality control of commercial herbal products, a problem that is a consequence of the Dietary Supplement Health and Education Act of 1994 (DSHEA), which markedly restricts the Food and Drug Administration’s (FDA’s) authority to regulate dietary supplements. As Berman and Straus stated (8), “Herbal medicines are plagued by contamination with heavy metals and filth, by adulteration with prescription drugs, wide divergence from labeled content, interference with the pharmacokinetics of life-saving drugs, and even some inherent toxicities,” an assessment that is supported by many reviews (15, 16).

To improve the quality of natural products used in clinical trials, NCCAM recommended chromatographic analysis of extracts and of their putative active ingredients (17). However, the number and identity of the active ingredients of most herbal remedies are unknown, and chromatographic standardization would not ensure standardization of biological activity or stability. Moreover, because there are few regulations governing herbal products, manufacturers can sell the public products that differ from the research materials. We see little reason, therefore, for NCCAM to continue to finance expensive clinical trials of plant extracts (18).

Two clinical trials supported by NCCAM deserve comment. In collaboration with the National Heart, Lung, and Blood Institute,
NCCAM is funding a 5-year $30 million trial of EDTA (ethylenediaminetetraacetic acid) chelation therapy for coronary artery disease (19). It is being carried out at more than 100 sites and involves over 2300 patients. The justification for this study is that many patients are receiving chelation therapy, although it is not approved by the FDA and off-label use for treating heart disease is currently illegal. The American Heart Association and other national medical organizations have issued statements concerning the lack of evidence for its benefit (20), and smaller controlled trials (21–24) have found chelation therapy to be ineffective. Will another negative trial modify the practice of individuals who choose to ignore existing negative evidence and risk legal sanctions?

Another clinical trial compares the use of the chemotherapeutic agent gemcitabine with the Gonzalez regimen in patients with stages II to IV pancreatic cancer (25). The beliefs that underlie this regimen are that cancer is caused by a deficiency of pancreatic proteolytic enzymes that would normally eliminate cancer cells and their toxic products, and that environmental toxins cause imbalances in the body that lead to cancer (26). Patients are treated with porcine pancreatic enzymes, coffee enemas twice daily, and nutritional supplementation that includes Papaya Plus, vitamins, minerals, “animal glandular products,” and other products four times daily. Severe adverse effects have been associated with the Gonzalez regimen (26, 27).

Two important criteria used by scientific review groups to evaluate grant proposals are scientific plausibility and promising preliminary data. No evidence in peer-reviewed journals supports either the plausibility or the efficacy of chelation therapy or the Gonzalez protocol. We believe that funding these projects confers undeserved legitimacy on alternative medicine research.

Review Groups and Advisory Panels

Because of its charter, NCCAM review groups include individuals whose primary training is in alternative therapies, as well as representatives of the botanical industry. In terms of training and publications in medical and scientific journals, their scientific credentials are limited; also, some have potential conflicts of interest. Well-qualified scientists also serve on NCCAM review panels, but their influence is constrained by the narrow NCCAM agenda that emphasizes trials of alternative therapies.

Another problem is that a handful of individuals have been influential in shaping the agenda of OAM and NCCAM. Since the inception of OAM in 1992, those who have written policy papers (28) also have served on review panels and advisory groups and have received numerous grants for research and education.

Evaluation of NCCAM

Oversight of extramural programs is the responsibility of the advisory councils of institutes and centers. The extramural program of NCCAM has escaped critical evaluation because its charter requires a preponderance of proponents of alternative medicine on its council.

In 2002, the Institute of Medicine (IOM) was commissioned by NIH and the Agency for Healthcare Research and Quality (29) to “explore scientific, policy and practice questions that arise from the significant and increasing use of CAM [complementary and alternative medicine] therapies by the American public.” One of three tasks assigned to the IOM Committee was to “Identify major scientific, policy and practice issues related to CAM research.” Seven of the 17 committee members were CAM practitioners or directed CAM and integrative medicine centers. The IOM report identified problems in CAM research, such as the variable composition of herbal medicines and limited number of individuals with research training in the CAM community. Unfortunately, the IOM committee did not evaluate the quality of NCCAM-funded trials or the value of spending hundreds of millions of dollars on CAM research.

Conclusions

We believe that NCCAM funds proposals of dubious merit; its research agenda is shaped more by politics than by science; and it is structured by its charter in a manner that precludes an independent review of its performance. The central issue is not whether research into alternative therapies should be supported by NIH. In view of the popularity of alternative therapies, it is appropriate to evaluate the efficacy and safety of selected treatments. The issue is that the administration of research by NCCAM falls below the standards of other NIH institutes and that the evaluation of alternative therapies could be performed by mechanisms that are already in place at NIH. We do not question the qualifications or integrity of Stephen Straus and his staff. However, because of the constraints under which it operates, NCCAM is unable to implement a research agenda that addresses legitimate scientific opportunities or health-care needs (30). Applicants for NCCAM grants must follow the center’s guidelines that stipulate which therapies are eligible for study. In contrast, applicants to NIH institutes can propose any project that may provide new insights into human biology or the pathogenesis or treatment of disease.

Recommendations

We propose that the IOM appoint an independent panel of scientists to review NCCAM. The panel should evaluate the center’s unique charter as well as its research portfolio, and its members should not include NIH or NCCAM staff, NCCAM grantees, and other stakeholders. An independent review is likely to be strongly opposed by members of Congress whose beliefs led to the creation of NCCAM and the passage of the DSHEA. Therefore, scientists and professional organizations should communicate to Congress and to Elias Zerhouni, the director of NIH, their strong support for an external assessment of NCCAM.

References and Notes

25. Gemcitabine compared with pancreatic enzyme therapy plus specialized diet (Gonzalez regimen) in treating patients who have stage II, stage III, or stage IV pancreatic cancer (http://clinicaltrials.gov).
27. S. Green (www.quackwatch.org/01QuackeryRelatedTopics/Cancer/kg.html).

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