

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

**NATIONAL ADVISORY COUNCIL FOR COMPLEMENTARY
AND INTEGRATIVE HEALTH
MINUTES OF THE FIFTY-FOURTH MEETING
February 6, 2015**

NACCIH Members Present

Dr. Martin Blaser, New York, NY^{1, 2}
 Dr. David Borsook, Waltham, MA
 Dr. Donald Brater, Indianapolis, IN
 Dr. Alice Clark, University, MS¹
 Dr. Stephen Ezeji-Okoye, Palo Alto, CA
 Dr. Tracy Gaudet, Washington, DC
 Dr. Christine Goertz, Davenport, IA¹
 Dr. Jane Guiltinan, Seattle, WA
 Dr. Scott Haldeman, Santa Ana, CA
 Dr. Bin He, Minneapolis, MN¹
 Dr. Frances Henderson, Jackson, MS
 Dr. Steven Hersch, Charleston, MA²
 Dr. Janice Kiecolt-Glaser, Columbus, OH
 Dr. Helene Langevin, Boston, MA¹
 Dr. Richard Niemtow, Alexandria, VA
 Dr. Deborah Powell, Minneapolis, MN
 Dr. Lynda Powell, Chicago, IL
 Dr. Eric Schoomaker, Bethesda, MD
 Dr. Reed Tuckson, Sandy Springs, GA¹
 Dr. Chenchen Wang, Boston, MA

¹Ad-hoc

²Telephone

SPEAKER

Dr. Lloyd Michener, Durham, NC

NACCIH Members Not Present

Dr. John Licciardone, Fort Worth, TX

NIH Staff Present

Barbara Sorkin, ODS, NIH

Members of the Public

Erin Boar
 John Bingham

Kennita Carter
Warren Goldstein
Blake Jones
Perry Kirkhan
Maggie O'Haire
Josheph Pahira
Silvia Stan
Barbara Stefanska
Karen Yehle

I. Closed Session

The first portion of the fifty-third meeting of the National Advisory Council for Complementary and Integrative Health (NACCIH) 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 110 applications were assigned to NCCIH. Of these, 36 were reviewed by NCCIH, 74 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 55 applications, requesting \$ 17,988,608 in total costs.

II. Open Session—Call to Order

The open session convened at 9:45 a.m. Dr. Martin Goldrosen, NACCIH Executive Secretary, called the meeting to order. The minutes of the October 2014 NACCIH meeting were approved unanimously.

III. NCCIH Director's Welcome and Report to Council

Dr. Briggs began her report to Council by welcoming the new members. She led her legislative update with information on the new Congress and the appropriations and authorizing committees for NIH. A budget overview from Fiscal Years (FYs) 2012 to 2016 was provided. The FY 2016 President's budget figure for NCCIH is \$127.5 million. The Consolidated and Further Continuing Appropriations Act, 2015, which was signed by President Obama on December 16, 2014, appropriated funds for FY 2015 and included changing the name of the National Center for Complementary and Alternative Medicine (NCCAM) to the National Center for Complementary and Integrative Health (NCCIH). Dr. Briggs noted that this is a change of name, not mission, Center staff are delighted with the change, and the process of the change includes awaiting Secretary Burwell's final signature and implementing various communications and administrative changes.

The House Appropriations HELP (Health, Employment, Labor, and Pensions) Subcommittee members and staff visited NIH in January 20, 2015, and the Senate HELP Committee held a hearing on January 29 on "Employer Wellness Programs: Better Health Outcomes and Lower Costs." Dr. Briggs invited Council's input on the Center's portfolio in the area of wellness. In

other congressional news, the American Chiropractic Association will sponsor a congressional briefing in spring 2015 on integrative approaches to pain management. NCCIH will emcee this event, which will offer the Center the opportunity to speak about pain management before congressional staff.

Dr. Briggs explained the budget mechanism table, an important tool for understanding NCCIH's budgetary decisions. Out of the NIH budget of \$30.15 billion in FY 2015, NCCIH's budget is \$124.13 million, which, though small, is likely the world's largest public-sector investment in this kind of research. In response to a query from Dr. Borsook on how NCCIH measures "bang for the buck" in research relative to other Institutes/Centers, Dr. Briggs mentioned the upcoming discussion on strategic planning and commented that metrics to quantify the value of research is a complex, widely-discussed topic that NCCIH approaches very thoughtfully. Dr. Briggs noted that NCCIH's extramural investments in FY 2012 for the areas of mind and body approaches and natural products were about the same (\$44 million and \$42 million respectively).

The President has launched a new Precision Medicine Initiative, and Dr. Briggs provided a brief overview. Dr. Briggs expressed hope that the initiative will create the kind of research infrastructure and tools allowing precision medicine to become a reality in those areas where it truly helps, and to help identify when tested measures are **not** predictive. An aspect of the initiative relevant to NCCIH is that of being able to build large electronic datasets using health records, and NCCIH may pursue a cooperative activity related to this with the VA.

Dr. Briggs praised Dr. Shurtleff's service for 7 months as Acting Associate Director for Science Policy in the NIH Office of Science Policy, prior to Dr. Carrie Wolinetz's appointment. Other personnel news included the appointment of Dr. Robert Califf, vice chancellor of clinical and translational research at Duke University, as Deputy Commissioner of the U.S. Food and Drug Administration (FDA).

Upcoming lecture events for NCCIH include the Stephen E. Straus Distinguished Lecture in the Science of Complementary and Integrative Health (an event originally scheduled for January 2015 but postponed due to weather), which will feature Drs. Jerome Groopman and Pamela Hartzband of Harvard Medical School. The NCCIH Integrative Medicine Research Lecture Series, and the Division of Intramural Research Pain Seminar Series have confirmed several noted speakers for their spring lectures.

In research news, the Creatine Safety, Tolerability and Efficacy in Huntington's Disease (CREST-E) Trial, a trial funded by NCCIH and conducted by the Huntington Study Group, was discontinued in October 2014. The decision to stop early was made because the first interim analysis for efficacy review by the Data Safety Monitoring Board showed, with high confidence, that the study would not show a significant benefit of creatine for slowing loss of function in early symptomatic disease. Although this finding was disappointing, Dr. Briggs expressed confidence that the study will offer a very valuable dataset. She then highlighted a report and accompanying editorial in a recent issue of the *New England Journal of Medicine* (2014; 371[25]) on a randomized, controlled trial in New Zealand on cytosine—a natural product that has been sold for decades in Eastern Europe as an inexpensive aid to smoking cessation but is not available elsewhere. Further studies of cytosine are needed to learn more about its efficacy compared with the current pharmaceutical treatments for smoking cessation, and its safety. NCCIH has begun contract-based work with a manufacturer to develop materials for an

Investigational New Drug application, which is needed if U.S. trials are to be sponsored either by industry or the Center.

Dr. Briggs closed her report by summarizing the Center's achievements in leading the 2014 Combined Federal Campaign for all of NIH.

IV. NIH and the BRAIN Initiative: An Update

Dr. David Shurtleff, Ph.D., NCCIH Deputy Director, provided an update on NIH and NCCIH activities related to the President's BRAIN Initiative. Dr. Shurtleff opened with an overview of the initiative and the high burden of brain disorders—e.g., mental and behavioral disorders far surpass any other chronic disease, especially in the first 50 years of life, in number of cumulative disability-adjusted life years. It is hoped that understanding the brain mechanisms in greater detail that contribute to these diseases and conditions will change that trajectory in the long run. NCCIH is one of the Institutes and Centers (ICs) supporting BRAIN activities, including because (1) more tools, biomarkers, and computational approaches are needed for understanding the neural basis of pain, which is also a huge public-health problem, and (2) better understanding is also needed of the brain mechanisms associated with nonpharmacologic interventions (such as mind and body approaches), which could have potential benefit for pain patients.

To tackle this large challenge, in June 2013 the NIH Director formed a subcommittee of the Advisory Council to the Director to develop a 10-year plan for the NIH BRAIN Initiative. The subcommittee released its final report in June 2014, and Dr. Shurtleff provided highlights, including the seven high-priority research areas: discovering diversity, maps at multiple scales, the brain in action, demonstrating causality, identifying fundamental principles, advancing human neuroscience, and [from] the BRAIN Initiative to the brain. Actual and proposed investments were presented along with examples of deliverables for 5 years and 10 years. Minimally or noninvasive technologies for monitoring and modulating brain activity was identified as a high-need area. To help track milestones and contribute additional expertise, a new working group, the BRAIN Multi-council Working Group, has been formed, with Dr. He as NCCIH's representative.

In FY 2014, NIH funding for the BRAIN Initiative was \$46 million in 58 projects across 5 RFAs. In FY 2015, total funding is about \$35 million, which includes about \$23 million for five reissued FOAs and \$12 million for four new FOAs.

Discussion. Dr. He commented that he thought NCCIH could play a greater role in (1) how we understand the dynamics of the whole brain and (2) movement toward viewing the brain in an integrative manner, and he will continue to bring those points to the working group. Dr. Briggs emphasized that the aim of the BRAIN Initiative is to be transformative and game-changing, and its funds build upon and are above existing neuroscience commitments rather than cutting into them. She anticipated that tools emerging from BRAIN could benefit the Center's portfolio over time, adding that NCCIH also benefits from being an active player in the neurosciences at NIH. Dr. Shurtleff noted a goal of thinking about the whole brain in NCCIH's mind and body portfolio. Dr. Niemtzow commented that the area of deep brain stimulation for psychological disorders is intriguing; Dr. Briggs responded that NCCIH's intramural investigators are using some of those tools, and Dr. Shurtleff mentioned an RFA in this direction as well as a hope to be able to also record brain activity over time. Dr. L. Powell recommended more crosstalk between

the neuroscientists involved in the initiative and the applied behavioral interventionists. Dr. Tuckson commented that he views the partnerships in BRAIN as a way of augmenting NCCIH's budget through collaboration, and he would like to see discovery of "highways we can drive other cars across." Dr. Brater commented that there could be more diversity on the NIH subcommittee, as only the U.S. coasts were represented.

V. Data from the 2012 National Health Interview Survey—Child and Adult

Dr. Richard Nahin, Lead Epidemiologist at NCCIH, presented data from a supplement to the 2012 National Health Interview Survey (NHIS) addressing the use of complementary health approaches by American adults and children. Dr. Nahin, NCCIH Statistician Ms. Barbara Stussman, and their colleagues from the Centers for Disease Control and Prevention (CDC) National Center for Health Statistics have been analyzing data from the supplements included in the 2002, 2007, and 2012 editions of the NHIS.

The NHIS is a study in which tens of thousands of Americans answer questions about their health. It is a large, nationally representative, in-person, household survey of the non-institutionalized U.S. population and is conducted by the CDC. NCCIH uses this data as one piece in its decisions about its research agenda, prioritization, and strategic planning. Questions for the complementary/integrative health supplement are developed through a systematic and iterative process, including literature reviews, community feedback, expert panels/workshops, and interviewing/focus groups. Thus, the therapies/modalities included can undergo changes between editions, but many remain the same, allowing for some analysis of trends. The surveys have shown high impact, as can be seen from mainstream media coverage and more than 120 publications to date.

Dr. Nahin then addressed whether use of complementary health approaches has changed over time in 2012 data as compared to 2002 and 2007 data.¹² In 2012, the most commonly used complementary approach for U.S. adults and children was natural products. Within adults' use of natural products: fish oil was the most-used product in 2012; use of fish oil, probiotics/prebiotics, and melatonin increased from 2007 to 2012; and use of glucosamine/chondroitin, echinacea, and garlic fell from 2007 to 2012. Within adults' use of mind and body approaches: the most commonly used approaches in 2012 included yoga, chiropractic or osteopathic manipulation, meditation, and massage therapy, and the percentage of adults who practice yoga rose substantially from 2002 to 2007 and again from 2007 to 2012. This finding on yoga was also seen in children. With respect to children's natural-product use, fish oil was the most-used product in 2012 (in 2007, it was echinacea); melatonin was number 2, and its use significantly increased from 2007 to 2012. Dr. Nahin added that some real sociodemographic differences were also seen in the data—e.g., users of any complementary approach in 2012 were more likely to be female (vs. male), White (vs. Black or Hispanic), have private health insurance (vs. public insurance), and/or have a poverty status of not poor (vs. poor).

¹Clarke TC, Black LI, Stussman BJ, et al. Trends in the use of complementary health approaches among adults: United States, 2002–2012. National health statistics reports; no. 79. Hyattsville, MD: National Center for Health Statistics. 2015.

²Black LI, Clarke TC, Barnes PM, et al. Use of complementary health approaches among children aged 4–17 years in the United States: National Health Interview Survey, 2007–2012. National health statistics reports; no. 78. Hyattsville, MD: National Center for Health Statistics. 2015.

Dr. Nahin's final topic was the use of complementary health approaches in the military population compared with the civilian population. Dr. Nahin identified the best and most-recent data on the topic as being from a 2005 survey by the Department of Defense on health-related behaviors among active-duty military personnel; Council member Dr. Goetz was lead author (Goertz C, Marriott BP, Finch MD, et al. Military report more complementary and alternative medicine use than civilians. *Journal of Alternative and Complementary Medicine*. 2013;19(6):509-17). Dr. Nahin provided key findings from that study and concluded that there are opportunities for NCCIH to collaborate with the Department of Defense.

Discussion. Dr. Gaudet asked about NHIS findings on mind and body approaches; Dr. Nahin showed the slide where that data was located, noted that prevalence for some approaches was too low to show up on the graph, and noted that the full paper with comprehensive tables would be published in several days. Dr. L. Powell wondered whether the marked differences between adult and child use could be because the adults are beginning to experience symptoms, whereas for children the symptoms/ailments may often be subclinical. Dr. Nahin responded that many questions in the 2012 edition were not disease-specific, given its wellness emphasis, but researchers will be investigating further the differences between the use rates for children and adults and it may be the case that adult use inclines more toward treatment or management of diseases/conditions. Dr. Powell also asked whether there were any questions on ailments and symptoms that could link to treatments. Dr. Nahin responded that Ms. Stussman is working on an analysis of that topic now. Dr. Powell made a suggestion to stratify within socioeconomic strata in that analysis.

Dr. Hersh inquired whether children who used a therapy were asked whether their parents also use the therapy. Dr. Nahin clarified that, in the NHIS, a parent answers on behalf of his or her child. In the 2007 edition it was found that if a parent is using a therapy, his or her child was 4 times as likely to use that therapy compared to when parents do not use the therapy. Dr. Borsook asked whether there is ability to look at the data in terms of disease entity and whether there are the same entities within parents and children. Dr. Nahin responded that he is confident that researchers (whether his team or others) will work on this question.

Dr. Schoomaker commented that there is a common question to why the military population uses complementary/integrative approaches—is it because they are dissatisfied with conventional medicine or is it a true preference. He was not convinced that it is the former, but rather that it may arise from multiple factors such as diversity within the military, the individual armed services not being the same (he said he would find a breakdown by service interesting), and worldwide deployments. He suggested that one way (albeit an unusual one) to look at this question could be to study what people impose on their pets in the way of complementary approaches, and to break down the use by sociodemographic factors. Dr. Brater commented that electronic medical records (EMRs) in health systems will increasingly be used, and encouraged NCCIH to catalyze a more accurate recording of complementary/integrative therapy use in EMRs. Dr. Briggs was supportive, adding that herb-drug interactions would be another concern to record. She added that NCCIH has been active for many years in development of tools for the NIH-funded Patient Reported Outcomes Measurement Information System (PROMIS), and that Dr. Tuckson will also be helpful in thinking about this topic area.

VI. Council Operating Procedures

Dr. Goldrosen reviewed Council operating procedures, including processes for NCCIH reports to Council, secondary review of grant applications, concepts for research initiatives, and appeals. Council unanimously passed a motion approving the operating procedures as presented. Dr. Briggs commented that NCCIH may make some last-minute decisions toward the end of the fiscal year that it may not have presented in detail to Council, but in October each year NCCIH provides Council with the full list of proposals funded the previous year and explains any grants funded out of order from the usual priority scores.

VII. 2015 Biennial Report Certifying Compliance with NIH Policy on Population Inclusion Guidelines

Dr. Catherine Meyers, Director of the Office of Clinical and Regulatory Affairs, presented the 2015 biennial report certifying NCCIH's compliance with NIH policy on inclusion guidelines for women and members of minority groups in clinical research. The goal of this policy is not to satisfy quotas for proportional representation based on census data, but to conduct research so that findings will be generalizable to the U.S. population. Councils are asked to review this information and verify that ICs are operating in compliance. The number of women, men, and/or racial/ethnic subpopulations included in any study depends on the scientific question, and the prevalence of the condition under investigation.

Data for this year's report by NCCIH was provided by investigators in annual progress reports for all clinical-research studies having enrollment activity. Dr. Meyers presented a table of NCCIH summary data for FYs 2009 through 2014 and the 2012 NHIS, and noted some trends: enrollment of women and minorities increased following the American Recovery and Reinvestment Act, and this has been sustained; NIH has been moving away from R21 study solicitations toward larger studies; and NCCIH has seen an increase in the number of women in its clinical studies, possibly from growth of the mind and body portfolio. Relative participation levels by women and minorities in the NHIS stayed stable over all three years. NCCIH did not fund any Phase III trials for FYs 2013 and 2014, but rather placed more emphasis on studies (1) characterizing biological effects, translational tools, and biomarker interventions and/or (2) characterizing interventions, optimizing outcome measures, and defining the target population best served by those interventions.

NIH has made changes to its population-tracking, inclusion-management system, including how principal investigators enter data (NIH is now completely paperless), program and grants-management reviews, and the enrollment form. There is Federal Government interest in assembling a single table for reporting all this information.

A motion was made to pass the report, and it passed unanimously.

Discussion. Dr. Tuckson suggested that he does not think it is useful to combine minority numbers into one category. Dr. Meyers said that she would break those numbers out and provide them. Dr. Tuckson added that this information would provide an opportunity to compare, contrast, and learn about different cultures' use of complementary/integrative approaches.

VIII. Report by the Council Working Group on Strengthening Collaborations with the DoD and VA: Effectiveness Research on Mind and Body Interventions

Dr. Kristen Huntley, Program Director, opened this session. She noted that, since 9/11, many returning military service members are reporting significant symptoms and conditions, and it has become clear that additional strategies are needed to address this large public-health issue. Both the U.S. Department of Veterans Affairs (VA) and the U.S. Department of Defense (DoD) have been very interested in exploring complementary/integrative approaches, and NCCIH has been encouraging research in this area. NCCIH is using a phased approach to build capacity and its portfolio, especially with respect to pain and comorbid conditions. Dr. Huntley gave a history of the program announcements and requests for applications in which NCCAM has participated to date. She described these collaborative efforts with sister agencies (the DoD, VA, National Institute on Drug Abuse, and National Institute on Alcohol Abuse and Alcoholism) and noted that they have been educational and beneficial for all involved.

In FY 2014, about two-thirds of grants in this area used the R01 mechanism and one-third the R34, and the military-research portfolio was 6.4% of the NCCIH extramural investment. Dr. Huntley provided several examples of funded projects, commenting that they are moving ahead and NCCIH is very excited. However, it is also important to note that the sizes of projects so far have been modest. Future opportunities exist to leverage health-system, patient-care, and medical-records data in the DoD and VA systems, which are among the best in the country.

In 2014, Dr. Briggs formed a Council working group on this topic, which held five meetings. The group was chaired by Dr. Michener, with Drs. Ezeji-Okoye, Gaudet, Niemtow, and Schoomaker as members, and Dr. Huntley as the designated Federal official. The group's charge was to provide recommendations to NCCIH regarding development of a large-scale initiative, suggest strategies for collaboration among Federal agencies, and provide recommendations for implementation of such an initiative. Each meeting featured one or more speakers, drawn from a range of government and non-government agencies/organizations, followed by discussion. The focus was the aspirational goal of clinical care of pain and associated symptoms in military personnel and veterans, but the group also kept in mind that these are major health problems for the general public as well.

Dr. Michener opened the second half of the presentation with the high burden in the military and general U.S. populations of chronic pain and the limitations of current therapies for it—the major therapy is opioids, but the risk of opioid overuse and death is a serious public-health problem, and veterans are the group most affected by and at risk for this. With respect to the evidence about complementary and integrative approaches for chronic pain, Dr. Michener reported that there is a paucity of well-designed studies and the existing evidence may be complex and mixed, while the evidence that opioids work for chronic pain is lacking but the evidence that they do damage is clear. The big picture is that conventional care is not doing a good job of managing chronic pain, and there is a need for other approaches.

Challenges exist in conducting research in military and veteran settings, such as competition with the operational mission, time limitations of health-care providers, mobility of military personnel, and a lack of uniform enthusiasm for nonpharmacologic approaches. However, there are also opportunities, including:

- a commitment of the DoD and VA to serve;
- a focus on pain research and improved management of pain and comorbid conditions;

- a shift away from treating people when they are ill toward an aspirational approach to health and healing (i.e., what would it take to have people be healthy, not just free of disease?);
- more positivity toward innovative study designs in addition to individual randomized controlled trials;
- the value of pragmatic studies in real-world settings where care is usually delivered;
- significant DoD and VA resources that could be leveraged for research;
- and special considerations involved in working within a military environment.

He added that the DoD Defense Health Agency (DHA) is responsible for increasing the integration of health care provided by the individual armed services and is interested in working on pain. He noted that the topics discussed in this session are not only a military but a civilian issue and fit within a number of Secretary Burwell's stated top priorities.

The conclusions reached by the working group were as follows: (1) NCCIH should further assess the feasibility of undertaking one or more large-scale studies in cooperation with the VA and DoD; excellent work has been done to this point, and it is time to scale it up. DHA may particularly be able to help answer important policy and patient-care questions about the use of integrative approaches in pain management. (2) Primary outcome measures should be the impact of pain on patients' personal function and quality-of-life. (3) The research could focus on an integrated package (vs. single interventions) of nonpharmacologic modalities that could be individualized, an integrative model of care that could include complementary health approaches, and/or a holistic or personalized approach to health care. (4) Patients who are in early stages of chronic pain (vs. end-stage illness) may be the most appropriate population to study, to try to break the pain and illness trajectory. (5) Natural experiments and existing resources should be leveraged whenever possible. (6) Studies should be pragmatic, and research should be embedded in the delivery of care. (7) Chronic pain and conditions related to it are a major societal problem affecting large numbers of Americans, but particularly the military and veteran populations. (8) Although [those conditions] may disproportionately affect those who are serving or have served in the military, they are widespread in the civilian population as well. (9) Future initiatives encouraging larger-scale studies may provide evidence that could improve quality of life and increase options for safe, effective pain management for military personnel and veterans first, and also for the millions of other Americans who struggle with chronic pain.

Discussion. Dr. Borsook asked whether, in the context of adding or enhancing integrative approaches, the group had considered temporal sequence in capturing patients. Dr. Schoomaker answered affirmatively and expanded the point with several examples (e.g., whether it is possible to identify personnel predeployment who are more prone to being injured). Dr. Borsook commented that a major problem is that, in clinics and hospitals, there is not an integrated process to follow patients. Dr. Schoomaker agreed, noting that the group grappled with this problem and commenting that the group's name offered "a very wide aperture" that they successfully narrowed to look at (1) pain and (2) a particular temporal portion of the spectrum of pain, in time and intensity. He added that, in the military community, complementary/integrative modalities have typically been a "court of last resort" for patients who have had a lifetime of chronic pain and failed other treatments. The working group moved away from approaching the topic in that way, since it appeared to carry a failure prospect and they wanted the approach to be highly integrative—recognizing, for example, that there are some very effective drug approaches for acute pain that should not be abandoned, but also that the "zone of chronicification" is where

there could be the most impact. Dr. Borsook recommended not overlooking the acute phase, where chronification starts. Dr. Schoomaker said that he did not disagree, and gave examples of effectively managing pain at the point of injury. He added that it was important to place emphasis upon the areas where DoD and VA saw the most need.

Dr. Wang commented that the report seemed to be missing some key points. Important questions that it needs to consider, she said, include: What is the mind and body intervention being used to reduce pain? What are its ingredients? (Western medicine understands the pain mechanism and model well, but mind and body interventions not as well.) What shall we teach about it, who is qualified to do so, and how should it be done? How can these kinds of interventions be generalized and standardized for delivery to patients with chronic pain? Instructors of tai chi, for example, often differ in how they deliver the modality; some do not have a medical education and/or know how to teach their intervention to patients with chronic pain. Dr. Briggs responded that those pragmatic issues are large challenges in mounting this kind of research—a key question is how much a therapy can be standardized and optimized compared with implementing it in a more real-world settings (where it may be more individualistic and variable).

Dr. Goertz commented that her institution has a study with the DoD on a pragmatic approach integrating chiropractic care with conventional care to treat low-back pain in the military setting, and she hopes data collection will be complete by August 2015. She added that the feasibility issues in that kind of research are indeed substantial. She also commented that she felt the working group stopped too soon in its report, because there was no discussion of information dissemination. Dr. Michener noted that the report was intended as a recommendation to Dr. Briggs and Council about moving forward, and a framing document. He added that the opportunity and timing were important for NCCIH, VA, and the DoD to come together and work through these kinds of issues, as the need is so great. Dr. Huntley said that as the work moves forward NCCIH will work with DoD and VA including on the dissemination of information.

Council unanimously approved a motion to accept the report as presented.

IX. NCCIH Strategic Plan: Background, Plans for Development, and Proposed Areas of Focus

As background for work on the upcoming strategic plan for NCCIH, Dr. Briggs presented her perspective on the last 5 years at the Center. She opened by explaining the legislative mandates for NCCAM and NCCIH and the authorization for NCCIH. The authorities and mandates are very broad with respect to types of research, and the charge does not actually define “complementary” or “alternative.” She presented the Center’s current definitions of alternative medicine, complementary health care, and integrative health care.

Dr. Briggs then summarized the mission, vision, goals, and major strategic objectives in the Center’s last strategic plan (2011-2015). The criteria for priority setting from that plan, she said, still fits quite well: (1) scientific promise, (2) amenability to rigorous scientific inquiry, (3) potential to change health practices, and (4) relationship to use and practice. Two criteria that have been added are: (5) Is the topic appropriate to NCCIH’s mission and legislative mandate? (6) Will the research meet a need not filled by other NIH programs?

Dr. Briggs also provided examples of the Center's activities in the past 5 years to meet each of the 5 strategic objectives outlined in the 2011-2015 plan: (1) advance research on natural products; (2) advance research on mind and body interventions, practices, and disciplines; (3) increase understanding of "real world" patterns and outcomes of use of complementary practices and their integration into health care and health promotion; (4) improve the capacity of the field to carry out rigorous research; and (5) develop and disseminate objective, evidence-based information on complementary and alternative [and integrative] medicine interventions.

Examples were provided of past NCCIH-funded major clinical trials on natural products, including the Trial to Assess Chelation Therapy (TACT). The first publication on TACT results found some fairly-significant beneficial effects from the chelation regimen upon rates of cardiovascular events in one subgroup: diabetics. When further analysis looked at diabetics and nondiabetics, marked benefit was seen in the diabetic population and no benefit in nondiabetics. Dr. Briggs described this data as very striking and said it adds plausibility to a hypothesis that interactions with lead or other heavy metals may cause cardiovascular injury and removing them might change vascular pathology. NCCIH and the National Heart, Lung and Blood Institute are working with the TACT investigators to consider a replication trial with ancillary investigation of the heavy-metal question.

Dr. Briggs also noted that NCCIH's information links to FDA safety information and that NCCIH posts natural-product safety concerns of which it is aware. Furthermore, Dr. Briggs noted that she thinks historic trends in use of natural products show at least some impact from the work NCCIH supports, and industry sales data appear to support this point.

Dr. Briggs commented that in the past 5 years mind and body approaches have coalesced as a focus for the Center, particularly with respect to their impact on pain. Funding for NCCIH pain research has grown into a large part of the Center's portfolio. Dr. Borsook commented at this point that a difficult challenge in the field is knowing which patients are responders or not, and the fact that some "get stuck" no matter what is tried. Dr. Briggs agreed that it is a challenge that needs to be addressed. Finally, she summarized NCCAM's interest in research in military populations.

Dr. Karin Lohman, Director of the NCCIH Office of Policy, Planning, and Evaluation, delivered Part 2 of the presentation, leading with a process overview and timeline for the new strategic plan. Dr. Lohman described that the Center views the next plan as a high-level, long-range, strategic vision for establishing research priorities and future scientific directions, building research capacity and multidisciplinary collaborations, and disseminating information to scientists, health care providers, and general public. The guiding principles for the plan are that it will be transparent, open, driven by science and data, and reflective of input from NCCIH's diverse stakeholder communities. It will not be an action plan but will rather articulate hopes for research outputs, to be followed by implementation and execution.

The plan timeline started in spring 2014 with planning and will continue with gathering of input, such as more assessment of the portfolio, accomplishments in the past 5 years, state of the science, gaps, public-health needs, and other emerging opportunities. This data will help establish a baseline. The plan process has six major steps (including seeking stakeholder input) and will conclude with a finalized plan presented to Council in February 2016. Input from its many diverse stakeholder groups is very important to the Center, and technology will be used as much as possible to gather input. Major planning activities accomplished so far include the

Council working group on collaborations with the DoD and VA, a strategic plan completed in 2014 for the NCCIH Intramural Division, and a number of internal portfolio assessments. The planning process is an opportunity to look at areas either where the Center has a footprint, that need refinement, or that could be expanded.

Discussion. Dr. Briggs opened a discussion on five draft white papers of topics representing potential areas of focus for the strategic plan. These drafts were developed largely by Extramural Division Director Dr. Emmeline Edwards with Division staff, and then were proposed to Dr. Briggs and edited by her. The resulting papers have three to five strategic questions for each topic. The session goal was to jumpstart a conversation that would continue, including among working groups to be appointed. Dr. Briggs expressed interest in hearing not only “30,000-foot” but “10,000-foot” views.

Topic 1: Probiotics and the Brain-Gut Microbiome Pathways. Dr. Briggs called on Dr. Blaser, who expressed support for the topic and urged that it be expanded beyond the brain-gut microbiome to the immune-gut and metabolic-gut microbiomes as well. Dr. Briggs commented that NCCIH is not the only funder of probiotic work at NIH, and focusing this topic area is a challenge. Dr. Blaser added that he thinks there will be probiotics in the form of microbes that know how to “talk” to the immune system and can recruit various kinds of immune cells useful for patients with various illnesses—he saw this as a winning area and an opportunity to also develop methodologies for evaluation. Dr. Briggs agreed on the usefulness of methodologies, e.g., to look for markers for probiotic action. Dr. Clark expressed support for this line of inquiry. Dr. Briggs saw as another interesting question the way probiotics may influence the gut metabolism of natural products.

Topic 2: Network Pharmacology, Natural Products, and the Inflammatory Pain Pathways.

Dr. Briggs said that NCCIH had had internal debate about whether to focus more on inflammatory pain or on systems-biology/network-pharmacology approaches. Dr. Borsook commented that, in general, Topic 2 was broad and impactful, and elaborated on two dimensions: (1) We don’t know how many pharmaceuticals work on the central nervous system and pain, and many new technologies are beginning to dissect this; (2) in recent literature, the neuroimmune system or inflammatory components in the peripheral nerves and brain seem to be a major and promising area. Dr. Clark expressed support for Topic 2, noting that natural products have an important role to play, in a systematic and innovative way, in understanding of pain and inflammation both mechanistically and therapeutically. In responding to a comment from Dr. L. Powell about earlier negative trial results in natural products, Dr. Briggs responded that NCCIH has come to expect efficacy trials in natural products to have more mature scientific underpinnings such as markers, and that she considers knowing more about natural products—including those in our diets—important. Dr. Powell suggested setting milestones as justification for moving forward in research. Dr. Briggs mentioned two upcoming initiatives in the natural-products portfolio: (1) herb-drug interactions and (2) increased focus on methodology in the NCCIH-Office of Dietary Supplements Botanical Research Centers.

Dr. Langevin urged clarity on use of the term “inflammatory pain;”—is one referring to neuroinflammation or components in the body’s periphery? She added that it is important in integrative health to not focus only on the brain and nervous system but also on the rest of the body including the periphery. Dr. Briggs responded that NCCIH has been thinking about both central and peripheral mechanisms, and that it is often not known where an agent is working. Dr.

Kiecolt-Glaser also supported having clarity on the term “inflammatory pain” and asked whether the work would mean targeting natural products that have been shown to be anti-inflammatory. Dr. Briggs responded that the Center would particularly be asking which natural products are of interest for their measurable impact on inflammatory pathways.

Topic 3: Employer and Community-based Health and Wellness Programs. Dr. Briggs described this topic as huge and intriguing, and a central question is where NCCIH’s impact could be greatest. She discussed the NIH Collaboratory as a helpful model of impactful partnerships that leverage resources powerfully. Many employers are implementing programs to try to improve health behaviors of their employees and families, she said, and complementary approaches can be part of the “hook,” but the evidence is quite sparse. The idea would be for the NIH to come up with research dollars but not actual implementation. Dr. Tuckson commented that what employers care most about at this time are rapidly escalating costs; any idea for partnership should demonstrate a clear-cut return on investment, and they should not be expected to bear the brunt of costs. He mentioned other questions and topics that are of interest to employers—including Dr. Wang’s earlier point on reproducibility and how to know if a provider is “good”; NCCIH can inform about things to look for and questions to ask when considering a study; an intervention should be framed as medical rather than as a wellness/feel-good approach; and NCCIH should show that it also cares about what **does not** work. The more that health benefits are shifting health care costs to the individual, he said, the more positive employers will feel toward information that aids decision making. When reaching out for a potential collaborative clinical-research opportunity, the initial contact should demonstrate NCCIH’s credibility and relevance.

Dr. Schoomaker commented that the military does not run a health care system, but rather a health-promotion system for an all-volunteer force. He added that more of a focus is needed nationwide on a transition to health promotion, not on health care delivery, and to make that change we must engage across a multidisciplinary spectrum that includes community. Dr. Briggs supported the point on community, adding that she does not believe NCCIH’s resources should be applied toward employee programs in the direction of “spa wellness.” Dr. Schoomaker added that he is equally interested not only in low-income and underserved communities, but also in high-end employers and what relatively-well-paid employees are being offered in terms of complementary and integrative approaches. He also saw the major challenge as behavior change, not science literacy. Dr. Michener commented that employers have access to data on productivity and absenteeism, which matter in addition to cost, and suggested several settings of potential research interest: inner-city academic health centers (which are large inner-city employers that self-insure, and are represented among lead members of the NIH Collaboratory) and also city and state employers.

Topic 4: Mind and Body Clinical Trials. This topic was especially focused on pain. Among the major questions, Dr. Briggs said, are (1) Dr. Wang’s earlier point about which interventions are ready (e.g., described and protocolized well enough) for pragmatic research on a sizeable scale, and (2) whether more mechanistic work or the classic randomized controlled trial would be more impactful.

Dr. Haldeman led the comments with the topic of the “primary spine clinician,” which his institution is implementing—a provider who knows the evidence and can deliver modalities (e.g., acupuncture, manipulation, other mind and body modalities, etc.). This idea is also being

discussed in journals such as *BMJ* and in training institutions for complementary practitioners. Its major aspects include that the clinician is someone other than an M.D., and a uniform treatment is emphasized rather than fringe ideas/beliefs attached to some complementary/integrative modalities. He suggested that to move from where we are now, we must ask how to put those providers in the community and make it work, what their qualifications should be, etc. Dr. Briggs commented that she does not view this as an “either/or conversation.” She added that the opioid epidemic is defining and impactful, including for the Center, and she is eager to have a discussion of interventions at all levels from basic science up to health care systems. Dr. Goertz described a tension between needing to focus vs. understanding the huge knowledge gap on the entire continuum from basic science to pragmatic trials; there is definitely a need for more pragmatic trials (relatively little has been done). She noted that a decade ago she was typically asked how a complementary/integrative modality works and how much it costs, whereas today she is more often asked how to find a good provider of the modality—this also pertains to what the criteria should be used to evaluate clinicians. Dr. Briggs commented that one way she has thought about study ideas for this portfolio is the question “Is it PCORI-ready?” (i.e., is it ready for an application to be funded by the Patient-Centered Outcomes Research Initiative?) One question with which Council could help is what the Center should fund vs. what others should fund.

Dr. Schoomaker mentioned that, in his setting, there has been a problem of being so focused on mechanistic work and on basic science that the fundamental question of “As it is being applied, does it work?” gets lost. He was concerned that the area is so focused on pain, when the constellation of symptoms that surrounds pain is also important. Dr. L. Powell commented that she often has seen in Council meetings an application of the natural-products paradigm to the mind-and-body paradigm, which seems to her presumptuous (e.g., having to identify the mechanism before an intervention can be tested in efficacy and effectiveness trials). She pointed out that some of her group’s biggest successes have been in multicomponent, multidimensional treatments, where the mechanism of effectiveness could be any of a number of components in the study or even be unknown. She urged that the Center not hold back in moving toward trials for pain of the most promising complementary interventions, comparing them with drugs, and looking at long-term (not just short-term) effects on pain. Dr. Briggs responded that NCCIH gets few applications with this approach and may need to specifically solicit them.

Dr. Tuckson added the idea of appropriateness—e.g., it is paramount to describe for whom the intervention is appropriate and under what circumstances. This is critical for getting it into the delivery system. Secondly, he added that it is important that NCCIH clarify the field, including what is and is not understood, and doing this would be a major public-health service. Dr. Borsook brought up the importance of allostatic load and suggested needs for “a sort of allostatic meter” and a new way of thinking about how the pain patient presents.

Topic 5: Science Communications. Ms. Alyssa Cotler, NCCIH Director of Communications, joined the panel. Dr. Briggs described that when people come to the Center looking for health information, it also presents an opportunity to help them better understand the scientific-research process, but Council should discuss other communications challenges/opportunities as well. Dr. D. Powell had described this topic as a very important one for public and health-care-provider education, as did Dr. Tuckson. Dr. Haldeman commented that health care providers were missing in the draft topic; for providers to obtain the kind of information that NCCIH provides and stay up-to-date on it are both difficult, and NCCIH has credibility. Dr. Henderson mentioned two

projects that she is working on in this area and emphasized the importance of NCCIH including input from the community. Dr. Ezeji-Okoye expressed concern that there may be too much focus in this topic toward treatment rather than prevention—e.g., talk about research can perpetuate the notion that any medical issue is curable or fixable by the medical provider with pills, surgery, etc. This was contrasted with willingness for providers to say more bluntly and openly what is not known, what could be done outside the medical field, and education on patient choice.

Dr. Wang offered two suggestions to improve NCCIH's information: (1) better understanding of the history, theoretical foundation, and principles of modalities (e.g., tai chi and yoga), which would also add to scientific knowledge and improve communication to patients, and (2) use international collaborations to better understand why a modality works. Dr. Guiltinan commented that understanding disciplines and whole practices is very important, as is providing training in science communication for complementary and integrative providers, health students (in pre-professional training and earlier), and consumers. Dr. Briggs noted that complementary/integrative practitioners can have an important role in promoting healthy behaviors, and there are some integration models that have brought traditional practitioners into public-health priorities; this area is complex but worth exploring in the strategic-planning effort.

In closing, Dr. Briggs was appreciative that these conversations had been launched and invited members' continuing input.

X. Public Comment and Adjournment

No public comments were offered.

The meeting adjourned at 3:45 p.m.

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

Martin Goldrosen, Ph.D.
Executive Secretary
National Advisory Council for
Complementary and Integrative
Health

Josephine Briggs, M.D.
Chairperson
National Advisory Council for
Complementary and Integrative
Health