

2016 NCCIH Strategic Plan

March 25, 2016

– Discussion Draft –

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FOREWORD

Mapping the Path Forward

During an 18-month planning process, the National Center for Complementary and Integrative Health (NCCIH) carefully assessed how recent developments in science, medicine, and health care have affected the Center's strategic approaches in the diverse arena of complementary and integrative health. With input from NCCIH staff, stakeholders, and scientific advisors, and guidance from the broader National Institutes of Health (NIH) strategic plan, the Center took stock of its existing programs and priorities; the growing evidence base, research capacity, and scientific opportunities; and public health needs going forward.

The NCCIH Plan takes into account scientific gaps and opportunities subsumed under three scientific and two cross-cutting objectives:

- Objective 1: Advance Fundamental Science and Methods Development
- Objective 2: Improve Care for Hard-to-Manage Symptoms
- Objective 3: Foster Health Promotion and Disease Prevention
- Objective 4: Enhance the Complementary and Integrative Health Research Workforce (cross-cutting)
- Objective 5: Disseminate Objective Evidence-based Information on Complementary and Integrative Health Interventions (cross-cutting)

In addition, the Plan contains a section on the Center's Top Scientific Priorities. This section will be "living," as it will be updated based on public health needs, new scientific opportunities, research results, changes in the Center's grant portfolio, and budgetary considerations. The set of Top Scientific Priorities does not encompass all of NCCIH's research interests, and the Center will also continue to rely on and will support highly meritorious grant applications covering an array of research highlighted in the broader Strategic Plan.

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2016 NCCIH Strategic Plan

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- *Develop new and improved research methods and tools for conducting rigorous studies of complementary health approaches and their integration into health care.*

Objective 2: Improve Care for Hard-to-Manage Symptoms

- *Develop and improve complementary health approaches and integrative treatment strategies for managing symptoms such as pain, anxiety, and depression.*
- *Conduct studies in “real world” clinical settings to test the safety and efficacy of complementary health approaches, including their integration into health care.*

Objective 3: Foster Health Promotion and Disease Prevention

- *Investigate mechanisms of action of complementary and integrative health approaches in health resilience and practices that improve health and prevent disease.*
- *Study complementary health approaches to promote health and wellness across the lifespan in diverse populations.*
- *Explore research opportunities to study and assess the safety and efficacy of complementary health approaches in non-clinical settings such as community- and employer-based wellness programs.*

Objective 4: Enhance the Complementary and Integrative Health Research Workforce

- *Support research training and career development opportunities to increase the number and quality of scientists trained to conduct rigorous, cutting-edge research on complementary and integrative health practices.*
- *Foster interdisciplinary collaborations and partnerships.*

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Objective 5: Disseminate Objective Evidence-based Information on Complementary and Integrative Health Interventions

- *Disseminate evidence-based information on complementary and integrative health approaches to health care providers, researchers, policymakers, and the public.*
- *Develop methods and approaches to enhance public understanding of basic scientific concepts and biomedical research.*

Top Scientific Priorities

- Nonpharmacologic Management of Pain
- Neurobiological Effects and Mechanisms
- Innovative Approaches for Establishing Biological Signatures of Natural Products
- Disease Prevention and Health Promotion Across the Lifespan
- Clinical Trials Utilizing Innovative Study Designs to Assess Complementary Health Approaches and Their Integration into Health Care
- Communications Strategies and Tools to Enhance Scientific Literacy and Understanding of Clinical Research.

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Introduction

Mission: *The mission of NCCIH is to define, through rigorous scientific investigation, the usefulness and safety of complementary and integrative health interventions and their roles in improving health and health care.*

Vision: *Scientific evidence informs decisionmaking by the public, by health care professionals, and by health policymakers regarding the use and integration of complementary and integrative health approaches.*

The National Center for Complementary and Integrative Health (NCCIH) is the lead Federal agency for scientific research on the usefulness and safety of complementary and integrative health practices. To address the need for objective evidence as to the safety and efficacy of many of these approaches, NCCIH supports rigorous scientific investigation to better understand how these interventions work, for whom, and the optimal methods of practice and delivery.

NCCIH supports research on a broad range of practices, interventions, and natural products that have an origin outside of conventional Western medicine. The research supported spans the continuum of basic, translational, efficacy, and effectiveness research. Continued emphasis on both basic research to understand biological effects and mechanisms of action and on efficacy studies to determine specific clinical effects of interventions is essential in developing the scientific evidence base. “Complementary” health approaches include mind and body interventions, such as massage, acupuncture, yoga, and meditation, and natural products, such as herbs, fish oil, melatonin, and probiotics. Many of these products and practices are in widespread use by the public, as shown by the 2012 National Health Interview Survey (NHIS), though most people who use complementary health approaches use them in conjunction with conventional health care.

NCCIH also supports research on integrative health approaches that bring conventional and complementary approaches together in a coordinated way. The use of integrative approaches to health and wellness has grown within care settings across the United States. The evidence base on integrative approaches, however, is limited, but growing. For example, researchers are currently exploring the potential benefits of integrative health in a variety of situations, including for pain management for military personnel and Veterans, relief of symptoms in cancer patients and survivors, and programs to promote healthy behaviors.

Use of Complementary and Integrative Approaches in the United States

The National Health Interview Survey (NHIS), conducted by the Centers for Disease Control and Prevention (CDC), provides the most comprehensive data available on Americans’ health. In 2002, 2007, and 2012, the NHIS included a special section, developed jointly by the NCHS and NCCIH and supported by NCCIH, on the use of complementary and integrative health approaches.

NHIS data show that about one in three U.S. adults (33.2 percent) used complementary health approaches in 2012, as did about one in nine children age 4 to 17 (11.6 percent). Natural products (dietary supplements other than vitamins and minerals) were used by 17.7 percent of adults and 4.9 percent of children. Fish oil, glucosamine and/or chondroitin, probiotics/prebiotics, and melatonin were among the most widely used natural products. Mind and body approaches in widespread use included

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yoga (used by 9.5 percent of adults and 3.1 percent of children), chiropractic or osteopathic manipulation (8.4 percent of adults; 3.3 percent of children), meditation (8.0 percent of adults; 1.6 percent of children), and massage therapy (6.9 percent of adults; 0.7 percent of children).

Foster Discovery and Innovation by Setting Priorities and Enhancing Stewardship

NCCIH strives to invest in research that will drive new discoveries that may lead to improved public health and health care. The Center's research priorities reflect public health needs, scientific promise, amenability of topics to rigorous scientific inquiry, potential to impact health care practices, and relationship to use and practice.

The relative burden of a disease or condition on human health and well-being is an important consideration in priority setting. According to the Institute for Health Metrics and Evaluation, the top five leading causes of years lived in less than ideal health (YLDs) include low-back and neck pain, other musculoskeletal disorders, depressive disorders, and anxiety disorders. Complementary and integrative health interventions have shown promise in treating and managing these conditions, but additional research is needed to identify and optimize beneficial interventions.

Consistent with this principle, NCCIH has made pain management a major emphasis in its research efforts. Pain is a major public health problem and is the most common reason why Americans use complementary and integrative health practices. Chronic pain affects about 100 million American adults—more than the total affected by heart disease, cancer, and diabetes combined. Conventional care often fails to manage chronic pain effectively, and other approaches to relieve or reduce pain and increase functional ability are needed. Research studies have shown that some complementary health modalities may reduce pain associated with some conditions; examples include massage, spinal manipulation, and yoga for chronic back pain and tai chi for fibromyalgia pain.

NCCIH also seeks to identify strategies for promoting health and preventing disease. Behavioral risk factors, including an unhealthy diet, being overweight or obese, living a sedentary life, smoking or using tobacco products, and the excessive consumption of alcohol, are linked to increased rates of cardiovascular disease, cancer, and diabetes. Preliminary evidence indicates that some complementary health approaches may be useful in encouraging improved self-care, an improved personal sense of well-being, and a greater commitment to a healthy lifestyle. For example, analysis of the 2012 NHIS data indicates that many people who practiced yoga reported that it motivated them to practice healthier behaviors, including eating better and exercising more regularly. While causal relationships between the practice of complementary approaches and healthy behaviors have not been established, further research is needed to explore, clarify, and examine their relationship.

Scientific Plausibility and Rigor

Maximizing the Center's research investments by focusing on areas where they will have the greatest impact is a key to priority-setting for NCCIH. This means prioritizing research topics that show scientific opportunity and promise and are amenable to rigorous scientific inquiry. No matter how interesting an approach may be, if the evidence favoring it is too limited to support the scope and direction of a proposed study, or if reliable, rigorous methods of measurement do not exist, that topic is not suitable for full-scale investigation. NCCIH supports studies to generate the required evidence, such as examining the mechanisms of action of interventions.

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As a responsible steward of its publicly provided resources, NCCIH is highly selective in the choice of topics for major clinical trials. Decisions about which large-scale trials to support must be based on the strength, reliability, and reproducibility of signals from clinical experience and preliminary, smaller pilot studies, as well as on evidence of scientific plausibility obtained from mechanistic studies. Adequate methods and tools to accurately and effectively measure clinical outcomes are equally important to sound research design. Objective, validated measurement tools are essential, and so are processes and procedures to ensure quality control, whether the intervention is mind and body-based or a natural product. For example, NCCIH has a strict natural product integrity policy to ensure that all natural products used in research supported by the Center are fully identified, characterized, and standardized.

Priority Setting Framework

NCCIH is committed to funding research in areas that will have an impact on health and health care. When considering funding a potential research project, the Center asks whether it is reasonably likely that the results of the research could lead to changes in the health practices of American consumers or health care providers or in the decisions of health policymakers. The Center also asks whether the research addresses an important public health concern or need for scientific information regarding the safety, efficacy, or effectiveness of complementary and integrative health approaches.

Framework for priority setting:

- ***Scientific promise:*** Does a reasonable body of evidence support the potential of the proposed research to lead to improved (1) options or strategies to treat troubling or prevalent health conditions or symptoms or (2) approaches to promote better health and well-being? Is evidence sufficient to support the scope and direction of the proposed research? If not, what research is needed to establish such evidence?
- ***Amenability to rigorous scientific inquiry:*** Are the key research goals achievable, and are the key research questions amenable to rigorous scientific investigation, given needed and available methods for measurement, translational tools, and technologies? Are potential approaches feasible and scientifically plausible? Do they lend themselves to rigorous quality control? If not, does the proposed research focus appropriately on developing needed methods, tools, and technologies?
- ***Potential to change health practices:*** Is it reasonably likely that the results of the research or program could lead to changes in the health practices of consumers or health care providers or in the decisions of health policymakers?
- ***Relationship to use and practice:*** Does the proposed project address an important public health concern or scientific information need regarding efficacy, safety, or public use of complementary and integrative health approaches?

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Objective 1: Advance Fundamental Science and Methods Development

Fundamental scientific inquiry is essential to the progress of biomedicine by enhancing the understanding of how living systems work. This understanding serves as a foundation for translational and clinical studies that can lead to improved approaches to the management, treatment, and prevention of diseases and symptoms.

Fundamental science plays a key role in fulfilling NCCIH's mission. The Center provides strong support for basic and mechanistic research on complementary health approaches. NCCIH's basic research is aimed at understanding the nature of complementary health approaches, such as their biology, physiology, and physical, chemical, and behavioral properties. NCCIH also supports the development of tools, models, and methodologies for studying these approaches. NCCIH mechanistic research is focused on identifying and understanding the active components of a complementary health approach and how those components produce effects. Depending upon the question, basic and mechanistic studies may be performed *in vitro*, in animals, or with human volunteers.

NCCIH also supports research studies characterizing the active elements of complex interventions. These studies frequently use state-of-the-art techniques in areas such as neuroscience, immunology, pharmacognosy, proteomics, genetics, and epigenomics. Understanding the mechanisms by which complex complementary or integrative interventions exert their effects is critical for the development of optimized interventions.

Strategies:

1. Advance understanding of basic biological mechanisms of action of natural products, including probiotics.

NCCIH has a broad interest in studying the biological activities of natural products, including the potential effects of these products on a variety of clinical conditions, and their potential to promote wellness or resilience. Many of the natural products used in this context, especially herbs, are very complex, with multiple molecular constituents that may contribute to their effects. To fully understand the activity of a complex product, it is necessary to identify the individual components responsible for a specific activity and determine how those components interact with other components. Preclinical model systems are valuable for these studies.

Going forward, NCCIH will continue to sponsor research on compounds isolated from natural products, as well as on the complex mixtures from which they originate. Future studies may focus on both the beneficial and harmful effects of natural products, including their interactions with medications. NCCIH-funded studies may also include the characterization of novel natural products or their chemical constituents.

Additionally, NCCIH will continue to support research to elucidate the effects of probiotics and prebiotics on the microbiota naturally present in the human body. The Center is interested in the role of gut microbiota and the potential for pre- and probiotics to modulate gut microbiota to prevent and treat a variety of diseases and disorders, including those that may be associated with the brain-gut axis (e.g., pain and anxiety). Through these efforts, NCCIH seeks to address fundamental knowledge gaps, including those pertaining to microbiota molecular mechanisms of action and potential interactions with pre- and probiotics and their impact on processes in the

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human body. This research may provide a sound basis for developing probiotic and prebiotic products that can enhance or restore health. NCCIH aligns its probiotics research program with trans-NIH microbiome initiatives such as the Human Microbiome Project. NCCIH will continue to work closely with other NIH Institutes and Centers (ICs), the Food and Drug Administration, and the Department of Agriculture to leverage its investments in this research area.

2. Advance understanding of the mechanisms through which mind and body approaches affect health, resiliency, and well-being.

Mind and body approaches, such as meditation, spinal manipulation, massage, yoga, tai chi, hypnosis, and acupuncture, are being studied for their effects on a variety of symptoms and on resiliency and well-being. To design and carry out rigorous clinical research on these approaches, it is important to have insight into their biological effects and the mechanisms of action by which these approaches impact physiology. Going forward, NCCIH investments will emphasize fundamental research to advance the understanding of the mechanisms through which mind and body approaches affect health.

An important focus of research on mind and body interventions is the central nervous system—the brain and spinal cord. NCCIH seeks to advance research aimed at elucidating the effects of interventions such as meditation and acupuncture on central mechanisms of pain perception, processing, and control. In addition, the Center also is interested in how factors such as emotion, attention, environment, and genetics affect pain perception.

Studying how mind and body approaches affect the nervous system is scientifically challenging. This challenge is compounded by individual variability attributable to genetic, epigenetic, and environmental differences. Nevertheless, recent transformative advances in genomic science, neuroscience, stem cells, systems biology, neuroimaging, and predictive computational modeling offer excellent resources and opportunities for neural mechanistic studies of complementary health approaches.

3. Develop new and improved research methods and tools for conducting rigorous studies of complementary health approaches and their integration into health care.

Rigorous research on complementary health approaches requires well-established methodology, including valid, reliable, and relevant research tools and outcome measures. NCCIH seeks to support fundamental science that will lead to the development of improved methodologies for complementary health research, especially those that can be used to assess symptoms such as pain, depression, and anxiety. Studies that identify and validate objective endpoints or biomarkers, assess and measure adherence or treatment fidelity, or will otherwise strengthen the design of clinical trials of complementary health approaches are particularly important.

a. Catalyze advances in natural products methodology

Natural products have a long and impressive history as sources of medicine and as important resources for biological research. However, many of the techniques for studying complex mixtures of natural products have remained unchanged for many years and have yet to leverage advances in biological and chemical methodologies.

To move the field forward, NCCIH is placing a renewed emphasis on overcoming methodological and technological hurdles that hinder advances in natural products

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research. For example, “omics-based” and other high-throughput technologies may help researchers evaluate the validity of hypothesized additive or synergistic effects that are at the core of many traditional herbal medicines. In addition, the use of network pharmacology—the study of the web of biologic targets for any bioactive substance—will enable researchers to investigate the complex effects of natural products on multiple targets in ways that were never before possible.

b. Support development of novel technologies and instruments, including diagnostic methods, tools, and sensors.

To carry out rigorous research on symptom management and functional changes, scientists need valid, reproducible ways to assess symptoms.

- ***Biosensors and Mobile Health:*** Rapid advances in technology and bioengineering are facilitating the development of increasingly sophisticated and versatile sensors. These sensors should enable improved reporting of symptoms and functional outcomes, as well as contribute to improved data capture. For example, wearable biosensors such as bracelets, patches, and caps can collect data on movement and physical activity, blood sugar levels, heart rates, and neural activity.
- ***Patient-Reported Outcomes:*** Patient Reported Outcomes Measurement Information System (PROMIS) tools are well suited for use as endpoints in clinical studies on the effectiveness of treatment. Further refinement and testing of PROMIS and other patient-reported outcome tools will lead to improved ways to assess pain, depression, anxiety, and other symptoms not easily measured with other diagnostics.
- ***Imaging and Neurotechnologies:*** Improved methods and tools are needed to understand the neurological aspects of symptoms such as pain, depression, and anxiety. Advances in imaging and other neurotechnologies may provide an improved means of measuring and understanding the neurologic circuits that underlie symptoms. For example, electrophysiological recordings, single photon emission computed tomography (SPECT), positron emission tomography (PET), and functional magnetic resonance imaging (fMRI) show promise for advancing what is known about neurologic and other biologic factors associated with pain and other symptoms. With NCCIH’s participation, some of these advances may be realized through the NIH B.R.A.I.N. (Brain Research through Advancing Innovative Neurotechnologies®) initiative.
- ***Biomarkers:*** There is an urgent need for the identification of biomarkers that can be used to assess pain and other symptoms. Advances in high-throughput technology and bioinformatics are providing new tools to simultaneously measure many metabolites, thus facilitating the identification of metabolites and other molecules associated with changes in symptom severity and functionality.

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Objective 2: Improve Care for Hard-to-Manage Symptoms

Managing symptoms—particularly recurring or chronic symptoms such as back, neck, or joint pain, anxiety, headache, and insomnia—is challenging. Symptoms may change over time, and patients may experience multiple symptoms in clusters (e.g., pain, sleep difficulties, and mood changes) rather than a single symptom in isolation. Current approaches to symptom management often have limitations. Despite medical treatment, some patients continue to experience troublesome levels of symptoms and a diminished quality of life. Moreover, medications used to treat symptoms may have significant risks and side effects.

Learning more about how complementary health approaches might improve symptom management in both the short- and long-term is a priority for NCCIH’s future research investments. There is a growing body of basic and clinical research on complementary health approaches for symptom management that employs the methods, tools, and technology of neuroscience, psychoneuroimmunology, psychology, behavioral medicine, physical medicine, and biomechanics. For example, research studies have revealed that interventions like meditation and acupuncture affect central mechanisms of pain perception and processing; regulation of emotion and attention; and placebo responses. Although not yet fully understood, these effects point toward scientifically plausible mechanisms—often unrelated to traditional mechanistic explanations—by which these interventions might be effective.

Strategies:

1. **Develop and improve complementary health approaches and integrative treatment strategies for managing symptoms such as pain, anxiety, and depression.**

NCCIH is particularly interested in clinical studies of interventions for pain, anxiety, and depression, as treatment options for these conditions are limited and some have deleterious side effects. NCCIH is also interested in better understanding the transition from acute to chronic pain and testing and developing interventions that may prevent it.

Rigorous study of any clinical intervention requires the use of well-established methodology. Well-powered randomized clinical studies are recognized as an essential component of the evidence base regarding clinical efficacy or effectiveness. To implement such studies, the magnitude and nature of treatment effects must be estimated in preliminary studies; treatment algorithms must be developed and validated; and feasibility of volunteer recruitment must be established. Methods are needed to measure consistency and fidelity of protocol implementation, practitioner variability, and adherence of participants to the interventions being studied. In addition, well-characterized and meaningful clinical and laboratory outcome measures are needed to fully determine safety and to definitively measure benefit or the lack thereof.

Although the scientific literature may provide the rationale for conducting a clinical trial, investigators often lack critical information about the intervention, outcome, or recruitment strategy necessary to design an informative trial. Preliminary studies to refine the intervention, determine the appropriate outcome measure, or adapt the intervention to a specific patient population are usually needed before a full-scale clinical trial can be conducted.

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Mind and Body Practices

Emerging evidence of promising clinical effects of many mind and body approaches points toward important opportunities to advance the science and improve the practice of symptom management. In many cases the evidence is strengthened by results from basic and clinical research that employ the tools and technology of neuroscience, immunology, psychology, behavioral and physical medicine, and biomechanics. Addressing the scientific and operational challenges confronting the study of promising mind and body interventions requires continued efforts to foster multidisciplinary collaborations that engage the expertise and experience of complementary health practitioners and use the tools and technologies of a variety of scientific disciplines.

Natural Products, Probiotics

NCCIH seeks to support clinical studies of the use of natural products for symptom management. The aim of such research is to confirm the link between the impact of the natural product on a biological signature (i.e., mechanism of action) and demonstrate an association between the change in the biological signature and clinical outcomes in humans. Large clinical trials are warranted only when basic and translational research enables rigorous testing of evidence-based hypotheses.

2. Conduct studies in “real world” clinical settings to test the safety and efficacy of complementary health approaches, including their integration into health care.

The Center is particularly interested in the efficacy and effectiveness of complementary and integrative health approaches aimed at managing pain, anxiety, and depression. There are many practical questions emerging from the NCCIH pain portfolio that could be studied using a pragmatic approach. For example, there is growing evidence, reflected in systematic reviews, that a number of mind and body therapies are beneficial for pain management, including acupuncture and meditation for the management of chronic low-back pain.

Many research organizations, including NIH, support the concept of a learning health care system in which research is embedded into the delivery of care. In this type of system, data are collected every time a patient receives care, and over time, the system “learns” whether and how well the care worked. Whenever something is learned with this approach, it can be quickly applied and adopted.

Integrating an effectiveness study within a health care system is often challenging. Research and patient care have long been conceptualized as separate activities that take place in different locations under different types of oversight, and the types of recordkeeping used in clinical care, including electronic health records, may not always meet research needs. However, these challenges are beginning to be overcome, and innovative approaches are being developed allowing for informative pragmatic research to be conducted in the actual settings where integrative health care is practiced.

Given the widespread use of complementary health approaches, opportunities exist to employ clinical outcomes and effectiveness research methodologies to collect “real world” evidence about the use of specific complementary approaches for health care and health promotion. Pursuing this type of research requires creative collaboration with those who provide care in settings where integration of complementary health approaches could be studied. The “real-world” settings for such research may be quite varied, and could include schools, nursing homes, hospices, cancer treatment facilities, and settings that provide care for military personnel and Veterans. NCCIH seeks

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to build upon the success of initiatives taking on this challenge, such as the NIH Health Care Systems Research Collaboratory, a NIH Common Fund initiative that is co-led by NCCIH.

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Objective 3: Foster Health Promotion and Disease Prevention

Individual behavior plays a key role in health promotion and disease prevention. It is well established that adopting and maintaining healthy behaviors (e.g., good eating habits and regular physical exercise) and modifying unhealthy behaviors (e.g., quitting smoking) reduce risks of major chronic diseases.

Additionally, a small but growing evidence base suggests a potential benefit of complementary health approaches for the purposes of wellness, health promotion, and disease prevention. More research is needed to better understand how certain complementary health approaches can be useful in encouraging better self-care, improving a personal sense of well-being, and promoting a greater commitment to a healthy lifestyle.

The use of complementary health approaches to promote wellness is a relatively new research focus area for NCCIH, but wellness is a familiar concept to many people who use these approaches. In fact, national survey data indicate that more people use complementary approaches to promote health and wellness than to treat a specific illness. In the 2012 NHIS, 94 percent of respondents who practiced yoga and 89 percent of those who used natural product supplements said that they did so for reasons related to wellness; much smaller numbers used these approaches as a treatment. Seventy-two percent of respondents who practiced yoga cited its focus on the whole person—mind, body, and spirit—as one of their reasons for using this practice.

NCCIH is committed to exploring the potential of complementary health approaches to foster health promotion and disease prevention across the lifespan, to better understand which interventions work best for whom and under which conditions, and to examine which strategies may promote long-term adherence to the most promising interventions. In addition, the Center is interested in exploring the potential of “omics” technologies to identify optimal health promotion and disease prevention strategies at the individual level.

Strategies:

- 1. Investigate mechanisms of action of complementary and integrative health approaches in health resilience and practices that improve health and prevent disease.**

Resilience

The concept of resilience—the capacity to withstand, grow, or recover from change and stress—is important in health, wellness, and prevention research. The study of resilience can help scientists learn why some people are better able than others to resist disease risks posed by stressful or adverse experiences, and it may lead to the development of approaches that will help individuals adapt in a more positive manner to negative life events.

NCCIH seeks to support research on complementary health approaches and resilience across the continuum from basic and mechanistic studies through clinical trials that examine efficacy and effectiveness of interventions. NCCIH is interested in understanding the mechanisms of action and potential effects of complementary health approaches in the context of resilience. These efforts will build upon extant data involving mind and body practices, such as mindfulness-based stress reduction or meditation. Future studies will help determine the value of complementary health approaches in enhancing cognitive, emotional, and behavioral resilience in people who are

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subjected to stressful or adverse circumstances. NCCIH also is interested in the role that some natural products may play in increasing resilience to psychological stressors. In addition, substances from some natural products may promote metabolic resilience—that is, the ability to maintain health despite the presence of stressors such as a high-fat diet or inflammation. Similarly, the potential role of the microbiome in the development and maintenance of resilience is of interest to NCCIH.

Promoting health and preventing disease

NCCIH’s research investments in understanding the role of complementary and integrative approaches in promoting health and preventing disease are, in part, informed by data on the complementary products and practices people use. These data include what groups of people use them, why they use them, how their use has changed over time, and how their use relates to health outcomes.

Survey data have revealed that people who use complementary approaches for wellness differ in significant ways from those who use them to treat an illness. For example, an analysis of NHIS data showed that wellness-oriented users of complementary approaches were generally healthier, had a lower rate of use of conventional health services, and had healthier behaviors overall, including greater physical activity and a lower likelihood of obesity, than those who used complementary approaches to treat illnesses. In addition, analyses of insurance claims data in the state of Washington showed that children who receive care from complementary health practitioners are less likely to receive recommended pediatric immunizations and that women who receive care from these practitioners are less likely to receive some, but not all, types of recommended screening tests. Findings like these can help guide the development of targeted information to ensure that all population groups receive needed preventive services.

Surveys are only a first step in gaining knowledge about health-related behavior. More focused research is needed to understand why people make healthy, unhealthy, or risky choices; find out what choices people are making on a day-to-day basis; and elucidate the impact these choices may have on short- and long-term health. Ever-changing technologies have improved the ways in which data can be obtained on a variety of behaviors. For example, wearable devices can monitor physical activity and physiologic measures such as heart rate. Current studies can also harness state-of-the-art technologies and approaches from the neurobiological, biomechanical, and biological sciences to elucidate biological effects and identify mechanisms of action of behaviors and interventions of interest. Researchers conducting studies may leverage existing databases such as electronic health records to provide real-world insights into health and health care.

2. Study complementary health approaches to promote health and wellness across the lifespan in diverse populations.

NCCIH seeks to foster research to develop, test, and refine interventions and to find ways to adapt interventions to meet the needs of different populations, including those most vulnerable. The Center plans to foster research that examines the potential contributions of complementary approaches in promoting healthy behaviors and preventing diseases and disorders across the life course. Most use of complementary health approaches in the United States is aimed at improving general health and well-being, but most complementary health research to date has focused on the application of those approaches to specific conditions or symptoms. Although the scientific and operational challenges in pursuing a health-promotion research agenda are significant, compelling

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opportunities exist to explore the potential role of complementary and integrative interventions for health promotion and prevention.

For example, preliminary evidence suggests that nurturing mindfulness in children and youth may be a feasible and effective method of building resilience in universal populations, such as students at a school. However, the evidence base is quite small. Larger, more rigorous studies are needed to determine the efficacy of these interventions, and if they are efficacious, further research will be needed to determine who benefits, at what age, and how the interventions can be implemented with fidelity at scale by trained providers. Another example of health promotion and prevention research is examining the potential of mindfulness approaches to reduce stress, anxiety, and depression in pregnant women and improve birth outcomes.

3. Explore research opportunities to study and assess the safety and efficacy of complementary health approaches in non-clinical settings such as community- and employer-based wellness programs.

Employer- and community-based health and wellness programs are widespread, even though little is known about their effectiveness. Some offer healthy lifestyle promotion, while others focus on disease management. An increasing number of these programs incorporate complementary health approaches, but very few studies have evaluated the potential benefit of complementary approaches in these settings.

NCCIH is interested in developing research partnerships and priorities to assess the safety and efficacy of complementary health approaches in workplace and community settings, with an emphasis on programs in medically underserved communities. NCCIH's experience with the Health Care Systems Research Collaboratory has demonstrated the feasibility of public-private partnerships. NCCIH will draw on this experience to build partnerships with employers or community health centers to expand and prioritize research on the effectiveness of wellness programs.

Leveraging the existing investments of employers and communities in these programs may facilitate comparative effectiveness trials of wellness programs with and without complementary or integrative components. Such trials could answer important research questions. For example, trials could be designed to find out whether workplace-based mindfulness training decreases stress and improves workplace satisfaction and productivity or whether workplace yoga classes enhance the effectiveness of conventional weight management programs.

This is a relatively new area of research for NCCIH, so it is important to investigate feasibility and identify infrastructure needs before attempting large-scale trials. Data need to be collected on the types of complementary approaches that are most commonly included in employer- and community-based wellness programs, the reasons why these approaches are chosen, the demographics of individuals engaged in the programs, the ways in which programs are marketed to potential participants, and the outcomes of greatest interest to employers and community organizations. In addition, there will need to be an assessment of various trial methodologies and evaluation criteria that could be used in clinical studies in "real world" settings.

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Objective 4: Enhance the Complementary and Integrative Health Research Workforce

Researchers from many different biomedical and behavioral disciplines are the key holders of scientific knowledge and technologies required for in-depth investigation of the basic biological, physiological, and clinical effects and safety of complementary health approaches and their integration with conventional medicine. Over the years, NCCIH has also targeted resources aimed at attracting well-trained and experienced scientists into complementary and integrative health research and in supporting their development as scientific leaders in the field.

NCCIH continues its commitment to training researchers with the expertise needed to conduct successful basic, translational, and clinical studies on complementary health approaches. For example, NCCIH supports a variety of training and career development awards that provide funding for new and early-stage investigators as well as mid-career investigators. Recently, a special Working Group of the National Advisory Council on Complementary and Integrative Health examined the topic of the complementary and integrative health research workforce. The [Working Group Report on Clinician-Scientist Workforce Development](#), which focuses specifically on ways to expand and strengthen the clinician-scientist workforce, was presented and discussed at the February 5, 2016 Council meeting.

Strategies:

1. Support research training and career development opportunities to increase the number and quality of scientists trained to conduct rigorous, cutting-edge research on complementary and integrative health practices.

NCCIH supports a range of research training and career development programs aimed at increasing the number, quality, and diversity of well-prepared, skilled investigators with knowledge and expertise in both complementary and integrative health and state-of-the-art research methods. Because complementary and integrative health approaches include a wide variety of modalities and specializations, NCCIH's training strategies must include innovative approaches that incorporate an understanding of this diversity to ensure that future workforce needs for the universe of modalities and the various combinations of these modalities are met.

In particular, the Center will focus on:

- Clinician-scientists, including conventionally trained physicians, complementary health practitioners, and other health care professionals (e.g., clinical psychologists, nurses) who conduct research across a wide range of complementary and integrative health approaches.
- Scientists trained in key biomedical and behavioral research disciplines necessary for rigorous, state-of-the-art scientific investigation of complementary and integrative health interventions, practices, and disciplines.
- Individuals from groups who are underrepresented in scientific research (e.g., racial and ethnic minority populations) and are interested in careers in complementary and integrative health research.

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2. Foster interdisciplinary collaborations and partnerships.

Across the fields of biomedical and behavioral research it has become clear that clinical investigation aimed at providing scientific evidence useful to the public, health care providers, and health policymakers is an inherently interdisciplinary enterprise that often requires a team of researchers with different areas of expertise. This is particularly true of the field of complementary and integrative health research. Rigorous investigation in this field requires cross-disciplinary and multidisciplinary teams, both within and across institutions and health care settings.

For example, NCCIH is currently working with a number of other NIH ICs, the Department of Veterans Affairs, and the Department of Defense on designing studies of complementary and integrative approaches for the management of pain in military and Veteran populations. These studies will require multidisciplinary teams of scientists working in either military or Veterans' health care systems.

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Objective 5: Disseminate Objective Evidence-based Information on Complementary and Integrative Health Interventions

It is critical that the public, health care providers, researchers, and policymakers be informed and knowledgeable about the safety and effectiveness of complementary and integrative health interventions. They also should have access to information about ongoing research and research results, as well as information about NCCIH's scientific priorities and funding initiatives.

NCCIH faces several unique challenges with regard to translating and disseminating complex scientific information to an interested and engaged public. First, the landscape of complementary and integrative health is inundated with information, some of it overtly promotional, and much of it either not based on evidence or of questionable quality and reliability. Second, there is evidence that individuals who use complementary health approaches often do not discuss their use with their conventional health care providers. Instead, they rely on other sources, including family and friends, practitioners of complementary health approaches, and information gleaned from the Internet, popular media, and advertising.

Going forward, NCCIH must continue to ensure that its presentation of evidence-based information on complementary health interventions is scientifically objective and appropriately balances what is known and not known about their safety and effectiveness. By extension, NCCIH also must develop methods and approaches to enhance the public's understanding of basic scientific concepts and biomedical research to lay a foundation of knowledge for the better understanding of information and improved decisionmaking. Importantly, NCCIH must provide information that is engaging, accessible, and of value to the public, health care providers, researchers, and policymakers, given the flood of information in the public domain and the frequent self-care use of complementary health approaches.

Strategies:

1. Disseminate evidence-based information on complementary and integrative health approaches to health care providers, researchers, policymakers, and the public.

NCCIH seeks to provide unbiased, reliable, authoritative resources on complementary and integrative health approaches and research results for health care providers, researchers, policymakers, and the public. The Center uses a variety of communication techniques and technologies to bring evidence-based information about complementary health approaches to these audiences and to provide a scientifically accurate perspective on the potential promise, as well as the risks, of using these interventions. NCCIH provides information to its audiences through multiple channels, including the Web, broadcast and print media, a research blog, and a social media program.

The Center recognizes the importance of engagement with the scientific research community. The NCCIH Web site provides current information about ongoing research, research results, strategic directions, high- and low-priority research areas, policies, and grant funding opportunities. In addition, information is disseminated at scientific conferences and meetings.

Health care professionals regularly face many challenges in providing their patients with advice and education about complementary and integrative health approaches. Recognizing these challenges,

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NCCIH continues to develop information resources targeted toward the needs of this important audience. These resources include specialized communications, outreach to professional societies, and online tools, including a dedicated Web portal and a monthly e-newsletter that summarizes the current evidence base of specific complementary health interventions and provides links to relevant clinical practice guidelines.

NCCIH will continue to work actively with its diverse community of stakeholders to identify, understand, and address the information needs of health care providers, researchers, policymakers, and the general public, and their concerns about accuracy or interpretation of research results and health messages.

2. Develop methods and approaches to enhance public understanding of basic scientific concepts and biomedical research.

NCCIH recognizes the importance of the general public having knowledge and understanding of basic scientific facts, concepts, and vocabulary related to health research. Those who possess such knowledge have the capacity to obtain, process, and understand the basic information about scientific research needed to make informed health care decisions. There is a particular need for an improved understanding of the science of health for those who use complementary and integrative health approaches. Because so many of these approaches are readily available in the marketplace, and so many individuals choose self-care options for their health, NCCIH sits at the crossroads between research and real-world consumer use.

To meet these needs, NCCIH will plan and implement a collaborative effort to educate the public about the importance of understanding basic scientific concepts and biomedical research. The Center will also provide consumers with the information they need to be discerning about what they hear and read and to make well-informed health care decisions. The information developed should equip the public with the ability to read, understand, and critically evaluate a variety of research reports, from commercial advertisements to articles in the popular press to publications in scientific journals. Tools and informational resources include engaging short videos, podcasts, infographics, interactive modules, and links to other creditable resources, and would be fully integrated into the NCCIH Web site.

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Top Scientific Priorities

March 25, 2016

- Nonpharmacologic Management of Pain
- Neurobiological Effects and Mechanisms
- Innovative Approaches for Establishing Biological Signatures of Natural Products
- Disease Prevention and Health Promotion Across the Lifespan
- Clinical Trials Utilizing Innovative Study Designs To Assess Complementary Health Approaches and Their Integration Into Health Care
- Communications Strategies and Tools To Enhance Scientific Literacy and Understanding of Clinical Research

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Nonpharmacologic Management of Pain

Introduction and Explanation of Need:

Pain is the condition for which adults in the United States most often use complementary and integrative health approaches. This includes musculoskeletal pain (back pain, neck pain, joint pain, etc.), headache, and pain associated with specific conditions (e.g., arthritis). Although pain is a normal, vital response to actual or potential tissue injury, in some cases pain can become chronic and a condition unto itself, leading to biological changes in the central nervous system as well as changes in peripheral tissues.

Chronic pain is a debilitating condition with high societal and economic costs. Growing evidence indicates that some complementary health approaches may help in its treatment and management. Now that self-management of chronic pain is recognized as a component of an overall treatment strategy, it is important to better understand how to best integrate effective complementary approaches into care and how to optimize interventions for individuals and groups. Discovering the mechanisms by which a complementary approach exerts its effects could help in the design of better treatments and predict which people are most likely to respond. Hence, there is a need for rigorous research on complementary and integrative health approaches for pain that spans basic, mechanistic, translational, and clinical domains.

What does success look like?

- There is increased understanding of the approaches for pain management that are most efficacious or effective for various conditions and populations, and which can best be integrated into overall pain treatment and management strategies.
- There is increased understanding of the mechanisms by which these approaches exert their effects.
- Research standards for studies on chronic low-back pain are broadly accepted and used, as shown by their inclusion in grant applications and research publications.

Objectives:

- Elucidate biological targets and pathways by which complementary health approaches (e.g., natural products, mind and body interventions) have clinical benefits, including analgesic effects for chronic pain conditions.
- Conduct basic and clinical research aimed at understanding the role of nonspecific effects (e.g., expectancy, context, placebo) and whether they can be used to enhance the effectiveness of pain management.
- Improve understanding of the higher-order neural mechanisms underlying pain perception and pain modulation by the environment, emotional and cognitive states, expectation, and context in both animal models and humans.
- Develop further understanding of the mechanisms of action and the biophysical characteristics of noninvasive neuromodulation (e.g., transcranial direct current stimulation and ultrasound) in preclinical model systems and in human laboratory studies.
- Develop understanding of brain-gut-microbiome signaling pathways that may be involved in chronic pain conditions and functional pain syndromes (e.g., functional abdominal pain syndrome).
- Examine interactions of nonpharmacologic and pharmacologic interventions for potential additive effects, possible synergy, and potential for safe reduction of opioids and other analgesics.
- Examine interactions of multiple nonpharmacologic interventions (e.g., meditation and probiotics) to determine whether they can increase effect size and enhance resilience.

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- Conduct large, pragmatic studies of pain management addressing important clinical or health systems questions.
- Develop and validate objective pain measures for complementary and integrative health approaches in the treatment of pain.

Areas of Low Programmatic Priority

- Research comparing clinical outcomes of verum and sham acupuncture.
- Research comparing individualized to standardized acupuncture treatment protocols.
- Research on antioxidants and pain.
- Preclinical studies of voluntary exercise for mitigating acute pain and/or nerve injury.

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Neurobiological Effects and Mechanisms

Introduction and Explanation of Need:

Complementary and integrative health approaches have been commonly used by the general public to treat or manage disorders or symptoms relevant to the nervous system. These range from pain, sleep disturbance, stress, anxiety, and behavioral disorders to more serious neurological or mental health conditions. Commonly used complementary health approaches include mind and body interventions such as meditation, spinal manipulation, yoga, massage, tai chi, and acupuncture. A variety of natural products, including herbs, dietary supplements, and prebiotic or probiotic products are also commonly used. Despite their broad usage by the general public, the therapeutic benefits of these approaches are, at best, modest and often not significantly better than placebo when subjected to rigorous efficacy studies. In-depth understanding of the mechanisms by which complementary and integrative health approaches may impact physiological systems, including the central nervous system (CNS), becomes critical for developing strategies to optimize the beneficial effects of these approaches.

Whether and how complementary health approaches directly modulate or modify the structure and/or function of the entire or part of the nervous system and other associated physiological systems, such as organs and tissues, remains understudied. Such studies are scientifically challenging for both the complementary and integrative health and the biomedical research communities. This challenge is further compounded by individual differences (e.g., genetic and epigenetic differences, psychosocial and environmental factors). Nevertheless, recent transformative advances in genomics, neuroscience, stem cells, system biology, neuroimaging, and predictive computational modeling offer excellent technological and conceptual resources and opportunities for innovative and impactful mechanistic studies of complementary health approaches.

What does success look like?

Successful mechanistic studies of complementary and integrative health approaches include two separate but interoperable accomplishments in model systems/organisms and/or human/clinical populations:

- Identification of modifiable mechanisms of complementary health approaches that may optimize the beneficial effects of these approaches alone or in combination with other therapies.
- Identification of predictive mechanisms or biomarkers that can differentiate responders from non-responders to these approaches.

Objectives:

- Develop or utilize innovative (1) humanized cellular or organ systems or (2) transgenic or preclinical animal models to investigate neural mechanisms of complementary and integrative health approaches.
- Ascertain the sensory neural basis or anatomical and physiological pathways of acupoints in various forms of acupuncture, acupoint-based stimulation interventions, or manual therapies in animal models or human subjects.
- Determine and analyze the neural pathways by which acupuncture, acupoint-based stimulation interventions, or manual therapies, such as massage, exert their analgesic effects or therapeutic effects on various physiological systems (e.g., immune system, vascular system, musculoskeletal system, or internal organs such as brain, heart, and gut) in animal models or human subjects.

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- Investigate top-down neural pathways underlying the effects of meditation, expectancy, placebo effects, and other mindfulness interventions (i.e., meditative yoga, tai chi, qi gong, hypnosis, and guided imagery), ranging from high-order brain functional regions to the peripheral tissues and organs, such as immune cells, gut, muscles, bone, heart, and microbiome.
- Assess the neural pathways or other physiological mechanisms by which meditative movement and related therapies impact the structure and function of the central nervous system.
- Examine innovative neural mechanisms by which candidate natural products, such as cannabinoids and some Chinese Traditional Medicine herbs or patches, generate analgesic effects.
- Pilot test neural mechanistic effects of combined natural products and mind and body interventions for acute and/or chronic pain management, other symptom management, or behavioral change.

Areas of Low Programmatic Priority

- A replicative mechanistic study of complementary and integrative health approaches in different clinical populations.

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Innovative Approaches for Establishing Biological Signatures of Natural Products

Introduction and Explanation of Need:

Natural products, whether as herbal supplements or as part of a diet, are frequently consumed as a complex mixture. This complexity is further amplified by potential interactions with endogenous metabolic pathways, including those associated with the microbiome. The result is a collection of natural products and their metabolites that, individually and/or collectively, are associated with a network of biological activity. Importantly, in addition to direct action on biological targets, the activity of natural products can be influenced by an individual's health and metagenomic background. The purpose of this research priority therefore is to advance the characterization and categorization of the biologic activity of complex natural products broadly, with an emphasis on determining metabolomic profiles.

Many of the techniques for studying complex mixtures of natural products have remained largely unchanged for many years and have not taken full advantage of innovative advances in biological and chemical methodologies and technologies. Understanding biological signatures of complex natural products requires innovative approaches and tools beyond those traditionally used for analyzing a single molecule against a single mechanistic target. To move the field forward, there must be a renewed emphasis on multidisciplinary high-impact approaches to overcome conceptual, methodological, and technological hurdles that hinder advances in natural products research.

One promising method is the incorporation of network pharmacology, an innovative approach that seeks to define the web of biologic targets for bioactive substances. This tool will facilitate the characterization and categorization of complex natural products. Information gleaned from network pharmacologic analyses may help predict pharmacological and biological mechanisms of action, including their influence on the microbiome.

What does success look like?

Researchers who are at the leading edge of science successfully incorporate novel natural products technologies in their research activities. In addition, these new technologies help elucidate pharmacological and metabolomic signatures that may provide a basis for understanding natural products' biological activities.

Objectives:

- Establish a state-of-the-art data repository of the chemical and biological signatures of natural products as a resource to aid researchers.
- Develop new and innovative technologies to better understand the effects of natural products on the human biome.
- Develop innovative bioinformatic technologies to better predict potential toxicities of dietary supplements, including pre-/probiotics.
- Identify and develop novel bioassays to evaluate natural products and their analogs for their complementary effects in alleviating pain, symptoms of depression, or signs of anxiety.

Areas of Low Programmatic Priority

- Research focused on a single compound or well-characterized mechanistic target.
- Screening of natural product libraries in subcellular assays.
- Bioactivity-guided fractionation projects.

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Disease Prevention and Health Promotion Across the Lifespan

Introduction and Explanation of Need:

Research on theory-based prevention interventions has been applied across the lifespan, from interventions to prevent difficulties early in life (e.g., to prevent maternal substance abuse during pregnancy, infant mortality, and child abuse and neglect), through prevention strategies for childhood (e.g., to reduce violence, mental health problems, and obesity), adolescence (e.g., to prevent delinquency, bullying, drug abuse, and suicidal ideation and behaviors), young adulthood (e.g., to prevent risky sexual behaviors and sexual assault), and adulthood (e.g., to prevent substance use disorders). While the targeted developmental stage may change, the primary focus of these interventions is on reducing risk and increasing protective factors that can modify proximal outcomes (e.g., self-regulation, skill development) as well as long-term, distal outcomes including psychological health, substance abuse, physical health, and other important areas (e.g., improved academic achievement and employment). Indeed, interventions designed to prevent mental illnesses and substance abuse disorders have shown efficacy and effectiveness in modifying a wide array of individual outcomes, such as improving cognitive ability, emotional regulation, and physical health, and reducing risky behavior). These interventions have also been shown to improve other outcomes not targeted by the interventions (e.g., risky sexual behaviors and suicidal ideation and behaviors).

There has been a growing interest in the use of complementary health approaches, especially meditative approaches, for the prevention of mental, emotional, and behavioral disorders, and for the promotion of psychological and physical health, well-being, and resilience. Studies have shown efficacy primarily for mindfulness-based stress reduction (MBSR) for improving factors related to many physical and mental health conditions in adults, including indices of immune, endocrine, and neurological function. However, the evidence for the use of complementary modalities in the context of prevention and health promotion is modest. Furthermore, a small body of research examining the use of complementary and integrative approaches for the prevention of substance abuse, mental health problems, and obesity in youth exists, though the evidence base is quite small.

There is a great interest in determining whether these approaches have an impact on a wide array of behaviors that promote health and prevent disease, particularly for children, adolescents, families, and young adults. Rigorously designed, developmentally appropriate studies are needed to determine the efficacy and effectiveness of complementary and integrative health approaches for health promotion and disease prevention across the lifespan. It is also essential to gain a better understanding of the mechanisms of action of these interventions and to determine what works, for whom, and under what conditions. NCCIH, therefore, seeks to support research that could expand the evidence base on meditative approaches for preventing mental, emotional, and behavioral disorders and for the promotion of psychological and physical health.

What does success look like?

Over the course of the next 5 to 10 years, the research NCCIH supports in this area will lead to an increased number of efficacious and effective life-course specific complementary health-promoting and disease-prevention approaches (e.g., mind and body interventions) that can be delivered at different levels (e.g., universal, selective, indicated), in different contexts (e.g., family, school, community, medical centers, child welfare and juvenile justice system) that also include populations at risk (e.g., families living in poverty, children who have experienced abuse, and military families).

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Objectives:

- Develop and test theory-based interventions that are, in general, developmentally appropriate and that also target vulnerable populations¹ across levels of intervention in different settings.² The interventions should be designed to have an impact on a broad array of outcomes, including cognitive, emotional, behavioral, and physical health.
- Investigate mechanisms of action, including underlying behavioral processes and the underlying biological and neurobiological mechanisms that are modified by an intervention.
- Develop and refine sensors and other innovative technologies (e.g., smartphone apps and wearable activity monitors) that can be used to deliver and measure prevention intervention effects and outcomes.

Prenatal through Young Adulthood:

- Develop and test complementary and integrative prevention approaches that include the adults most influential in children's lives (e.g., teachers, parents, and other caregivers), with the goal of improving the development and well-being of children.
- Utilize outcome measures that employ multiple methods (e.g., neurobiological, behavioral) for those involved in, or the focus of, the intervention (e.g., students, teachers, parents).
- Develop and test theory-based prevention mind-body interventions for adolescents and young adults, including universal interventions for the general population and selective, indicated interventions for those who are particularly vulnerable.

Older populations:

- Develop and test theory-based mind and body prevention interventions focused on older populations, including the general population and those at increased risk for depression, anxiety, and other mental health disorders.

Areas of Low Programmatic Priority

- Natural products interventions for prevention and health promotion across the lifespan.

¹ Examples of vulnerable populations include children and families living in poverty, including high-risk pregnant women; racial/ethnic minorities; and sexual minorities.

² Examples of settings include families, schools, health care, child welfare, juvenile justice, and the workplace (e.g., employer-based wellness settings).

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Clinical Trials Utilizing Innovative Study Designs To Assess Complementary Health Approaches and Their Integration Into Health Care

Introduction and Explanation of Need:

To achieve the NCCIH mission of defining the usefulness and safety of complementary and integrative health care interventions (i.e., both mind and body modalities and use of natural products) and their roles in disease prevention, improving health, and managing symptoms, NCCIH supports clinical trials to assess the safety, efficacy, and effectiveness of these approaches. Efficacy studies supported by the NCCIH clinical research portfolio use standard randomized controlled trial designs. In general, however, a pilot or feasibility study is conducted prior to an efficacy study, and it typically focuses on establishing the frequency and duration of the intervention; selection of the appropriate patient population and outcome measures; ability of the participants to adhere to the study intervention requirements; and demonstration that the team can recruit and retain participants. For natural product clinical investigations, additional pharmacokinetics studies, identification of biological signatures, and determination of appropriate dosing may be needed before launching a larger efficacy study.

For larger scale studies, NCCIH can take advantage of recent innovations in designs and methodologies. Examples include establishing optimal doses using Bayesian dosing studies and assessing effectiveness in a more generalizable population and in real world settings using pragmatic cluster randomized trials or stepped wedge designs. Electronic record data within health care systems can also be used to leverage extant patient-centered data for generating hypotheses and examining the use and possible effectiveness of complementary and integrative health approaches. If these interventions are found to be beneficial, there are also innovative methods for investigators to study how they can be integrated into health care systems effectively and efficiently with dissemination and implementation studies. A targeted approach for which innovative study designs can be utilized and when they are appropriate will assist in shaping a strong NCCIH clinical portfolio.

What does success look like?

The clinical portfolio will comprise standard randomized controlled trial designs to assess the safety and efficacy of complementary health approaches, and when appropriate, trials with innovative designs to address unique hypotheses about what complementary health approaches are most effective, for whom, and under what conditions. Pragmatic clinical trials conducted within health care systems will be able to address hypotheses that inform the delivery of health care to patients and inform health policy decisions that have the potential to improve health care outcomes.

The incorporation of innovative designs in early-phase clinical studies will result in more optimized interventions and a better understanding of the dosages of natural products needed to be able to detect benefit (if it exists). The utilization of innovative effectiveness studies will result in leveraging existing infrastructures for data collection and reducing costs for trials, thus allowing NCCIH to fund more large-scale trials.

Objectives:

Early-Stage Clinical Studies

- Utilize innovative early-phase methods, such as Bayesian estimation dose-finding approaches, that are flexible, involve fewer participants, and can be used to identify safe and tolerable doses for natural products.

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- Encourage Multiphase Optimization Strategy (MOST) designs when mind and body interventions need to be refined, to determine which components are necessary to achieve the benefit, or when interventions are being combined, to determine which components need to be maintained.

Efficacy or Effectiveness Studies

- Conduct pragmatic clinical trials to address questions about the integration of complementary health approaches into health care systems, or to study the effectiveness of complementary or integrative approaches in comparison to standard care.
- Apply lessons learned from the Health Care Systems Research Collaboratory pragmatic clinical trials initiative, such as biostatistical guidelines for cluster randomization and recommended methods for data extraction from electronic medical records, to study the impact of complementary health approaches, such as interventions for pain management and comorbid conditions, in health care systems such as the Veterans Health Administration and the Department of Defense's TRICARE.
- Utilize innovative designs such as Sequential Multiple Assignment Randomized Trials (SMART) for developing treatment algorithms or stepped-care strategies to determine the sequence of interventions, or at what times an intervention should be reassessed and modified.

Areas of Low Programmatic Priority

- Large-scale clinical trials of mind and body interventions when there are no preliminary data to determine appropriate dose, duration, and frequency or whether the patient population can adhere to the proposed intervention.
- Large-scale clinical trials of natural products when there are no preliminary data demonstrating the availability, bioavailability, and pharmacokinetics of the product; a replicable effect on a biologic signature; and dosing studies to determine the appropriate dose to impact the biologic signature.
- Pragmatic trials of interventions that do not have preliminary data demonstrating clinical efficacy or effectiveness in large controlled trials.

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Communications Strategies and Tools To Enhance Scientific Literacy and Understanding of Clinical Research

Introduction and Explanation of Need:

Surveys conducted in the United States and Europe reveal that many citizens do not have a firm grasp of basic scientific facts and concepts, nor do they have an understanding of the scientific process. Without an understanding of the science of health, many consumers will continue to value anecdotes over evidence, believe excessive claims made by supplement manufacturers or TV doctors touting the latest “miracle cure,” and potentially make unwise and unsafe decisions about their health. Those who do possess basic knowledge of the science of health have the capacity to obtain, process, and understand basic information about scientific research needed to make appropriate decisions about their health. Given the current health policy and research emphasis on shared decisionmaking with patients, enhanced patient understanding of the science of health is also a system-level priority. Health care professionals will bear a growing onus to explain and engage in dialogue with patients about treatment options. Promoting understanding of the science of health among a broad consumer base may ultimately make those discussions and decisions easier.

There is also a particular need for an improved understanding of the science of health for those who use complementary and integrative health approaches. Because many of these approaches are readily available in the marketplace, and so many individuals choose self-care options for their health, NCCIH sits at the crossroads between research and real-world consumer use. Further, to enhance the value and impact of NCCIH’s efforts in disseminating information, a basic understanding of the research enterprise is needed.

What does success look like?

Planning and implementing a collaborative effort to educate the public about the importance of understanding biomedical research so they may make informed, evidence-based decisions about their health. A successful strategic effort would include partner identification and development, needs assessment, content development (e.g., potential topics include absolute risk, levels of evidence, causation versus correlation, randomization in trials), qualitative and quantitative evaluation, support for scientific spokespeople, and outreach and dissemination.

Objectives:

- To establish a collaboration of partners within and external to the Federal Government committed to enhancing consumers’ understanding of the science of health
- To develop and evaluate easy-to-understand materials in a variety of platforms
- To promote the use of materials among the general public via direct outreach and targeting influential stakeholders.

Areas of Low Programmatic Priority

- Development of content with the specific goal of improving clinical trial recruitment
- Dissemination of materials and content at various reading levels for people with low literacy skills
- Development of communications strategies pertaining to the understanding of medical brochures, physician instructions, and consent forms, and the ability to navigate complex health care systems.