Complementary and Integrative Health Research: Priorities and Funding Opportunities from NCCIH

PAHO/WHO Regional Meeting

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Emmeline Edwards, Ph.D.
Dr. Edwards is a Title 42 federal employee who is required to disclose all financial holdings as public record, and has no outside activities to disclose.
Outline

- NIH and NCCIH - Mission and Strategic Plans
- NCCIH High Priority Topics
- Complementary & Integrative Health Approaches Utilization in the US
- Highlights from the NCCIH Portfolio
- Research & Training Opportunities for Investigators
NIH seeks fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability.
Your Application Could Be Funded by One of 24 NIH Institutes or Centers

- National Institute on Aging
- National Institute on Alcohol Abuse and Alcoholism
- National Institute of Allergy and Infectious Diseases
- National Institute of Arthritis and Musculoskeletal and Skin Diseases
- National Cancer Institute
- Eunice Kennedy Shriver National Institute of Child Health and Human Development
- National Institute on Deafness and Other Communication Disorders
- National Institute of Dental and Craniofacial Research
- National Institute of Diabetes and Digestive and Kidney Diseases
- National Institute on Drug Abuse
- National Institute of Environmental Health Sciences
- National Eye Institute
- National Institute of General Medical Sciences
- National Heart, Lung, and Blood Institute
- National Human Genome Research Institute
- National Institute of Mental Health
- National Institute of Neurological Disorders and Stroke
- National Institute of Nursing Research
- National Institute of Biomedical Imaging and Bioengineering
- National Center for Complementary and Integrative Health
- John E. Fogarty International Center
- National Center for Advancing Translational Research
- National Library of Medicine
- National Institute on Minority Health and Health Disparities

- Clinical Center
- Center for Information Technology
- Center for Scientific Review
 NIH-Wide Strategic Framework

**Setting Priorities**
- Incorporate disease burden as important, but not sole factor
- Foster scientific opportunity; need for nimbleness
- Advance research opportunities presented by rare diseases
- Consider value of permanently eradicating a pandemic

**Fundamental Science**
- Foundation for progress
- Consequences often unpredictable
- Advances in clinical methods stimulate progress
- Technology leaps catalyze advances
- Data science increases impact/efficiency

**Health Promotion/Disease Prevention**
- Importance of studying healthy individuals
- Advances in early diagnosis/detection
- Evidence-based elimination of health disparities

**Treatments/Cures**
- Opportunities based on molecular knowledge
- Breakdown of traditional disease boundaries
- Breakthroughs need partnerships, often come from unexpected directions

**Enhancing Stewardship**
- Recruit/retain outstanding research workforce
- Enhance workforce diversity
- Encourage innovation
- Optimize approaches to inform funding decisions
- Enhance impact through partnerships
- Ensure rigor and reproducibility
- Reduce administrative burden
- Employ risk management strategies

**Overview**
- Mission of NIH
- Unique moment of opportunity in biomedical research
- Current NIH-supported research landscape
- Constraints confronting the community in the face of lost purchasing power
Alignment of NCCIH Research Objectives with NIH-Wide Strategic Plan

NIH

Health Promotion/Disease Prevention

Treatments/Cures

Fundamental Science

NCCIH

Advance Fundamental Science

Foster Health Promotion & Disease Prevention

Improve Care for Hard to Manage Symptoms
The NCCIH Mission

Define, through rigorous scientific investigation, the usefulness and safety of complementary and integrative interventions and their roles in improving health and health care.
Overview
NCCIH Mission and Vision
Priority Setting

- Advance Fundamental Science
- Foster Health Promotion & Disease Prevention
- Improve Care for Hard to Manage Symptoms
- Enhance Research Workforce
- Disseminate Evidence-based Information
Overview
NCCIH Mission and Vision
Priority Setting

Objectives:
NCCIH Strategic Framework

Enhance Research Workforce
Disseminate Evidence-based Information

Advance Fundamental Science
Foster Health Promotion & Disease Prevention
Improve Care for Hard to Manage Symptoms

Priority Topics:
Pain Management
Probiotics & the Gut-Brain Axis
Neurobiological Effects & Mechanisms
Biological Signatures of Natural Products
Health Promotion & Disease Prevention
Innovative Clinical Trial Designs
Science Literacy & Clinical Research
When setting research priorities NCCIH asks

- Is the topic appropriate to our mission and legislative mandate?
- Will the research meet a need not filled by other NIH programs?

1. **Scientific Promise**
   How strong is the body of evidence supporting the concept?

2. **Amenability to Rigorous Scientific Inquiry**
   Are there reliable and reproducible methods—e.g., diagnostics, outcome measures, biological effects, quality control, etc.?

3. **Potential To Change Health Practices**
   Is it reasonably likely that the results will make a difference to consumers, providers, or policymakers?

4. **Relationship to Use and Practice**
   Do the methods and approaches actually address the most important questions about use or practice in the real world?
What Does NCCIH Fund?

- Mind and Body Practices
  - acupuncture, massage, meditation, spinal manipulation, deep-breathing exercises, hypnotherapy, qi gong, tai chi, etc.
- Natural Products
  - herbs, botanicals, dietary supplements, probiotics, etc.
- pain
- interactions & safety
- biological effects
- mechanisms
- healthy behaviors
- stress, anxiety, & other symptoms
NCCIH Strategic Plan Range of Research Questions

- **Basic and Mechanistic**: How does it work?
- **Translational**: Can the biological effect be reliably measured?
- **Intervention Refinement**: Can the intervention be modified to enhance impact or adherence?
- **Efficacy/Effectiveness**: Does it work in comparison to an appropriate control?
- **Pragmatic Studies and Dissemination**: Is it still effective when implemented in “real world” conditions?
NCCIH is unique within NIH because we focus on *interventions* rather than a disease.
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New Directions for Mind and Body Research

- Develop and validate objective outcome measures
- Develop precise criteria or standards for specific practices
- Identify (neuro)biological mechanisms
- Research collaborations with other agencies
New Directions for Natural Products Research

- **Center for Advancing Natural Products Innovation and Technology**
  - Develop and/or adapt cutting edge, innovative approaches and technologies that will impact on the chemical and biological investigation of natural products

- **Natural Product-Drug Interactions**
  - Identify natural products with potential to exhibit clinically significant interactions with commonly used medications
  - Establish a set of best practices
  - Provide data infrastructure to disseminate results

- **Natural Products Mechanisms of Actions**
  - Botanicals
  - Probiotics
  - Marine organisms
  - Compounds affecting brain responses
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National Health Interview Survey: Supplement on Complementary and Integrative Health Utilization

NHIS Sample

- All 50 states and D.C., year-round
- Oversamples Black, Hispanic, and Asian persons
- Civilian, non institutionalized population
Background Information

U.S. population in 2012
318 million individuals:

75.8% adults (18 or older)
24.2% children (under 18)
Key Findings

33.2% of adults
11.6% of children

used a complementary health approach in 2012
10 most common complementary health approaches among adults—2012

- Natural Products*: 17.7%
- Deep Breathing: 10.9%
- Yoga, Tai Chi, or Qi Gong: 10.1%
- Chiropractic or Osteopathic Manipulation: 8.4%
- Meditation: 8.0%
- Massage: 6.9%
- Special Diets: 3.0%
- Homeopathy: 2.2%
- Progressive Relaxation: 2.1%
- Guided Imagery: 1.7%

*Dietary supplements other than vitamins and minerals.

13-year trends for complementary approaches where questions are very similar across years


Most Used Natural Products by U.S. Adults

7.8%  Fish oil/omega 3/DHA, EPA fatty acids
2.6%  Glucosamine and/or chondroitin
1.6%  Probiotics/Prebiotics
1.3%  Melatonin
1.3%  Coenzyme Q10
0.9%  Echinacea
0.8%  Cranberry (pills or capsules)
0.8%  Garlic supplements
0.7%  Ginseng
0.7%  Ginkgo biloba
Diseases/conditions for which complementary health approaches are most frequently used among adults—2012

- Back Pain: 14.9%
- Neck Pain: 7.1%
- Joint Pain or Stiffness: 6.7%
- Cardiovascular Conditions: 5.5%
- Arthritis, Gout, Lupus, or Fibromyalgia: 4.1%
- Anxiety or Depression: 2.9%

Source: Clarke TC; approaches among National Center for Health Statistics. 2015.
Use of Complementary Health Approaches in the U.S.
National Health Interview Survey (NHIS)

Out-of-Pocket Spending on Complementary Health Approaches in the U.S.

Total Health Care Spending, 2012
$2.82 trillion

Conventional Out-of-Pocket* $328.8 billion
Complementary Health Approaches Out-of-Pocket $30.2 billion
Reimbursed*† $2.46 trillion

Other Conventional Care‡ $225.1 billion
Prescription Drugs* $54.1 billion
Nonvitamin, Nonmineral Natural Products $12.8 billion
Self-Care Purchases† $2.7 billion
Complementary Practitioner Visits $14.7 billion
Physician Visits* $49.6 billion

† Self-care purchases includes, for example, homeopathic medicines and self-help materials such as books or CDs related to complementary health topics.
‡ Other conventional care includes dental care, nursing homes, home health care, nondrug medical products, hospital care, and other professional services.

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NIH Launches TACT2

- Replication trial to assess marked benefits of chelation therapy noted in first trial
- Clinical Coordinating Center - Mount Sinai Medical Center of Florida
- Data Coordinating Center - Duke Clinical Research Institute
- Primary funding from NCCIH and NHLBI
- Major contributions from NIDDK and NIEHS
- Heavy metal testing performed by CDC
Primary Endpoint, Diabetes vs No Diabetes

Kaplan-Meier Estimates of the Primary Composite Endpoint
EDTA Chelation Therapy vs. Placebo
Subset of Patients with Diabetes: Hx, Med Use or Baseline Glucose≥126

Hazard Ratio 95% CI P-value (log-rank)
EDTA:Placebo 0.59 0.44, 0.79 .0002

Kaplan-Meier Estimates of the Primary Composite Endpoint
EDTA Chelation Therapy vs. Placebo
Subset of Patients without Diabetes (Hx, Med Use or Baseline Glucose≥126)

Hazard Ratio 95% CI P-value (log-rank)
EDTA:Placebo 1.02 0.81, 1.28 .8768


TACT
Kaplan-Meier Estimate of the Primary Composite Endpoint
EDTA Chelation Therapy vs. Placebo
Superimposed Graphs: Subset of Patients with Diabetes & Subset of Patients without Diabetes
NIH Centers for Advancing Research on Botanical and Other Natural Products (CARBON) Program

- Supported by Office of Dietary Supplements and NCCIH
- Promote collaborative, transdisciplinary research on the safety, effectiveness, and mechanisms of action of botanical dietary supplements that have a high potential to benefit human health
  - Identify and characterize botanicals
  - Assess the bioavailability and bioactivity of chemical components of botanicals
  - Explore their mechanisms of action
  - Conduct preclinical and clinical evaluations
  - Provide a rich environment for training and career development
NIH Centers for Advancing Research on Botanical and Other Natural Products (CARBON) Program

- Botanical Dietary Supplements Research Centers
  - Dietary Botanicals in the Preservation of Cognitive and Psychological Resilience, Icahn School of Medicine at Mount Sinai, New York City
  - Botanicals and Metabolic Resiliency, Pennington Biomedical Research Center, Louisiana State University, Baton Rouge
  - Botanical Dietary Supplements for Women’s Health, University of Illinois at Chicago

- Centers for Advancing Natural Products Innovation and Technology
  - Center for High-throughput Functional Annotation of Natural Products, University of Texas Southwestern Medical Center, Dallas; Simon Fraser University, Burnaby, British Columbia, Canada
  - Center for Natural Products Technologies, University of Illinois at Chicago
One of the many faces of NIH-supported innovation, Stanford’s Christina Smolke is exploring how synthetic biology and microbes can be used to produce new drugs. She is a 2012 Pioneer Award winner.

Credit: Linda Cicero/Stanford News Service
Chronic pain: a major public health problem

NCCIH research is tackling the problem of chronic pain:

- We spend about 30% of our research budget on pain
- We bring cutting-edge tools to the study of pain
- Our research results affect guidelines for and practice of medical care
- We are building knowledge about the placebo effect

Pain 30%
Other research 70%
NCCIH Research Budget
Original Investigation

Effect of Mindfulness-Based Stress Reduction vs Cognitive Behavioral Therapy or Usual Care on Back Pain and Functional Limitations in Adults With Chronic Low Back Pain: A Randomized Clinical Trial

Daniel C. Cherkin, PhD; Karen I. Sherman, PhD; Benjamin H. Balderson, PhD; Andrea J. Cook, PhD; Melissa L. Anderson, MS; Rene J. Hawkes, BS; Kelly E. Hansen, BS; Judith A. Turner, PhD
Chronic Pain and Opioid Use in Soldiers After Combat Deployment

Toblin, et. al., 2011
Toblin, et. al., 2014
Severe Pain in Veterans: The Effect of Age and Sex, and Comparisons With the General Population

Richard L. Nahin

National Center for Complementary and Integrative Health, National Institutes of Health, Bethesda, Maryland.
Partnering on Pain Research: NIH, DoD, and VA Announce Pain Management Collaboratory Funding Initiative

- NCCIH, NINDS, NIAAA, NICHD, ORWH, NINR
- Develop the capacity to implement cost-effective, large-scale clinical research in military and veteran health care delivery organizations focusing on nonpharmacologic approaches to the management of pain and comorbid conditions. The program will:
  - Establish a Coordinating Center to provide leadership and technical expertise
  - Support the design and execution of a set of high-impact demonstration projects that will involve pragmatic clinical trials
  - Make data, tools, best practices, and resources from these and other projects available.
- Applications will be reviewed in June 2017
What is Needed

- Mind and Body Research
  - Need for strong feasibility data and intervention refinement for developmental appropriateness
  - Larger well-controlled studies to demonstrate efficacy or effectiveness
  - Cluster randomized or group delivered interventions need special power calculation and data analysis approaches

- Natural Product Research
  - Need to demonstrate a product that has replicable biological signature to enhance rigor and reproducibility of early studies
  - Selection of dose based on optimizing biological signature
  - Product quality and consistency is important
  - Large scale well-controlled studies are needed
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NCCIH Grants and Funding Information

- https://nccih.nih.gov/grants

- NCCIH Funding Opportunities
- Types of Grants and Contracts
- NCCIH Clinical Research Toolbox
- Grant Application Resources
- Awarded Grants and Contracts
NCCIH TRAINING

- https://nccih.nih.gov/training
- Research Training and Career Development
- Awards and Opportunities
- Institutional Training Sites
- Grant Application, Review, and Award Processes
- More Training Resources
Description of Current Funding Opportunities

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<th>Individual Training</th>
<th>Institutional Training</th>
<th>Career Development</th>
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<tbody>
<tr>
<td>• F30: dual-degree pre-doctoral (*new)</td>
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<tr>
<td>• F31: pre-doctoral</td>
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<tr>
<td>• F32: post-doctoral</td>
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<tr>
<td>• T32: training for pre- and post-doctoral</td>
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<tr>
<td>• T35: short-term training</td>
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<th>Administrative Supplements</th>
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<td>• Diversity: undergraduate through faculty</td>
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<td>• Re-Entry: post-doctoral or faculty at time of interruption</td>
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<tr>
<td>• CAM Practitioner: ND, DC, L. Ac., MT, or similar</td>
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- **K01**: research scientist
- **K08**: clinician scientist
- **K23**: patient-oriented clinician scientist
- **K99/R00**: post-doctoral to independence
- **K24**: mid-career health-professional doctoral degree
Take Home Message

- Integration of Complementary and Integrative Health Therapies with Conventional Practice in the Management of hard to treat conditions
- Utilize the NCCIH Research Framework for staging intervention research
- **Capitalize on Current Funding Opportunity Announcements**
- Contact NCCIH Program Staff to discuss your research concept!

http://nccih.nih.gov/grants/contact
Questions?
https://nccih.nih.gov
edwardse@mail.nih.gov